ISOELECTRONIC ANALOGS OF INDOLIZINE

V. Derivatives of Pyrrolo[1, 2-a]Benzimidazole*

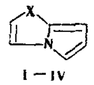
F. S. Babichev and A. F. Babicheva

Khimiya Geterotsiklicheskikh Soedinenii, Vol. 3, No. 5, pp. 917–922, 1967

UDC 547.74+547.785.5+543.422

A new method is offered for synthesizing hitherto unknown compounds of the pyrrolo[1, 2-a]benzimidazole series, involving heating quaternary salts prepared from 1, 2-dialkylbenzimidazoles and α-halogenoketones with sodium carbonate solution. The method is used to prepare 6 bases iso-electronic with the corresponding indolizine derivatives. The salts of the pyrrolo[1, 2-a]benzimidazoles give 2 series of cyanine dyes, those with a chain at the 1, 1' positions, and those with one at the 3, 3' positions. The anomalous value of the vinylene shift of the absorption maximum observed on passing from monomethine- to trimethinecyanines, is due to steric hindrance in molecules of monomethinecyanines.

Starting from the formula of indolizine, which is one of the nonbenzenoid heteroaromatic compounds, it is theoretically possible to pass to formulas of a series of compounds iso-electronic with it, and containing two heteroatoms. The formulas of the iso-electronic analogs of indolizine can be arrived at by replacing a vinylene group in the latter by the heteroatoms O, S, Se, or an NR group (R = H, Alk, Ar), when the formulas of compounds **I–IV** are obtained, where the indolizine 10 π-electron system is obtained by the coupling of two 5 electron rings.

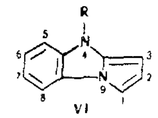


I—IV

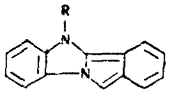
I X=O
II X=S
III X=Se
IV X=NR

Previous papers described the preparation of pyrrolo[2, 1-b]thiazole (II) [1, 2] and iso-indolo[1, 2-b]-benzothiazole (V) [3, 4]. Hitherto compounds of types I, **III**, and **IV** have not been described in the literature. Compounds of the pyrrolo[1, 2-a]benzimidazole (**VI**) and iso-indolo[1, 2-a]benzimidazole (**VII**) series are also unknown. Compounds of structures whose skeletons closely resemble **VII** are known [5–8], but they are not iso-electronic analogs of indolizine and do not have its characteristic system of bonds.

V

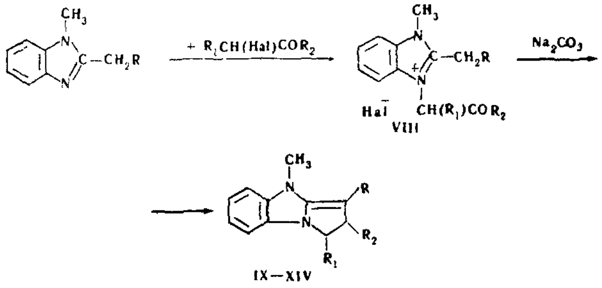


VI



VII

In the present work it is shown that derivatives VI can be obtained by the same method as pyrrolo[2, 1-b]-thiazoles [1]. Heating 1, 2-dialkylbenzimidazoles with α-halogeno ketones gives quaternary salts **VIII** and treatment of these with sodium carbonate converts them to pyrrolo[1, 2-a]benzimidazoles **IX–XIV**.

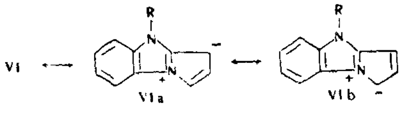


	R	R_1	R_2
IX	H	H	CH_3
X	H	H	C_6H_5
XI	CH_3	H	CH_3
XII	H	CH_3	C_6H_5
XIII	H	CH_3	CH_3
XIV	CH_3	H	C_6H_5

If sodium bicarbonate or triethylamine is used instead of sodium carbonate, pyrrolo[1, 2-a]benzimidazoles are not formed. The bases obtained are purer if sodium sulfite, inhibiting oxidation of the products, is present during the heating of quaternary salts **VIII** with sodium bicarbonate. The benzimidazole ring being highly basic, quaternary salts with α-halogenketones are very easily obtained (rather more easily than in the thiazole and benzothiazole series), so that here it is possible to synthesize the most diverse substituted pyrrolo[1, 2-a]benzimidazoles.

Unlike pyrrolo[2, 1-b]thiazoles and pyrrolo[1, -2-b]benzothiazoles, pyrrolo[1, 2-a]benzimidazoles are rather strong bases, giving with mineral acids salts which can be crystallized from water*. With picric acid they form picrates.

The structure of pyrrolo[1, 2-a]benzimidazole, and those of the other 10 π-electron heterocyclic compounds, are not only represented by the nonpolar formulas VI, but also by dipolar structures **VIa**, VIb where the entire ring has an aromatic sextet of electrons. Such compounds, with enhanced electron density in the pyrrole part of the molecule,



should react readily with electrophilic reagents.

Preliminary experiments showed that **VI** derivatives lacking a substituent at position 1 or 3, indeed

---

*For previous parts see [1-4].

*The question of the structure of the salts will be considered in a subsequent paper.

react with electrophilic reagents, and that their salts give cyanine dyes with the appropriate intermediates. Heating **XI** with acetic anhydride gives a 1-acetyl derivative **XV**, and **XIII** gives a 3-acetyl derivative **XVI**. The IR spectrum of this compound has an intense absorption band at 1620–1640 cm^{-1}, corresponding to a carbonyl group. Both 1- and 3-acetyl derivatives are easily hydrolyzed with hot hydrochloric acid, with splitting off of an acetyl group, and formation of a salt of XI and XIII respectively. In this respect the acetyl derivatives of pyrrolo[1,2-a]benzimidazole resemble the acyl derivatives of iso-indolo[1,2-b]-benzothiazole [3], and 5- and 7-acyl derivatives of pyrrolo[2,1-b]thiazole [1]. Similar properties are possessed by all compounds with an acyl group on a carbon atom where there is enhanced electron density (1- and 3-acyl derivatives of indolizine, acylmethylene bases, etc).

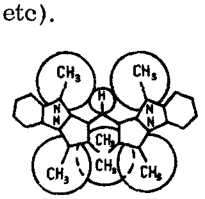
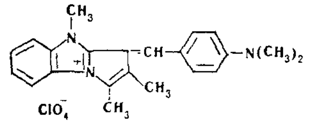
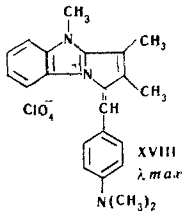


Fig. 1. Steric hindrance in a molecule of dye XIX (plane projection).

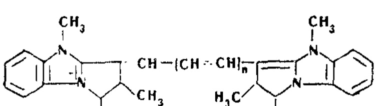
Derivatives of pyrrolo[1,2-a]benzimidazole give two series of cyanine dyes. XI gives cyanine dyes when the polymethine chain starts at position 1, while isomeric **XIII** gives dyes with the chain at position 3. There is a substantial difference in the colors of these two types of dyes. Lengthening of the internal chain by two carbon atoms in molecules of dyes which are styrenes (see compounds **XVII**, **XVIII**), quite unexpectedly results not in a bathochromic, but in a hypsochromic shift of the absorption maximum (by 13 mμ). With the symmetrical monomethine dyes **XIX** and **XX**, the transition leads, as would be expected, to deepening of the color (by 44 mμ).

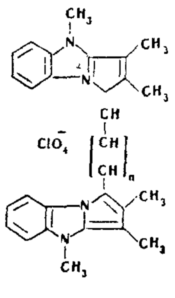


XVII λmax 528 mμ



XVIII λmax 515 mμ





XIX, $n=0$, λmax 569 mμ
XXI, $n=1$, λmax 608 mμ

XX, $n=0$, λmax 613 mμ
XXII, $n=1$, λmax 678 mμ

Trimethinecyanines **XXI** and **XXII** were prepared by condensing the perchlorates of XIII and XI, respectively, with β-ethoxyacroleindiethylacetal in dimethylformamide. Comparison of absorption maxima of trimethinecyanines and monomethinecyanines shows the vinylene shift for dyes with a polymethine chain at positions 1,1' to be 65 mμ, and with 3,3'-cyanines, to be 39 mμ. Obviously the difference found for the vinylene absorption maxima is considerably less than that usually found for cyanine dyes. For example in the case of thiacyanines, the vinylene shift of the absorption maximum on passing from monomethinethiacyanines to trimethinethiacyanines is 135 mμ, and on passing from trimethinethiacyanines to pentamethinethiacyanine, it is 94 mμ [9]. Possibly such an abnormally low value of the vinylene difference for dyes which are derivatives of **VI** is connected with steric hindrance in the molecules of monomethinecyanines. Projections of molecules of monomethinecyanines drawn with the right covalent and interference radii, and valence angles (Figs. 1 and 2), show that there is really steric hindrance in the molecules of these dyes.

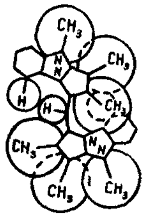


Fig. 2. Steric hindrance in molecule of dye XX (plane projection).

EXPERIMENTAL

QUATERNARY SALTS

1-Acetonyl-2,3-dimethylbenzimidazolium bromide (XXV). 2 g (0.014 mole) 1,2-Dimethylbenzimidazole [10] and 1.9 g (0.014 mole) bromoacetone in 10 ml toluene were heated for 10 min at 100°. The crystals were washed with benzene, then with ether, yield 3.2 g (0.011 mole, 82%), mp 234° (ex PrOH). Found: Br 28.07, 28.19%, calculated for $C_{12}H_{15}BrN_2O$: Br 28.21%.

1-methyl-2-ethylbenzimidazole bromophenylacylate (XXVI). Prepared similarly to XXV, using 7 g (0.044 mole) 1-methyl-2-ethylbenzimidazole and 8.7 g (0.044 mole) bromoacetophenone in 25 ml toluene (40 min heating). Yield 13.4 g (0.037 mole, 85%), colorless prisms, mp 239° (ex PrOH). Found: Br 22.06, 21.98%, calculated for $C_{18}H_{19}BrN_2O$: Br 22.24%.

1-Methyl-2-ethylbenzimidazole was obtained by methylating 2-ethylbenzimidazole with Me_2SO_4, similarly to [10], yield 45%, mp 62°.

1-Methyl-2-ethyl-3-acetonylbenzimidazolium bromide (XXVII). Prepared from 11.4 g (0.071 mole) 1-methyl-2-ethylbenzimidazole and 9.8 g (0.071 mole) bromoacetone. The product was washed repeatedly with acetone and ether, yield 14.4 g (0.049 mole, 68%), mp 266° (ex PrOH). Found: Br 27.06, 27.09%, calculated for $C_{13}H_{17}BrN_2O$: Br 26.88%.

1,2-Dimethyl-3-(butan-2'-on-3'-yl) benzimidazolinium bromide (XXVIII). 15 g (0.102 mole) 1,2-dimethylbenzimidazole, 15.6 g (0.103 mole) methyl-α-bromoethyl ketone, and 20 ml toluene were heated together for 45 min at 100°. The product which came down after 14 hr was recrystallized, and washed with acetone and ether.

Yield 20 g (0.067 mole, 65%), mp 255° (ex iso-PrOH). Found: Br 27, 27.13; 27.00%, calculated for $C_{13}H_{17}BrN_2O$: Br 26.88%.

PYRROLO[1, 2-a]BENZIMIDAZOLES

2, 4-Dimethylpyrrolo[1, 2-a]benzimidazole (IX). 4 g **XXV** was heated for 2 hr at 80°–90° with 180 ml 0.7% Na_2CO_3 solution, containing 1.6 g sodium sulfite. A pale yellow oil formed, which crystallized on cooling. It was extracted with ether, yield 1.2 g (46%), colorless plates, mp 90° (ex MeOH). Found: N 15.19; 15.25%, calculate for $C_{12}H_{12}N_2$: N 15.21%.

2, 4-Dimethylpyrrolo[1, 2-a]benzimidazolium perchlorate (XXIX). 3 g impure base **IX** was dissolved in 6 ml hot HC1 (1:1), 2.5 ml 42% $HClO_4$ added, and after cooling the product filtered off, washed with water, acetone, and ether. Yield 4.3 g (93%), colorless needles, mp 199°–200° (ex EtOH). Found: Cl 12.33; 12.29; N 10.02; 10.20%, calculated for $C_{12}H_{12}N_2 \cdot HClO_4$: Cl 12.45; N 9.84%.

2-Phenyl-4-methylpyrrolo 1, 2-a benzimidazole (X). Prepared similarly to base **IX**, colorless needles, mp 114° (ex EtOH). Found: N 11.51; 11.68%, calculated for $C_{17}H_{14}N_2$:H 1:N 11.39%.

2-Phenyl-4-methylpyrrolo[1, 2-a]benzimidazolium chloride. mp 273° (ex water). Found: Cl 12.48; 12.34%, calculated for $C_{17}H_{14}N_2 \cdot HCl$. Cl 12.54%.

2-Phenyl-4-methylpyrrolo[1, 2-a]benzimidazolinium iodide, obtained by treating the hydrochloride with KI, yellow needles, mp 276°. Found: N 7.37; 7.23%, calculated for $C_{17}H_{14}N_2 \cdot HI$:N 7.48%.

2, 3, 4-Trimethylpyrrolo[1, 2-a]benzimidazole (XI). 3 g **XXVII** was heated with 120 ml 0.7% Na_2CO_3 solution for 40 min at 90–95°. Yield 1 g (50%), colorless plates, mp 99° (ex MeOH), which turned green on keeping in air. Found: N 14.12; 14.32%, calculated for $C_{13}H_{14}N_2$: N 14.13%.

Picrate, yield 84%, yellow plates, mp 164° (ex EtOH). Found: N 16.50; 16.47%, calculated for $C_{13}H_{14}N_2 \cdot C_6H_3N_3O_7$:N 16.39%.

2, 3, 4-Trimethylpyrrolo 1, 2-a benzimidazolium perchlorate (XXX), from the base and $HClO_4$, yield 92%, mp 212°, (ex water). Found: Cl 11.90; 12.03%, calculated for $C_{13}H_{14}N_2 \cdot HClO_4$:Cl 11.87%.

1-Acetyl-2, 3, 4-trimethylpyrrolo[1, 2-a]benzimidazole (XV). 0.4 g base **XI** and 3 ml Ac_2O were refluxed together for some minutes. The product which came down on cooling filtered off and washed with Ac_2O and EtOH. Yield 0.25 g (52%), colorless needles, mp 199° (ex EtOH). Found: N 11.84; 11.99%, calculated for $C_{15}H_{16}N_2O$: N 11.66%.

Hydrolysis of product XV. 0.15 g compound **XV**, 1 ml conc HC1, and 3 ml water were refluxed together for 5 min, then 0.8 ml 42% $HClO_4$ added. The crystals that precipitated were filtered off, washed with water, then with EtOH, and finally with ether, yield 0.2 g, mp 212° (ex water). Undepressed mixed mp with **XXVII.**

1, 4-Dimethyl-2-phenylpyrrolo[1, 2-a]benzimidazole (XII). 3 g 1, 2-dimethylbenzimidazole, 4.4 g phenyl-α-bromoethyl ketone, and 7 ml toluene were heated together for 30 min at 100°. On long standing the oil that had formed solidified. It was washed with ether, whereupon it gave 5.5 g (74%), quaternary salt. 5.3 g of the salt was dissolved in 200 ml 0.8% Na_2CO_3 solution, the suspension formed extracted with ether, and the transparent solution heated for 1 hr at 90°–95°. Base **XII** came down as a pale yellow oil, which solidified on cooling, yield 3.2 g (85%). Recrystallization from MeOH gave 1.84 g (53%) large yellow plates, mp 145°–146°. Found: N 10.51; 10.60%, calculated for $C_{18}H_{16}N_2$: N 10.76%

Picrate, yield 95%, yellow needles mp 185° (ex EtOH). Found: N 14.44; 14.51%, calculated for $C_{18}H_{16}N_2 \cdot C_6H_3N_3O_7$: N 14.31%.

Hydroxide of base XII. 1 g Base was dissolved in hot HCl (1 : 1), a small amount of sodium sulfite added, and 0.9 g KI. The salt came down as an oil, which rapidly crystallized. The product was washed with water, EtOH, Me_2CO, and ether. Yellow needles, yield 1.06 g (75%), mp 245° (ex acidified water). Found: N 7.43; 7.31%, calculated for $C_{18}H_{16}N_2 \cdot HI$: N 7.22%.

1, 4-Dimethyl-2-phenylpyrrolo[1, 2-a]benzimidazolium perchlorate, pale yellow crystals, mp 208° (ex water, acidified with HCl). Found: Cl 9.53; 9.62%, calculated for $C_{18}H_{16}N_2 \cdot HClO_4$: Cl 9.83%.

1, 2, 4-Trimethylpyrrolo[1, 2-a]benzimidazole (XIII). Prepared from 7 g **XXVIII** (heated for 1 1/2 hr at 80°), yield 3.2 g (69%), recrystallization from MeOH gave 1.1 g (24%), colorless plates, mp 96°, which slowly turned red in air. Found: N 14.02; 14.16%, calculated for $C_{13}H_{14}N_2$: N 14.13%.

1, 2, 4-Trimethylpyrrolo[1, 2-a]benzimidazolium perchlorate (XXXI), prepared similarly to **XXIX**, yield 99%, colorless needles, mp 178° (ex EtOH). Found: Cl 11.96; 12.02%, calculated for $C_{13}H_{14}N_2$ · C1 11.78%.

3-Acetyl-1, 2, 4-trimethylpyrrolo[1, 2-a]benzimidazole (XVI), prepared similarly to XV, colorless long needles, mp 131° (ex EtOH). Found: $C_{13}H_{14}N_2 \cdot C_6H_3N_3O_7$, calculated for $C_{15}H_{16}N_2O$: N 11.66%. Heating the acetyl derivative with HC1 for 5 min led to splitting off of the acetyl group and formation of **XXXI.**

3, 4-Dimethyl-2-phenylpyrrolo[1, 2-a]benzimidazole (XIV), prepared* from 1 g XXVI by heating with NaOEt in EtOH, yield 66%, mp 36° (ex EtOH). Found: N 10.58; 10.60%, calculated for $C_{18}H_{16}N_2$: N 10.76%.

CYANINE DYES

3-(p-Dimethylaminobenzylidene)-1, 2-4-trimethylpyrrolo 1, 2-a benzimidazolium perchlorate (XVII). 0.2 g salt **XXXI**, 0.1 g p-dimethylaminobenzaldehyde, and 2 ml Ac_2O, were boiled together for 10 min, the dye was filtered off and washed with Ac_2O, then with EtOH, and finally with ether. Yield 0.12 g (41%), mp 236° (ex EtOH). Found: Cl 8.37; 8.41%, calculated for $C_{22}H_{24}ClN_3O_4$: Cl 8.25%.

1-(p-Dimethylaminobenzylidene)-2, 3, 4-trimethylpyrrolo[1, 2-a]-benzimidazolium perchlorate (XVIII), prepared similarly to the above dye, from salt **XXX**. Yield 69%, mp 232° (ex EtOH). Found: Cl 8.08; 7.96; N 9.97%, calculated for $C_{22}H_{24}ClN_3O_4$: Cl 8.25; N 9.77%.

Bis(1, 2, 4-trimethylpyrrolo[1, 2-a]benzimidazole-3)monomethinecyanine perchlorate. (XIX). 0.3 g perchlorate **XXXI**, 0.3 g orthoformic ester, and 2 ml pyridine were refluxed together for 15 min. The dye was then precipitated with ether, and recrystallized from EtOH, yield 0.04 g (16%), mp 210°. Found: Cl 7.07; 7.10%, calculated for $C_{27}H_{27}ClN_4O_4$: Cl 6.99%.

Bis(2, 3, 4-trimethylpyrrolo[1, 2-a]benzimidazole-1)monomethinecyanine perchlorate. 0.3 g perchlorate **XXX**, 0.3 g dimethylformamide dimethylacetal [11, 12] and 2 ml dimethylformamide were refluxed together for 10 min. Dye yield 0.15 g (58%), dark-green crystals, mp 290° (ex EtOH). Found: Cl 7.14; 7.20%, calculated for $C_{27}H_{27}ClN_4O_4$: Cl 6.99%.

Bis(1, 2, 4-trimethylpyrrolo[1, 2-a]benzimidazole-3)trimethinecyanine perchlorate. (XXI). A solution of 0.3 g perchlorate **XXXI**, 0.3 g β-ethoxyacroleindiethylacetal, 4 drops Et_3N in 2 ml dimethylformamide was refluxed for 10 min. After 12 hr the dye was filtered off, carefully washed with dimethylformamide, EtOH, and ether. Yield 0.14 g (56%), dark green needles, mp 245°. Found: Cl 6.87; 7.00%, calculated for $C_{29}H_{29}ClN_4O_4$: Cl 6.65%.

Bis(2, 3, 4-trimethylpyrrolo[1, 2-a]benzimidazole-1)trimethinecyanine perchlorate (XXII). 0.3 g perchlorate **XXX** and 0.3 g β-ethoxyacroleindiethylacetal were dissolved in 3 ml dimethylformamide, and 4 drops Et_3N added. The dye formed without heating, green needles, yield 0.17 g (63%), mp > 350° (ex dimethylformamide). Found: Cl 6.96; 7.02%, calculated for $C_{29}H_{29}ClN_4O_4$: Cl 6.65%.

REFERENCES

1. V. K. Kibirev and F. S. Babichev. Ukr. khim. zh., 30, 488, 1964.

2. F. S. Babichev, V. K. Kibirev, and L. G. Khil'ko, Ukr. khim. zh., 32, 79, 1966.

3. F. S. Babichev and V. K. Kibirev, ZhOKh, 33, 2000, 1963.

---

*G. P. Kutrov.

4. F. S. Babichev and V. K. Kibirev, ZhOKh, **33**, 3646, 1963.

5. A. Bistricki and W. Schmutz, Ann., **415**, 11, 1918.

6. M. Betrabet and G. Chakravarti, J. Indian Chem. Soc., 7, 495, 1930; C., II, 3025, 1930.

7. F. Spartore and G. Bignardi, Gazz. chim. ital., 92, 606, 1962.

8. W. Mosby, Heterocyclic Systems with Bridgehead Nitrogen Atoms, Part 1, N. Y., 1961.

9. I. I. Levkov, A. F. Vompe, and N. N. Sveshnikov, Khim. nauka i prom., 3, 597, 1958.

10. M. Le Bris, H. Wahl, and T. Jambu, Bull. soc. chim. France, 343, 1959.

11. H. Meermein, W. Florian, N. Schön and G. Stopp, Ann., **641**, 1, 1961.

12. Z. Arnold and M. Kornilow, Coll., **29**, 649, 1964.

11 January 1966

Kiev State University