SULFENYLATION AND SELENYLATION OF NITRILES

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We have examined the reaction of α -lithiated nitriles with dimethyl disulfide,¹ diphenyl diselenide,^{2,3} and phenylselenyl bromide.³ These reagents have recently been found to react with α -lithiated ketones,^{1,2} esters,¹⁻³ and lactones⁴ to yield α -methylthio¹ or α -phenylseleno²⁻⁴ carbonyl compounds. Oxidation to the α -sulfoxide or α -selenoxide, followed by pyrolytic elimination yields α,β -unsaturated ketones, esters, or lactones.

We have found that nitriles may be similarly sulfenylated or selenylated provided that two equivalents of base are used to form the nitrile anion. A typical procedure for the conversion of octanonitrile (1) to (E and Z)-2-octenonitrile (3 and 4) via 2-phenylselenooctanonitrile (2) follows:



Preparation of (E and Z)-2-octenonitrile:

To a stirred, cold (0°C) solution of N-isopropylcyclohexylamine (2.83 g, 20 mmoles) in 20 ml of freshly distilled, anhydrous THF, under N₂, is added

dropwise a solution of n-butyllithium in hexane (9.31 ml, 2.145 M, 20 mmoles).⁵ The reaction mixture is allowed to warm to room temperature over a 30 min period, and is then cooled to -75°. Octanonitrile (1.25 g, 10 mmoles) is added dropwise over a 10 min period and the solution is kept at -75° for an additional 30 min, then allowed to warm to room temperature. A solution of diphenyl diselenide (3.12 g, 10 mmoles) in 4 ml anhydrous THF is added dropwise over a 10 min period. After 1.5 hrs, the reaction mixture is poured into 30 ml of cold, saturated NHACl solution. The resulting mixture is extracted with 20 ml of ethyl acetate. After washing the ethyl acetate solution with 5% HCl, 5% NaOH, and water, it is dried over K2CO3 and diluted with 70 ml of ethyl acetate and 45 ml of THF. This solution is stirred at room temperature while 30% aqueous H₂O₂ (2.6 ml, 30 mmoles) is added dropwise over a 20 min period. After an additional 2 hrs, the mixture is washed with water and 5% Na₂CO₃, and is then dried over K2CO3. Evaporation of solvent affords 1.18 g (96%) of crude product, shown by glpc to consist of 54% E-2-octenonitrile (2) and 46% Z-2octenonitrile (3). The ir, pmr, and low resolution mass spectra of the products fully define their structures.

Essentially the same results are obtained using phenylselenyl bromide instead of diphenyl diselenide. In that case, the selenylation is carried out at -78°. In a similar manner, the α -lithiated octanonitrile reacts with dimethyldisulfide to yield 2-methylthiooctanonitrile (5) in 94% yield.



If only one equivalent of base is used in either the sulfenylation or selenylation reaction, the initial α -sulfenylated or selenylated product rapidly equilibrates with unreacted α -lithiated nitrile. In the case of dimethyl disulfide, a completely statistical mixture of starting nitrile, α -methylthionitrile 5 and α -bis(methylthio)nitrile 6 (1:2:1) results, even with inverse addition.



In the case of phenylselenyl bromide and diphenyl diselenide, only partial selenylation results. After oxidation and elimination, substantial quantities of starting octanonitrile are recovered. The results obtained in several runs are summarized in the Table.

| Base | Equivalents of base | Electrophile | Mode of Addition | <pre>% Yield</pre> | Ratio $\frac{3+4}{1}$ |
|-------------------------------|------------------------|-----------------------|----------------------|--------------------|-----------------------|
| LDA ^a | 1.0 | ØSeBr ^C | inverse ^e | 80 | 38/62 |
| LDA | 1.0 | ØSeBr ^C | normal | 76 | 25/75 |
| $\mathtt{LICHA}^{\mathtt{b}}$ | 1.0 | ØSeBr ^C | inverse | 83 | 40/60 |
| LICHA | 1.0 | ØSeBr ^C | normal | 81 | 30/70 |
| LICHA | 2.0 | ØSeBr ^C | inverse | ∿100 | 100/0 |
| LICHA | 1.0 | ØSeSeØ ^C | inverse | 85 | 72/28 |
| LICHA | 1.0 | EtSeBr ^{c,f} | inverse | 87 | 40/60 |
| LICHA | 1.0 | ØSe0Ac ^d | inverse | 82 | 30/70 |
| LICHA | 2.0 | ØSeSeØ ^d | inverse | 96 | 100/0 |

a) Lithium diisopropylamide b) lithium isopropylcyclohexylamide c) selenylation carried out at -78° d) selenylation carried out at 25° e) nitrile anion added to selenylating agent f) EtSeBr is prepared by the bromination of EtSeSeEt, a reagent that has a stench so vile as to preclude its use in almost all cases.

The proton transfer from the α -sulfenylated or α -selenylated nitrile to the starting nitrile anion is apparently very fast relative to sulfenylation or selenylation. In the case of the dialkyl disulfide, a random product mixture results. With the various selenylating reagents, although bisselenylation does not occur, part of the electrophile appears to be siphoned off by reaction with some other species in the reaction mixture, probably the dialkylamine.

Table

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