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Article

On the Reactivity of Triphenylphosphoranylidenesuccinic Anhydride with Nitrogen Nucleophiles: A New Synthetic Route to Nitrogen-Containing Phosphonium Salts

Silvio Cunha and Albert Kascheres*

Instituto de Química, Universidade Estadual de Campinas, CP 6154, 13083-970, Campinas - SP, Brazil

As reações do anidrido trifenilfosforanilidenossuccínico frente a aminas, hidrazinas e nucleófilos nitrogenados dipolares foram investigadas, o que levou ao desenvolvimento de um novo método de síntese de sais de fosfônio contendo o fragmento $RNHC(C=O)CH_2CH_2PPh_3$.

The reactions of triphenylphosphoranylidenesuccinic anhydride with amines, hydrazines and dipolar nitrogen nucleophiles were investigated, and a new method of synthesis of phosphonioum salts containing the fragment $RNHC(C=O)CH_2CH_2PPh_3$ is described.

Keywords: triphenylphosphoranylidenesuccinic anhydride, phosphonium salts

Introduction

Phosphorus ylides have been intensively used in organic synthesis, mainly in olefination reactions[1]. Recently, stabilized triphenylphosphonium ylides have attracted attention and new methods of preparation[2], their behavior under pyrolysis conditions[3] and structural elucidation[4] still demand investigation. When carrying out a transformation with stabilized triphenylphosphonium ylides their nucleophilicity has been the prime consideration[5]. However, some ylides contain electrophilic stabilizing functions which are reactive toward oxygen and nitrogen nucleophiles[6].

The ambiphilic triphenylphosphoranylidenesuccinic anhydride (**1**, TPPSA) is readily prepared by the reaction of maleic anhydride with triphenylphosphine[7], and its reactions with water (eq. 1, Scheme 1), methanol, and ethanol (eq. 2) were reported as examples of behavior towards oxygen nucleophiles[8]. There is only one example of reaction of TPPSA with a nitrogen nucleophile, diethylamine (eq. 3), wherein the phosphinoxide **4** was reportedly obtained in low yield[8]. In view of the limited data available concerning the reactivity of TPPSA, a study of the chemical behavior of **1** toward a broad spectrum of nitrogen nucleophiles was considered to be appropriate. Herein we report our results on the reactivity of TPPSA with such derivatives, in search of more complex systems.

*Current address: Instituto de Química, Universidade Federal de Goiás, CP 131, Campus II, Goiânia-Go, 74001-970, Brazil.
e-mail: silvio@quimica.ufg.br

Results and Discussion

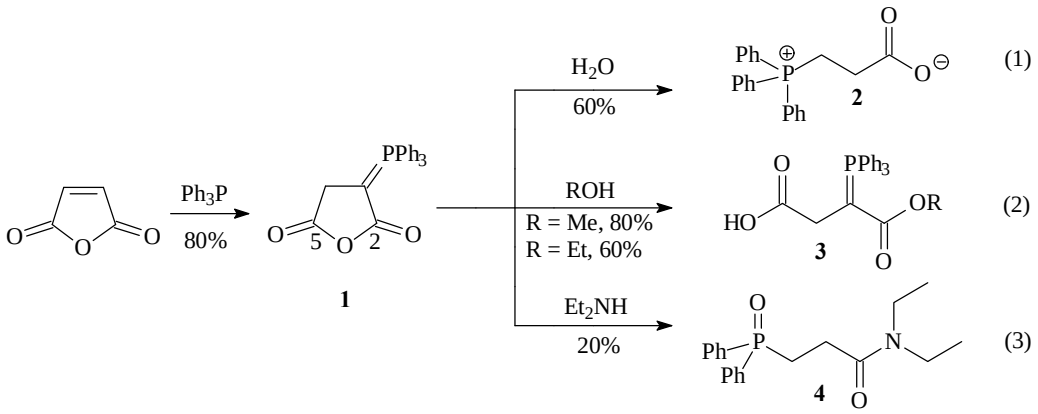
TPPSA may act as an ambident electrophile, as suggested by its reactions at C-2 with alcohols to afford **3** (eq. 2, Scheme 1), while reacting at C-5 with diethylamine to produce **4** (eq. 3)[8]. To provide insight into the reactivity of TPPSA we began our study varying the steric hindrance and the electronic nature of the nitrogen-nucleophiles. When a solution of TPPSA in CH_2Cl_2 was treated with an equimolar quantity of *tert*-butylamine, no reaction could be detected even after 8 days, while reaction with methylamine, benzylamine, cyclohexylamine and pyrrolidine afforded a complex mixture after 1 day, with no absorption characteristic of TPPSA being observed in the ^1H NMR spectrum of the crude residue[9]. Using this same reaction condition no transformation was observed using diethylamine (in our hands, using the literature procedure, the phosphinoxide **4** never was obtained). These results suggest a strong steric dependence for the reactions of TPPSA with aliphatic amines, where primary non sterically hindered and secondary cyclic amines are very reactive, while primary sterically crowded and secondary acyclic amines are not.

We next studied the reaction of TPPSA with aromatic amines. TPPSA underwent a smooth reaction with aniline (14 days), *p*-anisidine (6 days) and *p*-toluidine (6 days), but the purification of the products proved to be very difficult. Only in the reaction with *p*-toluidine could a pure solid product be obtained after tedious recrystallization, which allowed evidence for the structural assignment to be

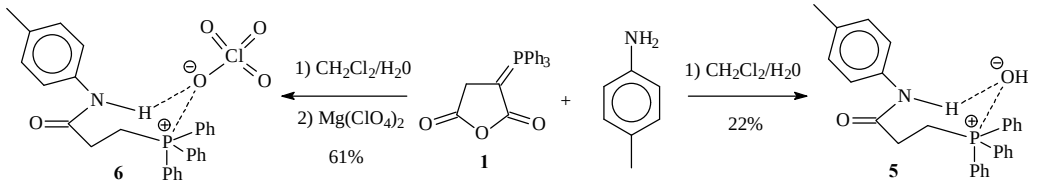
obtained from the spectral data. The IR spectrum showed absorptions characteristic of amide NH (3456 cm^{-1}) and C=O (1661 cm^{-1}) and the phosphonium group (1437 and 1114 cm^{-1})[10]. The NMR spectrum contained a pair of multiplets at δ 3.15 and δ 3.79 (2H each) and integration for 19 aromatic protons, indicating that a 1:1 adduct had formed. The presence of the phosphonium group was confirmed by the ^{31}P NMR spectrum which showed the characteristic positive signal (δ 25.0)[11]. Finally, the ^{13}C NMR spectrum showed two CH_2 fragments as doublets ($^1J_{P\text{-}C}$ = 54.0 Hz and $^2J_{P\text{-}C}$ = 3.4 Hz) and an amide carbonyl (doublet, $^3J_{P\text{-}C}$ = 13.6 Hz). On the basis of the above spectral evidence structure **5** was assigned to this product (Scheme 2) with hydroxide as counter-ion, as indicated by the alkaline pH of a dilute aqueous solution of **5**. There is a strong interaction of the organic moiety of **5** with its counter-ion, suggested by the low field amide hydrogen (δ 11.02) in the ^1H NMR spectrum.

Unfortunately, since **5** was not sufficiently stable to successive recrystallization and/or chromatographic purification, an analytical sample could not be obtained. To overcome this problem another procedure was developed whereby $Mg(ClO_4)_2$ was used to precipitate the phosphonium salt (see Experimental). Using this modification the phosphonium salt **6** was obtained with improved yield and elemental analysis in agreement with its structure (as the hydrate). The presence of the counter-ion perchlorate was indicated by the characteristic strong and wide absorption of this anion at 1115 cm^{-1} in the IR spectrum[12], and its association with the organic moiety of **6** was suggested by the chemical shift of the amide hydrogen (δ 8.87).

The behavior of TPPSA toward ambident nucleophiles was also investigated. Thus, TPPSA was treated with hydrazine derivatives (*N*,*N*-dimethylhydrazine, phenylhydrazine and 2,4-dinitrophenylhydrazine) but only with hydrazine itself did a reaction take place. In this case, a hygroscopic solid of difficult purification was obtained after 24h, and its ^1H NMR and IR spectra showed absorption of a free NH_2 from hydrazine. Reaction of TPPSA with hydrazine hydrate followed by successive treatment with anhydrous $MgSO_4$ and aromatic aldehydes afforded products **7-9** (Scheme 3). The presence of sulfate as counter-ion in **7-9** was assigned on the basis of a positive qualitative test for this anion (with $BaCl_2$)[13] and the presence of absorption at ~1113 cm^{-1} in the IR spectra of the solids obtained, characteristic of the sulfate anion[12,14]. Moreover, elemental analyses of **7-9** (as the hydrate) are in agreement with the proportion of 1:2 sulfate anion to organic moiety. Here again, the low field chemical shift of the amide hydrogen in **7-9** (δ 13.0, D_2O exchangeable) suggests a strong interaction of the organic moiety with sulfate anion as indicated in Scheme 3. The other spectral features observed for **5** are also present in compounds **7-9**. The serendipitous sulfate incorporation into **7-9** proved to be crucial to successful purification, and it should be pointed out that the use of drying agents other than $MgSO_4$ (Na_2SO_4, $CaCl_2$, K_2CO_3) did not yield solid compounds.



Scheme 1.



Scheme 2.

The above results prompted us to study the reactivity of TPPSA with dipolar nitrogen nucleophiles. With nitrones and pyridine *N*-oxide complex mixtures were observed, but when TPPSA was reacted with pyridinium *N*-imine **10**, generated in situ by reaction of *N*-aminopyridinium iodide **11**[15] with K_2CO_3, compound **12** was isolated in reasonable yield (Scheme 4).

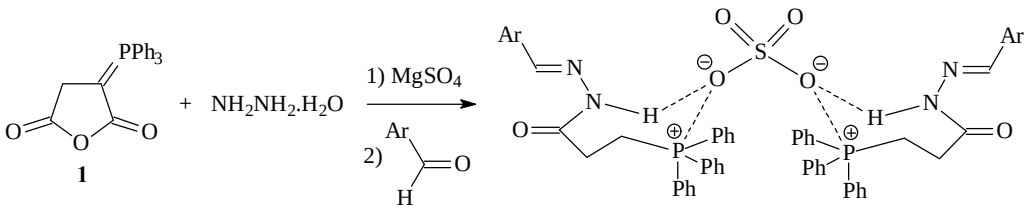
Compounds **5-9** and **12** have the same spacing between the phosphorus and nitrogen atoms, thus their aliphatic fragments present similar ^1H, ^{13}C and ^{31}P NMR data. The pyridinium ring in **12** could be defined by comparison with analogues described in the literature[16], and iodine as counter-ion was confirmed by a qualitative test[13] and elemental analysis of **12** (as the hydrate).

The formation of **5-9** and **12** may be visualized as occurring by reaction of the nitrogen nucleophile at the eletrophilic carbon **5** of TPPSA, followed by ring opening and CO_2 elimination forming the nonstabilized ylide intermediate that is trapped by water (Scheme 5).

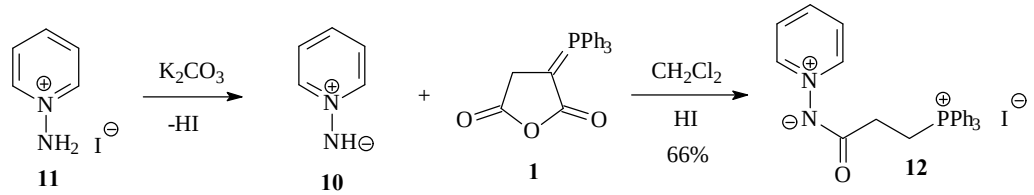
The results of the present study indicate that TPPSA is very reactive with a broad spectrum of nitrogen nucleophiles, and the formation of **5-9** and **12** demonstrate the potential of this new synthetic method for preparation of phosphonium salts containing the organic fragment $RNHC(C{=}O)CH_2CH_2PPh_3$. Recently, the design of new phosphonium salts has attracted attention due to their ability to form inclusion complexes with high molecular recognition[17]. The synthesis of chiral phosponium salts using the method described here and their use in chiral recognition are under investigation in our laboratory.

Experimental

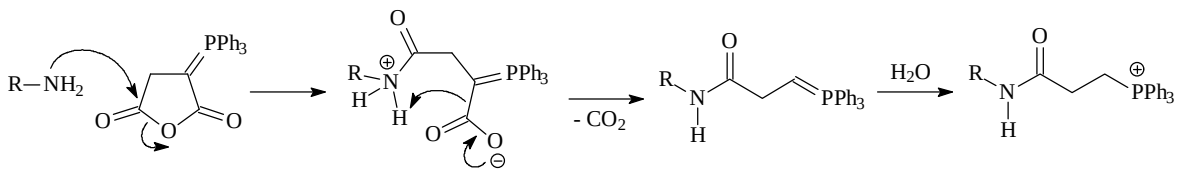
Melting points were determined on a Hoover-Unimelt apparatus and are uncorrected. Infrared spectra were recorded as KBr discs on a Perkin Elmer FT-IR 1600 instrument. NMR spectra were obtained for ^1H at 300 MHz, for ^{13}C at 75 MHz, and for ^{31}P at 121.4 MHz using a Varian Gemini 300(^1H, ^{13}C) or a Bruker AC300-P (^1H, ^{13}C, ^{31}P) spectrometer. All spectra were run in $CDCl_3$ solutions with internal TMS as reference for ^1H and ^{13}C and external 85% H_3PO_4 for ^{31}P. Chemical shifts are reported in δ (ppm) units downfield from reference, and the coupling constants in the ^{13}C NMR are $J_{P\text{-}C}$. Elemental analyses were performed on a Perkin Elmer 2401 Elemental Analysis by Instituto de Química, Universidade Estadual de Campinas, Brazil. The



Scheme 3.



Scheme 4.



Scheme 5.

triphenylphosphoranylidenesuccinic anhydride is available from Aldrich, but was prepared according to the literature procedure in 76-88% yield. *N*-aminopyridinium iodide **11** was prepared by Gösls's method[15].

Reaction of TPPSA with p-toluidine

Method A: A solution of 368.7 mg (1.0 mmol) of TPPSA and 109.1 mg (1.0 mmol) of *p*-toluidine in 5 cm^3 of CH_2Cl_2 was allowed to stand at room temperature for 6 days. After this time, the reaction mixture was allowed to cool in the freezer (-25°C) and a solid precipitated. The solvent was separated from the solid, which was recrystallized from ethyl acetate/CH_2Cl_2 /petroleum ether (1 cm^3 of ethyl acetate, CH_2Cl_2 dropwise until a clear solution was obtained, followed by petroleum ether) to give 98.0 mg (22%) of **5** (mp 214-216 ºC). IR: ν_{max}/cm^{-1} 3456, 1661, 1600, 1540, 1510, 1437, 1114 . ^1H NMR: δ 2.24 (s, 3H, CH_3), 3.15 (m, 2H, CH_2), 3.79 (m, 2H, CH_2), 6.98 (d, ^3J 8.4 Hz, 2H), 7.59 (d, ^3J 8.4 Hz, 2H), 7.62-7.79 (m, 15H), 11.02 (s, 1H, NH). $^{31}P\{^1H\}$ NMR: δ 25.0. ^{13}C NMR: δ 19.9 (d, ^1J (PC) 54 Hz, CH_2), 20.9 (s, CH_3), 29.7 (d, ^2J (PC) 3.4 Hz, CH_2), 117.7 (d, ^1J (PC) 86.5 Hz, C), 120.0 (s, CH), 128.9 (s, CH), 130.5 (d, ^3J (PC) 12.7 Hz, CH), 132.9 (s, C), 133.7 (d, ^2J (PC) 10.2 Hz, CH), 135.2 (d, ^4J (PC) 2.8 Hz, CH), 136.3 (s, C), 167.8 (d, ^3J (PC) 13.6 Hz, C).

Method B: A solution of 380.3 mg (1.1 mmol) of TPPSA and 117.0 mg (1.1 mmol) of *p*-toluidine in 5 cm^3 of CH_2Cl_2 was allowed to stand at room temperature for 6 days. After this time, the solvent was removed by rotatory evaporation and the residue was extracted with 10 cm^3 of hot water, the insoluble material was filtered off, and the filtrate allowed to cool to room temperature. An excess of saturated $Mg(ClO_4)_2$ solution was added to the filtrate yielding an insoluble white solid which was filtered and air-dried overnight. The solid was recrystallized from ethanol to give 304.3 mg (61%) of 6. IR: ν_{max}/cm^{-1} 3300, 1648, 1603, 1540, 1512, 1438, 1115 cm^{-1} (strong and wide). ^1H NMR: δ 2.26 (s, 3H, CH_3), 3.00 (m, 2H, CH_2), 3.53 (m, 2H, CH_2), 7.02 (d, ^3J 8.2 Hz, 2H), 7.41 (d, ^3J 8.2 Hz, 2H), 7.67-7.81 (m, 15H), 8.87 (s, 1H, NH). $^{31}P\{^1H\}$ NMR: δ 25.1. ^{13}C NMR: δ 19.3 (d, ^1J (PC) 55.6 Hz, CH_2), 20.9 (s, CH_3), 29.0 (d, ^2J (PC) 2.5 Hz, CH_2), 117.5 (d, ^1J (PC) 86.3 Hz, C), 119.9 (s, CH), 129.2 (s, CH), 130.7 (d, ^3J (PC) 12.5 Hz, CH), 133.5 (d, ^2J (PC) 10.1 Hz, CH), 133.5 (s, C), 135.4 (d, ^4J (PC) 3.0 Hz, CH), 167.1 (d, ^3J (PC) 13.4 Hz, C). Anal. Calcd. for $C_{28}H_{27}PNClO_5.H_2O$: C, 62.05; H, 5.36; N, 2.59. Found: C, 61.97; H, 5.11; N, 2.29.

Reaction of TPPSA with $NH_2NH_2.H_2O$ and benzaldehyde

A mixture containing 999.1 mg (2.75 mmol) of TPPSA in 10 cm^3 of CH_2Cl_2 and 1 cm^3 of 80% $NH_2NH_2.H_2O$ was left at room temperature with stirring overnight and then dried over anhydrous $MgSO_4$, filtered, and the solvent evaporated. The residual yellow oil was dissolved in 10 cm^3 of CH_2Cl_2 and 313.2 mg (2.95 mmol) of benzaldehyde was added and the solution was allowed to stand at room temperature for 24 hours after which time the solvent was evaporated. The crude solid was recystallized as described for **5** to give a white solid. Trituration with acetone afforded 711.8 mg (54%) of **7**, mp 253.5-255.5 ºC. IR (KBr): ν_{max}/cm^{-1} 3428, 1684, 1566, 1438, 1246, 1113 cm^{-1}. ^1H NMR: δ 3.10 (m, 2H), 3.80 (m, 2H), 7.32-7.35 (m, 3H), 7.69-7.86 (m, 17H), 8.59 (s, 1H), 12.97 (s, 1H, NH). $^{31}P\{^1H\}$ NMR: δ 24.9. ^{13}C NMR: δ 20.4 (d, ^1J (PC) 54.0 Hz, CH_2), 28.1 (d, ^2J (PC) 3.5 Hz, CH_2), 117.6 (d, ^1J (PC) 87.0 Hz, C), 127.9 (s, CH), 128.3 (s, CH), 129.9 (s, CH), 130.7 (d, ^3J (PC) 13.0 Hz, CH), 133.7 (d, ^2J (PC) 10.0 Hz, CH), 134,3 (s, C), 135.4 (d, ^4J (PC) 3.0 Hz, CH), 149.3 (s, CH), 166.0 (d, ^3J (PC) 15.0 Hz, C). Anal. Calcd. for $(C_{28}H_{26}PN_2O)_2SO_4$: C, 69.28; H, 5.36; N, 5.77. Found: C, 68.95; H, 5.34; N, 5.47.

Reaction of TPPSA with $NH_2NH_2.H_2O$ and p-chlorobenzaldehyde

As described for **7**, utilizing 187.2 mg (0.52 mmol) of TPPSA in 5 cm^3 of CH_2Cl_2 and 74.4 mg (0.55 mmol) of *p*-chlorobenzaldehyde. Yield 117.1 mg (44%) of **8**, mp 233-235 ºC. IR: ν_{max}/cm^{-1} 3500, 3450, 1696, 1439, 1244, 1115 cm^{-1}. ^1H NMR: δ 3.08 (m, 2H), 3.80 (m, 2H), 7.28 (d, ^3J 8.6 Hz, 2H), 7.65 (d, ^3J (PC) 8.6 Hz, 2H), 7.66-7.84 (m, 15H), 8.6 (s, 1H), 13.08 (s, 1H, NH). $^{31}P\{^1H\}$ NMR: δ 24.9. ^{13}C NMR: δ 20.1 (d, ^1J (PC) 54.4 Hz, CH_2), 28.0 (d, ^2J (PC) 3.2 Hz, CH_2), 117.5 (d, ^1J (PC) 86.3 Hz, C), 128.6 (s, CH), 129.0 (s, CH), 130.7 (d, ^3J (PC) 12.6 Hz, CH), 132.8 (s, C), 133.7 (d, ^2J (PC) 10.3 Hz, CH), 135.4 (d, ^4J (PC) 3.0 Hz, CH), 135.7 (s, C), 147.9 (s, CH), 166.1 (d, ^3J (PC) 14.8 Hz, C). Anal. Calcd. for $(C_{28}H_{25}PN_2ClO)_2SO_4.H_2O$: C, 63.58; H, 4.92; N, 5.30. Found: C, 63.04; H, 4.87; N, 5.21.

Reaction of TPPSA with $NH_2NH_2.H_2O$ and furfural

As described for **7**, using 373.2 mg (1.0 mmol) of TPPSA in 5 cm^3 of CH_2Cl_2, and 116.0 mg (1.2 mmol) of furfural. Yield 270.3 mg (55%) of **9**, mp 200-201 ºC. IR: ν_{max}/cm^{-1} 3422, 1684, 1438, 1234, 1114 cm^{-1}. ^1H NMR: δ 3.05 (m, 2H), 3.78 (m, 2H), 6.42 (dd, ^3J 3.3 and ^3J 1.7 Hz, 1H), 6.72 (d, ^3J 3.3 Hz, 1H), 7.45 (d, ^3J 1.7 Hz, 1H), 7.69-7.86 (m, 15H), 8.48 (s, 1H), 13.02 (s, 1H, NH). $^{31}P\{^1H\}$ NMR: δ 25.0. ^{13}C NMR: δ 20.2 (d, ^1J (PC) 54.3 Hz, CH_2), 28.0 (d, ^2J (PC) 3.4 Hz, CH_2), 111.6 (s, CH), 113.9 (s, CH), 117.5 (d, ^1J (PC) 86.7 Hz, C), 130.7 (d, ^3J (PC) 12.9 Hz, CH), 133.7 (d, ^2J (PC) 10.0 Hz, CH), 135.4 (d, ^4J (PC) 3.0 Hz, CH), 138.5 (s, CH), 144.0 (s, CH), 149.6 (s, C), 165.6 (d, ^3J (PC) 15.4 Hz, C). Anal. Calcd. for $(C_{26}H_{24}PN_2O_2)_2SO_4$: C, 65.68; H, 5.05; N, 5.89. Found: C, 65.46; H, 5.33; N, 5.63%.

Reaction of TPPSA with pyridinium N-*imine* **10**

A stirred suspension of 195.3 mg (0.54 mmol) of TPPSA, 116.8 mg (0.53 mmol) of N-aminopyridinium iodide **11** and 181.1 mg (1.31 mmol) of anhydrous K_2CO_3 was left at room temperature overnight, filtered and the solvent evaporated. The crude solid was recrystallized from ethanol/hexane to give a solid which was triturated with acetone yielding 190.8 mg (66%) of **12**, mp 168-170 ºC. IR: ν_{max}/cm^{-1} 3472, 1618, 1593, 1466, 1438, 1350, 1261, 1114 cm^{-1}. ^1H NMR: δ 2.67 (m, 4H; 2H after D_2O exchange, CH_2), 3.84 (m, 2H), 7.70-7.89 (m, 17H), 8.11 (t, ^3J (PC) 7.7 Hz, 1H), 8.48 (d, ^3J (PC) 6.7 Hz, 2H). $^{31}P\{^1H\}$ NMR: δ 25.0. ^{13}C NMR: δ 20.0 (d, ^1J (PC) 52.8 Hz, CH_2), 28.6 (d, ^2J (PC) 3.3 Hz, CH_2), 118.0 (d, ^1J (PC) 86.5 Hz, C), 126.8 (s, CH), 130.6 (d, ^3J (PC) 12.8 Hz, CH), 133.6 (d, ^2J (PC) 10.1 Hz, CH), 135.3 (d, ^4J (PC) 3.0 Hz, CH), 138.8 (s, CH), 142.9 (s, CH), 172.0 (d, ^3J (PC) 11.9 Hz, C). Anal. Calcd. for $C_{26}H_{24}PN_2IO.H_2O$: C, 56.12; H, 4.68; N, 5.04. Found: C, 56.09; H, 4.19; N, 4.89.

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References

1. Kelly, S. E. In *Alkene Synthesis*; Trost, B. M.; Fleming, I., Eds. *Comprehensive Organic Synthesis* Vol. 1; Pergamon Press: Oxford, 1991.
2. Meshram, H. M.; Reddy, G. S.; Reddy, M. M.; Yadav, J. S. *Tetrahedron Lett.* **1998**, *39*, 4107.
3. Aitken, R. A.; Karodia, N. *Liebigs Ann. Recl.* **1997**, 779.
4. Aitken, R. A.; Karodia, N. *Tetrahedron* **1998**, *54*, 9223.
5. Smith, M. B. *Organic Synthesis*; McGraw-Hill, Inc.: Singapore, 1994, p. 782.
6. Johnson, A. W.; Kaska, W. C.; Starzewski, K. A. O.; Dixon, D. A. *Ylides and Imines of Phosphorus*; Jonh Wiley & Sons, Inc.: New York, 1993.
7. Schonberg, A.; Ismail, A. F. A. *J. Chem. Soc.* **1940**, 1374.
8. Hudson, R. F.; Chopard, P. A. *Helv. Chim. Acta* **1963**, *46*, 2178.
9. When a solution of TPPSA in CH_2Cl_2 was allowed to stand at room temperature it acquired a brown coloring after a few minutes, but no significant decomposition was observed during 8 days, as determined by analysis of the ^1H NMR spectrum of the crude residue.
10. Flick, E. *Topics in Phosphorus Chemistry* V. 4; John Wiley: New York, 1967.
11. (a) Verkade, J. G.; Quin, L. D. *Phosphorus-31 NMR Spectroscopy in Stereochemical Analysis*; VCH: Florida, 1987. (b) Crutchfield, M. M.; Dugan, C. H.; Letcher, J. H.; Mark, V.; van Mazer, J. R. *Topics in Phosphorus Chemistry* V. 5; John Wiley: New York, 1967.
12. Nakamoto, K. *Infrared and Raman Spectra of Inorganic and Coordination Compounds* 4th. Ed.; John Wiley: New York, 1986.
13. Bacan, N.; Godinho, O. E. S.; Aleixo, L. M.; Stein, E. *Introdução à Semimicroanálise Qualitativa* 2nd Ed.; Editora da UNICAMP: Campinas, 1988.
14. Colthup, N. B.; Daly, L. H.; Wiberly, S. E. *Introduction to Infrared and Raman Spectroscopy*, 3rd. Ed.; Academic Press: California, 1990, p. 376.
15. Gösl, R.; Neuwsen, A. *Org. Synth.* **1963**, *43*, 1.
16. Balasubramanian, A.; McIntosh, J. M.; Snieckus, V. *J. Org. Chem.* **1970**, *35*, 433.
17. Toda, F.; Tanaka, K.; Sawada, H. *J. Chem. Soc., Perkin Trans.* 1 **1995**, 3065.

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