**ISSN 0009–2940**
**CHBEAM 123**
**1990 (7) 1453–1596, I–XV**

# Chemische Berichte

## A Teil A: Anorganische und elementorganische Chemie / Part A: Inorganic and Organometallic Chemistry

### Notizen / Notes

### Berichtigung / Correction

### Querverweise / Cross References

## B Teil B: Organische Chemie / Part B: Organic Chemistry

### Nachruf / Obituary

▶ Publikationssprache ▶ Language of Publication

Fortsetzung: bitte umblättern / Continued: please turn over

## Inhalt (Fortsetzung)

## Contents (Continued)

### Notizen / Notes

### Kurzmitteilung / Short Communication

### Berichtigung / Correction

### Querverweise / Cross References

▶ Publikationssprache ▶ Language of Publication

## Notizen / Notes

# Synthesis of β-Oxo Esters from Silyl Enol Ethers and Dichlorobis(phenoxy)methane

**Herbert Mayr***, **Anton Cambanis, and Englbert Bäuml**

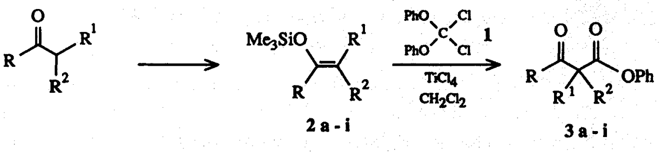
Institut für Chemie, Medizinische Universität zu Lübeck,
Ratzeburger Allee 160, D-2400 Lübeck 1, Federal Republic of Germany

Received February 2, 1990

**Key Words:** Carboxylation / Aryloxycarbonylation / Siloxyalkenes / Silyl Enol Ethers / Acetals, dichloro / β-Oxo esters

**Dichlorobis(phenoxy)methane (1) reacts with trimethylsiloxyalkenes in the presence of 1.2 equiv. of $TiCl_4$ to give β-oxo esters in 44–82% yield. The title compound 1 is thus employed as a $PhO_2C^{\oplus}$ equivalent.**

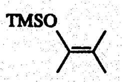
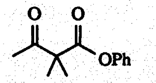
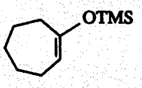
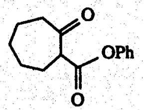
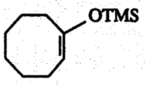
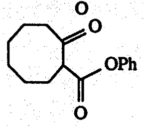
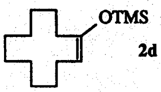
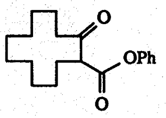
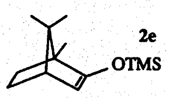
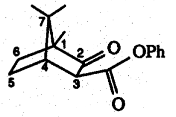
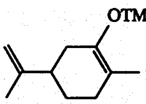
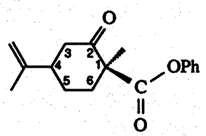
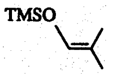
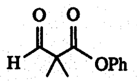
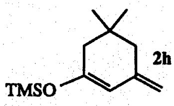
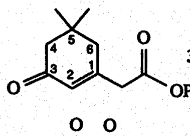
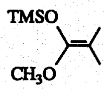
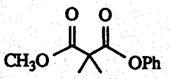
Bis(aryloxy)dichloromethanes (e. g. **1**) are readily available by radical-induced chlorination of formaldehyde diaryl acetals[1]. Like 2,2-dichloro-1,3-benzodioxol, which is used for the electrophilic carboxylation of aromatic compounds[2] and of alkenes[3], they represent $RO_2C^{\oplus}$ equivalents and have been employed for the synthesis of β,γ-unsaturated esters from allylsilanes[4]. In this paper we report on the reaction of bis(aryloxy)dichloromethanes with silyl enol ethers under Lewis-acidic conditions yielding β-oxo esters in moderate to good yields. Since silyl enol ethers may regioselectively be synthesized from the corresponding ketones[5], the two-step sequence according to eq. (1) represents a useful alternative for the generation of β-oxo esters from ketones, which has previously been carried out under strongly basic conditions using dialkyl carbonates[6], dialkyl oxalates[7], methyl methoxymagnesium carbonate[8], or methyl cyanoformate[9].



The experimental conditions of the reaction of **1** with the silyl enol ether **2g** have been optimized. Poor yields of **3g** are obtained, when **1** is treated with **2g** in $CH_2Cl_2$ in the presence of $ZnCl_2/Et_2O$[10] (1.5 equiv.) or in the presence of 0.1 equiv. of $TiCl_4$ (<20%). With $SnCl_4$ (1.3 equiv.) in $CH_2Cl_2$, 27% of **3g** is isolated, and an almost quantitative yield of crude **3g** is obtained, when 1.2 equiv. of $TiCl_4$ is added to a mixture of **1** and **2g** in $CH_2Cl_2$ at $-78°C$[11].

Table 1 (entries a–f) shows that silyl enol ethers, generated from saturated ketones, may efficiently be converted into β-oxo esters according to this method. Only one of the possible diastereoisomers is obtained from compounds **2e** and **2f**. Though some of these compounds are enolizable (**3b–e**), the NMR spectra, taken immediately after dissolving these compounds in $CDCl_3$, indicate the presence of pure keto compounds, and only in the case of **3b**, 10–15% of an enol has been detected. After several days, a ketone-to-enol ratio of 60:40 is observed for **3c**, while the spectra of the other compounds have remained unchanged[12].

Table 1. Titanium(IV) chloride promoted reactions of dichlorobis(phenoxy)methane (**1**) with trimethylsiloxyalkenes **2**

| Reactants | | Products | | Yield (%) | IR ν(CO) [cm⁻¹] |
|---|---|---|---|---|---|
|  | **2a** |  | **3a** | 71 | 1758, 1714 |
|  | **2b** |  | **3b** | 81 | 1764, 1701 |
|  | **2c** |  | **3c** | 68 | 1763, 1696 |
|  | **2d** |  | **3d** | 75 | 1748, 1708 |
|  | **2e** |  | **3e** | 54 | 1772, 1731 |
|  | **2f** |  | **3f** | 46 | 1757, 1708 |
|  | **2g** |  | **3g** | 74 | 1761, 1727 |
|  | **2h** |  | **3h** | 44 | 1755, 1670 |
|  | **2i** |  | **3i** | 82 | 1760, 1738 |

Chem. Ber. **123** (1990) 1571–1573 © VCH Verlagsgesellschaft mbH, D-6940 Weinheim, 1990 0009–2940/90/0707–1571 $ 03.50+25/0

Examples g–i suggest that **1** may also be used for the carboxylation of silyl enol ethers derived from aldehydes (**2g**), of siloxy dienes (**2h**), and ketene silyl acetals (**2i**), but experiments with 1-(trimethylsiloxy)indene and 1-(trimethylsiloxy)-1,3-butadiene have not been successful.

## Experimental

IR: IR-435 (Shimadzu). – NMR: XL 200 (Varian), internal standard TMS; for spectra of higher order, virtual couplings are listed. – MS: 70-250E (VG-Instruments).

Dichlorobis(phenoxy)methane (**1**) was prepared by chlorination of bis(phenoxy)methane[1]. The silyl enol ethers **2a–h** were synthesized from the corresponding carbonyl compounds by treatment with $Me_3SiCl$, NaI, and $(C_2H_5)_3N$ in $CH_3CN$ according to the procedures A and D described by Cazeau et al.[13]. The silylated ketene acetal **2i** is commercially available (Fluka).

***Caution:*** Because of the known toxicity of chloro ethers, all operations should be carried out in an efficient hood, and skin contact should be avoided.

*Phenyl 2,2-Dimethyl-3-oxobutyrate* (**3a**). – *General Procedure:* Compounds **1** (0.80 g, 3.0 mmol) and **2a** (0.52 g, 3.3 mmol) were dissolved in 25 ml of $CH_2Cl_2$ at –78°C. A solution of $TiCl_4$ (0.76 g, 4.0 mmol) in 10 ml of $CH_2Cl_2$ was added dropwise with stirring (ca. 5 min), and the mixture was kept at –78°C. After 10 h, the dark brown solution was washed with cold 3% aqueous HCl to give a colorless mixture. The organic layer was concentrated to yield an oily residue which was dissolved in pentane and repeatedly washed with 5% aqueous $Na_2CO_3$ solution to remove phenol. After drying with $Na_2CO_3$ and evaporation of pentane, the residue was purified by layer chromatography [silica gel, hexane/ether (95:5)] yielding 0.51 g of product. Distillation [73–76°C (bath)/0.1 mbar] afforded 0.44 g (71%) of **3a**. – $^{1}$H NMR ($CDCl_3$): $\delta$ = 1.52 (s, 6H), 2.30 (s, 3H), 7.05–7.40 (m, 5H). – $^{13}$C NMR ($CDCl_3$): $\delta$ = 21.86 (q, 2-$CH_3$), 25.77 (q, C-4), 56.02 (s, C-2), 121.11 (d, $C_o$), 126.10 (d, $C_p$), 129.49 (d, $C_m$), 150.50 (s, $C_i$), 172.18 (s, C-1), 205.32 (s, C-3). – MS (70 eV): *m/z* (%) = 206 (28) [$M^+$], 164 (34), 113 (51), 94 (100), 85 (56), 70 (53), 57 (31), 43 (98).

$C_{12}H_{14}O_3$ (206.2) Calcd. C 69.89 H 6.84
Found C 69.87 H 6.73

*Phenyl 2-Oxocycloheptanecarboxylate* (**3b**): A mixture of compounds **1** (0.80 g, 3.0 mmol) and **2b** (0.61 g, 3.3 mmol) was treated with 0.76 g (4.0 mmol) of $TiCl_4$ as described before and worked up after 20 h. Layer chromatography [silica gel, hexane/ether (3:1)] afforded 0.62 g of **3b**, which was distilled to yield 0.56 g (81%) of an analytically pure material with bp 110–115°C (bath)/0.1 mbar. – $^{1}$H NMR ($CDCl_3$): $\delta$ = 1.35–2.13, 2.17–2.34, 2.47–2.46 (3 m, 10H), 3.84 (dd, *J* = 10.1 Hz, *J* = 3.7 Hz, 0.9H, keto tautomer), 7.08–7.48 (m, 5H), 12.53 (br. s, 0.1 H, enol tautomer). – $^{13}$C NMR ($CDCl_3$): $\delta$ = 24.04, 27.47, 28.22, 29.45, 43.29 (5 t, C-3, C-4, C-5, C-6, C-7), 58.67 (d, C-1), 121.45 (d, $C_o$), 125.94 (d, $C_p$), 129.38 (d, $C_m$), 150.57 (s, $C_i$), 169.35 (s, $CO_2Ph$), 208.66 (s, C-2); signals for the enol species (<15%): $\delta$ = 24.56, 24.63, 31.95, 35.61 (t), 101.21 (s), 121.79 (d), 125.74 (d), 129.51 (d), 150.49 (s), 172.12 (s). – MS (70 eV): *m/z* (%) = 232 (1) [$M^+$], 139 (58), 94 (100).

$C_{14}H_{16}O_3$ (232.3) Calcd. C 72.39 H 6.94
Found C 72.20 H 7.02

*Phenyl 2-Oxocyclooctanecarboxylate* (**3c**): Compound **1** (1.2 g, 4.5 mmol) was treated with **2c** (1.0 g, 5.1 mmol) in the presence of $TiCl_4$ (1.1 g, 5.8 mmol) for 18 h to give **3c**. Distillation [125–130°C (bath)/0.2 mbar] afforded 0.75 g (68%) of oily **3c** which solidified; mp 70–72°C (pentane/ether). – $^{1}$H NMR ($CDCl_3$, 40°C): $\delta$ = 1.25–2.27, 2.48–2.76 (2 m, 12H), 3.86 (dd, *J* = 8 Hz, *J* = 7 Hz, 1H), 7.01–7.40 (m, 5H). – $^{13}$C NMR ($CDCl_3$): $\delta$ = 24.49, 24.66, 24.74, 27.30, 29.48, 42.36 (6 t, C-3, C-4, C-5, C-6, C-7, C-8), 56.34 (d, C-1), 121.34 (d, $C_o$), 125.97 (d, $C_p$), 129.38 (d, $C_m$), 150.45 (s, $C_i$), 168.81 (s, $CO_2Ph$), 211.71 (s, C-2); signals for the enol species: $\delta$ = 24.06, 26.05, 26.54, 28.77, 30.04, 32.59 (6 t, C-3, C-4, C-5, C-6, C-7, C-8), 98.79 (s, C-1), 121.78 (d, $C_o$), 125.77 (d, $C_p$), 171.70 (s, $CO_2Ph$), 178.60 (s, C-2). – MS (70 eV): *m/z* (%) = 246 (1) [$M^+$], 153 (100), 94 (32), 55 (54).

$C_{15}H_{18}O_3$ (246.3) Calcd. C 73.15 H 7.37
Found C 73.13 H 7.27

*Phenyl 2-Oxocyclododecanecarboxylate* (**3d**): Compound **1** (0.80 g, 3.0 mmol) was treated with **2d** (0.84 g, 3.3 mmol) and $TiCl_4$ (0.76, 4.0 mmol) for 24 h according to the described procedure. The residue, obtained after evaporation of pentane (0.90 g), was recrystallized from hexane to give 0.67 g (75%) of **3d** with mp 81–83°C. – $^{1}$H NMR ($CDCl_3$): $\delta$ = 1.05–2.08, 2.10–2.56, 2.62–2.91 (3 m, 20H), 3.87 (dd, *J* = 11.0 Hz, *J* = 3.7 Hz, 1H), 6.97–7.46 (m, 5H). – $^{13}$C NMR ($CDCl_3$): $\delta$ = 22.01, 22.31, 22.83, 23.85, 24.07 (high intensity), 25.26, 25.58, 26.77, 38.38, (9 t, C-3–C-12), 57.57 (d, C-1), 121.24 (d, $C_o$), 126.07 (d, $C_p$), 129.46 (d, $C_m$), 150.39 (s, $C_i$), 168.51 (s, $CO_2Ph$), 206.06 (s, C-2). – MS (70 eV): *m/z* (%) = 302 (1) [$M^+$], 209 (100), 94 (23), 77 (23), 55 (27), 41 (21).

$C_{19}H_{26}O_3$ (302.4) Calcd. C 75.46 H 8.67
Found C 75.37 H 8.57

*Phenyl Camphor-3-carboxylate* (**3e**) was synthesized by reaction of **1** (1.2 g, 4.5 mmol) with **2e** (1.1 g, 4.9 mmol) in the presence of $TiCl_4$ (1.1 g, 5.8 mmol) at –78°C for 20 h. Chromatographic purification of the product [silica gel, hexane/ether (4:1)] gave 0.65 g (54%) of **3e** which was recrystallized from hexane; mp 69–70°C. – $^{1}$H NMR ($CDCl_3$): $\delta$ = 0.94, 0.98, 1.06 (3 s, 9H), 1.48–2.07 (m, 4H), 2.60 (br. t, *J* = 4.4 Hz, 1H), 3.58 (dd, *J* = 1.9 Hz, *J* = 4.7 Hz, 1H), 7.00–7.43 (m, 5H). – $^{13}$C NMR ($CDCl_3$): $\delta$ = 9.55 (q, 1-$CH_3$), 18.79, 19.54 (2 q, 7-$CH_3$), 22.52 (t, C-5), 29.40 (t, C-6), 45.88 (d, C-4), 47.23 (s, C-7), 55.50 (d, C-3), 58.59 (s, C-1), 121.46 (d, $C_o$), 126.01 (d, $C_p$), 129.41 (d, $C_m$), 150.33 (s, $C_i$), 168.17 (s, $CO_2Ph$), 210.81 (s, C-2). – MS (70 eV): *m/z* (%) = 272 (5) [$M^+$], 179 (100), 151 (45), 123 (18), 94 (20), 83 (37), 55 (17), 41 (24).

$C_{17}H_{20}O_3$ (272.3) Calcd. C 74.97 H 7.40
Found C 74.95 H 7.46

*Phenyl 1-Methyl-4-(1-methylvinyl)-2-oxocyclohexanecarboxylate* (**3f**) was prepared by treatment of **1** (0.80 g, 3.0 mmol) with **2f** (0.74 g, 3.3 mmol), and $TiCl_4$ (0.76 g, 4.0 mmol) at –78°C for 17 h. Purification of the product by column chromatography [silica gel, hexane/ether (95:5)] gave 0.45 g of **3f** which was further purified by distillation yielding 0.37 g (46%) of product with bp 130 to 135°C/0.15 mbar. – $^{1}$H NMR ($CDCl_3$): $\delta$ = 1.53 (s, $CH_3$), 1.74 to 2.05 (m, superimposed by br. s at 1.77, 7H), 2.42–2.58 (m, 1H), 2.63 ($m_c$, 2H), 4.76, 4.86 (2 br. s, 2H), 7.05–7.45 (m, 5H). – $^{13}$C NMR ($CDCl_3$): $\delta$ = 20.48, 21.20 (2 q, 1-$CH_3$, $CH_3C$=), 25.40 (t, C-5), 33.68 (t, C-6), 43.35 (t, C-3), 44.22 (d, C-4), 57.19 (s, C-1), 111.27 (t, $CH_2$=), 121.40 (d, $C_o$), 125.96 (d, $C_p$), 129.42, (d, $C_m$), 145.48 (s, $C$=$CH_2$), 150.73 (s, $C_i$), 171.92 (s, $CO_2Ph$), 208.34 (s, C-2). – MS (70 eV): *m/z* (%) = 272 (12) [$M^+$], 179 (83), 151 (15), 123 (30), 109 (51), 107 (55), 97 (100), 94 (41), 81 (51), 69 (38), 67 (30), 55 (72), 41 (60).

$C_{17}H_{20}O_3$ (272.3) Calcd. C 74.97 H 7.40
Found C 74.92 H 7.37

*Phenyl 2,2-Dimethyl-3-oxopropanoate* (**3g**): The crude material obtained from **1** (1.2 g, 4.5 mmol), **2g** (0.79 g, 5.5 mmol), and $TiCl_4$ (1.1 g, 5.8 mmol) according to the general procedure was purified by column chromatography [silica gel, hexane/ether (4:1)] to yield 0.75 g of **3g**. Distillation [84–88°C (bath)/0.4 mbar] afforded 0.63 g (74%) of analytically pure **3g**. – $^1$H NMR ($CDCl_3$): $\delta$ = 1.50 (s, 6H), 7.05–7.41 (m, 5H), 9.80 (s, 1H). – $^{13}$C NMR ($CDCl_3$): $\delta$ = 19.71 (q, 2-$CH_3$), 54.03 (s, C-2), 121.24 (d, $C_o$), 126.21 (d, $C_p$), 129.51 (d, $C_m$), 150.32 (s, $C_i$), 171.30 (s, C-1), 198.50 (d, C-3). – MS (70 eV): *m/z* (%) = 192 (12) [$M^+$], 164 (25), 99 (49), 94 (100), 71 (47), 70 (43), 43 (82).

$C_{11}H_{12}O_3$ (192.2) Cacld. C 68.74 H 6.29
Found C 68.70 H 6.33

*Phenyl (5,5-Dimethyl-3-oxo-1-cyclohexen-1-ylacetate)* (**3h**): Compound **1** (0.80 g, 3.0 mmol) was treated with **2h** (0.70 g, 3.3 mmol) and $TiCl_4$ (0.76 g, 4.0 mmol) for 18 h to give crude **3h** which was purified by column chromatography [silica gel, ether/hexane (2:1)] and distillation [145–150°C (bath)/0.08 mbar] yielding 0.40 g of product. Recrystallization from hexane afforded 0.34 g (44%) of **3h** with mp 68–69°C. – $^1$H NMR ($CDCl_3$): $\delta$ = 1.09 (s, 6H), 2.28 (s, 2H), 2.38 (br. s, 2H), 3.47 (br. s, 2H), 6.09 (br. s, 1H), 7.05–7.50 (m, 5H). – $^{13}$C NMR ($CDCl_3$): $\delta$ = 28.13 (q, 5-$CH_3$), 33.73 (s, C-5), 43.12, 43.56 (2 t, C-6, $O_2CCH_2$), 50.85 (t, C-4), 126.26 (d, $C_o$), 126.13 (d, $C_p$), 128.17 (d, C-2), 129.49 (d, $C_m$), 150.29 (s, $C_i$), 154.01 (s, C-1), 167.86 (s, $CO_2Ph$), 199.39 (s, C-3). – MS (70 eV): *m/z* (%) = 258 (4) [$M^+$], 165 (100), 109 (12), 108 (25), 94 (22), 77 (7), 67 (10), 53 (10).

$C_{16}H_{18}O_3$ (258.3) Calcd. C 74.40 H 7.02
Found C 74.31 H 7.10

*Methyl Phenyl (2,2-Dimethylmalonate)* (**3i**): The product generated from **1** (0.80 g, 3.0 mmol) and **2i** (0.58 g, 3.3 mmol) in the presence of $TiCl_4$ (0.76 g, 4.0 mmol) within 14 h was purified by layer chromatography [silica gel, hexane/ether (95:5)] to yield 0.60 g of **3i**. Distillation [74–78°C (bath)/0.1 mbar] afforded 0.54 g (82%) of analytically pure **3i**. – $^1$H NMR ($CDCl_3$): $\delta$ = 1.59 (s, 6H), 3.81 (s, 3H), 7.04–7.45 (m, 5H). – $^{13}$C NMR ($CDCl_3$): $\delta$ = 22.75 (q, 2-$CH_3$), 50.08 (s, C-2), 52.69 (q, $OCH_3$), 121.21 (d, $C_o$), 125.99 (d, $C_p$), 129.43 (d, $C_i$), 150.67 (s, $C_i$), 171.36, 172.99 (2 s, $CO_2CH_3$, $CO_2Ph$). – MS (70 eV): *m/z* (%) = 222 (30) [$M^+$], 129 (97), 101 (100), 94 (80), 73 (45), 41 (27).

$C_{12}H_{14}O_4$ (222.2) Calcd. C 64.85 H 6.35
Found C 64.48 H 6.57

### CAS Registry Numbers

**1**: 4885-03-4 / **2a**: 17510-44-0 / **2b**: 22081-48-7 / **2c**: 50338-42-6 / **2d**: 51584-36-2 / **2e**: 56613-17-3 / **2f**: 72311-10-5 / **2g**: 6651-34-9 / **2h**: 80239-27-6 / **2i**: 31469-15-5 / **3a**: 103439-34-5 / **3b**: 126256-23-3 / **3c**: 126256-24-4 / **3d**: 126256-25-5 / **3c**: 126256-26-6 / **3f**: 126256-27-7 / **3g**: 89635-72-3 / **3h**: 126256-28-8 / **3i**: 126256-29-9

---

[1] A. Cambanis, E. Bäuml, H. Mayr, *Synthesis* **1988**, 961; Bayer AG (H. Mayr, A. Cambanis, E. Bäuml, Inv.), D.A.S. 3821 130.0.

[2] H. Gross, J. Rusche, M. Mirsch, *Chem. Ber.* **96** (1963) 1382.

[3] H. Mayr, U. von der Brüggen, *Chem. Ber.* **121** (1988) 339.

[4] H. Mayr, A. Cambanis, E. Bäuml, *Synthesis*, **1988**, 962.

[5] [5a] E. W. Colvin, *Silicon Reagents in Organic Synthesis*, p. 99, Academic Press, London 1988. – [5b] E. W. Colvin, *Silicon in Organic Synthesis*, p. 198, Butherworths, London 1981. – [5c] W. P. Weber, *Silicon Reagents for Organic Synthesis*, p. 255, Springer Verlag, Berlin 1983.

[6] [6a] A. P. Krapcho, J. Diamanti, C. Cayen, R. Bingham, *Org. Synth., Coll.* Vol. V (1973) 198. – [6b] S. B. Soloway, F. B. La-Forge, *J. Am. Chem. Soc.* **69** (1947) 2677.

[7] C. R. Hauser, F. W. Swamer, J. T. Adams, *Org. React.* **8** (1954) 59.

[8] [8a] M. Stiles, *J. Am. Chem. Soc.* **81** (1959) 2598. – [8b] S. W. Pelletier, R. L. Chappell, P. C. Parthasarthy, N. Lewin, *J. Org. Chem.* **31** (1966) 1747. – [8c] A. Pavia, F. Winternitz, R. Wylde, *C. R. Acad. Sci.* **261** (1965) 1026. – [8d] S. Julia, C. Huynh, *C. R. Acad. Sci., Ser. C*, **270** (1970) 1517.

[9] L. N. Mander, S. P. Sethi, *Tetrahedron Lett.* **24** (1983) 5425.

[10] H. Mayr, W. Striepe, *J. Org. Chem.* **50** (1985) 2995.

[11] Similar conditions have previously been applied for the tertiary alkylation of silyl enol ethers: M. T. Reetz, W. F. Maier, H. Heimbach, A. Giannis, G. Anastassious, *Chem. Ber.* **113** (1980) 3734.

[12] Detailed studies on keto-enol equilibria of the corresponding ethyl and methyl esters have been described: [12a] S. J. Rhoads, C. Pryde *J. Org. Chem.* **30** (1965) 3212. – [12b] S. J. Rhoads *J. Org. Chem.* **31** (1966) 171. – [12c] K. R. Kallury, U. J. Krull, M. Thompson *J. Org. Chem.* **53** (1988) 1320.

[13] P. Cazeau, F. Duboudin, F. Moulines, O. Babot, J. Dunogues, *Tetrahedron* **43** (1987) 2075.

[45/90]