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A USEFUL POLYMERIC DESULFURIZATION REAGENT[1]

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Polymeric support systems have received considerable attention over the past several years,[2a-d] however very little has been accomplished using polymers which are themselves active reagents.[2e,f]

Aminophosphines 1 have recently found use in selectively removing sulfur from compounds of the type shown below.[3] The most widely used aminophosphines for this purpose are the tris-

$$\text{R-X-S-R'} + \underset{\underline{1}}{(\text{R}''_2\text{N})_3\text{P}} \rightarrow \text{R-X-R'} + (\text{R}''_2\text{N})_3\text{P=S}$$

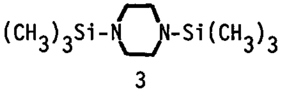
$$\text{X} = \text{-S, -S}_2\text{, -S(O), -S(O}_2\text{), -N(COCH}_2)_2$$

$$\text{R} = \text{R}' = \text{alkyl, aryl; R}'' = \text{-CH}_3\text{, -CH}_2\text{CH}_3$$

diethyl or dimethyl derivatives. In these cases, the product phosphine sulfides are liquids and at times their presence causes difficulty in product isolation.

We wish to report the synthesis and properties of two new polymeric and one crystalline aminophosphine and comment on their usefulness in desulfurization.

Treatment of the trimethylsilyl derivatives of piperazine (3)[4] and homopiperazine (4)[5] with PCl_3 effected the formation of the two polymeric reagents 5 and 6 in 99 and 96% yield



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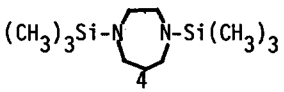

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respectively. Similar treatment of N-trimethylsilyl-1,2,3,4-tetrahydroisoquinoline[6] yielded (79%) a very reactive aminophosphine 7.[7]

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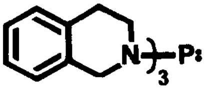

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The polymeric aminophosphines (5 and 6) exhibited the expected properties of aminophosphines[8] reacting with CCl_4, alcohols and water.

In addition, they display great insolubility in the usual organic solvents. The polymers are branched and are believed to be of high molecular weight though no convenient method of molecular weight determination is available owing to their extreme insolubility. As they slowly decompose under normal atmospheric conditions, they must be stored under nitrogen. A unique property of solvent absorption on formation of the aminophosphine polymer was noted. The piperazine phosphine polymer was found to have absorbed as much as six times its weight in benzene, while still remaining a fluffy, dry, white powder. Less dramatically, homopiperazine absorbed about 150% of its weight in solvent, though still exhibiting a dry powdery appearance. After the polymers are heated in vacuum to constant weight, they are able to readsorb solvent to the extent of only 50-60% by weight. Presumably the polymer structure is collapsed when dried and does not permit further entrapment of solvent.

The solvent-expanded polymer shows a much greater reactivity towards desulfurization compared with the dry polymer.[9] Again, this may be explained in that the phosphorus atoms are more available than in the collapsed polymer.

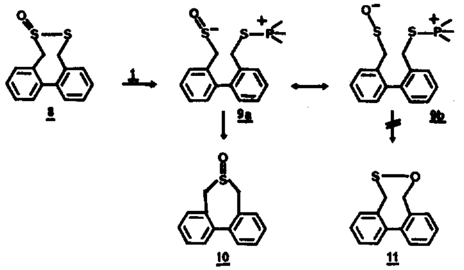
The desulfurization experiments are summarized in the Table. In general, the aminophosphine polymers 5 and 6 are less reactive than tetrahydroisoquinoline)phosphine 7 which is of the same order of reactivity as the *tris*(dialkylamino)phosphine 1. In the case of the polymers, an excess amount of reagent was required to obtain best results (*ca*. 200%).

Several advantages of the new aminophosphine reagents over the conventional aminophosphines are apparent. When using phosphines 1, reaction products often must be tediously separated by column or thin layer chromatography, and in some cases, separation even by these methods could not be achieved; by comparison, a simple filtration sufficed with the polymeric reagents.

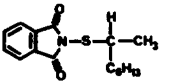
Although chromatographic separation was used in isolation of the products with reagent 7 the isoquinoline phosphine sulfide underwent slow decomposition on the column and did not readily elute.

While some of the desulfurization reactions were of a routine variety (e.g., RSSR, Table), two are worthy of special note. Thiosulfinate esters potentially have two possible desulfurization products, *via* the likely[3b,h] phosphonium salt intermediate 9 Ring closure through 9a would provide sulfoxide 10 while through 9b, a cyclic sulfenate ester (sultene) 11 .[10] In this reaction, only sulfoxide was found (66%).

Another interesting desulfurization was performed on the imide system 12. We have previously reported[3e] the easy desulfurization of this functional group to give N-alkyl imides,



precursors to amines by hydrolysis or hydrazinolysis. The mechanism of this reaction has not been elucidated although if it follows the pathway of the disulfide[3i] and thiosulfonate desulfurizations,[3b,h] it would be predicted that a phosphonium salt intermediate would be formed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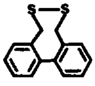
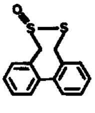
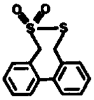
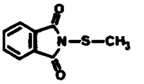
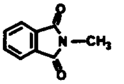
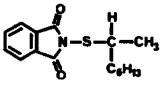
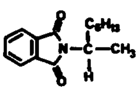
and inversion of configuration should occur at the chiral carbon. This was realized in that when(S)(+)-N-(2-octyl)thio phthalimide (12)[11] was treated with phosphine 1 a 65% yield of (R)(-)-N-(2-octyl) phthalimide (13) was obtained. The optical rotation of this product[12] compared most favorably with the highest reported value in the literature[13] for its enantiomer. Thus, the desulfurization of N-alkyl thiophthalimides proceeds with complete inversion of configuration and permits the conversion of thiols of one chirality into amines of the opposite.

DESULFURIZATION OF R-S-X-R

Substrate	amino-phosphine	Product	% yield	Reaction Time (hr) rt[b]
$(C_6H_5CH_2S)_2$	6	-S-	88	24
$(C_6H_5CH_2S)_2S$	5,6,7	-S-S-	90,90,97[a]	288,72,1
$(CH_3O\overset{O}{\overset{\|}{C}}CH_2S)_2$	6	-S-	99	24
$C_6H_5SSCH_3$	6	C_6H_5-S-CH_3	80	144
	6	-S-	58	48 (reflux)
	1	$-\overset{O}{\overset{\|}{S}}-$	66	24
	5,7	$-\underset{O}{\underset{\|}{\overset{O}{\overset{\|}{S}}}}-$	82,73	120,124
	5		97[a]	144
	(±)5,(+)6		(±)70[a],(-)71	3

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[a] Yield by nmr.

[b] Reaction solvent was benzene; reagents 5,6 used in 2-fold excess, 1,7 in 10% excess

[c] Crude

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REFERENCES

1. Organic Sulfur Chemistry. XXX. For Part XXIX see D.N. Harpp, B. Friedlander, C. Larsen, K. Steliou and A. Stockton, manuscript submitted. Presented in part at the 2nd Joint CIC/ACS Conference, Montreal, Canada, May 1977.

2. (a) "Solid Phase Synthesis", E.C. Blossey and D.C. Neckers, Ed., Halsted Press, New York, 1975; (b) C.C. Leznoff, Chem. Soc. Rev., 65 (1974); (c) "Biochemical Aspects of Reactions on Solid Supports", G.R. Stark, Ed., Academic Press, New York, 1971; (d) K. Horiki, Tetrahedron Lett., 4103 (1976); (e) W. Heitz and R. Michels, Angew. Chem. Int. Ed., 11, 298 (1972); (f) W. Heitz and R. Michels, Justus Leibig's Ann. Chem., 227 (1973).

3. (a) D.N. Harpp, J.G. Gleason and J.P. Snyder, J. Am. Chem. Soc., 90, 4181 (1968), X = S; R, R' = aryl, alkyl; (b) J.G. Gleason and D.N. Harpp, Tetrahedron Lett., 1447 (1969), X = SO_2; R, R' = alkyl; (c) D.N. Harpp and J.G. Gleason, J. Org. Chem., 35, 3259 (1970), X = SO_2; R, R' = alkyl; (d) D.N. Harpp and D.K. Ash, Chem. Commun., 811 (1970), X = SS; R, R' = benzyl; (e) D.N. Harpp and B.A. Orwig, Tetrahedron Lett., 31, 2691 (1970), X = $N(COR)_2$; R, R' = allyl, alkyl; (f) V. Boekelheide and J.L. Mondt, Tetrahedron Lett., 1203 (1970), X = S; R, R' = benzylic cyclophane; (g) D.N. Harpp and J.G. Gleason, J. Org. Chem., 36, 73 (1971), X = S; R, R' = alkyl; (h) D.N. Harpp, J.G. Gleason and D.K. Ash, J. Org. Chem., 36, 322 (1971), X = SO_2; R, R' = alkyl; (i) D.N. Harpp and J.G. Gleason, J. Am. Chem. Soc., 93, 2437 (1971), X = S; R, R' = alkyl, aryl; (j) J.E. McCormick and R.S. McElhinney, J. Chem. Soc. Perkin Trans. I, 2795 (1972), X = SO; R, R' = alkyl; (k) D.N. Harpp and R.A. Smith, Org. Syn., 57, 0000 (1978) in press, X = S; R, R' = benzyl.

4. (a) Formed in 89% yield, b.p. 205-208°/760 mm; lit.[4b]bp 210-216°, 34%; (b) L.W. Breed, W.J. Haggarty, Jr., and J. Harvey, J. Org. Chem., 25, 1804 (1960).

5. This derivative was prepared in 52% yield; b.p. 115-117°/15 mm.

6. Prepared in 51% yield; b.p. 190-210°/760 mm.

7. m.p. 89-91 ; nmr $CDCl_3$ δ 2.70 (t,2H), 3.25 (m,2H), 4.05 (d,2H), 7.02(s,4H).

8. R. Burgada, Ann. Chim., 8, 347 (1963); D.Hoalla, M. Sanchez and R. Wolf, Bull. Soc. Chim. Fr., 2368 (1965).

9. The desulfurization of benzyl disulfide could only be achieved with solvent expanded polymer (as opposed to dry polymer).

10. Only one sultene has been reported to date, G.W. Astrologes and J.C. Martin, J. Am. Chem. Soc., 97, 6909 (1975); ibid., 99, 4390 (1977).

11. 12 ; $[\alpha]_D^{20}$ + 18.3°(C = 2.9, C_6H_6); satisfactory C/H/N/S analysis.

12. In this case with phosphine 1 (R" =Et) separation of the alkylimide from the phosphine sulfide could not be achieved whereas with 1 (R" =Me) clean products easily resulted from silica gel chromatography; $[\alpha]_D^{20} = -25.3°$ (C = 3.9, C_6H_6); $[\alpha]_{545}^{20} = -30.3°$ (C = 3.9, C_6H_6). Further, desulfurization with polymer 6 gave $[\alpha]_D^{20} = -26.2°$ (C = 1.5, C_6H_6).

13. $[\alpha]_D^{20}$ +15.2° (C = 4.1, EtOH); D. Landini and F. Rolla, Synthesis, 389 (1976); we obtained 13 with $[\alpha]_D^{20}$ +19.0°(C = 3.0, EtOH); $[\alpha]_{546}^{20}$ +22.4°(C = 3.0, EtOH); $[\alpha]_D^{20}$ +24.9°(C = 3.13, C_6H_6); $[\alpha]_{546}^{20}$ +29.6°(C = 3.13, C_6H_6) by the method of O. Mitsunobi, M. Wada and T. Sano, J. Am. Chem. Soc., 94, 679 (1972).

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