

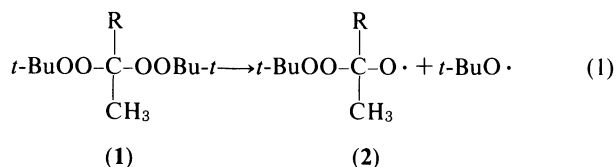
Simultaneous Generation of *t*-BuO· and *t*-BuOO· from the Decomposition of 2,2-Bis(*t*-butyldioxy)propane. A New Synthetic Method for Introducing a *t*-BuOO Group into Organic Molecules

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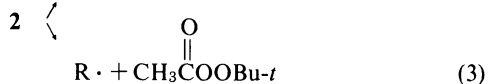
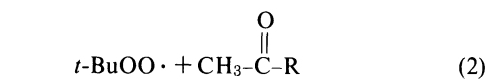
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A free-radical synthetic method for introducing a *t*-BuOO group into various organic substrates has been developed using 2,2-bis(*t*-butyldioxy)propane (**1a**) which can efficiently give two oxygen-centered radicals, *t*-BuO· and *t*-BuOO·, by thermolysis. The thermal reaction of **1a** with cumene afforded the desired dialkyl peroxide, *t*-butyl 1-methyl-1-phenylethyl peroxide, in good yield (53% based on **1a** reacted) together with an appreciable amount of a dimer, 2,3-dimethyl-2,3-diphenylbutane, as a by-product. The addition of *t*-BuOOH increased the yield of the dialkyl peroxide to as high as 82%, by suppressing the dimer formation (<10%). Also, reaction with isobutyronitrile and isopropyl methyl ketone gave good yields of dialkyl peroxides. The present method makes it possible to prepare unsymmetrical dialkyl peroxides containing functional groups, if the substrates are good hydrogen donors.

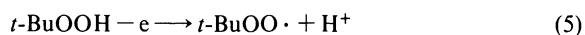
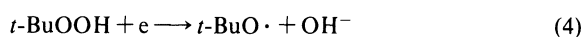
Recently, we reported a series of studies on the thermolysis mechanism of 2,2-bis(*t*-butyldioxy)alkanes (**1**) in various solvents.^{1–3} It was shown that the thermolysis of **1** proceeds stepwise and 1-(*t*-butyldioxy)alkoxy radicals (**2**) resulting from an O–O homolysis of **1** undergo facile β -scission. The rate of β -scission of **2** significantly depended on the substituent R in **1**. For example, the relative rates of β -scission of **2** to form radicals were *i*-Pr:Et:*t*-BuOO:Me=133:33:7:1 in cumene at 100 °C.² The facile formation of *t*-BuOO relative to Me indicates that the thermolysis of 2,2-bis(*t*-butyldioxy)propane (**1a**) proceeds mainly by Eqs. 1 and 2 along with a minor contribution by Eq. 3.



R=Me(**1a**), Et, *i*-Pr

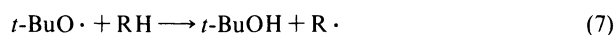
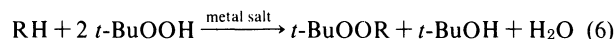


The thermolysis of **1a** is interesting in that two oxygen-centered radicals (i.e., *t*-BuO· and *t*-BuOO·) can be generated almost quantitatively from one molecule of **1a**. Participation of the two radicals reminded us of the redox reactions of *t*-BuOOH (Eqs. 4 and 5). Kharasch et al.⁴ applied this redox reaction to



introduction of a *t*-BuOO group into a variety of organic molecules using metal salts as a catalyst (Eq. 6). Two free-radical reactions of *t*-BuO· and *t*-BuOO·

participate in the *t*-BuOO introduction processes, that is, hydrogen abstraction from substrates (RH) by *t*-BuO· (Eq. 7) followed by the combination of *t*-BuOO· and R· (Eq. 8).



We expected that such reactions could be accomplished by the use of the single precursor **1a** instead of the combined use of *t*-BuOOH and a metal salt, since the thermolysis of **1a** can give the two oxygen-centered radicals at the same time. In the present paper, we report a new synthetic method for introducing a *t*-BuOO group into various organic molecules using **1a** as a precursor of the free radicals.

Results and Discussion

The reaction of **1a** with cumene was carried out at 120 °C under nitrogen. *t*-Butyl 1-methyl-1-phenylethyl peroxide (**3a**) and 2,3-dimethyl-2,3-diphenylbutane (**3b**) were obtained as major reaction products. Concentration changes of **3a**, **3b**, and the starting material **1a** with reaction time are shown in Fig. 1. While dehydro dimer **3b** increased with reaction time, the amount of peroxide **3a** reached a plateau at 4 h before **1a** decomposed completely. This was because **3** was slightly unstable under the present conditions. So, a reaction time of 2 h (about 50% conversion of **1a**) is suitable for obtaining highly selective dialkyl peroxides. Reactions with other alkylbenzenes (i.e., toluene and ethylbenzene) possessing benzylic hydrogens were carried out at 120 °C for 2 h. The desired dialkyl peroxides were obtained in good yields (50–65%), but appreciable amounts of the corresponding dehydro dimers were also produced (Table 1). Although acetone, *t*-butyl alcohol, and *t*-butyl peracetate due to the decomposition of

Table 1. Introduction of a *t*-BuOO Group into Alkylbenzenes with Benzylic Hydrogens^{a)}

Substrate	[<i>t</i> -BuOOH] ^{b)} M	Product yield ^{c)}			
		Dialkyl peroxide (%)		Dimer (%)	
PhCH ₃	0	PhCH ₂ OOBu ^t	(63)	[PhCH ₂ -] ₂	(22)
PhCH ₂ CH ₃	0	Ph(CH ₃)CHOOBu ^t	(53)	[Ph(CH ₃)CH-] ₂	(32)
PhCH(CH ₃) ₂	0	Ph(CH ₃) ₂ COOBu ^t	(53)	[Ph(CH ₃) ₂ C-] ₂	(32)
	0.05	(3a)	(76)	(3b)	(15)
	0.10		(82)		(9)

a) The reactions were carried out with 0.1 M of **1a** in substrates at 120 °C for 2 h under nitrogen. The conversion of **1a** for each reaction was about 50%. b) Concentrations of *t*-BuOOH added.

c) Values in parentheses are product yields (mol %) based on reacted **1a**. Yields were determined by GLC with authentic samples.

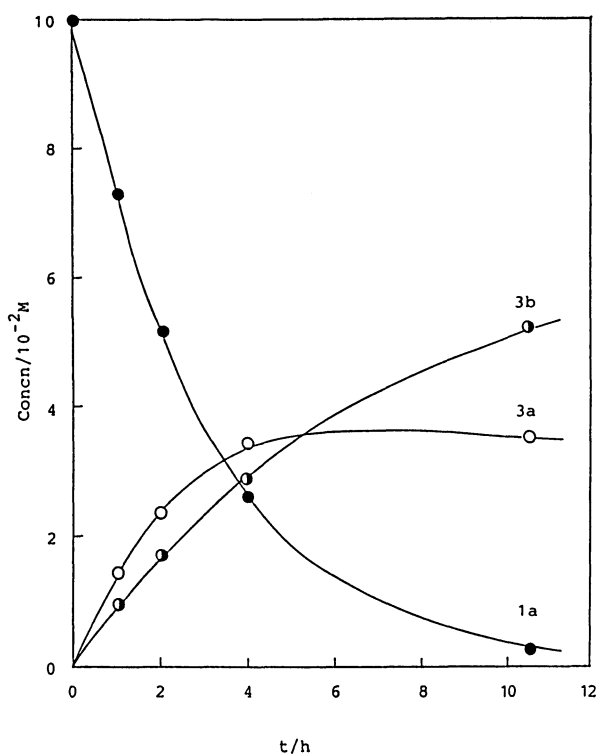


Fig. 1. Concentration changes of **3a**, **3b**, and **1a** with reaction time for the reaction with cumene at 120 °C. O: *t*-butyl 1-methyl-1-phenylethyl peroxide (**3a**), ●: 2,3-dimethyl-2,3-diphenylbutane (**3b**), ●: 2,2-bis(*t*-butyldioxy)propane (**1a**)

1a were also included in the reaction mixture, these products and **1a** were volatile enough to be removed easily by evaporation.

The reaction with cumene was also carried out in the presence of *t*-BuOOH in order to reduce the formation of dimer **3b**. Scaiano et al.⁵⁾ reported the absolute rate constants for hydrogen abstraction from *t*-BuOOH and cumene by *t*-BuO· to be 2.5×10^8 and 8.7×10^5 M⁻¹s⁻¹, respectively, at 21 ± 2 °C. The larger value for *t*-BuOOH indicates that the addition of even a small amount of *t*-BuOOH can increase the concentration of *t*-BuOO· and makes the cross-coupling of *t*-BuOO· and R· prevail over the self-coupling of R·. The effect

of added *t*-BuOOH on the reaction with cumene is shown in Table 1. The addition of 0.1 M (1 M = 1 mol dm⁻³) of *t*-BuOOH increased the yield of dialkyl peroxide up to as high as 82%, by suppressing dimer formation (<10%). Thus, it was demonstrated that the addition of *t*-BuOOH lead to a successful preparation of dialkyl peroxides.

We further attempted to introduce a *t*-BuOO group into various substrates such as isobutyronitrile, isopropyl methyl ketone, and 1,4-dioxane. The results are listed in Table 2. The highly selective introduction of *t*-BuOO was achieved for isobutyronitrile and isopropyl methyl ketone to yield 2-(*t*-butyldioxy)-2-methylpropanenitrile (**4a**) and 3-(*t*-butyldioxy)-3-methyl-2-butanone (**5a**), respectively. The high selectivity is interpreted in terms of the high reactivity of *t*-BuO· toward the tertiary carbon-hydrogen bond adjacent to the functional groups.⁶⁾

The reaction with 1,4-dioxane was expected to yield a dialkyl peroxide retaining the dioxane ring, that is, 2-(*t*-butyldioxy)-1,4-dioxane (**6**). However, the major reaction products were ring-opened dialkyl peroxide (**9a**) and bi-1,4-dioxane (**9b**). Probably, initially-formed **6** decomposes to alkoxyl radicals by O-O homolysis (Eq. 9) because of the thermal instability under the present conditions, and the resulting cycloalkoxyl radical (**7**) is readily converted to the more stable ring-opened radical (**8**) by β -scission (Eq. 10). Ultimately, the coupling of **8** and *t*-BuOO· affords the ring-opened dialkyl peroxide **9a** (Eq. 11). The β -scission of **7** is likely since five- or six-membered cycloalkoxyl radicals with ring strain are known to undergo facile β -scission leading to ring-opened radicals.⁷⁾

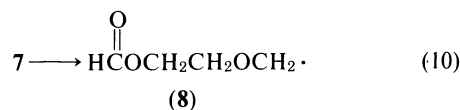
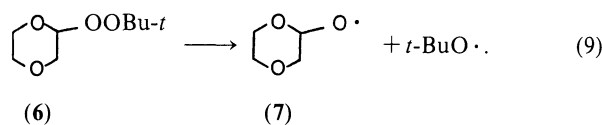


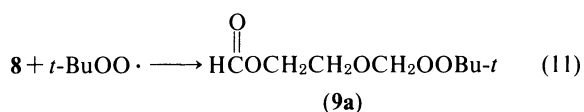


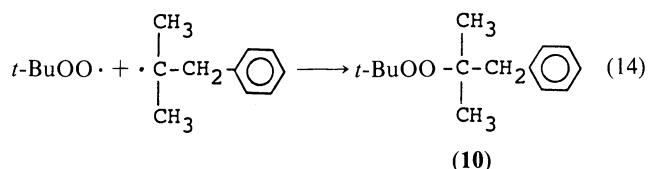
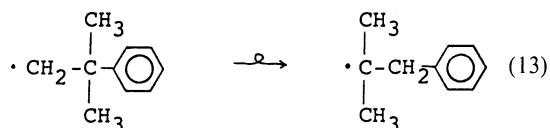
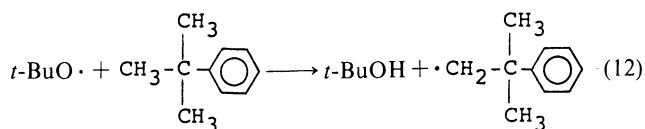
Table 2. Introduction of a *t*-BuOO Group into Substrates with Various Functional Groups^{a)}

Substrate	[<i>t</i> -BuOOH] ^{b)} M	Product yield ^{c)}		
		Dialkyl peroxide (%)		Dimer (%)
(CH ₃) ₂ CHCN	0	(CH ₃) ₂ C(CN)OOBu ^t (4a)	(49)	[(CH ₃) ₂ C(CN)-] ₂ (4b) (20)
	0.1		(77)	(6)
CH ₃ C(=O)CH(CH ₃) ₂	0.05	CH ₃ C(=O)C(CH ₃) ₂ OOBu ^t (5a)	(54)	[(CH ₃ C(=O)C(CH ₃) ₂)-] ₂ (5b) (26)
	0.05	HCOCH ₂ CH ₂ OCH ₂ OOBu ^t (9a)	(44)	[] ₂ (14) ^{d)} (9b)
PhC(CH ₃) ₃	0.05	PhCH ₂ C(CH ₃) ₂ OOBu ^t (10)	(7)	(e)

a) The reactions were carried out with 0.1 M of **1a** in substrates at 120 °C for 2 h under nitrogen. The conversion of **1a** for each reaction was about 50%. b) Concentrations of *t*-BuOOH added. c) Values in parentheses are product yields (mol%) based on reacted **1a**. Yields were determined by GLC, using isolated products as authentic samples. d) Total yield of *meso* and *dl* forms (*meso*/*dl*=1:1). e) Not determined.



In the case of *t*-butylbenzene, the formation of several reaction products was confirmed by GLC analysis, but the amount of each product was quite small. One major product among them was isolated and identified as *t*-butyl 1,1-dimethylphenethyl peroxide (**10**). The formation process of **10** may include the "neophyl rearrangement"⁸⁾ of the 2,2-dimethylphenethyl radical that was primarily formed by hydrogen abstraction by *t*-BuO[•] from *t*-butylbenzene (Eqs. 12 and 13). This rearrangement has been used as a free-radical clock and the activation parameters ($E_a=13.6$ kcal mol⁻¹, $A=10^{11.7}$ s⁻¹) were reported by Maillard and Ingold.⁹⁾ The absolute rate constant of 1.4×10^4 s⁻¹ at 120 °C can be calculated by extrapolation by using these parameters. In view of this relatively large value, it is reasonable that the 2,2-dimethylphenethyl radical undergoes neophyl rearrangement before it couples with *t*-BuOO[•].



Apparently, the yield of peroxide **10** was much lower than the yields of peroxides from the other substrates in this study. This is because *t*-BuO[•] can not abstract the primary hydrogen of *t*-butylbenzene efficiently. In principle, the present method for introduction of *t*-BuOO can be applied to substrates with a lower C-H bond energy whose hydrogens are easily abstracted by *t*-BuO[•].

The present reaction does not proceed catalytically like the redox reaction developed by Kharasch et al.⁴⁾ But our method without metal salts has some advantages. The post-treatment of catalysts is not needed and even substrates having functional groups sensitive to oxidation or reduction can be used if they are good hydrogen donors.

Experimental

IR and NMR spectra were recorded on JASCO A-3 and JEOL JNM-GSX270 spectrometers, respectively. GLC analyses were performed with a Shimadzu GC-14A gas chromatograph with a flame ionization detector using a 15 m flexible fused silica capillary column (0.53 mm in diameter) coated with silicone OV-1 or a column packed with SE-30 (20%). A Shimadzu Chromatopac C-R4A integrator was used for quantitative analyses. Mass spectra were obtained on a JEOL JMS-DX300 mass spectrometer by the EI or CI(methane) method. Preparative HPLC was carried out with a Shimadzu SPD-6A UV detector using a 20×250 mm ODS column. Wakogel C-200 was used for preparative column chromatography.

Materials. 2,2-Bis(*t*-butyldioxy)propane (**1a**) was prepared by the method previously described.²⁾

Toluene, ethylbenzene, cumene, and *t*-butylbenzene were purified by distillation after washing with concentrated sulfuric acid. The other substrates were purified by distillation.

Reaction Procedure. For all the reactions, one of the substrates was used as a reaction solvent. Reactions of **1a** with toluene, ethylbenzene, and cumene were carried out by

the following procedure. A 2 ml substrate solution containing 0.1 M of **1a** or a mixture of **1a** and *t*-BuOOH was placed in a glass ampoule. The ampoule was purged with nitrogen, sealed, and immersed in a constant temperature bath at 120 °C for 2 h. The reaction products were analyzed by GLC and/or GC-MS in comparison with authentic samples.

Likewise, reactions of isobutyronitrile, isopropyl methyl ketone, 1,4-dioxane, and *t*-butylbenzene were carried out in the presence of *t*-BuOOH. Yields of reaction products were determined by GLC using isolated products as authentic samples. Large scale (50 ml) reactions were carried out in order to isolate reaction products. After a given reaction time, low volatile materials were removed by evaporation under reduced pressure, and the remaining reaction products were isolated by column chromatography or preparative HPLC, and identified by the following analyses data.

2-(*t*-Butyldioxy)-2-methylpropanenitrile (4a): ¹H NMR (CDCl₃) δ=1.25(s, 9H) and 1.57(s, 6H); MS(70 eV) *m/z* 158(M⁺+1).

2,2,3,3-Tetramethylbutanedinitrile (4b): ¹H NMR (CDCl₃) δ=1.55(s); IR(KBr) 3000, 2950, 2900, 2350, 1470, 1390, and 1160 cm⁻¹; MS(70 eV) *m/z* 137(M⁺+1), 121, 94, and 69.

3-(*t*-Butyldioxy)-3-methyl-2-butanone (5a): ¹H NMR (CDCl₃) δ=1.23(s, 9H), 1.29(s, 6H), and 2.26(s, 3H); MS(70 eV) *m/z* 174(M⁺), 131, 73, and 57.

3,3,4,4-Tetramethyl-2,5-hexanedione (5b): ¹H NMR (CDCl₃) δ=1.22(s, 12H) and 2.18(s, 6H); MS(70 eV) *m/z* 170(M⁺) and 152.

2-[4-(*t*-Butyldioxy)methoxy] formate (9a): ¹H NMR (CDCl₃) δ=1.27(s, 9H), 3.80(t, *J*=4.3 Hz, 2H), 4.33(t, *J*=4.6 Hz, 2H), 4.81(s, 2H), and 8.09(s, 1H); ¹³C NMR (CDCl₃) δ=28.53(CH₃), 63.11(CH₂), 64.85(CH₂), 74.55(C), 89.96(CH₂), and 160.89 (C=O); IR(neat) 2950, 1725, 1367, 1180, 1052, and 1010 cm⁻¹; MS(Cl, methane) *m/z* 193 (M⁺+H).

2,2'-Bi-1,4-dioxane (9b): Two forms (*meso* and *dl*) of **9b**

were isolated. *meso* form: Mp 156—157 °C (lit.¹⁰) 157.5—158.0 °C; ¹H NMR (CDCl₃) δ=3.59—3.85(br); MS(70 eV) *m/z* 174(M⁺), 87, 73, and 59. *dl* form: Mp 131—132 °C (lit.¹⁰) 133.5—134.0 °C; ¹H NMR (CDCl₃) δ=3.40—3.90(br); MS(70 eV) *m/z* 174(M⁺), 87, 73, and 59.

***t*-Butyl 1,1-Dimethylphenethyl Peroxide (10):** ¹H NMR (CDCl₃) δ=1.16(s, 6H, CH₃), 1.23(s, 9H, *t*-Bu), 2.84(s, 2H, CH₂), and 7.24(m, 5H, Ph); MS(70 eV) *m/z* 222(M⁺), 149, 131, 91, and 73.

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