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CHEMISTRY OF HETEROCYCLIC COMPOUNDS. 13. REACTIONS OF N-(2-PYRIDYLMETHYLENE)ANILINE. EVIDENCE OF TRACES OF CYANIDE ION IN N,N-DIMETHYLFORMAMIDE

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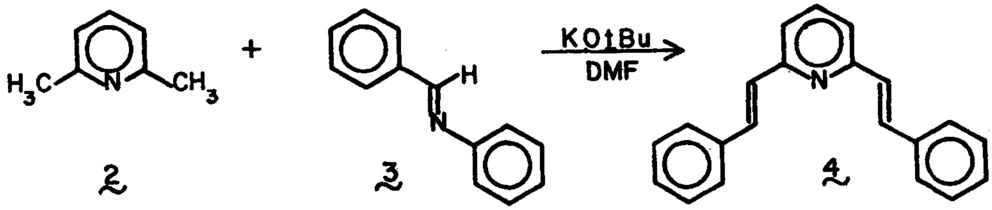
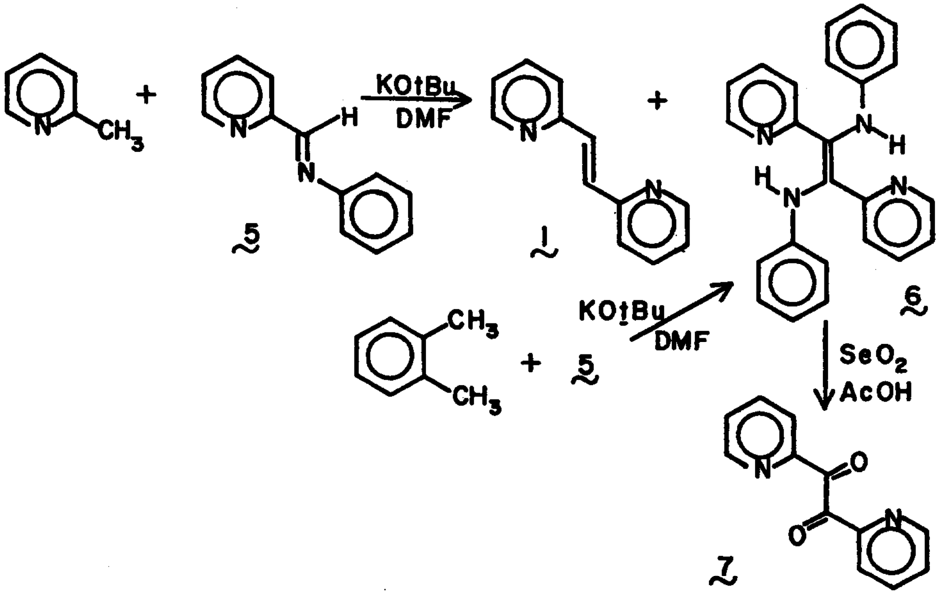
In connection with projects underway in our laboratories we required large quantities of *cis*- and *trans*-1,2-di(2-pyridyl)ethene (1). The *trans*-1 has been generally prepared by condensation of 2-methylpyridine with 2-pyridinecarboxaldehyde in refluxing acetic anhydride (*ca.* 140°C) usually resulting in yields of less than 50%. The *in situ* oxidation[2] of 2-hydroxymethylpyridine with 2-methylpyridine N- oxide to the corresponding aldehyde, followed by base-catalyzed condensation offers little advantage in the synthesis of these olefins. It has been shown[3] that utilization of anil intermediates in related condensations leads to increased yields of the desired olefinic products. Therefore before attempting the synthesis of *trans*-1, a test of the "anil synthesis" was conducted on a 2-pyridylmethyl system. A mixture of 2,6-dimethylpyridine (2), benzalaniline (3) and only one-half the suggested ratio of potassium *tert*-butoxide in N,N-dimethylformamide at 90°C for *ca.* 2 hours easily afforded (78%) the desired 2,6-distyrylpyridine [4; m.p. 165-166.5° (lit.[4a] m.p. 166.5°)], which had been previously obtained[4] (<45%) from the corresponding aldehyde.



With the initial success of this double condensation, N-(2-pyridylmethylene)aniline (5) was prepared from either 2-pyridinecarboxaldehyde[5a] or 2-hydroxymethylpyridine.[5b] The reaction of 5 with 2-methylpyridine in DMF with potassium *tert*-butoxide gave the expected *trans*-1 [m.p. 118-122° (lit.[6] m.p. 118-119°), 30-20%] along with *E* - 1,2-dianilino-1,2-di(2-pyridyl)ethene [6; m.p. 227-235° (dec); 40-50%] and unreacted starting materials. Similarly from reaction of the less reactive *o*-xylene with 5, the anil dimer 6 was isolated (36%). In fact, when a solution of 5 and potassium *tert*-butoxide in DMF was refluxed, the anil dimer slowly formed. Excellent yields (>90%) of 6 can be realized by a benzoin-type condensation of 5 in DMF with a catalytic amount of cyanide ion at room temperature within a few hours.

Although spectral and analytical data are consistent for 6, the oxidative hydrolysis of 6 by selenium dioxide in acetic acid afforded (60%) 2,2′-pyridil [7; m.p. 156-157° (lit.[7] m.p. 154-155°); i.r. ($CHCl_3$) 1705, 1685 (C=O) cm^{-1}; n.m.r. ($CDCl_3$) δ8.51 (6-pyr-H, d, J = 4Hz), 8.14 (3-pyr-H, d, J = 8Hz), 7.84 (4-pyr-H, ddd, J = 8, 8, 1Hz), and 7.40 (5-pyr-H, ddd, J = 8, 4, 1Hz)].



This anil dimerization can be rationalized by a benzoin-type condensation of 5; therefore, cyanide ion was liberated from the N,N-dimethylformamide solvent (redistilled from calcium hydride) upon addition of base. We have also utilized Trisler's trapping agent, 4-nitrobenzil[8], to detect cyanide ion in our redistilled commercial DMF. These latter data could negate the use of 2-pyridinecarboxaldehyde as an analytical reagent, which has been reported[9] capable of detecting cyanide ion at concentrations down to 5 μg per ml (*ca.* 10^{-4}M), since it gave a negative test for 35 reagents *including* *DMF*. Since Trisler can detect (and isolate derivatives of) cyanide in commercial DMF at concentrations of 10^{-6}M or less,[10] the visual test for cyanide ion *via* the formation of the insoluble α-pyridoin should be questioned or at least reevaluated.

The "anil synthesis" with **5** is currently being pursued in cyanide-free DMF[8] as well as alternate solvent systems. Since Becker[11] demonstrated that benzalaniline afforded the corresponding dimer in DMF with catalytic amounts of DMSO or dimethylsulfone, the role of alternate nucleophiles and cyanide liberating reagents will also be examined.

REFERENCES

1. This work was supported by the Public Health Service grant from the National Institute of Neurological Diseases and Stroke, the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Research Corporation.
2. S. Miyano and N. Abe, *Chem. Pharm. Bull.*, **15**, 511 (1967).
3. A. E. Siegrist, *Helv. Chem. Acta.*, **50**, 906 (1967); *ibid.*, **52**, 1282, 2521 (1969).
4. (a) J. Stanek and M. Horak, *Collect. Czech. Chem. Commun.*, **15**, 1037 (1950); (b) B. F. Putney and T. O. Soine, *J. Amer. Pharm. Assoc.*, **44**, 17 (1955) and references 18-20 therein.
5. (a) E. Schumaker and R. Taubenst, *Helv. Chem. Acta.*, **49**, 1455 (1966); B. P. Lugovkin, *Khim. Geterotsikl. Soldin., Sb. 1: Azotsoderzhashchie Geterotsiky*, 224 (1967), *Chem. Abstr.* **70**, 77722q (1969); (b) S. Miyano, A. Uno, and N. Abe, *Chem. Pharm. Bull.*, **15**, 515 (1967); S. Miyano, N. Abe, *ibid.*, **18**, 511 (1970); (c) An alternate and even more convenient method for the preparation of **5** would be from the readily available 2-methylpyridine. Adaptation of the method of Chardonnens and Heinrich [*Helv. Chem. Acta.*, **22**, 1471 (1939)], which uses N,N-dimethyl-*p*-nitrosoaniline and an activated methylene, may prove eventually to be a superior route to heterocyclic anils.
6. (a) H.-H. Perkampus and G. Kassebeer, *Justus Liebigs Ann. Chem.*, **696**, 1 (1966); (b) C. Harries and G. H. Lénart, *ibid.*, **410**, 95 (1915).
7. W. Mathes, W. Sauermilch, and T. Klein, *Chem. Ber.*, **84**, 452 (1951).

8. J. C. Trisler, B. F. Freasier, and S-M. Wu, accompanying publication.

9. E. J. Poziomek, M. E. Kronenberg, and E. Havinga, *Rec. Trav. Chim. Pays-Bas.*, **85**, 834 (1966).

10. Professor John C. Trisler, private communcation.

11. H-D. Becker, *J. Org. Chem.*, **29**, 2891 (1964).