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A NEW REAGENT FOR ALDEHYDE SYNTHESIS. 1-TRIMETHYLSILYL-1-PHENYLSELENOMETHYL-LITHIUM, A SYNTHETIC EQUIVALENT OF FORMYL CARBANION.

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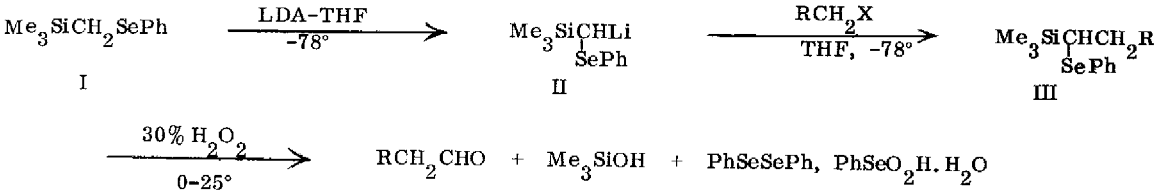
Due to a continued interest in the development of new organosilicon[1] and organoselenium[2] reagents, several recent studies have been reported which document the synthetic versatility of the carbanions stabilized by silicon[3] or by selenium.[4] However, to date no information is available on the chemical characteristics of the carbanions stabilized simultaneously by silicon and selenium. Also, little is known[5] concerning the chemistry of the reaction products of such anions.

In this communication it is shown that the phenylselenomethyltrimethylsilane (I), which can be prepared conveniently in a quantitative yield by the reaction of diphenyl diselenide with two equivalents of sodium borohydride in methanol followed by the addition of chloromethyltrimethyl silane,[6] is a valuable reagent for the transformation of halides to aldehydes as indicated in Scheme A. In view of the current interest in the reagents which act as nucleophilic "carbonyl anion" equivalents,[7] the lithio reagents generated from silyl-selenyl methanes I and III offer useful synthetic equivalents of a protected formyl anion and an acyl anion respectively.

Scheme A



$$\underset{\text{I}}{Me_3SiCH_2SePh} \xrightarrow[-78^\circ]{\text{LDA-THF}} \underset{\text{II}}{Me_3Si\underset{SePh}{C}HLi} \xrightarrow[\text{THF, } -78^\circ]{RCH_2X} \underset{\text{III}}{Me_3Si\underset{SePh}{C}HCH_2R}$$

$$\xrightarrow[0-25^\circ]{30\%\ H_2O_2} RCH_2CHO + Me_3SiOH + PhSeSePh,\ PhSeO_2H.H_2O$$

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The lithio reagent II derived from I with lithium diisopropylamide (LDA) reacts smoothly with primary alkyl bromides and iodides to give the corresponding monoalkylation products III in good to excellent yields. These products when treated with 30% H_2O_2 at 0-25° in THF-ether (conditions generally used for the olefin-forming syn-elimination of alkylphenyl selenoxides[2]) afford directly the corresponding aldehydes. To our knowledge, no examples of this kind of reaction have been reported in the literature.

This procedure has been applied successfully to the aldehyde homologation of primary halides. The results of a representative series are summarized in Table 1.

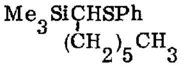
Table 1

Halide	III[a]	(Yield, %)	Aldehyde[b]	(Yield, %)
$CH_3(CH_2)_3CH_2Br$	$R=CH_3(CH_2)_3$-	(94)	$CH_3(CH_2)_4CHO$	(80)
$CH_3(CH_2)_4CH_2I$	$R=CH_3(CH_2)_4$-	(90)	$CH_3(CH_2)_5CHO$	(80)
$CH_3(CH_2)_{12}CH_2Br$	$R=CH_3(CH_2)_{12}$-	(90)	$CH_3(CH_2)_{13}CHO$	(90)
$C_6H_5(CH_2)_2CH_2Br$	$R=C_6H_5(CH_2)_2$-	(88)	$C_6H_5(CH_2)_3CHO$	(75)

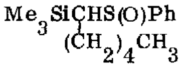
a. All new compounds possessed nmr and mass spectral data consistent with the assigned structures. Yields are based on the isolated products.

b. The aldehydes were identified by their spectral characteristics (nmr and mass spec) and comparison with authentic samples wherever available. The product mixtures were analyzed by vpc on a 6 ft. x 1/8 in. glass column packed with 3% SE-30 on Gas Chrom Q.

In this one step aldehyde synthesis from III, the intermediacy of vinylsilanes which are known[8] to provide convenient routes to the synthesis of carbonyl compounds (via epoxidation followed by hydrolysis under acidic conditions) seems unlikely on the basis of the observation that the sulphur analog IV[9] when treated with sodium periodate (2 equiv) in methanol-acetone at 25° for 20 hr gave the corresponding aldehyde (in low yield), while the *sulfoxide V[10] was recovered unchanged under similar conditions or when refluxed in acetonitrile for 9 hr.*

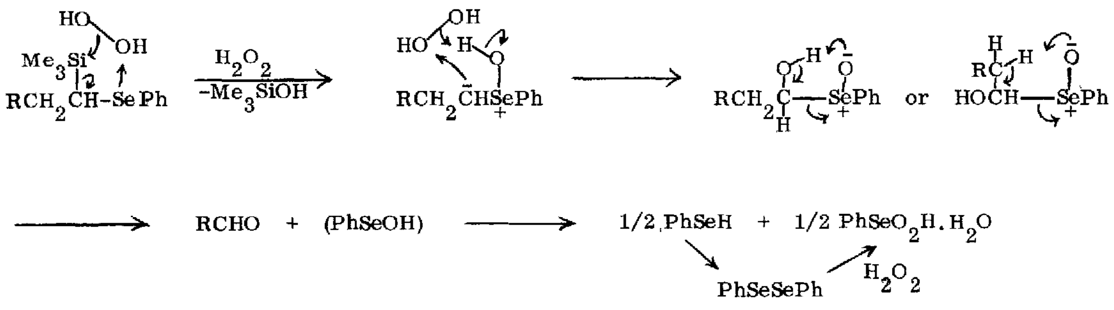

$Me_3SiCH(SPh)(CH_2)_5CH_3$

IV


$Me_3SiCH(S(O)Ph)(CH_2)_4CH_3$

V

One tentative mechanism is presented here: however, studies on this aspect and further synthetic applications of this new reaction are in progress.[11]



Preparation of I. To a stirred solution of diphenyl diselenide (9.36 g, 30 mmole) in 50 ml of methanol was added 2.4 g (63 mmole) of $NaBH_4$ at 0° under argon. When the yellow color had discharged (*ca.* 30 min) the mixture was treated with 7.7 g (64 mmole) of chloromethyltrimethylsilane in 20 ml of methanol. After 2 hr at 25° most of the solvent was removed by evaporative distillation and the mixture was diluted with 1:1 ether-pen-ane (250 ml) and then filtered through Celite 545. The filtrate was concentrated and the residue distilled at 90° 1.0 mm) to give I as a pale colored oil (12.9 g, 90%): nmr ($CDCl_3$, TMS), 0.1 (*s*, $SiMe_3$), 2.1 (*s*, $SeCH_2Si$), and 7.03-7.5 ppm (*m*, aromatic protons).

Monoalkylation of the lithio reagent II. A representative experimental procedure is as follows. To a stirred olution of LDA in dry THF (5 ml) at -78° prepared from 0.72 ml (5 mmole) of diisopropylamine (freshly dis-illed from CaH_2) and 2.4 M *n*-butyllithium in hexane (2.2 ml) in a 50-ml, three-necked, round-bottomed flask was added 1.2 g (5 mmole) of I in dry THF (10 ml) under argon. After 45 min at -78°, 1-bromopentane (0.76 g, mmole) in THF (10 ml) was added dropwise. After 3 hr the reaction was kept at 25° for 4 hr when it was oured into 2:1 ether-water (15 ml). The organic layer was separated and the aqueous portion was extracted with two 10 ml portions of ether. The combined extracts were washed with brine, dried ($MgSO_4$), concentrated nd distilled at 115-117° (0.12 mm) to yield III (R=$CH_3(CH_2)_3$-) as a colorless oil (1.45 g, 94%): nmr ($CDCl_3$, MS), 0.1 (*s*, $SiMe_3$), 0.62-1.83 (11 H, aliphatic protons), 2.4 (partially resolved triplet, SeCHSi) and 7.1-.63 ppm (pair of multiplets, aromatic protons).

reatment of III (R=$CH_3(CH_2)_3$-) with 30% H_2O_2 at 0-25°; isolation of 1-hexanal. To a stirred solution of the ove product (0.62 g, 2 mmole) in 4:6 THF-ether (10 ml) (only THF was used for higher molecular weight ompounds) at 0° was added 30% H_2O_2 (0.5 ml, *ca.* 2 equiv). After 10 min the colorless reaction mixture was lowed to warm to ambient temperature which caused a brisk reaction resulting in yellow color. During 1 hr 25° a white solid was deposited which was filtered and washed with ether to give 0.25 g, identified as $Se(OH)_3$, m.p. 115°d. The filtrate was washed with brine, dried ($MgSO_4$) and the solvent removed by distilla-on. The residue was transferred under reduced pressure into a cold trap to give a colorless liquid (0.3 g) hich was identified as a mixture of trimethylsilylol and 1-hexanal by nmr and vpc analysis. Me_3SiOH was parated by washing an ether solution of the mixture with cold 0.1 N sodium hydroxide (in the cases of higher iling aldehydes, i.e., $Ph(CH_2)_3CHO$ and $CH_3(CH_2)_{13}CHO$, silylol was separated by fractional distillation). e yellow pot residue was identified as diphenyl diselenide.

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REFERENCES

1. R. F. Cunico, *J. Organometal. Chem.*, **109**, 1 (1976).
2. K. B. Sharpless *et al*, *Chem. Scr.*, **8A**, 9 (1975), and the literature cited therein.
3. (a) E. J. Corey, D. Seebach and R. Freedman, *J. Amer. Chem. Soc.*, **89**, 434 (1967); (b) E. J. Corey, D. Enders and M. G. Bock, *Tetrahedron Letters*, 7 (1976); (c) F. A. Carey and A. S. Court, *J. Org. Chem.*, **37**, 939, 1926 (1972); (d) H. Yamamoto *et al*, *J. Amer. Chem. Soc.*, **96**, 1620 (1974).
4. D. Seebach and N. Peletier, *Angew. Chem.*, **81**, 465 (1969); K. B. Sharpless, R. F. Lauer and A. Y. Taranishi, *J. Amer. Chem. Soc.*, **95**, 6137 (1973); D. Seebach and A. K. Beck, *Angew. Chem. Int. Ed.*, **13**, 806 (1974); W. Dumont, P. Bayet and A. Krief, *ibid.*, 804; *ibid.*, **14**, 350 (1975).
5. Products analogous to III have recently been obtained from selenoketals and employed for generating α-silylcarbanions by the cleavage of the carbon-selenium bond with *n*-butyllithium at 0° in THF. W. Dumont and A. Krief, *Angew. Chem. Int. Ed.*, **15**, 161 (1976).
6. A condensation of phenylselenol (Pfaltz and Bauer) with chloromethyltrimethylsilane according to the procedure of G. D. Cooper, *J. Amer. Chem. Soc.*, **76**, 3713 (1954) for phenylthiomethyltrimethylsilane gave 76% of I (H. S. Sachdev and J. Sheu).
7. E. J. Corey and D. Seebach, *Angew. Chem.*, **77**, 1134 (1965); D. Seebach and M. Kolb, *Chem. and Ind.*, 687 (1974); J. E. Baldwin, *et al*, *J. Amer. Chem. Soc.*, **96**, 7125 (1974) and references cited therein.
8. G. Stork and E. Colvin, *J. Amer. Chem. Soc.*, **93**, 2080 (1971); B. T. Grobel and D. Seebach, *Angew. Chem. Int. Ed.*, **13**, 83 (1974).
9. Colorless liquid, b.p. 110-115° (0.1 mm), prepared in 60% yield by the alkylation of 1-trimethylsilyl-1-phenylthiomethyllithium[3c] with 1-iodohexane in THF at -20° to 25° for 14 hr.
10. Prepared in 95% yield by the sequential treatment of methyl phenyl sulfoxide in THF with an equivalent each of *n*-butyllithium (30 min, -78°), 1-iodopentane (3 hr, -78°; 30 min, 20°), *n*-butyllithium (30 min, -78°), chlorotrimethylsilane (3 hr, -78°; 1 hr, 20°) followed by the usual workup and purification by tlc.
11. The following interesting oxidative rearrangement has been brought to our attention by the referee K. B. Sharpless and M. W. Young, unpublished results.