# ACTION OF ALKALI METALS IN LIQUID AMMONIA ON SUBSTITUTED THIOPHENES

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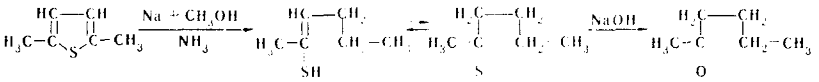
The simultaneous action of lithium and alcohol on α-alkyl- or α-(ω-carboxyalkyl)thiophenes in liquid ammonia results in the elimination of sulfur and the formation of ketones, and, respectively, the corresponding ketoalkanoic acids in yields of 40-75%. Unsubstituted thiophene gives only an insignificant amount of a carbonyl compound.

In recent years, the preparation of aliphatic and alicyclic compounds by the reductive desulfurization of thiophene derivatives has assumed great importance [1, 2]. Up until now, Raney nickel has remained practically the only agent for this process, although its use involves certain inconveniences and may not always prove to be economically justified. In searching for other routes for the conversion of thiophene compounds to compounds of the aliphatic series, we decided to study the action of alkali metals in liquid ammonia on the former. The reduction of thiophene with sodium and alcohol in liquid ammonia was first realized by Birch and McAllan [3]; the reduction product was a complex mixture of polymeric and low-molecular-weight substances. Depending on the amount of metal, dihydrothiophenes or more profound reduction products – butenethiols or butenes – predominated in the latter. The yield of 2,5-dihydrothiophene was twice that of 2,3-dihydrothiophene. The following were detected in the butenethiols: 15% $CH_2=CHCH_2CH_2SH$, 35-40% $CH_3CH=CHCH_2SH$, and only traces of $CH_3CH_2CH=CHSH$. Birch and McAllan also studied the reduction of 2-methyl-, 3-methyl-, and 2,5-dimethylthiophene in liquid ammonia [4]. In a number of the reduction products of 2-methyl- and 2,5-dimethylthiophene, insignificant amounts (less than 1%) of carbonyl-containing compounds, which proved to be 2-pentanone and 2-hexanone, respectively, were also detected. Birch and McAllan depict the formation of the ketone from 2,5-dimethylthiophene by the following scheme:



It must be noted that the reduction of methylthiophenes was carried out stepwise in [4]. In the first stage, only two equivalents of sodium, i.e., an amount that is insufficient for complete desulfurization, was introduced. The thiol fraction isolated by distillation was then treated with three equivalents of sodium. The ketones mentioned above were obtained in both the first and second stages of the reduction.

In a study of the action of sodium in liquid ammonia on ω-(2-thienyl)caproic acid, we observed that a carbonyl-containing reaction product – 7-ketocapric acid – is obtained when 10 equivalents of metal are used. The reaction proceeded in the same direction also in the case of several other thienylalkanoic acids. In our first experiments, the proton donor (ethanol), in contrast to the Birch method, was introduced 2-2.5 h after the addition of the sodium rather than at the start of the process. We later found that the yield of the keto acid can be raised if the acidified reaction mixture is heated on a water bath for 1.5-2 h (method A, Table 1). The results of this part of the investigation are set forth in general outline in a preliminary communication [5].

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TABLE 1. Keto Carboxylic Acids [n-$C_3H_7CO(CH_2)_nCOOH$] from 2-(ω-Carboxyalkyl)thiophenes

| $n$ | Method | Yield, % | mp, °C (from hexane) | Semicarbazone, mp, °C (from methanol) |
|---|---|---|---|---|
| 3 | A | 39 | 32,5—33,5[6, 7] | 186—188 |
|  | B | 61 |  |  |
| 4 | A | 34 | 36,5—37,5[8] | 153—154 |
|  | B | 42 |  |  |
| 5 | A | 60 | 40—41[9] | 156—158 |
|  | B | 73 |  |  |
| 9 | A | 55 | 66,5—67[10] | 97—99 |
|  | B | 65 |  |  |

TABLE 2. Ketones [$R(CH_2)_3CO(CH_2)_nCH_3$] from Alkylthiophenes

| R | $n$ | Yield, % | bp, °C (mm) | $n_D^{20}$ | Semicarbazone, mp, °C (from methanol) |
|---|---|---|---|---|---|
| H | 0 | 59 | 43—44,5 (92) | 1,3905 | 109—110[11] |
| $CH_3$ | 0 | 44 | 59 (70) | 1,4010 | 118—119,5[11] |
| H | 1 | 56 | 59—59,5 (80) | 1,4015 | 109,5—111[11] |
| H | 2 | 56 | 48—49 (23) | 1,4061 | 133—134[11] |
| H | 6 | 74* | 117—118 (20) | 1,4270 | 49—52[12] |

*The reduction was carried out in the presence of sodium.

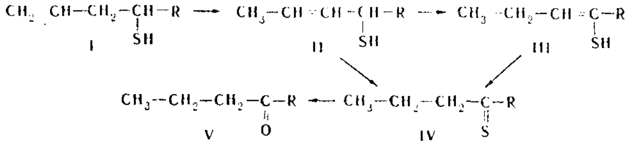
We subsequently established that the yields of the keto acids can be raised even somewhat more if lithium is used in place of sodium and the proton donor is introduced simultaneously with the starting compound (method B, Table 1).

The results of research on the reductive cleavage of thienylalkanoic acids compelled us to investigate the action of alkali metals in liquid ammonia on α-alkylthiophenes, although the results in [4] were not encouraging if one bears in mind our goal of obtaining aliphatic compounds. We carried out experiments with alkylthiophenes under the same conditions as in the preparation of keto acids, except that the amount of lithium (and alcohol) was 6 g-eqs per mole of starting compound rather than 10. Under these conditions, 2-alkylthiophenes and 2,5-dimethylthiophene are smoothly converted to the corresponding ketones in satisfactory yields (Table 2).

It should be noted here that lower alkylthiophenes are contained in the products of the refinement of several forms of fuel minerals, for example, shales [13, 14]. Thus, from our results, one can speak of new possibilities for the use of these products of the refinement of fuel shales.

When lithium is replaced by sodium, the yields of ketones decrease substantially. However, the reverse was observed in the case of 2-n-heptylthiophene: the yield of undecanone in the reduction with lithium was only 38%.

The sharp difference in the results of the hydrogenation of methylthiophenes that we obtained and the results obtained by Birch and McAllan is apparently due to the difference in the experimental conditions. We assume that the essential moment in the process is the reaction of the intermediate products of the reduction with the acid agents. As we established in the case of the reduction of thienylalkanoic acids, there is a direct relationship between the acid-treatment conditions and the yields of desulfurization products. In our experiments, the reduction products were subjected to the action of mineral acid while heating to 90-100°. The transformations of the possible intermediate reduction products (unsaturated thiols) should apparently be facilitated under these conditions, as depicted in the scheme



The III→IV conversion corresponds to the Birch scheme (see above). Thiol II, which is the thio analog of a substituted allyl alcohol, can also apparently be converted to thioketone IV in the presence of acid (probably through the intermediate formation of III) as a result of a prototropic transformation similar to the known rearrangement of allyl alcohols to saturated ketones [15]. Finally, thiol I, if it is present in appreciable amounts in the mixture,* could be isomerized to II as a result of the equilibrium migration of the double bond to the center of the chain, which is characteristic for 1-alkenes [15]. To this it should be added that heating with a mineral acid leads to rapid and irreversible hydrolysis of thioketone IV [16], and buildup of ketone V in the reaction mixture should thus be the overall result of the indicated isomeric transformations.

Of course, the proposed explanation cannot be considered to be exhaustive; other factors, for example, the nature of the metal, undoubtedly play a definite role.

An attempt to realize the desulfurization of thiophene in a direction similar to that for alkylthiophenes was unsuccessful. The carbonyl-containing desulfurization product – butyraldehyde – was isolated in insignificant quantities as the semicarbazone.

## EXPERIMENTAL

5-Ketocaprylic Acid. A mixture of dry liquid ammonia (400 ml), 13.8 g (0.3 mole) of technical-grade absolute ethanol, and 5.1 g (0.03 mole) of ω-(2-thienyl)butyric acid [17] in 50 ml of absolute ether was placed in a flask through which dry nitrogen had been blown. The flask was cooled to −65°, and 2.08 g (0.3 g-atom) of fine lithium clippings was added to the vigorously stirred mixture. The reaction mass was then stirred for 2.5 h and carefully diluted with 100 ml of water. The ammonia was evaporated on a water bath, and the residue was acidified with dilute hydrochloric acid and allowed to stand overnight. The acidified mixture was stirred on a boiling-water bath for 2 h, during which the evolved hydrogen sulfide was drawn off with a water aspirator. The mixture was then cooled and extracted with ether. Distillation of the residue from the ether extract gave, in addition to 5-ketocaprylic acid with bp 110° (0.1 mm) and mp 32.5-33.5° [6], a fraction with bp 80° (0.1 mm) and $n_D^{20}$ 1.4330, which proved to be ethyl 5-ketocaprylate [18]. Found: C 64.5; H 9.8%; M 186 (mass spectrometrically). $C_{10}H_{18}O_3$. Calculated: C 64.5; H 9.7%; M 186. After saponification of the ester with 10% NaOH solution at 80° for 1.5 h and isolation and purification of the acid by recrystallization from hexane, the overall yield of 5-ketocaprylic acid was 2.9 g (61%). The experiments with other acids were carried out similarly, with the exception that the crude reduction product, without distillation, was treated with alkali as indicated above, after which the keto acid was isolated and purified by recrystallization from hexane.

4-Undecanone. A total of 6.9 g (0.3 g-atom) of fine sodium clippings was added slowly to a stirred solution of 13.8 g (0.3 mole) of technical-grade absolute ethanol, 9.1 g (0.05 mole) of 2-n-heptylthiophene [19, 20], and 70 ml of absolute ether in 500 ml of liquid ammonia. The mixture was stirred at −33° for 2 h, after which it was heated slowly until the ammonia had evaporated completely. It was then cooled with ice and diluted with 150 ml of water, and the mixture was acidified with dilute hydrochloric acid. The following day, the mixture was stirred on a boiling-water bath for 1.5 h, during which the hydrogen sulfide was drawn off by suction with a water aspirator. The mixture was then cooled and extracted with ether. The residue after removal of the solvent by distillation was filtered away from fine yellow crystals (0.05 g), which proved to be elementary sulfur. The filtrate was vacuum-distilled to give 6.3 g (74%) of 4-undecanone with bp 127° (35 mm) and $n_D^{20}$ 1.4270. The semicarbazone had mp 49-52° [12] (from methanol).† The other alkylthiophenes were similarly reduced, except that an equivalent amount of lithium was used in place of sodium, and the reaction was carried out at −65°.

Reduction of Thiophene. An 8.4-g (0.1 mole) sample of thiophene was reduced by the action of 4.18 g (0.6 g-atom) of lithium and 27.6 g (0.6 mole) of ethanol in 500 ml of liquid ammonia under the conditions of the desulfurization of 2-alkylthiophenes. The ether and low-boiling substances were removed from the ether extract of the reduction product by distillation in a stream of nitrogen. The distillate, which, according to gas-liquid chromatography (at 80° with a column filled with polyethylene glycol adipate on Chromosorb W), contains an insignificant amount of butyraldehyde, was stirred at 30-35° for 3 h with 10 ml of an aqueous solution of 1 g of semicarbazide hydrochloride and 1.5 g of sodium acetate. The ether layer was evaporated, and butyraldehyde semicarbazone with mp 100-103° [21] (from hexane) was isolated from the residue. The major portion of the product of the reduction of thiophene (6.2 g) was an orange oil with an unpleasant odor, which we did not investigate further.

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*Birch and McAllan could not detect this form in the acid products isolated in the intermediate stage of the reduction of 2-methylthiophene.

†The semicarbazone crystallized poorly from both methanol and other solvents.

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