Registry No. 6-*p*-OCH_3, 115245-15-3; 6-*p*-CH_3, 115245-16-4; 6-*p*-H, 115269-71-1; 6-*p*-CF_3, 115245-17-5; 6-3,5-$(CF_3)_2$, 115245-18-6; **13**, 82638-98-0; **14**, 115245-19-7; **16**, 115245-20-0.

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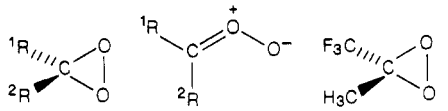
Received March 15, 1988

On the Isolation and Characterization of Methyl(trifluoromethyl)dioxirane

Summary: The title dioxirane **1f**, generated by the reaction of CF_3COCH_3 with potassium peroxomonosulfate, has been isolated and fully characterized spectroscopically; it displays a remarkable reactivity in oxygen transfer reactions.

Sir: Isolable[1] dioxirane species (the smallest ring peroxides containing carbon)[2] are known. As an alternative to steric stabilization effected by alkyl groups,[1-4] we wished to try "electronic stabilization", often exhibited by the trifluoromethyl group on highly strained compounds.[5] Dioxiranes **1** and their isomeric counterparts "carbonyl oxides" **2** have been shown to be involved as key intermediates in a number of oxidation processes.[6-8] Only recently, however, did it become possible to provide spectral data and reactivity tests that allow one to differentiate between these elusive entities.[1-4,9-11]



1 **2** **1f**

a, $^1R = {}^2R = H$; **b**, $^1R = {}^2R = CH_3$; **c**, $^1R = {}^2R = Ph$; **d**, $^1R = {}^2R = CF_3$; **e**, $^1R = Ph$, $^2R = CF_3$

The trifluoromethyl group can be expected to influence the stability of the small ring in several ways. For one, by drawing electron density from the negative oxygen pole toward the α-carbon, it would discourage formation of dipolar isomers **2**; then, any reaction that is initiated via carbon-oxygen bond rupture in **1**, e.g., dimerization to 1,2,4,5-tetraoxane ("ketone diperoxide"),[1] would be unfavored.

The title compound **1f** was synthesized by the known ketone/caroate method,[1-4] starting with trifluoroacetone (**3**).[12] In order to isolate the dioxirane, we followed a published procedure,[1,4] which was only slightly modified to suit the case at hand.[13] Thus, we were able to collect yellow solutions of **1f** in the parent ketone having concentrations ranging from 0.65 to 0.82 M.[14] This is over 6 times higher than the concentrations of dimethyldioxirane (**1b**) solutions usually attainable by using the same general procedure.[1-4]

The novel dioxirane has a UV absorption with λ_{max} 347 nm ($\epsilon \sim 9$, at 0 °C) that, characteristically,[1-4,10] tails into the visible to over 440 nm (hence its yellow color); it might be ascribed to n-π^* excitation.[2,15] Dioxiranes should not exhibit strong infrared bands;[11,15] however, in the difference IR spectrum (vapor phase) of **1f**, significant absorption could be located at 1259, 1189, 971 (w), 839 (w), 731 (w), and 669 (w) cm^{-1}.[16] By way of comparison, the difference IR spectrum of dioxirane **1e** (generated from $PhCCF_3$ via carbonyl oxide **2e** in oxygen-doped argon matrix) presents bands at 1213, 944, 720, 684, and 643 cm^{-1}.[11b] The salient NMR spectral data of **1f** are summarized in Table I; a comparison with those already reported for **1b** (and for **1d**) corroborates the dioxirane structure. Interestingly, **1d** (UV absorption with λ_{max} 306 nm, extending into the visible)[17] appears to have been generated by the reaction of fluorine gas with the dilithium or the monolithium salt of hexafluoroacetone hydrate, $(CF_3)_2C(OH)_2$.[17]

The yellow solutions of **1f** could be stored at -20 °C with only minor loss of dioxirane content (~6%, 48 h); the decrease in peroxide titer was ca. 30% during 120 h at 0 °C, while a half-life of ~20 h was estimated at 15 °C.[18] Thus, the stability of **1f** appears to be at least comparable to that of **1b**.[1,4] However, in contrast to the dimethyldioxirane case,[1] the loss of **1f** in solution does not lead to the formation of the corresponding ketone diperoxide dimer in any significant extent; rather, NMR analyses showed that the (exothermic) decomposition of **1f** yields mainly methyl trifluoroacetate (CF_3COOCH_3) and trifluoroacetic acid (the hydrolysis product of the latter).[19,20]

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(12) Commercial (Aldrich) 1,1,1-trifluoro-2-propanone: bp 22 °C; at -20 °C, pure liquid; ^1H NMR (Me_4Si) δ 2.44 (s); ^{19}F NMR ($CFCl_3$) δ -80.4 (s); $^{13}C(^1H)$ NMR (Me_4Si) δ 23.78 (s, CH_3), 117.1 (q, CF_3, ^1J = 291 Hz), 190.3 (q, $C{=}O$, ^2J = 36 Hz); ^{17}O NMR (H_2O, external) δ 577.7; IR (vapor) 1781 (C=O stretch), 1434, 1376, 1329, 1225, 1163, 1115, 1024, 968, 724, 614 cm^{-1}.
(13) Batch temperature 5-8 °C, no carrier gas, slight aspiration (water pump, 680-700 mmHg), spiral condenser cooled at -75 °C.
(14) Both iodometry and reaction with PhSMe (^1H NMR analysis) (cf. ref 4) were employed to estimate the dioxirane content of solutions, affording the same results within ±3%. The NMR spectra (Table I) indicated that **1f** was the only peroxide species present in solution.
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(16) Solutions of **1f** in trifluoroacetone (**3**) and, separately, the pure solvent were vaporized at 22 °C into an 8-cm gas-sampling cell (KBr windows) and FT IR spectra run on a Perkin-Elmer 1710 spectrophotometer; difference spectra were then obtained on a connected P.E. PC7350 data acquisition unit.
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(18) In order to obtain reproducible decomposition data, it is important that impurities and trace metals be carefully excluded (cf. ref 6).
(19) We find the following for methyl trifluoracetate (bp 43 °C): ^1H NMR (CF_3COCH_3, Me_4Si) δ 4.00; ^{19}F NMR (CF_3COCH_3, $CFCl_3$) δ -75.56. Trifluoroacetic acid: ^{19}F NMR (CF_3COCH_3, $CFCl_3$) δ -76.36.

0022-3263/88/1953-3890$01.50/0

Table I. NMR Chemical Shifts[a] of Some Dioxiranes $^1R^2RCO_2$

compd	^1R	^2R	temp, °C	^1H NMR	$^{13}C\{^1H\}$ NMR	^{19}F NMR [^{17}O NMR]	ref
1b	CH_3	CH_3	0	1.65 (s)	22.6 (CH_3)		1, 3, 4
					102.2 (>CO_2)	[302 (s)][b]	
1d	CF_3	CF_3	-		-	-76.8 (s)[c]	17
1f	CH_3	CF_3	-20	1.97 (s)	14.51 (CH_3)[d]		this
					97.32 (>CO_2)[d,e]	[297 (s)][g]	work[h]
					122.2 (CF_3)[d,f]	-81.5 (s)	

[a] Chemical shifts (δ) in parts per million are relative to Me_4Si for ^1H NMR (200 MHz) and for ^{13}C NMR (50.309 MHz, unless noted otherwise); in ^{17}O NMR (27.120 MHz, unless noted otherwise), chemical shifts were measured from external $Me_2C{=}O$ and referred to H_2O (cf. ref 3), while ^{19}F NMR (188.220 MHz) δ are relative to internal $CFCl_3$; a Varian XL200 instrument was employed. [b] $\Delta\nu_{1/2}$ = 113 Hz. [c] Compare $(CF_3)_2C{=}O$: ^{19}F NMR (MeCN, $CFCl_3$) δ -76.1 (Redwood, M. E.; Willis, C. J. *Can. J. Chem.* **1967**, *45*, 389-395). [d] At 100.577 MHz (Bruker AM400). [e] Quartet, J_{CCF} = 40.2 Hz. [f] Quartet, J_{CF} = 280.7 Hz. [g] At 54.227 MHz (Bruker AM400); $\Delta\nu_{1/2}$ = 270 Hz. [h] In all of the NMR experiments, it was verified that the resonance signals attributed to the dioxirane instantly disappear upon quenching of the reactive peroxide in solution with $PhSCH_3$ (cf. ref 4).

The screening of the reactivity presented by **1f** in selective oxidations of organic substrates has begun. We find that this dioxirane is able to perform the effective oxygen transfer reactions reported for dimethyldioxirane,[1] *but at a much higher rate.* For instance, phenanthrene could be converted by **1f** into the corresponding 9,10-oxide[1] efficiently (80% conversion, ≥93% yield) within just 5 min at -20 °C; by way of comparison, we observed that 50% conversion of the said arene into the same epoxide requires about 20 h at 22 °C by using **1b**.[21] As for alkene epoxidations, dioxirane **1f** reacts rapidly (ca. 1 min, at -20 °C) and in a completely stereospecific manner with *cis*-2-octene and *trans*-β-methylstyrene to form *cis*-2,3-epoxyoctane[22] and *trans*-β-methylstyrene oxide,[23] respectively (yield ≥90%).[21] Product isolation is attractively simple since trifluoroacetone (**3**) (the solvent and the reduction product of **1f**) is quite volatile. Efficient oxidations of saturated carbon C-H bonds can also be performed; as an example, cyclohexane reacts readily with dioxirane **1f** solutions at -20 °C by a 1:2 stoichiometry, yielding cyclohexanone (≥95% yield, 30 min).[21] Under similar conditions, during ca. 45 min, *n*-heptane is oxidized (30% conversion, ~95% yield) by **1f** to yield a mixture of 4-heptanone (20%), 3-heptanone (40%), and 2-heptanone (40%).[21]

We shall soon report in detail on more cases which will further illustrate the finding that, in performing selective oxidations, dioxirane **1f** is remarkably more reactive than dimethyldioxirane (**1b**). It is unlikely that this is due solely to solvent effects (i.e., trifluoroacetone (**3**) vs acetone). Rather, the considerable difference in acid strength existing between $(CF_3)(CH_3)C{=}O^+H$ (pK = -14.9) and $(CH_3)_2C{=}O^+H$ (pK = -7.6)[24] suggests that it should be ascribed to the better leaving-group ability of CF_3COCH_3 with respect to acetone (and to incipient charge separation in the transition state) during nucleophilic displacement at the dioxirane O-O bond (electrophilic oxidation).[6a] Then, it is perhaps not surprising that doxirane **1f** should be so "ripe"[25] for oxygen transfer to organic substrates.

Acknowledgment. This work was supported in part by the Ministry of Public Education of Italy (MPI 40). One of us (R.M.) was the recipient of an Accademia Nazionale "Lincei" fellowship, which was made available by Montefluos S.p.A. (Milan, Italy). Thanks are due to Prof. V. Lucchini (University of Venice, Italy) and to Dr. Song Shu-Zhong (Dalian Institute, Academia Sinica) for help in performing NMR and oxidation experiments, respectively.

(20) The decomposition kinetics of **1f** (iodometric titer) at 0 °C appears to follow a mixed first-order and second-order rate law; this suggests that the decomposition might also involve some oxygen production, i.e., $2\,\mathbf{1f} \rightarrow 2\,(CH_3)(CF_3)C{=}O + O_2$ (cf. ref 6).

(21) Reactions were monitored and product yields determined by GC (OV 101 or SE 30, 30 m × 0.25 μm i.d. capillary column, internal standard $CFCl_2CFCl_2$) or HPLC (reverse-phase, 10 μm C-18, 25 cm × 4.6 mm i.d. analytical column, MeCN/water or MeOH/water); the reaction products were identified upon comparison of their ^1H NMR and/or GC/MS (Hewlett-Packard 5970) spectra with those of authentic samples.

(22) Bp 70-72 °C (18 mmHg); ^1H NMR ($CDCl_3$, Me_4Si) δ 0.88 (t, 3 H, $CH_3(CH_2)_4$, J = 6 Hz), 1.25 (d, 3 H, $OCHCH_3$, J = 5.5 Hz), 1.26-1.48 (m, 8 H, $(CH_2)_4$), 2.87 (complex m, 1 H, $C_5H_{11}CHO$), 3.02 (d of q, 1 H, $CHOCHCH_3$, J_{HCH_3} = 5.5, J_{HH}(cis) = 4.3 Hz).

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(25) Our group has given this reactive species the laboratory name of Mello ("mellow") dioxirane.

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Received April 1, 1988

Enzymic Regioselectivity in the Hydroxylation of Cholesterol Catalyzed by a Membrane-Spanning Metalloporphyrin

Summary: The hydroxylation of simple alkanes and the selective C-25 hydroxylation of cholesterol have been achieved with a membrane-spanning Mn(III) porphyrin positioned in a synthetic bilayer assembly by appended steroidal substituents.

Sir: Cytochrome P-450 enzymes occur widely in nature and function as the monooxygenation catalysts of many lipophilic compounds. Among the oxidations this enzyme catalyzes, perhaps the most unique is the hydroxylation of saturated hydrocarbons. This reaction is important in the conversion of natural substrates such as cholesterol to corticosteroids and in the hydrophilization of foreign compounds such as petroleum products.[1] It has been shown in recent years that synthetic iron(III) and manganese(III) porphyrins are capable of mimicking the hydroxylation activity of the natural enzyme.[2,3] Although

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