Stereoselective Substitution at Phenyl-Substituted γ-Lactols with Organometallic Compounds

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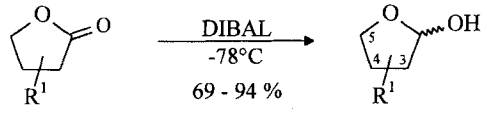
A variety of monosubstituted γ-lactols **4**–**6** were prepared in good yields by DIBAL reduction of the corresponding γ-lactones **1**–**3**. The monophenyl-substituted lactols **4b**–**6b** were transformed into disubstituted tetrahydrofuran derivatives by replacement of the hydroxyl group by the alkyl residue of organometallic compounds used as nucleophiles. The diastereoselectivity of the substitution was found to depend strongly on the substitution pattern of the γ-lactols. For the reaction of the 3- and 4-substituted derivatives **4b** and **5b**, respectively, good to excellent *trans* selectivity was observed, while the 5-substituted derivative reacted without any diastereoselectivity. These results were interpreted by means of the Felkin-Anh model.

The stereoselective synthesis of substituted tetrahydrofuran derivatives has received much attention[2], since they occur as building blocks in many interesting natural products such as pheromones[3] or polyether antibiotics[4]. Although widely used in carbohydrate chemistry[5], the Lewis acid-promoted substitution at the anomeric centre of simple γ-lactols (tetrahydrofuran-2-ols) via oxocarbenium ions[6] was rarely applied to the diastereoselective synthesis of these compounds[7]. Meanwhile, it is known which nucleophiles can be employed in this reaction, but there is a lack of systematic studies of the stereochemical outcome of the reaction and the dependence of the diastereoselectivity on both the substitution pattern of the γ-lactol and the nucleophile. Recently, we reported on the diastereoselective synthesis of highly substituted tetrahydrofuran derivatives employing silylated nucleophiles[8]. In this paper we disclose our results on the Lewis acid-induced reaction of monophenyl-substituted γ-lactols **4b**–**6b** with organometallic species as nucleophiles[9].



1 - 3 **4 - 6**

R^1

1 **a** = 3-Me **b** = 3-Ph **c** = 3-*tert*-Bu **4**
2 **a** = 4-Me **b** = 4-Ph **c** = 4-*tert*-Bu **5**
3 **a** = 5-Me **b** = 5-Ph **c** = 5-*tert*-Bu **6**

γ-Lactols **4**–**6** required for this and the subsequent studies were straightforwardly prepared by reduction of the corresponding γ-butyrolactones **1**–**3** with DIBAL (diisobutylaluminium hydride) at low temperature[10]. We modified the procedure for this reduction in order to obtain more reliable results for simple monosubstituted lactones. The γ-lactols **4**–**6** were obtained as mixtures of anomers.

The phenyl-substituted γ-lactols **4b**–**6b** were treated with several organometallic reagents with or without addition of Lewis acid.

Dialkylzinc compounds seem to be reagents of choice for the direct replacement of the hydroxyl group of γ-lactols by an alkyl group. While diethylzinc did not react with γ-lactols in the absence of a Lewis acid (entry 7), the introduction of an ethyl group smoothly proceeded in the presence of boron trifluoride (entries 2, 3, 8) to afford the tetrahydrofuran derivatives **8**, **9**, and **11** in high yields. Ethylation could also be achieved by treatment of the lactol with triethylaluminium (entry 4), while diethylaluminium chloride reacted rather sluggishly (entry 9). The reaction of γ-lactols **4b** and **6b** with dimethylcuprate in the presence of boron trifluoride (entries 1, 5) afforded the 2-methyl-substituted tetrahydrofuran derivatives **7** and **10** in moderate yields only. According to Lipshutz and coworkers[11] the reaction of organocuprates with boron trifluoride leads to a mixture of organometallic species containing inter alia $R-Li \cdot BF_3$. The moderate yields of the expected products might be due to the presence of this reagent, which is known to react with γ-lactols[7c] to give complex product mixtures.

Introduction of a methyl group at position 2 of the tetrahydrofurans was also achieved by use of methyltitanium trichloride (entry 6). This reagent did not display significant chemoselectivity with regard to which of the two carbon-oxygen bonds was cleaved. Besides the expected 2-methylated tetrahydrofuran **10** (55% yield) the diol **12** was ob-

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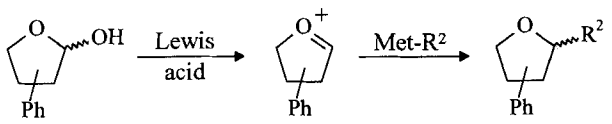
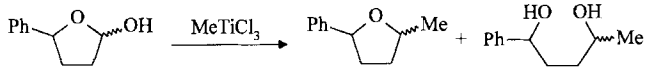


4b, 5b, 6b **7 - 11**

Entry	Lactol	Met-R²	Lewis acid	Product		R²	Yield (%)	*trans* : *cis*
1	**4b**	Me_2CuLi	$BF_3{\cdot}Et_2O$	**7**	3-Ph	Me	37	65 : 35
2	**4b**	$ZnEt_2$	$BF_3{\cdot}Et_2O$	**8**	3-Ph	Et	96	90 : 10
3	**5b**	$ZnEt_2$	$BF_3{\cdot}Et_2O$	**9**	4-Ph	Et	85	≥ 95 : 5
4	**5b**	$AlEt_3$	$BF_3{\cdot}Et_2O$	**9**	4-Ph	Et	62	94 : 6
5	**6b**	Me_2CuLi	$BF_3{\cdot}Et_2O$	**10**	5-Ph	Me	39	70 : 30
6	**6b**	$MeTiCl_3$	–	**10**	5-Ph	Me	55	42 : 58
7	**6b**	$ZnEt_2$	–	**11**	5-Ph	Et	–	–
8	**6b**	$ZnEt_2$	$BF_3{\cdot}Et_2O$	**11**	5-Ph	Et	94	49 : 51
9	**6b**	Et_2AlCl	–	**11**	5-Ph	Et	25	52 : 48

tained in 41% yield. The formation of **12** was rather surprising[12] since methyltitanium trichloride was expected to be sufficiently acidic to induce the heterolytic cleavage of the hydroxyl group of the γ-lactol to yield the intermediate oxocarbenium ion.



6b **10** **12**

Configurational Assignments

The assignment of the diastereoisomers was based on their ^{1}H- and ^{13}C-NMR spectroscopic data and on NOE experiments. Since in the 2,3-disubstituted *trans* isomers the protons in the positions 2 and 3 of the tetrahydrofuran ring are shielded by the vicinal substituent and their signals are observed at higher field than those of the corresponding *cis* isomer. For the same reason one observes for the alkyl protons of the substituent an upfield shift in spectrum of the *cis* isomer. According to Eliel et al.[13] the signals of the ring carbon atoms of *trans*-2,3-disubstituted tetrahydrofuran derivatives appear at lower field than those of the corresponding *cis* compounds. Thus, the major diastereoisomers of **7** and **8** are *trans*-configurated. In addition to these criteria, the major isomer of **8** was unambiguously characterized as *trans* compound by NOE experiments.

For 2,4-disubstituted tetrahydrofuran derivatives, the stereochemical assignment can be carried out on the basis of the ^{13}C-NMR spectroscopic data[13] since all ring carbon atoms of the *trans* diastereoisomer except C-5 show a downfield shift, while the signal of C-5 appears at higher field compared to that of the *cis* compound. The major diastereoisomer of **9** is therefore *trans*-configurated.

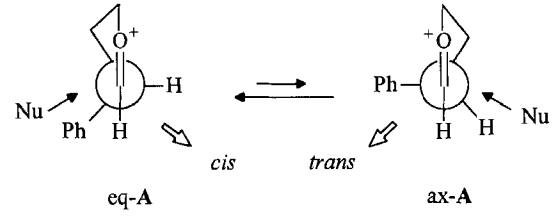
For the assignment of the 2,5-disubstituted derivatives ^{13}C-NMR spectroscopic data are of no use since the dependence of the chemical shift on the nature of the substituents is too strong[13]. However, in this case the configuration can be easily determined on the basis of the chemical shift of the protons in the positions 2 and 5 of the tetrahydrofuran ring. Due to a 1,3-deshielding effect of the alkyl substituent on the proton in γ-position[14] the signals of 2-H and 5-H of the *cis* compounds appear at higher fields than those of the corresponding *trans* derivatives. Therefore, the major diastereoisomer of **10** was assigned the *trans*, and that of **11** the *cis* configuration.

Discussion

Since the nature of the reactive species in the cuprate/Lewis acid mixture is not clear, the discussion of the diastereoselectivity will be limited to the transformations employing diethylzinc as nucleophile. In the case of the 3- and 4-phenyl-substituted γ-lactols **4b** and **5b** replacement of the hydroxyl group by this reagent proceeded with very high *trans* diastereoselectivity (entries 2, 3). For the 4-substituted derivative **5b** the reaction almost exclusively led to the *trans* product **9**. Lactol **5b** and triethylaluminium also reacted with excellent diastereoselectivity (entry 4). In contrast, replacement of the hydroxyl group of the 5-substituted γ-lactol **6b** by an ethyl group of diethylzinc proceeded without any diastereoselectivity.

These results can be explained by taking into account that one of the two possible conformations of the intermediate oxocarbenium ion is thermodynamically preferred and by applying the Felkin-Anh model[15] to predict the reactivity of each conformer. Force-field calculations[16] show that the conformations of the oxocarbenium ions derived from **4b**–**6b** bearing the phenyl substituent in an equatorial position are by 6.2–9.7 kJ/mol more stable than those bearing the substituent in an axial position. The application of these considerations to the reaction of 3-substituted γ-lactol **4b** leads to Scheme 1:

Scheme 1

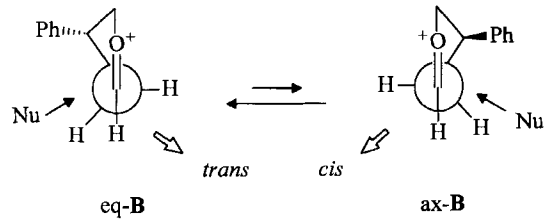


eq-A ax-A

According to the Felkin-Anh model, the attack of the nucleophile on oxocarbenium ion **A** generated from lactol **4b** occurs preferentially on ax-**A** since the phenyl group in eq-**A** significantly hinders the attack. Thus, by purely regarding the different reactivities of the two conformers the formation of the *trans* product should be highly favoured. On the other hand, eq-**A** is the thermodynamically preferred conformation of **A**; hence this conformer is present in a "higher concentration" leading to the formation of the *cis* product. Therefore, one observes two opposing effects, but the influence of the reactive conformation turned out to

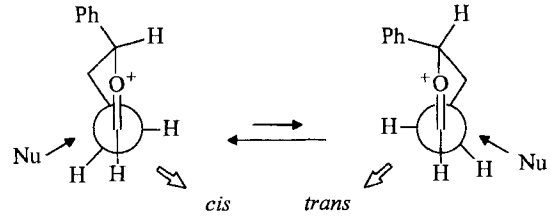
be dominant since *trans*-**8** was formed with high selectivity.

Scheme 2



For the 4-substituted oxocarbenium ion **B** derived from **5b** (Scheme 2), eq-**B** is the thermodynamically preferred and, since in ax-**B** the phenyl group strongly hinders the attack of the nucleophile, also the more reactive conformer. Both effects converge to lead to the preferential formation of *trans*-**9** giving in fact rise to an excellent *trans*-to-*cis* ratio (≥95:5).

Scheme 3



In the case of the 5-substituted oxocarbenium ion **C** derived from **6b** (Scheme 3) the situation is slightly more complex. As with the other examples, eq-**C** is thermodynamically preferred with respect to ax-**C**, but according to the Felkin-Anh model the two conformers differ in their reactivity to a smaller extent, since the phenyl substituent is situated in a rather remote position from the reaction centre. Consequently, one expects no selectivity or slight preference for the formation of the *cis* compound. In fact, the reaction of **6b** with diethylzinc afforded *cis*-**11** and *trans*-**11** in essentially equal amounts. In contrast, high *trans* selectivities were observed[7c] when a 5-substituted γ-lactol with the bulky (*tert*-butyldiphenylsilyloxy)methyl group was reacted with organozinc and organotin compounds in the presence of BF_3.

Our results demonstrate that the synthesis of 2-alkyl substituted tetrahydrofuran derivatives can be achieved in high yields by replacement of the hydroxyl group of γ-lactols by the alkyl group of organometallic reagents. 1,2- and 1,3-induction by a single phenyl substituent leads to excellent *trans* selectivities in the formation of these tetrahydrofuran derivatives, while there is essentially no selectivity in the synthesis of 2,5-disubstituted tetrahydrofuran derivatives. Reactions with other nucleophiles will be described in subsequent publications[17] and the mechanisms involved in these reactions will be discussed in great detail.

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Experimental

All reactions were carried out under nitrogen (1 atm) in flame-dried flasks by adding the compounds by means of syringes. All solvents were dried by standard methods. – ^{1}H NMR: Bruker WM 300 or AC 300 (300 MHz). Solvent $CDCl_3$, internal standard tetramethylsilane (δ = 0.00). ^{13}C NMR: Bruker WM 300 or AC 300 (75 MHz). Solvent $CDCl_3$, internal standard tetramethylsilane (δ = 0.00) or chloroform (δ = 77.0). Higher order NMR spectra were interpreted as first-order spectra where justified. Missing signals of minor isomers were hidden or too weak. – IR: Perkin-Elmer 1420 (films). – Boiling points: Temperature in the oven of a Büchi GKR50 bulb-to-bulb distillation apparatus (kugelrohr oven). – Elemental analysis: Perkin-Elmer CHN 240B.

The lactones **1**–**3** were prepared according to literature procedures except for **1a** which was purchased from Lancaster Co.: **1b**[18,19], **1c**[18,20], **2a**[21,22], **2b**[23], **2c**[24], **3a**[25], **3b**[25,26], **3c**[21], **3d**[27].

Reduction of γ-Lactones **1**–**3** *to the Corresponding γ-Lactols* **4**–**6**. – *General Procedure:* To a solution of the lactone in dry toluene (1.2 ml/mmol) cooled to −90 °C 1.2 equiv. of a 1.5 M solution of DIBAL in toluene was added by means of a syringe pump during 30 min. The reaction mixture was stirred for 3 h at −78 °C and subsequently poured into a stirred 1 M aqueous solution of tartaric acid (0.5 ml/mmol). The heterogeneous mixture was stirred for about 15 min and filtered over Celite followed by extraction with MeO*t*Bu and drying ($MgSO_4$) of the combined organic extracts. After evaporation of the solvent, the residue was purified by bulb-to-bulb distillation (except for the phenyl-substituted derivatives **4b**–**6b**). Scaling up of this procedure for the reduction of more than 2.00 g of lactone in one run led to a considerable decrease of the yield.

3-Methyltetrahydrofuran-2-ol (**4a**): Reduction of 2.00 g (20.0 mmol) of **1a** with DIBAL according to the general procedure afforded 1.60 g (78%) of **4a** as a mixture of the anomers in a ratio of 75:25. – B.p. 40 °C/0.75 Torr. Ref.[28]: 74–75 °C/15 Torr. – The ^{1}H- and ^{13}C-NMR spectroscopic data correspond to those reported in ref.[28].

3-Phenyltetrahydrofuran-2-ol (**4b**): Reduction of 2.00 g (12.3 mmol) of **1b** with DIBAL according to the general procedure afforded 1.62 g (80%) of **4b** as a mixture of the anomers in a ratio of 77:23. – Distillation led to decomposition of **4b** but the NMR spectra of the crude product showed no impurities. Ref.[29]: B.p. 135 °C/2 Torr, ^{1}H-NMR data (60 MHz) given. ^{1}H NMR (major anomer): δ = 7.40–7.20 (m, 5H, Ph), 5.44 (d, *J* = 2.5 Hz, 1H, 2-H), 4.21–4.07 (m, 2H, 5-H), 3.70–3.10 (m, 2H, 3-H, OH), 2.56–2.45 (m, 1H, 4-H), 2.05–1.94 (m, 1H, 4-H); minor anomer: δ = 7.40–7.20 (m, 5H, Ph), 5.51 (d, *J* = 4.5 Hz, 1H, 2-H), 4.27 (dt, *J* = 2.5, 8.5 Hz, 1H, 5-H), 3.98 (dt, *J* = 9.0, 7.5 Hz, 1H, 5-H), 3.92–3.37 (m, 1H, 3-H), 2.56–2.40 (m, 1H, 4-H), 2.29–2.19 (m, 1H, 4-H). – ^{13}C NMR (major anomer): δ = 141.7, 128.6, 127.2, 126.7 (s, 3 d, Ph), 103.9 (d, C-2), 67.4 (t, C-5), 52.0 (d, C-3), 32.8 (t, C-4); minor anomer: δ = 137.5, 128.8, 128.3, 127.0 (s, 3 d, Ph), 98.4 (d, C-2), 67.2 (t, C-5), 49.9 (d, C-3), 28.1 (t, C-4).

3-tert-Butyltetrahydrofuran-2-ol (**4c**): Reduction of 2.00 g (14.1 mmol) of **1c** with DIBAL according to the general procedure afforded 1.40 g (69%) of **4c** as a mixture of the anomers in a ratio of 95:5. – B.p. 60 °C/0.60 Torr. – IR: $\tilde{\nu}$ = 3600–3100 cm^{-1} (OH), 3000–2800 (CH), 1080–980 (acetal). – ^{1}H NMR: δ = 5.35 (d, *J* = 8.0 Hz, 0.05H, 2-H), 5.30 (d, *J* = 2.5 Hz, 0.95H, 2-H), 4.75–4.50 (broad s, 1H, OH), 4.02–3.89 (m, 1.9H, 5-H), 3.86–3.75 (m, 0.1H, 5-H), 2.00–1.55 (m, 3H, 3-H, 4-H), 0.92 (s, 8.55H, *tert*-Bu), 0.90 (s, 0.45H, *tert*-Bu). – ^{13}C NMR (major anomer): δ = 99.9 (d, C-2), 67.0 (t, C-5), 57.4 (d, C-3), 30.9, 27.9 (s,

q, *tert*-Bu), 23.7 (t, C-4); minor anomer: δ = 99.4 (d, C-2), 66.8 (t, C-5), 54.4 (d, C-3), 30.7, 28.9 (s, q, *tert*-Bu), 23.7 (t, C-4). – $C_8H_{16}O_2$ (144.2): calcd. C 66.63, H 11.18; found C 66.27, H 11.37.

4-Methyltetrahydrofuran-2-ol (**5a**): Reduction of 2.00 g (20.0 mmol) of **2a** with DIBAL according to the general procedure afforded 1.50 g (73%) of **5a** as a mixture of the anomers in a ratio of 60:40. – B.p. 50°C/0.75 Torr. Ref.[29]: 65–66°C/11 Torr, ^{1}H-NMR data (60 MHz) partially given. – ^{1}H NMR: δ = 5.53 (m_c, 1H, 2-H), 4.64 (d, *J* = 3.5 Hz, 0.6H, OH), 4.56 (d, *J* = 2.5 Hz, 0.4H, OH), 4.15 (t, *J* = 7.5 Hz, 0.6H, 5-H), 3.93 (t, *J* = 7.5 Hz, 0.4H, 5-H), 3.55 (t, *J* = 8.5 Hz, 0.4H, 5-H), 3.36 (t, *J* = 7.5 Hz, 0.6H, 5-H), 2.55 (m_c, 0.6H, 4-H), 2.28 (m_c, 0.8H, 3-H, 4-H), 2.02 (ddd, *J* = 13.0, 7.0, 1.0 Hz, 0.6H, 3-H), 1.57 (ddd, *J* = 13.0, 9.0, 5.0 Hz, 0.6H, 3-H), 1.44 (m_c, 0.4H, 3-H), 1.10 (d, *J* = 6.5 Hz, 1.2H, Me), 1.04 (d, *J* = 6.5Hz, 1.8H, Me). – ^{13}C NMR (major anomer): δ = 98.7 (d, C-2), 74.2 (t, C-5), 41.7 (t, C-3), 31.4 (d, C-4), 17.8 (q, Me); minor anomer: δ = 99.3 (d, C-2), 73.4 (t, C-5), 41.6 (t, C-3), 33.3 (d, C-4), 17.2 (q, Me).

4-Phenyltetrahydrofuran-2-ol (**5b**): Reduction of 2.00 g (12.3 mmol) of **2b** with DIBAL according to the general procedure afforded 1.90 g (94%) of **5b** as a mixture of the anomers in a ratio of 65:35. – Distillation led to decomposition of **5b** but the NMR spectra of the crude product showed no impurities. – Ref.[30]: ^{1}H-NMR data partially given. – ^{1}H NMR (major anomer): δ = 7.45–7.07 (m, 5H, Ph), 5.72 (dd, *J* = 5.0, 1.0 Hz, 1H, 2-H), 5.01 (broad s, 1H, OH), 4.43 (dd, *J* = 8.0, 7.0 Hz, 1H, 5-H), 3.80 (t, *J* = 8.0 Hz, 1H, 5-H), 3.73 (broad quint, *J* = 9.0 Hz, 1H, 4-H), 2.34 (ddd, *J* = 13.0, 7.0, 1.0 Hz, 1H, 3-H), 2.09 (ddd, *J* = 13.0, 9.5, 5.0 Hz, 1H, 3-H); minor anomer: δ = 7.45–7.07 (m, 5H, Ph), 5.71 (dd, *J* = 5.5, 3.5 Hz, 1H, 2-H), 5.01 (broad s, 1H, OH), 4.17 (dd, *J* = 8.5, 8.0 Hz, 1H, 5-H), 3.96 (dd, *J* = 10.0, 8.5 Hz, 1H, 5-H), 3.37 (broad quint, *J* = 9.0 Hz, 1H, 4-H), 2.60 (ddd, *J* = 13.5, 9.5, 5.5 Hz, 1H, 3-H), 2.04 (ddd, *J* = 13.5, 9.0, 3.5 Hz, 1H, 3-H). – ^{13}C NMR (major anomer): δ = 141.7, 128.6, 127.2, 126.4 (s, 3 d, Ph), 99.6 (d, C-2), 74.0 (t, C-5), 42.4 (d, C-4), 41.8 (t, C-3); minor anomer: δ = 140.7, 127.6, 126.6 (s, 2 d, Ph), 99.2 (d, C-2), 72.7 (t, C-5), 45.6 (d, C-4), 41.6 (t, C-3).

4-tert-Butyltetrahydrofuran-2-ol (**5c**): Reduction of 1.00 g (7.05 mmol) of **2c** with DIBAL according to the general procedure afforded 865 mg (85%) of **5c** as a mixture of the anomers in a ratio of 74:26. – B.p. 60°C/0.30 Torr. Ref.[31]: 63°C/0.1 Torr. – ^{1}H NMR: δ = 5.57–5.50 (m, 1H, 2-H), 4.05 (t, *J* = 8.0 Hz, 0.74H, 5-H), 4.00–3.50 (broad s, 1H, OH), 3.85–3.70 (m, 0.52H, 5-H), 3.63 (t, *J* = 8.0 Hz, 0.74H, 5-H), 2.42 (dq, *J* = 10.5, 8.0 Hz, 0.74H, 4-H), 2.20–2.00 (m, 0.26H, 4-H), 1.90–1.50 (m, 2H, 3-H), 0.91 (s, 2.34H, *tert*-Bu), 0.88 (s, 6.66H, *tert*-Bu). – ^{13}C NMR (major anomer): δ = 98.7 (d, C-2), 68.4 (t, C-5), 46.7 (d, C-4), 34.6 (t, C-3), 30.9, 27.2 (s, q, *tert*-Bu); minor anomer: δ = 98.9 (d, C-2), 67.3 (t, C-5), 49.5 (d, C-4), 35.0 (t, C-3), 30.4, 27.5 (s, q, *tert*-Bu).

5-Methyltetrahydrofuran-2-ol (**6a**): Reduction of 2.00 g (20.0 mmol) of **3a** with DIBAL according to the general procedure afforded 1.53 g (75%) of **6a** as a mixture of the anomers in a ratio of 60:40. – B.p. 60°C/0.75 Torr. Ref.[29]: 60–62°C/12 Torr, ^{1}H-NMR data (60 MHz) partially given. – ^{1}H NMR: δ = 5.56 (dd, *J* = 5.0, 2.0 Hz, 0.6H, 2-H), 5.47 (broad d, *J* = 3.0 Hz, 0.4H, 2-H), 4.35 (sext, *J* = 6.5 Hz, 0.6H, 5-H), 4.20–3.92 (m, 1.4H, 5-H, OH), 2.21–1.69 (m, 4H, 3-H, 4-H), 1.31 (d, *J* = 6.0 Hz, 1.2H, Me), 1.22 (d, *J* = 6.5 Hz, 1.8H, Me). – ^{13}C NMR (major anomer): δ = 98.3 (d, C-2), 74.1 (d, C-5), 33.1, 31.2 (2 t, C-3, C-4), 22.7 (q, Me); minor anomer: δ = 76.5 (d, C-5), 34.2, 31.0 (2 t, C-3, C-4).

5-Phenyltetrahydrofuran-2-ol (**6b**): Reduction of 2.00 g (12.3 mmol) of **3b** with DIBAL according to the general procedure afforded 1.90 g (94%) of **6b** as a mixture of the anomers in a ratio of 60:40. – Distillation led to decomposition of **6b** but the NMR spectra of the crude product showed no impurities. Ref.[32]: ^{1}H-NMR data given. – ^{1}H NMR: δ = 7.44–7.21 (m, 5H, Ph), 5.69 (dd, *J* = 5.0, 2.0 Hz, 0.6H, 2-H), 5.57 (dd, *J* = 4.0, 1.0 Hz, 0.4H, 2-H), 5.22 (t, *J* = 7.0 Hz, 0.6H, 5-H), 4.99–4.94 (m, 0.4H, 5-H), 4.38 (broad s, 1H, OH), 2.48–1.68 (m, 4H, 3-H, 4-H). The following signals were assigned to the open-chain tautomer (content <5%): δ = 9.68 (s, 1H, CHO), 4.68–4.56 (m, 2H), 3.59–3.49 (m, 1H). – ^{13}C NMR (major anomer): δ = 142.3, 128.3, 127.4, 125.6 (s, 3 d, Ph), 98.8 (d, C-2), 82.9 (d, C-5), 34.4, 32.9 (2 t, C-3, C-4); minor anomer: δ = 142.7, 127.5, 126.4 (s, 2 d, Ph), 98.5 (d, C-2), 79.6 (d, C-5), 32.9, 32.8 (2 t, C-3, C-4).

5-tert-Butyltetrahydrofuran-2-ol (**6c**): Reduction of 1.00 g (7.05 mmol) of **3c** with DIBAL according to the general procedure afforded 758 mg (75%) of **6a** as a mixture of the anomers in a ratio of 63:37. – B.p. 55°C/0.30 Torr. Ref.[33]: no data given. – ^{1}H NMR: δ = 5.60–5.55 (m, 0.63H, 2-H), 5.50–5.47 (m, 0.37H, 2-H), 4.46 (broad s, 0.63H, OH), 4.11 (broad s, 0.37H, OH), 3.94 (t, *J* = 7.0 Hz, 0.63H, 5-H), 3.71 (dd, *J* = 10.0, 6.0 Hz, 0.37H, 5-H), 2.05–1.55 (m, 4H, 3-H, 4-H), 0.93 (s, 3.33H, *tert*-Bu), 0.87 (s, 5.67H, *tert*-Bu). The following signals are due to the open-chain tautomer (content <5%): δ = 4.21 (dd, *J* = 9.0, 7.0 Hz, 1H), 2.58 (m_c, 2H), 2.20–2.05 (m, 1H), 0.96 (s, 9H, *tert*-Bu). – ^{13}C NMR (major anomer): δ = 98.5 (d, C-2), 86.2 (d, C-5), 32.2, 25.6 (s, q, *tert*-Bu), 33.1, 24.5 (2 t, C-3, C-4); minor anomer: δ = 97.7 (d, C-2), 89.6 (d, C-5), 33.9, 24.2 (s, q, *tert*-Bu), 33.1, 25.9 (2 t, C-3, C-4).

Methylation of γ-Lactols with Dimethylcuprate. – General Procedure: To a solution of the corresponding lactol in dry diethyl ether (2 ml/mmol) $BF_3 \cdot Et_2O$ (3 equiv.) was added at –78°C. Then dimethylcuprate[34] prepared in a second reaction flask (2 equiv.) was added by means of a syringe and the mixture was stirred at this temperature until the mixture turned bright yellow (formation of dimethylcopper). After addition of water (2 ml/mmol of lactol) the mixture was warmed up to room temp. and extracted with diethyl ether (3 × 20 ml). Drying ($MgSO_4$) of the combined organic extracts, evaporation of the solvent and bulb-to-bulb distillation of the residue afforded 2-methyl-substituted tetrahydrofurans **7** and **10**.

2-Methyl-3-phenyltetrahydrofuran (**7**): Reaction of dimethylcuprate with 300 mg (1.83 mmol) of **4b** afforded 110 mg (37%) of **7** (*trans*:*cis* = 65:35) as a colourless oil of b.p. 80°C/0.07 Torr. Ref.[35]: ^{1}H-NMR data (60 MHz) partially given. – ^{1}H NMR: *trans*-**7**: δ = 7.48–7.20 (m, 5H, Ph), 4.25–3.80 (m, 3H, 2-H, 5-H), 2.75 (q, *J* = 9.0 Hz, 1H, 3-H), 2.50–2.20 (m, 2H, 4-H), 1.22 (d, *J* = 6.0 Hz, 3H, 2-Me); *cis*-**7**: δ = 7.48–7.20 (m, 5H, Ph), 4.25–3.80 (m, 3H, 2-H, 5-H), 3.35 (q, *J* = 9.0 Hz, 1H, 3-H), 2.50–2.20 (m, 2H, 4-H), 0.84 (d, *J* = 6.0 Hz, 3H, 2-Me). – ^{13}C NMR (*trans*-**7**): δ = 141.6, 128.6, 127.8, 126.6 (s, 3 d, Ph), 82.8 (d, C-2), 67.4 (t, C-5), 53.0 (d, C-3), 35.4 (t, C-4), 19.0 (q, 2-Me); *cis*-**7**: δ = 141.8, 128.4, 128.2, 126.3 (s, 3 d, Ph), 78.2 (d, C-2), 66.9 (t, C-5), 48.4 (d, C-3), 32.7 (t, C-4), 16.9 (q, 2-Me).

2-Methyl-5-phenyltetrahydrofuran (**10**): Reaction of dimethylcuprate with 300 mg (1.83 mmol) of **6b** afforded 116 mg (39%) of **10** (*trans*:*cis* = 70:30) as a colourless oil of b.p. 110°C/1.0 Torr. Ref.[36]: 110°C/15 Torr, ^{1}H-NMR data (60 MHz) partially given. – ^{1}H NMR (*trans*-**10**): δ = 7.35–7.17 (m, 5H, Ph), 5.00 (d, *J* = 8.0, 6.5 Hz, 1H, 5-H), 4.32 (dquint, *J* = 8.0, 6.0 Hz, 1H, 2-H), 2.42–1.50 (m, 4H, 3-H, 4-H), 1.34 (d, *J* = 6.0 Hz, 3H, 2-Me); *cis*-**10**: δ = 7.35–7.17 (m, 5H, Ph), 4.84 (t, *J* = 7.0 Hz, 1H, 5-H), 4.13 (broad sext, *J* = 6.5 Hz, 1H, 2-H), 2.42–1.50 (m, 4H, 3-H, 4-H), 1.29 (d, *J* = 6.0 Hz, 3H, 2-Me). – ^{13}C NMR (*trans*-**10**): δ = 143.5,

129.1, 126.2, 125.0 (s, 3 d, Ph), 79.7 (d, C-2), 75.7 (d, C-5), 36.0, 34.5 (2 t, C-3, C-4), 21.8 (q, 2-Me); *cis*-**10**: δ = 143.0, 129.0, 126.5, 125.2 (s, 3 d, Ph), 80.5 (d, C-2), 75.4 (d, C-5), 34.0, 32.5 (2 t, C-3, C-4), 20.7 (q, 2-Me).

Methylation of **6b** *with* $MeTiCl_3$: To a solution of $MeTiCl_3$ prepared from 1.41 g (9.15 mmol) of $TiCl_4$ and 5.72 ml (9.15 mmol) of methyllithium (1.6 M in hexane) in 20 ml of diethyl ether[37] 300 mg (1.83 mmol) of **6b** was added at −50 °C. During 1 h the temp. was raised to −20 °C, the mixture was stirred for 2 h, then allowed to warm up to −10 °C, and stirred for further 3 h. After treatment with water the mixture was brought to room temp. and extracted with diethyl ether (3 × 20 ml). Drying ($MgSO_4$) of the combined organic extracts, evaporation of the solvent, and bulb-to-bulb distillation of the residue afforded 162 mg (55%) of **10** (*trans*:*cis* = 42:58) and 135 mg (41%) of *1-phenylpentan-1,4-diol* (**12**) as a mixture of diastereoisomers (88:12) with b.p. 110 °C/0.3 Torr. Ref.[36]: 127−131 °C/0.05 Torr, ^{1}H-NMR data (60 MHz) partially given. − ^{1}H NMR data of **12** (major diastereoisomer): δ = 7.36−7.19 (m, 5H, Ph), 4.66 (dd, *J* = 8.0, 5.0 Hz, 1H, 1-H), 3.80 (sext, *J* = 6.0 Hz, 1H, 4-H), 3.30 (s, 2H, OH), 1.90−1.75, 1.62−1.50 (2 m, 4H, 2-H, 3-H), 1.15 (d, *J* = 6.0 Hz, 3H, 5-H). The ^{1}H-NMR signals of the minor diastereomer are too weak for correct assignment. − ^{13}C NMR data of **12** (major diastereoisomer): δ = 144.5, 128.2, 126.9, 125.9 (s, 3 d, Ph), 74.5, 68.2 (2 d, C-1, C-4), 35.8, 35.6 (2 t, C-2, C-3), 23.3 (q, C-5); minor diastereoisomer: δ = 74.0, 67.7 (2 d, C-1, C-4), 23.2 (q, C-5).

Alkylation of γ-Lactols **4**−**6** *Affording 2-Alkyl-Substituted Tetrahydrofurans* **8**, **9**, *and* **11**. − *General Procedure:* To a solution of the lactol in dry dichloromethane (2 ml/mmol) 3 equiv. of $BF_3 \cdot Et_2O$ were added by means of a syringe at −78 °C. Then 2 equiv. of the organometallic compound were added at this temp. and the mixture was stirred for 12 h while warming up to room temp. After addition of water the mixture was extracted with dichloromethane (3 × 20 ml) and the combined organic extracts were dried ($MgSO_4$). Evaporation of the solvent and bulb-to-bulb distillation of the residue yielded the pure tetrahydrofurans **8**, **9**, and **11**.

2-Ethyl-3-phenyltetrahydrofuran (**8**): According to the general procedure 300 mg (1.83 mmol) of **4b** was treated with diethylzinc to yield 310 mg (96%) of **8** (*trans*:*cis* = 90:10) as a colourless oil of b.p. 75 °C/0.07 Torr. − IR: $\tilde{\nu}$ = 3080−3010 cm^{-1} (=CH), 2950−2880 (CH), 1550 (C=C). − ^{1}H NMR (*trans*-**8**): δ = 7.33−7.17 (m, 5H, Ph), 4.09−3.92 (m, 2H, 5-H), 3.73 (td, *J* = 8.0, 4.5 Hz, 1H, 2-H), 2.89 (q, *J* = 8.5 Hz, 1H, 3-H), 2.35 (dddd, *J* = 12.5, 8.5, 7.0, 5.0 Hz, 1H, 4-H), 2.10 (dddd, *J* = 12.5, 9.0, 8.5, 7.5 Hz, 1H, 4-H), 1.59−1.48 (m, 2H, CH_2CH_3), 0.92 (t, *J* = 7.5 Hz, 3H, CH_2CH_3); *cis*-**8**: δ = 7.33−7.17 (m, 5H, Ph), 4.16 (td, *J* = 8.5, 7.0 Hz, 1H, 2-H), 3.93−3.78 (m, 2H, 5-H), 3.31 (ddd, *J* = 8.5, 6.0, 5.0 Hz, 1H, 3-H), 1.29−1.02 (m, 2H, CH_2CH_3), 0.82 (t, *J* = 7.5 Hz, 3H, CH_2CH_3). − ^{13}C NMR (*trans*-**8**): δ = 142.3, 128.6, 127.6, 126.5 (s, 3 d, Ph), 87.5 (d, C-2), 67.5 (t, C-5), 50.8 (d, C-3), 35.8 (t, C-4), 26.9, 10.5 (t, q, Et); *cis*-**8**: δ = 142.3, 128.5, 128.1, 126.2 (s, 3d, Ph), 84.4 (d, C-2), 66.8 (t, C-5), 47.6 (d, C-3), 33.5 (t, C-4), 24.8, 10.8 (t, q, Et). − $C_{12}H_{16}O$ (176.3): calcd. C 81.77, H 9.15; found C 81.46, H 9.27.

Preparation of 2-Ethyl-4-phenyltetrahydrofuran (**9**) *Employing Diethylzinc:* According to the general procedure 400 mg (2.44 mmol) of **5b** was treated with diethylzinc to yield 364 mg (85%) of **9** (*trans*:*cis* ≥ 95:5) as a colourless oil of b.p. 70 °C/0.07 Torr. − IR: $\tilde{\nu}$ = 3070−3010 cm^{-1} (=CH), 3000−2900 (CH), 1545 (C=C). − ^{1}H NMR (*trans*-**9**): δ = 7.33−7.13 (m, 5H, Ph), 4.21 (dd, *J* = 8.5, 7.5 Hz, 1H, 5-H), 4.05 (broad quint, *J* = 7.0 Hz, 1H, 2-H), 3.70 (t, *J* = 8.5 Hz, 1H, 5-H), 3.39 (broad quint, *J* = 8.0 Hz, 1H, 4-H), 2.10−1.93 (m, 2H, 3-H), 1.67 (m_c, 2H, CH_2CH_3), 0.96 (t, *J* = 7.5 Hz, 3H, CH_2CH_3); *cis*-**9**: δ = 7.33−7.13 (m, 5H, Ph), 4.31 (t, *J* = 8.0 Hz, 1H, 5-H), 4.00−3.90 (m, 1H, 2-H), 3.79 (t, *J* = 8.5 Hz, 1H, 5-H), 2.45−2.27 (m, 2H, 3-H), 1.40−1.15 (m, 2H, CH_2CH_3), 0.98 (t, *J* = 7.5 Hz, 3H, CH_2CH_3). − ^{13}C NMR (*trans*-**9**): δ = 142.8, 128.6, 127.3, 126.4 (s, 3 d, Ph), 80.9 (d, C-2), 74.5 (t, C-5), 44.7 (d, C-4), 39.9 (t, C-3), 28.9, 10.3 (t, q, Et); *cis*-**9**: δ = 81.8 (d, C-2), 74.2 (t, C-5), 45.6 (d, C-4), 40.6 (t, C-3), 28.6, 8.0 (t, q, Et). − $C_{12}H_{16}O$ (176.3): calcd. C 81.77, H 9.15; found C 81.81, H 9.11.

Preparation of 2-Ethyl-4-phenyltetrahydrofuran (**9**) *Employing Triethylaluminium:* According to the general procedure, 400 mg (2.44 mmol) of **5b** was treated with triethylaluminium to yield 268 mg (62%) of **9** (*trans*:*cis* = 94:6).

Preparation of 2-Ethyl-5-phenyltetrahydrofuran (**11**) *Employing Diethylzinc:* According to the general procedure, 400 mg (2.44 mmol) of **6b** was treated with diethylzinc to yield 402 mg (94%) of **11** (*trans*:*cis* = 49:51) as a colourless oil of b.p. 70 °C/0.07 Torr. − IR: $\tilde{\nu}$ = 3080−3000 cm^{-1} (=CH), 2980−2880 (CH), 1550 (C=C). − ^{1}H NMR (*trans*-**11**): δ = 7.40−7.20 (m, 5H, Ph), 4.96 (dd, *J* = 8.0, 6.5 Hz, 1H, 5-H), 4.10 (dq, *J* = 8.0, 6.5 Hz, 1H, 2-H), 2.37 (dddd, *J* = 12.0, 7.5, 6.5, 3.5 Hz, 1H, 4-H), 2.11 (dddd, *J* = 11.0, 8.0, 7.5, 3.5 Hz, 1H, 3-H), 1.86 (ddt, *J* = 12.0, 9.5, 8.0 Hz, 1H, 4-H), 1.60 (dddd, *J* = 11.0, 9.5, 7.5, 6.5 Hz, 1H, 3-H), 1.67, 1.50 (2 m_c, 2H, CH_2CH_3), 0.97 (t, *J* = 7.5 Hz, 3H, CH_2CH_3); *cis*-**11**: δ = 7.40−7.20 (m, 5H, Ph), 4.84 (t, *J* = 7.0 Hz, 1H, 5-H), 3.93 (quint, *J* = 6.5 Hz, 1H, 2-H), 2.27 (dddd, *J* = 12.0, 8.0, 7.0, 6.0 Hz, 1H, 4-H), 2.05 (ddt, *J* = 11.5, 8.0, 6.5 Hz, 1H, 3-H), 1.85−1.70 (m, 2H, 4-H, CH_2CH_3), 1.70−1.50 (m, 2H, 3-H, CH_2CH_3), 1.01 (t, *J* = 6.0 Hz, 3H, CH_2CH_3). − ^{13}C NMR (*trans*-**11**): δ = 143.9, 128.3, 127.1, 125.8 (s, 3 d, Ph), 81.5, 80.3 (2 d, C-2, C-5), 35.4, 31.9 (2 t, C-3, C-4), 28.9, 10.4 (t, q, Et); *cis*-**11**: δ = 143.4, 128.2, 126.2, 125.0 (s, 3 d, Ph), 81.4, 80.9 (2 d, C-2, C-5), 34.5, 30.8 (2 t, C-3, C-4), 28.9, 10.3 (t, q, Et). − $C_{12}H_{16}O$ (176.3): calcd. C 81.77, H 9.15; found C 81.63, H 9.06.

Preparation of 2-Ethyl-5-phenyltetrahydrofuran (**11**) *Employing Diethylaluminium Chloride:* Treatment of 400 mg (2.44 mmol) **6b** with diethylaluminium chloride according to the general procedure but without addition of $BF_3 \cdot Et_2O$ yielded 107 mg (25%) of **11** (*trans*:*cis* = 52:48).

Reaction of **6b** *with Diethylzinc without Addition of Lewis Acid:* Treatment of 400 mg (2.44 mmol) of **6b** with diethylzinc according to the general procedure but without addition of $BF_3 \cdot Et_2O$ led to recovery of lactol **6b** in quantitative yield.

[1] A. Schmitt, Dissertation, Technische Hochschule Darmstadt **1992**.

[2] Reviews: T. L. B. Bovin, *Tetrahedron* **1987**, *43*, 3309−3362. − G. Cardillo, M. Orena, *Tetrahedron* **1990**, *46*, 3321−3408. − J.-C. Harmange, B. Figadère, *Tetrahedron: Asymmetry* **1993**, *4*, 1711−1754. − U. Koert, *Synthesis* **1995**, 115−132. − For recent publications with further leading references: H. C. Brown, A. S. Phadke, *Synlett* **1993**, 927−928. − K. Horita, I. Noda, K. Tanaka, T. Miura, Y. Oikawa, O. Yonemitsu, *Tetrahedron* **1993**, *49*, 5979−5996. − R. D. Walkup, S. W. Kim, S. D. Wagy, *J. Org. Chem.* **1993**, *58*, 6486−6490. − V. H. Rawal, S. P. Singh, C. Dufour, S. Michoud, *J. Org. Chem.* **1993**, *58*, 7718−7727. − P. Mohr, *Tetrahedron Lett.* **1993**, *34*, 6251−6254. − Y. Zhao, R. L. Beddoes, P. Qualye, *Tetrahedron Lett.* **1994**, *35*, 4183−4186. − G. Adiwidjaja, H. Flörke, A. Kirschning, E. Schaumann, *Liebigs Ann.* **1995**, 501−507.

[3] K. Mori, *Tetrahedron* **1989**, *45*, 3233−3298.

[4] Review: M. D. Ruff in *Polyether Antibiotics: Naturally occuring Acid Ionophors* (Ed.: I. W. Westley), Marcel Dekker, New York, **1982**, vol. 1, chapter 6.

[5] R. R. Schmidt in *Comprehensive Organic Synthesis* (Eds.: B. M.

Trost, I. Fleming), Pergamon Press, Oxford, **1991**, vol. 6, p. 33. – M. H. D. Postema, *Tetrahedron* **1992**, *48*, 8545–8599.

[6] According to Olah the correct term may be alkoxycarbenium ion or alkyloxonium ion (G. A. Olah, *Angew. Chem.* **1973**, *85*, 183–234; *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 173–211), however, in the recent literature the term oxocarbenium ion is generally accepted (e.g. T. Sammakia, R. S. Smith, *J. Am. Chem.Soc.* **1992**, *114*, 10998–10999).

[7] [7a] G. A. Kraus, K. A. Frazier, B. D. Roth, M. J. Taschner, K. Neuenschwander, *J. Org. Chem.* **1981**, *46*, 2417–2419. – G. A. Kraus, M. T. Molina, J. A. Walling, *J. Chem. Soc., Chem. Commun.* **1986**, 1568–1569. – G. A. Kraus, M. T. Molina, *J. Org. Chem.* **1988**, *53*, 752–753. – [7b] S. A. Barbirad, Y. Wang, Y. Kishi, *J. Org. Chem.* **1987**, *52*, 1370–1372. – [7c] K. Tomooka, K. Matsuzawa, K. Suzuki, G.-i. Tsuchihashi, *Tetrahedron Lett.* **1987**, *28*, 6339–6342. – [7d] K. T. Mead, S. K. Pillai, *Tetrahedron Lett.* **1993**, *34*, 6997–7000. – [7e] J. F. Gil, D. J. Ramón, M. Yus, *Tetrahedron* **1994**, *50*, 3437–3446. – [7f] For reactions of 5-substituted γ-lactols with organometallic compounds such as MeLi, MeMgBr, Me_3Al, $MeTiCl_3$, and $MeTi(OiPr)_3$ giving 1,4-diols in moderate to excellent *syn*-selectivities see: K. Tomooka, T. Okinaga, K. Suzuki, G.-i. Tsuchihashi, *Tetrahedron Lett.* **1987**, *28*, 6335–6338. Also see: K. Tomooka, T. Okinaga, K. Suzuki, G.-i. Tsuchihasi, *Tetrahedron Lett.* **1989**, *30*, 1563–1566. These reactions proceed via γ-hydroxy aldehydes which are present as open chain tautomers of γ-lactols in low concentrations.

[8] C. Brückner, H.-U. Reißig, *J. Chem. Soc., Chem. Commun.* **1985**, 1512–1513. – C. Brückner, H. Lorey, H.-U. Reißig, *Angew. Chem.* **1986**, *98*, 559–560; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 556–557. – C. Brückner, H. Holzinger, H.-U. Reißig, *J. Org. Chem.* **1988**, *53*, 2450–2456. – H.-U. Reißig, H. Holzinger, G. Glomsda, *Tetrahedron* **1989**, *45*, 3139–3150. – A. Schmitt, H.-U. Reißig, *Synlett* **1990**, 40–41.

[9] In principle, all reactions described for γ-lactols **4b**–**6b** should also be applicable to γ-lactols **4a**–**6a** and **4c**–**6c**, respectively. However, due to the expected high volatility of the resulting products when ethyl or methyl groups are introduced, we omitted these experiments.

[10] E. Winterfeldt, *Synthesis* **1975**, 617–630.

[11] B. H. Lipshutz, E. L. Ellsworth, T. J. Siahaan, *J. Am. Chem. Soc.* **1988**, *110*, 4834–4845. – B. H. Lipshutz, E. L. Ellsworth, T. J. Siahaan, *J. Am. Chem. Soc.* **1989**, *111*, 1351–1358. – B. H. Lipshutz, E. L. Ellsworth, S. H. Dimock, *J. Am. Chem. Soc.* **1990**, *112*, 5869–5871.

[12] Reactions of Grignard compounds with γ-lactols often exclusively provide 1,4-diols: H. Yoda, Y. Nakagami, K. Takabe, *Tetrahedron: Asymmetry* **1994**, *5*, 169–172.

[13] E. L. Eliel, V. Satyanarayana Rao, K. M. Pietrusiewicz, *Org. Magn. Reson.* **1979**, *12*, 461–466.

[14] E. L. Eliel, M. H. Gianni, T. H. Williams, *Tetrahedron Lett.* **1962**, 741–747. – D. Gagnair, P. Monzeglio, *Bull. Soc. Chim. Fr.* **1965**, 474–480. – M. Anteunis, D. Daneels, *Org. Magn. Reson.* **1975**, *7*, 345–348.

[15] M. Cherest, H. Felkin, N. Prudent, *Tetrahedron Lett.* **1968**, 2199–2204. – M. Cherest, H. Felkin, *Tetrahedron Lett.* **1968**, 2205–2208. – N. T. Anh, *Top. Curr. Chem.* **1980**, *88*, 145–162.

[16] K. E. Gilbert, J. J. Gajewski, program MMX, version 89.000, MM2 & P1, QCPE 395 + 318 (P1), Serena software.

[17] A. Schmitt, H.-U. Reißig, *Liebigs Ann.*, in preparation.

[18] P. L. Creger, *Org. Synth.* **1970**, *50*, 58–62.

[19] S. Karlsson, A. Hallberg, S. Gronowitz, *J. Organomet. Chem.* **1991**, *403*, 133–144.

[20] D. J. Canney, J. H. Levine, H.-F. La, D. F. Covey, *Synth. Commun.* **1990**, *20*, 2065–2073.

[21] E. Grimm, H.-U. Reißig, *J. Org. Chem.* **1985**, *50*, 242–244.

[22] C. F. Seidel, M. Stoll, *Helv. Chim. Acta* **1959**, *42*, 1830–1844.

[23] J.-J. Bourguignon, A. Schoenfelder, M. Schmitt, C.-G. Wermuth, V. Hechler, B. Charlier, M. Maitre, *J. Med. Chem.* **1988**, *31*, 893–897.

[24] A. de Boer, J. A. Hunter, *J. Org. Chem.* **1973**, *38*, 144–146.

[25] S. Hünig, G. Märkl, J. Sauer, *Integriertes organisches Praktikum*, Verlag Chemie: Weinheim, **1979**, p. 538.

[26] J. Cousseau, M. Lamant, *Bull. Soc. Chim. Fr.* **1967**, 4702–4707.

[27] T. Kunz, H.-U. Reißig, *Angew. Chem.* **1988**, *100*, 297–298; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 268–269. – H.-U. Reißig, H. Angert, T. Kunz, A. Janowitz, G. Handke, E. Bruce-Adjei, *J. Org. Chem.* **1993**, *58*, 6280–6285.

[28] D. J. Collins, A. M. James, *Aust. J. Chem.* **1989**, *42*, 223–228.

[29] C. Botthegi, *Gazz. Chim. Ital.* **1975**, *105*, 233–245.

[30] A. Arcadi, E. Bernocchi, S. Cacchi, F. Marinelli, *Tetrahedron* **1991**, *47*, 1525–1540.

[31] C. Botthegi, G. Consiglio, G. Ceccarelli, A. Stefani, *J. Org. Chem.* **1972**, *37*, 1835–1837.

[32] T. Lee, W. Holtz, R. L. Smith, *J. Org. Chem.* **1982**, *47*, 4750–4757.

[33] R. W. Bates, D. Diéz-Martin, W. J. Kerr, J. G. Knight, S. V. Ley, A. Sakellaridis, *Tetrahedron* **1990**, *46*, 4063–4082.

[34] G. H. Posner, C. E. Whitten, P. E. Mac Farland, *J. Am. Chem. Soc.* **1972**, *94*, 5106–5108.

[35] L. Graßhoff, R. Haller, *Arch. Pharm. (Weinheim, Ger.)* **1968**, *319*, 493–500.

[36] G. Dana, J.-P. Gireault, *Bull. Soc. Chim. Fr.* **1972**, 1650–1656.

[37] M. T. Reetz, S. H. Kyung, M. Hüllmann, *Tetrahedron* **1986**, *42*, 2931–2935.

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