

Organic Sulfur Chemistry. I. The Disulfide-Phosphine Reaction. Desulfurization with Tris(diethylamino)phosphine

Sir:

Desulfurization of organic disulfides by phosphines^{1,2} and phosphites^{3,4} has been reported; however, the reaction is by no means general.^{1,3}



Previous workers have shown that, in the reaction with trivalent phosphorus compounds, most organic disulfides are either unreactive or are desulfurized with accompanying rearrangement.^{1,3}

We have found that tris(diethylamino)phosphine (I)



smoothly desulfurizes a wide variety of disulfides without rearrangement, thus considerably broadening the scope of the reaction. These disulfides include cyclic, benzylic, aralkyl, and dialkyl derivatives. The results are summarized in Table I. For example, when di-

ment of the latter with phosphine I at room temperature for 28 hr results in a quantitative (vpc) conversion to tetrahydrothiophene (III). Extrusion of a sulfur atom from a cyclic compound under these mild conditions seems to have no close precedent.⁵ Moreover, the reaction appears to be a competitive general method for the preparation of such compounds.⁶

In addition, diamyl, tolyl benzyl, and methyl phenyl disulfides are cleanly desulfurized under conditions conducive to an ionic process.⁷ It should be noted that unsymmetrical aralkyl systems, as exemplified by tolyl benzyl and methyl phenyl disulfides, desulfurize exothermically at room temperature to give only the corresponding unsymmetrical sulfide.⁸ In contrast, the symmetrical aliphatic systems react very slowly under similar conditions. Of those disulfides studied, only *p*-tolyl disulfide failed to desulfurize easily, affording a mixture of products at elevated temperatures.¹⁰

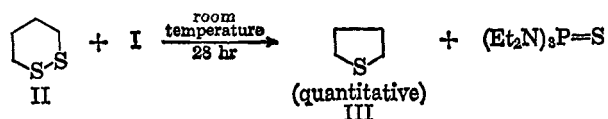
The mechanism of desulfurization is of considerable importance relative to the unsettled question of the exact pathway taken by nucleophiles in disulfide cleav-

Table I. $\text{RSSR}' + (\text{Et}_2\text{N})_3\text{P} \rightarrow \text{RSR}' + (\text{Et}_2\text{N})_3\text{P}=\text{S}$

Disulfide	Reaction time, hr	Reaction temp, °C ^a	% RSR' ^b	(Et ₂ N) ₃ P=S ^b
1,2-Dithiacyclohexane	28	25	101 ^{d,e}	
C ₆ H ₁₁ SSC ₆ H ₁₁	140	80	63	91 ^d
CH ₃ C ₆ H ₄ SSC ₆ H ₄ CH ₃	24	140 ^c	~1	
CH ₃ C ₆ H ₄ SSCH ₂ C ₆ H ₅	0.1	Exothermic	86	
CH ₃ C ₆ H ₄ SSCH ₃	0.1	Exothermic	86	70
C ₆ H ₅ CH ₂ SSCH ₂ C ₆ H ₅	1.5	80	80	89, ^f 87 ^d
BrC ₆ H ₄ CH ₂ SSCH ₂ C ₆ H ₅	3	80	22 ^{e,d} 38 ^{b,d} 11 ^{c,d}	85

^a Benzene solvent. ^b Unless otherwise noted, yields indicated are of isolated, recrystallized, or distilled product. ^c Neat. ^d By vpc, using internal standards. ^e Tetrahydrothiophene was isolated and proved to be identical with an authentic sample. ^f Crude yield. ^g (*p*-BrC₆H₄CH₂)₂S. ^h *p*-BrC₆H₄CH₂SSCH₂C₆H₅. ⁱ (C₆H₅CH₂)₂S.

benzyl disulfide is treated with a 10% excess of phosphine I in refluxing benzene for 1.5 hr, benzyl sulfide is isolated in 80% yield. Another facile desulfurization reaction obtains in the case of disulfide II. Treat-



(1) Only acyl, thioacyl, and vinylogous acyl "disulfides" desulfurize with triphenylphosphine, whereas benzyl and diethyl disulfides (among others) failed to react.² *p*-N,N-Dimethylamino phenyl disulfide was desulfurized, but only at elevated temperatures where a free-radical reaction undoubtedly took place;^{2b} alkylidene alkyl disulfides have been desulfurized but undergo allylic type rearrangement en route.^{2d}

(2) (a) A. Schönberg, *Chem. Ber.*, **68**, 163 (1935); (b) A. Schönberg and M. Barakat, *J. Chem. Soc.*, 892 (1949); (c) F. Challenger and D. Greenwood, *ibid.*, 26 (1950); (d) C. Moore and B. Trego, *Tetrahedron*, **18**, 205 (1962).

(3) When phosphites are used in this reaction, either irradiation is necessary for the reaction to take place;^{4c,d,i} Arbuzov rearrangement occurs ($\text{RSSR} + (\text{EtO})_3\text{P} \rightarrow \text{RSEt} + (\text{EtO})_2\text{P(O)SR}$);^{4a,b,d,f-h,j} or, when allylic type disulfides are employed, allylic rearrangement results.^{4e,g}

(4) (a) H. Jacobson, R. Harvey, and E. V. Jensen, *J. Am. Chem. Soc.*, **77**, 6064 (1955); (b) A. Poskus and J. Herweh, *ibid.*, **79**, 4245 (1957); (c) C. Walling and R. Rabinowitz, *ibid.*, **79**, 5326 (1957); (d) C. Walling and R. Rabinowitz, *ibid.*, **81**, 1243 (1959); (e) C. Moore and B. Trego, *J. Chem. Soc.*, 4205 (1962); (f) H. Jacobson, R. Harvey, and E. Jensen, *J. Am. Chem. Soc.*, **85**, 1618 (1963); (g) K. Pilgram, D. Phillips, and F. Korte, *J. Org. Chem.*, **29**, 1844 (1964); (h) K. Pilgram and F. Korte, *Tetrahedron*, **21**, 203 (1965); (i) A. J. Kirby, *ibid.*, **22**, 3001 (1966); (j) R. S. Davidson, *J. Chem. Soc.*, 2131 (1967).

age reactions.⁹ The behavior of disulfide IV is suggestive¹¹ of the mechanistic pathway taken by dialkyl disulfides with phosphine I.

All three possible sulfides are found to be products (Table I). The collapse of a tight ion pair, V, or the

(5) B. P. Stark and A. J. Duke, "Extrusion Reactions," Pergamon Press, London, 1967, pp 91-107.

(6) For other preparative schemes see E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. 3, Chemical Publishing Co., Inc., New York, N. Y., 1960, pp 11-147.

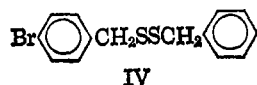
(7) (a) The possibility of a radical process was minimized as the reactions were carried out in the dark, in the presence of hydroquinone, and at temperatures considerably less than those reported^{2b} to homolytically cleave disulfides; (b) E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. 3, Chemical Publishing Co., Inc., New York, N. Y., 1960, pp 369-372.

(8) The high reaction rate as well as the absence of the dialkyl sulfides as products in these cases is not completely clear at this time (*cf.* ref 4f vs. 9a).

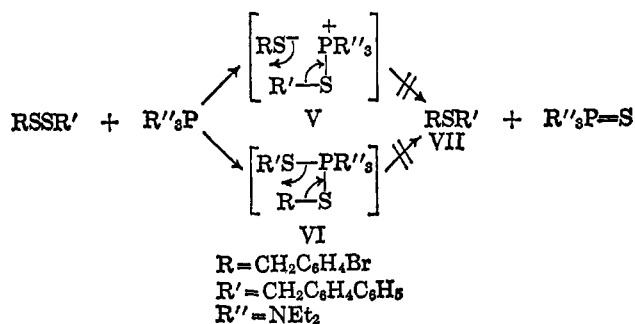
(9) (a) R. G. Hiskey and D. N. Harpp, *J. Am. Chem. Soc.*, **86**, 2014 (1964); (b) A. J. Parker and N. Kharasch, *ibid.*, **82**, 3071 (1960); (c) A. J. Parker and N. Kharasch, *Chem. Rev.*, **59**, 583 (1959); (d) J. L. Kice, *Accounts Chem. Res.*, **1**, 58 (1968), and references cited therein.

(10) A variety of products were observed by vpc and very low yields of tolyl sulfide and tolyl phosphorothioate ((CH₃C₆H₄S)₂P=O) were isolated, the latter compound probably being formed by oxidation of tolyl phosphorothioate ((CH₃C₆H₄S)₂P) on chromatographic work-up. The products of this reaction and those of other diaryl disulfides can be readily explained by invoking a radical mechanism initiated by thermal homolytic cleavage of the disulfide.

(11) Although it would appear that a mixture of phosphonium salts is involved, the prior or subsequent formation of intermediate VI cannot be precluded. In addition, the unsymmetrical distribution of sulfides in this reaction (Table I) is difficult to rationalize.



concerted breakdown of a pentacovalent species, VI, are thus ruled out as primary product-determining reaction modes.



If either transformation depicted by V or VI were exclusively operating, only sulfide VII would have been observed.¹¹ Preliminary observations on the kinetics of this reaction have indicated that the mechanism is, however, more complicated than originally anticipated. Work is continuing in this area.

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(12) Author to whom correspondence should be addressed.

David N. Harpp,¹² John G. Gleason
Department of Chemistry, McGill University
Montreal, Quebec, Canada

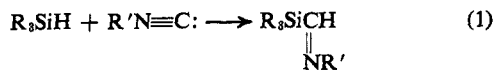
James P. Snyder
Department of Chemistry, Belfer Graduate School of Science
Yeshiva University, New York, New York 10037

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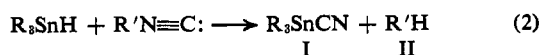
Radical Reaction of Isocyanide with Organotin Hydride

Sir:

Recently we reported a novel insertion reaction of isocyanide into a silicon-hydrogen linkage by a copper catalyst, a new type of hydrosilation.¹



Attempted copper-catalyzed insertion of isocyanide into the tin-hydrogen linkage of organotin hydrides proved unsuccessful. Instead, we found a new radical reaction of isocyanide with trialkyltin hydride in which trialkyltin (iso)cyanide² (I) and the hydrocarbon II were produced in fairly high yields.



Under a nitrogen atmosphere, a mixture of benzyl isocyanide (14.0 mmol), tri-*n*-butyltin hydride (14.0 mmol), and di-*t*-butyl peroxide (6 mol % for isocyanide) was stirred at 120–130° for 8 hr. The reaction mixture, which solidified on cooling at room tempera-

(1) T. Saegusa, Y. Ito, S. Kobayashi, and K. Hirota, *J. Am. Chem. Soc.*, **89**, 2240 (1967).

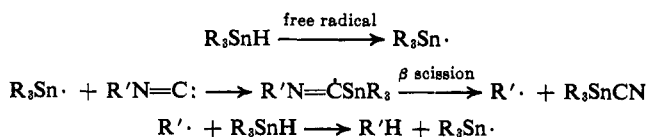
(2) J. S. Thayer and R. West, *Advan. Organometal. Chem.*, **5**, 183 (1967).

ture, was washed with cold ether. The insoluble crystalline solid on recrystallization from ether gave 3.63 g (11.5 mmol, 82%) of tri-*n*-butyltin (iso)cyanide (III), mp 88–89° (lit.³ 88.5°). *Anal.* Calcd for C₁₃H₂₇NSn: C, 49.40; H, 8.61; N, 4.43. Found: C, 49.11; H, 8.80; N, 4.26. The ir spectrum and the glpc retention time of III were identical with those of an authentic sample prepared from tri-*n*-butyltin chloride and potassium cyanide.⁴ The ether washings of the cooled reaction mixture were analyzed by glpc and contained 1.25 g (13.6 mmol, 97%) of toluene.

Similarly, the reaction of cyclohexyl isocyanide with tri-*n*-butyltin hydride induced by azobis(isobutyronitrile) in benzene produced III (52%) and cyclohexane (47%).

Reaction 2 requires a free-radical initiator. Heat treatment of a mixture of isocyanide and tri-*n*-butyltin hydride without a radical initiator under nitrogen gradually produced hexa-*n*-butyldistannane. Perhaps isocyanide played the role of a base catalyst for the coupling reaction of trialkyltin hydride.⁵ In the radical-initiated reaction of isocyanide with trialkyltin hydride, distannane was formed only in small quantities.

Considering the necessity of a radical initiator and the generally known, high reactivity of organotin hydride toward free radicals,⁵ the following scheme may outline the course of reaction.



As to the nature of the radical R'· in the above scheme, the reaction of *t*-butyl isocyanide with tri-*n*-butyltin hydride with the aid of azobis(isobutyronitrile) was examined. In the reaction at the reflux temperature of benzene as solvent for 24 hr the products were isobutane (45% yield) and III (51% yield). Isobutylene was not detected here. This observation has an interesting bearing on the character of the radical reaction of isocyanide.

Detailed mechanistic investigation will be the subject of future studies.

(3) J. Lorberth, *Ber.*, **98**, 1201 (1965).

(4) J. G. A. Luijten and G. J. M. van der Kerk, *J. Appl. Chem.*, **6**, 49 (1956).

(5) Reviewed by H. G. Kuivila, *Advan. Organometal. Chem.*, **1**, 47 (1964).

Takeo Saegusa, Shiro Kobayashi
Yoshihiko Ito, Naohiko Yasuda

Department of Synthetic Chemistry, Faculty of Engineering
Kyoto University, Kyoto, Japan

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Mass Spectrometry of Nucleic Acid Components. Trimethylsilyl Derivatives of Nucleotides, Nucleosides, and Bases¹

Sir:

Although the potential value of mass spectrometry in the structure elucidation of nucleosides and related

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