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STUDY OF FRIEDEL–CRAFTS ACETYLATION OF INDOLOBENZO[*b*]FURANS, INDOLOBENZO[*b*]THIOPHENES, PYRROLOCARBAZOLE, AND PYRROLOPHENOTHAZINE DIOXIDE BY ^{1}H NMR SPECTROSCOPY

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The reactivity towards Friedel-Crafts acetylation of the new heterocyclic systems indolo[5,6-d]- and indolo[5,4-d]benzo[d]furans, 3H-pyrrolo[2,3-c]carbazole, indolo[7,6-d]-, indolo[4,5-d]- and indolo[5,4-d]benzo-[b]thiophenes and 3H-pyrrolo[2,3-c]phenothiazine-11,11-dioxide have been studied. Under acid conditions these heterocycles behave like indole to give dimerization products, but anomalies were observed in a number of cases. These principles have been established by detailed analysis of the ^{1}H NMR spectra of the reaction products.

As part of a study of the reactivity of a number of heterocyclic systems we have synthesized [1-5] together with an examination of acetylation methods [6-9], we have examined the behavior of some of these systems in the widely studied Friedel–Crafts acetylation reaction [10-13].

The heterocycles whose structures are shown below have been used as model compounds (the positions bearing hydrogen atoms are labelled with letters which are used in discussion of the ^{1}H NMR spectra).

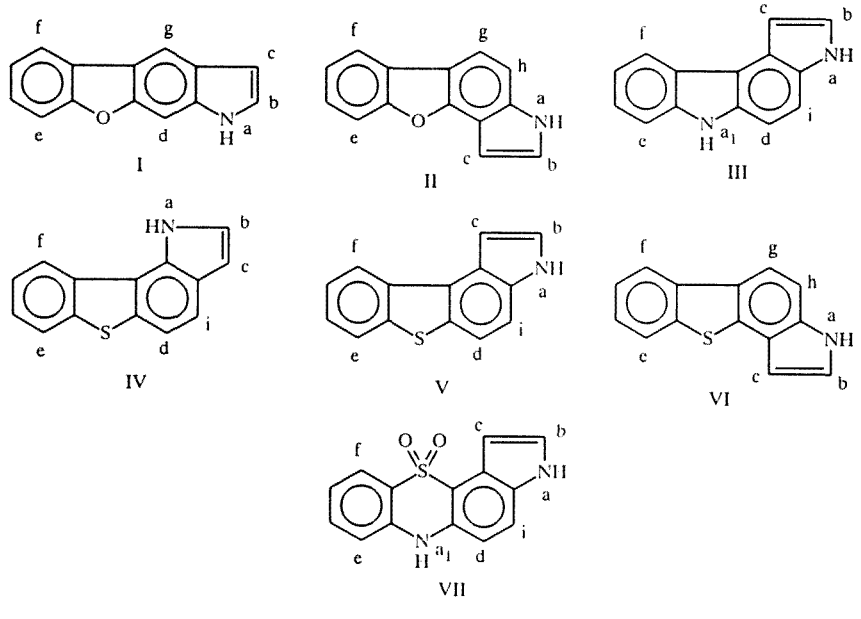

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TABLE 1. Chemical Shifts (δ, ppm) for Compounds I-XVI in DMSO-D_6

Compound	δ, ppm										
	a	a_1	b	b_1	c	c_1	c_2	d	d_1	e	e_1
I*	10,3	—	7.36	—	6,59	—	—	7,55	—	7,50	—
II	11,4	—	~7,40	—	6,73	—	—	—	—	7,64	—
III*	10,0	10,2	7,39	—	7,00	—	—	7,23	—	7,42	—
IV	11,5	—	7,44	—	6,65	—	—	7,73	—	8,00	—
V*	10,6	—	7,54	—	7,22	—	—	7,62	—	7,94	—
VI*	10,6	—	~7,40	—	6,65	—	—	—	—	7,90	—
VII*	10,6	9,7	7,44	—	7,02	—	—	7,04	—	*2	—
VIII*4	10,5	11,5	7,08	—	7,45	—	—	7,29	—	7,53	7,95
IXa	10,7	5,9	6,73	~5,4	—	~3,3	~3,60	7,50	*2	7,50	7,40
IXb*3	—	—	6,25	—	—	—	—	—	—	—	—
Xa	10,5	5,2	6,80	~5,8	—	3,5	4,00	—	—	7,70	7,60
Xb*3	—	—	6,70	—	—	—	—	—	—	—	—
XIa	11,3	6,3	6,91	~5,6	—	3,50	4,00	—	—	7,66	7,43
XIb*3	—	—	6,76	—	—	—	—	—	—	—	—
XII*4	11,0	—	7,10	6,10	—	3,30	3,97	7,50	8,38	*2	*2
XIII*4	11,4	—	7,04	6,15	—	3,76	4,33	7,60	*2	8,00	7,85
XIV	11,4	5,6	6,59	5,55	—	3,24	3,66	7,80	~7,5	7,98	7,85
XV*4	11,9	10,4	—	—	7,95	—	—	7,27	—	7,27	—
XVI*4	11,7	—	8,24	—	—	—	—	7,63	—	~7,50	—

TABLE 1 (continued)†

Compound	δ, ppm							
	f	f_1	g	g_1	h	h_1	i	i_1
I*	8,01	—	8,15	—	—	—	—	—
II	7,98	—	7,72	—	7,31	—	—	—
III*	8,19	—	—	—	—	—	7,44	—
IV	8,73	—	—	—	—	—	7,55	—
V*	8,52	—	—	—	—	—	7,62	—
VI*	8,16	—	7,95	—	7,54	—	—	—
VII*	7,96	—	—	—	—	—	7,66	—
VIII*4	8,79	—	—	—	—	—	7,52	—
IX*3a,b	8,01	7,90	8,19	7,70	—	—	—	—
X*3a,b	8,00	7,90	7,76	7,70	7,42	*2	—	—
XI*3a,b	7,98	7,79	7,99	7,91	7,49	*2	—	—
XII*4	8,70	8,27	~7,90	~7,90	—	—	—	—
XIII*4	8,50	8,20	—	—	—	—	7,50	8,33
XIV	8,70	8,30	—	—	—	—	7,50	*2
XV*4	7,87	—	—	—	—	—	7,49	—
XVI*4	8,02	—	8,79	—	—	—	—	—

*Spectra recorded in acetone-D_6.

*2Fall in the region of the aromatic protons at 7.3-7.5 ppm.

*3Shifts for the protons of the a and b isomers are similar except for the "b" protons.

*4The shifts of the methyl protons for compounds VIII, XII, XIII, XV and XVI were at 2.16, 2.71, 2.21, 2.51 and 2.15 ppm respectively.

†See next page.

Acyl chlorides were normally used as the acylating agents and aluminum chloride as the catalyst. The active complex $[R-C^+=O][AlCl_4^-]$ reacted by electrophilic substitution with the aromatic compound at the atom with the highest electron density.

TABLE 1. Coupling Constants (J, Hz) in the Spectra of Compounds I-XV in DMSO-D_6

Compound	Coupling constants, J, Hz.
I	$J_{ac} = 2,0$, $J_{ab} = 2,2$ $J_{bc} = 3,1$, $^5J_{dc} \approx J_{dg} = 0,8$
II	$J_{ac} = 2,2$, $J_{bc} = 3,3$, $J_{ch} = 0,4$, $J_{gh} = 8,7$
III	$J_{ab} = 2,2$, $J_{ac} = 1,8$, $J_{bc} = 3,3$, $J_{ci} = 0,8$, $J_{di} = 8,9$
IV	$J_{ab} = 1,8$, $J_{ac} = 1,5$, $J_{bc} = 2,7$, $J_{di} = 8,2$
V	$J_{ac} = 1,9$, $J_{ab} = 2,2$, $J_{bc} = 3,0$, $J_{ci} = 0,5$, $J_{di} = 8,4$
VI	$J_{ab} = 2,4$, $J_{ac} = 2,1$, $J_{bc} = 3,0$, $J_{ch} = 0,8$, $J_{gh} = 8,7$
VII	$J_{ab} = 2,5$, $J_{ac} = 2,0$, $J_{bc} = 3,0$, $J_{di} = 8,7$, $^5J_{ci} = 0,9$
VIII	$J_{ac} = 2,2$, $J_{ab} = 2,5$, $J_{bc} = 3,3$, $J_{ci} = 0,5$, $J_{ci} = 0,5$, $J_{ee_1} = 8,5$, $J_{ef} = 1,0$, $J_{e_1f} = 1,6$, $J_{di} = 8,7$
IXa	$J_{b_1c_1} \approx J_{b_1c_2} = 8,4$, $J_{c_1c_2} = 15,0$
IXb	$J_{ab} = 2$
Xa	$J_{b_1c_1} \approx J_{b_1c_2} = 9,0$, $J_{c_1c_2} = 15,5$
XIa	$J_{b_1c_1} \approx J_{b_1c_2} = 9,0$, $J_{c_1c_2} = 15,5$
XII	$J_{b_1c_2}$ (cisoid) = 1, , $J_{b_1c_1}$ (transoid) = 9,1
XIII	$J_{b_1c_2}$ (cisoid) = 2,0, $J_{b_1c_1}$ (transoid) = 9,0, $J_{c_1c_2} = 15,0$
XIV	$J_{b_1c_1} \approx J_{b_1c_2} = 8,7$, $J_{c_1c_2} = 15,3$
XV	$J_{ac} = 1,7$, $J_{di} = 8,8$

TABLE 2. UV and IR Spectra of Compounds I-XVI

Compound	UV spectra, λ_{max}, nm (lg ε)	IR spectra, cm^{-1}	
		CO	NH
I	208 (4,50), 243 (4,70), 252 (4,80), 268 (4,15), 282 (4,08), 308 (4,41), 320 (4,43)	—	3410
II	250 (5,03), 297 (4,43), 301 (4,36), 315 (4,19)	—	3380
III	234 (4,47), 262 (4,22), 271 (4,10), 317 (4,30), 353 (3,75)	—	3400, 3430
IV	206 (4,29), 215 (4,29), 225 (4,34), 236 (4,39), 246 (4,50), 251 (4,56), 254 (3,99), 293 (3,97), 305 (4,09), 327 (3,83), 340 (3,79)	—	3490
V	213 (4,23), 248 (4,66), 255 (4,63), 286 (4,14), 303 (4,23), 321 (3,75)	—	3440
VI	217 (4,39), 252 (4,77), 285 (4,24), 303 (3,36)	—	3350
VII	213 (4,31), 270 (4,25), 304 (3,87), 340 (3,82)	—	3310, 3420
VIII	212 (4,54), 307 (4,71)	1700	3390, 3400
IX	202 (4,95), 211 (4,97), 226 (4,99), 245 (4,92), 253 (5,02), 274 (4,54), 282 (4,48), 325 (4,82)	—	3385, 3430
X	221 (4,68), 251 (4,75), 271 (4,34), 296 (4,34), 308 (4,33), 318 (4,31)	—	3380, 3420
XI	203 (5,24), 242 (5,32), 255 (5,39), 295 (4,98), 327 (4,69)	—	3350, 3415
XII	202 (5,00), 210 (5,02), 226 (4,98), 243 (4,93), 252 (5,00), 268 (4,62), 283 (4,52), 303 (4,78), 315 (4,98), 323 (4,90)	1640	3330
XIII	211 (5,10), 241 (5,38), 252 (5,32), 267 (5,15), 285 (4,96), 301 (4,73), 315 (4,86), 331 (4,76), 343 (4,73)	1650	3320
XIV	202 (5,07), 237 (5,09), 253 (5,05), 286 (4,48), 311 (4,42)	—	3355, 3460
XV	213 (4,29), 270 (4,27), 339 (3,83), 353 (3,72)	1726	3330, 3400
XVI	208,5 (5,17), 220 (5,26), 229 (5,28), 248 (5,41), 287 (4,91), 317 (5,17), 328 (5,16)	1640	3200

Acetylation of these heterocycles (I-VII) was accompanied by transformations of the indole, dibenzofuran, carbazole, dibenzothiophene and phenothiazine which are structurally related compounds. In this connection the behavior of indole and the specified tricyclic systems under Friedel–Crafts conditions will be described briefly.

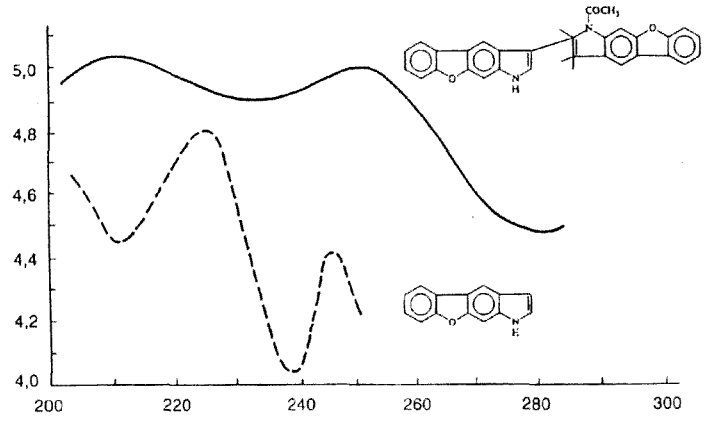


Fig. 1. UV absorption spectra of compounds I and XII in ethanol.

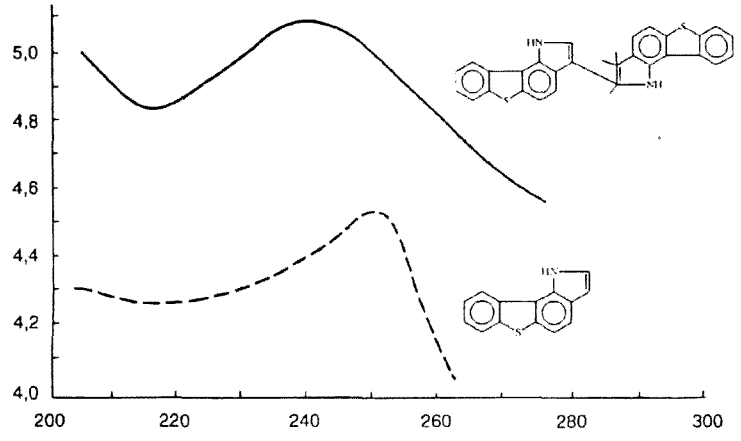


Fig. 2. UV absorption spectrum of compounds IV and XIV in ethanol.

It is well known that unsubstituted indole resinifies in the presence of Lewis acids, whereas 1,3-diacetylindole does not react with acetyl chloride in the presence of aluminum chloride [12]. Acetylation of 1-acetyl-2,3-dimethylindole gave the 6-acetyl derivative [13], i.e., substitution occurred in the benzene ring. It is also known that, under sufficiently acid conditions indole forms dimers and trimers depending on the acidity of the medium [14, 15]. When dibenzothiophene and dibenzofuran substituted in one ring react with acetyl chloride in the presence of aluminum chloride, acetylation occurs in the substituted benzene ring [16] which is completely different from the behavior of carbazole under similar conditions. Carbazole substituted in one ring underwent acetylation in the unsubstituted benzene ring [17, 18]. V. P. Lopatinskii and his coworkers have studied the Friedel–Crafts acylation of carbazole in greater detail [19].

We have observed completely analogous behavior of indolobenzo[b]furans (I, II) and indolobenzo[b]thiophenes (IV-VI) under Friedel–Crafts conditions, whereas pyrrolocarbazole (III) behaved quite differently.

The tetracyclic condensed systems containing pyrrole which we have synthesized — indolobenzo[*b*]furans, indolobenzo[*b*]thiophenes, pyrrolocarbazoles and pyrrolophenothiazine dioxides — behaved differently in the Friedel–Crafts reaction from dibenzofuran, carbazole, dibenzothiophene and phenothiazine. For example, 3H-pyrrolo[2,3-*c*]carbazole (III), unlike indole and carbazole, is acetylated quite readily at 0-5°C under Friedel–Crafts conditions to give the monosubstituted product (VIII) in which the acetyl group enters the unsubstituted benzene ring. Both the indolobenzo[*b*]furans I and II and the indolobenzo[*b*]thiophenes IV-VI give dimers of the initial tetracyclic systems with small amounts of the products of acetylation of the dimers at the nitrogen atom of the indole ring. Evidently the unsubstituted heterocycles I, II, IV-VI, like indole, are readily protonated under the reaction conditions, as a result of which formation of the corresponding dimer occurs.

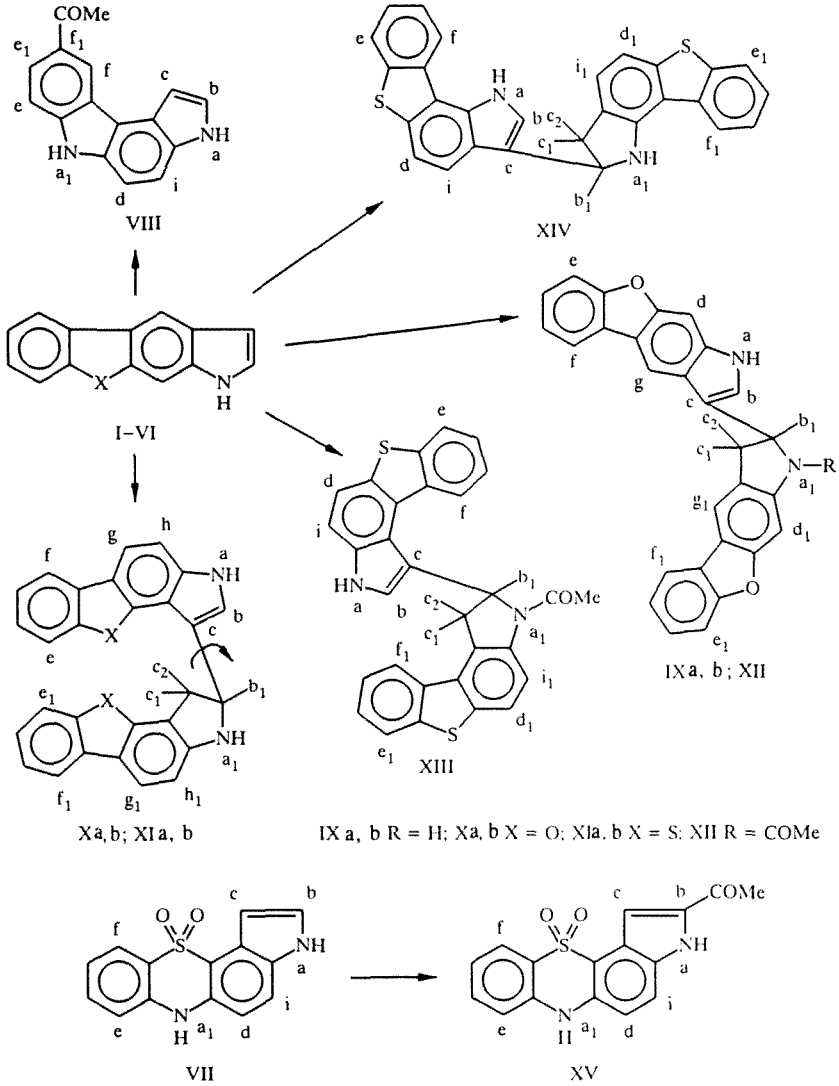
Dimerization of the linear heterocycles I occurs considerably more readily than for their angular isomers II, IV-VI. This apparently arises from the greater reactivity (easier protonation) of the former which is confirmed by kinetic studies of

azo-coupling [20] and ^{1}H NMR spectroscopic data (the difference in chemical shifts in the β-position in linear and angular isomers) [1-5]. The linear isomers are more sterically accessible than their angular analogs.

3H-Pyrrolo[2,3-*c*]phenothiazine-11,11-dioxide (VII), like phenothiazine itself [21], readily undergoes the Friedel–Crafts reaction in conditions described for the formally analogous (both having two NH groups) 3H-pyrrolo[2,3-*c*]carbazole (III), but whereas the acetyl group enters the unsubstituted benzene ring of III, with 3H-pyrrolo[2,3-*c*]phenothiazine-11,11-dioxide (VII) acetylation occurs in the α-position of the pyrrole ring.

These reactions are shown in Scheme 1:

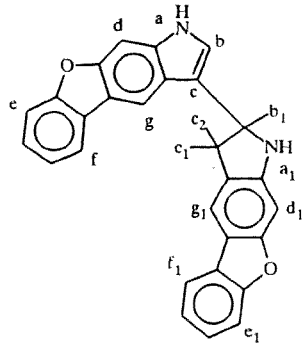
Scheme 1



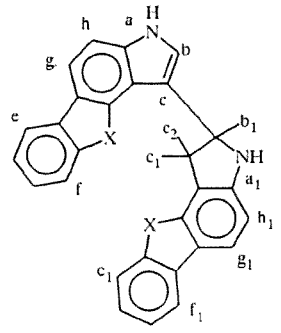
According to their ^{1}H NMR spectra (Table 1), compounds IX, X and XI are formed as mixtures of two stereoisomers. Depending on the experimental conditions products IXa, Xa, and XIa are accompanied by isomers IXb, Xb, and XIb with the structures shown below. The quantitative ratios of the dimers IXa and IXb, Xa and Xb, and XIa and XIb are 60:40, 50:50 and 50:50 respectively.

It has been demonstrated experimentally that prolonging the reaction under otherwise identical conditions has a marked effect on the ratio of the geometric isomers of the dimer for the linear heterocycles (IXa, b) but does not affect the ratio for the angular heterocycles (Xa and Xb, and XIa and XIb). For example, prolonging the acylation of indolo[5,6-*d*]benzo[*b*]furan (I) with acetyl chloride in the presence of anhydrous aluminum chloride to 2.5-3 h caused complete conversion IXb to IXa. At the same time a small amount of the acetyl derivative XII is formed with the acetyl group attached to the nitrogen atom in

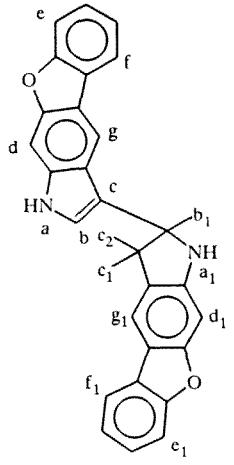
the fully reduced ring. Prolonging the reaction time for the angular heterocycles (II, VI) had no effect on the ratio of the geometric isomers Xa and Xb and XIa and XIb.



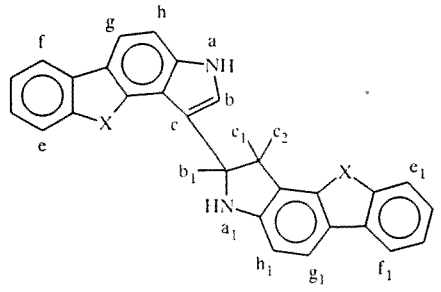
IXa



Xa X = O; XIa X = S



IXb



XbX = O; XIbX = S

Structures of the compounds synthesized were determined by ^{1}H NMR spectroscopy and confirmed by mass spectroscopy in the case of the N-acyl derivatives of the dimers XII and XIII. UV and IR spectra did not contradict the proposed structures.

The absence of a signal for proton "c" in the ^{1}H NMR spectrum of compound IXa and the shift of the singlet for proton "b" to higher field in comparison with the starting material, indolo[5,6-*d*]benzo[*b*]furan (I), shows the presence of an electron withdrawing group at position 3 of the heterocycle. The shift to high field of the signal of proton "b" may be explained by the spatial structure of dimer IXa, suggesting a diamagnetic shift from the aromatic ring of the hydrogenated part of the dimer molecule.

The ^{1}H NMR spectrum of compound IXb is also characterized by the absence of a signal for proton "c" and a shift of the signal for proton "b" to still higher field than for compound IXa. The difference in chemical shift for this proton in the two isomers IXa and IXb is $\Delta\delta$ = 0.5 ppm.

As noted above, the signal for proton "b" for compound IXa is a singlet, i.e., steric strain causes the NH group to move out of the plane of the molecule (J_{ab} is sharply reduced), whereas in the ^{1}H NMR spectrum of compound IXb spin–spin interaction is observed ($J \approx 2$ Hz). Apparently the structure of the indole portion of compound IXb is more planar and consequently more strained than the corresponding portion of compound IXa, which may explain the smaller yield of IXb. It is probable that this is also the reason for the conversion of compound IXb to the less strained IXa when the reaction is prolonged. The presence of the reduced pyrrole ring in compound IX is indicated by the signals of protons "c_1" and "c_2" (3.3 and 3.6 ppm respectively with geminal coupling J_{c1c2} = 15.0 Hz) and proton "b_1" (5.4 ppm, $J_{b1c1} = J_{b1c2} \approx 8.4$ Hz).

Friedel–Crafts acetylation of indolo[5,4-*d*]benzo[*b*]furan (II) and its structural analog indolo[5,4-*d*]benzo[*b*]thiophene (VI) also gave pairs of geometric isomers — the dimers Xa and Xb (X = O) and XIa and XIb (X = S) — but, in distinction from compound IX, the isomeric dimers were formed in equal amounts.

The steric structure of the angular dimers X and XI indicates a strong diamagnetic contribution to the chemical shift of proton "b" from the ring currents of the aromatic rings of the reduced section of the molecule. Consequently the signals for proton "b" in dimers X and XI are at higher field than the signals for the same proton in the starting materials II and VI (Table 1). Absence of spin–spin coupling for proton "b" is probably a result of particularly large steric strain in compounds Xa, Xb, XIa and XIb in consequence of the angular condensed rings. The barrier to rotation about the C_3-C_2 bond is very high: the difference in chemical shift of the α-protons "b" of the two isomers did not change at temperatures up to 120°C. This is evidently the reason why increasing the reaction time has no effect on the ratio of the geometric isomers of compounds X and XI in contrast with stereoisomers IXa and IXb.

The signal for proton "c" is absent from the ^{1}H NMR spectra of compounds X and XI, but signals for protons "c_1" and "c_2" (3.5 and 4.0, 3.5-4.0 ppm respectively with J_{c1c2} = 15.5 Hz) and "b_1" (5.8 and 5.6 ppm respectively with J_{b1c1} = J_{b1c2} = 9.0 Hz) appear at high field. This indicates the replacement of the proton in position 3 of the starting materials indolo[5,4-*d*]benzo[*b*]furan (II) and indolo[5.4-*d*]benzo[*b*]thiophene (VI) by an analogous tetracyclic system, but with a reduced pyrrole ring. The signals of the aromatic protons in the nonreduced sections of molecules IX, XI and XII have similar chemical shifts to the corresponding aromatic protons of compounds I, II and VI (Table 1).

The observation of signals for protons "a" and "a_1" (10.7 and 5.9, 10.5 and 5.2, and 11.3 and 6.3 ppm respectively) in the ^{1}H NMR spectra of compounds IX, X and XI indicates the presence of an unsubstituted NH group, which is confirmed by bands at 3385 and 3430, 3380 and 3420, and 3350 and 3415 cm^{-1} respectively in their IR spectra.

Comparison of the UV spectra of the dimers IX, X and XI with the UV spectra of indolo[5,6-*d*]- (I), indolo[5,4-*d*]benzo[*b*]furan (II), indolo[5,4-*d*]benzo[*b*]thiophene (VI), dibenzofuran, dibenzothiophene and indole shows that the number of absorption maxima in the spectra of the dimers is superficially greater than in the spectra of the starting materials I, II and VI (Table 2). The difference is only in the intensities of the absorptions. It was not possible to determine the molecular masses of compound IX or the other unsubstituted dimers X, XI and XIV by mass spectroscopy. In each case the molecular ions of the starting materials, indolo[5,6-*d*]- (I), indolo[5,4-*d*]benzo[*b*]furan (II), indolo[7,6-*d*]- (IV) and indolo[5,4-*d*]benzo[*b*]thiophene (VI), were observed possibly as a result of destruction of the dimers. A similar result was obtained for the dimers of indole and 2-methylindole which readily decomposed to the indole and 2-methylindole starting materials on heating [4]. It proved impossible to determine the molecular masses of the dimers by other known methods.

The structure of compound IX was determined by retrosynthesis as well as by spectroscopy. In particular, by saponification of the N-acylated dimer, the structure of which is in no doubt, we isolated a product identical with dimer IX. Mixed melting points of samples of compound IX made by different routes gave no depression.

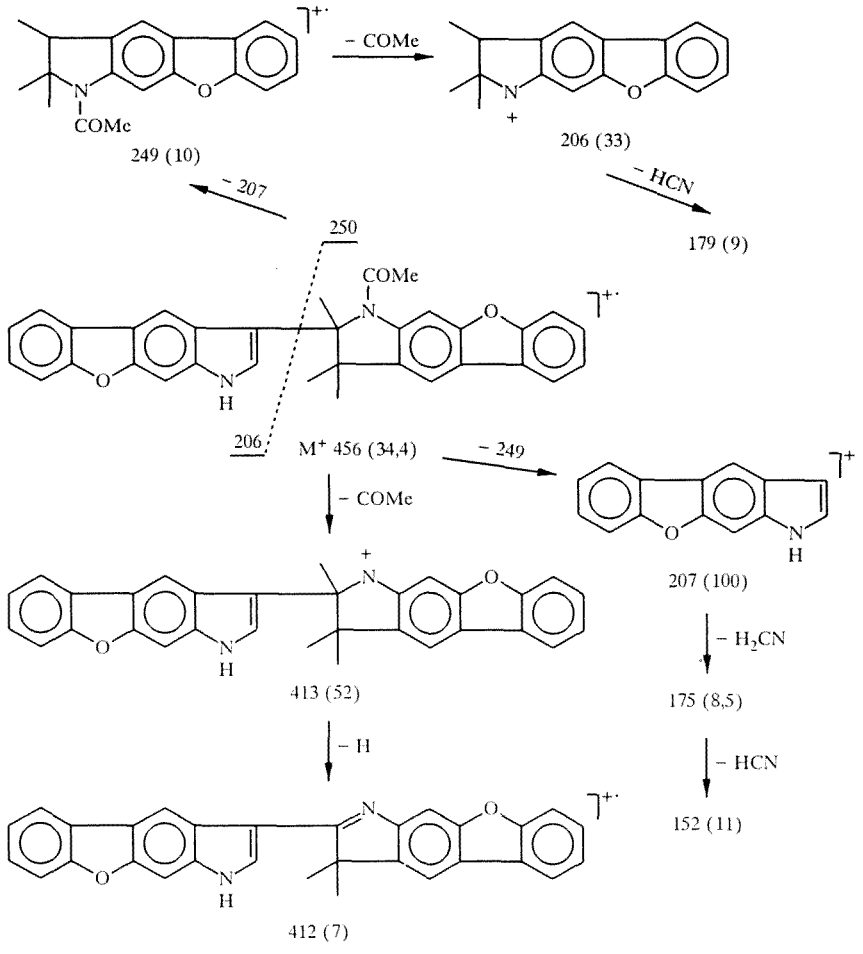
The absence of a signal for proton "a_1" and the appearance of a high field singlet at 2.2 ppm, characteristic of a methyl group, in the ^{1}H NMR spectrum of compound XII indicated the presence of an acetyl group in the molecule of this dimer. The presence of an acetyl group attached to the nitrogen atom of the reduced pyrrole ring of dimer XII is also indicated by the shift of the signal of proton "d_1" to weak field (by about 0.9 ppm) in comparison with the starting material I (7.6 ppm) as a result of the anisotropic effect of the carbonyl group. The presence of the acetyl group in compound XII leads to increased strain, i.e, the system becomes more sterically hindered. This is indicated by the change in angles in the reduced pyrrole ring (see the change in coupling constants, Table 1) and the weak field shift of the "b" signal.

The simultaneous presence of bands at 1640 (C=O stretch) and 3330 cm^{-1} (NH stretch) in the IR spectrum show the presence of NH and CO groups in compound XII.

Comparison of the UV spectrum of compound XII with that of the unsubstituted compound I shows that, as in the case of N-acylated indolo[5,6-*d*]benzo[*b*]furan which we synthesized earlier [10], the UV spectrum of the N-acylated dimer XII differs from that of the starting material I by somewhat increased intensity and a hypsochromic shift of the absorption especially in the shortwave region. This change in the spectrum is caused by the creation of a new conjugated system formed by attachment of the electron withdrawing acetyl group to the nitrogen atom in the reduced section of the dimer molecule (Fig. 1).

The structure of compound XII was confirmed by mass spectrometry. The molecular ion corresponded to the calculated molecular mass and the fragmentation pattern did not disagree with the structure proposed (Scheme 2).

Scheme 2



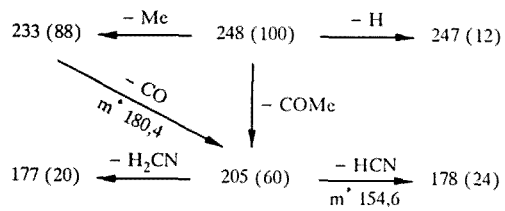
Since the fragmentation of the molecular ions of compounds XII and XIII are of the same type, only the fragmentation for compound XII is shown.

In the ^{1}H NMR spectrum of acetylpyrrolocarbazole VIII (Table 1), in which the acetyl group replaces hydrogen "f_1," a second AB spectrum appears for protons "e" and "e_2" with a characteristic *ortho* coupling constant, J_{ee1} = 8.5 Hz, and the signal for proton "f_1" is absent. The weak field shift by 0.6 ppm of the signal for proton "f" in comparison with the unsubstituted heterocycle III (δ_f = 8.2 ppm) is explained by the *ortho* position of the acceptor group relative to proton "f."

The absorption at 1700 cm^{-1} in the IR spectrum of compound VIII corresponds to the C=O stretch.

The UV spectrum of VIII differs from that of the unsubstituted heterocycle III by the presence of two absorption bands: a high intensity band at 307 nm and a moderate intensity band at 212 nm (Table 2).

The peak with maximum intensity in the mass spectrum of compound VIII is the molecular ion [M$^+$] 248. Further fragmentation and some decomposition processes, confirmed by metastable transitions, conform to the proposed structure:



The broadening of the corresponding interacting signals and the small coupling constants ($^5J_{ci}$) in the ^{1}H NMR spectrum of 2-acetyl-3H-pyrrolo[2,3-*c*]phenothiazine-11,11-dioxide (XV) show that position "c" is devoid of a hydrogen atom. The electron withdrawing and anisotropic properties of the substituent cause the corresponding weak field shifts of the signals of the groups closest to the substituent (Table 1).

Indolo[7,6-*d*]- (IV) and indolo[4,5-*d*]benzo[*b*]thiophene (V) behave analogously in the Friedel–Crafts reaction to indolo[5,6-*d*]- (I), indolo[5,4-*d*]benzo[*b*]furan (II) and indolo[5,4-*d*]benzo[*b*]thiophene (VI) discussed above. In both cases dimers are formed (XIV and XIII respectively) with small amounts of acetylated dimers in which the acetyl group (in compound XIII) is bonded to the nitrogen atom of the reduced pyrrole ring.

Unfortunately because of the difficulty in separating the products and the small yields, it was not possible in all cases to isolate enough of the products even for analysis. For example we were only able to separate the unsubstituted dimer in small yield in the case of compound XIV. In contrast the N-acetyl derivative of compound XIII was isolated and the unsubstituted dimer was only observed chromatographically.

Naturally this limited the spectroscopic data needed to determine the behavior of the heterocycles in our reactions. Nevertheless, the changes in the protons of the acetyl groups in the ^{1}H NMR spectra (and in some cases the UV and IR spectra) allowed us to draw some general conclusions about the structure of the reaction products from the sulfur containing heterocycles XIII and XIV in comparison with the oxygen containing heterocycles IX, X and XI.

For example, the absence of the signal for proton "c" in the ^{1}H NMR spectrum of dimer XIV and the appearance at high field of signals for protons "c_1" and "c_2" (at 3.7 and 3.2 ppm respectively with J_{c1c2} = 15.3 Hz) as in the spectra of compounds IX and X permitted the conclusion that the β-hydrogen of the pyrrole ring had been substituted in the respective dimers of the heterocycles IV and V, i.e., the product is analogous to the starting heterocycle with the substituent in the tetracyclic fragment with the hydrogenated pyrrole ring. The presence of signals for protons "a" and "a_1" (at 11.4 and 5.6 ppm respectively) in the ^{1}H NMR spectrum of compound XIV indicates the presence of an unsubstituted NH group in this dimer. This conclusion is confirmed by the presence of two NH stretching bands at 3355 and 3460 cm^{-1} in the IR spectrum of compound XIV.

The electronic spectrum of compound XIV differs from that of the unsubstituted heterocycle IV only in some increase in band intensity (Fig. 2).

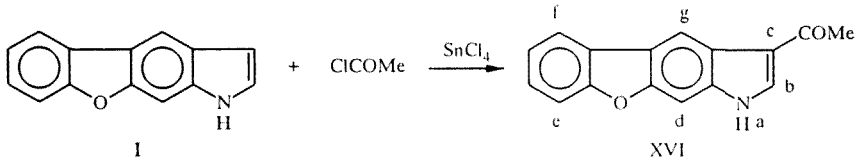
Compound XIII, like compound XII, is an N-acylated dimer with the acyl groups also on the nitrogen atom of the hydrogenated pyrrole ring as the absence of the signal for proton "a_1," the appearance at high field of the characteristic singlet of a methyl group at 2.2 ppm, and the considerable weak field shift of the signal for proton "i," caused by the anisotropy of the carbonyl group (Table 1), in the ^{1}H NMR spectrum of compound XIII all demonstrate.

The UV spectrum of compound XIII shows hypsochromic shifts and a considerable hyperchromic effect which indicates the creation of a new conjugated system caused by the presence of the electron withdrawing acetyl group in the molecule of dimer XIV.

This new system has a much greater effect than in the oxygen containing analog XII.

It was of interest to study the behavior of these heterocycles in the Friedel–Crafts acetylation with $SnCl_4$ in place of $AlCl_3$. Indolo[5,6-*d*]benzo[*b*]furan (I) was chosen as an example.

The synthesis was carried out as follows:



I XVI

The choice of a linear heterocycle is explained by its greater reactivity in comparison with its angular isomer and its greater tendency to undergo dimerization as shown in reactions with $AlCl_3$.

It was established that the use of a weaker Lewis acid precluded the formation of a dimer. The product obtained was the acetylated tetracycle with the $COCH_3$ group on the β-carbon of the pyrrole ring.

Substitution of the β-hydrogen by the acetyl group was shown by the absence of a signal for proton "c" and the appearance of a characteristic methyl singlet at 2.2 ppm in the ^{1}H NMR spectrum of compound XVI. The presence of the acetyl group also caused shifts of the signals of protons "b" and "g," to weak field (by 0.8 and 0.6 ppm respectively) in comparison with the starting material (7.4 and 8.2 ppm respectively).

Bands at 1640 (C=O) and 3200 cm^{-1} (NH) in the IR spectrum of compound XVI show the presence of NH and CO groups.

Some general conclusions can be drawn from the experimental results.

1. Indolobenzo[*b*]furans and indolobenzo[*b*]thiophenes, like indole under acid conditions, react with acetyl chloride and anhydrous aluminum chloride under Friedel–Crafts conditions to give dimers predominantly.

2. The unsubstituted dimers are formed as a mixture of geometric isomers in all the cases described, but the percentage composition of the mixture depends on the type of annelation of the pyrrole ring relative to the central heterocycle and on the prolongation of the reaction in the case of dimers with linear structure.

3. N-acetyl derivatives are formed with only one of the geometric forms, apparently as a result of steric factors.

4. In distinction from indolobenzo[*b*]furans and indolobenzo[*b*]thiophenes, 3H-pyrrolo[2,3-*c*]carbazole (III) and 3H-pyrrolo[2,3-*c*]phenothiazine-11,11-dioxide (VII) are acetylated on treatment with acetyl chloride in the presence of aluminum chloride: acetylation occurs in the unsubstituted benzene ring in the pyrrolocarbazole, but at the α-position of the pyrrole ring in heterocycle VII.

5. When aluminum chloride is replaced by $SnCl_4$ in the Friedel–Crafts reaction of indolo[5,6-*d*]benzo[*b*]furan (I) with acetyl chloride the β-hydrogen of the pyrrole ring is replaced by the acetyl group.

EXPERIMENTAL

Ultraviolet spectra were measured in ethanol in 1 cm cuvette on a Specord UV-Vis spectrometer: λ_{max} in nm and lg ε are cited. IR spectra in Nujol mulls were recorded with a UR-20 spectrophotometer with NaCl and LiF prisms. ^{1}H NMR spectra were recorded in deuterated solvents on a WP-200 SY (200 MHz) machine. Chemical shifts were measured with a precision of 0.01 ppm relative to tetramethylsilane as internal standard, coupling constants were measured to 0.1 Hz. Mass spectra were measured on an MX-1303 machine with direct insertion of the sample into the ion source, cathode emission voltage 1.5 μV, ionizing voltage 50 eV. Purification of samples and separation of isomers were carried out by thin layer and column chromatography on silica gel (100/400) in 1:4 ether–hexane.

2′-(Indolo[5,6-*d*]benzo[*b*]furan-3-yl)-2′,3′-dihydroindolo[5′,6′-*d*]benzo[*b*]furan (IXa, b). Method A. Freshly distilled acetyl chloride (0.12 cm^3, 0.0015 mol) was added slowly dropwise at 0°C to $AlCl_3$ (0.2 g, 0.0015 mol) in methylene chloride (2.5 cm^3). The complex was stirred for 0.5 h and then indolo[5,6-*c*]benzo[*b*]furan (I) (0.1 g, 0.0005 mol) dissolved in methylene chloride (5 cm^3) was added at 0°C and stirred at 0°C for 1 h. The reaction mixture was then decomposed with water, a small amount of HCl added, and it was then extracted with ethyl acetate. The extract was carefully washed with water until neutral and then dried. The reaction product was purified on a column packed with silica gel. According to ^{1}H NMR spectroscopy (Table 1) the isolated product was a 60:40 mixture of isomers IXa and IXb. Yield of mixture 15%. M.p. of IXa: 199-201°C. M.p. of IXb: 203-205°C. Found %: C 81.0, H 4.1, N 6.5. Calc. for $C_{28}H_{18}N_2O_2$, %: C 81.2, H 4.3, N 6.8.

Method B. Freshly distilled acetyl chloride (0.12 cm^3, 0.0015 mol) was added slowly dropwise at 0°C to $AlCl_3$ (0.2 g, 0.0015 mol) in methylene chloride (2.5 cm^3). The complex was stirred for 0.5 h and then compound (I) (0.1 g, 0.0005 mol) dissolved in methylene chloride (5 cm^3) was added at 0°C and stirred at 0°C for 1 h and then at room temperature for 2 h. The reaction mixture was treated as in method A. Two products, IXa and XII, were separated after purification on a silica gel column. Yield of compound XII 3%. M.p. 195-197°C. Found, %: C 78.9, H 4.2, N 6.3. Calc. for $C_{30}H_{20}N_2O_3$, %: C 78.9, H 4.4, N 6.1.

9-Acetyl-3H-pyrrolo[2,3-*c*]carbazole (VIII) was prepared by method A from 3H-pyrrolo[2,3-*c*]carbazole (III) analogously to IX. Yield 63%. M.p. 290-291°C. Found %: C 77.2, H 5.1, N 11.1. Calc. for $C_{16}H_{12}N_2O$, %: C 77.4, H 4.8, N 11.3.

2′-(Indolo[5,4-*d*]benzo[*b*]furan-3-yl)-2′,3′-dihydropyrrolo[5′,4′-*d*]benzo[*b*]furan, (Xa,b) was made by method A from indolo[5,4-*d*]benzo[*b*]furan (II) analogously to the synthesis of compound IX. Yield of mixture 17%. Ratio of isomer Xa to Xb: 50:50. M.p. of isomer Xa: 236-238°C. M.p. of isomer Xb: 241-243°C. Found, %: C 81.3, H 4.5, N 6.6. Calc. for.

$C_{28}H_{18}N_2O_2$, %: C 81.2, H 4.3, N 6.8. Changing the reaction conditions (method B) did not affect the ratio of isomers Xa and Xb.

2′-(Indolo[5,4-*d*]benzo[*b*]thiophen-3-yl)-2′,3′-dihydropyrrolo[5′,4′-*d*]benzo[*b*]thiophene, (XIa, b) was obtained by method A from indolo[5,4-*d*]benzo[*b*]thiophene (VI) analogously to compound IX. Yield of mixture: 25%. Ratio of isomers XIa and XIb: 50:50. M.p. of isomer XIa: 231-233°C. M.p. of isomer XIb: 242-244°C. Found, %: C 75.5, H 4.3, N 6.5, S 14.1. Calc. for $C_{28}H_{18}N_2S_2$, %: C 75.3, H 4.0, N 6.3, S 14.3. Change in the conditions of reaction (method B) did not affect the ratio of isomers XIa and XIb.

2′-(Indolo[4,5-*d*]benzo[*b*]thiophen-3-yl)-1′-acetyl-2′,3′-dihydropyrrolo[4,5-*d*]benzo[*b*]thiophene (XIII) was prepared by method A from indolo[4,5-*d*]benzo[*b*]thiophene (V) analogously to compound IX. Yield 20%. M.p. 326-328°C. Found, %: C 74.0, H 4.1, N 5.8, S 13.3. Calc. for $C_{30}H_{20}N_2OS_2$, %: C 73.8, H 4.1, N 5.7, S 13.1.

2′-(Indolo[7,6-*d*]benzo[*b*]thiophen-3-yl)-2′,3′-dihydropyrrolo[7,6-*d*]benzo[*b*]thiophene (XIV) was made by method B from indolo[7,6-*d*]benzo[*b*]thiophene (IV) analogously to compound IX. Yield 25%. M.p. 205-207°C. Found, %: C 75.3, H 4.2, N 6.1, S 14.0. Calc. for $C_{28}H_{18}N_2S_2$, %: C 75.3, H 4.0, N 6.3, S 14.3.

2-Acetyl-3H-pyrrolo[2,3-*c*]phenothiazine-11,11-dioxide (XV) was prepared by method B from 3H-pyrrolo[2,3-*c*]phenothiazine-11,11-dioxide analogously to compound IX. Yield 19%. M.p. 274-276°C. Found, %: C 61.6, H 3.8, N 8.8, S 10.1. Calc. for $C_{16}H_{12}N_2O_3S$, %: C 61.5, H 3.8, N 8.9, S 10.3.

2-Acetylindolo[5,6-*d*]benzo[*b*]furan (XVI). Acetyl chloride (0.024 cm^3, 0.003 mol) was added dropwise slowly to $SnCl_4$ (0.8 g, 0.003 mol) in methylene chloride (5 cm^3) at 0°C. The mixture was stirred for 0.5 h and then indolo[5,6-*d*]benzo[*b*]furan (I) (0.2 g, 0.001 mol) in methylene chloride was added at 0°C and the mixture was stirred at this temperature for 1 h. The reaction mixture was decomposed with water, HCl was added (0.1 cm^3) and the mixture was extracted with ethyl acetate. Product XVI was purified on a silica gel column. Yield 42%. M.p. 312-314°C. Found, %: C 77.3, H 4.7, N 5.7. Calc. for $C_{16}H_{11}NO_2$, %: C 77.1, H 4.4, N 5.6.

^1H NMR, UV and IR spectroscopic data are presented in Tables 1 and 2.

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