

5-Propyl-3-(dimethylaminomethyl)-4-thiolen-2-one (Va). A mixture of 5 g (0.035 mole) of thiolene IIa, 2.1 g (0.07 mole) of paraform, 1.6 g (0.035 mole) of dimethylamine hydrochloride, 80 ml of ethanol, and 1 ml of hydrochloric acid was heated at 90°C for 6 h with mixing. The ethanol was removed, and the residue recrystallized from acetone to give 4.8 g (49%) of Va. Compounds Vb-d were obtained analogously (Table 2).

5-Isobutyl-3-(dimethylaminomethyl)furan-2-one (Vf). To a solution of 5.6 g (0.04 mole) of furanone IIg in 15 g ethanol, 7.2 g (0.08 mole) of paraform, and 1.8 g (0.04 mole) of dimethylamine at 90°C was added with mixing over 1 h, 1.7 g of KOH in 10 ml of ethanol. The mixture was maintained at this temperature for 20 h, and when cool extracted with ether. After drying over Mg₂SO₄ the ether was removed and the residue was evaporated in vacuum (Table 1).

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REDUCTIVE ACYLATION OF 5-NITRO-2R-THIOPHENES

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A study was made of the kinetics of the reduction of eleven 5-nitro-2-substituted thiophenes to acetylaminothiophenes using Raney nickel in acetic anhydride. The dependence of the rate of the reaction both on the induction effect of the substituents and on the ratio of the adsorption constants of the reaction products and substrate was determined.

In [1] we studied the nitration of 2-substituted thiophenes with nitric acid in acetic anhydride. The experimental data indicated that the substituents have an appreciable effect on the activity of the reaction center. In the present work, the effect of the nature of the substituents in the nitrothiophene molecule on the reactivity of the nitrogroup under conditions of heterogeneous catalytic reduction have been studied. Publications on the synthesis of aminothiophenes [2-5] by the reduction of nitrothiophenes are limited to determinations of yields of reaction products. Kinetic studies of the reaction have not been carried out before.

In accordance with [6], the reaction was carried out in acetic anhydride, which ensures that only the nitro group is reduced, to give the stable acetyl form of the corresponding amine.

A study was made of the reduction of the 2-nitrothiophene and ten of its derivatives: 2-tert-butyl-5-nitrothiophene, 5-nitro-2-ethylthiophene, 2-iodo-5-nitrothiophene, 2-bromo-5-nitrothiophene, 5-nitro-2-acetothienone, 5-nitrothiophen-2-carboxylic acid, 5-nitrothiophen-2-aldehyde, diacetate of 5-nitrothiophen-2-aldehyde, 2,5-dinitrothiophene, and 5,5'-dinitro-2,2'-dithienyl.

At 323 K, the reaction was determined to be first order with respect to the catalyst, zero order for acetic anhydride and of a fractional order for the substrate. The rate of reduction is nonlinear and increases with increase in concentration of the nitrocompound (Fig. 1a). A linear relationship between c/v_0 and c (Fig. 1b) confirms that the adsorption of the nitrocompound on the catalyst appears to conform to the Langmuir equation.

At 293 K, the reduction of the majority of compounds does not go to completion; only about 50-80% of the starting material is reduced. The relationship between the reaction rate

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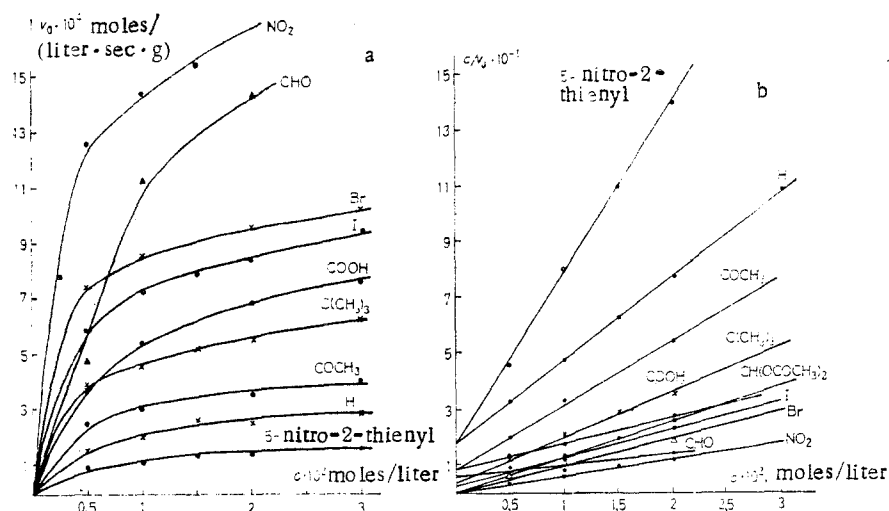


Fig. 1. Relationship between v_0 and the concentration of the substrate (a) and between c/v_0 and the concentration of the nitrocompound (b). Reaction temperature 323 K, concentration of catalyst 0.1782 mole/liter.

TABLE 1. Dependence of Adsorption Constants of Reaction Products and Substrate on Temperature in Reduction of 2R-5-nitrothiophenes by Raney Nickel

2-R	b_{pr}/b_{sub}					
	293 K	308 K	323 K	338 K	353 K	363 K
H	0.5751 ± 0.0580	0.1876 ± 0.0221	0.4706 ± 0.0277	0.8661 ± 0.0398	1.0720 ± 0.0536	1.2126 ± 0.0573
$C(CH_3)_3$	—	0.1100 ± 0.0231	0.1608 ± 0.0337	0.3150 ± 0.0456	0.5400 ± 0.0421	0.5850 ± 0.1579
C_2H_5	1.2900 ± 0.1305	0.2845 ± 0.0204	0.3500 ± 0.0154	0.4056 ± 0.0440	0.5623 ± 0.0331	0.6870 ± 0.1467
$CH(OCOCH_3)_2$	0.9706 ± 0.0569	0.1800 ± 0.0222	0.2606 ± 0.0360	0.2962 ± 0.0212	0.4027 ± 0.0805	0.4467 ± 0.0670
Br	0.4510 ± 0.0905	0.1843 ± 0.0221	0.1897 ± 0.0231	0.2146 ± 0.0366	0.2265 ± 0.0339	0.2477 ± 0.0371
I	0.6909 ± 0.1727	0.4870 ± 0.0584	0.3160 ± 0.0312	0.4460 ± 0.0179	0.5201 ± 0.0540	0.6607 ± 0.1189
$COCH_3$	0.5340 ± 0.0061	0.1649 ± 0.0145	0.2464 ± 0.0258	0.5166 ± 0.0019	0.7328 ± 0.0072	0.8313 ± 0.1081
COOH	0.5106 ± 0.0199	0.3310 ± 0.0243	0.3804 ± 0.0293	0.6208 ± 0.0853	0.8128 ± 0.1219	0.9661 ± 0.1449
CHO	0.6971 ± 0.0444	0.7776 ± 0.0741	1.4428 ± 0.0675	1.8495 ± 0.0530	2.5230 ± 0.2018	2.9850 ± 0.4477
NO_2	0.1888 ± 0.0320	1.6643 ± 0.0712	0.9963 ± 0.0774	0.8447 ± 0.1098	0.5888 ± 0.1877	0.5012 ± 0.0751
5-Nitro-2-thienyl	2.8456 ± 0.4183	0.9400 ± 0.0905	0.8479 ± 0.0807	1.2427 ± 0.0910	2.0736 ± 0.5600	2.3440 ± 0.5500

v and the degree change x in the temperature range 293–363 K varies. As an example, in Fig. 2 curves for 5-nitrothiophene are given. It can be seen that at 293–323 K the relationship between the reduction rate and the amount of reacted nitrocompound indicates that there is no appreciable retardation of the reaction as reaction products are formed; with increase in temperature, this relationship becomes linear, indicating that the reaction products affect the reaction rate [7].

This type of relationship is the result of a change in the ratio of the adsorption constants (b_{pr}/b_{sub}) for the reaction products and substrate at higher temperatures (Table 1). The values for b_{pr}/b_{sub} were determined from Eq. (1), both graphically and by the method of least squares.

$$r = k \frac{b_{sub} c_{sub}}{b_{sub} c_{sub} + b_{pr} c_{pr}} \quad (1)$$

The rates of reaction were calculated from kinetic experiments obtained by introducing different amounts of reaction products into the starting mixture, and also by following the course of a single kinetic experiment. Calculations of b_{pr}/b_{sub} for all the compounds were carried out in the same way. Graphic analysis of the relationship between the rate of reaction and the degree of change for the whole series shows that when $b_{pr}/b_{sub} < 1$, the curve r vs. x is convex, and when $b_{pr}/b_{sub} > 1$, r vs. x becomes linear.

The rate constants K_{all} were determined by the least squares method using Eq. (1). Values of the constant were also obtained from the relationship:

TABLE 2. Rate Constants and Activation Parameters for the Reduction of 2-R-5-nitrothiophenes by Raney Nickel

2-R	$k_{all} \cdot 10^4, \text{sec}^{-1} \cdot [\text{cat}]^{-1}$						$E_{all}, \text{kJ/mole}$		$\lg K_0$	
	293 K	308 K	323 K	338 K	353 K	363 K	293-323 K	338-363 K	293-323 K	338-363 K
H	2,974	4,984	9,668	13,611	18,462	22,317	30.81 ± 0.71	20.39 ± 0.08	1.95 ± 0.11	0.28 ± 0.01
$\text{C}(\text{CH}_3)_3$	1,308	3,357	8,090	15,850	20,310	21,450	41.78 ± 3.22	13.89 ± 1.59	3.60 ± 0.55	-0.94 ± 0.24
C_2H_5	2,706	5,839	7,340	9,430	11,928	13,617	$37.97 \pm 2.84^*$	16.41 ± 0.33	2.30 ± 0.49	-0.45 ± 0.05
$\text{CH}(\text{OCOCH}_3)_2$	4,100	7,748	12,349	14,903	17,700	19,700	28.93 ± 0.42	11.43 ± 0.04	1.78 ± 0.07	-1.05 ± 0.01
Br	2,761	4,881	6,913	8,841	11,071	12,730	24.12 ± 0.58	14.98 ± 0.08	0.75 ± 0.10	-0.73 ± 0.01
I	1,654	3,759	4,925	7,251	8,474	9,329	28.80 ± 1.71	10.34 ± 0.04	1.38 ± 0.29	-1.53 ± 0.01
COCH_3	3,959	5,800	11,070	15,520	26,990	35,120	28.01 ± 0.46		1.56 ± 0.07	1.56 ± 0.07
COOH	3,583	5,479	9,127	16,586	25,310	32,910	27.88 ± 0.46		1.49 ± 0.07	1.49 ± 0.07
CHO	4,270	8,213	11,817	17,746	22,698	26,443	26.75 ± 0.83	16.41 ± 0.08	1.42 ± 0.14	-0.21 ± 0.01
NO_2	3,025	5,346	8,039	11,788	13,548	14,770	25.66 ± 0.37	9.37 ± 0.12	1.06 ± 0.06	-1.47 ± 0.02
5-Nitro-2-thienyl	1,093	1,829	3,002	4,118	5,976	7,140	26.25 ± 0.42	18.73 ± 1.01	0.71 ± 0.07	-0.48 ± 0.15

*For temperatures 292-308 and 308-363 K.

$$k_{all} = \frac{1}{\tau[\text{cat}]} \left[(1 - b_{pr}/b_{sub})x - b_{pr}/b_{sub} a \ln \frac{a-x}{a} \right], \quad (2)$$

where a is the starting concentration of the substrate in moles/liter; x is the amount of substance reacted in moles/liter; $[\text{cat}]$ is the weight of the catalyst in grams; and τ is the time in seconds.

The values k_{all} calculated from Eq. (2) are given in Table 2.

The Arrhenius relationship for the majority of nitrothiophenes has a break at 323-338 K; for 5-nitro-2-ethylthiophene, the break occurs at 293-308 K. However, there is no break in the straight-line Arrhenius plot for 5-nitro-2-acetothienone and 5-nitrothiophene-2-carboxylic acid.

For the part of the curve corresponding to the higher temperature, the apparent energy of activation is appreciably less than for the other part (Table 2). In addition, over the whole temperature range a linear relationship between ΔH^\ddagger vs. ΔS^\ddagger (Fig. 3) and $\lg k_0$ vs. E is observed indicating that a single mechanism operates to control the effect of the substituents on the reaction center. Thus it appears that the observed break in the straight-line Arrhenius plot is due to an internal-diffusion retardation that occurs on going to a higher temperature [8].

The Hammett relation between the half-wave potential ($E_{1/2}$) and the σ -constant of the substituent for the polarographic reduction of the same compounds was determined in [9]. The activity of the substituents can be ordered as follows: $\text{NO}_2 > \text{COCH}_3 > \text{CHO} > \text{COOH} > \text{Br} > \text{I} \geq \text{C}_2\text{H}_5 > \text{C}(\text{CH}_3)_3$.

At a temperature of 293 K, this relationship is also observed in reductions with Raney nickel. An exception is 2,5-dinitrothiophene, where both groups are reduced, and the ratio of the rate constant for the reduction of 2,5-dinitrothiophene to the rate constant for the unsubstituted nitrothiophene lies between COOH and Br . At higher temperatures, the reaction series is disordered (see Table 2) because of changes in the relationship between the constant b_{pr}/b_{sub} and rate of chemical reaction for different compounds.

EXPERIMENTAL

The reduction was carried out in a thermostatted glass reaction-vessel, fitted with a vibration device and supplied with a continuous current of hydrogen. The course of the reaction was followed by observing the rate of absorption of hydrogen; the flow-rate was noted each minute. All the nitrothiophenes used in the work were obtained by the method given in [1, 10, 11]; polarographic and chromatographic data showed them to be at least 99.7% pure.

Commercial Raney nickel, grade TU 6-02-1019-75, with a specific surface area of $93.5 \text{ m}^2/\text{g}$ and a particle size of 2-4 microns was used as a catalyst. Grade A GOST 3022-61 hydrogen, containing less than 0.01% of oxygen, was used.

After purification by crystallization from aqueous-alcoholic solutions the yield of synthesized compounds was: 2-acetylaminothiophene - 84%, 5-acetylmino-2-ethylthiophene - 73%,

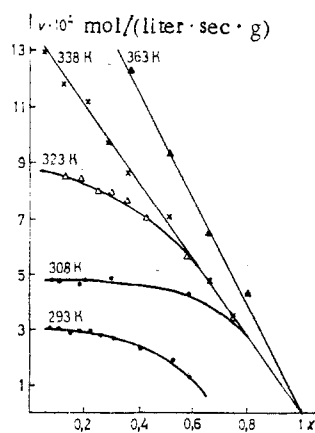


Fig. 2

Fig. 2. Relationship between reaction rate and extent of reduction of 2-nitrothiophene.

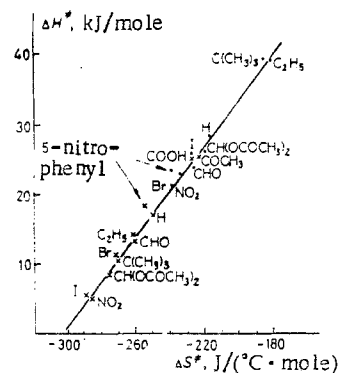


Fig. 3

Fig. 3. Relationship between enthalpy and entropy for Raney nickel reduction: ● — for temperature 293-323 K; × — for temperature 338-363 K.

5-acetylamino-2-acetothienone — 80%, 5-acetylaminothiophene-2-carboxylic acid — 3%, methyl ester of 5-acetylaminothiophene-2-carboxylic acid — 32%, ethyl ester of 5-acetylaminothiophene-2-carboxylic acid — 95%, 5-acetylaminothiophene-2-aldehyde — 7%, 5,5'-diacetyldiamine-2,2'-dithienyl — 70%. Owing to tarring, the reduction product of 2,5-dinitrothiophene could not be isolated in the pure form. Reduction of nitrohalogenothiophene gave a mixture of acetylaminothiophene and 5,5'-diacetyldiamine-2,2'-dithienyl [12].

All the synthesized compounds were characterized by melting point, PMR spectral data, and mass spectra. The nitrothiophene introduced into the reactor was first dissolved in DMFA. Special experiments showed that the rate of reduction of nitrothiophenes did not depend on the ratio of DMFA-acetic anhydride 1:0.001-7.5 mole/mole or on the rate at which the reaction vessel was shaken (>300 vibrations/minute). It was also shown that on increasing the concentration of Raney nickel from 0.1 to 0.3 mole/liter, the rate of reaction increased linearly; further increase in concentration did not produce any change. Accepting that, to a first approximation, with vigorous mixing (500 vibrations/minute) and a concentration of Raney nickel 0.178 mole/liter, the reaction occurs without diffusion limits; further kinetic studies were carried out under these conditions. Calculation of the rate constants and activation parameters was done on an M-222 computer using the specially developed program "ADASTRA." The mean square deviation was 4-15%, and the maximum deviation in individual tests was 20-25%.

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SYNTHESIS OF DERIVATIVES OF 2-ACYLAMINO-7-OXYBENZO[b]THIOPHENE.

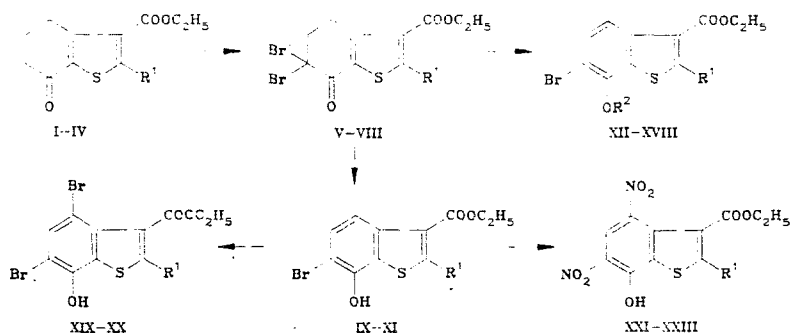
BROMINATION AND NITRATION

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Bromination of 2-acylamino-3-ethoxycarbonyl-7-oxo-4,5,6,7-tetrahydrobenzo[b]-thiophenes has been studied. This reaction affords 2-acylamino-6,6-dibromo-3-ethoxycarbonyl-7-oxo-4,5,6,7-tetrahydrobenzo[b]thiophene, which on dehydrobromination gives 6-bromo-7-oxybenzo[b]thiophene derivatives. The 4,6-dibromo- and 4,6-dinitro-7-oxybenzo[b]thiophenes were also obtained.

Bromination of the 7-oxo-4,5,6,7-tetrahydrobenzo[b]thiophenes (I-IV) [1] with 2 moles of bromine gave the 6,6-dibromoderivatives (V-VIII), the structures of which were confirmed by PMR spectra. The PMR spectrum of the 6,6-dibromoderivative V contained a multiplet at 3.19 ppm from the two CH₂ groups at positions 4 and 5. In order to synthesize 6-bromo-7-oxybenzo[b]thiophenes (IX, X), the dibromosubstituted compounds V and VII were dehydrobrominated using potassium carbonate. The PMR spectrum of the oxybenzo[b]thiophene IX contained doublets at 7.59 and 7.50 ppm corresponding to the two aromatic protons 4-H and 5-H, respectively. The structures of the compounds were also confirmed from IR spectra. In the spectra of compounds IX, the OH group absorbed at 3360 cm⁻¹, and the CO group absorbed at 1700-1650 cm⁻¹. We also prepared methoxy (XII, XIII), benzyloxy- (XIV), p-bromophenacyloxy- (XV, XVI), and acetoxy derivatives (XVII, XVIII) of benzo[b]thiophene. Bromination of compounds IX and X gave the 4,6-dibromoderivatives XIX, XX, which is in agreement with literature data [2]. Nitration of the 6-bromobenzo[b]thiophenes IX and X, and the previously obtained [1] XI, with nitric acid, takes place at the 4 position; replacement of the bromine by a nitro group also occurs. The PMR spectra of compounds XIX and XXI contained singlets at 7.72 and 8.67 ppm, respectively, arising from the aromatic protons at the 5 position. Nitration of compound XI occurred also at the benzene ring, confirmed by the presence of singlets in the PMR spectra of compound XXII at 8.53 and 8.75 ppm from the protons at positions 2 and 5.



I, V, IX, XII, XIV, XV, XVII, XIX, XXI R¹=NHCOCH₃; II, VI R¹=NHCOCH₂CH₃;
 III, VII, X, XIII, XVI, XVIII, XX, XXIII R¹=NHCOCH₂Cl; IV, VIII R¹=NHCOCH₂Cl;
 XI, XXII R¹=H; XII, XIII R²=CH₃; XIV R²=CH₂C₆H₅; XV, XVI R²=CH₂COC₆H₄Br-(p);
 XVII, XVIII R²=COCH₃

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