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ALDOL-ADDITIONS TO α- AND β-ALKOXY ALDEHYDES: THE EFFECT OF CHELATION ON SIMPLE DIASTEREOSELECTIVITY

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Abstract - The $TiCl_4$ or $SnCl_4$ mediated reaction of enol silanes with chiral α- and β-alkoxy aldehydes constitutes the only presently known, general way to perform aldol additions with chelation-control (asymmetric induction >90%). If the enol silane is prochiral, the additional stereoselection (simple diastereoselectivity) is surprisingly good. This unusual effect has been traced to syn-type of complexation of the aldehyde function.

Introduction

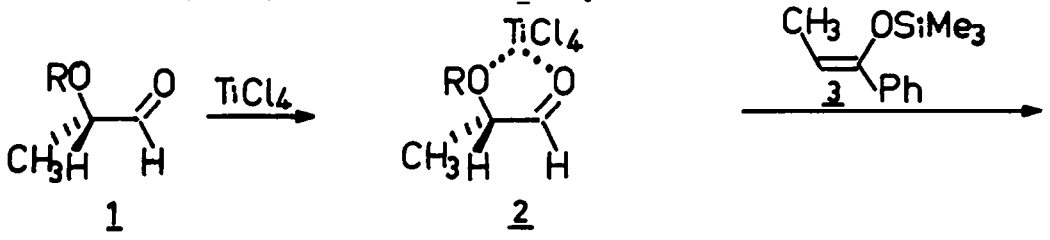
The extensive amount of recent research directed toward stereocontrol in aldol additions has focused on simple diastereoselectivity, i.e., on the relative stereochemistry of the two newly created chiral carbon centers formed by the union of two prochiral sp^2-hybridized C-atoms[1]. Less is known concerning a second type of stereoselectivity which may become relevant, namely diastereofacial selectivity[1]. In this case a chiral center in the aldehyde affects the formation of the new asymmetric C-atom, i.e., 1,n-asymmetric induction is involved. Obviously, if the enolate is prochiral, both types of stereoselection pertain.

Several cases of pronounced 1,2 asymmetric inductions in aldol additions to α-chiral aldehydes devoid of hetero-atoms have been reported and explained on the basis of Cram's model or more recent theories[1,2]. In case of α-alkoxy aldehydes, the situation is different because diastereofacial selectivity (1,2 asymmetric induction) is determined by chelation- or non-chelation-control[3]. Work by Heathcock has shown that lithium enolates from ketones tend to afford non-chelation-controlled products preferentially, although the degree of stereoselectivity is generally not very high[1,4]. Thus, it appeared challenging to devise methods which result in the opposite stereoselectivity, i.e., in efficient chelation-control.

Methods and Results

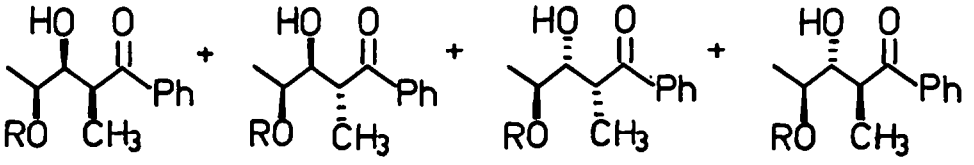
We recently reported the first and presently only known methodology for chelation-controlled aldol additions to α-chiral α-alkoxy aldehydes[5] and β-chiral β-alkoxy counterparts[6]. It involves $TiCl_4$ or $SnCl_4$ mediated Mukaiyama-type additions[7] of enol silanes. For example, adding $TiCl_4$ to the aldehyde 1 results in the octahedral complex 2, which reacts with a variety of enol silanes derived from ketones or esters to afford chelation-controlled aldol addition products with >95% stereoselectivity[5]. In case of prochiral 3, not only chelation-control is excellent, but

also the degree of simple diastereoselectivity. Thus, of four possible diastereomers practically only one (4) is formed[5]. In case of 1/$SnCl_4$ stereoselectivity is even better, i.e., the minor isomer 6 is present to<3%.



1 2

R = Benzyl; Ph = Phenyl; Me = Methyl throughout this paper.

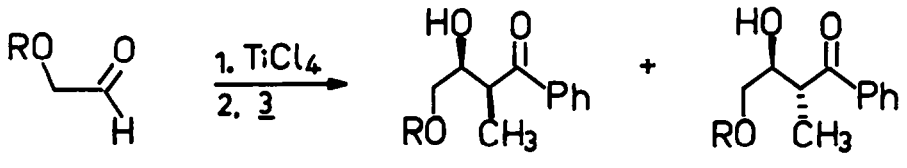


4 5 6 7

4	:	5	:	6	:	7
97		0		3		0
(chelation/syn)		(chelation/anti)		(non-chelation/syn)		(non-chelation/anti)

The fact that pronounced simple diastereoselectivity is observed surprises, because Mukaiyama additions of prochiral enol silanes to normal aldehydes generally afford mixtures of diastereomers[7]. For example, the $TiCl_4$ mediated reaction of propanal with 3 leads to a 66 : 34 product ratio of syn and anti adducts[6] (Masamune nomenclature). The mechanism of these reactions has not been elucidated. We have previously suggested that the above difference in behavior may be related to the different types of aldehyde-$TiCl_4$ complexation[5]. In case of simple aldehydes RCHO, complexation occurs anti to the R group, whereas chelation as in 2 necessarily involves syn-complexation. In this publication we report novel synthetic and mechanistic aspects concerning the influence of chelation on simple diastereoselectivity. Such a correlation has not been observed in case of other enolate systems (e.g., Li-enolates), i.e., the rules governing simple diastereoselectivity generally apply to all aldehydes[1].

If chelation of the type 2 is in fact the cause of increased simple diastereoselectivity, achiral 8 should also show this effect. Indeed, adding 3 to the $TiCl_4$ complex of 8 results in a product ratio of 9 : 10 = 90 : 10. Thus, simple diastereoselectivity is syn, as in the case of the addition of 3 to 2. The $SnCl_4$ induced addition of 3 to 8 is even more selective (9 : 10 = >95 : <5), but other metal systems are less so (Table 1).



8 9 10

Table 1 Formation of 9/10 from 8

Lewis Acid	Solvent	Reaction time (min)	9 : 10	Conversion (%)
$TiCl_4$ [a]	CH_2Cl_2	60	90 : 10	>95
$SnCl_4$ [a]	CH_2Cl_2	60	>95 : <5	>95
BF_3-etherate [a]	CH_2Cl_2	120	50 : 50	82
Li [b]	THF	90	66 : 34	85
$Ti(OCHMe_2)_3$ [c]	THF	90	83 : 17	81

a) The Lewis acid was reacted with 8 at -78 °C and after 10 min 3 added at the same temperature.

b) The lithium enolate corresponding to 3 was reacted with 8 in the absence of Lewis acids.

c) The lithium enolate corresponding to 3 was treated with $ClTi(OCHMe_2)_3$ at -78 °C and the resulting titanium enolate reacted with 8.

In order to shed more light on the mechanism of chelation-controlled additions, the effect of the geometry of the enolate on simple diastereoselectivity was studied. Adding 11 (the E-isomer of 3) to 2 resulted in complete diastereofacial selectivity via chelation and in an appreciable degree of simple diastereoselectivity (syn : anti = 85 : 15). Thus, the sense of simple diastereoselectivity is independent of the geometry of the enol silane.

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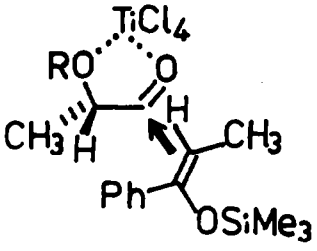
The results do not prove any one mechanism, but are in line with an acyclic transition state[8] 12 (for the Z-enolate) and 13 (for the E-enolate) in which the methyl group of the incoming C-nucleophile avoids steric interaction with the substituents of the five-membered chelate. In case of normal aldehydes of the type propanal, such an approach of the enol silane is no longer preferred, because the methyl group conflicts with the $TiCl_4$ (see 14 in case of the Z-enolate)*. This results in low diastereoselectivity.



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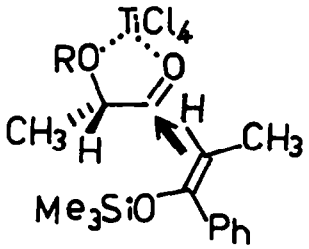

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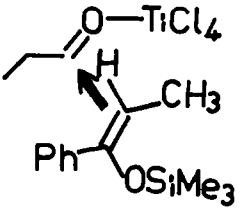

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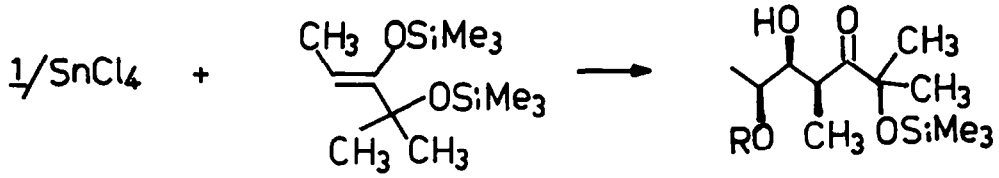
*) This is a simplification, because $TiCl_4$ may complex two aldehydes, i.e., it is likely to be octahedrally complexed. Chlorine bridging is also possible[9].

Further experiments show that the reactions described so far do not proceed via prior Si-Ti or Si-Sn exchange. According to Kuwajima, Z-configurated enol silanes from acyclic ketones react rapidly and stereospecifically with $TiCl_4$ to form Z-configurated Cl_3Ti-enolates, while the E-isomers interact sluggishly to afford low yields of mixtures of E- and Z-Ti-enolates[10]. The Z-isomers were shown to react with aldehydes to form syn-adducts preferentially (∿80 : 20 ratios)[10]. We therefore treated 3 with $TiCl_4$ and then added the preformed Cl_3Ti-enolate to 1[5]. The resulting product distribution 4 : 5 : 6 : 7 = 89 : 3 : 0 : 8 is different from the one observed in the addition of 3 to 2. Kuwajima also showed that certain enol silanes interact with $SnCl_4$ to form α-trichlorostannyl ketones, which react with achiral aldehydes to produce syn aldol adducts[10] preferentially. We observed that treatment of 3 with $SnCl_4$ followed by the addition of 1 (-78 °C, 1 h) results in 4 : 5 : 6 : 7 = 94 : 0 : 6 : 0 (70%). Apart from mechanistic aspects, pretreatment of 3 with $SnCl_4$ or $TiCl_4$ is inferior to the original method involving chelation of the aldehyde 1 with these Lewis acids.

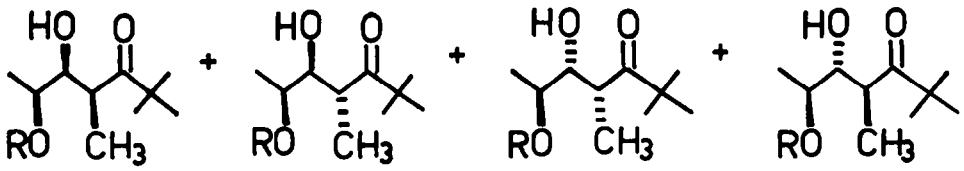
In order to extend the scope of the method, we reacted the enol silane 15[11] with 2 and 1/$SnCl_4$. In the former case (-78 °C/1 h), neither the aldol adduct nor starting material 15 was observed, possibly due to some sort of interaction of $TiCl_4$ with the silylated carbinol function. In contrast, the $SnCl_4$ mediated reaction delivered a single diastereomer 16 (∿84% conversion). This reaction is synthetically significant, because aldol adducts having such a carbonyl group[11] can easily be converted into other functionalities such as ester, aldehyde or ketone moieties. The corresponding Li-enolate is known to afford a 1 : 2 mixture of chelation- and non-chelation-controlled products[11].



15 16

In view of the results presented thus far, the reactions of the enol silane 17a are surprising (Table 2). 2 and 1/$SnCl_4$ both lead to complete chelation control, but simple diastereoselectivity is ∿1 : 1. Thus, not only the methyl group at the enolate double bond affects the sense of simple diastereoselectivity, but also the nature of the other enolate substituents. Their influence is difficult to assess, even if the hypothesis of an acyclic transition state is accepted[12], because the precise direction of enol approach is unknown. The interpretation is also difficult in case of the preformed Cl_3Ti-enolate, which reacts stereorandomly with respect to chelation- or non-chelation-control, but syn-selectively with respect to simple diastereoselectivity. Further manipulation of stereoselecitivity is possible by adding the preformed Cl_3Ti-enolate to 2. The α-$SnCl_3$-ketone fails to react. Also, the t-butyldimethylsilyl derivative 17b reacts with 2 to produce a product distribution which is different from the result of the analogous reaction of 17a (Table 2). This shows that the nature of the silyl group has some effect on the stereochemical outcome.

17 a) M = $SiMe_3$
b) M = $SiMe_2t$-Bu



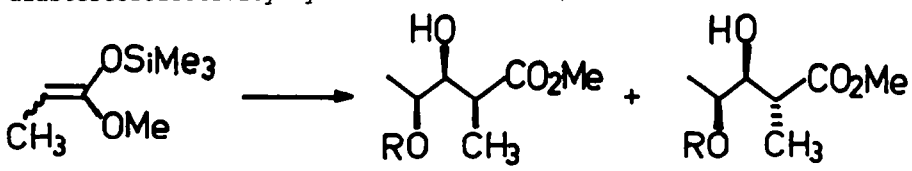
18 19 20 21

Table 2 Stereoselective Reactions[a] of 17

Aldehyde component	M in 17	Ratio 18 : 19 : 20 : 21
2	$SiMe_3$	45 : 55 : 0 : 0
1/$SnCl_4$	$SiMe_3$	56 : 44 : 0 : 0
1/BF_3[b]	$SiMe_3$	7 : 7 : 36 : 50
1	$TiCl_3$	52 : 2 : 46 : 0
2	$TiCl_3$	29 : 71 : 0 : 0
1	$SnCl_3$[c]	no addition
1/$SnCl_4$	$SnCl_3$[c]	no addition
2	$Si(CH_3)_2t$-Bu	39 : 61 : 0 : 0

a) All reactions in CH_2Cl_2 at -78 °C; conversion >80%
b) BF_3-etherate was used
c) The α-$SnCl_3$-ketone is probably involved.

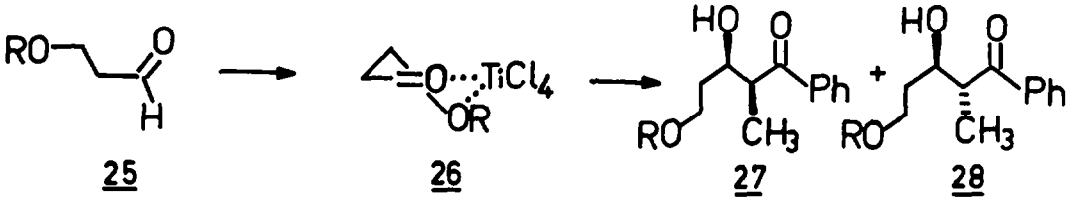
The above results underline the mechanistic complexity, and also demonstrate that 17a-b are not ideal synthetic reagents. We also tested the ester Si-enolate 22. Using an 83 : 17 E/Z mixture of 22, 2 or 1/$SnCl_4$ led to complete chelation-control and to useful levels of simple diastereoselectivity in favor of the syn-adduct. The other two diastereomers were not detected. In contrast, the Li-enolate delivers a mixture of all four diastereomers (chelation : non-chelation = 20 : 80; simple diastereoselectivity syn : anti = 68 : 32[13]).



22 23 24

$TiCl_4$	77	:	23
$SnCl_4$	80	:	20

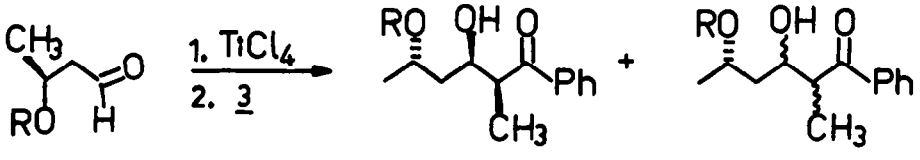
Turning from α- to β-alkoxy aldehydes , the achiral aldehyde 25 was treated with $TiCl_4$ and the complex 26 reacted with 3. The ratio of syn/anti adducts turned out to be >94 : <6. Similarly, the E-isomer 11 gave almost the same results. Thus, β-chelation 26 has the same effect on simple diastereoselectivity as α-chelation (see above). 25/$SnCl_4$ +11 affords a 1 : 1 mixture, possibly due to the longer Sn-O bond.



25 26 27 28

3	94	:	6
11	90	:	10

Finally, the β-chiral β-alkoxy aldehyde 29 was complexed with $TiCl_4$ and reacted with 3. Of the four possible diastereomers, 30 was formed to ∿92%. This means excellent 1,3 asymmetric induction via chelation control as well as unusually high simple diastereoselectivity (syn). The analogous reaction using $SnCl_4$ is stereorandom, a statistical mixture of all four diastereomers being formed. The Li-enolate also reacts stereorandomly at -78 °C in THF.



29 30 31

>92	:	<8

In summary, $TiCl_4$ or $SnCl_4$ mediated additions of enol silanes to chiral α- and β-alkoxy aldehydes constitute the only currently known way to perform aldol additions with efficient chelation-control. Thus, 1,2 and 1,3 asymmetric induction is >90%. In case of α-alkoxy aldehydes, $SnCl_4$ is more efficient than $TiCl_4$. The opposite is true for the β-alkoxy aldehydes. If the enol silane is prochiral, the additional type of stereoselectivity (simple diastereoselectivity) is syn. The latter is also generally high, although exceptions occur. The results are in line with acyclic transition states such as 12 and 13, but do not rigorously prove such a mechanism. Recently, Danishefsky reported $TiCl_4$ mediated cyclocondensations of chiral α-alkoxy aldehydes with siloxybutadiene derivatives[14]; these are related to our previous[5,6] and present results. Masamune has previously described stereoselective aldol additions of Li-enolates to certain β-alkoxy α-chiral aldehydes[15].

Configurational Assignments

Configurational assignments regarding simple diastereoselectivity were made in all cases using ^{13}C NMR data as delineated by Heathcock[1]. Accordingly, the ^{13}C-signals of the methyl group α to the carbonyl function of the syn-adducts appear at higher fields than the corresponding signals of the anti-adducts. Assignments pertaining to diastereofacial selectivity were also made using ^{13}C NMR spectroscopy. In case of compounds formed from 1, the ^{13}C signals of the methyl group α to the benzyloxy moiety of the chelation-controlled adducts consistently appear at lower field than the corresponding signals of the non-chelation-controlled adducts. This also applies to

the adducts resulting from the reactions of CH_3TiCl_3 and other Lewis acidic nucleophiles with 1; they were transformed chemically to known diols[5,16]. This general rule was also checked in case of several aldol adducts. Thus, the X-ray structure[5] of 4 proves the assignment made on the basis of ^{13}C NMR data. The configurations of 4, 6, 20 and 23 were also determined by chemical correlation[13]. For example, the known adduct 16 was transformed into 23. In case of chelation-controlled adducts of 29 resulting from reactions with enol silanes, CH_3TiCl_3 or allylsilane/$TiCl_4$, the ^{13}C-signals of the C-atom bearing the benzyloxy group consistently appear at higher field than the corresponding signals of the non-chelation-controlled adducts[6,17]. Jäger has made similar observations in case of amino-alcohols[18].

Generally, H-NMR data were found not to be a reliable criterion[13].

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Experimental Section

All reactions were carried out in dry flasks under an atmosphere of nitrogen. Solvents were dried using standard techniques. NMR spectra were recorded on Bruker WH 400 and WH 90 and Varian XL 100 instruments. The CH-analyses were performed in the Analytical Department (Fachbereich Chemie, Marburg) and Beller-Laboratory (Göttingen).

Preparation of Enol Silanes

Enol silanes were generally prepared by quenching the lithium enolate (made by LDA-induced deprotonation) with chlorosilanes according to standard procedures. In case of 11[19], the procedure of Matsuda was utilized[20].

Preparation of the Aldehydes

Compound 1 was prepared from (+)-lactic acid ethylester according to a known procedure[4]. 8[21] and 25[22] have also been described in the literature. 29 was made by ozonolysis of racemic 4-benzyloxy-1-pentene according to Geueke[23].

Z-3,4-Bis(trimethylsiloxy)-4-methyl-2-pentene (15):

To a solution of 55 mmol lithium diisopropylamid (LDA) in 150 ml THF was added at -78 °C 2-methyl-2-trimethylsiloxy-3-pentanone (9.42 g; 50 mmol)[11]. After 30 min the resulting enolate solution was treated with trimethylchlorosilane (8.69 g; 80 mmol), stirred for 30 min and then allowed to come to room temp. After 2 h the mixture was worked up with sat. $NaHCO_3$, extracted with pentane and dried over $MgSO_4$. The solvent was stripped off and the crude product distilled (91-92 °C/ 12 torr) to yield 11.03 g (85%) of a colorless liquid. Found: C 55.34, H 10.71; calcd. for $C_{12}H_{28}O_2Si_2$ (260.5) C 55.32, H 10.83. H NMR ($CDCl_3$): δ = 0.12(s,9H), 0.21(s,9H), 1.33(s,6H), 1.51(d, J=7 Hz,3H), 4.87(q,J=7 Hz,1H). ^{13}C NMR (C_6D_6): δ = 1.1, 2.8, 11.4, 29.1, 75.4, 98.9, 156.7.

Z-4,4-Dimethyl-3-(t-butyldimethylsiloxy)-2-pentene (17b):

To a solution of 55 mmol LDA in 150 ml THF was added at -78 °C 2,2-dimethyl-3-pentanone (5.71 g; 50 mmol). After 30 min a solution of t-butyldimethylchlorosilane (8.29 g; 55 mmol) in 30 ml hexamethylphosphoric acid triamide (HMPT) was

added and the mixture stirred for 30 min. The solution was warmed up to room temp. (2 h), poured on H_2O and extracted with pentane. After drying over $MgSO_4$ and removing the solvent, fractional distillation (80 °C/ 12 torr) yielded 7.85 g (69%) of a colorless liquid. Found: C 68.49, H 12.34; calcd. for $C_{13}H_{28}OSi$ (228.5) C 68.35, H 12.35. H NMR ($CDCl_3$): δ = 0.17(s,6H), 0.97(s,9H), 1.04(s,9H), 1.51(d, J=7 Hz,3H), 4.55(q,J=7 Hz,1H). ^{13}C NMR (C_6D_6): δ = -2.6, 12.1, 19.4, 26.7, 29.1, 36.8, 97.2, 159.0.

General Procedure of Lewis Acid Mediated Additions of Enol Silanes to α- and β-Alkoxy Aldehydes

5.0 mmol of the alkoxy aldehyde in 50 ml of dry CH_2Cl_2 is treated with 5 mmol of a Lewis acid at -78 °C. After 5-10 min 5 mmol of an enol silane is added using a syringe. In case of the more reactive ketene ketals, cooled (-78 °C) CH_2Cl_2 solutions are added to the aldehyde/Lewis acid complex. After addition is complete, the mixture is stirred for an additional 1 - 2 h. Sometimes the initially formed aldehyde/Lewis acid complex precipitates. In these cases final stirring (after the enol silane has been added) is prolonged (up to 5 h) and/or the temp. is raised to -50 or even -20 °C. The reaction is always complete within 30 min after the solution has become homogeneous. The mixture is then poured onto H_2O, extracted with ether twice and the combined organic phases neutralized with $NaHCO_3$-solution. In case of acid-sensitive products (16), sat. $NaHCO_3$ is poured onto the reaction mixture. After drying over $MgSO_4$ the solvent is stripped off and the crude product analyzed with NMR spectrscopy. Conversion is >85% in all cases. The same applies to reactions on a 10-20 mmol scale.

The crude products were purified by column chromatography (silica gel, pet.ether (40-60)/ether 2:1) which provided analytically pure diastereomeric mixtures, of which the CH-analyses were performed. Separation of diastereomers was accomplished in all cases (except 23/24) using HPLC (silica gel, pet.ether (40-60)/ether 5:1).

4-Benzyloxy-3-hydroxy-2-methyl-1-phenyl-pentan-1-one

Using 2 or 1/$SnCl_4$ and 3: 89-91% yield of a mixture of 4/5 (Kugelrohrdistillation at 160 °C/ 0.1 torr). The Zn-enolate[5] at 0 °C (5 h) delivers all four isomers 4-7 which can be separated by HPLC. Found: C 76.70, H 7.23; calcd. for $C_{11}H_{22}O_3$ (298.4): C 76.48, H 7.43.

^{13}C NMR ($CDCl_3$) data (δ)*):

4: 14.4, 16.0, 43.7, 70.8, 75.3, 76.4, 203.6
5: 15.1, 15.7, 42.5, 70.6, 74.7, 77.6, 204.8
6: 11.9, 15.6, 41.4, 70.7, 74.3, 74.9, 204.7
7: 15.6, 15.7, 39.8, 70.8, 76.9, 78.1, 206.6

4-Benzyloxy-3-hydroxy-2-methyl-1-phenyl-butan-1-one

Using 8/$SnCl_4$ and 3: 69% yield of a mixture of 9/10 (column chrom.). Found: C 76.02, H 7.02; calcd. for $C_{18}H_{20}O_3$ (284.4): C 76.03, H 7.09

^{13}C NMR ($CDCl_3$) data (δ) :

9: 12.9, 42.6, 71.2, 71.7, 73.4, 204.3
10: 14.8, 42.2, 72.1, 73.0, 73.4, 204.9

*) Here and in the following cases the signals of the phenyl groups have been left off. They are of no diagnostic value. H NMR data are listed in lit.[13].

6-Benzyloxy-5-hydroxy-2,4-dimethyl-2-trimethylsiloxy-heptan-3-one (16)

Using 1/$SnCl_4$ and 15 (1 h at -78 °C to -40 °C); 84% conversion (60-65% isolated by column chromatography). NMR data identical with lit.[11].

6-Benzyloxy-5-hydroxy-2,2,4-trimethyl-heptan-3-one

Using 2 or 1/$SnCl_4$ and 17a: 80-82% yield of a mixture of 18-21 (column chrom.). Found: C 73.14, H 9.29; calcd. for $C_{17}H_{26}O_3$ (278.4): C 73.35, H 9.41.

^{13}C NMR ($CDCl_3$) data (δ):

18: 14.7, 16.3, 26.4, 42.5, 44.9, 70.6, 75.6, 76.0, 219.5

19: 15.2, 15.9, 26.3, 42.2, 44.8, 70.4, 72.9, 77.3, 219.1

20: 11.0, 15.7, 26.0, 38.9, 44.8, 70.3, 74.1, 74.2, 221.8

21: 14.3, 15.9, 26.5, 39.9, 45.0, 70.6, 76.3, 76.9, 222.6

4-Benzyloxy-3-hydroxy-2-methylpentanoic acid methyl ester

Using 2 or 1/$SnCl_4$ and 22: 75-77% yield (column chrom.). Found: C 66.44, H 8.04; calcd. for $C_{14}H_{20}O_4$ (240.3): C 66.55 H 7.99

^{13}C NMR ($CDCl_3$) data (δ):

23: 12.6, 15.8, 42.3, 51.5, 71.1, 75.3, 75.9, 175.3

24: 11.7, 15.1, 41.1, 51.7, 70.6, 74.0, 75.0, 176.5

5-Benzyloxy-3-hydroxy-2-methyl-1-phenyl-pentan-1-one

Using 26 and 3: 70% of a mixture of 27/28 (column chrom.). Found: C 76.29, H 7.40; calcd. for $C_{19}H_{22}O_3$ (298.4): C 76.48, H 7.43

^{13}C NMR ($CDCl_3$) data (δ):

27: 11.8, 33.9, 45.0, 67.8, 70.2, 72.6, 204.1

The α-methyl signal of the anti-isomer 28 appears at δ = 13.9 (not enough material was present to identify all other signals).

5-Benzyloxy-3-hydroxy-2-methyl-1-phenyl-hexan-1-one

Using 29/$TiCl_4$ and 3: 65% of a mixture of 30/31 (column chrom.). Found: C 76.65, H 7.50; calcd. for $C_{20}H_{24}O_3$ (312.4) : C 76.89, H 7.74

^{13}C NMR ($CDCl_3$) data (δ):

30: 11.8, 19.4, 41.1, 45.2, 68.7, 70.4, 72.4, 204.8

Footnotes

1) C.H. Heathcock in J.D. Morrison, Asymmetric Synthesis, Vol. III, Part B, 1984; D.A. Evans, J.V, Nelson, T.R. Taber, Top. Stereochem. 13 (1982) 1.

2) C.H. Heathcock, L.A. Flippin, J. Am. Chem. Soc. 105 (1983) 1667.

3) Review: M.T. Reetz, Angew. Chem., in press.

4) C.H. Heathcock, M.C. Pirrung, J. Lampe, C.T. Buse, S.D. Young, J. Org. Chem. 46 (1981) 2290.

5) M.T. Reetz, K. Kesseler, S. Schmidtberger, B. Wenderoth, R. Steinbach, Angew. Chem. 95 (1983) 1007; Angew. Chem., Int. Ed. Engl. 22 (1983) 989; Angew. Chem. Suppl. 1983, 1511; M.T. Reetz, K. Kesseler, A. Jung, Tetrahedron Lett. 25 (1984) 729.

6) M.T. Reetz, A. Jung, J. Am. Chem. Soc. 105 (1983) 4833.

7) T. Mukaiyama, K. Banno, K. Narasaka, J. Am. Chem. Soc. 96 (1974) 7503; T. Mukaiyama, Org. React. 28 (1982) 203.

8) Acyclic transition states have been considered in other additions: Y. Yamamoto, H.Yatagai, Y. Naruta, K. Maruyama, J. Am. Chem. Soc. 102 (1980) 7107; M.T. Reetz, M. Sauerwald, J. Org. Chem. 49 (1984) 2292; and lit. cited therein.

9) $TiCl_4$ forms dimeric adducts with ethyl acetate in which chlorine bridges between two Ti-atoms; X-ray structure: L. Brun, Acta Crystallogr. 20 (1966) 739.

10) E. Nakamura, I. Kuwajima, Tetrahedron Lett. 24 (1983) 3343.

11) C.H. Heathcock, C.T. Buse, W.A. Kleschick, M.C. Pirrung, J.E. Sohn, J. Lampe, J. Org. Chem. 45 (1980) 1066.

12) Alternative mechanisms have been discussed[5,6].

13) K. Kesseler, projected PhD Thesis, Universität Marburg, 1985.

14) S.J. Danishefsky, W.H. Pearson, D.F. Harvey, J. Am. Chem. Soc. 106 (1984) 2456.

15) S. Masamune, J.W. Ellingboe, W. Choy, J. Am. Chem. Soc. 104 (1982) 5526.

16) S. Schmidtberger, Diplomarbeit, Universität Marburg, 1983.

17) A. Jung, Diplomarbeit, Universität Marburg, 1983.

18) V. Jäger, V. Buß, Liebigs Ann. Chem. 1980, 101.

19) R. Noyori, I. Nishida, J. Sakata, J. Am. Chem. Soc. 105 (1983) 1598.

20) I. Matsuda, S. Sato, Y. Izumi, Tetrahedron Lett. 24 (1983) 2787.

21) C.A. Grob, F. Reber, Helv. Chim. Acta 33 (1950) 1785.

22) A. Gaiffe, C. Launay, C.R. Acad. Sc., Ser. C, 266 (1968) 1379.

23) K.-J. Geueke, Dissertation, Universität Marburg, 1981.