AN ANOMALOUS DEALKYLATION-ACYLATION OF N,N-DIALKYLANILINES

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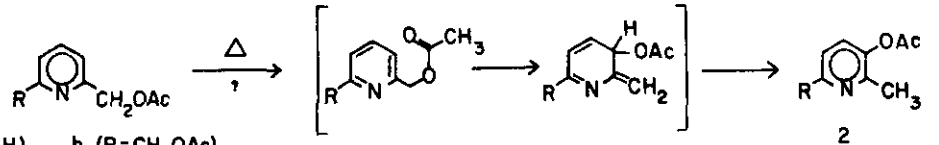
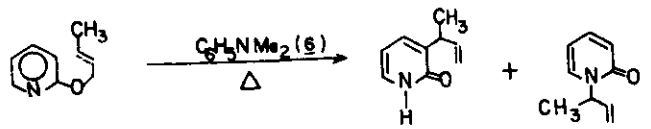
Abstract. N,N-Dialkylaniline undergoes a thermal N-dealkylation and acylation in the presence of 2-acetoxypyridines.

Activation of α-methyl groups on electron-deficient heterocyclic compounds can best be accomplished by the treatment of α-methyl-N-oxides with acetic anhydride[2,3], from which the α-acetoxymethyl derivatives along with minor amounts of ring substituted isomers[4] can be obtained. Few rearrangements in heterocyclic chemistry have been as extensively studied as this particular reaction, known as the Boekelheide Rearrangement. During our studies to functionalize the α-methyl moiety on diverse heterocycles, it appeared that the ring acetoxy isomers were generated from the subsequent rearrangement of the α-acetoxymethyl precursor, thus we attempted the thermolysis of 2-acetoxymethylpyridines (1) in order to evaluate this concept.

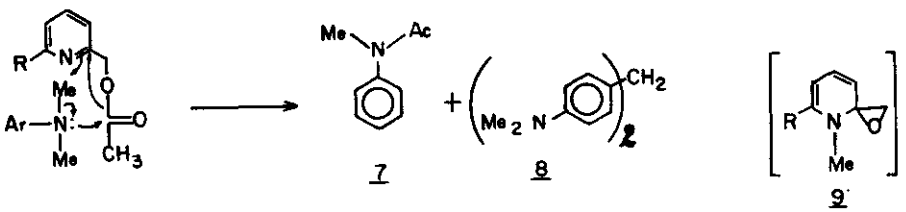


1a (R=H) b (R=CH_2OAc) 2

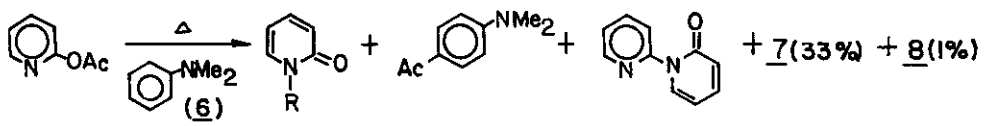
When 1 was pyrolyzed at temperatures up to 240°C, none of the anticipated rearrangement products (e.g. 2) were detected. At temperatures in excess of 240°C, 1 underwent extensive decomposition and added acetate ion had no obvious effect. Since the related 2-crotyloxypyridine (3) rearranges smoothly to 4 and 5 at 250°C in N,N-dimethylaniline (6)[5], pyrolysis of 1(a or b)[6] in 6, as solvent, gave the unexpected N-methylacetanilide (7) along with bis-(dimethylaminophenyl)methane (8; 10%; mp 84°C, lit.[7] mp 84-86°C]. Ring acetoxy product(s), e.g. 2, were not detected. Mechanistically, albeit naively, nucleophilic attack of the amine at the carbonyl group of the acetoxy group, followed by N-methylation can be envisioned. The resultant intermediate 9 subsequently can undergo a cyclopropylcarbinyl-type rearrangement to afford ethereal products. In order to simplify the reaction course, 2-acetoxypyridine [10; bp 58°C (0.8mm), lit.[8] bp 74-76°C (0.9mm)] was heated (255°C) in N,N-dimethylaniline (6) resulting in the generation of an equal within experimental error ratio of 7 and N-methylpyridinone (11). Other degradation products such as: 12 [mp 93-96°C, lit.[9] mp 90°C] via p-acetylation of 6 and loss of 2-pyridinone (13), and N-2-pyridinyl-2-pyridinone (14; mp 52°C, lit.[10c] mp



3 4 5



55°C) by the self-condensation of 10[10], followed by loss of acetic anhydride The necessity of pyridine N-electrons was supported by the fact that benzyl acetate does not transfer the acetyl group under comparable conditions.



Anilines	Acetanilides (%); Mp/Bp.
H,N,N-DiMe	H,N-Me (35%); Mp 98-100°C (lit.[11]mp 98-101°C)
3,N,N-TriMe	3,N-DiMe (42%); Mp 75-76°C (lit.[12]mp75-76°C)
4,N,N-TriMe	4,N-DiMe (41%); Mp 79-80°C (lit.[13]mp 80°C)
4-Cl-N,N-DiMe	4-Chloro-N-Me (47%); Mp 91-92°C (lit.[14]mp92-93°C)
4-MeO-N,N-DiMe	4-Methoxy-N-Me (48%); Mp 55-56°C (lit.[14]mp 51-53°C)
H,N,N-DiEt	H,N-Et (32%) Mp 50-50°C (lit.[15]mp 51°C)
4-Me-N,N-DiEt	4-Me-N-Et (43%); bp 220°C (lit.[16]bp 222°C)

Although the reaction conditions were not herein maximized, this one-step demethylation-acylation sequence demonstrated by these heterocyclic acetoxy compounds may have overall general synthetic utility[17,18].

REFERENCES

1. On leave from the Lanchow Institute of Chemical Physics, Academia Sinica, Lanchow, China, 1981-1982. 2. Boekelheide, V.; Linn, V. J. J. Am. Chem. Soc. 1954, 76, 1286. 3. Review: Traynelis, V. J. in "Mechanisms in Molecular Migrations", Vol. II, B. S. Thyagarajan, ed., Interscience Publishers, New York, N. Y., 1969, p.1. 4. Ford, P. W.; Swan, J. M. Aust. J. Chem. 1965, 18, 867; Cohen, T.; Deets, G. L. J. Am. Chem. Soc. 1967, 89, 3939. 5. Dinan, F. J.; Tieckelmann, H. J. Org. Chem. 1964, 29, 892. 6. Baker, W.; Buggle, K. M.; McOmie, J. G. W.; Watkins, D. A. M. J. Chem. Soc. 1958, 3594. 7. Horner, L.; Nickel, H. Chem. Ann. 1955, 597, 20. 8. Weinstein, B.; Brattesani, D. N. J. Org. Chem. 1967, 32, 4107. 9. Kumler, W. D., J. Am. Chem. Soc. 1946, 68,1184. 10. For related examples: (a) Ramirez, F.; von Ostwalden, P. Chem. Ind. (London) 1957, 46. (b) Takada, K.; Hamamoto, K. J. Pharm. Soc. Japan 1953, 73, 1158. (c) Takada, K.; Hamamoto, K.; Tone, H. ibid. 1952, 72, 1427. 11. Brehme, R. Synthesis 1976, 113. 12. Roberts, R. M.; Vogt, P. J. J. Am. Chem. Soc. 1956, 78, 4778. 13. Mills, W. H.; Kelham, R. M. J. Chem. Soc. 1937, 274. 14. Foues, U. S. J. Org. Chem. 1949, 14, 1099. 15. Horner, L.; Winkelmann, E.; Knapp, K. H.; Ludwig, W. Chem. Ber. 1959, 92, 288. 16. Siddall, T. H.; Prohaska, C. A. J. Am. Chem. Soc. 1966, 88, 1172. 17. The N-demethylation of 6 has recently been reported [Döpp, D.; Heufer, J. Tetrahedron Lett. 1982, 23, 1553. 18. Acknowledgment is made to the National Institute of Health for partial support of this research.

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