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Addition to Electron Deficient Olefins of α-Oxy Carbon-Centered Radicals, Generated from Cyclic Ethers and Acetals by the Reaction with Alkylperoxy- λ³-iodane

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Abstract: Thermal decomposition of 1-*tert*-butylperoxy-1,2-benziodoxol-3(1*H*)-one in cyclic ethers and acetals at 50 °C generates α-oxy carbon-centered radicals, which undergo an addition reaction with vinyl sulfones and unsaturated esters.

Keywords: Radical, iodane, ether, vinyl sulfone, maleate

Introduction

Commercially available crystalline 1-*tert*-butylperoxy-1,2-benziodoxol-3(1*H*)-one (**1**) serves as a versatile oxidizing agent [1]; thus, sulfides, secondary and tertiary amines and amides are readily oxidized with the *tert*-butylperoxy -λ³-iodane **1** to the corresponding sulfoxides, imines, *tert*-butyl-peroxyamino acetals and imides, respectively [2]. Oxidation of 4-substituted phenols affords 4-(*tert*-butylperoxy)-2,5-cyclohexadien-1-ones in good yields [3].
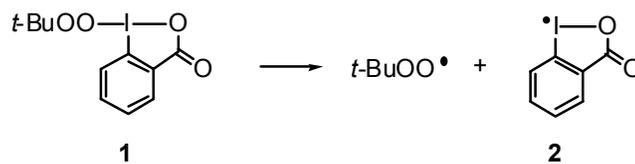
The λ³-iodane **1** is stable in the solid state but gradually decomposes in solution at ambient temperature to generate *tert*-butylperoxy radical and [9-I-2] iodanyl radical **2** through homolytic

cleavage of the hypervalent iodine(III)-peroxy bond. These radicals are responsible for the oxidation of benzyl and allyl ethers with the λ^3-iodane **1** in the presence of alkali metal carbonates, yielding the corresponding esters *via* the intermediacy of benzylic and allylic radicals [4]. Recently, we found that the gentle heating of a THF solution of the peroxy-λ^3-iodane **1** at 50 °C for 10 h under argon produced a mixture of *o*-iodobenzoic acid (**5**, 55%) and the acid-labile 2-tetrahydrofuranyl *o*-iodobenzoate (**6**, 45%) (Scheme 2) [5]. The formation of *o*-iodobenzoate **6** probably involves the following sequence: (a) α-hydrogen atom abstraction from THF by the *tert*-butylperoxy radical and/or the iodanyl radical **2** to give the α-tetrahydrofuranyl radical **3**, (b) a single-electron transfer from α-THF radical **3** to the peroxy-λ^3-iodane **1** (or *tert*-butylperoxy radical and the iodanyl radical **2**), generating the oxonium ion **4**, and finally, (c) nucleophilic attack of *o*-iodobenzoic acid **5**, generated *in situ* on **4**, yielding the ester **6**. This mechanism was supported by the finding that the decomposition of the λ^3-iodane **1** in THF in the presence of an alcohol results in a competition between the formation of **6** and the tetra-hydrofuranylation of the alcohol.

Scheme 1
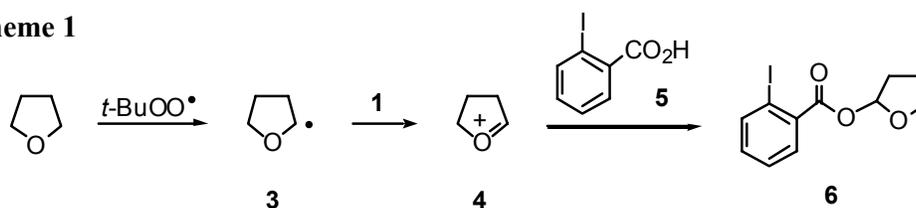
Since α-THF radical **3** is nucleophilic in nature and undergoes addition to electron-deficient olefins such as maleate esters [6] and vinyl sulfones [7], it seems reasonable to assume that, when the decomposition of the peroxy-λ^3-iodane **1** in THF is carried out in the presence of an electrophilic olefin, addition of α-THF radical **3** to the double bond would take place, if the radical addition is faster than a single-electron transfer from α-THF radical **3** to the peroxy-λ^3-iodane **1**. We report herein the λ^3-iodane-induced addition of α-oxy carbon-centered radicals generated from cyclic ethers and acetals to electron deficient olefins, which proceeds under mild conditions.

Results and Discussion

Exposure of phenyl vinyl sulfone (**7**) to an equivalent amount of the peroxy-λ^3-iodane **1** in THF at 50 °C for 24 h under argon resulted in an addition reaction of THF with formation of 2-[2-(phenyl-sulfonyl)ethyl]tetrahydrofuran (**8a**) in 83% yield (Scheme 2 and Table 1, Entry 2). Use of 0.3 equivalents of **1** decreased the yield of **8a** to 66%. 1,3-Dioxolane serves as an excellent hydrogen donor for the attack of electrophilic radicals such as *t*-BuO· [8]. Thus, in 1,3-dioxolane with the use of 0.3 equivalents of **1**, the addition product **8c** was obtained in 76% yield. Less reactive tetrahydropyran (THP) and 1,4-dioxane afforded moderate yields (50-52%) of 2-alkylated ethers **8b** and **8d**, respectively (Table 1, Entries 3 and 5). These reactivity differences seem to correlate well with their corresponding C-H bond dissociation energies: THF (2-H), 89.8 kcal/mol; 1,3-dioxolane (2-H), 90.0 kcal/mol; THP (2-H), 92.1 kcal/mol; 1,4-dioxane, 93.2 kcal/mol [8a]. Attempted addition of 1,3-dioxolane to (*E*)-1-propenyl phenyl sulfone was found to be fruitless [7c,d].

Scheme 2

7   **8a**
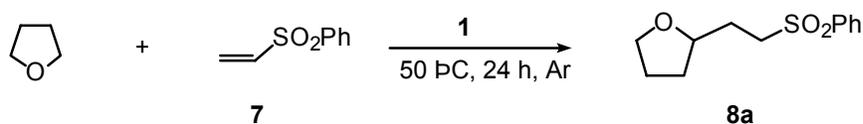
The formation of the 2-alkylated 1,3-dioxolane **8c** in good yield is very interesting, because 2-alkyl- and 2-aryl-1,3-dioxolanes undergo oxidative ring cleavage by the reaction with the peroxy-λ^3-iodane **1** in the presence of *tert*-butyl hydroperoxide and potassium carbonate in benzene at room temperature, yielding glycol monoesters [9].

Table 1. Addition of cyclic ethers to phenyl vinyl sulfone **7** [a]

Entry	λ^3-Iodane 1 (equiv)	Ether	Product		
			Structure	8	Yield (%) [b]
1	0.3	THF		**8a**	66
2	1	THF		**8a**	83
3	1	THP		**8b**	50
4	0.3	1,3-dioxolane		**8c**	76
5	1	1,4-dioxane		**8d**	52
6	1 [c]	1,3-dioxolane		**8e**	0
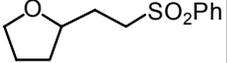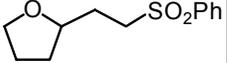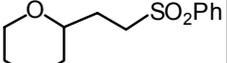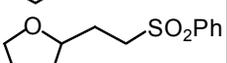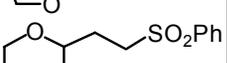
[a] Reactions were carried out at 50 °C for 24 h under argon. [b] Isolated yields.
[c] Reaction with (*E*)-1-propenyl phenyl sulfone.

Unsaturated esters serve as efficient acceptors for α-oxy carbon-centered radicals generated from cyclic ethers and acetals [10]. The reaction with diethyl fumarate (*E*)-(**9**) in the presence of the peroxy-λ^3-iodane **1** (1 equiv.) in THF at 50 °C for 24 h under argon afforded diethyl 2-tetrahydrofuranylsuccinate (**10a**) as a 1:1 mixture of diastereoisomers in 47% yield (Table 2). With diethyl maleate (*Z*)-(**9**), a higher yield (61%) of the succinate **10a** (a 1:1 mixture of diastereoisomers) was obtained. 1,3-Dioxolane also undergoes an addition reaction toward the unsaturated diesters to give diethyl (1,3-dioxolan-2-yl)succinate (**10b**) in high yields (Table 2, Entries 3 and 4). In these reactions, diethyl maleate (*Z*)-(**9**) served as a more efficient acceptor of α-oxy carbon-centered radicals than diethyl fumarate (*E*)-(**9**) [10a,b].

Scheme 3
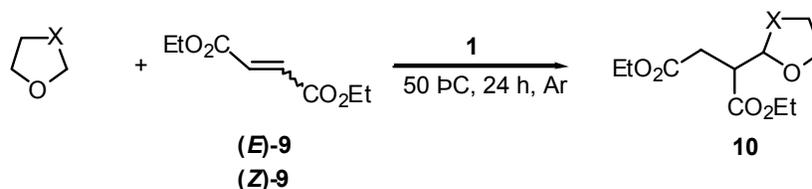
Table 2. Addition of cyclic ethers to unsaturated esters **9** [a]

Entry	Olefin	Ether	Product	
			10	**Yield (%)** [b]
1	(*E*)-**9**	THF	**10a**	47 (53) [c]
2	(*Z*)-**9**	THF	**10a**	61 (70) [c]
3	(*E*)-**9**	1,3-dioxolane	**10b**	81
4	(*Z*)-**9**	1,3-dioxolane	**10b**	88

[a] Reactions were carried out using one equiv. of the peroxy-λ^3-iodane **1** at 50 °C for 24 h under argon. [b] Isolated yields. Values in parentheses are GC yields. [c] A 1:1 mixture of stereoisomers.

The addition of cyclic ethers to the electron-deficient olefins probably involves the reaction sequence shown in Scheme 4. Addition of the nucleophilic α-oxy carbon-centered radical **3** to the electron-deficient olefins produces the carbon radicals **11** bonded to the electron-withdrawing group (EWG). This process may compete with a single-electron transfer from α-THF radical **3** to the peroxy-λ^3-iodane **1** (or *tert*-butylperoxy radical and the iodanyl radical **2**), generating the oxonium ion **4**.

Scheme 4
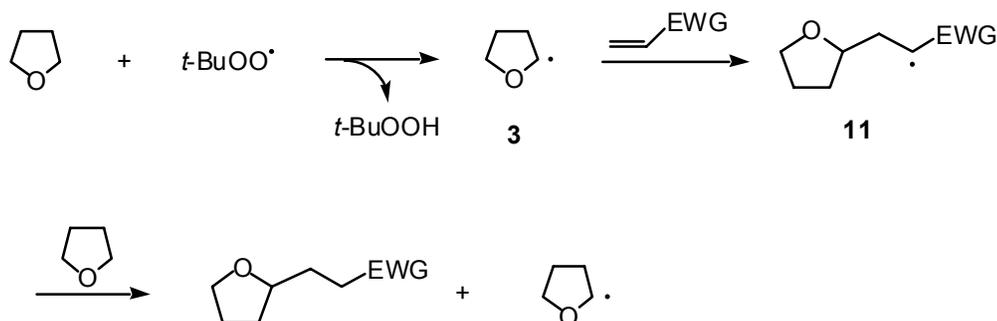
Experimental

General

^{1}H-NMR spectra were recorded in CDCl$_3$ on JEOL AL 300 or JNM GX-400 spectrometers using tetramethylsilane as an internal standard. The IR spectra were recorded on a Jasco FT-IR 420

spectrometer. The mass spectra were taken on a JEOL JMS-DX300 spectrometer. Analytical gas chromatography (GC) was carried out on a Shimazu GC-8A gas chromatograph with a column of 10% silicone SF-96 on Chromosorb W (AW-DMCS). Preparative thin-layer chromatography (TLC) was carried out on Kieselgel 60 F$_{254}$ (Merk).

General Procedure for Addition of Cyclic Ethers to Phenyl Vinyl Sulfone (**2**). *A Typical Example: 2-[2-(Phenylsulfonyl)ethyl]tetrahydrofuran* (**8a**) *(Table 1, Entry 2).*

To a mixture of *tert*-butylperoxy-λ^3-iodane **1** (67 mg, 0.2 mmol) and phenyl vinyl sulfone (**2**, 34 mg, 0.2 mmol) was added THF (1.2 mL) at room temperature under argon and the stirred mixture was heated at 50 °C for 24 h. The reaction was quenched by addition of a 5% aqueous K$_2$CO$_3$ solution and the mixture extracted with dichloromethane. The combined organic extracts were washed with water and brine, dried over anhydrous Na$_2$SO$_4$, and concentrated *in vacuo* to give an oil which was purified by preparative TLC (hexane-ethyl acetate 6:4) to give the sulfone **8a** (39.7 mg, 83%)[7a]; ^{1}H-NMR (300 MHz): δ 7.92 (2H, d, *J*= 7.7 Hz), 7.67 (1H, t, *J*= 6.9 Hz), 7.57 (2H, dd, *J*= 6.9, 7.7 Hz), 3.90-3.63 (3H, m), 3.37-3.23 (1H, m), 3.20-3.08 (1H, m), 2.07-1.76 (5H, m), 1.53-1.39 (H, m).

2-[2-(Phenylsulfonyl)ethyl]tetrahydropyran (**8b**): ^{1}H-NMR (400 MHz) δ 7.91 (2H, d, *J*= 8.0 Hz), 7.65 (1H, t, *J*= 8.0 Hz), 7.56 (2H, t, *J*= 8.0 Hz), 3.88 (1H, br d, *J* = 12.0 Hz), 3.37-3.23 (3H, m), 3.20-3.10 (1H, m), 1.96-1.85 (1H, m), 1.85-1.72 (2H, m), 1.56-1.39 (4H, m), 1.30-1.17 (1H, m); IR (neat) ν (cm^{-1}) 3063, 2935, 2847, 1585, 1446, 1308, 1146, 1086, 1047, 880, 742, 690; EIMS m/z (%) 254 (M$^+$, 24), 225 (19), 143 (15), 112 (100), 85 (42), 77 (33); HRMS (EI) calcd. for C$_{13}$H$_{18}$O$_3$S (M$^+$): 254.0977, found 254.0990.

2-[2-(Phenylsulfonyl)ethyl]-1,3-dioxolane (**8c**) [7b]: ^{1}H-NMR (300 MHz): δ 7.92 (2H, d, *J*= 7.7 Hz), 7.67 (1H, t, *J*= 6.9 Hz), 7.57 (2H, dd, *J*= 6.9, 7.7 Hz), 4.97 (1H, t, *J*= 3.6 Hz), 3.95-3.79 (4H, m), 3.31-3.14 (2H, m), 2.13-2.03 (2H, m).

2-[2-(Phenylsulfonyl)ethyl]-1,4-dioxane (**8d**) [7b]: ^{1}H-NMR (300 MHz): δ 7.91 (2H, br d, *J*= 7.7 Hz), 7.67 (1H, br t, *J*= 6.9 Hz), 7.58 (2H, dd, *J*= 6.9, 7.7 Hz), 3.73-3.08 (9H, m), 1.90-1.66 (2H, m).

General Procedure for Addition of Cyclic Ethers to Unsaturated Ester (**9**). *A Typical Example: Diethyl (Tetrahydrofuran-2-yl)succinate* (**10a**) *(Table 2, Entry 1).*

To a stirred suspension of *tert*-butylperoxy-λ^3-iodane **1** (50 mg, 0.15 mmol) in THF (1.5 mL) was added diethyl fumarate (*E*)-(**9**) (26 mg, 0.15 mmol) at room temperature under argon and the mixture was heated at 50 °C for 24 h. The reaction was quenched by addition of a 5% aqueous K$_2$CO$_3$ solution and the mixture was extracted with diethyl ether. The combined organic extracts were washed with water and brine, dried over anhydrous Na$_2$SO$_4$, and concentrated *in vacuo* to give an oil, which was purified by preparative TLC (hexane-ethyl acetate 6:4) to give the ester **10a** (17.2 mg, 47%) as a 1:1 mixture of diastereoisomers (as determined by analytical GC) [6]. Ester **10a** with a larger Rf value: ^{1}H-NMR (300 MHz): δ 4.17 (2H, q, *J*= 6.9 Hz), 4.13 (2H, q, *J*= 6.9 Hz), 4.00 (1H, q, *J*= 6.9 Hz),

3.87-3.67 (2H, m), 2.93-2.86 (1H, m), 2.78 (1H, dd, J= 8.8, 16.5 Hz), 2.69 (1H, dd, *J*= 5.2, 16.5 Hz), 2.07-1.67 (4H, m), 1.27 (3H, t, *J*= 6.9 Hz), 1.24 (3H, t, *J*= 6.9 Hz). Ester **10a** with a smaller Rf value: ^{1}H-NMR (300 MHz): δ 4.19 (2H, q, *J*= 6.9 Hz), 4.13 (2H, q, *J*= 6.9 Hz), 4.12-4.02 (1H, m), 3.92-3.81 (1H, m), 3.79-3.68 (1H, m), 3.13-3.03 (1H, m), 2.75 (1H, dd, *J*= 9.6, 16.5 Hz), 2.47 (1H, dd, *J*= 4.1, 16.5 Hz), 2.0-1.81 (3H, m), 1.73-1.61 (1H, m), 1.27 (3H, t, J= 6.9 Hz), 1.25 (3H, t, J= 6.9 Hz).

Diethyl (1,3-Dioxolan-2-yl)succinate (**10b**) [10a]: ^{1}H-NMR (300 MHz): δ 5.21 (1H, d, *J*= 3.9 Hz), 4.21 (2H, q, *J*= 6.9 Hz), 4.14 (2H, q, *J*= 6.9 Hz), 4.05-3.84 (4H, m), 3.23 (1H, dt, *J*= 9.4, 3.9 Hz), 2.78 (1H, dd, *J*= 9.4, 17.1 Hz), 2.61 (1H, dd, *J*= 3.9, 17.1 Hz), 1.28 (3H, t, *J*= 6.9 Hz), 1.26 (3H, t, *J*= 6.9 Hz).

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