chromatographed on a column (5 × 60 cm) of silica gel (L 100/250), eluent ether. The eluate was concentrated to 25 ml, the porphyrin (IX) precipitated with hexane, filtered off, and dried in air at room temperature to give 0.32 g (63%) of IX.

Tetra-(4-hydroxyphenyl)porphin (X) was obtained similarly from tetra-(4-aminophenyl)porphin, yield 0.36 g (72%).

Tetra[2-(p-hydroxyphenylazo)phenyl]porphin (XI). To a solution of 0.5 g (0.74 mmole) of tetra-(2-aminophenyl)porphin in a mixture of 0.5 ml of conc. sulfuric acid and 30 ml of water was added dropwise with stirring and cooling at 5°C a solution of 0.2 g (2.9 mmoles) of sodium nitrite in 1 ml of water. The resulting diazonium salt solution was added dropwise to a stirred solution of 0.3 g (3.2 mmole) of phenol and 1 g of KOH in 10 ml of water. The mixture was diluted to 150 ml with water, and filtered. The filtrate was neutralized with conc. HCl to pH 7, and the porphyrin filtered off, washed with 100 ml of 10% ammonia and water, and dried in the vacuum desiccator. The porphyrin was purified by dissolving it in 200 ml of boiling ether, and chromatography on a column (5 × 60 cm) of silica gel (L 100/250), eluent ether. The eluate was concentrated to 25 ml, the porphyrin precipitated with hexane, filtered off, and dried in air at room temperature to give 0.6 g (74%) of XI.

Tetra-[3-(p-Hydroxyphenylazo)phenyl]porphin (XII) was obtained similarly from tetra-(3-aminophenyl)porphin, yield 0.72 g (89%), as was tetra-[4-(n-hydroxyphenylazo)phenyl)porphin (XIII) from tetra-(4-aminophenyl)porphin, yield 0.78 g (98%).

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ETHYL 1,4-DIHYDROPYRIDINECARBODITHIOATES AND THE ELECTRONIC EFFECTS OF SULFUR-CONTAINING ESTER SUBSTITUENTS

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Methods have been developed for the synthesis of the ethyl esters of 2,6-dimethyl-1,4-dihydropyridine-3,5-bis(carbodithioic) and 4-aryl-2-methyl-5-oxo-4,5-dihydro-1H-indeno[1,2-b]pyridine-3-carbodithioic acids. From the physicochemical properties (acid dissociation constants and electrochemical oxidation potentials of the 1,4-dihydropyridines with sulfur-containing substituents in the β-positions, the electronic effects of these groups in the 1,4-dihydropyridine system have been determined. The inductive and resonance constants of these substituents in aromatic compounds have been found by ^{13}C and ^{19}F NMR spectroscopy.

Much attention has recently been devoted to 1,4-dihydropyridines (1,4-DHP) and hydrogenated nitrogenous heterocycles, with their unique chemical properties [1, 2] and manifold biological activity [3].

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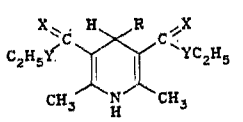
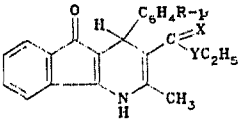
In studying 1,4-DHP with sulfur-containing ester substituents in the β-positions, we set ourselves the task of determining the electronic effects of these substituents. We have previously described [4-6] 1,4-DHP and dihydroindenopyridines with alkylthiocarbonyl, benzylthiocarbonyl, and ethoxythiocarbonyl groups in the β-positions (I, II X = O, Y = S; X = S, Y = O). We here describe methods of synthesis and properties of 1,4-DHP and 4,5-dihydro-1H-indeno[1,2-b]pyridine-5-ones bearing ethylthio(thiocarbonyl)substituents (I, II, X = Y = S) in the β-position.

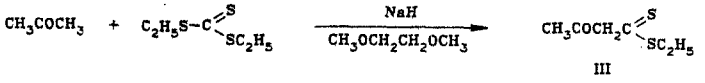


I



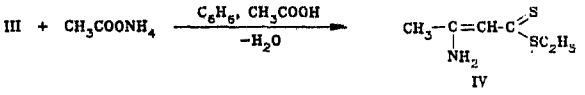
II

The key compound, ethyl acetodithioacetate (III) has been described in the literature [7, 8], but in order to simplify the synthesis and increase the yields we have developed a new method for its synthesis, as follows:



III

Ethyl β-aminodithiocrotonate (IV) has been synthesized for the first time by reaction of the dithioester III with ammonium acetate in the presence of acetic acid:



IV

From monocyclic dithioesters of the 1,4-dihydropyridine series we have only been able to obtain a 4-unsubstituted product (I R = H, X = Y = S) and a 4-p-nitrophenyl derivative (I R = $C_6H_4NO_2$-p, X = Y = S), which were synthesized by a modification of Hansch's method [9]. The condensation of the dithioester III with other aromatic aldehydes in glacial acetic acid was unsuccessful, since the prolonged heating required for cyclocondensation to 1,4-DHP resulted in decomposition of the dithioester III.

Polycyclic 1,4-DHP with an (ethylthio)thiocarbonyl group in the 3-position (II X = Y = S) were obtained from 2-arylideneindan-1,3-diones by two routes, either by boiling with the dithiocrotonic ester IV in acetic acid (method A), or by condensation with the dithio-ester III in the presence of an excess of ammonium acetate (method B). Method B is preferred, substantially higher yields of products being obtained.

The UV, IR, and PMR spectra of the products I and II (X = Y = S) (Table 1) confirmed the structures of these compounds. The UV spectra of the dithioesters (II = Y = S) the long-wavelength maximum (Table 1) undergoes a bathochromic shift by 20-40 nm in comparison with the corresponding thiol and thione esters [4-6]. In the IR spectrum of the 1,4-DHP I (R = H, H = Y = S), the only absorption present in the double bond region is seen at 1610 cm^{-1}, assigned to the double $>C=C<$ bonds of the dihydropyridine system. In the polycyclic dithioesters (II, X = Y = S), in addition two bands are present for the cyclic benzoylene moiety of the molecule, at around 1640 and 1670 cm^{-1} (Table 1).

In order to evaluate the electronic properties of the sulfur-containing ester groups, the pK values (Table 2) of the 1,4-DHP with an (ethylthio)thiocarbonyl β-substituent were found. For comparison, values were measured, previously determined values for known compounds were used for thiolo (I, II, X = O, Y = S), thiono (I, II, X = S, Y = O) and oxygen esters (I, II, X = Y = O) [4-6].

The pK values of compounds (I) and (II) were determined by the transmetallation method in DMSO [10], and for the dihydroindenopyridines (II) additionally by a spectrophotometric method [11] in 50% ethanol.

As will be seen from Table 2, replacement of an ether or carbonyl oxygen by sulfur increases the acidity by practically the same amount (~1.2 pK units) in compounds with struc-

TABLE 1. Ethyl Esters of 2,6-Dimethyl-1,4-dihydropyridine-3,5-bis(carbodithionic) (I X = Y = S) and 2-Methyl-5-oxo-4,5-dihydro-1H-indeno[1,2-b]pyridine-3-carbodithionic) (II X = Y = S) Acids

Compound	R	mp, °C	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max}, nm	PMR spectrum δ, ppm (in DMSO-d_6)						Found, %				Empirical formula	Calculated, %				Yield, %
					CH_2CH_3†, t	CH_2CH_3†, q	C—CH_3, s	4-H, s	N—H, s	H_{arom}, nm	C	H	N	S		C	H	N	S	
Id	H	94	1610, 3365	207, 309, 500	1,18	3,13	2,27	3,76	9,27	—	48,9	6,2	4,3	40,0	$C_{13}H_{19}NS_4$	49,2	6,0	4,4	40,4	35
Ia	p-$NO_2C_6H_4$	111	1615, 3380	207, 310, 470	1,16	3,17	2,32	6,26	9,72	7,20—8,45	52,4	5,0	6,7	28,8	$C_{19}H_{22}N_2O_2S_4$	52,0	5,1	6,4	29,2	41
IId	H	200	1610, 1620, 1640, 1670, 3200	207, 232, 262, 320, 497	1,13	3,11	2,18	5,04	10,15	7,10—7,70	70,4	4,9	3,5	16,7	$C_{22}H_{19}NOS_2$	70,0	5,1	3,7	17,0	75 (A), 90 (B)
IIg	CH_3O	183	1610, 1620, 1635, 1670, 3180	207, 235, 262, 317, 496	1,14	3,11	2,15	5,10	10,15	7,05—7,80 ‡	67,4	5,1	3,1	15,3	$C_{23}H_{21}NO_2S_2$	67,8	5,2	3,4	15,7	68 (A), 84 (B)
IIi	Br	195	1610, 1620, 1640, 1670, 3180	207, 235, 262, 322, 495	1,13	3,11	2,13	4,96	10,13	7,04—7,60	58,1	4,2	3,1	14,3	$C_{22}H_{18}BrNOS_2$	57,9	4,0	3,1	14,1	55 (A), 75 (B)
IIl	NO_2	199	1610, 1620, 1640, 1675, 3200	207, 231, 266, 320 (пл.), 498	1,13	3,11	2,16	5,11	10,22	7,27—8,27	62,2	4,5	6,3	14,9	$C_{22}H_{18}N_2O_3S_2$	62,5	4,3	6,6	15,2	71 (A), 82 (B)

*A full list of compounds is given in Table 3.
†The coupling constant with the ethyl group is 7.6 Hz.
‡For the CH_3O group, δ 3.60 ppm, s.

TABLE 2. Equilibrium Constants (K_{equil}) for the Reaction of the 1,4-DHP (I), (V), and (VI) and 4,5-Dihydroindenopyridines (II) with Potassium-Substituted Indicator Acids, Long-Wave Absorption of Their Anions, and pK Values in DMSO, together with the pK of (II) in 50% Ethanol

Compound*	Indicator (pK)	K_{equil}	λ_{max}, nm	$\varepsilon \cdot 10^{-4}$	pK	
					DMSO	50% ethanol
Ia	2-Methylimidazole (19.9)	0,66±0,1	475	2,64	20,1	—
Ib	2-Phenylimidazole (18.1)	2,4±0,3	522	1,60	17,7	—
Ic	2-Methylimidazole (18.1)	6,5±0,3	625	1,18	17,3	—
Id	1,2,4-Triazole (15.4)	3,6±0,4	705	2,76	14,8	—
IIa	1,2,4-Triazole (15.4)	1,7±0,2	578	1,02	15,2	12,74
IIb	1,2,4-Triazole (15.4)	24,3±0,4	584	1,04	14,0	12,52
IIc	1,2,4-Triazole (15.4)	20,7±1,2	620	1,20	14,0	12,52
IId	Benztriazole (12.6)	0,086±0,004	638	0,88	13,7	12,4
IIg	Benztriazole (12.6)	—	—	—	—	12,6
IIi	Benztriazole (12.6)	—	—	—	—	12,4
IIj	Benztriazole (12.6)	—	—	—	—	11,7
V	1,2,4-Triazole (15.4)	0,06±0,01	435	1,04	16,7	—
VI	2-Methylimidazole (19.9)	2,6±0,3	520	1,74	19,5	—

*A full list of compounds is given in Table 3.

ture II (IIa-c), and by ~2.5 pK units in monocyclic 1,4-DHP (Ia-c). The twice greater value of the change for compounds I is due to the fact that replacement of the oxygen atom by sulfur occurs simultaneously in two groups. Measurement of the pK of the dihydroindenopyridines II in ethanol gives closely concordant values for all the sulfur-containing substituents. It is important to stress that there is a good qualitative agreement between the sequence of changes in pK values of type II compounds in ethanol and in DMSO. The substantially lower differences in the pK values obtained for dihydropyridoindenes in ethanol as compared with DMSO is due to the leveling-out effect of the hydroxylated solvent [12]. The formation of a hydrogen bond between the ethanol and the N-anion stabilizes the latter, thereby increasing the strength of the conjugate NH-acid. The greater the basicity of the anion, the greater is the stabilizing effect of this specific solvation, and the greater is the decrease in the pK value in the hydroxylated solvent as compared with the aprotic solvent. Therefore, the range of acidity (pK values) in alcohol for a series of NH-acids is usually smaller than in DMSO [12].

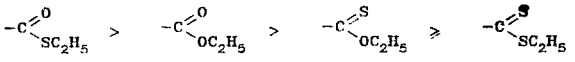
The introduction of (ethylthio)thiocarbonyl substituents into the β-position of 1,4-DHP (Table 2, Id) results in an increase in acidity of 5.3 pK units. Hence, in the magnitude of their effects on the acidity of 1,4-DHP these substituents can be arranged in the sequence:

In type II structures, however, the (ethylthio)thiocarbonyl substituent increases acidity in DMSO by only 1.5 pK units over the oxygen-containing ester, and by as little as 0.3 pK units in comparison with the thiolo and thionoesters (Table 2, IIa-d). The comparatively small differences in the pK values on varying the β-substituent in II is due to the fact that in the indene moiety the whole of the β-aminovinylcarboline five-membered chain lies in one plane, resulting in strong conjugation of the unshared electron pair of the nitrogen atom. On the other hand, the effect of the non-fixed β-substituent in II is to a large extent evened out, since for steric reasons it must be largely withdrawn from conjugation. Replacement of the ethoxycarbonyl group by the more highly electron-accepting nitrile group (in 2,6-dimethyl-3,5-dicyano-1,4-DHP, (V)) increases acidity by 3.4 pK units, whereas the acetyl group in 3,5-diacetyl-2,6-dimethyl-1,4-DHP (VI) is similar in its effect on acidity to the ethoxycarbonyl grouo (Table 2).

The increased acidifying effects of the ethoxythiocarbonyl and (ethylthio)thiocarbonyl substituents is doubtless due to intramolecular interactions between these groups and the N-anionic center, but it is difficult to arrive at an unambiguous interpretation of the effect. It may be that it is due to participation of the 3d sulfur orbitals in stabilizing the N-anion, but it is also possible that the ready polarizability of the sulfur atom is important [13]. The possible involvement of free 3d-orbitals of sulfur in charge delocalization at the N-anions

has been suggested to explain the enhanced acidity of N-phenylcarbamates on replacement of the carbonyl oxygen by sulfur [14]. The participation of sulfur in the stabilization of carboanions, or inclusion in conjugation of vacant 3d-orbitals of sulfur is well known in compounds containing sulfonyl, sulfide, or thioamide groups [15-20]. At the same time, it should be pointed out that the 1,4-DHP system is a very complex system for the unambiguous evlauation of intramolecular interactions of the β-substituents examined here with the π-electron system of the ring, in view of the complex interactions of polar and steric factors.

According to the conclusions of Stradyn' et al. [21], the electron-acceptor strength of β-substituents in 1,4-DHP and their electrochemical oxidation (EO) potentials vary in the same way. Consequently, the EO potentials provide a measure of the electronic effects of these sulfur-bearing ester substituents in the 1,4-dihydropyridine system. For this reason, we have determined the potentials of a wide range of compounds and II (Table 3). The introduction of a methyl or aryl substituent into the 4-position of 1,4-DHP (I) with sulfur-containing β-substituents resulted in an increase of 70-200 mV in the EO potentials (Table 3). A similar effect has been observed in a series of oxygen analogs [22, 23]. There was no discussion of the mechanism of EO on 1,4-dihydropyridines in these reports. The problem has been considered in the case of the simplest oxygen esters [23]. According to Vigante et al. [4], replacement of the oxygen atom of an alkoxy-group in a single ester substituent by sulfur increases the EO potential (E_P) by 30-40 mV. The introduction of sulfur atoms in place of oxygen in both ester groups doubles the effect [4] (Table 3), indicating that the (alkylthio)thiocarbonyl substituent has a stronger electron-acceptor effect than its oxygen analog. Thiono- and dithio-esters of 1,4-DHP (Table 3) are oxidized more readily than the carbonyl esters to the extent of 30-120 mV, indicating that electron-acceptor effects of the groups in this reaction series are weaker than with the ethoxy-carbonyl substituent. In the indenodihydropyridines (II), differences in the EO potentials depending on the nature of the β-substituent are less pronounced [6] (Table 3). To summarize, from the results given in Table 3, the ester substituents may be arranged in order of decreasing passivating effects on EO:



Hence, these results for acidity equilibria and EO give differing series of changes in the electron-acceptor properties of ester substituents. The reason for this is concealed in changes in the reaction center in these reaction series, since measurements of pK involve the N-anion, whereas EO involves the initial removal of an electron to give the cation-radical [23].

Finally, we measured the reactivity constants σ_I and σ_R° of the sulfur-containing ester substituents for aromatic compounds, by ^{19}F and ^{13}C NMR spectroscopy. For this purpose, the ^{13}C chemical shifts (CS) of substituted benzenes relative to unsubstituted benzene are normally used (method a) [24]:

$$\sigma_R^0 = -0.05\Delta\delta C_m + 0.05\Delta\delta C_p, \quad (1)$$

$$\sigma_I = 0.42\Delta\delta C_m + 0.028\Delta\delta C_p, \quad (2)$$

together with the ^{19}F CS of para- and meta-substituted fluorobenzenes [25, 26] relative to fluorobenzene (method b):

$$\Delta\delta F_m = -7.10\sigma_I + 0.6, \quad (3)$$

$$\Delta\delta F_p - \Delta\delta F_m = -29.5\sigma_R^0 \quad (4)$$

or a combination of these methods [27]: σ_I was obtained from Eq. (3), and σ_R° from the ^{13}C chemical shifts for the para-carbon atom in the substituted benzene allowing for the solvent (method c). For solutions of the compounds in deuterochloroform,

$$\sigma_R^0 = 0.047\Delta\delta C_p - 0.211\sigma_I. \quad (5)$$

The ^{13}C and ^{19}F CS found are given in Table 4. The values for σ_I and σ_R° calculated by these methods are reported in Table 5. There are some divergences between the values of σ_I and σ_R° obtained by different methods, although the general tendencies of the changes as oxygen is progressively replaced by sulfur persist. The greatest electron-acceptor properties are shown by the (ethylthio)carbonyl substituent, largely on account of its inductive effect (σ_I), then

TABLE 3. Half-Wave Potentials ($E_{1/2}$) in the EO of 1,4-Dihydropyridines (I) and 5-Oxo-4,5-dihydroindenopyridines (II)

Compound	R	X	Y	$E_{1/2}$, V	Compound	R	X	Y	$E_{1/2}$, V
Ia	H	O	O	0,89	IIa	H	O	O	1,10
Ib	H	O	S	0,97	IIb	H	O	S	1,10
Ic	H	S	O	0,83	IIc	H	S	O	1,08
Id	H	S	S	0,81	IId	H	S	S	1,07
Ie	CH_3	O	O	0,96	IIe	CH_3O	O	O	1,15
If	CH_3	O	S	1,08	IIf	CH_3O	S	O	1,05
Ig	CH_3	S	O	0,93	IIg	CH_3O	S	S	1,12
Ih	C_6H_5	O	O	1,08	IIh	Br	O	O	1,20
Ii	C_6H_5	O	S	1,10	IIi	Br	S	S	1,09
Ij	C_6H_5	S	O	0,98	IIj	NO_2	O	O	1,23
Ik	p-$NO_2C_6H_4$	O	O	1,18	IIk	NO_2	S	O	1,16
Il	p-$NO_2C_6H_4$	O	S	1,20	III	NO_2	S	S	1,14
Im	p-$NO_2C_6H_4$	S	O	1,06					

follows oxygen analog, the ethoxycarbonyl group; the (ethylthio)thiocarbonyl and ethoxythiocarbonyl groups display approximately the same electronic effects, the inductive effect being greater in the (ethylthio)thiocarbonyl substituent, i.e., the NMR method gives the following order of electron-acceptor properties for the ester groups:

$$-C\overset{O}{\underset{SC_2H_5}{<}} > -C\overset{O}{\underset{OC_2H_5}{<}} > -C\overset{S}{\underset{SC_2H_5}{<}} > -C\overset{S}{\underset{OC_2H_5}{<}}$$

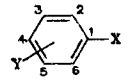
Thus, the (ethylthio)carbonyl group in 1,4-DHP in all the reaction series (pK, EO, oxidation kinetics, and alkylation [4]) and in aromatic systems (NMR for ^{13}C and ^{19}F nuclei) is a stronger electron-acceptor substituent than its oxygen analog. The (ethylthio)carbonyl group promotes reactions involving removal of a proton (pK), and retards reactions involving removal of an electron (oxidation), which is in agreement with the values of its Hammet σ-constant found by us previously [5] from the experimental pK values of substituted benzoic acids [28, 30, 31]. It will be seen from these that the deciding factor in the total electron-acceptor effect is the greater inductive effect of the (ethylthio)carbonyl group.

On the other hand, compounds containing thione sulfur in the β-substituent ($-C\overset{S}{\underset{YC_2H_5}{<}}$, Y = O, S) behave differently, depending on the experimental subject (anionic and neutral forms of 1,4-DHP or the aromatic system). When the thione group can participate in delocalization of the negative charge (acid ionization), the ethoxythiocarbonyl and (ethylthio)thiocarbonyl groups display stronger electron-acceptor properties than the ethoxycarbonyl group. However, in reactions of 1,4-DHP not involving loss of a proton (in particular EO), and when the σ-constant is measured in aromatic systems, the (ethylthio)thiocarbonyl and ethioxythiocarbonyl groups are weaker electron-acceptors than the ethoxycarbonyl and (ethylthio)carbonyl groups.

EXPERIMENTAL

IR spectra were obtained on a UR-20 (in Nujol), electronic absorption spectra on a Specord UV-VIS spectrophotometer (in ethanol), and PMR spectra on a WH-90 spectrometer (90 MHz) in $CDCl_3$ and DMSO-D_6, internal standard TMS. ^{13}C NMR spectra were obtained on a WH 90/DS (22.63 MHz) (for the 10% solutions in $CDCl_3$, internal standard TMS) at 35°C. The accuracy of measurement of the CS was ±0.04 ppm. ^{19}F NMR spectra were obtained on a Perkin-Elmer R-12A (10% solutions in CCl_4, temperature 36°C, internal standard fluorobenzene. Accuracy of measurement ±0.03 ppm). Melting points were determined on a Kofler block.

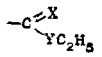
Ethyl Acetodithioacetate (III). To a suspension of 9.6 g (0.4 mole) of sodium hydride in 200 ml of dry 1,2-dimethoxyethane was added slowly 33.3 g (200 mmoles) of SS-diethyl trithiocarbonate under argon, with stirring at room temperature. After 1 h, 11.6 g (200 mmoles) of thoroughly purified and dried acetone was added dropwise. Stirring was continued for 1 h at room temperature, then the mixture was boiled for 6 h on the water bath. The reaction mixture, after cooling, was poured onto ice and acidified with cold 1 N hydrochloric acid. The mixture was extracted with methylene chloride, the extract dried over anhydrous magnesium sulfate, and distilled under reduced pressure to give 25.9 g (80%) of product, bp 120°C (15 mm Hg), the spectral properties and bp being in accordance with those reported previously [7, 8].

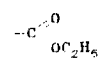
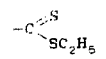
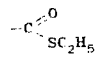
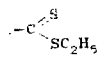
TABLE 4. ^{13}C and ^{19}F Chemical Shifts in Substituted Benzenes (VII)* 

Compound	Y	X	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	C_X			$\Delta\delta F$
									C_α	CH_2	CH_3	
VIIa	H	$-COOC_2H_5$	130,89	129,78	128,52	132,94	128,52	129,78	166,86	60,99	14,40	—
VIIb	H	$-C(=S)OC_2H_5$	138,92	128,97	128,26	132,77	128,26	128,97	211,80	68,63	13,81	—
VIIc	H	$-C(=O)SC_2H_5$	137,62	127,37	128,75	133,33	128,75	127,37	192,05	23,46	14,79	—
VIId	H	$-C(=S)SC_2H_5$	145,58	127,06	128,49	132,35	128,49	127,06	225,74	31,55	12,32	—
VIIe	4-F	$-COOC_2H_5$	127,35 (2,9)†	132,45 (8,8)	115,68 (22,1)	166,17 (253,7)	115,68 (22,1)	132,45 (8,8)	165,76	61,22	14,40	6,24
VIIf	4-F	$-C(=S)OC_2H_5$	135,15 (2,9)	131,42 (9,6)	115,20 (22,1)	166,10 (255,2)	115,20 (22,1)	131,42 (9,6)	209,98	68,73	13,78	5,90
VIIg	4-F	$-C(=O)SC_2H_5$	133,85 (2,9)	129,90 (9,6)	115,84 (22,1)	166,11 (254,4)	115,84 (22,1)	129,90 (9,6)	190,68	23,62	14,79	7,18
VIIh	4-F	$-C(=S)SC_2H_5$	141,65 (2,9)	129,30 (8,8)	115,36 (22,1)	165,86 (254,4)	115,36 (22,1)	129,30 (8,8)	226,23	31,65	12,32	5,25
VIIi	3-F	$-COOC_2H_5$ H	133,19 (7,4)	116,71 (22,8)	163,00 (247,1)	120,03 (22,1)	130,03 (8,1)	125,56 (2,9)	165,66 (2,9)	61,45	14,33	0,28
VIIj	3-F	$-C(=S)OC_2H_5$	140,67 (7,4)	115,64 (24,3)	162,66 (246,3)	119,52 (22,1)	129,67 (8,1)	124,69 (2,9)	209,73 (2,9)	68,92	13,71	−0,20
VIIk	3-F	$-C(=O)SC_2H_5$	139,52 (6,6)	114,24 (22,8)	163,03 (248,6)	120,28 (21,3)	130,48 (7,4)	123,15 (2,9)	190,91 (2,9)	23,72	14,69	1,05
VIIl	3-F	$-C(=S)SC_2H_5$	147,05 (5,1)	114,22 (23,5)	162,74 (247,1)	118,95 (21,3)	129,90 (8,1)	122,52 (2,2)	226,67 (2,2)	31,65	12,19	0,19
VIIm	F		124,24 (2,2)	130,24 (7,4)	115,57 (21,3)	162,29 (245,6)			—	—	—	0,00

*The ^{13}C CS for benzene is 128.38 ppm.
†The ^{13}C—^{19}F coupling constants (Hz) are given in brackets.

TABLE 5. σ_I and σ_R^0 Values of Substituents



Substituent	Method of calculation				
	a		b		c
	σ_I	σ_R^0	σ_I	σ_R^0	σ_R^0
	0,19	0,22	0,12	0,22	0,19
	0,07	0,23	0,06	0,20	0,22
	0,30	0,23	0,23	0,21	0,16
	0,16	0,20	0,11	0,17	0,16

*Literature values for the ethoxycarbonyl group: σ_I 0.37 [28], 0.30 [29] (from the pK values of substituted benzoic acids), 0.11 (CCl_4), 0.35 (CF_3COOH) [25] (from NMR on ^{19}F nuclei in substituted benzenes); σ_R^0 0.08 [28], 0.19 ($CHCl_3$) [26].

Ethyl β-Aminodithiocrotonate (IV). A mixture of 13 g (80 mmoles) of the dithioester III and 17 g of ammonium acetate was boiled with stirring in 5 ml of glacial acetic acid and 90 ml of dry benzene, in a Dean and Stark apparatus. Benzene (50 ml) was distilled off during 30 min. The remaining solution was washed with water, dried over anhydrous magnesium sulfate, and fractionated under reduced pressure to give 8.5 g (65%) of an orange oil, bp 157°C (10 mm). PMR spectrum (DMSO-D_6) 1.15 (3H, t, SCH_2CH_3, J = 7.6 Hz), 1.89 (3H, s, CH_3CO), 3.45 (2H, q, CH_2, J = 7.6 Hz), 5.60 (1H, s, =CH—), 8.76 (1 H, s, N—H), 10.7 ppm (1 H, s, N—H). Found: C 44.9; H 6.7; N 8.3; S 39.9%. Calculated: C 44.7; H 6.8; N 8.7; S 39.5%.

Diethyl 2,6-Dimethyl-1,4-dihydropyridine-3,5-bis(carbodithioate) (Id). A mixture of 3.3 g (20 mmoles) of the dithioester III, 0.7 g of urotropine, and 0.5 g of ammonium acetate in 3 ml of glacial acetic acid was heated for 10 min on the water bath. After cooling, the mixture was poured into water, extracted with ether, dried over anhydrous sodium sulfate, and the solvent removed under reduced pressure. The residue was crystallized from methanol (deep red crystals). Yield 1.1 g (35%) (Table 1).

Diethyl 2,6-dimethyl-4-(4-nitrophenyl)-1,4-dihydropyridine-3,5-bis(carbodithioate) (In). The dithioester III (3.3 g; 20 mmoles) was heated on the water bath for 1 h with 1.4 g (10 mmoles) of p-nitrobenzaldehyde and 5 ml of glacial acetic acid. The cooled reaction mixture was poured into water, extracted with ether, and dried over anhydrous magnesium sulfate. After removal of the ether, the residue was chromatographed on a column of Brockman grade II alumina, and eluted with a mixture of chloroform, hexane, and acetone (9:7:1). Crystallization from methanol gave 1.8 g (41%) of In as deep red crystals (Table 1).

General Method for the Preparation of Ethyl 4-Aryl-2-methyl-5-oxo-4,5-dihydro-1H-indeno-[1,2--b]pyridine-3-carbodithioates (IId,g,i,l). A. To a boiling solution of 5 mmoles of the 2-aryldeneindandione-1,3 in 20 ml of glacial acetic acid was added 0.81 g (5 mmoles) of the β-aminodithiocrotonate IV, and the mixture boiled for 5 min. Deep red crystals separated on cooling, and these were crystallized from acetic acid (Table 1).

B. The 2-arylideneindandione-1,3 (10 mmoles) and 3.3 g (20 mmoles) of ethyl acetodithioacetate III were boiled in 25 ml of acetic acid in the presence of 7.7 g (100 mmoles) of ammonium acetate for 10 min. After cooling, the mixture was diluted with water to 30 ml, and the red solid which separated was filtered off and crystallized from acetic acid (Table 1).

Synthesis of Esters and Sulfur-Containing Esters of Benzoic, p-Fluoro-, and m-Fluorobenzoic Acids (VII). Ethyl p-fluoro- (VIIe) and m-fluoro- ((VIIi) benzoates were obtained by sterifying the fluorobenzoic acids as described in [32]. The thiolo-esters of benzoic (VIIc) [33] and p-fluorobenzoic (VIIg) acids were obtained by reacting the acid anhydrides with ethyl mercaptan in the presence of pyridine, as described in [33]. The above method was used to obtain the novel thioethyl m-fluorobenzoate (VIIk), yield 69%, bp 115°C (10 mm). PMR spectrum ($CDCl_3$):

1.25 (3H, t, J = 7.6 Hz, CH_3); 3.07 (2H, q, J = 7.6 Hz, CH_2), 7.11-7.76 ppm (4H, m, arom. protons).

The thiono-esters of benzoic (VIIb) [35], p-fluorobenzoic (VIIf), and m-fluorobenzoic (VIIj) acids were obtained by direct thionylation of the esters of the acids with Lawessön's reagent (molar proportions 1:1.2) in boiling toluene, as described in [36].

O-Ethyl p-Fluorothiobenzoate (VIIf). Yield 85%, bp 132°C (11 mm). PMR spectrum ($CDCl_3$): 1.44 (3H, t, J = 7.6 Hz, CH_2), 4.62 (2H, q, J = 7.6 Hz, CH_2), 6.89-8.18 ppm (4H, m, arom. protons).

O-Ethyl m-Fluorothiobenzoate (VIIj). Yield 80%, bp 100°C (5 mm). PMR spectrum ($CDCl_3$): 1.46 (3H, t, J = 7.6 Hz, CH_3), 4.62 (2H, q, J = 7.6 Hz, CH_2), 7.04-7.87 ppm (4H, m, arom. protons).

Obtained similarly were ethyl dithiobenzoate (VIId) [37] and the previously unknown ethyl p-fluoro- (VIIh) and m-fluoro- (VIIℓ) dithiobenzoates, by boiling the thiolo-esters of benzoic, p-fluoro- and m-fluorobenzoic acids in toluene with Lawessön's reagent [36] in a molar ratio of 1:0.8.

Ethyl p-Fluorodithiobenzoate (VIIh). Yield 79%, bp 151°C (15 mm). PMR spectrum ($CDCl_3$): 1.37 (3H, t, J = 7.6 Hz, CH_3), 3.27 (2H, q, J = 7.6 Hz, CH_2), 6.84-8.00 ppm (4H, arom. protons).

Ethyl m-Fluorodithiobenzoate (VIIℓ). Yield 75%, bp 137°C (5 mm). PMR spectrum ($CDCl_3$): 1.40 (3H, t, J = 7.6 Hz, CH_3), 3.31 (2H, q, J = 7.6 Hz, CH_2), 7.07-7.67 ppm (4H, m, arom. protons).

The pK values in DMSO were measured by the transmetallation method, which is based on the spectrophotometric determination of the concentration equilibrium constants for the reaction of the 1,4-dihydropyridines with the alkali derivatives of indicators [10]. The method for the determination of the K_{equil} values in carefully purified DMSO in an all-brazed vacuum apparatus was similar to that described previously [10, 38]. The mean of four measurements was taken, the pK values of the indicators being obtained from [38].

The ionization constant of (II) in 50% (vol.) ethanol was determined spectrophotometrically [11], using the analytical wavelengths of the anion in the region of 600 nm.

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FORMATION OF A DERIVATIVE OF 3,3,5-TRICARBONYL-1,2,3,4-TETRAHYDROPYRIDINE UNDER THE CONDITIONS OF THE HANTZSCH SYNTHESIS

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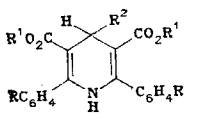
An ester of p-nitrobenzoylacetic acid is cyclized under the action of hexamethylenetetramine and ammonium acetate to 3,5-diethoxycarbonyl-3-p-nitrobenzoyl-6-p-nitrophenyl-1,2,3,4-tetra-hydropyridine, the structure of which has been established by NMR, UV, IR, and mass spectra and also by its chemical reactions.

Esters of β-ketocarboxylic acids form, in different variants of the Hantzsch synthesis, 1,4-dihydropyridines. Esters of benzoylacetic acid are not excluded in this respect, although in general the reactions take place with some difficulty [1]. From an ester of p-nitrobenzoylacetic acid, 4-substituted 1,4-dihydropyridines (I, R = p-NO_2, $R^2 \neq H$) are obtained.



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