6. A. N. Kost and A. P. Terent'ev, Zh. Obshch. Khim., 26, 1992 (1956).
7. P. Waykole and R. N. Usgaonkar, Indian J. Chem., A21, 272 (1982).
8. R. Elderfield (ed.), Heterocyclic Compounds [Russian translation], Vol. 1, Inostr. Lit., Moscow (1953), p. 273.
9. V. P. Sevodin, V. S. Velezheva, and N. N. Suvorov, Khim. Geterotsikl. Soedin., No. 8, 1125 (1982).
10. R. W. Daisley and Z. A. Elagbar, J. Heterocycl. Chem., 19, 1013 (1982).
11. C. D. Nenitzescu and D. Raileanu, Chem. Ber., 91, 1141 (1958).
12. V. S. Velezheva, V. P. Sevodin, Yu. V. Erofeev, N. K. Genkina, T. A. Kozik, V. V. Vampilova, and N. N. Suvorov, Khim. Geterotsikl. Soedin., No. 3, 360 (1977).

INDOLOBENZOTHIOPHENES.

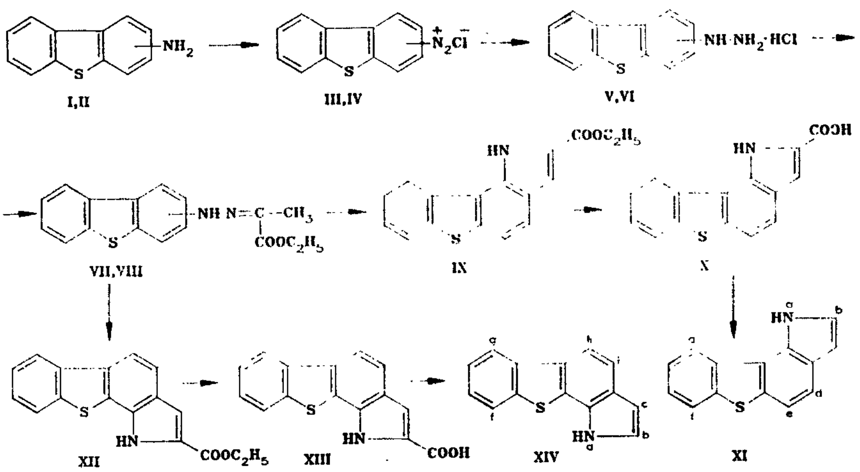
3.* SYNTHESIS AND PROPERTIES OF INDOLO[7,6-d]- AND INDOLO[6,7-d]BENZO[b]THIOPHENES

T. E. Khoshtariya, L. N. Kurkovskaya,
L. N. Kulesheva, and N. N. Suvorov

UDC 547.736'759.4.07:543.422

Precursors of a new heterocyclic system, indolo[7,6-d]- and indolo[6,7-d]benzo[b] thiophenes, have been synthesized using the Fischer reaction. Some physicochemical characteristics of the compounds are reported.

Continuing our research into tetracyclic compounds with a pyrrole ring system [1], we have synthesized some previously unreported isomeric indolobenzo[b]thiophenes using the Fischer reaction:



The 1- and 4-aminobenzothiophenes were used as starting compounds; 1-aminodibenzothiophene (I) was synthesized by the reduction of 1-nitrodibenzothiophene, obtained from 2-aminodibenzothiophene [2]. The reaction of the lithium derivative of dibenzothiophene with O-methylhydroxylamine [3] gave 4-aminodibenzothiophene (II). Compounds I and II were converted via the diazonium salts III and IV to the corresponding hydrazine hydrochlorides V, VI, which on treatment with ethyl pyruvate gave the hydrazones VII and VIII. Examination by TLC

---

*Communication 2, see [1].

I. G. Kutateladze Institute of Pharmaceutical Chemistry, Academy of Sciences of the Georgian SSR, Tbilisi.380059. D. I. Mendeleev Moscow Institute of Chemical Technology, Moscow 125047. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 236-240, February, 1985. Original article submitted January 2, 1984; revison submitted June 18, 1984.

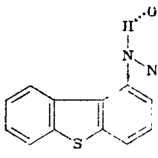
0009-3122/85/2102-0196$09.50

TABLE 1. NMR Spectra of Hydrazones VII and VIII (in $CDCl_3$)

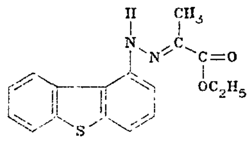
Compound	Chemical shift, δ, ppm				$J_{CH_2CH_3}$, Hz
	CH_3	CH_2—Et	CH_3—Et	NH	
VIIa	2,24	4,35	1,38	12,7	7,2
VIIb	2,28	4,22	1,27	9,4	7,0
VIIIa	2,30	4,41	1,40	12,1	7,1
VIIIb	2,27	4,25	1,31	9,1	7,0

showed that in all cases a mixture of syn (VIIa and VIIIa) and antiforms (VIIb and VIIIb) was formed, the antiform always predominating.

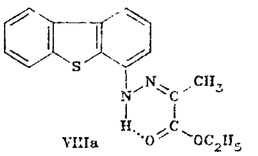
The NMR spectra of the geometric isomers differed significantly (Table 1). In both cases, signals from the NH protons in the synform of the hydrazones VIIa and VIIIa in $CDCl_3$ occurred downfield (12.7 and 12.1 ppm) from those of the corresponding signals from the anti-isomers VIIb and VIIIb (9.4 and 9.1 ppm), respectively. This shift is explained by strong intramolecular hydrogen bonding of the NH proton in the synconfiguration.



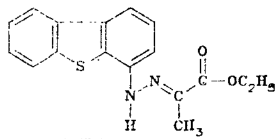
VIIa



VIIb



VIIIa



VIIIb

In the ultraviolet spectra, absorption maxima of the synforms of the hydrazones VIIa and VIIIa show bathochromic shifts of 33 and 23 nm, respectively, relative to their antiforms, confirming the conclusions made based on the NMR spectra. In the infrared, the CO and NH groups of the synisomers absorbed at lower frequencies than those of the antiisomers.

The hydrazone VII was cyclized by the Fischer reaction using ethyl polyphosphate [4] to give the ethyl ester of indolo[7,6-d]benzo[b]thiophene-2-carboxylic acid (IX); this was hydrolyzed to the corresponding acid X, which on thermal decarboxylation gave indolo[7,6-d] benzo[b]thiophene (XI).

Cyclization of the hydrazone VIII gave the ethyl ester of indolo[6,7-d]benzo[b]thiophene-2-carboxylic acid (XII), which on hydrolysis and decarboxylation yielded the unsubstituted indolo[6,7-d]thiophene (XIV).

The NMR spectra (Table 2) of compounds IX-XIV contained signals characteristic of the indole system. Steric interactions of the α-H and d-H protons in compound XI and its derivatives caused a strong down-field shift of the d-H proton in comparison with derivatives of the isomer XIV.

The infrared spectra for the isomers of compounds IX-XIV also showed certain characteristics. Thus, for compounds XIV, the formation of a five-membered ring by intramolecular hydrogen bonding (NH...S) causes the NH bond to be strongly polarized and consequently to absorb at a lower frequency compared with compound XI. The formation of intramolecular hydrogen bonds (of the type NH...O=CO) in the esters and acids (IX and X) causes the carbonyl group to absorb at a lower frequency; for the isomers XII and XIII, however, the NH...S bond is apparently retained.

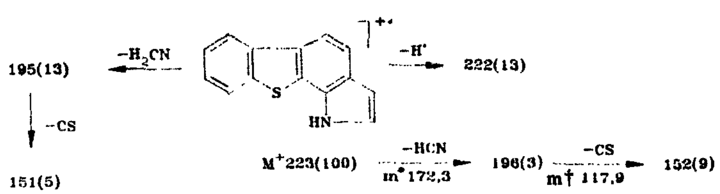
TABLE 2. NMR Spectra of Compounds IX–XIV (in DMSO-D_6)

Compound	Chemical shift, δ, ppm									J, Hz
	a-H	b-H	c-H	d-H	e-H	f-H	g-H	h-H	i-H	
IX	11,7	4,38; 1,39 (Et)	7,39	7,65	7,80	8,00	9,05	—	—	$J_{CH_2CH_3}=7{,}0$; $J_{a,c}=2{,}0$; $J_{d,e}=8{,}8$
X	11,7	*	7,31	7,63	7,78	7,99	9,03	—	—	$J_{d,e}=8{,}0$
XI	11,5	7,44	6,65	7,55	7,73	8,00	8,73	—	—	$J_{a,c}=1{,}5$; $J_{a,b}=1{,}8$; $J_{b,c}=2{,}7$; $J_{d,e}=8{,}2$
XII	12,5	4,37; 1,37 (Et)	7,28	—	—	8,25	7,97	7,99	7,70	$J_{CH_2CH_3}=7{,}0$; $J_{a,c}\approx 2{,}0$; $J_{h,i}=8{,}2$
XIII	12,5	*	7,22	—	—	8,35	7,99	7,97	7,68	$J_{h,i}=8{,}2$
XIV	11,5	7,35	6,58	—	—	8,20	7,95	7,87	7,61	$J_{a,i}=0{,}5$; $J_{a,c}=2{,}2$; $J_{a,b}=2{,}5$; $J_{b,c}=2{,}7$; $J_{h,i}=8{,}4$

---

*Signal from COOH broadened because of exchange.

Strong peaks due to the molecular ion [M^+] 223 are found in the mass spectra of the isomeric indolobenzo[b]thiophenes, but further fragmentation of the molecule involves metastable transitions; this does not disagree with the proposed structure. A possible scheme for the fragmentation of indolo[6,7-d]benzo[b]thiophene* is as follows:



EXPERIMENTAL

The course of the reaction and the purity of the products were checked by TLC using Silufol UV-254 plates in 1:3 ether:benzene. Ultraviolet spectra were recorded on a Specord spectrophotometer (in ethanol); infrared spectra, on a UR-20 with NaCl or LiF prisms (in mineral oil), scan rate 160, aperture 4 cm^{-1}. Mass spectra were obtained on a MKh-1303 with direct introduction of the sample into the ion source, cathode current 1.5 μA, ionization potential 50 eV. NMR spectra were taken on a Varian CFT-20 spectrometer (80 MHz), internal standard — TMS.

1-Dibenzothiophenylhydrazone of Ethyl Pyruvate (VII). A solution of 1.52 g (0.022 mole) of $NaNO_2$ in 6 ml of water was added dropwise to a mixture of 3.98 g (0.02 mole) of compound I, 40 ml of water, and 18.8 ml of concentrated HCl at −5 to −10°C over a period of 20 min. The solution of the diazonium salt was maintained at this temperature with stirring for 1.5 h, a solution of 7.58 g (0.04 mole) of stannous chloride in 40 ml of concentrated HCl was added, and mixing continued for a further 3 h. The precipitated hydrazine hydrochloride V was filtered off, dissolved in 200 ml of hot water, and quickly filtered. The filtrate was brought to pH 3 by the addition of a saturated solution of sodium acetate, and 2.2 ml (0.02 mole) of ethyl pyruvate in 5 ml of ethanol was added, and the mixture stirred for a further 30 min. The yellow hydrazone VII was filtered off, washed with water, and dried to give 3.1 g (50%) of unpurified hydrazone.

The stereoisomers of the hydrazone VII were separated on a silica gel column (ether–hexane, 1:3). The first fraction yielded 0.47 g (8%) of the synisomer VIIa with mp 120-122°. IR spectrum: 3320 (NH), 1680 cm^{-1} (CO). UV spectrum, λ_{max} (log ε): 206 (4.84), 230 (5.23), 246 (5.06), 283 (4.79), 296 (4.64), 351 nm (4.80). Found: C 65.3; H 5.2; N 9.0; S 10.3%. $C_{17}H_{16}N_2O_2S$. Calculated: C 65.4; H 5.1; N 9.0; S 10.2%. The second fraction consisted of

---

*Values of m/z are given; in parentheses — relative intensity of peaks in % of the maximum.
†Metastable transition.

antiisomer VIIb, yield 2.4 g (38%), mp 195-196°. IR spectrum: [3330 (NH), 1710 cm^{-1} (CO)]. UV spectrum: λ_{max} (logε): 203 (5.07), 219 (5.25), 239 (5.05), 266 (5.27), 285 (4.74), 318 nm (5.00). Found: C 65.4; H 5.0; N 9.2; S 10.4%. $C_{17}H_{16}N_2O_2S$. Calculated: C 65.4; H 5.1; N 9.0; S 10.2%.

4-Dibenzothiophenylhydrazone of Ethyl Pyruvate (VIII). This compound was obtained by the same method as compound VII from the thiophene II. Yield of unpurified hydrazone, 3.5 g (56%). The stereoisomers VIIIa and VIIIb were separated in the same way as VIIa and VIIb. Yield of synisomer VIIIa, 0.51 g (8%), mp 138-139°. IR spectrum: 3350 (NH), 1700 cm^{-1} (CO). UV spectrum, λ_{max} (log ε): 208 (4.44), 220 (4.90), 231 (5.23), 239 (5.00), 255 (5.05), 278 (4.85), 326 (4.66), 347 nm. Found: C 65.5; H 5.2; H 5.2; N 9.1; S 10.5%. $C_{17}H_{16}N_2O_2S$. Calculated: C 65.4; H 5.1; N 9.0; S 10.2%. Yield of antiisomer VIIIb 2.8 g (45%), mp 176-177°. IR spectrum: 3365 (NH), 1720 cm^{-1} (CO) . UV spectrum, λ_{max} (log ε): 205 (4.31), 222 (4.56), 235 (5.00), 242 (5.15), 251 (5.25), 260 (5.22), 277 (4.95), 324 nm (5.05). Found: C 65.7; H 5.4; N 9.0; S 10.4%. $C_{17}H_{16}N_2O_2S$. Calculated: C 65.4; H 5.1; N 9.0; S 10.2%.

Ethyl Ester of Indolo[7,6-d]benzo[b]thiophene-2-carboxylic Acid (IX). A mixture of 3.12 g (0.01 mole) of the hydrazone VII and 30 g of ethyl polyphosphate was heated to 80° and stirred for 1 h, cooled, and diluted with water. The precipitated material was filtered off, washed with water, and dried to give compound IX, which was purified on a silica gel column (ether—hexane, 1:3); 2.15 g (73%) of the ester IX, mp 110-111°, was obtained. IR spectrum: 3490 (NH), 1680^{-1} (CO). UV spectrum, λ_{max} (log ε): 203 (5.29), 213 (5.27), 247 (5.11), 259 (5.15), 270 (5.21), 291 (4.93), 303 (4.87), 3.16 (4.98), 331 (5.05), 346 nm (5.14). Found: C 69.2; H 4.7; N 4.9; S 11.0%. $C_{17}H_{13}NO_2S$. Calculated: C 69.2; H 4.4; N 4.7; S 10.8%.

Ethyl Ester of Indolo[6,7-d]benzo[b]thiophene-2-carboxylic Acid (XII). This compound was prepared from the hydrazone VIII by the method used for compound IX. A yield of 1.85 g (63%) of the ester XII with mp 221-222° was obtained. IR spectrum: 3300 (NH), 1720 cm^{-1} (CO). UV spectrum, λ_{max} (log ε): 208 (4.58), 216 (4.60), 224 (4.63), 232 (4.71), 242 (4.77), 249 (4.84), 256 (4.88), 267 (481), 274 (4.78), 286 (4.49), 297 (4.53), 317 nm (4.73). Found: C 69.4; H 4.5; N 4.9; S 10.8%. $C_{17}H_{13}NO_2S$. Calculated: 69.2; H 4.4; N 4.7; S 10.8%.

Indolo[7,6-d]benzo[b]thiophene-2-carboxylic Acid (X). A suspension of 2.95 g (0.01 mole) of the ester IX in 150 ml of water and 60 ml of ethanol, and 1.7 g (0.03 mole) of KOH was refluxed for 2 h. The solution was cooled, filtered, and the filtrate brought to pH 7-8 with dilute HCl. After refiltration the filtrate was brought to pH 1. The product was washed with water and dried to give 2.3 g (86%) of compound X with mp 330° (decomp.). IR spectrum: 3480 (NH), 1680 cm^{-1} (C). UV spectrum, λ_{max} (log ε): 203 (5.27), 210 (5.29), 227 (5.09), 246 (5.15), 254 (5.22), 265 (5.27), 270 (5.27), 291 (4.98), 301 (4.89), 314 (4.98), 331 (5.00), 345 nm (5.12). Found: C 67.2; H 3.4; N 5.2; S 12.0%. $C_{15}H_9NO_2S$. Calculated: C 67.4; H 3.4; N 5.2; S 12.0%.

Indolo[6,7-d]benzo[b]thiophen-2-carboxylic Acid (XIII). This compound was obtained by the same method as compound X, yield 2.35 g (88%) and mp 290° (decomp.). IR spectrum: 3420 (NH), 1680 cm^{-1} (CO). UV spectrum, λ_{max} (log ε): 206 (5.12), 220 (5.13), 240 (5.43), 256 (5.35), 273 (5.23), 284 (5.03), 295 (5.03), 315 nm (5.16). Found: C 67.8; H 3.9; N 5.6; S 12.2%. $C_{15}H_9NO_2S$. C 67.4; H 3.4; N 5.2; S 12.0%.

Indolo[7,6-d]benzo[b]thiophene (XI). This compound was obtained by heating 1 g (0.004 mole) of the acid X at 310-350° in a current of inert gas. The product was purified on a silica gel column (ether—hexane, 1:3) to give 0.5 g (60%) of XI with mp 150-151°. IR spectrum: 3480 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 206 (4.29), 215 (4.29), 225 (4.34), 236 (4.39), 246 (4.50), 251 (4.56), 264 (3.99), 293 (3.97), 305 (4.09), 327 (3.83), 340 nm (3.79). Found: C 75.0; H 3.9; N 6.0; S 14.1%. $C_{14}H_9NS$. Calculated: C 75.3; H 4.0; N 6.3; S 14.3%.

Indolo[6,7-d]benzo[b]thiophene (XIV). This compound was obtained by the same method as compound XI, yield 0.42 g (51%), mp 260-261°. IR spectrum: 3410 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 213 (4.35), 234 (4.45), 242 (4.61), 249 (4.74), 256 (4.76), 267 (4.12), 274 (4.66), 287 (4.36), 297 (4.41), 317 nm (4.61). Found: C 75.7; H 4.3; N 6.8; S 14.8%. $C_{14}H_9NS$. Calculated: C 75.3; H 4.0; N 6.3; S 14.3%.

LITERATURE CITED

1. L. A. Kintsurashvili, T. E. Khoshtariya, L. N. Kurkovskaya, and N. N. Suvorov, Khim. Geterotskikl.Soedin., No. 2, 211 (1981).
2. I. Johnson, E. Ebslager, and L. Werbel, J. Heterocycl. Chem., 14, 1209 (1977).
3. H. Gilman and S. Avakian, J. Am. Chem. Soc., 68, 1514 (1946).
4. V. Kanaoka, V. Ban, K. Miyashita, K. Irie, and O. Vonemitsu, Chem. Pharm. Bull. Jpn., 14, 934 (1966).

REACTIONS OF 5,6-DIAMINO-1,3-DIMETHYLURACIL WITH CARBONYL COMPOUNDS

V. D. Orlov and I. Z. Papiashvili

UDC 547.854.4'857.4'859.1'892:542.953.2

The first step in the acid-catalyzed reaction of 5,6-diamino-1,3-dimethyluracil with carbonyl compounds is the formation of an azomethine at the 5-amino group. Chalcone derivatives undergo a further substitution; the 6-amino group is replaced by a hydroxyl group with subsequent ring closure and the formation of a 2,3-dihydro-1,5-oxazepine ring. Azomethines based on arylidenacetones forms 2,3-dihydropyrimidino[5,6-b]-1,5-diazepine derivatives.

In earlier work [1] we found that derivatives of pyrimidinohydrooxazepine, theophylline, and pyrimidinodihydrodiazepine can be prepared by the reaction of 5,6-diamino-1,3-dimethyluracil (I) with aromatic α,β-unsaturated ketones. The aim of the present work is to study the effect of a number of factors (catalyst, temperature, nature of carbonyl component) on these reactions.

The first experiments involved the reaction of the diamine (I) with chalcones using 1-2 drops of acetic or concentrated hydrochloric acid as catalyst [1]. In the present work it was shown that if the diamine I monohydrochloride was used in place of diamine (I) the yield of the product, dihydropyrimidinooxazepines (VII), increased by 10-20% and reached 90-97%. On the other hand, if the catalytic acid content was reduced to 1-5 mg (calculated for 1 mmole of reagent), two products were formed. Colorless crystals of a derivative of dihydropyrimidinoxazepine VII were first to separate from the hot reaction solution; on cooling the solution, yellow crystals of a second product (II) form along with the colorless crystals. If the filtrate is diluted with water, a mixture of products II and VII separates. An analogous result is achieved by carrying out the reaction at room temperature or at 0°, but in this case the time required to complete the reaction is increased to 3-4 days. Formation of a mixture of compounds IIa and VIIa is observed if the reaction of chalcone with the diamine is catalyzed by 1-5 mg of sulfuric acid of HBF_4; for example, when one drop of 3% HBF_4 was added per 10 ml of reaction mixture containing 1 mmole of reagents.

It was not possible to separate the products II and VII by the usual method of crystallization because during purification the yellow product II was converted to the corresponding compound VII; separation of the mixture of these products by crystallization from absolute methanol was ineffective. Pure yellow material could be isolated mechanically (i.e., by Pasteur's method of sorting crystals under a magnifying glass). This method is laborious and was used only to obtain pure compound IIa — the product of the reaction of chalcone with the diamine I. The IR spectrum of compound IIa contained a sharp doublet at 3415 and 3315 cm^{-1} due to the amino group. A characteristic feature of the UV absorption spectrum of IIa is a strong absorption band with λ_{max} 362 nm. These results, together with the elemental analysis (Table 1), suggest that compound IIa is an azomethine.

A. M. Gor'kii Kharkov State University, Kharkov 310077. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 241-246, February, 1984. Original article submitted January 17, 1984; revison submitted July 10, 1984.

0009-3122/85/2102-0200$09.50