Ring-opening Reactions of Heterocyclic Metal-organics

II. On the Ring-opening of 2,5-Dimethyl-3-thienyllithium and 2,5-Dimethyl-3-selenienyllithium

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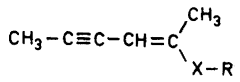
We have previously found[1] that 4-methyl-3-selena-4-octene-6-yne (IIa) is formed in the reaction between ethereal ethyllithium and 2,5-dimethyl-3-iodoselenophene (I) at −70°C. On decreasing the reaction temperature to −100°C we now find that 2,5-dimethyl-3-selenienyllithium (III) is stable enough to be trapped as the carboxylic acid upon carbonation.

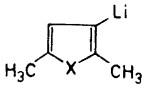
This result indicates that IIIa is an intermediate, which undergoes ring-opening to hex-2-en-4-yne-2-selenolate IVa. S_N2 type attack by IVa on ethyl iodide, formed during the halogen-metal exchange leads to IIa. The importance of trapping the anion IVa can be demonstrated by using methyllithium instead of ethyllithium in the reaction. In this case methyl iodide, a better alkylating agent than ethyl iodide, is generated during halogen-metal exchange. Reaction between I and methyllithium even at −100°C yielded no carboxylic acid upon carbonation. Work-up of the neutral fraction at room temperature yielded 3-methyl-2-selena-3-heptene-5-yne (IIb) in 82 % yield. The structure was evident from NMR and mass spectra and from comparison with the homologous IIa.[1]

It was of interest to determine if this facile ring-opening reaction in the selenophene series could be achieved in the thiophene series as well. Some evidence for this can be found in the work of Moses and Gronowitz [2] on halogen-metal exchange in the thiophene series. When ethereal solutions of 3-thienyllithium derivatives were allowed to stand at room temperature for longer periods, they detected the formation of unsaturated products. However, it has been shown that 2,5-dimethyl-3-thienyllithium is stable enough at −70°C to be a useful intermediate for the preparation of other thiophene derivatives.[3] We



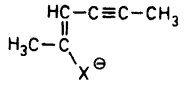
II

a X=Se R=C_2H_5
b: X=Se R=CH_3
c: X=S R=CH_3



III

a: X=Se
b: X=S



IV

a: X=Se
b. X=S

have now investigated the stability of 2,5-dimethyl-3-thienyllithium obtained through halogen-metal exchange between 2,5-dimethyl-3-iodothiophene and methyllithium at −70°C more closely. We find that 2,5-dimethyl-3-thienyllithium was unchanged after 6 h at −70°C, since carbonation produced 76 % of 2,5-dimethyl-3-thiophenecarboxylic acid, and no traces of 3-methyl-2-thia-3-heptene-5-yne (IIc) were detected in the neutral phase. However, when reacting 2,5-dimethyl-3-iodothiophene with methyllithium in refluxing ether IIc was obtained in 42 % yield, in addition to 14 % of 2,3,5-trimethylthiophene. The structure of IIc was evident from its spectral data and by comparison of NMR data for the ethyl homologue, prepared by Russian workers through the reaction of potassium ethyl mercaptide with dimethyl acetylene.[4] Our experiments clearly demonstrate the more facile ring-opening of 3-selenienyllithium than of 3-thienyllithium derivatives.

It is possible that an equilibrium exists between the aromatic lithium derivatives (III) and the ring-opened selenolate and thiolate IV, in which III predominates. However, IVa and IVb are removed from the equilibrium by alkylation and this provides the driving force for the formation of II. Of course, the other alternative is that the anions are irreversibly formed. The stability of 2,5-dimethyl-3-thiophene magnesium iodide [5] and of 2,5-dimethyl-3-selenophene magnesium iodide (demonstrated in this work), during the preparation of which no alkylating agent is formed,

could be taken as support for this view. Our attempts to prepare IIIa or IIIb through direct reaction with metallic lithium in ether have hitherto failed.

However, by carrying out the halogen-metal exchange reaction with phenyllithium, in which case the non-reactive iodobenzene would be obtained, we hoped to get additional information on the ring-opening. Attempts to react I with ethereal phenyllithium at room temperature gave no acids upon carbonation. Analyses of the neutral phase by VPC showed that about equal amounts of iodobenzene and 2,5-dimethylselenophene were formed. This indicates that halogen-metal exchange has indeed taken place and that the IIIa formed has ring-opened completely since no acid was obtained. The formation of 2,5-dimethylselenophene in aqueous alkaline medium can be explained by ring-closure of the selenolate (IVa) (in a kind of Michael addition). Similar ring-opening and closure has recently been observed by Iddon and Dickinson during the reaction of 3-bromobenzo[b]thiophene and butyllithium.[6]

If our interpretation of the mechanism of formation of 2,5-dimethylselenophene in the experiment with phenyllithium is correct, this would indicate either that the selenolate anion IVa has the *cis* configuration indicated in the formula, or that rapid rotation occurs around the formal C=C bond. Recent measurements on the rotation barriers in di(alkylthio)-ethylenes[7] seem to indicate that the barrier in IV could be quite high.

From the sharp melting point of spectral and VPC data of IIb and IIc, it is very probable that only one stereoisomer is obtained. Further study of the stereochemistry of II is necessary. We are continuing our study on the mechanism scope and limitations of this ring-opening reaction and its preparative usefulness for the stereospecific synthesis of conjugated enynes.

Experimental. 2,5-Dimethyl-3-selenophenecarboxylic acid. (Method a). The Grignard reagent was prepared in the usual manner from 112 g (0.393 mole) of 2,5-dimethyl-3-iodoselenophene[1] in 250 ml of anhydrous ether, 10.8 g (0.444 mole) of magnesium and 1 ml of ethyl bromide. When spontaneous reflux had stopped the mixture was refluxed for half an hour and then poured onto solid carbon dioxide covered with ether. When the mixture had reached room temperature 200 ml 1 N hydrochloric acid was added. The ether phase was separated and the aqueous layer was extracted with ether several times. The combined ether phases were extracted with 0.5 N potassium hydroxide solution. Upon acidification of the combined alkaline solutions with 2.5 N hydrochloric acid, 45 g of crude acid was precipitated. Recrystallization from acetic acid-water-methanol (1:20:4) yielded 41.5 g (52 %) of 2,5-dimethyl-3-selenophenecarboxylic acid, m.p. 118°C. NMR (acetone): $\tau_{2\text{-}CH_3}=7.22$ ppm, $\tau_{5\text{-}CH_3}=7.53$ ppm, $\tau_4=2.74$ ppm; $J_{5\text{-}CH_3\text{-}4}=1.2$ c/s, $J_{CH_3\text{-}CH_3}=0.6$ c/s. [Found: M.wt. 203; C 41.18; H 4.01. Calc. for $C_7H_8O_2Se$ (203.1): C 41.40; H 3.97].

Method b. To 5.00 g (0.0175 mole) of 2,5-dimethyl-3-iodoselenophene in 25 ml of anhydrous ether cooled to −100°C, ethereal ethyllithium (22 ml, 1.09 N) was added dropwise under nitrogen and with stirring. After stirring for additional 15 min powdered carbon dioxide was added at such a rate that the temperature did not rise above −100°C. Analogous work-up as described above yielded 1.82 g (51 %) of 2,5-dimethyl-3-selenophenecarboxylic acid with the same physical properties (m.p., IR spectrum) as described above. 1.42 g of 2,5-dimethyl-3-iodoselenophene was recovered.

3-Methyl-2-selena-3-heptene-5-yne. To a solution of 15.0 g (0.0526 mole) of 2,5-dimethyl-3-iodoselenophene[1] cooled to −110°C, methyllithium solution (100 ml, 0.7 N) was added drop-wise at such a rate that the temperature did not rise over −100°C. When the reaction was complete an aliquot was carbonated, but no carboxylic acid was isolated in the usual work-up. An IR spectrum of the neutral product showed absorption at 2200 cm^{-1} assigned to C≡C-stretching. The reaction mixture was allowed to reach room temperature and poured into water. The ether phase was separated and the aqueous layer extracted with ether. The combined ether phases were washed with water and dried over magnesium sulphate. Evaporation of the ether yielded 7.5 g (82 %) of the title compound, which according to VPC was homogeneous, m.p. 30°C after recrystallization from aqueous ethanol. IR: C≡C; 2220 cm^{-1}, C=C; 1590 cm^{-1}. NMR (CCl_4): $\tau(A)_{\equiv C\text{-}CH_3}=8.03$ ppm, $\tau(B)_{=C\text{-}CH_3}=7.90$ ppm, $\tau(C)_{Se\text{-}CH_3}=7.87$ ppm, $\tau(D)_{CH}=4.45$ ppm; $J_{AB}=0.6$ c/s, $J_{AD}=2.4$ c/s, $J_{BD}=1.4$ c/s. [Found: M. wt. 174; C 48.94; H 5.86. Calc. for $C_7H_{10}Se$ (174): C 48.57; H 5.82].

3-Methyl-2-thia-3-heptene-5-yne. Methyllithium solution (90 ml, 0.7 N) was added dropwise while stirring and under nitrogen to a solution of 10.0 g (0.0420 mole) of 2,5-dimethyl-3-iodothiophene[3] in 40 ml of anhydrous ether at room temperature. After

addition was complete, the mixture was refluxed for 2 h, cooled and poured into water and worked up as described above. Fractionation yielded 0.73 g (14 %) of 2,3,5-trimethylthiophene, b.p. 60–65°C/14 mmHg, identified by combined VPC-mass spectrometry and 2.26 g (42 %) of the title compound, b.p. 89–90°C/14 mmHg, m.p. 34–35°C. IR: C≡C 2220 cm^{-1}, C=C 1590 cm^{-1}. NMR (CCl_4): τ_{C-CH_3}=8.02 ppm, τ_{S-CH_3}=7.72 ppm, τ_{CH}=4.75 ppm. [Found: M.wt. 126; C 66.62; H 8.05; S 25.08. Calc. for $C_7H_{10}S$ (126): C 66.61; H 7.99; S 25.40].

2,5-Dimethyl-3-thiophenecarboxylic acid. Ethereal methyllithium (50 ml, 0.7 N) was added drop-wise under nitrogen with stirring to a solution of 5.00 g (0.0210 mole) of 2,5-dimethyl-3-iodothiophene in 40 ml of anhydrous ether cooled to −70°C. The mixture was allowed to stand at −70°C for 6 h and was then carbonated. The usual work-up yielded 2.51 g (76 %) of 2,5-dimethyl-3-thiophenecarboxylic acid, m.p. 117–118°C. Literature value,[5] m.p. 119–120°C.

The neutral phase contained 0.35 g of a mixture of 2,5-dimethylthiophene and 2,5-dimethyl-3-iodothiophene but no ring-opened product.

NMR spectra were recorded with a Varian A60 or a Varian HR-100 NMR spectrometer. Mass spectra were obtained with an LKB A 900 combined gas chromatograph mass-spectrometer. IR spectra were recorded on a Perkin-Elmer 257 grating infra-red spectrophotometer. Gas chromatographic analysis was carried out with a Perkin-Elmer model 900 gas chromatograph using an NPGS (5 %) column.

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Pyrolysis Products of Poly(2,6-dimethoxy-1,4-phenylene ether)

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Direct GLC analysis of the products of pyrolysis of methoxy-substituted polyphenylene oxides detects only partly demethylated fragments. To achieve a more complete analysis, we have studied by combined gas chromatography and mass spectrometry acetylated products of pyrolysis of poly(2,6-dimethoxy-1,4-phenylene ether) (PPOO). In addition, the oligomers formed were fractionated by gel permeation chromatography and their molecular weight distribution was investigated by vapour pressure osmometry (VPO).

Experimental. About 300 mg of PPOO (M_n=8000), synthetized as described in Ref. 2, was pyrolyzed at 500°C for 25 min in a nitrogen atmosphere as reported earlier.[1] The volatile reaction products were collected in a receiver held in a salt-ice bath. The pyrolysis residue was eluted with chloroform and the resulting solution was evaporated to dryness. The combined fractions were acetylated with a pyridine-acetic anhydride mixture for 6 h at 60–70°C.

The acetylated fractions were dissolved in chloroform and a sample of the solution was analyzed at 70 eV on a Perkin-Elmer Model 270 GC-DF mass spectrometer combined with a Model 900 gas chromatograph. A 3 % SE-30 column (length 1.5 m. diameter 6 mm) was used. The fractions were identified by comparing their mass spectra and retention times with those of model compounds.

Another sample of the mentioned solution was fractionated on a Sephadex LH-20 column using chloroform as eluent and the fractions were analyzed by UV spectroscopy at 260 and 270 nm. The column was calibrated with polystyrene standards. In addition molecular weights of representative oligomeric fractions of the pyrolyzed PPOO were investigated by VPO using a Hitachi-Perkin Elmer Model 115 instrument and chloroform as solvent.[3]

Non-aromatic degradation products were not analyzed.

Results. The principal results of the MS analysis are collected in Table 1 and those of the GPC analysis in Table 2.