2,2′,4,4′,6-Penta-*tert*-butylbenzil: an unexpected product in the attempted coupling of tri-*tert*-butylbenzoyl chloride with magnesium–magnesium iodide

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Reduction of 2,4,6-tri-*tert*-butylbenzoyl chloride with Mg–MgI$_2$ in 1:1 diethyl ether–benzene under ultrasonic irradiation gives the hexa-*tert*-butyl-benzil and -benzoin and also 2,2′,4,4′,6-penta-*tert*-butylbenzil. Possible mechanisms for the loss of the Bu^t group are discussed.

The highly bulky 2,4,6-tri-*tert*-butylphenyl group (dubbed 'supermesityl', Sup)[1] is widely used for kinetic stabilization of otherwise unstable highly reactive molecules.[2] This group has scarcely been used in enol chemistry, however, while preparing deoxybenzoin SupCH$_2$COSup Kawashima and Okazaki[3] isolated a benzofuran, presumably formed by oxidation of the enol SupCH=C(OH)Sup, the tautomer of the deoxybenzoin. Attempts to prepare *gem*-disupermesityl-substituted ethenols have failed since the generation of the Sup$_2$C moiety has so far proven impossible.

1,2-Diarylethenediols **1** have been studied by Fuson.[4] They can undergo tautomerization to the isomeric benzoin **2** or oxidation to the corresponding α-diketone **3** (Scheme 1). The bulkier the aryl substituent, the more stable the ene-1,2-diols are towards oxidation, the order of stability being **1d** > **1c** > **1b** > **1a** (not isolated).[4] Faraggi has shown that **1d** is less stable than its tautomer **2d**; reflux of a hexane solution of **1d** for 114 h gave only **2d**.[5]

Anticipating that a further increase in the bulk of the aryl group would increase the thermodynamic stability of the ene-1,2-diol, we attempted to synthesize 1,2-bis(supermesityl)-ethene-1,2-diol **1e**. Two routes have been previously applied to the synthesis of 1,2-diarylethene-1,2-diols; (i) Mg–MgI$_2$ (Gomberg–Bachman)[6] mediated reductive coupling of acyl chlorides **4** (Scheme 2)[7] and (ii) reduction of the corresponding α-diketone **3** either by molecular hydrogen[8] or by the Mg–MgI$_2$ mixture (Scheme 2).[7]
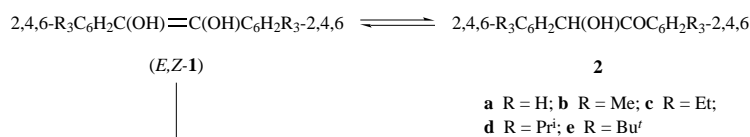
The highly crowded 2,2′,4,4′,6,6′-hexa-*tert*-butylbenzil **3e** has not hitherto been reduced. It was synthesized by Lauer and

Staab[9a] by reducing 2,4,6-tri-*tert*-butylbenzoyl chloride **4** (R = Bu^t) with Mg–MeI. Its crystal structure indicates severe distortions of the aryl rings.[10] In an attempt to prepare **1e** by both approaches we were unable to isolate it. Instead, side reactions took place.
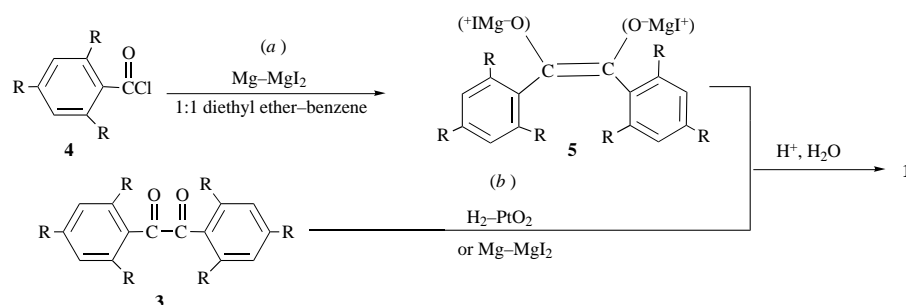
A Gomberg–Bachman reduction of **4** (R = Bu^t) did not take place (Scheme 2). However, under ultrasonic irradiation, both the symmetrical benzil **3e** and the unsymmetrical 2,2′,4,4′,6-penta-*tert*-butylbenzil **6** were formed, together with a small amount of benzoin **2e** and an unidentified compound (Scheme 3). Enediol **1e** was not observed.

Assignment of **6** as a 2,2′,4,4′,6- rather than as its 2,2′,4,6,6′-isomer is based on several considerations. First, it is reasonable that the Bu^t group in the more crowded *ortho* position will be lost. Second, the ^{1}H NMR spectrum displays four types of aromatic protons in a 2:1:1:1 ratio with coupling constants for the single proton signals corresponding to J_{ortho}, J_{meta} and $J_{ortho,meta}$ couplings, consistent with structure **6**. Third, the two distinct ^{13}C=O signals at 191.2 and 201.2 ppm indicate an unsymmetrical substitution pattern around the α-diketone moiety. The steric effect of the *o*-Bu^t group on the ^{13}C=O resonance causes deshielding. The higher field signal is probably due to the C=O adjacent to the trisubstituted ring since in **3e** $\delta(^{13}$C=O$) = 203.3$ ppm.[11]
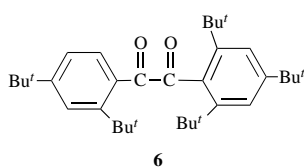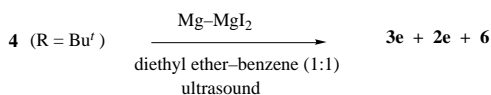
The room temp. ^{1}H NMR spectrum of **3e** (400 MHz) displays two distinct *o*-Bu^t signals indicating a hindered rotation. A rotational barrier of 16.7 kcal mol^{-1} (1 cal = 4.184 J) at 335 K was measured and assigned to a rotation about the Ar–C=O bond.[9a] A similar rotation in **6** is also hindered at room temp. as

$$2,4,6\text{-R}_3\text{C}_6\text{H}_2\text{C(OH)}\!=\!\text{C(OH)C}_6\text{H}_2\text{R}_3\text{-}2,4,6 \;\rightleftharpoons\; 2,4,6\text{-R}_3\text{C}_6\text{H}_2\text{CH(OH)COC}_6\text{H}_2\text{R}_3\text{-}2,4,6$$

(*E,Z*-**1**)   **2**

a R = H; **b** R = Me; **c** R = Et;
d R = Pr^i; **e** R = Bu^t

$$2,4,6\text{-R}_3\text{C}_6\text{H}_2\text{COCOC}_6\text{H}_2\text{R}_3\text{-}2,4,6$$

3

Scheme 1

Scheme 2

indicated by the appearance of two *o*-Bu^t groups of the tetra-substituted ring. However, the barrier was not measured.

The most likely reason why the *tert*-butyl group is lost is steric crowding in **3e**. An aromatic *tert*-butyl group may undergo electrophilic protio-[12a] or bromo-de-*tert*-butylation [12b] and a Bu^t ⟶ H replacement by adventitious HCl seems reasonable. However, when **3e** was reacted with a saturated solution of HCl in benzene, **6** was not formed. Furthermore, **6** was neither detected in the reaction of **3e** with Mg–MgI$_2$ in 1:1 diethyl ether–benzene under sonication nor in its catalytic hydrogenation with Adam's catalyst in high boiling light petroleum, CH$_3$CO$_2$H or EtOH. We conclude that the *tert*-butyl group is not lost by an electrophilic protio-de-*tert*-butylation or by reductive de-*tert*-butylation.

Since the *tert*-butyl group could have been lost earlier, *e.g.* from **4** (R = Bu^t), we searched in the acidic fraction of the reaction mixture for di- or mono-*tert*-butylbenzoic acid, but we detected only 2,4,6-tri-*tert*-butylbenzoic acid.[13] Moreover, no tetra-*tert*-butylbenzil, which would have been formed by a reductive coupling of two 2,4-di-*tert*-butylbenzoyl moieties, was observed. Consequently, we do not know at what stage the *o-tert*-butyl group is being lost (however, see below).

The catalytic hydrogenation which gave **1b–d** from **3b–d** did not give enediol **1e** from **3e**. A reduction–reoxidation sequence is excluded since when the reduction was conducted in the presence of the enediolate traps Ac$_2$O and Me$_3$SiCl no enediol diacetate or bis(trimethylsilyl) ether were formed.

However, reduction of **3e** with Mg–MgI$_2$ in 1:1 diethyl ether–benzene under sonication gave a product with a ^{1}H NMR spectrum identical to that of benzoin **2e** isolated according to Scheme 3. This result strongly suggests that enediol **1e**, or its salt **5**, is initially formed but is either mainly reoxidized in the reaction mixture (explaining I$_2$ release during the reaction) or isomerizes to the tautomeric **2e**.

This raises the possibility that a different oxidation course of **1e** or the salt **5** might account for the formation of **6**. The enol 1,1-bis(2,4,6-triisopropylphenyl)-3,3-dimethylbut-1-en-2-ol **7** undergoes facile oxidative cyclization in air with loss of an Pr^i group yielding the benzofuran **8**.[14] Similarly Kawashima and Okazaki obtained the benzofuran **9** with loss of a Bu^t group, as mentioned above.[3] Although we can speculate that enediol **1e** or its enediolate **5** (R = Bu^t) cyclizes and then isomerizes to a benzofuranone with loss of an *o-tert*-butyl group, an unknown, subsequent ring-cleavage of the benzofuranone is required to yield **6**. We therefore regard the mechanism of formation of **6** as unknown at present.†
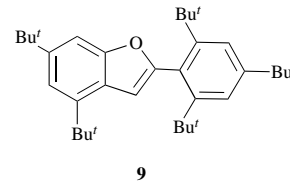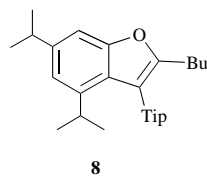
Experimental

General

Mps were measured on a Thomas-Hoover apparatus and are uncorrected. NMR Spectra were recorded on a Bruker AMX

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† Note added in proof: the editor has suggested an equally plausible radical de-*tert*-butylation mechanism, initiated by electron transfer from the Mg to **4**, coupling of the anion radical formed and loss of Cl$^-$ and *tert*-butyl radical.
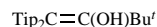
400 pulsed FT spectrometer operating at 400.13 MHz for ^{1}H and 100.62 MHz for ^{13}C, respectively and δ values are given in ppm downfield from Me$_4$Si and J values are in Hz. UV/VIS Spectra were recorded on a Uvikon 930 spectrometer and FT Infrared spectra on a Nicolet Impact 400 spectrometer. EI and CI mass spectra were recorded with Finnigan MAT 4600 and HRMS on Finnigan MAT 711 spectrometers. Light petroluum refers to that boiling in the range 60–80 °C.

Reduction of 2,4,6-tri-*tert*-butylbenzoyl chloride

To a suspension of Mg turnings (150 mg, 6.2 mmol) in 1:1 diethyl ether–benzene (30 ml), iodine (900 mg, 3.55 mmol) was added in small portions. The solution was refluxed until it became almost colourless, then it was cooled to room temp. in an Ar atmosphere. 2,4,6-Tri-*tert*-butylbenzoyl chloride [9b] (1 g, 3.23 mmol) in dry diethyl ether (10 ml) was added and the mixture was sonicated for 40 h at room temp. under a constant nitrogen flow. The colour became deep red upon I$_2$ release during the reaction. The mixture was filtered into 5% aqueous AcOH (50 ml), washed successively with water (30 ml), saturated brine (30 ml), 5% aqueous NaHCO$_3$ (30 ml) and water (30 ml), dried (MgSO$_4$) and the solvent was evaporated. The yellow residue was dissolved in light petroleum (20 ml). A white precipitate (135 mg, 13%) was isolated and identified by NMR spectroscopy as 2,4,6-tri-*tert*-butylbenzoic acid, mp 288–290 °C (lit.,[13] 297 °C).

The filtrate was evaporated to dryness, the residue dissolved in warm MeOH (20 ml) and upon cooling a bright yellow precipitate of 2,2′,4,4′,6,6′-hexa-*tert*-butylbenzil **3e** (69 mg, 7.8%) formed, mp 202–204 °C (lit.,[9a] 202–204 °C). This was further characterized by NMR and IR spectroscopy.

When the filtrate was evaporated again and the residue redissolved in MeOH a new precipitate was formed. Recrystallization from MeOH yielded yellow crystals of 2,2′,4,4′,6-penta-*tert*-butylbenzil **6** (105 mg, 13%), mp 147–148 °C; δ_H(400 MHz, CDCl$_3$) 1.31 (18 H, s, *p*-Bu^t), 1.35, 1.37, 1.45 (3 × 9 H, 3 × s, 3 × *o*-Bu^t), 7.37 (1 H, dd, J 8.5, 1.9, H-5′), 7.45 (2 H, s, H-3, H-5), 7.74 (1 H, d, J 1.9, H-3′), 8.32 (1 H, d, J 8.5, H-6′); δ_C(100.64 MHz, CDCl$_3$) 31.7 (Me), 32.2 (Me), 34.5 (CMe$_3$), 35.6 (CMe$_3$), 38.0 (CMe$_3$), 38.2 (CMe$_3$), 122.6, 123.6, 126.7, 136.3, 147.9, 150.7, 154.8 (Ar-C), 191.2 (C=O), 201.2 (C=O); ν_{max}(Nujol)/cm^{-1} 1708, 1680 (s, C=O), 1600 (m, Ar); m/z (EI) 273 (100%, Bu$^t_3$C$_6$H$_2$CO$^+$), 217 (7, Bu$^t_2$C$_6$H$_3$CO$^+$); m/z (CI, NH$_4^+$) 491 (M + H$^+$) (Found: C, 82.85; H, 10.13. C$_{34}$H$_{50}$O$_2$ requires C, 83.21; H, 10.27%).

Chromatography of the residual filtrate on silica gel using light petroleum–CH$_2$Cl$_2$ gradient as eluent gave additional 2,2′,4,4′,6,6′-hexa-*tert*-butylbenzil (6 mg, 0.7%) and 2,2′,4,4′,6-penta-*tert*-butylbenzil (27.5 mg, 3%).

A fourth compound was isolated from the chromatographic elution. After dissolution in MeOH, 2,2′,4,4′,6,6′-hexa-*tert*-butylbenzoin (12 mg) was precipitated as a white solid, mp 189 °C; δ_H(400 MHz, CDCl$_3$) 0.68, 0.98, 1.25, 1.26, 1.43 (5 × 9 H, 5 × s, 5 × Bu^t), 1.56 (9 H, s, Bu^t), 4.05 (1 H, s, OH), 6.06 [1 H, s, C*H*(OH)], 7.09 (1 H, d, J 1.9, Ar-H), 7.19 (1 H, d, J 2.1, Ar-H), 7.39 (1 H, d, J 1.9, Ar-H), 7.48 (1 H, d, J 2.1, Ar-H); δ_C(100.64 MHz, CDCl$_3$) 31.1 (Me), 31.2 (Me), 32.5 (Me), 33.0 (Me), 33.5 (Me), 34.2 (Me), 34.6 (CMe$_3$), 34.7 (CMe$_3$), 37.5

(CMe$_3$), 37.8 (CMe$_3$), 37.9 (CMe$_3$), 39.6 (CMe$_3$), 80.53 (C-OH), 122.4, 123.4, 123.6, 125.3, 130.1, 134.0, 146.2, 146.7, 148.9, 149.5, 151.8, 152.4 (Ar-C), 212.6 (C=O); ν_{max}(Nujol)/cm^{-1} 3500 (s, OH), 1690 (m, C=O), 1600 (m, Ar) [Found: (M − OBu^t)$^+$ 474.3894. C$_{34}$H$_{50}$O requires M, 474.3861; Found: (Bu$^t_3$C$_6$-H$_2$CO)$^+$ 273.2202. C$_{19}$H$_{29}$O requires M, 273.2218]; m/z (CI, isobutane) 475 (43%, MH$^+$ − OBu^t), 273 (100, Bu$^t_3$C$_6$-H$_2$CO$^+$); m/z (Negative CI) 547 (M − H), 491 (M − Bu^t).

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