

# DUAL REACTIVITY OF 1,2-DISUBSTITUTED DIHYDRO-N-HETEROAROMATIC SYSTEMS

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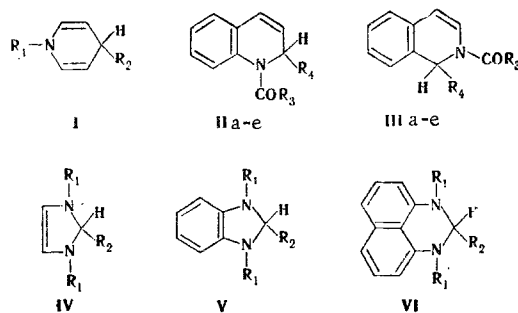
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The effect of the nature of the electrophile and the heteroring on the direction of reactions involving the aromatization of  $\alpha$ -substituted N-acyl dihydro-N-heterocycles with perchlorates of various organic cations was studied. It is shown that hard and intermediate electrophilic agents (triphenylmethyl, triindolylmethyl, and acetylium perchlorates) split out the  $\alpha$  substituent from the dihydroheterocycles to give stable N-acyl salts of the corresponding bases. Soft acceptors (2,2,6,6-tetramethyl-1-oxopiperidinium perchlorate) split out a hydride ion in all cases to give  $\alpha$ -substituted N-acyl salts of the corresponding bases.

The hydride-ion activity of diverse dihydro-N-heteroaromatic systems as models of NAD-H in reactions involving nonenzymatic homogeneous hydrogenation has been studied extensively [1] and is still under investigation [2]. In addition, some 1,2-disubstituted dihydro-N-heteroaromatic systems are ambident nucleophiles in which heterolytic cleavage of either a carbon-hydrogen bond with detachment of a hydride ion or of a carbon-carbon bond with splitting out of the  $\alpha$  substituent in the form of a carbanion and simultaneous aromatization of the heterocycle occurs [3, 4]. Splitting out of a substituent has been observed for 1,2-disubstituted dihydroquinolines [5] and perimidines [6]; however, the authors made no attempt to explain this phenomenon or to analyze the literature data. With the present communication we will inaugurate a series of studies devoted to the investigation of the dual reactivity of dihydro-N-heteroaromatic systems and the effect of various factors on the direction of their reactions with electrophiles.

We investigated the behavior of these systems in reactions that are controlled by the charge, i.e., in reactions with strong or intermediate acceptors such as  $R_3C^+$ ,  $H^+$ ,  $R^+$ , etc., and in reactions with weak electrophiles [7]. We assumed that, in conformity with general perturbation theory [7] and Pearson's concept [8], heterolytic cleavage of the carbon-hydrogen bond with detachment of a hydride ion, which is the softest of all the known nucleophiles [7], will occur in the reaction of these systems with soft electrophiles. However, detachment of the substituent in the form of both a carbanion and a hydride ion is possible in reactions of intermediate or hard electrophiles, depending on the nature of the geminal substituent.

With this goal in mind, we studied the reactivities of N-acyl  $\alpha$ -( $\gamma$ )-substituted dihydro-N-heterocycles (I-VI) in the case of aromatization under the influence of perchlorates of various organic cations, viz., the



I, IV, V, VI  $R_1 = COC_6H_5$ ;  $R_2 = 3$ -indolyl; II, III a, d, e  $R_3 = C_6H_5$ ; b  $R_3 = CH_3$ ;  
c  $R_3 = 2$ -thienyl; a, b, c  $R_4 = R^+$ ; d  $R_4 = CH_2CO$ -thienyl-2; e  $R_4 = CH_2COC_6H_5$

triphenylmethyl (VII), acetylium (VIII), triindolylmethyl (IX), and 2,2,6,6-tetramethyl-1-oxopiperidinium (X) cations. We used the oxopiperidinium cation (X) [9], which displays high dehydrogenating activity [10], as the softest electrophile.

TABLE 1. Salts of N-Heteroaromatic Cations

Compound	mp., °C (acetonitrile)	IR spectrum, $\nu_{\text{C=O}}$ $\text{cm}^{-1}$	Found, %			Empirical formula	calc., %			Yield, %
			C	H	N		C	H	N	
XIa	128—130	1755	57.5	3.7	4.2	$\text{C}_{16}\text{H}_{12}\text{NO}_5\text{Cl}$	57.8	3.6	4.2	97.7
XIb	135—136	1680	48.9	3.9	5.1	$\text{C}_{11}\text{H}_{10}\text{NO}_5\text{Cl}$	48.6	3.7	5.2	74.1
XIc <sup>a</sup>	195—198	1710	49.8	3.0	3.9	$\text{C}_{14}\text{H}_{10}\text{NO}_5\text{SCl}$	49.5	2.9	4.1	88.1
XIIb	179—180	1685	48.5	3.8	5.2	$\text{C}_{11}\text{H}_{10}\text{NO}_5\text{Cl}$	48.6	3.7	5.2	62.3
XIc <sup>b</sup>	174—176	1740	49.5	2.7	4.1	$\text{C}_{14}\text{H}_{10}\text{NO}_5\text{SCl}$	49.5	2.9	4.1	86.6
XIII	232—233	1695	60.0	4.0	7.1	$\text{C}_{20}\text{H}_{15}\text{N}_2\text{O}_5\text{Cl}$	60.2	3.8	7.0	71.7
XIVa	255—258 <sup>c</sup>	1750 <sup>d</sup>	64.2	4.1	6.3	$\text{C}_{24}\text{H}_{17}\text{N}_2\text{O}_5\text{Cl}$	64.4	3.8	6.3	98.8
XIVc <sup>e</sup>	174—175	1740	58.9	3.3	3.1	$\text{C}_{22}\text{H}_{11}\text{NO}_5\text{SCl}$	59.1	3.5	3.2	76.1
XIVe	210—211	1760	62.4	6.4	2.9	$\text{C}_{21}\text{H}_{28}\text{NO}_5\text{Cl}$	62.6	6.1	3.0	37.6
XVa	257—259 <sup>f</sup>	1745 <sup>d</sup>	64.5	4.0	6.2	$\text{C}_{24}\text{H}_{17}\text{N}_2\text{O}_5\text{Cl}$	64.4	3.8	6.3	95.4
XVb	220—221	1720	57.0	3.8	7.4	$\text{C}_{19}\text{H}_{15}\text{N}_2\text{O}_5\text{Cl}$	56.9	3.9	7.2	89.8
XVc <sup>g</sup>	178—180	1710	59.0	3.8	3.1	$\text{C}_{22}\text{H}_{11}\text{NO}_5\text{SCl}$	59.1	3.5	3.2	79.0
XVe	175—177	1745	62.6	6.4	3.2	$\text{C}_{24}\text{H}_{28}\text{NO}_5\text{Cl}$	62.6	6.1	3.0	54.2
XVIa	259—263	—	59.3	3.8	8.1	$\text{C}_{17}\text{H}_{13}\text{N}_2\text{O}_4\text{Cl}$	59.3	3.8	8.1	94.8
XVIIa	257—260	—	59.4	3.9	8.0	$\text{C}_{17}\text{H}_{13}\text{N}_2\text{O}_4\text{Cl}$	59.3	3.8	8.1	91.2

a) Found: S 9.2%. Calculated: S 9.4%. b) Found: S 9.5%. Calculated: S 9.4%. c) According to the data in [10], this compound has mp 196–198°C. d) In KBr pellets. e) Found: S 7.4%. Calculated: S 7.3%. f) According to the data in [10], this compound has mp 176–177°C. g) Found: S 7.4%. Calculated: S 7.3%.

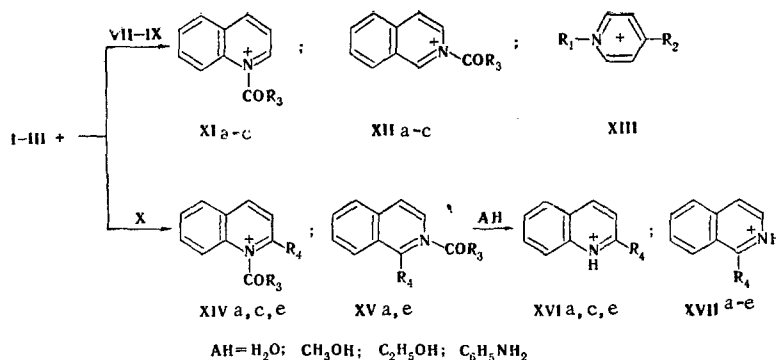
It was found that in the reaction with triphenylmethyl perchlorate (VII) dihydroquinolines and isoquinolines (II and III) split out substituent  $R_4$  in almost all cases, as we had assumed, to give stable N-acylquinolinium (XI) and isoquinolinium (XII) perchlorates (Table 1), which were heretofore assumed to be extremely hard-to-obtain and unstable compounds [11]. The substituents that are split out react with triphenylmethyl perchlorate to give triphenyl(3-indolyl)methane. When  $R_4$  was a phenacyl residue, acetophenone and triphenylcarbinol were detected as side products; these side products are evidently formed as a consequence of penetration of the reaction medium by moisture.

Perchlorates XI–XII are insoluble in nonpolar solvents and are slowly hydrolyzed in water to give the free bases and the corresponding acids. The absorption band of the carbonyl group in the IR spectra of these compounds is shifted  $100\text{ cm}^{-1}$  to the higher-frequency region as compared with the starting compounds (II–III), and this constitutes evidence for bonding between the acyl residue and the ammonium nitrogen atom (Table 1).

Under similar conditions dihydropyridines I split out a hydride ion and are converted to stable N-acylpyridinium salts (XIII), as we have observed for other dihydroheterocycles (IV–VI) [12, 13].

The acetylium (VIII) and triindolylmethyl (IX) cations and other hard and intermediate electrophiles also reacted in the same way as triphenylmethyl perchlorate. Soft acceptors such as, e.g., 2,2,6,6-tetramethyl-1-oxopiperidinium perchlorate (X), in all cases split out only a hydride ion to give the previously unknown stable  $\alpha$ -substituted N-acylquinolinium (XIV) and isoquinolinium (XV) salts (Table 1).

The synthesized acylquinolinium and isoquinolinium perchlorates (XIV and XV) are extremely reactive. They are readily hydrolyzed under the influence of water, alcohols, and primary and secondary amines and are thereby converted to the corresponding hydropchlorates (XVI and XVII) of  $\alpha$ -substituted benzopyridines.



In view of the high chemical activity of salts XIV and XV, their preparative yields depend not only on the purity of the reagents but also on the degree of purification and drying of the solvents. A difficult-to-separate

TABLE 2. Absorption Bands in the Electronic and IR Spectra of Benzopyrylium Salts XIVa-XVIIa\*

Compound	Electronic spectrum		IR spectrum, $\nu$ , $\text{cm}^{-1}$
	$\lambda_{\text{max}}$ , nm	$\epsilon \cdot 10^{-3}$	
XIVa	430	$18.0 \pm 0.1$	625 s, 1100 vs ( $\text{ClO}_4^-$ )
	333 sh	$5.6 \pm 0.1$	1422 s, 1452 m, 1462 m, 1493 m, 1535 s,
	299 sh	$10.3 \pm 0.1$	1570 m, 1602 s (In and $\text{X}^+$ )
	255	$28.1 \pm 0.1$	1750 s (C=O)
	225 sh	$31.3 \pm 0.4$	329 vs (N—H)
XVa	408	$7.5 \pm 0.05$	625 s, 1100 vs ( $\text{ClO}_4^-$ )
	332	$4.9 \pm 0.1$	1430 s, 1452 m, 1465 m, 1496 m, 1537 s,
	267 sh	$17.9 \pm 0.5$	1560 s, 1595 s, 1625 s (In and $\text{X}^+$ )
	241 sh	$32.0 \pm 1.0$	1745 s (C=O)
	225 sh	$37.3 \pm 0.7$	3260 (N—H)
	211	$53.1 \pm 0.3$	
XVIa	410	$22.0 \pm 0.1$	625 s, 1100 vs ( $\text{ClO}_4^-$ )
	300	$8.9 \pm 0.1$	1409 s, 1437 s, 1455, 1490 m, 1555 s, 1610 s,
	269	$18.7 \pm 0.2$	1630 s (In and $\text{X}^+$ )
	254	$17.8 \pm 0.2$	3290 s (N—H)
	216	$49.0 \pm 0.2$	
XVIIa	398	$13.1 \pm 0.1$	627 s, 1100 vs ( $\text{ClO}_4^-$ )
	333	$4.1 \pm 0.1$	1430 s, 1445 m, 1465 w, 1495 m, 1532 s,
	282 sh	$8.4 \pm 0.1$	1590 s, 1613 m, 1635 s (In and $\text{X}^+$ )
	270	$11.1 \pm 0.3$	3280 s (N—H)
	240 sh	$21.1 \pm 0.6$	
	244 sh	$47.6 \pm 0.6$	
	216	$53.1 \pm 0.2$	

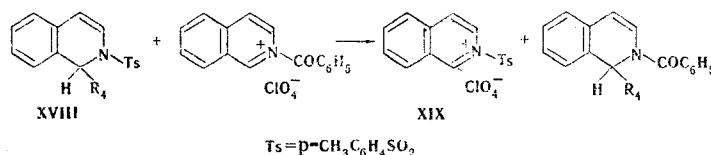
\* Abbreviations: In is the indole ring, and  $\text{X}^+$  is the quinolinium or isoquinolinium ring.

mixture of salts XIV and XVI or XV and XVII is therefore always obtained when moist solvents are used.

The electronic spectra of salts XIVa-XVIIa in the 200-800 nm region contain a number of overlapped bands (Table 2) that are associated primarily with the absorption of conjugated indole and benzopyridinium chromophores [14]. The yellow color of these compounds is due to the intense absorption band at 390-430 nm. In the case of the spectra of benzoyl derivatives XIVa and XVa this band is found in the longer-wave region and has a lower intensity than in the case of hydroperchlorates XVIa and XVIIa.

The IR spectra of salts XIVa-XVIIa are the superimposition of the bands at 625 and 1100  $\text{cm}^{-1}$  of the  $\text{ClO}_4^-$  anion and of the bands that correspond to the cations (Table 2). A number of bands at 1400-1650  $\text{cm}^{-1}$ , which are associated with the stretching vibrations of the indole and benzopyridinium rings, are characteristic for the cations. In addition, strong and broad bands of the NH vibrations of the indole fragment are present at 3250-3300  $\text{cm}^{-1}$ . The spectra of benzoyl salts XIVa and XVa also contain strong bands of stretching vibrations of a carbonyl group at 1750  $\text{cm}^{-1}$ .

Thus in the case of the behavior of dihydroquinolines IIa-e and isoquinolines IIIa-e our qualitative observations provide evidence that a substituent is primarily split out in charge-controlled reactions. In this connection, it seems possible to realize a new variant of transhetarylation in which conversion of the substituent from a less electrophilic cation to a more electrophilic cation may be realized by the action of a more electrophilic,\* as compared with the cation formed in the process (for example, XIX) N-acyl heteroaromatic cation (for example, XII). In fact, as a concrete example we were able to realize this sort of reaction:



## EXPERIMENTAL

The mass spectra were obtained by direct introduction of the samples into the ion source of a Varian MAT-311 spectrometer (the accelerating voltage was 3 kV, the cathode emission current was 1.0 mA, and the

\* In this case we understand electrophilicity to be the magnitude of the orbital electronegativity of the cations in accordance with the Pearson-Klopmann concept [7].

ionizing voltage was 70 eV). The IR spectra of mineral oil suspensions and KBr pellets of the compounds were recorded with a UR-20 spectrometer. The electronic spectra of acetonitrile solutions were recorded with a Specord UV-vis spectrophotometer.

**N-Benzoylisoquinolinium Perchlorate (XIIa).** A 0.35-g (0.01 mole) sample of N-benzoyl-1-(3-indolyl)-1,2-dihydroisoquinoline (IIIa) was added in portions at 25°C to a solution of 0.34 g (0.01 mole) of triphenylmethyl perchlorate (VIII) in 5 ml of dry acetonitrile. At the end of the reaction (30 min), 50 ml of dry ether was added to the reaction mixture, and the precipitated XIIa was removed by filtration and recrystallized from acetonitrile to give 0.33 g (98.5%) of a product with mp 174-175°C. IR spectrum: 1760 (C=O). Found: C 57.6; H 3.3; Cl 10.9; N 4.5%.  $C_{16}H_{12}ClNO_5$ . Calculated: C 57.8; H 3.6; Cl 10.6; N 4.2%.

After separation of the crystals of the salt, the filtrate was evaporated, and the residue was washed with methanol and recrystallized from butanol to give 0.28 g (78%) of triphenyl(3-indolyl)methane with mp 208-209°C, the IR spectrum and melting point of which were identical to those of the genuine compound.

Salts XIa-c, XIIb,c, and XIII, the principal characteristics of which are presented in Table 1, were similarly obtained.

**N-Benzoyl-1-(2-thenoylmethyl)isoquinolinium Perchlorate (XVd).** A 0.72-g (0.02 mole) sample of N-benzoyl-1-(2-thenoylmethyl)-1,2-dihydroisoquinoline (IIIId) was added in portions in the course of 10 min at 25°C to a solution of 0.77 g (0.03 mole) of 2,2,6,6-tetramethyl-1-oxopiperidinium perchlorate (X) in 10 ml of dry acetonitrile. At the end of the reaction (1.5-2 h), 100 ml of dry ether was added to the mixture, during which yellow salt XVd crystallized out. The crystals were removed by filtration and recrystallized from acetonitrile to give 1.2 g (85%) of a product with mp 204-205°C. IR spectrum: 1680 (C=O) and 1760  $cm^{-1}$  (C=O). Found: C 57.5; H 3.5; N 3.2; S 7.1%.  $C_{22}H_{16}ClNO_6S$ . Calculated: C 57.7; H 3.5; N 3.1; S 6.9%.

Salts XIVa,c,e and XVa-e, the principal characteristics of which are presented in Table 1, were similarly obtained.

**Reaction of N-Benzoyl-1-(2-thenoylmethyl)isoquinolinium Perchlorate (XVd) with Aniline.** A mixture of 0.46 g (0.01 mole) of XVd, 0.09 g (0.01 mole) of aniline, and 5 ml of dry acetonitrile was refluxed for 1-1.5 h, after which it was cooled, and the resulting precipitate was removed by filtration and recrystallized from methanol to give 0.06 g (28%) of benzaniline with mp 161-162°C, the IR spectrum and melting point of which were identical to those of the genuine compound. Ether (50 ml) was added to the filtrate, and the resulting resinous precipitate was removed by filtration, washed with chloroform, and recrystallized from acetonitrile to give 0.30 g (87%) of 1-(2-thenoylmethyl)isoquinolinium hydropерchlorate (XVIIId) with mp 167-169°C. Found: C 49.4; H 3.3; N 4.1; S 9.5%.  $C_{15}H_{12}ClNO_5S$ . Calculated: C 49.5; H 3.5; N 4.1; S 9.3%. A 0.35-g (0.01 mole) sample of hydropерchlorate XVIIId was treated with an aqueous alcohol solution of alkali, and the resulting yellow crystals were separated and recrystallized from acetonitrile to give 0.25 g (98%) of 1-(2-thenoylmethyl)-isoquinoline with mp 145-147°C. IR spectrum: 1670 (C=O) and 1650  $cm^{-1}$  (C=N). Mass spectrum, \* m/e: 83.0 (5.77); 105.0 (3.08); 111.1 (38.51); 113.1 (3.05); 114.1 (2.38); 115.1 (12.93); 140.2 (2.45); 141.3 (2.45); 141.3 (2.45); 141.3 (2.45); 142.4 (3.18); 180.2 (1.55); 226.3 (1.29); 253.2 (6.03). Found: C 72.2; H 4.4; N 5.6; S 12.3%.  $C_{15}H_{11}NOS$ . Calculated: C 72.0; H 4.4; N 5.5; S 12.6%.

**Reaction of N-p-Tolylsulfonyl-1-(3-indolyl)-(1,2-dihydroisoquinoline (XVIII) with N-Benzoylisoquinolinium Perchlorate (XIIa).** A mixture of 0.83 g (0.02 mole) of XVIII, 0.67 g (0.02 mole) of salt XIIa, and 10 ml of dry acetonitrile was refluxed for 2-3 h, after which it was cooled, and white crystals of N-benzoyl-1-(3-indolyl)-1,2-dihydroisoquinoline (IIIa) precipitated. The IR spectrum and melting point of the product were identical to those of the genuine compound. Dry ether (100 ml) was added to the acetonitrile filtrate, during which N-p-tolylsulfonylisoquinolinium perchlorate (XIX) crystallized out. The crystals were removed by filtration and recrystallized from acetonitrile to give 0.65 g (85%) of a product with mp 179-180°C. IR spectrum 1350 ( $SO_2$ )<sub>as</sub> and 1170  $cm^{-1}$  ( $SO_2$ )<sub>s</sub>. Found: C 50.2; H 3.3; N 3.7; S 8.5%.  $C_{16}H_{14}ClNO_6S$ . Calculated: C 50.0; H 3.6; N 3.6; S 8.3%.

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\* The intensities of the ion peaks in percent of the maximum peak in the spectrum are presented in parentheses.

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## SYNTHESIS OF 9-DIAZO-4-AZAFLUORENES

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Stable diazo compounds of the azafluorene series, viz., 9-diazo-4-azafluorenone and 1,3-diphenyl-4-azafluorene, were obtained from 4-azafluorenone and 1,3-diphenyl-4-azafluorene tosylhydrazones. 1',2'-Dicarbomethoxyspiro(4-azafluorene-9,3'-cyclopropane) was obtained from 4-azafluorenone tosylhydrazone, and 4',5'-dicarbomethoxyspiro(4-azafluorene-9,3'-pyrazolenine) was obtained from 9-diazo-4-azafluorene. It is assumed that the product in the latter case is obtained as a result of reaction of a carbene, viz., 4-azafluorenylidene carbene, which is formed from 9-diazo-4-fluorene, with dimethyl acetylenedicarboxylate.

2,4,7-Trinitrodiazafluorene has proved to be a very stable compound [1], and this fact constitutes an exception in the diazo series. Its stability is evidently due to the electron-acceptor effect of the nitro groups. Proceeding from the presence in the azafluorene molecule of a pyridine ring, the effect of which is similar to the effect of a nitro group, one may assume that diazo compounds of azafluorenes will also be stable. The synthesis of compounds of this type is of theoretical interest and also opens up a pathway for the preparation of new azafluorene derivatives that possibly have practically useful properties.

To prepare the diazo compounds of the azafluorene series we used the accessible 4-azafluorenone (I) and 1,3-diphenyl-4-azafluorenone (II) [3], from which we obtained their tosylhydrazones III and IV. Treatment of tosylhydrazone III with sodium isopropoxide in benzene gave the stable 9-diazo-4-azafluorene (V) (in higher than 60% yield) in the form of slightly red crystals with mp 68-69°C (mp 55-59°C [4]), the isolation of which was accomplished by a chromatographic method. In this experiment bis(4-aza-9-fluorenylidene) (VII) was also isolated in ~10% yield in the form of dark-red crystals with mp 284-286°C; this compound is evidently obtained from diazo compound V through a step involving the formation of a carbene, viz., 4-aza-9-fluorenylidene carbene. Compound VII was previously synthesized from 9-bromo-4-azafluorene by treatment with potassium hydroxide. 9-Diazo-1,3-diphenyl-4-azafluorene (VI), which is also a stable substance and was obtained in the form of light-pinkish crystals with mp 140-141°C, was obtained in considerably lower yield (8%) from tosylhydrazone IV and UV irradiation of a solution in tetrahydrofuran (THF) in the presence of sodium hydride. Azafluorenone II, which is evidently formed from diazo compound VI, was also obtained during the chromatographic separation of diazo compound VI.

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