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Unexpected Conversions of Selected Heteroorganic Compounds

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ABSTRACT: *A few unexpected conversions of selected heteroorganic compounds are described, including the formation of N-sulfonyl sulfenamide derivatives and the mixed phosphinyl-sulfenyl anhydrides in the reactions of sulfinyl chlorides with α-phenylethylamine or t-butyl-phenylphosphine oxide, respectively. Unexpected reactions of the ortho hydroxyalkyl-substituted diaryl sulfoxides and hypervalent sulfur and selenium derivatives, induced by triphenylphosphine, are also presented. Attempts to rationalize the observed reaction courses are briefly discussed.* © 2002 Wiley Periodicals, Inc. Heteroatom Chem 13:437–442, 2002; Published online in Wiley Interscience (www.interscience.wiley.com). DOI 10.1002/hc.10077

INTRODUCTION

In spite of the fact that the recent enormous progress in theory and experimental studies has made organic chemistry a much more logical and predictable subject, unexpected conversions and observations however, made by serendipity still constitute a vital part of everyday laboratory work. In this account, a few such unexpected conversions of selected heteroorganic compounds are presented, together with attempts to rationalize the observed reaction courses. Among them, we discuss the following:

(a) Formation of *N*-sulfonyl sulfenamide derivatives by the condensation of sulfinyl chlorides with optically active α-phenylethylamine;
(b) The formation of mixed phosphinyl-sulfenyl anhydrides in the reaction of *t*-butylphenylphosphine oxide with sulfinyl chlorides;
(c) Unexpected reactions of the ortho hydroxyalkyl-substituted diaryl sulfoxides.

Some uncommon reactions of hypervalent sulfur and selenium derivatives, induced by triphenylphosphine, are also presented.

FORMATION OF N-SULFONYL SULFENAMIDE DERIVATIVES BY THE CONDENSATION OF SULFINYL CHLORIDES WITH OPTICALLY ACTIVE α-PHENYLETHYLAMINE

A very clean formation of diastereomeric *N*-α-phenylethyl-*p*-toluenesulfinamides was found to occur in the reaction of *p*-toluenesulfinyl chloride with optically active α-phenylethylamine [1]. A similar reaction course was observed in the condensation of adamantanesulfinyl chloride **1** with this same optically active amine **2**, carried out in the presence of an equivalent amount of triethylamine as an HCl scavenger [2, J. Drabowicz, M. Mikołajczyk, manuscript

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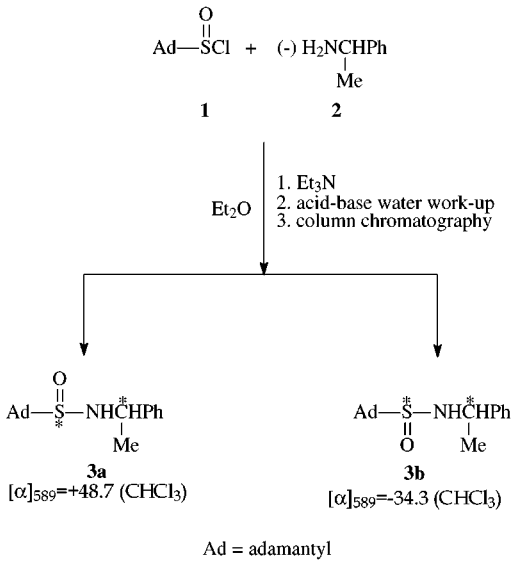
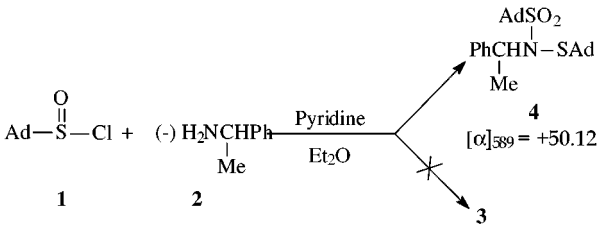


SCHEME 1

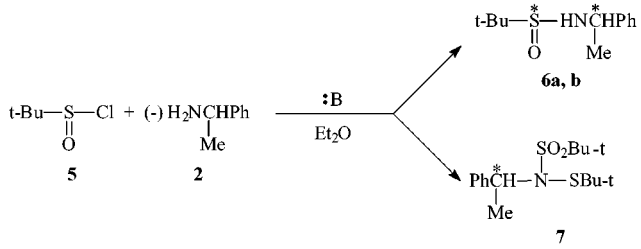
in preparation]. Moreover, the pure diasteoromers of sulfinamide **3** were isolated by column chromatography on silica gel (Scheme 1).

To find out whether the nature of the tertiary amine used has an influence on the selectivity of this condensation, an independent experiment, in which triethylamine was replaced by pyridine, was carried out. Its outcome was, however, completely unexpected. Instead of the expected diastereomeric sulfinamide **3** *N*-adamantanesulfonyl-*N*′-α-phenylethyl-adamantane-sulfenamide (**4**) was isolated as a single reaction product (Scheme 2).

The structure of **4** is fully supported by elemental analysis and spectroscopic techniques, including X-ray analysis. In a similar set of experiments, *t*-butanesulfinyl chloride **5** was found to react with the amine **2** in the presence of a variety of tertiary amines (used as the HCl scavenger) with the simultaneous formation of the expected sulfinamide **6** (as a mixture of diastereomers) and *N*-*t*-butanesulfonyl *N*′-α-phenylethyl-*t*-butane sulfenamide (**7**) (Scheme 3 and Table 1).



SCHEME 2



SCHEME 3

It is evident from the results given in Table 1 that the amount of the sulfenamide **7** formed is strongly influenced by the nature of the tertiary amine used. Simultaneously, this new asymmetric synthesis of diastereomeric sulfinamides **6** is modestly efficient in terms of chemical yields and diastereomeric excess values. The de values of **6** were found to be close to a 2:1 ratio. It should be noted here that, with diisopropylethylamine and tetramethylethylenediamine, exclusive formation of the sulfinamide **6** was observed.

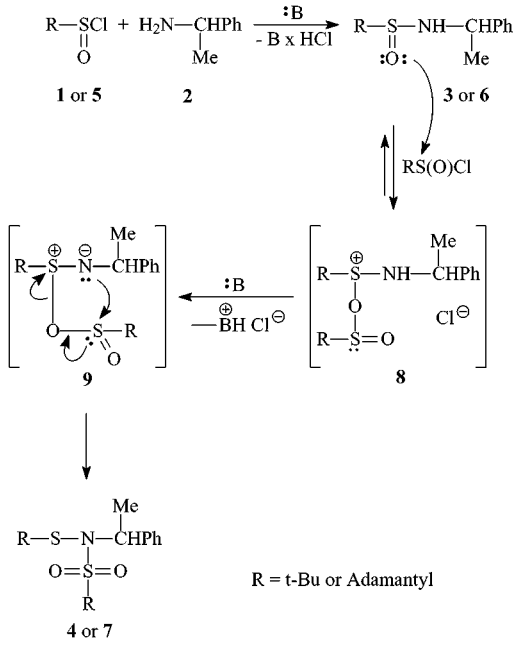
Exclusive and simultaneous formation of the sulfenamides **4** or **7** in the reactions between adamantanesulfinyl chloride **1** or *t*-butanesulfinyl chloride **5** with optically active α-phenylethylamine **2** may be rationalized by the sequence of events shown in Scheme 4.

Formation of the sulfenamide **4** or **7** is believed to proceed in two steps. The initial step involves the generation of the corresponding sulfinamide (**3** or **6**). In the second step, the sulfinamide **3** or **6** reacts with the appropriate sulfinyl chloride (**1** or **5**) to give the aminosulfonium salt **8**. Deprotonation of the salt **8** by an external base gives the ylide-like structures **9**, which finally rearranges to form the sulfenamide **4** or **7**. This mechanistic proposal was strongly supported by additional experiments which confirmed that the sulfenamide **4** is formed in the reactions between

TABLE 1 Condensation of *t*-Butanesulfinyl Chloride (**5**) with (-)-α-Phenylethylamine **2** in the Presence of Tertiary Amines

	6a,b		
Base	*Yield (%)*	*a/b Ratio*	***7***
(-) Me_2NαPEA	53	7:3	27
iPr_2NEt	85	30:12	0
TMEDA	90	16.2:7.7	0
K_2CO_3	68	18.7:10.8	21.0
2-MCH[a]	29	15.6:9.7	40.0
Et_2NPh	48	13.4:8.5	32
4-Me_2N-Pyridine	82	2.0:1.0	4

[a]2-MCH = 2-methylquinoline.



SCHEME 4

the diastereomerically pure sulfinamides **3a** or **3b** and adamantanesulfinyl chloride **1** carried out in the presence of pyridine (Scheme 5).

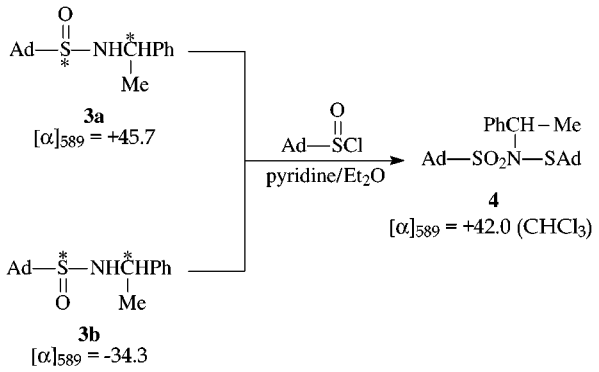
FORMATION OF THE MIXED PHOSPHINYL-SULFENYL ANHYDRIDES IN THE REACTIONS OF t-BUTYLPHENYLPHOSPHINE OXIDE WITH SULFINYL CHLORIDES

Among many substrates for the synthesis of a variety of enantiomerically pure compounds structurally related to phosphine oxides, the enantiomeric forms of the secondary *tert*-butylphenylphosphine oxide **10** are the most useful and promising ones. It was recently reported that the lithiated derivatives of **10** are configurationally stable and react with various electrophilic reagents to give the corresponding P—O derivatives without the loss of configurational integrity at phosphorus [3–6]. Similarly, additions of elemental sulfur and selenium to enantiomeric phosphine oxides **10** in the presence of triethylamine proceeds with a complete retention of configuration at phosphorus and gives the enantiomeric phosphinothioic acid and phosphinoselenoic acids, respectively [7,8].

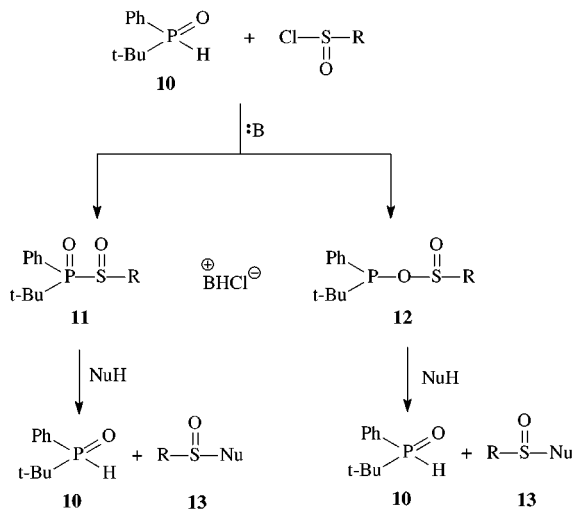
With optically active **10** in hands (obtained via formation of diastereomeric complexes with enantiomers of mandelic acid [9,10]) we envisaged a possibility of the preparation of the mixed anhydrides **11** and **12** and their use as chiral substrates for the synthesis of optically active sulfinyl derivative according to the general reaction sequence shown in Scheme 6.

However, preliminary experiments (J. Drabowicz, unpublished results) carried out with equimolar amounts of the oxide **10** and the *t*-butanesulfinyl chloride **5** in the presence of pyridine have shown that the expected anhydrides **11a** and **11b** were not present in the postreaction mixture, from which the mixed phosphinyl-sulfenyl anhydride **14** was isolated in 85% yield. It was accompanied by *t*-butylphenylphosphinyl chloride **15** and *S*-*t*-butyl-*t*-butanethiosulfonate **16** (Scheme 7).

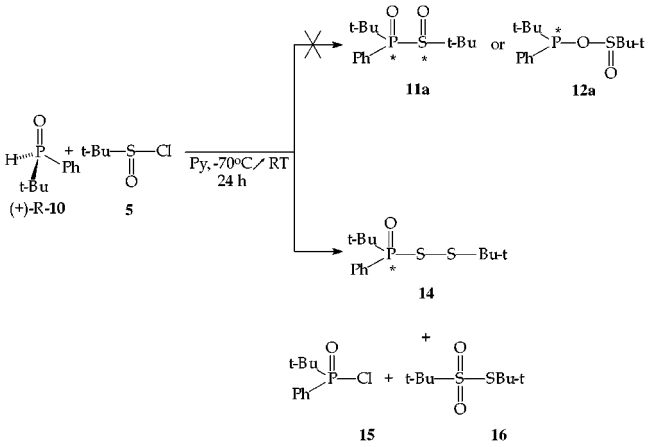
It is interesting to note that the anhydride **14** was simultaneously formed with the corresponding sulfinyl-phosphinyl anhydride **17** in the reaction of *t*-butanesulfinyl chloride **5** with *t*-butylphenylphosphinothioic acid **18** (Scheme 8). Formation of the sulfenyl anhydride **14** results most probably from the deoxygenation of the sulfinyl analogue **17** by *t*-butanesulfinyl chloride with the simultaneous generation of *t*-butanesulfenyl chloride.



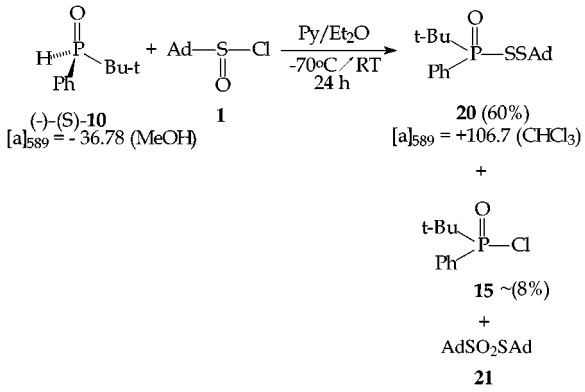
SCHEME 5



SCHEME 6



SCHEME 7

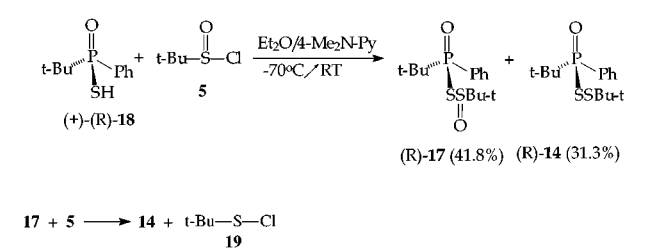


SCHEME 9

Condensation of adamantanesulfinyl chloride **1** with the levorotatory enantiomer of the oxide **10** gave in 40% yield the sulfenyl-phosphinyl anhydride **20**. It was accompanied by the phosphinyl chloride **15** and *S*-adamantyl adamantanethiosulfonate **21** (Scheme 9).

In this context, it is interesting to note that the similar condensation between the oxide **10** and methanesulfinyl chloride **22** gave only the phosphinyl chloride **15** having the inverted configuration at phosphorus, and even traces of the corresponding sulfenyl-phosphinyl anhydride **23** could not be detected among the crude reaction products (Scheme 10).

By consideration of the chlorination ability of sulfinyl chlorides toward the phosphine oxide **10**, it should be noted that this oxide upon dissolving in carbon tetrachloride can be converted into the phosphinyl chloride **15**, with very high stereoselectivity [10]. This reaction is explained in Scheme 11. A similar mechanism has been postulated earlier for the acid-catalyzed exchange of the active hydrogens of dialkyl phosphonates [11] and it seems possible that the actual species reacting with halogen is the phosphite, trivalent tautomer [12].



SCHEME 8

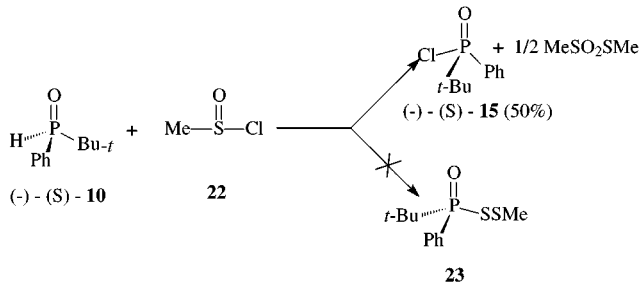
An unexpected course was found for the reaction between the sodium salt of (−)-(S)-**10** and methyl bromoacetate in methanol [9]. This conversion gave, not the expected alkylation product, but rather (−)-(*S*)-methyl *t*-butylphenylphosphinate **25**. Its formation can be explained by the reaction sequence shown in Scheme 12.

UNEXPECTED REACTIONS OF THE ORTHOHYDROXYALKYL SUBSTITUTED-DIARYL SULFOXIDES

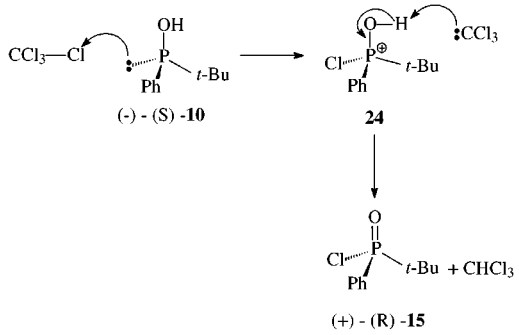
Recently we prepared a few optically active aryl(alkyl) (ortho-hydroxyalkyl)aryl sulfoxides, among them was di-trifluorohydroxymethyl analogue **26**, which was found to exist in solution in an equilibrium with the corresponding hydroxysulfurane structure **27** [13] (Scheme 13).

Most probably, because of the existence of this equilibrium, we were able to observe somewhat uncommon reactivity of the sulfoxide **26**. First of all, this compound, upon treatment with *O*-mesitylsulfonylhydroxylamine gave, instead of the expected optically active sulfoximine **28** (the product of oxidation), the achiral sulfone **29** (Scheme 14).

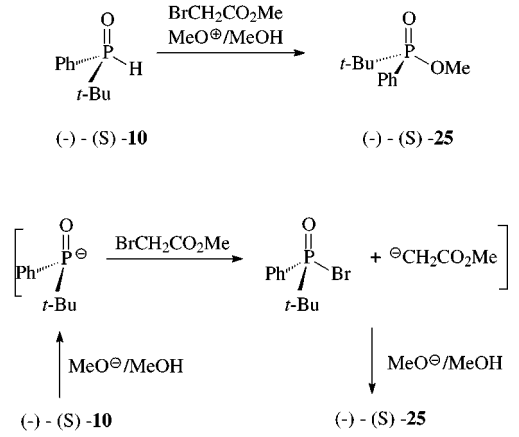
The second reaction which shows unexpected reactivity of the sulfoxide **26** is the HCl-catalyzed



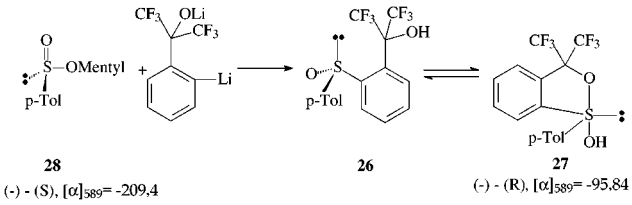
SCHEME 10



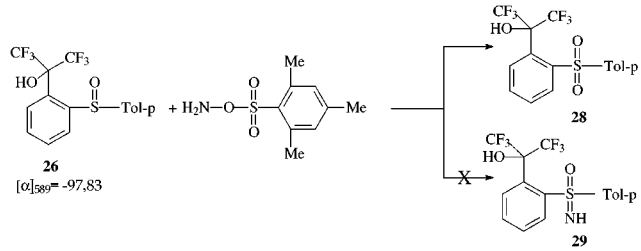
SCHEME 11



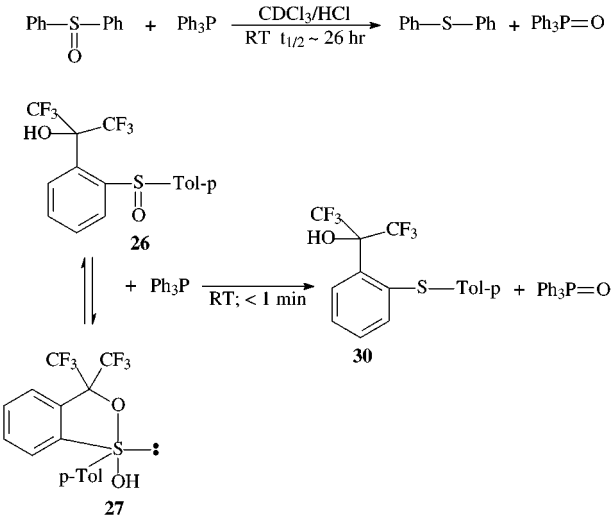
SCHEME 12



SCHEME 13



SCHEME 14

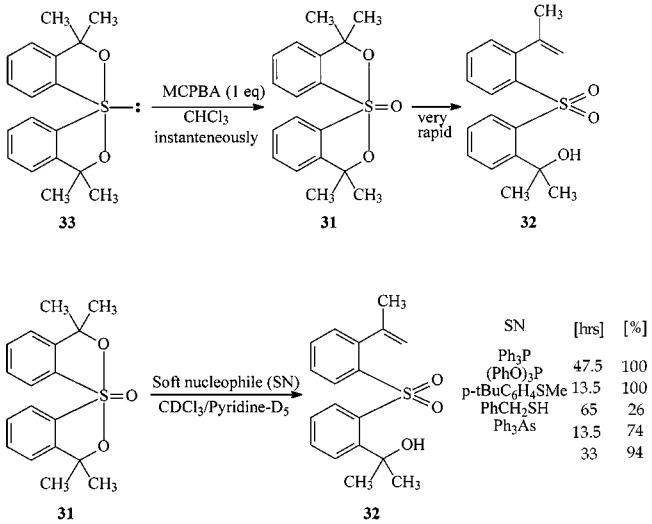


SCHEME 15

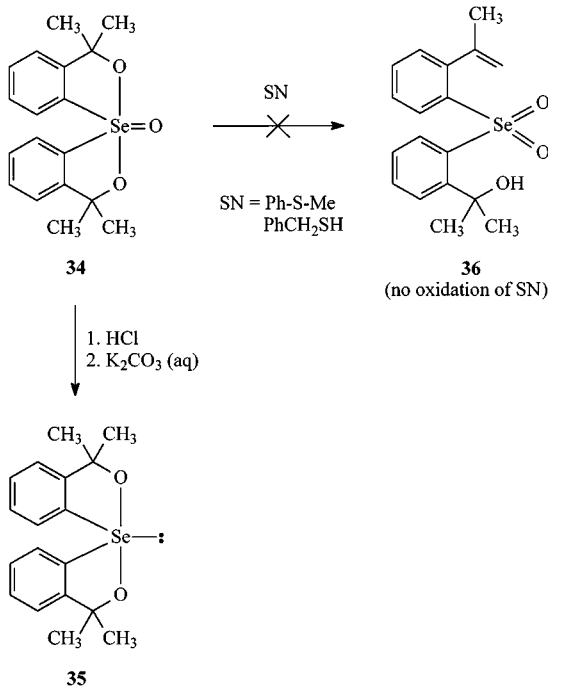
reduction by triphenylphosphine. It was found that this reaction is completed at room temperature after 1 min whereas the reduction of diphenyl sulfoxide under the same reaction conditions has a half-time equal approximately to 26 h (Scheme 15).

UNEXPECTED REACTIONS OF HYPERVALENT SULFUR AND SELENIUM DERIVATIVES

Acid-catalyzed rearrangement of spirosulfurane oxide **31**, derived from the bidentate cumyl ligand of the unsaturated sulfone **32**, was reported by Martin

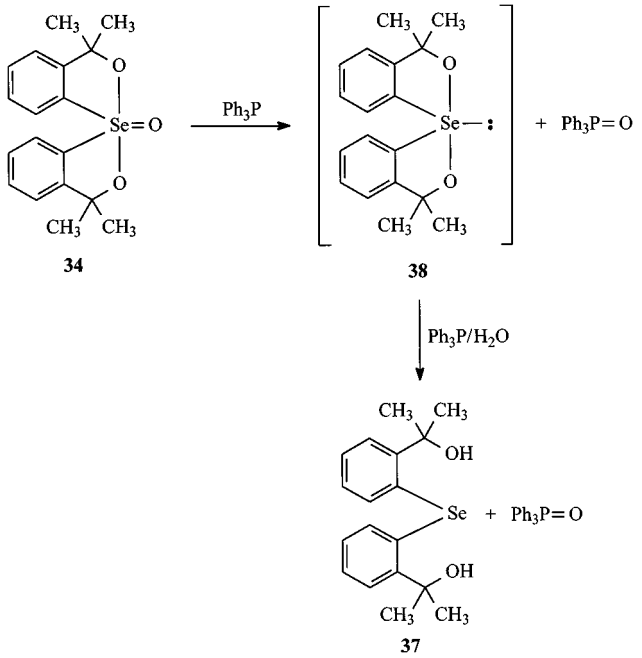


SCHEME 16



SCHEME 17

and Adzima [14]. We have found that this reaction can be catalyzed by a few so-called soft nucleophiles, but the speed of the conversion is very low (J. Drabowicz, unpublished results) (Scheme 16).



SCHEME 18

In a sharp contrast to the sulfurane oxide **31**, the analogous selenurane oxide **34** does not undergo such a rearrangement, even in the presence of gaseous HCl. As a matter of fact, it is unexpectedly reduced under these conditions to the parent selenurane **35** (Scheme 17).

Also, in sharp contrast to the sulfurane oxide **31**, which is opened upon treatment with Ph_3P to the unsaturated sulfone **32**, the selenurane oxide **34** is converted by treatment with two equivalents of Ph_3P, and in the presence of water, into the symmetrical hydroxyalkyl selenide **37** with simultaneous oxidation of triphenylphosphine to the corresponding oxide (Scheme 18). An independent experiment has shown that the selenurane **38** is also converted to the selenide **37** upon treatment with an equivalent amount of Ph_3P and water.

ACKNOWLEDGMENT

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