Alkylative Eliminations. Scope of the Activating Group

Summary: Reaction of alkyl, allyl, and benzyl halides with the anions from benzyl, 3,4-methylenedioxybenzyl, phenylthiomethyl, phenylsulfinylmethyl, and cyanomethyl phenyl sulfoxide leads directly to the corresponding alkylated and eliminated products in a convenient one-pot olefin synthesis

Sir: The observation that the rate of elimination of sulfoxides is appreciably affected by (1) the presence of substituents on the carbon bearing the sulfinyl group, (2) the leaving group ability of sulfur, and (3) the acidity of the hydrogen being abstracted makes this olefin-forming reaction much more synthetically useful.[1,2] In our previous work, we noted that a carbonyl group lowers the activation energy so that eliminations occur between room temperature and 110° at reasonable rates.[2,3] We have been able to combine this mild olefin-forming reaction with the alkylation of the anion of methyl 2-phenylsulfinylacetate to generate a counterpart to the Wittig olefination.[4] In this paper, we explore the generality of this alkylative elimination as a function of activating group.

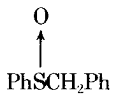
The sulfoxides **1–5** form the corresponding anions on treatment with lithium *N*-isopropylcyclohexylamide; the anions from **4** and **5** were also generated using sodium hydride. In most cases, the alkylation was performed at room temperature in dry THF or DME and the elimination effected by raising the temperature to reflux. The results are summarized in Table I.

The alkylation proceeds smoothly in every case[6,8,9] except the nitrile in which dialkylation was a severe problem.[10] It is quite interesting to note that a single stereoisomer, assigned the *Z* stereochemistry depicted in **7** (entry 13), results from this dialkylation–elimination. This assignment is based upon comparison of the chemical shifts of H_b (δ 6.69) and H_c (δ 6.11) compared to the corresponding shifts in the *E* and *Z* isomers of **6**. In particular, (*E*)-**6** shows H_b downfield and H_c upfield (δ 5.93) from the absorptions for the corresponding protons in (*Z*)-**6** (H_c, δ 6.32). Furthermore, dialkylation was suppressed by adding the anion inversely to warm geranyl bromide. The sluggishness of alkylation of the anion from **4** with an unactivated alkylating agent dictated the use of elevated temperatures (~80°), although no complications were encountered.

The temperatures for elimination in several instances were determined by pyrolyzing the isolated sulfoxides. The conditions determined in this way were incorporated into the one-pot alkylative elimination and are summarized in Table I. In some cases, a scavenger of phenylsulfenic acid, trimethyl phosphite,[11] was employed to avoid decomposition and facilitate isolation of product. Aryl, phenylthio, and cyano on the α carbon facilitate the elimination; however, phenylsulfinyl decelerates elimination. Ease of hydrogen abstraction decreases in the order allylic > benzylic > secondary > tertiary. Thus, in the absence of conformational restraints, the possibility for regioselectivity exists. The stereochemistry of the double bonds is *E* in the reactions using the anions from **1**, **2**, and **4** as determined by NMR (see Table I). As indicated above, monoalkylation of the anion of **5** gave, on elimination, a 1:1 *E*:*Z* mixture[12] in contrast to the corresponding alkylation of the carboxylic ester.[2-4] Alkylation with the anion of **3** gives predominantly the *E* isomer.

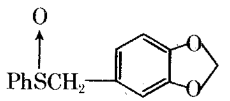
These results demonstrate the utility of the method for making a variety of olefins (aryl ethylenes and butadienes, vinyl thioethers, α,β-unsaturated sulfoxides, and α,β-un-

Table I
Alkylative Elimination[a,b]

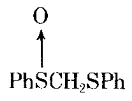


$PhS(\rightarrow O)CH_2Ph$

1,[5] mp 120–122°

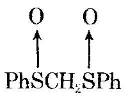


2, mp 85–86°



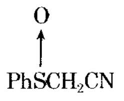
$PhS(\rightarrow O)CH_2SPh$

3[6]



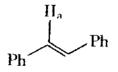
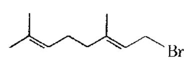
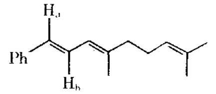
$PhS(\rightarrow O)CH_2S(\rightarrow O)Ph$

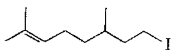
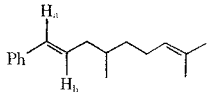
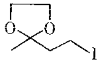
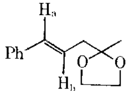
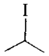
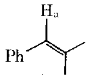
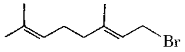
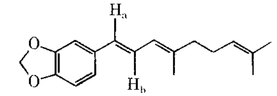
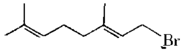
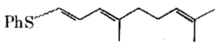
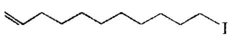
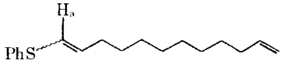
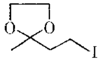
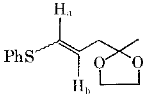
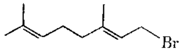
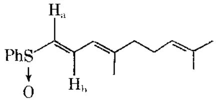
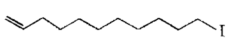
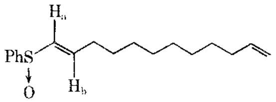
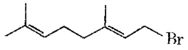
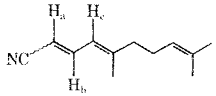
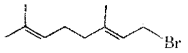
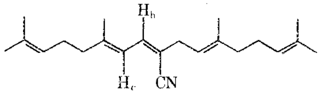
4[5]



$PhS(\rightarrow O)CH_2CN$

5,[7] mp 63–64°

Entry	Sulfoxide	Halide	Reaction conditions, temp, °C (time, hr)	Solvent	Product	% yield[c]	δH_a	δH_b	J_{AB}, Hz
1[d,e]	1	$PhCH_2Br$	0 (1), 20 (1), 85 (1)	DME		79	7.10		
2[d]	1		20 (1), 65 (8)	THF		87	6.35	6.93	15

$3^{d,e}$	1		20 (3), 85 (16)	DME		65	6.35	6.19	16
4^{d}	1		20 (4), 85 (16)	DME		57	6.45	6.22	16
5^{d}	1		20 (20), 180 (10 min)[g]	THF		41	6.25		
$6^{d,e}$	2		0 (1), 20 (1), 85 (1)	DME		67	6.32	*i*	16
$7^{d,e}$	3		0 (1), 20 (1), 85 (2)	DME		66	*j*	*j*	*j*
$8^{d,e}$	3		20 (4), 85 (16)	DME		67	6.12	*k*	15
9^{d}	3		20 (4), 85 (16)	DME		47	(*Z*) 6.44 (*E*) 6.32	5.98 6.04	9.5 15
$10^{e,f}$	4		20 (2), 140 (3.5)	Diglyme		60	6.15	7.13	15
$11^{e,f}$	4		80 (6), 165 (3)	HMPA		45	6.12	6.48	16
$12^{d,e}$	5		65 (4)[h]	THF	 **6**	49	(*Z*) 5.05 (*E*) 5.18	7.06 7.24	11 15
$13^{e,f}$	5	 (2 equiv)	20 (2), 85 (2)	HMPA	 **7**	42		6.69	

---

[a] All new compounds have satisfactory spectral properties. [b] All experiments were performed on a 1-mmol scale. [c] Isolated yields of pure materials. No attempts were made to optimize yields. [d] Anion generated with lithium *N*-isopropylcyclohexylamide. [e] Trimethyl phosphite added just prior to raising temperature for elimination. [f] Anion generated with sodium hydride. [g] Intermediate sulfoxide was pyrolyzed dry with olefin being distilled as formed. In decalin, pyrolysis of sulfoxide required 3 hr at 135°. [h] Carbanion generated in THF added *to* alkylating agent in refluxing THF. [i] H_b coincident with aromatic multiplet. [j] Multiplet of vinyl region in the NMR spectrum precludes interpretation. [k] Mainly *E*. H_b not discernible from terminal vinyl protons.

saturated nitriles) even without optimization of reaction conditions. The gentleness of the method is illustrated both by the sensitive nature of the systems that can be formed, as well as its compatibility with various functionality. Several of the compounds formed using geranyl bromide and citronellyl iodide have interest as juvenile hormone mimics.[13]

Acknowledgment. We wish to thank the National Science Foundation and the National Institutes of Health, General Medical Sciences, for their generous support of our work. A.B. thanks the Science Research Council of the U.K. for a fellowship. We also thank Dr. H. Gswend for informing us of his independent work on the alkylative elimination of phenylthioacetonitrile with benzylic halides.

References and Notes

(1) For earlier work on sulfoxide eliminations, see N. Grabowsky, *Justus Liebigs Ann. Chem.*, **175**, 348 (1875); C. A. Kingsbury and D. J. Cram, *J. Am. Chem. Soc.*, **82**, 1810 (1960); C. Walling and L. Bollyky, *J. Org. Chem.*, **29**, 2699 (1964); D. N. Jones and M. A. Saeed, *Proc. Chem. Soc. London,* 81 (1964); S. I. Goldberg and M. S. Sahli, *J. Org. Chem.*, **32,** 2059 (1967); D. W. Emerson and T. J. Korniski, *ibid.*, **34,** 4115 (1969); D. N. Jones, E. Helmy, and A. C. F. Edmonds, *J. Chem. Soc. C,* 833 (1970); T. Colclough and J. I. Cunneen, *Chem. Ind. (London),* 626 (1960); A. Deljac, Z. Stefanac, and K. Balenovic, *Tetrahedron, Suppl.,* **No. 8** (1), 33 (1966).

(2) B. M. Trost and T. N. Salzmann, *J. Am. Chem. Soc.*, **95,** 6840 (1973).

(3) B. M. Trost and T. N. Salzmann, *J. Org. Chem.*, **40,** 148 (1975).

(4) B. M. Trost, W. P. Conway, P. E. Strege, and T. J. Dietsche, *J. Am. Chem. Soc.*, **96,** 7165 (1974).

(5) R. L. Shiner, H. C. Strock, and W. J. Jorison, *J. Am. Chem. Soc.*, **52,** 2060 (1930).

(6) K. Ogara and G. Tsuchihashi, *Bull. Chem. Soc. Jpn.*, **45,** 2203 (1972).

(7) F. T. Bruderlein, U.S. Patent 3,334,137; *Chem. Abstr.*, **68,** 59328v (1968).

(8) For alkylation of sulfinyl stabilized anions, see P. G. Gassman and G. D. Richmond, *J. Org. Chem.*, **31,** 2355 (1966); T. Durst, R. Viau, and M. R. McClory, *J. Am. Chem. Soc.*, **93,** 3077 (1971); K. Nishihata and M. Nishio, *Chem. Commun.*, 958 (1971); K. Nishihata and M. Nishio, *J. Chem. Soc., Perkin Trans. 2,* 1730 (1972); S. Bory, R. Lett, B. Moreaw, and A. Marquet, *Tetrahedron Lett.*, 4921 (1972); R. Viau and T. Durst, *J. Am. Chem. Soc.*, **95,** 1346 (1973); S. Bory and A. Marquet, *Tetrahedron Lett.*, 4155 (1973); T. Durst and M. Mohn, *ibid.*, 63 (1975).

(9) J. E. Richman, J. L. Herrmann, and R. H. Schlessinger, *Tetrahedron Lett.*, 3267, 3271, 3275 (1973).

(10) Similar problems were encountered with anions of nitriles. See D. S. Watt, *Tetrahedron Lett.*, 707 (1974).

(11) For various thiophiles, see D. A. Evans and G. C. Andrews, *Acc. Chem. Res.*, **7,** 147 (1974). For use of an arylthiol as a sulfenic acid trap, see K. Iwai, M. Kawai, H. Kosugi, and H. Uda, *Chem. Lett.*, 385 (1974), Japanese Transl.

(12) Cf. D. N. Brattesani and C. H. Heathcock, *Tetrahedron Lett.*, 2279 (1974).

(13) For a review see M. Jacobson et al. in "Insect Juvenile Hormones", J. J. Menn and M. Beroza, Ed., Academic Press, New York, N.Y., 1972, pp 249–302, and F. M. Pallos and J. J. Menn, pp 303–316.

(14) Camille and Henry Dreyfus Teacher Scholar Grant Recipient, 1970–1975.

Department of Chemistry
University of Wisconsin
Madison, Wisconsin 53706

Barry M. Trost[*14]
Alex J. Bridges

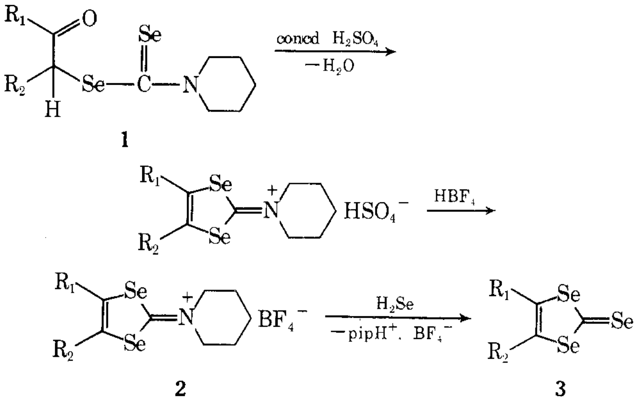
Received March 31, 1975

A Safe Preparation of Mono- and Disubstituted 1,3-Diselenole-2-selones

Summary: The preparation of 2-(*N,N*-pentamethylenimino)-1,3-diselenolium fluoroborate as nonhazardous intermediates in the synthesis of 1,3-diselenole-2-selones and tetraselenafulvalenes is described.

Sir: 1,3-Diselenole-2-selones[1–4] have recently gained in interest as intermediates in the synthesis of certain tetraselenafulvalenes, which form highly conducting organic solids with 7,7′,8,8′-tetracyanoquinodimethane.[2,3,5,6] Two different synthetic routes to 1,3-diselenole-2-selones have been reported. The first[2,4] involves the reaction of selenium and carbon diselenide with sodium acetylides leading to unsubstituted or monosubstituted selones. In the second[1,3] mono- and disubstituted 1,3-diselenole-2-selones are obtained by passing hydrogen selenide through a methanolic solution of 2-(*N,N*-pentamethylenimino)-1,3-diselenolium perchlorates. These salts do, however, detonate upon ignition, heating, and shock and, although we have not so far observed any spontaneous detonations as reported for related systems,[7] their handling in larger quantities constitutes a potential hazard. In spite of this, the use of perchlorates as intermediates was justified by their ready isolation in high yield and purity.

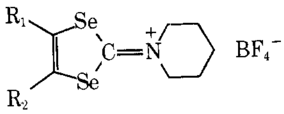
Scheme I



Previous attempts to prepare the fluoroborates (2) by treating the hydrosulfates, obtained by ring closure of 2-oxoalkyl piperidinodiselenocarbamates (1),[1,3] in concentrated H_2SO_4 with an excess of an ethanolic solution of 48% aqueous HBF_4 resulted in a rather poor yield of a deliquescent product.[8]

We have now found that addition of the reaction mixture containing the hydrosulfate to a stirred ethanolic solution containing a 2–3-fold molar excess of HBF_4, prepared from an ethereal solution of HBF_4 (54%, Merck-Schuchardt, Munich), gives well-defined, nonhygroscopic fluoroborates in excellent yields (Table I). This procedure makes the corresponding selones available in large quantities without the safety hazards of the earlier procedure.

Table I
2-(*N,N*-Pentamethylenimino)-1,3-diselenolium Tetrafluoroborates



2

R_1	R_2	Yield, %[a]	Mp, °C
CH_3	H	90[b]	111–112
CH_3	CH_3	91	178–179
Ph	H	93	176–177
$-CH_2CH_2CH_2-$		89	210–212 dec

[a] Satisfactory analytical data (±0.3% for C, H, N) were obtained for all compounds listed in the table. [b] A crystalline product was obtained by addition of ether until turbidity, followed by storage overnight at −30°.

In the general procedure, 0.05 mol of the 2-oxoalkyl piperidinodiselenocarbamate (1)[1,3] (Scheme I) was dissolved slowly in 50 g of concentrated H_2SO_4 over 1 hr. Enough ethyl acetate to cause starting precipitation of the hydrosulfate was added cautiously to the now cooled reaction mixture, which was then filtered through a