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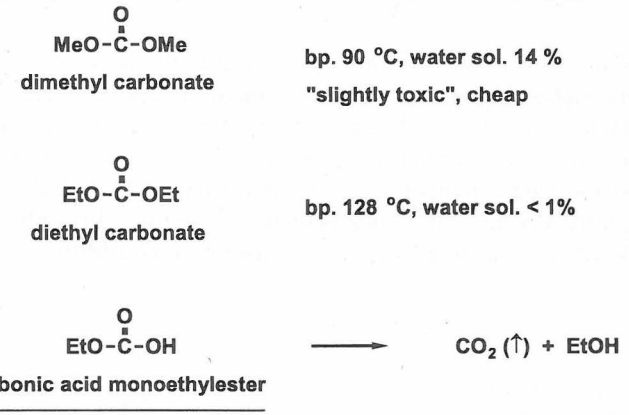
Lipase-catalyzed conversions with diethyl and dimethyl carbonate in oleochemistry[1]

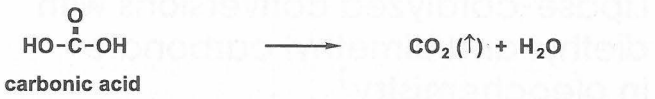
Siegfried Warwel, Mark Rüsch gen. Klaas and Ricarda Grothey
Institute for Biochemistry and Technology of Lipids, H.P. Kaufmann-Institute, Federal Centre for Cereal, Potato and Lipid Research
Piusallee 68, D-48147 Münster, Germany
Phone: +49-251-43510; Fax: +49-519275; E-mail: ibtfett@uni-muenster.de

Introduction

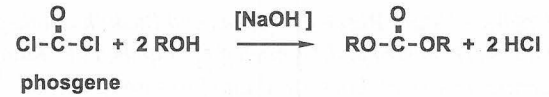
Dialkyl carbonates are acyclic diesters of carbonic acid. The short-chain compounds diethyl and dimethyl carbonate are common solvents in organic chemistry. Whereas the dialkyl carbonates are fairly stable under neutral and acidic conditions, the corresponding monoesters decompose, analogously to carbonic acid itself, to carbon dioxide and the alcohol.



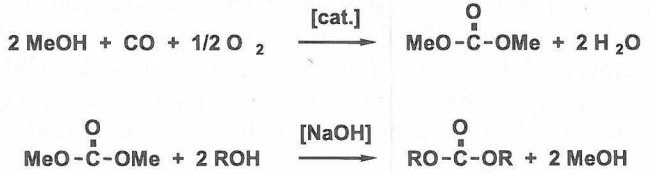
1 The original title "Fatty Alcohol Carbonates and Epoxy Fatty Alcohols by Lipase-Catalyzed Conversions with Diethyl Carbonate" has been enhanced to cover the entire presentation.



All dialkyl carbonates were formerly produced in industry from phosgene and the alcohol /1/:



Although this process is versatile in respect of the alcohol the disadvantage of dealing with phosgene as a starting material is obvious /2/; additionally, it is difficult to obtain a chlorine-free product this way. The modern production of dialkyl carbonates is based on the catalytic carbonylation of methanol /3/:

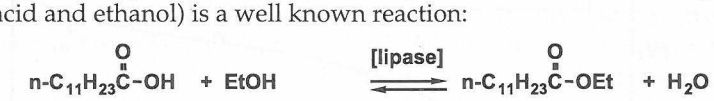


Because this process is only carried out with methanol, all other dialkyl carbonates are made by alkaline transesterification of dimethyl carbonate. Hence, dimethyl carbonate is by far the cheapest (~ 1 $/kg).

We now used dimethyl and diethyl carbonate for a variety of lipase-catalyzed conversions in oleochemistry to obtain fatty acid methylester, fatty alcohol carbonates, which are used in lubricants and cosmetics, as well as oleochemical epoxides for polymer-additives.

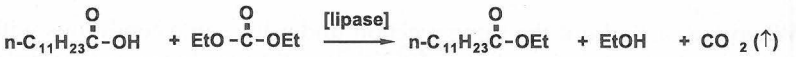
Lipase-catalyzed esterifications of fatty acids and transesterifications of plant oils

The lipase-catalyzed esterification of fatty acids with an alcohol (e.g. lauric acid and ethanol) is a well known reaction:

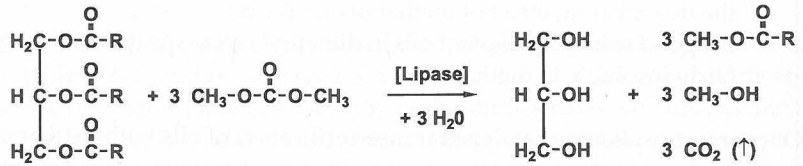


Its intrinsic disadvantage for technical applications is, that it is an equilibrium reaction and a lot of lipase chemistry is dealing with ways to shift this equilibrium to the desired side. The same is also true for the transesterification of a fatty acid with a short-chain ester, e.g. ethyl acetate:

In comparison the transesterification of a fatty acid with an dialkyl carbonate is not an equilibrium reaction, because the intermediate co-product (carbonic acid monoalkyl ester) decomposes immediately to carbon dioxide and one mol alcohol:



The situation is quite similar for the transesterification of plant oils with dialkyl carbonates.



As an example we chose the transesterification of high oleic sunflower oil with dimethyl carbonate under severe conditions (150 mmol plant oil / 1 solvent = 15 weight-%; 50 mmol plant oil / g enzyme). After 72 h (fig. 1) at 50 °C we obtained about 80 % oleic acid methylester and at 20 °C still 40-50 %.

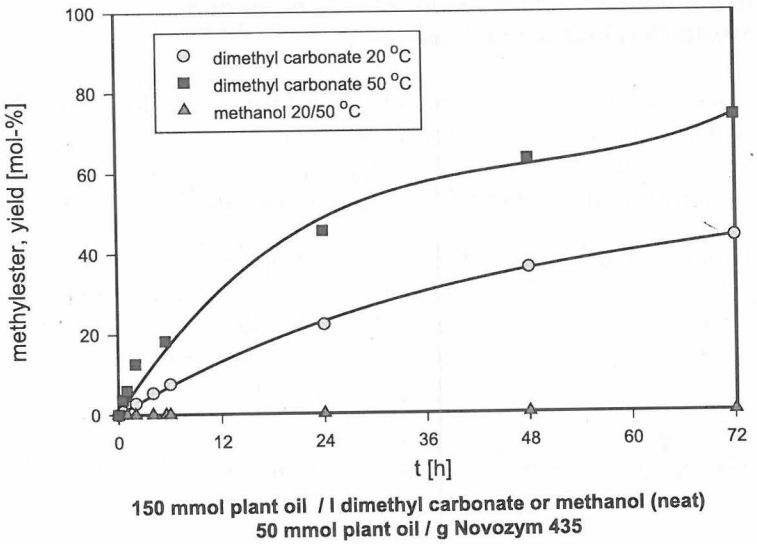


Fig. 1: Oleic acid methylester by lipase-catalyzed transesterification of high-oleic unflower oil with dimethyl carbonate or methanol

When we carried out the same reaction under the same conditions with methanol instead of dimethyl carbonate, we did not obtain any methylesters at all. This may be explained by the following reasons:

- the difference between an equilibrium reaction and a irreversible transesterification as explained above;
- the deactivating effect of methanol on lipases;
- the good solubility of plant oils in dimethyl carbonate (plant oils are fairly insoluble in methanol).

Of course, the alkaline catalyzed transesterification of oils with methanol to obtain fatty acid methyl esters is one of the basic reactions in industrial oleochemistry and it is carried out without any problem in most cases. For sensitive substances, however (tung oil, calendula, fish oils), lipase-catalyzed transesterification using dimethyl or diethyl carbonate may provide a viable alternative.

Fatty alcohol carbonates by lipase-catalyzed esterification of fatty alcohols with diethyl carbonate

In principle, fatty alcohol carbonates can be synthesized by transesterification of short chain dialkyl carbonates (fig. 2). If only one acyl group is substituted by a long chain fatty alcohol, the result is a so-called unsymmetric fatty alcohol carbonate; if both sides are substituted, the reaction product is a symmetric fatty alcohol carbonate.

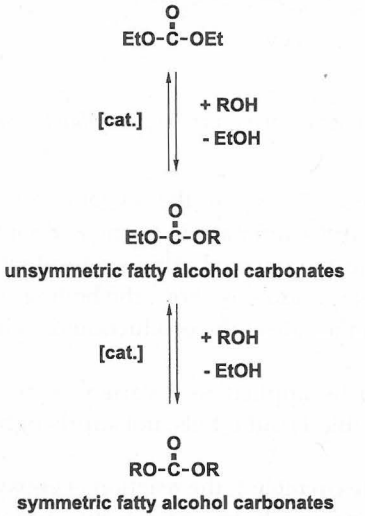


Fig. 2: Synthesis of unsymmetric and symmetric fatty alcohol carbonates by transesterification of diethyl carbonate with fatty alcohols

Fatty alcohol carbonates have been synthesized by lipase-catalysis before, but either reaction times have been extremly long /4/ or particularly reactive substrates had to be used /5/ or the studies have been only dealing with kinetics /6/ and not with product preparation. Therefore we tried to find simple, preparative useful reactions /7/. In an short enzyme screening, we found, that Novozym ® 435, a commercial immobilized lipase from *Candida antarctica*, is the most suitable biocatalyst for this purpose.

The lipase-catalyzed synthesis of unsymmetric fatty alcohol carbonates can be realized in the following way. A fatty alcohol (e.g. lauryl alcohol, fig. 3) is heated to 80 °C in the presence of the lipase for three hours in

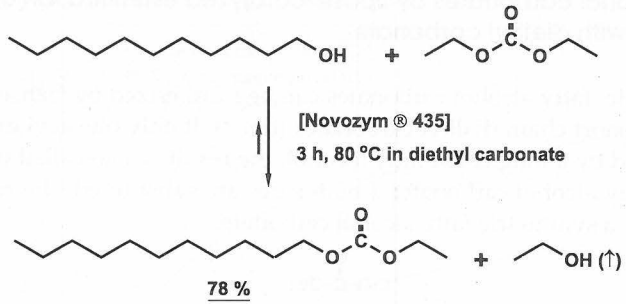


Fig. 3: Lipase-catalyzed preparation of ethyllauryl carbonate

diethyl carbonate (bp. 127 °C) as the solvent. An equilibrium is established and ethyllauryl carbonate is formed. Because of the excess of diethyl carbonate and the removal of the co-product ethanol by destillation – the reaction temperature is above the boiling point of ethanol – the equilibrium is far on the side of the products and a yield of 78 % ethyllauryl carbonate is achieved.

The reaction can be applied to a variety of primary alcohols with yields of 64-100 % (table 1) but it fails, not suprisingly, for secondary and tertiary alcohols.

Of all the examples in table 1, the reaction of epoxystearyl alcohol may be the most interesting one, because a selective preparation of the corresponding carbonate is only possible by lipase-catalysis. If the transesterification of diethyl carbonate with an epoxy alcohol were initiated by an alkaline catalysts, there would be side reactions by epoxide ring opening.

The lipase-catalyzed preparation of symmetric fatty alcohol carbonates can be carried out on two ways. First, two mols of a fatty alcohol carbonate – again, lauryl alcohol was chosen as an example – and one mol of diethyl carbonate can be converted at 80 °C in a high boiling solvent to yield 72 % dilauryl carbonate (fig. 4; lower part).

Second (fig. 4, upper part), two mols of ethyl lauryl carbonate, prepared as described above, can be "disproportionated" to one mol of dilauryl and diethyl carbonate each; by removal of diethyl carbonate via destillation under reduced pressure (80 °C, 50 mbar) a quantitative yield can be obtained.

Table 1: Fatty alcohol carbonate by Novozym ® 435 catalyzed esterification of various fatty alcohols with diethyl carbonate /7/

substrate	product	yield
1-butanol	butylethyl carbonate	70 %
1-heptanol	ethylheptyl carbonate	81 %
1-octanol	ethyloctyl carbonate	87 %
lauryl alcohol	dodecylethyl carbonate	78 %
stearyl alcohol	ethyloctadecyl carbonate	85 %
allyl alcohol	allylethyl carbonate	64 %
10-undecen-1-ol	ethyl-10-undecen-1-yl carbonate	84 %
oleyl alcohol	ethyl-9-octadecen-1-yl carbonate	100 %
epoxystearyl alcohol	ethylepoxystearyl carbonate	87 %
iso-butanol	iso-butylethyl carbonate	60 %
2-butanol	ethylisobutyl carbonate	29 %
cyclohexanol	eyclohexylethyl carbonate	21 %
tert-butanol		0 %

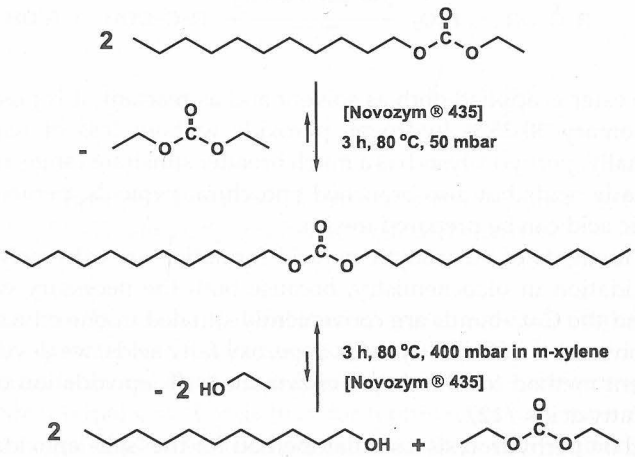
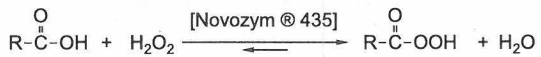


Fig. 4: Two procedures for lipase-catalyzed preparation of dilauryl carbonate

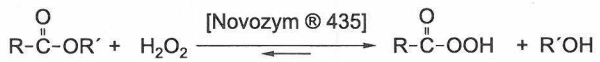
The substrate range of these two reactions was not yet evaluated. However, it can reasonably be expected, that it is the same as for the preparation of unsymmetric fatty alcohol carbonates.

Lipase-mediated epoxidation via peroxy carbonic acid

A new way to prepare peroxy acids has been discovered by Novo Nordisk, DK /8-10/. They have shown, that some lipases – and again, Novozym ® 435 is the most active and stable biocatalyst for this purpose – catalyze the conversion of fatty acids with hydrogen peroxide (preferably 60 %) to peroxy fatty acids:



Recently, we found, that Novozym ® 435 is also capable to catalyze perhydrolysis /11/, i.e. the reaction of carboxylic acids esters with hydrogen peroxide to percarboxylic acids:



If the ester is applied both as solvent and as reactant, it is possible to use customary 30-35 % hydrogen peroxide without loss of reactivity. Additionally, perhydrolysis has a much broader substrate range: not only peroxy fatty acids but also branched and chiral peracids, peracetic and peracrylic acid can be prepared in-situ.

Both methods of biocatalytic peracid formation are extremely useful for epoxidation in oleochemistry, because both the necessary carboxyl group and the C=C-bonds are conveniently situated in one educt. Based on the conversion of free fatty acids to peroxy fatty acids, we developed a convenient method for the chemo-enzymatic "self-"epoxidation of unsaturated fatty acids /12/.

Based on perhydrolysis a similar method for the "self-"epoxidation of plant oils yields 88-96 % epoxides with a selectivity ≥ 92 % /13,14/. The method is characterized by the use of 35 % hydrogen peroxide and the addition of a small amount of free fatty acids, which is necessary not for

peroxy acid formation but to prevent the formation of mono- and diglycerols by (per-)hydrolysis.

Now, while continuing our studies of the substrate range of Novozym ® 435 catalyzed perhydrolysis, we found that dialkyl esters of carbonic acid can also be perhydrolyzed and that olefins present were epoxidized (fig. 5) /15/. We suspect, that the peroxy acid, that is generated in situ, is monoperoxy carbonic acid monomethylester, but there is no spectroscopic evidence so far. In any case there is no acidic co-product but only methanol and carbon dioxide.

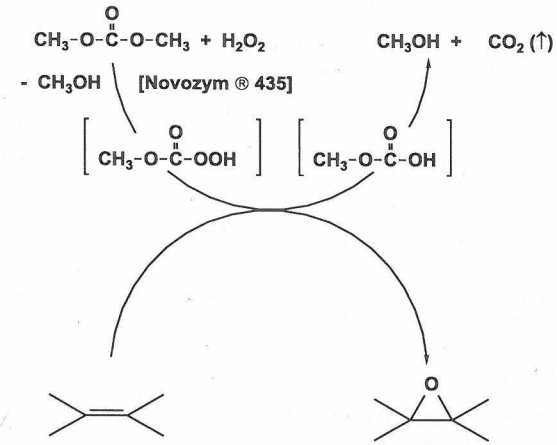


Fig. 5: Chemo-enzymatic epoxidation via "percarbonic acid" by Novozym ® 435 catalyzed perhydrolysis of dimethyl carbonate

Table 2 shows the results of the chemo-enzymatic epoxidation of various olefins by "percarbonic" and peracetic acid in situ. Yields of 60-100 % are obtained and – as usually in Prileshajev-epoxidations – they are generally higher for internal C=C-bonds than for terminal ones. In most cases the yields are equally good for both peracids, but there is one remarkable exception. b-Pinene, which is very sensitive to acid-catalyzed rearrangement, can not be epoxidized by peracetic acid, whereas by using our

"acid-free percarbonic acid", we achieved a yield of 77 % with a selectivity of more than 98 %.

Table 2: Chemo-enzymatic epoxidation of olefins by "percarbonic" and peracetic acid in situ

olefin	yield of epoxide (mol-%) peroxy acid generated from (solvent):	
	dimethyl carbonate[a]	ethyl acetate[b]
1-octene	67	61-81
4-octene	92	94
1-tetradecene	69	71
7-tetradecene	100	90
styrene	78	73-92
norbornene	83	92
α-pinene	85	72
β-pinene	77	3
cyclohexene	83	64

0.1 mol/l alkene in dimethyl carbonate / ethyl acetate; 16 h
C=C : H_2O_2 (60%) = 1 : 5;
20 °C for internal C=C; 40° for terminal C=C

a. 5 mmol C=C / g Novozym ® 435
b. 10-50 mmol C=C / g Novozym ® 435

As mentioned above perhydrolysis can also be used for the "self-epoxidation" of unsaturated plant oils. In an inert solvent the result is an epoxidized plant oil. Now we epoxidized a plant oil (high oleic sunflower oil, fig. 6) in dimethyl carbonate.

The overall reaction is a combination of the transesterification of plant oil by dimethyl carbonate and chemo-enzymatic "self-"epoxidation resulting in the formation of epoxidized methylesters directly from plant oils. In our particular case the yield was 82 % 9,10-epoxystearic acid methylester. This amounts to an overall selectivity of 94 % for this one-pot-two-step procedure (the oil contains about 87 % oleic acid methylester), which will be difficult to obtain by other methods.

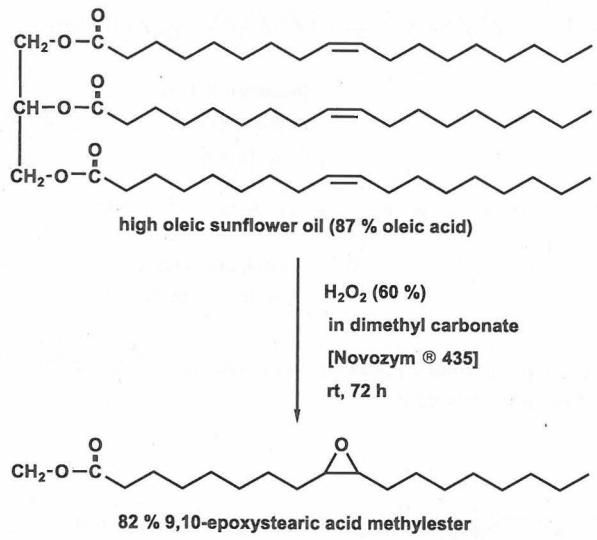


Fig. 6: Epoxidized fatty acid methylesters by lipase-catalyzed on-pot transesterification / epoxidation of plant oils with dimethly carbonate

Unsaturated fatty alcohols can also be epoxidized by lipase-catalyzed perhydrolysis /16/. Perhydrolysis of carboxylic acid esters leads directly and selectively to epoxy alkanol acylates in a three-step-one-pot reaction. However, by using "percarbonic acid" generated in situ from dimethyl carbonate and hydrogen peroxide, oleylalkohol is epoxidized with a very high selectivity (fig. 7); the hydroxyl group is not esterified, simply because there is no acid as a co-product (see also fig. 5).

The same principle can be applied and extended to chemo-enzymatic conversions of unsaturated fatty alcohol trimethylsilylethers. By choosing the acidic compound generated by lipase-catalyzed perhydrolysis or hydrolysis, the TMS-group can be removed or replaced by an acyl group and the C=C-bond can be epoxidized with removal or replacement of the TMS-group or without any attack on the TMS-group at all (fig. 8) /17/.

Although these last examples may not belong to core oleochemistry, they exemplify the versatility of lipase-catalysis for a variety of conversions outside the classic ester-hydrolysis / ester-synthesis scheme.

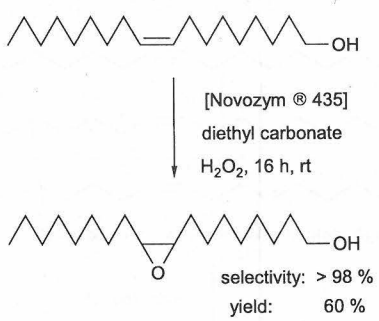


Fig. 7: Chemo-enzymatic epoxidation of oleylalcohol via perhydrolysis of dimethyl carbonate

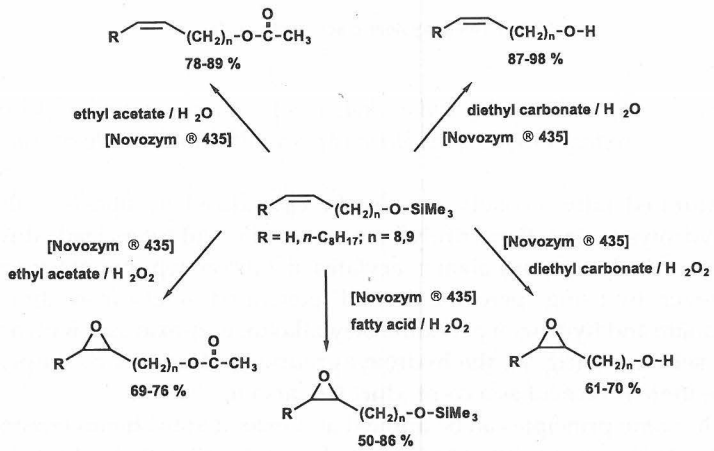


Fig. 8: Lipase-mediated conversions of fatty alcohol trimethyl silylethers /17/

Acknowlegdement

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