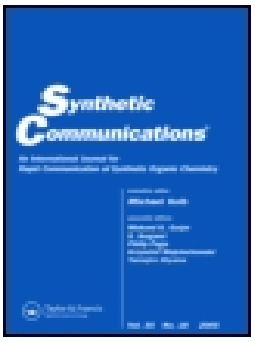

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Oxidative Cleavage of 1,3-Diaryl/(heteroaryl)benzo[*c*]furans into 1,2-Diaroyl/(heteroaroyl)benzenes using Selenium dioxide

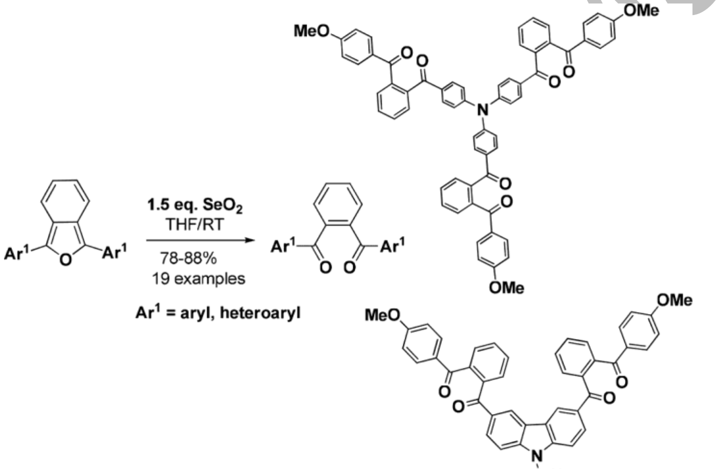
Jayachandran Karunakaran[1], Elumalai Sankar[1], Arasambattu K Mohanakrishnan[1]

[1]Department of Organic Chemistry, School of Chemistry, University of Madras, Chennai, Tamil Nadu, India

Corresponding author to A. K Mohanakrishnan: E-mail: mohanakrishnan@unom.ac.in/mohan_67@hotmail.com

Abstract

Reaction of 1,3-disubstituted isobenzofurans (IBFs) with selenium dioxide in THF at room temperature led to the formation of 1,2-diaroyl/(heteroaroyl)benzenes in good to excellent yields.



KEYWORDS: Isobenzofuran, Oxidative cleavage, Selenium dioxide, 1,2-Diaroylbenzenes

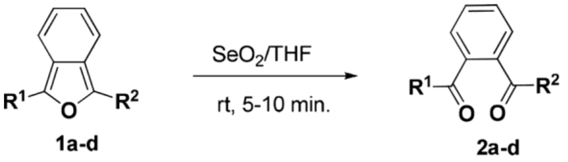
INTRODUCTION

Over the years, the 1,3-diarylbenzo[*c*]furan analogues have been exploited as diene in the Diels-Alder reaction for the syntheses of π-conjugated carbocycles[1] as well as heterocycles[2]. The benzo[*c*]furans have also been utilized as an ideal precursor for the synthesis of 1,3-disusbtituted benzo[*c*]selenophenes[3]. The synthesis of stable benzo[*c*]furan based cyanovinylenes as near-IR fluorophores have also been explored[4]. Nevertheless, the photochemical degradation of 1,3-diarylbenzo[*c*]furan analogues has been considered as a potential drawback, severally minimizing their optical applications[5]. In further exploitation of their utility, recently, a facile synthetic transformation of isobenzofurans into the annulated arenes and heteroarenes have also been reported[6].

Oxidative transformation of the 1,3-disubstituted benzo[*c*]furans (IBFs) into their respective diaroylbenzenes are achieved using lead tetraacetate (LTA)[7], singlet oxygen[8], *m*-CPBA[9] and active MnO_2.[10] Even though, these methods were employed for the synthetic transformation of 1,3-diarylbenzo[*c*]furans into 1,2-diaroylbenzenes, each one of them are having inherent disadvantageous[10]. The unstable nature of 1,3-diarylbenzo[*c*]furans coupled with undesired oxidation of thiophene unit[9] prompted us to explore the oxidative cleavage of these heterocycles with other oxidizing agents. Over the years, selenium dioxide (SeO_2) has been employed for smooth oxidation of allylic as well as methyl ketone[11] functions of organic compounds. An efficient synthesis of triarylethanones was achieved by Myrboh and coworkers through SeO_2-BF_3.OEt_2 promoted[12] bis-arylation of acetophenones at room temperature. Recently, Liu et al. reported the synthesis of *N*-arylisatins involving SeO_2-mediated oxidative-amidation[13] of 2-arylaminoacetophenone. Encouraged by these recent reports and also based on synthetic utility of 1,2-diaroylbenzenes,[6] a systematic study on oxidation of 1,3-disubstitued benzo[*c*]furans using SeO_2 were initiated.

RESULTS AND DISCUSSION

As a representative case, the reaction of symmetrical 1,3-diarylbenzo[*c*]furan **1a**/1,3-diheteroaryl **1b** with 1.5 eq. of SeO_2 in dry THF at room temperature for 5 minutes afforded the known diketone **2a/2b**[9] in an excellent yield. While stirring at room temperature, the sudden change of an orange-yellow fluorescent color of isobenzofuran **1a**/**1b** confirmed its transformation into the respective diketone **2a/2b**. Similarly, the aryl substituted unsymmetrical isobenzofuran **1c/1d** also underwent smooth oxidative cleavage to give the corresponding diketone **2c/2d**.

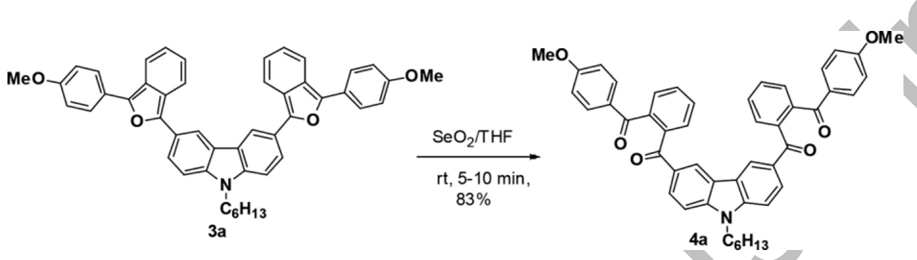


2a R^1, R^2 = phenyl, phenyl (84%)
2b R^1, R^2 = 2-thienyl, 2-thienyl (81%)
2c R^1, R^2 = phenyl, *p*-anisyl (85%)
2d R^1, R^2 = *p*-tolyl, 1-naphthyl (80%)

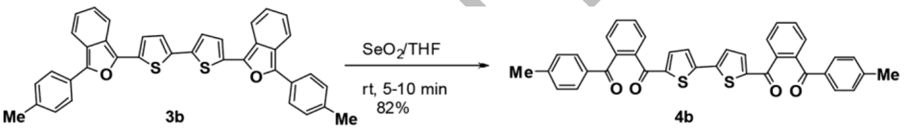
The facile transformation of the isobenzofurans **1a-d** into the respective diketones **2a-d** using SeO_2 encouraged us to do the oxidative cleavage of various types of unsymmetrical isobenzofuran derivatives **1e-n**, Table 1.

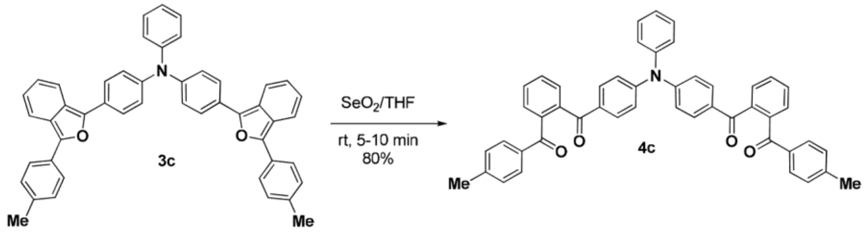
The SeO_2-mediated oxidative cleavage was found to be successful with dibenzoheterocycle as well as triphenylamine based isobenzofuran derivatives **1e-g** (entries 1-3). The pyrene, bithiophene and dihexylfluorene tethered benzo[*c*]furans **1h-j** are also underwent facile oxidative cleavages using SeO_2 to afford respective diketones **2h-j** (entries 4-6). Next, the oxidative ring opening reaction was also performed with diphenylmethane as well as dibenzofuran incorporated isobenzofurans **1k** and **1l** (entries 7, 8). Finally, the biphenyl and benzo[*b*]thiophene based isobenzofuran **1m, 1n** also participated in the SeO_2-mediated ring opening reaction to afford the corresponding diketone **2m** and **2n** in good yields (entries 9, 10).

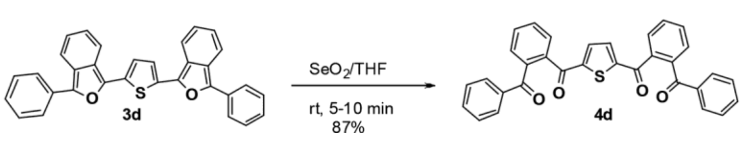
Next, the reaction of *N*-hexylcarbazole tethered bis-benzo[*c*]furan **3a** with 3 eqs. of SeO_2 at room temperature led to the formation of the respective tetra ketone **4a** in 83% yield.



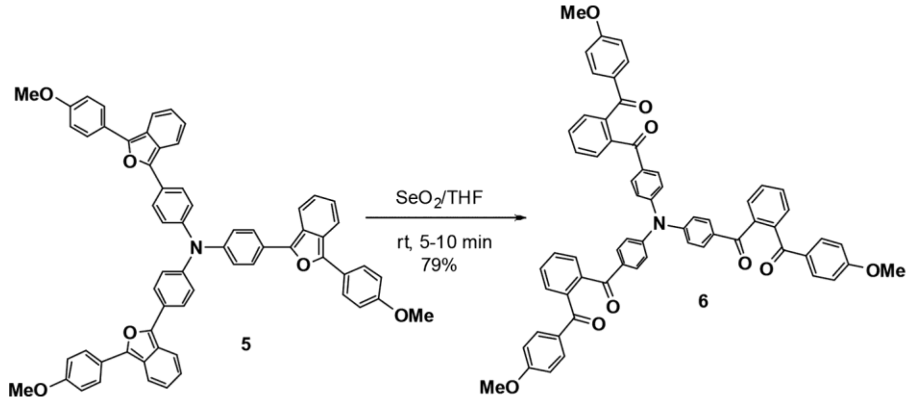
Under same conditions, the bithiophene-, triphenylamine- and thiophene based bis-benzo[*c*]furans **3b-d** could be smoothly converted into the respective tetra ketones **4b-d** in good yields.



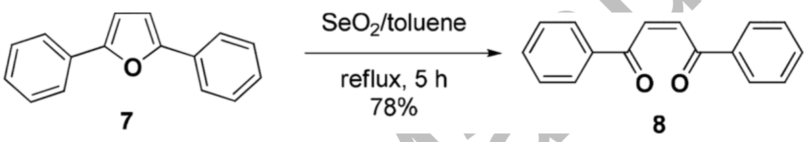




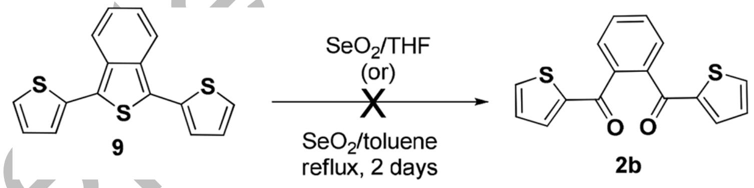
The triphenylamine based tris-benzo[*c*]furan **5** also underwent the facile SeO_2 mediated oxidative cleavage to afford tris-diketone **6** in 79% of yield.



The classical 2,5-diphenylfuran **7** also underwent SeO$_2$-mediated oxidative cleavage in toluene at reflux to give the respective *cis*-diketone **8**[10] in 78% yield.



Finally, an attempted cleavage of 1,3-dithienylbenzo[*c*]thiophene **9** using 1.5 eq. of SeO$_2$ in THF at room temperature and also at refluxing condition of toluene failed to give the expected diketone **2b**.



A plausible mechanism for the formation of 1,2-diaroylbenzenes from benzo[*c*]furans using SeO$_2$ is shown in the Scheme 1. The benzo[*c*]furans **1a-n** upon reaction with SeO$_2$ led to the formation of Diels-Alder type of adducts **10,** which upon elimination of divalent selenoxide furnished the diketones **11**. The observed failure to cleave the non-classical thiophene unit of 1,3-dithienyl benzo[*c*]thiophene **9** using SeO$_2$ clearly confirmed the relatively enhanced aromatic character of non-classical thiophene than that of the respective furan. Obviously, the reduced diene character of the non-classical thiophene unit disfavors the cycloaddition reaction of **9** with SeO_2.

EXPERIMENTAL

All melting points were uncorrected. Solvents were dried by standard procedures. The progression of reaction was monitored by TLC using hexane/ethyl acetate mixture as an eluent. Column chromatography was carried out on silica gel (230-400 mesh, Merck) by using increasing polarity. The ^{1}H, ^{13}C and DEPT-135 spectra were recorded in $CDCl_3$ using TMS as an internal standard on a 300 MHz NMR spectrometer at room temperature. Chemical shift values were quoted in part per million (ppm) and coupling constants (*J*) were quoted in hertz (Hz). Selenium dioxide purchased from Sigma-Aldrich was used as such for oxidation. The required benzo[*c*]furans/thiophenes **1a-n, 7** and **9** were prepared using the published procedures [3, 6, 9, 10].

General Procedure For Oxidation Of Benzo[*C*]Furans Into Diketones Using Seo$_2$:

To a stirred solution of benzo[*c*]furan (1.0 mmol) in dry THF (20 mL), SeO_2 (1.5 mmol) was added and stirred at room temperature until the disappearance of fluorescent color of benzo[*c*]furan (~5-10 minutes). After that, the reaction mixture was filtered through celite bed and washed with ethyl acetate (2 x 10 mL). The combined organic layer was washed with water (2 x 30 mL) and dried (Na_2SO_4). Removal of solvent followed by column chromatographic purification (Silica gel, 20% EA/Hexane) afforded diketone.

Oxidative Cleavage Of Benzo[*C*]Furan 1a Using Seo$_2$:

The oxidative cleavage of benzo[*c*]furan **1a** (0.23 g, 0.85 mmol) using SeO$_2$ (0.15 g, 1.35 mmol) adopting the general procedure gave known diketone **2a**[9] as a colorless solid (0.21 g, 84%); mp 137-138 °C; ^{1}H-NMR (300 MHz, CDCl$_3$): δ 7.63 (d, *J* = 7.2 Hz, 4H, C2-H & C3-H of 1,2-phenylene), 7.54 (s, 4H, C2-H of phenylmethanone), 7.44 (t, *J* = 7.2 Hz, 2H, C4-H of phenylmethanone) 7.32-7.27 (m, 4H, C3-H of phenylmethanone) ppm. ^{13}C-NMR (75 MHz, CDCl$_3$): δ 196.6 (C=O), 140.0 (C), 137.2 (C), 133.0 (C-H), 130.4 (C-H), 129.8 (C-H), 129.7 (C-H), 128.3 (C-H) ppm.

1,2-Phenylenebis(Thiophen-2-Ylmethanone) 2b[9]:

Yield: 0.47 g (81%); colorless solid; mp 152-153 °C ; ^{1}H-NMR (300 MHz, CDCl$_3$): δ 7.66-7.64 (m, 2H, C3-H of 1,2-phenylene), 7.58-7.56 (m, 4H, C2-H of 1,2-phenylene & C5-H of thiophene), 7.39-7.38 (m, 2H, C3-H of thiophene), 6.99-6.96 (m, 2H, C4-H of thiophene) ppm. ^{13}C-NMR (75 MHz, CDCl$_3$): δ 188.3 (C=O), 144.0 (C), 139.4 (C), 135.1 (C-H), 135.0 (C-H), 130.6 (C-H), 129.2 (C-H), 128.1 (C-H) ppm.

Procedure For Oxidation Of Furan 7 Into Diketone 8[10]:

To a stirred solution of 2,5-diphenylfuran **7** (0.24 g, 1.0 mmol) in dry toluene (10 mL), SeO$_2$ (0.18 g, 1.52 mmol) was added and refluxed for 5 h. After that, the reaction mixture was filtered through celite bed and washed with ethyl acetate (2 x 10 mL). The combined organic layer was washed with water (2 x 30 mL) and dried (Na$_2$SO$_4$). Removal of solvent followed by column chromatographic purification (Silica gel, 15% EA/Hexane) furnished diketone **8** as a pale yellow solid (0.20 g, 78%); mp 129 °C; ^{1}H-

NMR (300 MHz, $CDCl_3$): δ 7.85 (d, *J* = 7.8 Hz, 4H, C2-H of phenylmethanone), 7.50-7.46 (m, 2H, C4-H of phenylmethanone), 7.39-7.34 (m, 4H, C3-H of phenylmethanone), 7.07 (s, 2H, vinylic CH) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): *δ* 192.5 (C=O), 136.1 (C), 135.6 (C-H), 133.6 (C-H), 128.8 (C-H), 128.6 (C-H) ppm.

CONCLUSION

In summary, we have demonstrated that the mono-, bis- as well as tris-isobenzofurans can be efficiently transformed into their respective diaroyl/diheteroaroylbenzenes using SeO_2 mediated oxidative cleavage at room temperature. The methodology was found to be useful for the synthesis of complex diaroyl/diheteroaroylbenzenes in excellent yields and also the reaction proceeded with shorter reaction time compared to the existing procedures.

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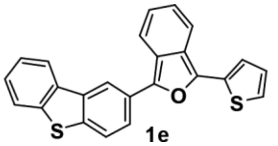
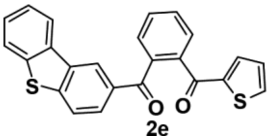
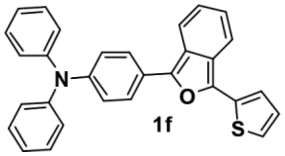
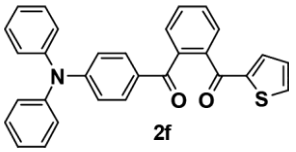
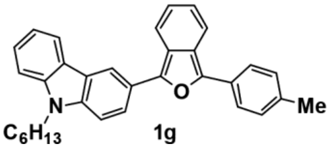
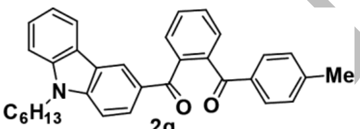
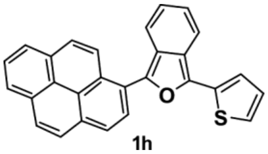
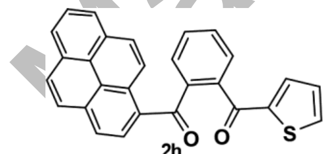
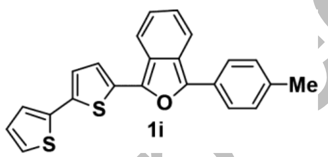
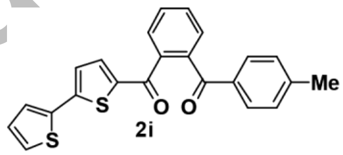
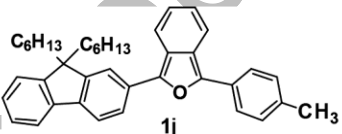
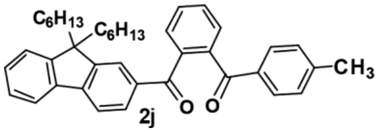
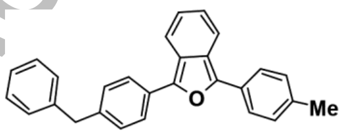
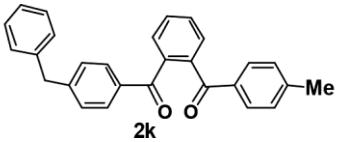
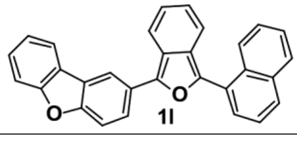
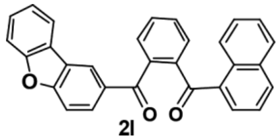
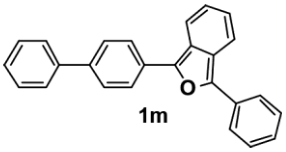
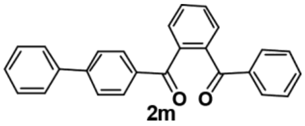
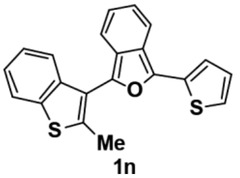
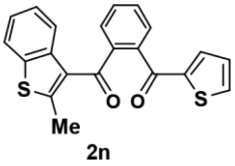
Table 1. Oxidative ring opening of isobenzofurans **1e-n** using SeO_2

entry	Substrate	Product	Time (min.)	Yield (%)
1	 **1e**	 **2e**	10	82
2	 **1f**	 **2f**	6	80
3	 **1g**	 **2g**	8	83
4	 **1h**	 **2h**	4	88
5	 **1i**	 **2i**	5	88
6	 **1j**	 **2j**	5	78
7		 **2k**	6	83
8	**1k**  **1l**	 **2l**	5	85

9	 **1m**	 **2m**	5	82
10	 **1n**	 **2n**	6	81

[a] Isolated yield by column chromatography.

Scheme 1. Mechanism for oxidative cleavage of 1,3-disubstituted benzo[*c*]furans using SeO_2