

Figure 1. Phthaloyl peroxide matrix isolated in argon at 8°K before irradiation.

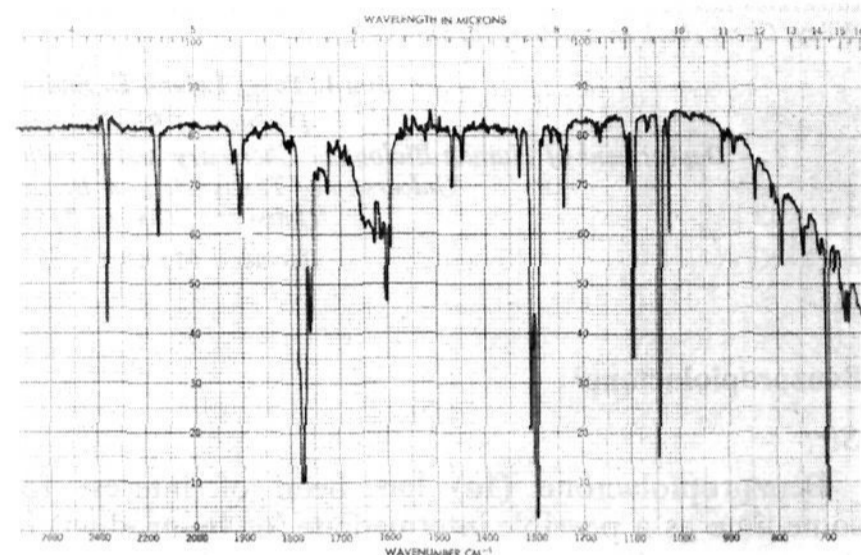
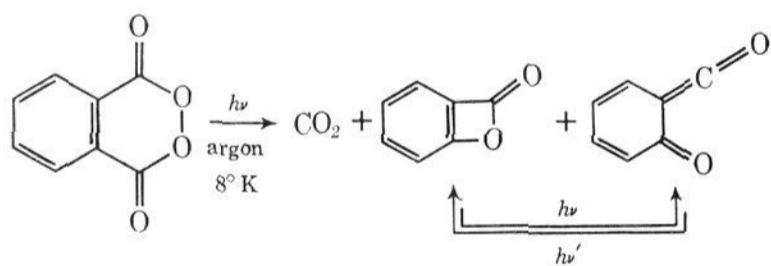


Figure 2. Phthaloyl peroxide matrix isolated in argon at 8°K after irradiation with light of wavelength $>3400 \text{ \AA}$.

Irradiation ($>3400 \text{ \AA}$) of phthaloyl peroxide matrix isolated in argon at 8°K gives rise to bands (Figure 2) characteristic of carbon dioxide ($2340, 665 \text{ cm}^{-1}$), the ketoketene ($2139, 1650 \text{ cm}^{-1}$), and a new species with carbonyl absorption at 1904 cm^{-1} . All three products



are primary products within the limits of our detection. The ratio of the ketoketene to the new species depends strongly on the wavelength of the light used in the irradiation. Long wavelength ($>3400 \text{ \AA}$) light favors the 1904-cm^{-1} species and shorter wavelength ($>3150 \text{ \AA}$) light favors the ketoketene. The wavelength dependence is a consequence of the photochemical interconversion of the ketoketene and the 1904-cm^{-1} species. Light of sufficiently short wavelength converts essentially all of the 1904-cm^{-1} species to the ketoketene. Conversely, irradiation of the ketoketene with long wavelength light regenerates the 1904-cm^{-1} species. Irradiation ($>3150 \text{ \AA}$) of phthaloyl peroxide in a matrix which contains methanol gives the ketoketene (Figure 3). Warming causes concurrent loss of the ketoketene bands and appearance of bands character-

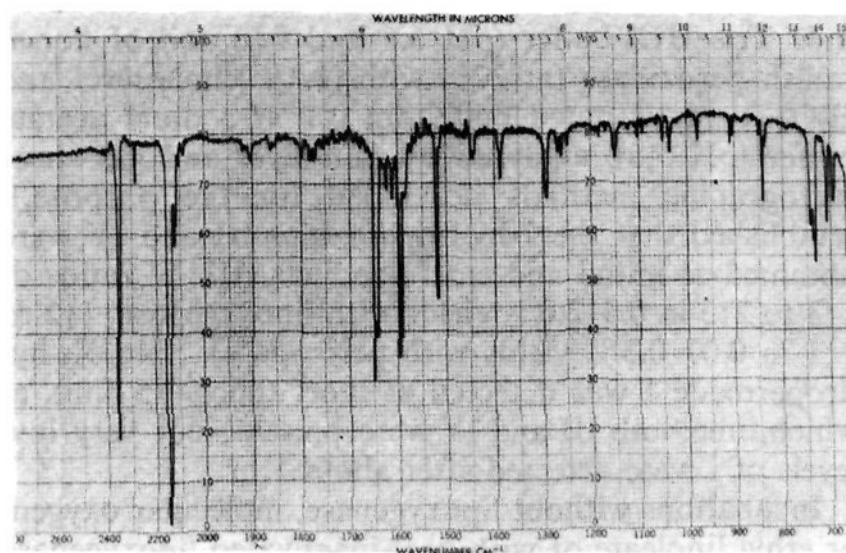


Figure 3. Phthaloyl peroxide matrix isolated in argon at 8°K after irradiation with light of wavelength $>3150 \text{ \AA}$.

istic of methyl salicylate. This observation firmly identifies the ketoketene. The photochemical interconversion of the ketoketene and the 1904-cm^{-1} species leads us to conclude that the 1904-cm^{-1} species is the elusive benzpropiolactone (1a). Attempts to define the thermal chemistry of benzpropiolactone have been uniformly unsuccessful.

Acknowledgment. This research was supported in part by Grant GP-28152X from the National Science Foundation and by the donors of the Petroleum Research Fund, administered by the American Chemical Society. The authors are indebted to Professor J. Michl for informing us of his results prior to publication.

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Received November 3, 1972

Intramolecular Oxidative Coupling of Monophenolic Benzylisoquinolines. Quinonoid Oxoaporphines¹

Sir:

Oxidative cyclization of benzyltetrahydroisoquinolines has long been considered as a biogenetic route to aporphine alkaloids.² In 1957, Barton and Cohen³ suggested that phenolic oxidation of diphenolic benzyltetrahydroisoquinoline precursors may generate the bond between the aporphine rings A and D, and this proposal has been amply supported by the results of numerous subsequent biosynthetic and synthetic studies.^{4,5} We wish to report herewith a second oxidative route, efficient intramolecular coupling of monophen-

(1) This investigation was supported by a grant from the National Cancer Institute (CA-12059).

(2) R. Robinson, "The Structural Relations of Natural Products," Clarendon, Oxford, 1955, and numerous earlier references cited therein.

(3) D. H. R. Barton and T. Cohen in "Festschrift A. Stoll," Birkhäuser, Basel, 1957, p 117.

(4) A. R. Battersby in "Oxidative Coupling of Phenols," W. I. Taylor and A. R. Battersby, Ed., Marcel Dekker, New York, N. Y., 1967.

(5) T. Kametani and K. Fukumoto, *Synthesis*, 657 (1972).

olic benzyloquinolines such as **1** to novel quinonoid oxoaporphines such as **5**.⁶

Quinonoid oxoaporphine **5** was first encountered as the unexpected product of a classical cyclization. Having demonstrated the advantageous effect of a phenolic group upon Pschorr ring closure of 1-(2'-aminobenzyl)-1,2,3,4-tetrahydro-2-methylisoquinolines,⁷ we examined the cyclization of the corresponding phenolic benzyloquinoline derivatives. Treatment with copper powder of the diazonium salt prepared *in situ* after acid hydrolysis of the acetate ester **3** (mp 79–81°)^{8–10} yielded the oxoaporphine **5** (orange needles, 55% from **3**): mp 236–238°; uv $\lambda_{\text{max}}^{\text{EtOH}}$ (ϵ) 231 (37,000), 246 (sh) (27,000), 274 (sh) (15,000), 284 (sh) (13,000), 295 (sh) (10,500), 406 (9500), 462 (8000) nm; ir $\lambda_{\text{max}}^{\text{KBr}}$: 6.14, 6.67, 6.97, 7.72, 7.90, 8.16, 8.93, 9.10 μ ; nmr (CF_3COOH) δ 9.02 (s, *H*-11), 8.52 (d, *J* = 6 Hz, *H*-5), 8.50 (s, *H*-7), 7.63 (d, *J* = 6 Hz, *H*-4), 7.00 (s, 1 H, ArH), 6.72 (s, 1 H, ArH), 3.74, 3.69, 3.68 (3-OCH₃); mass spectrum *m/e* (%) 321 (70, M⁺), 290 (100). It is probable that **4**, the expected product, is transient in this reaction and suffers immediate aerial oxidation, initiated by abstraction of a hydrogen atom from the methylene carbon of ring C, to the fully conjugated, planar product, **5**.^{11–13}

During routine examination of intermediates on analytical silica gel plates sprayed with 3% ceric sulfate in 3 *N* sulfuric acid as a visualizing aid, we were surprised to observe that the phenol **1** developed an orange-red coloration reminiscent of the quinonoid oxoaporphine **5**. Indeed, in a subsequent preparative experiment, conducted at 0° by adding **1** to ceric sulfate (4 mol equiv) in 10% sulfuric acid, **5** was isolated in 25% yield. The remarkable facility with which this novel cyclization occurred was further demonstrated by the variety of oxidants found to promote coupling,¹⁴ resulting in yields of **5** of up to 62% (Table I).

Trifluoroacetic acid was found to be a valuable medium for carrying out these oxidations, particularly where moisture-sensitive oxidants were involved. In a representative experiment, VOF₃ (2.7 g, 22 mmol) was added to a solution of **1** (0.975 g, 3 mmol) in trifluoroacetic acid (30 ml) at 0° and protected from moisture. After 3 hr stirring the mixture showed negligible amounts of **1** (tlc on alumina) and was poured into cold water (60 ml) containing citric acid (10 g, to reduce excess oxidant and to complex metal ions during subsequent basification). Basification (5% NH₄OH) and extraction with CHCl₃ until no further

(6) A parallel sequence from the appropriate precursors has yielded the C-9,10-dioxymethylene analog, mp 255° dec, and the corresponding products (±)-nordomesticine, mp 204–206°, and (±)-domesticine.

(7) S. M. Kupchan, V. Kameswaran, and J. W. A. Findlay, *J. Org. Chem.*, **38**, 405 (1973).

(8) All new compounds were characterized by concordant analytical and ir, uv, nmr, and mass spectral data.

(9) Compound **3** was prepared by acetylation of **1**,¹⁰ followed by nitration *in situ* to **2**, mp 203–205°, and reduction (Pd/C).

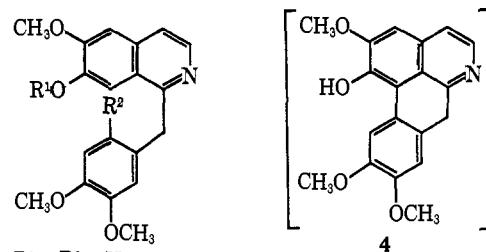
(10) E. Brochmann-Hanssen and K. Hirai, *J. Pharm. Sci.*, **57**, 940 (1968).

(11) Cf. M. P. Cava and I. Noguchi, *J. Org. Chem.*, **38**, 61 (1973).

(12) Catalytic reduction of **5** gave (±)-wilsonirine (**6**),¹³ mp 202–204° dec, and methylation (NaBH₄-CH₂O) of **6** afforded (±)-thalicmidine (**7**).⁷

(13) K. C. Stuart and C. Chambers, *Tetrahedron Lett.*, **42**, 4135 (1967).

(14) For recent examples of the usefulness of these reagents in oxidative coupling of diphenols, see, e.g., M. A. Schwartz, R. A. Holton, and S. W. Scott, *J. Amer. Chem. Soc.*, **91**, 2800 (1969); M. A. Schwartz and R. A. Holton, *ibid.*, **92**, 1090 (1970); and ref 5.



- 1, R¹ = R² = H
2, R¹ = COCH₃; R² = NO₂
3, R¹ = COCH₃; R² = NH₂

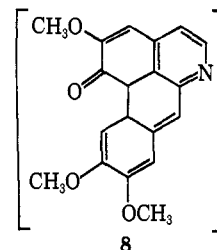
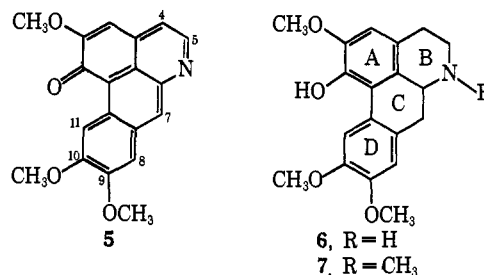


Table I

Oxidant	Medium	Yield, % of 5
Ce(SO ₄) ₂	10% aq H ₂ SO ₄ ^a	25
Co(OH) ₃	10% aq H ₂ SO ₄ ^b	15
MnO ₂	CF ₃ COOH ^a	30
CrO ₃	Aq H ₂ SO ₄ -HOAc ^a	25
Tl(CF ₃ COO) ₃	CF ₃ COOH ^b	12
Pb ₂ O ₄	CF ₃ COOH ^a	22
VOF ₃	CF ₃ COOH ^a	59
MoOCl ₄	CF ₃ COOH-CHCl ₃ ^b	62

^a 0°. ^b 25°.

color was apparent in the extract, followed by concentration and filtration of the CHCl₃ extract through a column of alumina, afforded **5** in 59% yield.

Among the useful reagents are recognized both one-electron and two-electron transfer oxidants, as well as some reagents of variable characteristics. These observations render difficult firm conclusions concerning the mechanism.¹⁵ The reaction may proceed by abstraction of hydrogen atoms from the activated diarylmethylene function and the phenolic hydroxyl group to yield an intermediate such as **8**, and subsequent further oxidation to **5**. However, alternative mechanisms cannot be precluded.

The smooth intramolecular oxidative coupling of monophenolic benzyloquinolines contrasts notably with the results of most prior studies of oxidative

(15) Thallium(III) trifluoroacetate has recently been used in a two-electron oxidation which gave rise to intramolecular phenol-aryl ether coupling, apparently *via* a phenoxonium ion: M. A. Schwartz, B. F. Rose, and B. Vishnurajala, *J. Amer. Chem. Soc.*, **95**, 612 (1973).

cyclization of diphenolic benzyltetrahydroisoquinoline derivatives.^{4,5} Investigations are in progress to determine the possible implications of these observations for aporphine alkaloid biosynthesis and for intermolecular oxidative coupling.

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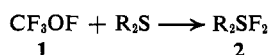
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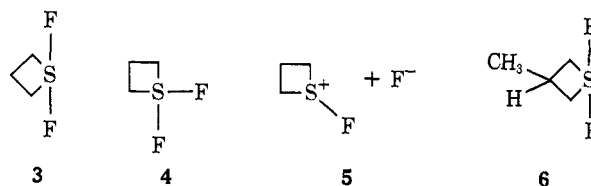
Alkyl and Aryl Difluorosulfuranes¹

Sir:

There has been considerable interest in sulfuranes in the past few years. Several have been isolated and a number have been postulated as reaction intermediates.² Despite this interest little is known about simple aliphatic sulfuranes with α protons. In fact there is only one report of the preparation of such a material, $\text{CH}_3\text{-CH}_2\text{CH}_2\text{CHFSF}_3$.^{2h} It has now been found that reaction of trifluoromethyl hypofluorite (1) with sulfides at low temperatures yields difluorosulfuranes, 2. ¹⁹F nmr studies of these difluorosulfuranes have provided significant structural information and have indicated that they undergo ionization under some conditions. Ionization can be inhibited by neutralizing acid which is formed during the preparation of the sulfuranes.



Reaction of trimethylene sulfide with 1 in methylene chloride at -78° yielded a solution to which was added solid calcium hydride.³ The sample was allowed to warm with agitation. Gas was evolved. The sample was cooled and then allowed to warm several times until no more gas was evolved. The ¹⁹F nmr spectrum showed one major absorption at $+5.76$ ppm relative to fluorotrichloromethane. The ¹H nmr spectrum of another sample at -78° showed two broad absorptions at δ 3.85 and 3.58 in the ratio of *ca.* 2:1. A reaction mixture was hydrolyzed with aqueous bicarbonate solution to give trimethylene sulfoxide, *ca.* 60%, which was identified by glpc, ¹H nmr, and infrared spectroscopy. The results strongly suggest that the difluoro-sulfurane, 3, is the species present in solution. The finding that the fluorines are equivalent on the nmr time scale is in accord with structure 3; however, 4 can



also account for the results if equatorial-apical switching "pseudorotation" is occurring. Finally fast ionization, 5, could account for the equivalency. A choice was made between these possibilities by allowing 3-methylthiacyclobutane⁴ to react with 1 at -78° . The ¹⁹F nmr spectrum after calcium hydride treatment showed two doublets at $\delta -7.03$ and $+16.3$, $J_{\text{F-S-F}} = 167$ Hz. Structure 6 uniquely meets the requirements of two nonequivalent fluorines coupled to each other. A "pseudorotating" structure, 4, with the added methyl group would have given two singlets. There would have been two diastereoisomers if equatorial-apical switching of fluorines and the ring was occurring. Rapid ionization would have led to equivalent fluorines or two noncoupled nonequivalent fluorines. Finally it should be noted that 6 is not pseudorotating rapidly at -78° . The ¹H nmr spectrum of 6 was in agreement with the assigned structure; a doublet for the absorptions of the hydrogens of the methyl group was found at δ 1.46, $J_{\text{HCH}} = 5$ Hz, and two other complex absorptions were found at δ 3.5 and 4.0. Hydrolysis afforded a mixture of the *cis* and *trans* sulfoxides in high yield.⁵

The ¹⁹F nmr spectrum of 6 varied with solvent and reaction conditions. For example, in methylene chloride with no treatment to remove acid, there was found two broad absorptions at -80° centered at $\delta -2.6$ and $+19.1$. When 6 was prepared in methylene chloride-trichlorofluoromethane (1:1), the ¹⁹F nmr spectrum at -80° showed two poorly resolved doublets at δ 5.3 and $+17.5$. Addition of trimethyl-*N,N*-diethylaminosilane changed the spectrum to two well resolved doublets as was found with the calcium hydride treated reaction mixture. In another experiment 6 was prepared in a solvent mixture which was primarily trichlorofluoromethane. The ¹⁹F nmr spectrum at -80° showed fairly well resolved doublets; on warming to higher temperatures, *ca.* -40 to -20° , the doublets collapsed into "mound-like" absorptions. These experiments suggest that ionization of 6 can occur. No evidence for pseudorotation has been found; however, it cannot be excluded. Other workers have not found pseudorotation in similar compounds.^{2a,e,o,p}

Tetrahydrothiophene (7), di-*n*-propyl sulfide (8), diphenyl sulfide (9), and perfluorodiphenyl sulfide (10) have been allowed to react with 1 at -78° . Hydrolysis of the reaction mixtures from 7, 8, and 9 led to isolation of the corresponding sulfoxides, and in the case of 8 substantial amounts of sulfone was isolated which suggests that some $(\text{CH}_3\text{CH}_2\text{CH}_2)_2\text{SF}_4$ was formed. The ¹⁹F nmr spectrum also suggested that this compound was present. The sulfuranes from 7 and 8 were much less thermally stable than 3 and 6 and they also underwent intermolecular fluorine exchange to much lower temperatures than did 3 and 6. As might have been expected the sulfuranes from 9 and 10 were relatively stable. The product from 10, *i.e.*, 11, had absorptions

(1) This research has been supported by the National Science Foundation and by a Public Health Service Research Grant No. CA-10737 from the National Cancer Institute.

(2) (a) R. J. Arhart and J. C. Martin, *J. Amer. Chem. Soc.*, **94**, 4997 (1972). (b) R. J. Arhart and J. C. Martin, *ibid.*, **94**, 5003 (1972). (c) I. C. Paul, J. C. Martin, and E. F. Perozzi, *ibid.*, **94**, 5010 (1972). (d) J. I. Musher, *Advan. Chem. Ser.*, No. 110, 44 (1972). (e) D. T. Sauer and J. M. Shreeve, *J. Fluorine Chem.*, **1**, 1, 1971. (f) R. W. La Rochelle and B. M. Trost, *J. Amer. Chem. Soc.*, **93**, 6077 (1971). (g) C. R. Johnson and J. J. Rigan, *ibid.*, **91**, 5398 (1969). (h) W. A. Sheppard, *ibid.*, **84**, 3058 (1962). (i) W. A. Sheppard, *ibid.*, 5597 (1971). (j) I. Kapovitz and A. Kalman, *Chem. Commun.*, 649 (1971). (k) D. Harrington, J. Weston, J. Jacobus and K. Mislow, *J. Chem. Soc., Chem. Commun.*, 1079 (1972). (l) D. C. Owskey, G. K. Helmkamp, and R. F. Rettig, *J. Amer. Chem. Soc.*, **91**, 5239 (1969). (m) G. E. Wilson, Jr., and M. M. Yang Chang, *Tetrahedron Lett.*, 875 (1971). (n) D. Swern, I. Ikeda, and G. F. Whitfield, *ibid.*, 2635 (1972). (o) W. A. Sheppard and D. W. Ovenall, *Org. Magn. Resonance*, **4**, 695 (1972). (p) D. G. Ibbott and A. F. Janzen, *Can. J. Chem.*, **50**, 2428 (1972).

(3) The use of calcium hydride and the alternate warming and cooling procedure resulted from variations in a number of experimental variables. In subsequent experiments trimethyl-*N,N*-diethylaminosilane has been used to remove acid.^{2p}

(4) F. G. Bordwell and W. A. Hewett, *J. Org. Chem.*, **23**, 636 (1958).
(5) R. Tang and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 5644 (1969).