Structures of Some Alleged Diels–Alder Adducts from 2,3-Dimethylquinoxaline[1]

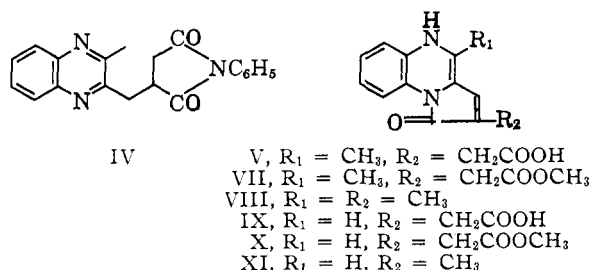BY EDWARD C. TAYLOR AND E. SMAKULA HAND

Frequent reference is made in the literature[3] to the Diels–Alder reaction of 2,3-dimethylquinoxaline (purportedly reacting in its tautomeric dimethylene form) with maleic anhydride and N-phenylmaleimide to give adducts of type Ia or Ib. We have shown that the latter reaction leads, in fact, to the simple Michael addition product IV, and that the alleged 2,3-dimethylquinoxaline–maleic anhydride "adduct" is the tricyclic acid V. Novel and simple entries into the 1,4-dihydroquinoxaline system (e.g., V, IX, XXIX) have been found in the reaction of 2-methylquinoxalines with maleic anhydride or maleic acid, and in the dehydrative cyclization of β-quinoxal-2-ylpropionic acids.

It is well known that maleic anhydride undergoes three general types of reactions: condensation with dienes across its double bond to give Diels–Alder adducts, addition to the double bond with formation of succinic anhydride derivatives, or reaction at one of the carbonyl groups with (generally) concomitant cleavage of the anhydride system.[2] With 2,3-dimethylquinoxaline these several reaction paths would lead to products such as Ia, II, and IIIa and IIIb, some of which could undergo further reactions. Structure Ia (or Ib) has already been proposed for the yellow product derived from maleic anhydride and 2,3-dimethylquinoxaline,[3] and the analogous structure, where the succinic anhydride ring is replaced by N-phenylsuccinimide, was postulated

Ia

II

Ib

IIIb

IIIa
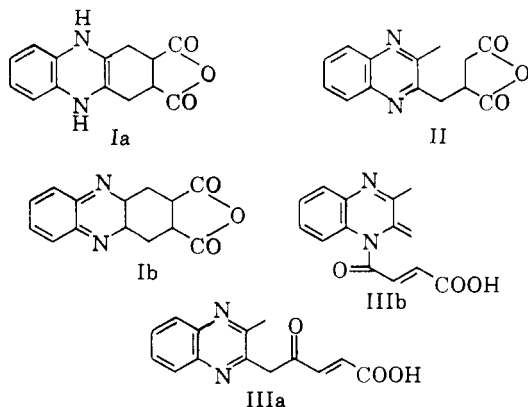
for the colorless product of the reaction between N-phenylmaleimide and 2,3-dimethylquinoxaline.[4] Since one of these products is yellow and the other is colorless, the structure of one of them was immediately suspect. Furthermore, the "adduct" obtained from maleic anhydride and 2,3-dimethylquinoxaline is reported[3] to be sublimable, recrystallizable from acetic acid, soluble in 10% sodium hydroxide, and recoverable after refluxing for one hour in aqueous 10% sodium hydroxide. The extraordinary stability of this compound as indicated by these properties seemed at variance not only with the presence of the dihydroquinoxaline systems in Ia or Ib, but also with the presence of an anhydride ring. We have reinvestigated both reactions and have shown that the N-phenylmaleimide–2,3-dimethylquinoxaline "adduct" has in fact structure IV (analogous to II) and that the

maleic anhydride–2,3-dimethylquinoxaline "adduct"[5] has structure V derivable from II or IIIb.[5a]

IV

V, R_1 = CH$_3$, R_2 = CH$_2$COOH
VII, R_1 = CH$_3$, R_2 = CH$_2$COOCH$_3$
VIII, R_1 = R_2 = CH$_3$
IX, R_1 = H, R_2 = CH$_2$COOH
X, R_1 = H, R_2 = CH$_2$COOCH$_3$
XI, R_1 = H, R_2 = CH$_3$

The colorless "adduct" of 2,3-dimethylquinoxaline and N-phenylmaleimide,[6] prepared according to the described procedure,[4] had the correct melting point and the reported analysis of $C_{20}H_{17}N_3O_2$. In the infrared it showed bands at 5.64(w), 5.86(s), 5.97(sh) and 6.25 μ similar to those of N-phenylsuccinimide (5.62(w), 5.87-(s), 5.97(sh) and 6.26 μ), and its ultraviolet spectrum could be attributed to a 2,3-dialkylquinoxaline system (see Table I, compound IV). Its n.m.r. spectrum (CDCl$_3$) is in excellent accord with the simple Michael addition product IV; the complex multiplet extending from 1.8–2.7 τ[7] accounts for the nine aromatic hydrogens, the unsplit band at 7.24 τ accounts for the three methyl hydrogens (the methyl groups of 2,3-dimethylquinoxaline absorb at 7.42 τ (CCl$_4$) and the aromatic methyl group in compound XXV absorbs at 7.29 τ (CDCl$_3$)), the multiplet (six or more peaks) at 6.97 τ is due to the two methylenic hydrogens of the succinimide ring (the methylene groups in N-phenylsuccinimide absorb at 6.93 τ (CDCl$_3$)), the other two methylenic hydrogens absorb at 6.38 τ, and on this last peak is superimposed another multiplet due to the single tertiary hydrogen which couples with the non-equivalent methylenic hydrogens of the succinimide ring. Only IV can satisfy the requirements of all the spectral data and the analysis.

The maleic anhydride–dimethylquinoxaline "adduct," prepared according to the reported procedure,[3] was yellow, did not melt below 300°, had the correct analysis, $C_{14}H_{12}N_2O_3$, and could be recovered from aqueous sodium hydroxide solution as previously described. However, its infrared spectrum (perfluorocarbon oil) lacked the typical anhydride absorption bands, but showed the presence of NH or OH (3.07 μ), a carboxylic acid group (3.4–5.5, 5.87(s) μ), a double bond (5.99 μ), and possibly a vinylogous amide (6.19, 6.26, 6.39

(1) This work was supported by a grant (CY-2551) to Princeton University from the National Cancer Institute, National Institutes of Health, Public Health Service.

(2) L. H. Flett and W. H. Gardner, "Maleic Anhydride Derivatives," John Wiley and Sons, Inc., New York, N. Y., 1952.

(3) (a) A. Schönberg and A. Mustafa, J. Chem. Soc., 654 (1953), cited in (b) ref. 2, p. 153; (c) E. H. Rodd, ed., "Chemistry of Carbon Compounds," Vol. IVB, Elsevier Publishing Co., Amsterdam, 1959, p. 1349; (d) A. Albert, "Heterocyclic Chemistry," The Athlone Press, University of London, 1959, p. 89; (e) M. C. Kloetzel, "Organic Reactions," R. Adams, et al., ed., Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 39; (f) J. C. E. Simpson, "The Chemistry of Heterocyclic Compounds: Condensed Pyridazine and Pyrazine Rings," Interscience, New York, N. Y., 1953, p. 278.

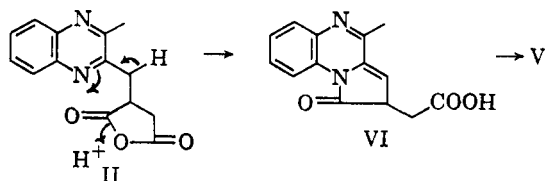(4) A. Mustafa and M. Kamel, J. Am. Chem. Soc., 77, 1828 (1955).

(5) The structure proof for V has been presented in a preliminary Communication (E. C. Taylor and E. S. Hand, Tetrahedron Letters, 25, 1189 (1962).

(5a) Note Added in Proof.—A revised but incorrect formulation (A) for the "adduct" of 2,3-dimethylquinoxaline and maleic anhydride very recently has

A
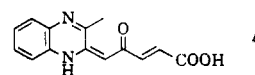
been advanced (C. W. Bird and G. W. H. Cheeseman, J. Chem. Soc., 3037 (1962)). The N-phenylmaleimide "adduct" was correctly formulated as IV.

(6) We thank the U. S. Rubber Co. for their generous gift of this material.

(7) Band positions are expressed in τ-values (G. V. D. Tiers, J. Phys. Chem., 62, 1151 (1958)), where tetramethylsilane has τ = 10.00 p.p.m.

(8) N. H. Cromwell, F. A. Miller, A. R. Johnson, R. L. Frank and D. J. Wallace (J. Am. Chem. Soc., 71, 3337 (1949)) have reported infrared spectral data on vinylogous amides.

and 6.43(s), 6.54 μ).[8] Thus, Ia, Ib and II must be excluded as possible structures for the "adduct." Since the double bond of maleic anhydride is as reactive as that of maleimide, and since the anhydride ring is more susceptible toward cleavage than the succinimide ring, it was thought that the maleic anhydride analog of the "adduct" IV, i.e., compound II, might be an intermediate which could react further to give VI or V. The latter contains the structural features necessary for interpretation of the infrared spectrum of the "adduct."

TABLE I: ULTRAVIOLET DATA OF 2,3-DIALKYLQUINOXALINES IN ABSOLUTE ETHANOL

Compound	λ_{max}, mμ (ϵ)	λ_{max}, mμ (ϵ)	λ_{min}, mμ (ϵ)
2,3-Dimethyl-quinoxaline	236 (25,400) 240^a (20,300)	305^a (5600) 316 (7100) 324^a (5500)	260 (1600)
IV	237 (27,600)	298^a (4300) 305^a (5400) 310^a (6100) 316 (6900) 323^a (5700)	
XII	240	310^a 320 328^a	283
XIV	238 (26,400)	308^a (6300) 320 (7700)	274 (2500)
XIX	236 (26,600)	308^a (6100) 316 (7100)	260 (1900)
XXVI	237 (26,800)	307^a (6000) 318 (7500)	260 (1700)
XXVIII	235 (21,900)	306^a (5000) 316 (5900)	260 (1600)
XXX	237 (27,600)	307^a (6300) 318 (7800)	263 (1900)
XXXI	237 (25,000)	305^a (5500) 318 (7100)	Plateau 257–275 (2000)
XXXII	235 (27,600) 240^a (20,000)	308^a (6300) 315 (7100)	258 (1900)
XXXIII	237 (29,800) 240^a (25,500)	306^a (6200) 317 (7500)	264 (2000)
XXXIV	236 (31,300) 240^a (26,500)	310^a (6800) 318 (8100)	262 (1900)

^{a} Approximate inflection points.

The n.m.r. spectrum of the "adduct" (D$_2$O/KOH) also is consistent with structure V: the unsplit resonance lines at 8.06, 6.67, 3.39, 3.22 and 1.2 (broad) τ (approximate area ratio 3:2:1:4:1, respectively) are assigned to the methyl group, the methylene group adjacent to the carboxylic acid group, the vinyl hydrogen, the aromatic hydrogens and the NH hydrogen, respectively.

Other data in agreement with structure V are: (i) The "adduct" was soluble in aqueous dilute base and could be recovered on acidification. (ii) It reacted with diazomethane to give a monomethyl ester (VII), $C_{15}H_{14}N_2O_3$. (iii) Titration in 50% aqueous ethanol gave a pK_a value of 5.7 and a neutral equivalent weight of

231 (calcd. 256). Comparison with data in the literature[9] indicated that this acidity constant is reasonable for a carboxylic acid group such as is present in V. (iv) Two of the three oxygen atoms present in the "adduct" are accounted for by the carboxylic acid group. Since the "adduct" did not form a semicarbazone or a 2,4-dinitrophenylhydrazone, the third oxygen atom must be present as an amide, or less likely as an alcohol or an ether function. (v) A Kuhn–Roth determination indicated the presence of at least one C–CH$_3$ group (found 4.3%, required 5.9%).[10] (vi) On heating in vacuo at 240–270° a material sublimed which, according to its infrared spectrum, no longer contained a carboxyl group. The analysis of this "sublimate" showed that the elements of CO$_2$ had been lost, and a Kuhn–Roth determination showed the presence of two C–CH$_3$ groups (found 9.4%, required 14.2%). The formation of a second C–CH$_3$ group on decarboxylation indicates that the –CH$_2$COOH group was present in the "adduct." (vii) Independent evidence for the fact that the carboxylic acid group is insulated from the chromophoric system came from ultraviolet data: the complex spectra of the "adduct," its methyl ester and the "sublimate" are all nearly the same (see Table II). From Table II it is apparent that the yellow or yellow-orange color of these substances is due to the intense absorption band at about 420 mμ. The long wave length absorption maximum of these compounds appears to be characteristic of 1,4-dihydroquinoxalines and 1,4-dihydropyrazines which have a carbonyl group in conjugation with the double bond.[11]

As regards the structure of the "sublimate," the data given above together with the infrared spectrum (3.11, 3.17, 3.24, 3.8–4.4, 5.98(m), 6.23(s), 6.38(s, broad), 6.55(s) and 6.69(s) μ) justify the assignment of VIII to this compound.

Further evidence for structure V rests on the formation of an "adduct" from 2-methylquinoxaline and maleic anhydride, an oxidative degradation, and the synthesis of a model compound. These several aspects will be discussed in turn.

When an acetic acid solution of 2-methylquinoxaline and maleic anhydride was refluxed for several hours, a yellow "adduct" (IX), $C_{13}H_{10}N_2O_3$, was formed. On treatment with diazomethane it gave a methyl ester (X), $C_{14}H_{12}N_2O_3$, and on heating in vacuo at 240° it decarboxylated to form XI, $C_{12}H_{10}N_2O$. The ultraviolet spectra of these compounds are again nearly the same as the spectrum of the "adduct" V (see Table II), and their infrared spectra are similar to the respective compounds obtained from 2,3-dimethylquinoxaline and maleic anhydride. Since 2-methylquinoxaline and maleic anhydride form an "adduct" whose spectral data show it to have the same chromophores as are present in the "adduct" obtained from 2,3-dimethylquinoxaline, only one methyl group can be involved in the reaction.

Alkaline ferricyanide oxidation of the "adduct" V gave a dicarboxylic acid which had an approximate analysis of $C_{14}H_{14}N_2O_5$. Its infrared spectrum showed that, besides the carboxylic acid groups (3.7–4.5, 5.0–

(9) Cf. H. C. Brown, D. H. McDaniel and O. Häfliger in "Determination of Organic Structures by Physical Methods," ed. by E. A. Braude and F. G. Nachod, Academic Press, Inc., New York, N. Y., 1955: the solvent effect in changing from water to 50% aqueous ethanol on the pK_a of a carboxylic acid causes a rise in the dissociation constant of ca. 1.5 units (p. 619); acetic acid and butyric acid in water have pK_a's of 4.8 (p. 578); an α,β-double bond lowers the pK_a by ca. 0.35 unit (p. 580); a β-ketone or ester group lowers the pK_a by ca. 0.3 unit (p. 578).

(10) B. Franck and J. Knoke, Ber., 95, 579 (1962).

(11) (a) J. A. Barltrop, C. G. Richards and D. M. Russell, J. Chem. Soc., 1423 (1959); (b) F. E. King and J. W. Clark-Lewis, ibid., 3030 (1951); (c) W. Pfleiderer and E. C. Taylor, J. Am. Chem. Soc., 82, 3765 (1960); (d) H. I. X. Mager and W. Berends, Rec. trav. chim., 79, 282 (1960), and preceding papers in this series.
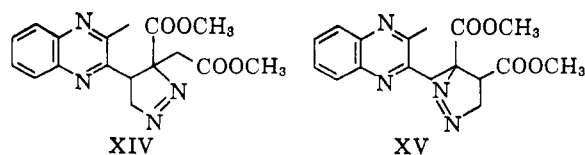
TABLE II

ULTRAVIOLET DATA OF THE "ADDUCTS" AND RELATED COMPOUNDS IN ABSOLUTE ETHANOL

Compound				λ_{max}, mμ (ϵ)			
V	233 (24,900)	258 (7000)	291 (9400)	299 (9900)	325 (2900)	420 (12,900)
VII	234 (21,800)	259 (5700)	291 (8300)	299 (8500)	325 (2500)	415 (11,300)
VIII	233 (26,300)	258 (7900)	291 (10,000)	299 (10,500)	325 (3100)	422 (13,500)
IX	232 (25,200)	257 (6500)	291 (9800)	300 (9800)	326 (2600)	420 (12,500)
X	231 (24,700)	257 (7100)	290 (9600)	300 (10,000)	326 (2500)	422 (12,600)
XI	234	259	292	302	330	417
XXIX	231 (24,900)	257 (8100)	288 (9600)	297 (10,400)	323 (2700)	421 (11,700)

5.5, 5.85(broad) and 6.0(sh) μ), an OH group was present (2.87 μ), and its ultraviolet spectrum (see Table I, compound XII) indicated the presence of a 2,3-dialkylquinoxaline system. On the basis of the spectral data and the following evidence, structure XII is assigned to this substance. Titration gave a neutral equivalent weight of 154 (calcd. 145) and approximate pK_a values of

XII

XIII
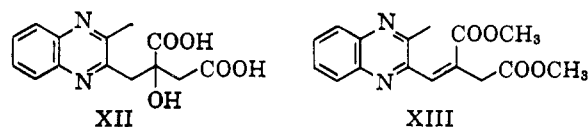
5.4 and 6.7 (50% aqueous ethanol). For comparison the acidity constants of malic acid in water,[12] 3.4 and 5.1, may be cited. It should be recalled (vide supra) that acidity constants are considerably higher in 50% aqueous ethanol than in water. Treatment of the oxidation product XII with diazomethane gave a mixture of products from which two dimethyl esters were isolated. One was obtained as a viscous yellowish liquid, $C_{16}H_{18}N_2O_4$, which on prolonged standing changed to a gummy solid. According to its infrared spectrum it contained a saturated ester (5.75(s) μ) and an unsaturated ester function (5.82(s) and 5.99(w) μ) and its ultraviolet spectrum was similar to that of β-quinoxal-2-yl-α-propenoic acid (XXVII) (see Table III). The n.m.r. spectrum (CCl$_4$) had bands at 7.24, 6.43, 6.20, 6.06 and 2.33 (multiplet) τ (area ratio approximately 3:3:3:2:5), consistent with the C–CH$_3$ group, the OCH$_3$ groups of the saturated and unsaturated esters, the methylene group, and the vinyl and aromatic hydrogens present in structure XIII, which is now proposed for this ester. Since the ester could not be obtained as well-defined crystals, it may have been a mixture of the cis and trans isomers. The other dimethyl ester, $C_{17}H_{18}N_4O_4$, obtained in low yield, had infrared bands at 5.75 and 5.78 μ and exhibited a 2,3-dialkylquinoxaline ultraviolet spectrum (see Table I, compound XIV). Since no NH band could be detected in the infrared, structure XIV is proposed for this substance.[13] However, in the absence of other data, alternative structures such as XV cannot be excluded.

XIV

XV

Heating of the oxidation product XII at its melting point gave a monocarboxylic acid, $C_{13}H_{12}N_2O_2$, which exhibited the β-quinoxal-2-yl-α-propenoic acid spectrum in the ultraviolet (see Table III, compound XVIII). A reasonable mode of formation of such a compound from XII is initial loss of water to give XVI, followed

by decarboxylation to XVII and rearrangement to the thermodynamically more stable conjugated unsaturated system XVIII. The n.m.r. spectrum of the acid (D$_2$O/K$_2$CO$_3$) is in excellent accord with structure XVIII:

XVI → XVII + CO$_2$

XVIII
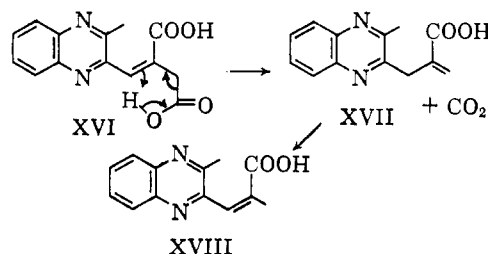
the multiplet centering about 2.8 τ is due to the aromatic hydrogens, the aromatic C–CH$_3$ absorbs at 7.80 τ, and the vinyl hydrogen and the hydrogens of the unsaturated methyl group, whose spins are coupled, ap-

TABLE III

ULTRAVIOLET DATA OF α,β-UNSATURATED QUINOXALINES IN ABSOLUTE ETHANOL

Compound		λ_{max}, mμ (ϵ)		λ_{min}, mμ (ϵ)
XIII	224[a]	262	230
	241[a]	331	287
XVIII	224[a] (14,100)	259 (23,000)	230 (13,000)
	243[a] (18,100)	330 (10,700)	286 (4600)
XXVII	222[a] (15,000)	260 (25,800)	232 (12,200)
	242[a] (14,300)	335 (11,300)	286 (3500)
		342 (11,100)	

[a] Approximate inflection points.

pear at 3.02 (quartet, $J \sim 2$ c.p.s.) and 8.23 (doublet, $J \sim 2$ c.p.s.) τ, respectively. The protons in the non-aromatic system CH=C—CH are known to have coupling constants of 1–2 c.p.s.[14] Although compound XVII was not obtained in the pure state, there is good evidence for its formation as an intermediate. A second substance isolable from the decarboxylation reaction mixture had the characteristics expected of XVII (contaminated with XVIII). In the infrared it showed absorption bands at 5.48 (very weak), 6.13(m) and 7.18 μ, attributable to =CH$_2$ vibrations.[15] Its ultraviolet spectrum indicated it to be a 1:2 mixture of XVIII and a 2,3-dialkylquinoxaline (assuming extinction coefficients approximately equal to those of 2,3-dimethyl-quinoxaline). The material melted partially at 142° without gas evolution, resolidified, and then melted at 180° (pure XVIII melts at 185–186°), and was converted in 70% yield to compound XVIII on short heating at 144°. Hydrogenation of XVIII gave a dihydro compound, XIX, $C_{13}H_{14}N_2O_2$, which had a 2,3-dialkylquinoxaline ultraviolet absorption spectrum (see Table I).

(12) F. Auerbach and E. Smolczyk, Z. physik. Chem., 110, 65 (1924).

(13) In the products from α,β-unsaturated esters and diazomethane nitrogen is invariably attached to the α-carbon atom (J. D. Loudon in "Chemistry of Carbon Compounds," ed. by E. H. Rodd, Vol. IVA, Elsevier Publishing Co., Amsterdam, 1957, p. 263.

(14) Cf., for example, J. D. Roberts, "Nuclear Magnetic Resonance," McGraw–Hill Book Co., Inc., New York, N. Y., 1959, p. 54; J. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, Ltd., London, 1959, p. 125.

(15) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Second Edition, John Wiley and Sons, Inc., New York, N. Y., 1958, p. 34.

XX
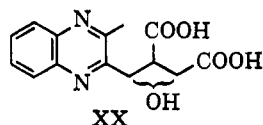
The facile formation of α-methyl-β-(3-methylquin-oxal-2-yl)-propenoic acid (XVIII) from the oxidation product establishes the partial structure XX for the latter compound. Although the position of the hydroxyl group is not known, we favor the tertiary position for the following reason. Even though very little is known about the mechanism of ferricyanide oxidation,[16] it is clear that the oxidation will take place at an electron-rich center. Removal of two electrons from the basic nitrogen in the "adduct" V would lead to structure XXI which, on reaction with base, could give rise to XXII. Cleavage of the lactam ring would then give compound XII in which the hydroxyl group is attached to the tertiary carbon atom. However, regardless of where the hydroxyl group is attached, the partial structure XX


XXI   XXII
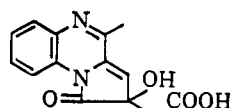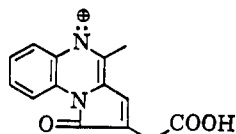
supports the skeleton of the "adduct" as shown in XXIII and the total structure V. The only other structure possibly compatible with the data given earlier, namely XXIV, which is derived from IIIa, must therefore be excluded.



XXIII   XXIV
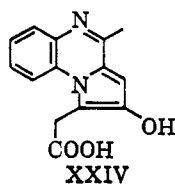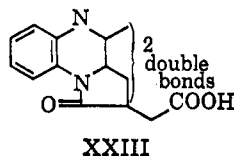
Finally, the model compound XXIX, containing the five-membered lactam ring present in V, was synthesized according to the scheme outlined below. This synthesis was realized only with some difficulty. Sodium borohydride reduction of XXV under some conditions gave mixtures of the expected hydroxy ester XXVI, $C_{14}H_{18}N_2O_3$, the diol XXX, $C_{12}H_{14}N_2O_2$, and/or starting material; under other conditions the diol was the sole product. Although sodium borohydride generally does not attack ester groups,[17] instances of the reduction of esters to alcohols by this reagent are known.[18] The dehydration–hydrolysis, best accomplished by heating XXVI with concentrated sulfuric acid on the steam-bath, proceeded in very poor yield to give XXVII, $C_{12}H_{10}N_2O_2$. From the reaction of XXVI with concentrated sulfuric acid at room temperature only the hydroxy acid XXXI could be isolated. Hydrogenation of XXVII in the presence of palladium-on-carbon gave XXVIII which had a 2,3-dialkylquinoxaline ultraviolet spectrum (see Table I), but crystallized with a quarter of a mole of ethyl acetate according to its analysis, and showed peculiar melting point behavior. Its methyl ester XXXII, however, had the correct analysis ($C_{13}H_{14}N_2O_2$) as well as the expected ultraviolet (see Table I) and infrared spectra. Cyclization of the saturated acid XXVIII to compound XXIX,

$C_{12}H_{10}N_2O$, took place when the acid was treated with acetic anhydride in the presence of sulfuric acid. The model compound XXIX had very nearly the same ultraviolet spectrum as the "adducts" V and IX, their

XXV → XXVI

XXVII

XXXI

XXVIII → XXIX   XXX
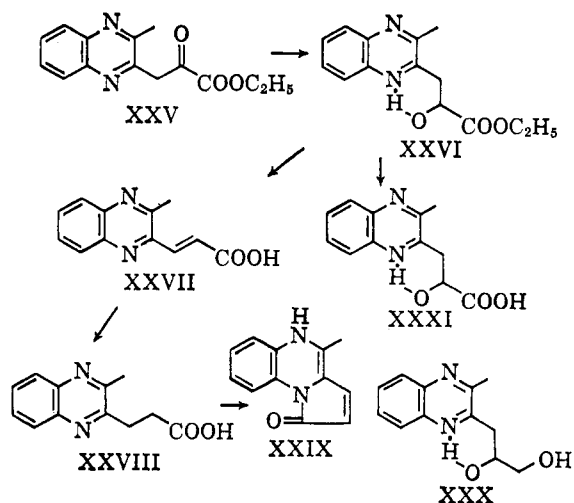
methyl esters and their decarboxylation products (see Table II). Furthermore, its infrared spectrum was very similar in the region 2–7 μ to the spectra of the decarboxylation products VIII and XI.

The unsaturated acid XXVII was more readily prepared from the addition product XXXIII of 2,3-dimethylquinoxaline and chloral.[19] Depending upon conditions, either the mono- or the dichloral addition product (XXXIV) could be prepared. The ultraviolet spectra of these compounds are included in Table I. Treatment of XXXIII with aqueous sodium hydroxide caused hydrolysis of the —CCl_2 group with concurrent dehydration to give the unsaturated acid XXVII directly.[20]

XXXIII   XXXIV
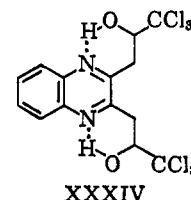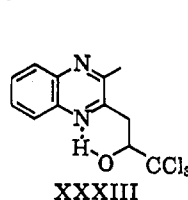
The infrared spectra (solid state) of the "adducts," their derivatives and the model compound merit some further comment. In the carboxylic acids V and IX the NH bands at 3.07 and 3.03 μ, respectively, are stronger than the C–H bands, whereas in the methyl esters VII and X, in the decarboxylated compounds VIII and XI, and in the model compound XXIX this band is weaker. The spectra of the latter group of compounds also show a weak, very broad band in the region 3.6–4.5 μ. We are inclined to attribute these changes to hydrogen bonding. The carboxylic acid group in the "adducts" V and IX is undoubtedly the main source of hydrogen bonding; once this group is removed only the NH groups can contribute to hydrogen-bonded interactions, and the very broad band (3.6–4.5 μ) is apparently due to such interactions.

Although it is not directly relevant to the material discussed above, some mention should be made of the structural implications of the spectral properties of ethyl 3-methylquinoxal-2-ylpyruvate (XXV). On theoretical grounds one might predict that this compound

(16) B. S. Thyagarajan, *Chem. Revs.*, **58**, 439 (1958).

(17) H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962, p. 243.

(18) (a) M. L. Wolfrom and H. B. Wood, *J. Am. Chem. Soc.*, **73**, 2933 (1951); (b) M. L. Wolfrom and K. Anno, *ibid.*, **74**, 5583 (1952); (c) J. Kollonitsch, O. Fuchs and V. Gabor, *Nature*, **173**, 125 (1954); (d) H. Heymann and L. F. Fieser, *J. Am. Chem. Soc.*, **73**, 5252 (1951).

(19) For condensations of chloral with methyl groups adjacent to ring nitrogen atoms in similar heterocyclic systems, see R. G. Jones, E. C. Kornfeld and K. C. McLaughlin, *ibid.*, **72**, 3539 (1950), and references cited therein.

(20) R. B. Woodward and E. C. Kornfeld, *ibid.*, **70**, 2508 (1948); Jones, *et al.* (ref. 19).

should exist in the enolized form XXXV (R = C_2H_5), and its n.m.r. spectrum (CCl_4) could indeed be interpreted in terms of this structure. The resonance lines occur at 8.56 (triplet, $J \sim$ 7 c.p.s.), 7.29, 5.72 (quartet, $J \sim$ 7 c.p.s.), 3.52, 2.5 (center of multiplet), −5.1 (very broad) τ and have an area ratio of 3:3:2:1:4 (:1?). Ultraviolet data are shown in Table IV, and infrared absorption patterns in three media are summarized in Table V. The ultraviolet spectrum of the ester is seen to resemble very closely the spectrum of 3-methylquinoxal-2-ylpyruvic acid (XXXVI).[21] Neither spectrum bears any resemblance to the spectra of the α,β-unsaturated quinoxalines in Table III or the alkyl-

TABLE IV

ULTRAVIOLET ABSORPTION DATA

Compound XXV (XXXVII, R = C_2H_5) $\lambda_{max}^{CCl_4}$, mμ	λ_{max}^{EtOH}, mμ (ϵ)	Compound XXXVI (XXXVII, R = H) λ_{max}^{EtOH}, mμ (ϵ)
	221 (23,500)	221 (23,400)
280[b]	253 (6270)	253 (4950)
288	279[a] (10,200)	280[a] (9540)
313	287 (11,500)	286 (10,600)
325	312 (8120)	313 (7360)
339	330[a] (6550)	332[a] (5520)
371	367[a] (9120)	367[a] (8400)
382	382 (10,200)	382 (9300)
420	418[a] (9270)	418[a] (8280)
441	438 (13,100)	437 (11,500)
468	462 (11,000)	461 (9200)

[a] Approximate inflection points. [b] Epsilon values are not reported, for XXV does not obey Beer's law in CCl_4 solution.

TABLE V

INFRARED ABSORPTION DATA

| Compound XXV (XXXVII, R = C_2H_5) CCl_4	HCCl$_3$	Nujol	Compound XXXVI (XXXVII, R = H) Nujol
5.73(m)		5.75(m)	5.71(s)
5.79(s)	5.79(s)	5.83(s)	5.86(m)
6.05–	6.23(s)	6.22(s)	6.25(s)
6.5	6.38(s)	6.38(s)	6.40(s)
		6.51(s)	6.50(s)

quinoxalines in Table I, but both spectra exhibit a complexity and long wave length absorption reminiscent of the spectrum of the "adduct" V. A similar observation can be made in regard to the infrared spectra: the bands in the 6.0–6.6 μ region of the spectra of XXV and XXXVI are not present in the α,β-unsaturated or saturated quinoxalines, but strong bands in this region were observed in the spectra of the "adducts" V and IX and their derivatives, and are known to be present in the spectra of vinylogous amides.[8] The implication of these observations is, of course, that ethyl 3-methylquinoxal-2-ylpyruvate (XXV) and the corresponding acid XXXVI exist primarily in the tautomeric form XXXVII (R = C_2H_5 and H, respectively) both in the solid state and in solution. The n.m.r. spectrum given above could be interpreted in terms of either structure XXXV or XXXVII (R = C_2H_5) but since the band at

XXXV   XXXVII
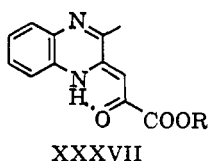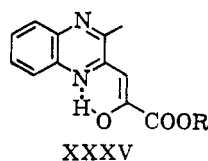
−5.1 τ is exceedingly broad, rapid exchange of the proton between oxygen and nitrogen probably takes place.

(21) W. Börsche and W. Doeller, *Ann.*, **537**, 39 (1939).

It is interesting to note that the OH hydrogen of acetylacetone, XXXVIII, also absorbs at very low field, namely −5.3 τ.[22]

XXXVIII
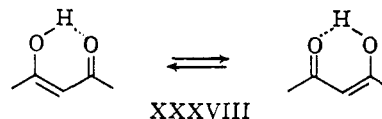
Experimental

2,3-Dimethylquinoxaline–N-Phenylmaleimide "Adduct" (IV). —This material was prepared according to Mustafa and Kamel,[4] and after several crystallizations from benzene had m.p. 185.5–186.5° (reptd. 184°); infrared bands: 5.64(w), 5.86(s), 5.97(sh), 6.25 μ; n.m.r. (CDCl$_3$): 7.24, 6.97 (center of multiplet), 6.38 underneath which lies a multiplet, and a complex multiplet extending from 1.8–2.7 which has a sharp peak at 2.53 τ; area ratio 3:2:3:9.

Anal. Calcd. for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68. Found: C, 72.67; H, 5.21; N, 12.56.

The 12% yield of pure product could be increased to 27% by tripling the time of reflux. The remaining material appeared to be a mixture of starting materials and product.

2,3-Dimethylquinoxaline–Maleic Anhydride "Adduct" (V).— The best yield of product was obtained when an acetic acid solution (100 ml.) of the quinoxaline (15 g., 95 mmoles) and maleic anhydride (15 g., 150 mmoles) containing 5 ml. of water was refluxed gently for 3 hr. The dark solution, which contained a yellow solid, was then allowed to stand for 3 hr., and the solid was filtered and rinsed with acetic acid followed by ether. The product (12 g.) retains acetic acid and does not melt below 300°. An analytical sample crystallized from acetic acid as dull yellow needles and was dried at 118° (0.025 mm.) for 7 hr.; infrared bands (perfluorocarbon oil): 3.07, 3.13, 3.21, 3.4–5.5, 5.87(s), 5.99(s), 6.19(m), 6.26(m), 6.39 and 6.43(s), 6.54(s), 6.67(s) μ and others; n.m.r. (D$_2$O/KOH): 8.06, 6.67, 3.39, 3.22 and 1.2 (broad) τ with approximate area ratio of 3:2:1:4:1, respectively; pK_a (50% aq. ethanol) 5.7.

Anal. Calcd. for $C_{14}H_{12}N_2O_3$: C, 65.62; H, 4.72; N, 10.93; C–CH$_3$, 5.9; neut. equiv. wt., 256. Found: C, 65.56; H, 4.93; N, 10.79; C–CH$_3$, 4.3; neut. equiv. wt., 231.

The same compound was also obtained (a) on refluxing a toluene solution of dimethylquinoxaline and maleic anhydride for 7 hr.[3a]; (b) on refluxing a toluene solution of dimethylquinoxaline and maleic acid for 20 min.; (c) on heating for 10 min. at 130–140° the complex, m.p. 123–124°, obtained when equimolar ethereal solutions of dimethylquinoxaline and maleic acid are mixed. Under most reaction conditions the product was obtained as a dark brown solid which was best purified by treatment with aq. dil. base and Norit, followed by acidification with acetic acid.

2,3-Dimethylquinoxaline–Maleic Acid Complex.—After mixing filtered ethereal solutions of pure dimethylquinoxaline (0.64 g., 4 mmoles) and maleic acid (0.47 g., 4 mmoles), colorless needles (0.38 g., 35%) separated slowly. The compound, which turns yellow at 120° and gives a red melt at 123–124°, was analyzed without further purification; infrared bands: 3.28, broad bands at 4.0, 4.25 and 5.2, 5.79(sh), 5.86(s), 6.08(m), 6.3(w, broad), 6.66 μ; λ_{max}^{EtOH}: 236 mμ (ϵ 25,700), 240 (infl.) (21,000), 305 (infl.) (5500), 316 (6800), 324 (infl.) (5200), λ_{min} 262 (2000).

Anal. Calcd. for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.15; N, 10.21. Found: C, 61.30; H, 5.22; N, 10.20.

Evaporation of the ether gave an additional 0.72 g. (100% total) with the same melting point.

Methyl Ester (VII) of the "Adduct."—A mixture of finely powdered V, ethanol and a large excess of ethereal diazomethane was left to stand overnight. The solid was filtered and recrystallized from ethanol to give glistening yellow needles which do not appear to melt, but turn black by 250°; infrared bands (perfluorocarbon oil): 3.11, 3.16, 3.23, 3.8–4.5, 5.77(s), 5.86 (sh), 5.97(m), 6.23(s), 6.35(s, broad), 6.53(s), 6.68(s) μ.

Anal. Calcd. for $C_{15}H_{14}N_2O_3$: C, 66.65; H, 5.22; N, 10.37. Found: C, 66.33; H, 5.50; N, 10.22.

Decarboxylation of V: Formation of VIII.—When the crude "adduct" (0.50 g., 2 mmoles) was heated at 240–270° and 0.5 mm. for 6 hr., an orange compound (0.18 g., 43%) sublimed. Crystallization from acetic acid afforded glistening orange-yellow needles, m.p. > 300°. The analytical sample was dried at 118° (0.05 mm.) for 12 hr.; infrared bands (perfluorocarbon oil): 3.11,

(22) G. O. Dudek and R. H. Holm, *J. Am. Chem. Soc.*, **83**, 2099 (1961).

(23) Melting points are uncorrected; ultraviolet absorption maxima are accurate to ±2 mμ; infrared spectra were taken as Nujol mulls unless otherwise specified and the bands in the 5.6–6.6 μ region were corrected by calibration against the 6.11 μ band of atmospheric water vapor. We are indebted for the microanalyses to the Scandinavian Microanalytical Laboratory, Box 25, Herlev, Denmark.

3.17, 3.24, 3.8–4.4, 5.98(m), 6.23(s), 6.38(s, broad), 6.55(s), 6.69(s) μ.

Anal. Calcd. for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20; C–CH₃, 14.2. Found: C, 73.28; H, 5.72; N, 13.41; C–CH₃, 9.4.

2-Methylquinoxaline–Maleic Anhydride "Adduct" (IX).—A mixture of 2-methylquinoxaline (7.2 g., 50 mmoles), maleic anhydride (3.9 g., 40 mmoles) and acetic acid (50 ml.) was refluxed for 5 hr. The black solution was cooled, scratched, and left to stand for several hours. The solid was filtered (6 g.) and purified by dissolving it in excess aq. 10% potassium hydroxide, treatment with Norit, followed by filtration and acidification of the filtrate with acetic acid. Several crystallizations from acetic acid gave an analytical sample as yellow needles, m.p. 229° dec. (darkens > 200°), dried at 100° *in vacuo;* infrared bands: 3.03, 3.16, 3.25, 3.7–4.4, 5.82(s), 5.94(s), 6.19(s), 6.26(s), 6.30(s), 6.6(s, broad), 6.74(s) μ.

Anal. Calcd. for $C_{13}H_{10}N_2O_3$: C, 64.46; H, 4.16; N, 11.57. Found: C, 64.36; H, 4.30; N, 11.51.

The methyl ester X of IX was formed with ethereal diazomethane in the presence of methanol and purified to lustrous yellow needles by crystallization from ethanol. It does not appear to melt, but darkens above 230° and is black by 240°; infrared bands: 3.10(sh), 3.17, 3.25, 3.6–4.4, 5.75(s), 5.97(m), 6.20(sh), 6.26(s), 6.39(s), 6.54(s), 6.69 μ.

Anal. Calcd. for $C_{14}H_{12}N_2O_3$: C, 65.62; H, 4.72; N, 10.93. Found: C, 65.56; H, 4.76; N, 10.93.

The decarboxylation product XI was prepared from IX by sublimation at 240° and 0.2 mm., followed by crystallization from ethanol. The yellow needles darken above 235° and turn black at 250°; infrared bands: 3.10, 3.17, 3.27, 3.6–4.5, 5.97 (m), 6.20(sh), 6.27(s), 6.39(s), 6.60(s), 6.69(s) μ.

Anal. Calcd. for $C_{12}H_{10}N_2O$: C, 72.71; H, 5.09; N, 14.13. Found: C, 72.34; H, 5.30; N, 13.96.

Oxidation of V: Formation of XII.—A solution of V (10 g., 39 mmoles) in aq. 15% potassium hydroxide (100 ml.) was stirred during the addition of an aq. concd. potassium ferricyanide (26 g., 79 mmoles) solution. The mixture was left to stand for *ca.* 10 min. and then filtered through Celite. The filtrate was stirred and aq. dil. sulfuric acid was slowly added to pH 4. After a few minutes the brownish solid was filtered and rinsed with water. The filtrate was treated with more dil. acid to pH 1, some of the black gum that separated was removed with a stirring rod, and the mixture was left to stand *ca.* 20 min. The second crop was filtered and rinsed with water to give a total of 7.7 g. The product was dissolved in ethanol (*ca.* 200 ml.), treated with a large amount of Norit, and the filtered solution concentrated *in vacuo* to about 25 ml. The pale yellow solid (4.0 g., 35%) had m.p. 124° dec. After several crystallizations from aqueous ethanol, it was colorless and had m.p. 143° dec.; infrared bands: 2.87, 3.7–4.5, 5.0–5.5, 5.85(s, broad), 6.0(sh), 6.70 μ; pK_a (50% aq. ethanol): 4.5 and 6.7.

Anal. Calcd. for $C_{14}H_{14}N_2O_5$: C, 57.93; H, 4.86; N, 9.65; neut. equiv. wt., 145. Found: C, 59.24, 57.39; H, 4.95, 5.10; N, 9.84, 8.81; neut. equiv. wt., 154.

Treatment of XII with Diazomethane: Formation of XIII and XIV.—The once-recrystallized compound XII (0.60 g.) was treated with an excess of ethereal diazomethane in the presence of methanol. When all of the solid had dissolved, the solvent was evaporated and the residual dark red oil was put on a column of Merck alumina (35 g.) in benzene. From the first five 40-ml. fractions liquids were obtained which had the same infrared spectrum (neat, 5.75(s), 5.82(s), 5.99(w) μ) and which solidified on standing for 2 weeks (130 mg., 22%). Since the solids could not be crystallized, the combined fractions were "molecularly" distilled to a viscous pale yellow liquid, compound XIII.

Anal. Calcd. for $C_{16}H_{16}N_2O_4$: C, 63.99; H, 5.37; N, 9.33. Found: C, 63.60; H, 5.54; N, 9.81.

Later fractions eluted with ether–benzene (2–10% ether) contained liquids whose infrared spectra differed slightly from that above (160 mg.) (neat, 5.75(s), 5.82(s), 6.10(w) μ). A mixture of 50% ether–benzene and ether eluted nearly pure compound XIV (60 mg., 10%) which after crystallization from ether had m.p. 128.5–129°; infrared bands: 5.75 and 5.78 (same intensity), 6.37(m) μ.

Anal. Calcd. for $C_{17}H_{18}N_4O_4$: C, 59.64; H, 5.30; N, 16.37. Found: C, 59.65; H, 5.43; N, 16.33.

Decarboxylation–Dehydration of XII to XVIII.—The decarboxylation product XVIII was first obtained in very poor yield on sublimation of XII at 150–170° and 0.5 mm. It crystallized from aq. ethanol to give faintly yellow fluffy needles which after drying had m.p. 185–186° dec.; infrared bands: 3.7–4.4, 5.92(s), 6.04(sh), 6.17(w) μ; n.m.r. (D₂O/K₂CO₃): 8.23 (doublet, $J \sim 2$ c./s.), 7.80, 3.02 (quartet, $J \sim 2$ c.p.s.), 2.80 (multiplet) τ with area ratio 3:3:1:4, respectively.

Anal. Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.29; H, 5.36; N, 12.19.

The same product was best prepared by heating a mixture of XII (0.50 g.) and xylene (*ca.* 40 ml.) for 15 min. in an oil-bath preheated to 145°. On cooling, the product crystallized as pale yellow fluffy needles (0.21 g., 53%, m.p. 184–185° dec.). Evaporation of the mother liquor to dryness under reduced pressure and treatment of the residue with some ether gave 0.16 g. (93% total) of a substance[24] which melted partially at 142°, then resolidified and melted at 180° dec.; infrared bands: 3.7–4.4, 5.48(very w), 5.88(sh), 5.91(s), 6.13(m), 7.18 μ; ultraviolet maxima: 236, 240(sh), 262 and 318 mμ. When this substance (0.16 g.) was heated in refluxing xylene (20 ml.) for 15 min. and the solution was cooled, compound XVIII separated as light brown needles (0.11 g., 69%, m.p. 185–186° dec., infrared and ultraviolet spectra identical to those above).

Hydrogenation of XVIII to XIX.—Compound XVIII (0.18 g., 0.79 mmole) in ethyl acetate was allowed to react with hydrogen in the presence of prereduced 5% Pd/C until 1.2 equiv. (23 ml.) had been consumed. The reduction mixture almost immediately assumed a deep reddish-brown color (presumably due to the formation of some 1,4-dihydroquinoxaline) which rapidly faded when the reduction mixture was exposed to air. The catalyst was filtered, the filtrate evaporated *in vacuo* to an oil, and the residue left to crystallize in the presence of ether. The product (90 mg., 50%, m.p. 135–137°) was recrystallized from ether to sturdy colorless crystals, m.p. 136–137°; infrared bands: 3.7–4.4, 5.87(s) μ.

Anal. Calcd. for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.90; H, 6.24; N, 12.23.

Ethyl 3-Methylquinoxal-2-ylpyruvate (XXV).[21,25]—Diethyl oxalate (14.6 g., 0.1 mole) was added to a solution of sodium (2.3 g., 0.1 mole) in absolute ethanol (50 ml.) in an erlenmeyer flask, followed by 2,3-dimethylquinoxaline (15.8 g., 0.1 mole) dissolved in warm ethanol (*ca.* 80 ml.). Almost at once a yellow solid separated. The solid paste was left to stand overnight and then filtered. The solid was rinsed with ethanol and ether, and then treated with 2 N sulfuric acid (*ca.* 35 ml.) and chloroform. The layers were separated, the aqueous layer was extracted twice more with chloroform, and the combined extracts were washed with water, dried over sodium sulfate, and stripped of solvent under reduced pressure. Ether was added to the residue and the canary-yellow solid was filtered (17 g., m.p. 113–119°). Crystallization from absolute ethanol gave fine yellow needles, m.p. 127–129° (lit. 129–130°,[21] 129°[25]). For infrared bands, see Table V; n.m.r. (CCl₄): 8.56 (triplet), 7.29, 5.72 (quartet) 3.52, 2.5 (center of multiplet), −5.1 (broad) τ, with area ratio of 3:3:2:1:-4(:1?), respectively.

Sodium Borohydride Reduction of XXV: Formation of XXVI and XXX.—Sodium borohydride (0.15 g., 4 mmoles) was dissolved in water (15 ml.), and ethanol (15 ml.) and compound XXV (1.0 g., 3.9 mmoles) were added. When most of the solid had gone into solution, the mixture was filtered, the filtrate treated with a little acetic acid and then concentrated *in vacuo.* Water was added, the mixture extracted three times with benzene, the extract dried over sodium sulfate and stripped of solvent. The residue was dissolved in ether, treated with Norit, and the solvent evaporated to give a yellow solid, m.p. 73–76° (0.62 g.). After six crystallizations from carbon tetrachloride with great losses, the product XXVI still retained a yellow tinge (m.p. 77.5–78°); infrared bands: 3.18(m), 5.71(s) μ.

Anal. Calcd. for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.26; H, 6.29; N, 10.60.

The diol XXX was always formed to some extent, but it remained in the aqueous layer when XXVI was extracted with benzene. It was formed exclusively when XXV (0.78 g., 3 mmoles) was treated with solid sodium borohydride (0.30 g., 7.9 mmoles) in ethanol and the mixture was heated on the steam-bath for a few minutes. The almost colorless solution was cooled, acetic acid was added until hydrogen evolution ceased, and the solvent was evaporated under reduced pressure. The residue was dissolved in water (10 ml.) and the solution extracted twice with chloroform. After the extract was dried over sodium sulfate, it was evaporated *in vacuo* to an oil which readily crystallized on scratching and treating with ether (0.62 g., 92%, m.p. 123–124.5°). The product XXX was recrystallized from ethyl acetate; infrared bands: 2.95 (s), 3.12(s), 3.7–4.4 μ.

Anal. Calcd. for $C_{12}H_{14}N_2O_2$: C, 66.03; H, 6.47; N, 12.84. Found: C, 65.88; H, 6.57; N, 12.67.

Dehydration of XXVI: Formation of XXVII and XXXI.—The crude hydroxyester XXVI (3.1 g., 14 mmoles) was heated with concd. sulfuric acid (25 ml.) on the steam-bath for 25 min. The dark solution was cooled, poured on ice, and the solution made

(24) Comparison of its ultraviolet spectrum with the spectra of XVIII and 2,3-dimethylquinoxaline indicated it to be a mixture of XVIII and XVII (approximately 1:2).

(25) G. M. Bennett and G. H. Willis, *J. Chem. Soc.,* 1960 (1928).

alkaline with aq. 15% potassium hydroxide. The solution was extracted three times with chloroform, the aq. layer reacidified with 2 N sulfuric acid and the brown solid filtered (1.2 g.). The product XXVII was purified by dissolving it in dil. base, treating with Norit, and reprecipitating with sulfuric acid (0.52 g., 20%, m.p. 210–213° dec.). An analytical sample, m.p. 213° dec., was prepared by crystallization from aq. acetic acid; infrared bands: 3.7–4.4, 5.1–5.6, 5.70(m), 5.87(s), 6.08(m), 6.70(m) μ.

Anal. Calcd. for $C_{12}N_{10}N_2O_2$: C, 67.28; H, 4.71; N, 13.08. Found: C, 67.07; H, 4.67; N, 13.20.

Treatment of the hydroxyester XXVI with concd. sulfuric acid at room temperature for 1 hr. and the same work-up as above did not give a precipitate on reacidification. The acidified solution was therefore extracted three times with chloroform and the chloroform evaporated under reduced pressure. The residue was an almost colorless powder (50%) which was recrystallized from small amounts of ethanol to give the colorless hydroxyacid XXXI, m.p. 171–173°; infrared bands: 2.86, 3.7–4.4, 5.0–5.6, 5.85 (broad) μ.

Anal. Calcd. for $C_{12}H_{12}N_2O_3$: C, 62.06; H, 5.21; N, 12.06. Found: C, 62.08; H, 5.30; N, 11.94.

An attempt to dehydrate XXVI by heating with acetic anhydride on the steam-bath for 15 hr. gave a liquid which could not be crystallized. Base hydrolysis of the liquid led to the formation of both the hydroxyacid XXXI and the α,β-unsaturated acid XXVII. Treatment of XXVI with thionyl chloride on the steam-bath for 1 hr. gave an intractable dark oil which was not further investigated.

2,3-Dimethylquinoxaline–Chloral Addition Compounds, XXXIII and XXXIV. A solution of the quinoxaline (7.0 g., 44 mmoles) in pyridine (50 ml.) was heated to 60° on the steam-bath and chloral (6.0 g., 40 mmoles) was added dropwise with vigorous swirling. The solution was heated for 50 min., and then freed of pyridine under reduced pressure. The dark residue was dissolved in ethanol and somewhat less than one volume of water was added (too much water gives very impure product). The nearly colorless solid that slowly separated (5.1 g., m.p. 131–143°) was recrystallized from carbon tetrachloride (2.3 g., 19%, m.p. 143–146°; second crop, 13%, m.p. 139–144°). An analytical sample of XXXIII, m.p. 147.5–148°, was obtained as a colorless powder.

Anal. Calcd. for $C_{12}H_{11}N_2OCl_3$: C, 47.15; H, 3.62; N, 9.16; Cl, 34.81. Found: C, 46.98; H, 3.56; N, 9.22; Cl, 35.37.

When an excess of chloral and a small amount of pyridine were used, a mixture of two compounds (m.p. 148–151°) was obtained from which the dichloral addition compound XXXIV could be separated by several crystallizations from benzene and benzene-pentane. The product crystallized as colorless solid kernels, m.p. 175–179° dec. (depending upon the rate of heating). The material in the mother liquors was a mixture, which could nevertheless be used for the preparation of XXVII.

Anal. Calcd. for $C_{14}H_{12}N_2O_2Cl_6$: C, 37.11; H, 2.67; N, 6.18; Cl, 46.94. Found: C, 37.64; H, 2.88; N, 6.10; Cl, 46.81.

The monochloral addition product was readily converted to the dichloral addition product on treatment with chloral and pyri-

dine. The infrared bands distinguishing between the two compounds are at 8.63, 8.80, 9.11 (sharp), and 13.18 μ for XXXIII and at 8.74, 8.84, 8.98 and *ca*. 9.17 and 13.10 μ for XXXIV.

Base Treatment of XXXIII: Formation of XXVII. When an aqueous solution of sodium hydroxide (2.4 g., 60 mmoles, in 10 ml. of water) was slowly added to a gently boiling ethanolic solution (12 ml.) of XXXIII (3.4 g., 11 mmoles), vigorous ebullition occurred. The dark solution was cooled, treated with charcoal, and acidified with dil. sulfuric acid to pH 3. The resulting light brown precipitate (1.7 g.) was recrystallized from aq. acetic acid and then was the same in all respects as the acid, m.p. 213° dec., obtained from the hydroxyester XXVI.

Hydrogenation of XXVII: Formation of XXVIII.—A solution of XXVII (1.1 g., 5.1 mmoles) in ethyl acetate (200 ml.) was stirred with hydrogen in the presence of 5% Pd/C (200 mg.) until 1.04 equiv. (132 ml.) was consumed. The same color changes took place as were observed in the formation of XIX. The catalyst was filtered, and the solvent was removed under reduced pressure. The residue was crystallized from ethyl acetate and then had m.p. 148–167° which did not change on repeated crystallization from the same solvent or from ethanol–pentane; infrared bands: 3.6–4.4, 5.75(sh), 5.81 μ. The analytical sample was dried at room temperature and 0.05 mm. for 12 hr.

Anal. Calcd. for $C_{12}H_{12}N_2O_2 \cdot 0.25\ EtOAc$: C, 65.53; H, 5.92; N, 11.76. Found: C, 65.55, 65.74; H, 5.99, 5.90; N, 11.75, 11.91.

When the acid was sublimed under reduced pressure it became yellow and then had m.p. 167–168°. After crystallization from ethyl acetate it was colorless and had m.p. 152–168°. It was dried at 80° and 0.025 mm. for 24 hr.

Anal. Calcd. for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.09; H, 5.86; N, 12.28.

The methyl ester XXXII of XXVIII was prepared with ethereal diazomethane and purified by sublimation (80–90°, 0.04 mm.) to fine colorless needles, m.p. 97–98°; infrared band: 5.78(s) μ.

Anal. Calcd. for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.78; H, 6.16; N, 12.24.

Cyclization of XXVIII to XXIX.—The finely powdered acid XXVIII (0.50 g.) was added to hot (70°) acetic anhydride (40 ml.) containing a few drops of concd. sulfuric acid, and the solution was heated for 20 min. on the steam-bath. It was then concentrated to a small volume, the residue was thoroughly cooled, and water was added. When 10% KOH was added to pH 5, an orange fluffy material precipitated. After filtration and air-drying, the compound was bright red (0.47 g.). It was recrystallized several times from acetic acid (a small amount of dark compound insoluble in hot acetic acid was filtered and discarded) to give orange-yellow needles, m.p. >340°, darkens above 190°. The analytical sample was dried at 100° and 0.20 mm. for 12 hr. and then was deep orange. After standing for several weeks, the compound became brown; infrared bands: 3.11, 3.17, 3.24, 3.6–4.4, 6.00(w), 6.17, 6.23, 6.38(s), 6.56(s), 6.70 μ.

Anal. Calcd. for $C_{12}H_{10}N_2O$: C, 72.71; H, 5.09; N, 14.13; C–CH₃, 7.6. Found: C, 72.52; H, 5.12; N, 13.94; C–CH₃, 1.9.

Photochemical Dimerization of 2-Aminopyridines and 2-Pyridones[1,2]

BY EDWARD C. TAYLOR AND ROBERT O. KAN

Ultraviolet irradiation of 2-aminopyridine, 2-amino-5-chloropyridine, 2-amino-3-methyl-, 4-methyl-, 5-methyl- and 6-methylpyridines, and of N,6-dimethyl-2-iminopyridine in hydrochloric acid solution resulted in the formation of 1,4-dimers. A similar series of photodimers (XIII) has been prepared from the corresponding 2-pyridones, and the two series have been directly interrelated by alkaline hydrolysis of the tetrahydro dimer of 2-aminopyridine to the tetrahydro dimer of 2-pyridone. Assignment of the *anti-trans* configuration to all dimers has been made on the basis of a detailed study of their n.m.r. spectra. The unusual chemical and physical properties of these dimers are discussed.

Valence-bond tautomerism is now a well-established phenomenon, and although most examples involve the bridging of a seven-membered ring to give a bicyclo-(3.2.0)heptene or heptadiene system, several instances of the conversion of cyclic hexadienes incorporated into rigid polycyclic systems into bicyclo(2.2.0)hexenes have been reported.[3] It seemed to us that a possible monocyclic system which upon irradiation might be expected to undergo valence-bond tautomerism in the above sense would be a salt of 2-aminopyridine, since the formation of a cyclic amidine salt (2-aminopyridine is known to protonate on the ring nitrogen rather than on the exocyclic amino group)[4] might give partial diene

(3) (a) W. H. Schuller, R. N. Moore, J. E. Hawkins and R. V. Lawrence, *J. Org. Chem.*, **27**, 1178 (1962); (b) W. G. Dauben and G. J. Fonken, *J. Am. Chem. Soc.*, **81**, 4060 (1959).

(4) A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," Methuen and Co., Ltd., London, 1962, p. 143.