which the mixture was cooled, and the resulting precipitate was removed by filtration and washed with acetic acid and ether.

3-Acetyl-2,5,7-trimethylpyrazolo[1,5-*a*]pyrimidine (VI). A 0.005-mole sample of salt IIb or IIc and a solution of 0.01 mole of potassium in 8 ml of tert-butyl alcohol were added successively to a solution of 0.0075 mole of acetylacetone in 5 ml of tert-butyl alcohol, after which the mixture was refluxed for 45 min, and the hot solution was filtered. The filtrate was cooled to precipitate VI, which was removed by filtration and washed with ether.

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ACTION OF ALKALI METALS IN LIQUID AMMONIA ON SUBSTITUTED THIOPHENES

III.* PREPARATION OF AMINO KETONES OF THE ALIPHATIC SERIES FROM 2-(ω-DIALKYLAMINOALKYL)THIOPHENES

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The action of lithium and alcohols in liquid ammonia on α-substituted thiophenes with subsequent hydrolysis of the products leads to conversion of the thiophene fragment of the molecule to a butyryl group. A number of amino ketones of the aliphatic series were obtained from α-(ω-dialkylaminoalkyl)thiophenes.

Currently one of the most nearly universal methods for the preparation of derivatives of the aliphatic and cycloparaffin series, especially those with long straight and branched chains of carbon atoms, is reductive desulfuration of substituted thiophenes with Raney nickel. This method, as a rule, proves to be effective in all cases and leads to the conversion of the thiophene ring to a hydrocarbon chain made up of four carbon atoms. Another reductive agent – sodium or lithium in liquid ammonia [1, 2] – acts on α-alkyl-, α-(ω-hydroxyalkyl)-, and α-(ω-carboxyalkyl)-substituted thiophenes in such a way that, in addition to hydrogenation of the unsaturated bonds, the ring is cleaved at the bond between the sulfur atom and the unsubstituted ring carbon atom. Thus in all of the cases that we investigated we observed (after hydrolysis of the reaction mixture) the formation of compounds having a butyryl group.

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*See [1] for communication II.

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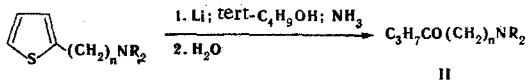
TABLE 1. 2-(ω-Diethylaminoalkyl)thiophenes

Compound	bp, °C (mm)	n_D^{20}	d_4^{20}	Mol. wt. from mass spectrum	Empirical formula	Found, %			Calc., %		
						C	H	S	C	H	S
Ib	96—98 (8)	1,5080	0,9692	183	$C_{10}H_{17}NS$	65,3	9,3	17,4	65,5	9,3	17,5
Ic	106—107 (6,5)	1,5043	0,9596	197	$C_{11}H_{19}NS$	66,8	9,8	16,2	66,9	9,7	16,2
Id	104—104,5 (3)	1,5021	0,9501	211	$C_{12}H_{21}NS$	68,2	10,1	15,3	68,2	10,0	15,1
Ie	132—133 (5,5)	1,5000	0,9423	225	$C_{13}H_{23}NS$	69,3	10,3	14,3	69,3	10,3	14,2
If	125,5—126 (1,5)	1,4978	0,9368	239	$C_{14}H_{25}NS$	70,3	10,5	13,5	70,2	10,5	13,4

The differences that are observed in the reduction in liquid ammonia of α-alkyl-substituted thiophenes having a functional grouping at the end of the chain are associated with the degree of remoteness of the latter from the ring. In particular, we observed [1] the effect of this factor during a study of the reaction of lithium and tert-butyl alcohol with ω-(2-thienyl)alkanols in liquid ammonia.

Reduction of the side chain to four (or less) carbon atoms brought about a sharp decrease in the yields of aliphatic keto alcohols; in our opinion, this is associated with the effect of the negative charge of the alkoxide ion that is formed as a result of the reaction of the thienylalkanol with lithium and ammonia.

In commencing our study of the reduction of 2-(ω-dialkylaminoalkyl)thiophenes (I), we assumed that the tendency toward a decrease in the yield of the aliphatic reaction product as the magnitude of n decreases that was noted in the case of thienylalkanols would not be observed here or at least would be manifested to a considerably lesser extent. In fact, in the reduction of amines I a successive reduction in the number of methylene links from six to three did not appreciably affect the yields of amino ketones (70-80%). However, a further shortening of the methylene chain (n=2) led to a decrease in the yield to 37%. Here, one should note that the yield in the reduction of 2-(2-thienyl)ethanol was only 6% (the bulk of the starting material was recovered unchanged), and thus in this case also the amine proved to be much more active than the corresponding alkanol.



II

n=1-6; R=CH_3 or C_2H_5

We were previously [1] unable to obtain an aliphatic keto ester from 2-methoxymethylthiophene by the action of lithium and tert-butyl alcohol in liquid ammonia on the latter, inasmuch as the C—O bond was cleaved in the initial stage of the reaction, as in the case of benzyl esters [3]. It is known [3] that tertiary amines of the benzyl type are not cleaved at the N-benzyl bond during Birch reduction. One therefore might have expected that the corresponding compound of the thiophene series – 2-dimethylaminomethylthiophene – in analogy with benzylamines, would prove to be resistant to cleavage at the N-thienyl bond. However, a high-molecular-weight substance that cannot be distilled on heating to 210° at a pressure of 1 mm proved to be practically the only product of the reaction carried out by the standard method (see below). In a control experiment in which we used insufficient lithium for complete reduction, the product contained a small amount of 2-methylthiophene. This fact constitutes evidence that reductive cleavage at the N-thienyl bond nevertheless does occur. Replacement of lithium by the less active sodium made it possible to obtain the desired product – 1-dimethylamino-2-pentanone – but the yield was only ~13%.

Thus the reduction of aminoalkylthiophenes I with alkali metals in liquid ammonia, just as in the case of thienylalkanols, is complicated when the length of the methylene chain connecting the functional group to the thiophene ring is insufficient to ward off the effect of this group on ring opening. However, the essential character of these effects in any case remains as yet unclear.

EXPERIMENTAL

The structures of the compounds obtained for the first time in this research were confirmed by their IR [1720 cm^{-1} (CO)] and mass spectra [m/e 71 ($C_3H_7CO^+$), 43 ($C_3H_7^+$), 86 [$(C_2H_5)_2N^+=CH_2$], etc.]. Gas–liquid chromatography (GLC) was used both to monitor the course of the reactions and to confirm the purity of the isolated products (an LKh-M 8 MD chromatograph with a flame-ionization detector, helium as the carrier gas, a column temperature of 100-160°, a 100 by 0.3 cm stainless-steel column with 10% Versamid on silanized Celite-545 and 5% polyethylene glycol adipate on Chromosorb G was used).

TABLE 2. Amino Ketones n-$C_3H_7CO(CH_2)_nNR_2$ from 2-(ω-Dialkylaminoalkyl)thiophenes

Compound	bp, °C (mm)	n_D^{20}	Empirical formula	Found, %			Calc., %			Yield, %	Derivative mp, °C[a]
				C	H	N	C	H	N		
IIa[b]	67—68 (23)	1,4231	$C_7H_{15}NO$	64,9	11,7	10,8	65,1	11,7	10,8	13	P, 58—59[c]
IIb[12]	89—90 (11)	1,4375	$C_{10}H_{21}NO$	69,9	12,4	8,4	70,1	12,4	8,2	37	P, 80—81[d]
IIc[11]	76 (3,5)	1,4395	$C_{11}H_{23}NO$	71,4	12,5	7,2	71,3	12,5	7,5	78	O, 71,5—72
IId	120—120,5 (10)	1,4434	$C_{12}H_{25}NO$	72,4	12,6	7,1	72,3	12,6	7,0	69	O, 75—76
IIe	120 (5)	1,4454	$C_{13}H_{27}NO$	73,2	12,7	6,5	73,2	12,8	6,6	70	O, 77—78
IIf	126—127 (3,5)	1,4469	$C_{14}H_{29}NO$	74,1	12,8	6,5	74,0	12,9	6,1	82	O, 88,5—89

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[a] Derivatives: P indicates picrate and O indicates oxalate. The oxalates were purified by reprecipitation from alcohol by the addition of absolute ether. The derivatives had satisfactory analytical data for nitrogen.

[b] Only the melting point of the picrate is presented in [13].

[c] From ether–petroleum ether.

[d] From methanol.

2-Dimethylaminomethylthiophene (Ia). Amine Ia [35.2 g (83%)], with bp 60-61° (10 mm) and n_D^{20} 1.5180 [4], was obtained by the Leuckart reaction from 33.6 g (0.3 mole) of 2-formylthiophene, 22.0 g (1.8 mole) of DMF, and 70 ml of 85% formic acid.

2-(2-Diethylaminoethyl)thiophene (Ib, Table 1). Amine Ib was obtained in 47% yield by the method in [6] from 29.3 g (0.2 mole) of 2-(2-chloroethyl)thiophene [7], 32.2 g (0.44 mole) of diethylamine, and 150 ml of DMF.

2(3-Diethylaminopropyl)thiophene (Ic, Table 1). As in the preceding experiment, Ic was obtained in 87% yield from 2-(3-chloropropyl)thiophene [7].

2-(4-Diethylaminobutyl)thiophene (Id, Table 1). The acid diethylamide, with bp 155-158° (3 mm), was obtained in 94% yield by reaction of 4-(2-thienyl)butyryl chloride [8] and diethylamine in ether at −10°. The diethylamide was reduced with lithium aluminum hydride by the method in [9] to give amine Id (94% yield).

2-(5-Diethylaminoamyl)thiophene (Ie, Table 1). The acid diethylamide [91% yield, bp 155-156° (2.5 mm)] and amine Ie (90% yield) were obtained successively by the method described above from 5-(2-thienyl)valeryl chloride [10].

2-(6-Diethylaminohexyl)thiophene (If, Table 1). The acid diethylamide [93% yield, bp 168-170° (3 mm)] and amine If (94% yield) were obtained successively from 6-(2-thienyl)caproyl chloride [10].

1-Diethylamino-4-heptanone (IIc, Table 2). Fine pieces of lithium [1.67 g (0.24 g-atom)] were added at −60° in the course of 10 min to a stirred solution of 7.9 g (0.04 mole) of Ic and 17.8 g (0.24 mole) of tert-butyl alcohol in 300 ml of liquid NH_3, after which the mixture was stirred at −60° for 2 h. Solid NH_4Cl [12.9 g (0.24 mole)] was added in very small portions to the mixture, and the ammonia was evaporated. The residue was dissolved in water, and the solution was extracted repeatedly with ether. The combined organic extracts were washed with concentrated NaCl solution and dried with $MgSO_4$. Distillation gave 6.1 g of ketone IIc [11].

1-Diethylamino-5-octanone (IId, Table 2). Ketone IId (6.9 g) was obtained as described above from 10.6 g (0.05 mole) of Id, 18.5 g (0.25 mole) of tert-butyl alcohol, and 1.73 g (0.25 g-atom) of lithium in 300 ml of liquid NH_3.

1-Diethylamino-6-nonanone (IIe, Table 2). Ketone IIe (3.61 g) was obtained from 6.75 g (0.03 mole) of Ie, 11.1 g (0.15 mole) of tert-butyl alcohol, and 1.04 (0.15 g-atom) of lithium in 200 ml of liquid NH_3.

1-Diethylamino-7-decanone (IIf, Table 2). Ketone IIf (9.36 g) was obtained from 12.0 g (0.05 mole) of If, 22.2 g (0.3 mole) of tert-butyl alcohol, and 2.08 g (0.3 g-atom) of lithium in 400 ml of liquid NH_3.

1-Diethylamino-3-hexanone (IIb, Table 2). The reduction of 9.1 g (0.05 mole) of Ib by means of 2.08 g (0.3 g-atom) of lithium, 22.2 g (0.3 mole) of tert-butyl alcohol, and 300 ml of liquid NH_3 was carried out by the method described above. Distillation yielded 4.4 g of a viscous liquid with bp 127-132° (0.7 mm). According to analysis, the product contained more than 10% sulfur, had a molecular weight approximately twice that of the original molecular weight, and apparently was the product of incomplete reduction. The same amounts of the starting reagents were used in a repeated experiment. After evaporation of the NH_3, the crude product was dissolved in dilute hydrochloric acid, and the solution was allowed to stand overnight. It was then washed with petroleum ether, made alkaline to pH 9, and extracted repeatedly with petroleum ether. Distillation yielded 3.15 g of IIb [12].

1-Dimethylamino-2-pentanone (IIa, Table 2). A) The product of the reaction of 4.2 g (0.03 mole) of amine Ia with 1.25 g (0.18 g-atom) of lithium and 13.3 g (0.18 mole) of tert-butyl alcohol in 100 ml of liquid NH_3 was worked up as described for the preparation of ketone IIb, and 0.1 g of a substance with amine character and bp 65° (20 mm) was isolated by distillation. The remainder of the reaction product could not be distilled without decomposition even on heating to 210° at a pressure of 1 mm. In a control experiment only 2 equivalents of lithium and tert-butyl alcohol were used for the reduction of Ia, and the crude reaction product was analyzed by GLC (with a column filled with polyethylene glycol adipate on Chromosorb G and programming from 40 to 165°). A small peak due to 2-methylthiophene was recorded along with several other peaks, the largest of which is affiliated with starting Ia.

B) The reaction of 9.86 g (0.07 mole) of Ia with 7.6 g (0.33 g-atom) of sodium, 24.4 g (0.33 mole) of tert-butyl alcohol, and 300 ml of liquid NH_3 was carried out at −40° (the reaction proceeds very slowly below −45°), and the product was worked up as described in the preparation of IIb. Distillation yielded 1.18 g of IIa [13].

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