φ, between the C_2–H bond and the C_1–C_2–C_3 plane. (A positive value of φ corresponds to bending of the C_2–H bond in the endo direction.) Calculated results are shown in Figure 4. The comparison between the observed hyperfine coupling constants and the calculated results shows that the angle φ of **1** is about +20°, that is the C_2–H bond is bent out of the C_1–C_2–C_3 plane about 20° to the endo direction, and that the angle of **2** is about 10° larger than φ of **1**.

The pyramidal structure of the radical-center carbon of the present radicals should be, at least, one of the dominant factors which controls the stereoselectivity of these radicals in transfer reactions, and the present results support the proposal of Fujimoto and Fukui.[3]

* Address correspondence to this author c/o Dr. J. K. Kochi, Department of Chemistry, Indiana University, Bloomington, Ind. 47401.

Takashi Kawamura,* Tohru Koyama, Teijiro Yonezawa

Department of Hydrocarbon Chemistry
Faculty of Engineering, Kyoto University
Sakyo-ku, Kyoto, Japan

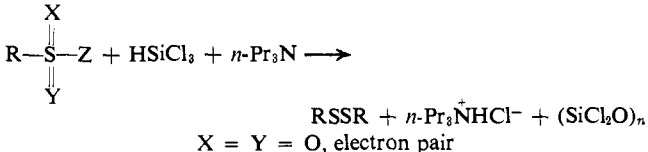
Received September 22, 1970

Reductive Formation of Disulfides from Sulfenyl, Sulfinyl, and Sulfonyl Derivatives Using Tri-*n*-propylamine and Trichlorosilane

Sir:

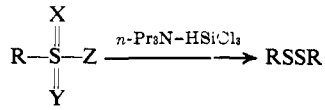
Disulfides are generally prepared by the oxidative coupling of thiols.[1] Recently however, nucleophilic substitution of sulfenylthiocyanates,[2] thiolsulfonates,[3] sulfenylhydrazo compounds,[4] and sulfenimides[5] with thiols have also been reported as general routes to disulfides. In the course of our studies on the deoxygenation of sulfur compounds,[6] we have found that the sulfur–sulfur linkage is not cleaved by trichlorosilane.[7] This leads to the possibility that disulfides may be prepared reductively from sulfur compounds of higher oxidation state.

We wish to report that good to excellent yields of symmetrical disulfides can be obtained from the reduction of the corresponding sulfenyl, sulfinyl, and sulfonyl chlorides as well as sulfenate and sulfinate esters with the tri-*n*-propylamine–trichlorosilane system (*n*-Pr_3N–$HSiCl_3$)[8] (Table I). Thus to a mixture of

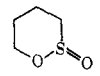
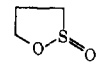


X = Y = O, electron pair
Z = Cl, OR′ (see Table I, footnote *a*)

Table I. Reduction of Various Sulfur Compounds with *n*-Pr_3N–$HSiCl_3$



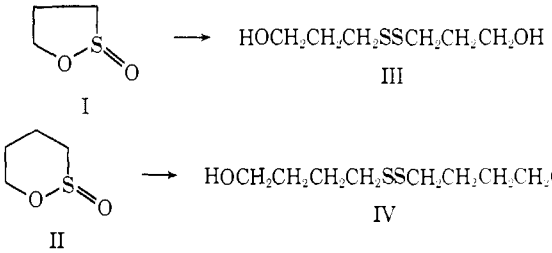
X = Y = O, electron pair
Z = Cl, OR′ [a]

Compound	Time, hr (T, °C)[b]	Product	% yield
C_6H_5S–Cl	4 (20)	$C_6H_5SSC_6H_5$	53
C_6H_5S–OCH_3	4 (20)	$C_6H_5SSC_6H_5$	88
p-$CH_3C_6H_4SO$–Cl	5 (20)	*p*-$CH_3C_6H_4SSC_6H_4CH_3$-*p*	91
C_6H_5SO–OCH_3	4 (20)	$C_6H_5SSC_6H_5$	85
	4 (20)	$HO(CH_2)_4SS(CH_2)_4OH$	60
	4 (20)	$HO(CH_2)_3SS(CH_2)_3OH$	80
$C_6H_5SO_2Cl$	20 (20) 6 (80)	$C_6H_5SSC_6H_5$	67 85
$C_6H_5SO_2OCH_3$	15 (20) 70 (80)		*a*, *c*

[a] Sulfonate esters (X = Y = O; Z = OR′) do not react. [b] All reactions were carried out in benzene solution. [c] Starting material recovered.

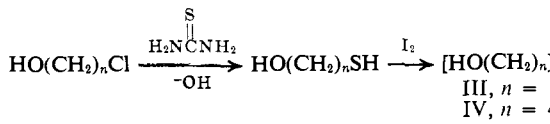
methyl benzenesulfinate (0.04 mol) and trichlorosilane (0.06 mol) in 70 ml of benzene at 20°, tri-*n*-propylamine (0.042 mol) in 50 ml of benzene was added dropwise. After a stirring period of 4 hr, the mixture was hydrolyzed with water (20 ml) and extracted, affording an 85% yield of diphenyl disulfide. Similarly, disulfides were obtained from sulfonyl chlorides (RSO_2Cl), sulfinyl chlorides (RSOCl), sulfenyl chlorides (RSCl), and sulfenates (RSOR′) in high yield (Table I).

The generality and utility of this method of disulfide preparation is illustrated by the reaction of two cyclic sulfinate esters (1,2-oxathiolane 2-oxide (I) and 1,2-oxathiane 2-oxide (II))[9] with *n*-Pr_3N–$HSiCl_3$. In both cases, rupture of the heterocycle occurred along with reduction of the sulfinyl oxygen to give the symmetrical hydroxy disulfides III and IV in 80 and 60% yield, respectively. The identity of structures III and IV was



established by correct elemental analysis, spectral properties, and synthesis by an independent route according to Scheme I.

Scheme I



The mechanistic details of the reduction of organic functional groups with trichlorosilane are far from

(1) E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. I, Chemical Publishing Co., New York, N. Y., 1958.
(2) R. G. Hiskey, F. I. Carroll, R. M. Babb, R. M. Bledsoe, R. T. Puckett, and B. W. Roberts, *J. Org. Chem.*, **26**, 1152 (1961).
(3) L. Field, H. Harle, T. C. Owen, and A. Ferretti, *ibid.*, **29**, 1632 (1964).
(4) T. Mukaiyama and K. Takahashi, *Tetrahedron Lett.*, 5907 (1968).
(5) K. S. Boustany and A. B. Sullivan, *ibid.*, 3547 (1970); D. N. Harpp, D. K. Ash, T. G. Back, J. G. Gleason, B. A. Orwig, W. F. Van Horn, and J. P. Snyder, *ibid.*, 3551 (1970).
(6) T. H. Chan, A. Melnyk, and D. N. Harpp, *ibid.*, 201 (1969); T. H. Chan and A. Melnyk, *J. Amer. Chem. Soc.*, **92**, 3718 (1970).
(7) T. H. Chan and A. Melnyk, unpublished results.
(8) For the reduction of other functional groups by these reagents see R. A. Benkeser and J. M. Gaul, *J. Amer. Chem. Soc.*, **92**, 720 (1970), and references cited therein.
(9) D. N. Harpp and J. G. Gleason, *Tetrahedron Lett.*, 1447 (1969).

clear. Benkeser has proposed that in the n-Pr_3N–$HSiCl_3$ system, the trichlorosilyl anion ($SiCl_3^-$) is the reactive intermediate and reported nmr evidence in support of this.[10] On the other hand, Mislow suggested that n-Pr_3N–$HSiCl_3$ is an extremely complicated system and that perchloropolysilane is formed and is likely to be the reactive agent.[11] In the absence of definitive work we offer the following observations. The reaction does not occur without the addition of the tertiary amine. Thus deoxygenation of the S=O group by trichlorosilane alone, similar to the reduction of sulfoxides to sulfides,[6] does not take place. Secondly, a 1:1 adduct between sulfinate esters and trichlorosilane occurs almost instantaneously after mixing the two reagents. For example, the adduct (II:$HSiCl_3$) has quite different spectroscopic properties from either of the starting materials but decomposed on distillation. The sulfinate ester II could, however, be recovered quantitatively on hydrolysis of the adduct. It seems reasonable to suggest that it is the adduct which reacts with the amine on the pathway to product.

We are in the process of exploring the generality and mechanism of these reactions.

Acknowledgments. We thank the National Research Council and the Defense Research Board of Canada for financial support of this work. Acknowledgment is also made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial financial support.

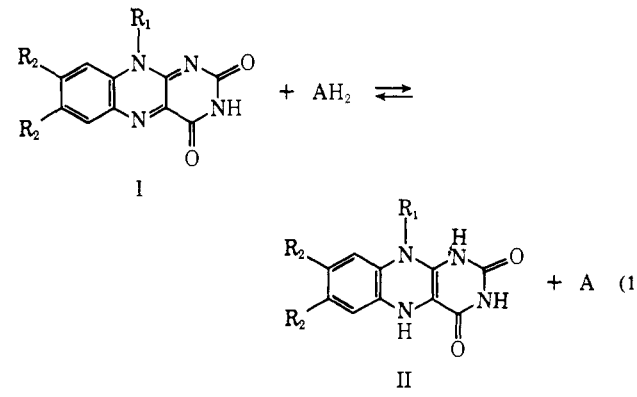
(10) R. A. Benkeser, K. M. Foley, J. B. Grutzner, and W. E. Smith, *J. Amer. Chem. Soc.*, **92**, 697 (1970).
(11) K. Naumann, G. Zon, and K. Mislow, *ibid.*, **92**, 697 (1969).
(12) Visiting Scientist, Bishops University, Lennoxville, Quebec.
* Authors to whom correspondence may be addressed.

T. H. Chan,* J. P. Montillier
William F. Van Horn,[12] David N. Harpp*
Department of Chemistry, McGill University
Montreal, Canada
Received September 1, 1970

Some Model Reactions and a General Mechanism for Flavoenzyme-Catalyzed Dehydrogenations[1]

Sir:

Although the flavin coenzymes participate in many enzymic dehydrogenation reactions,[2] the mechanism of the dehydrogenation step (eq 1) has remained unclear. Several classes of such reactions, with enzymic examples in parentheses, are: (1) alcohol dehydrogenation (glucose oxidase, lactate dehydrogenase), (2) amine dehydrogenation (amino acid oxidases), (3) dehydrogenation α,β to a carbonyl



I + AH_2 ⇌ II + A (1)

(succinate dehydrogenase, acyl-CoA dehydrogenases), (4) dihydronicotinamide dehydrogenation (NADH dehydrogenases), (5) dithiol dehydrogenation (lipoamide dehydrogenase). Nonenzymic reactions related to classes 3–5 have been studied.[3-10] In this communication we report the first successful duplication of the reactions in classes 1 and 2 in a nonenzymic system in the dark. Also, a general mechanism for flavoenzyme-catalyzed reactions is suggested.

When 10-phenylisoalloxazine (I, R_1 = phenyl; R_2 = H) is allowed to react under anaerobic basic conditions with either methyl mandelate ($C_6H_5CHOHCO_2CH_3$, III) or methyl phenylglycine ($C_6H_5CH(NH_2)CO_2CH_3$, IV) in anhydrous dimethylformamide–*tert*-butyl alcohol the spectrum (solid line) shown in Figure 1 is obtained. This spectrum, especially the low absorption at 437 nm, is characteristic of the fully reduced flavin II;[11] the shoulders at 475 and 355 nm are attributable to the presence of small amounts of flavin radical anion.[12] Upon addition of dry air the reaction solution immediately turns yellow and a spectrum (Figure 1) characteristic of oxidized flavin (I) is obtained; the observed optical density at 437 nm indicates that I is regenerated in greater than 90% yield.

No spectral change is observed in the absence of *tert*-butoxide. In the absence of III and IV, *tert*-butoxide causes a shift of the 437-nm peak of I to a broad peak centered at 400 nm; this shift is reversed by acid but not by O_2. Therefore, under the reaction conditions *tert*-butoxide alone does not effect the reduction of I to II.

The expected dehydrogenation products of III and IV are $C_6H_5COCO_2CH_3$ (V) and $C_6H_5C(=NH)CO_2CH_3$ (VI), respectively. At pH 9, V is hydrolyzed to $C_6H_5COCOOH$ (VII) and the same is expected for VI. Following treatment of anaerobic reaction mixtures, which initially contained either III or IV, with aqueous

(1) This research was supported in part by a research grant (AM 13448) from the National Institute of Arthritis and Metabolic Diseases, Public Health Service, and in part by a Predoctoral Fellowship (1967–1970) to L. E. B. from the National Institute of General Medical Sciences (GM 37,741). Presented at the 160th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1970, Abstract No. BIOL 50.
(2) For reviews see: (a) P. Hemmerich, G. Nagelschneider, and C. Veeger, *FEBS (Fed. Eur. Biochem. Soc.) Lett.*, **8**, 69 (1970); (b) A. H. Neims and L. Hellerman, *Annu. Rev. Biochem.*, **39**, 867 (1970); (c) E. C. Slater, Ed., "Flavins and Flavoproteins," Elsevier, Amsterdam, 1966; (d) K. Yagi, Ed., "Flavins and Flavoproteins," University Park Press, Baltimore, Md., 1968; (e) T. P. Singer, Ed., "Biological Oxidations," Interscience, New York, N. Y., 1968; (f) P. D. Boyer, H. Lardy, and K. Myrbaeck, Ed., "Enzymes," Vol. 7, 2nd ed, Academic Press, New York, N. Y., 1963, pp 275–648.
(3) T. P. Singer and E. B. Kearney, *J. Biol. Chem.*, **183**, 409 (1950).
(4) C. H. Suelter and D. E. Metzler, *Biochem. Biophys. Acta*, **44**, 23 (1960).
(5) G. K. Radda and M. Calvin, *Biochemistry*, **3**, 384 (1964).
(6) J. L. Fox and G. Tollin, *ibid.*, **5**, 3865, 3873 (1966).
(7) F. Y. Wu, R. E. Mackenzie, and D. B. McCormick, *ibid.*, **9**, 2219 (1970).
(8) I. M. Gascoigne and G. K. Radda, *Biochim. Biophys. Acta*, **131**, 498 (1967).
(9) M. J. Gibian and D. V. Winkleman, *Tetrahedron Lett.*, 3901 (1969).
(10) G. D. Weatherby and D. O. Carr, *Biochemistry*, **9**, 351 (1970).
(11) A similar spectrum in the 400–500-nm region is observed on catalytic reduction (H_2 and Pd/C) of an anaerobic, anhydrous solution of I and potassium *tert*-butoxide in DMF–*tert*-BuOH.
(12) A. Ehrenberg, F. Muller, and P. Hemmerich, *Eur. J. Biochem.*, **2**, 286 (1967).