The Photorearrangement of 3-Acetamidopyridine

John T. Edward and Lucy Y-S. Mo

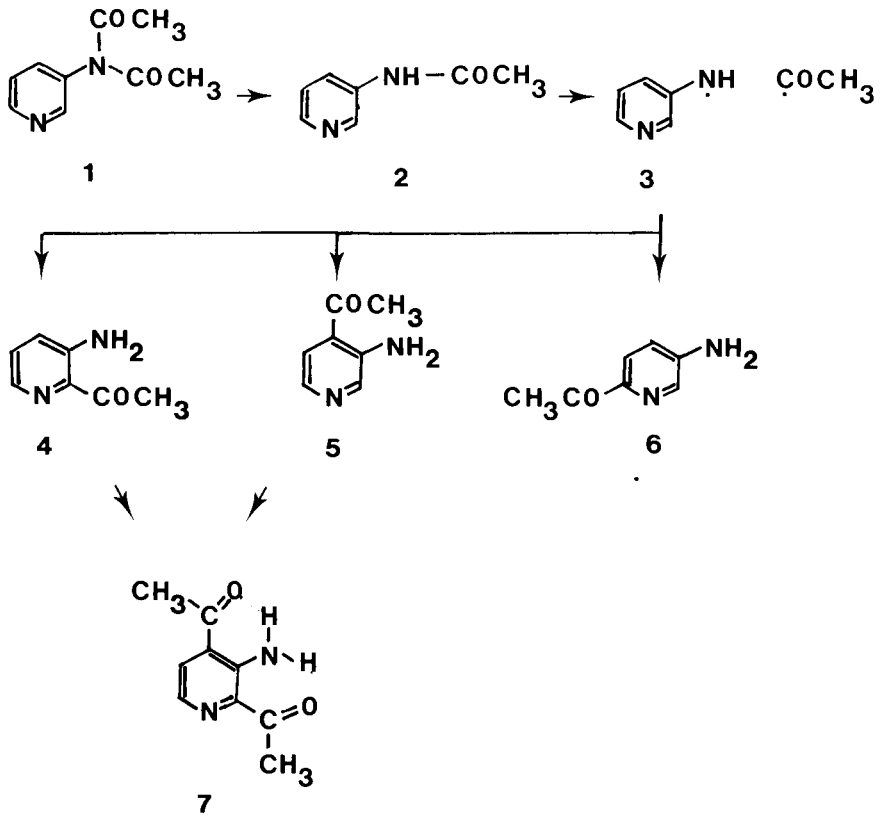
Department of Chemistry, McGill University, P.O. Box 6070, Montreal 101, Canada

Received March 12, 1973

The hitherto unknown 4-acetyl-3-aminopyridine (**5**), required as a starting material in certain projected syntheses, has been prepared by photorearrangement of the readily available 3-acetamidopyridine (2). This reaction, modeled on the photorearrangement of acetanilide (1; *cf.* refs. 2 and 3), afforded in addition the isomeric products **4** and **6**, 3-aminopyridine, and a trace of a diacetyl compound, probably **7**.

The isolation of these products was monitored by tlc, which showed in the reaction mixture (in order of decreasing Rf) five compounds A-E, followed by 3-acetamidopyridine, and (near the origin) some dark (polymeric?) material. Compound C was present in traces only, and was not investigated further. Compounds B, D and E were isolated by column chromatography and/or preparative thick-layer chromatography, and shown to be three isomers of empirical formula $C_7H_8N_2O$. This accorded with their mass spectra, which showed peaks at m/e 136 for the parent ions ($=\overset{+}{M}$). The presence of acetyl groups was evident from strong peaks at m/e 43 (CH_3CO^+) 93 (M^+-$COCH_3$), and 121 (M^+-CH_3). This pointed to the structures **4**, **5**, and **6** for B, D and E, when account was taken of the probable mechanism of photorearrangement (1,2).

Assignment of a unique structure to each of B, D and E could be done on the basis of their uv and nmr spectra. The uv spectrum of E was similar to that of 4-aminoacetophenone (Table I), indicating the structure 6 for this compound; the spectra of B and D were similar to that of 2-aminoacetophenone, indicating for them structures 4 or 5. These structural distinctions were confirmed by the nmr spectra (Table II), the chemical shift of the



amino protons of E being at higher field than those for the amino protons of B and D, indicating hydrogen bonding to adjacent carbonyl groups in the latter, and hence structures **4** or **5**. Further distinction between B and D was possible by a more detailed analysis of the chemical shifts and coupling constants (Table II) which conformed to well-established patterns (4), and which served to identify B with **4** and D with **5**.

Compound A was isolated in a minute amount only, possibly because it is more volatile than the other compounds. It was assigned the structure **7** on the basis of its mass spectrum, which showed strong peaks for M^+, M^+-CH_3, and M^+-$COCH_3$, and its nmr spectrum which indicated a 1,2,3-trisubstituted pyridine (4).

The probable mechanism for the formation of **4**, **5**, and **6** involves the photolysis of **2** to the acetyl radical and the amino radical **3** (1-3); the odd electron of the latter is delocalized to positions 2, 4, and 6 of the ring, thus accounting for the formation of three of the four possible isomers. 3-Aminopyridine presumably arises through hydrogen-abstraction from the solvent by **3**, and 2,4-diacetyl-3-aminopyridine (**7**) by escape of acetyl radical from the solvent cage and attack on **4** or **5**. In an attempt to increase the yield of **7**, the photorearrangement of 3-diacetamidopyridine (**1**) was investigated. However, thin layer chromatography of the reaction mixture indicated the formation of A-E in about the same proportions as previously obtained from **2**. It seems likely that in ethanol the excited state of **1** undergoes ready ethanolysis to **2**, which then undergoes photorearrangement.

TABLE I

Uv Peaks (in nm) of Analogous Benzene and Pyridine Compounds in Ethanol

Benzene Compounds		Pyridine Compounds	
Substituents	λ max	λ max	Structure
CH_3CONH	242,280	231,271	**2**
2-NH_2-1-$COCH_3$	257,358	260,362	**4** ≡ B
		253,362	**5** ≡ D
4-NH_2-1-$COCH_3$	233,317	220,318	**6** ≡ E

EXPERIMENTAL (5)

A solution of 3-acetamidopyridine (2.54 g.) in absolute ethanol (600 ml.) was deoxygenated in a quartz vessel by bubbling nitrogen through it for 15 minutes. It was then sealed off and irradiated for 20 hours in a Rayonet photochemical chamber reactor with light of 2537 Å wavelength. The ethanol was removed at reduced pressure, and the resultant brown gum was extracted with hot benzene. The benzene-insoluble residue was unreacted 3-acetamidopyridine, which on recrystallization from ethanol amounted to 490 mg., identified by m.p. and mixed m.p.

The solvent was removed from the benzene solution and the gum taken up in chloroform and percolated through a short Florosil column. The percolate was collected in three fractions, which on evaporation afforded 513 mg. of I, 380 mg. of II and 540 mg. of III (gum).

Fraction I was chromatographed on a column of grade III alumina (50 g.). Elution with ligroin-benzene 1:1 removed first 2,4-diacetyl-3-aminopyridine (**7**) (*ca.* 10 mg.), white needles subliming on warming; ir 3420, 3310 (NH_2), 1680, 1650 (hydrogen-bonded C=O), 1600, 1560, 1530 cm^{-1}; uv λ max 240 (sh), 287, 407 nm; mass spectrum m/e (relative intensities in parentheses) 178 (100), 163 (21), 161 (29), 150 (16), 149 (16), 136 (21), 135 (29), 124 (16), 121 (21), 108 (16), 93 (42), 66 (16) and 43 (50).

Further elution removed 2-acetyl-3-aminopyridine (4) (312 mg.), m.p. 66-67°; ir 3475, 3340 (NH_2), 1940 (*ortho*-substituted pyridine), 1670 cm^{-1} (C=O); uv λ max 260, 362 nm; mass spectrum m/e 136 (100), 121 (20), 108 (16), 94 (40), 93 (63), 67 (27), 66 (23) and 43 (27). The picrate crystallized from 50% aqueous ethanol as yellow prisms, m.p. 200-201°.

Anal. Calcd. for $C_{13}H_{11}N_5O_8$: C, 42.8; H, 3.0; N, 19.4. Found: C, 42.7; H, 3.2; N, 19.2.

Further elution removed 4-acetyl-3-aminopyridine (**5**)(32 mg.), m.p. 91-92°. More of this compound (325 mg.), along with a further 29 mg. of **4** was obtained by chromatography of fraction II on alumina, grade III (65 g.), and elution with benzene; ir 3480 and 3360 (NH_2), 1945 (*ortho*-disubstituted pyridine), and 1665 cm^{-1} (C=O); uv λ max 253, 362 nm; mass spectrum m/e 136 (100), 121 (72), 93 (52), 66 (26) and 43 (26). Its picrate

TABLE II

Chemical Shifts (τ) and Coupling Constants of Photorearrangement Products

Compound	H-2	NH_2	H-4	H-5	H-6	CH_3
A ≡ **7**	-----	1.24	-----	2.38 (a)	2.07 (a)	7.28, 7.38
B ≡ **4**	-----	3.66	3.01 (b)	2.82 (b,c)	2.02 (c)	7.29
D ≡ **5**	1.80	3.70	-----	2.58 (d)	2.09 (d)	7.43
E ≡ **6**	1.96 (e)	5.60	3.05 (e,f)	2.14 (f)	------	7.38

(a) $J_{5,6}$ 5.0 Hz. (b) $J_{4,5}$ 8.2 Hz. (c) $J_{5,6}$ 4.2 Hz. (d) $J_{5,6}$ 5.8 Hz. (e) $J_{2,4}$ 2.5 Hz. (d) $J_{4,5}$ 8.0 Hz.

crystallized from 50% aqueous ethanol as yellow leaflets, m.p. 189-191°.

Anal. Calcd. for $C_{13}H_{11}N_5O_8$: C, 42.8; H, 3.0; N, 19.4. Found: C, 42.9; H, 3.0; N, 19.3.

Preparative thick-layer chromatography of fraction III on silica using chloroform-ethanol 10:1 for development gave 3-aminopyridine (271 mg.), identified by m.p. and mixture m.p., and 6-acetyl-3-aminopyridine (**6**) (304 mg.), m.p. 108-109°; ir 3490, 3400 (N-H), 1680 cm^{-1} (C=O); uv λ max 318 nm; mass spectrum m/e 136 (100), 121 (43), 108 (13), 94 (38), 93 (57), 67 (25), 66 (53) and 43 (28). Its picrate crystallized from 50% ethanol as yellow needles, m.p. 191-192°.

Anal. Calcd. for $C_{13}H_{11}N_5O_8$: C, 42.8; H, 3.0; M, 19.4. Found: C, 42.9; N, 3.2; N, 19.3.

Acknowledgment.

We are grateful to V. Yu and Dr. A. Taurins who suggested this problem, and to the National Research Council of Canada for financial support.

REFERENCES

(1) D. Elad, D. V. Rao and V. I. Sternberg, *J. Org. Chem.*, **30**, 3252 (1965); D. V. Rao and V. Lamberti, *ibid.*, **32**, 2896 (1967); J. S. Bradshaw, R. D. Knudsen and E. L. Loveridge, *ibid.*, **35**, 1219 (1970).

(2) H. Shizuka, *Bull. Chem. Soc. Japan*, **42**, 52, 57, 909 (1969); H. Shizuka and I. Tanaka, *ibid.*, **41**, 2343 (1968).

(3) B. S. Thyagarajan, N. Kharasch, H. B. Lewis and W. Wolf, *Chem. Commun.*, 614 (1967).

(4) J. W. Emsley, J. Feaney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, London, 1966, Vol. 2, pp. 795, 797.

(5) Melting points are uncorrected. Infrared spectra were taken in chloroform solution using a Perkin Elmer 337 instrument. Ultraviolet absorption spectra were obtained with a Unicam SP600 spectrophotometer using ethanol solutions. Nuclear magnetic resonance spectra were measured with a Varian A-60 instrument using deuterochloroform solutions and TMS as internal reference. Mass spectra were obtained at 70 eV using an AEI MS 902 mass spectrometer. Elemental Analyses were by Bernhardt, West Germany.