14. T. G. Beamont and K. M. C. Davis, J. Chem. Soc. B, No. 9, 1010 (1968).
15. T. G. Beamont and K. M. C. Davis, J. Chem. Soc. B, No. 4, 592 (1970).
16. S. S. Gitis and A. Ya. Kaminskii, Usp. Khim., 47, 1971 (1978).
17. R. Foster and C. A. Fyfe, J. Chem. Soc. B, 53 (1966).
18. V. N. Drozd, N. V. Tokmakova, I. V. Stankevich, and Yu. M. Udachin, Zh. Org. Khim., 18, 124 (1982).

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

8.* AROMATIZATION OF N-ACYL PARTLY HYDROGENATED PYRAZINE AND QUINOXALINE DERIVATIVES

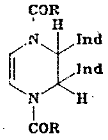
Kh. Ya. Lopatinskaya, Z. M. Skorobogatova,
A. K. Sheinkman, and T. A. Zaritovskaya

UDC 547.861.3'863.13'866:543.422'51'52

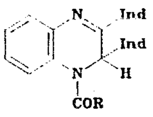
N-mono- and N,N-diacyl 2,3-diindolyl-substituted 1,2-dihydro- and 1,2,3,4-tetrahydropyrazines and quinoxalines were aromatized with triphenylmethyl perchlorate and 2,2,6,6-tetramethyl-1-oxo-piperidinium perchlorate. The hitherto unknown N-acylquinoxalinium perchlorates were obtained.

Continuing our study of the aromatization of N-acyl partly hydrogenated N-heteroaromatic systems [2, 3], we have studied the reactivity of the most difficulty aromatizable N-acyl derivatives of di- and tetrahydro-1,4-diazinium bases, having substituents at the *sp*^{3} carbons of the heterocycle, under the influence of perchlorates of various organic cations. Moreover we have studied the synthesis by aromatization (by analogy with the synthesis of stable N-acyl pyridinium and benzopyridinium salts [2]) of hitherto unknown N-acyl salts of 1,4-diazines. Their participation *in situ*, however, was postulated for the synthesis of Reissert's compounds [4] and in the heteroarylation of nucleophilic organic compounds under the simultaneous action of acyl chlorides and diazines [5]. Until now, aromatization has been described for N-methyl and N-hydro derivatives of di- and tetrahydro-1,4-diazine systems [6-10], by the action of neutral oxidants of various strengths: chloranil, oxygen, sulfur, and $KMnO_4$. From the data of [6-10] it follows that the ease of aromatization of these systems decreases substantially in going from their N-methyl to their N-hydro derivatives, from dihydro to tetrahydro derivatives, and from the products of mono-addition of various nucleophiles to the products of binucleophilic addition to quaternary and protonated 1,4-diazine salts.

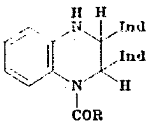
We aromatized a series of 2,3-diindolyl-substituted N,N-diacyl-1,2,3,4-tetrahydropyrazines (I), mono-N-acyl-1,2-dihydro- (II), 1,2,3,4-tetrahydro- (III), and N,N-diacyl-2,3-di(indolyl-3)-1,2,3,4-tetrahydroquinoxalines (IV) by the action of various hydride ion acceptors.



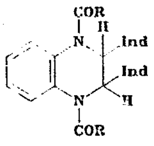
Ia,b



IIa-e



III a-e



IV b

I—IV Ind=3-indolyl; I—III a $R=C_6H_5$; I—IV b $R=CH_3$; II, III c $R=C_6H_4-Cl$-*p*; d $R=C_6H_4-NO_2$-*p*; e $R=C_6H_4-CH_3$-*o*

---

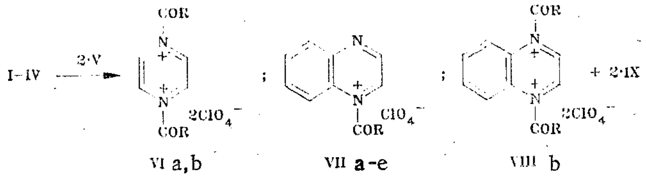
*For Communication 7, see [1].

Institute of Physical Organic Chemistry and Coal Chemistry, Academy of Sciences of the Ukrainian SSR, Donetsk 340114. Dnepropetrovsk Civil Engineering Institute, Dnepropetrovsk 320361. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 810-815, June, 1985. Original article submitted June 5, 1984.

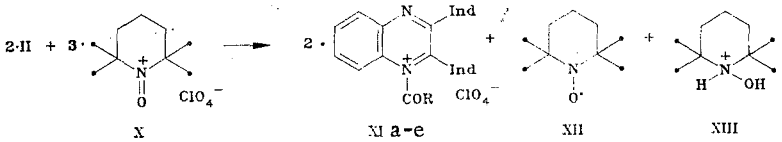
0009-3122/85/2106-0675$09.50

As we have previously shown [5], chloranil does not show aromatizing activity toward compounds I, II, or IV; under relatively mild conditions it easily dehydrogenates the mono-N-acyl tetrahydro derivatives III to the respective N-acyl-1,2-dihydroquinoxalines II.

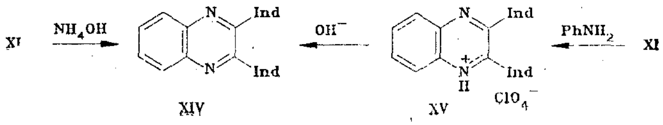
In the reaction with triphenylmethyl perchlorate (V), all compounds I-IV, even under mild conditions, split off both indole substituents to give the extremely unstable di-N-acyl pyrazinium (VI) and mono- and di-N-acyl quinoxalinium (VII, VIII) perchlorates attemps to isolate them individually from the acetonitrile solution were unsuccessful; when the white crystalline salts came in contact with air they instantly deliquesced and turned dark. What confirms the formation of VI-VIII is the separation in almost quantitative yield (from the calculated stoichiometry of the reaction: 2 mole of perchlorate V per mole of I-IV) of the byproduct triphenyl(indolyl-3)methane IX, which forms by the reaction of the split-off substituent with V.



A milder aromatizing agent, viz., 2,2,6,6-tetramethyl-1-oxopiperidinium perchlorate (X) [11] shows a dehydroaromatizing effect when it reacts with I-IV, just as in analogous reactions with N-acyl monoazine derivatives [3]. But we isolated the corresponding salts XI only from reactions with the mono-N-acyl derivatives II and III. With the 1,4-diacyl derivatives I and IV, the yellow crystalline precipitates of diacyl salts instantly deliquesced when we tried to filter them off. We were able to decide that in all cases a hydride ion, and not the indole substituent, was split off from the isolation of the calculated amounts (allowing for the difference in stoichiometry of aromatization of di- II and the tetrahydroderivatives I, III, and IV) of 2,2,6,6-tetramethyl-piperidine-oxyl XII and the hydroxypiperidinium cation XIII which forms by reduction of the oxopiperidinium cation X [3, 12].



The perchlorates XIa-e are insoluble in nonpolar solvents and quickly hydrolyze in aqueous ammonia to release the free base 2,3-di(indolyl-3)quinoxaline (XIV), the structure of which was confirmed by IR and mass spectra. Salts XIa-e acylate aniline easily and are thereby converted to the hydroperchlorate XV, which by treatment with alkali is converted to the bas XIV.



The electron spectra of XIa-e and XV contain in the 220-450 nm region a series of overlapping bands due to absorption by the conjugated indole and quinoxaline nuclei. As Table 1 shows, the long-wave band (λ_{max} = 420 nm) of the $\pi \rightarrow \pi^*$ transition of XIa, corresponding to overall excitation of the molecule [13], is shifted to a higher frequency than the same band in 3-(quinoxalyl-2)-indole ethiodide described in [13] (λ_{max} = 490 nm), despite the presence in XIa of an additional chromophore, viz., the second indole residue at the 3-position of the N-acyl-quinoxalinium cation. In the visible region the difference between the yellow color of perchlorates XIa-e and XV and the dark red of the iodides corresponds fundamentally with this phenomenon. These facts are explainable by the known difference [14] between the effects of ClO_4^- and I^- on the UV spectra of the respective salts, which is related to the different capabilities of these anions to form charge-transfer complexes. The nature of the substituent at the N-acyl residue of XIa-e has very little effect on the location of the maximum of the long-wave $\pi \rightarrow \pi^*$ transition band (the difference is 2-4 nm in all). But this affects more strongly the second, higher-frequency absorption band of XIa-e (λ_{max} = 312 nm for XIa), which corresponds to the excitation (and consequently local electron transitions) of the quinoxalinium cation. For example, going from XIa to XIc to XId is accompanied by bathochromic shifts of 8 and 12 nm, respectively. This also corresponds to the visual ob-

TABLE 1. 1-Acyl-2,3-di(indolyl-3)quinoxalinium Perchlorates XIa-e and XV

Compound	mp, °C (from acetonitrile)	UV spectrum, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)	IR spectrum*, ν, cm^{-1}	Found			Empirical formula	Calculated			Yield, %
				C	H	N (Cl)		C	H	N (Cl)	
XIa	231—233	420 (44±0,1), 375 sh (21±0,4), 312 (13±0,1), 229 (56±0,2)	625 s, 1100 v.s (ClO$_4^-$), 1450 s, 1520 m, 1560 s 1615 m (IndandX+), 1695 s (C=O), 3430 m (H)	66,7	4,0	9,8	$C_{31}H_{21}ClN_4O_5$	65,9	3,7	9,9	53
XIb	195—198	430 (32±0,1), 373 sh (28±0,3), 314 (16±0,1), 225 (58±0,3)	625 s, 1100 v.s (ClO$_4^-$), 1410 m, 1430 m, 1490 s, 1510 m, 1560 s, 1595 m, 1615 s, 1620 m (IndandX+), 1690 s (C=O), 3435 (NH)	60,9	3,6	12,0	$C_{26}H_{19}ClN_4O_5$	62,1	3,8	11,1	64
XIc	210—214	430 (40±0,1), 320 (14±0,2), 295 sh (20±0,4)	625 s, 1100 v.s (ClO$_4^-$), 1435 s, 1485 m, 1500 m, 1562 s, 1600 s, 1615 s (IndandX+); 1700 s (C=O), 3430 w (NH)	62,7	3,4	9,4 (11,4)	$C_{31}H_{20}Cl_2N_4O_5$	62,1	3,3	9,3 (11,8)	32
XId	245—246	432 (46±0,1), 380 sh (22±0,4), 324 (14±0,1), 226 (58±0,2)	625 s, 1100 v.s (ClO$_4^-$), 1430 m, 1450 m, 1505 m, 1560 s, 1595 s, 1610 m (IndandX+), 1705 s (C=O), 3430 m (NH)	61,1	3,0	11,3	$C_{31}H_{20}ClN_5O_7$	61,1	3,3	11,5	58
XIe	201 (decomp.)	431 (46±0,1), 400 sh (36±0,5), 322 (17±0,1), 228 (53±0,2)	625 s, 1100 v.s (ClO$_4^-$), 1450 s, 1525 m, 1615 s (IndandX+), 1690 s (C=O), 3432 m (NH)	65,8	4,3	9,6	$C_{32}H_{23}ClN_4O_5$	66,3	3,9	9,7	21
XV	296—298	429 (39±0,2), 373 sh (24±0,4), 306 (10±0,1), 228 (42±0,2)	625 s, 1100 v.s (ClO$_4^-$), 1415 m, 1452 s, 1500 s, 1560 s, 1600 m, 1610 m (IndandX+), 3290 s (NH), 3432 m (NH)								

*Ind, indole ring; X$^+$, quinoxalinium ring.

servations; in this series of salts the color changes from yellow to orange-red. In going from the N-acyl salts XI to the hydroperchlorate XV the electron spectra show a hypsochromic shift of the band at 312 nm, and a hypsochromic shift of the longer wave $\pi-\pi^*$ transition band.

The IR spectra of XIa-e (Table 1) show an overlapping of bands in the ClO_4^- region, 625 and 1100 cm^{-1}, and bands corresponding to the cations. Typical of the latter are the bands at 1400-1620 cm^{-1} that are related to the stretching vibrations of the indole and quinoxaline rings, and the broad medium-strength band at 3430-3450 cm^{-1} of the indole NH vibrations. Moreover, the spectra of XIa-e have strong bands in the 1690-1705 cm^{-1} region, which we have assigned to the valence vibrations of the carbonyl located at the nitrogen of the 2,3-diindolylquinoxalinium cation. The location of these bands does not agree with that of the carbonyl bands in amides I-IV (where they are at 1640-1670 cm^{-1}). Such a small increase (20-35 cm^{-1}) in carbonyl vibration frequency in going from amide to salt (in pyridinium salts this shift is 90-100 cm^{-1}) is apparently related to the presence in the quinoxalinium cation of the two π-donor indole substituents, which promote additional possibilities for the delocalization of the positive charge.

Thus it follows from what has been presented that 1,2,3-trisubstituted di- and tetrahydro-1,4-diazines, like the 1,2-disubstituted dihydropyridines and dihydrobenzopyridines [2] are ambidentate nucleophiles; by the action of various electrophiles heterolytic scission occurs either of a carbon—hydrogen bond with detachment of a hydride ion, or of a carbon—carbon bond with splitting out of the α-substituent as a carbanion and simultaneous aromatization of the heterocycle.

EXPERIMENTAL

Mass spectra were obtained by direct introduction of the sample into the ion source of a Varian MAT-311 spectrometer (3 kV accelerating voltage, 1.0 mA cathode emission current, 70 eV ionizing voltage.) IR spectra were obtained on a UR-20 spectrometer in mineral oil in dry argon atmosphere. Electron spectra were obtained on a Specord UV-Vis spectrometer in acetonitrile solution, at $2 \cdot 10^{-6}$ M.

Compounds I-IV were synthesized by the procedure of [5].

Reaction of 1,4-Diacetyl-2,3-di(indolyl-3)-1,2,3,4-tetrahydropyrazine, Ib, with Triphenylmethyl Perchlorate, V. To a solution of 0.68 g (2 mmole) of V in 5 ml of dry acetonitrile at 10° was added 0.40 g (1 mmole) of Ib in one portion. After the reaction was complete (20 min), 50 ml of dry ether was added to the mixture, and the precipitate was quickly crystallized from abs. acetonitrile. White needles of VIb were obtained. When rapidly heated over a flame the salt explodes, as is typical of perchlorates. Melting point, elemental composition, and spectrum could not be determined because the sample deliquesces and darkens. After removal of the salt precipitate, the ether solution was evaporated, and the residue was washed with alcohol and crystallized from butanol. There was obtained 0.60 g (83%) of triphenyl(indolyl-3)methane, mp 208°; IR spectrum and melting point were identical with those of a known material.

Compound Ia, II-IV behave similarly in reaction with V.

1-Benzoyl-2,3-di(indolyl-3)quinoxalinium Perchlorate (XIa) (Table 1). A. To a solution of 0.77 g (3 mmole) of oxopiperidinium perchlorate X in 15 ml of dry acetonitrile was added 0.47 g (1 mmole) of tetrahydroquinoxaline derivative of IIIa at 25° over 10 min portionwise. After the reaction was complete (3-5 h at 50°), 100 ml of ether was added to the mixture. The yellow precipitate was cryatallized from acetonitrile to give perchlorate XIa. The ether mother liquor was evaporated at 25°, the tarry residue was triturated with 30 ml of pentane, and the crystalline product was recrystallized from ethanol—ether mixture. Hydroxypiperidinium perchlorate, XIII, was obtained. Yield 0.12 g (50% based on starting IIIa), mp 189-191° (100-191 [15]). The pentane extract was evaporated to give red crystals of piperidine oxyl XII, identified by comparison of IR spectrum and mp with a known sample; yield 0.072 g (90%).

XIb-e were obtained similarly (Table 1).

B. Similarly to method A, but starting from 1.5 mmole of X and 1 mmole of the mono-N-acyldihydroquinoxalines IIa-e, the same salts XIa-e were obtained.

Reaction of N-acetyl-2,3-di(indolyl-3)quinoxalinium Perchlorate XIb with Aniline. A mixture of 0.5 g (1 mmole) of XIb and 0.09 g (1 mmole) of aniline in 10 ml of dry acetonitrile was boiled for 2 h. After cooling and evaporation to half the volume, the precipitate was crystallized from water. There was obtained 0.04 g (32%) of acetanilide; mp 113°, identical with known sample. To the acetonitrile filtrate was added 30 ml of ether. The resin that separated was treated with ether several times, then crystallized (quickly!) from dry acetonitrile. Hydroperchlorate XV was obtained (Table 1).

Reaction of Salts XIa-e and XV with Ammonia. To 1 mmole of XIa-e and XV in 10 ml of acetonitrile was added 10 ml of 25% NH_4OH and the mixture was stirred at room temperature for 10 min. The yellow precipitate was crystallized from aqueous ethanol. The yield of 2,3-di(indolyl-3)quinoxaline XIV varied from 67 to 84%, mp 185-186°. Found: C 79.6; H 4.15; N 15.76%. $C_{24}H_{16}N$. Calculated: C 80.0; H 4.44; N 15.55%. IR spectrum: 3430 and 3450 (NH); 1550 cm^{-1} (C=N). UV spectrum (in alcohol), λ_{max} ($\varepsilon \cdot 10^{-3}$): 230 (60 ± 0.2), 235 sh (44 ± 0.2), 311 (20 ± 0.2), 330 nm (19 ± 0.1). Mass spectrum m/z* (%): 77 (11), 89 (6), 104 (12), 105 (6), 115 (16), 116 (14), 128 (12), 232 (7), 233 (5), 243 (80), 244 (31), 360 ($M^{+\cdot}$, 100).

LITERATURE CITED

1. A. K. Sheinkman, T. S. Chmilenko, G. G. Vdovkina, and A. I. Chernishev, Khim. Geterotsikl. Soedin., No. 6, 806 (1985).
2. T. V. Stupnikova, Z. M. Skorobogatova, and A. K. Sheinkman, Khim. Geterotsikl. Soedin., No. 7, 946 (1979).
3. A. K. Sheinkman, Z. M. Skorobogatova, and L. V. Luk'yanenko, Khim. Geterotsikl. Soedin., No. 3, 367 (1982).
4. F. D. Popp, Heterocycles, 14, 1033 (1980).
5. A. K. Sheinkman, Kh. Ya. Lopatinskaya, N. A. Klyuev, and Zh. K. Torosyan, Khim. Geterotsikl. Soedin., No. 2, 234 (1980).
6. V. M. Rudenko, A. Ya. Il'chenko, and Yu. S. Rozum, Dokl. Akad. Nauk Ukr. SSR, Ser. B, No. 2, 159 (1970).
7. O. N. Chupakhin, E. O. Sidorov, and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., No. 10, 1433 (1975).
8. V. N. Charushin, O. N. Chupakhin, and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., No. 8, 1146 (1976).
9. O. N. Chupakhin, E. O. Sidorov, I. I. Bil'kis, and S. M. Shein, Zh. Org. Khim., 12, No. 11, 2464 (1976).
10. A. Marxer, H. Salzman, and F. Hofer, Helv. Chim. Acta, 54, 2507 (1971).
11. T. V. Stupnikova, Z. M. Skorobogatova, A. K. Sheinkman, and V. A. Golubev, Dokl. Akad. Nauk Ukr. SSR, Ser. B, No. 2, 144 (1978).
12. Z. M. Skorobogatova, V. A. Golubev, and A. K. Sheinkman, Khim. Geterotsikl. Soedin., No. 1, 76 (1981).
13. T. V. Stupnikova, Kh. Ya. Lopatinskaya, B. P. Zemskii, and Yu. B. Vysotskii, and R. S. Sagitullin, Khim. Geterotsikl. Soedin., No. 10, 1365 (1980).
14. E. M. Kosower, in: New Problems in Physical Organic Chemistry [Russian translation], Mir, Moscow (1969), p. 40.
15. V. A. Golubev, R. O. Zhdanov, V. M. Giba, and É. G. Rozantsev, Izv. Akad. Nauk SSSR, Ser. Khim., No. 4, 853 (1971).

---

*The ten most intense peaks are given.