sulfones from the reaction of aryldiazonium salts with sulfones.

(16) G. R. Chalkley, D. J. Snodin, G. Stevens, and M. C. Whiting, *J. Chem. Soc. C*, 682 (1970).

(17) ^{1}H NMR (CD_2Cl_2) δ 1.62 (s, 6 H), 1.92 (m, 3 H), 4.47 (m, 1 H), 4.73 (broad s, 1 H), 5.04 (m, 1 H), 7.20–8.10 (m, 8 H). Elemental analyses, infrared and mass spectra were also consistent with sulfone **4**.

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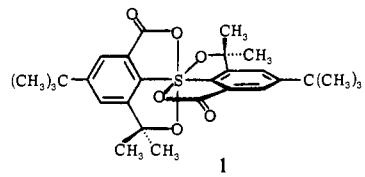
A Diaryldiacyloxydialkoxypersulfurane.[1] The First Example of a Hexacoordinated Organosulfur Derivative Lacking Fluorine Ligands, a Sulfone Bisketal

Sir:

Derivatives of SF_6 in which one or two of the fluorine ligands have been replaced by aryl, vinyl, ethynyl, or perfluoroalkyl groups have been known[2] for many years. The first persulfuranes with two simple alkyl or aryl ligands and four fluorines bound to sulfur were only recently prepared, and found to be stable at −78 °C, by Denney et al.[3]

We now report the isolation and characterization of the first[4] persulfurane[5] lacking fluorine ligands, diaryldiacyloxydialkoxypersulfurane (**1**), a compound of surprising stability.



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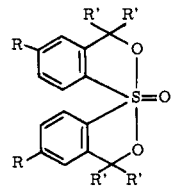
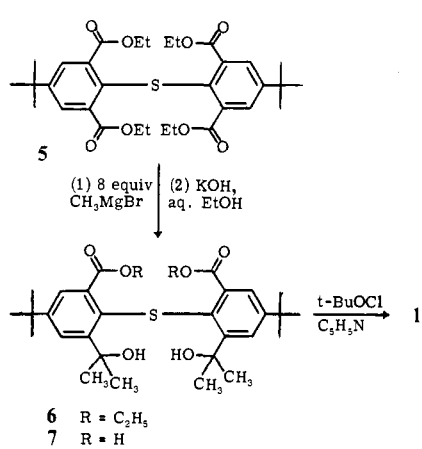
By analogy to the spirobicyclicsulfurane oxide **4a**,[6] the first reported monoketal analogue of a sulfone, persulfurane **1**, can be considered the first bisketal analogue of a sulfone.



4a R = $(CH_3)C$; R' = CF_3
4b R = H; R' = CH_3

Reaction of tetraester **5**[7] with methyl Grignard (8 equiv, 3 h) in ether gave diester diol **6** in 86% yield (mp 154–156 °C). Saponification of **6** with 15% KOH in aqueous ethanol (1:1) gave diacid diol **7** (mp 268–270 °C). Treatment of a CCl_4 suspension of **7** and pyridine (2 equiv) with *tert*-butyl hypochlorite (5 equiv) at 0 °C afforded white powdery **1** in 90–95% yield. The product, **1**, was recrystallized from ether–pentane or THF–pentane, mp 166–170 °C dec.[8] The crystalline **1** is stable indefinitely at room temperature. The two peaks at δ 1.799 and 1.782 in its ^{1}H NMR spectrum[8] clearly indicate the diasterotopic nature of the two geminal methyl groups on the five-membered heterocyclic ring, as expected for the pictured octahedral structure of **1**.



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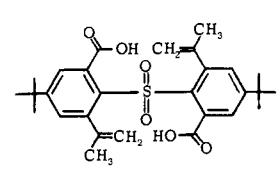
(1) 8 equiv CH_3MgBr; (2) KOH, aq. EtOH

6 R = C_2H_5
7 R = H

The solid persulfurane **1** is stable and unreactive toward atmospheric moisture. However, **1** was found to decompose completely at room temperature (<30 min) in ordinary $CDCl_3$ and (3 days) in pyridine-d_5 solvent, as evidenced by the ^{1}H NMR spectra. The product from decomposition of **1** was identified as the isomeric sulfone diene diacid (**8**) by elemental analysis, infrared, NMR, and mass spectrometry.[9] The decomposition of persulfurane **1** to give **8** is analogous to the acid-catalyzed fragmentation[10] of spirobicyclicsulfurane oxide **4b**, to give **9**, another fragmentation deriving its driving force



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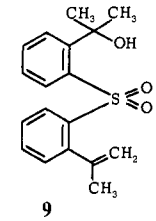

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from the formation of the stable sulfone functional group. In the case of persulfurane **1**, fragmentation is catalyzed either by a trace of HCl present in ordinary chloroform or by a trace of water present in the pyridine-d_5. When a drop of D_2O was added to a sample of **1** in pyridine-d_5, the rate of fragmentation was greatly enhanced (complete reaction within minutes at room temperature).

The spectroscopic and chemical evidence presented here provides a compelling case for the proposed structure for persulfurane **1**. Further work on the structure and reactivity of persulfuranes is underway in our laboratory.

Acknowledgment. This research was supported in part by a grant from the National Science Foundation, MPS 75-17742.

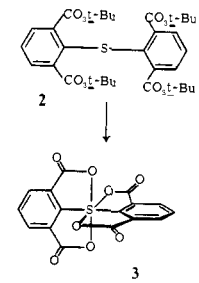
References and Notes

(1) Paper 25 in a series on sulfuranes. For paper 24 see the preceding paper, L. J. Adzima and J. C. Martin, *J. Am. Chem. Soc.*, preceding paper in this issue.

(2) (a) R. D. Dresdner and T. R. Hooper, *Fluorine Chem. Rev.*, (1969) **4**; (b) H. L. Roberts, "Inorganic Sulfur Chemistry", G. Nickless, Ed., Elsevier, New York, N.Y., 1968, Chapter 12; (c) W. A. Sheppard and C. M. Sharts, "Organic Fluorine Chemistry", W. A. Benjamin, New York, N.Y., 1969.

(3) D. B. Denney, D. Z. Denney, and Y. F. Hsu, *J. Am. Chem. Soc.*, **95**, 8191 (1973).

(4) It has been reported by M. M. Chau, Ph.D. Thesis, University of Illinois, 1975 (manuscript, with J. C. Martin, in preparation), that decomposition of tetraperester **2** gave a compound for which structure **3**, a persulfurane, was proposed. Evidence for its structure was, however, incomplete.



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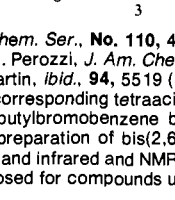

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(5) J. I. Musher, *Adv. Chem. Ser.*, **No. 110**, 44–52 (1972).

(6) J. C. Martin and E. F. Perozzi, *J. Am. Chem. Soc.*, **96**, 3155 (1974); E. F. Perozzi and J. C. Martin, *ibid.*, **94**, 5519 (1972).

(7) Prepared from the corresponding tetraacid, which was synthesized from 2,6-dimethyl-4-*tert*-butylbromobenzene by a procedure similar to that described[4] for the preparation of bis(2,6-dicarboxyphenyl) sulfide. The elemental analyses and infrared and NMR spectra are all consistent with the structures proposed for compounds used in the preparation of **1**.

(8) Anal: Calcd for $C_{28}H_{34}O_6S$: C, 67.45; H, 6.87; S, 6.43. Found C, 67.68; H, 6.93; S, 6.34. IR (Nujol mull): 1709 cm^{-1} (s). ^1H NMR (pyridine-d_5, 220 MHz): δ 8.342 and 8.098 (d of d, 4, J_{AB} = 1.3 Hz, aromatic C*H*), 1.799 (s, 6, OCCH_3), 1.782 (s, 6, OCCH_3), 1.318 (s, 18, *t*-BuCH_3). The chirality of **1** was evidenced by the addition of optically active 2,2,2-trifluoro-1-phenylethanol, purchased from Burdick and Jackson Laboratories, Inc., to a CD_2Cl_2 solution of **1** (−30 °C) in the 220-MHz NMR spectrum. The methyl singlet at δ 1.782 and the *tert*-butyl singlet were each resolved into two singlets. For a discussion of the use of this chiral alcohol in NMR spectroscopy of racemic mixtures, see W. H. Pirkle, *J. Am. Chem. Soc.*, **88**, 1837 (1966) and W. H. Pirkle and S. D. Beare, *ibid.*, **90**, 6250 (1968).

(9) Anal. Calcd for $C_{28}H_{34}O_6S$: C, 67.45; H, 6.87; S, 6.43. Found C, 67.18; H, 6.78; S, 6.63. IR (Nujol mull): 3400 (m), 1710 (s), 1320 (s) and 1165 cm^{-1} (s). ^1H NMR (pyridine-d_5): δ 7.805 and 7.340 (d of d, 4, J_{AB} = 2.1 Hz, aromatic C*H*), 5.277 (br s, 2, olefinic C*H*), 4.818 (br s, 2, olefinic C*H*), 1.939 (s, 6, CH_3 at olefinic carbon), 1.316 (s, 18, *t*-BuCH_3).

(10) J. C. Martin and L. J. Adzima, preceding communication.

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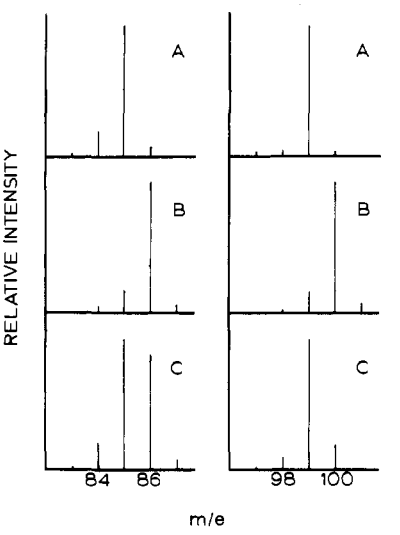


Figure 1. (left panel) Mass spectrometer scans of the molecular-weight region of the γ-butyrolactam formed by enzymatic decarboxylation of glutamic acid at pL 4.6, 22 °C (A) in H_2O; (b) in D_2O; (C) in 50:50 H_2O:D_2O. (right panel) Same, for the γ-valerolactam formed by enzymatic decarboxylation of α-methylglutamic acid at pL 4.6, 22 °C.

A Solvent Isotope Effect Probe for Enzyme-Mediated Proton Transfers

Sir:

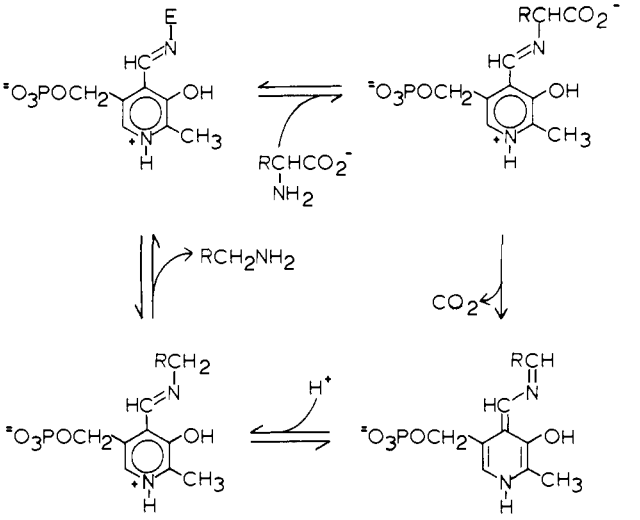
A crucial step in a number of enzyme-catalyzed reactions is the transfer of a proton from the solvent to a carbon atom of the substrate. Examples of such reactions include decarboxylations and other carbon-carbon bond cleavage reactions, some hydration and dehydration reactions, and a variety of others. The proton transfer may occur either directly from the solvent or else through the mediation of some catalytic group of the enzyme. We show here that a distinction between these two possibilities can sometimes be made by measuring the hydrogen isotope discrimination which occurs when the reaction is conducted in 50:50 H_2O:D_2O.

Proton transfers to and from carbon are ordinarily subject to hydrogen isotope effects[1,2] in the range k^H/k^D = 2-10. If a proton transfer from the solvent to a carbon atom of the substrate occurs during the course of an enzymatic reaction, then such an isotope effect is expected to occur in that proton transfer step. If the reaction is conducted in 50:50 H_2O:D_2O the isotopic composition of the product will reflect this isotope effect, provided that (1) the proton transfer occurs either directly from the solvent or from a catalytic group of the enzyme which undergoes rapid hydrogen exchange with the solvent and (2) the enzyme does not catalyze hydrogen exchange between solvent and product under the conditions of the experiment.

On the other hand, this isotope discrimination may not be observed if the proton transfer occurs through the mediation of a monoprotic[3] catalytic group which is shielded from hydrogen exchange with the solvent. Under such conditions the only proton available for transfer to the intermediate is the hydrogen attached to that catalytic group and the isotopic content of the product will reflect only the equilibrium isotope fractionation between the solvent and the catalytic group. For imidazole and carboxyl groups, this equilibrium fractionation is near unity,[4] and no hydrogen isotope discrimination in the product is expected.[5] Thus, the absence of hydrogen isotope discrimination in the protonation of an enzyme-substrate complex may serve as evidence for mediation of the proton transfer by a monoprotic catalytic group of the enzyme which is shielded from proton exchange with the solvent during the lifetime of the appropriate intermediate.[6]

The pyridoxal 5′-phosphate dependent amino acid decarboxylases function by a mechanism involving an enzyme-bound Schiff base between the coenzyme and the substrate[7] (Scheme I). Decarboxylation produces a quinoid intermediate which

Scheme I



is protonated almost exclusively on the terminal carbon of the conjugated system.[8] No evidence has been provided for the existence of an enzyme catalytic group which mediates this protonation.

L-Glutamic acid (0.03 M in 3 ml of 0.2 M pyridinium chloride buffer, pH 4.6, containing 1.7×10^{-6} M dithiothreitol, 1.7×10^{-6} M pyridoxal 5′-phosphate, and 0.2 M total chloride ion) was decarboxylated completely by treatment for 18 h with 320 units of purified glutamate decarboxylase from *E. coli*.[9] Similar experiments were conducted at the same pL in D_2O and in 50:50 H_2O:D_2O. The product γ-aminobutyric acid formed in each case was isolated, washed repeatedly with water, and converted by pyrolysis to γ-butyrolactam.[10] Mass spectra of the lactam samples so obtained are shown in Figure 1. When the decarboxylation was conducted in D_2O, 1.00 deuterium atom was incorporated into the product.[11] The sample from the mixed solvent contained 0.48 deuterium atom. Six repetitions of this procedure gave 1.00 ± 0.02 deuterium for experiments conducted in D_2O and 0.48 ± 0.03 deuterium in the mixed solvent. The results were independent of acidity over the range pL 4.1-5.1. Because glutamate decarboxylase does not catalyze hydrogen exchange in γ-aminobutyric acid[12,13] the results of the isotope discrimination experiments