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Synthesis of Highly Hindered 1,2-Diaryl Diketones and of *cis*- and *trans*-1,2-Diacetoxy-1,2-bis(aryl)ethenes†

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Highly hindered 1,2-diaryl diketones can be synthesized in good yields by the reaction of 1-aryllithium with CO in THF solution at atmospheric pressure; preparation of *cis*- and *trans*-1,2-diacetoxy-1,2-bis(Mes)ethene can be also afforded by a similar procedure and further quenching with Ac_2O.

Symmetrical α-diketones, RCOCOR, are useful intermediates for the synthesis of oxygenated fine chemicals,[1] and several methods have been recently attempted for their preparation. Most of the reported methods for the synthesis of aromatic α-diketones are based on the coupling of carbonyl compounds, promoted by different means.[2,3] Novel routes to aryl 1,2-diketones utilise treatment of benzotriazole derivatives with butyllithium and subsequent reaction with esters; no diaryl compounds were reported.[4] Since coupling of *ortho*-substituted derivatives is unfavourable because of steric hindrance, a strategy based on the formation of an oxycarbene that would favor coupling is proposed here, as a procedure for the synthesis of highly hindered aromatic α-diketones under mild reaction conditions.

The reaction of 1-aryllithium **1** with CO at atmospheric pressure allowed the synthesis of hindered 1,2-diaryl diketones **2** in good yields; giving in some cases also the diarylketone **3** as a side product [eqn. (1)]. A careful search of conditions was carried out for the reactions of 2,4,6-trimethylphenyllithium, (MesLi) **1a**, which was prepared from mesityl bromide and *n*-butyllithium.

$$\underset{\mathbf{1}}{\mathrm{ArLi}} + \mathrm{CO} \longrightarrow \underset{\mathbf{2}}{\mathrm{ArCOCOAr}} + \underset{\mathbf{3}}{\mathrm{ArCOAr}} \qquad (1)$$

In this case, only the 1,2-diaryl diketone **2a** is produced in yields > 50%; to the best of our knowledge, **2a** was previously obtained in only 8% yield.[5] The reaction mixture contains also variable amounts of the corresponding hydrocarbon **4a** [eqn. (2)] plus some other trace products (Table 1).

$$\underset{\mathbf{1a}}{\mathrm{MesLi}} + \mathrm{CO} \longrightarrow \underset{\mathbf{2a}}{\mathrm{MesCOCOMes}} + \underset{\mathbf{4a}}{\mathrm{MesH}} \qquad (2)$$

In a previously reported mechanistic study of the reaction of phenyllithium with CO,[6] the reaction is shown to be initiated by electron transfer from PhLi to CO, giving the radical cation–radical anion pair **5** (Ar = Ph); further reaction within the cage gives the transient acyl anion intermediate **6**,[7] which is in equilibrium with an oxycarbene species [eqn. (3)].

$$\mathrm{ArLi} + \mathrm{CO} \longrightarrow \underset{\mathbf{5}}{\left[(\mathrm{ArLi})^{\bullet+}, (\mathrm{CO})^{\bullet-}\right]} \longrightarrow \underset{\mathbf{6}}{\left[\mathrm{ArC(O)Li} \rightleftharpoons \mathrm{Ar\ddot{C}OLi}\right]} \qquad (3)$$

Table 1 Carbonylation of MesLi **1a** in THF quenching with 50 μL of aqueous NH_4Cl

			Products(%)[a]	
1a/mmol	Volume$_{CO}$/mL	T/°C	**2a**	**4a**
0.8	10	−50	67	27
0.3	5	0	54	42
1.2	14	25	52	36
0.4	8	35	44	56

[a] Determined by GC, against decalin as internal standard.

Table 2 Carbonylation of MesLi **1a** quenching with 50 μL of acetic anhydride

			Products(%)		
1a/mmol	Volume$_{CO}$/mL	T/°C	**4a**	**8a**	**8b**
0.8[a]	35	−78	30	46	0
1.2[a]	17	−35	60	20	2
0.4[a]	8	25	36	41	11
0.6[b]	20	45	39	25	38
4.5[c]	18	80	64	6	5
4.5[c]	27	100	30	8	15
4.5[c]	39	130	43	10	14

[a] [**1a**]=0.4 M in THF. [b] [**1a**]=0.3 M in THF. [c] MesLi (solid phase reaction).

In the present study, the finding of mesitylene in the reaction mixture could, in principle, be explained in analogy to a transmetallation reaction, which was reported to yield the π-stabilised benzyl anion at temperatures higher than −10 °C.[8] Nevertheless, formation of **4a** can be better explained by a partial escape of $(\mathrm{MesLi})^+$ from the cage, **5** (Ar = Mes), and subsequent H abstraction from THF by the mesityl radical formed.

Treatment of the reaction mixture with acetic anhydride before quenching produces *cis*- and *trans*-1,2-diacetoxy-1,2-bis(2,4,6-trimethylphenyl)ethene **8** [eqn. (4)]. This is a further proof for the reaction mechanism mentioned above and indicates that the intermediate is the 1,2-dilithiumdiolate **7** formed by dimerization of **6a** (Ar = Mes).[9]

$$2\,[\mathbf{6a}] \longrightarrow \underset{\mathbf{7}}{\left[\mathrm{Mes(LiO)C{=}C(OLi)Mes}\right]} \xrightarrow{\mathrm{Ac_2O}} \underset{\mathbf{8}}{\left[\mathrm{Mes(AcO)C{=}C(OAc)Mes}\right]} \qquad (4)$$

It can be seen from Table 2 that the production of isomers **8a** (*cis*) and **8b** (*trans*) is strongly dependent on the temperature. At relatively high temperature the yield of **8b** is slightly higher than those of the *cis* isomer **8a**, while at lower temperatures the *cis/trans* ratio increases, and reaction at −78 °C yields only the *cis*-isomer (Table 2). These isomers were characterized by analogy with the *cis, trans* isomers of 1,2-diacetoxy-1,2-bis(phenyl)ethene.[10] The *cisoid* configuration of the transition state in which

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Table 3 Carbonylation of 1-aryllithium **1** in THF quenching with 50 µL of saturated NH_4Cl[a]

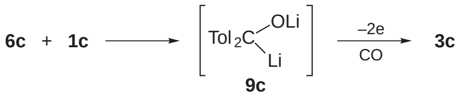
	Mesityllithium **1a**		Xylyllithium **1b**		*o*-Tolyllithium **1c**	
T/°C	**2a**	**3a**	**2b**	**3b**	**2c**	**3c**
−78	94	0	96	< 1	67	30
0	96	0	96	0	32	67
25	90	0	98	0	30	70

[a]The yields represent % conversion. Variable amounts of the respective hydrocarbon were also found.

both oxygens are coordinated to both lithium atoms requires less energy and thus formation of the *cis* isomer **7a** is favoured at low temperatures.

Recently, increasing interest has focused on reactions carried out in the solid state,[11] and we have reported earlier that performing the reaction of PhLi with CO in the absence of solvent could be an efficient method for the synthesis of α, α-diphenylacetophenone in yields > 90%.[12] The carbonylation of **1a** was therefore tested in the solid phase, at several temperatures, and results are shown in Table 2 (see footnote *c*). In this case, no improvement in the yields of **8** was found, and a major production of **4a** and by-products was observed at $T \geq 80$ °C.

In order to expand the scope of this work, the carbonylation of other hindered aryllithiums, namely (2,6-dimethyphenyl)lithium **1b** and (2-methyphenyl)lithium **1c** (Ar = Tol), was examined (Table 3). It can be observed that with **1c**, the least hindered of the three reagents, variable amounts of the diarylketone **3c** were also obtained. The highest formation of **3c** was observed at 25 °C, and can be rationalized by the oxidation of the dilithium dianion **9c** produced from the reaction of the corresponding transient intermediate **6c** with another molecule of **1c**, as observed previously in the case of Ar = Ph,[10] [eqn. (5)].



(5)

The corresponding 1,2-diacetoxy compounds **8** for *o*-tolyl and xylyl derivatives could be obtained as described for the mesityl compounds.

In conclusion, hindered diaryl diketones **2** can be obtained in good yields by the reaction of the corresponding aryllithium with CO in THF at temperatures < 25 °C at atmospheric pressure. For 1,2-diacetoxy-1,2-bis(aryl)ethenes, it is possible to tune the selectivity of the reaction by varying the temperature, in order to obtain the desired compound in major yield.

Experimental

The reactions of **1** with carbon monoxide were carried out according to the general procedure reported previously.[13] A stirred solution of **1** is exposed to CO at *ca*. 1013 mbar at the working temperature until absorption is complete. The reaction mixture was treated with a saturated aqueous solution of NH_4Cl (to obtain **2**) or with 50 µL of acetic anhydride (to prepare **8**). Quantitative analysis of the compounds was carried out by GC.

1,2-*Dimesityldiketone* **2a** was isolated by column chromatography, mp 118–120 °C (lit.[5] 122 °C).

Bis(2,6-*dimethylphenyl*)*glyoxal* **2b** was obtained from the reaction of CO with **1b** in THF at −78 °C and was crystallised from hexane, giving yellow plates, mp 151–153 °C (lit.[14] 153–154 °C).

Bis(2-*methylphenyl*)*glyoxal* **2c** was independently prepared by the method described by Shacklett and Smieth[15] and crystallised from ethanol, mp 90–92 °C (lit. 92–94 °C).

2,2′-*Dimethylbenzophenone* **3c** was prepared by reaction of 1.5 mmol of *o*-tolyllithium with 180 mg (1.5 mmol) of *o*-tolualdehyde in THF at 0 °C. The resulting alcohol was isolated by column chromatography. The alcohol was converted to the benzophenone by reaction with Jones solution; **3c** was isolated by chromatography and crystallised from ethanol, mp 64–66 °C (lit.[16] 64–67 °C).

1,2-*Diacetoxy*-1,2-*bis*(2,4,6-*trimethylphenyl*)*ethene* **8** was characterised as follows: FT IR(KBr)/cm^{-1} 3025, 3001, 2946, 2920, 2850, 2721, 1630, 1605, 1461, 1370, 876, 615, 600. ^{1}H δ_H(CDCl$_3$) 6.66 (s, 4H), 2.13 (s, 18H), 2.07 (s, 6H). MS: *m*/*z*, (rel. int.) 380 (21), 338 (50), 296 (100), 235 (10), 220 (12), 176 (21), 158 (8), 148 (55), 147 (73), 133 (31), 105 (15), 103 (13), 79 (10), 77 (20), 65 (9), 43 (50). mp **8a** 155 °C (lit.[17] 164–165 °C).

General Procedure for Reactions with Carbon Monoxide in the Solid State.—A septum-capped reaction flask containing **1a** as a powder was immersed in a silicone-oil bath at the working temperature and was exposed to CO at atmospheric pressure. When the absorption was complete the reaction mixture was worked-up by adding THF and subsequently Ac_2O. The product composition was determined by GC.

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