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THE GENERATION OF UNCOMPLEXED PHENYL SELENIDE ANION AND ITS APPLICABILITY TO S_N2 - TYPE ESTER CLEAVAGES

Dennis Liotta*, William Markiewicz and Hector Santiesteban

Department of Chemistry, Emory University, Atlanta, Georgia 30322

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The utility of aryl selenide anions for effecting a wide variety of synthetic transformations is now well-established.[1] In this communication we wish to report a new method for generating a reactive phenyl selenide anion and the application of this anion to the facile, high-yield cleavage of alkyl esters.

The standard conditions used in generating an aryl selenide anion typically involve reduction of the appropriate diaryl diselenide or aryl selenocyanate with sodium borohydride in ethanol, followed by addition of the substrate in tetrahydrofuran (THF).[1a] Because a number of the systems under investigation in our laboratory are sensitive to sodium borohydride, it seemed advisable to find another method for generating these anions. Reaction of diphenyl diselenide (<u>1</u>) with sodium metal in dry refluxing THF for three to four hours produces a copious precipitate which is insoluble in absolute ethanol/THF solution.[2] This is quite surprising in that phenyl selenide anion, generated under standard conditions (<u>vide supra</u>), yields a colorless, homogeneous solution. When the precipitate formed from reaction of <u>1</u> with sodium is solubilized by the addition of a small amount of hexamethylphosphoramide (HMPA) and to this solution is added a molar equivalent of n-decyl bromide at room temperature, a quantitative yield of n-decyl phenyl selenide (<u>2</u>) is obtained. Thus, although both methods ultimately yield the same product, the anions which are responsible for the reaction are obviously quite different.

In order to understand the differences in the generation of phenyl selenide anion, it is of interest to examine the stoichiometry of the two reductions (see Eqs. 1 and 2).

$$\mathrm{PhSeSePh} + 2\,\mathrm{Na}^{o} \xrightarrow{\mathrm{THF}} 2\,\mathrm{Na}^{+}\,{}^{-}\mathrm{SePh} \qquad (1)$$

$$\mathrm{PhSeSePh} + 2\,\mathrm{NaBH}_4 \xrightarrow[\mathrm{THF}]{\mathrm{EtOH}} 2\,\mathrm{Na}^{+}[(\mathrm{PhSe})\mathrm{BH}_3]^{-} + \mathrm{H}_2 \qquad (2)$$

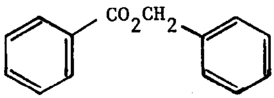
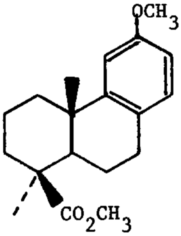
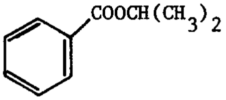
Besides the hydrogen evolved in the sodium borohydride reduction, the only difference in the products of these two processes is the presence of the excess elements B_2H_6 in Eq. 2. Thus, the stoichiometry, as written in Eq. 2, implies that *the reduction of diphenyl diselenide with sodium borohydride generates a phenyl selenyl/borane complex.*[3] Consistent with this, we have found that the addition of both absolute ethanol and diborane in THF immediately converts the precipitate, generated according to Eq. 1, to a colorless, homogeneous solution, which, upon addition of n-decyl bromide, gives 2 in 93% yield.[5] Furthermore, reaction of benzeneselenol and sodium hydride in THF at room temperature (see Eq. 3) produces an anion which in every respect resembles the anion generated by the process given in Eq. 1.

$$\mathrm{PhSeH} + \mathrm{NaH} \xrightarrow{\mathrm{THF}} \mathrm{Na}^{+}\,{}^{-}\mathrm{SePh} + \mathrm{H_2} \qquad (3)$$

Since the phenyl selenide anion, generated according to either Eqs. 1 or 3, is not a complex, it should be substantially more reactive than the anion generated under standard conditions. In accord with this, we have been able to effect S_N2-type ester cleavages on a wide variety of alkyl esters using this uncomplexed anion (see Table I).[6] A generalized experimental procedure for this process is as follows: To a solution of 0.1 mole of diphenyl diselenide in dry THF (20 ml) is added 0.22 gram atom of sodium metal and the resulting mixture is allowed to reflux for three to four hours. After allowing the mixture to cool to room temperature, the flask is sequentially charged with HMPA (2 ml) and 0.2 mole of the alkyl ester. The deep orange/brown solution is allowed to reflux for a number of hours during which time a copious precipitate forms. After cooling to room temperature the mixture is quenched with 10 ml of methanol and poured into 150 ml of water and extracted with ether. The basic aqueous solution is then acidified, washed with ether, dried and stripped of solvent. In general, the acid obtained by this procedure is essentially pure. Evaporation of the original ether extract yields the appropriate alkyl phenyl selenide which was isolated for all the listings in Table I with the exception of 8.[7] Interestingly, the relatively low reaction temperatures and short reaction times required for this procedure make it one of the mildest methods now available for S_N2-type ester cleavage reactions.[8]

In conclusion, we believe that we have presented compelling evidence that "phenyl selenide

TABLE I. The Reaction of Alkyl Esters with Uncomplexed Phenyl Selenide Anion.

Ester	% Yield of[a] Acid	Reflux[b] Time	Ester	% Yield of[a] Acid	Reflux[b] Time
$(CH_3)_3C\,COOCH_3$ 3	98%	7 hrs.	$CH_3(CH_2)_3CO_2CH_2CH_3$ 6	99%	8 hrs.
 4	96%	8 hrs	$(CH_3)_2CHCH_2CO_2(CH_2)_2CH(CH_3)_2$ 7	92.4%	12 hrs.
 5	100%	10 hrs.	 8	99%	24 hrs.

[a] % yields refer to isolated yields of the corresponding carboxylic acid. Products were identified by analysis of their ir, nmr and mass spectra as well as comparison of their physical properties with authentic samples.

[b] Reflux times have not been optimized.

anion", generated by borohydride reduction of 1, is actually a borane complex.[9] Furthermore, we have demonstrated that uncomplexed phenyl selenide anion is a potent nucleophile which is capable of cleaving esters in high yield under mild conditions.

FOOTNOTES AND REFERENCES

(1) (a) K. B. Sharpless and R. F. Lauer, J. Amer. Chem. Soc., 95, 2697 (1973); K. B. Sharpless, R. F. Lauer and A. Y. Teranishi, J. Amer. Chem. Soc., 95, 6137 (1973); P. A. Grieco, S. Gilman, M. Nishizawa, J. Org. Chem., 41, 1485 (1976); R. Ahmad, J. Saa and M. P. Cava, J. Org. Chem., 42, 1228 (1977).

(2) Even twenty times the quantity of ethanol used in Ref. 1a would not dissolve the precipitate.

(3) Since it is known (Ref. 4) that in borohydride reductions, hydrides are replaced by alkoxy groups derived from the alcohol solvent, it is reasonable to assume that the soft acid, BH_3, preferentially interacts with the soft base, phenyl selenide, rather than the harder alcohol solvent.

(4) D. C. Wigfield and F. W. Gowland, Tetrahedron Lett., 3373 (1976).

(5) The quantities of reagents were chosen to closely mimick the anion obtained under standard conditions.

(6) If the anion is generated according to Eq. 2, no reaction is obtained with a variety of simple alkyl esters after three hours of reflux.

(7) The reaction of phenyl selenide with 8 may not be an S_N2 process, but may instead proceed by acyl/oxygen cleavage or E2 elimination.

(8) J. McMurry, Org. Reac., 24, 187 (1977).

(9) The exact nature of this complex is not known. However, the addition of a molar equivalent of triethyl borate failed to dissolve the uncomplexed sodium phenyl selenide anion.