

SULFENYLATION AND SELENYLATION OF NITRILES

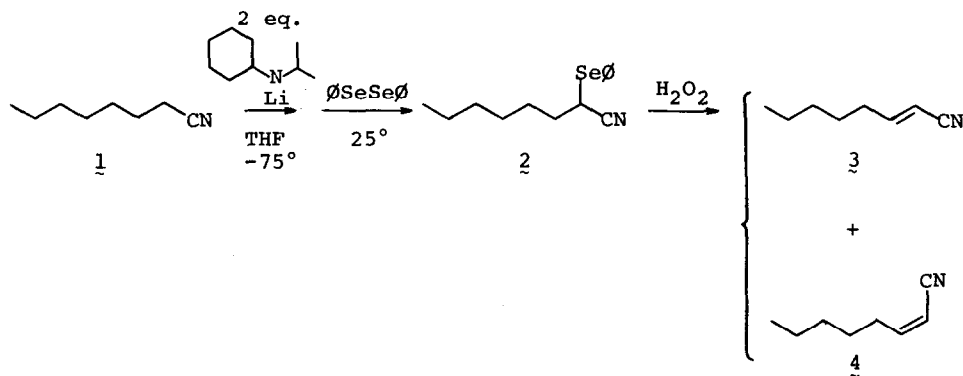
D.N. Brattesani and C.H. Heathcock\*

Department of Chemistry, University of California  
Berkeley, California 94720

(Received in USA 25 April 1974; received in UK for publication 20 May 1974)

We have examined the reaction of  $\alpha$ -lithiated nitriles with dimethyl disulfide,<sup>1</sup> diphenyl diselenide,<sup>2,3</sup> and phenylselenyl bromide.<sup>3</sup> These reagents have recently been found to react with  $\alpha$ -lithiated ketones,<sup>1,2</sup> esters,<sup>1-3</sup> and lactones<sup>4</sup> to yield  $\alpha$ -methylthio<sup>1</sup> or  $\alpha$ -phenylseleno<sup>2-4</sup> carbonyl compounds. Oxidation to the  $\alpha$ -sulfoxide or  $\alpha$ -selenoxide, followed by pyrolytic elimination yields  $\alpha,\beta$ -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:

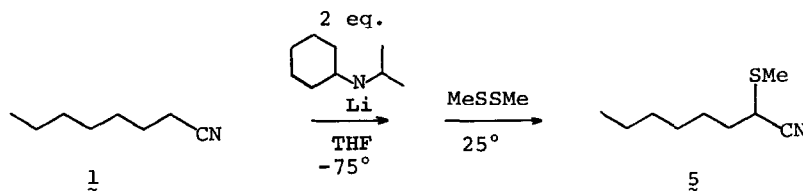


Preparation of (E and Z)-2-octenonitrile:

To a stirred, cold (0°C) solution of N-isopropylcyclohexylamine (2.83 g, 20 mmoles) in 20 ml of freshly distilled, anhydrous THF, under  $\text{N}_2$ , is added

dropwise a solution of n-butyllithium in hexane (9.31 ml, 2.145 M, 20 mmoles).<sup>5</sup> The reaction mixture is allowed to warm to room temperature over a 30 min period, and is then cooled to  $-75^{\circ}$ . Octanonitrile (1.25 g, 10 mmoles) is added dropwise over a 10 min period and the solution is kept at  $-75^{\circ}$  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  $\text{NH}_4\text{Cl}$  solution. The resulting mixture is extracted with 20 ml of ethyl acetate. After washing the ethyl acetate solution with 5%  $\text{HCl}$ , 5%  $\text{NaOH}$ , and water, it is dried over  $\text{K}_2\text{CO}_3$  and diluted with 70 ml of ethyl acetate and 45 ml of THF. This solution is stirred at room temperature while 30% aqueous  $\text{H}_2\text{O}_2$  (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%  $\text{Na}_2\text{CO}_3$ , and is then dried over  $\text{K}_2\text{CO}_3$ . Evaporation of solvent affords 1.18 g (96%) of crude product, shown by glpc to consist of 54% E-2-octenitrile (2) and 46% Z-2-octenitrile (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  $-78^{\circ}$ . In a similar manner, the  $\alpha$ -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  $\alpha$ -sulfenylated or selenylated product rapidly equilibrates with unreacted  $\alpha$ -lithiated nitrile. In the case of dimethyldisulfide, a completely statistical mixture of starting nitrile,  $\alpha$ -methylthionitrile 5 and  $\alpha$ -bis(methylthio)nitrile 6 (1:2:1) results, even with inverse addition.



Acknowledgement: We gratefully acknowledge financial support from the National Science Foundation.

References

1. B.M. Trost and T.N. Salzman, J. Amer. Chem. Soc., 95, 6840 (1973).
2. H.J. Reich, I.L. Reich, and J.M. Renga, ibid., 95, 5813 (1973).
3. K.B. Sharpless, R.F. Lauer, and A.Y. Teranishi, ibid., 95, 6137 (1973).
4. P.A. Grieco and M. Miyashita, J. Org. Chem., 39, 120 (1974).
5. M.W. Rathke and A. Kindert, J. Amer. Chem. Soc., 93, 2318 (1971).