Notiz / Note

Sterically Hindered Double-Bond Systems, VII[1]

On the Reaction of Succinic Esters with *tert*-Butyllithium

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Addition of *tert*-butyllithium to dimethyl (**1a**) and diethyl succinate (**1b**), respectively, provides 2,2,7,7-tetramethyl-3,6-octanedione (**3**) in good yield as well as the ketoesters **5a/b** and the cyclized products **6** and **7**. The mode of formation of these latter side products is discussed, and several published errors concerning these transformations are corrected.

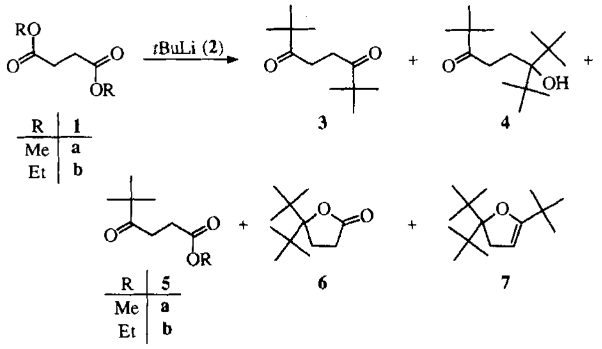
As a part of an ongoing investigation on the structural and chemical properties of highly substituted, especially *tert*-butylated di- and polyenes[2] we required a sample of 2,2,7,7-tetramethyl-3,6-octanedione (**3**), a diketone which has been described by Petrov et al.[3] as being readily available from the reaction of dimethyl succinate (**1a**) with *tert*-butyllithium. According to the Russian workers **3** is accompanied by small amounts of the tertiary alcohol **4**, a secondary product produced from **3** by addition of excess *tert*-butyllithium. On repeating this work we have not only been unable to reproduce the published results[3], we believe, moreover, that the published structure assignment for **3** is incorrect.

According to the original procedure[3] we added dimethyl succinate (**1a**) in diethyl ether to a solution of *tert*-butyllithium in ether at −40°C. Standard workup provided **3** and the mono-*tert*-butylated oxo ester **5a** as well as the γ-lactone **6** and the dihydrofuran derivative **7** in the yields given in Scheme 1.

When the diethyl diester **1b** is employed as the substrate the product spectrum and the yields of the different products are comparable. In no case could the hydroxy ketone **4** be detected. Furthermore, both from the analytical and spectroscopic data (cf. Experimental) we conclude that the reported "diketone" **3** is actually the lactone **6**. Whereas authentic **3** is an oily liquid, the isomeric **6** is a solid melting at 88−89°C; and a solid possessing the same m.p. (86−87°C) has been isolated by Petrov[3].

None of the experiments described so far provides **3** in preparatively satisfying amounts. However, when the addition is performed in a reverse manner by adding the organolithium compound to the diester, **3** becomes the predominating product regardless whether **1a** or **1b** is used as the substrate. Although the yield is somewhat lower in the latter experiment (see the table in Scheme 1) the material obtained is purer, **5b**, **6**, and **7** being only minor, easily separable products in this instance. As shown in Scheme 2 for **1a** the reaction begins with the formation of the oxo ester **5a**. In the next step the *tert*-butyllithium can either attack an ester or an oxo carbonyl group. Although the latter should be the preferred reaction site for electronic reasons it is disfavored sterically. Since **3** is the major product the steric effect is evidently predominating. Still, the oxo group also reacts with *tert*-butyllithium, and via **9** and its cyclic isomer **8** the lactone **6** is formed by terminal loss of methoxide. When **6** reacts with excess *tert*-butyllithium **11** is produced which after protonation and dehydration is converted into **7**. That this is not the only route to the cyclic enol ether though, was shown by treating diketone **3** with *tert*-butyllithium. Again **7** is formed (10%), but this time most likely by way of **10** which could also cyclize to **11**. Since either pathway involves the addition of *tert*-butyllithium to an ester function it is likely that its steric size will influence the outcome of the overall reaction. It hence comes as no surprise that with the "smaller" methyl ester **1a**, **6** and **7** are formed in larger amounts than with the sterically more demanding ethyl derivative **1b**.

Scheme 1. The reaction of *tert*-butyllithium with dimethyl (**1a**) and diethyl succinate (**1b**)



Starting compound	Yield (%)[a] of						Ref.
	3	**4**	**5a**	**5b**	**6**	**7**	
1a	11	4	-	-	-	-	[2]
1a	14	-	5	-	11	2	this work
1b	13	-	-	4	12	3	this work
1a[b]	47	-	4	-	17	15	this work
1b[b]	44	-	-	trace	4	5	this work

[a] Determined by GLPC. − [b] Inverse addition.

That the isolated yields in the normal addition mode (entries 1−3 in the table of Scheme 1) are lower than in the inverse case

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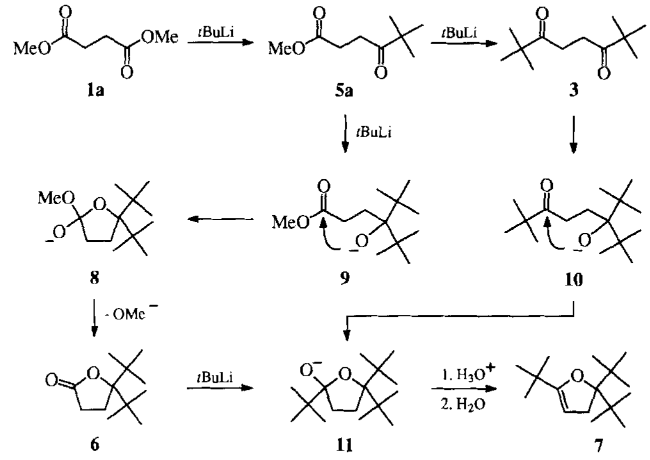
Scheme 2. Mode of formation of the side products **6** and **7**



(entries 4 and 5) is presumably caused by competing aldol-type condensations which should be more competitive when the base is present in excess during the course of the addition.

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Experimental

General: See ref.[4].

To a stirred solution of 0.6 mol of *tert*-butyllithium in 350 ml of hexane diluted with 400 ml of dry diethyl ether 0.15 mol (26.2 g, 25 ml) of diethyl succinate (**1b**) in 100 ml of diethyl ether was slowly added at −40°C under N_2. The reaction was allowed to reach room temp., and stirring was continued for 2.5 h at this temperature. For hydrolysis, ice/water, followed by dild. hydrochloric acid was added. Extraction with diethyl ether, drying ($MgSO_4$), and removal of the solvent by rotatory evaporation concluded the workup. The raw product mixture (5.1 g) was analyzed by analytical gas chromatography (15-m SPB-5 column, 60−200°C) providing the composition presented in the table of Scheme 1. Analytically pure samples of the different products were obtained by preparative gas chromatography (3-m SE 54 column, 140−180°C).

2,2,7,7-Tetramethyl-3,6-octanedione (**3**): Colorless oil, n_D^{20} = 1.4400. − ^1H NMR ($CDCl_3$, int. TMS): δ = 1.18 (s, 18H, *t*Bu), 2.77 (s, 4H, CH_2). − ^{13}C NMR ($CDCl_3$): δ = 214.8 (s, C-3), 43.9 (s, C-2), 30.5 (t, C-4), 26.6 (q, C-1). − IR (film): ṽ = 1704 cm^{-1} (vs, C=O). − MS (40 eV): *m/z* (%) = 141 (85) [$M^+ - C_4H_9$], 113 (100). − $C_{12}H_{22}O_2$ (198.31): calcd. C 72.68 H 11.18; found C 72.64 H 11.05.

Ethyl 4-Oxo-5,5-dimethylhexanoate (**5b**): ^1H NMR ($CDCl_3$): δ = 1.17 (s, 9H, *t*Bu), 1.25 (t, *J* = 7.14 Hz, 3H, CH_3), 2.56 (t, *J* = 6.5 Hz, 2H, CH_2CO_2), 2.82 (t, *J* = 6.5 Hz, 2H, CH_2COC), 4.12 (q, *J* = 7.17 Hz, 2H, CH_2). − IR (film): ṽ = 1771 cm^{-1} (vs), 1737 (vs), 1710 (vs). − MS (40 eV): *m/z* (%) = 141 (12) [$M^+ - OC_2H_5$], 129 (58), 101 (100).

5,5-Di-tert-butyl-tetrahydrofuran-2-one (**6**): Colorless needles, m.p. 88−89°C. − ^1H NMR ($CDCl_3$): δ = 1.09 (s, 18H, *t*Bu), 2.14−2.18 (AA'BB'-m, 2H), 2.52−2.56 (AA'BB'-m, 2H). − ^{13}C NMR ($CDCl_3$): δ = 177.9 (s, C-2), 96.6 (s, C-5), 41.8 (s, C-6), 30.6 (t, C-2), 28.2 (q, C-7), 25.3 (t, C-4). − IR (KBr): ṽ = 1744 cm^{-1} (vs). − MS (40 eV): *m/z* = 141 (100) [$M^+ - C_4H_9$], 113 (98), 576 (48). − $C_{12}H_{22}O_2$ (198.231): calcd. C 72.68 H 11.18; found C 72.64 H 11.11.

2,2,5-Tri-tert-butyl-2,3-dihydrofuran (**7**): Colorless oil, n_D^{20} = 1.4462. − ^1H NMR ($CDCl_3$): δ = 1.02 (s, 18H, *t*Bu), 1.1 (s, 9H, *t*Bu), 2.50 (m, 2H, CH_2), 4.32 (m, 1H, CH=). − ^{13}C NMR ($CDCl_3$): δ = 166.0 (s, C-5), 95.7 (s, C-2), 91.1 (d, C-4), 41.7 [s, 5-$\mathit{C}(CH_3)_3$], 35.5 (t, C-3), 32.2 {s, 2-[$\mathit{C}(CH_3)_3]_2$}, 28.2, 27.9 {q, 2-[$C(\mathit{C}H_3)_3]_2$, 5-$C(\mathit{C}H_3)_3$}. − IR (film): ṽ = 1663 cm^{-1} (vs), 1117 (s). − MS (40 eV): *m/z* (%) = 238 (1) [M^+], 181 (12), 125 (9), 57 (100). − In the elemental analysis the values for C and H were consistently too low, possibly because of uncontrolled decomposition of **7** (easy thermal loss of isobutene).

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[1] For part VI of this series see: H. Hopf, R. Hänel, P. G. Jones, P. Bubenitschek, *Angew. Chem.* **1994**, *106*, 1444−1445; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1369−1370.

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