發明專利說明書 200305422

（填寫本書件時請先行詳閱申請書後之申請須知，作※記號部分請勿填寫）

※ 申請案號：92105741 ※IPC分類：A61K31/546

※ 申請日期：92.3.17

壹、發明名稱

（中文）廣抗菌譜哌吩化合物

（英文）BROAD SPECTRUM CEFEM COMPOUNDS

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捌、聲明事項

☐ 本案係符合專利法第二十條第一項☐第一款但書或☐第二款但書規定之期間，其日期為：＿＿＿＿＿＿＿＿＿＿

☑ 本案已向下列國家（地區）申請專利，申請日期及案號資料如下：

【格式請依：申請國家（地區）；申請日期；申請案號　順序註記】

1. 日本　2002.03.18　特願 2002-073526
2.
3.

☑ 主張專利法第二十四條第一項優先權：

【格式請依：受理國家（地區）；日期；案號　順序註記】

1. 日本　2002.03.18　特願 2002-073526
2.
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☐ 主張專利法第二十五條之一第一項優先權：

【格式請依：申請日；申請案號　順序註記】

1.
2.
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☐ 主張專利法第二十六條微生物：

☐國內微生物　【格式請依：寄存機構；日期；號碼　順序註記】

1.
2.
3.

☐國外微生物　【格式請依：寄存國名；機構；日期；號碼　順序註記】

1.
2.
3.

☐熟習該項技術者易於獲得，不須寄存。

玖、發明說明

（發明說明應敘明：發明所屬之技術領域、先前技術、內容、實施方式及圖式簡單說明）

發明所屬之技術領域

本發明爲關於其醫藥組成物對各種病原性細菌有廣抗菌譜之哌吩化合物，及關於其製造方法及中間體製造方法。本發明化合物特對β-乙內醯胺酶安定，因而對包括綠膿菌之產生β-乙內醯胺酶之抗哌吩菌有效。

先前技術

對革蘭式陽性菌及包括綠膿菌之革蘭式陰性菌有抗菌力之廣域哌吩化合物，近來哌吩結構中7位爲胺噻唑或胺噻二唑之3位環狀之4級銨甲基化合物受人注目。例如7位爲胺噻唑者如cefepime鹽酸鹽(USP4,406,899)、cefpirome硫酸鹽(USP4,609,653，特開昭57-192394)、cefoselis硫酸鹽(特開平7-196665，WO97/41128)等，又同位爲胺噻二唑者如cefclidin[USP4,748,171]、cefozopran鹽酸鹽(USP 4,864,022，特開平62-149682、特開平3-47189)等。同型哌吩化合物亦揭示於文獻如特開昭58-4789中含3位「可取代之含2個以上N原子之雜環陽離子基」之哌吩化合物，及特開昭60-155183中有同位「含2個以上N原子之不飽和稠合雜環陽離子基」之哌吩化合物。

於特開昭60-97982、特開昭59-130294、特開昭60-34973、特開昭62-114990、特開昭64-42491及WO87/06232號等中揭示哌吩化合物其中7位胺噻唑環上有鹵素，或7位肟部分末端被COOH取代。但此文獻中並無任何具體記載

兼備 2 種構造特徵之哂吩化合物。

7 位胺噻唑環上有鹵素，而 7 位肟部分末端被 COOH 取代之哂吩化合物雖揭示於特開昭 60-231684，但具體揭示之化合物爲 7 位肟上亞甲基部分爲未取代亞甲基或二甲基取代亞甲基。於特開昭 57-131794、特開平 1-308286 中雖揭示化合物其 7 位肟上亞甲基部分被單甲基取代，但該甲基之立體配位無特定，且無記載 3 位亞甲基上取代基之 4 級銨基。且這些文獻中並無任何記載對哂吩抗性綠膿菌之效力。

3 位有 4 級銨基且 7 位胺噻唑-氧亞胺型側鏈之哂吩化合物被稱爲廣域哂吩藥，尤其已知特對含綠膿菌之革蘭式陰性菌有效。例如，報告指出 ceftazidime 爲對 β-乙內醯胺酶安定、對產生 β-乙內醯胺酶之綠膿菌有較強之活性 (Acta Microbiologica Hungarica35(4), pp. 327-359(1988) 等)。

此種狀況下，近來顯示革蘭式陰性菌中對廣域哂吩藥有抗性之菌有增加之趨勢，大量產生 β-乙內醯胺酶，尤其 C 型 β-乙內醯胺酶之哂吩抗性綠膿菌在臨床上分離出之頻率極高，因而造成世界性社會問題(「最近 β-乙內醯胺酶之分類及免疫學」，臨床微生物 Vol.26 No.21999.3 P103-109)。但至今尚無該哂吩抗性綠膿菌有高度抗菌活性之哂吩劑之報告。

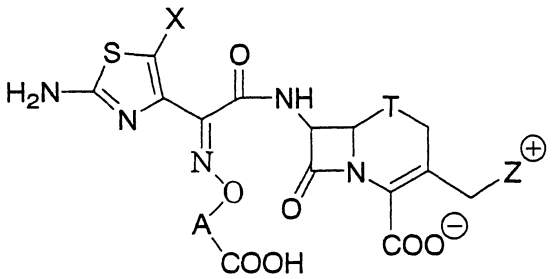
故極爲需要開發新穎廣域哂吩化合物，宜爲對產生 β-乙內醯胺酶之哂吩抗性綠膿菌有高度抗菌活性之哂吩化合

物，又宜爲注射用哂吩化合物。

發明內容

本發明者特意研發之結果，於哂吩化合物之7位側鏈之胺噻唑環中引入鹵素原子等，與α位碳原子結合之肟基末端中導入羧基，且3位中引入含有N原子之雜環基，尤宜爲4級銨基，則可增加對哂吩抗性綠膿菌所產出之β-乙內醯胺酶等安定性，而增強對該綠膿菌之抗菌活性。本發明之較佳之結構爲肟基中結合之伸低烷基，宜爲亞甲基上取代基爲單低烷基，尤宜將甲基導入α配位，則可更加提高抗菌活性，終於完成本發明。

1.式：



(I)

(式中，

T爲S、SO或O；

X爲鹵素、CN、低烷基可被取代之胺甲醯基、低烷基、低烷氧基、或低烷硫基；

A爲已取代低伸烷基(取代基：可有取代基之單低烷基、可有取代基之低亞烷基、或可有取代基之低伸烷基)；

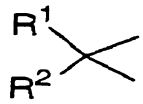
$Z^{\oplus}$爲可有取代基、且含陽離子基之含N原子之雜環基)所示化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物。

2.如上述 1 所示化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 T 爲 S。

3.如上述 1 所示化合物化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 T 爲 O。

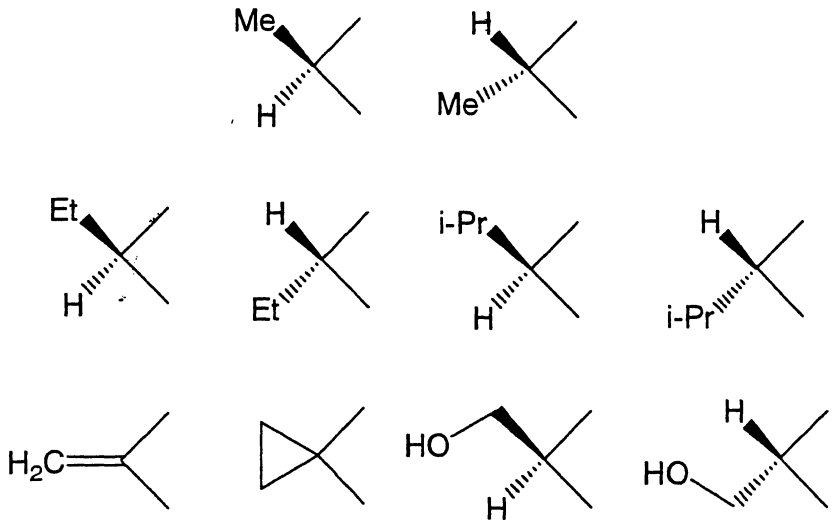
4.如上述 1 所示化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 X 爲鹵素或低烷基。

5.如上述 1 所示化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 A 爲下式：



(式中，R^1 及 R^2 爲不同、各爲氫或可有取代基之低烷基、或可共同形成可被取代低亞烷基或可被取代之伸低烷基)所示之 2 價基。

6.如上述 5 所示化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 A 爲如下所示 2 價基：

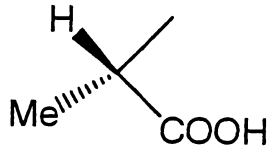


(式中，Me爲甲基；Et爲乙基；i-Pr爲異丙基。)

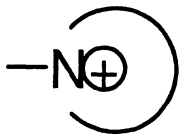
7.如上述5所示化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 R^1 及 R^2 爲不同、各爲氫或低烷基。

8.如上述5所示化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 R^1 及 R^2 爲不同、各爲氫或甲基。

9.如上述5所示化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中"-A-COOH"爲如下所示之基：

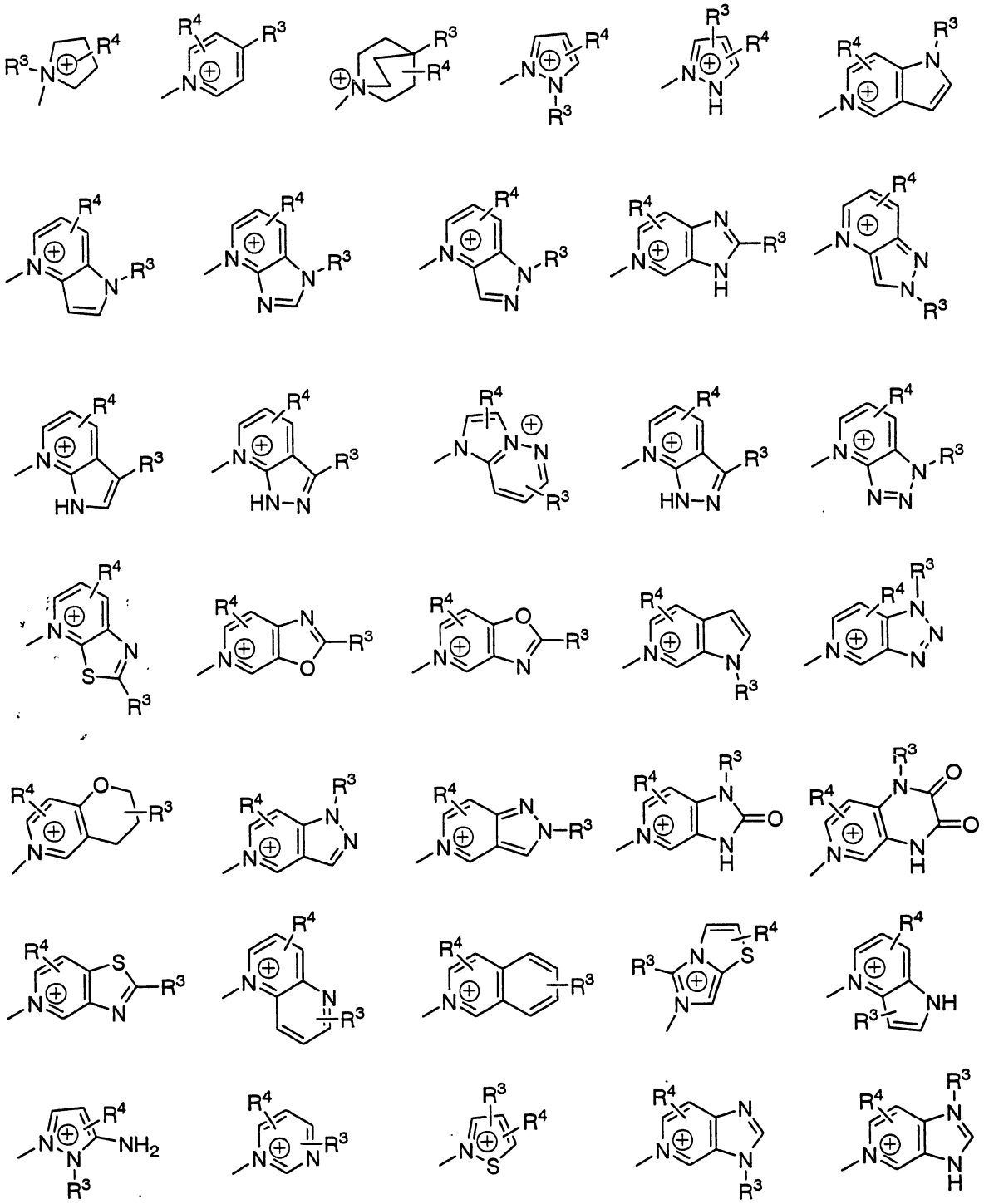


10.如上述1所示化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 $Z^{\oplus}$ 爲如下所示：



其含一以上N原子且可有1～4個取代基之飽和或不飽和、單環或稠合環之4級銨基。

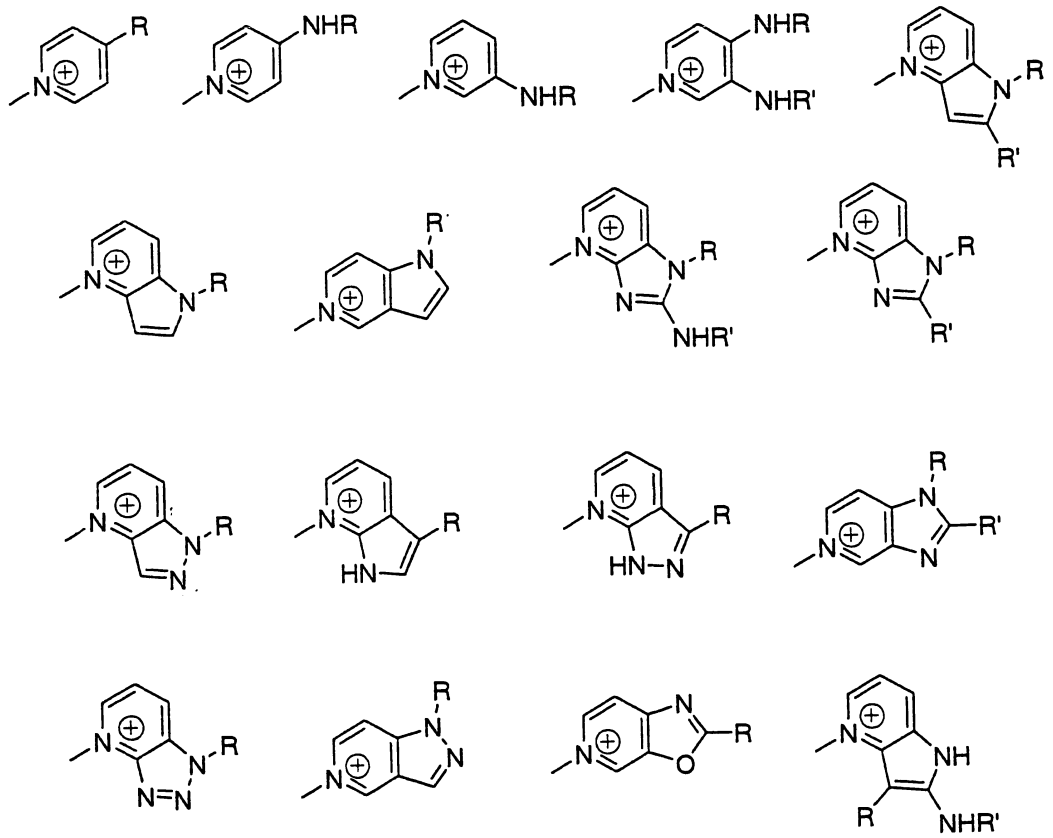
11.如上述1所示化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 $Z^{\oplus}$ 爲如下所示雜環基：



(式中，R^3 及 R^4 各爲氫、可取代之低烷基、可取代之環烷基、可取代之低烯基、可取代之胺基、羥基、鹵素、可取代之胺甲醯基、可取代之烷氧基、或可取代之雜環基)。

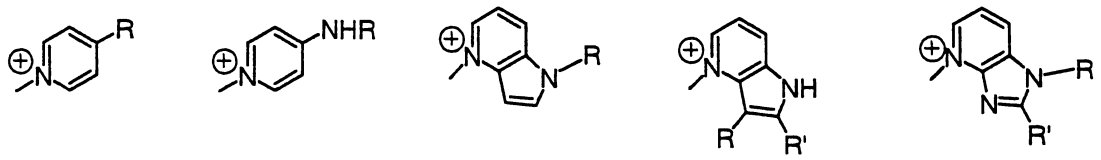
12.如上述 1 所示化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 $Z^{\oplus}$ 爲如下所示

雜環基：



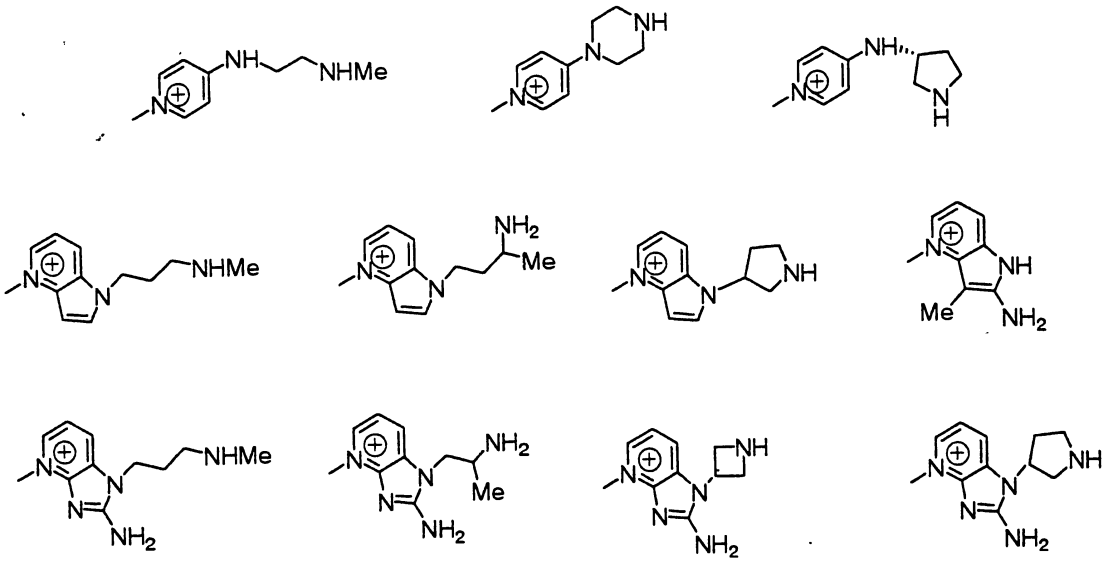
(式中，R及R'各爲氫、低烷基、胺基、單或二低烷胺基、低烯基、胺低烷基、低烷胺低烷基、低烷胺低烷胺基、胺低烷氧胺基、可有取代之雜環基取代之胺基、羥低烷基、羥低烷胺低烷基、低烷氧低烷基、胺甲醯低烷基、羧低烷基、低烷羰胺低烷基、低烷氧羰胺低烷基、低烷氧基、可有其他種種取代之低烷基、有2個取代基之低烷基、或可取代之雜環基)。

13.如上述1所示化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 $Z^{\oplus}$ 爲如下所示雜環基：



(式中，R各爲氫、低烷基、胺低烷基、低烷胺低烷基、可取代之雜環基取代之胺基、或可取代之雜環基；R'爲胺基)。

14.如上述1所示化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 $Z^{\oplus}$ 爲如下所示雜環基：



(式中，Me爲甲基)。

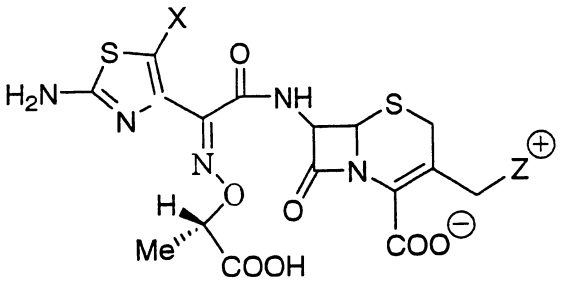
15.如上述1所示化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中T爲S；X爲鹵素；A可如上述5～9所示2價基。

16.如上述1所示化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中T爲S；X爲鹵素；A爲如上述8所示2價基；$Z^{\oplus}$ 爲如上述12所示雜環基。

17.如上述1所示化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中T爲S；X爲鹵素；A爲如上述9所示2價基；$Z^{\oplus}$ 爲如上述13或14所

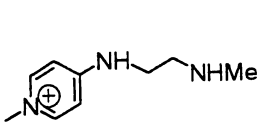
示雜環基。

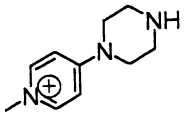
18.如上述1所示化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其係如下式所示：

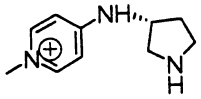


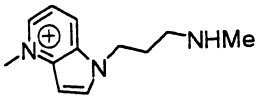
(I)

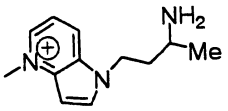
(式中，X爲鹵素；$Z^{\oplus}$爲如下之雜環基)

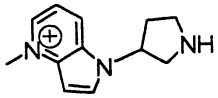


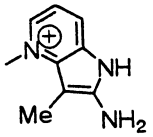


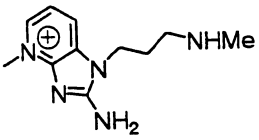


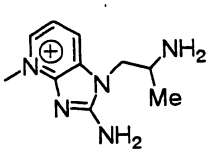


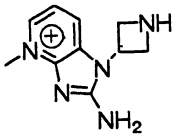


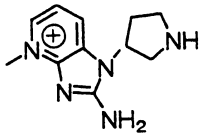






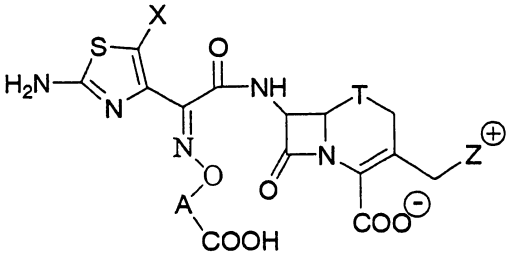






(式中，Me爲甲基)。

19.一種如下式化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物：



(I-A)

(式中，

T爲S、SO或O；

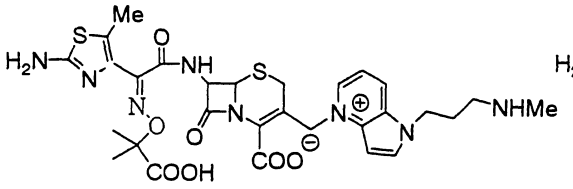
X 爲鹵素、CN、可有低烷基取代之胺甲醯基、低烷基、低烷氧基、或低烷硫基；

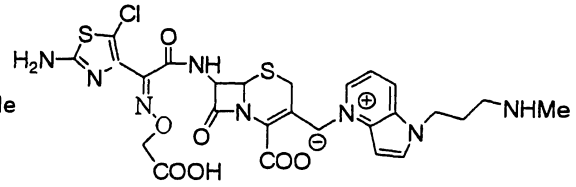
A 爲可有取代之低伸烷基(但不含取代基爲可取代之單低烷基、可取代之低亞烷基、或可取代之伸低烷基之情形)；

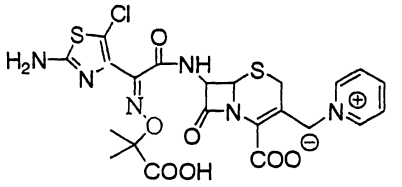
$Z^{\oplus}$ 爲可有取代基、且含陽離子基之含 N 原子之雜環基)所示化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物(但 T 爲 S；X 爲鹵素、1)A 爲亞甲基；$Z^{\oplus}$ 爲吡錠、或 2)A 爲二甲基亞甲基；$Z^{\oplus}$ 爲咪唑并[1,2-a]吡錠之情形除外)。

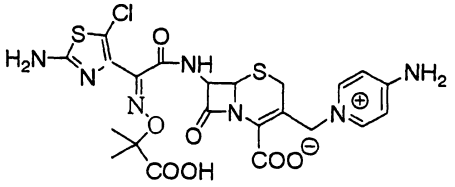
20.如上述19所示化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 T 爲 S、X 爲鹵素或低烷基；A 爲可有二低烷基取代之亞甲基。

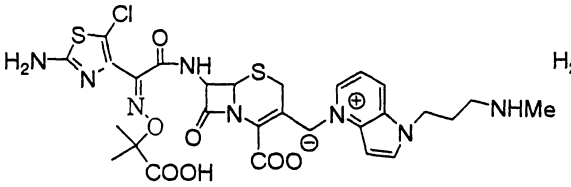
21.如上述 20 所示化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其係如下所示：

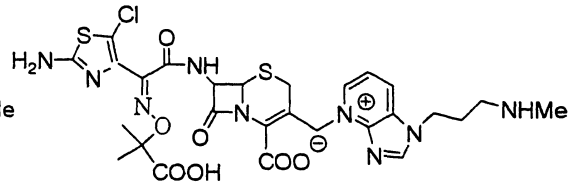


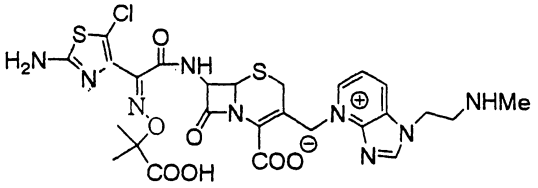


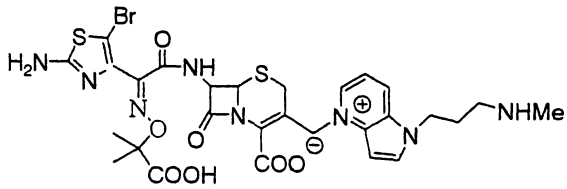








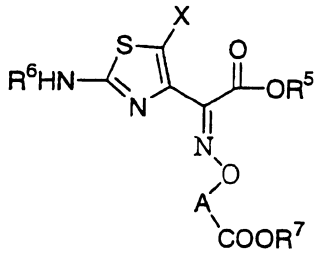




22.一種醫藥組成物，其係含如上述 1～21 所示化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物。

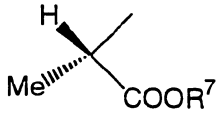
23.一種抗菌藥，其含如上述 1～21 所示化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物。

24.一種如下式化合物或其製藥容許鹽：



(IV)

(式中，X 爲鹵素、CN、可有低烷基取代之胺甲醯基、低烷基、低烷氧基、或低烷硫基；A 爲如下所示：



R^5 爲氫或羧基保護基；R^6 爲氫或胺基保護基；R^7 爲氫或羧基保護基)。

25.如上述 24 所示化合物或其製藥容許鹽，其中 X 爲鹵素或低烷基。

26.如上述 24 所示化合物或其製藥容許鹽，其中 X 爲鹵素。

本發明提供本發明化合物及其中間體之製造方法，投予本發明化合物以預防及治療細菌感染症之方法，及提供使用本發明化合物以製造抗菌劑。

實施方式

下面說明本文中用語，除另行規定者外，單獨或併用時皆共通。

(T之定義)

T爲S、SO或O，宜爲S或O，特宜爲S。

(X之定義)

X爲鹵素、CN、低烷基中可取代之胺甲醯基、低烷基、低烷氧基、或低烷硫基。

鹵素爲F、Cl、Br等。宜爲Cl或Br，特宜爲Cl。

低烷基爲直鏈或分岐鏈之C_{1-6}烷基，例如甲基、乙基、正丙基、異丙基、第三丁基、正戊基、正己基等。宜爲C_{1-3}烷基，特宜爲甲基。

低烷氧基爲上述低烷基結合以氧，例如甲氧基、乙氧基、正丙氧基、異丙氧基、第三丁氧基、正戊氧基、正己氧基等。宜爲C_{1-3}烷氧基，特宜爲甲氧基。

低烷硫基爲上述低烷基結合以硫基，例如甲硫基、乙硫基、正丙硫基、異丙硫基、第三丁硫基、正戊硫基、正己硫基等。宜爲C_{1-3}烷硫基，特宜爲甲硫基。

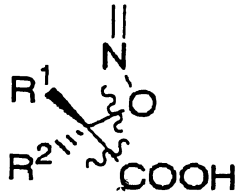
X宜爲鹵素(例如：Cl、Br)或低烷基(例如：甲基)，特宜爲鹵素。

(A之定義)

A爲對化合物(I)或化合物(I-A)之抗菌活性等無不良影響之2價基，並無特限，宜爲R^1及R^2等可取代之伸低烷基。化合物(I)中A爲取代伸低烷基。

該伸低烷基爲源自上述低烷基之 2 價基，宜爲 C_{1-3} 伸烷基，更宜爲亞甲基($-CH_2-$)。

A 宜爲如下述 R^1 及 R^2 取代之亞甲基，宜爲如下之立體配位。



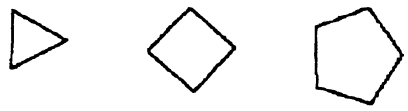
(R^1、R^2 之定義)

R^1 及 R^2 各爲氫、可取代之低烷基、或可共同形成可被取代低亞烷基或可被取代之伸低烷基。但，化合物(I)中 R^1 及 R^2 爲不同。

該低烷基可如上所例示之低烷基，宜爲 C_{1-4} 基，又更宜爲甲基、乙基或丙基(例如正丙基、異丙基)，特宜爲甲基。

該低亞烷基包含上述低烷基上相同碳原子失去 2 個氫原子所得 2 價基，例如 $=CH_2$、$=CHCH_3$、$=CHCH_2CH_3$、$=C(CH_3)_2$、$=CH(CH_3)_3$ 等。宜爲 $=CH_2$、$=CHCH_3$ 或 $=C(CH_3)_2$，特宜爲 $=CH_2$。

該伸低烷基爲含 $-(CH_2)_n-$(n 爲 2～4 之整數，宜爲 2)之基。R^1 及 R^2 共同形成伸低烷基之場合，其與相鄰碳原子共形成如下例示環烷基，宜爲環丙基或環丁基，特宜爲形成環丙基。

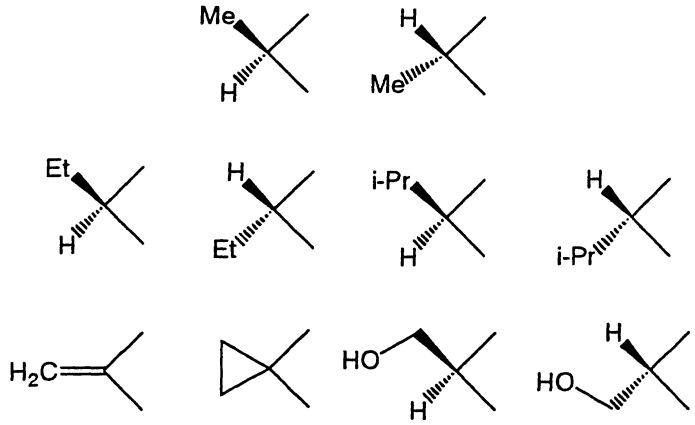


上述低烷基、低亞烷基或伸低烷基被取代時之取代基爲

鹵素(例如：F、Cl)、羥基、低烷氧基(例如：甲氧基、乙氧基)等，宜爲羥基。

(R^1，R^2)之組合特宜爲(甲基，氫)、(氫，甲基)、(甲基、甲基)或共同形成$=CH_2$、$-(CH_2)_2-$等。化合物(I)中特宜爲氫及低烷基，又宜爲(R^1，R^2)、(氫，甲基)，特宜爲(氫，甲基)。

化合物(I)中 A 宜爲如下所示含 2 價基之基。

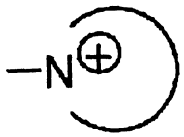


(式中，Me 爲甲基；Et 爲乙基：i-Pr 爲異丙基。)

(Z^+之定義)

Z^+爲可取代之有陽離子且含 N 原子之雜環基。對藥理活性無不良影響者並無特限，該取代基之數目及位置、陽離子之位置、及雜環種類並無特限。即 Z^+爲包含熟於此藝者習知哂吩化合物之各種 2 位雜環基。陽離子宜存在化合物(I)3 位亞甲基鄰接之 N 原子上。

Z^+宜爲下式：



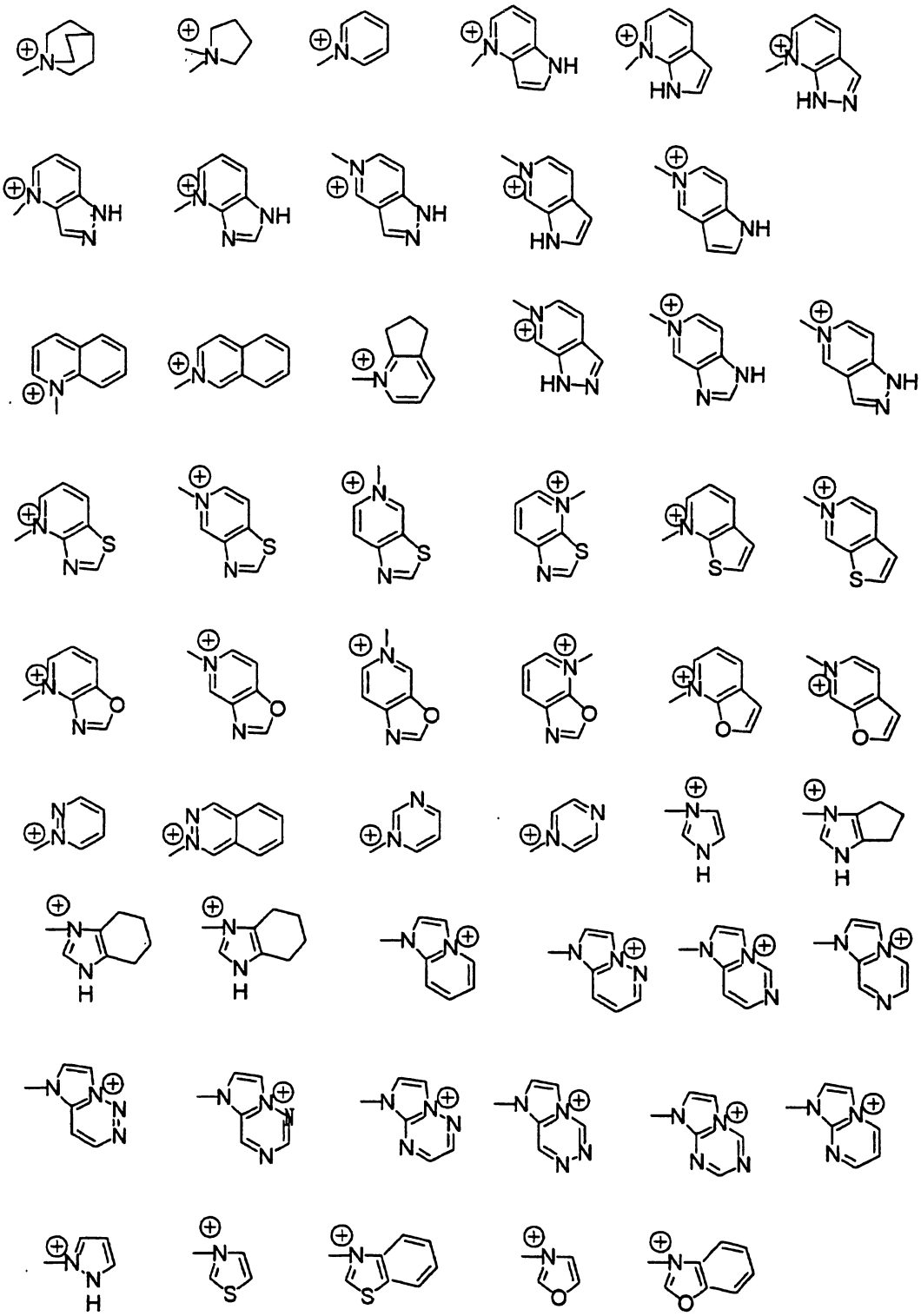
含一以上 N 原子(宜爲 1～4 個，更宜爲 1～3 個或 1～2 個)

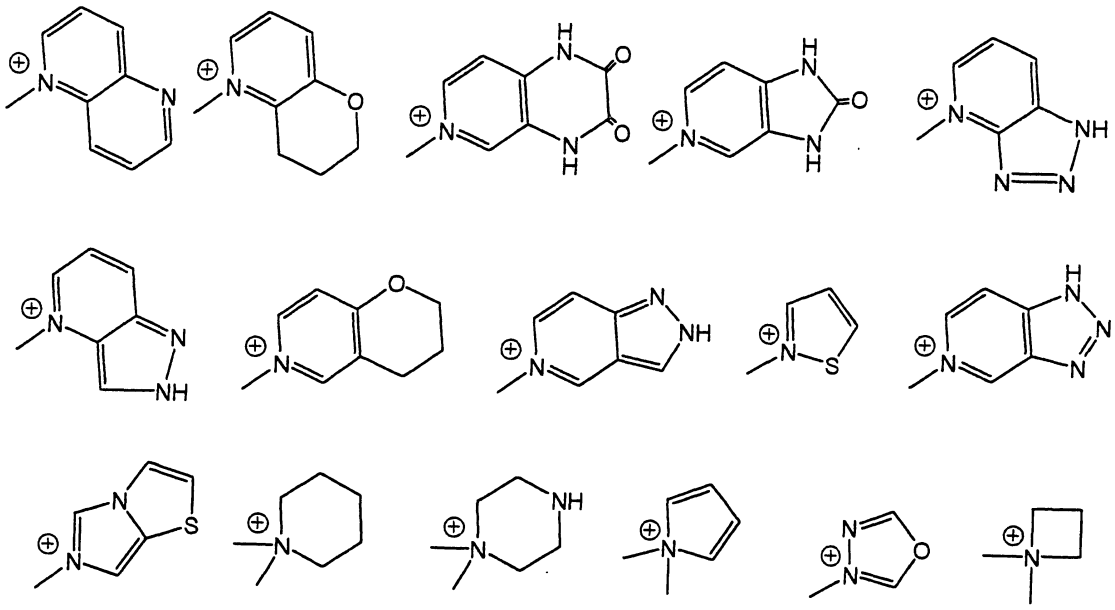
，可有 1～4 個(宜爲 1～2 個)取代基、之飽和或不飽和、單環或稠合環之 4 級銨基。該雜環可含 1 或 2 個以上 O 原子及/或 S 原子。該雜環宜爲 5～10 員環，更宜爲 5～6 員環。

含有 N 原子之飽和雜環爲吡咯啶基、吡唑啶基、噻唑啶基、噁唑啶基、咪唑啶基、哌啶基、哌啡基、嗎啉基、硫嗎啉基、及其稠合環。

含有 N 原子之不飽和雜環爲單環(例如：吡咯基、吡唑基、咪唑基、噁唑基、異噁唑基、噻唑基、異噻唑基、吡啶基、嗒啡基、嘧啶基、吡啡基、三啡基、三唑基)，及單環其環中含稠合 2 環(例如：吲哚基、引啡基、苯并咪唑基、苯并吡唑基、吲啡基、喹啉基、異喹啉基、啡啉基、萘基、酞基、喹唑啉基、喔啶基、苯并異噁唑基、苯并吡唑基、苯并噁唑基、苯并噁二唑、苯并異噻唑基、苯并噻唑基、苯并三唑基、嘌呤、吲哚基、吡唑并咪唑、嗒啡并咪唑、噻唑并咪唑、四氫吡喃并吡啶、噁唑并[4,5-c]吡啶、噁唑并[5,4-c]吡啶、1H-吡咯并[3,2-b]吡啶、1H-吡咯并[2,3-b]吡啶、1H-吡咯并[3,2-c]吡啶、1H-吡咯并[2,3-c]吡啶、1H-吡唑并[4,3-b]吡啶、1H-吡唑并[3,4-b]吡啶、1H-咪唑并[4,5-c]吡啶、1H-咪唑并[4,5-b]吡啶、噻唑并[4,5-c]吡啶、噻唑并[5,4-b]吡啶、1,4-二氫吡啶并[3,4-b]吡啡、1,3-二氫咪唑并[4,5-c]吡啶、二唑并吡啶等)。

Z^+之具體例含如下可取代之雜環基。



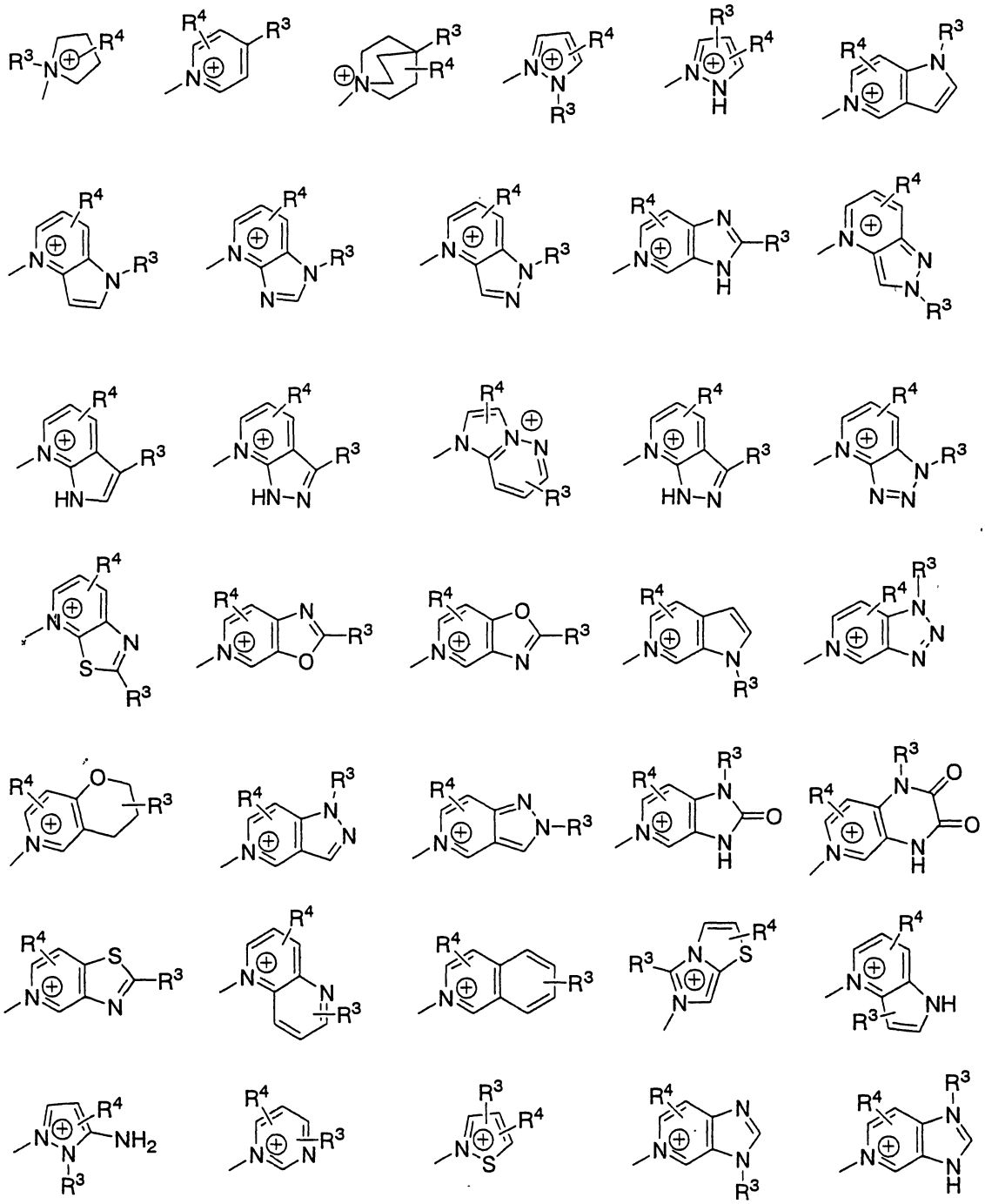


當上述雜環基含取代基時，該取代基可爲選自低烷基(例如：甲基、乙基、正丁基)、可取代之低烷基(取代基：胺基、低烷胺基(例如：$-NHCH_3$)、可取代之低烷胺基(例如：$-NHCH_2CH_2OH$)、可取代之雜環基(例如：2-吡咯啶基、3-吡咯啶基、5-(3-羥吡咯啶基))、羥基、環烷基、羧基、低烷氧基(例如：甲氧基)、$-OCOCH_3$、$-OCONH_2$、$-OCONHOCH_3$、$-OCONHOH$、$-OCONHCH_3$、$-OCON(CH_3)_2$、$-OCONHN(CH_3)_2$、$-ONHCOOCH_3$、$-CONH_2$、$-CONHOCH_3$、$-CONHOH$、低烷氧羰胺基(例如：$-NHCOOCH_3$)、低烷羰胺基(例如：$-NHCOCH_3$、$-NHCONH_2$、$-NHSO_2NH_2$、$-NHCHO$、$-N(CH_3)C=NH(NH_2)$、鹵素、氧等)；可取代之胺基(取代基：低烷基(例如：甲基、乙基、丙基)、胺低烷基(例如：$-CH_2CH_2NH_2$、$-CH_2CH(NH_2)CH_3$、$-CH_2CH_2CH_2NH_2$)、低烷胺低烷基(例如：$-CH_2CH_2NHCH_3$、$-CH_2CH_2CH_2NHCH_3$)、可取代之雜環基(例如：3-吡咯啶基、4-吡咯啶基、2-噻唑基、5-(1-(2-羥乙基)吡唑基)、5-(1-(2-胺乙基)吡唑基))、

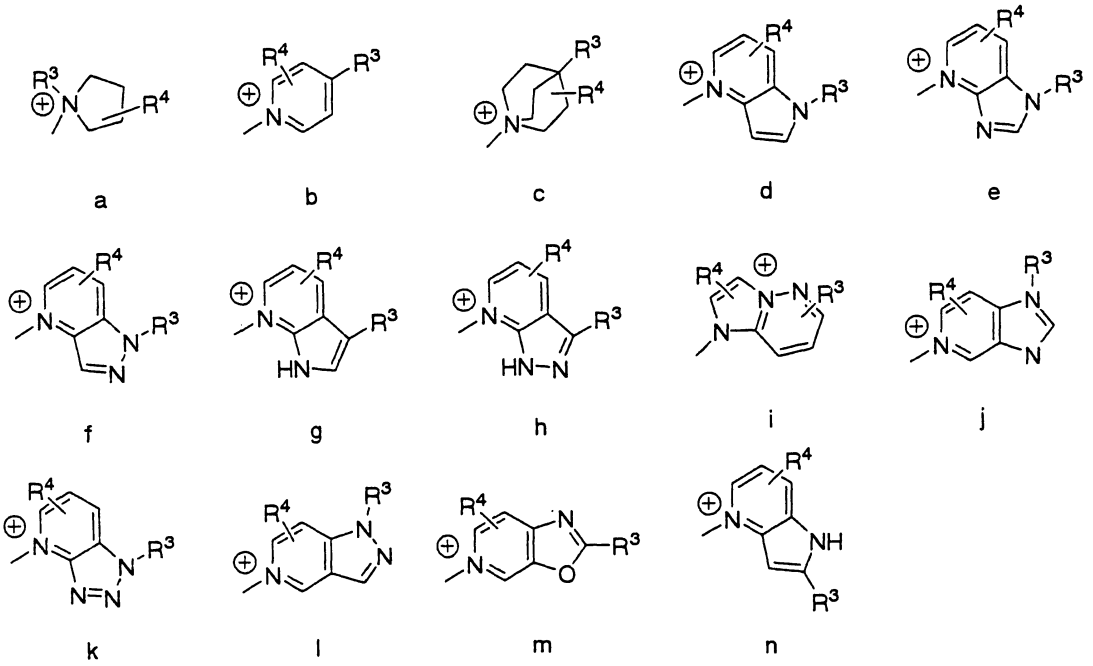
可取代之雜環基中取代低烷基(例如：(2-吡咯啶基)甲基、2-(5-胺基-1-(吡唑基)乙基))、胍低烷基(例如：$-CH_2CH_2NHC=NH(NH_2)$)、羥低烷基(例如：$-CH_2CH_2OH$、$-CH_2CH_2CH_2OH$)、羥低烷胺基低烷基(例如：$-CH_2CH_2NHCH_2CH_2OH$)、胺低烷氧基(例如：$-OCH_2CH_2NH_2$)、低烷胺低烷氧基(例如：$-OCH_2CH_2NHCH_3$、$-OCH_2CH_2CH_2NHCH_3$)、-CHO、$=CHN(CH_3)_2$、-NHCHO、可取代之胺甲醯基(例如：$-CONH_2$、$-CONHCH_2CH_2NHCH_3$、$-CONHCH_2CH_2NHC=NH(NH_2)$)、$-COOCH_2CH_3$、$-CH_2COOH$、醯基(例如：乙醯基)、胺醯基(例如：$-COCH_2CH(CH_3)NH_2$等)；可取代之胺甲醯基(取代基：甲基、乙基、-NHCHO等)；伸低烷基(例如：$-CH_2CH_2-$、$-CH_2CH_2CH_2-$)；可取代之低烯基(例如：$-CH_2CH=CH_2$)；可取代之環烷基(例如：環丙基)；羥基；硝基；氰基；醛基；可取代之烷氧基(例如：$-OCH_3$、$-OCH_2CH_3$、$-OCH_2CH_2NHCH_3$、$-OCH_2CH_2CH_2NHCH_3$)；低烷硫基(例如：$-SCH_3$)；低烷氧羰基(例如：$-COOCH_2CH_3$)；鹵素(例如：F、Cl、Br等)，及可取代之雜環基等一以上相同或不同取代基，宜爲1～4個，又宜爲1～3個，特宜爲1～2個之取代基。該「可取代之雜環基」可如上述Z所例示之雜環基、其結合位置並無特定。特宜爲含N原子之飽和4～6員環，例如吖丁啶基(例如：3-吖丁啶基)、吡咯啶基(例如：3-吡咯啶基)、哌啶基(例如：4-哌啶基、1-(4-胺哌啶基))、哌啡基(例如：1-哌啡基、1-(3-甲哌啡基))、吡咯基(例如：3-吡咯基、4-(2-胺甲醯吡咯基))、吡唑基

(例如：1-吡唑基、4-吡唑基)、噁二唑基(例如：2-噁二唑基)、三唑基(例如：1-三唑基)。上述"低"宜爲 C_{1-6}，又宜爲 C_{1-3}。該雜環基上取代基宜爲可取代之低烷基、可取代之低烯基、可取代之胺基及可取代之雜環基，及如下所示 R^3 及 R^4、及"-R"、"-NHR"等。

Z^+ 宜爲如下所示之雜環基。

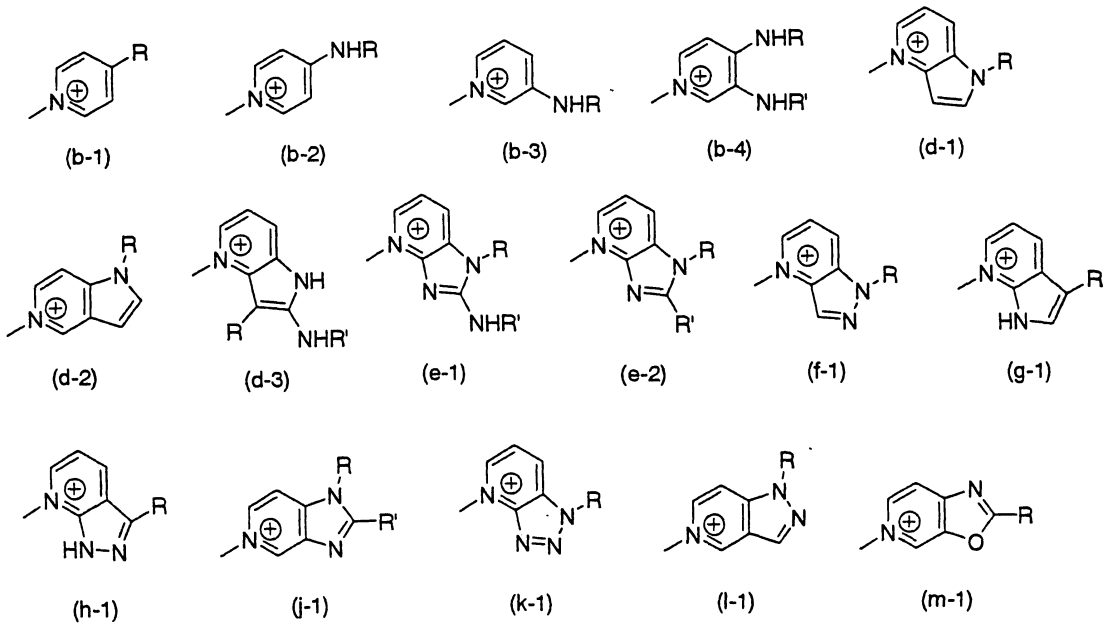


Z^+宜再選自如下之雜環基，又宜爲 b、d、e 及 n 所示之基等。



R^3 及 R^4 爲任意選自上述雜環之取代基，宜各爲氫，上述可取代之烷基、可取代之低烯基、可取代之胺基或可取代之雜環基等，包含以下之"-R"、"-R'"、"-NHR"、"-NHR'"。R^3 及 R^4 爲可任意於可取代位置取代而得。

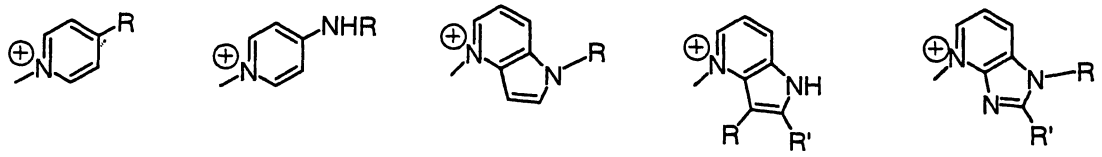
Z^+宜爲如下所示雜環基，宜爲 b-1、b-2、d-1、d-3、或 e-1 之基等。



R及R'可任意選自上述雜環基之取代基，宜各爲氫、可取代之低烷基、可取代之胺基、及可取代之雜環基等。又宜爲氫、低烷基、低烯基、胺低烷基、胺羥低烷基、低烷胺低烷基、羥低烷基、醯氧(胺基)低烷基、醯胺低烷基、磺醯胺低烷基、胺甲醯氧基低烷基、低烷肼氧低烷基、胺甲醯胺低烷基、烷氧羰胺氧低烷基、低烷氧低烷基、胺甲醯低烷基、可取代之環烷基、可取代之雜環基中取代低烷基、羧低烷基、低烷氧羰胺低烷基、鹵低烷基、低烷胺基、胺低烷胺基、低烷胺低烷胺基、羥低烷胺基低烷胺基、胺甲醯氧低烷胺基、胍低烷胺基、可取代之胺甲醯基、可取代之烷氧基、可取代之羰胺基、可取代之雜環基中取代以胺基、胺低烷氧基、及可取代之雜環基。R宜爲氫、甲基、乙基、環丙基、$-CH_2CH_2NH_2$、$-CH_2CH_2NHCH_3$、$-CH_2CH_2CH_2NHCH_3$、$-CH_2CH_2NHCH_2CH_2OH$、$-CH_2CH_2CH_2NHCH_2CH_2OH$、$-CH_2CH_2CH_2NH_2$、$-CH_2CH(NH_2)CH_3$、$-CH_2CH_2CH(NH_2)CH_3$、$-CH_2CH_2CH(NH_2)CH_2OH$、$-CH_2CH_2CH(NH_2)CH_2OCOCH_3$、$-CH_2CH(NHCH_3)CH_3$、$-CH_2CH_2OH$、$-CH_2CH_2OCONH_2$、$-CH_2CH_2OCONHOCH_3$、$-CH_2CH_2OCONHCH_3$、$-CH_2CH_2OCON(CH_3)_2$、$-CH_2CH_2OCONHN(CH_3)_2$、$-CH_2CH_2OCONHOH$、$-CH_2CH_2CH_2OCONH_2$、$-CH_2CH_2ONHCOOCH_3$、$-CH_2CH_2NHCOOH$、$-CH_2CH_2CONH_2$、$-CH_2CONHOCH_3$、$-CH_2CONHOH$、$-CH_2COOH$、$-CH_2CH_2NHCOCH_3$、$-CH_2CH_2NHCONH_2$、$-CH_2CH_2NHSO_2NH_2$、$-CH_2CH_2NHCOOCH_3$、

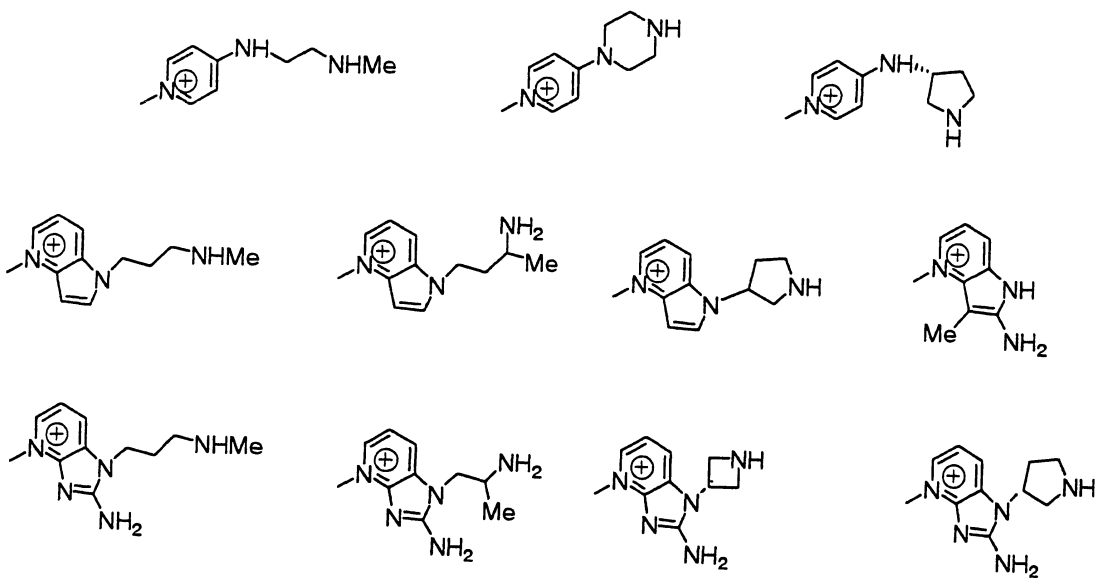
$-CH_2CH_2NHC(NH_2)=NH$、$-CH_2CH_2CH_2N(CH_3)C(NH_2)=NH$、$NH_2$、$-NHCH_2CH_2NH_2$、$-NHCH_2CH_2NHCH_3$、$-N(CH_3)CH_2CH_2NHCH_3$、$-N(CHO)CH_2CH_2NHCH_3$、$-NHCOCH_2CH(NH_2)CH_3$、$-CONHCH_2CH_2NHCH_3$、$-CONHCH_2CH_2NHC(NH_2)=NH$、$-OCH_2CH_2NHCH_3$、3-吖丁啶基、3-吡咯啶胺基、3-吡咯啶基、1-吡唑基、5-(1-(2-羥乙基)吡唑基、5-(1-(2-胺乙基)吡唑基)、2-(1-(5-胺吡唑基))乙基、4-吡唑基、3-吡咯基、4-(2-胺甲醯吡咯基)、2-吡咯啶基甲基、3-吡咯啶基甲基、5-(3-羥吡咯啶基)甲基、2-噻唑基、2-噁二唑基、1-三唑基、1-(3-甲基哌啡基)、1-(4-胺哌啶基)、及4-哌啶基等。R'宜爲氫或可取代之胺基。R'宜爲氫、$-NH_2$、$-NHCH_3$、$-N(CH_3)_2$、$-N=CHN(CH_3)_2$、$-N(CH_3)CH_2CH_2NH_2$、$-NHCH_2CH_2NHCH_2$、$-NHCOOCH_2CH_3$、$-NHOCH_3$、或$-NHCH_2COOH$。

Z^+宜爲下示基。



(式中，R各爲氫、低烷基、胺低烷基、低烷胺低烷基、可取代以胺基之已取代雜環基、或可取代之雜環基；R'爲胺基)

$Z^{\oplus}$特宜爲如下所示雜環基。



化合物(I)宜包含以下化合物。

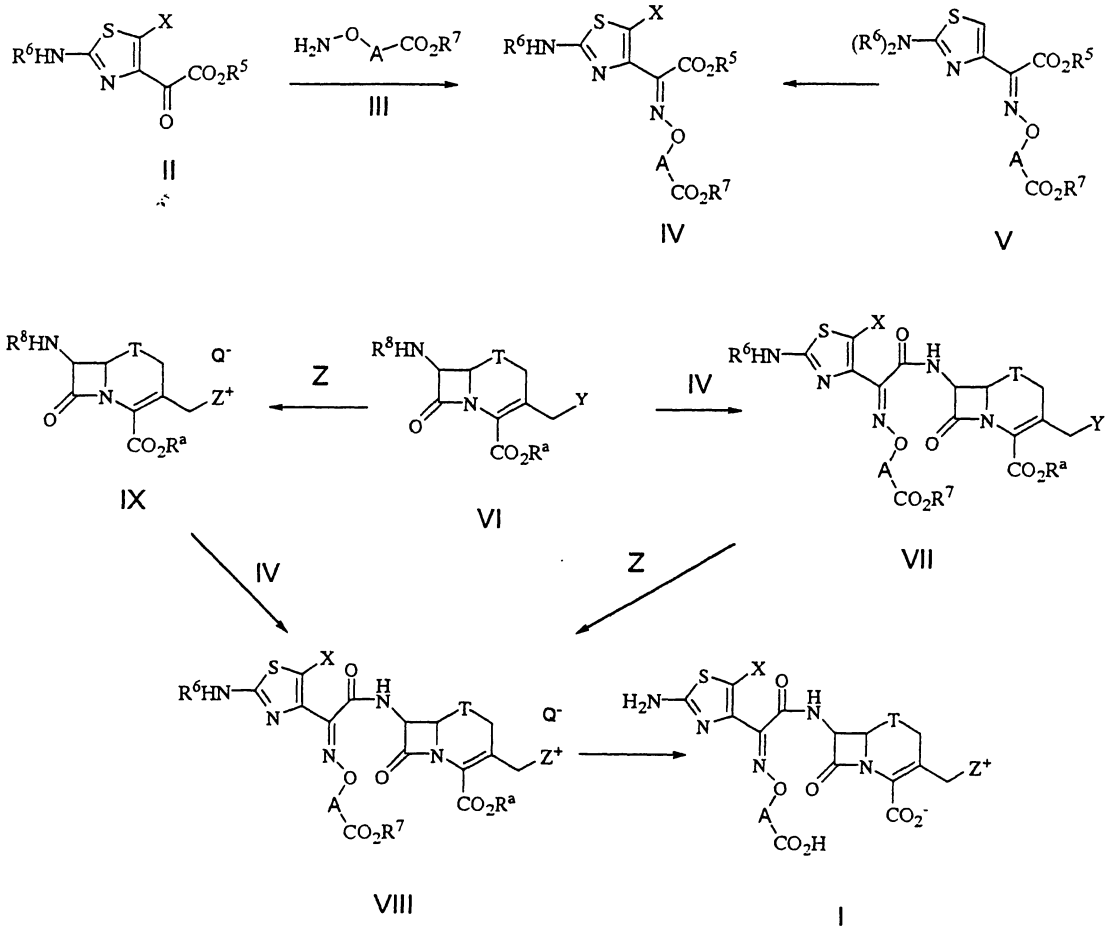
(a)T爲 S；X爲鹵素或低烷基；A爲如上述(5)～(9)所例示之 2 價基；Z^+爲如上述(10)～(14)所例示之雜環基之化合物。

(b)T爲 S；X爲鹵素或低烷基；A爲如上述(8)所例示之 2 價基；Z^+爲如上述(12)所例示之雜環基之化合物。又宜爲 x 爲鹵素，且 Z^+爲如上述(b-1)、(b-2)、(d-1)、(d-3)、(e-1)、或(e-2)之基。

(c)T爲 S；X爲鹵素或低烷基；A爲如上述(9)所例示之 2 價基；Z^+爲如上述(13)所例示之雜環基之化合物。

其中，宜爲實施例 1、3、4、5、8、9、18、19、20、79、98、111、112、124、128、132、161、164、185 等例示之化合物，更宜爲實施例 8、9、18、20、79、98、124、128、132、161、164 等例示之化合物。

次說明化合物(I)之代表製法如下。



(式中，T之定義如上；R^5爲氫或羧基保護基；R^6爲氫或胺基保護基；R^7爲氫或羧基保護基；R^8爲氫或胺基保護基；R^a爲氫或羧基保護基；Y爲離去基(例如：羥基、鹵素(Cl、Br、I等)、胺甲醯氧基、取代胺甲醯氧基、醯氧基、甲磺醯氧基、甲苯磺醯氧基等)；Q^-爲鹵素等陰離子)

(1)7位側鏈原料；化合物(IV)之製法

(A法)

將化合物(II)與化合物(III)反應可得化合物(IV)。此反應中，R^5宜爲氫；R^6宜爲胺基保護基；R^7爲羧基保護基。

化合物(III)使用量對化合物(II)1莫耳，通常爲約1～10莫耳，宜爲約1～2莫耳。

反應溶劑爲例如醚類(例如：二噁烷、四氫呋喃、乙醚、

第三丁基甲基醚、二異丙醚)、酯類(例如：甲酸乙酯、乙酸乙酯、乙酸正丁酯)、鹵化烴類(例如：二氯甲烷、氯仿、四氯化碳)、烴類(例如：正己烷、苯、甲苯)、醇類(例如：甲醇、乙醇、異丙醇)、醯胺類(例如：甲醯胺、N,N-二甲基甲醯胺、N,N-二甲基乙醯胺、N-甲基吡咯啶酮)、酮類(例如：丙酮、甲基乙基酮)、腈類(例如：乙腈、丙腈)、二甲亞碸、水等。此溶劑可單獨使用或混合2種以上來使用。

反應溫度通常約爲-20～100℃，宜爲約0～50℃。

(B法)

將化合物(V)鹵化後，視需要進行脫保護可得化合物(IV)。此反應中，R^5宜爲化合物(V)之羧基保護基，化合物(IV)宜爲氫；R^6宜爲胺基保護基；R^7宜爲羧基保護基。

鹵化劑爲N-氯丁二醯亞胺、N-氯酞醯亞胺、氯、N-溴丁二醯亞胺、N-溴酞醯亞胺、溴、碘等。

鹵化劑之使用量對化合物(V)1莫耳，通常爲約1～20莫耳，宜爲約1～2莫耳。

反應溶劑可如上所例示者。

反應溫度通常爲約-10～100℃，宜爲約0～50℃。

(2)7位醯化及3位側鏈形成；化合物(VII)及(VIII)之製法

1)7位醯化；令化合物(VI)而化合物(IV)反應可得化合物(VII)。此反應中，R^2宜爲羧基保護基；R^5宜爲氫；R^6宜爲胺基保護基；R^7宜爲羧基保護基；R^8宜爲氫。

化合物(IV)使用量對化合物(VI)1莫耳，通常爲約1～5

莫耳，宜爲約 1～2 莫耳。

反應溶劑爲例如醚類(例如：二噁烷、四氫呋喃、乙醚、第三丁基甲基醚、二異丙醚)、酯類(例如：甲酸乙酯、乙酸乙酯、乙酸正丁酯)、鹵化烴類(例如：二氯甲烷、氯仿、四氯化碳)、烴類(例如：正己烷、苯、甲苯)、醯胺類(例如：甲醯胺、N,N-二甲基甲醯胺、N,N-二甲基乙醯胺、N-甲基吡咯啶酮)、酮類(例如：丙酮、甲基乙基酮)、腈類(例如：乙腈、丙腈)、二甲亞碸、水等。

反應溫度通常約爲-40～100℃，宜爲約 0～30℃。

化合物(VI，VII，VIII，T=SO)可令化合物(VI，VII，VIII，T=S)氧化而得。宜爲化合物(VII，T=SO)可令化合物(VII，T=S)氧化而得。

氧化劑爲間氯過苯甲酸(m-CPBA)、過氧化氫、過乙酸等。

化合物(VI)可依文獻(例如：特開昭 60-231684、特開昭 62-149682 等)記載之方法而合成。

上述醯胺化反應爲將羧基部分以反應性衍生物(例如：無機鹼鹽、有機鹼鹽、醯鹵、醯胺、酐、混合酐、活化醯胺、活化酯、活化硫酯)進行轉換來施行。該無機鹼爲鹼金屬(例如：Na、K 等)、鹼土金屬(例如：Ca、Mg)等，有機鹼爲二甲胺、三乙胺、第三丁基二甲胺、二苄甲胺、苄基二甲胺、N-甲嗎啉、二異丙基乙胺等，醯鹵爲醯氯、醯溴等，混合酐爲單烷碳酸混合酐、脂族碳酸混合酐、芳族碳酸混合酐、有機磺酸混合酐等，活化醯胺可如含氮雜環化合物之醯胺等，活化酯可爲有機磷酸酯(例如：二乙氧磷酸酯

、二苯氧磷酸酯等)、對-硝苯酯、2,4-二硝苯酯、氰甲酯等，活化硫酯爲如芳族雜環硫化合物之酯(例如：2-吡啶硫酯)等。上述反應可視需要使用適當縮合劑。縮合劑可如1-二甲胺丙基-3-乙基碳化二亞胺・鹽酸鹽(WSCD・HCl)、N,N'-二環己基碳化二亞胺、N,N'-羰基二咪唑、N,N'-硫羰基二咪唑、N-乙氧羰基-2-乙氧基-1,2-二氫喹啉、氧氯化磷、烷氧乙炔、2-氯吡錠甲基碘、2-氟吡錠甲基碘、三氟乙酐等。

2)3位側鏈之形成；令化合物(VII)與Z(：含N原子之可被取代雜環)反應可得化合物(VIII)。此反應中，R^6宜爲胺基保護基；R^7宜爲羧基保護基；R^a宜爲羧基保護基。化合物(VIII)之Z上取代基存在胺基等功能基之場合下，可將保護基進行保護。

Z之使用量對化合物(VII)1莫耳，通常爲約1～10莫耳，宜爲約1～2莫耳。

反應溶劑爲例如醚類(例如：二噁烷、四氫呋喃、乙醚、第三丁基甲基醚、二異丙醚)、酯類(例如：甲酸乙酯、乙酸乙酯、乙酸正丁酯)、鹵化烴類(例如：二氯甲烷、氯仿、四氯化碳)、烴類(例如：正己烷、苯、甲苯)、醯胺類(例如：甲醯胺、N,N-二甲基甲醯胺、N,N-二甲基乙醯胺、N-甲基吡咯啶酮)、酮類(例如：丙酮、甲基乙基酮)、腈類(例如：乙腈、丙腈)、二甲亞碸、水等。

反應溫度通常約爲0～100℃，宜爲約0～50℃，又宜爲約10～30℃。

反應促進劑宜使用NaI等。

化合物(VIII，T=S)可令化合物(VIII，T=SO)還原而得。還原劑可如金屬(例如：鋅、錫等)、碘化物(例如：KI等)。

(3)形成3位側鏈及7位醯化：化合物(IX)及(VIII)之製法

1)3位側鏈之形成；令化合物(VI)與Z(：含N原子之可被取代雜環)反應可得化合物(IX)。此反應中，R^8宜爲氫；R^a宜爲羧基保護基。化合物(IX)之Z上取代基存在胺基等功能基之場合下，可將保護基進行保護。

Z之使用量對化合物(VI)1莫耳，通常爲約1～10莫耳，宜爲約1～2莫耳。

反應溶劑爲例如醚類(例如：二噁烷、四氫呋喃、乙醚、第三丁基甲基醚、二異丙醚)、酯類(例如：甲酸乙酯、乙酸乙酯、乙酸正丁酯)、鹵化烴類(例如：二氯甲烷、氯仿、四氯化碳)、烴類(例如：正己烷、苯、甲苯)、醯胺類(例如：甲醯胺、N,N-二甲基甲醯胺、N,N-二甲基乙醯胺、N-甲基吡咯啶酮)、酮類(例如：丙酮、甲基乙基酮)、腈類(例如：乙腈、丙腈)、二甲亞碸、水等。

反應溫度通常約爲0～100℃，宜爲約0～50℃，又宜爲約10～30℃。

反應促進劑宜使用NaI等。

化合物(IX，T=SO)可令化合物(IX，T=SO)氧化而得。

氧化劑可如間氯過苯甲酸(m-CPBA)、過氧化氫、過乙酸等。

2)7位醯化；可令化合物(IX)與化合物(IV)反應而得化合物(VIII)。此反應中，R^a宜爲羧基保護基；R^5宜爲氫；R^6宜

爲胺基保護基；R^7宜爲羧基保護基；R^8宜爲氫。

化合物(IV)之使用量對化合物(IX)1莫耳，通常爲約1～5莫耳，宜爲約1～2莫耳。

反應溶劑爲例如醚類(例如：二噁烷、四氫呋喃、乙醚、第三丁基甲基醚、二異丙醚)、酯類(例如：甲酸乙酯、乙酸乙酯、乙酸正丁酯)、鹵化烴類(例如：二氯甲烷、氯仿、四氯化碳)、烴類(例如：正己烷、苯、甲苯)、醯胺類(例如：甲醯胺、N,N-二甲基甲醯胺、N,N-二甲基乙醯胺、N-甲基吡咯啶酮)、酮類(例如：丙酮、甲基乙基酮)、腈類(例如：乙腈、丙腈)、二甲亞碸、水等。

反應溫度通常約爲-40～100℃，宜爲約0～30℃。

醯胺化反應爲將上述同樣羧基部分以反應性衍生物(例如：無機鹼鹽、有機鹼鹽、醯鹵、醯胺、酐、混合酐、活化醯胺、活化酯、活化硫酯)進行轉換來施行，可視需要使用適當縮合劑來進行。

(4)脫保護

令化合物(VIII)依習知方法進行脫保護反應可得化合物(I)。

反應溶劑爲例如醚類(例如：二噁烷、四氫呋喃、乙醚、第三丁基甲基醚、二異丙醚)、酯類(例如：甲酸乙酯、乙酸乙酯、乙酸正丁酯)、鹵化烴類(例如：二氯甲烷、氯仿、四氯化碳)、烴類(例如：正己烷、苯、甲苯)、醯胺類(例如：甲醯胺、N,N-二甲基甲醯胺、N,N-二甲基乙醯胺、N-甲基吡咯啶酮)、酮類(例如：丙酮、甲基乙基酮)、腈類

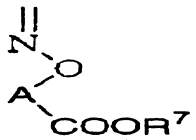
(例如：乙腈、丙腈)、硝類(例如：硝甲烷、硝乙烷、硝苯)、二甲亞碸、水等。此溶劑可單獨使用或混合 2 種以上來使用。

反應溫度通常約爲-30～100℃，宜爲約 0～50℃，又宜爲約 0～10℃。

觸媒可使用路易士酸(例如：$AlCl_3$、$SnCl_4$、$TiCl_4$)、質子酸(例如：鹽酸、硫酸、$HClO_4$、甲酸、酚)等。

所得化合物(I)可進行化學修飾而得其它化合物(I)、酯、及其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物。

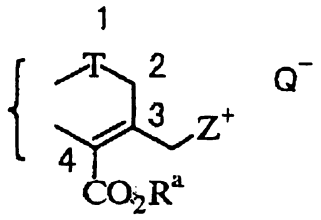
化合物(I)之酯宜包含 7 位側鏈上或 4 位羧基轉爲酯體。7 位側鏈上羧基轉爲酯體爲如下式：



(R^7 爲羧基保護基等酯殘基)

所示酯構造之化合物。該酯包含體內容易代謝之羧基之酯。

化合物(I)4 位羧基轉爲酯體中 4 位部分爲如下式：

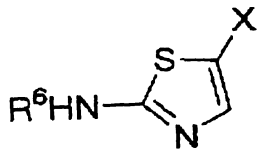


(R^a 爲羧基保護基等酯殘基；Q 爲鹵素等離子)所示酯構造之化合物。該酯包含體內容易代謝之羧基之酯。

上述羧基保護基爲如低烷基(例如：甲基、乙基、第三丁

基)，(取代)芳烷基(例如：苄基、二苯甲基、對-甲氧苄基、對-硝苄基)，矽烷基(第三丁基二甲矽烷基、二苯第三丁基矽烷基)等。

化合物(I)7位噻唑環上胺基之保護體意指該噻唑環形成如下式環：



(R^6為胺基保護基)之化合物。該胺基保護基含可易於體內代謝胺基之基。上述胺基保護基為低烷氧羰基(例如：第三丁氧羰基、苄氧羰、對-硝苄氧羰基)，(取代)芳烷醯基(例如：對-硝苄醯基)，醯基(例如：甲醯基、氯乙醯基)等。化合物(I)之製藥容許鹽為無機鹼、氨、有機鹼、無機酸、有機酸、鹼性胺基酸、鹵素離子等形成之鹽或分子內鹽。該無機鹼為鹼金屬(Na、K等)，鹼土金屬(Mg等)，有機鹼為普羅卡因、2-苯乙苄胺、二苄伸乙二胺、乙醇胺、二乙醇胺、參羥甲胺甲烷、聚羥烷胺、N-甲葡糖胺等。無機酸為氫氯酸、氫溴酸、硫酸、硝酸、磷酸等。有機酸為對-甲苯磺酸、甲磺酸、甲酸、三氟乙酸、順丁烯二酸等。鹼性胺基酸為離胺酸、精胺酸、鳥胺酸、組胺酸等。

化合物(I)之溶劑合物之溶劑為如水或醇。

本發明提供上述化合物(I-A)。化合物(I-A)中各基之定義及製法可如上述化合物(I)所述。

本發明亦提供上述化合物(IV)、(VII)及(IX)。此化合物

可作爲製造化合物(I)之中間體。特以化合物(IV)爲發揮化合物(I)抗菌活性之重要中間體。化合物(IV)中宜爲 X 爲鹵素或低烷基，更宜爲鹵素(例如：Cl、Br)。

本發明化合物具有廣抗菌活性，可用以預防或治療人(含各種哺乳動物)因病原性細菌所致各種疾病，例如呼吸道感染症、尿道感染症、呼吸器感染症、敗血症、腎炎、膽囊炎、口腔內感染症、心內膜炎、肺炎、骨髓膜炎、中耳炎、腸炎、蓄膿病、傷口感染、機會感染等。

本發明化合物特對含綠膿菌、大腸菌、流感菌等革蘭式陰性菌有高抗菌活性。尤其對哂吩抗性綠膿菌所產出β-乙內醯胺酶(特爲 C 型β-乙內醯胺酶)極具安定性，而對該抗性綠膿菌有效。可單獨不與β-乙內醯胺酶抑制劑併用仍有優異之治療效果。本發明化合物對包含甲基青黴素抗性黃色葡萄球菌(MRSA)、青黴素抗性肺炎葡萄球菌(PRSP)等革蘭式陽性菌有抗菌活性。更具優良體內循環、高血濃度、長效性、及顯著組織移動性等之特徵。本發明化合物具有高水溶性，特宜爲注射藥。

化合物(I)及(I-A)可以注射劑、膠囊劑、錠劑、顆粒劑等以非經口或經口投予，宜爲以注射劑投予。投予量對患者或動物 1 公斤體重，通常投予約 0.1～100 毫克/日，宜爲約 0.5～50 毫克/日，可視需要次分爲 1 日 2～4 回來投與。使用注射劑時載體可爲蒸餾水、生理食鹽水等，亦可用 pH 調節之鹼等。使用膠囊劑、顆粒劑、錠劑時載體可爲習用賦形劑(例如：澱粉、乳糖、白糖、碳酸鈣、磷酸鈣等)

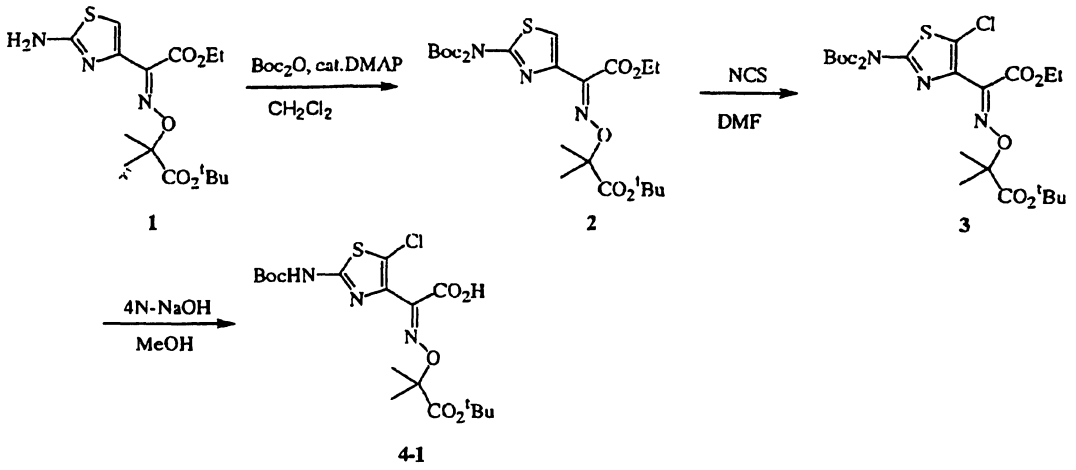
、結合劑(例如：澱粉、阿拉伯樹膠、羧甲基纖維素、羥丙基纖維素、結晶纖維素等)、潤滑劑(例如：硬脂酸鎂、滑石等)等。

以下爲參考例及實施例。

(簡寫)

Me：甲基；Et：乙基；iPr：異丙基；Bu：丁基；Ac：乙醯基；DMF：二甲基甲醯胺；THF：四氫呋喃；DMA：二甲基乙醯胺；WSCD：1-二甲胺丙基-3-乙基碳化二亞胺；m-CPBA：間-氯過苯甲酸；Boc：第三丁氧羰基；PMB：對-甲氧苄基；BH：二苯甲基；TBS：第三丁二甲矽烷基；Ph：苯基

參考例 1(7位側鏈之合成)



(1) 將含化合物 1(71.4克，200毫莫耳)之無水二氯甲烷714毫升溶液，於室溫下加入4-二甲胺吡啶(DMAP)2.44克(0.1當量)。再滴加入 Boc_2O 95.2毫升(2.1當量)。於室溫下攪拌21小時，加入1N-HCl 19毫升後注入飽和氯化銨水溶液，將有機層分層。將分層之有機層以食鹽水洗淨後，

於無水硫酸鈉下乾燥，減壓濃縮得化合物 2(112 克)。

^{1}H-NMR ($CDCl_3$) δ: 1.35(3H, t, J = 6.9 Hz), 1.43(9H, s), 1.51(6H, s), 1.53(18H, s), 4.36(2H, q, J = 6.9 Hz), 7.38(1H, s).

IR (KBr) cm^{-1}: 2979, 2938, 1781, 1743, 1722, 1494, 1457, 1369, 1346, 1328,1284, 1135.

MS(ESI):558$^+$($M+H^+$).

元素分析 $C_{25}H_{39}N_3O_9S$.

計算值： C,53.84 ; H,7.05 ; N,7.54 ; S,5.75 (%).

實驗值： C,53.70 ; H,6.91 ; N,7.49 ; S,5.81 (%).

(2) 將化合物 2 101 克(181 毫莫耳)溶在 DMF 400 毫升、於室溫下加入 N-氯丁二醯亞胺(NCS)9.65 克(0.4 當量)，於室溫下攪拌 3 小時。追加入 NCS 9.65 克(0.4 當量)後於室溫下攪拌 2 小時，再加入 NCS 9.65 克(0.4 當量)後於室溫下攪拌 4 小時。靜置於 4℃ 下過夜，將反應溶液以硫酸鈉 30 克並加入 1000 毫升水溶液，以乙酸乙酯萃取(500 毫升，2 次)。將所得有機層以食鹽水洗淨，於無水硫酸鈉下乾燥，減壓濃縮。以矽膠柱層析純化，減壓濃縮得化合物 3(104 克)。

^{1}H-NMR ($CDCl_3$) δ: 1.34(3H, t, J = 6.9 Hz), 1.44(9H, s), 1.52(6H, s), 1.53(18H, s), 4.33(2H, q, J = 6.9 Hz).

IR (KBr) cm^{-1}: 2979, 2938, 1781, 1743, 1722, 1494, 1457, 1369, 1346, 1328,1284, 1135.

MS(ESI):614$^+$($M+Na^+$).

元素分析 $C_{25}H_{38}ClN_3O_9S$.

計算值： C,50.71 ; H,6.47 ; N,7.10 ; S,5.42 ; Cl,5.99 (%).

實驗值： C,50.57 ; H,6.40 ; N,7.01 ; S,5.13 ; Cl,5.93(%).

(3) 將化合物 3 83.2 克(140 毫莫耳)溶在甲醇 160 毫升，於冰冷卻下滴加入 8N-氫氧化鈉 175 毫升。於冰冷卻下攪拌 0.5 小時，回溫至室溫再攪拌 5.5 小時。滴加入 5N-鹽酸 210 毫升(滴加入後反應溶液之 pH 爲 5.3)。於室溫下靜置過夜。減壓濃縮蒸除甲醇可析出白色沈澱物，加水 1000 毫升，過濾。將所得白色固體以冰水洗淨後，減壓濃縮得化合物 4-1 60.9 克。

^{1}H-NMR ($CDCl_3$) δ: 1.46(9H, s), 1.52(9H, s), 1.58(6H, s), 5.20-6.20(2H, brs).

IR (KBr) cm^{-1}: 3426, 3220, 3081, 2981, 2937, 1720, 1556, 1455, 1394, 1369, 1249, 1155.

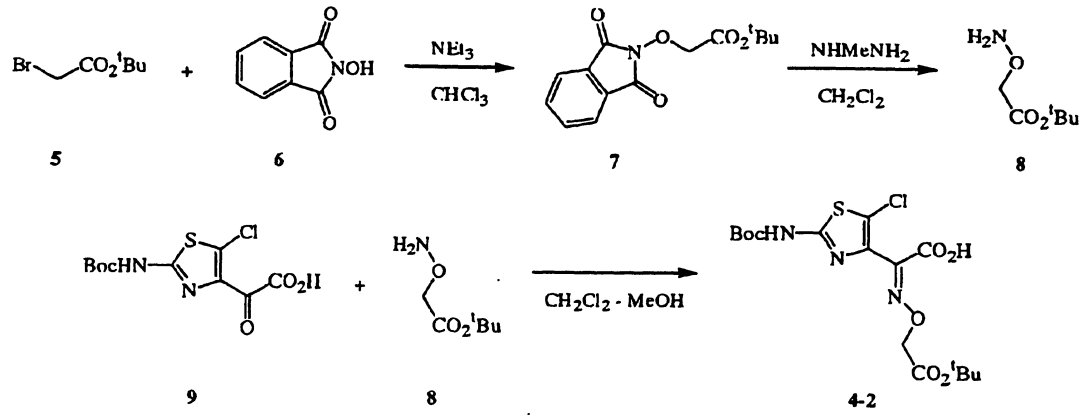
MS(ESI):464$^+$(M+H$^+$).

元素分析 $C_{18}H_{26}ClN_3O_7S \cdot 0.6\ H_2O$.

計算值： C,45.54 ; H,5.77 ; N,8.85 ; S,6.75 ; Cl,7.47 (%).

實驗值： C,45.38 ; H,5.59 ; N,8.82 ; S,6.67 ; Cl,7.75(%).

參考例 2(7 位側鏈之合成)



(1) 將含化合物 1(8.8 毫升，60 毫莫耳)及化合物 6(6.52 克，40 毫莫耳)之無水氯仿 180 毫升溶液，於冰冷卻下滴加入三乙胺 6.12 毫升，於室溫下攪拌 3 日。追加入三乙胺 0.3 毫升後，於室溫下攪拌 1 日，加入飽和碳酸氫鈉水溶

液後，以氯仿萃取。將所得有機層以飽和氯化銨水溶液洗淨後，於無水硫酸鎂下乾燥，減壓濃縮得化合物 7 10.5 克。

^{1}H-NMR ($CDCl_3$) δ: 1.49(9H, s), 4.71(2H, s), 7.70-7.90(4H, m).

IR (KBr) cm^{-1}: 2980, 2939, 1788, 1745, 1730, 1465, 1441, 1374, 1247, 1186, 1160, 1137, 1043.

MS(ESI):300^+($M+Na^+$).

元素分析 $C_{14}H_{15}NO_5 \cdot 0.2\ H_2O$.

計算值： C,59.87 ; H,5.53 ; N,4.99 (%).

實驗值： C,60.04 ; H,5.55 ; N,5.13 (%).

(2) 將含化合物 7(1.67 克，6 毫莫耳)之無水二氯甲烷 16 毫升溶液，於冰冷卻下加入甲肼 0.32 毫升，於冰冷卻下攪拌 15 分。濾除所析出之白色沈澱，濾液中得化合物 8。於冰冷卻下加入甲醇 6 毫升至濾液中，加入化合物 9(1.53 克，5 毫莫耳)。於冰冷卻下攪拌 10 分後，於室溫下攪拌 2.5 小時，再加熱回流下攪拌 1 小時，於室溫下靜置 3 日。靜置 3 日後濾集析出沈澱物、以乙醚洗淨得化合物 4-2 1.36 克。

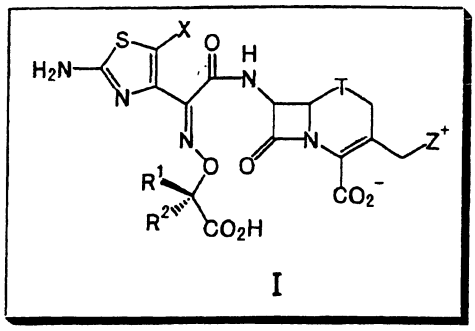
^{1}H-NMR(d_6-DMSO)δ：1.42(9H, s), 1.46(9H,s),4.36(2H,s), 6.0-9.0(1H, brs), 11.9(1H, brs).

IR (KBr) cm^{-1}: 3429, 3136, 2982, 2936, 1739, 1715, 1626, 1557, 1458, 1392, 1381, 1370, 1249, 1157.

MS(FAB):434^-($M-H^-$).

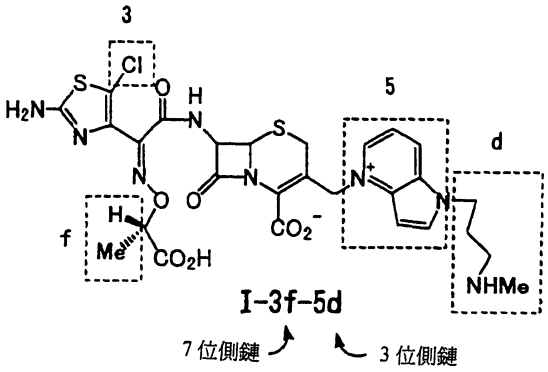
HR-MS(FAB): calcd for $C_{16}H_{21}Cl_1N_3O_7S$ 434.0789 found 434.0782.

實施例化合物之取代基之種類，及化合物 No 與構造之關係如下。



I

化合物 No 之例示



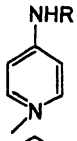
7 位側鏈

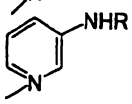
X	R^1	R^2
1: H	a: H	H
2: Me	b: =CH_2	
3: Cl	c: $-(CH_2)_2-$	
4: Br	d: Me	Me
	e: Me	H
	f: H	Me
	g: Et	H
	h: H	Et
	i: iPr	H
	j: H	iPr
	k: CH_2OH	H
	l: H	CH_2OH

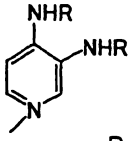
3 位側鏈

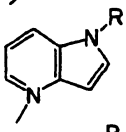
Z

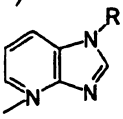
1: 

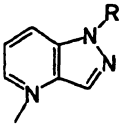
2: 

3: 

4: 

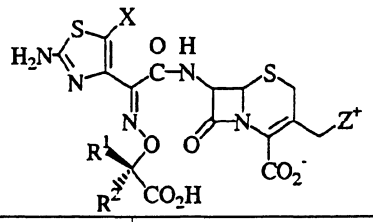
5: 

6: 

7: 

R =
a: H
b: Me
c: $(CH_2)_2NHMe$
d: $(CH_2)_3NHMe$

實施例 1～21 之化合物(I)之構造如下。

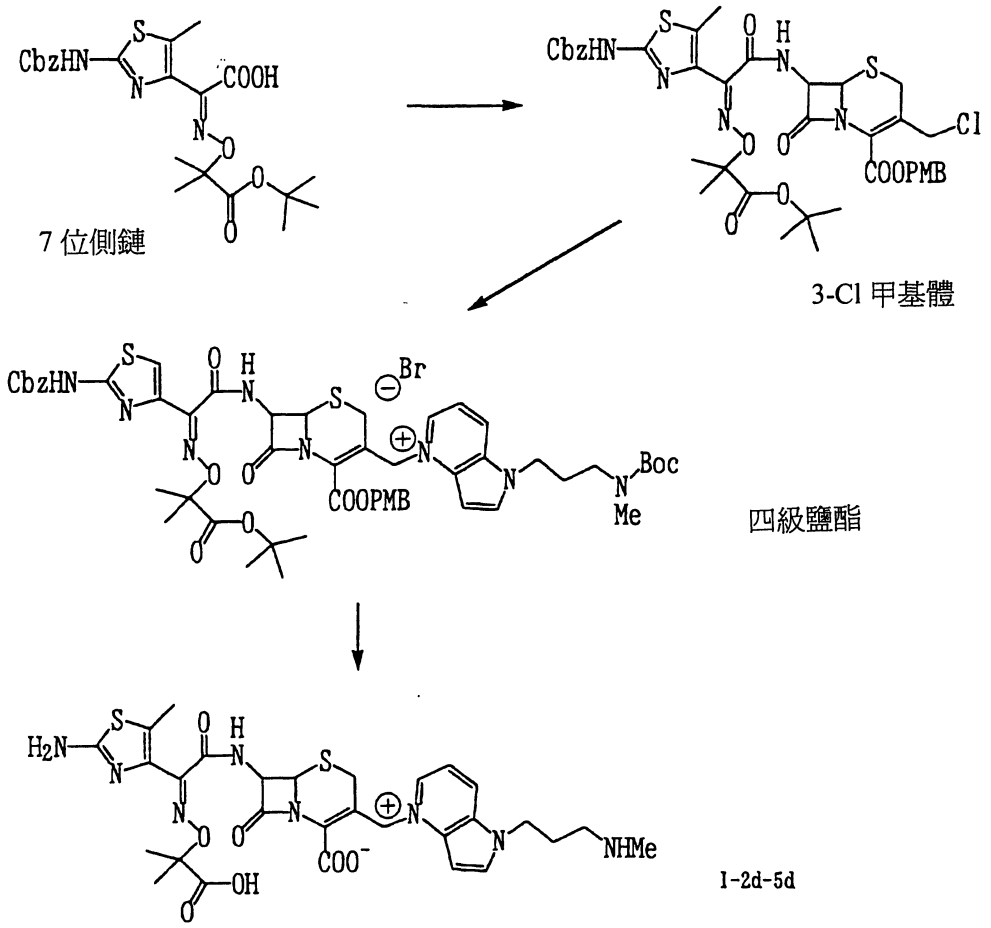


(I)

實施例	化合物No	X	R 1	R 2	Z
1	I-2d-5d	Me	Me	Me	5d
2	I-3a-5d	Cl	H	H	5d
3	I-3d-1	Cl	Me	Me	1
4	I-3d-2a	Cl	Me	Me	2a
5	I-3d-5d	Cl	Me	Me	5d
6	I-3d-6d	Cl	Me	Me	6d
7	I-3d-5c	Cl	Me	Me	5c
8	I-3e-5d	Cl	Me	H	5d
9	I-3f-5d	Cl	H	Me	5d
10	I-3g-5d	Cl	Et	H	5d
11	I-3h-5d	Cl	H	Et	5d
12	I-3i-5d	Cl	iPr	H	5d
13	I-3j-5d	Cl	H	iPr	5d
14	I-3k-5d	Cl	CH_2OH	H	5d
15	I-3l-5d	Cl	H	CH_2OH	5d
16	I-3f-2a	Cl	H	Me	2a
17	I-3c-2a	Cl	$-(CH_2)_2-$		2a
18	I-3c-5d	Cl	$-(CH_2)_2-$		5d
19	I-3b-5d	Cl	$=CH_2$		5d
20	I-4d-5d	Br	Me	Me	5d
21	I-4f-5d	Br	H	Me	5d

合成法及物性如下。化合物之合成仿實施例 2 及 5 施行。

實施例 1



I-2d-5d：

^{1}H-NMR (D_2O) δ: 1.46(6H, s), 2.27(3H, s), 2.31(2H, m), 2.69(3H, s), 3.06(2H, m), 3.18 及 3.39(2H, ABq, J = 17.7 Hz), 4.52(2H, t, J = 7.2 Hz), 5.18(1H, d, J = 4.8 Hz), 5.55 及 5.69(2H, ABq, J = 15.0 Hz), 5.82(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.6 Hz), 7.69(1H, dd, J = 6.0 及 8.4 Hz), 8.12(1H, d, J = 3.6 Hz), 8.59(1H, d, J = 8.4 Hz), 8.65(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}: 3413, 2983, 2458, 1774, 1610, 1498, 1467, 1392, 1359, 1288, 1195, 1162, 1122.

MS(ESI):671$^+$($M+H^+$).

元素分析 $C_{29}H_{34}N_8O_7S_2 \cdot 5.6\ H_2O$.

計算值： C,45.14 ; H,5.90 ; N,14.52 ; S,8.31 (%).

實驗值： C,45.15 ; H,5.32 ; N,14.36 ; S,8.49 (%).

四級鹽酯：

^{1}H-NMR (d_6-DMSO) δ: 1.37(9H, s), 1.38(6H, s), 1.42(9H, s), 2.03(2H, m), 2.41(3H, s), 2.78(3H, brs), 3.18(2H, m), 3.36 及 3.56(2H, m), 3.75(3H, s), 4.43(2H, m), 5.17(1H, d, J = 5.1 Hz), 5.21(2H, s), 5.22 及 5.29(2H, ABq, J = 11.4 Hz), 5.67 及 5.72(2H, ABq, J = 16.2 Hz), 5.96(1H, dd, J = 5.1 及 8.7 Hz), 6.90(2H, d, J = 8.7 Hz), 6.96(1H, d, J = 3.6 Hz), 7.33(2H, d, J = 8.7 Hz), 7.34-7.45(5H, 7.78(5H, m), 7.78(1H, m), 8.43(1H, d, J = 3.3 Hz), 8.62(1H, d, J = 6.0 Hz), 8.88(1H, d, J = 8.4 Hz), 9.49(1H, d, J = 8.7 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1}:3423, 3089, 2973, 2933, 1791, 1724, 1685, 1556, 1515, 1496, 1454, 1390, 1365, 1299, 1247, 1222, 1174, 1145, 1062, 1027.

MS(ESI): 1081$^+$($C_{54}H_{65}N_8O_{12}S_2^+$).

3-Cl 甲基體：

^{1}H-NMR ($CDCl_3$) δ: 1.42(9H, s), 1.57(3H, s), 1.58(3H, s), 2.48(3H, s), 3.47 and 3.64(2H, ABq, J = 18.3 Hz), 3.81(3H, s), 4.44 及 4.55(2H, ABq, J = 11.7 Hz), 5.04(1H, d, J = 5.1 Hz), 5.20 及 5.26(2H, ABq, J = 12.0 Hz), 5.25(2H, s), 6.04(1H, dd, J = 5.1 及 9.3 Hz), 6.90(2H, d, J = 9.0 Hz), 7.35(2H, d, J = 9.0 Hz), 7.30-7.40(5H, m), 7.90(1H, d, J = 9.3 Hz), 8.38(1H, brs).

IR (KBr) cm^{-1}: 3386, 3283, 2979, 2937, 1789, 1726, 1692, 1613, 1557, 1515, 1455, 1383, 1367, 1300, 1247, 1224, 1142, 1094, 1061.

MS(ESI): 828$^+$(M+H$^+$).

元素分析 $C_{38}H_{42}ClN_5O_{10}S_2 \cdot 0.05\ CHCl_3 \cdot 0.7\ H_2O$.

計算值： C,53.96 ; H,5.17 ; N,8.27 ; S,7.57 ; Cl,4.81 (%).

實驗值： C,54.03 ; H,5.14 ; N,8.16 ; S,7.29 ; Cl,4.81 (%).

7 位側鏈：

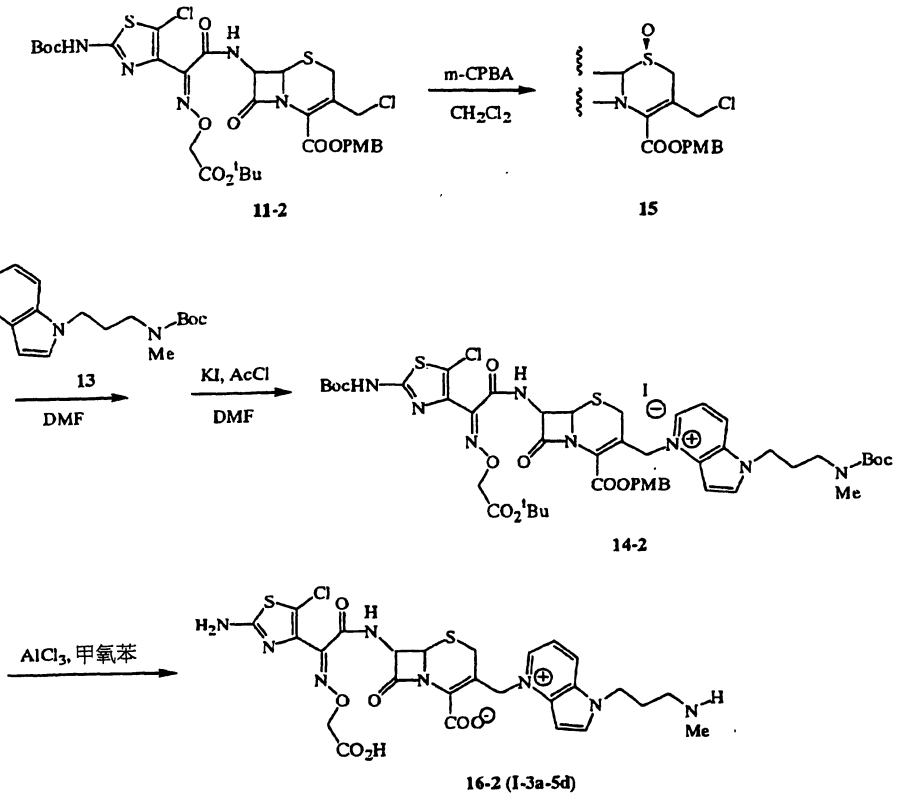
^{1}H-NMR (d_6-DMSO) δ: 1.39(9H, s), 1.41(6H, s), 2.43(3H, s), 5.22(2H, s),

7.30-7.40(5H, m), 12.0(1H, brs).

IR (KBr) cm^{-1}: 3430, 3193, 2981, 2937, 1731, 1614, 1596, 1562, 1455, 1392, 1369, 1299, 1228, 1187, 1141, 1062.

MS(ESI): $478^{+}(M+H^{+})$.

實施例 2



(1) 於氮氣下，將含化合物 11-2(1.20 克，1.53 毫莫耳)之二氯甲烷 12 毫升溶液於-50℃冷卻後，加入 65%m-CPBA (366 毫克，0.9 當量)之 2 毫升溶液，於-50℃～-40℃攪拌 15 分。將反應溶液加入飽和硫代硫酸鈉溶液，以氯仿萃取。將所得有機層以飽和碳酸氫鈉水溶液及食鹽水洗淨後，於無水硫酸鎂下乾燥，減壓濃縮得化合物 15(1.18 克)。將化合物 15(1.18 克，1.4 毫莫耳)於氮氣下溶在 DMF 2 毫升後，加入 NaBr(303 毫克，2 當量)，化合物 13(627 毫克，1.55 當量)之 DMF 2 毫升溶液並於室溫下攪拌 5 小時，於 4℃下靜置過夜。於氮氣下加入 DMF 20 毫升，KI 1.7 克，

於-50℃下冷卻後，滴加入 AcCl 0.523 毫升後於-50℃下攪拌 1 小時，再於-50℃～-10℃下攪拌 1.5 小時。加入硫代硫酸鈉 1 克，於冰冷卻下滴加入 5%NaCl 溶液可生成沈澱物。濾集沈澱，於減壓下以 P_2O_5 乾燥得粉末狀化合物 14-2 1.59 克。

化合物 14-2

^{1}H-NMR (d_6-DMSO) δ: 1.40(9H, s), 1.46(18H, s), 2.03(2H, m), 2.78(3H, brs), 3.18(2H, t, J = 7.2 Hz), 3.27 及 3.43(2H, ABq, J = 18.3 Hz), 3.75(3H, s), 4.43(2H, t, J = 6.6 Hz), 4.55(2H, s), 5.18(1H, d, J = 4.8 Hz), 5.21 及 5.28(2H, ABq, J = 12.0 Hz), 5.65 及 5.73(2H, ABq, J = 15.3 Hz), 5.95(1H, dd, J = 4.8 及 8.7 Hz), 6.89(2H, d, J = 8.7 Hz), 7.00(1H, d, J= 3.3 Hz), 7.35(2H, d, J = 8.7 Hz), 7.78(1H, dd, J = 6.3 及 8.1 Hz), 8.43(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 6.3 Hz), 8.88(1H, d, J = 8.1 Hz), 9.65(1H, d, J = 8.7 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1}: 3427, 3058, 2976, 2933, 1791, 1718, 1686, 1630, 1613, 1584, 1550, 1515, 1496, 1455, 1393, 1368, 1300, 1247, 1156, 1080, 1063, 1022.

MS(ESI): 1039$^+$($C_{48}H_{60}ClN_8O_{12}S_2^+$).

化合物 11-2

^{1}H-NMR ($CDCl_3$) δ: 1.44(9H, s), 1.53(9H, s), 3.47 及 3.63(2H, ABq, J = 18.0 Hz), 3.82(3H, s), 4.45(2H, s), 4.68 及 4.75(2H, ABq, J = 16.8Hz), 5.05(1H, d, J = 4.8 Hz), 5.20 及 5.27(2H, ABq, J = 12.0 Hz), 5.98(1H, dd, J = 4.8 及 9.3 Hz), 6.91(2H, d, J = 8.7 Hz), 7.35(2H, d, J = 8.7 Hz), 8.11(1H, brs), 8.49(1H, d, J = 9.3 Hz).

IR (KBr) cm^{-1}: 3382, 3277, 2979, 2935, 2837, 1791, 1722, 1613, 1551, 1515, 1455, 1369, 1302, 1246, 1157, 1085, 1062, 1036, 1021.

MS(FAB): 786$^+$(M+H$^+$).

HR-MS(FAB): calcd for $C_{32}H_{38}Cl_2N_5O_{10}S_2$ 786.1437 found 786.1434 .

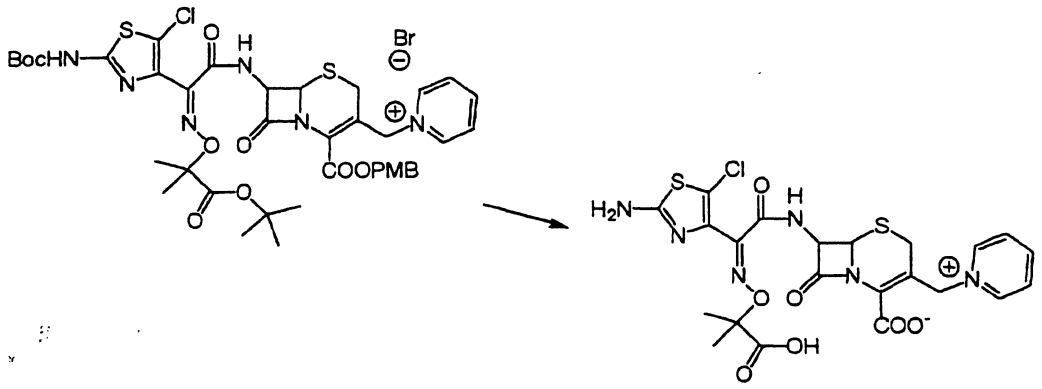
(2) 將化合物 14-2 1.59 克(約 1.47 毫莫耳)依實施例 5(3)之方法進行脫保護可得化合物 16-2(I-3a-5d，270 毫克)。

3.18(2H, t, J = 7.2 Hz), 3.27 及 3.43(2H, ABq, J = 18.3 Hz), 3.75(3H, s), 4.43(2H, t, J = 6.6 Hz), 4.55(2H, s), 5.18(1H, d, J = 4.8 Hz), 5.21 及 5.28(2H, ABq, J = 12.0 Hz), 5.65 及 5.73(2H, ABq, J = 15.3 Hz), 5.95(1H, dd, J = 4.8 及 8.7 Hz), 6.89(2H, d, J = 8.7 Hz), 7.00(1H, d, J = 3.3 Hz), 7.35(2H, d, J = 8.7 Hz), 7.78(1H, dd, J = 6.3 及 8.1 Hz), 8.43(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 6.3 Hz), 8.88(1H, d, J = 8.1 Hz), 9.65(1H, d, J = 8.7 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1}: 3427, 3058, 2976, 2933, 1791, 1718, 1686, 1630, 1613, 1584, 1550, 1515, 1496, 1455, 1393, 1368, 1300, 1247, 1156, 1080, 1063, 1022.

MS(ESI): $1039^{+}(C_{48}H_{60}ClN_8O_{12}S_2^{+})$.

實施例 3



I-3d-1 :

^{1}H-NMR (D_2O) δ : 1.54(6H, s), 3.22 and 3.64(2H, ABq, J = 17.7 Hz), 5.28(1H, d, J = 4.8 Hz), 5.34 and 5.58(2H, ABq, J = 14.4 Hz), 5.88(1H, d, J = 4.8 Hz), 8.09(2H, t like), 8.58(1H, t like), 8.96(2H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}: 3417, 3058, 2989, 2938, 2524, 1778, 1673, 1625, 1536, 1486, 1386, 1340, 1157.

MS(ESI):$581^{+}(M+H^{+})$.

元素分析 $C_{22}H_{21}ClN_6O_7S_2 \cdot 2.9\ H_2O$.

計算値： C,41.73 ; H,4.27 ; N,13.27 ; Cl,5.60; S,10.13 (%).

實驗值：C,41.74 ; H,3.99 ; N,13.16 ; Cl,5.53; S,10.20 (%).

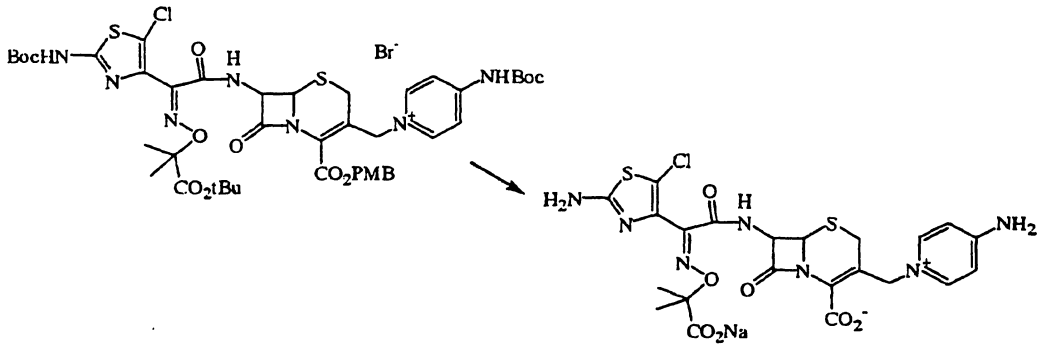
四級鹽酯：

^{1}H-NMR (d_6-DMSO) δ: 1.37(9H, s), 1.42(3H, s), 1.44(3H, s), 1.46(9H, s), 3.51(2H, brs), 3.77(3H, s), 5.20 及 5.26(2H, ABq, J = 12.0 Hz), 5.22(1H, d, J = 5.1 Hz), 5.58(2H, brs), 5.98(1H, dd, J = 5.1 及 9.0 Hz), 6.93(2H, d, J = 8.4 Hz), 7.35(2H, d, J = 8.4 Hz), 8.20(2H, t like), 8.66(1H, t like), 8.99(2H, d, J = 5.7 Hz), 9.57(1H, d, J = 9.0 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1}: 3428, 3054, 2979, 2935, 1791, 1718, 1629, 1614, 1548, 1515, 1481, 1455, 1392, 1369, 1299, 1247, 1153, 1064, 1029.

MS(ESI): 857$^+$($C_{39}H_{46}ClN_6O_{10}S_2^+$).

實施例 4



I-3d-2a：

^{1}H-NMR (D20) δ: 1.40(6H, s), 3.18 and 3.55(2H, ABq, J = 17.7 Hz), 4.88 及 5.02(2H, ABq, J = 14.7 Hz), 5.23(1H, d, J =4.8 Hz), 5.84(1H, d, J = 4.8 Hz), 6.83 及 8.05(4H, A2B2q, J = 7.5).

IR (KBr) cm^{-1}: 3400, 3189, 2993, 1770, 1654, 1604, 1537, 1398, 1361, 1165 .

元素分析 $C_{27}H_{21.2}N_7O_7S_2ClNa_{0.8}\cdot 5H_2O$

計算值： C,37.55; H,4.47; N,13.93; S,9.11; Cl,5.04; Na,2.61 (%).

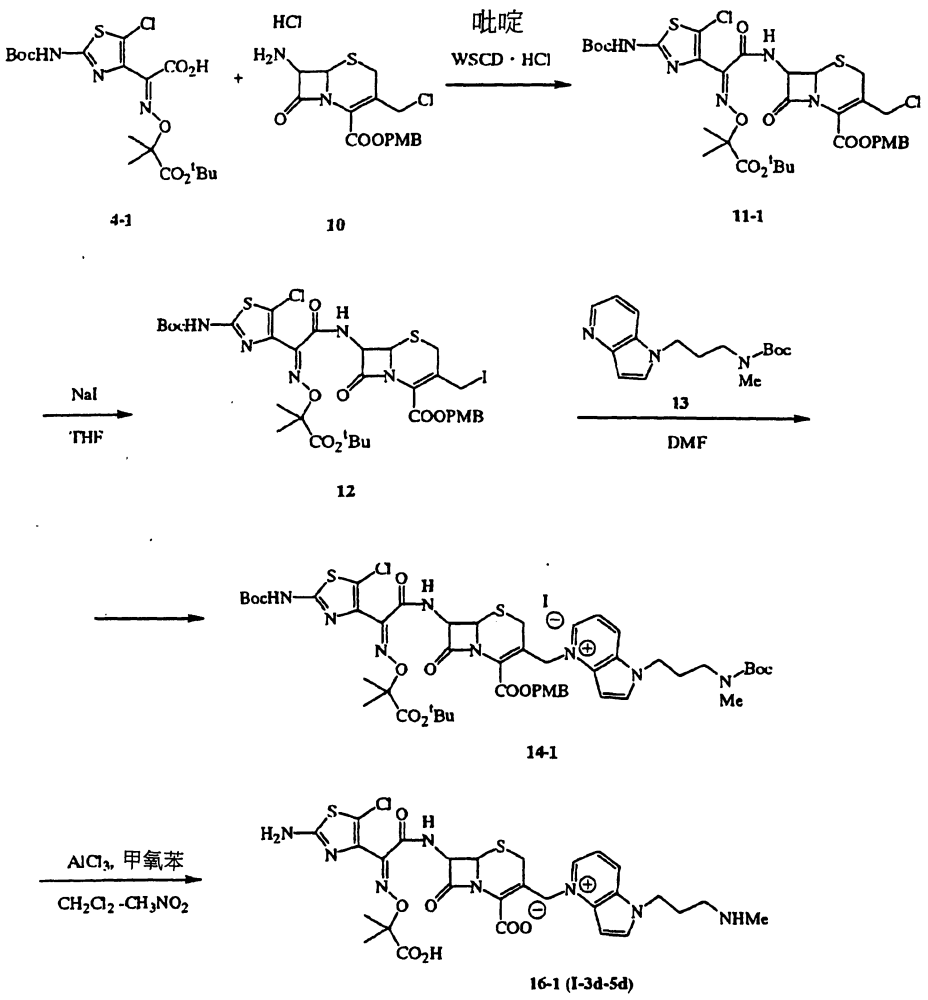
實驗值： C,37.34; H,4.28; N,13.73; S,9.07; Cl,4.97; Na,2.70 (%).

四級鹽酯：

^{1}H-NMR (CDCl3) δ: 1.43(9H, s), 1.51(9H, s), 1.55(9H, s), 1.58(3H, s), 1.59(3H, s), 3.35 及 3.92(2H, ABq, J = 19.2 Hz), 3.82(3H, s), 5.24 ~ 5.30(3H, m), 5.31 及 5.57(2H, Abq, J = 14.4 Hz), 6.01(1H, dd, J = 4.8, 8.7 Hz), 6.90 及 7.36(4H, A2B2q, J = 9 Hz), 8.04~8.12(3H, m), 8.35(1H,br s), 8.63(2H, J = 7.5 Hz), 8.98(1H, s).

IR (KBr) cm^{-1}: 3422, 3274, 2979, 2934, 1794, 1719, 1641, 1530, 1457, 1369, 1299, 1246, 1146, 842.

實施例 5



(1) 將含參考例 1 所得化合物 4-1(10.3 克，22.2 毫莫耳)與化合物 10(9.90 克，24.4 毫莫耳)之無水 DMF 100 毫升溶液，於冰冷卻下加入 WSCD・鹽酸(5.11 克，1.2 當量)，吡

啶(1.80毫升，1.0當量)，於室溫下攪拌1小時。將反應溶液加入冰水300毫升，以乙酸乙酯萃取(200毫升，2次)。將所得有機層以食鹽水洗淨後，於無水硫酸鎂下乾燥。減壓濃縮後，以矽膠柱層析純化，減壓濃縮得泡沫狀化合物11-1 13.7克。

^{1}H-NMR ($CDCl_3$) δ: 1.42(9H, s), 1.52(9H, s), 1.60(6H, s), 3.48 及 3.65(2H, ABq, J = 18.0 Hz), 3.82(3H, s), 4.45 及 4.55(2H, ABq, J = 11.7 Hz), 5.04(1H, d, J = 5.1 Hz), 5.20 及 5.27(2H, ABq, J = 12.0 Hz), 6.03(1H, dd, J = 5.1 及 9.3 Hz), 6.91(2H, d, J = 8.7 Hz), 7.35(2H, d, J = 8.7 Hz), 8.03(1H, d, J = 9.3 Hz), 8.13(1H, brs).

IR (KBr) cm^{-1}: 3396, 3284, 2979, 2937, 2836, 1791, 1722, 1614, 1550, 1515, 1455, 1384, 1369, 1301, 1247, 1155, 1035.

MS(ESI): $814^+(M+H^+)$.

元素分析 $C_{34}H_{41}Cl_2N_5O_{10}S_2 \cdot 0.2\ CHCl_3 \cdot 0.4\ H_2O$.

計算值: C,48.56 ; H,5.00 ; N,8.28 ; S,7.58 ; Cl,10.90 (%).

實驗值: C,48.51 ; H,4.85 ; N,8.11 ; S,7.56 ; Cl,11.00 (%).

(2) 於氮氣下，將含化合物11-1(5.0克，6.14毫莫耳)之THF 50毫升溶液冷卻至15℃，加入NaI 2.76(3當量)，於15℃下攪拌30分。將反應溶液加至冰水150毫升，以乙酸乙酯萃取。將所得有機層以飽和硫代硫酸鈉水溶液，及食鹽水洗淨後，於無水硫酸鎂下乾燥，減壓濃縮得泡沫狀化合物12(5.51克)。於氮氣下，將含化合物12(2.72克，3.01毫莫耳)之DMF 12毫升溶液，加入化合物13(868毫克，1當量)之DMF 3毫升溶液。於室溫下攪拌1小時後，於冰冷卻下將反應溶液滴加入5%NaCl溶液可生成淡黃色沈澱物。濾集沈澱，於減壓下以P_2O_5乾燥得粉末狀化合物14-1

3.26 克。

^{1}H-NMR (d_6-DMSO) δ: 1.37(9H, s), 1.43(6H, s), 1.46(18H, s), 2.03(2H, m), 2,78(3H, brs), 3.17(2H, m), 3.28 及 3.39(2H, ABq, J = 16.2 Hz), 3.76(3H, s), 4.43(2H, m), 5.18(1H, d, J = 5.1 Hz), 5.22 及 5.30(2H, ABq, J = 11.7 Hz), 5.70(2H, brs), 5.95(1H, dd, J = 5.1 及 8.7 Hz), 6.90(2H, d, J = 8.7 Hz), 6.95(1H, d, J = 3.3 Hz), 7.33(2H, d, J = 8.7 Hz), 7.78(1H, dd, J = 5.7 及 8.4 Hz), 8.43(1H, d, J = 3.3 Hz), 8.63(1H, d, J = 5.7 Hz), 8.88(1H, d, J = 8.4 Hz), 9.58(1H, d, J = 8.7 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1}: 3423, 2977, 2935, 1789, 1718, 1685, 1629, 1612, 1550, 1515, 1496, 1455, 1392, 1367, 1299, 1249, 1153.

MS(ESI): 1067$^+$($C_{50}H_{64}ClN_8O_{12}S_2^+$).

(3) 將化合物 14-1(3.20 克)溶在 $MeNO_2$ 30 毫升，甲氧苯 30 毫升之混液，於氮氣及冰冷卻下，加入 $AlCl_3$-$MeNO_2$ 溶液(1.5M，21 毫升)並攪拌 1 小時。加入冰及 1N 鹽酸、乙腈及乙醚並收集水層，減壓濃縮，以 HP-20 層析純化後真空冷凍乾燥，得化合物 16-1(I-3d-5d，900 毫克)。

^{1}H-NMR (D_2O) δ: 2.30(2H, m), 2.68(3H, s), 3.05(2H, m), 3.15 及 3.38 (2H, ABq, J = 17.7 Hz), 4.52(2H, t, J = 6.9 Hz), 4.54(2H, s), 5.16(1H, d, J = 4.8 Hz), 5.56 及 5.67(2H, ABq, J = 15.0 Hz), 5.83(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.6 Hz), 7.68(1H, dd, J = 6.0 及 8.1 Hz), 8.12(1H, d, J = 3.6 Hz), 8.59(1H, d, J = 8.1 Hz), 8.65(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}: 3394, 2817, 1773, 1604, 1539, 1498, 1466, 1391, 1361, 1317, 1163, 1121., 1055, 1033.

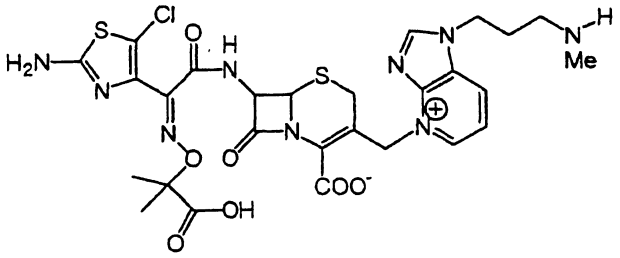
MS(ESI):663$^+$(M+H$^+$).

元素分析 $C_{26}H_{27}ClN_8O_7S_2 \cdot 3.7\ H_2O$.

計算值： C,42.79 ; H,4.75 ; N,15.35 ; Cl,4.86; S,8.79 (%).

實驗值： C,42.78 ; H,4.66 ; N,15.42 ; Cl,4.81; S,9.02 (%).

實施例 6



I-3d-6d：

^{1}H-NMR(D_6-DMSO-D_2O) δ:1.38(6H, brs), 2.23(2H, brs), 2.48(3H, s), 2.92(2H, brs), 3.13 及 3.52 (2H, ABq, J = 17.4 Hz), 4.55(2H, brs), 5.06(1H, d, J = 4.8 Hz), 5.59 及 5.70(2H, ABq, J = 12.9 Hz), 5.79(1H, d, J = 4.8 Hz), 7.71(1H, t like), 8.82(1H, d, J = 7.8), 9.04(1H, s), 9.19(1H, d, J = 5.1 Hz).

IR(KBr) cm^{-1} :3421, 2460, 1772, 1610, 1538, 1488, 1465, 1394, 1359, 1315, 1234, 1159.

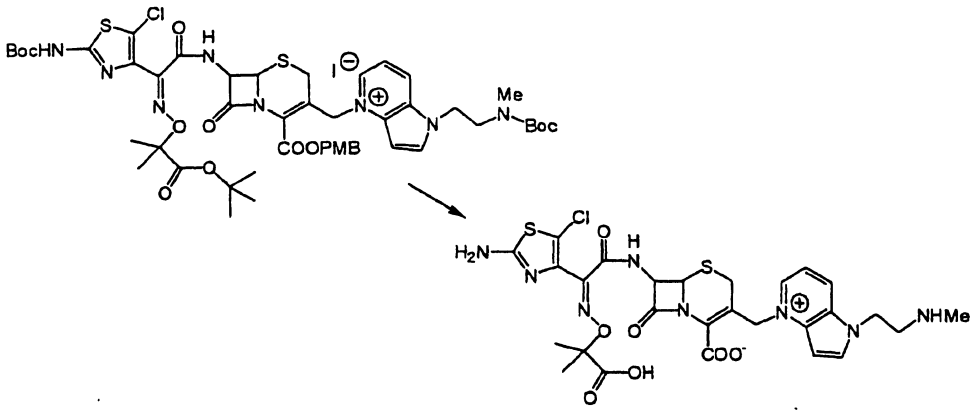
MS(ESI):692$^+$(M+H$^+$).

元素分析 $C_{27}H_{30}ClN_9O_7S_2 \cdot 5.3(H_2O)$.

計算值：C,40.98 ; H,5.18 ; N,15.93 ; Cl,4.93 ; S,8.10 (%).

實驗值：C,40.70 ; H,4.88 ; N,15.74 ; Cl,4.94 ; S,7.97 (%).

實施例 7



I-3d-5c：

^{1}H-NMR (D_2O) δ: 1.48(6H, s), 2.73(3H, s), 3.17 及 3.40(2H, ABq, J = 17.7 Hz),

3.61(2H, t, J = 6.0 Hz), 4.79(2H, t, J = 6.0 Hz), 5.17(1H, d, J = 5.1 Hz), 5.57 及 5.69(2H, ABq, J = 15.0 Hz), 5.81(1H, d, J = 5.1 Hz), 7.10(1H, d, J = 3.3 Hz), 7.70(1H, dd, J = 6.3 及 8.1 Hz), 8.14(1H, d, J = 3.3 Hz), 8.61(1H, d, J = 8.1 Hz), 8.69(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}: 3401, 2987, 2451, 1772, 1606, 1538, 1500, 1467, 1396, 1361, 1288, 1159, 1120.

MS(ESI):$677^{+}(M+H^{+})$.

元素分析 $C_{27}H_{29}ClN_8O_7S_2 \cdot 6.5\ H_2O$.

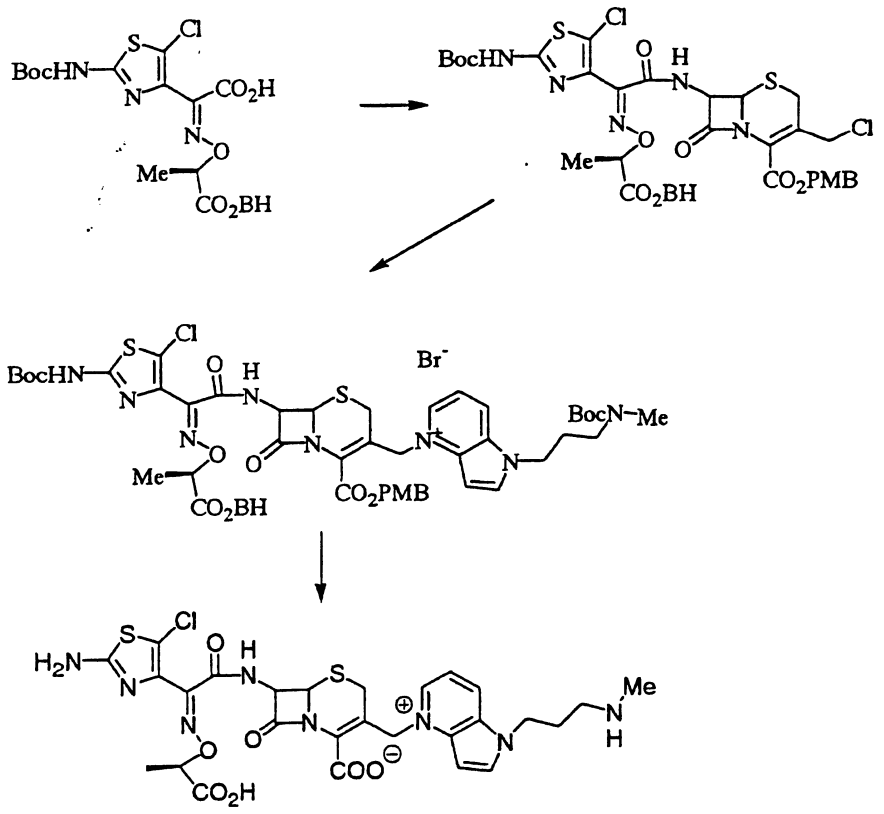
計算值： C,40.83 ; H,5.33 ; N,14.11 ; Cl,4.46; S,8.07 (%).

實驗值： C,40.82 ; H,5.14 ; N,14.12 ; Cl,4.57; S,8.03 (%).

四級鹽酯：

^{1}H-NMR (d_6-DMSO) δ : 1.37(9H, s), 1.39(3H, s), 1.43(3H, s), 1.46(18H, s), 2.80(3H, brs), 3.27 及 3.39(2H, m), 3.59(2H, m), 3.76(3H, s), 4.60(2H, brs), 5.17(1H, d, J = 5.1 Hz), 5.23 及 5.31(2H, ABq, J = 12.0 Hz), 5.72(2H, brs), 5.96(1H, dd, J = 5.1 及 8.7 Hz), 6.92(2H, d, J = 8.4 Hz), 7.02(1H, d, J = 3.6 Hz), 7.36(2H, d, J = 8.4 Hz), 7.82(1H, m), 8.31(1H, d, J = 3.6 Hz), 8.67(1H, m), 8.85(1H, m), 9.58(1H, d, J = 8.7 Hz), 12.1(1H, brs).

實施例 8



I-3e-5d：

^{1}H-NMR (D2O) δ：1.40(3H, d, J = 6.9 Hz), 2.31(2H, q like), 2.68(3H, s), 3.05(2H, t like), 3.14 及 3.39(2H, ABq, J = 17.7 Hz), 4.52(2H, t like), 4.61(1H, q, J = 6.9 Hz), 5.19(1H, d, J = 4.8 Hz), 5.57 及 5.67(2H, ABq, J = 15 Hz), 5.80(1H, d, J =4.5 Hz), 7.06(1H, d, J = 3.6), 7.69(1H, dd, J = 6.0, 8.1 Hz), 8.12(1H, d, J = 3.6 Hz), 8.59(1H, d, J = 8.1 Hz), 8.64(1H, d, J = 6.0Hz).

IR (KBr) cm^{-1}: 3411, 1774, 1606, 1539, 1498, 1392, 1363, 1034, 759 .

Positive ESIMS: m/z 677 [M+H]+ . Negative ESIMS: m/z 675 [M-H]- .

元素分析 $C_{27}H_{29}N_8O_7S_2Cl \cdot 6.2H_2O$

計算値： C,41.11; H,5.29; N,14.20; S,8.13; Cl,4.49 (%).

實驗値： C,40.99; H,5.07; N,14.15; S,8.21; Cl,4.76 (%).

四級鹽酯：

^{1}H-NMR (CDCl3) δ：1.48(9H, s), 1.51(9H, s), 1.60(3H, d, J =7.2 Hz), 2.22(2H,

t like), 2.91(3H, s), 3.17 及 3.73(2H, ABq, J = 18.6 Hz), 3.37(2H, t like), 3.81(3H, s), 4.44(2H, t like), 5.03(1H, q, J = 7.2 Hz), 5.17(1H, d, J = 5.1 Hz), 5.24 及 5.30(2H, ABq, J = 11.7 Hz), 5.63 及 5.75(2H, ABq, J = 15 Hz), 6.01(1H, dd, J = 5.1, 9 Hz), 6.87 (2H, d, J =8.7 Hz), 6.88(1H, s), 7.24~7.35 (12H, m), 7.59(1H, dd, J = 6,8.1 Hz), 7.78(1H, d, J =9 HZ), 8.24(1H, m), 8.34(1H, br s), 8.48(1H, d, J = 8.1 Hz), 8.53(1H, d, J = 6.0 Hz) .

IR (KBr) cm^{-1}: 3430, 3091, 3060, 1793, 1718, 1684, 1630, 1549, 1516, 1367, 1247, 1153, 1034, 754, 702 .

3-Cl 甲基體：

^{1}H-NMR (CDCl3) δ: 1.53(9H, s), 1.65(3H, d, J =7.2 Hz), 3.23 及 3.47(2H, ABq, J = 18.3 Hz), 3.82(3H, s), 4.39 及 4.55(2H, ABq, J = 12 Hz), 4.99(1H, d, J = 5.1 Hz), 5.10(1H, q, J= 7.2 Hz), 5.21 及 5.27(2H, ABq, J = 12 Hz), 5.99(1H, dd, J =5.1, 9.9 Hz), 6.91(3H, m), 7.16~7.37 (12H, m), 7.76 (1H,d, J= 9.9 Hz), 8.20(1H, br s).

IR (KBr) cm^{-1}: 3373, 3286, 2979, 2937, 1791, 1720, 1612, 1550, 1515, 1248, 1155, 1035, 700 .

7 位側鏈(NEt_3 鹽)：

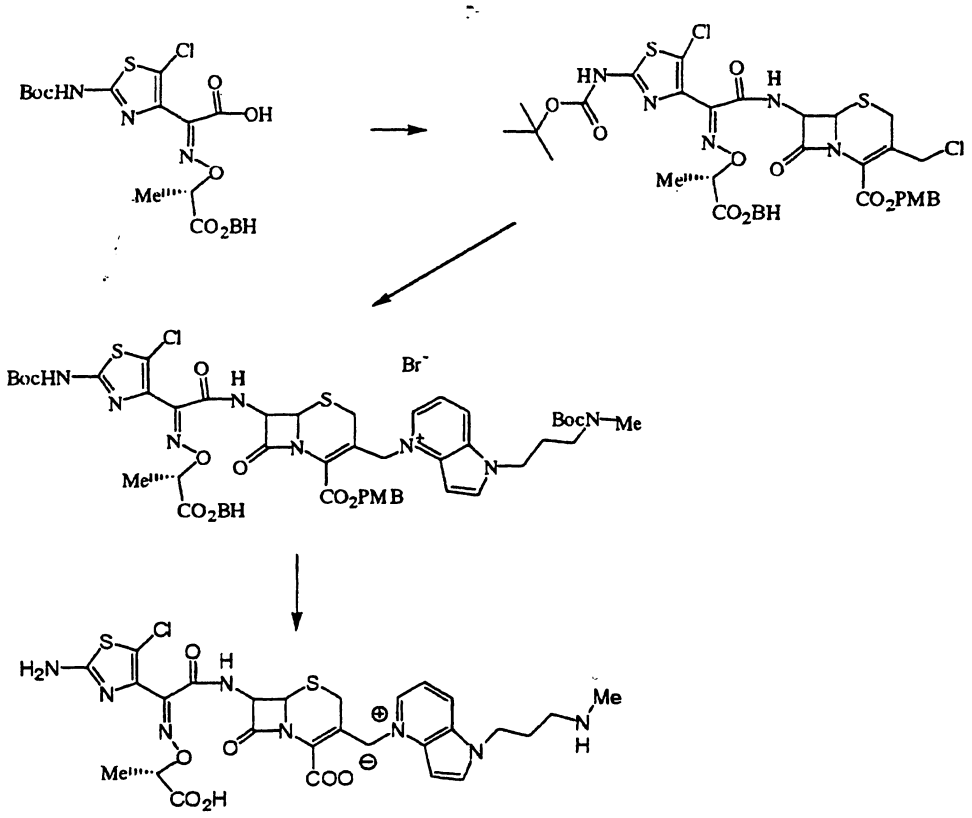
^{1}H-NMR (CDCl3) δ: 1.50(9H, s), 1.51(3H, d, J = 7.2 Hz), 4.94(1H, q, J = 7.2), 6.89(1H, s),7.23 ~ 7.35(10H, m).

IR (KBr) cm^{-1}: 3429, 2981, 2937, 1739, 1714, 1612, 1556, 1250, 1157, 1036, 964, 700 ,

Positive ESIMS: m/z 560[M+H]+, m/z 582[M+Na]+ .

Negative ESIMS: m/z 558[M-H]-, m/z 580[M+Na-2H]- .

實施例 9



I-3f-5d：

^{1}H-NMR (D20) δ: 1.43 (3H, d, J = 7.2 Hz), 2.31(2H, q like), 2.68(3H, s), 3.05(2H, t, J = 8 Hz), 3.18 及 3.37(2H, ABq, J = 18 Hz), 4.53(2H, t like), 4.65 (1H, q, J = 7.2 Hz), 5.17(1H, d, J = 4.8 Hz), 5.54 及 5.70(2H, ABq, J = 15 Hz), 5.86(1H, d, J =4.5 Hz), 7.03(1H, d, J = 3.6 Hz), 7.69(1H, dd, J = 6 , 8.4 Hz), 8.13(1H, d, J = 3.6 Hz), 8.60(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6 Hz).

IR (KBr) cm^{-1}: 3398, 1775,1603,1541,1392,1363,1320, 1286,1033,762.

Positive ESIMS: m/z 677 [M+H]+ . Negative ESIMS: m/z 675 [M-H]- .

元素分析 $C_{27}H_{29}N_8O_7S_2Cl \cdot 6.2H_2O$

計算值： C,41.11; H,5.29; N,14.20; S,8.13; Cl,4.49 (%).

實驗值： C,40.88; H,4.88; N,14.23; S,8.05; Cl,4.57 (%).

四級鹽酯：

^{1}H-NMR (CDCl3) δ: 1.48(9H, s), 1.51(9H, s), 1.62(3H, d, J = 7.2 Hz), 2.21(2H, m), 2.91(3H, s), 3.24 及 3.82(2H, ABq, J = 18.9 Hz), 3.36(2H, m), 3.81(3H, s),

4.43(2H, t like), 5.09(1H, q, J = 7.2 Hz), 5.16(1H, d, J = 5.1 Hz), 5.24 及 5.31(2H, ABq, J = 11.7 Hz), 5.58 及 5.75(2H, ABq, J = 14.7 Hz), 5.99(1H, dd, J = 5.1, 8.7 Hz), 6.86(1H, s), 6.87(2H, d, J = 8.7 Hz), 7.00(1H, br s), 7.24 −7.38(12H, m), 7.55(1H, t like), 7.78(H, d, J = 8.7 Hz), 8.25(1H, br s), 8.47(1H, d, J = 10.2 Hz), 8.50(1H, d, J = 6 Hz).

3-Cl 甲基體：

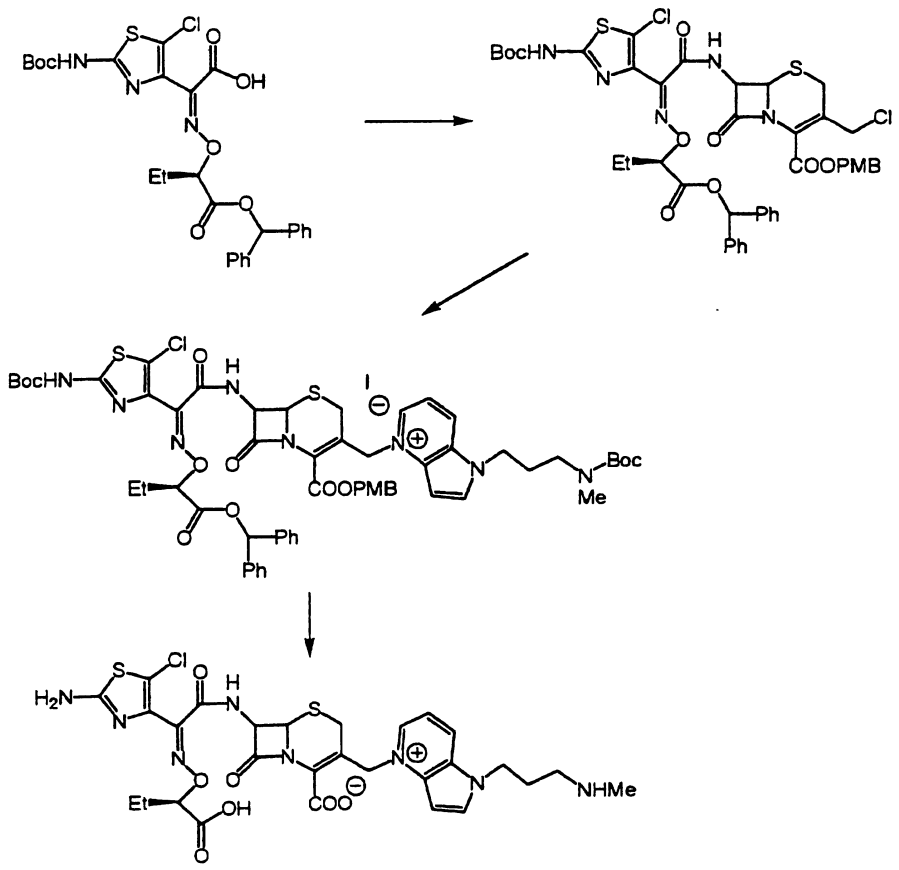
^{1}H-NMR (CDCl3) δ: 1.53(9H, s), 1.64(6H, d, J = 7.2 Hz), 3.39 及 3.58(2H, ABq, J = 18.3 Hz), 3.81(3H, s), 4.42 及 4.59(2H, ABq, J = 12 Hz), 4.97(1H, d, J = 5.1 Hz), 5.08(1H, q, J = 7.2 Hz), 5.20 及 5.27(2H, ABq, J = 11.7 Hz), 6.01(1H, dd, J =5.1, 9.3 Hz), 6.88− 6.91(3H, m), 7.06−7.35(12H, m), 7.85(1H, d, J = 9.3 Hz), 8.15(1H, br s).

IR (KBr) cm^{-1}: 3281, 2980, 2935, 2836, 1790, 1719, 1612, 1552, 1515, 1454, 1369, 1247, 1155,1035, 700 .

7 位側鏈：

^{1}H-NMR (CDCl3) δ: 1.47(9H, s), 1.49(3H, J = 7.2 Hz), 4.99(1H, q, J = 7.2 Hz) .

實施例 10



I-3g-5d :

^{1}H-NMR (D_2O) δ : 0.90(3H, t, J = 7.5 Hz), 1.79(2H, quintet-like), 2.31(2H, quintet-like), 2.69(3H, s), 3.05(2H, t, J = 8.1 Hz), 3.12 及 3.39 (2H, ABq, J = 18.0 Hz), 4.45(1H, t, J = 6.6 Hz), 4.52(2H, t, J = 7.2 Hz), 5.19(1H, d, J = 4.8 Hz), 5.58 及 5.66(2H, ABq, J = 14.7 Hz), 5.78(1H, d, J = 4.8 Hz), 7.06(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.0 and 8.1 Hz), 8.12(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.1 Hz), 8.65(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}:3397, 2967, 1774, 1604, 1537, 1497, 1459, 1390, 1361, 1315, 1159, 1120, 1051, 1031.

MS(ESI):691$^+$($M+H^+$).

元素分析　$C_{28}H_{31}ClN_8O_7S_2 \cdot 4.9\ H_2O$.

計算値： C,43.15 ; H,5.28 ; N,14.38 ; Cl,4.55 ; S,8.23 (%).

實驗值： C,43.02 ; H,5.01 ; N,14.51 ; Cl,4.54 ; S,8.27 (%).

四級鹽酯：

^{1}H-NMR (d_6-DMSO) δ : 0.90(3H, t, J = 7.2 Hz), 1.36(9H, brs), 1.45(9H, s), 1.85(2H, quintet-like), 2.03(2H, quintet-like), 2.78(3H, brs), 3.18(2H, t, J = 6.9 Hz), 3.28 及 3.34(2H, ABq, J = 15.9 Hz), 3.75(3H, s), 4.43(2H, t, J = 6.9 Hz), 4.71(1H, t, J = 6.6 Hz), 5.18(1H, d, J = 4.8 Hz), 5.21 及 5.30(2H, ABq, J = 11.7 Hz), 5.66 及 5.72(2H, ABq, J = 15.6 Hz), 5.99(1H, dd, J = 4.8 及 9.0 Hz), 6.84(1H, s), 6.88(2H, d, J = 8.7 Hz), 6.97(1H, d, J = 3.6 Hz), 7.20-7.44(12H, m), 7.76(1H, dd, J = 6.3 and 8.1 Hz), 8.42(1H, d, J = 3.6 Hz), 8.60(1H, d, J = 6.3 Hz), 8.88(1H, d, J = 8.1 Hz), 9.69(1H, d, J = 9.0 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1}:3414, 3062, 3032, 2975, 2935, 1791, 1717, 1686, 1630, 1613, 1585, 1550, 1515, 1495, 1455, 1393, 1367, 1248, 1154, 1018 .

MS(ESI): $924^+(M+H^+)$.

3-Cl 甲基體：

^{1}H-NMR ($CDCl_3$) δ : 1.08(3H, t, J = 7.2Hz), 1.53(9H, s), 1.90-2.10(2H, m), 3.26 及 3.50(2H, ABq, J = 18.3 Hz), 3.82(3H, s), 4.40 及 4.56(2H, ABq, J = 11.7 Hz), 4.91(1H, dd, J = 5.1 及 9.0 Hz), 4.99(1H, d, J = 5.1 Hz), 5.21 及 5.28(2H, ABq, J = 11.7 Hz), 5.98(1H, dd, J = 5.1 及 9.6 Hz), 6.91(2H, d, J = 8.7 Hz), 6.93(1H, s), 7.25-7.32(10H, m), 7.36(2H, d, J = 8.7Hz), 7.72(1H, d, J = 9.6Hz), 8.01(1H, brs).

IR (KBr) cm^{-1}: 3378, 3291, 3063, 3032, 2975, 2935, 1791, 1721, 1613, 1550, 1515, 1455, 1384, 1368, 1301, 1246, 1155, 1109, 1058, 1032, 1003.

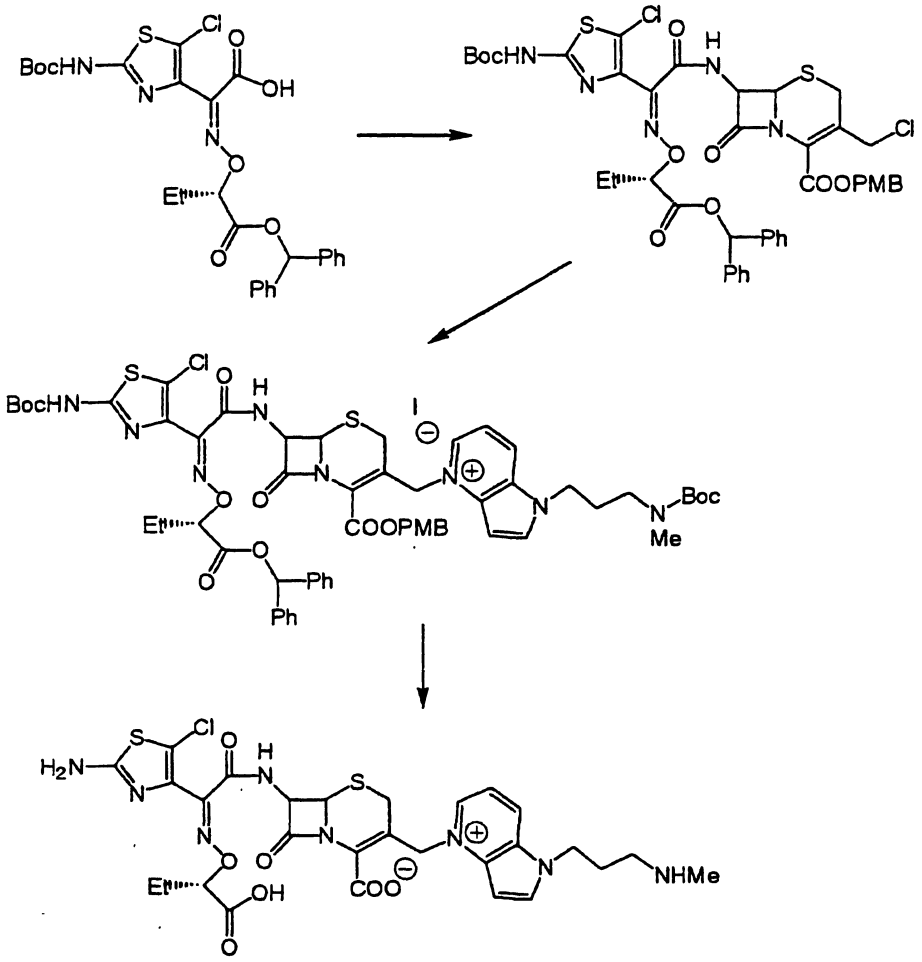
7 位側鏈：

^{1}H-NMR (d_6-DMSO) δ : 0.89(3H, t, J = 7.5 Hz), 1.46(9H, s), 1.78(2H, quintet like), 4.52(1H, t, J = 6.9 Hz), 6.84(1H, s), 7.23-7.46(10H, m), 12.0(1H, brs).

IR (KBr) cm^{-1}: 3428, 3164, 3063, 3032, 2978, 2936, 1717, 1623, 1557, 1496, 1455, 1392, 1370, 1292, 1251, 1210, 1157, 1105, 1056, 1036.

MS(ESI): $574^{+}(M+H^{+})$.

實施例 11



I-3h-5d :

^{1}H-NMR (D_2O) δ : 0.93(3H, t, J = 7.5 Hz), 1.83(2H, quintet-like), 2.30(2H, quintet-like), 2.69(3H, s), 3.05(2H, t, J = 8.1 Hz), 3.16 及 3.37 (2H, ABq, J = 17.7 Hz), 4.52(1H, t, J = 6.0 Hz), 4.52(2H, t, J = 6.3 Hz), 5.17(1H, d, J = 4.8 Hz), 5.55 及 5.68(2H, ABq, J = 15.0 Hz), 5.85(1H, d, J = 4.8 Hz), 7.03(1H, d, J = 3.6 Hz), 7.69(1H, dd, J = 6.0 及 8.4 Hz), 8.12(1H, d, J = 3.6 Hz), 8.58(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}:3388, 2970, 1775, 1602, 1539, 1498, 1463, 1392, 1362, 1316, 1160,

1121, 1061, 1032.

MS(ESI):691$^+$(M+H$^+$).

元素分析 $C_{28}H_{31}ClN_8O_7S_2 \cdot 5.6\ H_2O$.

計算值： C,42.46 ; H,5.37 ; N,14.15 ; Cl,4.48 ; S,8.10 (%).

実験値： C,42.38 ; H,5.02 ; N,14.25 ; Cl,4.41 ; S,8.02 (%).

四級鹽酯：

^{1}H-NMR (d_6-DMSO) δ : 0.86(3H, t, J = 7.2 Hz), 1.36(9H, brs), 1.46(9H, s), 1.83(2H, quintet-like), 2.03(2H, quintet-like), 2.77(3H, brs), 3.18(2H, t, J = 6.9 Hz), 3.29 及 3.39(2H, ABq, J = 18.9 Hz), 3.76(3H, s), 4.43(2H, t, J = 6.6 Hz), 4.73(1H, t, J = 6.6 Hz), 5.19(1H, d, J = 4.8 Hz), 5.21 及 5.30(2H, ABq, J = 11.7 Hz), 5.70(2H, brs), 5.98(1H, dd, J = 4.8 及 8.7 Hz), 6.84(1H, s), 6.89(2H, d, J = 9.0 Hz), 6.96(1H, d, J = 3.0 Hz), 7.20-7.44(12H, m), 7.78(1H, dd, J = 6.3 及 8.4 Hz), 8.42(1H, d, J = 3.0 Hz), 8.60(1H, d, J = 6.3 Hz), 8.88(1H, d, J = 8.4 Hz), 9.74(1H, d, J = 8.7 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1}:3423, 3061, 3032, 2974, 2934, 1791, 1718, 1686, 1630, 1613, 1585, 1549, 1515, 1495, 1455, 1392, 1367, 1247, 1154, 1123, 1060, 1029.

MS(ESI): 1177$^+$($C_{59}H_{66}ClN_8O_{12}S_2^+$).

3-Cl 甲基體：

^{1}H-NMR ($CDCl_3$) δ : 1.02(3H, t, J = 7.2Hz), 1.53(9H, s), 1.96-2.08(2H, m), 3.40 及 3.59(2H, ABq, J = 18.0 Hz), 3.81(3H, s), 4.43 及 4.58(2H, ABq, J = 11.7 Hz), 4.93(1H, t, J = 6.3 Hz), 4.99(1H, d, J = 5.1 Hz), 5.20 及 5.28(2H, ABq, J = 11.7 Hz), 6.01(1H, dd, J = 5.1 及 9.0 Hz), 6.90(2H, d, J = 9.0 Hz), 6.95(1H, s), 7.25-7.31(10H, m), 7.35(2H, d, J = 9.0 Hz), 7.91(1H, d, J = 9.0Hz), 7.93(1H, brs).

IR (KBr) cm^{-1}: 3283, 3063, 3031, 2976, 2936, 2836, 1791, 1721, 1613, 1550, 1515, 1455, 1384, 1369, 1301, 1246, 1155, 1058, 1033, 1004.

MS(ESI): 924$^+$(M+H$^+$).

元素分析　$C_{43}H_{43}Cl_2N_5O_{10}S_2 \cdot 0.3\ CHCl_3 \cdot 0.8\ H_2O$.

計算值： C,53.33 ; H,4.64 ; N,7.18 ; S,6.58 ; Cl,10.54 (%).

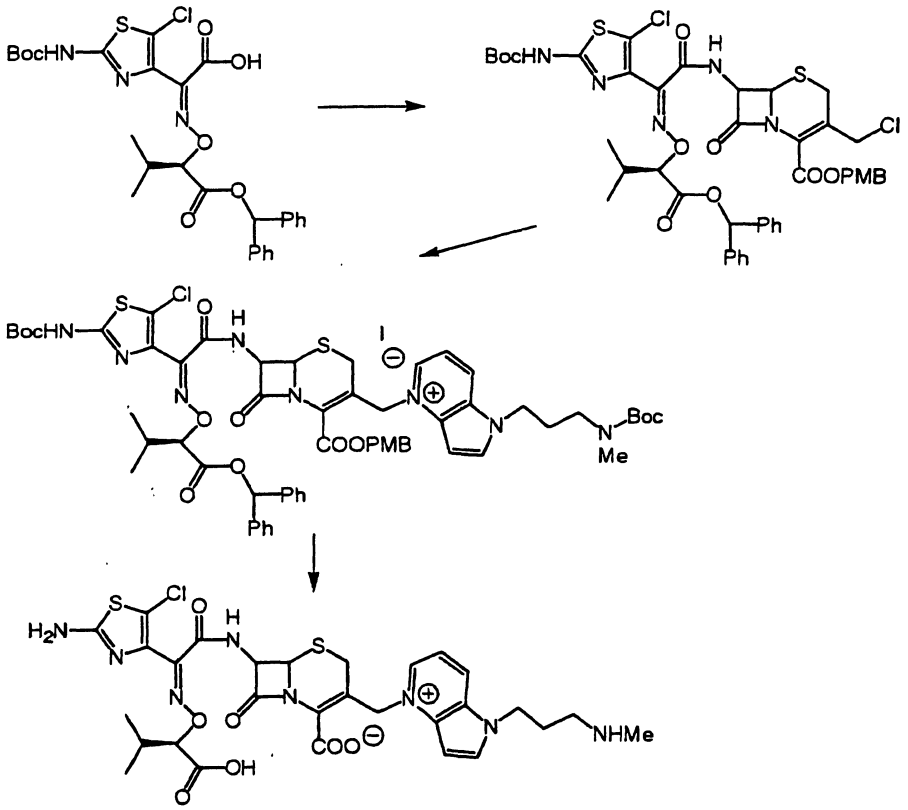
7位側鏈：

^{1}H-NMR (d_6-DMSO) δ : 0.89(3H, t, J = 7.5 Hz), 1.46(9H, s), 1.78(2H, quintet like), 4.52(1H, t, J = 6.9 Hz), 6.84(1H, s), 7.23-7.46(10H, m), 12.0(1H, brs).

IR (KBr) cm^{-1}: 3431, 3180, 3064, 3033, 2978, 2934, 1736, 1715, 1621, 1557, 1496, 1455, 1391, 1370, 1295, 1250, 1211, 1158, 1118, 1064, 1034.

MS(ESI): 574$^+$(M+H$^+$).

實施例 12



I-3i-5d：

^{1}H-NMR (D_2O) δ : 0.93(6H, d, J = 6.9 Hz), 2.09(1H, sextet-like), 2.31(2H, quintet-like), 2.68(3H, s), 3.04(2H, t, J = 8.1 Hz), 3.13 及 3.39 (2H, ABq, J = 17.7 Hz), 4.27(1H, d, J = 6.0 Hz), 4.53(2H, t, J = 6.9 Hz), 5.19(1H, d, J = 4.8 Hz), 5.58 及 5.66(2H, ABq, J = 15.0 Hz), 5.80(1H, d, J = 4.8 Hz), 7.07(1H,

d, J = 3.3 Hz), 7.69(1H, dd, J = 6.3 and 8.7 Hz), 8.12(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 8.7 Hz), 8.65(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3396, 2965, 1775, 1604, 1538, 1498, 1466, 1391, 1364, 1223, 1121, 1062, 1027.

MS(ESI):705^{+}($M+H^{+}$).

元素分析 $C_{29}H_{33}ClN_8O_7S_2 \cdot 4.28\ H_2O$.

計算值： C,44.52 ; H,5.35 ; N,14.32 ; Cl,4.53 ; S,8.20 (%).

實驗值： C,44.14 ; H,4.96 ; N,14.38 ; Cl,4.53 ; S,8.14 (%).

四級鹽酯：

^{1}H-NMR (d_6-DMSO) δ: 0.88(3H, d, J = 6.9 Hz), 0.90(3H, d, J = 6.6 Hz), 1.36(9H, brs), 1.45(9H, s), 2.02(2H, quintet-like), 2.15(1H, sextet-like), 2.77(3H, brs), 3.17(2H, t, J = 6.9 Hz), 3.26 及 3.40(2H, ABq, J = 18.3 Hz), 3.75(3H, s), 4.42(2H, t-like), 4.50(1H, t, J = 6.3 Hz), 5.18(1H, d, J = 5.1 Hz), 5.20 及 5.30(2H, ABq, J = 11.7 Hz), 5.65 及 5.71(2H, ABq, J = 15.6 Hz), 6.00(1H, dd, J = 5.1 及 8.4 Hz), 6.86(1H, s), 6.87(2H, d, J = 8.4 Hz), 6.97(1H, d, J = 3.3 Hz), 7.20-7.45(12H, m), 7.75(1H, dd, J = 6.0 及 7.8 Hz), 8.41(1H, d, J = 3.3 Hz), 8.58(1H, d, J = 6.0 Hz), 8.87(1H, d, J = 7.8 Hz), 9.72(1H, d, J = 8.4 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1}:3393, 3061, 3031, 2972, 2933, 1791, 1719, 1686, 1630, 1613, 1550, 1515, 1495, 1455, 1392, 1367, 1248, 1175, 1155, 1125, 1029.

3-Cl 甲基體：

^{1}H-NMR ($CDCl_3$) δ: 0.99(3H, d, J = 7.2 Hz), 1.02(3H, d, J = 7.2 Hz), 1.53(9H, s), 2.37(1H, sextet-like), 3.35 及 3.55(2H, ABq, J = 18.3 Hz), 3.82(3H, s), 4.42 及 4.54(2H, ABq, J = 12.0 Hz), 4.76(1H, d, J = 6.0 Hz), 4.99(1H, d, J = 5.1 Hz), 5.21 及 5.28(2H, ABq, J = 11.7 Hz), 5.95(1H, dd, J = 5.1 及 9.3 Hz), 6.91(2H, d, J = 8.7 Hz), 6.94(1H, s), 7.25-7.32(10H, m), 7.36(2H, d, J = 8.7Hz), 7.51(1H, d, J = 9.3 Hz), 8.03(1H, brs).

IR (KBr) cm^{-1}: 3292, 3063, 3031, 2970, 2935, 2876, 2836, 1792, 1722, 1613, 1550, 1515, 1454, 1387, 1369, 1333, 1302, 1247, 1155, 1096, 1031.

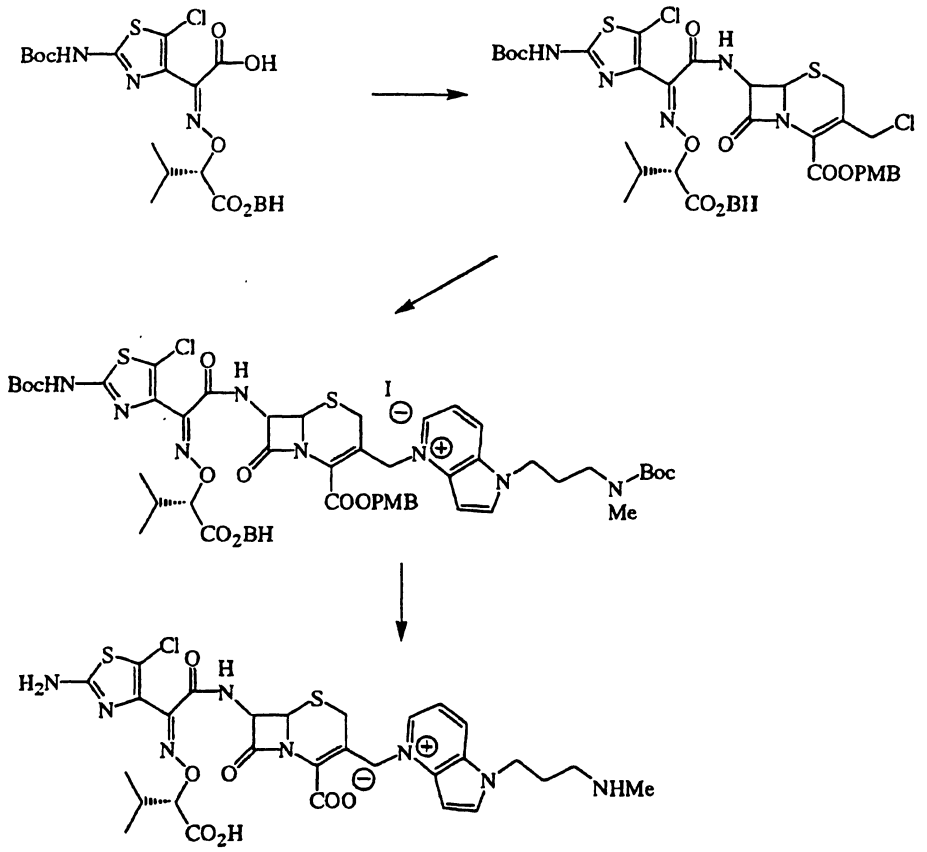
MS(ESI): $938^{+}(M+H^{+})$.

7位側鏈：

^{1}H-NMR(D_6-DMSO) δ:0.83(3H, d, J = 6.9 Hz), 0.93(3H, d, J = 6.6 Hz), 1.46(9H, s), 2.05(1H, sex., J = ca 6.9 Hz), 4.28(1H, d, J = 7.2 Hz), 6.86(1H, s), 7.24-7.31(6H, m), 7..43-7.45(4H, m).

IR(KBr) cm^{-1} :3431, 2971, 2934, 1740, 1715, 1619, 1555, 1371, 1251, 1157, 1034, 699.

實施例 13



I-3j-5d：

^{1}H-NMR (D_2O) δ: 0.94(3H, d, J = 7.2 Hz), 0.98(3H, d, J = 6.9 Hz), 2.13(1H,

sextet-like), 2.31(2H, quintet-like), 2.68(3H, s), 2.91(2H, t, J = 7.8 Hz), 3.15 及 3.37 (2H, ABq, J = 17.7 Hz), 4.35(1H, d, J = 5.4 Hz), 4.52(2H, t, J = 6.9 Hz), 5.17(1H, d, J = 4.8 Hz), 5.55 及 5.67(2H, ABq, J = 15.3 Hz), 5.87(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.0 及 8.1 Hz), 8.12(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.1 Hz), 8.64(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}:3389, 2965, 1777, 1601, 1539, 1498, 1466, 1391, 1364, 1223, 1120, 1062, 1019.

MS(ESI):$705^+(M+H^+)$.

元素分析 $C_{23}H_{33}ClN_8O_7S_2 \cdot 6.5\ H_2O$.

計算值： C,42.36 ; H,5.64 ; N,13.63 ; Cl,4.31 ; S,7.80 (%).

實驗值： C,42.01 ; H,4.82 ; N,13.51 ; Cl,4.26 ; S,7.89 (%).

7 位側鏈：

^{1}H-NMR (d_6-DMSO) δ: 0.85(3H, d, J = 6.6 Hz), 0.93(3H, d, J = 6.6 Hz), 1.46(9H, s), 2.07(1H, sextet-like), 4.35(1H, d, J = 7.2 Hz), 6.87(1H, s), 7.1-7.5(11H, m), 12.0(1H, brs).

IR (KBr) cm^{-1}: 3422, 3207, 3064, 3032, 2976, 2933, 2876, 1717, 1629, 1555, 1495, 1455, 1393, 1370, 1295, 1248, 1156, 1055, 1032.

MS(ESI):$588^+(M+H^+)$.

元素分析 $C_{28}H_{30}ClN_8O_7S_1 \cdot 1.04\ H_2O \cdot 0.12$ AcOEt.

計算值： C,55.41 ; H,5.39 ; N,6.81 ; Cl,5.74 ; S,5.19 (%).

實驗值： C,55.44 ; H,5.11 ; N,7.20 ; Cl,5.67 ; S,4.80 (%).

3-Cl 甲基體：

^{1}H-NMR ($CDCl_3$) δ: 0.95(3H, d, J = 7.2 Hz), 1.04(3H, d, J = 6.9 Hz), 1.53(9H, s), 2.35(1H, m), 3.43 及 3.59(2H, ABq, J = 18.3 Hz), 3.81(3H, s), 4.45 及 4.57(2H, ABq, J = 11.7 Hz), 4.84(1H, d, J = 4.5 Hz), 4.99(1H, d, J = 4.8 Hz), 5.21 及 5.28(2H, ABq, J = 12.0 Hz), 5.99(1H, dd, J = 4.8 及 9.0 Hz), 6.91(2H, d, J = 8.7 Hz), 6.98(1H, s), 7.25-7.32(10H, m), 7.35(2H, d, J = 8.7Hz), 7.92(1H,

s), 7.99(1H, d, J = 9.0 Hz).

IR (KBr) cm^{-1}: 3392, 3283, 3062, 3032, 2969, 2934, 2835, 1791, 1721, 1613, 1585, 1551, 1514, 1455, 1387, 1368, 1302, 1246, 1155, 1096, 1061, 1030.

MS(ESI): $938^{+}(M+H^{+})$.

元素分析 $C_{44}H_{45}Cl_2N_5O_{10}S_2 \cdot 0.1\ CHCl_3 \cdot 0.4\ H_2O \cdot 0.4$ AcOEt.

計算值： C,55.26 ; H,4.98 ; N,7.05 ; S,6.46 ; Cl,8.21 (%).

實驗值： C,55.22 ; H,4.64 ; N,6.90 ; S,6.20 ; Cl,8.37 (%).

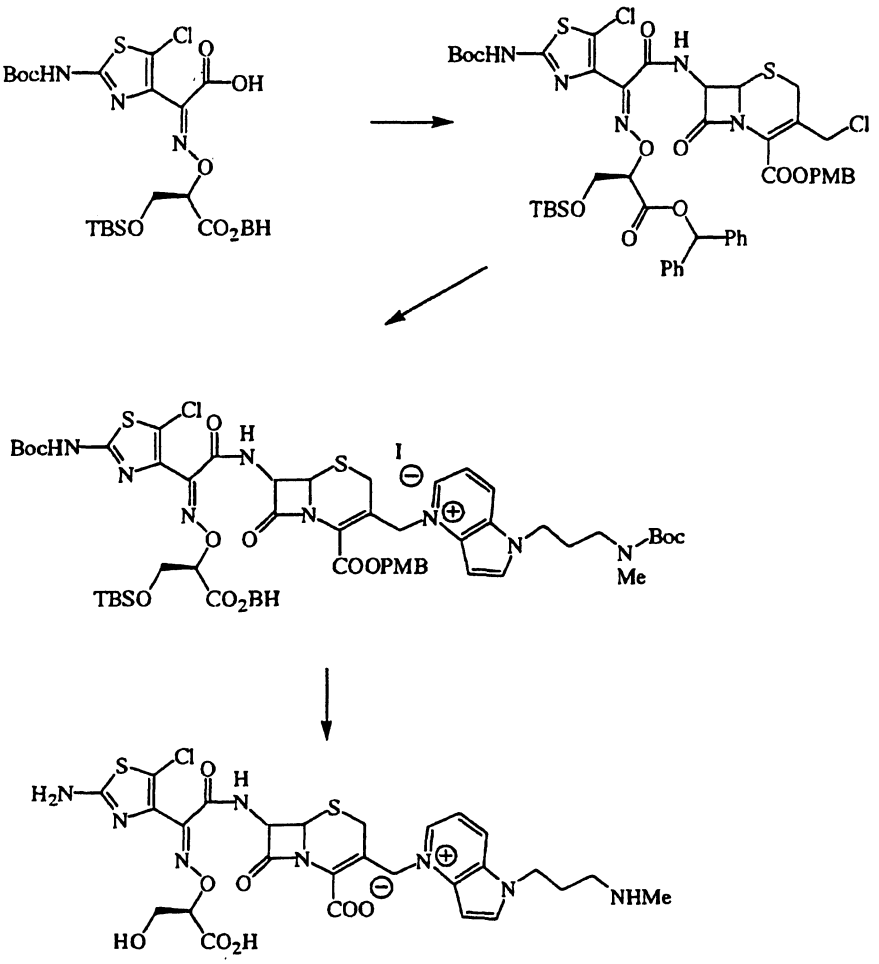
四級鹽酯：

^{1}H-NMR (d_6-DMSO) δ: 0.87(3H, d, J = 6.9 Hz), 0.89(3H, d, J = 7.2 Hz), 1.36(9H, brs), 1.46(9H, s), 2.03(2H, quintet-like), 2.15(1H, sextet-like), 2.78(3H, brs), 3.18(2H, t-like), 3.27 及 3.43(2H, ABq, J = 13.2 Hz), 3.76(3H, s), 4.43(2H, t-like), 4.56(1H, d, J = 6.0 Hz), 5.20(1H, d, J = 5.4 Hz), 5.21 及 5.30(2H, ABq, J = 11.7 Hz), 5.70(2H, brs), 6.00(1H, dd, J = 5.4 及 8.4 Hz), 6.86(1H, s), 6.89(2H, d, J = 8.7 Hz), 6.95(1H, d, J = 3.3 Hz), 7.21-7.44(12H, m), 7.78(1H, dd, J = 6.3 及 8.4 Hz), 8.41(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 6.3 Hz), 8.87(1H, d, J = 8.4 Hz), 9.74(1H, d, J = 8.4 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1}:3423, 3061, 3032, 2972, 2933, 1792, 1718, 1685, 1630, 1613, 1584, 1550, 1515, 1495, 1455, 1392, 1367, 1247, 1154, 1061, 1028.

MS(ESI): $1191^{+}(M-I^{+})$.

實施例 14



I-3k-5d :

^{1}H-NMR (D_2O) δ : 2.31(2H, quintet-like), 2.68(3H, s), 3.05(2H, t, J = 8.1 Hz), 3.14 及 3.40 (2H, ABq, J = 18.0 Hz), 3.91(2H, m), 4.53(2H, t, J = 6.9 Hz), 4.69(1H, m), 5.20(1H, d, J = 4.8 Hz), 5.58 及 5.67(2H, ABq, J = 14.7 Hz), 5.84(1H, d, J = 4.8 Hz), 7.06(1H, d, J = 3.6 Hz), 7.69(1H, dd, J = 6.3 及 8.4 Hz), 8.12(1H, d, J = 3.6 Hz), 8.60(1H, d, J = 8.4 Hz), 8.65(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3388, 1772, 1605, 1539, 1498, 1466, 1391, 1362, 1321, 1223, 1152, 1120, 1064, 1034.

MS(ESI):$693^+(M+H^+)$.

元素分析　$C_{27}H_{29}ClN_8O_8S_2 \cdot 5.62\ H_2O$.

計算値： C,40.82 ; H,5.11 ; N,14.11 ; Cl,4.46 ; S,8.07 (%).

實驗值： C,40.41 ; H,4.70 ; N,14.05 ; Cl,4.27 ; S,8.03 (%).

7位側鏈：

^{1}H-NMR (d_6-DMSO) δ: -0.03(3H, s), -0.01(3H, s), 0.77(9H, s), 1.46(9H, s), 3.86-3.99(2H, m), 4.62(1H, t-like), 6.83(1H, s), 7.20-7.50(11H, m), 11.1(1H, brs).

IR (KBr) cm^{-1}:3450, 3159, 3078, 2956, 2795, 1772, 1698, 1428, 1418, 1373, 1294, 1240, 1190, 1002.

MS(ESI):690$^+$(M+H$^+$).

3-Cl 甲基體：

^{1}H-NMR ($CDCl_3$) δ: 0.00(6H, s), 0.82(9H, s), 1.49(9H, s), 3.21 及 3.46(2H, ABq, J = 18.0 Hz), 3.77(3H, s), 4.12(2H, t-like), 4.36 及 4.52(2H, ABq, J = 12.0 Hz), 4.93(1H, d, J = 4.8 Hz), 5.04(1H, m), 5.16 及 5.24(2H, ABq, J = 11.7 Hz), 5.93(1H, dd, J = 4.8 及 9.3 Hz), 6.85(2H, d, J = 8.7 Hz), 6.89(1H, s), 7.22-7.29(10H, m), 7.32(2H, d, J = 8.7Hz), , 7.61(1H, d, J = 9.3 Hz), 8.22(1H, s).

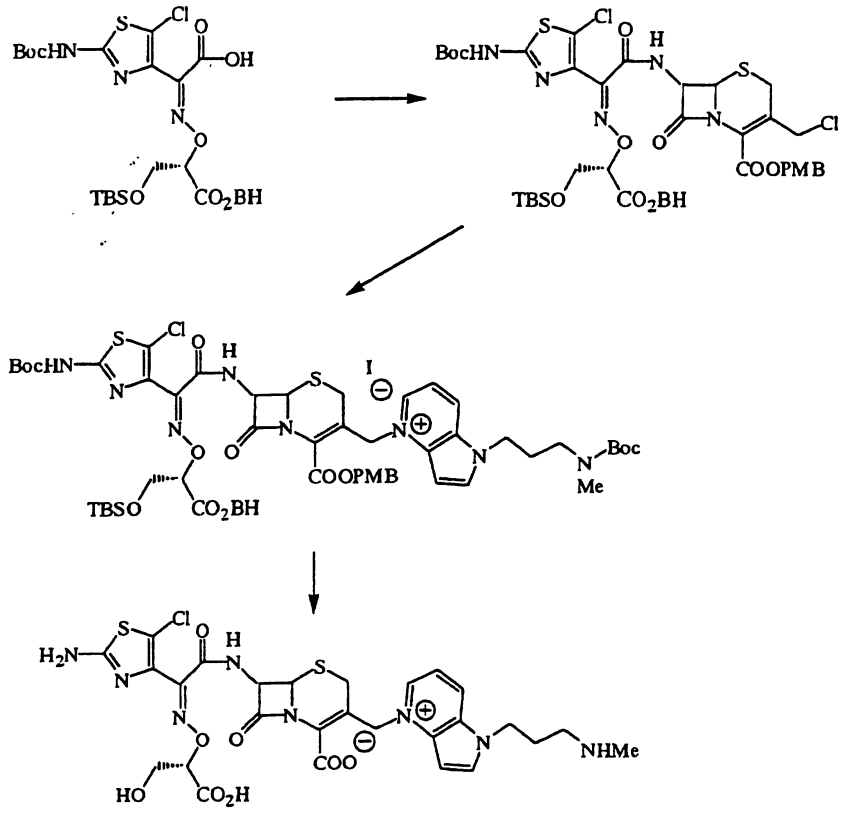
IR (KBr) cm^{-1}:3470, 3283, 2954, 2932, 1788, 1720, 1612, 1585, 1556, 1514, 1455, 1388, 1368, 1301, 1248, 1173, 1157, 1102, 1064, 1034.

四級鹽酯：

IR (KBr) cm^{-1}:3421, 3062, 3032, 2930, 2855, 1791, 1718, 1686, 1630, 1612, 1585, 1550, 1515, 1495, 1455, 1392, 1367, 1248, 1175, 1154, 1102, 1064, 1029.

MS(ESI):1293$^+$(M-I$^+$).

實施例 15



I-31-5d：

^{1}H-NMR (D_2O) δ：2.31(2H, quintet-like), 2.68(3H, s), 3.05(2H, t, J = 8.1 Hz), 3.17 及 3.38 (2H, ABq, J = 17.7 Hz), 3.94(2H, m), 4.53(2H, t, J = 7.2 Hz), 4.70(1H, m), 5.18(1H, d, J = 4.8 Hz), 5.55 及 5.68(2H, ABq, J = 15.0 Hz), 5.88(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.3 及 8.4 Hz), 8.12(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3398, 1774, 1603, 1538, 1498, 1466, 1392, 1362, 1320, 1064.

MS(ESI):693^+($M+H^+$).

元素分析　$C_{27}H_{29}ClN_8O_8S_2 \cdot 9.0\ H_2O$.

計算値：C,37.92 ; H,5.54 ; N,13.10 ; Cl,4.15 ; S,7.50 (%).

實驗値：C,37.77 ; H,4.42 ; N,13.09 ; Cl,4.24 ; S,7.49 (%).

7位側鏈：

^{1}H-NMR (d_6-DMSO) δ：-0.03(3H, s), -0.01(3H, s), 0.77(9H, s), 1.46(9H, s),

3.87-3.99(2H, m), 4.63(1H, t-like), 6.83(1H, s), 7.22-7.48(11H, m), 11.1(1H, brs).

IR (KBr) cm^{-1}:3450, 3159, 3078, 2955, 2794, 1772, 1697, 1428, 1417, 1373, 1294, 1240, 1191, 1002.

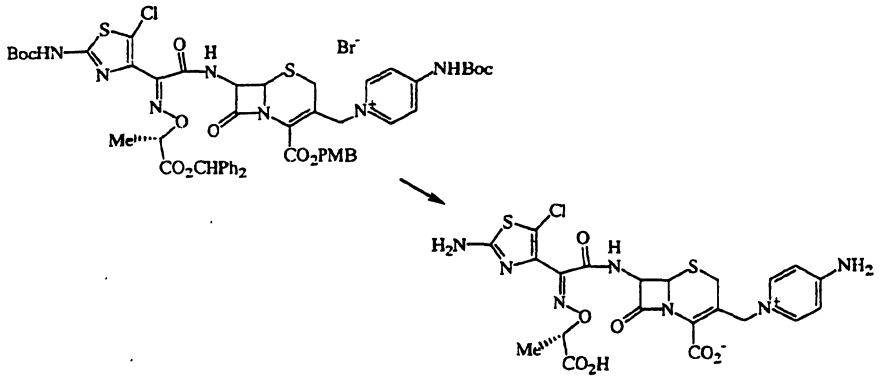
MS(ESI):690^{+}(M+H^{+}).

四級鹽酯：

IR (KBr) cm^{-1}:3423, 3062, 3032, 2930, 2855, 1792, 1718, 1687, 1630, 1613, 1585, 1550, 1515, 1495, 1455, 1392, 1367, 1248, 1174, 1154, 1102, 1064, 1030.

MS(ESI):1293^{+}(M-I^{+}).

實施例 16



I-3f-2a：

^{1}H-NMR (D6-dmso) δ: 1.39(3H, J = 7.2 Hz), 2.99 及 3.44(2H, ABq, J = 17.4 Hz), 4.56(1H, q, J = 7.2 Hz), 4.68 及 5.16(2H, ABq, J = 13.2 Hz), 5.05(1H, d, J = 4.8 Hz), 5.71(1H, dd, J =4.8, 8.4 Hz), 6.83 及 8.46(4H, A2B2q, J = 6.6 Hz), 7.42(2H, s), 8.19(2H, s), 9.71(1H, d, J = 8.4 Hz).

IR (KBr) cm^{-1}: 3409, 3205, 1776, 1656, 1539, 1375, 1168, 1035, 842 .

Positive ESIMS: m/z 582 [M+H]+ . Negative ESIMS: m/z 580 [M-H]- .

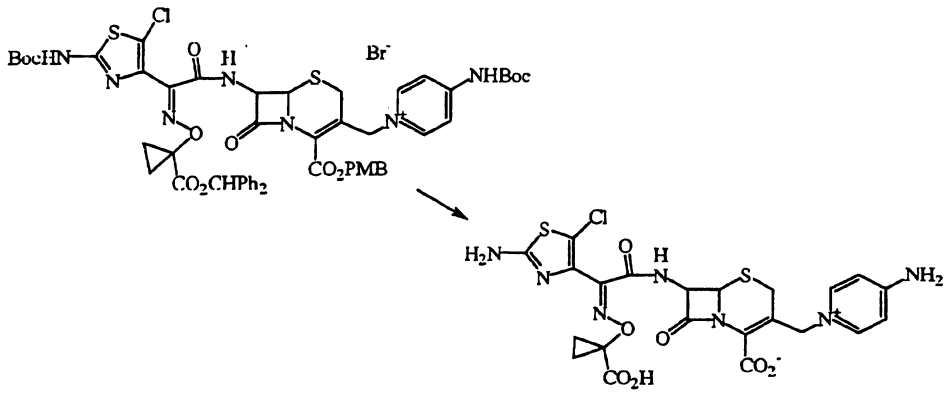
四級鹽酯：　　：

^{1}H-NMR (CDCl3-CD3OD) δ: 1.53(9H, s), 1.56(9H, s), 1.61(3H, d, J = 7.2 Hz), 3.18

及 3.75(2H, ABq, J = 18.6 Hz), 3.83(3H, s), 4.99(1H, q, J = 7.2 Hz), 5.09(1H, d, J = 5.1 Hz), 5.21 及 5.31(2H, ABq, J = 11.7 Hz), 5.27 及 5.47(2H, ABq, J = 13.8 Hz), 5.94(1H, d, J = 5.1 Hz), 6.90(2H, J = 9 Hz), 6.91 (1H, s), 7.3 1 −7.36(12H, m), 7.96(2H, m), 8.73(1H, d, J = 6.6 Hz) .

IR (KBr) cm^{-1}: 3401, 2978, 2935, 1793, 1741, 1719, 1642, 1587, 1532, 1247, 1148, 1063, 701 .

實施例 17



I-3c-2a :

^{1}H-NMR (D6-dmso) δ : 1.28 −1.36 (4H, m), 3.03 及 3.44(2H, ABq, J = 17.7 Hz), 4.72 及 5.12(2H, ABq, J = 13.8 Hz), 5.05(1H, d, J = 4.8 Hz), 5.71(1H, dd, J =4.8, 8.7 Hz), 6.85 及 8.40(4H, A2B2q, J = 6.6 Hz), 7.45(2H, s), 8.27(2H, s), 9.71(1H, m).

IR (KBr) cm^{-1}: 3349, 3199, 1776, 1656, 1538, 1376, 1170, 1035, 972 .

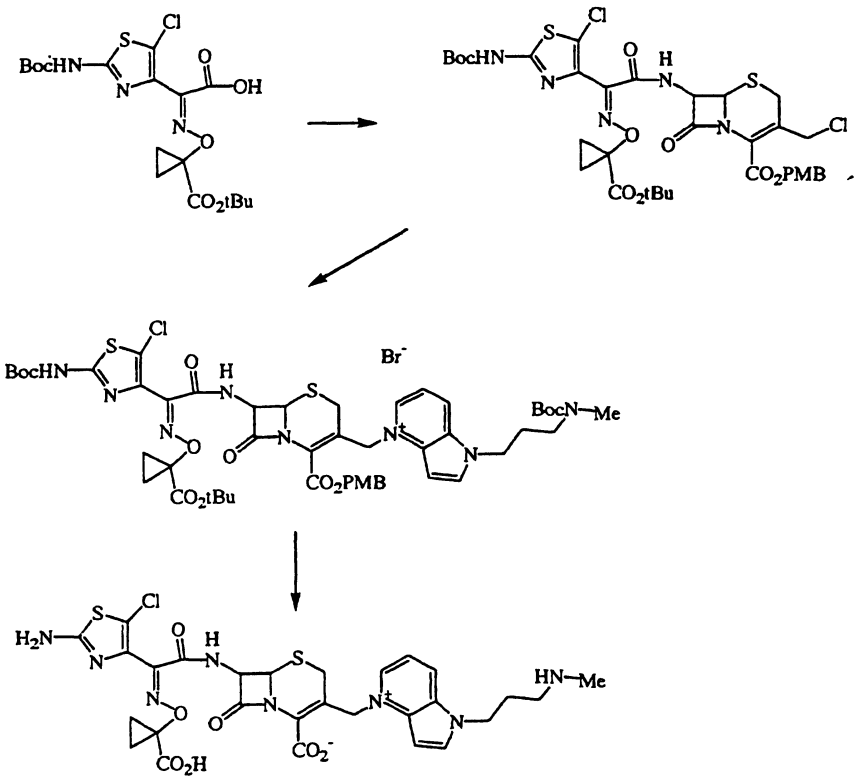
Positive ESIMS: m/z 594 [M+H]+ . Negative ESIMS: m/z 592 [M-H]- .

四級鹽酯：

^{1}H-NMR (CDCl3) δ:. 1.35(9H, s), 1.41 − 1.54(22H, m), 3.22 及 3.89(2H, ABq, J = 18.3 Hz), 3.83(3H, s), 5.12(1H, d, J = 5.1 Hz), 5.22 及 5.30(2H, ABq, J = 11.7 Hz), 5.48 及 5.64(2H, ABq, J = 8.4 Hz), 6.02(1H, dd, J = 5.1, 9 Hz), 6.91 及 7.34(4H, A2B2q, J = 8.4 Hz), 8.17(1H, br s), 8.38 及 8.93(4H, A2B2q, J = 7.5 Hz), 8.61(1H, d, J = 9 Hz), 10.2(1H, s) .

IR (KBr) cm^{-1}: 3425, 3249, 2979, 2935, 1794, 1718, 1642, 1586, 1532, 1458, 1370, 1247, 1149, 1031, 838 .

實施例 18



I-3c-5d :

^{1}H-NMR (D20) δ: 1.26-1.32 (4H, m), 2.31(2H, q like), 2.68(3H, s), 3.06(2H, t, J = 8.1 Hz), 3.15 及 3.39(2H, ABq, J = 17.7 Hz), 4.54(2H, t like), 5.17(1H, d, J = 4.5 Hz), 5.57 及 5.68(2H, ABq, J = 15 Hz), 5.80(1H, d, J =4.5 Hz), 7.05(1H, d, J = 3.3 Hz), 7.70(1H, t, J = ca7 Hz), 8.13(1H, d, J = 2.4 Hz), 8.60(1H, d, J = 8.4 Hz), 8.65(1H, d, J = 6 Hz).

IR (KBr) cm^{-1}: 3398, 2820, 1773, 1608, 1540, 1395, 1225, 1033, 968, 761 .

Positive ESIMS: m/z 689 [M+H]+ . Negative ESIMS: m/z 687 [M-H]- .

四級鹽酯：

^{1}H-NMR (CDCl3) δ: 1.41(9H, s), 1.46－1.52(22H, m), 2.23(2H, m), 2.92(3H, s), 3.35 及 3.78(2H, ABq, J = 18 Hz), 3.38(2H, m), 3.81(3H, s), 4.45(2H, t like),

5.20(1H, d, J = 5.1 Hz), 5.24 及 5.30(2H, ABq, J = 11.4 Hz), 5.76 及 5.90(2H, ABq, J = 14.1 Hz), 6.02(1H, dd, J = 5.1, 8.7 Hz), 6.87 及 7.33(4H, A2B2q, J = 8.4 Hz), 7.01 (1H, br s), 7.64 (1H, t like), 8.02(1H, br s), 8.30(2H, m), 8.51(2H, d like), 8.61(1H, d, J = 9 Hz) .

IR (KBr) cm^{-1}: 3424, 3253, 2976, 2932, 1793, 1716, 1685, 1632, 1613, 1549, 1516, 1455, 1392, 1367, 1248, 1152, 1031, 754 .

3-Cl 甲基體：

^{1}H-NMR (CDCl3) δ: 1.41(9H, s), 1.47－1.53(13H, m), 3.48 及 3.63(2H, ABq, J = 18.3 Hz), 3.82(3H, s), 4.49(2H, s), 5.06(1H, d, J = 5.1 Hz), 5.08(1H, q, J = 7.2 Hz), 5.21 及 5.28(2H, ABq, J = 11.7 Hz), 5.99(1H, dd, J =5.1, 9.3 Hz), 6.91 及 7.36(4H, A2B2q, J = 8.7 Hz), 8.13(1H, br s), 8.59(1H, d, J = 9.3 Hz) .

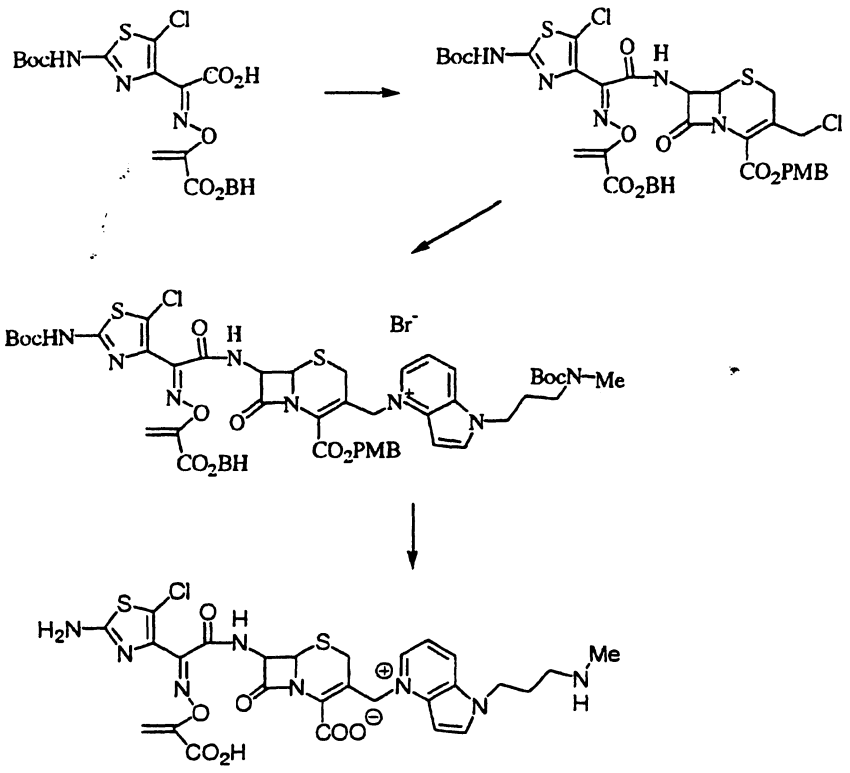
IR (KBr) cm^{-1}: 3378, 3268, 2979, 2935, 2838, 1793, 1719, 1613, 1550, 1517, 1457, 1369, 1248, 1154, 1032 .

7 位側鏈：

^{1}H-NMR (CDCl3) δ: 1.40(9H, s), 1.43－1.55(13H, m) .

IR (CHCl3) cm^{-1}:3405, 2983, 2935, 1719, 1626, 1550, 1153 .

實施例 19



I-3b-5d：

^{1}H-NMR (D20) δ: 2.31(2H, q like, J = 7.5 Hz), 2.68(3H, s), 3.04(2H, t like), 3.17 及 3.31(2H, ABq, J = 17.7 Hz), 4.53(2H, t like), 5.10(1H, d, J = 2.1 Hz), 5.12(1H, d, J = 4.5 Hz), 5.27(1H, d, J = 2.1 Hz), 5.51 及 5.76(2H, ABq, J = 15 Hz), 5.88(1H, d, J =4.5 Hz), 6.99(1H, d, J = 3.6), 7.67(1H, dd, J = 6.4, 8.1 Hz), 8.12(1H, d, J = 3.6 Hz), 8.59(1H, d, J = 8.1 Hz), 8.63(1H, d, J = 6.4Hz). IR (KBr) cm^{-1}: 3398, 1774, 1606, 1539, 1498, 1468, 1392, 1203, 759 .

Positive ESIMS: m/z 675 [M+H]+ .

元素分析 $C_{27}H_{27}N_8O_7S_2Cl \cdot 5.5H_2O$

計算值： C,41.89; H,4.95; N,14.47; S,8.28; Cl,4.58 (%).

實驗值： C,41.92; H,4.72; N,14.49; S,8.38; Cl,4.66 (%).

四級鹽酯：

^{1}H-NMR (CDCl3) δ: 1.48(9H, s),1.53(9H, s), 2.20(2H, m),2.90(3H, s) 3.19

及 3.64(2H, ABq, J = 18 Hz), 3.36(2H, t like), 3.78(3H, s), 4.42(2H, t like), 4.95(1H, d, J = 4.8 Hz), 5.20 及 5.28(2H, ABq, J = 11.7 Hz), 5.59(1H, d, J =1.5 Hz), 5.75(1H, d, J =1.5 Hz), 5.84(1H, dd, J = 4.8, 8.6 Hz), 6.83 (2H, d, J =8.7 HZ), 6.89(1H, s), 7.04(1H, br s), 7.23− 7.36 (12H, m), 7.62(1H, m), 8.20(1H, m), 8.46(1H, d, J = 9.3 Hz), 8.56(1H, d, J = 6.0 Hz), 8.65(1H, m) .

IR (CHCl3) cm^{-1}: 3403, 1793, 1720, 1685, 1632, 1613, 1551, 1517, 1154 .

3-Cl 甲基體：

^{1}H-NMR (CDCl3) δ: 1.53(9H, s), 3.23 及 3.43(2H, ABq, J = 18 Hz), 3.80(3H, s), 4.36 及 4.55(2H, ABq, J = 12 Hz), 4.75(1H, d, J = 5.1 Hz), 5.16 及 5.25(2H, ABq, J = 11.4 Hz), 5.61(1H, d, J =1.8), 5.81(1H, d, J =1.8), 5.88(1H, dd, J = 5.1, 9.0 Hz), 6.87− 6.92 (3H, m), 7.16 −7.39 (12H, m), 8.56(1H,br s).

IR (CHCl3) cm^{-1} : 3403, 1793, 1725, 1613, 1550, 1517, 1248, 1215, 1155.

7 位側鏈：

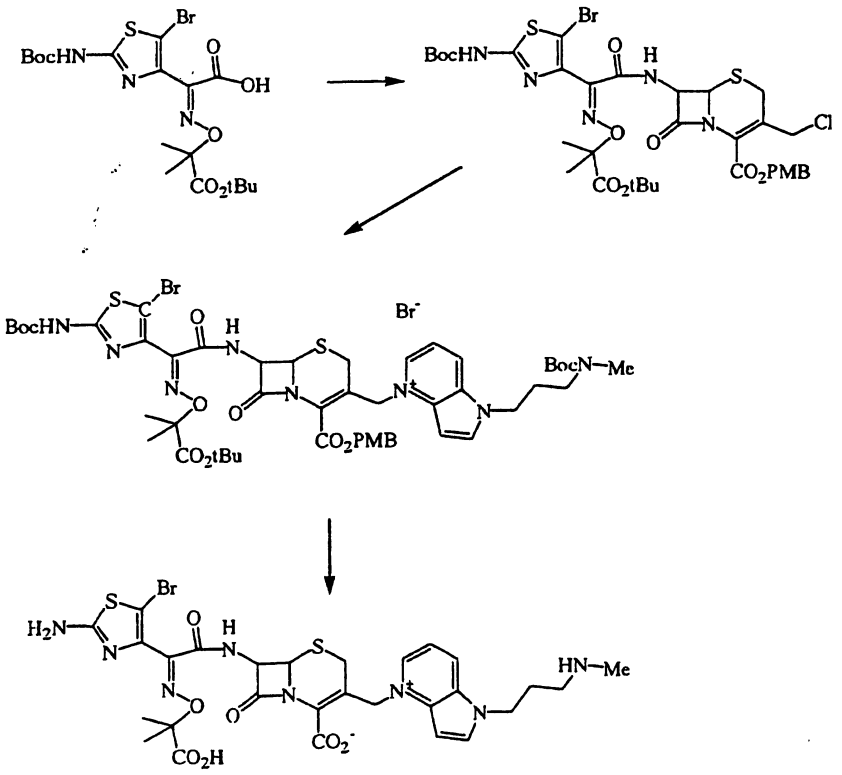
^{1}H-NMR (CDCl3) δ: 1.48(9H, s), 5.65(1H, d, J = 2.4), 5.75(1H, d, J = 2.4), 6.93(1H, s),7.27 −7.34(10H, m).

Positive FABMS(Matrix:m-NBA): m/z 558[M+H]+, 580[M+Na]+, 1115[2M+ H]+ .

Negative FABMS(Matrix:m-NBA): m/z 556[M-H]-, 1113[2M H]- .

IR (CHCl3) cm^{-1}: 3602, 3404, 1723, 1603, 1550, 1285, 1253, 1227, 1155 .

實施例 20



I-4d-5d：

^{1}H-NMR (D20) δ：1.47 (6H, s), 2.30(2H, q like), 2.68(3H, s), 3.06(2H, t, J = 8 Hz), 3.18 及 3.39(2H, ABq, J = 17.7 Hz), 4.52(2H, t like), 5.18(1H, d, J = 4.8 Hz), 5.56 及 5.68(2H, ABq, J = 15 Hz), 5.82(1H, d, J =4.8 Hz), 7.04(1H, d, J = 3.3 Hz), 7.68(1H, t like), 8.12(1H, d, J = 3.6 Hz), 8.58(1H, d, J = 8.1 Hz), 8.64(1H, d, J = 6 Hz).

IR (KBr) cm^{-1}: 3405, 1772, 1608, 1535, 1394, 1362, 1160, 790, 760 .

Positive ESIMS: m/z 735 [M+H]+ . Negative ESIMS: m/z 733 [M-H]- .

元素分析 $C_{28}H_{31}N_8O_7S_2Br \cdot 5H_2O$

計算值： C,40.73; H,5.00; N,13.57; S,7.77; Br,9.68 (%).

實驗值： C,40.67; H,4.91; N,13.39; S,7.50; Br,9.64 (%).

四級鹽酯：

^{1}H-NMR (CDCl3) δ：1.43(9H, s), 1.48(9H, s), 1.51(3H, s), 1.59(3H, s), 2.22(2H, m), 2.91(3H, s), 3.37(2H, t like), 3.31 及 3.80(2H, ABq, J = 18.6 Hz), 3.82(3H,

s), 4.45(2H, t like), 5.19(1H, d, J = 5.4 Hz), 5.23 及 5.30(2H, ABq, J = 11.4 Hz), 5.64 及 5.79(2H, ABq, J = 15 Hz), 6.07(1H, dd, J = 5.4, 9 Hz), 6.87 及 7.33(4H, A2B2q, J = 8.7 Hz), 7.04 (1H, br s), 7.67(1H, t like), 8.06 (1H, d, J = 9 Hz), 8.26(1H, br s), 8.39(1H, br s), 8.52(1H, d, J = 9 Hz), 8.58(1H, d, J = 6 Hz) .

3-Cl 甲基體；

^{1}H-NMR (CDCl3) δ: 1.43(9H, s), 1.52(9H, s), 1.62(6H, s), 3.48 及 3.65(2H, ABq, J = 18.3 Hz), 3.82(3H, s), 4.44 及 4.55(2H, ABq, J = 12 Hz), 5.04(1H, d, J = 4.8 Hz), 5.19 及 5.27(2H, ABq, J = 12 Hz), 6.03(1H, dd, J =5.1, 9 Hz), 6.91 及 7.35(4H, A2B2q, J = 8.7 Hz), 8.02(1H,d, J= 9 Hz), 8.17(1H, br s).

IR (KBr) cm^{-1}: 3280, 2980, 2935, 2837, 1789, 1720, 1614, 1549, 1516, 1369, 1248, 1155 .

7 位側鏈：

^{1}H-NMR (CDCl3) δ: 1.48(9H, s), 1.49(9H, s), 1.53(3H, s), 1.56(3H, s) .

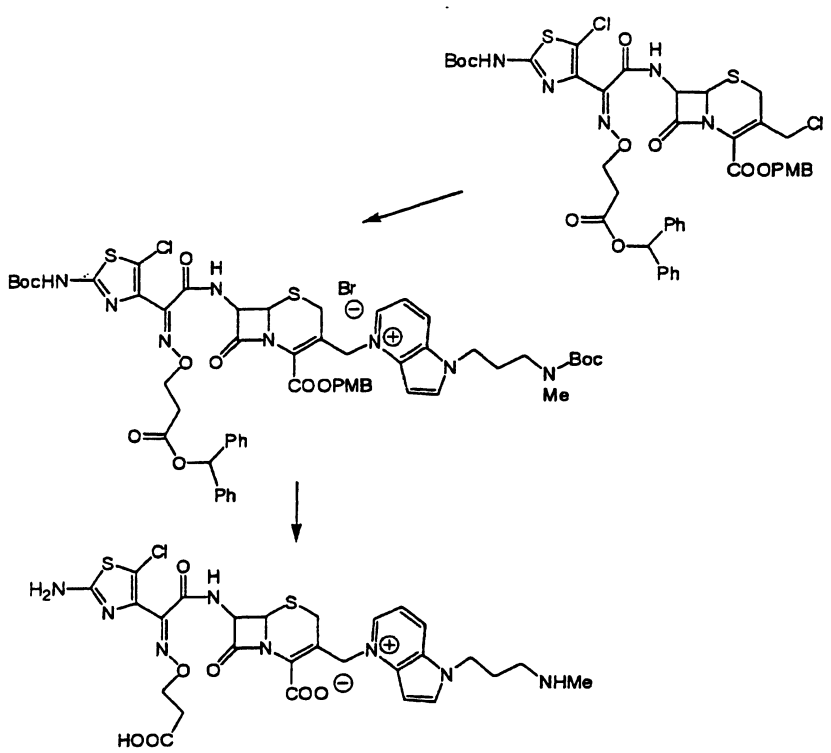
IR (CHCl3) cm^{-1}: 3406, 3019, 2983, 2937, 1724, 1544, 1369, 1226, 1151 .

Positive ESIMS: m/z 508[M+H]+, m/z 530[M+Na]+ .

Negative ESIMS: m/z 506[M-H]-, m/z 528[M+Na-2H]-

其他實施例化合物如下。

實 施 例 22



^{1}H-NMR (D_2O) δ : 2.31(2H, m), 2.59(2H, t, J = 6.9 Hz), 2.69(3H, s), 3.06(2H, m), 3.21 及 3.35 (2H, ABq, J = 17.7 Hz), 4.39(2H, m), 4.53(2H, t, J = 6.9 Hz), 5.14(1H, d, J = 5.1 Hz), 5.54 及 5.71(2H, ABq, J = 15.0 Hz), 5.76(1H, d, J = 5.1 Hz), 7.03(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.3 及 8.4 Hz), 8.13(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 8.4 Hz), 8.66(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}: 3397, 3132, 2458, 1775, 1615, 1540, 1499, 1466, 1389, 1223, 1164, 1122, 1063, 1027.

MS(ESI):677$^+$(M+H$^+$).

元素分析 $C_{27}H_{29}ClN_8O_7S_2 \cdot 2.8\ H_2O$.

計算值： C,44.57 ; H,4.79 ; N,15.40 ; Cl,4.87; S,8.81 (%).

實驗值： C,44.51 ; H,4.57 ; N,15.37 ; Cl,4.81; S,8.66 (%).

3-Cl 甲基體： ;

^{1}H-NMR ($CDCl_3$) δ : 1.52(9H, s), 2.89(2H, m), 3.28 及 3.53(2H, ABq, J = 18.3 Hz), 3.81(3H, s), 4.22 及 4.54(2H, ABq, J = 12.0 Hz), 4.59(3H, t, J = 6.6 Hz), 4.95(1H, d, J = 4.8 Hz), 5.17 及 5.26(2H, ABq, J = 11.7 Hz), 5.90(1H, dd, J = 4.8 and

8.7 Hz), 6.84(1H, s), 6.90(2H, d, J = 9.0 Hz), 7.24-7.38(12H, m), 7.48(1H, d, J = 8.7 Hz), 8.50(1H, brs).

IR (KBr) cm^{-1}: 3283, 3062, 3031, 2978, 2836, 1789, 1721, 1613, 1549, 1515, 1454, 1386, 1369, 1302, 1246, 1158, 1096, 1063, 1031.

MS(ESI): $910^{+}(M+H^{+})$.

元素分析 $C_{42}H_{41}Cl_2N_5O_{10}S_2 \cdot 0.3\ CHCl_3 \cdot 0.7\ H_2O$.

計算值： C,52.96 ; H,4.49 ; N,7.30 ; S,6.69 ; Cl,10.72 (%).

實驗值： C,52.91 ; H,4.34 ; N,7.33 ; S,6.64 ; Cl,10.74 (%).

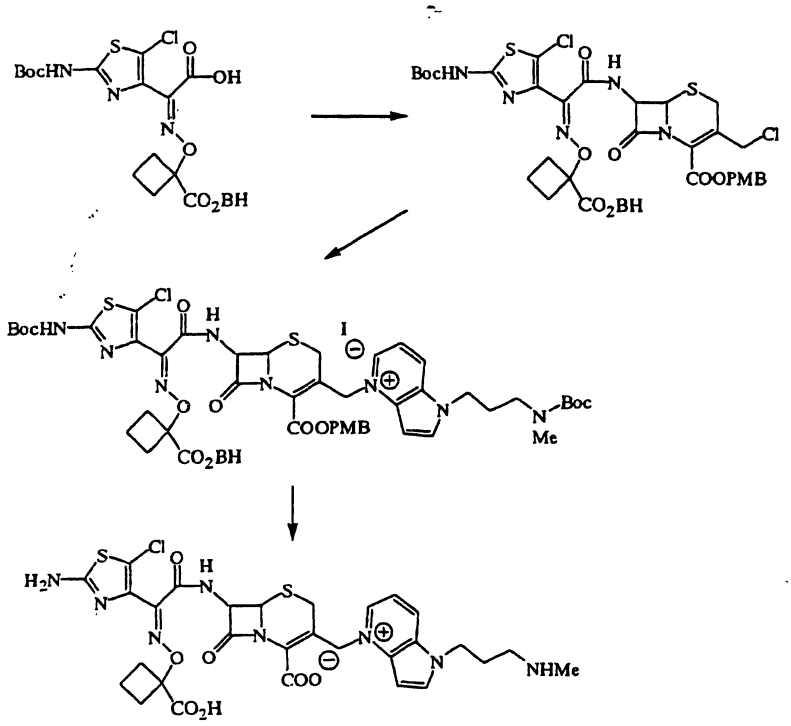
四級鹽酯：

^{1}H-NMR (d_6-DMSO) δ : 1.37(9H, s), 1.46(9H, s), 2.03(2H, m), 2.77(3H, brs), 2.87(2H, t, J = 6.6 Hz), 3.18(2H, t, J = 6.6 Hz), 3.28 及 3.35(2H, m), 3.75(3H, s), 4.36(2H, t, J = 6.3 Hz), 4.43(2H, t, J = 6.6 Hz), 5.15(1H, d, J = 4.8 Hz), 5.21 及 5.29(2H, ABq, J = 11.7 Hz), 5.66 及 5.72(2H, ABq, J = 15.0 Hz), 5.94(1H, dd, J = 4.8 及 9.0 Hz), 6.75(1H, s), 6.88(2H, d, J = 8.7 Hz), 6.99(1H, d, J = 3.3 Hz), 7.20-7.40(12H, m), 7.78(1H, dd, J = 6.0 and 8.1 Hz), 8.43(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 6.0 Hz), 8.88(1H, d, J = 8.1 Hz), 9.72(1H, d, J = 9.0 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1}: 3424, 3061, 3031, 2975, 2934, 1791, 1719, 1685, 1630, 1613, 1548, 1515, 1495, 1455, 1392, 1367, 1247, 1156, 1029.

MS(ESI): $1163^{+}(C_{58}H_{64}ClN_8O_{12}S_2^{+})$.

實施例 23



^{1}H-NMR (D_2O) δ: 1.90(2H, m), 2.31(4H, m), 2.44(2H, m), 2.68(3H, s), 3.05(2H, t, J = 8.1 Hz), 3.17 及 3.39 (2H, ABq, J = 18.0 Hz), 4.54(2H, t, J = 6.9 Hz), 5.20(1H, d, J = 4.8 Hz), 5.56 及 5.69(2H, ABq, J = 15.0 Hz), 5.83(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.3 及 8.4 Hz), 8.12(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3398, 2948, 1774, 1610, 1538, 1498, 1458, 1392, 1287, 1236, 1158, 1120, 1064, 1032.

MS(ESI):$703^+(M+H^+)$.

元素分析 $C_{29}H_{31}ClN_8O_7S_2 \cdot 6.5\ H_2O$.

計算値： C,42.46 ; H,5.41 ; N,13.66 ; Cl,4.32 ; S,7.82 (%).

實驗値： C,42.34 ; H,4.87 ; N,13.71 ; Cl,4.39 ; S,7.79 (%).

７位側鏈：

^{1}H-NMR (d_6-DMSO) δ: 1.47(9H, s), 1.75-2.00(2H, m), 2.20-2.38(2H, m), 2.44-2.54(2H, m), 6.82(1H, s), 7.1-7.5(10H, m), 12.0(1H, brs).

IR (KBr) cm^{-1}: 3209, 3064, 3031, 2980, 2955, 1719, 1619, 1554, 1495, 1454, 1394,

1370, 1295, 1249, 1204, 1155, 1067, 1037.

MS(ESI):586$^+$(M+H$^+$).

元素分析 $C_{28}H_{30}ClN_6O_7S_1 \cdot 1.3\ H_2O$.

計算值： C,55.18 ; H,5.06 ; N,6.89 ; Cl,5.82 ; S,5.26 (%).

實驗值： C,55.17 ; H,4.92 ; N,7.28 ; Cl,5.65 ; S,5.24 (%).

3-Cl 甲基體：

^{1}H-NMR ($CDCl_3$) δ: 1.53(9H, s), 2.05-2.18(2H, m), 2.47-2.78(4H, m), 3.26 及 3.51(2H, ABq, J = 18.3 Hz), 3.82(3H, s), 4.40 及 4.56(2H, ABq, J = 12.0 Hz), 4.96(1H, d, J = 4.8 Hz), 5.24(1H, d, J = 5.1 Hz), 5.21 及 5.27(2H, ABq, J = 12.0 Hz), 5.97(1H, dd, J = 5.1 及 9.6 Hz), 6.90(2H, d, J = 8.7 Hz), 6.92(1H, s), 7.25-7.31(10H, m), 7.35(2H, d, J = 8.7Hz), 7.44(1H, d, J = 9.6 Hz), 8.00(1H, s).

IR (KBr) cm^{-1}: 3378, 3285, 3063, 3031, 2978, 2836, 1790, 1722, 1613, 1585, 1549, 1515, 1454, 1385, 1368, 1300, 1247, 1203, 1156, 1112, 1098, 1063, 1034.

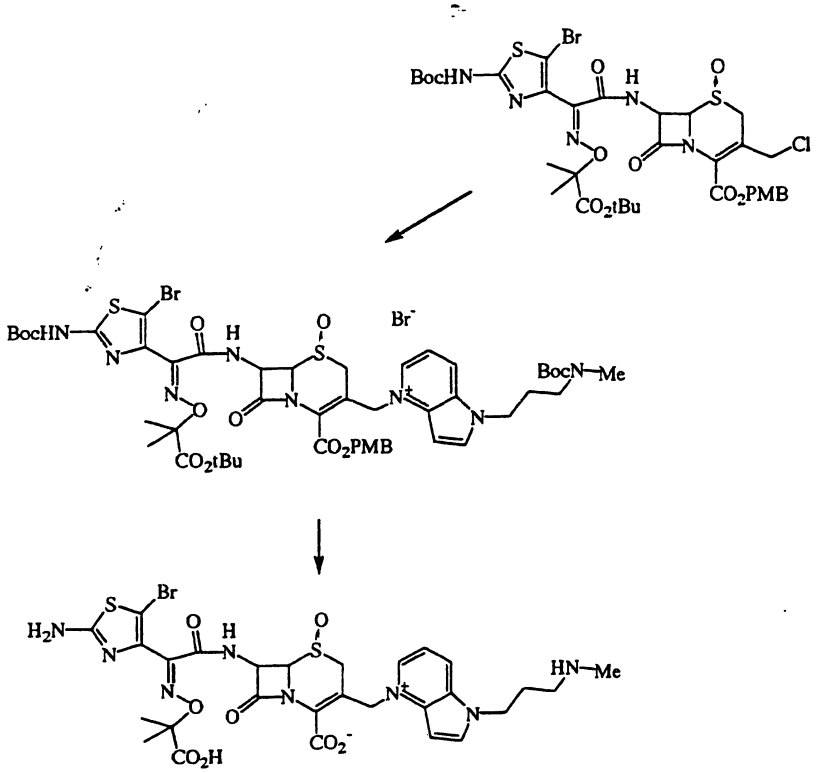
MS(ESI):936$^+$(M+H$^+$).

四級鹽酯：

^{1}H-NMR (d_6-DMSO) δ: 1.36(9H, brs), 1.46(9H, s), 1.79-2.09(2H, m), 2.03(2H, quintet-like), 2.30-2.61(4H, m), 2.77(3H, brs), 3.17(2H, t-like), 3.30 及 3.42(2H, ABq, J = 13.2 Hz), 3.76(3H, s), 4.43(2H, t-like), 5.21(1H, d, J = 4.8 Hz), 5.22 及 5.31(2H, ABq, J = 11.7 Hz), 5.71(2H, brs), 6.01(1H, dd, J = 4.8 及 8.7 Hz), 6.82(1H, s), 6.90(2H, d, J = 8.4 Hz), 6.96(1H, d, J = 3.3 Hz), 7.21-7.44(12H, m), 7.78(1H, dd, J = 6.3 及 8.1 Hz), 8.42(1H, d, J = 3.3 Hz), 8.63(1H, d, J = 6.3 Hz), 8.88(1H, d, J = 8.1 Hz), 9.77(1H, d, J = 8.7 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1}:3424, 3061, 2975, 1791, 1718, 1685, 1630, 1613, 1584, 1550, 1515, 1495, 1455, 1392, 1367, 1298, 1248, 1155, 1123, 1065, 1030, 1018.

實施例 24



^{1}H-NMR (D20) δ: 1.50 (6H, br s), 2.30(2H, q like), 2.69(3H, s), 3.06(2H, t, J =7.8 Hz), 3.38 及 3.63(2H, ABq, J = 18.3 Hz), 4.52(2H, m), 4.98(1H, d, J = 4.8 Hz), 5.63 及 5.75(2H, ABq, J = 15.3 Hz), 6.05(1H, d, J =4.8 Hz), 7.06(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.0 ,8.1 Hz), 8.13(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.1 Hz), 8.67(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}:3412, 1784, 1618, 1535, 1396, 1361, 1159, 858, 760 .

元素分析 $C_{28}H_{31}N_8O_8S_2Br \cdot 6.4H_2O$

計算值： C,38.79; H,5.09; N,12.93; S,7.40; Br,9.22 (%).

實驗值： C,38.82; H,4.85; N,12.90; S,7.43; Br,9.02 (%).

四級鹽酯 (S-Oxide)：

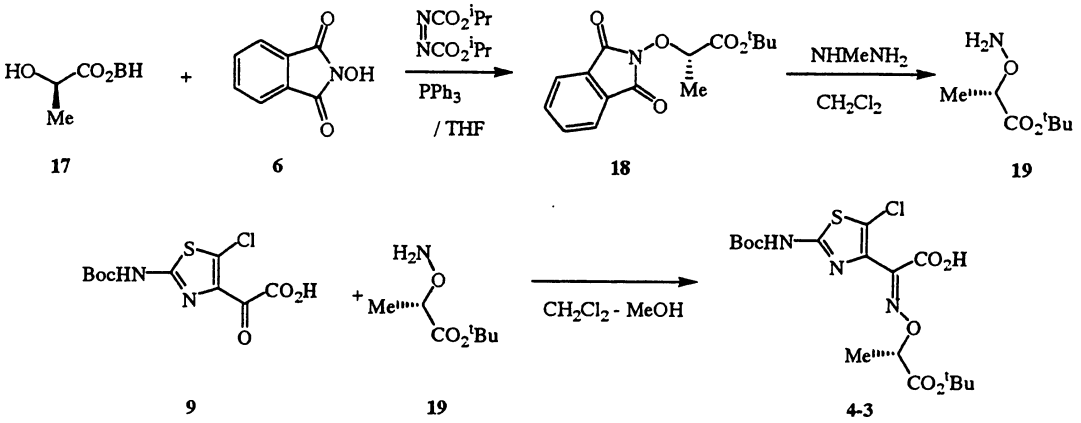
IR (KBr) cm^{-1}: 3427, 2978, 2935, 1802, 1722, 1687, 1549, 1516, 1458, 1390, 1367, 1250, 1153, 1030, 766 .

3-Cl 甲基體 (S-Oxide)：

^{1}H-NMR (CDCl3) δ: 1.42(9H, s), 1.52(9H, s), 1.61(6H, br s), 3.43 及 3.82(2H,

ABq, J = 18.6 Hz), 3.82(3H, s), 4.24 and 5.03(2H, ABq, J = 12.6 Hz), 4.59(1H, dd, J =1.2, 5.1 Hz), 5.24 and 5.30(2H, ABq, J = 12 Hz), 6.19(1H, dd, J =5.1, 9.6 Hz), 6.92 and 7.37(4H, A2B2q, J = 6.6 Hz), 7.94(1H,d, J= 10.2 Hz), 8.37(1H, br s).

實施例25



(1) 將含化合物 17(4.85 克)之無水 THF 38 毫升溶液，加入三苯膦(5.71 克)及羥酞醯亞胺(3.55 克)，於冰冷下攪拌，滴加入疊氮二羧酸二異丙酯(4.3 毫升)，於 4℃ 靜置過夜。減壓濃縮後以矽膠柱層析純化，以乙醚/己烷結晶得化合物 187.6 克。

^{1}H-NMR ($CDCl_3$) δ: 1.67(3H, d, J = 7.2 Hz), 5.05(1H, q, J = 7.2 Hz), 6.93 (1H, s), 7.22-7.32(10H, m), 7.70-7.79(4H, m).

IR (KBr) cm^{-1}: 1791, 1736, 1284, 700.

FABMS: m/z 402 [M+H]+, 803 [2M+H]+ .

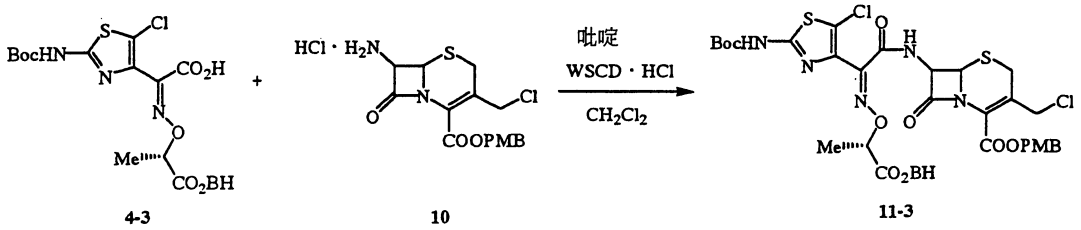
(2) 將含上述化合物 18(4.82 克)之二氯甲烷 12 毫升溶液，於 -25℃ 冷卻下加入甲肼 0.63 毫升並攪拌 1.5 小時。濾除析出結晶，將濾液以甲醇 25 毫升稀釋後，於冰冷卻下加入羧酸 9(3.7 克)並攪拌 2 小時，於 4℃ 靜置過夜。將反應液減壓濃縮後以溶在乙酸乙酯，依次以碳酸氫鈉水、鹽酸

、食鹽水洗淨，於無水硫酸鎂下乾燥，減壓蒸除得化合物 4-3 4.74 克。

^{1}H-NMR(d_6-DMSO)δ：1.46(3H, d, J=6.9H), 1.47(9H, s), 5.00(1H, q, J=6.9 Hz), 6.85(1H, s), 7.26-7.42(10H, m), 12.06(1H, s).

IR (KBr) cm^{-1}: 3422, 3193, 3062, 3032, 2983, 1740, 1719, 1602, 1554, 1453, 1370, 1250, 1155, 1096, 1038, 967, 744, 699.

FABMS: m/z 560 [M+H]+, 1119 [2M+H]+ .

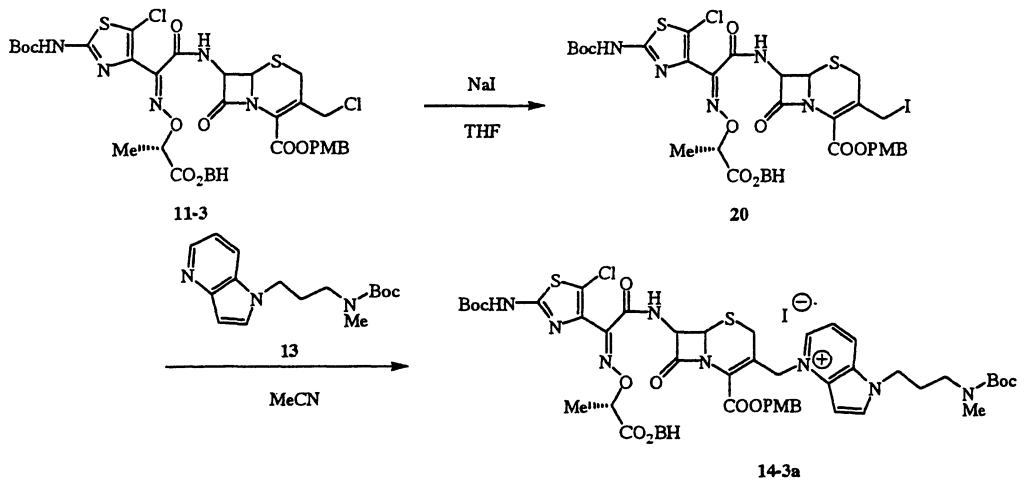


(3) 將含羧酸 4-3(3.50 克，6.25 毫莫耳)及 ACLE・鹽酸鹽 10(2.53 克，6.25 毫莫耳)之二氯甲烷 21 毫升溶液，於冰冷卻下加入 WSCD・鹽酸(1.20 克，1 當量)再加入吡啶(0.51 毫升，1.0 當量)，於同溫度下攪拌 1 小時。將反應液以食鹽水洗淨，於無水硫酸鎂下乾燥，減壓濃縮後以矽膠柱層析純化得泡沫狀殘渣 11-3 4.60 克。

H-NMR (CDCl3) δ: 1.53(9H, s), 1.64(3H, d, J = 7.2 Hz), 3.39 及 3.58(2H, ABq, J = 18.3 Hz), 3.81(3H, s), 4.42 及 4.59(2H, ABq, J = 12 Hz), 4.97(1H, d, J = 5.1 Hz), 5.08(1H, q, J = 7.2 Hz), 5.20 及 5.27(2H, ABq, J = 11.7 Hz), 6.01(1H, dd, J =5.1, 9.3 Hz), 6.88- 6.91(3H, m), 7.06-7.35(12H, m), 7.85(1H, d, J = 9.3 Hz), 8.15(1H, br s).

IR (KBr) cm^{-1}: 3281, 2980, 2935, 2836, 1790, 1719, 1612, 1552, 1515, 1454, 1369, 1247, 1155,1035, 700 .

FABMS: m/z 910 [M+H]+ .



(4) 於 13℃ 冷卻下，於含氯體 11-3(4.60 克，5.05 毫莫耳)之 THF 46 毫升溶液中加入 NaI(2.65 克，3.5 當量)，攪拌 30 分。將反應液注至硫代硫酸鈉水-乙酸乙酯中並分離有機層，以食鹽水洗淨，於無水硫酸鎂下乾燥後減壓濃縮得泡沫狀殘渣 20 5.07 克。

H-NMR (CDCl3) δ: 1.53(9H, s), 1.65(3H, d, J = 7.2 Hz), 3.39 及 3.67(2H, ABq, J = 17.7 Hz), 3.81(3H, s), 4.33 及 4.45(2H, ABq, J = 9.3Hz), 4.96(1H, d, J = 5.1 Hz), 5.08(1H, q, J = 7.2 Hz), 5.20 及 5.28(2H, ABq, J = 11.7 Hz), 5.95(1H, dd, J =5.1, 9.0 Hz), 6.88~ 6.92(3H, m), 7.23~7.39(12H, m), 7.78(1H, d, J = 9.0 Hz), 8.01(1H, br s).

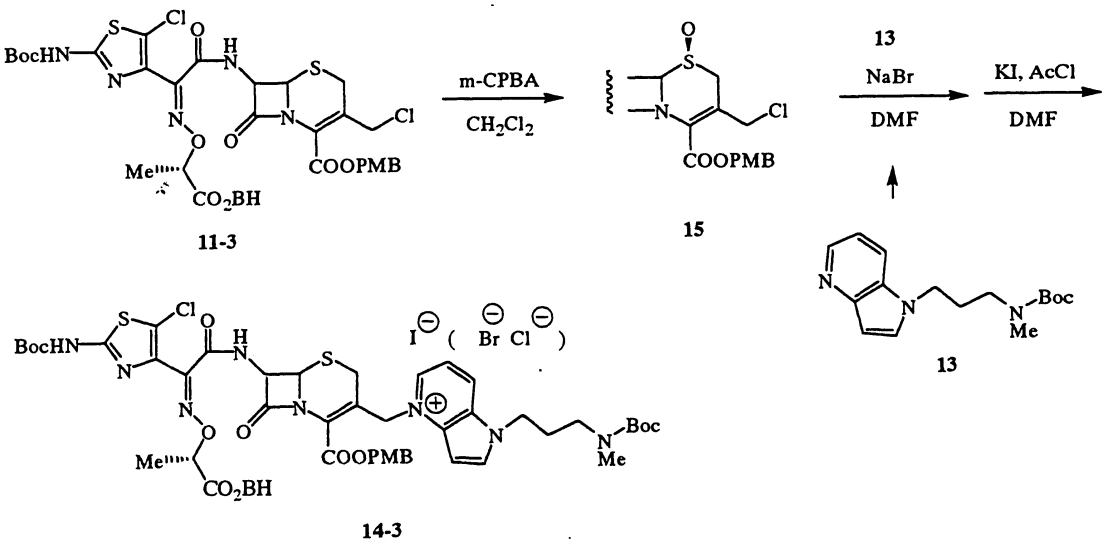
IR (KBr) cm^{-1}: 3383, 3284, 2980, 2836, 1790, 1719, 1613, 1551, 1516,1369, 1246, 1153, 1037, 700 .

ABMS: m/z 1002 [M+H]+ .

(5) 將含 3 位側鏈 13(174 毫克，0.60 毫莫耳)之乙腈 1 毫升溶液，於冰冷卻下加入碘體 20(570 毫克，純度換算爲 0.60 毫莫耳)，於同溫下攪拌 3 小時再於室溫下攪拌 2 小時。滴加入甲苯/乙醚/正己烷(1:30:30)之混合液，濾集析出之粉末得四級鹽 14-3a 675 毫克。

^{1}H-NMR ($CDCl_3$)δ: 1.46(9H, s), 1.51(9H, s), 1.61(3H, d, J = 7.2 Hz), 2.21(2H, m), 2.88(3H, s), 3.19 及 3.89(2H, ABq, J = 18.9 Hz), 3.33(2H, m), 3.80(3H, s), 4.42(2H, t like), 5.04-5.15(4H, m), 5.22 及 5.30(2H, ABq, J = 12 Hz), 5.84 and 5.75(2H, ABq, J = 14.7 Hz), 5.98(1H, dd, J = 5.1, 8.7 Hz), 6.89(3H,m), 7.25-7.36(12H, m), 7.54(1H, t like), 7.75(H, d, J = 7.8 Hz), 8.25(1H, m), 8.56(1H, d, J = 8.7 Hz), 8.95(1H, d, J = 5.7 Hz).

IR (KBr) cm^{-1}: 3423, 2976, 2932, 1792, 1718, 1687, 1613, 1550, 1515, 1496, 1454, 1367, 1248 1154, 759, 701 .



(6) 將含氯體 11-3(2.13 克，2.33 毫莫耳)之二氯甲烷 10 毫升溶液，於 -50℃ 冷卻下滴加入 m-CPBA(純度:>65%，495 毫克，0.81 當量)之二氯甲烷 8 毫升溶液，於同溫下攪拌 30 分。再加入 5%硫代硫酸鈉水，將有機層依次以碳酸氫鈉水、食鹽水洗淨後，於無水硫酸鎂下乾燥後減壓濃縮得泡沫狀殘渣。以乙醚/正己烷粉末得氧化物 15，約 2 克。

H-NMR (CDCl3) δ: 1.53(9H, s), 1.64(3H, d, J = 7.2 Hz), 3.29 及 3.70(2H, ABq, J = 18.6 Hz), 3.81(3H, s), 4.23 及 4.99(2H, ABq, J = 12.6 Hz), 4.44(1H, d, J = 5.1 Hz), 5.10(1H, q, J = 7.2 Hz), 5.26 (2H, m), 6.16(1H, dd, J =5.1, 9.6 Hz), 6.88- 6.94(3H, m), 7.25-7.375(12H, m), 7.90(1H, d, J = 9.6 Hz), 8.32(1H, br s).

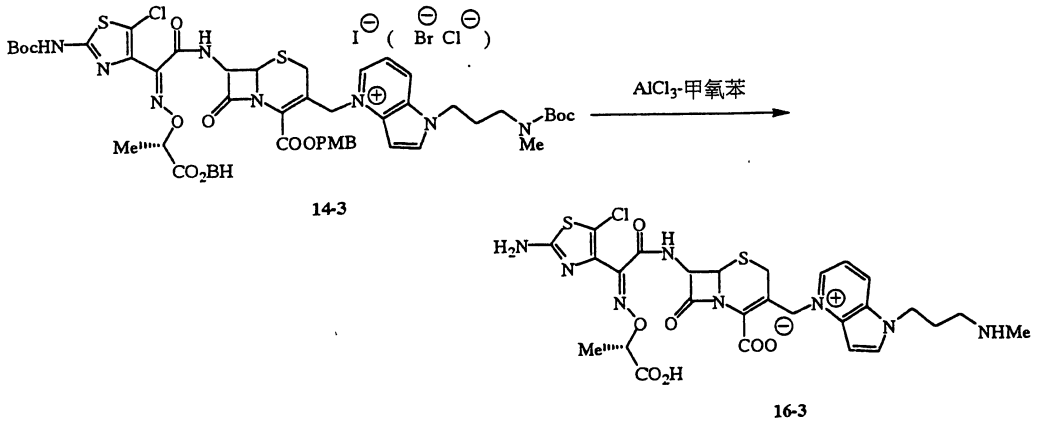
IR (KBr) cm^{-1}: 3425, 2979, 2937, 1804, 1720, 1613, 1553, 1516, 1454, 1369, 1249 1155, 1037, 701 .

(7-1) 將含 3 位側鏈 13(324 毫克，1.1 當量)之 DMF 1.8 毫升溶液中加入氧化物 15(1.22 克，1.31 毫莫耳)及 NaBr(271 毫克，2 當量)，於氮氣及室溫下攪拌 1.5 小時。加入 DMF 2 毫升及 KI 1.28 克，於 -40℃ 下冷卻後滴加入 AcCl 0.40 毫升，於 -10℃ 下攪拌 3 小時。加入含 NaCl 及硫代硫酸鈉之磷酸緩衝液，濾集結結後以丙酮溶解並減壓濃縮。以乙醚/正己烷粉末化得四級鹽 14-3 1.77 克。

^{1}H-NMR($CDCl_3$)δ: 1.48(9H, s), 1.51(9H, s), 1.62(3H, d, J=7.2Hz), 2.21(2H, m), 2.91(3H, s), 3.24 及 3.82(2H, ABq, J = 18.9 Hz), 3.36(2H, m), 3.81(3H, s), 4.43(2H, t like), 5.09(1H, q, J = 7.2 Hz), 5.16(1H, d, J = 5.1 Hz), 5.24 及 5.31(2H, ABq, J = 11.7 Hz), 5.58 及 5.75(2H, ABq, J = 14.7 Hz), 5.99(1H, dd, J = 5.1, 8.7 Hz), 6.86(1H, s), 6.87(2H, d, J = 8.7 Hz), 7.00(1H, br s), .7.24 - 7.38(12H, m), 7.55(1H, t like), 7.78(H, d, J = 8.7 Hz), 8.25(1H, br s), 8.47(1H, d, J = 10.2 Hz), 8.50(1H, d, J = 6 Hz).

IR (KBr) cm^{-1}: 3423, 2976, 2932, 1792, 1718, 1687, 1613, 1248 1154, 759, 701

(7-2) 將含 3 位側鏈 13(174 毫克，0.60 毫莫耳)之乙腈 1 毫升溶液中加入碘體 20(570 毫克，純度換算爲 0.60 毫莫耳)，於同溫下攪拌 3 小時再於室溫下攪拌 2 小時。滴加入甲苯/乙醚/正己烷(1:30:30)之混合液，濾集析出之粉末得四級鹽 14-3a 675 毫克。



(8) 將含四級鹽 14-3(約 1.3 毫莫耳)之二氯甲烷-$MeON_2$ 30 毫升及甲氧苯(1.7 毫升)溶液，於氮氣及冰冷卻下加入 $AlCl_3$-$MeNO_2$ 溶液(1.5M，7 毫升)，攪拌 1 小時。加入冰、1N 鹽酸-乙腈及乙醚並分離水層，減壓濃縮，以 HP-20 層析純化後真空冷凍乾燥，得粉末狀化合物 16-3(450 毫克)。

^{1}H-NMR (D20) δ: 1.43 (3H, d, J = 7.2 Hz), 2.31(2H, q like), 2.68(3H, s), 3.05(2H, t, J = 8 Hz), 3.18 及 3.37(2H, ABq, J = 18 Hz), 4.53(2H, t like), 4.65 (1H, q, J = 7.2 Hz), 5.17(1H, d, J = 4.8 Hz), 5.54 and 5.70(2H, ABq, J = 15 Hz), 5.86(1H, d, J =4.5 Hz), 7.03(1H, d, J = 3.6 Hz), 7.69(1H, dd, J = 6 , 8.4 Hz), 8.13(1H,

d, J = 3.6 Hz), 8.60(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6 Hz).

IR (KBr) cm^{-1}: 3398, 1775,1603,1541,1392,1363,1320, 1286,1033,762.

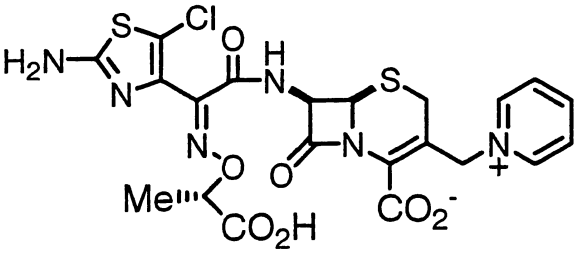
Positive ESIMS: m/z 677 [M+H]+ . Negative ESIMS: m/z 675 [M-H]- .

元素分析 $C_{27}H_{29}N_8O_7S_2Cl \cdot 6.2H_2O$

計算值： C,41.11; H,5.29; N,14.20; S,8.13; Cl,4.49 (%).

實驗值： C,40.88; H,4.88; N,14.23; S,8.05; Cl,4.57 (%).

實施例 26



^{1}H-NMR (D_2O) δ : 1.51 (3H, d, J = 7.25 Hz), 3.22 及 3.64 (Abq, J = 17.9 Hz), 4.83 (1H, q, J = 7.2Hz), 5.28 (1H, d, J = 4.8 Hz), 5.35 及 5.58 (2H, ABq, J = 14.6 Hz), 5.90 (1H, d, J = 4.8Hz), 8.09 (2H, t-like), 8.57 (2H, t, J = 7.8 Hz), 8.95 (2H, d, J = 5.7 Hz).

IR (KBr) cm^{-1}:3410, 3060, 1780, 1674, 1627, 1538, 1481, 1445, 1389, 1341, 1219, 1186, 1153, 1100, 1035.

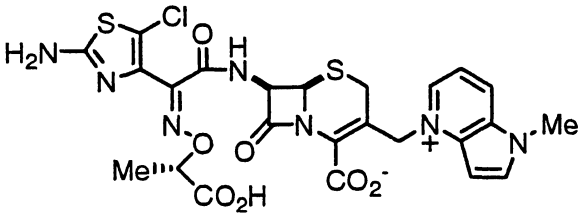
MS(ESI): 567^+ $(M+H)^+$.

元素分析 $C_{21}H_{19}ClN_6O_7S_2 \cdot 2.9\ H_2O$.

計算值： C,40.73 ; H,4.04 ; N,13.57 ; Cl,5.73; S,10.36 (%).

實驗值： C,40.67 ; H,3.87 ; N,13.45 ; Cl,5.50; S,10.36 (%).

實施例 27



^{1}H-NMR (d_6-DMSO) δ : 1.36 (3H, d, J = 7.1 Hz), 2.97 及 3.25 (2H, Abq, J = 17.3 Hz), 4.03 (3H, s), 4.55 (1H, q, J = 7.1 Hz), 4.97 (1H, d, J = 5.1 Hz), 5.61-5.72 (3H, m), 5.60 及

5.73 (2H, ABq, J = 15.2 Hz), 7.37 (1H, d, J = 3.3 Hz), 7.41 (1H, s), 7.78 (1H, dd, J = 6.3, 8.2 Hz), 8.28 (1H, d, J = 3.3 Hz), 8.74 (1H, d, J = 8.2), 9.16 (1H, d, J = 6.3 Hz), 9.61 (1H, brs).

IR (KBr) cm^{-1}:3423, 2986, 1778, 1674, 1618, 1538, 1500, 1469, 1416, 1368, 1324, 1281, 1222, 1187, 1154, 1094, 1062, 1032. ..

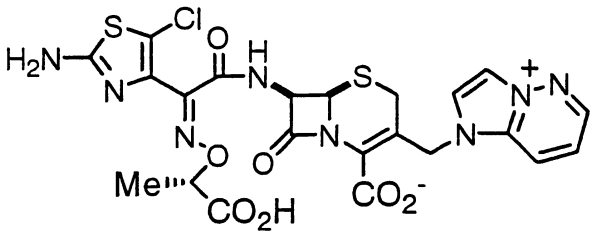
MS(ESI): 620^+ $(M+H)^+$.

元素分析　$C_{24}H_{22}ClN_7O_7S_2 \cdot 2.6\ H_2O$.

計算値：　C,43.22 ; H,4.11 ; N,14.70 ; Cl,5.32; S,9.62 (%).

實驗値：　C,43.16 ; H,3.99 ; N,14.88 ; Cl,5.12; S,9.61 (%).

實施例 28



^{1}H-NMR (D_2O) δ : 1.50 (3H, d, J = 6.9 Hz), 3.20 及 3.58 (2H, ABq, J = 17.7 Hz), 4.80 及 4.84 (2H, ABq, J = 6.9 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.37 及 5.42 (2H, ABq, J = 16.2 Hz), 5.87 (1H, d, J = 4.8 Hz), 7.90 (1H, dd, J = 4.5, 9.4 Hz), 8.25 (1H, d, J = 2.3Hz), 8.44 (1H, d, J = 2.3 Hz), 8.66 (1H, d, J = 9.4 Hz), 8.94 (1H, dd, J = 1.5, 4.5 Hz).

IR (KBr) cm^{-1}: 3416, 3136, 2939, 1776, 1674, 1625, 1535, 1447, 1383, 1346, 1317, 1232, 1185, 1155, 1100, 1066, 1035.

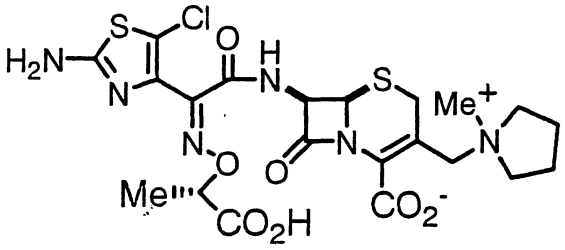
MS(FAB): 607^+ $(M+H)^+$.

元素分析　$C_{22}H_{19}ClN_8O_7S_2 \cdot 2.8\ H_2O$.

計算値：　C,40.19 ; H,3.77 ; N,17.04 ; Cl,5.39; S,9.75 (%).

實驗値：　C,40.10 ; H,3.56 ; N,17.01 ; Cl,5.20; S,9.73 (%).

實施例２９



^{1}H-NMR (D_2O) δ : 1.55 (3H, d, J = 7.2 Hz), 2.22 (4H, brs), 2.99 (3H, s), 3.46 及 3.92 (2H, ABq, J = 17.0Hz), 3.53 (4H, m), 3.99 及 4.74 (2H, ABq, J = 13.79 Hz), 4.85 (1H, q, J = 7.2 Hz), 5.36 (1H, d, J = 5.1 Hz), 5.90 (1H, d, J = 5.1 Hz).

IR (KBr) cm^{-1}: 3416, 1780, 1676, 1616, 1538, 1459, 1345, 1285, 1236, 1180, 1097, 1068, 1036.

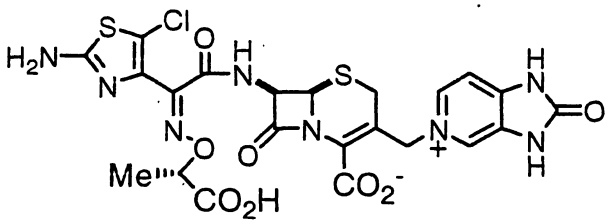
MS(FAB): 573$^+$ $(M+H)^+$.

元素分析 $C_{21}H_{25}ClN_6O_7S_2$ · 4.0 H_2O.

計算値： C,39.10 ; H,5.16 ; N,13.03 ; Cl,5.50; S,9.94 (%).

實驗値： C,38.86 ; H,4.64 ; N,13.00; Cl,5.30; S,9.90 (%).

實施例 30



^{1}H-NMR (d_6-DMSO) δ : 1.37 (3H, d, J = 7.1 Hz), 3.15 及 3.50 (ABq, J = 17.6 Hz), 4.54 (1H, q, J = 7.1 Hz), 4.96 及 5.58 (2H, ABq, J = 13.4 Hz), 5.11 (1H, d, J = 4.9 Hz), 5.73 (1H, dd, J = 4.9, 8.9 Hz), 7.41 (2H,s), 7.52 (1H, d, J = 6.6 Hz), 8.70 (2H, d, J = 6.6 Hz), 9.14 (1H, s), 9.75 (1H, brs).

IR (KBr) cm^{-1}: 3414, 3086, 1738, 1661, 1620, 1527, 1446, 1390, 1351, 1307, 1210, 1118, 1066, 1036.

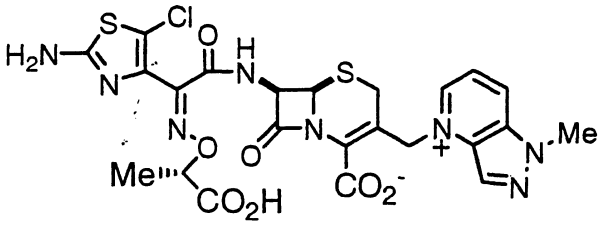
MS(ESI): 623$^+$ $(M+H)^+$.

元素分析 $C_{22}H_{19}ClN_8O_8S_2$ · 3.7 H_2O.

計算値： C,38.31 ; H,3.86 ; N,16.25 ; Cl,5.14; S,9.30 (%).

實驗值： C,38.18 ; H,3.51 ; N,16.22 ; Cl,4.85; S,9.24 (%).

實施例 31



^{1}H-NMR (d_6-DMSO) δ : 1.36 (3H, d, J = 7.1 Hz), 3.03 及 3.32 (ABq, J = 17.6 Hz), 4.29 (3H, s), 4.55 (1H, q, J = 7.1 Hz), 5.00 (1H, d, J = 5.0 Hz), 5.69 (1H, dd, J = 5.0, 8.6 Hz), 5.75 及 5.818 (2H, ABq, J = 14.1 Hz), 7.42 (2H,s), 8.12 (1H, dd, J = 5.6, 8.8 Hz), 9.08 (1H, d, J = 8.8 Hz), 9.15 (1H, s), 9.46 (1H, d, J = 5.6 Hz), 9.56 (1H, d, J = 8.6 Hz).

IR (KBr) cm^{-1}: 3415, 1779, 1675, 1617, 1538, 1483, 1442, 1392, 1372, 1348, 1291, 1236, 1188, 1155, 1100, 1063, 1034.

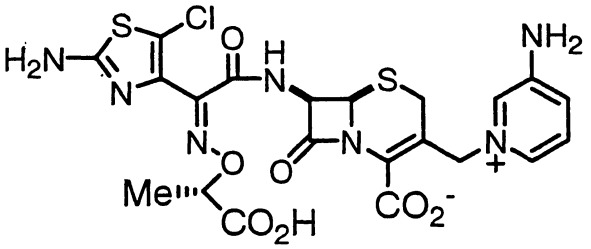
MS(ESI): 621^+ $(M+H)^+$.

元素分析 $C_{23}H_{21}ClN_8O_7S_2 \cdot 3.1\ H_2O$.

計算值： C,40.81; H,4.05; N,16.55; Cl,5.24; S,9.47 (%).

實驗值： C,40.85; H,3.85; N,16.73; Cl,5.01; S,9.46 (%).

實施例 32



^{1}H-NMR (d_6-DMSO) δ : 1.39 (3H, d, J = 7.1 Hz), 3.01 及 3.46 (2H, ABq, J = 17.6 Hz), 4.56 (1H, q, J = 7.1 Hz), 5.00 及 5.55 (2H, ABq, J = 13.4 Hz), 5.06 (1H, d, J = 5.1 Hz), 5.70 (1H, dd, J = 5.1 Hz), 6.74 (2H, brs), 7.42 (2H,brs), 7.55 (1H, d, J = 8.5 Hz), 7.68 (1H, dd, J = 8.5, 5.7 Hz), 8.38 (1H, d, J = 5.7 Hz), 8.51 (1H, brs), 9.67 (1H, brs).

IR (KBr) cm^{-1}: 3351, 3208, 1777, 1629, 1538, 1512, 1445, 1391, 1346, 1232, 1190, 1155, 1098, 1065, 1034.

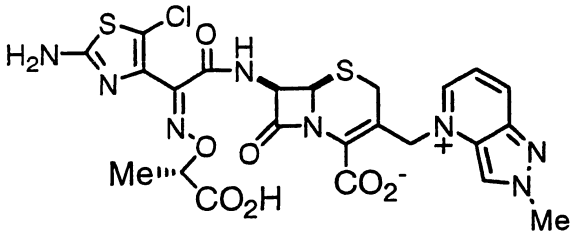
MS(ESI): 582^+ $(M+H)^+$.

元素分析　$C_{21}H_{20}ClN_7O_7S_2 \cdot 3.6\ H_2O$.

計算值：　C,38.99; H,4.24; N,15.16; Cl,5.48; S,9.91 (%).

實驗值：　C,38.84; H,3.84; N,15.23; Cl,5.34; S,9.67 (%).

實施例 33



^{1}H-NMR (d_6-DMSO) δ: 1.37 (3H, d, J = 6.9 Hz), 3.10 及 3.34 (2H, ABq, J = 17.3 Hz), 4.39 (3H, s), 4.55 (1H, q, J = 6.9 Hz), 5.01 (1H, d, J = 4.9 Hz), 5.60 及 5.73 (2H, ABq, J = 14.3 Hz), 5.68 (1H, dd, J = 4.9, 9.0 Hz), 7.42 (2H, s), 7.97 (1H,dd, J = 5.5, 8.6 Hz), 9.04 (1H, d, J = 8.6 Hz), 9.42 (1H, d, J = 5.5 Hz), 9.59 (2H, brs).

IR (KBr) cm^{-1}: 3419, 1778, 1634, 1615, 1538, 1454, 1408, 1356, 1329, 1295, 1235, 1176, 1156, 1100, 1073, 1035, 1011.

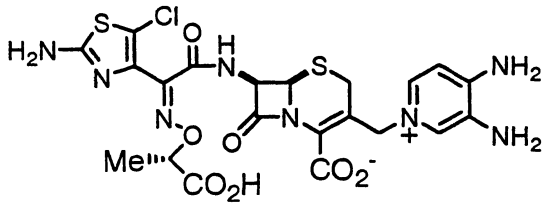
MS(ESI): 621^+ $(M+H)^+$.

元素分析　$C_{23}H_{21}ClN_8O_7S_2 \cdot 3.2\ H_2O$.

計算值：　C,40.70; H,4.07; N,16.51; Cl,5.22; S,9.45 (%).

實驗值：　C,40.48; H,3.61; N,16.42; Cl,5.16; S,9.46 (%).

實施例 34



^{1}H-NMR (d_6-DMSO) δ: 1.39 (3H, d, J = 7.1 Hz), 2.95 及 3.41 (2H, ABq, J = 17.7 Hz), 4.57 (1H, q, J = 7.1 Hz), 4.70 及 5.22 (2H, ABq, J = 13.8 Hz), 5.05 (1H, d, J = 4.89 Hz), 5.66 (2H, brs), 5.71 (1H, dd, J = 4.8, 8.7 Hz), 6.73 (1H, d, J = 6.9 Hz), 7.42 (4H, brs), 7.98 (2H, m).

IR (KBr) cm^{-1}: 3379, 3213, 1775, 1645, 1577, 1542, 1446, 1360, 1308, 1235, 1184, 1156, 1065, 1035.

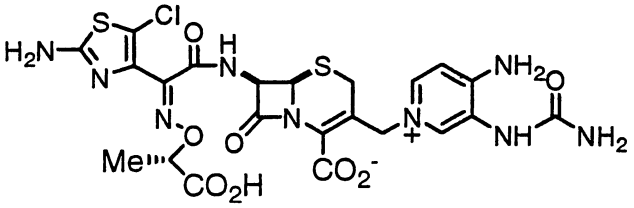
MS(ESI): $597^{+}(M+H)^{+}$.

元素分析 $C_{21}H_{21}ClN_8O_7S_2 \cdot 3.1\ H_2O$.

計算值： C,38.63; H,4.20; N,17.16; Cl,5.43; S,9.82 (%).

實驗值： C,38.51; H,3.83; N,17.22; Cl,5.41; S,9.75 (%).

實施例 35



^{1}H-NMR (d_6-DMSO) δ: 1.40 (3H, d, J = 7.1 Hz), 3.09 及 3.48 (2H, ABq, J = 17.7 Hz), 4.57 (1H, q, J = 7.1 Hz), 4.85 及 5.22 (2H, ABq, J = 13.8 Hz), 5.09 (1H, d, J = 4.9 Hz), 5.76 (1H, dd, J = 4.9 Hz), 6.58 (2H, brs), 6.95 (1H, d, J = 6.5 Hz), 7.40 (2H, s), 7.96 (2H,brs), 8.28 (1H, d, J = 6.5 Hz), 8.82 (1H, brs), 9.25 (1H, brs), 9.77 (1H, brs).

IR (KBr) cm^{-1}: 3364, 3205, 1775, 1657, 1540, 1493, 1447, 1355, 1270, 1182, 1146, 1109, 1066, 1034.

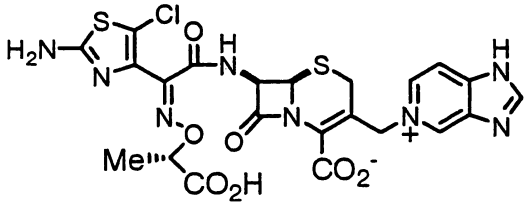
MS(ESI): $640^{+}(M+H)^{+}$.

元素分析 $C_{22}H_{22}ClN_9O_8S_2 \cdot 3.0\ H_2O$.

計算值： C,38.07; H,4.07; N,18.16; Cl,5.11; S,9.24 (%).

實驗值： C,37.72; H,3.67; N,17.97; Cl,5.03; S,9.02 (%).

實施例 36



^{1}H-NMR (d_6-DMSO) δ: 1.36 (3H, d, J = 7.0 Hz), 3.10 及 3.54 (2H, ABq, J = 17.6 Hz), 4.55 (1H, q, J = 7.0 Hz), 5.14 (1H, d, J = 5.0 Hz), 5.20 及 5.68 (2H, ABq, J = 13.8 Hz), 5.77 (1H, dd, J = 5.0, 9.1 Hz), 7.40 (2H, brs), 8.18 (1H, d, J = 6.6 Hz), 8.83 (1H, brs), 8.87 (1H, d,

J = 6.6 Hz), 9.68 (1H, d, J = 9.1 Hz), 9.80 (1H, brs).

IR (KBr) cm^{-1}: 3412, 1777, 1614, 1539, 1444, 1377, 1305, 1187, 1108, 1066, 1036.

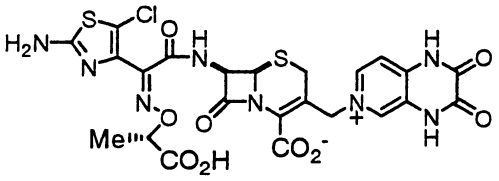
MS(ESI): 607^+ $(M+H)^+$.

元素分析 $C_{22}H_{19}ClN_8O_7S_2 \cdot 2.7H_2O$.

計算值： C,40.30; H,3.75; N,17.09; Cl,5.41; S,9.78 (%).

實驗值： C,40.22; H,3.55; N,17.05; Cl,5.35; S,9.57 (%).

實施例 37



^{1}H-NMR (d_6-DMSO) δ: 1.38 (3H, d, J = 7.1 Hz), 3.07 及 3.49 (2H, ABq, J = 17.4 Hz), 4.57 (1H, q, J = 7.1 Hz), 5.09 (1H, d, J = 4.8 Hz), 5.12 及 5.55 (2H, ABq, J = 13.5 Hz), 5.75 (1H, dd, J = 4.8, 8.2 Hz), 7.41 (2H, s), 7.48 (1H, d, J = 6.2 Hz), 8.70 (1H, d, J = 6.2 Hz), 8.90 (1H, brs), 9.62 (1H, d, J = 8.2 Hz).

IR (KBr) cm^{-1}: 3421, 3195, 3088, 2988, 1776, 1720, 1639, 1532, 1375, 1237, 1175, 1137, 1066, 1035..

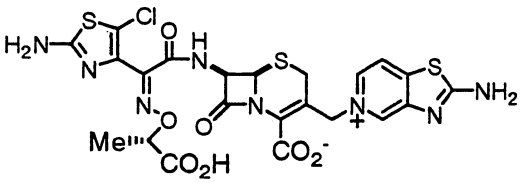
MS(ESI): 651^+ $(M+H)^+$.

元素分析 $C_{23}H_{19}ClN_8O_9S_2 \cdot 3.1H_2O$.

計算值： C,39.08; H,3.59; N,15.85; Cl,5.02; S,9.07 (%).

實驗值： C,39.05; H,3.44; N,15.81; Cl,4.84; S,8.83 (%).

實施例 38



^{1}H-NMR (d_6-DMSO) δ: 1.37 (3H, d, J = 6.9 Hz), 3.06 及 3.49 (2H, ABq, J = 17.6 Hz), 4.51 (1H, q, J = 6.9 Hz), 5.06 (1H, d, J = 4.7 Hz), 5.04 及 5.61 (2H, ABq, J = 12.9 Hz), 5.71 (1H, dd, J = 4.7, 8.9 Hz), 7.42 (2H, s), 8.40 (1H, d, J = 6.2 Hz), 8.64 (2H, s), 8.91 (1H, d, J =

6.2 Hz), 9.39 (1H, s), 9.60 (1H, brs).

IR (KBr) cm^{-1}: 3399, 3191, 1775, 1638, 1537, 1478, 1391, 1317, 1273, 1236, 1187, 1089, 1035.

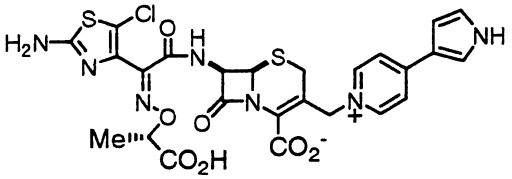
MS(ESI): 639^+ $(M+H)^+$.

元素分析 $C_{22}H_{19}ClN_8O_7S_3 \cdot 3.4H_2O$

計算值： C,37.73; H,3.71; N,16.00; Cl,5.06; S,13.74 (%).

實驗值： C,37.61; H,3.35; N,16.12; Cl,4.92; S,13.56 (%).

實施例 39 9



^{1}H-NMR (d_6-DMSO) δ : 1.37 (3H, d, J = 6.9 Hz), 3.06 及 3.50 (2H, ABq, J = 17.7 Hz), 4.53 (1H, q, J = 6.9 Hz), 5.06 (1H, d, J = 4.7 Hz), 4.91 及 5.45 (2H, ABq, J = 12.5 Hz), 5.70 (1H, dd, J = 4.7, 8.79 Hz), 6.85 (1H,s), 7.01 (1H, s), 7.41 (2H, s), 7.96 (1H, s), 8.15 (2H, d, J = 5.7 Hz), 9.08 (2H, d, J = 5.7 Hz), 9.73 (1H, brs), 11.85 (1H, brs).

IR (KBr) cm^{-1}: 3410, 1774, 1636, 1560, 1474, 1354, 1218, 1152, 1107, 1037.

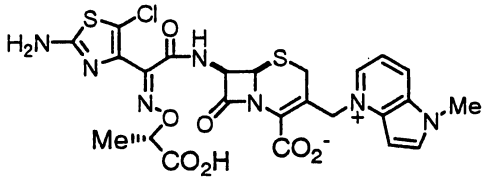
MS(ESI): 632^+ $(M+H)^+$.

元素分析 $C_{25}H_{22}ClN_7O_7S_2 \cdot 8.4H_2O$.

計算值： C,38.33; H,3.99; N,12.52; Cl,4.53; S,8.19 (%).

實驗值： C,37.89; H,3.62; N,12.41; Cl,4.41; S,7.93 (%).

實施例 40 0



^{1}H-NMR (d_6-DMSO) δ : 1.37 (3H, d, J = 7.1 Hz), 2.96 及 3.26 (2H, ABq, J = 17.6 Hz), 4.02 (3H, s), 4.50 (2H, brs), 4.98 (1H, d, J = 4.8 Hz), 5.67 (1H, brs), 7.34 (1H,d, J = 3.0 Hz), 7.41 (2H, brs), 7.78 (1H d, J = 6.0 Hz), 8.29 (1H, d, J = 3.0 Hz), 8.75 (1H, d, J = 7.9 Hz),

9.13 (1H, d, J = 6.0, 7.9 Hz), 9.75 (1H, brs).

IR (KBr) cm^{-1}: 3412, 1775, 1673, 1613, 1538, 1501, 1470, 1392, 1368, 1324, 1281, 1221, 1152, 1063, 1035..

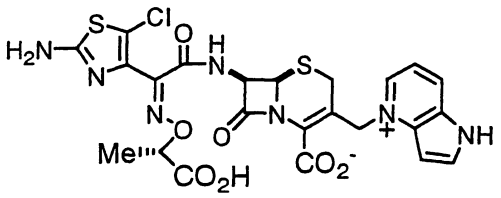
MS(ESI): 620^+ $(M+H)^+$.

元素分析 $C_{23}H_{20}ClN_7O_7S_2 \cdot 2.1H_2O$.

計算値： C,42.90; H,3.79; N,15.23; Cl,5.51; S,9.96 (%).

實驗値： C,42.91; H,3.76; N,15.34; Cl,5.47; S,9.90 (%).

實施例 41



^{1}H-NMR (d_6-DMSO) δ : 1.37 (3H, d, J = 7.1 Hz), 3.03 及 3.28 (2H, ABq, J = 17.4 Hz), 4.56 (1H, q, J = 7.1 Hz), 5.01 (1H, d, J = 4.8 Hz), 5.69 (3H, m), 7.32 (1H,d, J = 2.9 Hz), 7.41 (2H, s), 7.67 (1H t-like), 8.27 (1H, d, J = 2.9 Hz), 8.60 (1H, d, J = 8.4 Hz), 9.06 (1H, d, J = 5.7 Hz), 9.68 (1H, brs), 13.45 (1H, brs).

IR (KBr) cm^{-1}: 3410, 2938, 1777, 1673, 1613, 1537, 1457, 1385, 1361, 1225, 1185, 1156, 1114, 1033.

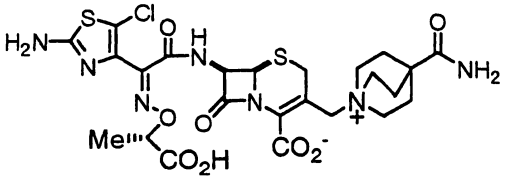
MS(ESI): 606^+ $(M+H)^+$.

元素分析 $C_{23}H_{20}ClN_7O_7S_2 \cdot 2.5H_2O$.

計算値： C,42.43; H,3.87; N,15.06; Cl,5.45; S,9.85 (%).

實驗値： C,42.44; H,3.69; N,14.90; Cl,5.24; S,9.94 (%).

實施例 42



^{1}H-NMR ($_{D2O}$) δ : 1.55 (3H, d, J = 7.1 Hz), 2.19 (6H, t-like), 3.39-3.56 (7H, m), 3.89 (1H, d, J = 16.8 Hz), 3.93 (1H, d, J = 13.9 Hz), 4.62 (1H, d, J = 13.9 Hz), 4.86 (1H, m), 5.36 (1H,d, J

= 5.0 Hz), 5.90 (1H, d, J = 5.6 Hz).

IR (KBr) cm^{-1}: 3371, 1779, 1671, 1614, 1538, 1466, 1389, 1343, 1236, 1183, 1099, 1070, 1035.

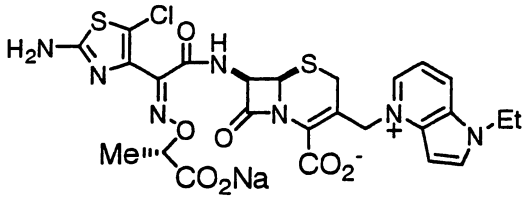
MS(ESI): $642^{+}(M+H)^{+}$.

元素分析 $C_{24}H_{28}ClN_7O_8S_2 \cdot 5.6H_2O$.

計算值： C,38.80; H,5.32; N,13.20; Cl,4.77; S,8.63 (%).

實驗值： C,38.57; H,4.76; N,13.24; Cl,4.56; S,8.32 (%).

實施例 43



^{1}H-NMR (d_6-DMSO) δ: 1.31 (3H, d, J = 7.1 Hz), 1.44 (3H, t, J = 7.2 Hz), 2.96 及 3.25 (2H, ABq, J = 17.1 Hz), 4.32 (1H, q, J = 7.1 Hz), 4.45 (2H, q, J = 7.2 Hz), 4.93 (1H, d, J = 5.1 Hz), 5.68 (2H, t-like), 5.75 (1H, dd, J = 5.1, 9.0 Hz), 7.31 (2H,s), 7.39 (1H, d, J = 3.5 Hz), 7.78 (1H, dd, J = 6.1, 8.1 Hz), 8.37 (1H, d, J = 3.5 Hz), 8.81 (1H, d, J = 8.1 Hz), 9.21 (1H, d, J = 6.1 Hz), 12.10 (1H, d, J = 9.0 Hz).

IR (KBr) cm^{-1}: 3409, 2982, 1772, 1604, 1539, 1496, 1460, 1394, 1362, 1317, 1289, 1230, 1185, 1153, 1106, 1033.

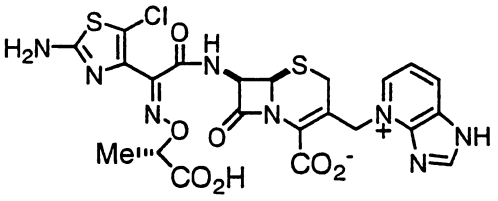
MS(ESI): $634^{+}(M+H)^{+}$.

元素分析 $C_{25}H_{23}ClN_7N_aO_7S_2 \cdot 3.7H_2O$.

計算值： C,41.55; H,4.24; N,13.57; Cl,4.91; S,8.87; Na,3.18 (%).

實驗值： C,41.48; H,3.96; N,13.60; Cl,4.84; S,8.87; Na, 3.26 (%).

實施例 44



^{1}H-NMR (d_6-DMSO) δ: 1.35 (3H, d, J = 6.9 Hz), 3.12 及 3.49 (2H, ABq, J = 17.9 Hz),

4.54 (1H, q, J = 6.9 Hz), 5.12 (1H, d, J = 4.8 Hz), 5.57 及 5.68 (2H, ABq, J = 14.1 Hz), 5.81 (1H, dd, J = 4.8, 8.9 Hz), 7.42 (2H,s), 7.52 (1H, t-like), 8.55 (2H, brs), 8.71 (1H, d, J = 6.6 Hz), 9.54 (1H, d, J = 8.9 Hz).

IR (KBr) cm^{-1}: 3416, 1777, 1674, 1608, 1538, 1449, 1387, 1311, 1230, 1187, 1158, 1102, 1072, 1032.

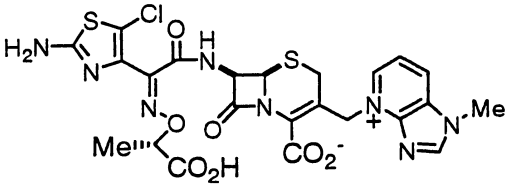
MS(ESI): 607^+ $(M+H)^+$.

元素分析 $C_{22}H_{19}ClN_8O_7S_2 \cdot 2.3H_2O$.

計算值： C,40.75; H,3.67; N,17.28; Cl,5.47; S,9.89 (%).

實驗值： C,40.72; H,3.55; N,17.35; Cl,5.51; S,9.90 (%).

實施例 45



^{1}H-NMR (d_6-DMSO) δ: 1.34 (3H, d, J = 6.9 Hz), 3.00 及 3.51 (2H, ABq, J = 17.6 Hz), 4.07 (3H, s), 4.53 (1H, q, J = 6.9 Hz), 5.02 (1H, d, J = 5.4 Hz), 5.68-5.74 (3H, m), 7.41 (2H,s), 7.97 (1H, t-like), 8.89 (1H, d, J = 7.8 Hz), 9.04 (1H, s), 9.66 (2H, m).

IR (KBr) cm^{-1}: 3416, 1778, 1674, 1615, 1538, 1497, 1464, 1362, 1316, 1266, 1235, 1188, 1155, 1100, 1063, 1033.

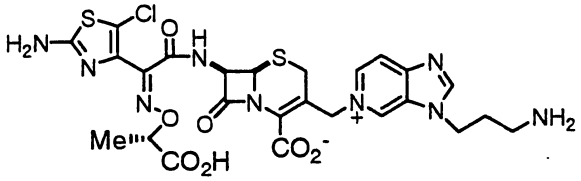
MS(ESI): 621^+ $(M+H)^+$.

元素分析 $C_{23}H_{21}ClN_8O_7S_2 \cdot 2.3H_2O$.

計算值： C,41.70; H,3.89; N,16.91; Cl,5.35; S,9.68 (%).

實驗值： C,41.67; H,3.85; N,16.90; Cl,5.27; S,9.60 (%).

實施例 46



^{1}H-NMR (D_2O) δ: 1.43 (3H, d, J = 7.2 Hz), 2.35 (2H, m), 3.12 (2H, t-like), 3.19 及 3.68

(2H, ABq, J = 17.7 Hz), 4.61 (3H, q-like), 5.28 (1H, d, J = 5.1 Hz), 5.33 及 5.67 (2H, ABq, J = 14.7 Hz), 5.86 (1H, d, J = 5.1 Hz), 8.21 (1H, d, J = 6.3 Hz), 8.70 (1H, d, J = 6.3 Hz), 8.90 (1H, brs), 9.71 (1H, s).

IR (KBr) cm^{-1}: 3410, 1773, 1606, 1538, 1478, 1450, 1384, 1315, 1284, 1214, 1170, 1117, 1083, 1033..

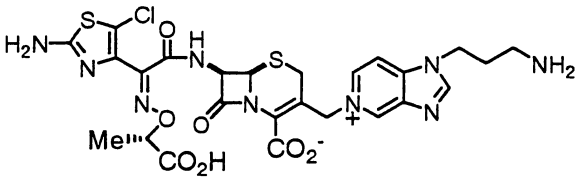
MS(ESI): 664^{+} $(M+H)^{+}$.

元素分析 $C_{25}H_{26}ClN_9O_7S_2 \cdot 3.6H_2O$.

計算值： C,41.19; H,4.59; N,17.29; Cl,4.86; S,8.80(%).

實驗值： C,41.25; H,4.49; N,17.07; Cl,4.87; S,8.50 (%).

實施例 47 7



^{1}H-NMR (D_2O) δ: 1.42 (3H, d, J = 6.9 Hz), 2.34 (2H, m), 3.10 (2H, t-like), 3.18 及 3.63 (2H, ABq, J = 17.9 Hz), 4.55-4.67 (3H, m), 5.27(1H, d, J = 5.0 Hz), 5.35 及 5.66 (2H, ABq, J = 14.3 Hz), 5.87 (1H, d, J = 5.0 Hz), 8.22 (1H, d, J = 6.9 Hz), 8.79 (2H, d,-like), 9.49 (1H, s).

IR (KBr) cm^{-1}: 3410, 1773, 1606, 1539, 1515, 1458, 1395, 1363, 1310, 1216, 1185, 1137, 1107, 1066, 1033.

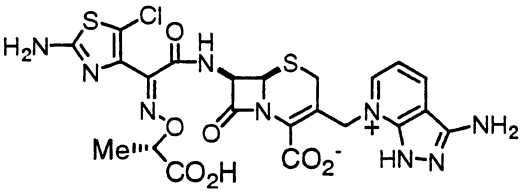
MS(ESI): 664^{+} $(M+H)^{+}$.

元素分析 $C_{25}H_{26}ClN_9O_7S_2 \cdot 3.2H_2O$.

計算值： C,41.60; H,4.52; N,17.47; Cl,4.91; S,8.89 (%).

實驗值： C,41.63; H,4.48; N,17.40; Cl,4.82; S,8.73 (%).

實施例 48 8



^{1}H-NMR (d_6-DMSO) δ: 1.34 (3H, d, J = 6.9 Hz), 2.84 及 3.51 (2H, ABq, J = 17.4 Hz), 4.51 (1H, q, J = 6.9 Hz), 5.11 (1H, d, J = 4.6 Hz), 5.14 及 5.54 (2H, ABq, J = 14.4 Hz), 5.72 (1H, dd, J = 4.6, 9.0 Hz), 6.59 (1H, brs), 7.34-7.40 (3H, m), 8.77 (2H, d,-like), 9.58 (1H, brs).

IR (KBr) cm^{-1}: 3414, 1774, 1638, 1574, 1538, 1446, 1391, 1367, 1334, 1227, 1182, 1078, 1036.

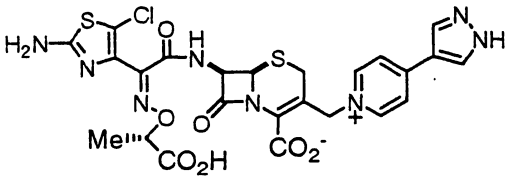
MS(ESI): 662^+ $(M+H)^+$.

元素分析 $C_{22}H_{20}ClN_9O_7S_2 \cdot 2.4H_2O$.

計算值： C,39.72; H,3.76; N,18.95; Cl,5.33; S,9.649 (%).

實驗值： C,39.77; H,3.69; N,19.04; Cl,5.27; S,9.49 (%).

實施例 49



^{1}H-NMR (d_6-DMSO) δ: 1.37 (3H, d, J = 7.0 Hz), 3.09 及 3.51 (2H, ABq, J = 17.6 Hz), 4.54 (1H, q, J = 7.0 Hz), 4.99 及 5.51 (2H, ABq, J = 12.8 Hz), 5.70 (1H, dd, J = 4.7, 8.7 Hz), 7.42 (2H, s), 8.30 (2H, d, J = 6.5 Hz), 8.59 (2H, brs), 9.58 (1H, d, J = 8.7 Hz), 13.7 (1H, brs).

IR (KBr) cm^{-1}: 3314, 3194, 1777, 1671, 1637, 1570, 1538, 1470, 1391, 1344, 1285, 1221, 1156, 1100, 1065, 1034.

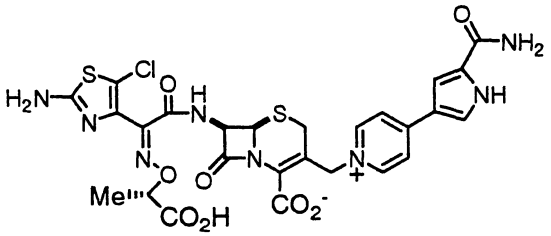
MS(ESI): 633^+ $(M+H)^+$.

元素分析 $C_{24}H_{21}ClN_8O_7S_2 \cdot 2.5H_2O$.

計算值： C,42.51; H,3.86; N,16.52; Cl,5.23; S,9.46 (%).

實驗值： C,42.44; H,3.67; N,16.68; Cl,5.36; S,9.36 (%).

實施例 50



^{1}H-NMR (d_6-DMSO) δ: 1.37 (3H, d, J = 7.1 Hz), 3.09 及 3.51 (2H, ABq, J = 17.4 Hz), 4.76 (1H, q, J = 7.1 Hz), 4.94 及 5.49 (2H, ABq, J = 12.5 Hz), 5.07 (1H, d, J = 4.7 Hz), 5.72 (1H, dd, J = 4.7, 8.6 Hz), 7.27 (1H, brs), 7.41 (2H, s), 7.62 (1H, brs), 7.94 (1H, brs), 8.06 (1H, brs), 8.18 (2H, d, J = 5.9 Hz), 9.16 (2H, d, J = 5.9 Hz), 9.81 (1H, brs), 12.5 (1H, brs).

IR (KBr) cm^{-1}: 3402, 1775, 1718, 1636, 1608, 1570, 1550, 1441, 1393, 1343, 1288, 1220, 1150, 1035.

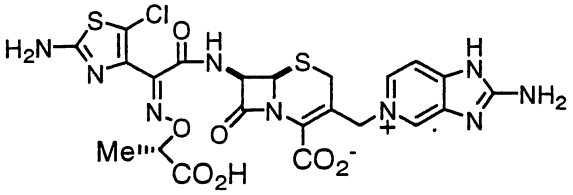
MS(ESI): 675$^+$ $(M+H)^+$.

元素分析 $C_{26}H_{23}ClN_8O_8S_2 \cdot 5.1H_2O$.

計算值： C,40.72; H,4.36; N,14.61; Cl,4.62; S,8.36 (%).

實驗值： C40 56; H,3.97; N,14.44; Cl,5.09; S,8.05(%).

實施例 51



^{1}H-NMR (d_6-DMSO) δ: 1.34 (3H, d, J = 7.0 Hz), 3.05 及 3.61 (2H, ABq, J = 17.9 Hz), 4.52 (1H, q, J = 7.0 Hz), 4.82 及 5.37 (2H, ABq, J = 14.4 Hz), 5.14 (1H, d, J = 5.0 Hz), 5.76 (1H, dd, J = 5.0, 8.9 Hz), 7.37 (2H, brs), 7.43 (1H, d, J = 6.9 Hz), 8.40 (2H, brs), 8.42 (1H, d, J = 6.9 Hz), 9.63 (2H, brs).

IR (KBr) cm^{-1}: 3336, 3192, 1774, 1662, 1617, 1573, 1539, 1489, 1393, 1332, 1246, 1188, 1153, 1119, 1066, 1034.

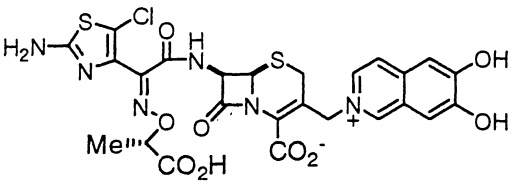
MS(ESI): 622$^+$ $(M+H)^+$.

元素分析 $C_{22}H_{20}ClN_9O_7S_2 \cdot 1.9H_2O$.

計算值： C,40.26; H,3.66; N,19.21; Cl,5.40; S,9.77 (%).

實驗值： C,40.48; H,3.69; N,19.26; Cl,5.10; S,9.48 (%).

實施例 52



^{1}H-NMR (d_6-DMSO) δ: 1.37 (3H, d, J = 7.0 Hz), 3.18 及 3.52 (2H, ABq, J = 18.0 Hz), 4.56 (1H, q, J = 7.0 Hz), 5.11 (2H. m), 5.48 (1H, q, J = 13.8 Hz), 5.81 (1H, q, J = 4.7, 8.8 Hz), 7.12 (1H, rs), 7.41 (2H, s), 7.53 (1H, s), 7.83 (1H, d, J = 6.0 Hz), 8.38 (1H, d, J = 6.0 Hz), 9.24 (1H, brs), 9.63 (1H, d, J = 8.8 Hz).

IR (KBr) cm^{-1}: 3420, 1778, 1672, 1623, 1535, 1480, 1445, 1395, 1308, 1184, 1154, 1131, 1065, 1035.

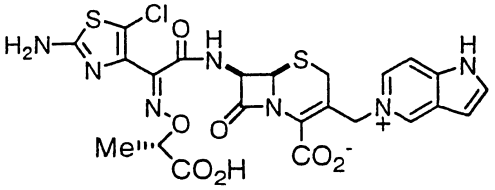
MS(ESI): 649^+ $(M+H)^+$.

元素分析 $C_{25}H_{21}ClN_6O_9S_2 \cdot 2.1H_2O$.

計算值： C,43.71; H,3.70; N,12.23; Cl,5.16; S,9.34 (%).

實驗值： C,44.06; H,3.69; N,12.31; Cl,5.00; S,9.94 (%).

實施例 533



^{1}H-NMR (d_6-DMSO) δ: 1.35 (3H, d, J = 7.0 Hz), 3.04 及 3.50 (2H, ABq, J = 17.7 Hz), 4.54 (1H, q, J = 7.0 Hz), 5.08 (1H, d, J = 5.1 Hz), 5.15 及 5.65 (2H, ABq, J = 13.7 Hz), 5.73 (1H, dd, J = 5.1, 8.6 Hz), 7.01 (1H, d, J = 3.3 Hz), 7.42 (2H, s), 7.94 (1H, d, J = 3.3 Hz), 8.03 (1H, d, J = 6.6 Hz), 8.88 (1H, d, J = 6.6 Hz), 9.71 (1H, brs), 13.4 (1H, brs).

IR (KBr) cm^{-1}: 3395, 3009, 2937, 1777, 1673, 1632, 1537, 1484, 1445, 1378, 1359, 1227, 1187, 1153, 1117, 1065, 1034.

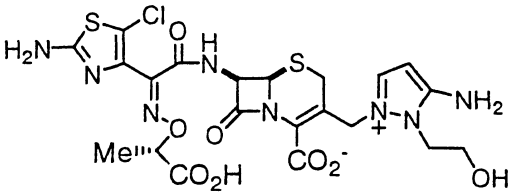
MS(ESI): 606^+ $(M+H)^+$.

元素分析 $C_{23}H_{20}ClN_7O_7S_2 \cdot 2.2H_2O$.

計算值： C,42.78; H,3.81; N,15.19; Cl,5.49; S,9.93 (%).

實驗值： C,42.87; H,3.81; N,15.20; Cl,5.30; S,9.86 (%).

實施例 54



^{1}H-NMR (d_6-DMSO) δ : 1.41 (3H, d, J = 7.0 Hz), 2.97 及 3.21 (2H, ABq, J = 17.6 Hz), 3.58 (2H, brs), 4.58 (1H, q, J = 7.0 Hz), 5.06 (1H, d, J = 4.9 Hz), 5.10 及 5.23 (2H, ABq, J = 15.9 Hz), 5.70 (1H, dd, J = 4.9, 8.6 Hz), 5.83 (1H, d, J = 3.0 Hz), 7.26 (2H, s), 7.43 (2H, s), 8.08 (1H, d, J = 3.0Hz), 9.75 (1H, brs).

IR (KBr) cm^{-1}: 3411, 2939, 1775, 1635, 1537, 1456, 1325, 1221, 1151, 1097, 1036.

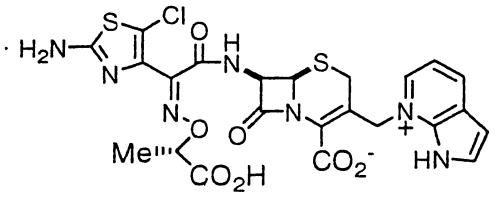
MS(ESI): 615^+ $(M+H)^+$.

元素分析 $C_{21}H_{23}ClN_8O_8S_2 \cdot 2.6H_2O$.

計算值： C,38.11; H,4.29; N,16.93; Cl,5.36; S,9.69 (%).

實驗值： C,38.04; H,3.93; N,16.67; Cl,5.49; S,9.68 (%).

實施例 555



^{1}H-NMR (d_6-DMSO) δ : 1.30 (3H, d, J = 7.0 Hz), 2.76 及 3.57 (2H, ABq, J = 18.0 Hz), 4.48 (1H, q, J = 7.0 Hz), 5.13 (1H, d, J = 4.9 Hz), 5.24 及 5.90 (2H, ABq, J = 14.3 Hz), 5.72 (1H, dd, J = 4.9, 8.4 Hz), 6.89 (1H, d, J = 3.3 Hz), 7.40 (2H, s), 7.58 (1H, dd, J = 6.0, 7.8 Hz), 7.92 (1H, d, J = 3.3 Hz), 8.71 (2H, m), 9.54 (1H, d, J = 8.4 Hz).

IR (KBr) cm^{-1}: 3413, 2934, 2718, 1777, 1675, 1616, 1537, 1480, 1461, 1362, 1230, 1189, 1112, 1034.

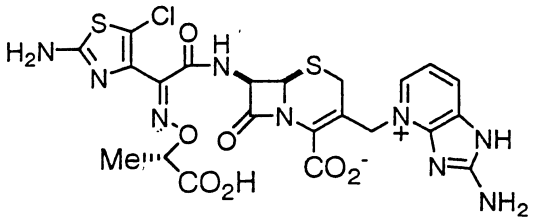
MS(ESI): 606^+ $(M+H)^+$.

元素分析 $C_{23}H_{20}ClN_7O_7S_2 \cdot 2.3H_2O$.

計算值： C,42.67; H,3.83; N,15.14; Cl,5.48; S,9.90 (%).

實驗值： C,42.65; H,3.82; N,15.18; Cl,5.40; S,9.74 (%).

実施例５６



^{1}H-NMR (d_6-DMSO) δ : 1.39 (3H, d, J = 7.1 Hz), 3.15 及 3.52 (2H, ABq, J = 17.7 Hz), 4.56 (1H, q, J = 7.1 Hz), 5.10 (1H, d, J = 4.9 Hz), 5.36 (2H, brs), 5.80 (1H, dd, J = 4.9, 8.6 Hz), 7.11 (1H, t, J = 7.2 Hz), 7.69 (1H, d, J = 7.2 Hz), 8.42 (3H, m), 9.84 (1H, brs).

IR (KBr) cm^{-1}: 3352, 3151, 2712, 1772, 1665, 1607, 1583, 1543, 1490, 1443, 1408, 1390, 1368, 1341, 1300, 1211, 1160, 1106, 1083, 1060, 1031.

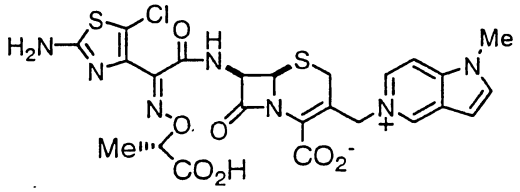
MS(ESI): 622$^+$ (M+H)$^+$.

元素分析　$C_{22}H_{20}ClN_9O_7S_2 \cdot 3.0H_2O$.

計算値：　C,39.08; H,3.88; N,18.65; Cl,5.24; S,9.49 (%).

實驗値：　C,39.26; H,3.83; N,18.75; Cl,5.33; S,9.19 (%).

實施例577



^{1}H-NMR (d_6-DMSO) δ : 1.34 (3H, d, J = 6.9 Hz), 2.97 及 3.48 (2H, ABq, J = 17.6 Hz), 3.98 (3H,s), 4.52 (1H, q, J = 6.9 Hz), 5.05-5.12 (2H, m), 5.63-5.72 (2H, m), 7.09 (1H, d, J = 3.1 Hz), 7.42 (2H, s), 7.94 (1H, d, J = 3.1 Hz), 8.17 (1H, d, J = 7.1 Hz), 9.49 (1H, d, J = 7.1 Hz), 9.64 (1H, brs), 9.7 (1H, brs).

IR (KBr) cm^{-1}: 3406, 3073, 2945, 1778, 1675, 1631, 1538, 1447, 1361, 1324, 1254, 1227, 1184, 1132, 1106, 1065, 1033.

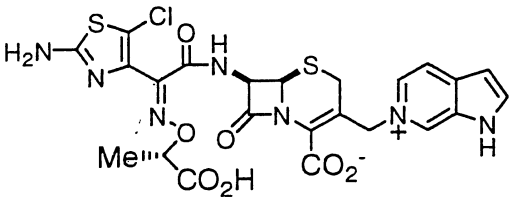
MS(FAB): 620 (M+H)$^+$.

元素分析　$C_{24}H_{22}ClN_7O_7S_2 \cdot 2.4H_2O$.

計算値：　C,43.46; H,4.07; N,14.78; Cl,5.34; S,9.67 (%).

實驗值： C,43.45; H,4.03; N,14.88; Cl,5.25; S,9.55 (%).

實施例 5 8



^{1}H-NMR (d_6-DMSO) δ: 1.35 (3H, d, J = 6.9 Hz), 3.04 及 3.56 (2H, ABq, J = 17.6 Hz), 4.53 (1H, q, J = 7.0 Hz), 5.09-5.15 (2H, m), 5.68-5.76 (2H, m), 6.92 (1H, d, J = 2.7 Hz), 7.40 (2H, s), 8.11 (1H, d, J = 6.9 Hz), 8.30 (1H, d, J = 2.7 Hz), 8.55 (1H, d, J = 6.9 Hz), 9.84 (2H, brs), 14.7 (1H, brs).

IR (KBr) cm^{-1}: 3326, 3195, 2938, 1777, 1674, 1612, 1537, 1461, 1375, 1312, 1234, 1187, 1145, 1065, 1034.

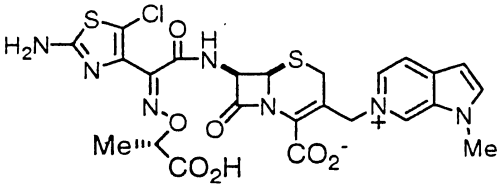
MS(ESI): 606 $(M+H)^+$.

元素分析 $C_{23}H_{20}ClN_7O_7S_2 \cdot 2.5H_2O$.

計算值： C,42.43; H,3.87; N,15.06 Cl,5.45; S,9.85 (%).

實驗值： C,42.46; H,3.74; N,15.01; Cl,5.33; S,9.93 (%).

實施例 59 9



^{1}H-NMR (d_6-DMSO) δ: 1.34 (3H, d, J = 7.0 Hz), 3.08 及 3.49 (2H, ABq, J = 17.6 Hz), 4.04 (3H, s), 4.52 (1H, q, J = 7.0 Hz), 5.05-5.12 (2H, m), 5.66-5.72 (2H, m), 6.92 (1H, d, J = 2.9 Hz), 7.42 (2H, brs), 8.14 (1H, d, J = 6.8 Hz), 8.28 (1H, d, J = 2.9 Hz), 8.97 (1H, d, J = 6.8 Hz), 9.64 (1H, brs), 9,80 (1H, brs).

IR (KBr) cm^{-1}: 3410, 1777, 1676, 1614, 1537, 1486, 1447, 1423, 1378, 1326, 1260, 1230, 1161, 1096, 1065, 1033.

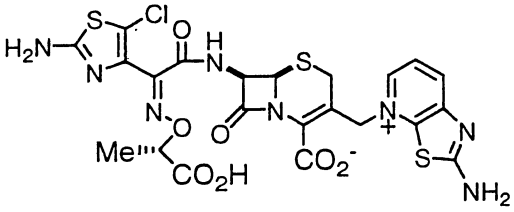
MS(ESI): 620 $(M+H)^+$.

元素分析 $C_{24}H_{22}ClN_7O_7S_2 \cdot 2.4H_2O$.

計算値： C,43.46; H,4.07; N,14.78; Cl,5.34; S,9.67 (%).

實驗値： C,43.47; H,3.97; N,14.79; Cl,5.21; S,9.59 (%).

實施例 6 0



^{1}H-NMR (d_6-DMSO) δ: 1.39 (3H, d, J = 7.1 Hz), 3.15 及 3.34 (2H, ABq, J = 17.6 Hz), 4.56 (1H, q, J = 7.1 Hz), 5.05 (1H, d, J = 4.8 Hz), 5.47 (1H, d, J = 14.1 Hz), 5.72-5.78 (2H,m), 7.41 (2H, brs), 7.84 (1H, dd, J = 5.9, 8.1 Hz), 8.21 (1H, d, J = 8.1 Hz), 8.83 (1H, d, J = 5.9 Hz), 8.89 (2H, brs), 9.87 (1H, brs).

IR (KBr) cm^{-1}: 3312, 3189, 1778, 1630, 1537, 1426, 1386, 1341, 1308, 1214, 1186, 1129, 1064, 1034.

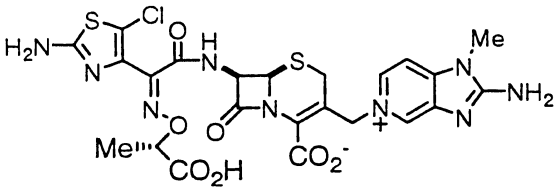
MS(FAB): 639$^+$ (M+H)$^+$.

元素分析 $C_{22}H_{19}ClN_8O_7S_3 \cdot 3.2H_2O$.

計算値： C,37.92; H,3.67; N,16.08; Cl,5.09; S,13.81(%).

實驗値： C,37.95; H,3.60; N,16.04; Cl,5.07; S,13.60 (%).

實施例 611



^{1}H-NMR (d_6-DMSO) δ: 1.35 (3H, d, J = 7.0 Hz), 2.90 及 3.46 (2H, ABq, J = 17.6 Hz), 3.66 (3H, s), 4.53 (1H, q, J = 7.0 Hz), 4.96 及 5.56 (2H, ABq, J = 13.7 Hz), 5.06 (1H, d, J = 4.9 Hz), 5.69 (1H, dd, J = 4.9, 8.9 Hz), 7.42 (2H, brs), 7.73 (2H, brs), 7.81 (1H, d, J = 6.6 Hz), 8.81 (1H, d, J = 6.6 Hz), 9.63 (1H, brs).

IR (KBr) cm^{-1}: 3346, 3180, 1775, 1664, 1613, 1567, 1538, 1508, 1448, 1389, 1352, 1311, 1271, 1179, 1100, 1065, 1034.

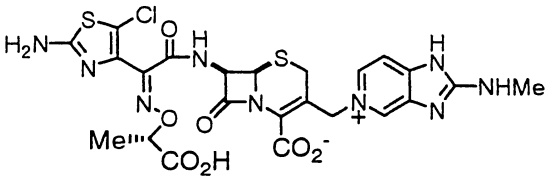
MS(FAB): 636⁺ (M+H)⁺.

元素分析　$C_{23}H_{22}ClN_9O_7S_2 \cdot 2.7H_2O$.

計算值：　C,40.35; H,4.03; N,18.41; Cl,5.18; S,9.37 (%).

實驗值：　C,40.32; H,3.90; N,18.39; Cl,5.14; S,9.35 (%).

實施例 62



^{1}H-NMR (d_6-DMSO) δ : 1.35 (3H, d, J = 7.0 Hz), 3.03-3.09 (4H, m), 3.61 (1H, d, J = 18.0 Hz), 4.52 (1H, q, J = 7.0 Hz), 4.83 及 5.40 (2H, ABq, J = 14.0 Hz), 5.14 (1H, d, J = 5.0 Hz), 5.77 (1H, dd, J = 5.0, 8.7 Hz), 7.36 (2H, brs), 7.48 (1H, d, J = 6.8 Hz), 8.43 (1H, d, J = 6.8 Hz), 9.33 (1H, brs), 9.59 (1H, brs), 9.70 (1H, brs).

IR (KBr) cm^{-1}: 3370, 1775, 1644, 1579, 1538, 1479, 1394, 1329, 1239, 1188, 1121, 1066, 1034.

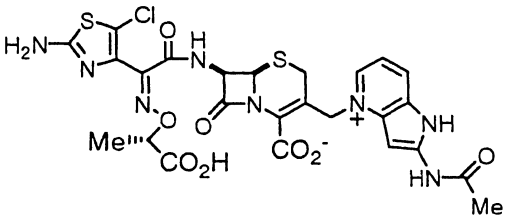
MS(FAB): 636⁺ (M+H)⁺.

元素分析　$C_{23}H_{22}ClN_9O_7S_2 \cdot 2.2H_2O$.

計算值：　C,40.88; H,3.94; N,18.66; Cl,5.25; S,9.49 (%).

實驗值：　C,41.07; H,4.21; N,18.30; Cl,4.86; S,8.86 (%).

實施例 63



^{1}H-NMR (d_6-DMSO) δ : 1.41 (3H, d, J = 7.0 Hz), 2.16 (3H, s), 3.10 (1H, d, J = 17.1 Hz), 4.59 (1H, q, J = 7.0 Hz), 5.08 (1H, d, J = 5.1 Hz), 5.51 (2H, brs); 5.76 (1H,dd, J = 5.1, 8.4 Hz), 6,87 (1H,s), 7.33 (1H, t-like), 7.39 (2H, brs), 8.01 (1H, brs), 8.59 (1H, d, J = 6.0 Hz), 9.70 (1H, brs), 12.7 (1H, brs).

IR (KBr) cm^{-1}: 3325, 1776, 1653, 1609, 1561, 1470, 1416, 1369, 1352, 1236, 1183, 1158, 1100, 1065, 1032.

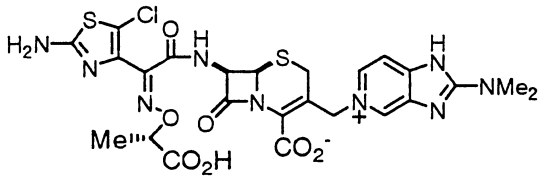
MS(FAB): 663^+ $(M+H)^+$.

元素分析　$C_{25}H_{23}ClN_8O_8S_2 \cdot 3.2H_2O$.

計算值：　C,41.66; H,4.11; N,15.55; Cl,4.92; S,8.90 (%).

實驗值：　C,41.79; H,4.14; N,15.37; Cl,4.82; S,8.75 (%).

實施例 64



^{1}H-NMR (d_6-DMSO) δ: 1.36 (3H, d, J = 7.1 Hz), 2.98 及 3.50 (2H, ABq, J = 17.3 Hz), 3.21 (6H,s), 4.54 (1H, q, J = 7.1 Hz), 5.00 及 5.48 (2H, ABq, J = 13.5 Hz), 5.16 (1H, d, J = 4.8 Hz), 5.72 (1H, dd, J = 4.8, 9.0 Hz), 7.39 (2H, brs), 7.49 (1H, d, J = 6.9 Hz), 8.44 (1H, d, J = 6.9 Hz), 9.09 (1H, brs), 9.85 (1H, brs).

IR (KBr) cm^{-1}: 3413, 2938, 1777, 1639, 1557, 1538, 1440, 1391, 1335, 1247, 1190, 1150, 1121, 1065, 1034.

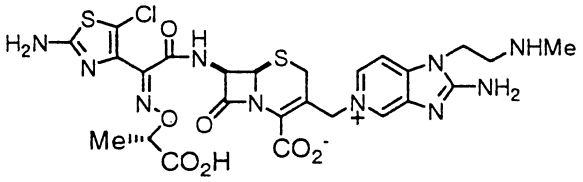
MS(FAB): 650^+ $(M+H)^+$.

元素分析　$C_{24}H_{24}ClN_9O_7S_2 \cdot 3.2H_2O$.

計算值：　C,40.73; H,4.33; N,17.81; Cl,5.01; S,9.06 (%).

實驗值：　C,40.73; H,4.24; N,17.75; Cl,5.08; S,9.10 (%).

實施例 65



^{1}H-NMR (D_2O + DCl) δ: 1.55 (3H, d, J = 7.1 Hz), 2.82 (3H, s), 3.36 及 3.75 (2H, ABq, J = 18.5 Hz), 4.72 (2H, t, J = 6.5 Hz), 4.99 (1H, q, J = 7.1 Hz), 5.36 (1H, d, J = 4.8 Hz), 5.40 及 5.86 (2H, ABq, J = 14.9 Hz), 5.94 (1H, d, J = 4.8 Hz), 8.09 (1H, d, J = 6.8 Hz), 8.83 (1H, d, J

= 6.8 Hz), 9.06 (1H, s).

IR (KBr) cm^{-1}: 3370, 3174, 1771, 1667, 1606, 1541, 1504, 1449, 1399, 1360, 1312, 1281, 1184, 1113, 1067, 1035.

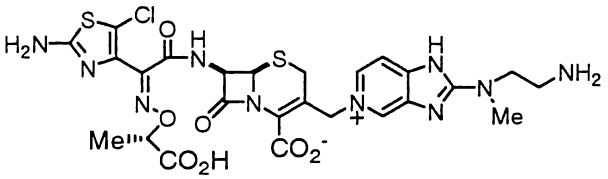
MS(FAB): 679^+ $(M+H)^+$.

元素分析　$C_{25}H_{27}ClN_{10}O_7S_2 \cdot 4.0H_2O$.

計算値：　C,39.97; H,4.70; N,18.65; Cl,4.72; S,8.54 (%).

實驗値：　C,40.02; H,4.64; N,18.79; Cl,4.60; S,8.31 (%).

實施例 66



^{1}H-NMR (D_2O + DCl)　δ : 1.55 (3H, d, J = 7.1 Hz), 3.29- 3.45 (6H, m), 3.69 (1H, d, J = 18.3 Hz), 4.04 (2H, t, J = 6.2 Hz), 4.98 (1H, q, J = 7.1 Hz), 5.28-5.35 (2H, m), 5.70 (1H, s), 5.93 (1H, d, J = 4.8 Hz), 7.68 (1H, d, J = 4.6 Hz), 8.45 (1H, dd, J = 1.2, 4.6 Hz), 8.73 (1H, d, J = 1.2 Hz).

IR (KBr) cm^{-1}: 3397, 1772, 1623, 1578, 1540, 1508, 1446, 1397, 1330, 1247, 1190, 1151, 1121, 1066, 1034.

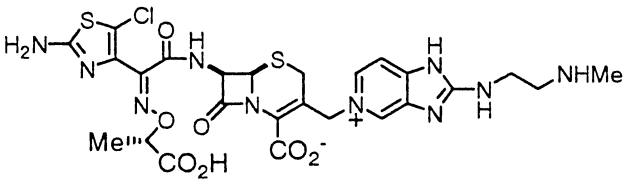
MS(FAB): 679^+ $(M+H)^+$.

元素分析　$C_{25}H_{27}ClN_{10}O_7S_2 \cdot 4.3H_2O$.

計算値：　C,39.69; H,4.74; N,18.51; Cl,4.69; S,8.48 (%).

實驗値：　C,39.77; H,4.70; N,18.43; Cl,4.59; S,8.48 (%).

實施例 67



^{1}H-NMR (D_2O + DCl)　δ : 1.54 (3H, d, J = 7.1 Hz), 2.80 (3H, s), 3.29 及 3.66 (2H, ABq, J = 18.3 Hz), 3.41 (2H, t, J = 5.8 Hz), 3.89 (2H, t, J = 5.8 Hz), 4.96 (1H, q, J = 7.1 Hz), 5.27-5.33

(2H, m), 5.61 (1H, d, J = 14.8 Hz), 5.93 (1H, d, J = 4.8 Hz), 7.67 (1H, d, J = 6.8 Hz), 8.43 (1H, d, J = 6.8 Hz), 8.71 (1H,s).

IR (KBr) cm^{-1}: 3388, 1773, 1626, 1540, 1477, 1395, 1361, 1238, 1186, 1152, 1120, 1065, 1035.

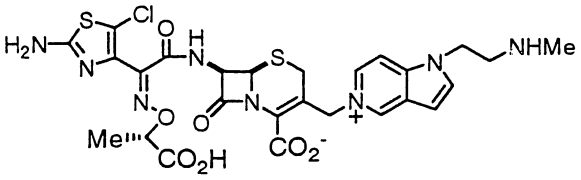
MS(FAB): 679^+ $(M+H)^+$.

元素分析　$C_{25}H_{27}ClN_{10}O_7S_2 \cdot 3.7H_2O$.

計算值：　C,40.26; H,4.65; N,18.78; Cl,4.75; S,8.60 (%).

實驗值：　C,40.23; H,4.60; N,18.76; Cl,4.79; S,8.51 (%).

實施例 68



^{1}H-NMR (D_2O) δ : 1.42 (3H, d, J = 6.9 Hz), 2.74 (3H, s), 3.17 (1H, d, J = 18.0 Hz), 3.56-3.61 (3H, m), 4.61-4.76 (3H, m), 5.23-5.31 (2H, m), 5.54 (1H, d, J = 14.7 Hz), 5.56 (1H, d, J = 4.5 Hz), 7.12 (1H, d, J = 3.4 Hz), 7.80 (1H, d, J = 3.4 Hz), 7.99 (1H, d, J = 7.0 Hz), 8.52 (1H, d, J = 7.0 Hz), 9.086 (1H, s).

IR (KBr) cm^{-1}: 3398, 2452, 1773, 1604, 1540, 1514, 1494, 1448, 1395, 1363, 1286, 1223, 1187, 1119, 1065, 1034.

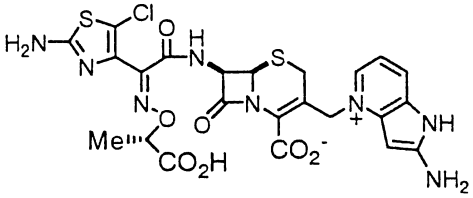
MS(FAB): 663^+ $(M+H)^+$.

元素分析　$C_{26}H_{27}ClN_8O_7S_2 \cdot 4.0H_2O$.

計算值：　C,42.48; H,4.80; N,15.24; Cl,4.82; S,8.72 (%).

實驗值：　C,42.45; H,4.57; N,15.20; Cl,4.86; S,8.70 (%).

實施例 69



^{1}H-NMR (d_6-DMSO) δ : 1.39 (3H, d, J = 7.0 Hz), 3.02 及 3.31 (2H ABq, J = 17.7 Hz), 4.57

(1H, q, J = 7.0 Hz), 5.05 (1H, d, J = 4.9 Hz), 5.22 及 5.35 (2H, ABq, J = 14.4 Hz), 5.75 (1H, dd, J = 4.9, 9.0 Hz), 5.87 (1H, s), 6,84 (1H, t-like), 7.39 (2H, brs), 7.49 (1H, d, J = 7.5 Hz), 7.82 (1H, brs), 8.09 (1H, d, J = 6.6 Hz), 9.86 (1H, brs), 12.9 (1H, brs).

IR (KBr) cm^{-1}: 3338, 3198, 1773, 1640, 1581, 1540, 1497, 1427, 1364, 1329, 1285, 1239, 1192, 1159, 1099, 1034.

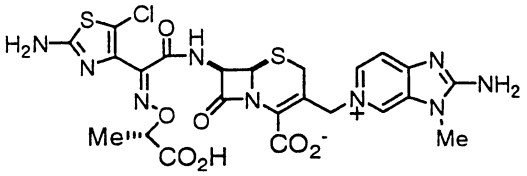
MS(FAB): 621^+ $(M+H)^+$.

元素分析 $C_{23}H_{21}ClN_8O_7S_2 \cdot 2.9H_2O$.

計算值： C,41.03; H,4.01; N,16.64; Cl,5.27; S,9.52 (%).

實驗值： C,41.01; H,3.90; N,16.64; Cl,5.37; S,9.49 (%).

實施例 70



^{1}H-NMR (d_6-DMSO) δ: 1.36 (3H, d, J = 7.1 Hz), 3.01 及 3.47 (2H, ABq, J = 17.7 Hz), 3.60 (3H, s), 4.53 (1H, q, J = 7.1 Hz), 4.90 及 5.50 (2H, ABq, J = 13.7 Hz), 5.04 (1H, d, J = 4.9 Hz), 5.69 (1H, dd, J = 4.9, 9.0 Hz), 7.40 (2H, brs), 7.51 (1H, d, J = 6.8 Hz), 8.14 (2H, brs), 8.82 (1H, d, J = 6.8 Hz), 9.13 (1H, brs), 9.68 (1H, brs).

IR (KBr) cm^{-1}: 3354, 3190, 1774, 1658, 1557, 1485, 1467, 1389, 1347, 1231, 1162, 1094, 1066, 1035.

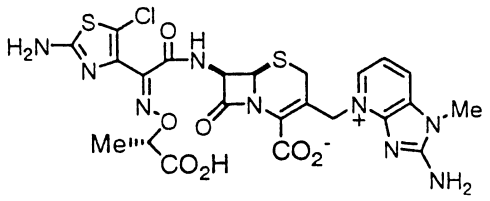
MS(FAB): 636^+ $(M+H)^+$.

元素分析 $C_{23}H_{22}ClN_9O_7S_2 \cdot 3.2H_2O$.

計算值： C,39.82; H,4.13; N,18.17; Cl,5.11; S,9.24 (%).

實驗值： C,39.85; H,4.07; N,18.08; Cl,5.02; S,9.12 (%).

實施例 71



^{1}H-NMR (D_2O + DCl) δ : 1.54 (3H, d, J = 7.2 Hz), 3.33 及 3.59 (2H ABq, J = 18.5 Hz), 3.67 (3H, s), 4.99 (1H, q, J = 7.2 Hz), 5.29 (1H, d, J = 4.8 Hz), 5.22 及 5.65 (2H, ABq, J = 15.2 Hz), 5.91 (1H, d, J = 4.8 Hz), 7.33 (1H, dd, J = 6.5, 7.8 Hz), 7.91 (1H, d, J = 7.8 Hz), 8.10 (1H, d, J = 6.5 Hz).

IR (KBr) cm^{-1}: 3455, 3351, 3288, 3041, 2949, 2899, 1746, 1699, 1671, 1651, 1625, 1606, 1579, 1533, 1494, 1462, 1447, 1422, 1404, 1364, 1354, 1303, 1275, 1254, 1227, 1209, 1189, 1173, 1155, 1140, 1091, 1076, 1064, 1026.

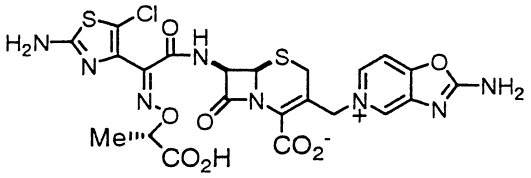
MS(FAB): 636^+ $(M+H)^+$.

元素分析 $C_{23}H_{22}ClN_9O_7S_2 \cdot 2.5H_2O$.

計算值： C,42.82; H,3.59; N,19.54; Cl,5.50; S,9.94 (%).

實驗值： C,42.84; H,3.55; N,19.51; Cl,5.43; S,10.00 (%).

實施例 72



^{1}H-NMR (d_6-DMSO) δ : 1.37 (3H, d, J = 7.1 Hz), 3.00 及 3.49 (2H, ABq, J = 17.7 Hz), 4.54 (1H, q, J = 7.1 Hz), 5.02 及 5.63 (2H, ABq, J = 13.7 Hz), 5.07 (1H, d, J = 5.0 Hz), 5.72 (1H, dd, J = 5.0, 8.7 Hz), 7.41 (2H, brs), 8.12 (1H, d, J = 7.1 Hz), 8.72 (2H, brs), 9.10 (1H, d, J = 7.1 Hz), 9.45 (1H, brs), 9.55 (1H, d, J = 8.7 Hz).

IR (KBr) cm^{-1}: 3385, 1776, 1692, 1617, 1538, 1492, 1363, 1287, 1223, 1188, 1150, 1103, 1066, 1036.

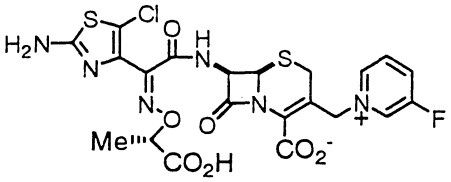
MS(FAB): 623^+ $(M+H)^+$.

元素分析 $C_{22}H_{19}ClN_8O_8S_2 \cdot 2.9H_2O$.

計算值： C,39.13; H,3.70; N,16.59; Cl,5.25; S,9.50 (%).

實驗值： C,39.04; H,3.55; N,16.69; Cl,5.12; S,9.52 (%).

實施例 73



^{1}H-NMR (d_6-DMSO) δ : 1.38 (3H, d, J = 7.0 Hz), 3.15 及 3.50 (2H, ABq, J = 17.6 Hz), 4.55 (1H, q, J = 7.0 Hz), 5.07 (1H, d, J = 5.1 Hz), 5.11 (1H, d, J = 13.2 Hz), 5.65-5.74 (2H, m), 7.41 (2H, brs), 8.24-8.31 (1H, m), 8.62-8.68 (1H, m), 9.46 (1H, d, J = 6.0 Hz), 9.52 (1H, d, J = 8.7 Hz), 9.89 (1H, brs).

IR (KBr) cm^{-1}: 3411, 3068, 2943, 1778, 1673, 1616, 1538, 1503, 1446, 1390, 1345, 1275, 1189, 1137, 1097, 1065, 1035.

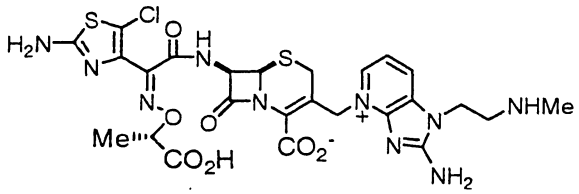
MS(FAB): 585$^+$ (M+H)$^+$.

元素分析 $C_{21}H_{18}ClFN_6O_7S_2 \cdot 2.9H_2O$.

計算値： C,39.58; H,3.76; N,13.19; Cl,5.56; S,10.06 (%).

實驗値： C,39.52; H,3.59; N,13.24; Cl,5.65; S,10.25 (%).

實施例 74



^{1}H-NMR (D_2O + DCl) δ : 1.54 (3H, d, J = 7.1 Hz), 2.78 (3H, s), 3.37 (1H, d, J = 18.3 Hz), 3.54-3.62 (3H, m), 4.57 (2H, t, J = 6.5 Hz), 4.98 (1H, q, J = 7.1 Hz), 5.27 (1H, d, J = 4.8 Hz), 5.49 及 5.71 (2H, ABq, J = 15.2 Hz), 5.91 (1H, d, J = 4.8 Hz), 7.34 (1H,t-like), 8.00 (1H, d, J = 7.8 Hz), 8.17 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}: 3398, 2451, 1771, 1666, 1603, 1562, 1493, 1396, 1362, 1315, 1387, 1224, 1165, 1090, 1034.

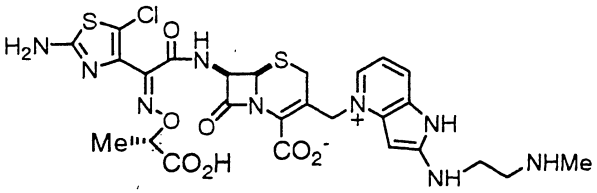
MS(FAB): 679$^+$ (M+H)$^+$.

元素分析 $C_{25}H_{27}ClN_{10}O_7S_2 \cdot 3.6H_2O$.

計算値： C,40.36; H,4.63; N,18.83; Cl,4.77; S,8.62 (%).

實驗値： C,40.32; H,4.68; N,18.84; Cl,4.87; S,8.77 (%).

實施例 755



^{1}H-NMR (D_2O + DCl) δ : 1.54 (3H, d, J = 7.1 Hz), 2.64 (3H, s), 3.25 及 3.45 (2H ABq, J = 18.3 Hz), 3.38 (2H, t, J = 5.9 Hz), 3.76 (2H, t, J = 5.9 Hz), 4.98 (1H, q, J = 7.1 Hz), 5.26 (1H, d, J = 4.8 Hz), 5.39 及 5.48 (2H, ABq, J = 15.5 Hz), 5.89 (1H, d, J = 4.8 Hz), 7.10 (1H, t-like), 7.73 (1H, d, J = 7.8 Hz), 7.94 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}: 3389, 1771, 1590, 1540, 1428, 1395, 1360, 1317, 1284, 1192, 1158, 1113, 1058, 1033.

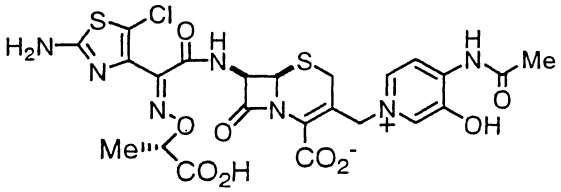
MS(FAB): 678^+ $(M+H)^+$.

元素分析 $C_{26}H_{28}ClN_9O_7S_2 \cdot 3.3H_2O$.

計算值： C,42.34; H,4.73; N,17.09; Cl,4.81; S,8.69 (%).

實驗值： C,42.11; H,4.67; N,17.00; Cl,4.94; S,9.09 (%).

實施例 76 6



^{1}H-NMR (d_6-DMSO) δ : 1.40 (3H, d, J = 7.1 Hz), 2.26 (3H,s), 3.12 及 3.45 (2H, ABq, J = 17.7 Hz), 4.59 (1H, q, J = 7.1 Hz), 5.20 (1H, d, J = 4.9 Hz), 5.78 (1H, dd, J = 4.9, 9.2 Hz),.7.41 (2H, brs), 8.12 (1H, d, J = 6.3 Hz), 8.39 (1H, brs), 8.47 (1H, d, J = 6.3 Hz), 9.60 (1H, d, J = 9.2 Hz), 10.05 (1H, brs).

IR (KBr) cm^{-1}: 3330, 1777, 1674, 1623, 1529, 1475, 1379, 1314, 1230, 1141, 1102, 1066, 1036.

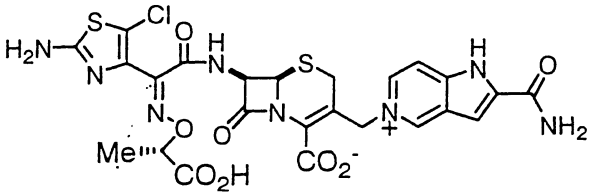
MS(ESI): 640^+ $(M+H)^+$.

元素分析 $C_{23}H_{22}ClN_7O_9S_2 \cdot 2.8H_2O$.

計算值： C,40.01; H,4.03; N,14.20; Cl,5.13; S,9.29 (%).

實驗值： C,39.92; H,3.90; N,14.32; Cl,5.27; S,9.31 (%).

實施例 77



^{1}H-NMR (d_6-DMSO) δ : 1.35 (3H, d, J = 6.9 Hz), 3.05 及 3.48 (2H, ABq, J = 17.6 Hz), 4.53 (1H, q, J = 6.9 Hz), 5.06 (1H, d, J = 4.8 Hz), 5.13 (1H, d, J = 13.8 Hz), 5.64-5.73 (2H, m), 7.40 (2H, brs), 7.66 (1H, s), 7.87 (1H, brs), 7.94 (1H, d, J = 6.9 Hz), 8.51 (1H, brs), 8.97 (1H, d, J = 6.9 Hz), 9.62 (1H, brs), 9.81 (1H, brs).

IR (KBr) cm^{-1}: 3327, 3195, 1775, 1677, 1613, 1540, 1375, 1335, 1240, 1182, 1152, 1116, 1066, 1036.

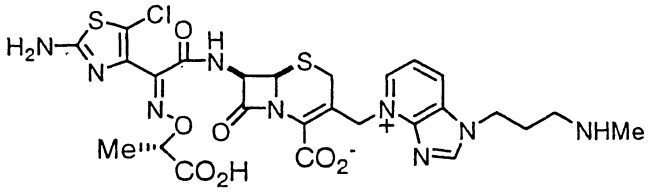
MS(ESI): 649$^+$ (M+H)$^+$.

元素分析 $C_{24}H_{21}ClN_8O_8S_2 \cdot 2.4H_2O$.

計算值： C,41.64; H,3.76; N,16.19; Cl,5.12; S,9.26 (%).

實驗值： C,41.70; H,3.71; N,16.24; Cl,5.00; S,9.063 (%).

實施例 78



^{1}H-NMR (D_2O) δ : 1.43 (3H, d, J = 7.1 Hz), 2.39 (2H, quint. J = 7.8 Hz), 2.72 (3H, s), 3.15 (2H, t, J = 7.8 Hz), 3.26 及 3.62 (2H, ABq, J = 18.0 Hz), 4.59-4.69 (3H, m), 5.23 (1H, d, J = 4.8 Hz), 5.62 (1H, d, J = 14.7 Hz), 5.70-5.75 (2H, m), 7.89 (1H,dd, J = 6.3, 8.3 Hz), 8.78 (1H, d, J = 8.3 Hz), 8.86 (1H, brs), 8.88 (1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}: 3397, 2464, 1773, 1602, 1541, 1490, 1463, 1389, 1313, 1287, 1237, 1187, 1159, 1115, 1064, 1034.

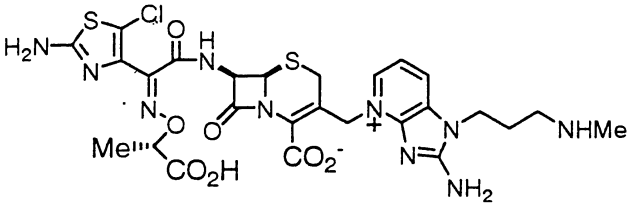
MS(ESI): 678$^+$ (M+H)$^+$.

元素分析 $C_{26}H_{28}ClN_9O_7S_2 \cdot 3.7H_2O$.

計算値： C,41.93; H,4.79; N,16.93; Cl,4.76; S,8.61 (%).

實驗値： C,41.93; H,4.74; N,16.89; Cl,4.53; S,8.58 (%).

實施例 79



^{1}H-NMR (D_2O) δ : 1.44 (3H, d, J = 7.0 Hz), 2.20 (2H, m), 2.70 (3H, s), 3.12 (2H, m), 3.24 及 3.50 (2H, ABq, J = 17.9 Hz), 4.22 (2H, t, J = 7.1 Hz), 4.55 (1H, q, J = 7.0 Hz), 5.18 (1H, d, J = 4.8 Hz), 5.25 及 5.56 (2H, ABq, J = 14.7 Hz), 5.84 (1H, d, J = 4.8 Hz), 7.30 (1H, t-like), 7.89 (1H, d, J = 7.8Hz), 8.12 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}: 3363, 3181, 1772, 1651, 1600, 1565, 1494, 1394, 1364, 1315, 1288, 1223, 1163, 1091, 1034.

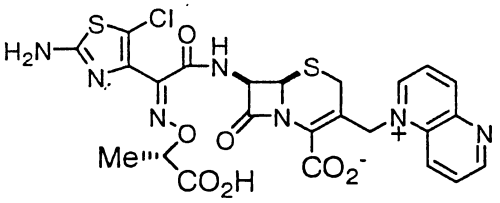
MS(ESI): 693$^+$ (M+H)$^+$.

元素分析 $C_{26}H_{29}ClN_{10}O_7S_2 \cdot 2.9H_2O$.

計算値： C,41.89; H,4.71; N,18.79; Cl,4.76; S,8.60 (%).

實驗値： C,41.93; H,4.73; N,18.81; Cl,4.51; S,8.51 (%).

實施例 80



^{1}H-NMR (D_2O + DCl) δ : 1.55 (3H, d, J = 7.1 Hz), 3.35 及 3.63 (2H ABq, J = 18.9 Hz), 5.39 (1H, d, J = 5.1 Hz), 5.98 (1H, d, J = 5.1 Hz), 6.03 及 6.24 (2H, ABq, J = 15.6 Hz), 8.40 (1H, dd, J = 5.7, 8.7 Hz), 9.04 (1H, d, J = 9.3 Hz), 9.29 (1H, d, J = 8.7 Hz), 9.17-9.20 (2H, m).

IR (KBr) cm^{-1}: 3411, 3197, 1778, 1675, 1617, 1538, 1521, 1456, 1376, 1339, 1285, 1230, 1189, 1152, 1098, 1066, 1035.

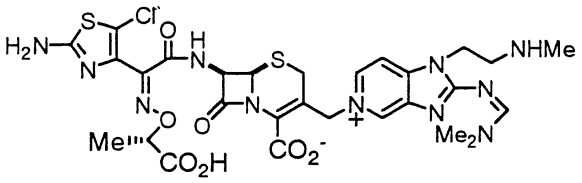
MS(ESI): 618$^+$ (M+H)$^+$.

元素分析 $C_{24}H_{20}ClN_7O_7S_2 \cdot 3.0H_2O$.

計算値： C,42.89; H,3.90; N,14.59; Cl,5.28; S,9.54 (%).

實驗値： C,42.91; H,3.97; N,12.66; Cl,5.18; S,9.51 (%).

實施例 81



^{1}H-NMR (D_2O + DCl) δ : 1.55 (3H, d, J = 7.2 Hz), 2.80 (3H, s), 3.38 及 3.77 (2H, ABq, J = 18.9 Hz), 3.38 (3H, s), 3.45 (3H, s), 3.64 (2H, t, J = 5.7 Hz), 4.76 (2H, t, J = 5.7 Hz), 4.99 (1H, q, J = 7.2 Hz), 5.37 (1H, d, J = 4.8 Hz), 5.42 及 5.88 (2H, ABq, J = 14.6 Hz), 5.95 (1H, d, J = 4.8 Hz), 8.13 (1H, d, J = 7.0 Hz), 8.68 (1H, brs), 8.84 (1H, dd, J = 1.2, 7.0 Hz), 9.14 (1H, d, J = 1.2 Hz).

IR (KBr) cm^{-1}: 3406, 1773, 1632, 1535, 1497, 1421, 1389, 1352, 1308, 1237, 1183, 1114, 1065, 1034.

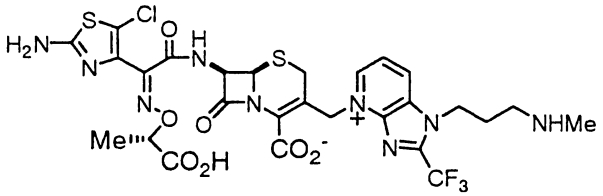
MS(FAB): 734$^+$ $(M+H)^+$.

元素分析 $C_{28}H_{32}ClN_{11}O_7S_2 \cdot 5.5H_2O$.

計算値： C,40.36; H,5.20; N,18.49; Cl,4.25; S,7.70 (%).

實驗値： C,40.38; H,5.03; N,18.36; Cl,4.52; S,7.89 (%).

實施例 82 2



^{1}H-NMR (D_2O + DCl) δ : 1.44 (3H, d, J = 6.9 Hz), 2.39 (2H, m), 2.73 (3H, s), 3.23 (2H, m), 3.30 及 3.68 (2H, ABq, J = 18.0 Hz), 4.59-4.69 (3H, m), 5.24 (1H, d, J = 5.0 Hz), 5.67 及 5.93 (2H, ABq, J = 14.7 Hz), 5.88 (1H, d, J = 5.0 Hz), 8.09 (1H,dd, J = 8.2, 6.1 Hz), 8.99 (1H, d, J = 8.2 Hz), 9.12 (1H, d, J = 6.1 Hz).

IR (KBr) cm^{-1}: 3403, 2467, 1776, 1604, 1540, 1482, 1458, 1437, 1394, 1352, 1317, 1269, 1195, 1155, 1121, 1096, 1065, 1034.

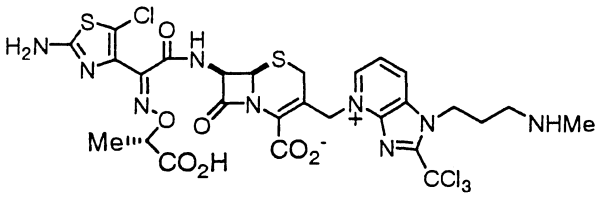
MS(FAB): 7462^{+} $(M+H)^{+}$.

元素分析　$C_{27}H_{27}ClF_3N_9O_7S_2 \cdot 3.7H_2O$.

計算値：　C,39.90; H,4.27; N,15.51; Cl,4.36; S,7.89 (%).

實驗値：　C,39.98; H,4.33; N,15.51; Cl,4.12; S,7.73 (%).

實施例 833



^{1}H-NMR (D_2O + DCl)　δ : 1.56 (3H, d, J = 6.9 Hz), 2.50 (2H, m), 2.77 (3H, s), 3.33 (2H, m), 3.59 及 3.72 (2H, ABq, J = 18.3 Hz), 4.93-5.04 (3H, m), 5.27 (1H, d, J = 5.1 Hz), 5.77 及 6.28 (2H, ABq, J = 14.9 Hz), 5.92 (1H, d, J = 5.1 Hz), 8.05 (1H,dd, J = 8.4, 6.3 Hz), 8.99 (1H, d, J = 8.4 Hz), 9.03(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}: 3400, 1776, 1604, 1539, 1450, 1392, 1350, 1321, 1287, 1224, 1159, 1063, 1033.

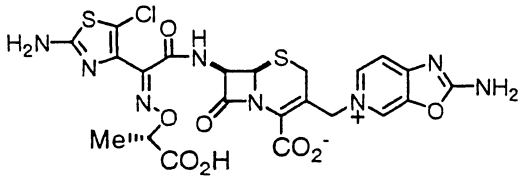
MS(FAB): 794^{+} $(M+H)^{+}$.

元素分析　$C_{27}H_{27}Cl_4N_9O_7S_2 \cdot 3.3H_2O$.

計算値：　C,37.93; H,3.96; N,14.74; Cl,16.59; S,7.50 (%).

實驗値：　C,38.26; H,4.00; N,14.96; Cl,15.25; S,7.46 (%).

實施例 844



^{1}H-NMR (d_6-DMSO)　δ : 1.37 (3H, d, J = 7.1 Hz), 3.02 及 3.48 (2H, ABq, J = 17.9 Hz), 4.54 (1H, q, J = 7.1 Hz), 4.90 及 5.50 (2H, ABq, J = 13.5 Hz), 5.05 (1H, d, J = 4.8 Hz), 5.70 (1H, dd, J = 4.8, 8.7 Hz), 7.41 (2H, brs), 7.69 (1H, d, J = 6.8 Hz), 9.01 (1H, d, J = 6.8 Hz), 9.33 (2H, brs), 9.58 (2H, brs).

IR (KBr) cm^{-1}: 3393, 1776, 1687, 1615, 1559, 1513, 1484, 1377, 1326, 1284, 1213, 1188,

1154, 1106, 1066, 1034.

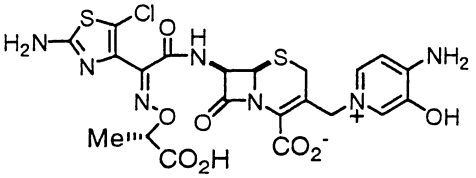
MS(FAB): 623^+ $(M+H)^+$.

元素分析　$C_{22}H_{19}ClN_8O_8S_2 \cdot 2.7H_2O$.

計算值：　C,39.34; H,3.66; N,16.68; Cl,5.28; S,9.55 (%).

實驗值：　C,39.35; H,3.67; N,16.61; Cl,5.26; S,9.48 (%).

實施例 85



^{1}H-NMR (d_6-DMSO)　δ : 1.39 (3H, d, J = 6.9 Hz), 2.95 及 3.42 (2H ABq, J = 17.4 Hz), 4.55 (1H, q, J = 6.9 Hz), 4.73 及 5.21 (2H, ABq, J = 13.8 Hz), 5.13 (1H, d, J = 4.8 Hz), 5.71 (1H, dd, J = 4.8, 8.7 Hz), 6.73 (1H, d, J = 6.9 Hz), 7.40 (2H, brs), 7.99 (1H, d, J = 6.9 Hz), 8.27 (1H, brs), 9.79 (1H, brs).

IR (KBr) cm^{-1}: 3343, 3202, 1776, 1644, 1546, 1446, 1370, 1309, 1258, 1179, 1147, 1065, 1036.

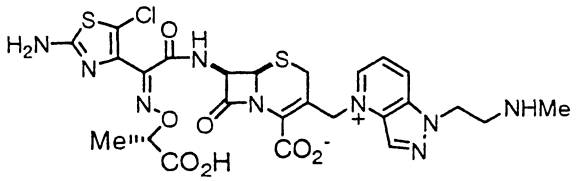
MS(FAB): 598^+ $(M+H)^+$.

元素分析　$C_{21}H_{20}ClN_7O_7S_2 \cdot 2.6H_2O$.

計算值：　C,39.11; H,3.949; N,15.20; Cl,5.50; S,9.94 (%).

實驗值：　C,39.18; H,3.74; N,15.14; Cl,5.38; S,9.82 (%).

實施例 86



^{1}H-NMR (D_2O + DCl)　δ : 1.44 (3H, d, J = 7.1 Hz), 2.80 (3H, s), 3.20 及 3.53 (2H, ABq, J = 17.9 Hz), 3.75 (2H, t, J = 5.5 Hz), 4.66 (1H, q, J = 7.1 Hz), 5.03 (2H, t, J = 5.5 Hz), 5.23 (1H, d, J = 5.0 Hz), 5.79 (2H, s), 5.88 (1H, d, J = 5.0 Hz), 8.07 (1H,dd, J = 8.7, 5.8 Hz), 8.82 (1H, s), 8.96 (1H, d, J = 8.7 Hz), 9.05 (1H, d, J = 5.8 Hz).

IR (KBr) cm^{-1}: 3408, 1773, 1604, 1540, 1476, 1447, 1394, 1352, 1316, 1289, 1222, 1187, 1159, 1080, 1034.

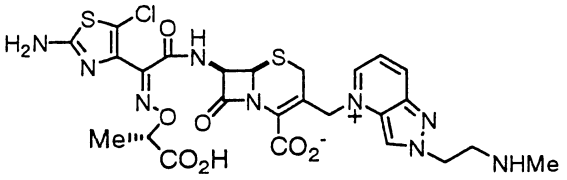
MS(FAB): 664^+ $(M+H)^+$.

元素分析　$C_{25}26_9ClN_9O_7S_2 \cdot 3.0H_2O$.

計算値：　C,41.81; H,4.49; N,17.55; Cl,4.94; S,8.93 (%).

實驗値：　C,41.86; H,4.45; N,17.66; Cl,4.81; S,8.71 (%).

實施例 87



^{1}H-NMR (D_2O + DCl) δ : 1.44 (3H, d, J = 7.1 Hz), 2.78 (3H, s), 3.11 及 3.52 (2H, ABq, J = 17.9 Hz), 3.78 (2H, t, J = 5.6 Hz), 4.66 (1H, q, J = 7.1 Hz), 5.09 (2H, t, J = 5.6 Hz), 5.23 (1H, d, J = 4.8 Hz), 5.63 及 5.81 (2H, ABq, J = 15.2 Hz), 5.85 (1H, d, J = 4.8 Hz), 7.95 (1H,dd, J = 9.0, 5.4 Hz), 8.97 (1H, d, J = 9.0 Hz), 9.07 (1H, d, J = 5.4 Hz), 9.21 (1H, brs).

IR (KBr) cm^{-1}: 3408, 1773, 1603, 1540, 1476, 1447, 1394, 1352, 1316, 1289, 1223, 1187, 1159, 1080, 1034.

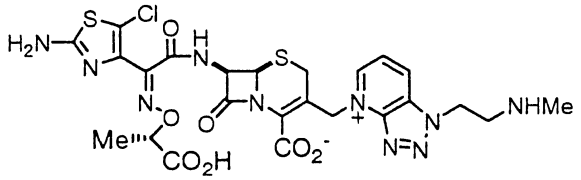
MS(FAB): 664^+ $(M+H)^+$.

元素分析　$C_{25}H_{26}ClN_9O_7S_2 \cdot 3.1H_2O$.

計算値：　C,41.71; H,4.51; N,17.51; Cl,4.92; S,8.91 (%).

實驗値：　C,41.75; H,4.39; N,17.57; Cl,4.64; S,8.71 (%).

實施例 88



^{1}H-NMR (D_2O + DCl) δ : 1.55 (3H, d, J = 7.2 Hz), 2.85 (3H, s), 3.53 及 3.80 (2H, ABq, J = 18.0 Hz), 3.91 (2H, t, J = 6.0 Hz), 5.34 (1H, d, J = 4.8 Hz), 5.40 (2H, t, J = 6.0 Hz), 5.96 (1H, d, J = 4.8 Hz), 6.07 及 6.29 (2H, ABq, J = 15.0 Hz), 8.28 (1H,dd, J = 5.4, 8.4 Hz), 9.25 (1H,

d, J = 8.4 Hz), 9.34(1H, d, J = 5.4 Hz).

IR (KBr) cm^{-1}: 3408, 2448, 1774, 1606, 1539, 1465, 1393, 1348, 1283, 1188, 1155, 1093, 1065, 1034.

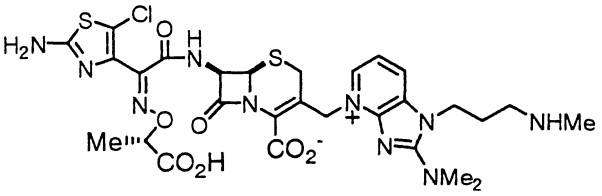
MS(ESI): 655 $(M+H)^+$.

元素分析　$C_{24}H_{25}ClN_{10}O_7S_2 \cdot 3.6H_2O$.

計算值：　C,39.49; H,4.45; N,19.19; Cl,4.86; S,8.79 (%).

實驗值：　C,39.50; H,4.42; N,19.21; Cl,4.80; S,8.67 (%).

實施例 89



^{1}H-NMR (D_2O) δ : 1.44 (3H, d, J = 7.0 Hz), 2.22 (2H, m), 2.70 (3H, s), 3.08 (2H, m), 3.27 及 3.51 (2H, ABq, J = 18.0 Hz), 3.36 (6H, s), 4.36 (2H, t,-like), 5.16 (1H, d, J = 4.5 Hz), 5.22 及 5.67 (2H, ABq, J = 14.7 Hz), 5.83 (1H, d, J = 4.5 Hz), 7.26 (1H, t-like), 7.85 (1H, d, J = 7.8 Hz), 8.08 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}: 3399, 1773, 1629, 1584, 1541, 1501, 1419, 1350, 1320, 1226, 1167, 1137, 1064, 1033.

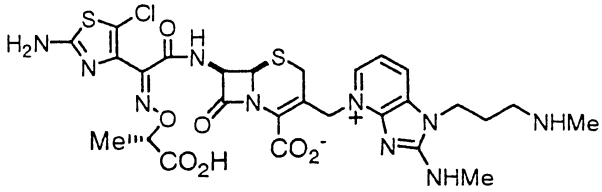
MS(FAB): 721^+ $(M+H)^+$.

元素分析　$C_{28}H_{33}ClN_{10}O_7S_2 \cdot 3.0H_2O$.

計算值：　C,43.38; H,5.07; N,18.07; Cl,4.57; S,8.27 (%).

實驗值：　C,43.43; H,5.05; N,18.07; Cl,4.36; S,8.10 (%).

實施例 90



^{1}H-NMR (D_2O+DCl) δ : 1.56 (3H, d, J = 7.5 Hz), 2.22 (2H, m), 2.72 (3H, s), 3.12-3.18 (5H, m), 3.46 及 3.60 (2H, ABq, J = 18.5 Hz), 4.22 (2H, t, J = 7.5 Hz), 5.01 (1H, q, J = 7.5 Hz),

5.27 (1H, d, J = 4.8 Hz), 5.27 (1H, d, J = 4.8 Hz), 5.43 (1H, d, J = 15.0 Hz), 5.85-5.91 (2H, m), 7.32 (1H, dd, J = 6.7, 7.6 Hz), 7.92 (1H, d, J = 7.6 Hz), 8.10 (1H, d, J = 6.7 Hz).

IR (KBr) cm^{-1}: 3398, 1773, 1642, 1596, 1541, 1496, 1412, 1392, 1366, 1316, 1222, 1165, 1139, 1099, 1064, 1034.

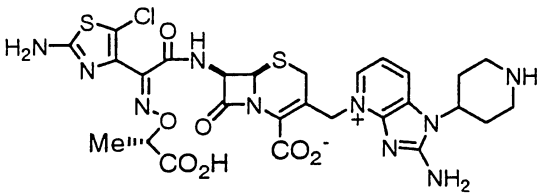
MS(ESI): 707^+ $(M+H)^+$.

元素分析　$C_{27}H_{31}ClN_{10}O_7S_2 \cdot 3.5H_2O$.

計算值：　C,42.10; H,4.97; N,18.18; Cl,4.60; S,8.33 (%).

實驗值：　C,42.09; H,4.97; N,18.19; Cl,4.44; S,8.18 (%).

實施例 91



^{1}H-NMR (D_2O+DCl)　δ : 1.55 (3H, d, J = 7.2 Hz), 2.33 (2H, d-like), 2.61 (2H, q-like), 3.25-3.39 (3H, m), 3.60 (1H, d, J = 18.3 Hz), 3.72 (2H, d-like), 4.99 (1H, q, J = 7.2 Hz), 5.29 (1H, d, J = 4.9 Hz), 5.50 及 5.69 (2H, ABq, J = 15.0 Hz), 5.92 (1H, d, J = 4.9 Hz), 7.33 (1H, t-like), 8.14 (2H, m).

IR (KBr) cm^{-1}: 3380, 3182, 1772, 1601, 1555, 1491, 1440, 1395, 1362, 1317, 1287, 1225, 1169, 1092, 1033.

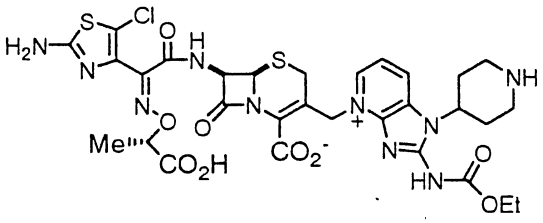
MS(ESI): 705^+ $(M+H)^+$.

元素分析　$C_{27}H_{29}ClN_{10}O_7S_2 \cdot 4.5H_2O$.

計算值：　C,41.25; H,4.87; N,17.81; Cl,4.51; S,8.16 (%).

實驗值：　C,41.38; H,4.79; N,17.71; Cl,4.19; S,7.50 (%).

實施例 92



^{1}H-NMR (D_2O + DCl) δ : 1.36 (3H, d, J = 7.1 Hz), 1.55 (3H, t, J = 7.3 Hz), 2.38 (2H, d-like), 2.62-2.72 (2H,m), 3.27-3.35 (2H m), 3.44 (1H, d., J = 18.6 Hz), 3.68-3.74 (3H, m), 4.37 (2H, q, J = 7.3 Hz), 4.99 (1H, q, J = 7.1 Hz), 5.31 (1H, d, J = 5.1 Hz), 5.73 (1H, d, J = 15.1 Hz), 5.90-5.95 (2H, m), 7.74 (1H, dd, J = 6.6, 7.9 Hz), 8.63 (1H, d, J = 6.6 Hz), 8.69 (1H, d, J = 7.9 Hz).

IR (KBr) cm^{-1}: 3409, 2982, 2527, 1775, 1607, 1538, 1468, 1385, 1283, 1223, 1174, 1094, 1033.

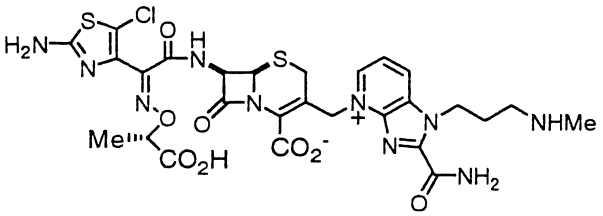
MS(ESI): 777^+ $(M+H)^+$.

元素分析　$C_{30}H_{33}ClN_{10}O_9S_2 \cdot 4.8H_2O$.

計算値：　C,41.72; H,4.97; N,16.22; Cl,4.10; S,7.43 (%).

實驗値：　C,41.68; H,4.86; N,16.33; Cl,4.08; S,7.46 (%).

實施例 93



^{1}H-NMR (D_2O+DCl) δ : 1.56 (3H, d, J = 5.4 Hz), 2.38 (2H, m), 2.74 (3H, s), 3.19 (2H, m), 3.54 (2H, m), 4.9 6(3H, m), 5.19 (1H, brs), 5.62-6.32 (2H, m), 5.87 (1H, brs), 7.99 (1H, m), 8.93 (1H, d, J = 7.5 Hz), 9.01(1H, d, J = 5.7 Hz).

IR (KBr) cm^{-1}: 3399, 1771, 1698, 1667, 1602, 1540, 1460, 1394, 1358, 1327, 1287, 1221, 1187, 1152, 1082, 1061, 1034.

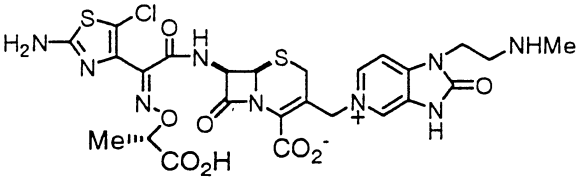
MS(ESI): $721^+$$(M+H^+)$.

元素分析　$C_{27}H_{29}ClN_{10}O_8S_2 \cdot 5.0\ H_2O$.

計算値：　C,39.97 ; H,4.85 ; N,17.27 ; Cl,4.37; S,7.91 (%).

實驗値：　C,39.88 ; H,4.45 ; N,17.07 ; Cl,4.40; S,7.99 (%).

實施例 94



^{1}H-NMR (D_2O + DCl) δ : 1.55 (3H, d, J = 7.1 Hz), 2.79 (3H, s), 3.35 及 3.54 (2H, ABq, J = 18.5 Hz), 3.54 (2H, t, J = 5.6 Hz), 4.44 (2H, t, J = 5.6 Hz), 4.99 (1H, q, J = 7.1 Hz), 5.36 (1H, d, J = 5.0 Hz), 5.31 及 5.79 (2H, ABq, J = 14.7 Hz), 5.94 (1H, d, J = 5.0 Hz), 7.79 (1H, d, J = 6.7 Hz), 8.65 (1H, dd, J = 1.2, 6.7 Hz), 8.72 (1H, brs).

IR (KBr) cm^{-1}: 3395, 3086, 1748, 1660, 1611, 1528, 1448, 1396, 1353, 1313, 1288, 1212, 1188, 1156, 1136, 1111, 1106, 1035.

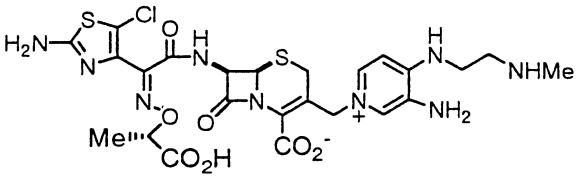
MS(ESI): 680^+ $(M+H)^+$.

元素分析 $C_{25}H_{26}ClN_9O_8S_2 \cdot 3.4H_2O$.

計算值： C,40.50; H,4.46; N,17.00; Cl,4.78; S,8.56 (%).

實驗值： C,40.73; H,4.45; N,17.10; Cl,4.65; S,8.35 (%).

實施例 95



^{1}H-NMR (D_2O + DCl) δ : 1.56 (3H, d, J = 7.1 Hz), 2.79 (3H, s), 3.31 及 3.66 (2H, ABq, J = 18.3 Hz), 3.40 (2H, t, J = 5.9 Hz), 3.85 (2H, t, J = 5.9 Hz), 4.96-5.03 (2H, m), 5.33 (1H, d, J = 5.1 Hz), 5.41 (1H, d, J = 14.7 Hz), 5.93 (1H, d, J = 5.1 Hz), 6.95 (1H, d, J = 7.2 Hz), 7.71 (1H, d, J = 1.8 Hz), 8.05 (1H, dd, J = 1.8, 7.2 Hz).

IR (KBr) cm^{-1}: 3368, 1773, 1627, 1556, 1455, 1395, 1349, 1321, 1287, 1190, 1158, 1093, 1065, 1034.

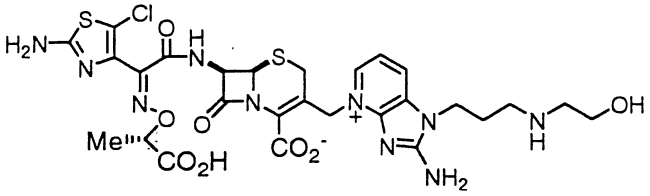
MS(ESI): 654^+ $(M+H)^+$.

元素分析 $C_{24}H_{28}ClN_9O_7S_2 \cdot 3.1H_2O$.

計算值： C,40.60; H,4.86; N,17.76; Cl,4.993; S,9.03 (%).

實驗值： C,40.63; H,4.81; N,17.74; Cl,4.891; S,8.88 (%).

實施例 96



^{1}H-NMR (D_2O + DCl) δ : 1.55 (3H, d, J = 7.0 Hz), 2.21-2.32 (2H, m), 3.20-3.25 (4H, m), 3.37 及 3.61 (2H, ABq, J = 18.5 Hz), 3.83 (2H, t, J = 5.0 Hz), 4.29 (2H, t, J = 7.1 Hz), 4.99 (1H, q, J = 7.0 Hz), 5.29 (1H, d, J = 4.5 Hz), 5.50 及 5.68 (2H, ABq, J = 15.2 Hz), 5.92 (1H, d, J = 4.5 Hz), 7.34 (2H, t-like), 7.66 (1H, d, J = 7.8 Hz), 8.13 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}: 3368, 1773, 1627, 1556, 1455, 1395, 1349, 1321, 1287, 1090, 1158, 1093, 1065, 1034.

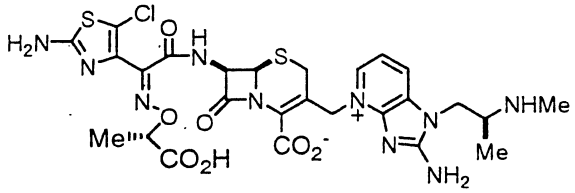
MS(ESI): 723^+ $(M+H)^+$.

元素分析 $C_{27}H_{31}ClN_{10}O_8S_2 \cdot 2.8H_2O$.

計算值： C,41.92; H,4.77; N,18.11; Cl,4.58; S,8.29 (%).

實驗值： C,41.93; H,4.73; N,18.06; Cl,4.46; S,8.17 (%).

實施例 97



^{1}H-NMR (D_2O + DCl) δ : 1.43 (3H, d, J = 6.9 Hz), 1.55 (3H, d, J = 7.2 Hz), 2.78 (3H, s), 3.40 及 3.61 (2H, ABq, J = 18.6 Hz), 3.83-3.95 (1H, m), 4.39-4.60 (2H, m), 5.00 (1H, q, J = 6.9 Hz), 5.29 (1H, d, J = 4.8Hz), 5.51 及 5.72 (2H, ABq, J = 15.2 Hz), 5.92 (1H, d, J = 4.8 Hz), 7.34 (1H, dd, J = 6.9, 8.1 Hz), 8.02 (1H, d, J = 8.1 Hz), 8.18 (1H, d, J = 6.9 Hz).

IR (KBr) cm^{-1}: 3372, 3185, 1772, 1667, 1600, 1563, 1493, 1394, 1353, 1317, 1287, 1225, 1166, 1090, 1033.

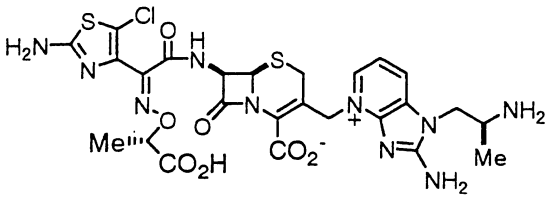
MS(ESI): 693 $(M+H)^+$.

元素分析 $C_{26}H_{29}ClN_{10}O_7S_2 \cdot 2.7H_2O$.

計算值： C,42.10; H,4.67; N,18.88; Cl,4.78; S,8.65 (%).

實驗值： C,42.15; H,4.72; N,18.88; Cl,4.61; S,8.40 (%).

實施例 98 8



^{1}H-NMR (D_2O+DCl) δ: 1.44 (3H, d, J = 6.3 Hz), 1.55 (3H, d, J = 7.2 Hz), 3.38 及 3.59 (2H, ABq, J = 18.6 Hz), 3.96 (1H, m), 4.41 (2H, d, J = 5.7 Hz), 4.98 (1H, q, J = 7.2), 5.27 (1H, d, J = 4.7 Hz), 5.47 及 5.71 (2H, ABq, J = 14.6 Hz), 5.91 (1H, d, J = 4.7 Hz), 7.35 (1H, m), 8.00 (1H, d, J = 8.1 Hz), 8.17 (1H, d, J = 6.9 Hz).

IR (KBr) cm^{-1}: 3358, 3184, 1771, 1651, 1563, 1494, 1396, 1365, 1317, 1288, 1225, 1166, 1090, 1034.

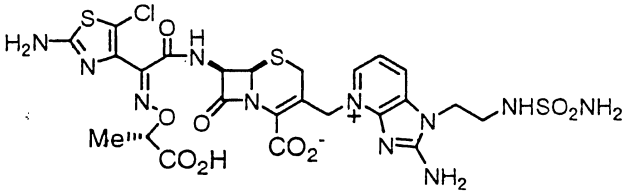
MS(ESI): $679^+(M+H^+)$.

元素分析 $C_{25}H_{27}ClN_{10}O_7S_2 \cdot 2.9\ H_2O$.

計算值： C,41.06 ; H,4.52 ; N,19.15 ; Cl,4.85; S,8.77 (%).

實驗值： C,41.06 ; H,4.46 ; N,19.14 ; Cl,4.75; S,8.62 (%).

實施例 99



^{1}H-NMR (d_6-DMSO) δ: 1.36 (3H, d, J = 7.0 Hz), 2.96 及 3.47 (2H, ABq, J = 17.7 Hz), 3.26 (2H, brs), 4.21 (2H, brs), 4.53 (1H, q, J = 7.0 Hz), 5.03 (1H, q, J = 5.1 Hz), 5.26 及 5.38 (2H, ABq, J = 13.5 Hz), 5.72 (1H, dd, J = 5.1, 9.0 Hz), 6.67 (2H, brs), 6.83 (1H, brs), 7.30 (1H, t-like), 7.41 (2H, brs), 7.93 (1H d, J = 7.5 Hz), 8.51 (1H, brs), 8.81 (1H, d, J = 6.6 Hz), 9.80 (1H, brs).

IR (KBr) cm^{-1}: 3382, 3194, 1766, 1667, 1651, 1609, 1568, 1496, 1444, 1389, 1345, 1304, 1214, 1156, 1076, 1036.

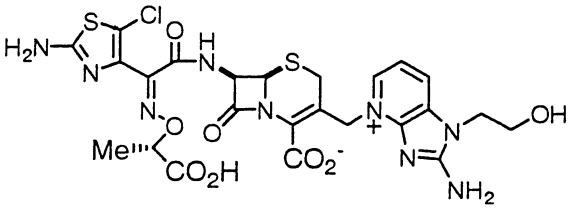
MS(ESI): $744^+(M+H)^+$.

元素分析　$C_{24}H_{26}ClN_{11}O_9S_3 \cdot 3.0H_2O$.

計算値：　C,36.11; H,4.04; N,19.30; Cl,4.44; S,12.05 (%).

實驗値：　C,35.88; H,3.93; N,19.18; Cl,4.54; S,12.17 (%).

實施例 100



^{1}H-NMR (D_2O + DCl)　δ : 1.54 (3H, d, J = 6.9 Hz), 3.36 及 3.61 (2H, ABq, J = 18.6 Hz), 3.97 (2H, t, J = 4.8 Hz), 4.30 (2H, t, J = 4.8 Hz), 5.29 (1H, d, J = 4.8 Hz), 5.54 及 5.68 (2H, ABq, J = 15.3 Hz), 5.92 (1H, d, J = 4.8 Hz), 7.34 (1H, t-like), 7.97 (1H d, J = 7.8 Hz), 8.14 (1H, d, J = 6.9 Hz).

IR (KBr) cm^{-1}: 3357, 3190, 1758, 1669, 1648, 1618, 1574, 1540, 1492, 1460, 1443, 1412, 1395, 1362, 1342, 1297, 1265, 1236, 1210, 1168, 1074, 1028.

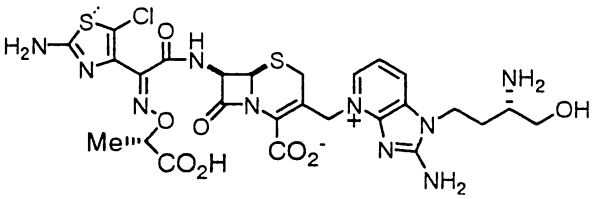
MS(ESI): 666^+ $(M+H)^+$.

元素分析　$C_{24}H_{24}ClN_9O_8S_2 \cdot 1.7H_2O$.

計算値：　C,41.37; H,3.96; N,18.09; Cl,5.09; S,9.20 (%).

實驗値：　C,41.53; H,3.80; N,18.19; Cl,4.64; S,8.79 (%).

實施例 101



^{1}H-NMR (D_2O + DCl)　δ : 1.55 (3H, d, J = 7.1Hz), 2.20 (2H, m), 3.37 (1H, d, J = 18.3 Hz), 3.50- 3.64 (2H, m), 3.77 (1H, dd, J = 6.0, 12.3 Hz), 3.94 (1H, dd, J = 4.2, 12.3 Hz), 4.30 (2H, t, J = 7.8 Hz), 5.30 (1H, d, J = 4.8 Hz), 5.51 及 5.68 (2H, ABq, J = 15.2 Hz), 5.92 (1H, d, J = 4.8 Hz), 7.35 (1H, t-like), 8.00 (1H d, J = 7.8 Hz), 8.14 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}: 3613, 3415, 3339, 3191, 1763, 1703, 1670, 1620, 1570, 1532, 1497, 1443, 1392, 1357, 1345, 1309, 1289, 1265, 1214, 1168, 1154, 1084, 1061, 1029.

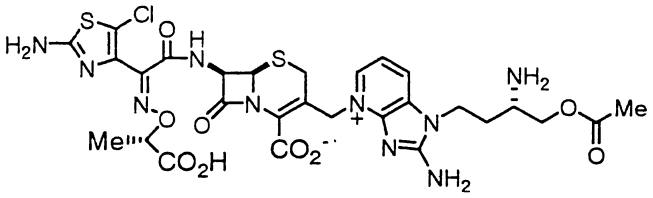
MS(ESI): 709^{+} $(M+H)^{+}$.

元素分析　$C_{26}H_{29}ClN_{10}O8_{7}S_{2}$・$2.3H_{2}O$.

計算値：　C,41.60; H,4.51; N,18.66; Cl,4.72; S,8.54 (%).

實驗値：　C,41.66; H,4.19; N,18.68; Cl,4.65; S,7.87 (%).

實施例 102



^{1}H-NMR ($D_{2}O$ + DCl)　δ : 1.55 (3H, d, J = 7.2 Hz), 2.13 (3H, s), 2.17-2.35 (2H, m), 3.38 及 3.61 (2H, ABq, J = 18.6 Hz), 3.74- 3.81 (1H, m), 4.24-4.44 (4H, m), 4.99 (1H, q, J = 7.2 Hz), 5.29 (1H, d, J = 4.8 Hz), 5.51 及　5.69 (2H, ABq, J = 15.0 Hz), 5.92 (1H, d, J = 4.8 Hz), 7.36 (1H, dd, J = 6.6, 8.1 Hz), 8.00 (1H d, J = 8.1 Hz), 8.15 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}: 3371, 3182, 1773, 1651, 1604, 1562, 1495, 1393, 1367, 1317, 1285, 1229, 1166, 1035.

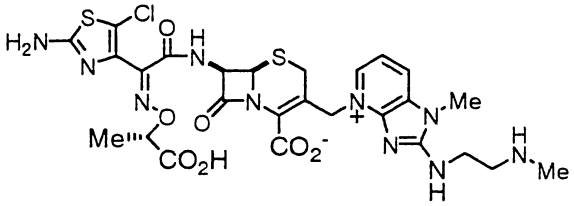
MS(ESI): 751^{+} $(M+H)^{+}$.

元素分析　$C_{28}H_{31}ClN_{10}O_{9}S_{2}$・$3.4H_{2}O$.

計算値：　C,41.39; H,4.69; N,17.24; Cl,4.36; S,7.89 (%).

實驗値：　C,41.23; H,4.31; N,17.10; Cl,4.01; S,7.97 (%).

實施例 103



^{1}H-NMR ($D_{2}O$+DCl)　δ : 1.55 (3H, d, J = 7.5 Hz), 3.37-3.57 (4H, m), 3.67 (3H, s), 3.93-4.02 (2H, m), 5.00 (1H, sept, J = 7.5 Hz), 5.25 (1H, d, J = 5.1 Hz), 5.46 及　5.93 (2H, ABq, J = 15.0 Hz), 5.91 (1H, d, J = 5.1), 7.53 (1H, t, J = 6.6 Hz), 7.94 (1H, d, J = 6.6 Hz), 8.15 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}:3309, 1773, 1636, 1598, 1539, 1501, 1452, 1390, 1357, 1317, 1285, 1142,

1093, 1072, 1034, 988.

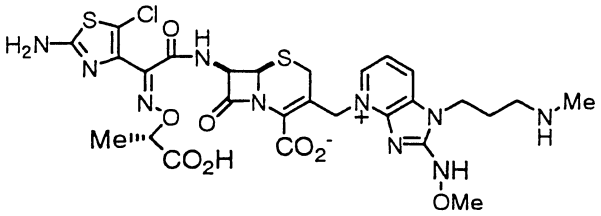
MS(ESI): 693^{+} $(M+H)^{+}$.

元素分析　$C_{26}H_{29}ClN_{10}O_7S_2 \cdot 3.9\ H_2O$.

計算值：　C,41.89 ; H,4.71 ; N,18.79 ; Cl,4.76; S,8.60 (%).

實驗值：　C,42.03 ; H,4.98 ; N,18.70 ; Cl,4.60; S,8.57 (%).

實施例 104



^{1}H-NMR (D_2O+DCl)　δ : 1.54 (3H, d, J = 7.2 Hz), 2.17-2.30 (2H, m), 2.72 (3H, s), 3.11-3.20 (2H, m), 3.36 及　3.66 (2H, ABq, J = 18.3 Hz), 3.94 (3H, s), 4.18-4.27 (2H, m), 4.97 (1H, sept, J = 7.2 Hz), 5.30 (1H, d, J = 5.1 Hz), 5.60 及　5.73 (2H, ABq, J = 15.2 Hz), 5.92 (1H, d, J = 5.1 Hz), 7.44-7.50 (1H, m), 8.14 (1H, d, J = 8.1 Hz), 8.28 (1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3398, 1775, 1599, 1490, 1393, 1315, 1223, 1162, 1095, 1063, 1035, 968.

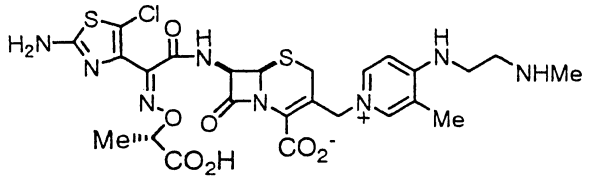
MS(ESI): 723^{+} $(M+H)^{+}$.

元素分析　$C_{27}H_{31}ClN_{10}O_8S_2 \cdot 3.7\ H_2O$.

計算值：　C,41.06 ; H,4.90 ; N,17.73 ; Cl,4.49; S,8.12 (%).

實驗值：　C,41.11 ; H,4.67 ; N,17.59 ; Cl,4.59; S,8.01 (%).

實施例 105



^{1}H-NMR (D_2O + DCl)　δ : 1.45 (3H, d, J = 6.9 Hz), 2.18 (3H, s), 2.76 (3H, s), 3.15 及　3.55 (2H, ABq, J = 18.0 Hz), 3.34 (2H, t, J = 6.0 Hz), 3.80 (2H, t, J = 6.0 Hz), 4.68 (1H, q, J = 6.9 Hz), 4.89 及　5.09 (2H, ABq, J = 14.7 Hz), 5.23 (1H, d, J = 4.8 Hz), 5.85 (1H, d, J = 4.8 Hz), 6.93 (1H, d, J = 7.2 Hz), 8.08 (1H, brs), 8.22 (1H, d, J = 7.2 Hz).

IR (KBr) cm^{-1}: 3383, 1773, 1649, 1554, 1449, 1395, 1288, 1213, 1190, 1154, 1094, 1065, 1035.

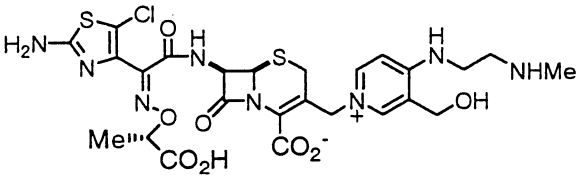
MS(ESI): 653^+ $(M+H)^+$.

元素分析　$C_{25}H_{29}ClN_8O_7S_2 \cdot 3.0H_2O$.

計算值：　C,42.46; H,4.99; N,1585; Cl,5.01; S,9.07(%).

實驗值：　C,42.47; H,4.77; N,15.81; Cl,5.86; S,8.84 (%).

實施例106



^{1}H-NMR (D_2O + DCl)　δ: 1.45 (3H, d, J = 7.2 Hz), 2.76 (3H, s), 3.16 及 3.58 (2H, ABq, J = 17.4 Hz), 3.36 (2H, t, J = 6.3 Hz), 3.82 (2H, t, J = 6.3 Hz), 4.64-4.72 (3H, m), 4.91 及 5.13 (2H, ABq, J = 14.7 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 7.02 (1H, d, J = 7.5 Hz), 8.24 (1H, brs), 8.29(1H, d, J = 7.5 Hz).

IR (KBr) cm^{-1}: 3366, 1772, 1651, 1588, 1551, 1457, 1395, 1288, 1205, 1150, 1094, 1035.

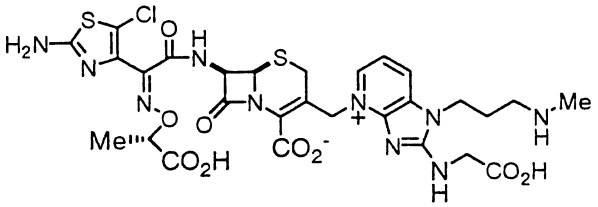
MS(ESI): 669^+ $(M+H)^+$.

元素分析　$C_{25}H_{29}ClN_8O_8S_2 \cdot 3.3H_2O$.

計算值：　C,41.21; H,4.93; N,15.38; Cl,4.87; S,8.80 (%).

實驗值：　C,41.38; H,4.73; N,15.53; Cl,4.77; S,8.51 (%).

實施例107



^{1}H-NMR (D_2O+DCl)　δ: 1.56 (3H, d, J = 6.9 Hz), 2.18-2.31 (2H, m), 2.71 (3H, s), 3.11-3.19 (2H, m), 3.43 及 3.51 (2H, ABq, J = 17.9 Hz), 4.25-4.35 (2H, m), 4.43 (2H, s), 4.18 (1H, sept, J = 6.9 Hz), 5.20 (1H, d, J = 4.8 Hz), 5.35 及 5.91 (2H, ABq, J = 15.2 Hz), 5.90 (1H, d, J = 4.8 Hz), 7.34-7.40 (1H, m), 8.02 (1H, d, J = 7.5 Hz), 8.18 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}:3409, 1774, 1635, 1593, 1540, 1496, 1390, 1314, 1228, 1188, 1165, 1112, 1073, 1034, 984, 759.

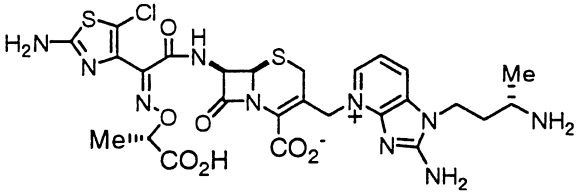
MS(FAB): 751^{+} $(M+H)^{+}$.

元素分析　$C_{28}H_{31}ClN_{10}O_9S_2 \cdot 2.3\ H_2O$.

計算値：　C,42.43 ; H,4.53 ; N,17.67 ; Cl,4.47; S,8.09 (%).

實驗値：　C,42.50 ; H,4.16 ; N,17.66 ; Cl,4.40; S,7.88 (%).

實施例108



^{1}H-NMR (D_2O+DCl) δ : 1.43 (3H, d, J = 6.9 Hz), 1.55 (3H, d, J = 7.1 Hz), 2.17 (2H, m), 3.35 及 3.59 (2H, ABq, J = 18.6 Hz), 3.51 (1H, m), 4.28 (2H, t -ike), 4.97 (1H, q, J = 7.1), 5.27 (1H, d, J = 4.8 Hz), 5.45 及 5.67 (2H, ABq, J = 15.0 Hz), 5.9 1(1H, d, J = 4.8 Hz), 7.3 (1H, t-like), 7.97 (1H, d, J = 7.8 Hz), 8.13 (1H, d, J = 6.9 Hz).

IR (KBr) cm^{-1}: 3408, 1773, 1650, 1601, 1565, 1495, 1395, 1363, 1317, 1287, 1224, 1165, 1090, 1034.

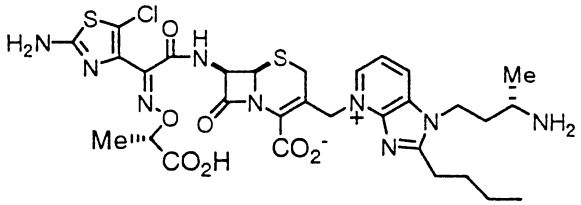
MS(ESI): $693^{+}$$(M+H^{+})$.

元素分析　$C_{26}H_{29}ClN_{10}O_7S_2 \cdot 3.7\ H_2O$.

計算値：　C,41.10 ; H,4.83 ; N,18.43 ; Cl,4.67; S,8.44 (%).

實驗値：　C,41.15 ; H,4.69 ; N,18.33 ; Cl,4.65; S,8.17 (%).

實施例109



^{1}H-NMR (D_2O+DCl) δ : 0.97 (3H, t, J = 7.4 Hz), 1.48 (2H, m), 1.55 (3H, d, J = 7.2 Hz), 1.91 (2H, q, J = 7.5 Hz), 2.23 (2H, m), 3.15 (2H, t, J = 7.5 Hz), 3.42 及 3.64 (2H, ABq, J = 18.3 Hz), 3.61 (1H, m), 4.58 (2H, t like), 4.99 (1H, q, J = 7.2), 5.28 (1H, d, J = 4.8 Hz), 5.73

and 6.02 (2H, ABq, J = 15.0 Hz), 5.73 (1H, d, J = 4.8 Hz), 7.79 (1H, t like), 8.67 (1H, d, J = 8.1 Hz), 8.72 (1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}: 3399, 2959, 2872, 1776, 1601, 1540, 1465, 1396, 1349, 1318, 1224, 1161, 1093, 1064, 1033.

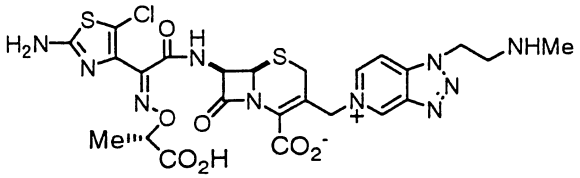
MS(ESI): $734^{+}(M+H^{+})$.

元素分析　$C_{30}H_{36}ClN_9O_7S_2 \cdot 3.8\ H_2O$.

計算値：C,44.89 ; H,5.47 ; N,15.70 ; Cl,4.42; S,7.99 (%).

實驗値：C,44.79 ; H,5.22 ; N,15.82 ; Cl,4.32; S,7.89 (%).

實施例110



^{1}H-NMR (D_2O+DCl) δ : 1.53 (3H, d, J = 7.2 Hz), 2.85 (3H, s), 3.39 及 3.80 (2H, ABq, J = 18.6 Hz), 3.88 (2H, t, J = 5.7 Hz), 4.97 (1H, q, J = 7.2 Hz), 5.31 (2H, t, J = 5.7 Hz), 5.37 (1H, d, J = 4.7 Hz), 5.54-6.00 (2H, m), 5.95 (1H, d, J = 4.7 Hz), 8.50 (1H, d, J = 7.2 Hz), 8.96 (1H, d, J = 7.2 Hz), 10.16(1H, s).

IR (KBr) cm^{-1}: 3407, 1774, 1609, 1539, 1483, 1447, 1394, 1359, 1287, 1190, 1155, 1104, 1066, 1034.

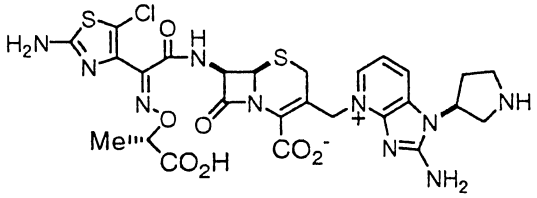
MS(ESI): $665^{+}(M+H^{+})$.

元素分析　$C_{24}H_{25}ClN_{10}O_7S_2 \cdot 3.2\ H_2O$.

計算値：C,39.88 ; H,4.38; N,19.38 ; Cl,4.91; S,8.87 (%).

實驗値：C,39.93 ; H,4.02 ; N,19.34; Cl,4.76; S,8.64 (%).

實施例111



^{1}H-NMR (D_2O+DCl) δ : 1.55 (3H, d, J = 7.2 Hz), 2.68 (2H, m), 3.36 及 3.60 (2H, ABq, J =

18.6 Hz), 3.57 及 3.97 (4H, m), 4.99 (1H, m), 5.29 (1H, d, J = 5.0 Hz), 5.50 及 5.69 (2H, ABq, J = 15.2 Hz), 5.92 (1H, d, J = 5.0 Hz), 7.34 (1H, t like), 8.06 (1H, d, J = 7.5 Hz), 8.16 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}: 3410, 1771, 1606, 1556, 1491, 1440, 1396, 1363, 1319, 1224, 1167, 1092, 1034.

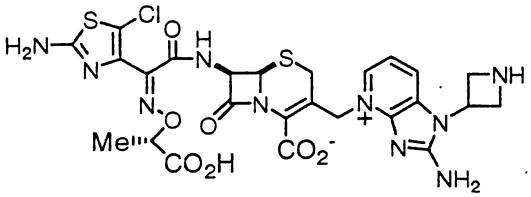
MS(FAB): $691^{+}(M+H^{+})$.

元素分析 $C_{26}H_{27}ClN_{10}O_7S_2 \cdot 4.6\ H_2O$.

計算值： C,40.35 ; H,4.71 ; N,18.10 ; Cl,4.58; S,8.29 (%).

實驗值： C,40.39 ; H,4.17 ; N,17.79 ; Cl,4.49; S,8.47 (%).

實施例112



^{1}H-NMR (D_2O+DCl) δ : 1.55 (3H, d, J = 7.5 Hz), 3.38 及 3.61 (2H, ABq, J = 18.6 Hz), 4.59-4.68 (2H, m), 4.92-5.03 (2H, m), 5.29 (1H, d, J = 4.8 Hz), 5.51 (1H, d, J = 15.0 Hz), 5.67-5.78 (2H, m), 5.92 (1H, d, J = 4.8 Hz), 7.40 (1H, dd, J = 6.6, 8.1 Hz), 8.21 (1H, d, J = 6.6 Hz), 8.29 (1H, d, J = 8.1 Hz).

IR (KBr) cm^{-1}: 3379, 1770, 1667, 1603, 1559, 1491, 1442, 1398, 1364, 1317, 1287, 1226, 1170, 1092, 1034.

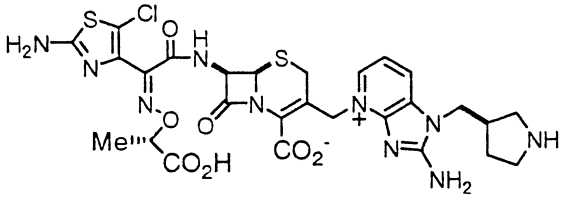
MS(ESI): $677^{+}(M+H)^{+}$.

元素分析 $C_{252}H_{25}ClN_{10}O_7S_2 \cdot 3.9H_2O$.

計算值： C,40.18; H,4.42; N,18.74; Cl,4.74; S,8.58 (%).

實驗值： C,40.36; H,4.32; N,18.37; Cl,4.76; S,8.39 (%).

實施例113



^{1}H-NMR (D_2O+DCl) δ: 1.55 (3H, d, J = 7.2 Hz), 1.83-2.37 (4H, m), 3.29-3.62 (4H, m), 4.07 (1H, m), 4.58 (2H, d, J = 7.2 Hz), 4.97 (1H, q, J = 7.2 Hz), 5.27 (1H, d, J = 5.0 Hz), 5.46 及 5.71 (2H, ABq, J = 15.3 Hz), 5.91 (1H, d, J = 5.0 Hz), 7.35 (1H, t-like), 8.02 (1H, d, J = 7.8 Hz), 8.17 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}: 3417, 1772, 1650, 1605, 1563, 1494, 1394, 1362, 1317, 1222, 1167, 1093, 1033.

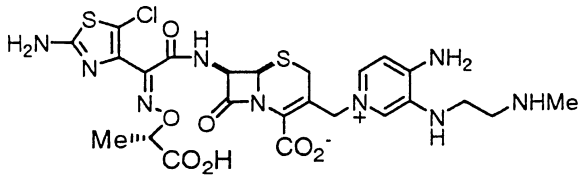
MS(ESI): $705^+(M+H^+)$.

元素分析 $C_{27}H_{29}ClN_{10}O_7S_2 \cdot 4.1\ H_2O$.

計算值： C,41.63 ; H,4.81 ; N,17.98 ; Cl,4.55; S,8.23 (%).

實驗值： C,41.73 ; H,4.66 ; N,17.70 ; Cl,4.74; S,8.37 (%).

實施例 114



^{1}H-NMR (D_2O) δ: 1.44 (3H, d, J = 6.9 Hz), 2.75 (3H, s), 3.11 及 3.57 (2H, ABq, J = 17.7 Hz), 3.32 (2H, t, J = 5.9 Hz), 3.51 (2H, t, J = 5.9 Hz), 4.66 (1H, q, J = 6.9 Hz), 4.77 及 5.12 (2H, ABq, J = 14.4 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.69 (1H, d, J = 4.8 Hz), 6.83 (1H, d, J = 6.3 Hz), 7.86-7.89 (2H, m).

IR (KBr) cm^{-1}: 3371, 1773, 1600, 1546, 1492, 1457, 1394, 1358, 1284, 1185, 1157, 1093, 1066, 1034.

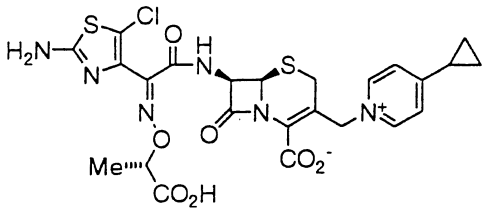
MS(FAB): 654^+ $(M+H)^+$.

元素分析 $C_{24}H_{28}ClN_9O_7S_2 \cdot 2.7H_2O$.

計算值： C,41.02; H,4.73; N,17.94; Cl,5.04; S,9.13 (%).

實驗值： C,41.14; H,4.53; N,17.91; Cl,4.73; S,8.55 (%).

實施例 115



^{1}H-NMR (d_6-DMSO) δ : 1.07-1.18 (2H, m), 1.38 (3H, d, J = 7.2 Hz), 1.38-1.47 (2H, m), 2.20-2.38 (1H, m), 3.02 (1H, d, J = 17.7 Hz), 3.48 (1H, d, J = 17.7 Hz), 4.55 (1H, q, J = 7.2 Hz), 4.99 (1H, d, J = 13.2 Hz), 5.05 (1H, d, J = 4.2 Hz), 5.52 (1H, d, J = 13.2 Hz), 5.70 (1H, dd, J = 4.2, 8.4 Hz), 7.37-7.57 (2H, m), 7.82 (2H, d, J = 6.0 Hz), 9.19 (2H, d, J = 6.0 Hz), 9.58-9.73 (1H, m).

IR (KBr) cm^{-1}: 3409, 3053, 1778, 1674, 1637, 1538, 1518, 1475, 1453, 1389, 1353,1215, 1185, 1158, 1100, 1034.

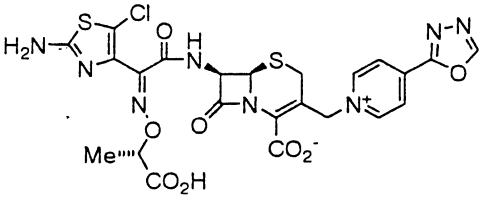
MS(FAB): $607^+(M+H^+)$.

元素分析　$C_{24}H_{23}ClN_6O_7S_2 \cdot 1.9\ H_2O$.

計算値：　C,44.95 ; H,4.21 ; N,13.10 ; Cl,5.53 ; S,10.00 (%).

實驗値：　C,44.93 ; H,4.35 ; N,13.09 ; Cl,5.44 ; S,10.08 (%).

實施例 116



^{1}H-NMR (d_6-DMSO) δ : 1.37 (3H, d, J = 6.9 Hz), 3.11 (1H, d, J = 17.7 Hz), 3.53 (1H, d, J = 17.7 Hz), 4.54 (1H, q, J = 6.9 Hz), 5.07 (1H, d, J = 4.8 Hz), 5.21 (1H, d, J = 13.8 Hz), 5.72 (1H, dd, J = 4.8, 8.4 Hz), 5.77 (1H, d, J = 13.8 Hz), 7.41 (2H, s), 8.73 (2H, d, J = 6.9 Hz), 9.51-9.82 (3H, m).

IR (KBr) cm^{-1}: 3413, 1777, 1671, 1615, 1538, 1510, 1457, 1391, 1346, 1237, 1189, 1152, 1103, 1083, 1035.

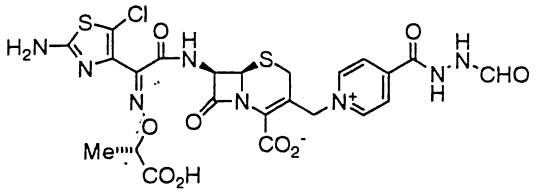
MS(FAB): $635^+(M+H^+)$.

元素分析　$C_{23}H_{19}ClN_8O_8S_2 \cdot 3.1\ H_2O$.

計算値：　C,39.98 ; H,3.68 ; N,16.22 ; Cl,5.13 ; S,9.28 (%).

實驗值： C,39.83 ; H,3.62 ; N,16.25 ; Cl,5.25 ; S,9.78 (%).

實施例 17



^{1}H-NMR (d_6-DMSO) δ: 1.37 (3H, d, J = 6.9 Hz), 3.12 (1H, d, J = 18.0 Hz), 3.50 (1H, d, J = 18.0 Hz), 4.55 (1H, q, J = 6.9 Hz), 5.06 (1H, d, J = 5.1 Hz), 5.19 (1H, d, J = 13.2 Hz), 5.68-5.79 (2H, m), 7.41 (2H, s), 8.16 (1H, s), 8.46 (2H, d, J = 6.6 Hz), 9.49-9.75 (3H, m).

IR (KBr) cm^{-1}: 3287, 3196, 3055, 2988, 1779, 1673, 1618, 1538, 1457, 1345, 1242, 1188, 1119, 1065, 1035.

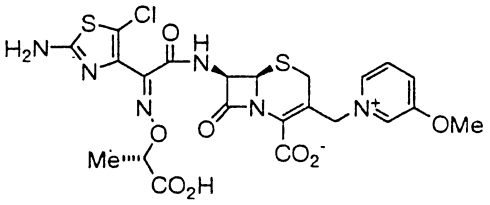
MS(FAB): 653$^+$(M+H$^+$).

元素分析 $C_{23}H_{21}ClN_8O_9S_2 \cdot 2.1\ H_2O$.

計算值： C,39.98 ; H,3.68 ; N,16.22 ; Cl,5.13 ; S,9.28 (%).

實驗值： C,39.97 ; H,3.75 ; N,16.57 ; Cl,4.72 ; S,8.79 (%).

實施例 118



^{1}H-NMR (d_6-DMSO) δ: 1.38 (3H, d, J = 6.9 Hz), 3.08 (1H, d, J = 17.7 Hz), 3.50 (1H, d, J = 17.7 Hz), 3.99 (3H, s), 4.55 (1H, q, J = 6.9 Hz), 5.06 (1H, d, J = 4.5 Hz), 5.08 (1H, d, J = 12.9 Hz), 5.62 (1H, d, J = 12.9 Hz), 5.71 (1H, dd, J = 4.5, 8.1 Hz), 7.41 (2H, s), 8.08 (1H, dd, J = 5.7, 8.7 Hz), 8.22 (1H, d, J = 8.7 Hz), 9.11 (1H, d, J = 5.7 Hz), 9.41 (1H, s), 9.54-9.66 (1H, m).

IR (KBr) cm^{-1}: 3410, 2942, 1778, 1674, 1618, 1539, 1509, 1444, 1389, 1340, 1290, 1235, 1188, 1148, 1099, 1041, 1009.

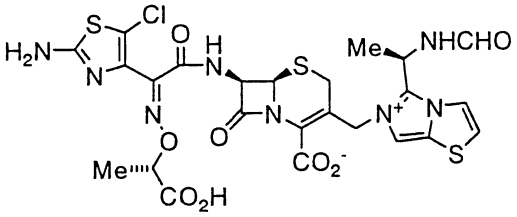
MS(FAB): 597$^+$(M+H$^+$).

元素分析　$C_{22}H_{21}ClN_6O_8S_2 \cdot 2.7\ H_2O$.

計算値：　C,40.92 ; H,4.12 ; N,13.02 ; Cl,5.49 ; S,9.93 (%).

實驗値：　C,40.94 ; H,4.01 ; N,13.12 ; Cl,5.36 ; S,9.91 (%).

實施例 119



^{1}H-NMR (d_6-DMSO) δ: 1.39 (3H, d, J = 7.2 Hz), 1.59 (3H, d, J = 7.2 Hz), 3.09 (1H, d, J = 17.4 Hz), 4.54 (1H, q, J = 7.2 Hz), 5.00 (1H, d, J = 5.4 Hz), 5.30 (1H, d, J = 13.8 Hz), 5.42 (1H, d, J = 13.8 Hz), 5.55-5.67 (1H, m), 5.72 (1H, dd, J = 5.4, 8.4 Hz), 7.41 (2H, s), 7.79 (1H, d, J = 4.2 Hz), 8.02-8.09 (2H, m), 8.30-8.39 (1H, m), 9.75 (1H, s).

IR (KBr) cm^{-1}: 3410, 2353, 1775, 1669, 1612, 1537, 1447, 1382, 1319, 1289, 1237, 1185, 1152, 1098, 1068, 1034.

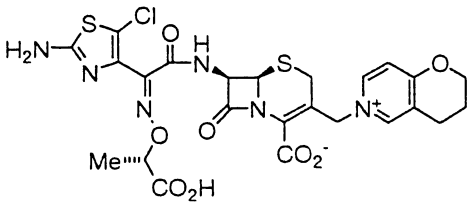
MS(FAB): $683^+(M+H^+)$.

元素分析　$C_{24}H_{23}ClN_8O_8S_3 \cdot 4.0\ H_2O$.

計算値：　C,38.17 ; H,4.14 ; N,14.84 ; Cl,4.69 ; S,12.74 (%).

實驗値：　C,38.05 ; H,4.10 ; N,14.78 ; Cl,4.97 ; S,12.98 (%).

實施例 120



^{1}H-NMR (d_6-DMSO) δ: 1.38 (3H, d, J = 6.6 Hz), 1.96-2.10 (2H, m), 2.79-2.90 (2H, m), 3.03 (1H, d, J = 17.7 Hz), 3.47 (1H, d, J = 17.7 Hz), 4.45-4.54 (2H, m), 4.54 (1H, q, J = 6.6 Hz), 4.86 (1H, d, J = 13.5 Hz), 5.04 (1H, d, J = 4.8 Hz), 5.43 (1H, d, J = 13.5 Hz), 5.70 (1H, dd, J = 4.8, 8.4 Hz), 7.38-7.48 (3H, m),

9.04 (1H, s), 9.08 (1H, d, J = 6.9 Hz), 9.64-9.82 (1H, m).

IR (KBr) cm^{-1}: 3412, 3057, 1779, 1674, 1641, 1538, 1516, 1489, 1468, 1444, 1351, 1287, 1220, 1168, 1135, 1034, 1008.

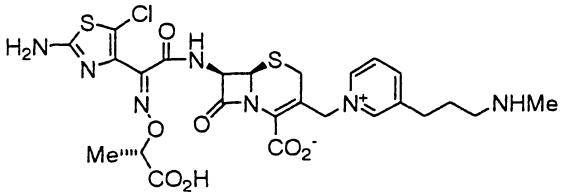
MS(FAB): $623^{+}(M+H^{+})$.

元素分析　$C_{24}H_{23}ClN_{8}O_{8}S_{2}\cdot 2.0\ H_{2}O$.

計算値：　C,43.74 ; H,4.13 ; N,12.75 ; Cl,5.38 ; S,9.73 (%).

實驗値：　C,43.71 ; H,3.94 ; N,12.94 ; Cl,5.13 ; S,9.49 (%).

實施例 121



^{1}H-NMR ($D_{2}O$) δ: 1.45 (3H, d, J = 7.2), 2.09 (2H, m), 2.71 (3H, s), 2.97 (2H, t, J = 8.1 Hz), 3.10 (2H, t, J = 8.1 Hz), 3.16 (1H, d, J = 18.0 Hz), 3.65 (1H, d, J = 18.0 Hz), 4.66 (1H, q, J = 7.2 Hz), 5. 25 (1H, d, J = 14.1 Hz), 5.28 (1H, d, J = 5.1 Hz), 5.56 (1H, d, J = 14.1 Hz), 5.88 (1H, d, J = 5.1 Hz), 8.01 (1H, dd, J = 6.6, 7.5 Hz), 8.45 (1H, d, J = 7.5 Hz), 8.82 (1H, d, J = 6.6 Hz), 8.93 (1H, brs).

IR (KBr) cm^{-1}: 3398, 2822, 1776, 1674, 1605, 1539, 1507, 1469, 1393, 1351, 1286, 1238, 1191, 1149, 1094, 1066, 1033.

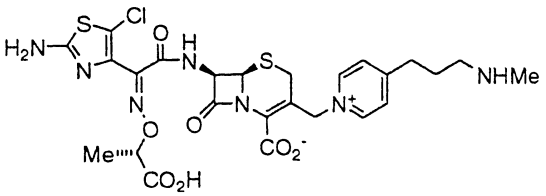
MS (ESI): 638 $(M+H)^{+}$, 660 $(M+Na)^{+}$.

元素分析　$C_{25}H_{28}ClN_{7}O_{7}S_{2}\cdot 4.0\ H_{2}O$.

計算値：　C, 42.28; H, 5.11; N, 13.81; Cl, 4.99; S, 9.03 (%).

實驗値：　C, 42.27; H, 5.09; N, 13.80; Cl, 5.00; S, 9.08 (%).

實施例 122



^{1}H-NMR (D_2O) δ: 1.36 (3H, d, J = 6.9), 2.04 (2H, m), 2.64 (3H, s), 2.95 (2H, t, J = 7.8 Hz), 3.03 (2H, t, J = 7.8 Hz), 3.11 (1H, d, J = 17.7 Hz), 3.55 (1H, d, J = 17.7 Hz), 4.58 (1H, q, J = 6.9 Hz), 5. 17 (1H, d, J = 14.7 Hz), 5.19 (1H, d, J = 4.8 Hz), 5.45 (1H, d, J = 14.7 Hz), 5.81 (1H, d, J = 4.8 Hz), 7.86 (2H, d, J = 6.9 Hz), 8.76 (2H, d, J = 6.9 Hz).

IR (KBr) cm^{-1}: 3397, 2821, 1776, 1606, 1538, 1467, 1394, 1350, 1287, 1231, 1187, 1152, 1094, 1066, 1033.

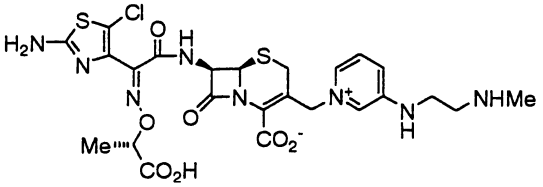
MS (ESI): 638 $(M+H)^+$, 660 $(M+Na)^+$.

元素分析 $C_{25}H_{28}ClN_7O_7S_2 \cdot 3.8\ H_2O$.

計算値： C, 42.50; H, 5.08; N, 13.88; Cl, 5.02; S, 9.08 (%).

實驗値： C, 42.34; H, 5.10; N, 13.97; Cl, 5.07; S, 9.29 (%).

實施例 123



^{1}H-NMR (d_6-DMSO) δ: 1.41 (3H, d, J = 6.9 Hz), 2.48 (3H, s), 2.81 (1H, d, J = 17.4 Hz), 2.94-3.06 (2H, m), 3.30-3.40 (2H, m), 3.50 (1H, d, J = 17.4 Hz), 4.47 (1H, q, J = 6.9 Hz), 4.87 (1H, d, J = 13.2 Hz), 5.12 (1H, d, J = 5.4 Hz), 5.41 (1H, d, J = 13.2 Hz), 5.82 (1H, dd, J = 5.4, 9.0 Hz), 7.35 (2H, s), 7.58-7.74 (3H, m), 8.23-8.32 (1H, m), 9.11 (1H, s), 11.10-11.23 (1H, m).

IR (KBr) cm^{-1}: 3362, 3086, 1774, 1593, 1539, 1511, 1458, 1394, 1353, 1288, 1184, 1154, 1095, 1065, 1033.

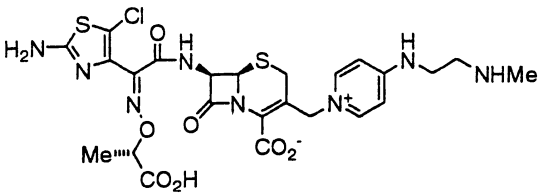
MS(ESI): $639^+(M+H^+)$.

元素分析 $C_{24}H_{27}ClN_8O_7S_2 \cdot 3.0\ H_2O$.

計算値： C,41.59 ; H,4.80 ; N,16.17 ; Cl,5.11 ; S,9.25 (%).

實驗値： C,41.54 ; H,4.67 ; N,16.18 ; Cl,5.17 ; S,9.45 (%).

實施例 124



^{1}H-NMR (D_2O) δ: 1.45 (3H, d, J = 6.9 Hz), 2.76 (3H, s), 3.17 (1H, d, J = 18.0 Hz), 3.33 (2H, t, J = 6.0 Hz), 3.58 (1H, d, J = 18.0 Hz), 3.75 (2H, t, J = 6.0 Hz), 4.66 (1H, q, J = 6.9 Hz), 4.89 (1H, d, J = 14.7 Hz), 5.09 (1H, d, J = 14.7 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 6.94 (2H, d, J = 6.3 Hz), 8.04-8.35 (2H, m).

IR (KBr) cm^{-1}: 3398, 3066, 1773, 1650, 1601, 1556, 1450, 1394, 1357, 1288, 1218, 1168, 1094, 1065, 1035.

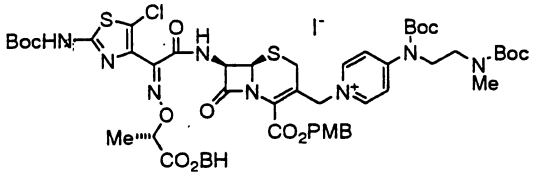
MS(FAB): $639^+(M+H^+)$.

元素分析 $C_{24}H_{27}ClN_8O_7S_2 \cdot 3.4\ H_2O$.

計算值： C,41.16 ; H,4.86 ; N,16.00 ; Cl,5.06 ; S,9.16 (%).

實驗值： C,41.14 ; H,4.69 ; N,16.00 ; Cl,4.97 ; S,9.36 (%).

四級鹽酯：

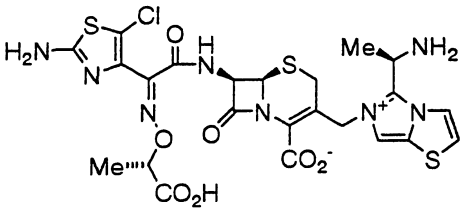


^{1}H-NMR (d_6-DMSO) δ: 1.15-1.40 (9H, m), 1.43-1.50 (12H, m), 1.54 (9H, s), 2.75-2.86 (3H, m), 3.20-3.38 (3H, m), 3.45 (1H, d, J = 17.7 Hz), 3.76 (3H, s), 4.00-4.16 (2H, m), 4.90 (1H, q, J = 6.9 Hz), 5.21 (1H, d, J = 12.6 Hz), 5.21 (1H, d, J = 5.1 Hz), 5.28 (1H, d, J = 12.6 Hz), 5.41 (2H, s), 5.97 (1H, dd, J = 5.1, 8.1 Hz), 6.83 (1H, s), 6.93 (2H, d, J = 8.1 Hz), 7.20-7.44 (12H, m), 8.09 (2H, d, J = 7.5 Hz), 8.73 (2H, d, J = 7.5 Hz), 9.73 (1H, d, J = 8.1 Hz), 12.08 (1H, s).

IR (KBr) cm^{-1}: 3425, 2978, 2934, 1793, 1724, 1693, 1638, 1613, 1551, 1516, 1479, 1455, 1393, 1369, 1249, 1223, 1153, 1065, 1036.

MS(FAB): 1225⁺(M⁺).

實施例 1 2 5



^{1}H-NMR (d_6-DMSO) δ: 1.39 (3H, d, J = 6.9 Hz), 1.47 (3H, d, J = 6.6 Hz), 3.15 (1H, d, J = 17.4 Hz), 3.40 (3H, d, J = 17.4 Hz), 4.55 (1H, q, J = 6.9 Hz), 4.99-50.6 (2H, m), 5.27 (1H, d, J = 13.8 Hz), 5.42 (1H, d, J = 13.8 Hz), 5.71 (1H, dd, J = 5.1, 9.0 Hz), 7.41 (2H, br s), 7.70 (1H, d, J = 4.2 Hz), 8.06 (1H, m), 8.45 (1H, d, J = 4.2 Hz), 9.78 (1H, br s).

IR (KBr) cm^{-1}: 3394, 1773, 1670, 1613, 1537, 1446, 1354, 1183, 1152, 1094, 1066, 1035.

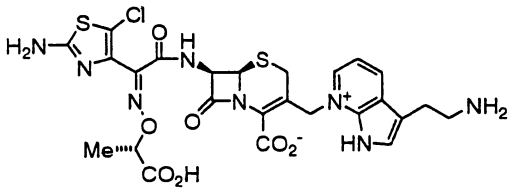
MS (FAB): 655 (M+H)⁺, 1309 (2M+H)⁺.

元素分析 $C_{23}H_{23}ClN_8O_7S_3 \cdot 3.6\ H_2O$.

計算値： C, 38.37; H, 4.23; N, 15.56; Cl, 4.92; S, 13.36 (%).

實驗値： C, 38.61; H, 4.01; N, 15.58; Cl, 4.92; S, 13.08 (%).

實施例 126



^{1}H-NMR (D_2O) δ: 1.38 (3H, d, J = 7.2), 2.89 (1H, d, J = 18.0 Hz), 3.17 (2H, t, J = 7.2 Hz), 3.33 (2H, t, J = 7.2 Hz), 3.70 (1H, d, J = 18.0 Hz), 4.62 (1H, q, J = 7.2 Hz), 5. 20 (1H, d, J = 15.0 Hz), 5.29 (1H, d, J = 4.8 Hz), 5.83 (1H, d, J = 4.8 Hz), 6.00 (1H, d, J = 15.0 Hz), 7.58 (1H, br t, J = 7.5 Hz), 7.64 (1H, s), 8.50 (1H, d, J = 6.0 Hz), 8.65 (1H, d, J = 7.5 Hz).

IR (KBr) cm^{-1}: 3396, 3184, 2821, 1772, 1598, 1539, 1445, 1384, 1361, 1288,

1219, 1188, 1157, 1093, 1061, 1035.

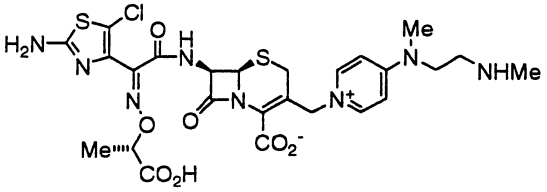
MS (FAB): 649 $(M+H)^+$, 1297 $(2M+H)^+$.

元素分析　$C_{25}H_{25}ClN_8O_7S_2 \cdot 3.8\ H_2O$.

計算値：C, 41.85; H, 4.58; N, 15.62; Cl, 4.94; S, 8.94 (%).

實驗値：C, 41.78; H, 4.34; N, 15.66; Cl, 4.98; S, 8.77 (%).

實施例 127



^{1}H-NMR (D_2O) δ: 1.46 (3H, d, J = 6.9), 2.76 (3H, s), 3.18 (1H, d, J = 18.0 Hz), 3.23 (3H, s), 3.36 (2H, t, J = 6.9 Hz), 3.58 (1H, d, J = 18.0 Hz), 3.95 (2H, t, J = 6.9 Hz), 4.68 (1H, q, J = 6.9 Hz), 4.91 (1H, d, J = 15.0 Hz), 5.10 (1H, d, J = 15.0 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 7.01 (2H, d, J = 7.5 Hz), 8.24 (2H, d, J = 7.5 Hz).

IR (KBr) cm^{-1}: 3408, 1775, 1650, 1606, 1556, 1450, 1404, 1359, 1286, 1235, 1164, 1106, 1064, 1034.

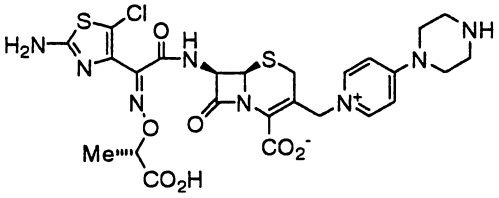
MS (FAB): 653 $(M+H)^+$, 1305 $(2M+H)^+$.

元素分析　$C_{25}H_{29}ClN_8O_7S_2 \cdot 3.7\ H_2O$.

計算値：C, 41.72; H, 5.10; N, 15.77; Cl, 4.93; S, 8.91 (%).

實驗値：C, 41.79; H, 4.94; N, 15.48; Cl, 4.92; S, 8.78 (%).

實施例 128



^{1}H-NMR (D_2O) δ: 1.45 (3H, d, J = 6.9), 3.17 (1H, d, J = 18.0 Hz), 3.45 (4H, m), 3.58 (1H, d, J = 18.0 Hz), 3.97 (4H, m), 4.66 (1H, q, J = 6.9 Hz), 4.92 (1H, d, J = 15.0 Hz), 5.13 (1H, d, J = 15.0 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.86 (1H,

d, J = 4.8 Hz), 7.15 (2H, d, J = 7.8 Hz), 8.27 (2H, d, J = 7.8 Hz).

IR (KBr) cm^{-1}: 3398, 1771, 1649, 1603, 1544, 1450, 1385, 1362, 1283, 1239, 1175, 1151, 1093, 1065, 1035.

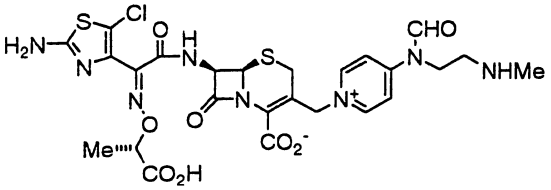
MS (ESI): 651 $(M+H)^+$, 673 $(M+Na)^+$.

元素分析 $C_{25}H_{27}ClN_8O_7S_2 \cdot 3.7\ H_2O$.

計算値： C, 41.83; H, 4.83; N, 15.61; Cl, 4.94; S, 8.93 (%).

實驗値： C, 41.79; H, 4.72; N, 15.71; Cl, 4.97; S, 8.96 (%).

實施例 129



^{1}H-NMR (D_2O) δ: 1.52 (3H, d, J = 7.2), 2.89 (3H/2, s), 3.04 (3H/2, s), 3.18 (1H, br d, J = 18.0 Hz), 3.52-3.62 (5H, m), 4.84 (1H, q, J = 7.2 Hz), 4.90 (1H, d, J = 15.0 Hz), 5.05 (1H, d, J = 15.0 Hz), 5.25 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 6.88 (2H, m), 7.88 (1H/2, s), 7.99 (1H/2, s), 8.02-8.19 (2H,m).

IR (KBr) cm^{-1}: 3406, 1778, 1650, 1554, 1446, 1391, 1352, 1219, 1170, 1096, 1064, 1034.

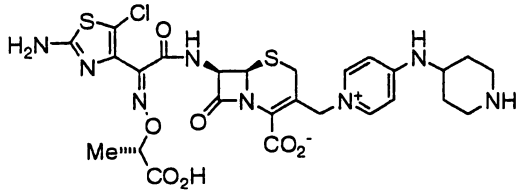
MS (ESI): 667 $(M+H)^+$.

元素分析 $C_{25}H_{27}ClN_8O_8S_2 \cdot 2.7\ H_2O$.

計算値： C, 41.95; H, 4.56; N, 15.66; Cl, 4.95; S, 8.96 (%).

實驗値： C, 41.93; H, 4.40; N, 15.73; Cl, 5.12; S, 8.93 (%).

實施例 130



^{1}H-NMR (D_2O) δ: 1.44 (3H, d, J = 6.6 Hz), 1.69-1.90 (2H, m), 2.20-2.34 (2H, m), 3.09-3.25 (3H, m), 3.44-3.62 (3H, m), 3.84-4.00 (1H, m), 4.65 (1H, q, J = 6.6

Hz), 4.86 (1H, d, J = 14.7 Hz), 5.06 (1H, d, J = 14.7 Hz), 5.23 (1H, d, J = 5.1 Hz), 5.86 (1H, d, J = 5.1 Hz), 6.80-7.00 (2H, m), 7.96-8.28 (2H, m).

IR (KBr) cm^{-1}: 3395, 2527, 1773, 1650, 1594, 1553, 1453, 1387, 1287, 1217, 1166, 1097, 1066, 1034.

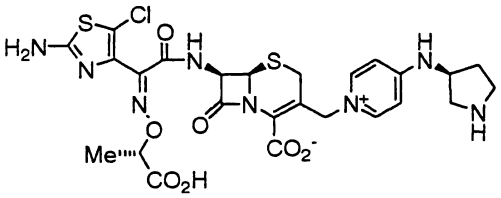
MS(FAB): $665^{+}(M+H^{+})$.

元素分析　$C_{26}H_{28}ClN_8O_7S_2 \cdot 6.2\ H_2O$.

計算値：　C,40.20 ; H,5.37 ; N,14.42 ; Cl,4.56 ; S,8.26 (%).

實驗値：　C,40.13 ; H,5.07 ; N,14.45 ; Cl,4.81 ; S,8.37 (%).

實施例 131



^{1}H-NMR (D_2O) δ : 1.56 (3H, d, J = 7.2Hz), 2.13-2.25 (1H, m), 2.45-2.58 (1H, m), 3.28 and 3.64 (2H, ABq, J = 18.3 Hz), 3.36-3.77 (4H, m), 4.53-4.60 (1H, m,), 4.96 (1H, q, J = 6.9 Hz), 4.99 and 5.25 (2H, ABq, J = 14.7 Hz), 5.30 (1H, d, J = 4.8 Hz), 5.90 (1H, d, J = 4.8 Hz), 6.82 (2H, d, J = 7.2 Hz), 8.18 (1H, m).

IR (KBr) cm^{-1}: 1773, 1650, 1597, 1551, 1446, 1391, 1286, 1217, 1167.

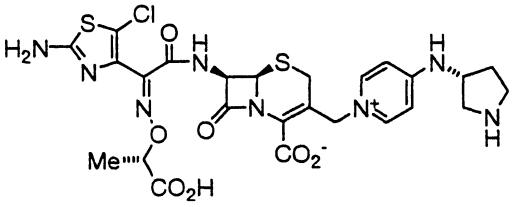
MS (ESI): 651 $(M+H)^{+}$, 673 $(M+Na)^{+}$.

元素分析　$C_{25}H_{27}ClN_8O_7S_2 \cdot 2.7\ H_2O$.

計算値：　C, 42.91; H, 4.67; N, 16.01; Cl, 5.07; S, 9.17 (%).

實驗値：　C, 42.98; H, 4.64; N, 15.99; Cl, 4.97; S, 9.29 (%).

實施例 132



^{1}H-NMR (D_2O) δ : 1.56 (3H, d, J = 7.2Hz), 2.16-2.24 (1H, m), 2.46-2.58 (1H, m), 3.29 and 3.64 (2H, ABq, J = 18.2 Hz), 3.37-3.78 (4H, m), 4.53-4.60 (1H, m,),

4.96 (1H, q, J = 7.2 Hz), 5.00 and 5.26 (2H, ABq, J = 14.7 Hz), 5.30 (1H, d, J = 4.8 Hz), 5.90 (1H, d, J = 4.8 Hz), 6.96 (2H, d, J = 7.5 Hz), 8.20 (1H, m).

IR (KBr) cm^{-1}: 1774, 1650, 1595, 1551, 1446, 1391, 1286, 1218, 1167.

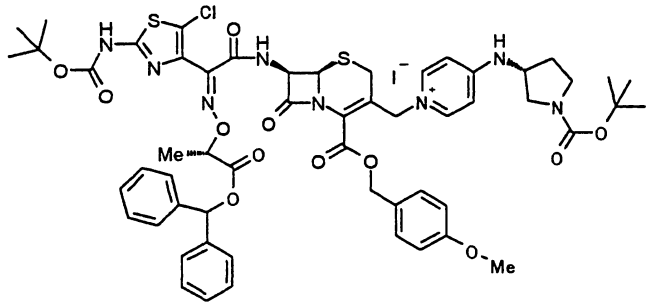
MS (ESI): 651 $(M+H)^+$, 673 $(M+Na)^+$.

元素分析 $C_{25}H_{27}ClN_8O_7S_2 \cdot 2.2\ H_2O$.

計算值： C, 43.47; H, 4.58; N, 16.22; Cl, 5.13; S, 9.28 (%).

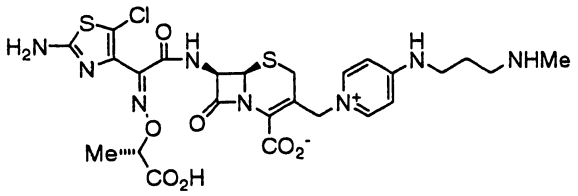
實驗值： C, 43.40; H, 4.60; N, 16.25; Cl, 5.07; S, 9.28 (%).

四級鹽酯：



^{1}H-NMR (DMSO) δ: 1.41 (9H, s), 1.46-1.48 (12H, m), 1.78-1.96 (1H, m), 2.10-2.30 (1H, m), 3.11-3.25 (1H, m), 3.37,3.49 (ABq, J=18.9Hz), 3.54-3.76 (2H, m), 3.76 (3H, s), 4.19-4.36 (1H, m), 4.90 (1H, q, J = 6.9 Hz), 5.04-5.15 (2H,m), 5.20(1H,d,J=5.1Hz),5.21,5.26(2H,Abq,J=11.7Hz),5.96(1H,dd,J=4.8Hz,J=8.1Hz),6.84(1H,s)6.866.97(4H,m),7.07(1H,d,J=7.8Hz),7.19,7.48(10H,m),8.07,8.09(1H,m), 8.27(1H,d,J=7.5Hz),8.92,8.94(1H,m),9.74(1H,J=8.4Hz),12.11(1H,s).

實施例 133



^{1}H-NMR (D_2O) δ: 1.45 (3H, d, J = 6.9), 2.04 (3H, m), 2.72 (3H, s), 3.12 (2H, t, J = 7.8 Hz), 3.16 (1H, d, J = 18.0 Hz), 3.44 (2H, t, J = 6.9 Hz), 3.56 (1H, d, J = 18.0 Hz), 4.66 (1H, q, J = 6.9 Hz), 4.86 (1H, d, J = 14.4 Hz), 5.05 (1H, d, J = 14.4 Hz), 5.23 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 6.85 (2H,

d, J = 7.5 Hz), 8.02-8.18 (2H, m).

IR (KBr) cm^{-1}: 3397, 1773, 1651, 1598, 1556, 1462, 1395, 1360, 1288, 1216, 1168, 1093, 1065, 1034.

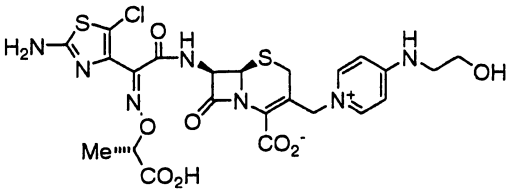
MS (ESI): 653 $(M+H)^+$, 675 $(M+Na)^+$.

元素分析　$C_{25}H_{29}ClN_8O_7S_2 \cdot 3.8\ H_2O$.

計算値：C, 41.61; H, 5.11; N, 15.53; Cl, 4.91; S, 8.89 (%).

實驗値：C, 41.47; H, 5.08; N, 15.63; Cl, 5.15; S, 8.98 (%).

實施例 134



^{1}H-NMR (d_6-DMSO) δ: 1.39 (3H, d, J = 6.9), 2.97 (1H, d, J = 18.0 Hz), 3.34 (2H, m), 3.46 (1H, d, J = 18.0 Hz), 3.59 (2H, t, J = 5.1 Hz), 4.56 (1H, q, J = 6.9 Hz), 4.65 (1H, d, J = 13.5 Hz), 5.05 (1H, d, J = 4.8 Hz), 5.16 (1H, d, J = 13.5 Hz), 5.70 (1H, dd, J = 4.8, 8.4 Hz), 6.94 (2H, m), 7.41 (2H, br s), 8.44 (1H, d, J = 6.9 Hz), 8.59 (1H, d, J = 7.5 Hz), 8.85 (1H, 5.4 Hz), 9.65 (1H, br).

IR (KBr) cm^{-1}: 3398, 1776, 1651, 1555, 1450, 1378, 1350, 1218, 1171, 1097, 1063, 1035.

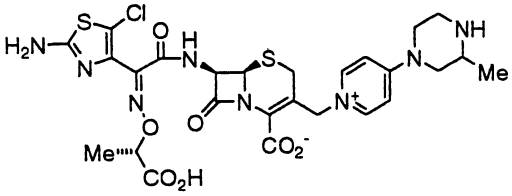
MS (ESI): 626 $(M+H)^+$, 1251 $(2M+H)^+$.

元素分析　$C_{23}H_{24}ClN_7O_8S_2 \cdot 2.3\ H_2O$.

計算値：C, 41.39; H, 4.32; N, 14.69; Cl, 5.31; S, 9.61 (%).

實驗値：C, 41.39; H, 4.34; N, 14.78; Cl, 5.11; S, 9.37 (%).

實施例 135



^{1}H-NMR (D_2O) δ: 1.40 (3H, d, J = 6.3), 1.45 (3H, d, J = 6.9 Hz), 3.17 (1H, d,

J = 18.0 Hz), 3.34 (1H, m), 3.55-3.61 (4H, m), 4.28-4.33 (2H, m), 4.66 (1H, q, J = 6.9 Hz), 4.91 (1H, d, J = 14.7 Hz), 5.12 (1H, d, J = 14.7 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 7.16 (2H, d, J = 7.2 Hz), 8.27 (2H, d, J = 7.2 Hz).

IR (KBr) cm^{-1}: 3408, 1773, 1649, 1605, 1546, 1449, 1386, 1360, 1284, 1239, 1158, 1107, 1065, 1036.

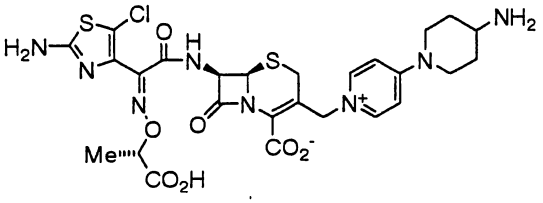
MS (ESI): 665 $(M+H)^+$, 687 $(M+Na)^+$.

元素分析 $C_{26}H_{29}ClN_8O_7S_2 \cdot 4.5\ H_2O$.

計算値： C, 41.85; H, 5.13; N, 15.02; Cl, 4.75; S, 8.59 (%).

實驗値： C, 41.86; H, 4.84; N, 15.06; Cl, 4.74; S, 8.48 (%).

實施例 136



^{1}H-NMR (D_2O) δ: 1.32 (3H, d, J = 6.9), 1.57 (2H, m), 2.08 (2H, m), 3.04 (1H, d, J = 17.4 Hz), 3.15 (2H, m), 3.48 (1H, m), 4.14 (2H, m), 4.53 (1H, q, J = 6.9 Hz), 4.74 (1H, d, J = 15.0 Hz), 4.94 (1H, d, J = 15.0 Hz), 5.12 (1H, d, J = 4.8 Hz), 5.73 (1H, d, J = 4.8 Hz), 6.96 (2H, d, J = 7.2 Hz), 8.02 (2H, d, J = 7.2 Hz).

IR (KBr) cm^{-1}: 3398, 1772, 1650, 1600, 1549, 1451, 1389, 1362, 1286, 1238, 1174, 1095, 1065, 1035.

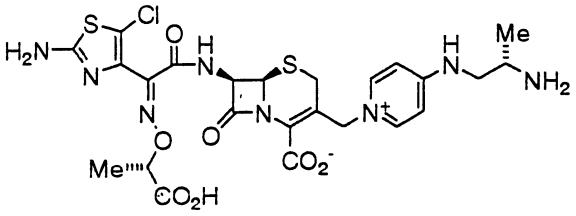
MS (ESI): 665 $(M+H)^+$, 687 $(M+Na)^+$.

元素分析 $C_{26}H_{29}ClN_8O_7S_2 \cdot 4.3\ H_2O$.

計算値： C, 42.05; H, 5.10; N, 15.09; Cl, 4.77; S, 8.64 (%).

實驗値： C, 42.12; H, 5.16; N, 14.95; Cl, 4.68; S, 8.50 (%).

實施例 137



^{1}H-NMR (D_2O) δ: 1.36 (3H, d, J = 6.3 Hz), 1.45 (3H, d, J = 6.6 Hz), 3.17 (1H, d, J = 18.0 Hz), 3.57 (1H, d, J = 18.0 Hz), 3.58-3.72 (3H, m), 4.65 (1H, q, J = 6.6 Hz), 4.87 (1H, d, J = 14.4 Hz), 5.09 (1H, d, J = 14.4 Hz), 5.23 (1H, d, J = 5.1 Hz), 5.86 (1H, d, J = 5.1 Hz), 6.93 (2H, d, J = 6.9 Hz), 8.05-8.38 (2H, m).

IR (KBr) cm^{-1}: 3294, 2983, 1774, 1650, 1592, 1555, 1456, 1395, 1360, 1287, 1218, 1167, 1092, 1065, 1034.

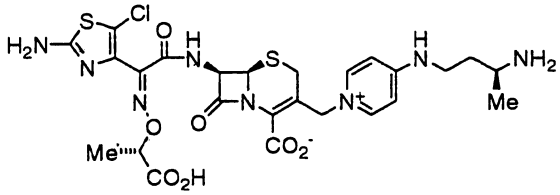
MS(ESI): $639^+(M+H^+)$.

元素分析　$C_{24}H_{27}ClN_8O_7S_2 \cdot 2.8\ H_2O$.

計算値：C,41.80 ; H,4.77 ; N,16.25 ; Cl,5.14 ; S,9.30 (%).

實驗値：C,41.83 ; H,4.64 ; N,16.29 ; Cl,4.96 ; S,9.22 (%).

實施例 138



^{1}H-NMR (D_2O) δ: 1.35 (3H, d, J = 6.3 Hz), 1.45 (3H, d, J = 6.6 Hz), 1.82-2.13 (2H, m), 3.16 (1H, d, J = 17.7 Hz), 3.35-3.50 (3H, m), 3.55 (1H, d, J = 17.7 Hz), 4.65 (1H, q, J = 6.6 Hz), 4.83 (1H, d, J = 14.4 Hz), 5.05 (1H, d, J = 14.4 Hz), 5.22 (1H, d, J = 4.2 Hz), 5.85 (1H, d, J = 4.2 Hz), 6.83 (2H, d, J = 6.3 Hz), 7.95-8.25 (2H, m).

IR (KBr) cm^{-1}: 3415, 3067, 2982, 1772, 1650, 1597, 1557, 1447, 1395, 1360, 1288, 1216, 1169, 1094, 1065, 1034.

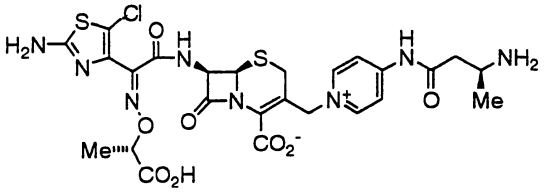
MS(FAB): $653^+(M+H^+)$.

元素分析　$C_{25}H_{29}ClN_8O_7S_2 \cdot 3.6\ H_2O$.

計算値：C,41.82 ; H,5.08 ; N,15.61 ; Cl,4.94 ; S,8.93 (%).

實驗値：C,41.89 ; H,4.95 ; N,15.54 ; Cl,4.57 ; S,8.60 (%).

實施例 139



^{1}H-NMR (D_2O) δ：1.40 (3H, d, J = 6.6 Hz), 1.44 (3H, d, J = 6.9 Hz), 2.88-3.02 (2H, m), 3.17 (1H, d, J = 17.7 Hz), 3.63 (1H, d, J = 17.7 Hz), 3.88 (1H, m), 4.66 (1H, q, J = 6.9 Hz), 5.13 (1H, d, J = 14.7 Hz), 5.26 (1H, d, J = 5.1 Hz), 5.40 (1H, d, J = 14.4 Hz), 5.87 (1H, d, J = 5.1 Hz), 8.07 (2H, d, J = 7.2 Hz), 8.71 (2H, d, J = 7.2 Hz).

IR (KBr) cm^{-1}: 3388, 1775, 1716, 1607, 1537, 1517, 1464, 1394, 1328, 1287, 1182, 1159, 1101, 1066, 1035.

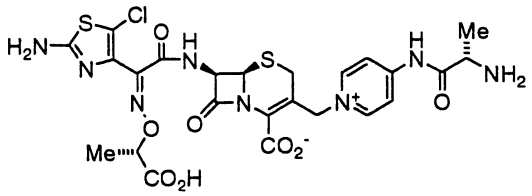
MS(FAB): 667 $(M+H)^+$, 1333 $(2M+H)^+$.

元素分析　$C_{25}H_{27}ClN_8O_8S_2 \cdot 3.7\ H_2O$.

計算値：C, 40.92; H, 4.73; N, 15.27; Cl, 4.83; S, 8.74 (%).

實驗値：C, 41.15; H, 4.46; N, 15.52; Cl, 4.57; S, 8.45 (%).

實施例 140



^{1}H-NMR (D_2O) δ：1.31 (3H, d, J = 7.2 Hz), 1.52 (3H, d, J = 6.9 Hz), 3.06 (1H, d, J = 18.1 Hz), 3.50 (1H, d, J = 18.1 Hz), 4.20 (1H, q, J = 6.9 Hz), 4.52 (1H, q, J = 7.2 Hz), 5.03 (1H, d, J = 14.4 Hz), 5.14 (1H, d, J = 5.1 Hz), 5.29 (1H, d, J = 14.4 Hz), 5.75 (1H, d, J = 5.1 Hz), 8.00 (2H, d, J = 7.2 Hz), 8.63 (2H, d, J = 7.2 Hz).

IR (KBr) cm^{-1}: 3398, 1775, 1730, 1612, 1538, 1516, 1466, 1397, 1356, 1327, 1288, 1197, 1158, 1110, 1066, 1035.

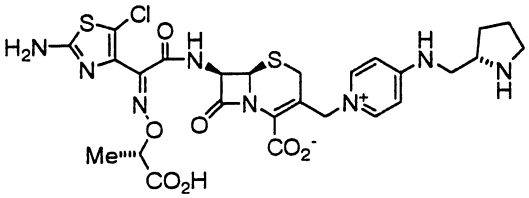
MS(ESI): 653 $(M+H)^+$.

元素分析　$C_{24}H_{25}ClN_8O_8S_2 \cdot 2.7\ H_2O$.

計算値：C, 41.08; H, 4.37; N, 15.97; Cl, 5.05; S, 9.14 (%).

實驗値：C, 41.13; H, 4.44; N, 15.94; Cl, 4.96; S, 8.94 (%).

實施例 141



^{1}H-NMR (D_2O) δ: 1.44 (3H, d, J = 7.5 Hz), 1.70-1.88 (1H, m), 1.98-2.20 (2H, m), 2.22-2.38 (1H, m), 3.17 (1H, d, J = 17.7 Hz), 3.30-3.42 (2H, m), 3.57 (1H, d, J = 17.7 Hz), 3.70 (2H, d, J = 6.3 Hz), 3.82-3.94 (1H, m), 4.66 (1H, q, J = 7.5 Hz), 4.87 (1H, d, J = 14.4 Hz), 5.10 (1H, d, J = 14.4 Hz), 5.23 (1H, d, J = 4.5 Hz), 5.85 (1H, d, J = 4.5 Hz), 6.93 (2H, d, J = 6.9 Hz), 8.05-8.30 (2H, m).

IR (KBr) cm^{-1}: 3398, 3065, 2983, 1774, 1650, 1602, 1556, 1447, 1394, 1360, 1287, 1218, 1168, 1096, 1064, 1034.

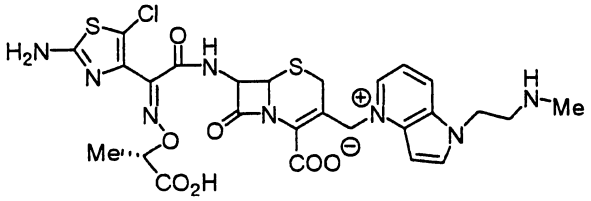
MS(FAB): $665^+(M+H^+)$.

元素分析　$C_{26}H_{29}ClN_8O_7S_2 \cdot 4.1\ H_2O$.

計算値：C,42.26 ; H,5.07 ; N,15.16 ; Cl,4.80 ; S,8.68 (%).

實驗値：C,42.29 ; H,4.82 ; N,15.26 ; Cl,4.67 ; S,8.53 (%).

實施例 142



^{1}H-NMR (D_2O) δ: 1.44(3H, d, J = 7.2 Hz), 2.73(3H, s), 3.17 及 3.38 (2H, ABq, J = 18.0 Hz), 3.63(2H, t, J = 6.0 Hz), 4.65(1H, q, J = 7.2 Hz), 4.80(2H, t, J

= 6.0 Hz), 5.17(1H, d, J = 4.8 Hz), 5.56 及 5.69(2H, ABq, J = 15.0 Hz), 5.85(1H, d, J = 4.8 Hz), 7.09(1H, d, J = 3.3 Hz), 7.73(1H, dd, J = 6.3 及 8.4 Hz), 8.15(1H, d, J = 3.3 Hz), 8.62(1H, d, J = 8.4 Hz), 8.68(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3407, 2452, 1773, 1603, 1539, 1500, 1467, 1392, 1364, 1287, 1184, 1120, 1089, 1063, 1032.

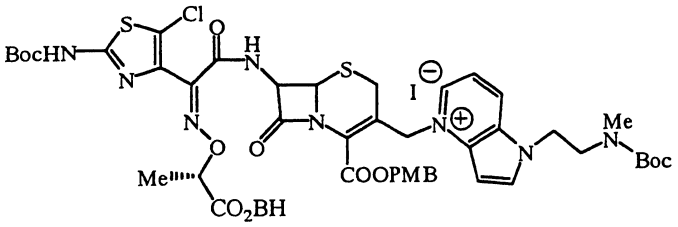
MS(FAB): $663^{+}(M+H^{+})$.

元素分析 $C_{26}H_{27}ClN_8O_7S_2 \cdot 5.2\ H_2O$.

計算值： C,41.26 ; H,4.98 ; N,14.81 ; Cl,4.68; S,8.47 (%).

實驗值： C,41.41 ; H,4.90 ; N,14.55 ; Cl,4.54; S,8.46 (%).

四級鹽酯：

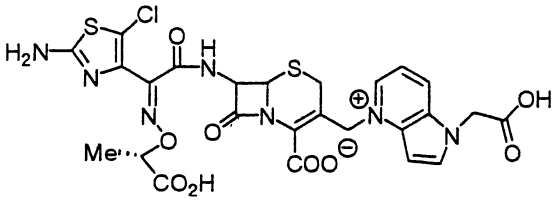


^{1}H-NMR (d_6-DMSO) δ : 1.04(9H, brs), 1.43(3H, d, = 7.2 Hz), 1.46(9H, s), 2.78(3H, brs), 3.21 及 3.40(2H, Abq, J = 18.6 Hz), 3.60(2H, m), 3.76(3H, s), 4.60(2H, t-like), 4.89(1H, q, J = 7.2 Hz), 5.20(1H, d, J = 5.1 Hz), 5.23 及 5.31(2H, Abq, J = 11.7 Hz), 5.71(2H, brs), 5.97(1H, dd, J = 5.1 and 8.7 Hz), 6.82(1H, s), 6.92(2H, d , J = 8.7 Hz), 7.01(1H, d, J = 3.3 Hz), 7.22-7.42(12H, m), 7.83(1H, brs), 8.30(1H, d, J = 3.3 Hz), 8.65(1H, brs), 8.84(1H, brs), 9.77(1H, d, J = 8.7 Hz), 12.1(brs).

IR (KBr) cm^{-1}:3422, 3061, 3032, 2977, 2935, 1791, 1717, 1690, 1631, 1613, 1584, 1550, 1515, 1495, 1455, 1392, 1367, 1248, 1155, 1118, 1100, 1065, 1032, 1018.

MS(FAB): $1149^{+}(C_{57}H_{62}ClN_8O_{12}S_2^{+})$.

實施例１４３



^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 7.2 Hz), 3.21 及 3.35 (2H, ABq, J = 18.0 Hz), 4.64(1H, q, J = 7.2 Hz), 5.01(2H, s), 5.17(1H, d, J = 4.8 Hz), 5.53 及 5.74(2H, ABq, J = 15.0 Hz), 5.89(1H, d, J = 4.8 Hz), 6.98(1H, d, J = 3.3 Hz), 7.67(1H, dd, J = 6.3 及 8.1 Hz), 8.04(1H, d, J = 3.3 Hz), 8.44(1H, d, J = 8.1 Hz), 8.62(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3415, 2989, 2527, 1778, 1725, 1672, 1630, 1537, 1500, 1467, 1373, 1328, 1229, 1162, 1129, 1063, 1035.

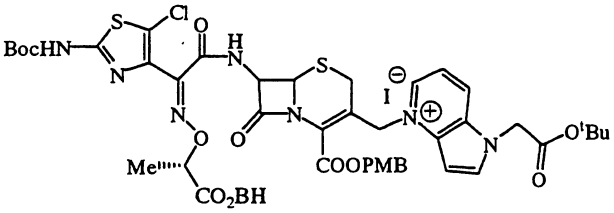
MS(ESI): $664^+(M+H^+)$.

元素分析 $C_{25}H_{22}ClN_7O_9S_2 \cdot 3.0\ H_2O$.

計算值： C,41.81 ; H,3.93 ; N,13.65 ; Cl,4.94; S,8.93 (%).

實驗值： C,41.75 ; H,3.89 ; N,13.71 ; Cl,5.08; S,8.84 (%).

四級鹽酯：



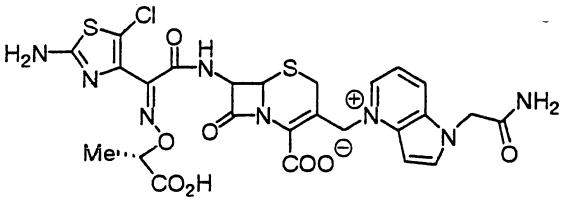
^{1}H-NMR (d_6-DMSO) δ: 1.42(3H, d, J = 7.2 Hz), 1.44(9H, s), 1.46(9H, s), 3.37(2H, brs), 3.75(3H, s), 4.89(1H, q, J = 7.2 Hz), 5.20(1H, d, J = 5.1 Hz), 5.21 及 5.29(2H, Abq, J = 12.0 Hz), 5.38(2H, brs), 5.72(2H, brs), 5.96(1H, dd, J = 5.1 及 8.7 Hz), 6.82(1H, s), 6.89(2H, d, J = 8.7 Hz), 7.00(1H, d, J = 3.3 Hz), 7.22-7.42(12H, m), 7.80(1H, dd, J = 6.3 及 8.4 Hz), 8.31(1H, d, J = 3.3 Hz), 8.62(1H, d, J = 6.3 Hz), 8.82(1H, d, J = 8.4 Hz), 9.76(1H, d, J = 8.7 Hz), 12.1(brs).

IR (KBr) cm^{-1}:3422, 3061, 3031, 2979, 2935, 1790, 1738, 1631, 1613, 1585,

1550, 1515, 1498, 1466, 1455, 1392, 1369, 1329, 1247, 1155, 1128, 1100, 1064, 1032.

MS(FAB): $1106^{+}(C_{55}H_{57}ClN_7O_{12}S_2^{+})$.

實施例１４４



^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 6.9 Hz), 3.20 及 3.37 (2H, ABq, J = 17.7 Hz), 4.64(1H, q, J = 6.9 Hz), 5.17(1H, d, J = 4.8 Hz), 5.27(2H, s), 5.56 及 5.73(2H, ABq, J = 15.0 Hz), 5.88(1H, d, J = 4.8 Hz), 7.06(1H, d, J = 3.3 Hz), 7.70(1H, dd, J = 6.3 及 8.1 Hz), 8.07(1H, d, J = 3.3 Hz), 8.51(1H, d, J = 8.1 Hz), 8.67(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3407, 3191, 2988, 1776, 1684, 1615, 1537, 1500, 1467, 1364, 1331, 1225, 1189, 1160, 1131, 1063, 1034.

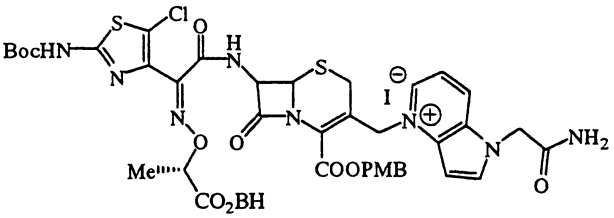
MS(ESI): $663^{+}(M+H^{+})$.

元素分析 $C_{25}H_{23}ClN_8O_8S_2 \cdot 3.9\ H_2O$.

計算値： C,40.95 ; H,4.23 ; N,15.28 ; Cl,4.83 ; S,8.74 (%).

實驗値： C,40.93 ; H,4.06 ; N,15.26 ; Cl,4.82 ; S,8.64 (%).

四級鹽酯：



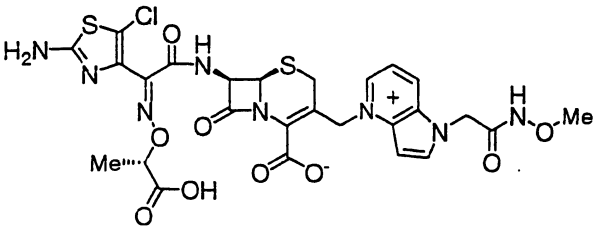
^{1}H-NMR (d_6-DMSO) δ: 1.45(3H, d, J = 6.9 Hz), 1.46(9H, s), 3.39(2H, brs), 3.75(3H, s), 4.89(1H, q, J = 6.9 Hz), 5.17(2H, brs), 5.20(1H, d, J = 4.8 Hz), 5.21 及 5.29(2H, Abq, J = 11.7 Hz), 5.70(2H, brs), 5.96(1H, dd, J = 4.8 及 8.7 Hz), 6.82(1H, s), 6.89(2H, d, J = 8.7 Hz), 6.96(1H, d, J = 3.3 Hz), 7.20-7.45(12H,

m), 7.76(1H, dd, J = 6.0 及 8.7 Hz), 7.79(2H, brs), 8.29(1H, d, J = 3.3 Hz), 8.58(1H, d, J = 6.0 Hz), 8.73(1H, d, J = 8.7 Hz), 9.76(1H, d, J = 8.7 Hz), 12.1(brs).

IR (KBr) cm^{-1}:3422, 3063, 2980, 2936, 1789, 1716, 1690, 1631, 1613, 1585, 1551, 1515, 1497, 1467, 1455, 1393, 1369, 1248, 1175, 1154, 1128, 1100, 1065, 1030, 1018.

MS(FAB): $1049^{+}(C_{51}H_{50}ClN_{8}O_{11}S_{2}^{+})$.

實施例１４５



^{1}H-NMR (D_2O) δ: 1.44(3H, d, J = 7.2 Hz), 3.20 及 3.37 (2H, ABq, J = 17.7 Hz), 3.73(3H, s), 4.65(1H, q, J = 7.2 Hz), 5.17(2H, s), 5.18(1H, d, J = 4.8 Hz), 5.56 及 5.73(2H, ABq, J = 15.0 Hz), 5.88(1H, d, J = 4.8 Hz), 7.06(1H, d, J = 3.3 Hz), 7.71(1H, dd, J = 6.3 及 8.1 Hz), 8.08(1H, d, J = 3.3 Hz), 8.53(1H, d, J = 8.1 Hz), 8.68(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3422, 2985, 2938, 1778, 1678, 1615, 1537, 1501, 1466, 1442, 1365, 1330, 1225, 1188, 1159, 1129, 1065, 1034.

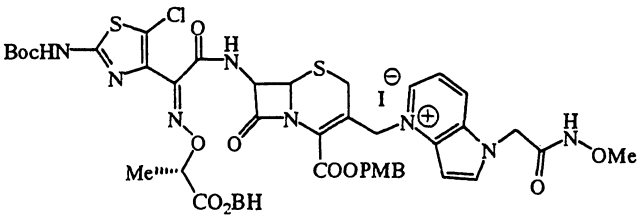
MS(FAB): $693^{+}(M+H^{+})$.

元素分析 $C_{26}H_{25}ClN_{8}O_{9}S_{2}\cdot 3.9\ H_2O$.

計算値： C,40.91 ; H,4.33 ; N,14.68 ; Cl,4.64 ; S,8.40 (%).

實驗値： C,40.78 ; H,4.14 ; N,14.77 ; Cl,4.67 ; S,8.54 (%).

四級鹽酯：

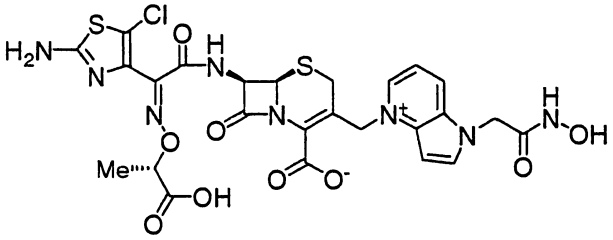


^{1}H-NMR (d_6-DMSO) δ : 1.44(3H, d, J = 7.2 Hz), 1.46(9H, s), 3.39(2H, brs), 3.68(3H, s), 3.76(3H, s), 4.89(1H, q, J = 7.2 Hz), 5.14(2H, brs), 5.20(1H, d, J = 4.8 Hz), 5.21 及 5.28(2H, Abq, J = 11.4 Hz), 5.71(2H, brs), 5.96(1H, dd, J = 4.8 及 8.7 Hz), 6.82(1H, s), 6.88(2H, d, J = 8.7 Hz), 6.98(1H, d, J = 3.0 Hz), 7.20-7.41(13H, m), 7.80(1H, dd, J = 6.0 及 8.1 Hz), 8.30(1H, d, J = 3.0 Hz), 8.59(1H, d, J = 6.0 Hz), 8.76(1H, d, J = 8.1 Hz), 9.76(1H, d, J = 8.7 Hz), 12.1(brs).

IR (KBr) cm^{-1}:3428, 3101, 3063, 3031, 2980, 2937, 1789, 1717, 1632, 1613, 1585, 1550, 1515, 1497, 1466, 1391, 1369, 1326, 1247, 1175, 1155, 1127, 1100, 1064, 1032, 1018.

MS(FAB): $1079^+(C_{52}H_{52}ClN_8O_{12}S_2^+)$.

實施例 146



^{1}H-NMR (D_2O) δ : 1.43(3H, d, J = 7.2 Hz), 3.19 及 3.37 (2H, ABq, J = 17.4 Hz), 4.65(1H, q, J = 7.2 Hz), 5.17(1H, d, J = 4.8 Hz), 5.19(2H, s), 5.56 及 5.72(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 4.8 Hz), 7.06(1H, d, J = 3.3 Hz), 7.71(1H, dd, J = 6.0 及 8.1 Hz), 8.08(1H, d, J = 3.3 Hz), 8.52(1H, d, J = 8.1 Hz), 8.68(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}:3415, 2988, 1777, 1675, 1615, 1537, 1500, 1466, 1365, 1330, 1225, 1188, 1161, 1129, 1064, 1036.

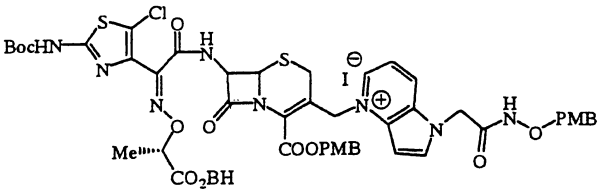
MS(FAB): $679^+(M+H^+)$.

元素分析 $C_{25}H_{23}ClN_8O_9S_2 \cdot 3.5\ H_2O$.

計算值： C,40.46 ; H,4.07 ; N,15.10 ; Cl,4.78 ; S,8.64 (%).

實驗值： C,40.45 ; H,4.00 ; N,15.08 ; Cl,4.72 ; S,8.57 (%).

四級鹽酯：

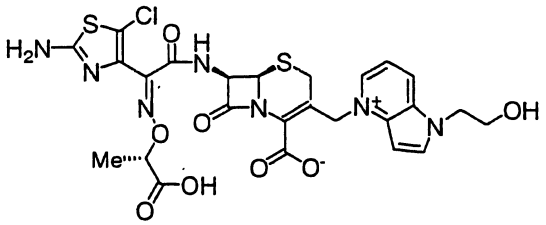


^{1}H-NMR (d_6-DMSO) δ : 1.45(3H, d, J = 7.2 Hz), 1.46(9H, s), 3.40(2H, brs), 3.75(6H, s), 4.74(2H, brs), 4.89(1H, q, J = 7.2 Hz), 5.13(2H, brs), 5.20(1H, d, J = 5.1 Hz), 5.21 及 5.28(2H, Abq, J = 12.0 Hz), 5.71(2H, brs), 5.96(1H, dd, J = 5.1 及 8.7 Hz), 6.82(1H, s), 6.89(2H, d, J = 8.7 Hz), 6.99(1H, d, J = 3.3 Hz), 7.19-7.49(13H, m), 7.79(1H, dd, J = 6.3 及 8.7 Hz), 8.29(1H, d, J = 3.3 Hz), 8.61(1H, d, J = 6.3 Hz), 8.71(1H, d, J = 8.7 Hz), 9.76(1H, d, J = 8.7 Hz), 12.1(brs).

IR (KBr) cm^{-1}:3421, 3063, 2978, 2936, 2836, 1790, 1716, 1631, 1612, 1585, 1549, 1514, 1497, 1465, 1369, 1325, 1248, 1176, 1154, 1125, 1100, 1064, 1030.

MS(FAB): 1185$^+$($C_{59}H_{58}ClN_8O_{13}S_2^+$).

實施例 147



^{1}H-NMR (D_2O) δ : 1.43(3H, d, J = 7.2 Hz), 3.18 及 3.34 (2H, ABq, J = 18.0 Hz), 3.97(2H, t, J = 4.8 Hz), 4.54(2H, t, J = 4.8 Hz), 4.64(1H, q, J = 7.2 Hz), 5.16(1H, d, J = 4.8 Hz), 5.53 及 5.71(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 4.8 Hz), 7.00(1H, d, J = 3.0 Hz), 7.67(1H, dd, J = 6.3 及 8.1 Hz), 8.12(1H, d, J = 3.0 Hz), 8.59(1H, d, J = 8.1 Hz), 8.62(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3408, 2938, 1776, 1670, 1615, 1539, 1496, 1466, 1447, 1362, 1322, 1240, 1187, 1159, 1130, 1072, 1034.

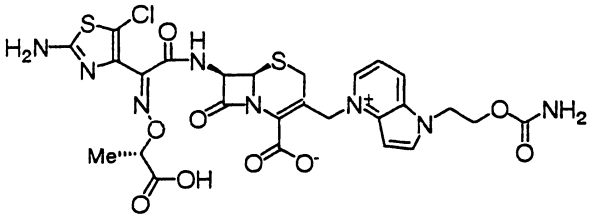
MS(FAB): 650$^+$(M+H$^+$).

元素分析 $C_{25}H_{24}ClN_7O_8S_2$ · 4.1 H_2O.

計算値： C,41.48 ; H,4.48 ; N,13.54 ; Cl,4.90 ; S,8.86 (%).

實驗値： C,41.48 ; H,4.40 ; N,13.59 ; Cl,5.07 ; S,8.88 (%).

實施例 148



^{1}H-NMR (D_2O) δ: 1.44(3H, d, J = 6.9 Hz), 3.16 及 3.31 (2H, ABq, J = 18.0 Hz), 4.43(2H, t, J = 4.5 Hz), 4.65(1H, q, J = 6.9 Hz), 4.68(2H, t, J = 4.5 Hz), 5.17(1H, d, J = 5.1 Hz), 5.54 及 5.71(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 5.1 Hz), 7.01(1H, d, J = 3.0 Hz), 7.69(1H, dd, J = 6.3 及 8.1 Hz), 8.12(1H, d, J = 3.0 Hz), 8.61(1H, d, J = 8.1 Hz), 8.63(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3415, 3193, 2987, 1777, 1718, 1673, 1614, 1537, 1497, 1466, 1447, 1364, 1328, 1225, 1188, 1135, 1080, 1034.

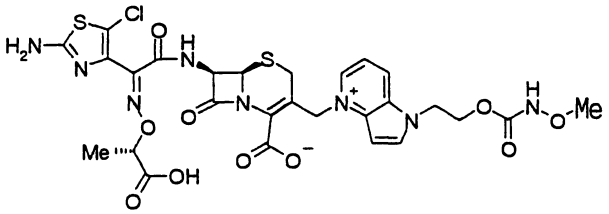
MS(FAB): $693^+(M+H^+)$.

元素分析 $C_{26}H_{25}ClN_8O_9S_2 \cdot 3.0\ H_2O$.

計算値： C,41.80 ; H,4.18 ; N,15.00 ; Cl,4.75 ; S,8.58 (%).

實驗値： C,41.68 ; H,4.19 ; N,14.79 ; Cl,4.78 ; S,8.91 (%).

實施例 149



^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 7.2 Hz), 3.15 及 3.31(2H, ABq, J = 17.7 Hz), 3.47(3H, s), 4.54(2H, t, J = 4.8 Hz), 4.64(1H, q, J = 7.2 Hz), 4.72(2H, t, J = 4.8 Hz), 5.17(1H, d, J = 4.8 Hz), 5.54 及 5.71(2H, ABq, J = 15.0 Hz), 5.87(1H,

d, J = 4.8 Hz), 7.02(1H, d, J = 3.3 Hz), 7.71(1H, dd, J = 6.3 及 8.4 Hz), 8.13(1H, d, J = 3.3 Hz), 8.62(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3416, 2984, 2939, 1778, 1731, 1674, 1615, 1538, 1498, 1466, 1445, 1364, 1326, 1286, 1264, 1189, 1123, 1035.

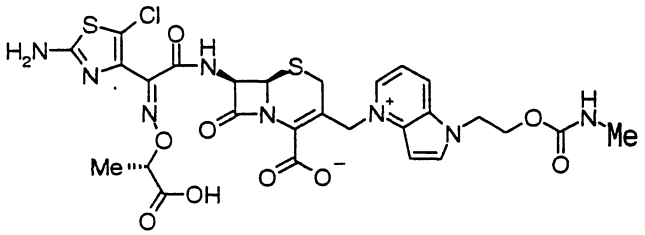
MS(FAB): $723^{+}(M+H^{+})$.

元素分析　$C_{27}H_{27}ClN_8O_{10}S_2 \cdot 3.7\ H_2O$.

計算値：　C,41.06 ; H,4.39 ; N,14.19 ; Cl,4.49 ; S,8.12 (%).

實驗値：　C,40.93 ; H,4.29 ; N,14.32 ; Cl,4.63 ; S,8.14 (%).

實施例 150



^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 7.2 Hz), 2.45(3H, s), 3.15 及 3.31(2H, ABq, J = 17.7 Hz), 4.44(2H, brs), 4.64(1H, q, J = 7.2 Hz), 4.69(2H, brs), 5.17(1H, d, J = 4.8 Hz), 5.54 及 5.71(2H, ABq, J = 15.3 Hz), 5.87(1H, d, J = 4.8 Hz), 7.01(1H, d, J = 3.0 Hz), 7.69(1H, dd, J = 6.0 及 8.4 Hz), 8.11(1H, d, J = 3.0 Hz), 8.60(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}:3401, 2984, 1779, 1710, 1676, 1617, 1538, 1498, 1466, 1364, 1326, 1265, 1187, 1135, 1097, 1033.

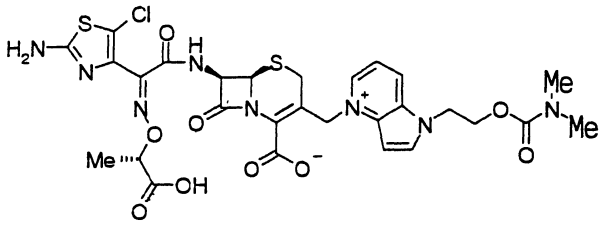
MS(FAB): $707^{+}(M+H^{+})$.

元素分析　$C_{27}H_{27}ClN_8O_9S_2 \cdot 3.5\ H_2O$.

計算値：　C,42.11 ; H,4.45 ; N,14.55 ; Cl,4.60 ; S,8.33 (%).

實驗値：　C,42.18 ; H,4.37 ; N,14.52 ; Cl,4.63 ; S,8.12 (%).

實施例 151



^{1}H-NMR (D_2O) δ : 1.43(3H, d, J = 7.2 Hz), 2.66(3H, s), 2.70(3H, s), 3.14 及 3.30(2H, ABq, J = 17.7 Hz), 4.46(2H, t, J = 4.8 Hz), 4.64(1H, q, J = 7.2 Hz), 4.72(2H, t, J = 4.8 Hz), 5.17(1H, d, J = 5.1 Hz), 5.55 及 5.71(2H, ABq, J = 15.3 Hz), 5.87(1H, d, J = 5.1 Hz), 7.02(1H, d, J = 3.3 Hz), 7.70(1H, dd, J = 6.6 及 8.1 Hz), 8.15(1H, d, J = 3.3 Hz), 8.64(1H, d, J = 8.1 Hz), 8.65(1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}:3422, 2938, 1779, 1690, 1617, 1538, 1497, 1466, 1363, 1325, 1287, 1190, 1135, 1098, 1066, 1034.

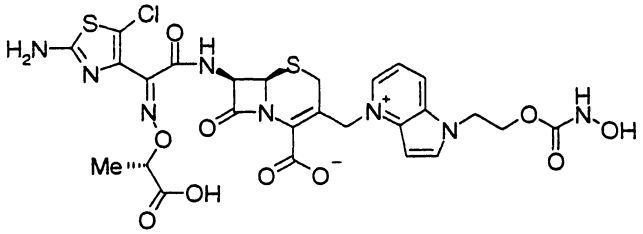
MS(FAB): $721^+(M+H^+)$.

元素分析 $C_{28}H_{29}ClN_8O_9S_2 \cdot 3.5\ H_2O$.

計算值： C,42.88 ; H,4.63 ; N,14.29 ; Cl,4.52 ; S,8.18 (%).

實驗值： C,42.81 ; H,4.62 ; N,14.23 ; Cl,4.50 ; S,8.38 (%).

實施例 152



^{1}H-NMR (D_2O) δ : 1.43(3H, d, J = 7.2 Hz), 3.17 及 3.32(2H, ABq, J = 17.7 Hz), 4.52(2H, t, J = 4.8 Hz), 4.65(1H, q, J = 7.2 Hz), 4.71(2H, t, J = 4.8 Hz), 5.17(1H, d, J = 4.8 Hz), 5.53 及 5.71(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 4.8 Hz), 7.00(1H, d, J = 3.3 Hz), 7.70(1H, dd, J = 6.0 及 8.4 Hz), 8.11(1H, d, J = 3.3 Hz), 8.61(1H, d, J = 8.4 Hz), 8.63(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}:3307, 2938, 1777, 1728, 1673, 1613, 1537, 1498, 1466, 1364, 1326, 1285, 1188, 1122, 1034.

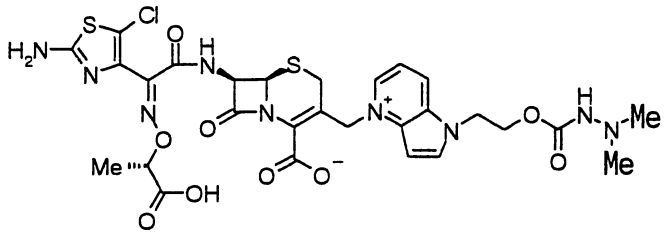
MS(FAB): $709^{+}(M+H^{+})$.

元素分析　$C_{26}H_{25}ClN_8O_{10}S_2 \cdot 3.5\ H_2O$.

計算值：C,40.44 ; H,4.18 ; N,14.51 ; Cl,4.59 ; S,8.31 (%).

實驗值：C,40.45 ; H,4.15 ; N,14.48 ; Cl,4.70 ; S,8.41 (%).

實施例 153



^{1}H-NMR (D_2O) δ: 1.44(3H, d, J = 7.2 Hz), 2.33(6H, s), 3.17 及 3.33(2H, ABq, J = 17.7 Hz), 4.48(2H, brs), 4.65(1H, q, J = 7.2 Hz), 4.69(2H, brs), 5.18(1H, d, J = 4.8 Hz), 5.54 及 5.71(2H, ABq, J = 14.7 Hz), 5.87(1H, d, J = 4.8 Hz), 7.03(1H, d, J = 3.3 Hz), 7.72(1H, dd, J = 6.0 及 8.7 Hz), 8.13(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 8.7 Hz), 8.64(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}:3412, 2900, 2960, 1779, 1723, 1671, 1626, 1541, 1498, 1466, 1449, 1427, 1364, 1326, 1286, 1244, 1187, 1163, 1135, 1114, 1035.

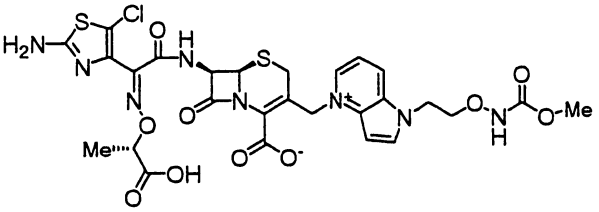
MS(FAB): $636^{+}(M+H^{+})$.

元素分析　$C_{28}H_{30}ClN_9O_9S_2 \cdot 4.2\ H_2O$.

計算值：C,41.42 ; H,4.77 ; N,15.53 ; Cl,4.37 ; S,7.90 (%).

實驗值：C,41.36 ; H,4.55 ; N,15.46 ; Cl,4.36 ; S,8.17 (%).

實施例 154



^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 6.9 Hz), 3.17 及 3.33(2H, ABq, J = 17.7 Hz), 3.62(3H, s), 4.29(2H, t, J = 4.8 Hz), 4.64(1H, q, J = 6.9 Hz), 4.69(2H, t, J

= 4.8 Hz), 5.17(1H, d, J = 4.5 Hz), 5.54 及 5.72(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 4.5 Hz), 7.02(1H, d, J = 3.3 Hz), 7.68(1H, dd, J = 6.3 及 8.4 Hz), 8.18(1H, d, J = 3.3 Hz), 8.61(1H, d, J = 8.4 Hz), 8.63(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3415, 2988, 2953, 1778, 1674, 1616, 1538, 1498, 1466, 1363, 1321, 1285, 1190, 1132, 1062, 1035.

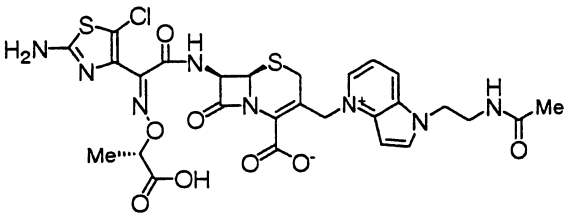
MS(FAB): $723^{+}(M+H^{+})$.

元素分析 $C_{27}H_{27}ClN_8O_{10}S_2 \cdot 4.1\ H_2O$.

計算值： C,40.69 ; H,4.45 ; N,14.06 ; Cl,4.45 ; S,8.05 (%).

實驗值： C,40.47 ; H,4.28 ; N,14.18 ; Cl,4.88 ; S,8.56 (%).

實施例 155



^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 6.9 Hz), 1.74(3H, s), 3.18 及 3.33(2H, ABq, J = 17.7 Hz), 3.62(2H, t, J = 5.4 Hz), 4.53(2H, t, J = 5.4 Hz), 4.65(1H, q, J = 6.9 Hz), 5.18(1H, d, J = 4.8 Hz), 5.53 及 5.71(2H, ABq, J = 14.7 Hz), 5.87(1H, d, J = 4.8 Hz), 6.99(1H, d, J = 3.0 Hz), 7.69(1H, dd, J = 6.3 及 8.4 Hz), 8.07(1H, d, J = 3.0 Hz), 8.57(1H, d, J = 8.4 Hz), 8.62(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3400, 2938, 1777, 1629, 1540, 1497, 1467, 1450, 1368, 1323, 1288, 1240, 1189, 1159, 1134, 1095, 1035.

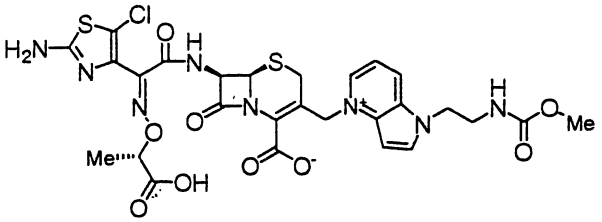
MS(FAB): $691^{+}(M+H^{+})$.

元素分析 $C_{27}H_{27}ClN_8O_8S_2 \cdot 4.1\ H_2O$.

計算值： C,41.51 ; H,4.77 ; N,14.34 ; Cl,4.54 ; S,8.21 (%).

實驗值： C,41.33 ; H,4.56 ; N,14.36 ; Cl,4.88 ; S,8.39 (%).

實施例 156



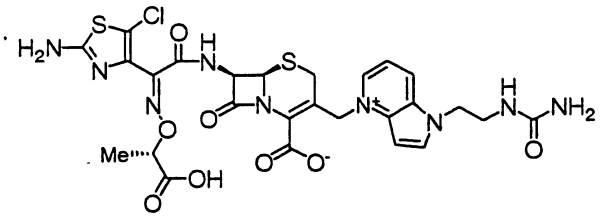
^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 7.5 Hz), 3.15 及 3.32(2H, ABq, J = 17.7 Hz), 3.91(3H, s), 3.57(2H, brs), 4.51(2H, m), 4.65(1H, q, J = 7.5 Hz), 5.17(1H, d, J = 4.8 Hz), 5.55 及 5.70(2H, ABq, J = 14.7 Hz), 5.87(1H, d, J = 4.8 Hz), 7.00(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.0 及 8.1 Hz), 8.09(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.1 Hz), 8.64(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}:3410, 2987, 2940, 1777, 1677, 1626, 1537, 1499, 1466, 1365, 1322, 1271, 1191, 1157, 1132, 1096, 1035.

MS(FAB): 07$^+$(M+H$^+$).

HR-MS(FAB): calcd for $C_{27}H_{28}ClN_8O_9S_2$ 707.1109 found 707.1106.

實施例 157



^{1}H-NMR (D_2O) δ: 1.44(3H, d, J = 6.9 Hz), 3.18 及 3.33(2H, ABq, J = 17.7 Hz), 3.54(2H, t, J = 4.5 Hz), 4.49(2H, t, J = 4.5 Hz), 4.65(1H, q, J = 6.9 Hz), 5.17(1H, d, J = 5.1 Hz), 5.52 及 5.70(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 5.1 Hz), 6.98(1H, d, J = 3.3 Hz), 7.67(1H, dd, J = 6.3 及 8.1 Hz), 8.07(1H, d, J = 3.3 Hz), 8.55(1H, d, J = 8.1 Hz), 8.60(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3375, 1773, 1660, 1609, 1543, 1497, 1466, 1451, 1362, 1288, 1240, 1188, 1159, 1133, 1098, 1035.

MS(FAB): 692$^+$(M+H$^+$).

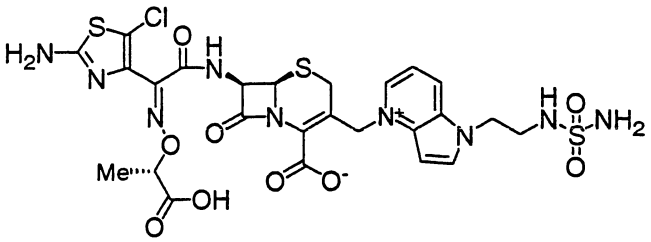
HR-MS(FAB): calcd for $C_{26}H_{27}ClN_9O_8S_2$ 692.1113 found 692.1100.

元素分析　$C_{26}H_{26}ClN_9O_8S_2 \cdot 4.3\ H_2O$.

計算值：　C,40.58 ; H,4.53 ; N,16.38 ; Cl,4.61 ; S,8.33 (%).

實驗值：　C,40.46 ; H,4.38 ; N,16.84 ; Cl,5.26 ; S,7.73 (%).

實施例 158



^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 7.2 Hz), 3.14 及 3.31(2H, ABq, J = 17.7 Hz), 3.53(2H, t-like), 4.57(2H, t-like), 4.64(1H, q, J = 7.2 Hz), 5.17(1H, d, J = 4.8 Hz), 5.54 及 5.70(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 4.8 Hz), 7.00(1H, d, J = 3.3 Hz), 7.68(1H, dd, J = 6.3 及 8.4 Hz), 8.13(1H, d, J = 3.3 Hz), 8.62(1H, d, J = 8.4 Hz), 8.62(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3316, 1775, 1671, 1611, 1538, 1497, 1467, 1448, 1363, 1326, 1241, 1157, 1134, 1097, 1035.

MS(FAB): $728^+(M+H^+)$.

元素分析　$C_{25}H_{26}ClN_9O_9S_3 \cdot 3.6\ H_2O$.

計算值：　C,37.86 ; H,4.22 ; N,15.90 ; Cl,4.47 ; S,12.13 (%).

實驗值：　C,37.88 ; H,4.10 ; N,15.92 ; Cl,4.37 ; S,12.00 (%).

IR (KBr) cm^{-1}:3316, 1775, 1671, 1611, 1538, 1497, 1467, 1448, 1363, 1326, 1241, 1157, 1134, 1097, 1035.

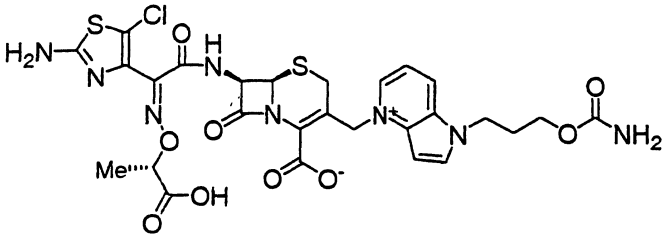
MS(FAB): $728^+(M+H^+)$.

元素分析　$C_{25}H_{26}ClN_9O_9S_3 \cdot 3.6\ H_2O$.

計算值：　C,37.86 ; H,4.22 ; N,15.90 ; Cl,4.47 ; S,12.13 (%).

實驗值：　C,37.88 ; H,4.10 ; N,15.92 ; Cl,4.37 ; S,12.00 (%).

實施例 159



^{1}H-NMR (D_2O) δ: 1.44(3H, d, J = 6.9 Hz), 2.25(2H, m), 3.17 及 3.33(2H, ABq, J = 17.7 Hz), 3.95(2H, t, J = 5.7 Hz), 4.54(2H, t, J = 6.3 Hz), 4.65(1H, q, J = 6.9 Hz), 5.17(1H, d, J = 5.1 Hz), 5.53 及 5.70(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 5.1 Hz), 7.00(1H, d, J = 3.3 Hz), 7.67(1H, dd, J = 6.3 及 8.4 Hz), 8.12(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.4 Hz), 8.61(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3402, 3193, 2985, 1777, 1710, 1673, 1612, 1539, 1497, 1457, 1362, 1331, 1239, 1189, 1132, 1103, 1078, 1036.

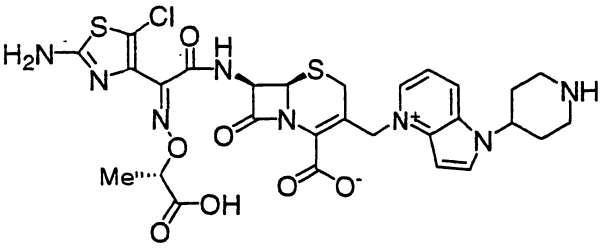
MS(FAB): $707^+(M+H^+)$.

元素分析 $C_{27}H_{27}ClN_8O_9S_2 \cdot 3.4\ H_2O$.

計算值： C,42.20 ; H,4.43 ; N,14.58 ; Cl,4.61 ; S,8.35 (%).

實驗值： C,42.19 ; H,4.34 ; N,14.60 ; Cl,4.54 ; S,8.23 (%).

實施例 160



^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 7.2 Hz), 2.26-2.42(4H, m), 3.15 及 3.34(2H, ABq, J = 17.7 Hz), 3.28(2H, dt, J = 3.0 及 12.6 Hz), 3.64(2H, d, J = 12.6 Hz), 4.65(1H, q, J = 7.2 Hz), 4.91-5.00(1H, m), 5.16(1H, d, J = 4.8 Hz), 5.55 及 5.69(2H, ABq, J = 15.0 Hz), 5.85(1H, d, J = 4.8 Hz), 7.06(1H, d, J = 3.6 Hz), 7.69(1H, dd, J = 6.3 及 8.4 Hz), 8.23(1H, d, J = 3.6 Hz), 8.64(1H, d, J = 8.4 Hz), 8.65(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3397, 2528, 1773, 1599, 1539, 1494, 1461, 1396, 1360, 1315,

1285, 1185, 1128, 1068, 1032.

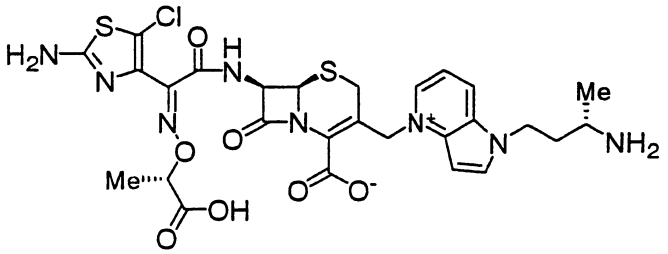
MS(FAB): $689^{+}(M+H^{+})$.

元素分析 $C_{28}H_{29}ClN_8O_7S_2 \cdot 6.5\ H_2O$.

計算值： C,41.71 ; H,5.25 ; N,13.90 ; Cl,4.40 ; S,7.95 (%).

實驗值： C,41.69 ; H,5.13 ; N,13.96 ; Cl,4.35 ; S,7.78 (%).

實施例 161



^{1}H-NMR (D_2O) δ : 1.36(3H, d, J = 6.9 Hz), 1.43(3H, d, J = 7.2 Hz), 2.10-2.37(2H, m), 3.16 及 3.36(2H, ABq, J = 17.7 Hz), 3.31-3.42(1H, m), 4.52(2H, t-like), 4.65(1H, q, J = 7.2 Hz), 5.17(1H, d, J = 4.8 Hz), 5.54 及 5.69(2H, ABq, J = 15.0 Hz), 5.85(1H, d, J = 4.8 Hz), 7.02(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.0 及 8.7 Hz), 8.14(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.7 Hz), 8.63(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}:3388, 2981, 1775, 1591, 1539, 1499, 1458, 1393, 1363, 1286, 1221, 1186, 1160, 1114, 1062, 1033.

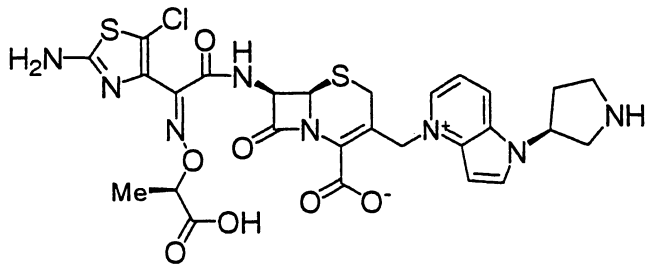
MS(FAB): $677^{+}(M+H^{+})$.

元素分析 $C_{27}H_{29}ClN_8O_7S_2 \cdot 5.4\ H_2O$.

計算值： C,41.87 ; H,5.18 ; N,14.47 ; Cl,4.58 ; S,8.28 (%).

實驗值： C,41.81 ; H,4.96 ; N,14.40 ; Cl,4.69 ; S,8.30 (%).

實施例 162



^{1}H-NMR (D_2O) δ : 1.42(3H, d, J = 6.9 Hz), 2.30(1H, m), 2.54(1H, m), 3.19 及 3.33(2H, ABq, J = 18.0 Hz), 3.42-3.59(2H, m), 3.72-3.78(1H, m), 3.88-3.94(1H, m), 4.63(1H, q, J = 6.9 Hz), 5.18(1H, d, J = 4.8 Hz), 5.36(1H, m), 5.53 及 5.72(2H, ABq, J = 15.3 Hz), 5.82(1H, d, J = 4.8 Hz), 7.00(1H, d, J = 3.6 Hz), 7.69(1H, dd, J = 6.0 及 8.4 Hz), 8.08(1H, d, J = 3.6 Hz), 8.62(1H, d, J = 6.0 Hz), 8.63(1H, d, J = 8.4 Hz).

IR (KBr) cm^{-1}:3387, 1770, 1667, 1605, 1543, 1495, 1461, 1399, 1359, 1321, 1285, 1202, 1149, 1131, 1081, 1058, 1029.

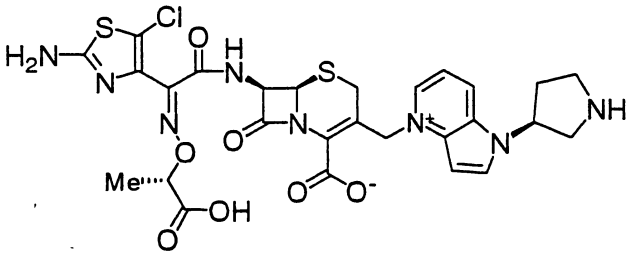
MS(ESI): $675^+(M+H^+)$.

元素分析 $C_{27}H_{27}ClN_8O_7S_2 \cdot 6.0\ H_2O \cdot 0.2(C_3H_7OH)$.

計算值： C,41.68 ; H,5.15 ; N,14.09 ; Cl,4.46 ; S,8.06 (%).

實驗值： C,41.53 ; H,5.05 ; N,14.16 ; Cl,4.35 ; S,7.82 (%).

實施例 163



^{1}H-NMR (D_2O) δ : 1.44(3H, d, J = 7.2 Hz), 2.30(1H, m), 2.53(1H, m), 3.19 及 3.33(2H, ABq, J = 17.7 Hz), 3.42-3.59(2H, m), 3.72-3.78(1H, m), 3.88-3.94 (1H, m), 4.66(1H, q, J = 7.2 Hz), 5.18(1H, d, J = 5.1 Hz), 5.38(1H, m), 5.52 及 5.71(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 5.1 Hz), 7.00(1H, d, J = 3.6 Hz),7.69(1H, dd, J = 6.3 及 8.4 Hz), 8.08(1H, d, J = 3.6 Hz), 8.62 (1H, d, J = 6.3 Hz), 8.64(1H, d, J = 8.4 Hz).

IR (KBr) cm^{-1}:3406, 2978, 1772, 1601, 1541, 1497, 1461, 1395, 1364, 1313, 1287, 1222, 1186, 1161, 1132, 1094, 1065, 1034.

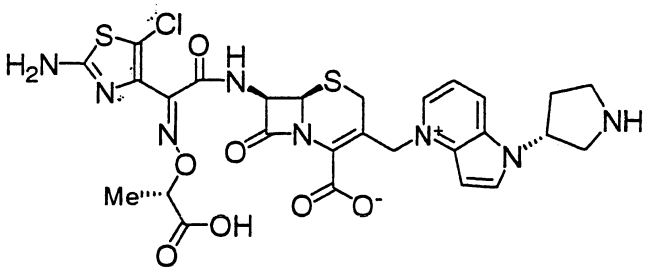
MS(ESI): $675^+(M+H^+)$.

元素分析 $C_{27}H_{27}ClN_8O_7S_2 \cdot 3.2\ H_2O \cdot 0.45(C_3H_7OH)$.

計算値： C,44.81 ; H,4.91 ; N,14.75 ; Cl,4.67 ; S,8.44 (%).

實驗値： C,44.79 ; H,4.97 ; N,14.64 ; Cl,4.61 ; S,8.28 (%).

實施例 164



^{1}H-NMR (D_2O) δ: 1.44(3H, d, J = 7.2 Hz), 2.30(1H, m), 2.54(1H, m), 3.19 及 3.33(2H, ABq, J = 18.0 Hz), 3.42-3.59(2H, m), 3.72-3.77(1H, m), 3.88-3.94 (1H, m), 4.65(1H, q, J = 7.2 Hz), 5.18(1H, d, J = 4.8 Hz), 5.38(1H, m), 5.52 及 5.72(2H, ABq, J = 14.7 Hz), 5.88(1H, d, J = 4.8 Hz), 7.00(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.0 及 8.4 Hz), 8.08(1H, d, J = 3.3 Hz), 8.62(1H, d, J = 6.0 Hz), 8.65(1H, d, J = 8.4 Hz).

IR (KBr) cm^{-1}:3397, 2982, 1773, 1602, 1540, 1497, 1462, 1395, 1364, 1316, 1287, 1186, 1132, 1092, 1064, 1034.

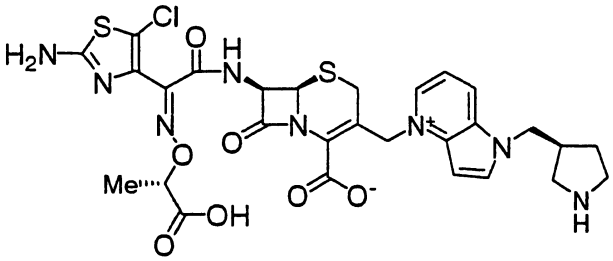
MS(ESI): $675^+(M+H^+)$.

元素分析 $C_{27}H_{27}ClN_8O_7S_2 \cdot 5.0\ H_2O \cdot 0.1(C_3H_7OH)$.

計算値： C,42.52 ; H,4.94 ; N,14.53 ; Cl,4.60 ; S,8.32 (%).

實驗値： C,42.54 ; H,4.95 ; N,14.29 ; Cl,5.01 ; S,8.09 (%).

實施例 165



^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 6.9 Hz), 1.76-1.89(1H, m), 2.08-2.18(1H, m), 2.98-3.52(5H, m), 3.18 及 3.37(2H, ABq, J = 18.3 Hz), 4.55(2H, d, J = 6.3Hz), 4.65(1H, q, J = 6.9 Hz), 5.18(1H, d, J = 4.8 Hz), 5.55 及 5.70(2H, ABq, J =

15.0 Hz), 5.86(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.3 Hz), 7.70(1H, dd, J = 6.3 及 8.1 Hz), 8.15(1H, d, J = 3.3 Hz), 8.63(1H, d, J = 8.1 Hz), 8.65(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3397, 2982, 1774, 1602, 1539, 1499, 1454, 1391, 1363, 1319, 1286, 1185, 1158, 1129, 1092, 1064, 1033.

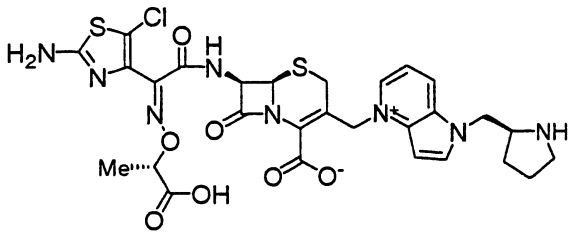
MS(FAB): $689^{+}(M+H^{+})$.

元素分析 $C_{28}H_{29}ClN_8O_7S_2 \cdot 4.9\ H_2O$.

計算值： C,43.26 ; H,5.03 ; N,14.41 ; Cl,4.56 ; S,8.25 (%).

實驗值： C,43.23 ; H,5.01 ; N,14.42 ; Cl,4.47 ; S,8.14 (%).

實施例 166



^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 6.9 Hz), 1.81-1.94(1H, m), 2.02-2.34(3H, m), 3.18 及 3.39(2H, ABq, J = 17.7 Hz), 3.26-3.49(2H, m), 4.09-4.19(1H, m), 4.65(1H, q, J = 6.9 Hz), 4.75(2H, brs), 5.18(1H, d, J = 4.8 Hz), 5.57 及 5.71(2H, ABq, J = 15.3 Hz), 5.86(1H, d, J = 4.8 Hz), 7.10(1H, d, J = 3.0 Hz), 7.74(1H, dd, J = 6.3 及 8.4 Hz), 8.17(1H, d, J = 3.0 Hz), 8.66(1H, d, J = 8.4 Hz), 8.69(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3396, 2982, 1775, 1602, 1540, 1501, 1465, 1391, 1364, 1287, 1186, 1158, 1131, 1092, 1064, 1033.

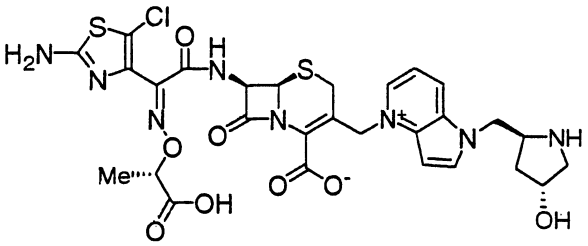
MS(FAB): $689^{+}(M+H^{+})$.

元素分析 $C_{28}H_{29}ClN_8O_7S_2 \cdot 4.9\ H_2O$.

計算值： C,43.26 ; H,5.03 ; N,14.41 ; Cl,4.56 ; S,8.25 (%).

實驗值： C,43.54 ; H,5.01 ; N,14.32 ; Cl,4.40 ; S,7.96 (%).

實施例 167



^{1}H-NMR (D_2O) δ: 1.44(3H, d, J = 7.2 Hz), 2.02-2.31(2H, m), 3.18 及 3.40(2H, ABq, J = 17.7 Hz), 3.30(1H, d, J = 12.9 Hz), 3.65(1H, dd, J = 4.8 及 12.9 Hz), 4.37-4.50(1H, m), 4.66(1H, q, J = 7.2 Hz), 4.63-4.74(1H, m), 4.86(2H, m), 5.19(1H, d, J = 5.1 Hz), 5.58 及 5.71(2H, ABq, J = 15.0 Hz), 5.86(1H, d, J = 5.1 Hz), 7.12(1H, d, J = 3.3 Hz), 7.75(1H, dd, J = 6.0 及 8.4 Hz), 8.19(1H, d, J = 3.3 Hz), 8.67(1H, d, J = 8.4 Hz), 8.69(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}:3395, 2984, 1774, 1603, 1539, 1502, 1465, 1392, 1364, 1322, 1287, 1221, 1186, 1132, 1091, 1066, 1034.

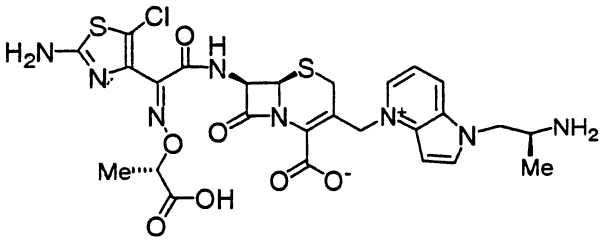
MS(FAB): $705^+(M+H^+)$.

元素分析 $C_{28}H_{29}ClN_8O_8S_2 \cdot 4.5\ H_2O$.

計算值： C,42.77 ; H,4.87 ; N,14.25 ; Cl,4.51 ; S,8.16 (%).

實驗值： C,42.69 ; H,4.51 ; N,14.46 ; Cl,4.36 ; S,8.04 (%).

實施例 168



^{1}H-NMR (D_2O) δ: 1.39(3H, d, J = 6.6 Hz), 1.43(3H, d, J = 6.9 Hz), 3.18 及 3.38(2H, ABq, J = 17.7 Hz), 3.99(1H, q-like), 4.65(1H, q, J = 6.9 Hz), 4.66(2H, t-like), 5.18(1H, d, J = 4.8 Hz), 5.57 及 5.71(2H, ABq, J = 15.0 Hz), 5.86(1H, d, J = 4.8 Hz), 7.11(1H, d, J = 3.0 Hz), 7.74(1H, dd, J = 6.3 及 8.4 Hz), 8.14(1H, d, J = 3.0 Hz), 8.64(1H, d, J = 8.4 Hz), 8.69(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3397, 2983, 1773, 1597, 1539, 1502, 1466, 1395, 1364, 1325,

1289, 1181, 1112, 1063, 1033.

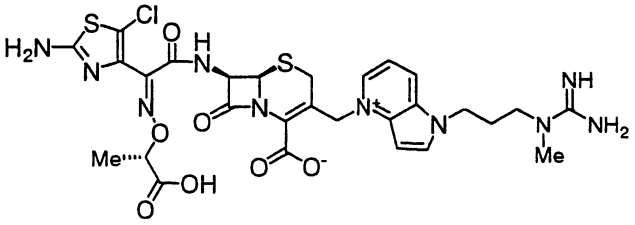
MS(FAB): 663⁺(M+H⁺).

元素分析 $C_{28}H_{27}ClN_8O_7S_2 \cdot 4.7\ H_2O$.

計算值： C,41.76 ; H,4.91 ; N,14.98 ; Cl,4.74 ; S,8.58 (%).

實驗值： C,41.81 ; H,4.80 ; N,14.92 ; Cl,4.70 ; S,8.59 (%).

實施例 169



^{1}H-NMR (D_2O) δ : 1.43(3H, d, J = 7.2 Hz), 2.31(2H, quintet, J = 7.2 Hz), 2.91(3H, s), 3.17 及 3.37(2H, ABq, J = 17.7 Hz), 3.38(2H, t, J = 7.2 Hz), 4.48(2H, t, J = 7.2 Hz), 4.65(1H, q, J = 7.2 Hz), 5.18(1H, d, J = 4.8 Hz), 5.56 及 5.69(2H, ABq, J = 15.0 Hz), 5.85(1H, d, J = 4.8 Hz), 7.05(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.0 及 8.7 Hz), 8.14(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.7 Hz), 8.64(1H, d, J = 6.0 Hz).

IR (KBr) cm⁻¹:3373, 1774, 1600, 1540, 1498, 1457, 1392, 1363, 1321, 1286, 1184, 1127, 1082, 1033.

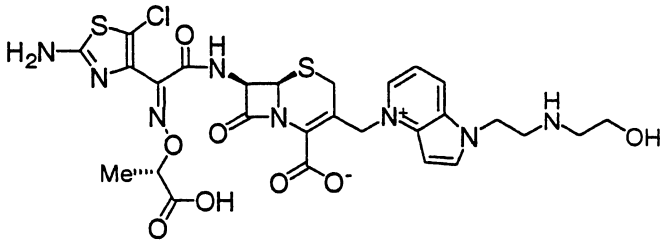
MS(FAB): 719⁺(M+H⁺).

元素分析 $C_{28}H_{31}ClN_{10}O_7S_2 \cdot 4.3\ H_2O$.

計算值： C,42.21 ; H,5.01 ; N,17.58 ; Cl,4.45 ; S,8.05 (%).

實驗值： C,42.28 ; H,4.87 ; N,17.55 ; Cl,4.19 ; S,7.84 (%).

實施例 170



^{1}H-NMR (D_2O) δ: 1. 43(3H, d, J = 7.2 Hz), 3.17 及 3.38(2H, ABq, J = 17.7 Hz), 3.22(2H, m), 3.69(2H, t, J = 6.3 Hz), 3.81(2H, m), 4.65(1H, q, J = 7.2 Hz), 4.83(2H, t, J = 6.3 Hz), 5.18(1H, d, J = 4.8 Hz), 5.57 及 5.71(2H, ABq, J = 15.0 Hz), 5.86(1H, d, J = 4.8 Hz), 7.10(1H, d, J = 3.3 Hz), 7.74(1H, dd, J = 6.0 及 8.4 Hz), 8.16(1H, d, J = 3.3 Hz), 8.64(1H, d, J = 8.4 Hz), 8.69(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1}:3385, 1773, 1601, 1539, 1500, 1466, 1393, 1364, 1287, 1186, 1139, 1112, 1064, 1033.

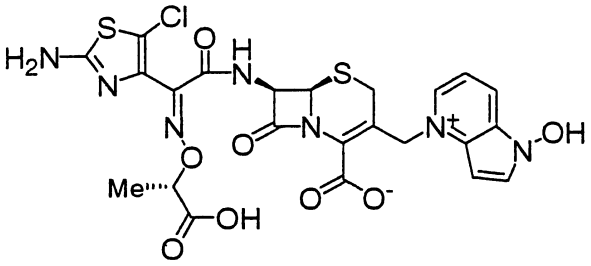
MS(FAB): $693^+(M+H^+)$.

元素分析 $C_{27}H_{29}ClN_8O_8S_2 \cdot 2.9\ H_2O$.

計算值： C,43.51 ; H,4.71 ; N,15.03 ; Cl,4.76 ; S,8.60 (%).

實驗值： C,43.61 ; H,4.80 ; N,15.12 ; Cl,4.48 ; S,8.21 (%).

實施例 171



^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 7.2 Hz), 3.19 及 3.28 (2H, ABq, J = 18.0 Hz), 4.64(1H, q, J = 7.2 Hz), 5.15(1H, d, J = 4.8 Hz), 5.41 及 5.65(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 4.8 Hz), 6.58(1H, d, J = 3.3 Hz), 7.43(1H, dd, J = 6.3 及 8.1 Hz), 7.90(1H, d, J = 3.3 Hz), 8.37(1H, d, J = 8.1 Hz), 8.40(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3468, 3144, 3116, 3099, 3080, 2980, 2951, 2924, 2870, 2341, 2276, 2256, 1934, 1891, 1754, 1618, 1580, 1499, 1449, 1429, 1365, 1345, 1309, 1237, 1227, 1208, 1187, 1159, 1114, 1054.

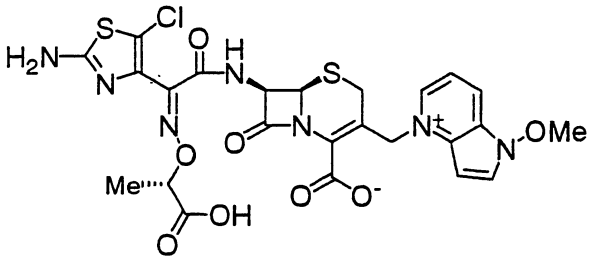
MS(FAB): $622^+(M+H^+)$.

元素分析 $C_{23}H_{20}ClN_7O_8S_2 \cdot 3.5\ H_2O$.

計算值： C,40.32 ; H,3.97 ; N,14.31 ; Cl,5.17 ; S,9.36 (%).

實驗值： C,40.38 ; H,3.90 ; N,14.23 ; Cl,5.36 ; S,9.25 (%).

實施例 172



^{1}H-NMR (D_2O) δ : 1.44(3H, d, J = 6.9 Hz), 3.18 及 3.37 (2H, ABq, J = 17.4 Hz), 4.26(s, 3H), 4.65(1H, q, J = 6.9 Hz), 5.18(1H, d, J = 4.8 Hz), 5.55 及 5.71(2H, ABq, J = 15.3 Hz), 5.88(1H, d, J = 4.8 Hz), 6.91(1H, d, J = 3.6 Hz), 7.74(1H, dd, J = 6.3 及 8.1 Hz), 8.31(1H, d, J = 3.6 Hz), 8.65(1H, d, J = 8.1 Hz), 8.68(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3410, 3134, 2941, 1778, 1674, 1614, 1537, 1457, 1364, 1234, 1211, 1188, 1155, 1120, 1058, 1034.

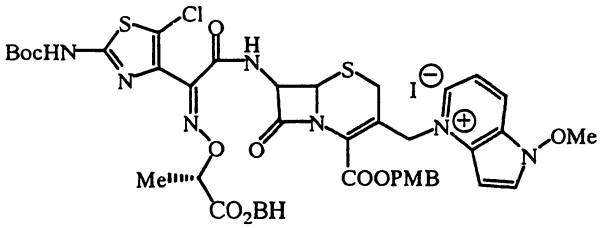
MS(ESI): $636^+(M+H^+)$.

元素分析 $C_{24}H_{22}ClN_7O_8S_2 \cdot 3.2\ H_2O$.

計算值： C,41.55 ; H,4.13 ; N,14.13 ; Cl,5.11 ; S,9.24 (%).

實驗值： C,41.62 ; H,4.21 ; N,14.26 ; Cl,4.90 ; S,9.08 (%).

四級鹽酯：



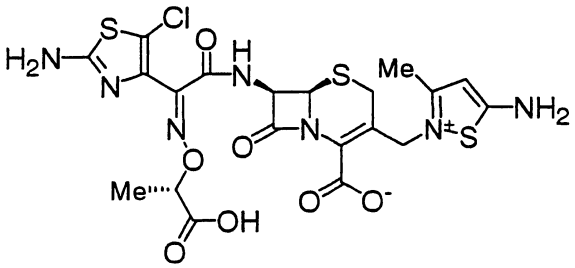
^{1}H-NMR (d_6-DMSO) δ : 1.44(3H, d, J = 6.9 Hz), 1.46(9H, s), 3.34 及 3.42(2H, Abq, J = 18.0 Hz), 3.76(3H, s), 4.26(3H, s), 4.89(1H, q, J = 6.9 Hz), 5.19(1H, d, J = 5.1 Hz), 5.22 及 5.29(2H, Abq, J = 11.7 Hz), 5.68 及 5.75(2H, Abq, J = 15.3 Hz), 5.97(1H, dd, J = 5.1 and 8.4 Hz), 6.82(1H, s), 6.89(2H, d, J = 9.0 Hz), 6.95(1H, d, J = 3.6 Hz), 7.20-7.42(12H, m), 7.84(1H, dd, J = 6.0 and 8.1

Hz), 8.67(1H, d, J = 6.0 Hz), 8.73(1H, d, J = 3.6 Hz), 8.86(1H, d, J = 8.1 Hz), 9.76(1H, d, J = 8.4 Hz), 12.1(brs).

IR (KBr) cm^{-1}:3394, 3131, 3091, 3061, 3031, 2978, 2937, 1789, 1719, 1632, 1613, 1549, 1515, 1495, 1455, 1391, 1368, 1247, 1176, 1154, 1119, 1063, 1032.

MS(FAB): $1222^{+}(C_{50}H_{49}ClN_7O_{11}S_2^{+})$.

實施例 173



^{1}H-NMR (D_2O) δ: 1.47(3H, d, J = 6.9 Hz), 2.43(3H, s), 3.26 及 3.62 (2H, ABq, J = 17.7 Hz), 4.66(1H, q, J = 6.9 Hz), 4.79 及 4.95(2H, ABq, J = 14.7 Hz), 5.26(1H, d, J = 4.8 Hz), 5.88(1H, d, J = 4.8 Hz), 6.26(1H, s).

IR (KBr) cm^{-1}:3312, 3190, 1776, 1671, 1617, 1535, 1460, 1392, 1337, 1187, 1134, 1100, 1064, 1034.

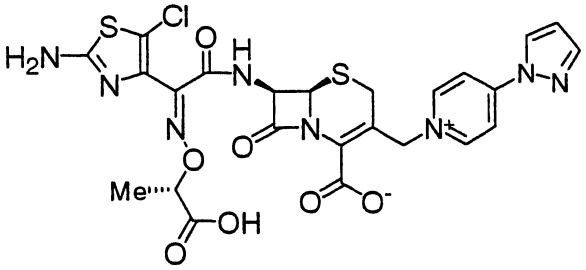
MS(FAB): $602^{+}(M+H^{+})$.

元素分析 $C_{20}H_{20}ClN_7O_7S_3 \cdot 2.5\ H_2O$.

計算值： C,37.12 ; H,3.89 ; N,15.15 ; Cl,5.48 ; S,14.87 (%).

實驗值： C,36.94 ; H,3.98 ; N,14.93 ; Cl,5.42 ; S,15.09 (%).

實施例 174



^{1}H-NMR (D_2O) δ: 1.44(3H, d, J = 7.2 Hz), 3.26 及 3.66(2H, ABq, J = 18.0 Hz), 4.64(1H, q, J = 7.2 Hz), 5.25 及 5.50(2H, ABq, J = 14.4 Hz), 5.28(1H, d, J =

4.8 Hz), 5.89(1H, d, J = 4.8 Hz), 6.78(1H, dd, J = 1.8 及 3.0 Hz), 8.04(1H, d, J = 1.8 Hz), 8.27 及 8.94(2H, ABq, J = 7.2 Hz), 8.53(1H, d, J = 3.0 Hz).

IR (KBr) cm^{-1}:3417, 3135, 1779, 1673, 1639, 1537, 1480, 1446, 1397, 1360, 1217, 1159, 1116, 1036.

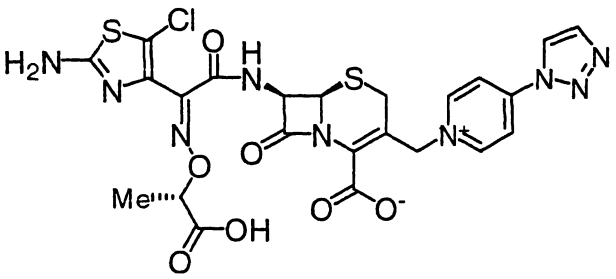
MS(FAB): $633^{+}(M+H^{+})$.

元素分析 $C_{24}H_{21}ClN_8O_7S_2 \cdot 2.7\ H_2O$.

計算值： C,42.29 ; H,3.90 ; N,16.44 ; Cl,5.20 ; S,9.41 (%).

實驗值： C,42.41 ; H,3.97 ; N,16.42 ; Cl,4.93 ; S,9.24 (%).

實施例 175



^{1}H-NMR (D_2O) δ: 1.44(3H, d, J = 6.9 Hz), 3.28 及 3.70(2H, ABq, J = 18.0 Hz), 4.65(1H, q, J = 6.9 Hz), 5.30(1H, d, J = 5.1 Hz), 5.36 及 5.63(2H, ABq, J = 14.7 Hz), 5.92(1H, d, J = 5.1 Hz), 8.07(1H, d, J = 1.8 Hz), 8.59 及 9.18(2H, ABq, J = 7.5 Hz), 8.85(1H, d, J = 1.8 Hz).

IR (KBr) cm^{-1}:3415, 3132, 1778, 1673, 1638, 1530, 1475, 1341, 1247, 1186, 1159, 1125, 1095, 1064, 1032.

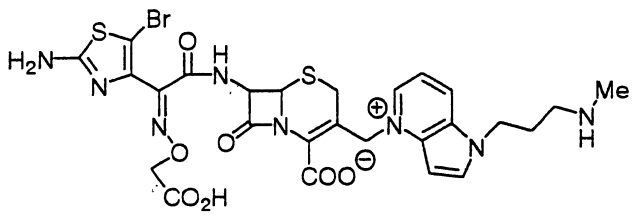
MS(FAB): $634^{+}(M+H^{+})$.

元素分析 $C_{23}H_{20}ClN_9O_7S_2 \cdot 2.6\ H_2O$.

計算值： C,40.57 ; H,3.73 ; N,18.51 ; Cl,5.21 ; S,9.42 (%).

實驗值： C,40.61 ; H,3.67 ; N,18.52 ; Cl,4.96 ; S,9.20 (%).

實施例 176



^{1}H-NMR (D_2O) δ: 2.30(2H, m), 2.67(3H, s), 3.0542H, m), 3.15 及 3.38 (2H, ABq, J = 17.7 Hz), 4.52(2H, t, J = 6.6 Hz), 4.55(2H, s), 5.17(1H, d, J = 4.8 Hz), 5.56 及 5.67(2H, ABq, J = 15.0 Hz), 5.85(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.3 Hz), 7.68(1H, dd, J = 6.3 及 8.1 Hz), 8.11(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.1 Hz), 8.64(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3418, 1771, 1607, 1534, 1497, 1466, 1391, 1360, 1317, 1152, 1119, 1052, 1020.

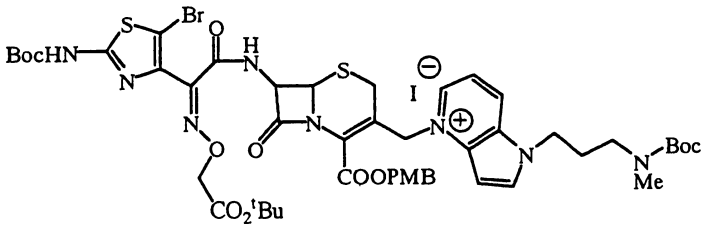
MS(ESI): $707^+(M+H^+)$.

元素分析 $C_{26}H_{27}BrN_8O_7S_2 \cdot 5.4\ H_2O$.

計算值： C,38.80 ; H,4.73 ; N,13.92 ; Br,9.93; S,7.97 (%).

實驗值： C,38.80 ; H,4.46 ; N,14.04 ; Br,9.66; S,8.01 (%).

四級鹽酯：

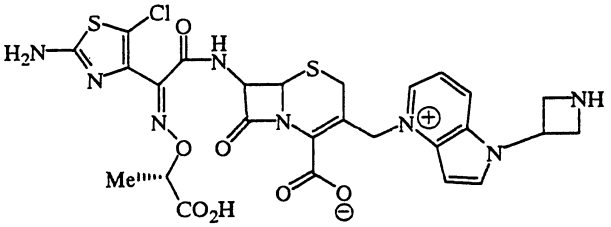


^{1}H-NMR (d_6-DMSO) δ: 1.40(9H, s), 1.46(18H, s), 2.03(2H, m), 2.78(3H, brs), 3.18(2H, t, J = 6.6 Hz), 3.26 及 3.43(2H, Abq, J = 18.3 Hz), 3.75(3H, s), 4.43(2H, t-like), 4.55(2H, s), 5.17(1H, d, J = 4.8 Hz), 5.21 及 5.28(2H, Abq, J = 11.7 Hz), 5.65 及 5.73(2H, ABq, J = 15.0 Hz), 5.94(1H, dd, J = 4.8 及 8.7 Hz), 6.88 及 7.32(4H, Abq, J = 8.7 Hz), 7.00(1H, d, J = 3.3 Hz), 7.79(1H, dd, J = 6.0 及 8.1 Hz), 8.43(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 6.0 Hz), 8.88(1H, d, J = 8.1 Hz), 9.61(1H, d, J = 8.7 Hz), 12.1(brs).

IR (KBr) cm^{-1}:3428, 3060, 2976, 2933, 1790, 1720, 1686, 1630, 1613, 1584, 1548, 1515, 1496, 1455, 1393, 1368, 1300, 1247, 1156, 1078, 1062, 1024.

MS(ESI): $1083^{+}(C_{48}H_{60}BrN_{8}O_{12}S_{2}^{+})$.

實施例 177



^{1}H-NMR (D_2O) δ: 1.43(3H, d, J = 6.9 Hz), 3.17 及 3.38(2H, ABq, J = 17.7 Hz), 4.65(1H, q, J = 6.9 Hz), 4.70-4.75(4H, m), 5.18(1H, d, J = 4.8 Hz), 5.57 及 5.71(2H, ABq, J = 15.3 Hz), 5.86(1H, d, J = 4.8 Hz), 5.95(1H, quintet-like), 7.20(1H, d, J = 3.6 Hz), 7.73(1H, dd, J = 6.3 及 8.4 Hz), 8.53(1H, d, J = 3.6 Hz), 8.60(1H, d, J = 8.4 Hz), 8.70(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}:3407, 2985, 2670, 1773, 1604, 1539, 1502, 1463, 1394, 1364, 1286,1185, 1136, 1090, 1064, 1032.

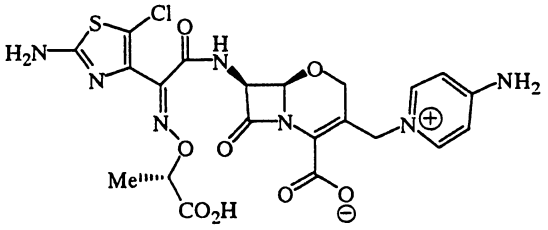
MS(FAB): $661^{+}(M+H^{+})$.

元素分析 $C_{26}H_{25}ClN_{8}O_{7}S_{2}\cdot 4.5\ H_{2}O$.

計算值： C,42.08 ; H,4.62 ; N,15.10 ; Cl,4.78 ; S,8.64 (%).

實驗值： C,42.05 ; H,4.60 ; N,15.23 ; Cl,4.50 ; S,8.34 (%).

實施例 178



^{1}H-NMR (D_2O) δ: 1.37(3H, d, J = 6.9 Hz), 4.34 及 4.41(2H, ABq, J = 17.4 Hz), 4.61(1H, q, J = 6.9 Hz), 4.87 及 5.21(2H, ABq, J = 14.7 Hz), 5.31(1H, d, J = 3.9 Hz), 5.65(1H, d, J = 3.9 Hz), 6.83 及 8.08(2H, ABq, J = 7.2 Hz).

IR (KBr) cm^{-1}:3344, 3197, 1781, 1655, 1538, 1444, 1402, 1372, 1349, 1279, 1240, 1210, 1171, 1109, 1064, 1034.

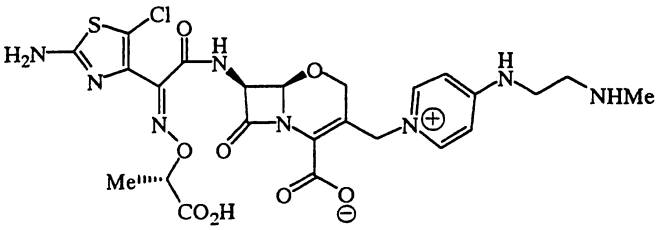
MS(FAB): $566^{+}(M+H^{+})$

元素分析 $C_{21}H_{20}ClN_7O_8S \cdot 3.0\ H_2O$.

計算値： C,40.68 ; H,4.23 ; N,15.81 ; Cl,5.72 ; S,5.17 (%).

實驗値： C,40.56 ; H,3.90 ; N,15.83 ; Cl,5.84 ; S,5.18 (%).

實施例 179



^{1}H-NMR (D_2O) δ: 1.38(3H, d, J = 7.2 Hz), 3.33(2H, t, J = 6.0 Hz), 3.73(2H, t, J = 6.0 Hz), 4.34 及 4.45(2H, ABq, J = 17.4 Hz), 4.63(1H, q, J = 7.2 Hz), 4.78 及 5.32(2H, ABq, J = 14.7 Hz), 5.33(1H, d, J = 3.9 Hz), 5.63(1H, d, J = 3.9 Hz), 6.83(2H, d-like), 8.08(2H, m).

IR (KBr) cm^{-1}:3396, 3067, 1779, 1649, 1601, 1556, 1448, 1403, 1371, 1350, 1279, 1217, 1171, 1107, 1063, 1033.

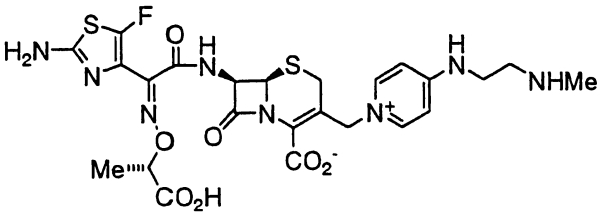
MS(FAB): $623^{+}(M+H^{+})$.

元素分析 $C_{24}H_{27}ClN_8O_8S \cdot 4.9\ H_2O$.

計算値： C,40.52 ; H,5.21 ; N,15.75 ; Cl,4.98 ; S,4.51 (%).

實驗値： C,40.36 ; H,4.96 ; N,15.90 ; Cl,5.12 ; S,4.67 (%).

實施例 180



^{1}H-NMR (D_2O) δ: 1.31 (3H, d, J = 7.2 Hz), 2.64 (3H, s), 3.03 (1H, d, J = 17.1

Hz), 3.21 (2H, t, J = 6.0 Hz), 3.45 (1H, d, J = 17.1 Hz), 3.61 (2H, t, J = 6.0 Hz), 4.51 (1H, q, J = 7.2 Hz), 4.76 (1H, d, J = 15.0 Hz), 4.97 (1H, d, J = 15.0 Hz), 5.10 (1H, d, J = 4.2 Hz), 5.70 (1H, d, J = 4.2 Hz), 6.81 (2H, d, J = 6.3 Hz), 8.01-8.13 (2H, m).

IR (KBr) cm^{-1}: 3388, 3066, 1773, 1650, 1590, 1557, 1533, 1450, 1394, 1355, 1320, 1289, 1217, 1169, 1094, 1064, 1036.

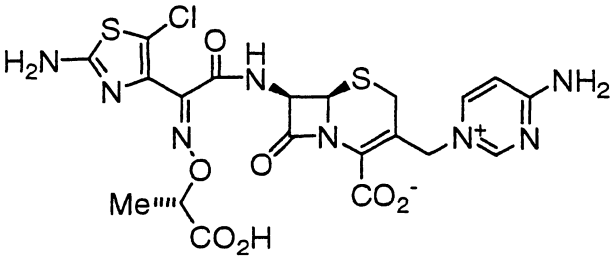
MS(FAB): 623^{+} $(M+H^{+})$.

元素分析 $C_{24}H_{27}FN_8O_7S_2 \cdot 3.8\ H_2O$.

計算値： C, 41.71; H, 5.05; N, 16.21; F, 2.75; S, 9.28 (%).

實驗値： C, 41.69; H, 4.92 ; N, 16.23; F, 2.51; S, 9.05 (%).

實施例 181



^{1}H-NMR (D_2O) δ : 1.52 (3H, d, J = 6.9 Hz), 3.25 (1H, d, J = 17.7 Hz), 3.63 (1H, d, J = 17.7 Hz), 4.84 (1H, q, J = 6.9 Hz), 4.88 (1H, d, J = 14.7 Hz), 5.06 (1H, d, J = 14.7 Hz), 5.26 (1H, d, J = 5.1 Hz), 5.87 (1H, d, J = 5.1 Hz), 6.85 (1H, d, J = 7.5 Hz), 8.21 (1H, dd, J = 1.5, 7.5 Hz), 8.68 (1H, d, J = 1.5 Hz).

IR (KBr) cm^{-1}: 3397, 3198, 1776, 1659, 1539, 1494, 1445, 1391, 1372, 1238, 1169, 1103, 1065, 1037.

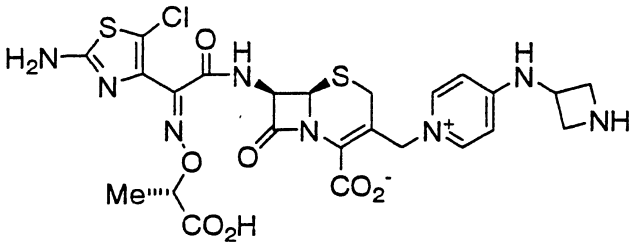
MS (FAB): 583 $(M+H)^{+}$, 1165 $(2M+H)^{+}$.

元素分析 $C_{20}H_{19}ClN_8O_7S_2 \cdot 2.1\ H_2O$.

計算値： C, 38.69; H, 3.77; N, 18.05; Cl, 5.71; S, 10.33 (%).

實驗値： C, 38.81; H, 3.70; N, 18.01; Cl, 5.54; S, 10.05 (%).

實施例 182



^{1}H-NMR (D_2O) δ: 1.44 (3H, d, J = 6.9 Hz), 3.16 (1H, d, J = 17.7 Hz), 3.57 (1H, d, J = 17.7 Hz), 4.21 (2H, m), 4.52 (2H, m), 5.11 (1H, d, J = 14.4 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 6.89 (2H, m), 8.23 (2H, m).

IR (KBr) cm^{-1}: 3399, 3059, 1772, 1649, 1601, 1551, 1445, 1361, 1288, 1217, 1167, 1095, 1065, 1035.

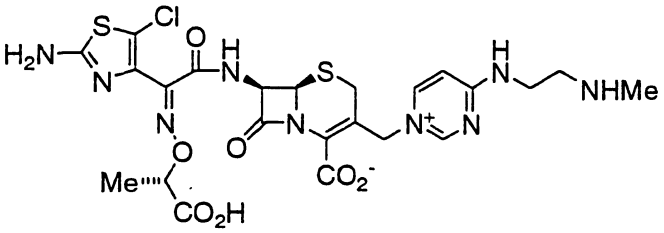
MS (FAB): 637 $(M+H)^+$, 1273 $(2M+H)^+$.

元素分析　$C_{24}H_{25}ClN_8O_7S_2 \cdot 2.2\ H_2O$.

計算値：　C, 42.60; H, 4.38; N, 16.56; Cl, 5.24; S, 9.48 (%).

實驗値：　C, 42.67; H, 4.31; N, 16.71; Cl, 5.16; S, 9.08 (%).

實施例 183



^{1}H-NMR (D_2O) δ: 1.33 (3H, d, J = 6.9 Hz), 2.62 (3H, s), 3.12 (1H, d, J = 18.0 Hz), 3.22 (2H, t, J = 5.7 Hz), 3.53 (1H, d, J = 18.0 Hz), 3.82 (2H, t, J = 5.7 Hz), 4.54 (1H, q, J = 6.9 Hz), 4.75 (1H, d, J = 14.7 Hz), 4.96 (1H, d, J = 14.7 Hz), 5.13 (1H, d, J = 5.1 Hz), 5.74 (1H, d, J = 5.1 Hz), 6.77 (1H, d, J = 7.5 Hz), 8.12 (1H, br d, J = 7.5 Hz), 8.70 (1H, br s).

IR (KBr) cm^{-1}: 3409, 1775, 1652, 1605, 1538, 1509, 1447, 1394, 1370, 1287, 1170, 1095, 1065, 1035.

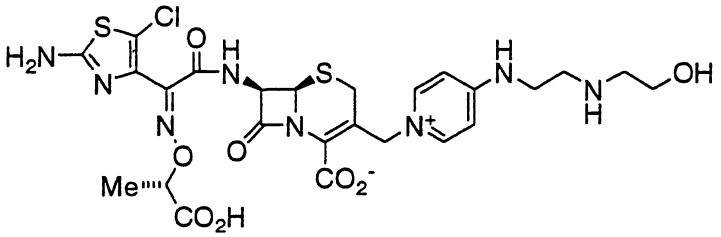
MS (FAB): 640 $(M+H)^+$, 1279 $(2M+H)^+$.

元素分析　$C_{23}H_{26}ClN_9O_7S_2 \cdot 3.5\ H_2O$.

計算値： C, 39.29; H, 4.73; N, 17.93; Cl, 5.04; S, 9.12 (%).

實驗値： C, 39.43; H, 4.68; N, 17.74; Cl, 5.00; S, 8.95 (%).

實施例 184



^{1}H-NMR (D_2O) δ : 1.45 (3H, d, J = 6.9 Hz), 3.17 (1H, d, J = 18.0 Hz), 3.24 (2H, t, J = 5.1 Hz), 3.39 (2H, t, J = 6.3 Hz), 3.57 (1H, d, J = 18.0 Hz), 3.77 (2H, t, J = 6.3 Hz), 3.85 (2H, t, J = 5.1 Hz), 4.66 (1H, q, J = 6.9 Hz), 4.88 (1H, d, J = 15.0 Hz), 5.09 (1H, d, J = 15.0 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 6.94 (2H, d, J = 6.9 Hz), 8.19 (2H, m).

IR (KBr) cm^{-1}: 3378, 1774, 1650, 1598, 1556, 1448, 1394, 1358, 1286, 1218, 1168, 1093, 1066, 1034.

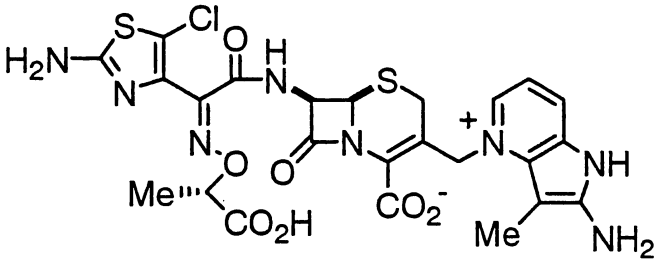
MS (FAB): 669 $(M+H)^+$.

元素分析 $C_{25}H_{29}ClN_8O_8S_2 \cdot 2.7\ H_2O$.

計算値： C, 41.83; H, 4.83; N, 15.61; Cl, 4.94; S, 8.93 (%).

實驗値： C, 41.76; H, 4.61; N, 15.80; Cl, 4.78; S, 8.65 (%).

實施例 185



^{1}H-NMR (d_6-DMSO) δ : 1.39 (3H, d, J = 6.9 Hz), 2.21 (3H, brs), 2.97 及 3.48 (2H, ABqt, J = 17.7 Hz), 4.57 (1H, q, J = 6.9 Hz), 5.09 (1H, d, J = 4.8 Hz), 5.41 (2H, brs), 5.77 (1H, dd, J = 4.8, 8.4 Hz), 6.75 (1H, t-like), 7.37-7.39 (3H, m), 7.70 (2H, brs), 8.05 (1H, d, J = 5.4 Hz), 9.96 (1H, brs), 13.5 (1H, brs).

IR (KBr) cm^{-1}:3339, 3195, 1773, 1646, 1603, 1567, 1479, 1424, 1394, 1338, 1286, 1227, 1190, 1161, 1094, 1035.

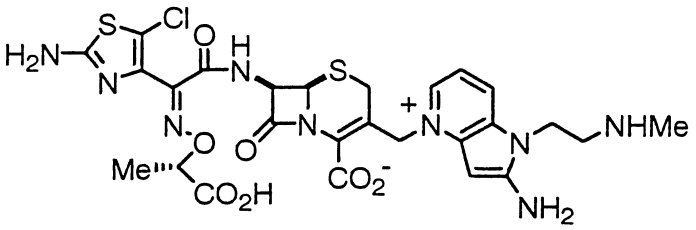
MS(FAB): 635^+ $(M+H)^+$.

元素分析　$C_{24}H_{23}ClN_8O_7S_2 \cdot 2.3\ H_2O$.

計算値：　C,42.61; H,4.11 ; N,16.56 ; Cl,5.24; S,9.48 (%).

實驗値：　C,42.72 ; H,4.27 ; N,16.53 ; Cl,5.02; S,9.13 (%).

實施例 186



^{1}H-NMR (D_2O + DCl) δ : 1.54 (3H, d, J = 7.5 Hz), 2.76 (3H, s), 3.24 及 3.46 (2H, ABqt, J = 18.6 Hz), 3.51 (2H, t, J = 6.3 Hz), 4.56 (2H, t, J = 6.3 Hz), 4.98 (1H, q, J = 7.5 Hz), 5.27 (1H, d, J = 4.8 Hz), 5.36 及 5.49 (2H, ABq, J = 15.9 Hz), 5.91 (1H, d, J = 4.8 Hz), 7.11 (1H, dd, J = 6.3, 7.8 Hz), 7.80 (1H, d, J = 7.8 Hz), 7.95 (1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}: 3369, 2457, 1761, 1646, 1564, 1475, 1435, 1398, 1360, 1317, 1284, 1191, 1164, 1092, 1036.

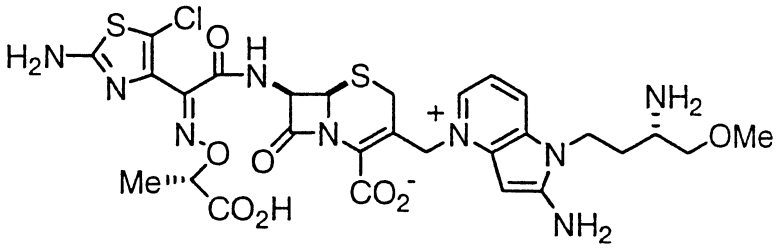
MS(FAB): 678^+ $(M+H)^+$

元素分析　$C_{26}H_{28}ClN_9O_7S_2 \cdot 3.2\ H_2O$.

計算値：　C,42.44; H,4.71 ; N,17.13 ; Cl,4.82; S,8.72 (%).

實驗値：　C,42.15 ; H,4.41 ; N,17.15 ; Cl,4.86; S,8.68 (%).

實施例 187



^{1}H-NMR (D_2O + DCl) δ : 1.55 (3H, d, J = 6.9 Hz), 2.16-2.24 (3H, m), 3.37 (1H, d, J = 18.3

Hz), 3.43 (3H, s), 3.57-3.76 (4H, m), 4.31 (2H, t, J = 8.1 Hz), 4.79 (1H, d, J = 5.1 Hz), 4.99 (1H, q, J = 6.9 Hz), 5.49 及 5.68 (2H, ABq, J = 15.0 Hz), 5.92 (1H, d, J = 5.1 Hz), 7.35 (1H, dd, J = 6.6, 7.8 Hz), 7.97 (1H, d, J = 7.8 Hz), 8.14 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}: 3378, 3183, 1773, 1650, 1565, 1495, 1441, 1395, 1352, 1316, 1287, 1223, 1165, 1095, 1034.

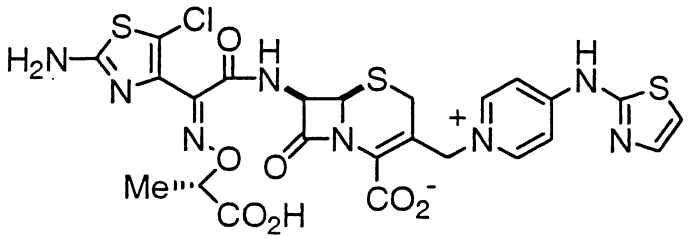
MS(FAB): 723^+ $(M+H)^+$

元素分析 $C_{27}H_{31}ClN_{10}O_8S_2 \cdot 2.6\ H_2O$.

計算值： C,42.11; H,4.74 ; N,18.19 ; Cl,4.60; S,8.33 (%).

實驗值： C,42.14 ; H,4.54 ; N,18.19 ; Cl,4.50; S,8.16 (%).

實施例 188



^{1}H-NMR (d_6-DMSO) δ : 1.39 (3H, d, J = 6.9 Hz), 3.07 及 3.49 (2H, d, J = 17.7 Hz), 4.56 (1H,q, J = 6.9 Hz), 4.92 及 5.38 (2H, ABq, J = 13.5 Hz), 5.07 (1H, d, J = 5.4 Hz), 5.73 (1H, dd, J = 5.4, 9.0 Hz), 7.35 (1H, d, J = 3.3 Hz), 7.40 (2H, brs), 7.54 (1H, d, J = 3.3 Hz), 8.05 (2H, brs), 8.90 (2H, brd, J = 7.2 Hz), 9.70 (1H, brs).

IR (KBr) cm^{-1}: 3416, 2984, 1777, 1643, 1547, 1515, 1476, 1461, 1348, 1204, 1161, 1102, 1063, 1036.

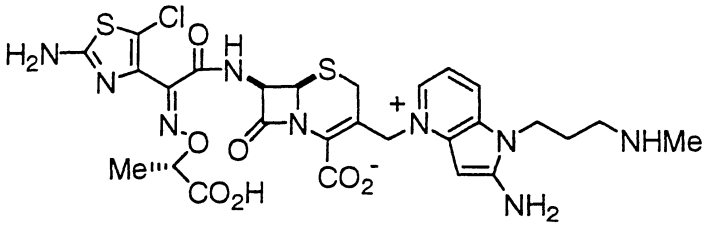
MS(FAB): 665^+ $(M+H)^+$.

元素分析 $C_{24}H_{21}ClN_8O_7S_3 \cdot 2.5H_2O$.

計算值： C,40.59; H,3.69; N,15.78; Cl,4.99; S,13.55 (%).

實驗值： C,40.41 ; H,3.62; N,16.01 ; Cl,5.03; S,13.25 (%).

實施例 189



^{1}H-NMR (D_2O + DCl) δ : 1.54 (3H, d, J = 6.9 Hz), 2.14-2.24 (2H, m), 2.71 (3H, s), 3.11 (2H, t, J = 8.4 Hz), 3.25 及 3.48 (2H, ABqt, J = 18.3 Hz), 4.28 (2H, t, J = 7.5 Hz), 4.99 (1H, q, J = 6.9 Hz), 5.29 (1H, d, J = 4.8 Hz), 5.34 及 5.51 (2H, ABq, J = 15.6 Hz), 5.91 (1H, d, J = 4.8 Hz), 7.08 (1H, dd, J = 6.6, 7.5 Hz), 7.78 (1H, d, J = 7.5 Hz), 7.91 (1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1}: 3341, 3177, 1772, 1646, 1564, 1473, 1439, 1394, 1346, 1284, 1190, 1162, 1092, 1058, 1034.

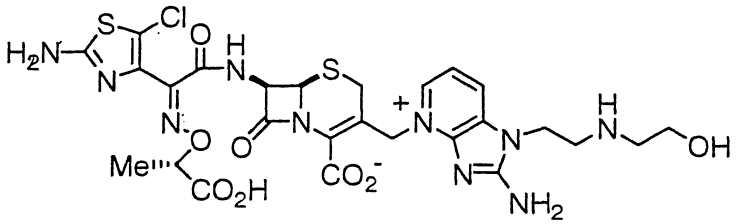
MS(FAB): 692^+ $(M+H)^+$.

元素分析 $C_{27}H_{30}ClN_9O_7S_2 \cdot 3.8\ H_2O$.

計算値： C,42.63; H,4.98 ; N,16.57 ; Cl,4.66; S,8.43 (%).

實驗値： C,42.69 ; H,4.81 ; N,16.49 ; Cl,4.67; S,8.51 (%).

實施例 190



^{1}H-NMR (D_2O+DCl) δ : 1.55 (3H, d, J = 6.9 Hz), 3.27 (2H, t, J = 8.3 Hz), 3.36 及 3.59 (2H, ABq, J = 18.3 Hz), 3.61 (2H, t, J = 6.8 Hz), 3.86 (2H, t, J = 8.3 Hz), 4.98 (1H, sept, J = 6.9 Hz), 5.27 (1H, d, J = 4.8 Hz), 5.47 及 5.70 (2H, ABq, J = 15.2 Hz), 7.32-7.38 (1H, m), 8.01 (1H, d, J = 7.5 Hz), 8.16 (1H, d, J = 6.9 Hz).

IR (KBr) cm^{-1}:3371, 3184, 1772, 1667, 1603, 1563, 1395, 1351, 1316, 1222, 1170, 1072, 1034, 984, 867, 758.

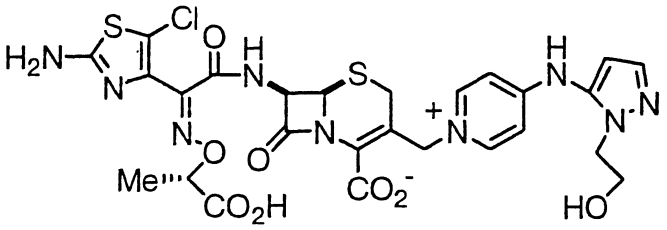
MS(FAB): 709^+ $(M+H)^+$.

元素分析 $C_{26}H_{29}ClN_{10}O_8S_2 \cdot 2.6\ H_2O$.

計算値： C,41.31 ; H,4.56 ; N,18.53 ; Cl,4.69; S,8.48 (%).

實驗値： C,41.22 ; H,4.37 ; N,18.51 ; Cl,5.27; S,8.25 (%).

實施例 191



^{1}H-NMR (d_6-DMSO) δ : 1.39 (3H, d, J = 6.9 Hz), 3.04 及 3.486 (2H, ABqt, J = 17.4 Hz), 3.67 (2H, t, J = 5.4 Hz), 4.07 (2H, t, J = 5.4 Hz), 4.57 (1H, q, J = 6.9 Hz), 4.84 及 5.30 (2H, ABq, J = 13.8 Hz), 5.06 (1H, d, J = 4.8 Hz), 5.72 (1H, dd, J = 4.8, 8.7 Hz), 6.31 (1H, d, J = 1.8 Hz), 7.14 (2H, brs), 7.41 (2H, brs), 7.57 (1H, d, J = 1.8 Hz), 8.72 (1H, d, J = 7.2 Hz), 9.65 (1H, brs), 10.8 (1H, brs).

IR (KBr) cm^{-1}: 3308, 2948, 1777, 1648, 1608, 1541, 1456, 1357, 1212, 1165, 1109, 1065, 1036.

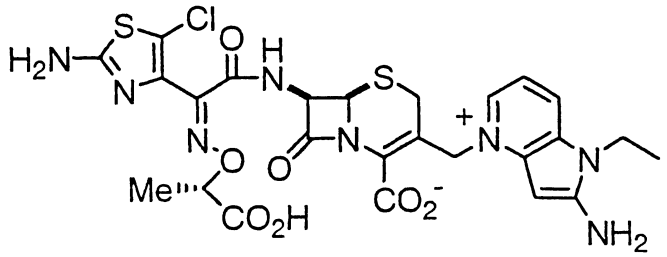
MS(FAB): 692^+ $(M+H)^+$.

元素分析 $C_{26}H_{26}ClN_9O_8S_2 \cdot 2.2\ H_2O$.

計算値： C,42.68; H,4.19 ; N,17.23 ; Cl,4.84; S,8.78 (%).

實驗値： C,42.79 ; H,4.10 ; N,17.32 ; Cl,4.47; S,8.45 (%).

實施例 192



^{1}H-NMR (d_6-DMSO) δ : 1.20 (3H, t, J = 6.9 Hz), 1.38 (3H, d, J = 7.2 Hz), 2.94 及 3.27 (2H, ABqt, J = 17.4 Hz), 4.16 (2H, q, J = 6.9 Hz), 4.55 (2H, q, J = 7.2 Hz), 5.00 (1H, d, J = 4.8 Hz), 5.22 及 5.34 (2H, ABq, J = 14.4 Hz), 5.68 (1H, dd, J = 4.8, 9.0 Hz), 6.05 (1H, s), 6.99 (1H, dd, J = 6.6, 7.5 Hz), 7.40 (2H, brs), 7.79 (1H, d, J = 7.5 Hz), 7.88 (2H, brs), 8.27 (1H, d, J =

6.6 Hz), 9.78 (1H, brs).

IR (KBr) cm^{-1}: 3346, 3189, 2985, 2936, 1777, 1646, 1594, 1563, 1474, 1441, 1386, 1342, 1285, 1191, 1162, 1098, 1036.

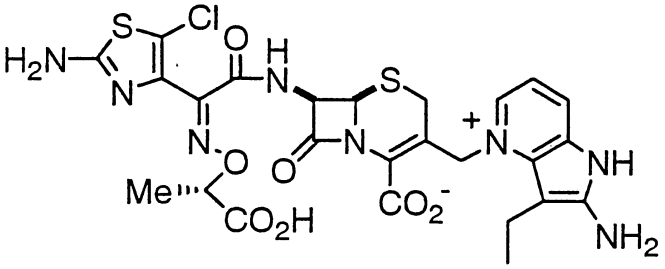
MS(FAB): 649^+ $(M+H)^+$.

元素分析　$C_{25}H_{25}ClN_8O_7S_2 \cdot 2.3\ H_2O$.

計算值：　C,43.48; H,4.32 ; N,16.23 ; Cl,5.13; S,9.29 (%).

實驗值：　C,43.48 ; H,4.21 ; N,16.28 ; Cl,4.80; S,8.98 (%).

實施例 193



^{1}H-NMR (d_6-DMSO) δ : 1.04 (3H, t, J = 7.2 Hz), 1.40 (3H, d, J = 6.9 Hz), 2.60-2.70 (2H, m), 2.97 及 3.49(2H, ABqt, J = 17.4 Hz), 4.57 (1H, q, J = 6.9 Hz), 5.10 (1H, d, J = 4.8 Hz), 5.24 及 5.46 (2H, ABq, J = 14.7 Hz), 5.78 (1H, dd, J = 4.8, 8.1 Hz), 6.75 (1H, t-like), 7.37-7.39 (3H, m), 7.72 (2H, brs), 8.00 (1H, brs), 9.92 (1H, brs), 13.1 (1H, brs).

IR (KBr) cm^{-1}: 3341, 3196, 2972, 2934, 1176, 1633, 1567, 1475, 1423, 1344, 1225, 1187, 1159, 1101, 1058, 1033.

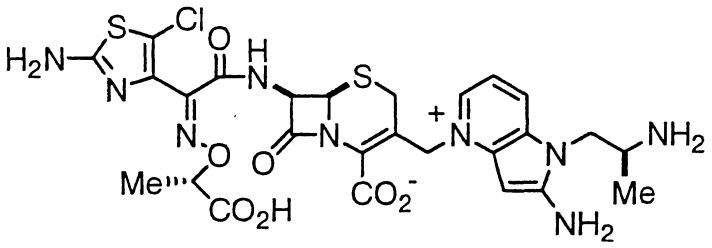
MS(FAB): 649^+ $(M+H)^+$.

元素分析　$C_{25}H_{25}ClN_8O_7S_2 \cdot 2.6H_2O$.

計算值：　C,43.15; H,4.37 ; N,16.10 ; Cl,5.09; S,9.21 (%).

實驗值：　C,43.25 ; H,4.18 ; N,16.06 ; Cl,4.81; S,8.86 (%).

實施例 194



^{1}H-NMR (D_2O + DCl) δ : 1.41 (3H, d, J = 6.3 Hz), 1.54 (3H., d, J = 6.9 Hz), 3.26 及 3.49 (2H, ABqt, J = 18.3 Hz), 3.87-3.99 (1H, m), 4.35-4.49 (2H, m),5.29 (1H, d, J = 4.8 Hz), 5.36 及 5.53 (2H, ABq, J = 15.3 Hz), 5.91 (1H, d, J = 4.8 Hz), 7.11 (1H, dd, J = 6.3, 7.8 Hz), 7.83 (1H, d, J = 7.8 Hz), 7.95 (1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1}: 3353, 3176, 1756, 1647, 1561, 1436, 1398, 1355, 1318, 1284, 1236, 1165, 1092, 1036.

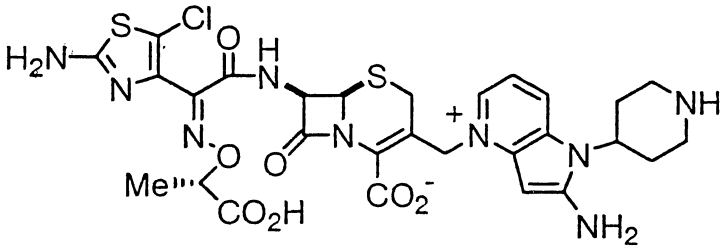
MS(FAB): 678^+ $(M+H)^+$.

元素分析 $C_{26}H_{29}ClN_9O_7S_2 \cdot 3.2\ H_2O$.

計算值： C,42.38; H,4.84 ; N,17.11 ; Cl,4.81; S,8.70 (%).

實驗值： C,42.46 ; H,4.69 ; N,17.11 ; Cl,4.58; S,8.47 (%).

實施例 195



^{1}H-NMR (D_2O+DCl) δ : 1.54 (3H, d, J = 6.9 Hz), 2.24 (3H, s), 2.26 (2H, d-like), 2.62-2.74 (2H, m), 3.19-3.34 (3H, m), 3.46 (1H, d, J = 18.3 Hz), 3.72 (2H, d-like), 4.69-4.78 (1H, m), 4.99 (1H, q, J = 6.9 Hz), 5.29 (1H, d, J = 4.8 Hz), 5.35 及 5.53 (2H, ABq, J = 15.6 Hz), 5.91 (1H, t-like), 7.08 (1H, t-like), 7.94 (2H, t-like).

IR (KBr) cm^{-1}: 3355, 3184, 1771, 1594, 1559, 1476, 1434, 1395, 1349, 1317, 1283, 1188, 1166, 1066, 1033, 1001.

MS(FAB): 704^+ $(M+H)^+$.

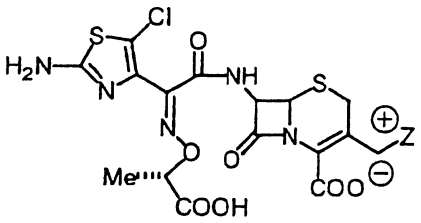
元素分析 $C_{28}H_{30}ClN_9O_7S_2 \cdot 3.6\ H_2O$.

計算值： C,43.73 ; H,4.88 ; N,16.39 ; Cl,4.61; S,8.34 (%).

實驗值： C,43.74 ; H,4.65 ; N,16.50 ; Cl,4.40; S,8.13 (%).

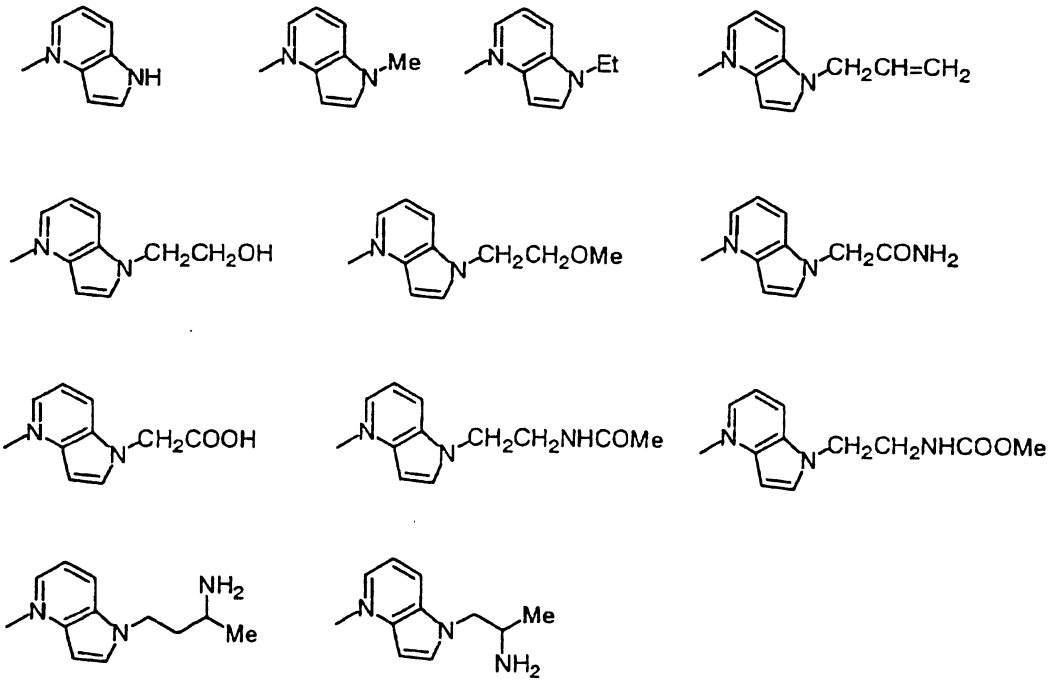
實 施 例 A

仿 前 述 實 施 例 合 成 以 下 化 合 物 (I)。

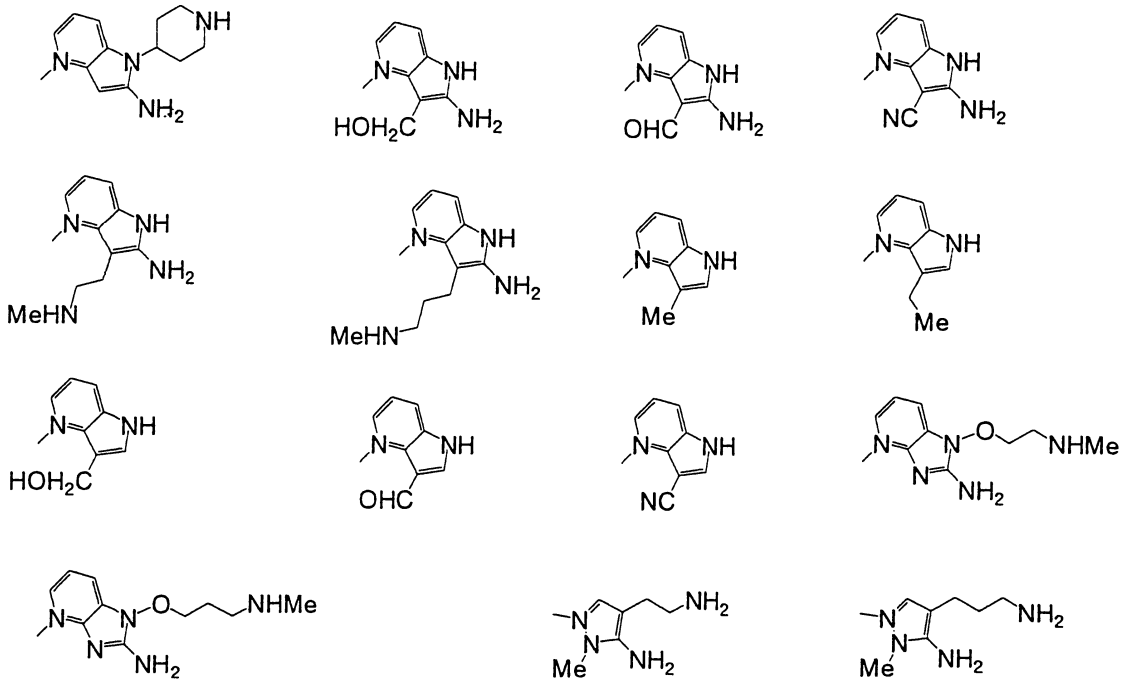


(I)

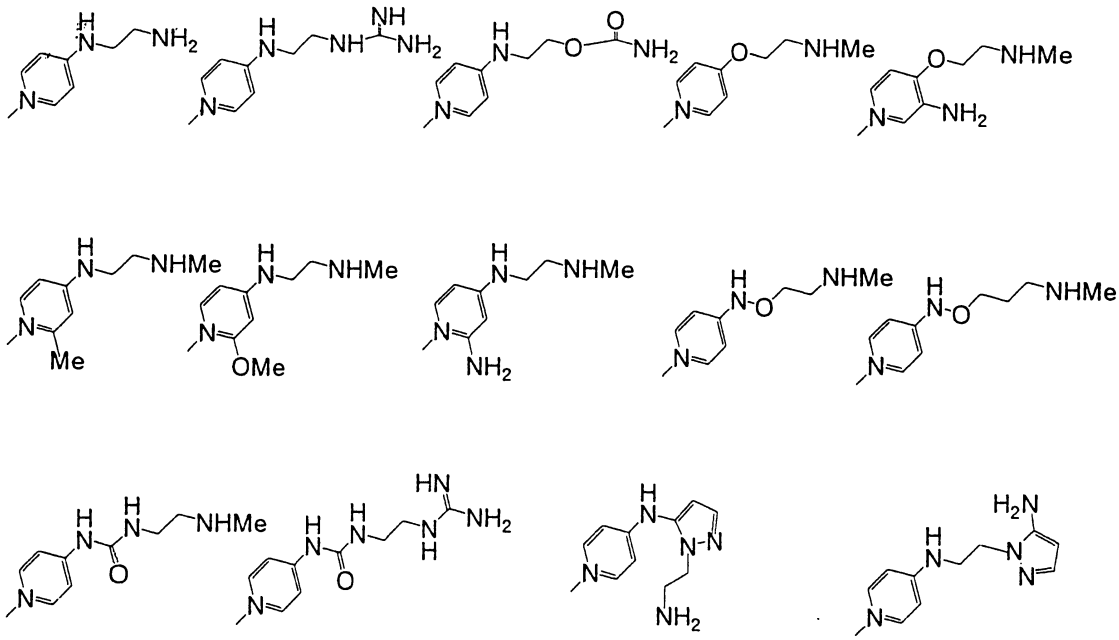
Z =

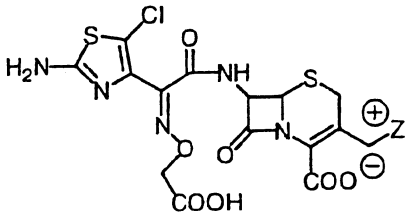


Z=



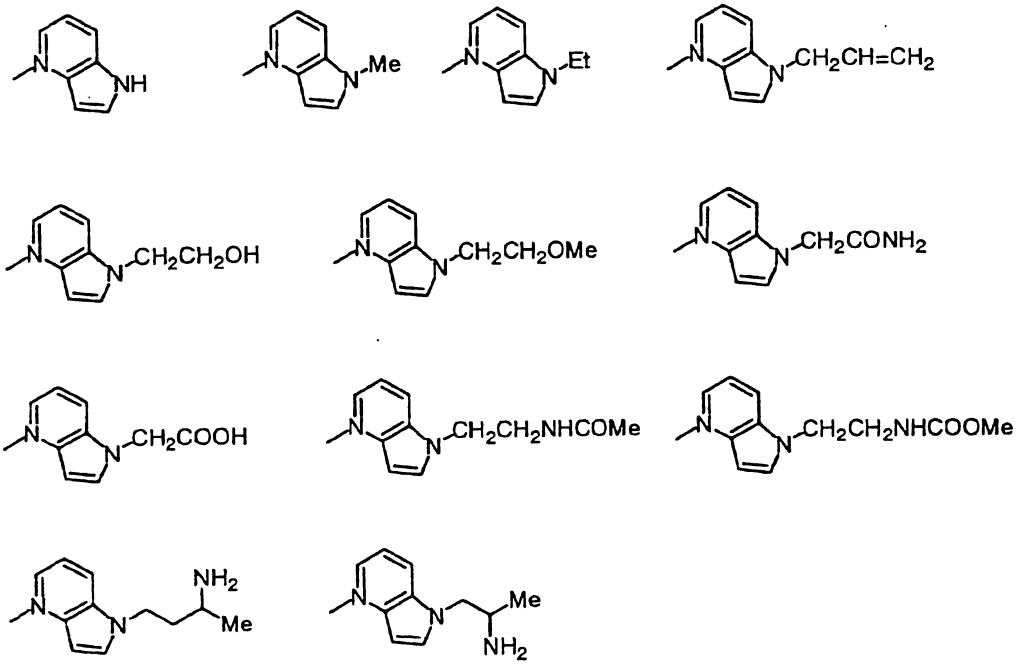
Z=





(I)

Z =



試驗例 1

本發明化合物之各種細菌之 MIC 值(最小生長制止濃度)依常法洋菜稀釋法求出，結果如表 1。

（表 1）

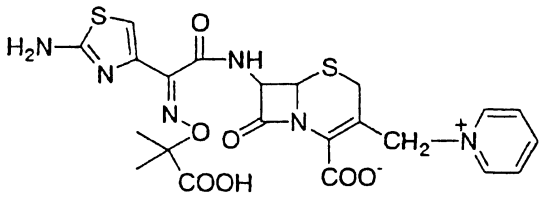
實施例編號	黃色葡萄球菌 SR3637 (H-MRSA) *1	表皮葡萄球菌 SR 25009(MRSE) *2	陰溝桿菌 SR4321 (Bla++) *3	綠膿菌 SR24-12 *3
比 1	>128	>128	64	64
實 1	64	32	16	8
實 3	32	32	16	8
實 4	16	8	4	8
實 5	16	8	8	-
實 8	32	32	4	4
實 9	16	8	2	4
實 18	8	4	2	4
實 19	16	8	1	8
實 20	16	16	8	4
實 79	8	8	2	4
實 98	8	8	2	2
實 124	16	8	4	4
實 132	16	8	4	4

*1 甲基青黴素高度耐性黃色葡萄球菌

*2 甲基青黴素高度耐性表皮葡萄球菌

*3 AmpC 高產生哂吩耐性株

比較例 1



由上述結果，與比較例 1 化合物(ceftazidime)相比，胺噻唑環部分有鹵素等取代基之本發明化合物顯示對有高度抗性之 MRSA 及 MRSE，及含綠膿菌之哂吩耐性株等各種細菌有強力抗菌作用。

製劑例 1

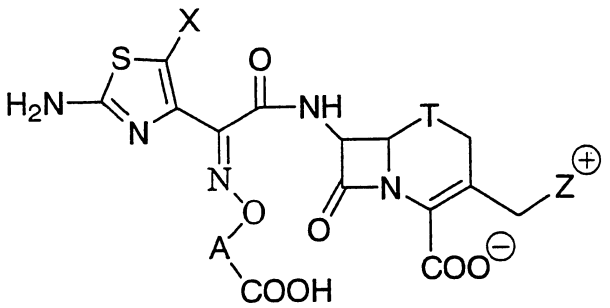
將實施例 1 之本發明化合物與 pH 調節劑用粉末填充或注射劑調製。

產業上之利用領域

本發明化合物對含革蘭式陰性菌各種細菌有強力抗菌作用。對 β-乙內醯胺酶安定，對包括產生 C 型 β-乙內醯胺酶之綠膿菌之哂吩抗性菌非常有效。且因優良體內循環，高水溶性，而特宜爲注射藥。

肆、中文發明摘要

本發明爲有關如下式所示化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物：



(I)

(式中，

T 爲 S、SO 或 O；

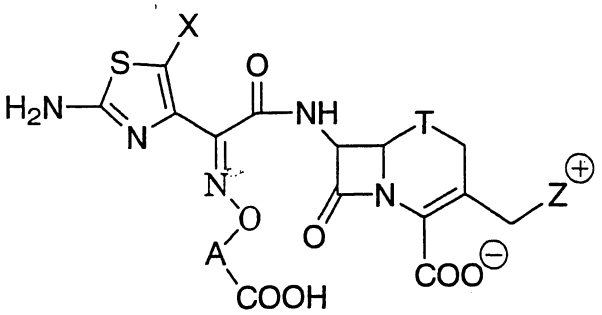
X 爲鹵素、CN、低烷基可被取代之胺甲醯基、低烷基、低烷氧基、或低烷硫基；

A 爲已取代低伸烷基(取代基：可有取代基之單低烷基、可有取代基之低亞烷基、或可有取代基之低伸烷基)；

$Z^{\oplus}$ 爲可有取代基、且含陽離子基之含 N 原子之雜環基)。

伍、英文發明摘要

A cephem compound having broad antibiotic spectrum



(I)

(wherein,

T represents S, SO or O;

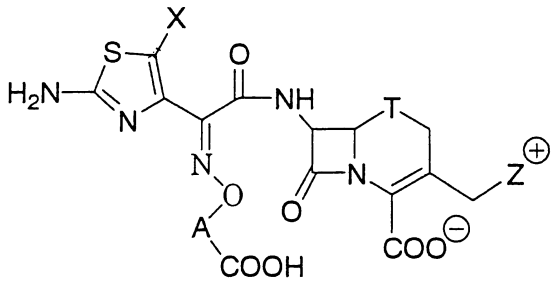
X represents a halogen atom, CN, a carbamoyl group optionally substituted by a lower alkyl group, a lower alkyl group, a lower alkoxyl group or a lower alkylthio group;

A represents a substituted lower alkylene group(substituting group: optionally substituted mono lower alkyl group, optionally substituted lower alkylidene group, or optionally substituted lower alkylene group);

$Z^{\oplus}$ represents a optionally substituted N-containing heterocyclic group having a cation group) or the ester, the compound protected on the amino group on 7-position of the thiazole ring, or the pharmaceutically acceptable salt or the solvate thereof is disclosed.

拾、申請專利範圍

1.一種如下式化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，



(I)

(式中，

T為S、SO或O；

X為鹵素、CN、可被低烷基取代之胺甲醯基、低烷基、低烷氧基、或低烷硫基；

A為已取代低伸烷基(取代基：可有取代基之單低烷基、可有取代基之低亞烷基、或可有取代基之低伸烷基)；

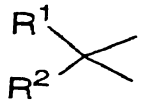
$Z^{\oplus}$為可有取代基、且含陽離子基之含N原子之雜環基)。

2.如申請專利範圍第1項之化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中T為S。

3.如申請專利範圍第1項之化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中T為O。

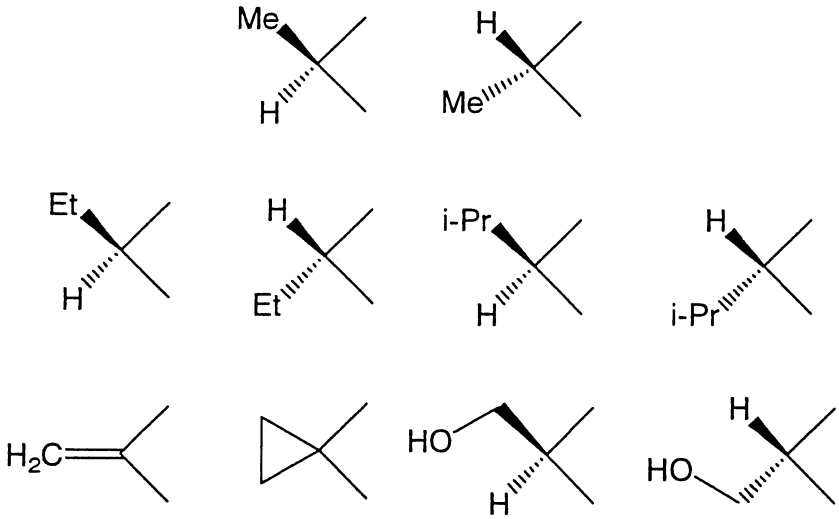
4.如申請專利範圍第1項之化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中X為鹵素或低烷基。

5. 如申請專利範圍第 1 項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 A 爲下式：



(式中，R^1 及 R^2 爲不同、各爲氫或可有取代基之低烷基、或可共同形成可被取代低亞烷基或可被取代之伸低烷基)所示之 2 價基。

6. 如申請專利範圍第 5 項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 A 爲如下所示 2 價基：



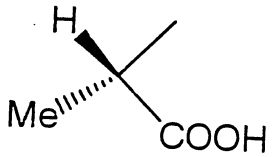
(式中，Me 爲甲基；Et 爲乙基；i-Pr 爲異丙基。)

7. 如申請專利範圍第 5 項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 R^1 及 R^2 爲不同、各爲氫或低烷基。

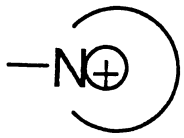
8. 如申請專利範圍第 5 項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中

R^1 及 R^2 爲不同、各爲氫或甲基。

9. 如申請專利範圍第 5 項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中"-A-COOH"爲如下所示之基：

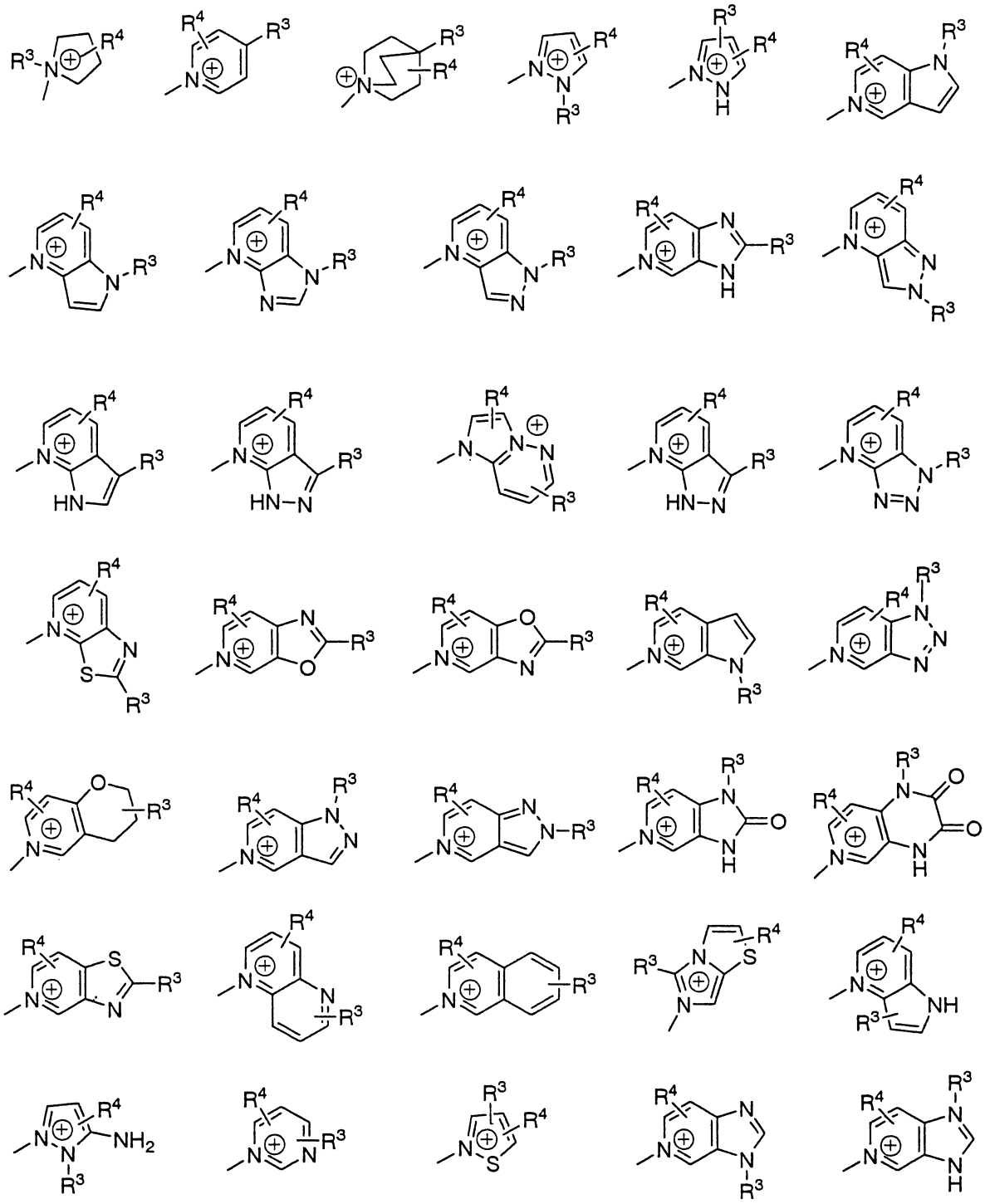


10. 如申請專利範圍第 1 項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 $Z^{\oplus}$ 爲如下所示：



其含一以上 N 原子且可有 1～4 個取代基之飽和或不飽和、單環或稠合環之 4 級銨基。

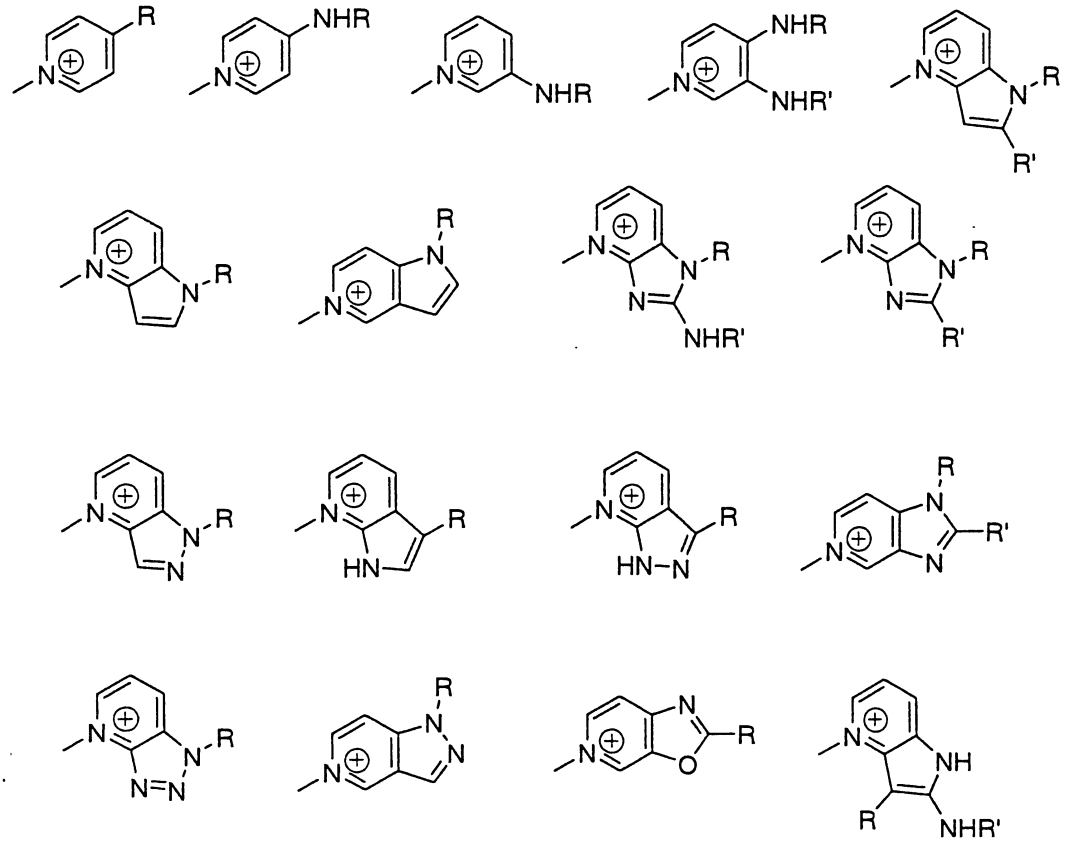
11. 如申請專利範圍第 1 項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 $Z^{\oplus}$ 爲如下所示雜環基：



(式中，R^3 及 R^4 各爲氫、可取代之低烷基、可取代之環烷基、可取代之低烯基、可取代之胺基、羥基、鹵素、可取代之胺甲醯基、可取代之烷氧基、或可取代之雜環基)。

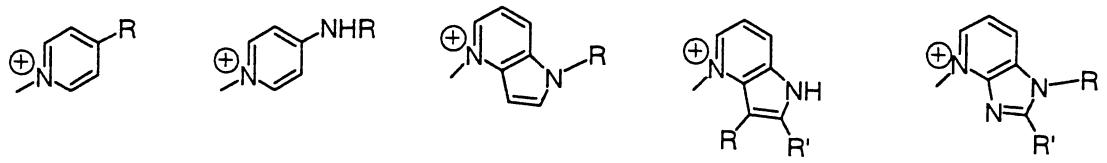
12.如申請專利範圍第 1 項之化合物、其酯、或其 7 位噻唑

環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 $Z^{\oplus}$ 爲如下所示雜環基：



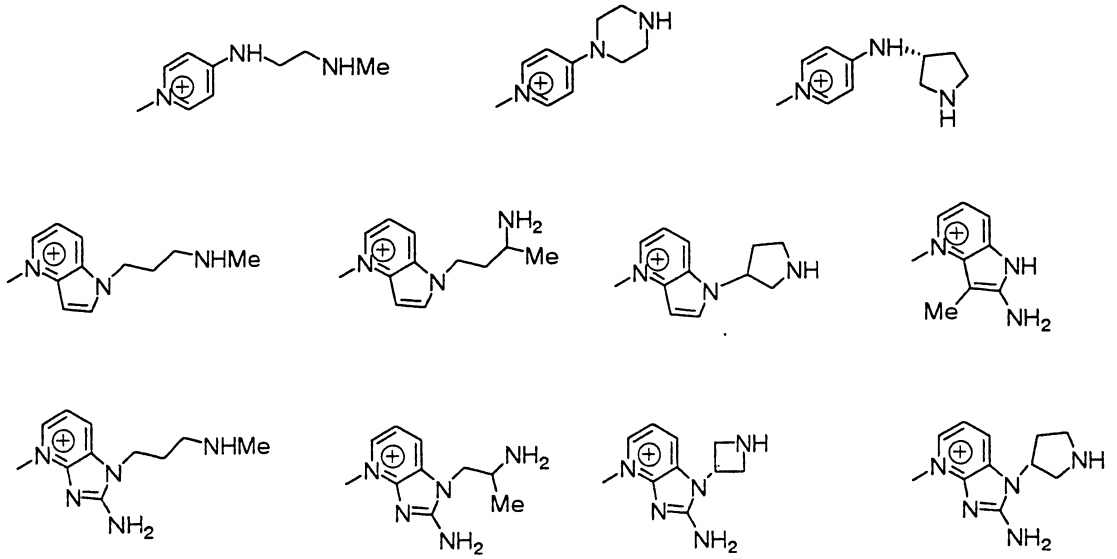
(式中，R及R'各爲氫、低烷基、胺基、單或二低烷胺基、低烯基、胺低烷基、低烷胺低烷基、低烷胺低烷胺基、胺低烷氧胺基、可有取代之雜環基取代之胺基、羥低烷基、羥低烷胺低烷基、低烷氧低烷基、胺甲醯低烷基、羧低烷基、低烷羰胺低烷基、低烷氧羰胺低烷基、低烷氧基、可有其他種種取代之低烷基、有2個取代基之低烷基、或可取代之雜環基)。

13. 如申請專利範圍第1項之化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 $Z^{\oplus}$ 爲如下所示雜環基：



(式中，R各爲氫、低烷基、胺低烷基、低烷胺低烷基、可取代之雜環基取代之胺基、或可取代之雜環基；R'爲胺基)。

14.如申請專利範圍第1項之化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中$Z^{\oplus}$爲如下所示雜環基：



(式中，Me爲甲基)。

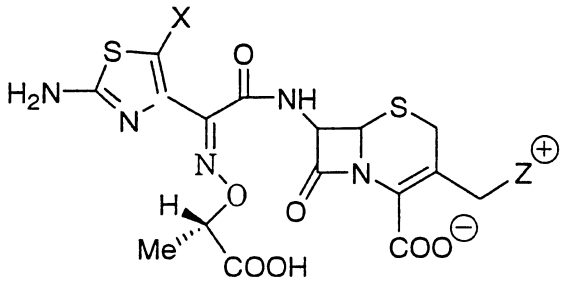
15.如申請專利範圍第1項之化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中T爲S；X爲鹵素；A爲如申請專利範圍第5～9項所示2價基，$Z^{\oplus}$爲如申請專利範圍第10～14項所示雜環基。

16.如申請專利範圍第1項之化合物、其酯、或其7位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中

T 爲 S；X 爲鹵素；A 爲如申請專利範圍第 8 項所示 2 價基；$Z^{\oplus}$ 爲如申請專利範圍第 12 項所示雜環基。

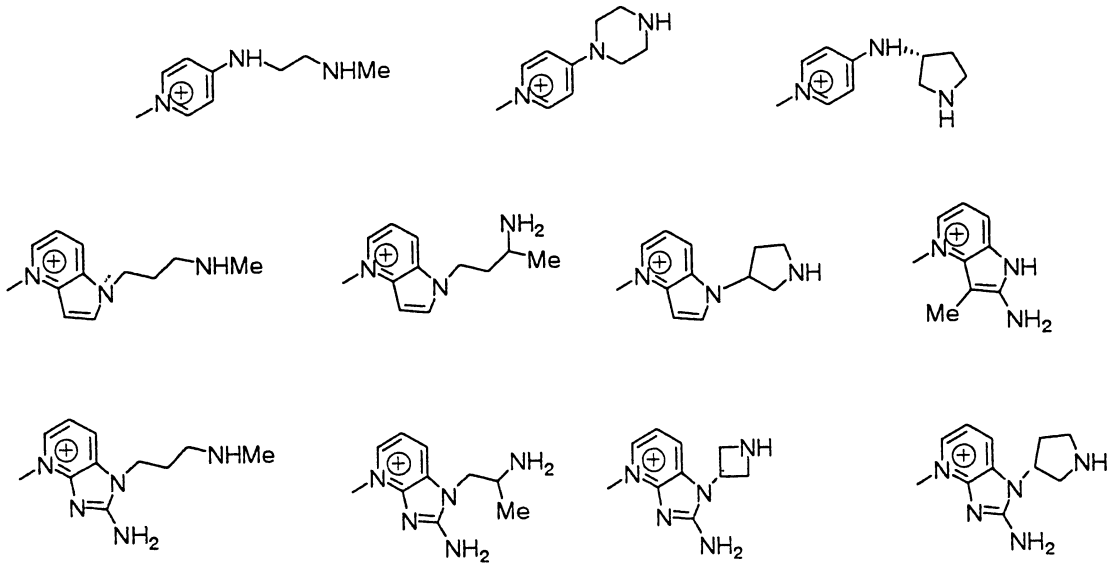
17. 如申請專利範圍第 1 項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 T 爲 S；X 爲鹵素；A 爲如申請專利範圍第 9 項所示 2 價基；$Z^{\oplus}$ 爲如申請專利範圍第 13 或 14 項所示雜環基。

18. 如申請專利範圍第 1 項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其係如下式所示：



(I)

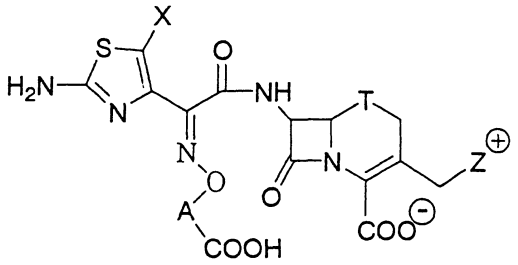
(式中，X 爲鹵素；$Z^{\oplus}$ 爲如下之雜環基)



(式中，Me 爲甲基)。

19. 一種如下式化合物、其酯、或其 7 位噻唑環上胺基之保

護體、或其製藥容許鹽或溶劑合物：



(I-A)

(式中，

T 爲 S、SO 或 O；

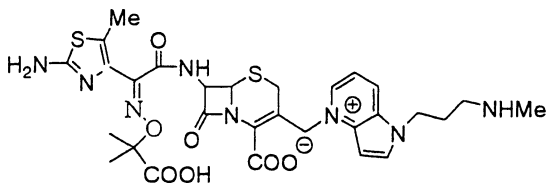
X 爲鹵素、CN、可有低烷基取代之胺甲醯基、低烷基、低烷氧基、或低烷硫基；

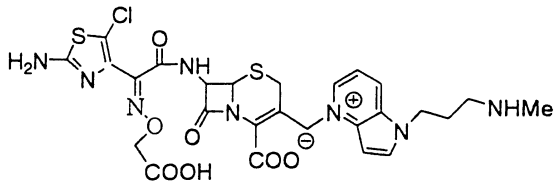
A 爲可有取代之低伸烷基(但不含取代基爲可取代之單低烷基、可取代之低亞烷基、或可取代之伸低烷基之情形)；

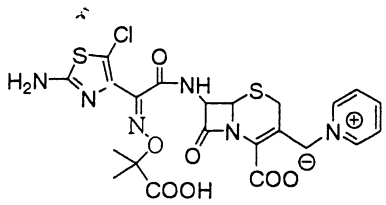
$Z^{\oplus}$ 爲可有取代基、且含陽離子基之含 N 原子之雜環基)(但 T 爲 S；X 爲鹵素、1)A 爲亞甲基；$Z^{\oplus}$ 爲吡錠、或 2)A 爲二甲基亞甲基；$Z^{\oplus}$ 爲咪唑并[1,2-a]吡錠之情形除外)。

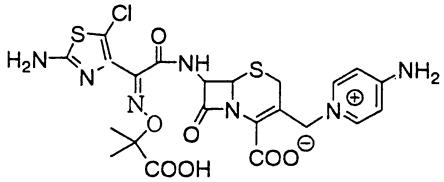
20. 如申請專利範圍第 19 項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其中 T 爲 S、X 爲鹵素或低烷基；A 爲可有二低烷基取代之亞甲基。

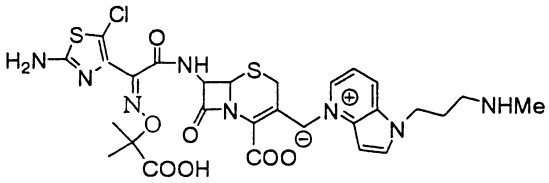
21. 如申請專利範圍第 20 項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物，其係如下所示：

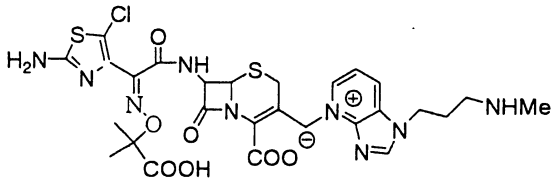


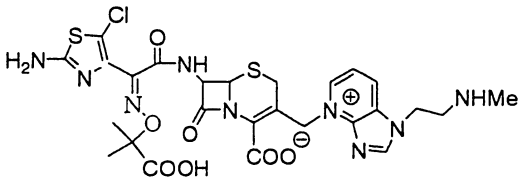


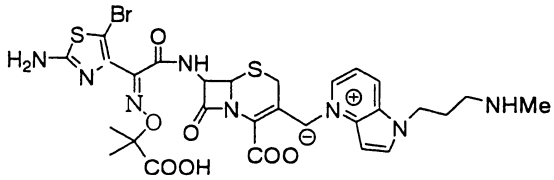








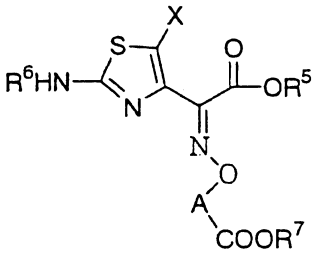




22.一種醫藥組成物，其係含如申請專利範圍第 1～21 項中任一項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物。

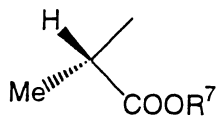
23.一種抗菌藥，其含如申請專利範圍第 1～21 項中任一項之化合物、其酯、或其 7 位噻唑環上胺基之保護體、或其製藥容許鹽或溶劑合物。

24.一種如下式化合物或其製藥容許鹽：



(IV)

(式中，X 為鹵素、CN、可有低烷基取代之胺甲醯基、低烷基、低烷氧基、或低烷硫基；A 為如下所示：



R^5 爲氫或羧基保護基；R^6 爲氫或胺基保護基；R^7 爲氫或羧基保護基)。

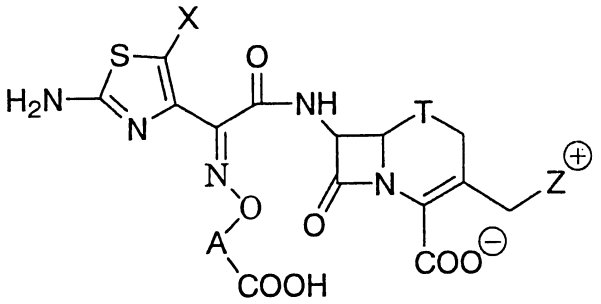
25. 如申請專利範圍第 24 項之化合物或其製藥容許鹽，其中 X 爲鹵素或低烷基。

26. 如申請專利範圍第 24 項之化合物或其製藥容許鹽，其中 X 爲鹵素。

陸、(一)、本案指定代表圖爲：第_____圖

(二)、本代表圖之元件代表符號簡單說明：

柒、本案若有化學式時，請揭示最能顯示發明特徵的化學式：



(I)