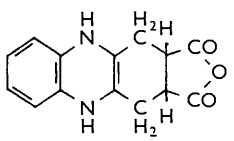
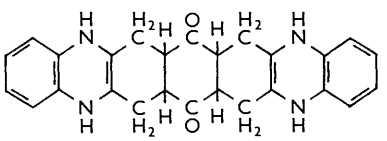
586. *The Nature of the Addition Reactions of Methyl-azines with Some Typical Dienophiles.*

By C. W. Bird and G. W. H. Cheeseman.

The adducts of 2,3-dimethylquinoxaline with maleic anhydride, *p*-benzoquinone, and *N*-phenylmaleimide have been reinvestigated and revised structures assigned. The reactions of *N*-phenylmaleimide with 2-methylquinoxaline, 2- and 4-methylquinoline, and 2- and 4-methylpyridine have also been examined.

2,3-Dimethylquinoxaline has been shown to form adducts with several typical dienophiles, namely, maleic anhydride, *p*-benzoquinone, and *N*-phenylmaleimide.[1,2] These products were formulated as (I), (II), and (III) primarily since analogous adducts were not isolated from reactions with other quinoxalines in which there was no possibility of tautomerism to a buta-1,3-diene system, as (IV). Alternative structures for these adducts as 2,3-dihydroquinoxalines were also suggested. The suggested structures seemed to be open to criticism on a number of grounds, *inter alia*, the apparent stability of these dihydroquinoxalines, and the results of the present investigation clearly vitiate the suggested structures.


(I)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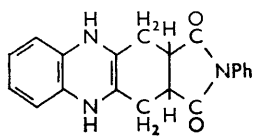
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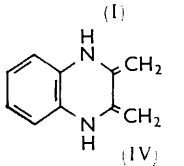
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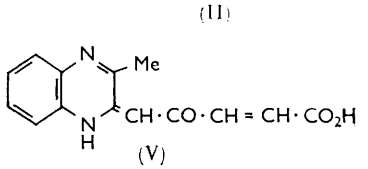
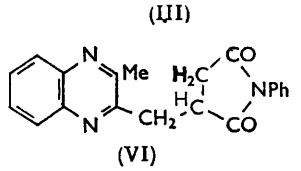

(V)


(VI)

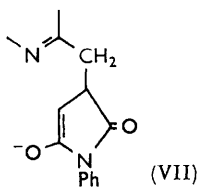
The reaction of maleic anhydride and 2,3-dimethylquinoxaline in refluxing toluene gave the reported adduct in poor yield. An improved yield was obtained when xylene was used as solvent. The adduct showed both acidic and basic properties. It was readily converted into a monomethyl ester and on hydrogenation, in acid solution and in the presence of a palladium–charcoal catalyst, it rapidly absorbed one mol. of hydrogen. Kuhn–Roth oxidation demonstrated the presence of at least one *C*-methyl group in the molecule. The brownish-yellow adduct had an absorption maximum in the visible region of the spectrum at 420 mμ (ε 12,150), indicating the presence of an extended conjugated system. The infrared spectrum of the adduct suggested the presence of a >NH group ($\nu_{max.}$ 3280 cm.$^{-1}$), a carboxyl-hydroxyl group ($\nu_{max.}$ *ca.* 2800 and *ca.* 2400 cm.$^{-1}$, absent in the methyl ester), two conjugated carbonyl groups ($\nu_{max.}$ 1700 and 1665 cm.$^{-1}$), and a *trans*-disubstituted double bond ($\nu_{max.}$ 945 cm.$^{-1}$). This evidence seems to lead to reformulation of

[1] Schönberg and Mustafa, *J.*, 1943, 654.
[2] Mustafa and Kamel, *J. Amer. Chem. Soc.*, 1955, **77**, 1828.

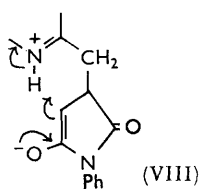
the adduct as (V, or a tautomer). Analogous adducts also appear to be formed by 2-methylquinoxaline and 2-methylquinoline but the products proved to be difficult to manipulate.

The " benzoquinone adduct " was obtained by the published method; large amounts of quinhydrone were also formed. The ultraviolet spectrum of the product was identical with that of 2,3-dimethylquinoxaline. The infrared spectrum showed no carbonyl absorption, and maxima at *ca.* 3100 and 1200 cm.$^{-1}$ are consistent with the presence of phenolic groups. Acetylation with acetic anhydride gave quinol diacetate. An identical product was obtained by crystallising quinol from toluene in the presence of an excess of 2,3-dimethylquinoxaline. Thus the adduct is a complex of two molecules of the quinoxaline and one of quinol. The reaction of 2-methylquinoline and benzoquinone has recently been shown to yield an analogous 2 : 1 2-methylquinoline–quinol adduct.[3]

The adduct prepared by the reported method from 2,3-dimethylquinoxaline and *N*-phenylmaleimide showed an ultraviolet spectrum closely similar to that of 2,3-dimethylquinoxaline itself, thus pointing to the survival of the quinoxaline nucleus. The infrared spectrum exhibited carbonyl absorptions at 1765w and 1700s cm.$^{-1}$ consistent with the presence of an *N*-phenylsuccinimide ring, as in (VI). An analogous *N*-phenylmaleimide adduct was prepared from 2-methylquinoxaline, demonstrating that tautomerism to a buta-1,3-diene type system is not a structural prerequisite for addition. It therefore appeared that these reactions were more correctly regarded as examples of Michael addition and that similar adducts should be formed by other compounds having activated methyl groups. In agreement with this conclusion 1 : 1 adducts were formed by both 2-methylquinoline and 2-methylpyridine. The ultraviolet spectra of the adducts were closely similar to those of the parent 2-methyl compounds, and the infrared spectra indicated the presence of the *N*-phenylsuccinimide ring. Much basic polymer was formed together with 1 : 1 adduct in all these reactions, but when 4-methylquinoline and 4-methylpyridine were used as substrates only basic polymer, and no adduct, could be isolated. This suggests that some additional factor is operative. If the intermediate (VII) formed by the addition of the heterocyclic anion to *N*-phenylmaleimide is protonated as shown, then intramolecular transfer of a proton in (VIII) gives the adduct (VIII would also result from direct



(VII)



(VIII)

addition of the tautomeric alkylidene form of the 2-methyl compound to *N*-phenylmaleimide). The polymer formed in these reactions could arise from interaction of either (VII) or (VIII) with further molecules of *N*-phenylmaleimide. The basicity of these polymers, which also show the expected infrared absorptions for *N*-phenylsuccinimide residues, supports the conclusion. The suggested mechanism of adduct formation is clearly not applicable to the 4-methyl compounds, though a similar mechanism for polymer formation could operate.

Experimental

Infrared spectra were recorded for Nujol mulls, unless otherwise stated, on a Perkin–Elmer model 137 instrument. Ultraviolet spectra were measured for ethanol solutions on a Unicam S.P. 500 or S.P. 700 instrument. Solutions for chromatography were prepared in benzene and chromatographed on silica gel with benzene containing increasing proportions of ethyl acetate. Xylene was dried by distillation before use.

[3] Bothner-By, *J. Amer. Chem. Soc.*, 1955, **77**, 749.

The Adduct of 2,3-Dimethylquinoxaline and Maleic Anhydride.—2,3-Dimethylquinoxaline [4] (3·16 g.) and maleic anhydride (2·0 g.) were stirred under reflux in xylene (50 ml.). The product rapidly crystallised from the hot solution and after 3 hr. the precipitate (1·15 g.) was collected. The filtrate was heated and stirred for a further 18 hr. and a second crop of slightly discoloured adduct (1·75 g.) obtained. Crystallisation of the product from glacial acetic acid (120 parts) gave brownish-yellow needles of compound (V), m. p. >300°, soluble in aqueous sodium hydrogen carbonate and dilute mineral acid (Found: *C*-Me, 4·0. Calc. for 1*C*-Me, 5·9%), $\lambda_{max.}$ 233 (ε 24,600), 298 (ε 9360), 420 mμ (ε 12,150), $\nu_{max.}$ 3280, *ca.* 2800, *ca.* 2400, 1700, 1665, 945, 765 cm.$^{-}$. The xylene mother-liquor was extracted successively with 2N-sodium carbonate and 2N-sulphuric acid. Basification of the acid extracts gave unchanged 2,3-dimethylquinoxaline (0·95 g.).

Hydrogenation of the adduct in acidic solution resulted in the rapid uptake of 1 mol. of hydrogen.

When dry hydrogen chloride was bubbled through a suspension of the adduct (1·4 g.) in dry methanol (50 ml.), the solid dissolved and then a crystalline hydrochloride separated. This was filtered off and triturated with an excess of 2N-sodium carbonate. Crystallisation from methanol (75 ml.) gave *methyl* 5-(1,2-*dihydro*-3-*methylquinoxalin*-2-*ylidene*)-4-*oxopent*-2-*enoate* (cf. V) as brownish-yellow needles or plates, decomposing indefinitely above 230° (Found: C, 66·5; H, 5·1; N, 10·4. $C_{15}H_{14}N_2O_3$ requires C, 66·6; H, 5·2; N, 10·4%).

Reaction of 2,3-Dimethylquinoxaline with Benzoquinone.—This was carried out as previously described.[1] The product had m. p. 188—190°, $\lambda_{max.}$ 236 (ε 52,200), 316 mμ (ε 14,400), $\nu_{max.}$ *ca.* 3100, 1240, 1200, 845, 835, 780, 755 cm.$^{-1}$. Acetylation with acetic anhydride gave *p*-diacetoxybenzene, identified by m. p. and mixed m. p.

An identical *adduct* was obtained by crystallising quinol from toluene containing an excess of 2,3-dimethylquinoxaline (Found: C, 73·5; H, 6·2; N, 13·1. $C_{26}H_{26}N_4O_2$ requires C, 73·2; H, 6·1; N, 13·1%).

N-*Phenylmaleimide.*—This was prepared from maleanilic acid by the recorded method,[5] except that the cyclisation was carried out in a mixture of acetic anhydride and acetic acid rather than in acetic anhydride alone. The product was purified by crystallisation from light petroleum (b. p. 60—80°; 40 parts). Maleanilic acid was prepared by the addition of maleic anhydride to a solution of aniline in ethanol.

Reactions with N-*Phenylmaleimide.*—(*a*) 2,3-Dimethylquinoxaline gave the reported adduct [2] (VI), m. p. 185—186°, $\lambda_{max.}$ 237 (ε 19,900), 316 mμ (ε 4670), $\nu_{max.}$ 1765w, 1700, 1180, 770, 710 cm.$^{-1}$.

(*b*) 2-Methylquinoxaline (4·3 g.) and *N*-phenylmaleimide (5·2 g.) in xylene (60 ml.) were heated under reflux for 24 hr. Most of the xylene was removed *in vacuo* and the residue dissolved in a little methanol and set aside to crystallise. The crude product (1·7 g.) was chromatographed. Crystallisation from ethanol (20 ml.) gave N-*phenyl*-α-*quinoxalin*-2-*ylmethylsuccinimide*, m. p. 132—133° (Found: C, 71·9; H, 4·9; N, 13·0. $C_{19}H_{15}N_3O_2$ requires C, 72·0; H, 4·7; N, 13·3%), $\lambda_{max.}$ 236 (ε 26,350), 316 mμ (ε 5150), $\nu_{max.}$ 1770w, 1705, 1180, 770, 700 cm.$^{-1}$.

(*c*) 2-Methylquinoline (4·8 g.) and *N*-phenylmaleimide (5·7 g.) in xylene (50 ml.) were heated under reflux for 24 hr. Most of the xylene was removed *in vacuo*, the residue dissolved in chloroform and extracted with 2N-hydrochloric acid, and the extract basified with sodium carbonate. The product (1·2 g.) was isolated by chloroform-extraction. Crystallisation from aqueous ethanol (1 : 1; 40 ml.) gave N-*phenyl*-α-2-*quinolylmethylsuccinimide*, m. p. 129—130° (Found: C, 75·9; H, 5·2; N, 8·8. $C_{20}H_{16}N_2O_2$ requires C, 76·0; H, 5·1; N, 8·9%), $\lambda_{max.}$ 267 (ε 3550), 300 (ε 2970), 313 mμ (ε 3650), $\nu_{max.}$ 1770w, 1710, 1180, 1170, 840, 790, 765, 745, 705 cm.$^{-1}$. The yield was increased to 1·8 g. by heating the mixture under reflux for 72 hr.; much basic polymer was also formed. The adduct formed a hydrochloride which readily crystallised from 2N-hydrochloric acid.

(*d*) The reaction of 4-methylquinoline with *N*-phenylmaleimide was conducted essentially as above. Large amounts of basic amorphous polymers were isolated but no 1 : 1 adduct could be detected.

(*e*) 2-Methylpyridine (10 ml.) and *N*-phenylmaleimide (3·5 g.) in xylene (30 ml.) were refluxed for 72 hr. Some amorphous solid which separated was filtered off. The solution was

[4] Leonard and Boyer, *J. Amer. Chem. Soc.*, 1950, **72**, 2980.
[5] Searle, U.S.P. 2,444,536; *Chem. Abs.*, 1948, **42**, 7340.

extracted with 2N-hydrochloric acid. More solid separated and was filtered off. The acid extract was basified with sodium carbonate, and the crude product (1·0 g.) isolated by chloroform-extraction. Further purification was effected by chromatography. Slow crystallisation from benzene–light petroleum gave *N-phenyl-α-2-pyridylmethylsuccinimide*, m. p. 71—72° (Found: C, 72·5; H, 5·5; N, 10·3. $C_{16}H_{14}N_2O_2$ requires C, 72·2; H, 5·3; N, 10·5%), $\lambda_{max.}$ 255 (ε 3080), 260 (ε 3320), 267 mμ (ε 2330), $\nu_{max.}$ 1770w, 1710, 1180, 760, 705 cm.$^{-1}$.

(*f*) The reaction of 4-methylpyridine with *N*-phenylmaleimide conducted as above gave only amorphous basic polymers.

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