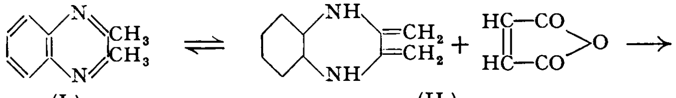
172. *The Diels–Alder Synthesis with 2 : 3-Dimethylquinoxaline. The Reaction between Maleic Anhydride and Anthranil.*

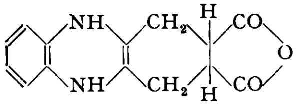
By A. Schönberg and Ahmed Mostafa.

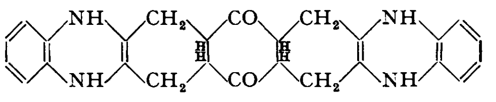
2 : 3-Dimethylquinoxaline, in the tautomeric form (II), reacts with maleic anhydride in the molecular proportion 1 : 1 and with *p*-benzoquinone in the proportion 2 : 1. Formulæ (III*a*) or (III*b*) and (IV*a*) or (IV*b*) respectively are advanced for the *products*. No reaction of this kind was observed between 2 : 3-dimethylquinoxaline and succinic anhydride or between maleic anhydride or *p*-benzoquinone and quinoxaline or its derivatives not capable of forming a diene system corresponding to (II). Anthranil reacts with maleic anhydride, forming a colourless *product* (VI*a* or VI*b*).

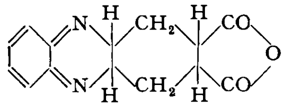
(I) 2 : 3-Dimethylquinoxaline (I), reacting in the tautomeric form (II) (Ogg and Bergstrom, *J. Amer. Chem. Soc.*, **1931**, **53**, 1846), gives *addition products* when heated with maleic anhydride or with *p*-benzoquinone in toluene, by addition in the molecular proportion 1 : 1 in the former case and 2 : 1 in the latter. Both products can be sublimed in a vacuum and do not react with diazomethane and formulæ (III*a*) or (III*b*) and (IV*a*) or (IV*b*) respectively are proposed for them. The addition product (III*a*) or (III*b*) is soluble in alkali and is precipitated unchanged on careful neutralisation.

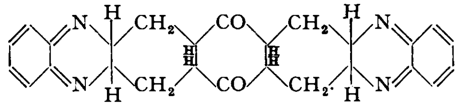
Further evidence that 2 : 3-dimethylquinoxaline can be applied in diene synthesis with maleic anhydride and *p*-benzoquinone was found in the fact that no reaction of this type occurred when quinoxaline, 2-methylquinoxaline, 2-phenyl-3-methylquinoxaline, and 2 : 3-diphenylquinoxaline were heated under the same conditions, or even more severe conditions, with maleic anhydride and with *p*-benzoquinone. The above-mentioned quinoxalines are not capable of forming a diene system. No reaction occurred when 2 : 3-dimethylquinoxaline was heated with succinic anhydride under similar conditions to those under which the reaction with maleic anhydride takes place, which shows that the double bond in maleic anhydride plays a part.


(I.) (II.)

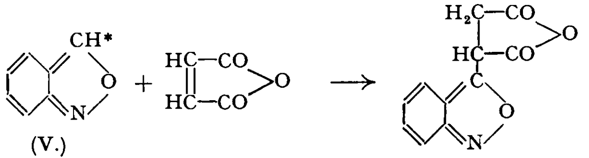
(IIIa.)


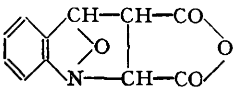

(IVa.)

(IIIb.)



(IVb.)

(II) A colourless *additive product* was obtained by reaction between maleic anhydride and anthranil (V) in molecular proportion. It sublimed without decomposition in a vacuum, decomposed when heated in air, yielding maleic anhydride and a red residue (a similar red residue is formed when anthranil is heated alone), was stable towards diazomethane, and dissolved in alkali and was precipitated unchanged on careful neutralisation. These properties do not allow us to state the structure of the addition product beyond doubt; we confine ourselves to the statement that, *inter alia*, formulæ (VI*a*) and (VI*b*) would explain the properties of the compound. Succinic anhydride did not react with anthranil to form an addition product under similar or even more severe conditions, possibly because it does not contain the necessary double bond. *C*-Phenylanthranil did not react with maleic anhydride, which may be explained by the fact that the hydrogen atom marked with an asterisk in (V) is essential for reaction (compare VI*a*); but the lack of reaction in this case may be due to steric hindrance. If (VI*b*) is the correct formula, the reaction is analogous to the action of maleic anhydride on furan (Diels and Alder, *Ber.*, 1929, **62**, 554); (VII), like the addition product of anthranil and maleic anhydride, decomposes on heating with the formation of maleic anhydride.


(V.) (VI*a*.)


(VI*b*.)


(VII.)

EXPERIMENTAL.

Maleic Anhydride and 2 : 3-Dimethylquinoxaline.—2 : 3-Dimethylquinoxaline free from water of crystallisation (Gabriel and Sonn, *Ber.*, 1907, **40**, 4833) (0·5 g.; 1 mol.) and maleic anhydride (1 mol.) were refluxed in dry toluene (20 c.c.) for 2½ hours, a brown sticky substance separating. The mixture was left overnight in the refrigerator, the toluene then decanted, and the sticky material dissolved in hot glacial acetic acid and kept in the refrigerator; yellowish (slightly green) crystals (III*a* or III*b*) were obtained from the mother-liquor (A). The *addition product* was readily soluble in tetralin and methyl alcohol, with difficulty in chloroform and acetone; the sample for analysis was crystallised several times from glacial acetic acid; m. p. above 305°, but darkening was observed at that temperature (Found: C, 65·8; H, 4·8; N, 10·6. $C_{14}H_{12}O_3N_2$ requires C, 65·5; H, 4·7; N, 10·8%). On further refluxing for 3 hours, the mother-liquor (A) deposited more of the brown substance (total yield, about 0·4 g.).

The addition product (0·5 g.) was heated under reduced pressure in a bath at 260° for 15 minutes. After 5 minutes a brown sublimate formed; it was crystallised from acetic acid and proved to be the addition product.

A solution of the addition product in aqueous sodium hydroxide (30%) was cooled and treated dropwise with concentrated hydrochloric acid. The precipitate formed (it was soluble in excess of hydrochloric acid) was collected, washed, and crystallised from glacial acetic acid, and proved to be the initial material.

Even after refluxing for 1 hour with 10% sodium hydroxide solution the addition product was recovered unchanged.

Succinic Anhydride and 2 : 3-Dimethylquinoxaline.—Equimolecular amounts of 2 : 3-dimethylquinoxaline (0·5 g.) and succinic anhydride were refluxed in dry toluene (20 c.c.) for 6 hours, and the mixture kept for one night in a cooling mixture; succinic anhydride separated. From the mother-liquor, after concentration, 2 : 3-dimethylquinoxaline was obtained.

Maleic Anhydride and Quinoxaline.—Solutions of quinoxaline (Chattaway and Humphrey, J., 1929, 645) (1 g.; 1 mol.)

and maleic anhydride (1 mol.), each in hot dry toluene (15 c.c.), were mixed, refluxed for 3 hours, and then kept overnight in the refrigerator; no crystals separated and on concentration the initial materials were recovered. The same result was obtained after refluxing in dry xylene for 6 hours.

Maleic Anhydride and 2-*Methylquinoxaline.*—2-Methylquinoxaline (Bennett and Willis, J., 1928, **1960**) (free from *o*-phenylenediamine; see below) and maleic anhydride in molecular proportion were dissolved in toluene (dried over sodium) and refluxed for 6 hours without formation of a deposit. The presence of unchanged 2-methylquinoxaline was shown by treating a portion of the product with *p*-nitrobenzaldehyde; the 2-*p*-nitrostyrylquinoxaline obtained did not depress the m. p. of an authentic specimen (Bennett and Willis, *loc. cit.*). Another portion, after removal of the toluene in a vacuum, left a brown liquid, from which a solid separated on cooling. This was washed with and crystallised from light petroleum, giving maleic anhydride (identified by mixed m. p.).

Maleic Anhydride and 2-*Phenyl*-3-*methyl- or* 2 : 3-*Diphenyl-quinoxaline.*—The quinoxaline (1 g.) and maleic anhydride (1 mol.) were refluxed in dry toluene (20 c.c.) for 3 hours, and the solution kept overnight in the refrigerator. No crystals separated and on concentration the initial materials were recovered.

The same results were obtained after 6 hours' refluxing in dry xylene.

Maleic Anhydride and o-*Phenylenediamine.*—To *o*-phenylenediamine (1 g.; 1 mol.) in toluene (10 c.c., dried over sodium) was added a hot solution of maleic anhydride (1 mol. in 10 c.c. of dry toluene); rapid precipitation of a yellow substance took place and the mixture was left in the refrigerator to complete the reaction. The *product*

$$C_6H_4(NH{\cdot}CO{\cdot}CH{:}CH{\cdot}CO_2H)_2$$

was collected and washed with dry toluene; it separated from methyl alcohol in colourless crystals, m. p. 189—190°, readily soluble in alkali, methyl alcohol, ethyl alcohol and acetone (Found: C, 55·4; H, 4·1; N, 9·2. $C_{14}H_{12}O_6N_2$ requires C, 55·3; H, 3·9; N, 9·2%). The same product was obtained when 2 mols. of maleic anhydride were used.

p-*Benzoquinone and* 2 : 3-*Dimethylquinoxaline.*—A solution of equimolecular amounts of 2 : 3-dimethylquinoxaline (1 g.) and *p*-benzoquinone in dry toluene (20 c.c.) became brown after refluxing for 2½ hours. It was left overnight in the refrigerator and the crystalline *addition product* (IV*a* or IV*b*) (about 0·6 g.) was then collected and recrystallised from toluene, forming colourless needles, m. p. 190° (brown melt after shrinking at 189°), soluble in ether and benzene (Found: C, 73·5; H, 5·9; N, 12·6. $C_{26}H_{24}O_2N_2$ requires C, 73·5; H, 5·6; N, 13·2%).

The same substance was obtained when 2 mols. of 2 : 3-dimethylquinoxaline were treated with 1 mol. of *p*-benzoquinone under similar conditions.

The addition product was heated (boiling nitrobenzene bath) in a sublimation apparatus through which carbon dioxide was passed. After 15 minutes a colourless sublimate of needles formed, m. p. 190°, not depressed by the original addition product.

p-*Benzoquinone and Quinoxaline.*—A solution of equimolecular amounts of quinoxaline (1 g.) and *p*-benzoquinone in dry benzene (20 c.c., thiophen-free) was heated in a sealed tube at 110° for 3 hours; the benzene was then evaporated in a vacuum, and the residue divided into two portions. One portion was extracted with water; from the aqueous solution ether extracted quinoxaline (0·8 g.). From the other portion, on concentration, *p*-benzoquinone was obtained.

p-*Benzoquinone and* 2 : 3-*Diphenylquinoxaline.*—The two substances were recovered unchanged after a solution of equimolecular amounts of 2 : 3-diphenylquinoxaline (Hinsberg and König, *Ber.*, 1894, **27**, 2181) (1 g.) and *p*-benzoquinone in dry xylene (20 c.c.) had been refluxed for 3 hours, concentrated, and cooled.

Anthranil and Maleic Anhydride.—Equimolecular amounts of anthranil (1 g.) and maleic anhydride in dry toluene (20 c.c.) were heated on a water-bath for ½ hour, and the mixture left for 1 day in the refrigerator. The *addition product* obtained separated from chloroform in fine colourless or almost colourless crystals, m. p. about 150° (some decomp.) (Found: C, 60·5; H, 3·1; N, 6·6. $C_{11}H_7O_4N$ requires C, 60·8; H, 3·2; N, 6·4%), readily soluble in benzene, carbon tetrachloride, and methyl alcohol. It dissolved in aqueous sodium hydroxide and was reprecipitated by concentrated hydrochloric acid. It sublimed when heated in a vacuum (bath temperature about 60°). When heated in a sublimation apparatus, at first without vacuum, it became red and melted; then, under vacuum, at a bath temperature of 210°, maleic anhydride condensed on the walls.

Succinic Anhydride and Anthranil.—Equimolecular amounts of anthranil (1 g.) and succinic anhydride were refluxed in toluene (20 c.c., dried over sodium) for 3 hours or in phenetole for 6 hours, but were recovered unchanged.

Maleic Anhydride and C-Phenylanthranil.—*C*-Phenylanthranil (Bamberger and Lindberg, *Ber.*, 1909, **42**, 1723) (1 g.) was recovered unchanged after being subjected to the procedure described in the case of anthranil and maleic anhydride.

FOUAD I UNIVERSITY, CAIRO, EGYPT.

[*Received, June* 11*th*, 1943.]