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O.N. Chupakhin on his 70th Anniversary

Reduction of Carbonyl Compounds with Polyethylsiloxane in the Presence of Titanium Compounds

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Abstract—Reduction of carbonyl compounds with polyethylsiloxane in the presence of titanium alkoxides gives the corresponding alcohols in high yields.

In the recent years, reduction of esters with silicon hydrides acquires increasing importance from the preparative viewpoint. Presumably, the most convenient reducing agents are polymeric silicon hydrides, for these compounds are widely used in industry and, unlike monomeric analogs, are not prone to undergo disproportionation leading to formation of explosive silane.

Breeden and Lawrence [1] studied the reduction of esters with excess polymethylsiloxane at a molar ratio of 1:10 in the presence of an equimolar amount of titanium isopropoxide or zirconium ethoxide on heating in boiling THF for 5 to 80 h. The yields of the reduction products ranged from 65 to 98%. Ridding and Buchwald [2] reported on the reduction of esters with polymethylsiloxane (molar ratio 1:2.5) in the presence of 25–100 mol % of titanium isopropoxide without a solvent at 23 to 70°C. The reaction time was 1.25 to 24 h, and the yields ranged from 8 to 99%. The reduction of some ketones was also examined in [1].

In the present work we effected reduction of esters with more accessible and more stable polyethylsiloxane in the presence of different titanium compounds at 100°C. Initially, we compared the results of reduction of butyl laurate with polymethylsiloxane (PMS) and polyethylsiloxane (PES). In the presence of an equimolar amount of butyl titanate as catalyst, the yields of lauryl alcohol were 95 and 88%, respectively. Although in the reduction with polyethylsiloxane the yield is somewhat lower, it nevertheless remains fairly high.

Preliminary experiments showed that during the reduction the reaction solution turns dark blue, which suggests formation of tervalent titanium compounds. We presumed that the presence of Ti(III) derivatives favors the reduction process and examined the catalytic activity of other titanium compounds. The results are summarized in Table 1. It is seen that decrease of the amount of butyl titanate from 100 to 5 mol % leads to considerable reduction of the yield. However, transformation of Ti(IV) derivative into Ti(III), regardless of the nature of Ti(III) compound, increases the yield to nearly quantitative.

The yield of the reduction products depends on the ester structure (Table 2). It decreases with increase in steric hindrance in the alkyl fragment of lauric acid esters. However, the above system ensures successful reduction of various esters derived from lower alcohols. As follows from the data given for ethyl esters, the lowest yield is observed for ethyl benzoate and ethyl 3-phenylpropionate. In order to estimate the

Table 1. Reduction of butyl laurate with polyethylsiloxane in the presence of titanium compounds (5 mol %)

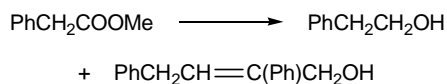
Titanium compound	Yield of lauryl alcohol, %
Ti(OBu) ₄	30
Ti(OBu) ₄ –Li–anthracene	88
Ti(OEt) ₄ –Li–naphthalene	95
LiTi(OPr- <i>i</i>) ₄	94
LiTiOC(CH ₃) ₂ CH(CH ₃) ₂	87

Table 2. Reduction of esters and lactones with polyethylsiloxane in the presence of 5 mol % of LiTi(OPr-*i*)₄

Ester or lactone	Yield of alcohol, %
Me(CH ₂) ₁₀ COOEt	93
Me(CH ₂) ₁₀ COOBu	88
Me(CH ₂) ₁₀ COOPr- <i>i</i>	57
Me(CH ₂) ₁₀ COOPh	50
Me ₃ CCOOEt	41
H(CF ₂) ₄ COOMe	57
Me(CH ₂) ₇ CH=CH(CH ₂) ₂ COOEt	74
Heteroauxin ethyl ester	49
Naproxen ethyl ester	95
PhCOOEt	39
PhCH ₂ COOEt	61
Ph(CH ₂) ₂ COOEt	26
Ph(CH ₂) ₃ COOEt	85
Butyrolactone	73
Valerolactone	52
Caprolactone	37

effect of aromatic radical in the acid fragment we examined a series of esters in which the benzene ring is located at different distances from the carboxy group. Provided that ethyl 3-phenylpropionate is excluded, the yield of the reduction product increases as the benzene ring becomes more distant from the carboxy group, i.e., conjugation between the carboxy group and benzene ring inhibits the process. However, the determining factor is steric hindrances. Actually, in keeping with the Newman rule, substituents at the β-carbon atom create greater steric hindrances than do α-substituents, and the yield in the reduction of ethyl 3-phenylpropionate is the lowest. As a rule, the yields given in Table 2 are not optimal. For example, prolonging the reduction of ethyl benzoate from 24 to 48 h leads to a quite satisfactory yield of benzyl alcohol (75%).

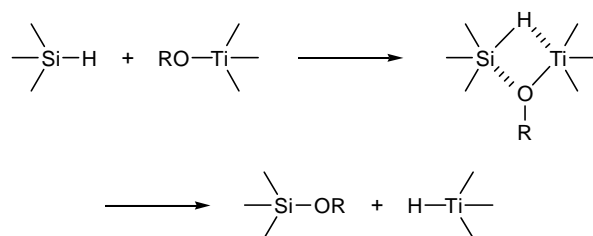
According to [1], the reduction of ethyl phenylacetate is accompanied by formation of 2,4-diphenyl-2-buten-1-ol as by-product.



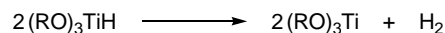
Analogous compound was isolated in the reduction of ethyl 2-thienylacetate [2] (here, the yield of the target product was as poor as 8%). Obviously, such

compounds could be formed only by self-condensation of the corresponding aldehydes. Therefore, the reduced yields of alcohols from aryl-substituted acetic acid esters may result not only from steric hindrances but also from side condensation processes. On the other hand, these findings indicate that the reduction involves intermediate formation of the corresponding aldehyde which is generally reduced at a higher rate and hence it does not accumulate in the system.

While discussing the reduction mechanism [1, 2], the authors tend to conclude that silicon hydride reacts with titanium alkoxide to give an intermediate which is then converted into titanium hydride. The latter was considered in [2] to be the active reducing species.

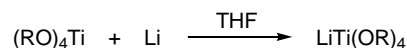


Breeden and Lawrence [1] believe that the observed color (typical of tervalent titanium compounds) originates from another side process:

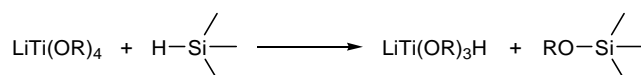


Taking into account the results of our experiments where Ti(III) derivatives showed the highest catalytic activity, we believe that just Ti(III) compounds act as reducing agents.

Reaction of titanium alkoxides with alkali metals was studied in detail by Vyshinskaya and co-workers [3], and the proposed mechanism is beyond doubt:



The alkoxide complex thus formed is reduced to hydride complex, and the latter is the active reducing species (i.e., catalyst):

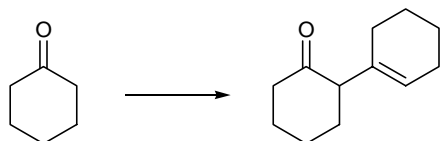


Analogous trialkoxyaluminum and trialkoxyboron hydrides are excellent reducing agents; for example, sodium trialkoxyboron hydrides are known to be more reactive than sodium tetrahydridoborate. Addition of anthracene (or naphthalene) accelerates dissolution of

lithium, but the yield of the reduction product remains essentially unaffected.

In order to compare the reduction patterns for aromatic and aliphatic esters we examined the reduction process by IR spectroscopy using $\text{Me}(\text{EtO})_2\text{SiH}$ as model reducing agent. In the reduction of ethyl benzoate, the carbonyl absorption intensity decreased at a lower rate than in the reduction of ethyl valerate. This suggests some chemoselectivity of the reducing agent. By reduction of a 1:1 mixture of ethyl benzoate and ethyl laurate we obtained benzyl alcohol and lauryl alcohol at a ratio of 12:80.

As noted above, reduction of aldehydes can be accompanied by their self-condensation catalyzed by titanium alkoxides [4]. Therefore, using cyclohexanone as an example, we preliminarily examined how the amount of the catalyst affects the yield of the reduction product. The yield of cyclohexyl alcohol was 46, 41, 40, and 25%, respectively, in the presence of 25, 50, 75, and 100 mol % of the catalyst. The low yield of the alcohol generally results from the concurrent self-condensation of cyclohexanone:



According to the GLC data, the still residue obtained after distillation of the reaction mixture contained 2-(1-cyclohexenyl)cyclohexanone and products of more profound condensation. The results showed that the use of an equimolar amount of titanium alkoxide is the least favorable. In the other cases, the yield may be regarded as constant within the experimental error. Therefore, in further experiments we used an average (50%) amount of the catalyst. No appreciable increase in the yield was observed in the presence of a complex catalyst. On the whole, satisfactory to good yields can be achieved (Table 3).

Aldehydes are reduced more readily than ketones, and the reaction successfully occurs at 50°C (Table 4). The yields of the reduction products are not high. In addition, various by-products are formed. In the reduction of benzaldehyde, the alkaline extract contained benzoic acid. Presumably, the process is accompanied by the Tishchenko reaction:

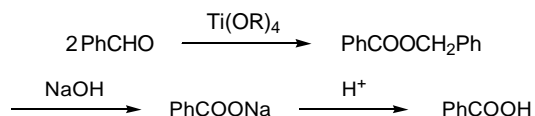


Table 3. Reduction of ketones with polyethylsiloxane in the presence of $\text{Ti}(\text{OBu})_4$

Ketone	Yield, %
$\text{Me}(\text{CH}_2)_5\text{COMe}$	67
$\text{Me}_2\text{CHCH}_2\text{COMe}$	44
Me_3CSOMe	44
PhCOMe	47
PhCOPh	30
$(\text{CF}_3)_2\text{CFCOCF}_2\text{CF}_3$	42
Cyclopentanone	38
Cyclohexanone	40
Tetrahydronaphthalen-1-one	68

Table 4. Reduction of aldehydes with polyethylsiloxane in the presence of $\text{Ti}(\text{OBu})_4$

Aldehyde	Yield, %
$\text{Me}_2\text{CHCH}_2\text{CHO}$	35
$\text{Me}(\text{CH}_2)_7\text{CHO}$	40
PhCHO	51
$p\text{-O}_2\text{NC}_6\text{H}_4\text{CHO}$	16
PhCH_2CHO	14–17
2-Furaldehyde	0

The low yield of the corresponding alcohol obtained from *p*-nitrobenzaldehyde is likely to result just from side reactions (it is known that nitro group is not reduced with silicon hydrides). In the reduction of furaldehyde, the reaction mixture solidified, presumably as a result of polycondensation.

IR spectroscopic study of the reduction of acetophenone and methyl isobutyl ketone with $\text{Me}(\text{EtO})_2\text{SiH}$ (following the change in the carbonyl absorption intensity) showed that the aromatic ketone is reduced at a lower rate. Analogous study of the reduction of isovaleraldehyde revealed that decrease in the carbonyl absorption intensity is accompanied by appearance of a new absorption band at 1692 cm^{-1} , which is typical of α,β -unsaturated compounds; its intensity increases with time. These data confirm the above assumptions concerning side condensation processes.

EXPERIMENTAL

GLC analysis was performed on a Tsvet-100 chromatograph equipped with a thermal conductivity detector; carrier gas helium, inlet pressure 2 atm;

100×0.6-cm column packed with 5% of tris(cyanoethoxy)propane on Chromaton AW (grain size 0.200–0.250 mm). The products were identified using authentic samples. The IR spectra were recorded on a Perkin–Elmer Spectrum-One spectrometer.

A mixture of the corresponding ester, silicon hydride, and titanium compound at a molar ratio of 1:3:(0.05–1) was heated for 24 h at 100°C (the reaction flask was plugged with wool). A 10% solution of sodium hydroxide was added (the mixture can be transferred into another flask by washing with THF), the mixture was heated for 3 h at the boiling point, cooled, and extracted with diethyl ether, and the

extract was subjected to fractional distillation. The silicon hydride-to-NaOH molar ratio was $\geq 1:3$. The products were identified by comparing their physical constants with published data.

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