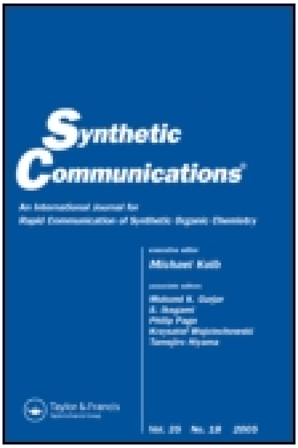

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Synthesis of 2-Hydroxybenzophenones by Oxidation of 3-Aryl-3H-benzofuran-2-ones

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Synthesis of 2-Hydroxybenzophenones by Oxidation of 3-Aryl-3H-benzofuran-2-ones

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ABSTRACT

Oxidation of 5,7-di-*tert*-butyl-3-aryl-3H-benzofuran-2-ones **1** with alkaline potassium hexacyanoferrate (III) affords 3,5-di-*tert*-butyl-2-hydroxybenzophenones **2** in good to moderate yields.

Key Words: 2-Hydroxybenzophenones; 3-Aryl-3H-benzofuran-2-ones; Oxidation; Potassium hexacyanoferrate (III).

RESULTS AND DISCUSSION

2-Hydroxybenzophenones have found use as intermediates in the synthesis of pharmaceuticals, dyes, agrochemicals, or as ultraviolet (UV) light absorbers for the protection of human skin or organic materials such

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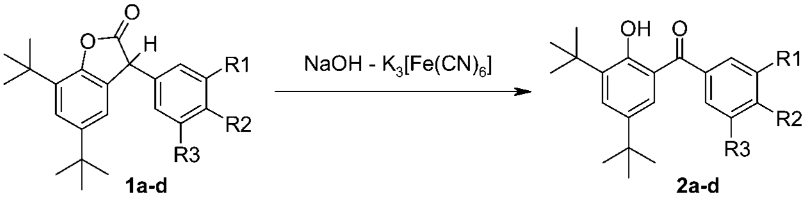
as polymers and coatings against UV-damage.[1] Different syntheses of 2-hydroxybenzophenones are known,[1] for example: Fries[2] or Photo-Fries rearrangement of *O*-aroylphenols, 2-aroylation[3] of *o*-lithiated phenoxides, Pd-catalyzed coupling[4] of 2-hydroxyaryl aldehydes with hypervalent iodonium salts or with aryl iodides,[5] or condensation[6] of trichloromethyl benzene with phenols in alkaline aqueous solution. Unfortunately, these methods are not ideal with respect to the scope of applicability, yield or readily available starting materials. New synthetic methods for 2-hydroxybenzophenones are therefore still of interest.

We would like to report in this paper that 3,5-di-*tert*-butyl substituted 2-hydroxybenzophenones **2** can be obtained easily in moderate to good yields by treatment of 3-aryl-5,7-di-*tert*-butyl-3H-benzofuran-2-ones **1** with an alkaline aqueous solution of potassium hexacyanoferrate (III) (Sch. 1 and Table 1). The starting 3-aryl-3H-benzofuran-2-ones are easily accessible[7] compounds. Particularly straightforward is the synthesis of 5,7-di-*tert*-butyl substituted benzofuranones **1** for which several methods starting from the cheap 2,4-di-*tert*-butyl-phenol (DBP) are available. Thus, **1a** was made by the condensation[7] of DBP with glyoxylic acid and *o*-xylene. Thermal condensation of DBP with the corresponding mandelic acids was employed[8] for the synthesis of **1b–d**.

To our knowledge, preparative oxidative transformation of 3-aryl-3H-benzofuran-2-ones into 2-hydroxybenzophenones was never reported. Only traces of 2-hydroxybenzophenone, among other products, were observed[9] when 3-phenyl-3H-benzofuran-2-one was UV-irradiated in the presence of singlet oxygen or when the DMF solution of its sodium enolate was exposed[10] to oxygen. The first step of the transformation of **1** into **2** is the alkaline hydrolysis of the lactone ring of **1** leading to the corresponding water soluble substituted diphenylacetic acid salt. This is manifested by the formation of a homogeneous solution from the water insoluble **1** upon heating with the aqueous NaOH. The site where the hexacyanoferrate (III) oxidation starts is not clear. It may be the phenolic or phenolate ion group; indeed oxidations of phenols with alkaline hexacyanoferrate (III) affording quinone



Scheme 1.

Table 1. Synthesis of 2-hydroxybenzophenones **2** by oxidation of 3-arylbenzofuranones **1**.

Entry	R1	R2	R3	Yield (%)
2a	Me	Me	H	87
2b	Me	OMe	Me	43
2c	H	OEt	H	66
2d	H	H	H	52

methides are well known.[11] On the other hand, oxidative decarboxylation of carboxylic acids under the same conditions is also known.[12] The scope of our new reaction in its current form seems to be limited to oxidation of 5,7-di-*tert*-butyl substituted benzofuranones **1**. Thus, 2-hydroxybenzophenones could not be isolated from the oxidation of 3-(4-ethoxy-phenyl)-5-methoxy-3H-benzofuran-2-one,[8] 5,7-*bis*-benzylsulfanyl-methyl-3-phenyl-3H-benzofuran-2-one[13] or 4,6,7-trimethyl-3-phenyl-3H-benzofuran-2-one.[14]

EXPERIMENTAL

The spectra were measured with the following equipments: ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75.37 MHz) on a Bruker 300 spectrometer in $CDCl_3$ with TMS as an internal standard, IR on a Nicolet Magna-IR 750 spectrometer using the ATR technique, MS (direct inlet, 70 eV) on a Finnigan SSQ 710 apparatus. The melting points were not corrected. The solvents and reagents were of p.a. grade from Fluka.

Typical Procedure for the Oxidation of 1

3,5-Di-*tert*-butyl-2-hydroxy-phenyl-(3,4-dimethyl-phenyl)-methanone (**2a**). To a solution of 0.8 g (0.040 mol) NaOH in 30 mL water were added 3.51 g (0.010 mol) of 5,7-di-*tert*-butyl-3-(3,4-dimethyl-phenyl)-3H-benzofuran-2-one **1a** and the stirred suspension was refluxed for 1 hr under nitrogen. The resulting slightly turbid solution was cooled to 70°C. Toluene (30 mL) was added and thereafter a solution of 13.17 g (0.040 mol) potassium hexacyanoferrate (III) and 1.2 g (0.030 mol) of NaOH in 30 mL water was added dropwise over 10 min. The mixture was stirred for 5 hr at 70°C, cooled to r.t. and diluted with toluene (20 mL). The organic layer was separated, washed with 5% HCl and water (20 mL each), dried over $MgSO_4$ and evaporated under reduced pressure. The yellow residue (3.41 g) was purified by chromatography on silica gel (380 g, hexanes: CH_2Cl_2, 1 : 1) to afford 2.95 g (87%) **2a**, mp 119–121°C (MeOH). Calculated/found for $C_{23}H_{30}O_2$ (338.49): C 81.61/81.46, H 8.93/9.14. MS, *m/e* (%): 338 (53, M^+), 323 (100), 217 (71). ^{1}H-NMR, δ ppm: 12.70 (s, OH), 7.61 (m, 1ArH), 7.53 (m, 2ArH), 7.45 (d, 1ArH, $J = 7.6$ Hz), 7.27 (d, 1ArH, $J = 7.6$ Hz), 2.39 (s, Me), 2.37 (s, Me), 1.60 (s, *t*-Bu), 1.29 (s, *t*-Bu). ^{13}C-NMR, δ ppm: 202.34, 160.49, 141.08, 139.57, 137.73, 136.69, 136.31, 130.80, 130.70, 129.29, 128.01, 127.25, 118.42, 35.22, 34.25, 31.35, 29.45, 19.97, 19.72. IR (νCO, cm^{-1}): 1615, 1596.

The following products were made in the similar manner.

(2b). 43%, mp 89–91°C (EtOH). calculated/found for $C_{24}H_{32}O_3$ (368.52): C 78.22/77.90, H 8.75/8.85. MS, *m/e* (%): 368 (M^+, 36), 353 (41), 217 (100). ^{1}H-NMR, δ ppm: 12.67 (s, OH), 7.61 (d, 1ArH, $J = 2.4$ Hz), 7.52 (d, 1ArH, $J = 2.4$ Hz), 7.51 (s, 2ArH), 3.83 (s, OMe), 2.38 (s, 2× Me), 1.50 (s, *t*-Bu); 1.29 (s, *t*-Bu). ^{13}C-NMR, δ ppm: 202.19, 160.81, 160.52, 139.94, 138.13, 134.48, 131.32, 131.15, 130.96, 128.40, 118.77, 60.16, 35.61, 34.63, 31.73, 29.84, 16.56. IR (νCO, cm^{-1}): 1612, 1576.

(2c). 66%, mp 99–101°C (EtOH). calculated/found for $C_{23}H_{30}O_3$ (354.49): C 77.93/78.04, H 8.53/8.70. MS, *m/e* (%): 354 (M^+, 30), 339 (28), 217 (100). ^{1}H-NMR, δ ppm: 12.64 (s, OH), 7.73 (m, 2ArH), 7.60 (d, 1ArH, $J = 2.4$ Hz), 7.51 (d, 1ArH, $J = 2.4$ Hz), 7.01 (m, 2ArH), 4.16 (q, 2H, $J = 7.2$ Hz), 1.49 (t, Me, $J = 7.2$ Hz), 1.48 (s, *t*-Bu), 1.30 (s, *t*-Bu). ^{13}C-NMR, δ ppm: 201.45, 162.51, 160.65, 139.98, 138.14, 132.27, 131.35, 130.97, 128.07, 118.92, 114.34, 64.15, 35.61, 34.65, 31.77, 29.86, 15.13. IR (νCO, cm^{-1}): 1607, 1588.

(2d). 52%, mp 59–61°C (EtOH). [15]mp 60–62°C (EtOH–H_2O). MS ($C_{21}H_{26}O_2$, M = 310.44), *m/e* (%): 310 (M^+, 37), 295 (100), 217 (23). ^{1}H-NMR, δ ppm: 12.73 (s, OH), 7.71–7.29 (m, 7ArH), 1.58 (s, *t*-Bu), 1.27 (s, *t*-Bu). ^{13}C-NMR, δ ppm: 202.54, 160.70, 139.81, 138.71, 137.91, 131.62, 131.23, 129.22, 128.18, 127.86, 118.23, 35.23, 34.24, 31.30, 29.43. IR (νCO, cm^{-1}): 1618, 1595, 1575.

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