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REACTION BETWEEN N-METHYL-2-PYRIDONE AND MALEIC ANHYDRIDE

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IN ORDER to determine the aromaticity in N-alkyl-2-pyridones, maleic anhydride was condensed with N-methyl 2-pyridone. The two reactants, when heated together at 100° without a solvent or in toluene, yield (24 per cent) a colourless crystalline compound which was isolated by repeated extraction of the reaction mixture with large volumes of petroleum ether (40–60°). The compound m.p. 99–100°, has a molecular weight 350 (± 2 per cent, determined by the X-ray crystallographic method) and analysed for $C_{14}H_{15}NO_9$ (Calc. C, 49·29; H, 4·39; N, 4·10. Found: C, 49·55, 49·70, 49·58, 49·60; H, 4·55, 4·19, 4·90, 4·63; N, 4·20, 4·24%). The compound has four carboxylic acid groups determined potentiometrically or by direct alkali titrations. (Equivalent weights = 88·69, 88·88, 86·82, 82·39). The U.V. absorption spectrum of the compound in alcohol or water is virtually identical with that of the starting pyridone and the compound dissociates readily into maleic acid and N-methyl-2-pyridone on dissolving in polar solvents. Indeed the N.M.R. spectrum of the compound measured in D_2O shows the presence of *two* molecules of maleic *acid* and *one* of the pyridone. Also, at the melting point and during sublimation the compound splits into two molecules of maleic acid and one of the pyridone. These results clearly indicate the presence of *two* molecules of maleic *acid* in combination with *one* of the N-methyl-2-pyridone and condensation between *one* molecule of each reactant failed and gave only starting materials. In a recent investigation[1] a similar condensation was attempted without success and the authors concluded no addition takes place between the reactants under the conditions employed.

The presence in the final adduct, of two molecules of maleic *acid* suggested the possibility of using the free acid instead of the anhydride but no reaction occurred and the starting materials were recovered. This clearly rules out the possibility of the adduct being a salt or a betain from malic acid and the pyridone. Similarly, any molecular complexes must be eliminated as only maleic anhydride and not the acid is capable of forming such complexes; whereas in the product obtained, four free carboxylic acid groups are present.

The great lability of the compound even on dissolution in polar solvents, rules out a possible double electrophilic substitution at the 3 and 5 positions of the pyridone molecule; and a straightforward Diels–Alder type addition cannot be considered because such an addition need not involve *two* molecules of the maleic acid. Besides N-methyl-5-cyano-1,2-dihydropyridine forms a highly stable normal Diels–Alder adduct with only one molecule of maleic anhydride.[2]

On the basis of the dipolar ground state of the N-methyl-2-pyridone (cf. its high dipole moment of 4·75 D and the blue shift observed in its U.V. spectrum in going from less polar to more polar solvents[3]), the following structure and the possible mechanistic pathway indicated in the accompanying chart are proposed.

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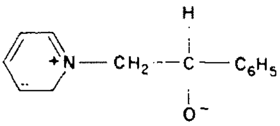
[1] J. A. Elvidge and L. M. Jackman, *J. Chem. Soc.* 859 (1961).

[2] K. Schenker and J. Druey, *Helv. Chim. Acta* **42**, 1961–70 (1959).

[3] S. F. Mason, *J. Chem. Soc.* 1254 (1959).

It has been shown by Krohnke[4] that N-methyl pyridinium halides undergo aldol type additions with aromatic aldehydes in the presence of piperidine as catalyst, resulting in labile adducts of the following type:

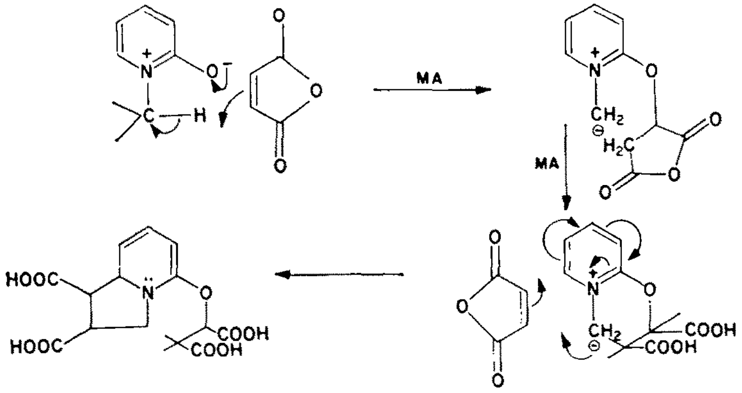


Such compounds dissociate so readily that they were considered to be molecular addition compounds until they were synthesized by alternative routes.*

Maleic anhydride being a good acceptor of anionic charges, could form an N-methyl-pyridinium adduct of a similar nature through the initial addition of one molecule of maleic anhydride to the oxygen anion. The second molecule of the anhydride could then add across the ylid[5] resulting in a dihydropyridine structure. The avidity to regain aromaticity may well provide the driving force for the reversal to the original components.[6]

N-Methyl-2-pyridone exchanges deuterium readily on refluxing with sodium deuteroxide, indicating the acidity of the N-methyl hydrogen atoms due to the cationoid aromaticity in the pyridone.

An investigation is in progress to test this observation and the mechanism of the addition and reversal. As no further chemical examination seems possible in view of the extraordinary lability of the adduct, an X-ray crystallographic analysis is currently being undertaken in the laboratories of Professor Dame Kathleen Lonsdale, FRS University College, London.



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* See *Pyridine and Derivatives* (Edited by E. Klingsberg) Part II; p. 26, Interscience, New York (1961).

[4] F. Krohnke and Vogt, *Liebigs Ann.* **589**, 26, 45 (1954).

[5] V. Boekhelheide and K. Fahrenholtz, *J. Amer. Chem. Soc.* **83**, 458 (1961).

[6] A. F. E. Sima and P. W. G. Smith, *Proc. Chem. Soc.* 282 (1958).