Copper-Catalyzed Oxidation of Deoxybenzoins to Benzils under Aerobic Conditions

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Received: 17.01.2013; Accepted after revision: 08.04.2013

Abstract: A novel copper-catalyzed approach to benzils from readily available deoxybenzoins under neutral conditions using air as the oxidant has been developed. The reaction tolerates a variety of useful substituents including chloro, bromo, iodo, keto, ester, and cyano groups.

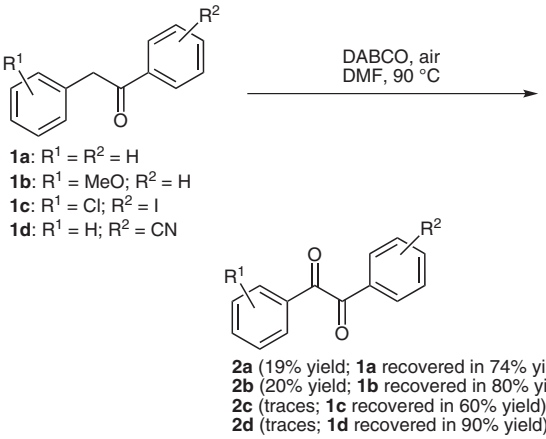
Key words: copper, catalysis, oxidation, deoxybenzoins, benzils

As part of our continuing interest in the synthesis of heterocycles,[1] we lately focused on the development of new approaches to heterocyclic derivatives starting from 1,2-diketones, a class of versatile synthetic intermediates.[2] Among the wide variety of methods described in literature for their preparation,[3] the recently reported conversion of readily available deoxybenzoins to benzils in the presence of DABCO and air[4] appeared to us particularly attractive and convenient as well as environmentally benign. Unfortunately, when the conversion of **1a** into **2a** was attempted under the described conditions, a reaction described to afford **2a** in 95% yield,[4] the desired product was isolated only in 19% yield and the starting material was recovered in 74% yield (Scheme 1). Similar disappointing results were also obtained with **1b**–**d** (Scheme 1).

We then turned our attention to the other methods that allow for the synthesis of benzils via oxidation of deoxybenzoins. However, they are all based on the use of stoichiometric amounts or an excess of oxidants such as selenium dioxide,[3a] thallium nitrate,[3b] pyridinium chlorochromate,[3g,h] potassium permanganate,[3i] and copper bromide adsorbed onto alumina.[3k] Furthermore, methods based on thallium and chromium salts suffer from the drawback of using toxic reagents. Therefore, it appeared to us of interest to explore an alternative, more environmentally friendly approach. Particularly, given the known ability of copper to catalyze oxidation reactions,[5,6] we settled to investigate the feasibility of a copper-catalyzed oxidation process.

The starting deoxybenzoins were prepared by Friedel–Crafts acylation reactions or palladium-catalyzed cross-coupling of aryl halides with acetophenones.[7]

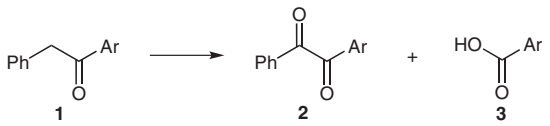
Our study was started by examining the oxidation of **1a** ($R^1 = R^2 = H$) with $Cu(OAc)_2$ and Ph_3P in *o*-xylene under a balloon of oxygen. An initial screening showed that **2a** could be isolated only in 15% yield at 80 °C, the main product being benzoic acid (50% yield) (Table 1, entry 1). The starting material was recovered in 35% yield. Pleasingly, increasing the reaction temperature to 100 °C led to the isolation of **2a** in 95% yield (entry 2). However, when these conditions were applied to **1b** ($R^1 = H$; $R^2 = 4$-MeO) the reaction afforded **2b** in 24% yield and *p*-anisic acid was isolated in 70% yield (entry 3). Thus, the reaction conditions were optimized for this substrate by exploring the influence of temperature, copper salts, ligands, and solvents on the reaction outcome. Increasing the reaction temperature to 130 °C led to the isolation of the desired oxidation product in 48% yield along with significant amounts of *p*-anisic acid (entry 4). The use of other copper salts and ligands gave similar results (entries 5–9). Similar results were also obtained in *m*-xylene (entry 10) whereas the starting material was recovered in almost quantitative yield using 1,4-dioxane, acetonitrile, and toluene (entries 11–13). An increase in the yield (57%) was observed in 1,2,4-trimethylbenzene and by substituting air for oxygen (entry 14). When the reaction was carried out under the latter conditions by decreasing the reaction temperature to 100 °C, **2b** could be isolated in a satisfactory 62% yield (entry 15). When the behavior of **1a** under these conditions was evaluated, it was found that **2a** was formed in high yield although lower than that observed in *o*-xylene under oxygen. Thus, it was decided to use both the oxidation protocols [$Cu(OAc)_2$, Ph_3P, *o*-xylene, O_2, 100 °C and $Cu(OAc)_2$, Ph_3P, 1,3,5-trimethylbenzene, air, 100 °C] when other substrates were investigated to explore the scope and generality of the reaction. Most probably, the



Scheme 1 Reaction of deoxybenzoins with DABCO under aerobic conditions

SYNTHESIS 2013, 45, 1701–1707
Advanced online publication: 15.05.2013
DOI: 10.1055/s-0033-1338451; Art ID: SS-2013-Z0055-OP

Table 1 Optimization Studies[a]



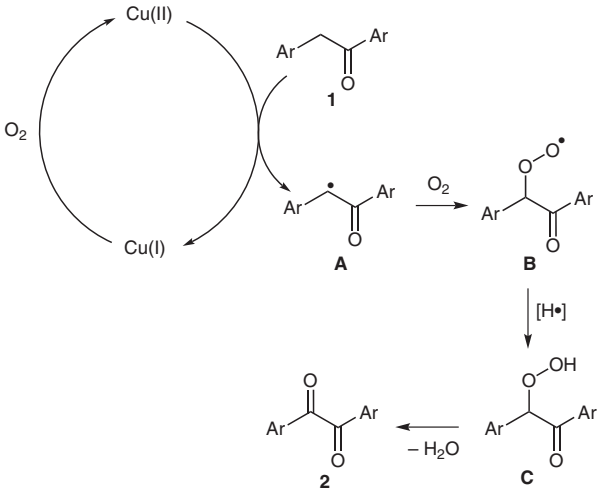
Entry	Ar		[Cu]	Ligand	Atmosphere	Solvent	Temp (°C)	Time (h)	**2** Yield (%)[b]		**3** Yield (%)[b]	
1	Ph	**1a**	$Cu(OAc)_2$ (15%)	Ph_3P (30%)	O_2	*o*-xylene	80	24	15	**2a**	50[c]	**3a**
2	Ph	**1a**	$Cu(OAc)_2$ (15%)	Ph_3P (30%)	O_2	*o*-xylene	100	4	95	**2a**	–	**3a**
3	4-$MeOC_6H_4$	**1b**	$Cu(OAc)_2$ (15%)	Ph_3P (30%)	O_2	*o*-xylene	100	4	24	**2b**	70	**3b**
4	4-$MeOC_6H_4$	**1b**	$Cu(OAc)_2$ (15%)	Ph_3P (30%)	O_2	*o*-xylene	130	0.75	48	**2b**	19	**3b**
5	4-$MeOC_6H_4$	**1b**	$Cu(OTf)_2$ (20%)	–	O_2	*o*-xylene	130	3	44	**2b**	31	**3b**
6	4-$MeOC_6H_4$	**1b**	CuI (15%)	Ph_3P (30%)	O_2	*o*-xylene	130	24	46	**2b**	6	**3b**
7	4-$MeOC_6H_4$	**1b**	CuI (20%)	proline (40%)	O_2	*o*-xylene	130	0.75	24	**2b**	30[d]	**3b**
8	4-$MeOC_6H_4$	**1b**	$CuCl_2$ (20%)	–	O_2	*o*-xylene	130	5.5	50	**2b**	8	**3b**
9	4-$MeOC_6H_4$	**1b**	$Cu(OAc)_2$ (15%)	CHDA[e] (30%)	O_2	*o*-xylene	130	2.25	48	**2b**	–	**3b**
10	4-$MeOC_6H_4$	**1b**	$Cu(OAc)_2$ (10%)	Ph_3P (30%)	O_2	*m*-xylene	130	0.75	48	**2b**	19	**3b**
11	4-$MeOC_6H_4$	**1b**	$Cu(OAc)_2$ (15%)	Ph_3P (30%)	O_2	1,4-dioxane	130	24	–	**2b**	–[f]	**3b**
12	4-$MeOC_6H_4$	**1b**	$Cu(OAc)_2$ (15%)	Ph_3P (30%)	O_2	MeCN	130	4	–	**2b**	–[f]	**3b**
13	4-$MeOC_6H_4$	**1b**	$Cu(OAc)_2$ (15%)	Ph_3P (30%)	O_2	toluene	130	0.75	–	**2b**	–[f]	**3b**
14	4-$MeOC_6H_4$	**1b**	$Cu(OAc)_2$ (15%)	Ph_3P (30%)	air	1,2,4-TMB[g]	130	0.75	57	**2b**	–	**3b**
15	4-$MeOC_6H_4$	**1b**	$Cu(OAc)_2$ (15%)	Ph_3P (30%)	air	1,2,4-TMB[g]	100	0.75	62	**2b**	–	**3b**
16	Ph	**1a**	$Cu(OAc)_2$ (15%)	Ph_3P (30%)	air	1,2,4-TMB[g]	100	0.75	83	**2a**	–	**3a**

[a] Reactions were carried out on a 0.4 mmol scale in 1.6 mL of solvent.
[b] Yields are given for isolated products.
[c] Starting material **1a** was recovered in 34% yield.
[d] Starting material **1a** was recovered in 9% yield.
[e] CHDA: cyclohexane-1,2-diamine.
[f] Starting material **1a** was recovered in 99% yield.
[g] 1,2,4-TMB: 1,2,4-trimethylbenzene.

best method is to evaluate the effectiveness of these protocols each time.

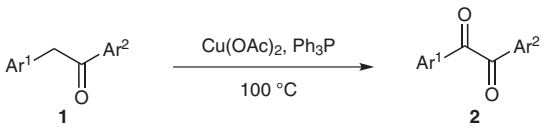
As shown by the results summarized in Table 2, the reaction affords benzils from deoxybenzoins in moderate to excellent yields and tolerates a variety of useful substituents including chloro, bromo, iodo, keto, ester, and cyano groups. Substituents in the ortho position of the benzylic fragment are also tolerated (Table 2, entry 19).

Although the detailed mechanism of this copper-catalyzed oxidation is unclear at the moment, it is likely that the reaction proceeds according to the following elementary steps (Scheme 2): initial formation of the benzylic radical **A** from the starting deoxybenzoin **1** combined with the reduction of the copper(II) catalyst to copper(I); subsequent reaction of **1** with oxygen to afford the peroxoradical **B**; conversion of the latter into the hydroperoxide **C** via capture of a hydrogen from the reaction medium; and elimination of water[8] to give the benzil derivative **2**. Copper(I) is reoxidized to the active copper(II) catalyst by oxygen.



Scheme 2 Proposed reaction mechanism for the copper-catalyzed oxidation of deoxybenzoins to benzyls

Table 2 Copper-Catalyzed Oxidation of Deoxybenzoins **1** to Benzyls **2**[a]



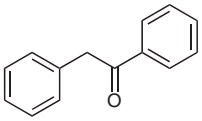
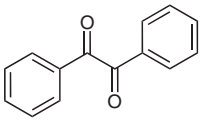
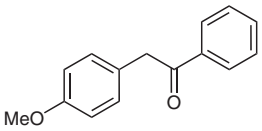
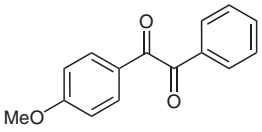
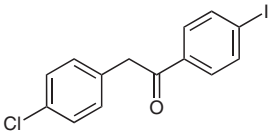
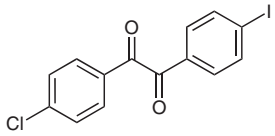
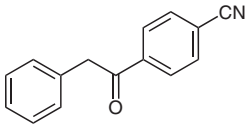
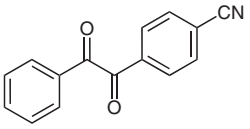
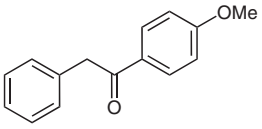
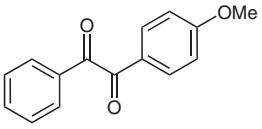
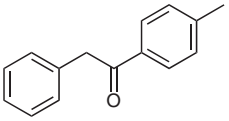
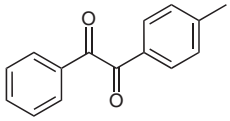
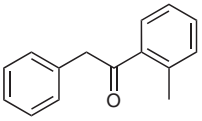
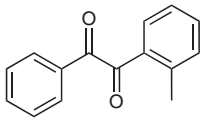
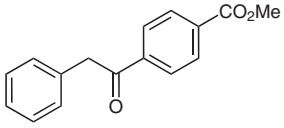
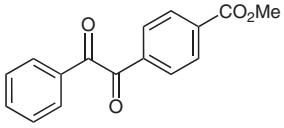
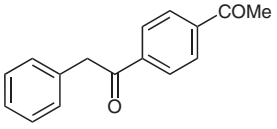
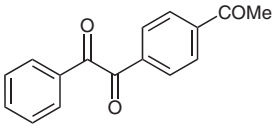
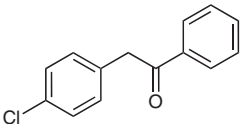
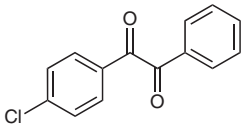
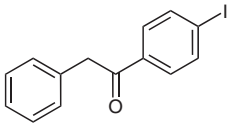
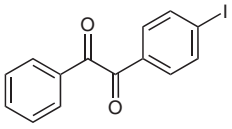
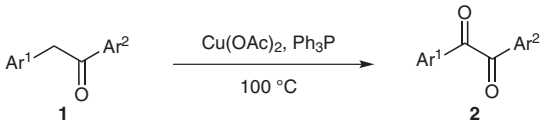
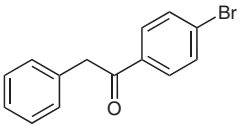
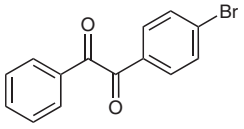
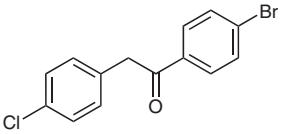
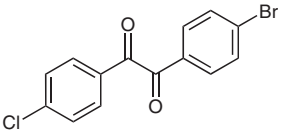
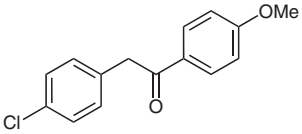
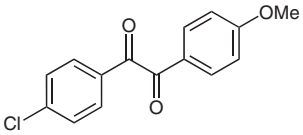
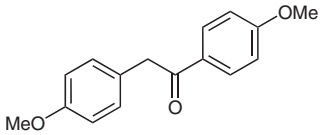
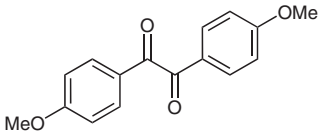
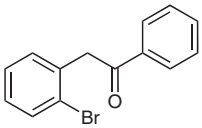
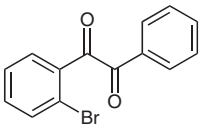
Entry	Deoxybenzoin **1**		Time (h)[b]	Benzil **2**, yield (%)[c,d]		
1		**1a**	4		**2a**	95[e]
2			0.75			83
3			0.75			85[f]
4		**1b**	0.75		**2b**	55
5		**1c**	2.5		**2c**	70
6		**1d**	1		**2d**	66
7		**1e**	0.75		**2b**	62
8		**1f**	7		**2e**	70
9		**1g**	0.5		**2f**	45
10		**1h**	1		**2g**	72
11		**1i**	5		**2h**	53
12		**1j**	1.5		**2i**	53
13			4.5			43[e]
14		**1k**	7		**2j**	60

Table 2 Copper-Catalyzed Oxidation of Deoxybenzoins **1** to Benzyls **2**[a] (continued)



1 2

Entry	Deoxybenzoin **1**		Time (h)[b]	Benzil **2**, yield (%)[c,d]		
15		**1l**	2.5		**2k**	75
16		**1m**	9		**2l**	60
17		**1n**	0.5		**2m**	56
18		**1o**	0.75		**2n**	51
19		**1p**	7		**2o**	62

[a] Unless otherwise stated, reactions were carried out on a 0.4 mmol scale in 1.6 mL of 1,2,4-trimethylbenzene at 100 °C under air using 15 mol% of $Cu(OAc)_2$ and 30 mol% of Ph_3P.
[b] Reaction times are for a 100% conversion.
[c] Yields are given for isolated products.
[d] Variable amounts of carboxylic acids were formed as well as other by-products that have not been investigated.
[e] Reactions carried out in *o*-xylene under a balloon of O_2.
[f] On a 10 mmol scale.

In summary, a simple and convenient copper-catalyzed oxidation of deoxybenzoins to benzils under neutral conditions using air as the oxidant has been developed. The reaction allows for the preparation of benzils in moderate to excellent yields and tolerates a variety of useful substituents including chloro, bromo, iodo, keto, ester, and cyano groups.

Melting points were determined with a Büchi B-545 apparatus and are uncorrected. Deoxybenzoins were prepared through Friedel–Crafts acylation reactions or palladium-catalyzed cross-coupling of aryl halides with acetophenones.[6] All the other reagents and solvents are commercially available and were used as purchased, without further purification. ^1H NMR (400.13 MHz) and ^{13}C NMR (100.6 MHz) spectra were recorded with a Bruker Avance 400 spectrometer. IR spectra were recorded on a JASCO FT/IR-430 spectrophotometer. Mass spectra were determined with a QP2010 gas chromatograph mass spectrometer (EI ion source).

Deoxybenzoins via Friedel–Crafts Acylation; 2-(4-Chlorophenyl)-1-phenylethanone (1j); Typical Procedure

A flask equipped with a magnetic stirring bar was charged with 2-(4-chlorophenyl)acetyl chloride (283.5 mg, 219 μL, 1.5 mmol), CH_2Cl_2 (2 mL), and benzene (234 mg, 267 μL, 3.0 mmol). The solution was stirred under N_2 at 0 °C before adding $AlCl_3$ (219 mg, 1.65 mmol). The reaction mixture was stirred at r.t. for 0.5 h. After this time, it was poured onto ice, extracted with CH_2Cl_2 (150 mL), and washed with brine (50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by gradient elution flash chromatography on silica gel (*n*-hexane–EtOAc mixtures) to give **1j** as a white solid; yield: 256 mg (88%); mp 132–134 °C (Lit.[9] mp 132–134 °C).

Deoxybenzoins via Palladium-Catalyzed Cross-Coupling of Aryl Halides with Acetophenones; 1-(4-Cyanophenyl)-2-phenylethan-1-one (1d); Typical Procedure

A Carousel reaction tube (Radley Discovery) was charged with $Pd(OAc)_2$ (7 mg, 0.03 mmol), XPhos (29 mg, 0.06 mmol), and toluene (2 mL). The solution was stirred under N_2 at r.t. for 10 min before adding *t*-BuONa (720 mg, 7.5 mmol), 4-acetylbenzonitrile (522 mg, 3.6 mmol), and bromobenzene (471 mg, 3 mmol) dissolved in toluene (2 mL). The reaction mixture was warmed at 90 °C and stirred for 5 h. After cooling, the mixture was diluted with

Et_2O (150 mL) and washed with H_2O (50 mL) and brine (150 mL). The organic layer was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by gradient elution flash chromatography (*n*-hexane–EtOAc mixtures) to afford **1d** as a white solid; yield: 471 mg (71%); mp 110–112 °C.

1,2-Diarylethanediones; Benzil (2a); Typical Procedure

A Carousel reaction tube (Radley Discovery) was charged with $Cu(OAc)_2$ (12 mg, 0.06 mmol), Ph_3P (31 mg, 0.12 mmol), and 1,2,4-trimethylbenzene (1 mL). The solution was stirred under air at r.t. for 10 min before adding 1,2-diphenylethanone (78.5 mg, 0.4 mmol) dissolved in 1,2,4-trimethylbenzene (0.6 mL). The reaction mixture was warmed at 100 °C and stirred for 1 h. After cooling, the mixture was diluted with Et_2O (150 mL) and washed with a sat. aq NH_4Cl (50 mL) and brine (50 mL). The organic layer was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by gradient elution flash chromatography on silica gel (*n*-hexane–EtOAc mixtures) to give **2a** as a pale yellow solid; yield: 71.4 mg (83%); mp 91–93 °C; R_f = 0.18 (*n*-hexane–EtOAc, 95:5).

IR (KBr): 2921, 2856, 1658, 1594, 1450, 1384, 1211, 1101, 875 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 7.2 Hz, 4 H), 7.67 (t, *J* = 7.6 Hz, 2 H), 7.53 (t, *J* = 7.6 Hz, 4 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 194.6, 134.9, 133.0, 129.9, 129.1.

MS: *m*/*z* (%) = 210 (M^+, 0.2), 64 (10.1), 105 (11.6), 51 (14.8), 92 (15.6), 77 (43.1), 135 (100).

Anal. Calcd for $C_{14}H_{10}O_2$: C, 79.98; H, 4.79. Found: C, 79.88; H, 4.78.

1-(4-Methoxyphenyl)-2-phenylethane-1,2-dione (2b)

Yield: 52.8 mg (55%); yellow oil; R_f = 0.19 (*n*-hexane–EtOAc, 90:10).

IR (neat): 2933, 2842, 1779, 1675, 1596, 1265, 1216, 1166, 1024, 875 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.96 (m, 4 H), 7.66 (t, *J* = 7.6 Hz, 1 H), 7.52 (t, *J* = 7.6 Hz, 2 H), 7.00 (d, *J* = 8.8 Hz, 2 H), 3.90 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 194.9, 193.2, 165.0, 134.7, 133.2, 132.4, 129.9, 129.0, 126.1, 114.4, 55.6.

MS: *m*/*z* (%) = 240 (M^+, 0.7), 64 (10.2), 105 (12.0), 92 (15.0), 51 (15.7), 77 (44.4), 135 (100).

Anal. Calcd for $C_{15}H_{12}O_3$: C, 74.99; H, 5.03. Found: C, 74.90; H, 5.04.

1-(4-Chlorophenyl)-2-(4-iodophenyl)ethane-1,2-dione (2c)

Yield: 103.8 mg (70%); yellow solid; mp 208–210 °C; R_f = 0.18 (*n*-hexane–EtOAc, 97:3).

IR (KBr): 3087, 2954, 2913, 1662, 1579, 1394, 1209, 1172, 1091, 881 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.94–7.91 (m, 4 H), 7.19 (d, *J* = 8.4 Hz, 2 H), 7.52 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 193.0, 192.3, 141.8, 138.5, 132.1, 131.3, 131.1, 131.0, 129.5, 103.9.

MS: *m*/*z* (%) = 370 (M^+, 6.0), 203 (18.3), 51 (18.7), 141 (35.3), 111 (58.1), 50 (71.5), 231 (85.1), 76 (85.6), 139 (100).

Anal. Calcd for $C_{14}H_8ClIO_2$: C, 45.38; H, 2.18. Found: C, 45.42; H, 2.17.

4-(2-Oxo-2-phenylacetyl)benzonitrile (2d)

Yield: 62.1 mg (66%); pale yellow solid; mp 110–112 °C; R_f = 0.20 (*n*-hexane–EtOAc, 85:15).

IR (KBr): 3112, 3073, 3046, 2225, 1683, 1660, 1594, 1172, 881 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 8.8 Hz, 2 H), 8.00 (dd, *J* = 8.4, 0.8 Hz, 2 H), 7.84 (d, *J* = 8.4 Hz, 2 H), 7.73 (t, *J* = 7.6 Hz, 1 H), 7.57 (t, *J* = 8.0 Hz, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 193.0, 192.4, 135.9, 135.4, 132.8, 132.5, 130.2, 130.0, 129.2, 117.9, 117.6.

MS: *m*/*z* (%) = 163 (6.3), 235 (M^+, 7.2), 102 (26.6), 51 (42.9), 77 (62.2), 105 (100).

Anal. Calcd for $C_{15}H_9NO_2$: C, 76.59; H, 3.86; N, 5.95. Found: C, 76.65; H, 3.87; N, 5.96.

1-Phenyl-2-*p*-tolylethane-1,2-dione (2e)

Yield: 62.8 mg (70%); yellow oil; R_f = 0.20 (*n*-hexane–EtOAc, 97:3).

IR (neat): 2923, 2854, 1674, 1604, 1450, 1384, 1214, 1174, 875 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 7.2 Hz, 2 H), 7.90 (d, *J* = 8.4 Hz, 2 H), 7.68 (t, *J* = 7.2 Hz, 1 H), 7.53 (t, *J* = 8.0 Hz, 2 H), 7.33 (d, *J* = 8.0 Hz, 2 H), 2.46 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 194.8, 194.3, 146.2, 134.8, 133.1, 130.6, 130.0, 129.9, 129.7, 129.0, 21.9.

MS: *m*/*z* (%) = 224 (M^+, 1.5), 51 (22.7), 65 (24.3), 105 (25.1), 77 (34.8), 91 (37.0), 119 (100).

Anal. Calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39. Found: C, 80.42; H, 5.40.

1-(2-Methoxyphenyl)-2-phenylethane-1,2-dione (2f)

Yield: 40.4 mg (45%); pale yellow solid; mp 53–55 °C; R_f = 0.20 (*n*-hexane–EtOAc, 97:3).

IR (KBr): 3064, 2969, 2929, 1994, 1820, 1679, 1596, 1452, 1205, 1166, 881 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 7.6 Hz, 2 H), 7.69–7.51 (m, 3 H), 7.38–7.29 (m, 4 H), 2.73 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 196.8, 194.8, 141.3, 134.7, 133.7, 133.2, 133.0, 132.6, 129.9, 129.0, 128.5, 126.0, 21.9.

MS: *m*/*z* (%) = 224 (M^+, 1.4), 51 (21.5), 65 (23.3), 105 (25.2), 77 (35.2), 91 (37.3), 119 (100).

Anal. Calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39. Found: C, 80.39; H, 5.38.

Methyl 4-(2-Oxo-2-phenylacetyl)benzoate (2g)

Yield: 77.2 mg (72%); pale yellow solid; mp 65–67 °C; R_f = 0.19 (*n*-hexane–EtOAc, 85:15).

IR (KBr): 2954, 2927, 2848, 1720, 1671, 1436, 1286, 1209, 1105, 885 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 8.4 Hz, 2 H), 8.06 (d, *J* = 8.0 Hz, 2 H), 8.00 (d, *J* = 7.6 Hz, 2 H), 7.70 (t, *J* = 7.6 Hz, 1 H), 7.54 (t, *J* = 7.6 Hz, 2 H), 3.97 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 193.7, 193.6, 165.8, 136.1, 135.3, 135.1, 132.8, 130.1, 130.0, 129.8, 126.3, 52.6.

MS: *m*/*z* (%) = 135 (9.1), 51 (22.1), 163 (24.7), 77 (51.3), 105 (100).

Anal. Calcd for $C_{16}H_{12}O_4$: C, 71.64; H, 4.51. Found: C, 71.59; H, 4.50.

1-(4-Acetylphenyl)-2-phenylethane-1,2-dione (2h)

Yield: 53.4 mg (53%); pale yellow solid; mp 78–80 °C; R_f = 0.20 (*n*-hexane–EtOAc, 85:15).

IR (KBr): 2923, 2852, 1677, 1436, 1213, 885 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.09–8.01 (m, 4 H), 7.99 (d, *J* = 1.2 Hz, 2 H), 7.69 (t, *J* = 7.6 Hz, 1 H), 7.54 (t, *J* = 7.6 Hz, 2 H), 2.65 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 197.1, 193.7, 193.6, 141.3, 136.0, 135.1, 132.7, 130.1, 129.9, 129.1, 128.7, 26.9.

MS: *m*/*z* (%) = 252 (M^+, 2.51), 91 (10.7), 147 (24.5), 77 (44.8), 105 (100).

Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.22; H, 4.78.

1-(4-Chlorophenyl)-2-phenylethane-1,2-dione (2i)
Yield: 51.9 mg (53%); pale yellow solid; mp 71–73 °C; R_f = 0.20 (*n*-hexane–EtOAc, 96:4).

IR (KBr): 2931, 1666, 1585, 1450, 1402, 1209, 1174, 1095, 875 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.93 (m, 4 H), 7.69 (t, *J* = 7.6 Hz, 1 H), 7.56–7.49 (m, 4 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 193.9, 193.0, 141.6, 135.1, 132.8, 131.4, 131.2, 129.9, 129.4, 129.1.

MS: *m*/*z* (%) = 245 (M^+, 0.6), 141 (10.5), 139 (29.8), 51 (35.8), 77 (56.8), 105 (100).

Anal. Calcd for $C_{14}H_9ClO_2$: C, 68.72; H, 3.71. Found: C, 68.69; H, 3.72.

1-(4-Iodophenyl)-2-phenylethane-1,2-dione (2j)
Yield: 80.7 mg (60%); yellow solid; mp 89–90 °C; R_f = 0.20 (*n*-hexane–EtOAc, 97:3).

IR (KBr): 3060, 2927, 2861, 1670, 1579, 1394, 1211, 1174, 879 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 7.6 Hz, 2 H), 7.91 (d, *J* = 8.4 Hz, 2 H), 7.71–7.68 (m, 3 H), 7.54 (t, *J* = 7.6 Hz, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 193.9, 193.7, 138.4, 135.1, 132.8, 132.3, 131.0, 130.0, 129.1, 103.7.

MS: *m*/*z* (%) = 336 (M^+, 0.5), 203 (6.5), 231 (19.1), 51 (32.7), 50 (33.7), 77 (56.7), 105 (100).

Anal. Calcd for $C_{14}H_9IO_2$: C, 50.03; H, 2.70. Found: C, 50.10; H, 2.71.

1-(4-Bromophenyl)-2-phenylethane-1,2-dione (2k)
Yield: 86.7 mg (75%); yellow solid; mp 81–83 °C; R_f = 0.18 (*n*-hexane–EtOAc, 97:3).

IR (KBr): 3087, 2967, 2927, 1668, 1579, 1450, 1398, 1209, 1174, 1070, 873 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 7.2 Hz, 2 H), 7.86 (d, *J* = 8.4 Hz, 2 H), 7.71–7.67 (m, 3 H), 7.54 (t, *J* = 7.6 Hz, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 193.9, 193.3, 135.1, 132.8, 132.5, 131.7, 131.3, 130.5, 130.0, 129.1.

MS: *m*/*z* (%) = 289 (M^+, 2.0), 183 (9.0), 155 (11.9), 51 (32.8), 77 (55.5), 105 (100).

Anal. Calcd for $C_{14}H_9BrO_2$: C, 58.16; H, 3.14. Found: C, 58.20; H, 3.13.

1-(4-Bromophenyl)-2-(4-chlorophenyl)ethane-1,2-dione (2l)
Yield: 77.7 mg (60%); yellow solid; mp 203–205 °C; R_f = 0.21 (*n*-hexane–EtOAc, 97:3).

IR (KBr): 2923, 1664, 1587, 1209, 1172, 835 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.4 Hz, 2 H), 7.86 (d, *J* = 8.4 Hz, 2 H), 7.69 (d, *J* = 8.4 Hz, 2 H), 7.52 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 192.6, 192.3, 141.8, 132.5, 131.5, 131.3, 131.1, 130.7, 129.5.

MS: *m*/*z* (%) = 237 (11.4), 51 (18.2), 155 (30.1), 141 (41.7), 185 (46.5), 111 (50.2), 50 (58.9), 75 (92.5), 139 (100).

Anal. Calcd for $C_{14}H_8BrClO_2$: C, 51.97; H, 2.49. Found: C, 52.02; H, 2.50.

1-(4-Chlorophenyl)-2-(4-methoxyphenyl)ethane-1,2-dione (2m)
Yield: 61.5 mg (56%); pale yellow solid; mp 127–128 °C; R_f = 0.19 (*n*-hexane–EtOAc, 90:10).

IR (KBr): 3093, 3002, 2937, 2838, 1670, 1654, 1598, 1267, 1214, 1168, 1027, 881 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96–7.92 (m, 4 H), 7.49 (d, *J* = 8.4 Hz, 2 H), 6.99 (d, *J* = 8.8 Hz, 2 H), 3.90 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 193.3, 192.4, 165.1, 141.4, 132.4, 131.6, 131.2, 129.4, 125.9, 114.4, 55.7.

MS: *m*/*z* (%) = 274 (M^+, 1.5), 139 (18.2), 77 (20.2), 141 (52.2), 135 (100).

Anal. Calcd for $C_{15}H_{11}ClO_3$: C, 65.58; H, 4.04. Found: C, 65.66; H, 4.03.

1,2-Bis(4-methoxyphenyl)ethane-1,2-dione (2n)
Yield: 55.1 mg (51%); yellow solid; mp 131–132 °C; R_f = 0.17 (*n*-hexane–EtOAc, 85:15).

IR (KBr): 3025, 2925, 2850, 1654, 1598, 1571, 1263, 1160, 1016, 879 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.8 Hz, 4 H), 7.00 (d, *J* = 8.8 Hz, 4 H), 3.91 (s, 6 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 193.5, 164.9, 132.4, 126.3, 114.3, 55.6.

MS: *m*/*z* (%) = 270 (M^+, 2.2), 77 (17.9), 207 (49.4), 44 (85.1), 135 (100).

Anal. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.18; H, 5.23.

1-(2-Bromophenyl)-2-phenylethane-1,2-dione (2o)
Yield: 71.7 mg (62%); yellow oil; R_f = 0.18 (*n*-hexane–EtOAc, 96:4).

IR (neat): 2923, 1677, 1585, 1450, 1253, 1027 860 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 0.8 Hz, 2 H), 7.85–7.83 (m, 1 H), 7.71–7.62 (m, 2 H), 7.58–7.44 (m, 4 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 194.2, 191.5, 136.0, 134.5, 134.4, 133.8, 132.7, 132.6, 130.4, 128.9, 127.8, 121.8.

MS: *m*/*z* (%) = 289 (M^+, 2.0), 183 (11.2), 155 (12.9), 51 (32.9), 77 (54.5), 105 (100).

Anal. Calcd for $C_{14}H_9BrO_2$: C, 58.16; H, 3.14. Found: C, 58.21; H, 3.13.

Acknowledgment

We gratefully acknowledge MURST and the University 'La Sapienza', Rome, for financial support.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

References

(1) (a) Battistuzzi, G.; Cacchi, S.; Fabrizi, G. *Eur. J. Org. Chem.* **2002**, 2671. (b) Battistuzzi, G.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Parisi, L. M. *Org. Lett.* **2002**, *4*, 1355. (c) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873. (d) Cacchi, S.; Fabrizi, G.; Goggiamani, A. *Curr. Org. Chem.* **2006**, *10*, 1423. (e) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2011**, *111*, PR215. (f) Cacchi, S.; Fabrizi, G.; Filisti, E. *Org. Lett.* **2008**, *10*, 2629. (g) Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Sferrazza, A. *Synlett* **2009**, 1277. (h) Bernini, R.; Cacchi, S.; Fabrizi, G.; Filisti, E.; Sferrazza,

A. *Synlett* **2009**, 1245. (i) Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Perboni, A.; Sferrazza, A.; Stabile, P. *Org. Lett.* **2010**, *12*, 3279. (j) Bagnoli, L.; Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Scarponi, C.; Tiecco, M. *J. Org. Chem.* **2010**, *75*, 2134. (k) Cacchi, S.; Fabrizi, G.; Goggiamani, A. *Org. Biomol. Chem.* **2011**, *9*, 641. (l) Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Sferrazza, A. *Org. Biomol. Chem.* **2011**, *9*, 1727. (m) Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Iazzetti, A.; Madec, D.; Poli, G.; Prestatt, G. *Org. Biomol. Chem.* **2011**, *9*, 8233.

(2) (a) Koike, T.; Murata, K.; Ikariya, T. *Org. Lett.* **2000**, *2*, 3833. (b) Deng, X.; Mani, N. S. *Org. Lett.* **2006**, *8*, 269. (c) Samai, S.; Nandi, G. C.; Singh, P.; Singh, M. S. *Tetrahedron* **2009**, *65*, 10155. (d) Das, P. J.; Sarkar, S. *Chem. Biol. Interface* **2011**, *1*, 95. (e) Kumar, D.; Kommi, D. N.; Bollineni, N.; Patel, A. R.; Asit, K.; Chakraborti, A. K. *Green Chem.* **2012**, *14*, 2038. (f) Ramesh, K.; Murthy, S. N.; Karnakar, K.; Nageswar, Y. V. D.; Vijayalakhshmi, K.; Prabavathi Devi, B. L.A.; Prasad, R. B. N. *Tetrahedron Lett.* **2012**, *53*, 1126.

(3) (a) Corey, E. J.; Schaefer, J. P. *J. Am. Chem. Soc.* **1960**, *82*, 917. (b) McKillop, A.; Swann, B. P.; Ford, M. E.; Taylor, E. C. *J. Am. Chem. Soc.* **1973**, *95*, 3641. (c) Bauer, D. P.; Macomber, R. S. *J. Org. Chem.* **1975**, *40*, 1990. (d) Wasserman, H. H.; Ives, J. L. *J. Am. Chem. Soc.* **1976**, *98*, 7868. (e) De Kimpe, N.; Verhé, R.; De Buyck, I.; Schamp, N. *J. Org. Chem.* **1978**, *43*, 2933. (f) Wasserman, H. H.; Ives, J. L. *J. Org. Chem.* **1985**, *50*, 3573. (g) Rathore, R.; Saxena, N.; Chandrasekaran, S. *Synth. Commun.* **1986**, *16*, 12. (h) Bonadies, F.; Bonini, C. *Synth. Commun.* **1986**, *18*, 1573. (i) Jiang, Q.; Joshi, B. S.; Pelletier, S. W. *Tetrahedron Lett.* **1991**, *32*, 5283. (j) Lee, J. C.; Park, H.; Park, J. Y. *Tetrahedron Lett.* **2002**, *43*, 5661. (k) Park, B. S.; Lee, H. M.; Cho, S. *Bull. Korean Chem. Soc.* **2007**, *28*, 871.

(4) Qi, C.; Jiang, H.; Huang, L.; Chen, Z.; Chen, H. *Synthesis* **2011**, 387.

(5) For selected references, see: (a) Gamez, P.; Aubel, P. G.; Driessen, W. L.; Reedijk, J. *Chem. Soc. Rev.* **2001**, *30*, 376. (b) Geisslmeir, D.; Jary, W. G.; Falk, H. *Monatsh. Chem.* **2005**, *136*, 1591. (c) Punniyamurthy, T.; Rout, L. *Coord. Chem. Rev.* **2008**, *252*, 134. (d) Conde, A.; Diaz-Requejo, M. M.; Perez, P. J. *Chem. Commun.* **2011**, *47*, 8154. (e) Liu, Q.; Wu, P.; Yang, Y.; Zeng, Z.; Liu, J.; Yi, H.; Lei, A. *Angew. Chem. Int. Ed.* **2012**, *51*, 4666. (f) Ahmad, J. U.; Raeisaenen, M. T.; Leskelae, M.; Repo, T. *Appl. Catal., A* **2012**, *411-412*, 180.

(6) For selected references on the oxidation of benzoins to benzils, see: (a) Macaione, D. P.; Wentworth, S. E. *Synthesis* **1974**, 716. (b) Depreux, P.; Bethegnies, G.; Marcincal-Lefebvre, A. *J. Chem. Educ.* **1988**, *65*, 553. (c) Varma, R. S.; Kumar, D.; Dahiya, R. *J. Chem. Res., Synop.* **1998**, 324. (d) Tymonko, S. A.; Nattier, B. A.; Mohan, R. S. *Tetrahedron Lett.* **1999**, *40*, 7657. (e) Sachdev, D.; Naik, M. A.; Dubey, A.; Mishra, B. G. *Catal. Commun.* **2010**, *11*, 684.

(7) Fox, J. M.; Huang, X.; Chieffi, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 1360.

(8) Bordwell, F. G.; Knipe, A. C. *J. Am. Chem. Soc.* **1971**, *93*, 3416.

(9) Prakash, O.; Kumar, R.; Sharma, D.; Pannu, K.; Kamal, R. *Synlett* **2007**, 2189.