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The Reaction of 2-Pyridones with Benzyne

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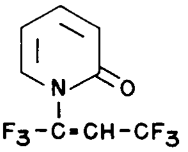
Sir:

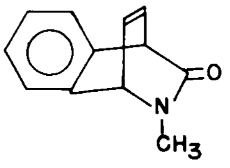
Previous attempts to use 2-pyridones as a dienoid system in Diels-Alder reactions have been unsuccessful. It was shown that 2-pyridone simply added to hexafluoro-2-butyne to give I (1) while 1-methyl-2-pyridone reacted with maleic anhydride yielding a high molecular weight product not involving a Diels-Alder reaction (2). Since the reaction of benzyne with a number of heterocyclic dienoid systems such as furans (3,4), pyrroles (5,6) and α-pyrone (7) has been reported, its reaction with 2-pyridones was explored.

When 1-methyl-2-pyridone was allowed to react with diazotized anthranilic acid under conditions which generate benzyne (8), the adduct II was obtained (10% yield), m.p. 98-100° (*Anal.* Calcd. for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.80; H, 6.03; N, 7.69). Its n.m.r. spectrum (9) showed the *N*-methyl signal at 2.82 δ (singlet), the two methine protons at 4.59 and 5.00 δ (each a doublet of doublets, J's 2.4, 4.8 and 2.6, 4.8) and the olefinic and aromatic protons as a complex multiplet between 6.8 and 7.4 δ. Its mass spectrum (even at 12 e.v.) was identical with that of naphthalene, molecular ion, m/e 128, indicating that the molecule decomposed under electron impact. It was shown subsequently that II also afforded naphthalene when pyrolyzed at 200°. An interesting byproduct of this reaction was acridone III (1.4%) which was later shown to be produced under identical conditions from diazotized anthranilic acid in the absence of 1-methyl-2-pyridone. This suggests the addition of anthranilic acid to benzyne, a reaction which is currently being investigated further.

When benzyne was generated from chlorobenzene and sodamide (10), the reaction with 1-methyl-2-pyridone took a different course. There was isolated 1-methyl-3-phenyl-2-pyridone (IV), m.p. 130-132° (5.4% yield), molecular ion, m/e 185. (*Anal.* Calcd. For $C_{12}H_{11}NO$: as above. Found: C, 78.04; H, 6.15; N, 7.46). Its n.m.r. spectrum (9) is consistent with the proposed structure: N-CH_3 resonance at 3.58 δ (singlet), H-5 signal at 6.22 δ (triplet, $J_{4,5} = J_{5,6} = 7.0$ c.p.s.), H-4, H-6 and phenyl protons between 7.2 and 7.9 δ (complex multiplet). Its formation would involve electrophilic attack of benzyne at one of the expected positions (C-3 in this case) followed by neutralization to give IV. A byproduct of this reaction was a small amount of 1,1'-dimethyl-2,2'-bipyrid-6,6'-dione (V), m.p. 206-210°, molecular ion, m/e 216. (*Anal.* Calcd. for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.95. Found: C, 66.69; H, 5.57; N, 12.91). Its n.m.r. spectrum (9) was analyzed by first order rules, and the chemical shifts and coupling constants were found to be analogous to those of 6-methyl-2-pyridone (11): N-CH_3 at 3.32 δ (singlet), H-3 at 6.27 p.p.m. (doublet), H-5 at 6.71 p.p.m. (doublet), H-4 at 7.54 p.p.m. (doublet of doublets) and couplings as follows: $J_{3,4} = 6.5$ c.p.s., $J_{4,5} = 9.0$ c.p.s. and



I



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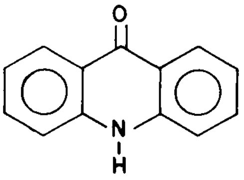

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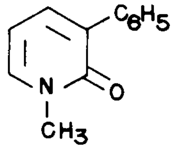

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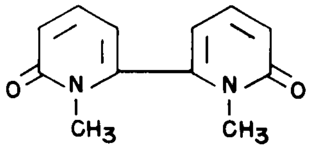

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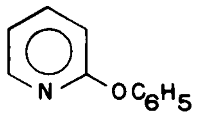
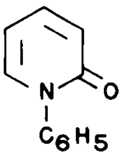


VII



VIII

$J_{3,5}$ = 1.5 c.p.s. A sample of V was synthesized from 2,2'-bipyridine by quaternizing it with methyl sulfate to the bis methosulfate followed by the Decker oxidation with potassium ferricyanide (12). It was found that the reaction of 1-methyl-2-pyridone with sodamide in liquid ammonia in the absence of chlorobenzene also gave rise to a small quantity of V. In that medium, however, ring opening of 1-methyl-2-pyridone was observed to give a pale yellow solid, m.p. 132-137° (6% yield), molecular ion, m/e 126, which we formulate to be the enamine amide, $CH_3NH-CH=CH-CH=CH-CONH_2$ (VI). (*Anal.* Calcd. for $C_6H_{10}N_2O$: C, 57.12; H, 7.99; N, 22.20. Found: C, 57.06; H, 8.19; N, 22.18.) Its n.m.r. spectrum (in DMSO-d_6 with TMS as internal reference) did not lend itself to first order interpretation but contained the following salient features: the $N-CH_3$ resonance was a doublet at 2.61 δ (J = 4.5 c.p.s.) but the olefinic and N-H protons were present in a complex pattern. Exchange with deuterium oxide converted the $N-CH_3$ signal into a singlet, and a total of three protons had exchanged which substantiated the structure VI.

In the reaction of 2-pyridone with benzyne (from diazotized anthranilic acid) no Diels-Alder adduct could be isolated, the products found being 2-phenoxypyridine (VII) (3.9%), m.p. 38-39° (undepressed on admixture with an authentic sample) and 1-phenyl-2-pyridone (VIII) (1.8%), m.p. 124-126°, lit. m.p. 128° (13), whose n.m.r. spectra were consistent with the proposed structures. The only other product found was acridone III (2.3%), m.p. 360-363°, lit. m.p. 350° (14) identical to the samples isolated above (M^+ = 195); u.v. identical to that in the literature (14).

The reactions of benzyne with other heterocyclic systems are being investigated further.

REFERENCES

(1) L. A. Paquette, *J. Org. Chem.*, 30, 2107 (1965).

(2) B. S. Thyagarajan and K. Rajagopalan, *Tetrahedron*, 19, 1483 (1963).

(3) G. Wittig and L. Pohmer, *Chem. Ber.*, 89, 1334 (1956).

(4) G. Wittig, W. Stilz and E. Knauss, *Angew. Chem.*, 70, 166 (1958).

(5a) G. Wittig and W. Behnisch, *Chem. Ber.*, 91, 2358 (1958).

(b) G. Wittig and B. Reichel, *ibid.*, 96, 2851 (1963).

(6) L. A. Carpino and D. E. Barr, *J. Org. Chem.*, 31, 764 (1966).

(7) G. Wittig and R. W. Hoffmann, *Chem. Ber.*, 95, 2718 (1962).

(8) L. Friedman and F. M. Logullo, *J. Am. Chem. Soc.*, 85, 1549 (1963).

(9) Determined in deuteriochloroform, chemical shifts reported in p.p.m. (δ) downfield from internal tetramethylsilane.

(10) W. W. Leake and R. Levine, *J. Am. Chem. Soc.*, 81, 1169 (1959).

(11) C. L. Bell, R. S. Egan and L. Bauer, *J. Heterocyclic Chem.*, 2, 420 (1965).

(12) E. A. Prill and S. M. McElvain, *Org. Syn.*, Coll. Vol. II, p. 419, John Wiley and Sons, Inc., New York, N. Y., 1943.

(13) A. E. Tschitschibabin and N. P. Jeletzky, *Ber.*, 57, 1159 (1924).

(14) R. M. Acheson, M. L. Burstall, C. W. Jefford and B. F. Sansom, *J. Chem. Soc.*, 3742 (1954).

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