of a similar series of experiments with 2-bromobutane gave a plot similar to Figure 1, with the difference that at the highest $[DCPH/Sn^-]_0$ value 17% 2-butyltrimethyltin was formed, suggesting some residual direct displacement (although any geminate reaction would also be included in this value).

1-Bromoadamantane reacts with (trimethyltin)sodium in THF to yield 95% trimethyladamantyltin. The same yield is obtained in liquid ammonia as solvent. Bromobenzene, which has been shown to react by way of phenyl anion intermediates, yields 95% benzene in liquid ammonia. Thus an anion mechanism is unlikely for bromoadamantane. Its reaction with (trimethyltin)sodium in THF in the presence of varying concentrations of DCPH resulted in a decrease in yield of the substitution product to ca. 2% and an increase in the yield of adamantane to 98% in the presence of a threefold or greater excess of DCPH over $(Me_3Sn)Na$ initial concentration. Consequently a possible multicenter mechanism can be excluded in favor of one involving free admantyl radicals, as in Scheme I. The simple tertiary triethylcarbinyl bromide yielded less unambiguous results. In the absence of trap the products were 46% 3-ethyl-2-pentene and 53% 3-ethylpentane. In the presence of excess (4.6-fold) DCPH the yields changed to 32% alkene and 67% alkane. The nearly equal product distribution in the first example suggested disporportionation of triethylcarbinyl radicals. However, only 14% of these were diverted to alkane by the DCPH as indicated by the increase in yield from 53% to 67%. It may be that adamantyl radicals, which should be more reactive, are less hindered from the front side because they are pyramidal, and do not undergo disporportionation, are efficiently trapped. The triethylcarbinyl radicals, being more stable, probably planar, and somewhat sterically hindered, react by disproportionation in effective competition with being trapped. The relatively high concentrations of radicals which might form in this fast reaction, and the low value of 60 kcal/mol[12] for the bond dissociation energy of the β-C–H bond in carbon radicals may be crucial in this case.

When we examined primary bromides under the reaction conditions used, only substitution was observed with simple cases such as *n*-butyl and isobutyl, both in the presence and absence of DCPH. These are presumably S_N2 reactions. When sufficient steric hindrance was introduced to slow down this mechanism sufficiently, as in the case of neopentyl bromide, the results changed. In the absence of trap, 99% substitution product and about 1% neopentane were formed. With a 4.1-fold excess of DCPH, 58% substitution product and 40% neopentane were observed as products. When *tert*-butylamine was present in 9-fold excess, 8% neopentane was formed.[13] As the amine did not function as a trap in the experiments cited above, this suggests that 8% of this reaction proceeded by an anion intermediate mechanism, 32% proceeded by the radical mechanism of Scheme I, and the remainder by S_N2 and geminate reactions.

Bock and Whitesides observed about 80% inversion in the reaction of (trimethyltin)lithium in THF at 0 °C with 1-bromo-3,3-dimethylbutane-*1,2-d*$_2$.[2e] The less than quantitative inversion may be due to the incursion of an electron-transfer mechanism due to the steric hindrance to the S_N2 mechanism introduced by the presence of the *tert*-butyl group.

Several control experiments were conducted to test the validity of the results reported above.[13] DCPH did not react with the halides under the reaction conditions. 1-Bromoadamantane was observed to react at a slightly slower rate in the presence of DCPH than in its absence. This implies that it functions as a trap only after the rate-determining step. Because the retardation in rate is relatively small, a free radical chain mechanism of the SR_N1 type is not involved. Also, in experiments in which either DCPH or 1-bromoadamantane was initially present in a concentration higher than that of Me_3SnNa, the amount of bromide which reacted did not exceed that of tin anion used.

In conclusion, we have shown that DCPH can function as an efficient free-radical trap and thus provide information on the minimum degree of participation of a free-radical mechanism in the reaction of halides with a trimethyltin anionoid. By extension it should be applicable to other nucleophiles whose conjugate acids have pK_a's less than that of DCPH (about 38) and to substrates other than halides.

Acknowledgment. We are grateful to the National Science Foundation for support of this work.

Registry No. Cyclohexane, 110-82-7; cyclohexene, 110-83-8; (trimethylcyclohexyl)tin, 3531-48-4; bromocyclohexane, 108-85-0; (trimethyltin)sodium, 16643-09-7; dicyclohexylphosphine, 829-84-5; 1-bromoadamantane, 768-90-1; (trimethyladamantyl)tin, 51533-74-5; bromobenzene, 108-86-1; benzene, 71-43-2; 2-bromobutane, 78-76-2; (2-butyltrimethyl)tin, 15095-79-1; adamantane, 281-23-2; triethylcarbinyl bromide, 73908-04-0; 3-ethyl-2-pentene, 816-79-5; 3-ethylpentane, 617-78-7; butyl bromide, 109-65-9; *iso*-butyl bromide, 78-77-3; neopentyl bromide, 630-17-1; (trimethyl neopentyl)tin, 55204-72-3; neopentane, 463-82-1.

Henry G. Kuivila,* Gary F. Smith
Department of Chemistry
State University of New York at Albany
Albany, New York 12222
Received March 24, 1980

(12) S. W. Benson, *J. Chem. Educ.*, **42**, 502 (1965).
(13) In the reaction of (trimethyltin)sodium with bromobenzene, *tert*-butylamine was shown to be as effective as *tert*-butyl alcohol[8] in trapping phenyl anions. Only 3% loss of (trimethyltin)sodium (p*Ka* ~25)[9] occurred in the presence of dicyclohexylphosphine in 24 h. The very fast reaction of the anion with 1-bromobutane to form 1-butyltrimethyltin quantitatively was used for analysis.

N-Nitrosoenamines, Versatile New Synthesis Intermediates[1]

Summary: *N*-Nitrosoenamines are reactive toward nucleophilic reagents such as dialkylcopper lithium and enolate ions, as well as being active in electrophilic reactions such as acid-catalyzed additions.

Sir: We have recently reported[2] several convenient preparations of *N*-nitrosoenamines (α,β-unsaturated nitrosamines). These novel substances have proven to be very useful intermediates for the synthesis of a number of interesting substances and hold the promise of much wider exploitation. We present here some representative reactions which will serve to illustrate the versatility of these reagents. It should be remembered that the nitroso

(1) This research was supported by the National Cancer Institute Contract No. N01-CO-75380 and was carried out in partial fulfillment of requirements for the Ph.D. degree of R.K. at the University of Nebraska—Lincoln.
(2) Kupper, R.; Michejda, C. J. *J. Org. Chem.* **1979**, *44*, 2326. Selected *N*-nitrosoenamines were also reported by other workers, whom we failed to cite: Seebach, D.; Enders, D. *Chem. Ber.* **1975**, *108*, 1293; Loeppky, R. N., Smith, D. H. *J. Org. Chem.* **1976**, *41*, 1578. Renger, B.; Seebach, D. *Chem. Ber.* **1977**, *110*, 2334. Seebach, D.; Enders, D.; Reuger, B. *Chem. Ber.* **1977**, *110*, 1852.

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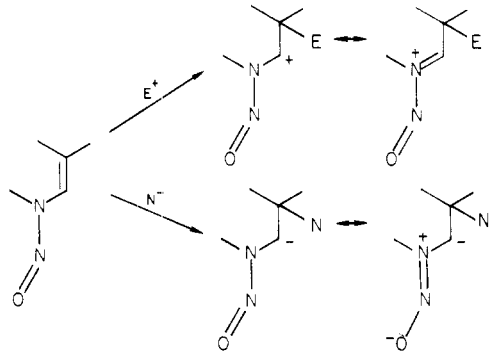
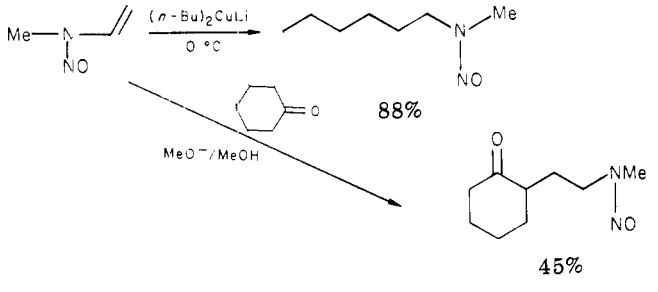
function can be readily cleaved from nitrosamines,[3] so that the *N*-nitroso group can be regarded as a protected secondary amine. Most nitrosamines are potent chemical carcinogens[4] and should be handled with proper care.[5]

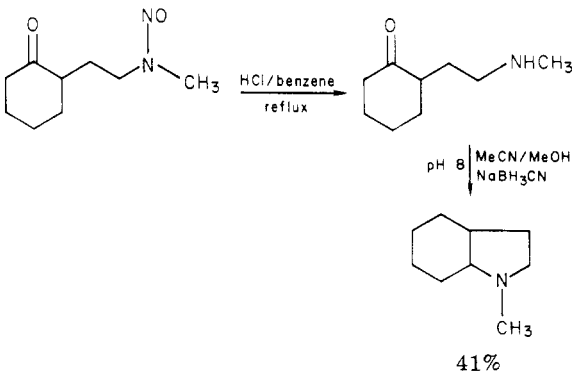
The nitroso function is unique in the fact that it can stabilize both a positive charge[6] and a negative charge[7] on the α-carbon. Consequently, it would be expected that both electrophilic and nucleophilic reagents should react with *N*-nitrosoenamines. This was, in fact, found to be



the case. Thus, methylvinylnitrosamine reacted with di-*n*-butylcopper lithium to form methylhexylnitrosamine in 88% yield and with the enolate of cyclohexanone to form the corresponding adduct in 45% yield.

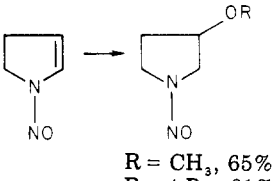


These nitrosamines can be denitrosated essentially quantitatively by using Raney nickel catalyzed hydrogenolysis, the newer procedure developed by Seebach and Wykypiel,[8] which involves one-pot reduction of the nitroso group to the hydrazine with lithium aluminum hydride, followed by Raney nickel catalyzed hydrogenolysis, or mineral acid catalyzed denitrosation, as illustrated below. The nitrosamines formed by the alkylation reaction need not be isolated, thereby minimizing the hazard associated with the handling of these substances. Thus, these reactions are examples of potentially very useful aminoethylations. When the nucleophile adding to the *N*-nitrosoenamine is an enolate ion, the resulting γ-amino alkanones can be cyclized under reductive conditions. Thus, in the above example, the alkylated product, after denitrosation, can be cyclyzed to perhydro-*N*-methylindole.



It is interesting to note that alkyl- and aryllithiums are not the reagents of choice in the Michael-type addition, presumably because reactions involving addition to the nitroso group[9] and the formation of the α-carbanion[7] become important. Thus, phenyllithium reacted with methylvinylnitrosamine to form methyl(2-phenylethyl)-nitrosamine in only a 15% yield, together with several other products.

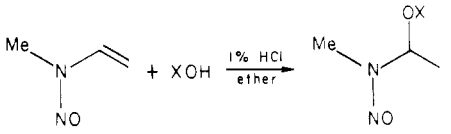
The cyclic *N*-nitrosoenamine 2,3-dehydro-*N*-nitrosopyrrolidine in a base-catalyzed reaction with alcohols yielded 3-alkyoxy-*N*-nitrosopyrrolidines. These reactions



R = CH_3, 65%
R = *t*-Bu, 61%

occurred very rapidly at room temperature.[10] The addition of alkoxide to the six-membered-ring analogue, 2,3-dehydro-*N*-nitrosopiperidine, was very slow. For example, 3-methoxy-*N*-nitrosopiperidine was formed in only an 8% yield after 4 weeks at room temperature. In fact, all additions to the unsaturated piperidine derivative proceeded much more slowly than those to the pyrrolidine or to the acyclic *N*-nitrosoenamines.

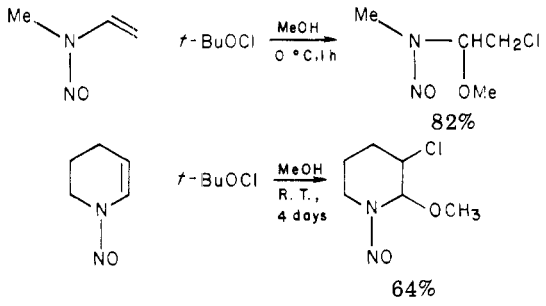
Electrophilic additions to the *N*-nitrosoenamines proceed rapidly. Thus, a mixture of acetic acid (4 equiv), methylvinylnitrosamine, and a catalytic quantity of dry hydrogen chloride in ether at 0 °C gave an excellent yield of methyl(1-acetoxyethyl)nitrosamine. In a similar vein, the acid-catalyzed addition of methanol gave a nearly quantitative yield of the corresponding 1-methoxy derivative. These compounds possess interesting biological properties because they are simple derivatives of α-hydroxylated nitrosamine, which are postulated to be the metabolically formed reactive intermediates involved in cancer initiation by nitrosamines.[11]



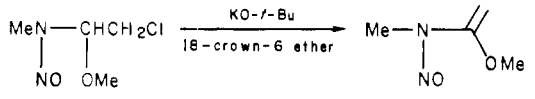
X = Ac, 86%
X = Me, 98%

(3) Eizember, R. F.; Vogler, K. R.; Souter, R. W.; Cannon, W. N.; Wege, P. M., II *J. Org. Chem.* **1979**, *44*, 784.
(4) Magee, P. N.; Montesano, R.; Preussmann, R. In "Chemical Carcinogens"; Searle, C. E., Ed.; American Chemical Society: Washington, D.C., 1976; p 491–625.
(5) It should be pointed out that many substances in current organic laboratory practice are also hazardous in that respect (e.g., benzene, chloroform, dioxane, most derivatives of hydrazine, and many aromatic amines). Experiments described herein were all carried out in an efficient fume hood with care being taken to dispose of nitrosamine wastes in a safe manner. In our case, all the wastes were burned in a high-temperature incinerator.
(6) Baldwin, J. E.; Scott, A.; Branz, S. E.; Tannenbaum, S. R.; Green, L. *J. Org. Chem.* **1978**, *43*, 2427.
(7) Keefer, L. K.; Fodor, C. H. *J. Am. Chem. Soc.* **1970**, *92*, 5747. Seebach, D.; Enders, D. *Chem. Ber.* **1975**, *108*, 1293.
(8) Seebach, D.; Wykypiel, W. *Synthesis* **1979**, 423.
(9) Michejda, C. J.; Schluenz, R. W. *J. Org. Chem.* **1973**, *38*, 2412.
(10) This reaction implies that the 2,3-dehydro-*N*-nitrosopyrrolidine cannot be obtained by isomerization of the 3,4-dehydro isomer.[2] While this is a convenient reaction for all the other systems examined, the five-ring *N*-nitrosoenamine is too reactive toward all manner of nucleophilic reagents. The best way to prepare this compound is via the α-phenylselenonitrosamine method.[2]
(11) Wiessler, M. In "*N*-Nitrosamines"; Anselme, J.-P., Ed.; American Chemical Society: Washington, D.C., 1979; p 57–75.

The reaction of *tert*-butyl hypochlorite with the nitrosoenamines in methanol gave good yields of β-chloro-α-methoxy derivatives. The chloromethoxy adducts allow



a convenient preparation of the heretofore unknown enol ethers of *N*-nitrosamides. Thus, treatment of methyl(1-methoxy-2-chloroethyl)nitrosamine with potassium *tert*-butoxide in ether in the presence of a catalytic quantity of 18-crown-6 ether resulted in a smooth dehydrohalogenation to the corresponding enol ether. Enol ethers of *N*-nitrosamides are potentially very interesting substances because they are readily hydrolyzed to *N*-nitrosamides in mild acid.



In forthcoming publications, applications of some of these reactions will be described.

Registry No. Methylvinylnitrosamine, 4549-40-0; methylhexylnitrosamine, 28538-70-7; cyclohexanone, 108-94-1; methyl(2-(cyclohexanon-2-yl)ethyl)nitrosamine, 73908-51-7; methyl(2-phenylethyl)nitrosamine, 13256-11-6; 2,3-dehydro-*N*-nitrosopyrrolidine, 70501-84-7; 3-methoxy-*N*-nitrosopyrrolidine, 61467-70-7; 3-*tert*-butoxy-*N*-nitrosopyrrolidine, 73908-52-8; methanol, 67-56-1; *tert*-butyl alcohol, 75-65-0; 2,3-dehydro-*N*-nitrosopiperidine, 70501-82-5; 3-methoxy-*N*-nitrosopiperidine, 73908-53-9; acetic acid, 64-19-7; methyl(1-acetoxyethyl)nitrosamine, 65986-79-0; methyl(1-methoxyethyl)nitrosamine, 61738-05-4; methyl(2-chloro-1-methoxyethyl)-nitrosamine, 73926-11-1; 3-chloro-2-methoxy-*N*-nitrosopiperidine, 73908-54-0; methyl(1-methoxyethenyl)nitrosamine, 73908-55-1.

Supplementary Material Available: Experimental detail for general reactions of selected *N*-nitrosoenamines (3 pages). Ordering information is given on any current masthead page.

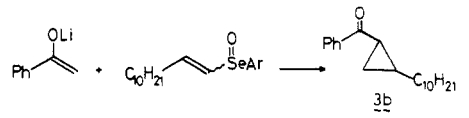
Robert Kupper, Christopher J. Michejda*
Chemical Carcinogenesis Program
Frederick Cancer Research Center
Frederick, Maryland 21701
Received November 6, 1979

Aryl Vinyl Selenoxide as a Versatile Reagent for Transfer of an Ethylene Unit to Enolates. New Synthetic Method of Formation of Cyclopropyl Ketones

Summary: The reaction between an aryl vinyl selenoxide and the lithium enolate of a ketone or an ester gave a cyclopropyl carbonyl compound in good yield.

Sir: Recent developments in organoselenium chemistry have realized a variety of useful reactions for constructing versatile synthetic intermediates.[1]

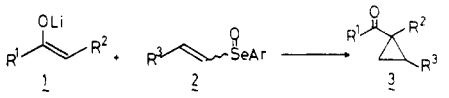
Table I. Effect of Aryl Substituents[a]



Ar	solvent	% yield of 3b[b]
C_6H_5	Et_2O	63
o-$CH_3C_6H_4$	THF	17
m-$CF_3C_6H_4$	Et_2O	73
o-$NO_2C_6H_4$	Et_2O	trace
p-ClC_6H_4	Et_2O	81
p-ClC_6H_4	THF	69
p-ClC_6H_4	THF[c]	91

[a] Reactions were carried out on 0.5-mmol scale with a reactant ratio, enolate-selenoxide = ~1.2-1.25:1.0. [b] Isolated yield. [c] Enolate (1.7 equiv) was used.

We examined the reactivity of aryl vinyl selenoxides[2,3] as 1,4-addition acceptors and found a novel cyclopropanation reaction between aryl vinyl selenoxides and ketone or ester enolates, as shown in eq 1, which consti-



(1)

tutes an efficient method for the transfer of an ethylene unit to ketones or esters to produce cyclopropyl carbonyl compounds.

The following example illustrates a typical procedure. To a solution of LDA (0.75 mmol) in ether (2 mL) was added a solution of acetophenone (66 mg, 0.55 mmol) in ether (3 mL) at −30 °C and the mixture was stirred at that temperature for 30 min. An ethereal (5 mL) solution of *p*-chlorophenyl 1-dodecenyl selenoxide[4] (164 mg, 0.44 mmol) was added to the solution of the enolate and the mixture was stirred at −30 °C for 1 h and then at room temperature for 5 h. The pale yellow mixture was washed with saturated aqueous NaCl and dried. Removal of the solvent followed by purification by preparative TLC gave 1-benzoyl-2-decylcyclopropane (102 mg, 81%) as a colorless oil.

As shown in Table I, significant effects of substituents on the aryl selenoxide moiety were observed in the present reaction. A *p*-chloro or *m*-trifluoromethyl substituent effectively enhanced the desired reaction. In contrast to their effects of enhancing the syn elimination reaction of alkyl aryl selenoxides,[5] *o*-nitrophenyl selenoxide gave poor results. Because *p*-chlorophenyl dodecenyl selenoxide afforded the corresponding cyclopropyl ketone in high

(1) For recent reviews, see: Sharpless, K. B.; Lauer, R. F.; Patrick, D. W.; Singer, S. P.; Young, M. W. *Chem. Scr.* **1975**, *8A*, 9; Clive, D. J. L. *Tetrahedron* **1978**, *34*, 1049; Reich, H. J. *Acc. Chem. Res.* **1979**, *12*, 22.

(2) The preparation of vinyl selenoxides and some of their reactions were reported: Sevrin, M.; Dumont, W.; Krief, A. *Tetrahedron Lett.* **1977**, 3835; see also footnote 7 of ref 6e.

(3) For the use of vinyl sulfoxide as conjugate addition acceptor, see: Tsuchihashi, G.; Mitamura, S.; Inoue, S.; Ogura, K. *Tetrahedron Lett.* **1973**, 323; Tsuchihashi, G.; Mitamura, S.; Ogura, K. *Ibid.* **1976**, 855; Koppel, G. A.; Kinnick, M. D. *J. Chem. Soc., Chem. Commun.* **1975**, 473.

(4) Aryl vinyl selenides were oxidized either by *m*-CPBA or $NaIO_4$. The yields of selenoxides were ~90–100%; see ref 2.

(5) An electron-withdrawing substituent on the aryl group enhances the selenoxide elimination reaction: Sharpless, K. B.; Young, M. W. *J. Org. Chem.* **1975**, *40*, 47; Grieco, P. A.; Masaki, Y.; Boxler, D. *J. Am. Chem. Soc.* **1975**, *97*, 1597; Grieco, P. A.; Noguez, J. A.; Masaki, Y. *Tetrahedron Lett.* **1975**, 4213; Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434.

(6) For the preparation of vinyl selenides, see: (a) Reich, H. J.; Chow, F. *J. Chem. Soc., Chem. Commun.* **1975**, *790*; (b) Raucher, S. *J. Org. Chem.* **1977**, *42*, 2950; (c) Raucher, S.; Hansen, M. R.; Colter, M. A. *Ibid.* **1978**, *43*, 4885; (d) Raucher, S.; Koolpe, G. A. *Ibid.* **1978**, *43*, 3794; (e) *Ibid.* **1978**, *43*, 4252; (f) ref 2; (g) Dumont, W.; Van Ende, D.; Krief, A. *Tetrahedron Lett.* **1979**, 485; (h) Sevrin, M.; Denis, J. N.; Krief, A. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 526.

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