Oxidative Cleavage of 1,3-Disubstituted Benzo[*c*]furans with Activated Manganese Dioxide: A Facile Preparation of 1,2-Di(het)aroylbenzenes

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Abstract: Manganese dioxide mediated oxidative cleavage of 1,3-disubstituted benzo[*c*]furans in dichloromethane at room temperature gave good yields of 1,2-di(het)aroylbenzenes.

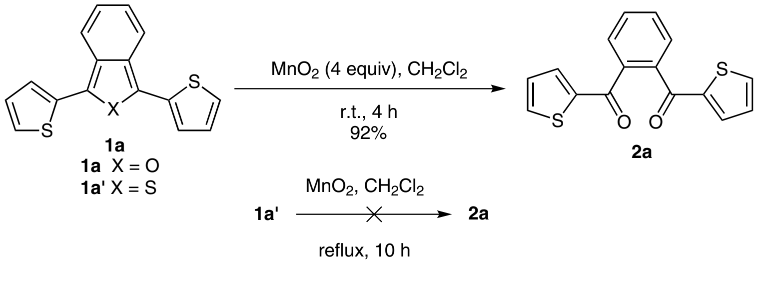
Key words: heterocycles, polycycles, diketones, ring opening, oxidation, manganese dioxide

Since the first report on 1,3-dithienylbenzo[*c*]thiophenes,[1] the syntheses and characterization of benzo[*c*]thiophene analogues have been well explored.[2] In comparison, the chemistry of the corresponding benzo[*c*]furans is less well explored because of their unstable nature. Swager and co-workers reported the first synthesis of benzo[*c*]furan-based cyanovinylenes as near-infrared fluorophores.[3] Over the years, 1,3-diarylbenzo[*c*]furans have been used as dienes in Diels–Alder reactions for the syntheses of a wide variety of π-conjugated molecules.[4] 1,3-Disubstituted benzo[*c*]furans have also been used as intermediates for the synthesis of benzo[*c*]selenophenes.[5] We recently reported the synthesis of annulated arenes and hetarenes from unsymmetrically substituted benzo[*c*]furans.[6]

In general, the oxidative transformation of 1,3-disubstituted benzo[*c*]furans into the corresponding diaroylbenzenes is achieved by using lead tetraacetate (LTA)[1b] or singlet oxygen.[7] We recently developed a simple oxidative ring opening of 1,3-disubstituted benzo[*c*]heterocycles by using 3-chloroperbenzoic acid (MCPBA).[8] Even though this procedure was successfully applied to a wide variety of benzo[*c*]heterocycles, undesired oxidation of the thiophene moiety also occurred in some cases. The synthetic utility of 1,2-diaroylbenzenes[6,9] prompted us to undertake a detailed study of the oxidative cleavage of benzo[*c*]heterocycles with other oxidizing agents. Over the years, activated manganese dioxide (MnO_2) has been used for the oxidation of a variety of heterocyclic compounds.[10] Garofalo and co-workers achieved an efficient synthesis of pyrroloindolones by a MnO_2-promoted intramolecular cyclization.[11] Recently, oxidation of arylmethylene compounds[12] with MnO_2 and the oxidation of benzylic alcohols with a substoichiometric quantity of MnO_2[13] have been reported. These reports encouraged us to explore the oxidation of 1,3-disubstitued benzo[*c*]furans with activated MnO_2.

In a representative case, treatment of 1,3-dithienylbenzo[*c*]furan (**1a**) with four equivalents of MnO_2 in dichloromethane at room temperature for four hours gave the corresponding diketone **2a** in 92% yield.[14] However, under identical conditions, the corresponding benzo[*c*]thiophene **1a′** failed to give diketone **2a** and, even under reflux conditions, the starting material **1a′** was recovered unchanged.

The ease with which benzo[*c*]furan **1a** underwent MnO_2-mediated oxidative ring opening prompted us to undertake a comprehensive study with various benzo[*c*]furan analogues. We were pleased to find that the MnO_2-mediated oxidative cleavage could be successful applied to a wide variety of 1,3-diaryl- and 1,3-dihetarylbenzo[*c*]furans (Table 1). The symmetrical benzo[*c*]furans **1b**–**d**, on treatment with four equivalents of MnO_2 in dichloromethane at room temperature, readily underwent oxidative ring cleavage to give the corresponding diaroylbenzenes **2b**–**d** in excellent yields (Table 1, entry 1). The nonsymmetrical 1,3-diarylbenzo[*c*]furans **1e**–**k** similarly underwent cleavage with MnO_2 in very good yields (entry 2). The MnO_2-mediated oxidative ring opening of the veratrole-tethered benzo[*c*]furans **3a**–**d** similarly gave the corresponding



Scheme 1 Attempted oxidations of furan **1a** and thiophene **1a′** with MnO_2

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diketones **4a**–**d** in 86–91% yield (entry 3). Cleavage of the dibenzothiophene-linked benzo[*c*]furans **5a** and **5b** with MnO_2 in dichloromethane at room temperature gave the corresponding 1,2-diaroylbenzenes **6a** and **6b** in 82 and 85% yield, respectively (entry 4). Note that the similar oxidative cleavage of benzo[*c*]furans **5a** and **5b** with MCPBA[8] gave the 1,2-diaroylbenzenes **6a** and **6b** in low yields as a result of oxidation of the dibenzothiophene unit. Obviously, the mild oxidizing nature of MnO_2 permits selective oxidation of the benzo[*c*]furan moiety without any effect on the dibenzothiophene unit. The MnO_2-mediated oxidative ring-opening reaction was also successfully applied to the bithiophene-containing benzo[*c*]furan **7**, to give the diketone **8** in 86% yield (entry 5), and to the biphenyl-containing benzo[*c*]furans **9a** and **9b** (entry 6). The benzo[*b*]thiophene-containing benzo[*c*]furans **11a** and **11b** also readily underwent the oxidative ring-opening reaction to give the corresponding products **12a** and **12b** in good yields (entry 7). As expected, the reactions of the triphenylamine-containing benzo[*c*]furans **13a** and **13b** and the *N*-hexylcarbazole-containing benzo[*c*]furans **15a** and **15b** with MnO_2 gave the corresponding diketones in 81–87% yield (entries 8 and 9). Under identical conditions, various other benzo[*c*]furans **17**, **19**, and **21** gave the corresponding diketones **18**, **20**, and **22** in 83–92% yields (entries 10–12). However, attempts at oxidative cleavage of the symmetrical 2,5-diarylfurans **23a** and **23b** with MnO_2 were unsuccessful and, even under reflux conditions, the starting materials were recovered unchanged (entry 13).

Table 1 Oxidations of Benzo[*c*]furans with MnO_2[a]

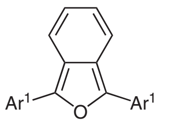
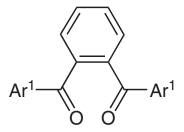
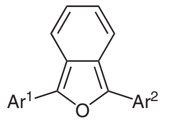
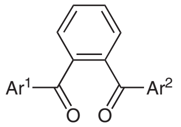
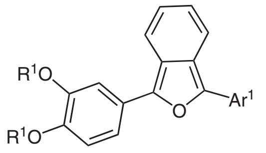
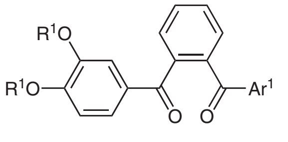
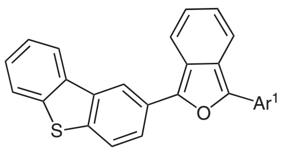
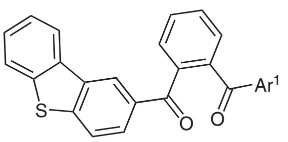
Entry	Substrate	Product	Yield (%)
1	 **1a** **1b** **1c**	 **2b** Ar^1 = Ph **2c** Ar^1 = 4-Tol **2d** Ar^1 = 1-naphthyl	94 95 92
2	 **1e** **1f** **1g** **1h** **1i** **1j** **1k**	 **2e** Ar^1 = 4-$MeOC_6H_4$; Ar^2 = Ph **2f** Ar^1 = 4-Tol; Ar^2 = 1-naphthyl **2g** Ar^1 = Ph; Ar^2 = 2-thienyl **2h** Ar^1 = 3,4-$Me_2C_6H_3$; Ar^2 = 4-$MeOC_6H_4$ **2i** Ar^1 = 2-methoxy-1-naphthyl; Ar^2 = Ph **2j** Ar^1 = 2-methoxy-1-naphthyl; Ar^2 = 1-naphthyl **2k** Ar^1 = 2,4-$Me_2C_6H_3$; Ar^2 = 1-naphthyl	93 90 90 96 90 91 93
3	 **3a** **3b** **3c** **3d**	 **4a** R^1 = Me; Ar^1 = 1-naphthyl **4b** R^1 = Me; Ar^1 = 4-Tol **4c** R^1 = $(CH_2)_5Me$; Ar^1 = Ph **4d** R^1 = $(CH_2)_5Me$; Ar^1 = 2-thienyl	91 88 89 86
4	 **5a** **5b**	 **6a** Ar^1 = 2-thienyl **6b** Ar^1 = 1-naphthyl	82 85

Table 1 Oxidations of Benzo[*c*]furans with MnO_2[a] (continued)

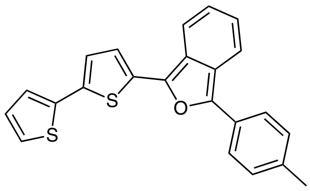
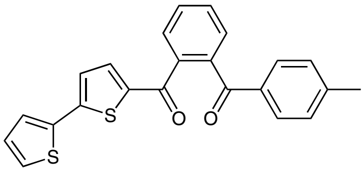
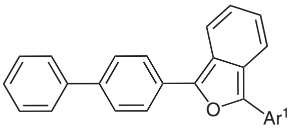
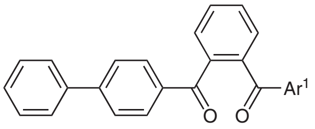
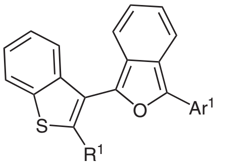
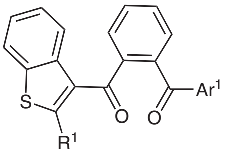
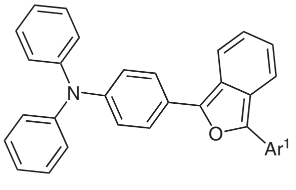
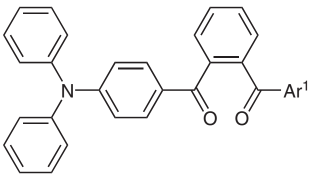
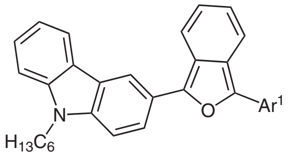
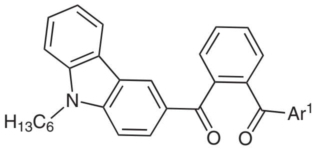
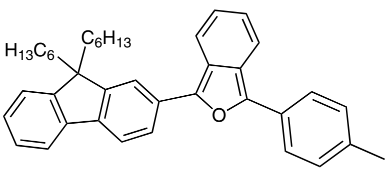
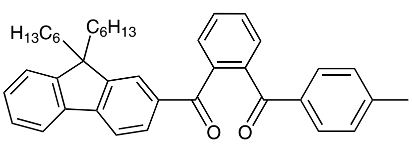
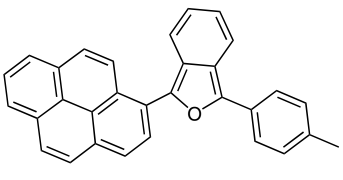
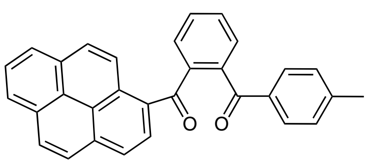
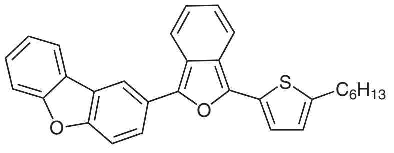
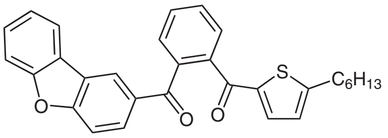
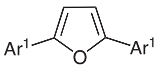
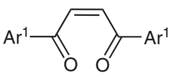
Entry	Substrate	Product	Yield (%)
5	 **7**	 **8**	86
6	 **9a** **9b**	 **10a** Ar^1 = Ph **10b** Ar^1 = 3-hexyl-2-thienyl	88 87
7	 **11a** **11b**	 **12a** R^1 = H; Ar^1 = 4-Tol **12b** R^1 = Me; Ar^1 = 2-thienyl	87 89
8	 **13a** **13b**	 **14a** Ar^1 = 2-thienyl **14b** Ar^1 = 4-$MeOC_6H_4$	84 87
9	 **15a** **15b**	 **16a** Ar^1 = 4-Tol **16b** Ar^1 = 4-$MeOC_6H_4$	81 85
10	 **17**	 **18**	83
11	 **19**	 **20**	92

Table 1 Oxidations of Benzo[*c*]furans with MnO_2[a] (continued)

Entry	Substrate	Product	Yield (%)
12	 **21**	 **22**	91
13	 **23a** **23b**	 **24a** Ar^1 = 2-thienyl **24b** Ar^1 = Ph	0 0

[a] *Reaction conditions*: substrate (1 equiv), MnO_2 (4 equiv), anhyd CH_2Cl_2, r.t., ~4 h.

To understand the efficacy of MnO_2-mediated oxidative cleavage in more detail we needed to compare the MnO_2-mediated ring-opening reactions of benzo[*c*]furans with those mediated by other oxidizing agents. Accordingly, we examined the reactions of representative benzo[*c*]furans with LTA, MCPBA, and MnO_2, and the yields obtained are shown in Table 2.

Table 2 Comparative Study on the Oxidation of Benzo[*c*]furans with LTA, MCPBA, and MnO_2

Entry	Substrate	Product	Yield[a] (%)		
			$Pb(OAc)_4$[b]	MCPBA[c]	MnO_2[d]
1	**1a**	**2a**	83	89	92
2	**1c**	**2c**	84	92	94
3	**5a**	**6a**	80	41	82
4	**5b**	**6b**	83	44	85
5	**13a**	**14a**	24	83	84
6	**15a**	**16a**	25	82	81

[a] Isolated yield

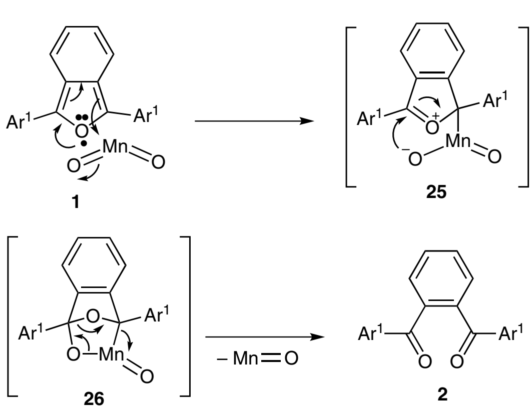
[b] Reactions were carried out by using LTA (2 equiv) in THF.

[c] Reactions were carried out by using MCPBA (1.5 equiv) in CH_2Cl_2.

[d] Reactions were carried out by using MnO_2 (4 equiv) in CH_2Cl_2.

In the case of the symmetrical 1,3-diarylbenzo[*c*]furans **1a** and **1c**, similar yields of diketones **2a** and **2c** were obtained with all three oxidizing agents (Table 2, entries 1 and 2). In the case of the dibenzothiophene-linked benzo[*c*]furans **5a** and **5b**, better yields of the diketones were obtained by using LTA or MnO_2 than with MCPBA (entries 3 and 4). Oxidative ring-opening reactions of the triphenylamine- and *N*-hexylcarbazole-capped benzo[*c*]furans **13a** and **15a** with MnO_2 and with MnO_2 gave comparable yields, whereas the corresponding reactions with LTA gave low yields of the corresponding diketones **14a** and **16a** (entries 5 and 6).

A plausible mechanism for the formation of 1,2-diaroylbenzenes **2** from benzo[*c*]furans **1** by MnO_2-mediated oxidation is shown in Scheme 2.



Scheme 2 Proposed mechanism for the oxidative cleavage of 1,3-disubstituted benzo[*c*]furans by MnO_2

Nucleophilic attack by MnO_2 on benzo[*c*]furan **1**, followed by intramolecular cyclization, gives intermediate **26**, which undergoes elimination of MnO to give the diaroylbenzene **2**.

In summary, we have developed a mild MnO_2-mediated oxidative ring opening of symmetrical or unsymmetrical 1,3-diarylbenzo[*c*]furans at room temperature. The reaction generally proceeds in excellent yields. In most cases, yields of the 1,2-di(het)aroylbenzenes obtained by the MnO_2-mediated oxidative cleavage are comparable to or better than those produced by existing methods.

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Supporting Information for this article is available online at http://www.thieme-connect.com/products/ejournals/journal/10.1055/s-00000083.

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(14) **1,2-Phenylenebis(2-thienylmethanone) (2a); Typical Procedure**
MnO_2 (0.57 g, 7.09 mmol) was added to a stirred solution of benzo[*c*]furan **1a** (0.5 g, 1.77 mmol) in CH_2Cl_2 (20 mL), and the mixture was stirred at r.t until the benzo[*c*]furan was consumed (~4 h). The mixture was then filtered through Celite and the residue was washed with CH_2Cl_2 (2 × 10 mL). The combined filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (silica gel; 5% EtOAc–hexane) to give a brown solid; yield: 0.48 g (92%); mp 150–152 °C (Lit. see ref. 1b 149–150 °C); IR (KBr): 1623, 1582, 1568, 1514, 1416 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.66–7.64 (m, 2 H, ArH), 7.58–7.56 (m, 4 H, ArH), 7.39–7.38 (m, 2 H, ArH), 6.99–6.96 (m, 2 H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.3, 144.0, 139.4, 135.1, 135.0, 130.6, 129.2, 128.1; DEPT-135 (75 MHz, $CDCl_3$): δ = 135.2, 135.0, 130.6, 129.2, 128.1; HRMS (EI): *m/z* [M^+] calcd for $C_{16}H_{10}O_2S_2$: 298.0122; found: 298.0121.