INVESTIGATION OF SELENIDES OF THE THIOPHENE AND FURAN SERIES

VII.* CLEAVAGE OF SOME ARYL HETARYL SELENIDES BY n-BUTYLLITHIUM OR BROMINE

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As in the case of alkyl 2-thienyl selenides, replacement of the alkylseleno group to form the corresponding lithium derivative is observed when n-butyllithium acts on alkyl 2-furyl and alkyl 2-selenienyl selenides. The alkylselenide function is also replaced when alkyl 2-thienyl selenides are treated with excess bromine. A scheme of the mechanism for the reaction of alkyl 2-hetaryl selenides with n-butyllithium is proposed. Alkyl 2-furyl selenides undergo the diene synthesis with maleic anhydride to give phthalic anhydride without a selenide function as the final product.

We have previously observed that, under the conditions of metallation with n-butyllithium, alkyl 2-thienyl selenides split out an alkylseleno group to form 2-thienyllithium [2,3]. It was of interest to ascertain the behavior of substituents (in the 2 position of the alkylseleno group) of other five-membered heterocycles – furan and selenophene – under similar conditions. We found also in this case that the alkylseleno group is replaced to form the corresponding Li derivative and dialkyl selenide. In particular, 2-methylselenofuran and 2-methylselenoselenophene form, respectively, furan- and selenophene-2-carboxylic acids as a result of the action of n-butyllithium and subsequent carbonation.

In order to ascertain the effect of the nature of the alkyl group bonded to the selenium atom on the elimination of an alkylseleno group, we made a study of the action of n-butyllithium on 2-butylselenothiophene. The yields of reaction products in this case are somewhat higher than in the case of 2-methylselenothiophene [2], which can apparently be explained by the relatively greater inductive effect of the butyl group as compared with the methyl group.

In order to compare the behavior of aromatic and heteroaromatic selenides under the conditions of the metallation with n-butyllithium, we studied the behavior toward the latter of selenoanisole under similar conditions. Replacement of an alkylseleno group did not occur in this case, and up to 82% of the starting selenoanisole was recovered. We note, however, that cleavage of the Ar–Se bond in selenoanisole does occur but under more severe conditions and to a much lesser degree [4, 5] than in the case of the cleavage of the hetaryl–selenium bond that we observed.

The process that occurs during the reaction of 2-alkylseleno derivatives of five-membered heterocycles with n-butyllithium can be depicted as shown by the following scheme. The proposed scheme differs from the mechanism for the elimination of an alkylmercapto group in alkyl phenyl sulfides [6] in that, in the latter case, metallation occurs at the α-carbon atom of the side chain, and a four-membered cyclic transition state then develops, and the Ar–Se bond is cleaved.

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*See [1] for communication VI.

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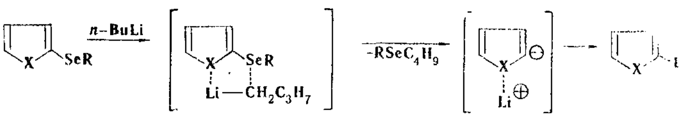
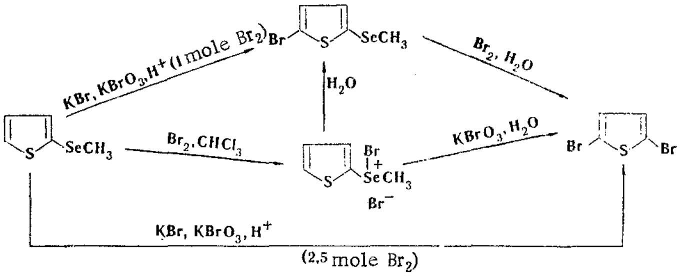


X=O, S, Se; R=Alk

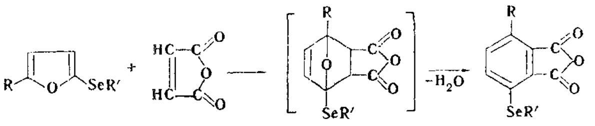
Since substitution of an alkylseleno group by lithium under the influence of n-butyllithium can, in principle, be used for the synthesis of difficult-to-obtain 2,3- and 2,4-derivatives of thiophene and, possibly, other five-membered heterocycles, we attempted to find a different method for cleaving the hetaryl–selenium bond since, in the case of alkyl hetaryl selenides bearing functional groups of the OH, CHO, COR, etc. type, attack of n-butyllithium can be directed primarily to these groups.

We observed another type of cleavage of the C–Se bond in a study of the bromination of alkyl 2-thienyl selenides. Proceeding from the noted analogy in the behavior of sulfides and selenides of the thiophene series in electrophilic substitution reactions [7, 8], it might have been expected that in the bromination of 2-methylselenothiophene, bromine would enter the free α position of the thiophene ring, as in the case of 2-methylmercaptothiophene [9]. In fact, the action of a bromide–bromate solution, in the amount necessary for the liberation of one equivalent of bromine, on 2-methylselenothiphene gave 40-45% 5-bromo-2-methylselenothiophene, which, however, according to gas-liquid chromatography, contains 10% 2,5-dibromothiophene, the formation of which was not noted in the bromination of 2-methylmercaptothiophene [9]. Moreover, the direct attack of the free α position is not observed in the action of bromine in chloroform at lower temperatures on 2-methylselenothiophene, but a quantitative yield of a colored, crystalline substance, which is the product of the addition of two bromine atoms to the selenium atom, is formed. 5-Methylseleno-2-methylthiophene behaves similarly under these conditions. The dibromides obtained apparently contain ionogenic bromine, since they titrate potentiometrically. The ionogenic character of bromine in dibromides of selenides has been reported (see, for example, [10, 11]), but, in addition, data on the poor conductivity of a solution of 4-methylselenoacetophenone dichloride served as a basis for the assumption of covalent character of the Hal–Se bond in such compounds [12].

We studied several transformations of the dibromides obtained. The alkylseleno group is replaced to form 2,5-dibromothiophene by the action of aqueous potassium bromate on the dibromide of 2-methylselenothiophene. However, on contact with water, the dibromide is slowly converted to 5-bromo-2-methylselenothiophene, which is converted to 2,5-dibromothiophene on reaction with bromine water. 2,5-Dibromothiophene is also formed by the action of a bromide-bromate solution (in the amount necessary for the liberation of 2.5 mole of bromine) on 2-methylselenothiophene.



Like the bromination of 2-alkylselenothiophene in the free α position of the ring under the influence of bromine, the clarification of the mechanism of the cleavage of the C–Se bond requires additional thorough investigation.



R=H, alkyl; R′= alkyl

Continuing our study of the properties of alkyl hetaryl selenides in comparison with the properties of the analogous sulfides, we investigated the reaction of alkyl furyl selenides with maleic anhydride. As in the case of the corresponding alkyl furyl sulfides [13, 14], adducts, which split out a molecule of water to give phthalic anhydrides containing a selenide function, are formed. This makes it possible to realize the transition from selenides of the furan series to selenides of the benzene series.

EXPERIMENTAL

Action of n-Butyllithium on 2-Methylselenofuran. A total of 5.1 ml of a 1.8 N ether solution of n-butyllithium was added under nitrogen to a solution of 1.5 g (93 mmole) of 2-methylselenofuran in 20 ml of absolute ether. The mixture was stirred for 2 h at room temperature and poured over finely crushed dry ice. The dry ice was evaporated, and the residue was dissolved in the minimum amount of water. The aqueous solution was extracted thoroughly with ether, and the extract was dried with anhydrous $MgSO_4$. Removal of the ether by distillation gave 0.84 g (64%) of methyl butyl selenide with bp 141-142° and n_D^{20} 1.4764 (bp 141° and n_D^{20} 1.4771 [15]). The aqueous layer was acidified with 1 N HCl and extracted thoroughly with ether. Removal of the ether by distillation gave 0.65 g (62%) of furan-2-carboxylic acid with mp 132-133° (from water) [16].

Action of n-Butyllithium on 2-Methylselenoselenophene. As above, 1.13 g (5 mmole) of 2-methylselenophene gave 0.77 g (88%) of selenophene-2-carboxylic acid with mp 120-121° (from water) [17]. Gas-liquid chromatography of the ether layer showed one peak that had the same retention time as the peak of methyl butyl selenide.

Action of n-Butyllithium on 2-Butylselenothiophene. An experiment with n-butyllithium and 2-butylselenothiophene was carried out under the conditions indicated above. After carbonation, the acidified aqueous layer gave 91% thiophene-2-carboxylic acid with mp 125.5-126° (from water). The ether layer from the carbonation product gave 90% dibutyl selenide with bp 102° (31 mm) and n_D^{20} 1.4763 (bp 82-83°, 13 mm, and n_D^{20} 1.4753 [18]).

The above acids were identified by comparison of their UV spectra with the spectra of genuine samples; the samples obtained did not depress the melting points of the genuine samples.

Action of n-Butyllithium on Selenoanisole. Under similar conditions, 0.86 g of selenoanisole gave 0.7 g (81%) of the starting compound with bp 94-95° (24 mm) and n_D^{20} 1.6047 [bp 202-203° (743.8 mm), n_D^{25} 1.6039 [19]]. The aqueous layer after acidification (no precipitate was observed) was extracted with ether. The ether was removed by distillation, but no residue was observed.

Action of n-Butyllithium on 2-Methylmercaptoselenophene. Under similar conditions, the metallation of 1.77 g (0.01 mole) of 2-methylmercaptoselenophene and subsequent carbonation gave 1.81 g (82%) of 5-methylmercaptoselenophene-2-carboxylic acid with mp 119-120° (from 20% alcohol). Found: C 32.7, 32.9; H 2.9, 3.0%. $C_6H_6O_2SSe$. Calculated: C 32.6; H 2.7%.

2-Methylselenothiophene Dibromide. A solution of 2.5 ml of bromine in 10 ml of $CHCl_3$ was added with vigorous stirring to a cooled (−40 to −20°) solution of 7.08 g (40 mmole) of 2-methylselenothiophene in 35 ml of $CHCl_3$. After 5-10 min, the resulting orange precipitate was removed by filtration and washed with cold ether to give 13.02 g (97%) of the unstable 2-methylselenothiophene dibromide with mp 64-65° (determined directly after preparation, since the melting point decreases with time). Found: C 18.2, 17.8; H 1.8, 1.6; Br (by potentiometric titration) 46.5; 47.5%. $C_5H_6Br_2SSe$. Calculated: C 17.8; H 1.8; Br 47.4%.

A mixture of 9.8 g (29 mmole) of 2-methylselenothiophene dibromide and saturated aqueous $KBrO_3$ in 75 ml of water was shaken in an open vial. The solution rapidly became turbid with slight warming and evolution of bromine vapors. The liberated oil was extracted thoroughly with ether, and the extract was washed with 10% NaOH and water and dried with anhydrous $MgSO_4$. Distillation gave 6.4 g (91%) of 2,5-dibromothiophene with bp 110-111° (26 mm) and n_D^{20} 1.6290 (n_D^{20} 1.6288 [20]). Found: C 19.6, 19.4; H 1.0, 1.0; Br 65.3, 66.1; S 13.1, 13.3%. $C_4H_2Br_2S$. Calculated: C 19.9; H 0.8; Br 66.1; S 13.3%.

A 10-g (30 mmole) sample of 2-methylselenothiophene dibromide was stirred with 120 ml of water for 5 h. After 2 days at 20°, the liberated oil was extracted thoroughly with ether. The extract was washed with 10% NaOH solution and water and dried with $MgSO_4$. Distillation gave 4 g (53%) of 5-bromo-2-methylselenothiophene with bp 95° (5 mm) and n_D^{20} 1.6576. Found: C 23.5, 23.6; H 2.0, 2.2; Br 31.2, 31.0; S 12.5, 12.4; Se 30.8, 30.6%. C_5H_5BrSSe. Calculated: C 23.5; H 2.0; Br 31.2; S 12.5; Se 30.8%.

5-Bromo-2-methylselenothiophene [bp 102-103° (6 mm), n_D^{20} 1.6556] was also obtained in 45% yield by the addition of 19 ml of concentrated hydrochloric acid in the course of 30 min to a mixture of 5.31 g (0.03 mole) of 2-methylselenothiophene, 50 ml of ether, and 60 ml of a bromide–bromate solution (0.08 g/ml of bromine) at 10-15° with subsequent stirring for 10 h at 20°. The identical character of the compounds obtained by these two methods was confirmed by gas-liquid chromatography and UV spectroscopy.

A solution of 3.3 g (13 mmole) of 5-bromo-2-methylselenothiophene in 200 ml of bromine water containing 2.5 ml of bromine was stirred at 20° for 5 h. After decoloration of the bromine water, the light-yellow ether layer was separated, and the aqueous layer was extracted three times with ether. The combined ether extracts were washed with 10% NaOH solution and water and dried with anhydrous $MgSO_4$. Distillation gave 2.86 g (92%) of 2,5-dibromothiophene with bp 93-94° (18 mm) and n_D^{20} 1.6300.

A total of 47 ml of concentrated hydrochloric acid was added with vigorous stirring in the course of 1 h to a cooled (10-15°) mixture of 5.31 g (0.03 mole) of 2-methylselenothiophene, 50 ml of ether, and 150 ml of a bromide–bromate solution (0.08 g/ml), and the mixture was stirred for 5 h. The mixture was then allowed to stand at 20° for 2 days. The ether layer was separated, and the aqueous layer was extracted thoroughly with ether. The combined ether extracts were washed with 10% NaOH solution and dried with $MgSO_4$ to give 3.3 g (46%) of 2,5-dibromothiophene with bp 99-101° (20 mm) and n_D^{20} 1.6288.

The identical character of all of the samples of 2,5-dibromothiophenes obtained was confirmed by gas-liquid chromatography and UV spectroscopy.

5-Methylseleno-2-methylthiophene Dibromide. This compound was similarly obtained in 87% yield and had mp 55-56° (for the uncrystallized dibromide; the product decomposed on attempts to recrystallize it. The dibromides also decomposed on standing at room temperature.) Found: C 20.3, 21.1; H 2.2, 2.4; Br (by potentiometric titration) 44.9, 45.1%. $C_6H_8Br_2SSe$. Calculated: C 20.5; H 2.3; Br 45.5%.

3-Methylselenophthalic Anhydride. A 4.9-g (0.05 mole) sample of maleic anhydride was dissolved by heating in 8 ml of benzene. The solution was then cooled to 20°, and 8.05 g (0.05 mole) of 2-methylselenofuran was added to it. The reaction mixture was refluxed on a water bath for 4 h and allowed to stand at 20° for 50 h. The resulting precipitate was removed by filtration and washed twice with ether to give 5 g (42%) of 3-methylselenophthalic anhydride with mp 176.5-177.5° (from chloroform). Found: C 44.7, 44.6; H 2.6, 2.5%. $C_9H_6O_3Se$. Calculated: C 44.8; H 2.5%.

6-Methylseleno-3-methylphthalic Anhydride. As in the preceding experiment, 5.8 g (46%) of 6-methylseleno-3-methylphthalic anhydride with mp 196-197° (from chloroform) was obtained from 4.9 g (0.05 mole) of maleic anhydride and 8.8 g (0.05 mole) of 5-methylseleno-2-methylthiophene. Found: C 46.9, 46.8; H 3.0, 2.9%. $C_{10}H_8O_3Se$. Calculated: C 47.1; H 3.2%.

LITERATURE CITED

1. V. S. Bogdanov, V. P. Litvinov, A. N. Sukiasyan, and Ya. L. Gol'dfarb, Zh. Organ. Khim., 7, 1257 (1971).
2. Ya. L. Gol'dfarb, V. P. Litvinov, and A. N. Sukiasyan, Izv. Akad. Nauk SSSR, Ser. Khim.,2585 (1967).
3. Ya. L. Gol'dfarb, V. P. Litvinov, and A. N. Sukiasyan, Dokl. Akad. Nauk SSSR, 182, 340 (1968).
4. H. Gilman and F. J. Webb, J. Am. Chem. Soc., 71, 4062 (1949).
5. H. Gilman and R. L. Bebb, J. Am. Chem. Soc., 61, 109 (1939).
6. D. A. Shirley and R. J. Reeves, J. Organomet. Chem., 16, 1 (1969).
7. A. N. Sukiasyan, V. P. Litivinov, and Ya. L. Gol'dfarb, Izv. Akad. Nauk SSSR, Ser. Khim., 1345 (1970).
8. Ya. L. Gol'dfarb, V. P. Litvinov, and A. N. Sukiasyan, Izv. Akad. Nauk SSSR, Ser. Khim., 1296 (1971).
9. L. I. Belen'kii, N. S. Ksenzhek, and Ya. L. Gol'dfarb, Khim. Geterotsikl. Soedin., 310 (1972).
10. O. K. Edwards, W. R. Gaytwaite, J. Kenyon, and H. Phillips, J. Chem. Soc., 2293 (1928).
11. P. Spinoglio and M. De Gasperi, Gazz. Chim. Ital., 67, 318 (1937).
12. E. Hannig and H. Ziebandt, Pharmazie, 23, 552 (1968).
13. Ya. L. Gol'dfarb, Ya. L. Danyushchevskii, and M. A. Marakatkina, USSR Author's Certificate No. 187,778 (1965); Byull. Izobr., No. 21, 39 (1966).
14. Ya. L. Danyushevskii, M. A. Marakatkina, and Ya. L. Gol'dfarb, Zh. Organ. Khim., 4, 474 (1968).
15. L. Chugaev, Ber., 42, 53 (1909).
16. Syntheses of Heterocyclic Compounds [in Russian], Vol. 1, Izd. Akad. Nauk Arm. SSSR, Erevan (1956), p. 54.
17. E. G. Kataev and M. F. Palkina, Uch. Zap. Kazansk. Univ., 113, 115 (1953).
18. G. Ayrey, D. Barnard, and D. T. Woodbridge, J. Chem. Soc., 2095 (1962).
19. M. Nardelli and L. Chierici, Ann. Chim. (Rome), 42, 111 (1952); Chem. Abstr., 47, 7454 (1952).
20. H. D. Hartough, Thiophene and Its Derivatives, New York (1952), p. 208.