

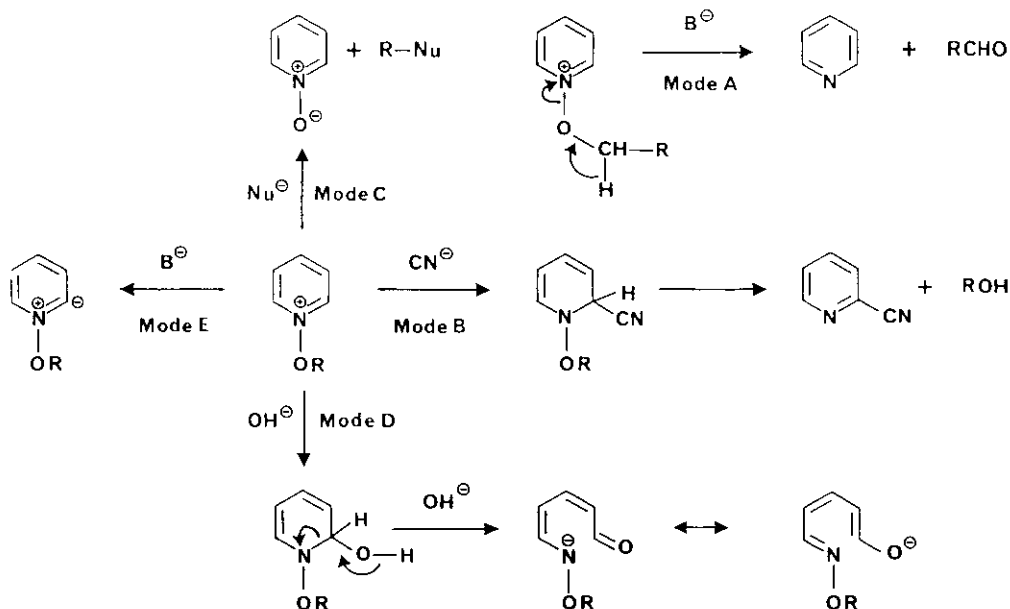
BASE-INDUCED CONVERSION OF N-ALKOXYPYRIDINIUM SALTS BEARING A FORMYL
GROUP IN THEIR ALKOXYL CHAIN

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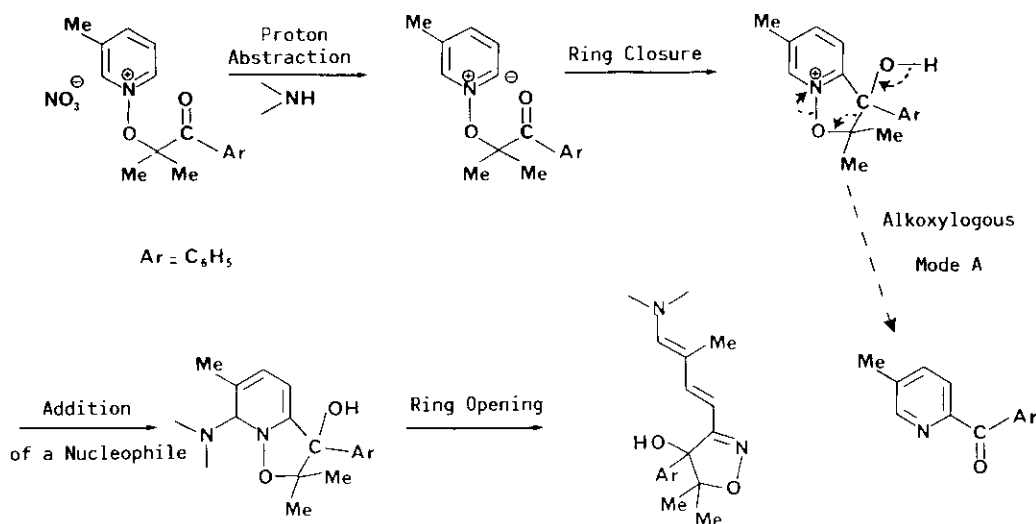
Abstract - Reaction of pyridine N-oxide with α -disubstituted 2-bromo-
aldehydes led to the expected N-alkoxypyridinium salts which were
converted to 2-(α -hydroxyacyl)pyridines on base treatment.

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



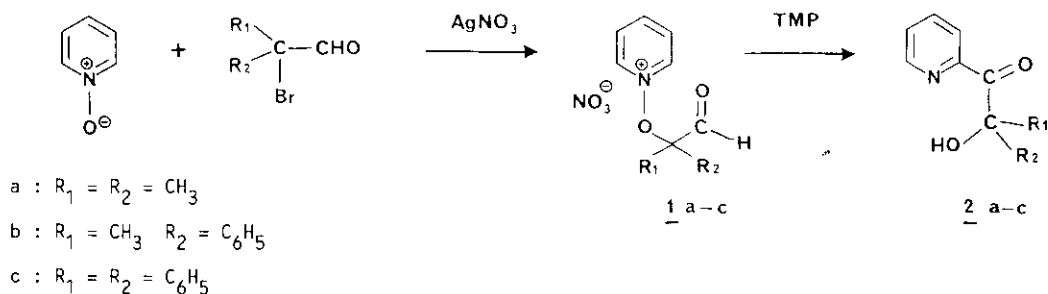
Scheme 1

We have taken advantage of this ylid formation according to Mode E to realize novel reactions of salts bearing a functionalized alkoxy chain. Our previous studies⁴⁻⁶ on such salts bearing an alkoxy carbonyl or a carbonyl group have led to a new heterocyclic ring conversion proceeding by the PARC-ANRO mechanism⁷ 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-alkoxy pyridinium salts 1 bearing a formyl group (Scheme 3). The study has been limited to salts which are disubstituted at the α -carbon on their alkoxy chain to prevent any competitive decomposition according to Mode A.



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-alkoxy pyridinium salts,^{8,9} i.e. by

treating pyridine N-oxide in acetonitrile with the appropriate 2-bromoaldehydes¹⁰ 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 ¹H nmr data which are reported in the Table and by ms study.

Infrared data, $\nu(\text{cm}^{-1})$.

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

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

Compound	Solvent	H ₃	H ₄	H ₅	H ₆	CH ₃	C ₆ H ₅	OH
<u>2a</u>	CDCl ₃	8.10	7.93	7.52	8.62	1.60	-	6.40
<u>2b</u>	DMSO-d ₆	7.97	7.94	7.53	8.53	1.69	7.16-7.47	7.08
<u>2c</u>	CDCl ₃	8.20	7.87	7.39	8.43	-	7.25-7.49	8.18

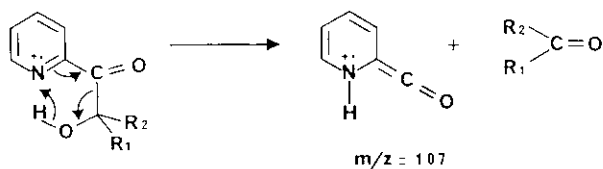
¹H Nmr data : Coupling constants¹¹ (Hz)

Compound	J ₃₋₄	J ₃₋₅	J ₃₋₆	J ₄₋₅	J ₄₋₆	J ₅₋₆
<u>2a</u>	7.4	1.6	0.9	7.4	1.75	4.6
<u>2c</u>	7.9	1.3	0.9	7.7	1.75	4.85

Table

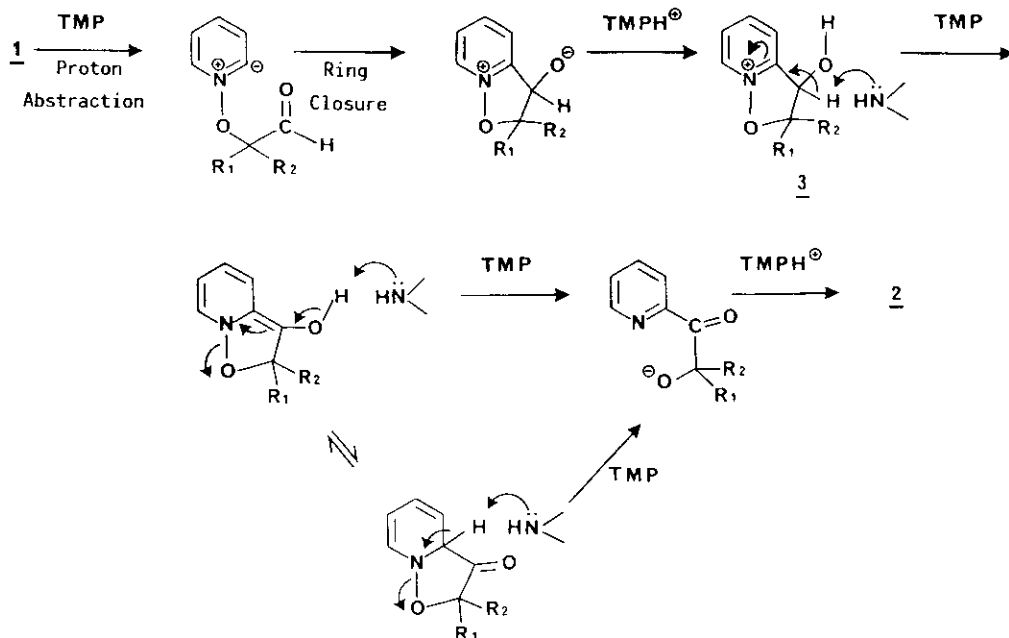
One can notice that the chemical shifts and coupling constants observed in ^1H nmr spectra clearly established the substitution pattern of the ring providing a 2-substituted pyridine.¹² Furthermore ir study indicates the presence of a conjugated carbonyl group together with a chelated hydroxyl group.

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 alkoxypridinium 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.

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