BASE-INDUCED CONVERSION OF N-ALKOXYPYRIDINIUM SALTS BEARING A FORMYL GROUP IN THEIR ALKOXYL CHAIN

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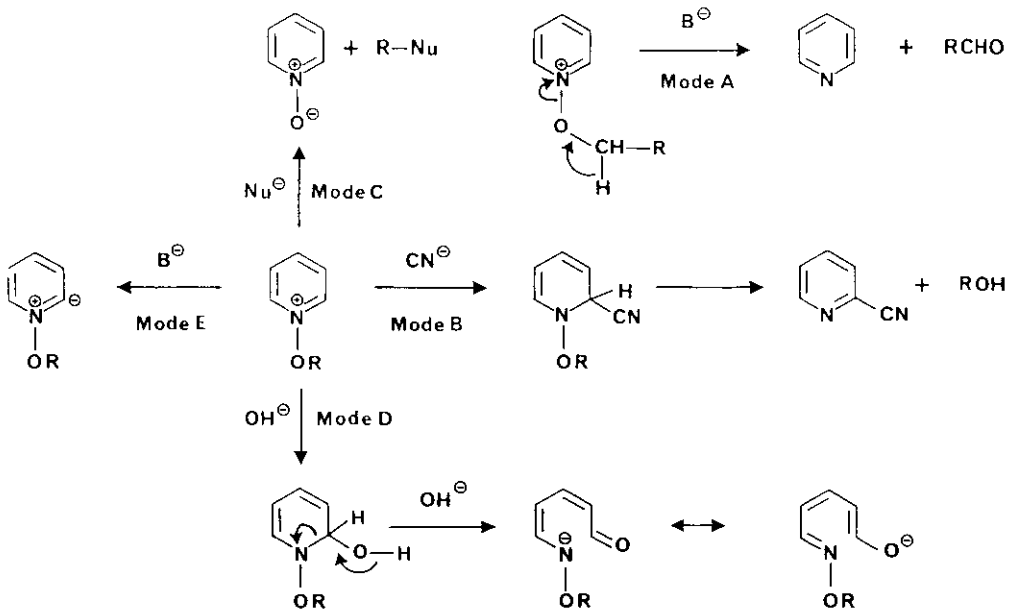
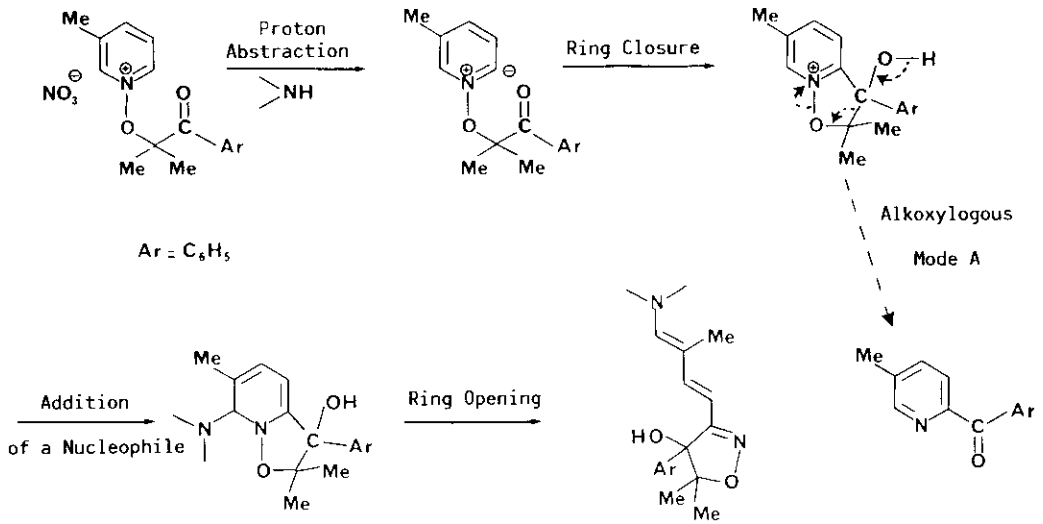
Abstract - Reaction of pyridine N-oxide with α-disubstituted 2-bromoaldehydes led to the expected N-alkoxypyridinium salts which were converted to 2-(α-hydroxyacyl)pyridines on base treatment.

N-Alkoxypyridinium salts are versatile compounds which undergo various types of reaction upon treatment with nucleophiles or bases.[1] In addition to the four classical modes of decomposition described by Katritzky (Modes A-D, Scheme 1)[2] a fifth mode of reaction involving nuclear proton abstraction from the 2-position has been proposed by Abramovitch (Mode E, Scheme 1).[3]



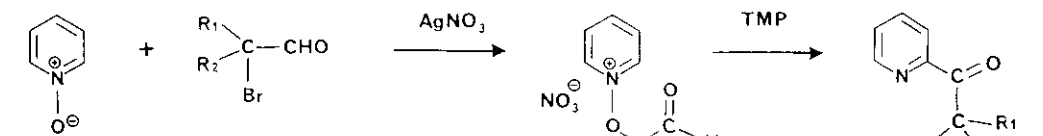
Scheme 1

We have taken advantage of this ylid formation according to Mode E to realize novel reactions of salts bearing a functionalized alkoxyl chain. Our previous studies[4-6] on such salts bearing an alkoxycarbonyl or a carbonyl group have led to a new heterocyclic ring conversion proceeding by the PARC-ANRO mechanism[7] and to a novel mode of decomposition described as "alkoxylogous" of Mode A (Scheme 2).



Scheme 2

The present report is concerned with the synthesis and the base-induced transformation of the N-alkoxypyridinium salts 1 bearing a formyl group (Scheme 3). The study has been limited to salts which are disubstituted at the α-carbon on their alkoxyl chain to prevent any competitive decomposition according to Mode A.



a : $R_1 = R_2 = CH_3$

b : $R_1 = CH_3$ $R_2 = C_6H_5$

c : $R_1 = R_2 = C_6H_5$

1 a–c

2 a–c

Scheme 3

The salts 1 have been prepared in good yields (90 %) by the general procedure that we have developed during our previous studies of functionalized N-alkoxypyridinium salts,[8,9] i.e. by

treating pyridine N-oxide in acetonitrile with the appropriate 2-bromoaldehydes[10] in the presence of silver nitrate. In order to avoid nucleophilic attack at the carbonyl group as well as a possible ring opening according to Mode D a sterically crowded base was chosen to generate the ylid.

Reaction of the salts 1 with 2,2,6,6-tetramethylpiperidine (TMP) in acetonitrile resulted in the formation of a precipitate of tetramethylpiperidinium nitrate which occurred in a few minutes. Filtration followed by solvent evaporation and subsequent distillation for 2a (bp 69°C (0.45 mmHg)) or recrystallization for 2b (ethanol, mp 78°C) and 2c (chloroform, mp 134°C) afforded the 2-(α-hydroxyacyl)pyridines 2 in 85,94 and 92 % yields, respectively. Their structures were ascertained by the ir and ^{1}H nmr data which are reported in the Table and by ms study.

Infrared data, ν(cm^{-1}).

Compound	OH (bonded)	C=O (conjugated)	C=C and C=N (ring)
2a	3350	1695	1580 ; 1565
2b	3240	1695	1580 ; 1565
2c	3240	1695	1580 ; 1560

^{1}H Nmr data : Chemical shifts, δ , ppm (TMS).

Compound	Solvent	H_3	H_4	H_5	H_6	CH_3	C_6H_5	OH
2a	$CDCl_3$	8.10	7.93	7.52	8.62	1.60	-	6.40
2b	DMSO-d_6	7.97	7.94	7.53	8.53	1.69	7.16-7.47	7.08
2c	$CDCl_3$	8.20	7.87	7.39	8.43	-	7.25-7.49	8.18

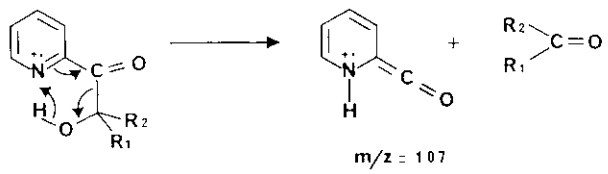
^{1}H Nmr data : Coupling constants[11] (Hz)

Compound	J_{3-4}	J_{3-5}	J_{3-6}	J_{4-5}	J_{4-6}	J_{5-6}
2a	7.4	1.6	0.9	7.4	1.75	4.6
2c	7.9.	1.3	0.9	7.7	1.75	4.85

Table

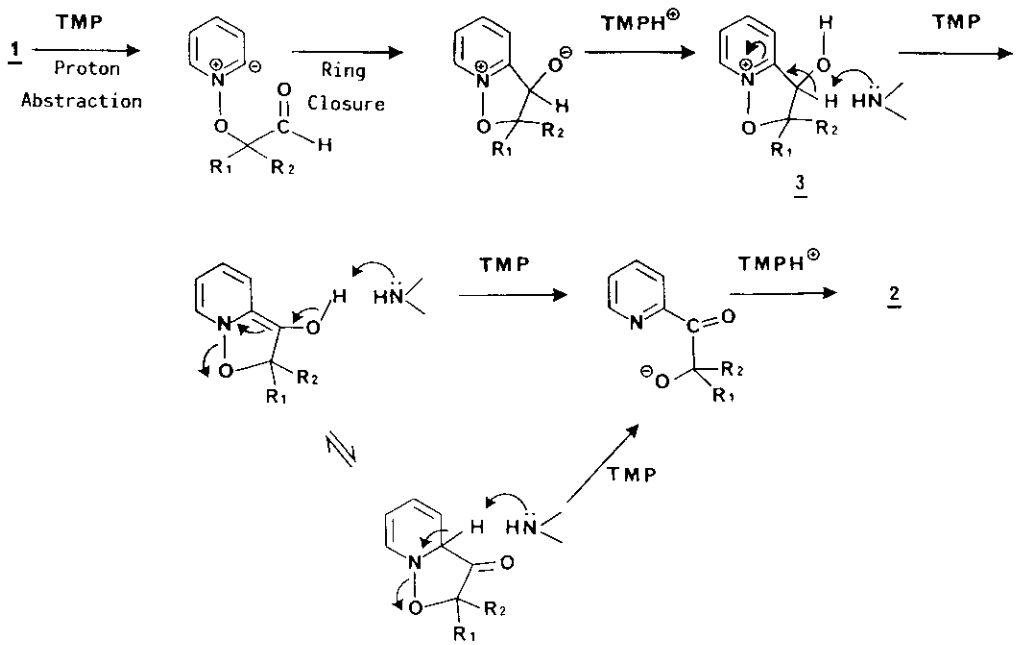
One can notice that the chemical shifts and coupling constants observed in ^1H nmr spectra clearly established the substitution pattern of the ring providing a 2-substituted pyridine.[12] Furthermore ir study indicates the presence of a conjugated carbonyl group together with a chelated hydroxyl group.

These findings are corroborated by mass spectroscopy analysis which shows a peak at m/z = 107 (the base peak for 2a). This fragment results from a Mac Lafferty-type rearrangement, as shown in Scheme 4, which is characteristic of 2-substituted azines.[13]



Scheme 4

The following Scheme 5 can be proposed to account for the formation of the α-hydroxyacyl-pyridines.



Scheme 5

Thus the reaction follows the first phase of the PARC-ANRO mechanism, but once the ring closure step has been realized, proton transfer between the reactive intermediates and the

acid-base pair $TMPH^+$/TMP leads to the α-hydroxyacylpyridines via anhydro base formation ; the ANRO step does not occur. It is noticeable that the isoxazolopyridinium ion 3 does not suffer the alkoxylogous Mode A fragmentation which occurred, as described in Scheme 2, in similar intermediates possessing a tertiary alcoholic function and which became exclusive in the quinoline and isoquinoline series.[6]

This fact is in accordance with the relatively high acidity of a hydrogen atom of an alkyl substituent attached to the 2-position of N-alkoxypyridinium salts. Indeed we have shown that anhydro base formation by abstraction of this proton occurs very readily during base decomposition of alkoxypyridinium salts derived from 2-picoline N-oxide.[9]

In conclusion the studied reaction illustrates the multifarious reactivity of N-alkoxypyridinium salts and is a promising new access to 2-(α-hydroxyacyl)pyridine derivatives.

REFERENCES AND NOTES

1. A. R. Katritzky and J. M. Lagowski, "Chemistry of the Heterocyclic N-oxides", ed. by A. T. Blomquist, Academic Press, London and New York, 1971, p. 550.
2. R. Eisenthal and A. R. Katritzky, Tetrahedron, 1965, 21, 2205.
3. R. A. Abramovitch, "Pyridine and its Derivatives", supplement Part 2 "The Chemistry of Heterocyclic Compounds", eds. by A. Weissberger and E. C. Taylor, John Wiley and Sons, New York, London, 1974, p. 81.
4. H. Sliwa and A. Tartar, Tetrahedron, 1979, 35, 341.
5. H. Sliwa and C. Raharimanana, Tetrahedron Lett., 1986, 27, 349.
6. H. Sliwa and L. Ouattara, Heterocycles, 1987, 26, 3065.
7. Proton Abstraction, Ring Closure - Addition of a Nucleophile and Ring Opening.
8. H. Sliwa and A. Tartar, J. Org. Chem., 1976, 41, 160.
9. H. Sliwa and A. Tartar, Tetrahedron, 1977, 33, 3111.
10. P. Duhamel, L. Duhamel, and J. Y. Valnot, Bull. Soc. Chim. France, 1973, 1465.
11. The coupling constants have not been determined for compound 2b owing to the fact that overlap of H_3 and H_4 signals does not allow first order analysis.
12. R. A. Abramovitch, "Pyridine and Its Derivatives", Supplement Part 1 in "The Chemistry of Heterocyclic Compounds", eds. by A. Weissberger and E. C. Taylor, John Wiley and Sons, New York, London, 1974, p. 11.
13. A. R. Katritzky, "Handbook of Heterocyclic Chemistry", Pergamon Press, Oxford, 1985, p. 43.

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