phenylindene-5,6-dicarboxylate gave the 1,1,3-trideuterio derivative.

6,8-Dimethyl-7-phenyl-7H-benzocyclohepten-7-ol (35).—Phenyllithium (4.0 ml of a solution in benzene–ether, 8.57 mmoles) was added slowly under nitrogen to a solution of 1.32 g (7.17 mmoles) of **5** in 15 ml of benzene at 10°. After 20 min at 25°, the reaction was treated with water and ether giving 1.75 g (6.67 mmoles, 93%) of colorless crystals, mp 109.5–110.5° (hexane).

Anal. Calcd for $C_{19}H_{18}O$: C, 86.98; H, 6.91. Found: C, 87.12; H, 7.19.

6,8-Dimethyl-7-phenylbenzotropylium Perchlorate (36).—Alcohol **35** (759 mg, 2.90 mmoles) in 6.0 ml of ether was treated with 1.0 ml of concentrated perchloric acid giving a yellow solid. Recrystallization from methylene chloride gave 942 mg (2.66 mmoles, 81.7%) of yellow, fluorescent crystals, mp 163–165°.

Anal. Calcd for $C_{19}H_{17}ClO_4$: C, 66.19; H, 4.97. Found: C, 66.38; H, 5.02.

6,8-Dimethyl-2,7-diphenyl-1,7-dihydrocyclohept[*f*]inden-7-ol (37).—A solution of **26** (605 mg, 2.03 mmoles) in 10 ml of benzene was treated with 2.10 ml (4.50 mmoles) of a phenyllithium solution in benzene–ether. After 45 min under nitrogen the reaction was treated with water and chloroform to give 577 mg (154 mmoles, 76%) of colorless crystals, mp 184–185° (chloroform).

Anal. Calcd for $C_{28}H_{24}O$: C, 89.32; H, 6.43. Found: C, 89.13; H, 6.42.

Attempts to dehydrate this alcohol with sodium methoxide in dimethyl sulfoxide or with alumina in benzene were unsuccessful.

6,8-Dimethyl-2,7-diphenyl-1H-cyclohept[*f*]indenium Perchlorate (36).—Concentrated perchloric acid (5.0 ml) was added to a solution of **37** (868 mg, 2.30 mmoles) in 40 ml of methylene chloride. Addition of 25 ml ether and cooling gave 959 mg (2.09 mmoles, 90.5%) of maroon crystals which did not melt at 300°.

Anal. Calcd for $C_{28}H_{23}ClO_4$: C, 73.29; H, 5.05. Found: C, 73.25; H, 5.29.

Attempted Synthesis of 6,8-Dimethyl-2,7-diphenylcyclohept[*f*]-indene.—Perchlorate **36** (166 mg) was suspended in 2.0 ml of dry methylene chloride and treated with 0.2 ml of dry triethylamine. After 1 min, the solution turned from dark red to yellow and the maroon crystals dissolved. Removal of solvents under vacuum gave 200 mg of a tan solid, whose infrared spectrum showed protonated amine and whose nmr spectrum showed aromatic, olefinic, and ethyl peaks with a reduced indene methylene peak.

Syntheses of Indolizino- and Dihydroindolizinoquinoxalines

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Received September 21, 1965

A 47% yield of the benzoindolizinoquinoxaline (**8**, Scheme I) was obtained in one step upon reaction of 2,3-dichloroquinoxaline (**1**) with ethyl cyanoacetate and isoquinoline. The assigned structure is based on the results of determinations of the molecular weight and infrared absorption spectrum as well as on analogies with related reactions carried out in these laboratories. An 80% yield of cyano ester **3** was obtained from ethyl cyanoacetate and 2,3-dichloroquinoxaline and a 74% yield of related dicyano compound **6** was obtained from malononitrile and 2,3-dichloroquinoxaline. Reaction of either **3** or **6** with isoquinoline gave **8**. Reaction of **3** with pyridine gave **23** (Scheme II), the expected analog of **8**, but reaction of **6** with pyridine gave dihydrodicyanoindolizinoquinoxaline **26** in 84% yield. Upon treating 2,3-dichloroquinoxaline with the sodium salt of 2-phenacylquinoline, a 24% yield of the benzoindolizinoquinoxaline (**2**, Scheme I) containing a ring system not available by the other methods was obtained. A number of analogs of the foregoing products were prepared and routes of reaction are proposed.

It has been found that 2,3-dichloroquinoxaline (**1**) reacts with isoquinoline and ethyl cyanoacetate to give a 47% yield of 14-cyanobenz[*a*]indolizino[2,3-*b*]-quinoxaline (**8**, Scheme I). Low yields of **8** and **9** were obtained when benzoylacetonitrile and ethyl acetoacetate were employed in place of the ethyl cyanoacetate. Here three bonds of the central pyrrole ring are established in one step. The molecular weight of **8** was found[3] to be close to the calculated value and bands ascribed to the cyano and carbonyl groups appeared at 2200 and 1675 cm^{-1} in the infrared absorption spectra of **8** and **9**. The close analogy of these reactions with the previously reported[4] reaction of 2,3-dichloro-1,4-naphthoquinone, isoquinoline, and ethyl cyanoacetate to give **12** supports the assigned structures. Other syntheses reported herein for **8**, and its analogs obtained with pyridines (**23**, **24**, and **25**; Scheme II), supply additional confirmation.

The one-step synthesis of **8** is most simply envisaged as proceeding *via* **1** → **3** → **10** → **11** → **8** (Scheme I). It was previously proposed[5] that the quinone analogs of **10** underwent solvolytic cleavage (*e.g.*, of the carbethoxyl group) before the cyclization (**10** → **11**), but such a cleavage or cleavage by loss of alkyl carbonate[6] appears improbable in the one-step synthesis of **8** since water, alcohols, and strong bases are absent. The isolation of compounds analogous to **11** (*cf.* **26** through **29**, Scheme II) further supports the proposal that the carbethoxyl group is eliminated (**11** → **8**) as ethyl formate.[7] This elimination is doubtlessly facilitated by the resonance stabilization of **8** involving contributing structures **13** and **14**. All seven of the indolizinoquinoxalines obtained are deeply colored, varying from orange to red, and hence may be of potential interest as dyes. No synthesis for these indolizinoquinoxaline ring systems was found in the literature.

The first reaction intermediate suggested above, compound **3**, and several of its analogs were readily obtained by interaction of 2,3-dichloroquinoxaline, an active methylene compound and potassium *t*-butoxide in *t*-butyl alcohol. The active methylene compounds used, the products, and the yields obtained under identical conditions were as follows: ethyl cyanoacetate, **3**, 80%; methyl cyanoacetate, **4**, 84%; *t*-butyl cyanoacetate, **5**, 59%; and malononitrile, **6**, 74%. Since the bands for the nitrile and carbonyl groups appeared in the infrared absorption spectra at

(1) From the Ph.D. Thesis of J. C. Keresztesy, Jr., July 1964.

(2) We wish to thank the National Institutes of Health for a Fellowship to J. C. K. for 1962–1964, which greatly aided the progress of this work.

(3) We wish to thank Mr. Donald Glover of the Naval Ordnance Laboratory for these determinations.

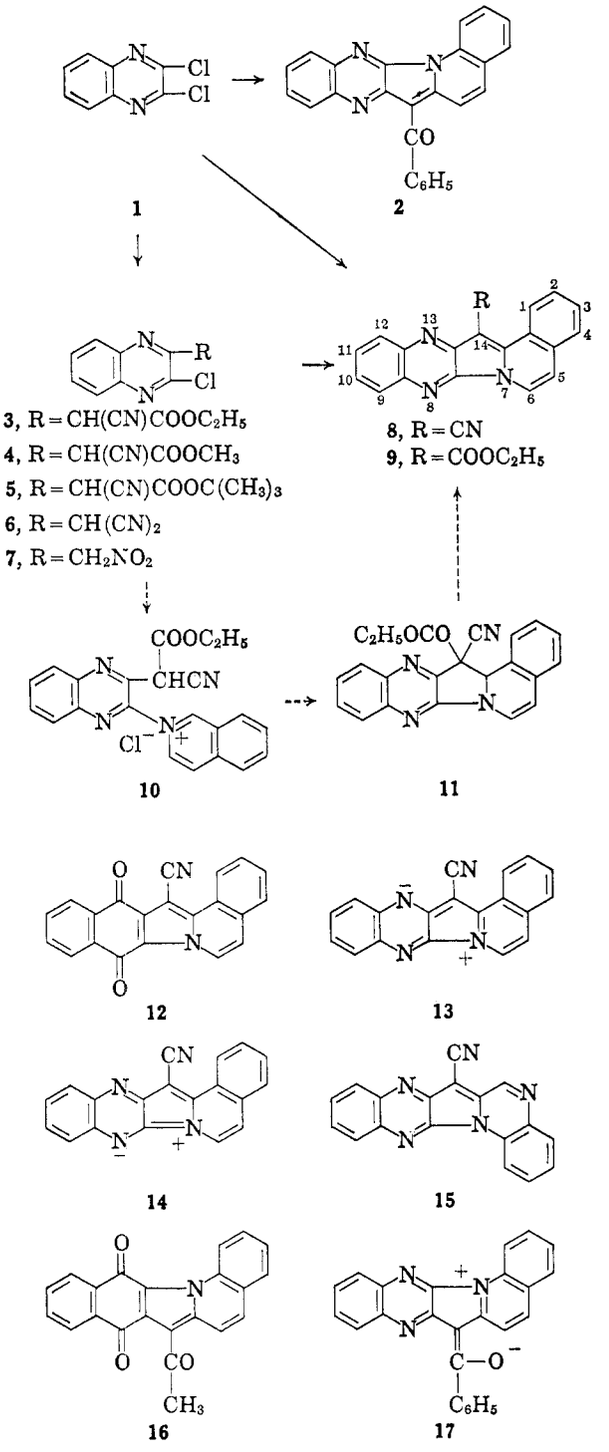
(4) E. F. Pratt, R. G. Rice, and R. W. Luckenbaugh, *J. Am. Chem. Soc.*, **79**, 1212 (1957).

(5) E. F. Pratt, R. W. Luckenbaugh, and R. L. Erickson, *J. Org. Chem.*, **19**, 176 (1954).

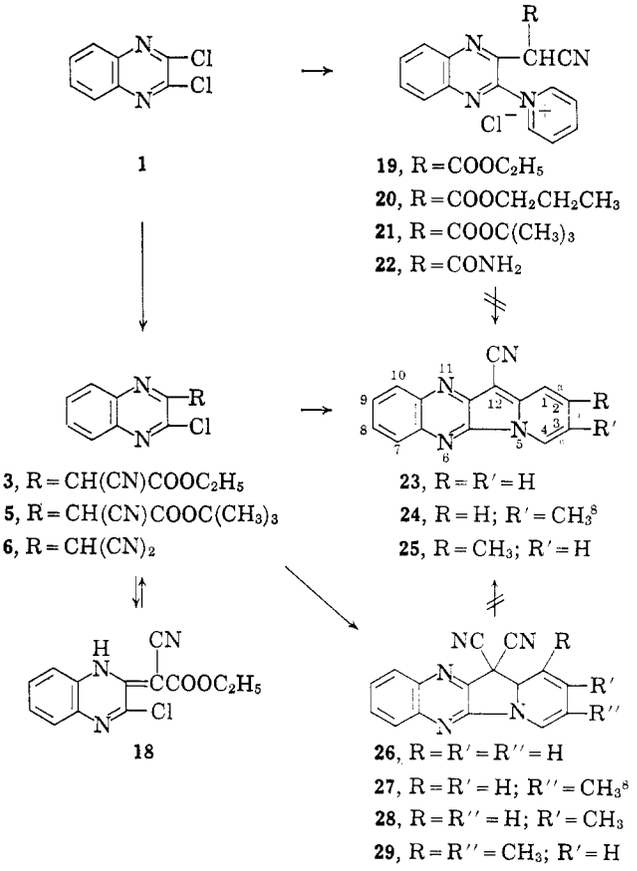
(6) A. C. Cope, H. L. Holmes, and H. O. House in *Org. Reactions*, **9**, 127 (1957).

(7) A related elimination for certain quinone analogs was first suggested by J. A. VanAllan, G. A. Reynolds, and R. E. Adel, *J. Org. Chem.*, **28**, 3520 (1963).

SCHEME I
SYNTHESES EMPLOYING QUINOLINES



SCHEME II
SYNTHESES EMPLOYING PYRIDINES



somewhat lower frequencies than normal, the tautomeric structures exemplified by **18** (Scheme II) may be correct. With nitromethane as the active methylene compound a 16% yield of the expected product (**7**) was obtained using a much longer reaction time. Attempts to employ several other highly active methylene compounds, such as dibenzoylmethane, were unsuccessful. Condensation of 2,3-dichloroquinoxaline with an active methylene compound appears not to have been reported previously.

In agreement with the reaction route proposed above, treatment of **3** or **6** with isoquinoline gave **8** as shown by the results of mixture melting point and infrared absorption spectra determinations.

As expected, treatment of **3** with pyridine gave **23** (Scheme II), and **24**[8] and **25** were obtained in analogous fashion using 3-picoline and 4-picoline in place of the pyridine. The molecular weight[3] of compound **23** was found to be close to the calculated value and bands ascribed to the nitrile group appeared in the infrared absorption spectra of all three products. Compound **23** was also prepared from the *t*-butoxynitrile **5** and pyridine. Although the results of analysis for nitrogen were not entirely satisfactory, a product believed to be **15** was obtained upon treatment of **3** with quinoxaline.

When ethanol was employed as the solvent in these syntheses of **23**, **24**, and **25**, the chlorine of **3** was solvolyzed to the ethoxyl group to a considerable extent. The yield of **23** almost doubled, to 42%, when benzene replaced the ethanol, but the yield of **25** remained low.

It was expected that dinitrile **6** would also react with pyridine to give **23**, but apparently the elimination step (**11** → **8**, Scheme I) did not occur; so dicyanodihydroindolizinoquinoxaline **26** was obtained. This is consistent with the foregoing interpretation that **11** eliminates ethyl formate to give **8** with no evidence of elimination of hydrogen cyanide to give **9**. Possibly a *trans* configuration of the carbethoxyl group and the adjacent hydrogen atom in **11** favors the elimination of ethyl formate. Attempts to eliminate hydrogen cyanide from **26** to give **23** were unsuccessful. Apparently, however, hydrogen cyanide was eliminated in the above-noted reaction of dinitrile **6**, with isoquinoline to give **8**, but the yield was only 8%.

(8) The possibility that the methyl group is at the 1 instead of the 3 position must be recognized, but steric considerations favor the latter.

The pyridines treated with dinitrile **6**, the products, and the yields were as follows: pyridine, **26**, 84%; 3-picoline, **27**,[8] 90%; 4-picoline, **28**, 86%; and 3,5-lutidine, **29**, 90%. Since the yields of these dicyanodihydroindolizinoquinoxalines were much higher than the yields of the just described indolizinoquinoxalines (**23**, **24**, and **25**), the elimination step may be the yield-determining one. Two bands ascribed to the nitrile groups were found in the infrared absorption spectra of compounds **26** through **29**. This would be expected since the hydrogen at the adjacent position (**12a**) would be *cis* to one nitrile group and *trans* to the other. Resonance involving a contributing structure analogous to **14** doubtlessly facilitates the formation of these compounds which varied in color from deep orange to deep red.

Substitution of pyridine for isoquinoline in the one-step synthesis of **8** outlined in the first paragraph did not give the expected indolizinoquinoxaline (**23**). The results of determinations of molecular weight and ionic halogen were somewhat anomalous, but on the basis of elemental analysis and ethoxyl content structure **19** is suggested. Attempts to convert **19** to **23** were unsuccessful. The active methylene compounds treated with 2,3-dichloroquinoxaline and pyridine, the suggested products, and the yields were as follows: ethyl cyanoacetate, **19**, 47%; *n*-propyl cyanoacetate, **20**, 34%; *t*-butyl cyanoacetate, **21**, 20%; and cyanoacetamide, **22**, 18%. Substitution of 3-picoline for the pyridine used in the preparation of **19** gave the expected analog in 22% yield.

7-Benzoylbenz[*c*]indolizino[2,3-*b*]quinoxaline (**2**, see Scheme I) was obtained in 24% yield by treatment of 2,3-dichloroquinoxaline with the sodium salt of 2-phenacylquinoline. This was the only route found to the ring system of **2** since quinoline could not be successfully substituted for isoquinoline in either of the two routes to the ring system of **8** described above (Scheme I). Compound **2** is probably formed *via* intermediates closely analogous to those previously suggested[4] for the formation of **16** and its pyridine analog by reaction of acetonylquinoline and acetonylpyridine with 2,3-dichloro-1,4-naphthoquinone. The infrared absorption spectrum of **2** contained little evidence of a carbonyl band suggesting that the contributing structure **17** is of major significance.

Experimental Section[9,10]

One-Step Synthesis of Benz[*a*]indolizinoquinoxalines 8 and 9.—A solution of 3.0 g of 2,3-dichloroquinoxaline, 42 ml of isoquinoline, 24 ml of ethyl cyanoacetate, and 150 ml of benzene was heated under reflux for 48 hr in an apparatus fitted with a Dean–Stark water trap to minimize hydrolysis of the dichloroquinoxaline. Removal of volatile material left a thick syrup which was chromatographed on alumina (800 g, Alcoa F-20) using 1.5 l. of benzene, 3.6 l. of 1:1 methylene chloride–benzene, and finally 7.0 l. of methylene chloride as eluents. The desired product which appeared as a broad, orange band was eluted by the methylene chloride. The residue obtained upon evaporating the solvent was extracted in a Soxhlet with about 300 ml of chloroform. Cooling the extract gave 2.06 g (47%) of 14-cyanobenz[*a*]indolizino[2,3-*b*]quinoxaline (**8**) which melted at 321–323°. The molecular weight determined with a Mechrolab osmometer[3] was 296 ± 6 while the calculated value is 294. This and several other compounds prepared in this study were very difficult to work with because of their low solubilities.

Anal. Calcd for $C_{19}H_{10}N_4$: C, 77.53; H, 3.42; N, 19.04. Found: C, 77.54; H, 3.23; N, 18.80.

Compound **8** was also synthesized, in 3% yield, from 0.5 g of 2,3-dichloroquinoxaline, 7 ml of isoquinoline, and 1.0 g of benzoylacetonitrile dissolved in 30 ml of benzene using the same general procedure. It melted at 319–320° both alone and when mixed with the product obtained from ethyl cyanoacetate. About 90% of the 2,3-dichloroquinoxaline was recovered from the benzene eluates.

Compound **9** was synthesized by heating a solution of 2.0 g of 2,3-dichloroquinoxaline, 28 ml of isoquinoline, 16 ml of acetoacetic ester, and 100 ml of absolute alcohol under reflux for 24 hr. Some 2,3-dichloroquinoxaline (0.19 g) was filtered from the cold (−20°) reaction mixture. Addition of 100 ml of petroleum ether (bp 30–60°) to the filtrate precipitated 0.60 g of isoquinoline hydrochloride. The alcohol and petroleum ether were distilled and the isoquinoline and acetoacetic ester were steam-distilled from the filtrate. The chloroform extract of the aqueous residue was dried and the volatile constituents were removed under reduced pressure. A solution of the residue in 50 ml of 1:1 petroleum ether (bp 30–60°)–benzene was chromatographed on 100 g of alumina (Merck acid washed) using about 100-ml portions of 1:1 petroleum ether (bp 30–60°)–benzene, benzene, 1:1 methylene chloride–benzene, and finally methylene chloride as eluents. Recrystallization from 1-nitropropane of the residue from the methylene chloride fractions gave 0.23 g (7%) of 14-14-carbethoxybenz[*a*]indolizino[2,3-*b*]quinoxaline (**9**) as orange needles which melted at 215–222°. Two more recrystallizations raised the melting point to 222–224°.

Anal. Calcd for $C_{21}H_{15}N_3O_2$: C, 73.83; H, 4.43; N, 12.31; C_2H_5O, 9.68. Found: C, 73.70: H, 4.59; N, 12.11; C_2H_5O, 11.0.

Synthesis of Compound 2.—2-Phenacylquinoline[11] (0.50 g) was added to a solution of sodium ethoxide prepared from 0.25 g of sodium and 50 ml of absolute alcohol and the mixture was stirred mechanically for 3 hr, just below the reflux temperature. Twenty milliliters of dry ether was added to the cooled reaction mixture and the sodium salt of 2-phenacylquinoline was filtered off, washed with dry xylene, and immediately transferred to a flask to which was added 40 ml of *o*-xylene and 0.40 g of 2,3-dichloroquinoxaline. The mixture was heated under reflux with magnetic stirring for 24 hr and cooled, the sodium chloride was filtered off, and the *o*-xylene was removed under reduced pressure. A benzene suspension of the residue was chromatographed on 100 g of alumina (Alcoa F-20) using 1250 ml of benzene, 150 ml of 1:1 benzene–chloroform, 150 ml of chloroform, and finally 30 ml of 1:1 chloroform–ethyl acetate as eluents. Over half of the 2,3-dichloroquinoxaline was recovered from the benzene fractions. The orange product could readily be followed visually on the column. Evaporation of the chloroform and ethyl acetate eluate gave 0.18 g (24%) of 7-benzoylbenz[*c*]indolizino[2,3-*b*]-quinoxaline (**2**) which melted at 285°. The analytical results are corrected for 0.4% of residue which apparently arose from the silicone lubricant employed.

Anal. Calcd for $C_{25}H_{15}N_3O_1$: C, 80.19; H, 4.05; N, 11.25. Found: C, 79.49; H, 4.19; N, 11.50.

Synthesis of 2-Chloro-3-Substituted Quinoxalines 3 through 7.—Ten milliliters of ethyl cyanoacetate was added with stirring to a solution prepared from 2.5 g of clean potassium and 150 ml of *t*-butyl alcohol. An additional 100 ml of *t*-butyl alcohol and 5.0 g of 2,3-dichloroquinoxaline were then added and the mixture was heated under reflux 1 hr. The resulting yellow solution was poured into 1500 ml of 0.4 *N* hydrochloric acid and the mixture was stirred 30 min while cooling in an ice bath. Recrystallization of the crude product gave 2-chloro-3-(carbethoxycyanomethyl)quinoxaline (**3**) as yellow needles which melted at 174–175°. Nitrile and carbonyl bands appeared at 2200 and 1630 cm^{-1} in the infrared absorption spectrum.

Anal. Calcd for $C_{13}H_{10}ClN_3O_2$: C, 56.63; H, 3.65; Cl, 12.86; N, 15.24; C_2H_5O, 16.34. Found: C, 56.34; H, 3.90; Cl, 13.08; N, 15.50; C_2H_5O, 16.55.

The foregoing procedure was employed for the synthesis of compounds **4**, **5**, and **6**, except that 10 ml of the required active methylene compound replaced the 10 ml of ethyl cyanoacetate. The 2-chloro-3-(carbomethoxycyanomethyl)quinoxaline (**4**) was obtained as yellow needles which melted at 198°. The infrared absorption spectrum showed nitrile and carbonyl bands at 2175 and 1640 cm^{-1}.

(9) All melting points are corrected.

(10) We are indebted to Dr. Franz J. Kasler for the elemental analyses.

(11) We wish to thank Mr. Kenneth Hyde for preparing this compound.

Anal. Calcd for $C_{12}H_8ClN_3O_2$: C, 55.08; H, 3.08; N, 16.06. Found: C, 55.48; H, 3.40; N, 16.03.

The 2-chloro-3-(carbo-*t*-butoxycyanomethyl)quinoxaline (**5**) was isolated as orange needles[12] which melted at 168–170° dec. Nitrile and carbonyl bands appeared at 2175 and 1630 cm^{-1} in the infrared absorption spectrum.

Anal. Calcd for $C_{15}H_{14}ClN_3O_2$: C, 59.31; H, 4.64; N, 13.83. Found: C, 59.09; H, 4.90; N, 13.74.

The gold needles of 2-chloro-3-(dicyanomethyl)quinoxaline (**6**) melted at 217° dec. The nitrile band appeared at 2200 cm^{-1} in the infrared absorption spectrum.

Anal. Calcd for $C_{11}H_5N_4Cl$: C, 57.78; H, 2.20; N, 24.50. Found: C, 58.05; H, 2.48; N, 24.27.

With nitromethane (10 ml) it was found necessary to extend the time of heating under reflux to 10 hr. The 2-chloro-3-(nitromethyl)quinoxaline (**7**) was obtained as tan plates which melted at 115° dec.

Anal. Calcd for $C_9H_6ClN_3O_2$: C, 48.34; H, 2.71; N, 18.79. Found: C, 48.39; H, 2.69; N, 18.50.

Synthesis of Indolizinoquinoxalines 15, 23, 24, and 25.—In the preparation of compound **25** a solution of 1.38 g (0.005 mole) of compound **3**, 7 ml of 4-picoline, and 50 ml of absolute alcohol was heated under reflux for 24 hr. Volatile material was removed and a solution of the dry residue in 20 ml of chloroform was chromatographed on 100 g of alumina (Alcoa F-20) employing 360 ml of chloroform, then 120 ml of 1:1 chloroform–ethyl acetate, and finally 240 ml of ethyl acetate as eluents. The product could readily be followed as a red band. Recrystallization from 1-nitropropane of the solid resulting from distillation of the solvent from the first half of the ethyl acetate eluate gave 0.08 g (6%) of 2-methyl-12-cyanoindolizino[2,3-*b*]quinoxaline (**25**) as square, red plates which melted at 291–292°. A nitrile band appeared at 2175 cm^{-1} in the infrared absorption spectrum. The analytical results were corrected for 0.3% of residue.

Anal. Calcd for $C_{16}H_{10}N_4$: C, 74.40; H, 3.90; N, 21.69. Found: C, 73.94; H, 4.20; N, 21.95.

Evaporation of volatile material from the chloroform eluate and recrystallization of the residue from absolute alcohol yielded 0.95 g (67%) of 2-ethoxy-3-(carbethoxycyanomethyl)quinoxaline as yellow needles which melted at 165–169°. Recrystallization raised the melting point to 170–171°.

Anal. Calcd for $C_{15}H_{15}N_3O_3$: C, 63.14; H, 5.29; N, 14.73; C_2H_5O, 31.55. Found: C, 62.93; H, 5.50; N, 14.98; C_2H_5O, 29.50.

When the preceding synthesis of **25** was repeated using 50 ml of benzene in place of the 50 ml of alcohol, a 7% yield was obtained.

This second procedure (benzene reaction medium) gave a 42% yield of 12-cyanoindolizino[2,3-*b*]quinoxaline (**23**) when 7 ml of pyridine replaced the 4-picoline. The product, isolated as for **25**, was obtained as red needles which melted at 281–282°. The molecular weight determined with a Mechrolab osmometer[3] was 241 ± 3 while the calculated value is 244. A nitrile band appeared at 2250 cm^{-1} in the infrared absorption spectrum.

Anal. Calcd for $C_{15}H_8N_4$: C, 73.75; H, 3.29; N, 22.94. Found: C, 73.84; H, 3.58; N, 23.50.

A 22% yield of **23** was obtained when 3.0 g of compound **3**, 21 ml of pyridine, and 150 ml of absolute alcohol were used as described for the synthesis of **25**. From the chloroform eluate a 33% yield of 2-ethoxy-3-(carbethoxycyanomethyl)quinoxaline was isolated.

Compound **23** was also prepared (24% yield) from 0.005 mole of the *t*-butoxy ester (**5**) and 7 ml of pyridine in 50 ml of absolute alcohol as described for **25**.

Compound **24** was prepared (alcohol reaction medium) and isolated as described for **25** except that 7 ml of 3-picoline replaced the 7 ml of 4-picoline. A 50% yield of 2-ethoxy-3-(carbethoxycyanomethyl)quinoxaline and 0.07 g (5%) of 3-methyl-12-cyanoindolizino[2,3-*b*]quinoxaline[3] (**24**) which melted at 263–264° were obtained. The red needles gave a nitrile band at 2180 cm^{-1} in the infrared absorption spectrum.

Anal. Calcd for $C_{16}H_{10}N_4$: C, 74.00; H, 3.90; N, 21.69. Found: C, 73.78; H, 4.20; N, 21.98.

Compound **15** was prepared and isolated as described for **25** (alcohol reaction medium) except that 2.0 g of quinoxaline was used in place of the 7 ml of 4-picoline. Three fractional crystallizations of the crude product from 1-nitropropane gave 0.05 g (3%) of 2-aza-14-cyanobenz[*c*]indolizino[2,3-*b*]quinoxaline (**15**) as red needles which melted at 276–280°. Attempts to improve the results of the nitrogen analysis were unsuccessful.

Anal. Calcd for $C_{18}H_9N_5$: C, 73.21; H, 3.07; N, 23.72. Found: C, 73.50; H, 3.30; N, 22.14.

Synthesis of Dicyanodihydroindolizinoquinoxalines 26 through 29.—The following procedure was used for all four of these compounds. To 0.005 mole of compound **6** were added 7 ml of the desired pyridine and 50 ml of absolute alcohol and the resulting solution was heated under reflux for 12 hr during which the product precipitated. It was filtered off and recrystallized from 1-nitropropane.

With pyridine 12,12-dicyano-12,12a-dihydroindolizino[2,3-*b*]-quinoxaline (**26**) was obtained as orange needles which melted at 342° dec. One nitrile group gave a band at 2170 and the other gave one at 2200 cm^{-1} in the infrared absorption spectrum.

Anal. Calcd for $C_{16}H_9N_5$: C, 70.86; H, 3.34; N, 25.82. Found: C, 70.98; H, 3.60; N, 26.10.

When 3-picoline was used 3-methyl-12,12-dicyano-12,12a-dihydroindolizino[2,3-*b*]quinoxaline[3] (**27**) was obtained as red plates which melted at 303° dec. The infrared absorption spectrum showed the two nitrile bands at 2120 and 2160 cm^{-1}.

Anal. Calcd for $C_{17}H_{11}N_5$: C, 71.56; H, 3.89; N, 24.54. Found: C, 71.37; H, 3.98; N, 24.30.

4-Picoline gave 2-methyl-12,12-dicyano-12,12a-dihydroindolizinoquinoxaline (**28**) as red plates which melted at 275–276°. The two nitrile bands appeared at 2170 and 2210 cm^{-1} in the infrared absorption spectrum.

Anal. Calcd for $C_{17}H_{11}N_5$: C, 71.56; H, 3.89; N, 24.54. Found: C, 71.55; H, 3.73; N, 24.68.

3,5-Lutidine yielded 1,3-dimethyl-12,12-dicyano-12,12a-dihyroindolizino[2,3-*b*]quinoxaline (**29**) as red needles which melted at 293–294°. The nitrile bands occurred at 2110 and 2180 cm^{-1} in the infrared absorption spectrum.

Anal. Calcd for $C_{18}H_{13}N_5$: C, 72.22; H, 4.37; N, 23.39. Found: C, 72.32; H, 4.54; N, 23.10.

Synthesis of Compound 8 from 3 and from 6.—Reaction of compound **3** with isoquinoline gave compound **8** in 19% yield. The reaction conditions and the isolation procedure were in general the same as those for compound **25** (alcohol reaction medium).

When **6** was treated with isoquinoline under the conditions just described for the synthesis of **26** through **29** and the product was isolated chromatographically as described for **25**, an 8% yield of compound **8** was obtained. In these two preparations compound **8** was recrystallized from 1-nitropropane and mixture melting points were used to establish its identity.

Reaction of 2,3-Dichloroquinoxaline, Pyridine, and Ethyl Cyanoacetate and Its Analogs.—The following procedure was used for the first three of these reactions. A solution of 150 ml of benzene, 3.0 g of 2,3-dichloroquinoxaline, 42 ml of pyridine, and 24 ml of the desired active methylene compound was heated for 48 hr under reflux in an apparatus fitted with a Dean–Stark water trap to ensure dryness. The reaction mixture was cooled in ice and the product was recrystallized from 1-nitropropane.

Ethyl cyanoacetate gave red plates which melted at 271–272° dec. Nitrile and carbonyl bands appeared at 2200 and 1695 cm^{-1} in the infrared absorption spectrum. The results of ultimate analysis agreed with those calculated for 2-pyridinium-3-(carbethoxycyanomethyl)quinoxaline chloride (**19**).

Anal. Calcd for $C_{18}H_{15}ClN_4O_2$: C, 60.93; H, 4.29; Cl, 9.99; N, 15.79; C_2H_5O, 12.69. Found: C, 60.79; H, 4.84; Cl, 10.21; N, 15.75; C_2H_5O, 11.68.

From *n*-propyl cyanoacetate red plates which melted at 264° dec were obtained. The nitrile band appeared at 2160 and the carbonyl band at 1680 cm^{-1} in the infrared absorption spectrum. The nitrogen content was low but the other analytical results agreed with those calculated for 2-pyridinium-3-(carbo-*n*-propoxycyanomethyl)quinoxaline chloride (**20**).

Anal. Calcd for $C_{19}H_{17}ClN_4O_2$: C, 61.87; H, 4.64; N, 15.18. Found: C, 61.84; H, 4.80; N, 14.05.

When *t*-butyl cyanoacetate[12] was used orange plates which melted at 222° dec were obtained. The infrared absorption spectrum showed a nitrile band at 2190 and a carbonyl band at 1685 cm^{-1}. Results of analysis agreed with those calculated for 2-pyridinium-3-(carbo-*t*-butoxycyanomethyl)quinoxaline chloride (**21**).

Anal. Calcd for $C_{20}H_{19}ClN_4O_2$: C, 62.74; H, 5.00; Cl, 9.26; N, 14.11. Found: C, 62.52; H, 5.20; Cl, 9.57; N, 14.36.

Since cyanoacetamide is a solid, 6.0 g of it was used in place of the 24 ml of active methylene compound in the foregoing

(12) We wish to thank Dr. Richard Minesinger for preparing the *t*-butyl cyanoacetate.

procedure. An 18% yield of orange needles which melted at 247–249° was obtained. A nitrile band appeared at 2195 cm^{-1} in the infrared absorption spectrum. The nitrogen content was low, but the other analytical results agreed satisfactorily with those calculated for 2-pyridinium-3-(carboxamidocyanomethyl) quinoxaline (**22**) when corrected for 0.3% of residue.

Anal. Calcd for $C_{16}H_{12}ClN_5O$: C, 58.81; H, 4.01; N, 21.43. Found: C, 58.51; H, 4.50; N, 20.42.

When 42 ml of 3-picoline was used in place of the 42 ml of pyridine together with 24 ml of ethyl cyanoacetate in the foregoing procedure, orange needles which melted at 254° dec were obtained. The infrared absorption spectrum had a nitrile band at 2200 and a carbonyl band at 1715 cm^{-1}. The results of elemental analysis agreed satisfactorily with those calculated for 2-(3-picolinium)-3-(carbethoxycyanomethyl)quinoxaline.

Anal. Calcd for $C_{19}H_{17}ClN_4O_2$: C, 61.87; H, 4.64; N, 15.18. Found: C, 61.95; H, 4.92; N, 15.40.

Quinoxalinediones. III. 1,4-Addition Reactions of 2,3-Dimethyl-5,8-quinoxalinedione and a Study of the Influence of Substituents on the Polarographic Half-Wave Potential of This System[1,2]

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Received June 8, 1966

The 1,4-addition reactions of 2,3-dimethyl-5,8-quinoxalinedione (**1**) with several amines and acids, in an aprotic solvent, were found to occur easily and to give higher yields of products than the corresponding reactions with 1,4-naphthoquinone. The higher yields may be attributed to the more desirable aprotic solvent used, 1,2-dimethoxyethane (1,2-DME). The polarographic half-wave potentials of the substituted 5,8-quinoxalinediones were measured and the two-step polarographic reduction mechanism of **1** was investigated. The polarographic reduction mechanism of **1** was found to be a composite of the known reduction mechanisms of quinones and quinoxalines. The effects of substituents on the $E^\circ_{1/2}$ of **1** could be determined quantitatively using a modified Hammett equation proposed by Zuman, thus testing the validity of this equation on this heterocyclic quinone system. A reaction constant, ρ, was determined and its value was analogous to the value obtained for the 1,4-naphthoquinone system which is the carbocyclic analog of **1**. Some new substituent constants ($\sigma_{p\text{-B}}$) were assigned using this modified Hammett equation.

In the previous papers in this series, the synthesis and a study of the dienophilic properties of 2,3-dimethyl-5,8-quinoxalinedione (**1**) were described.[2,4] As part of a program investigating the physical and chemical properties of heterocyclic quinones and their potential pharmacological applications, we now report on the 1,4-addition reactions of **1** and on the oxidation–reduction potentials of the substituted quinones obtained from these reactions.

The synthesis of **1** was first reported in 1964 by Levy and Joullié.[4] In the present investigation the original synthetic route was used with some modifications (see the Experimental Section).

1,4-Addition Reactions.—Although most 2-alkylamino-1,4-naphthoquinones were obtained by nucleophilic displacements of 1,4-naphthoquinonesulfonate with amines,[5] Plimpton studied the action of ammonia and amines on 1,4-naphthoquinone using water and alcohol as solvents.[6] In these protic solvents, it was necessary to add the amines dissolved in neutral solutions of acetic acid to obtain the products in reasonable yields. Aniline reacted with the same quinone, in ethanol, to yield 2-anilino-1,4-naphthoquinone and 1,4-dihydroxy-naphthalene.[7] We have found that by using the aprotic solvent, 1,2-dimethoxyethane (1,2-DME), **1** undergoes 1,4-addition reactions with ammonia, aniline, and various primary and secondary amines (Scheme I).

Low yields of substituted quinones were obtained in the reaction of **1** with ammonia and methylamine owing to the decomposition of **1** in the alkaline reaction media. Quinone **1** decomposes readily above pH 8 to yield unidentifiable products while the substituted aminoquinones appear to be more stable to basic conditions. Since secondary amines react considerably faster with **1** than primary amines the decomposition of **1** does not have as much time to occur. The weak basic character of aniline causes negligible decomposition of **1**.

When aziridine and ammonia were added to 6-chloro-2,3-dimethyl-5,8-quinoxaline dione (**12**), a 1,4-addition reaction occurred rather than the nucleophilic displacement of the chloro group as observed for certain halonaphthoquinones.[8] The corresponding aziridino (**9**), and amino (**10**) derivatives were obtained in good yields showing that the chloro group promoted the nucleophilic addition of these amines to the quinone ring by increasing the positive character of the 7 position. The isolation of the hydroquinone (**2**) in all of the reactions studied showed that all the reactions with amines involved product-starting material oxidation–reduction equilibration as expected for 1,4-addition reactions where electron-releasing groups are introduced.

Terentyev, Grinev, and Terentyev showed that quinones undergo 1,4-addition reactions with anhydrous halogen halides, in ether solution, to give the halogeno-substituted hydroquinones.[9] We have found that hydrogen halides add easily to **1**, in 1,2-DME,

(1) Presented before the Division of Organic Chemistry, First Middle Atlantic Regional Meeting of the American Chemical Society, Philadelphia, Pa., Feb 3, 1966, p 128.

(2) Paper II of this series: W. F. Gum, Jr., and M. M. Joullié, *J. Org. Chem.*, **30**, 2583 (1965).

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