Canadian Journal of Chemistry

Issued by THE NATIONAL RESEARCH COUNCIL OF CANADA

VOLUME 32 JULY 1954 NUMBER 7

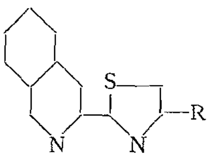
ANALOGUES OF 2,2′-BIPYRIDYL WITH ISOQUINOLINE AND THIAZOLE RINGS. PART II[1]

BY F. R. CROWNE AND J. G. BRECKENRIDGE

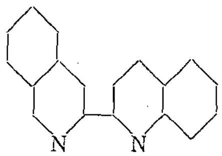
ABSTRACT

In continuation of the work reported in Part I, several more bipyridyl analogues have been prepared and the absorption spectra of the cuprous and ferrous complexes determined. The results follow the pattern of the previous series of compounds.

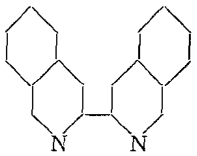
In an earlier paper (5) we reported the synthesis of a number of bipyridyl analogues and their reactions with cuprous and ferrous ion. Some of these were 1-isoquinolyl derivatives. In the present paper we report the synthesis of several analogues with the isoquinoline ring connected in the 3-position. Examples of this type in the literature are confined to 3,3′-biisoquinolyl, prepared by Case (1), who reported that it gave an orange color with ferrous ion, but gave no further details. We have repeated his synthesis, and have prepared in addition four new compounds; the structures of all these are shown below. In order to avoid confusion with those described earlier, the present compounds are numbered XVII to XXI, in continuation of the previous series.



XVII R = H
XVIII R = CH_3
XIX R = C_6H_5



XX



XXI

On the basis of our present knowledge of this type of compound, those with no "ortho" blocking groups (XVII, XXI) should react with ferrous ion, while the remainder should react only with cuprous ion; this was confirmed. Experimental work on the absorption spectra of the complexes was carried

---

[1] *Manuscript received March 16, 1954.*
Contribution from the Department of Chemical Engineering, University of Toronto, Toronto, Ont.
Condensed from the M.A.Sc. thesis of F. R. Crowne.

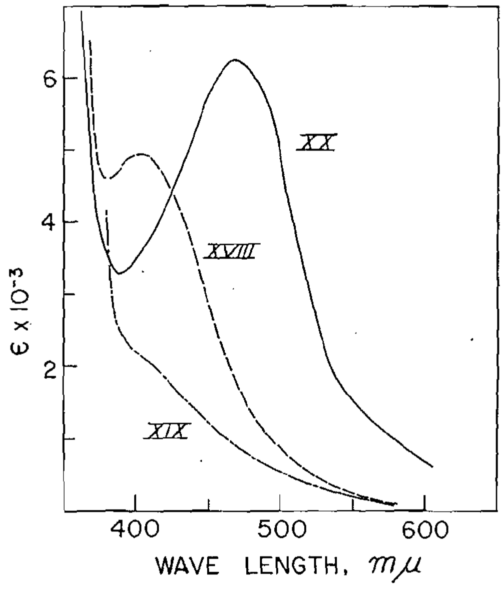
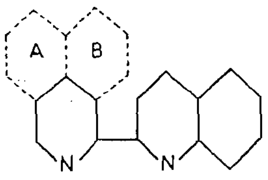


FIG. 1. Absorption spectra of copper complexes of compounds XVIII, XIX, XX.

out in the same manner as for the previous group; Fig. 1 shows the absorption spectra in the visible region for the cuprous complexes of compounds XVIII, XIX, and XX, all of which were extractable by isoamyl alcohol.

The depressing effect of a phenyl group in the "ortho" position (as compared to a methyl group) on the value for ϵ_{max} is evident (compare XVIII and XIX); this is the same as was observed in the previous series. The two compounds (XVII, XXI) with no "ortho" group gave weakly colored unstable complexes, the spectra of which were not determined. It is of interest to compare the value for ϵ_{max} for XX with that found by Hoste (3) for the isomeric 1-(2-quinolyl) isoquinoline:



Cuprous complexes
A—ϵ_{max} = 6230 at 470 mμ
B—ϵ_{max} = 2550 at 495 mμ

The fused ring in position B should not result in any appreciable hindrance to planarity, so that the steric situation in the immediate vicinity of the metal ion should be the same in both cases.

Compounds XVII and XXI behaved in a similar manner toward ferrous ion; both gave orange complexes which were highly dissociated, and we were unable to calculate accurate values for the molar extinction coefficients. The absorption spectra are shown in Fig. 2. Irving and Williams have predicted (4) that XXI should give an extractable complex with ferrous ion,

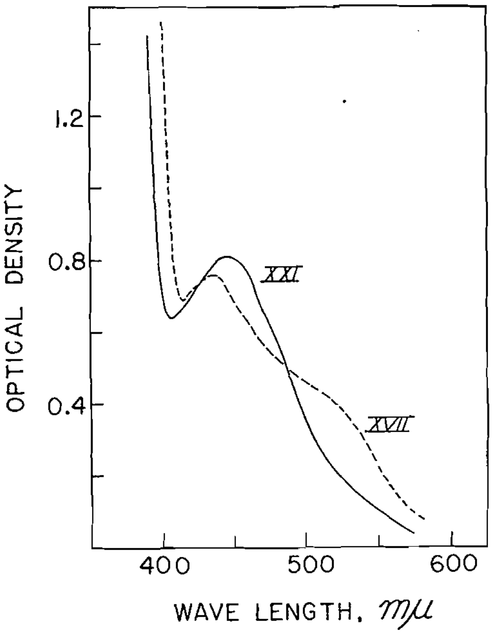


FIG. 2. Absorption spectra of iron complexes of compounds XVII, XXI.

and that it should be a more sensitive reagent than 2,2'-bipyridyl, which has a value of $\epsilon_{\max}$ of 8700 at 522 mμ (6). We have confirmed this, since the complex is indeed extractable by isoamyl alcohol, and an approximate value for $\epsilon_{\max}$ is 14200 at 445 mμ.

EXPERIMENTAL

Melting points are corrected: microanalyses by Micro-Tech Laboratories, Skokie, Ill.

Isoquinoline-3-aldoxime

Isoquinoline-3-carboxaldehyde, prepared from 3-methylisoquinoline by the method of Case (1), was condensed with an equimolar amount of hydroxylamine hydrochloride in aqueous ethanol. The mixture was made alkaline and poured into water, and the product recrystallized from ethanol. Yield nearly theoretical, m.p. 197–197.5°C. Calc. for $C_{10}H_8ON_2$: C, 69.75; H, 4.68; N, 16.27%. Found: C, 69.80, 69.83; H, 4.54, 4.65; N, 15.94, 16.07%.

3-Cyanoisoquinoline

The aldoxime, (19.5 gm.) was warmed with acetic anhydride (25 gm.), and after the vigorous reaction had subsided, the mixture was refluxed for two hours and then poured into water. The product was extracted with petroleum ether and recrystallized from ethanol in 80% yield, m.p. 127.5–128°C. Calc. for $C_{10}H_6N_2$: C, 77.90; H, 3.92; N, 18.17%. Found: C, 78.23, 78.34; H, 3.98, 3.97; N, 17.91, 18.00%.

Isoquinoline-3-thiocarboxamide

Five grams of the cyano compound was dissolved in 200 ml. ethanol, and ammonia was bubbled through the solution, followed by hydrogen sulphide. The yellow precipitate which appeared on standing was crystallized from ethanol. Yield theoretical, m.p. 198–198.5°C. Calc. for $C_{10}H_8N_2S$: C, 63.80; H, 4.28; N, 14.80%. Found: C, 63.90, 64.14; H, 4.48, 4.40; N, 14.97, 15.13%.

3-(2-Thiazole)isoquinoline (XVII)

Isoquinoline-3-thiocarboxamide (5 gm.) and ethyl α,β-dichloroethyl ether (5 gm.) were dissolved in 230 ml. 75% ethanol and the solution refluxed for 12 hr. A further 4 gm. of the ether was added and refluxing continued for eight hours more. The solution was concentrated to 100 ml., made alkaline, and extracted with petroleum ether. Evaporation of the extract left an orange oil, which was crystallized from petroleum ether. Yield 10%, m.p. 116–117°C. Calc. for $C_{12}H_8N_2S$: C, 67.90; H, 3.80; N, 13.20%. Found: C, 67.86, 68.06; H, 3.85, 3.94; N, 12.87, 12.77%.

3-(4-Methyl-2-thiazole)isoquinoline (XVIII)
3-(4-Phenyl-2-thiazole)isoquinoline (XIX)

These were prepared by condensation of the thiocarboxamide with chloroacetone and ω-chloroacetophenone in ethanol. The products were recrystallized from ethanol; yield about 80% in both cases. Data for XVIII: m.p. 150–151°C.; calc. for $C_{13}H_{10}N_2S$: C, 69.00; H, 4.46; N, 12.38%; found: C, 69.00, 69.01; H, 4.55, 4.53; N, 12.34, 12.11%. Picrate m.p. 184.5–185°C.; calc.; N, 15.38%; found: N, 14.92, 15.06%. Data for XIX: m.p. 173.5–174°C.; calc. for $C_{18}H_{12}N_2S$: C, 74.97; H, 4.20; N, 9.72%; found: C, 75.13, 75.15; H, 4.11, 4.16; N, 9.70, 9.84%. Picrate m.p. 191.5–192°C.; calc.: N, 13.54%; found: N, 13.40, 13.60%.

3-Acetylisoquinoline

To a Grignard reagent in ether prepared from 2.6 gm. magnesium and 14.8 gm. methyl iodide was added 11 gm. 3-cyanoisoquinoline in 600 ml. ether. The mixture was warmed gently and shaken, a voluminous precipitate appearing. Most of the ether was distilled off, 200 ml. dry benzene added, and the mixture refluxed for one hour and then cooled. Crushed ice and 50 ml. cold 50% sulphuric acid were added slowly, an orange precipitate appearing in the aqueous layer. The benzene layer was extracted with acid, and the combined acid portions made alkaline and steam-distilled. The product was recrystallized from ethanol, yield 60%, m.p. 92–92.8°C. Calc. for $C_{11}H_9ON$: C, 77.17; H, 5.30; N, 8.23%. Found: C, 77.21, 77.31; H, 5.18, 5.34; N, 8.21, 8.40%. Clemo and Popli (2) report m.p. 88°C. for this compound.

3-(2-Quinolyl)isoquinoline (XX)

To a solution of 3.4 gm. *o*-aminobenzaldehyde in 25 ml. 95% ethanol was added a solution of 4.5 gm. 3-acetylisoquinoline in 75 ml. 95% ethanol. Potassium hydroxide in ethanol (1.5 ml., 1 *N*) was added, and the mixture refluxed for two hours and cooled. The product was recrystallized from ethanol, yield 50%, m.p. 151.5–152°C. Calc. for $C_{18}H_{12}N_2$: C, 84.35; H, 4.72; N, 10.93%. Found: C, 84.40, 84.52; H, 4.80, 4.77; N, 11.11, 11.10%. Picrate m.p. 245.5–246°C.; calc.: N, 14.43%; found: N, 14.68, 14.55%.

ACKNOWLEDGMENT

We wish to acknowledge with thanks financial assistance provided by the Advisory Committee on Scientific Research, University of Toronto.

REFERENCES

1. Case, F. H. J. Org. Chem. 17: 471. 1952.
2. Clemo, G. R. and Popli, S. P. J. Chem. Soc. 1406. 1951.
3. Hoste, J. Anal. Chim. Acta, 4: 23. 1950.
4. Irving, H. and Williams, R. J. P. Analyst, 77: 813. 1952.
5. Knott, R. F. and Breckenridge, J. G. Can. J. Chem. 32: 512. 1954.
6. Moss, M. L. and Mellon, M. G. Ind. Eng. Chem. Anal. Ed. 14: 862. 1942.