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A NEW TYPE OF FUNCTIONALIZATION OF THE BENZYLIC-TYPE POSITIONS IN ALKYLPYRIDINES BY DMSO-AC$_2$O.

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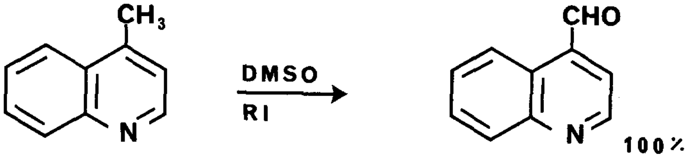
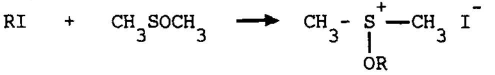
Abstract- 4-Methyl, 4-ethyl,4-isopropylpyridine and 4-methylquinoline react with DMSO-Ac$_2$O giving a new type of reaction of the C-H benzylic type bond, mainly involving the substitution of the hydrogen atom by the CH_2SCH_3 group.

Recently we[1] have reported a highly selective oxidation of lepidine to the corresponding 4-formylquinoline by using DMSO and alkyliodides as oxidant (eq. 1)

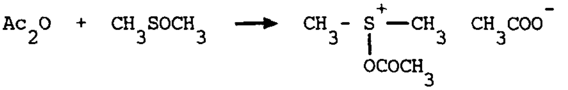


(1)

Since our attempt of interpretation involved the alkoxysulfonium salt (eq. 2) as real oxidizing agent, we thought it right to investigate the reaction with the well-known[2] oxidizing agent DMSO-Ac$_2$O which leads to a similar acetoxysulfonium salt intermediate (eq. 3)

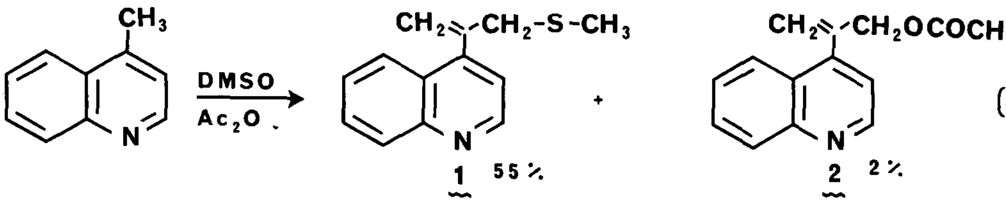


$$RI + CH_3SOCH_3 \longrightarrow CH_3-\underset{\displaystyle OR}{\overset{+}{S}}-CH_3 \; I^- \qquad (2)$$



$$Ac_2O + CH_3SOCH_3 \longrightarrow CH_3-\underset{\displaystyle OCOCH_3}{\overset{+}{S}}-CH_3 \; CH_3COO^- \qquad (3)$$

The results with lepidine and DMSO-Ac$_2$O, however are completely different: **1** and **2** are the main products isolated from the reaction (eq. 4)

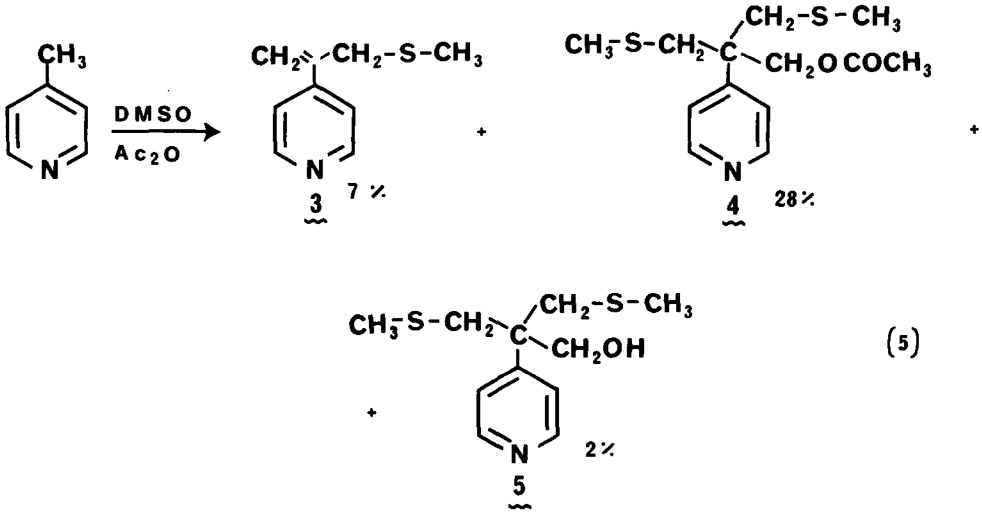


(4)

The amount of **2** increases during the reaction, compared with **1**; it seems that **2** is formed from **1** by further reaction with AcOH and Ac$_2$O.

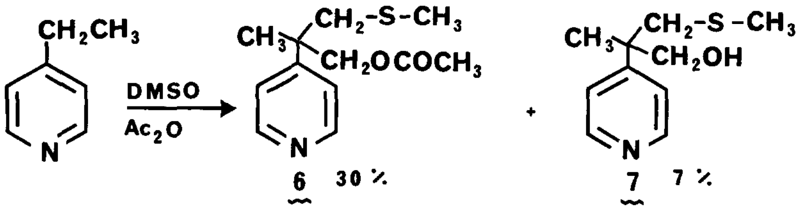
In an attempt to determine the range of application of this new reaction, 4-methyl-, 4-ethyl- and 4-isopropyl-pyridine were subjected to the reaction with DMSO-Ac_2O under the same conditions.

3, 4 and 5 are the main products isolated from the reaction with 4-methylpyridine (eq. 5)



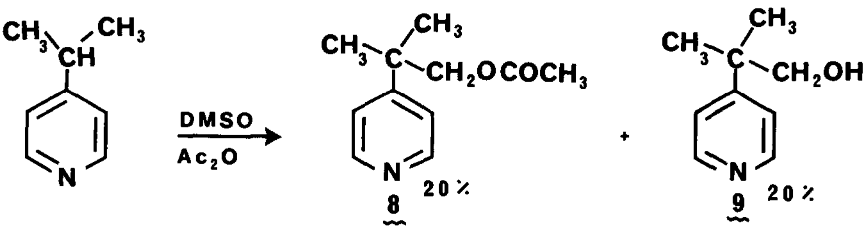
(5)

4 -Ethylpyridine similarly gives 6 and 7 as the main products isolated from the reaction (eq. 6)



(6)

8 and 9 are the products isolated with 4-isopropylpyridine (eq. 7)



(7)

The hydroxymethylderivatives 5, 7 and 9 very probably are not primary products of the reaction, but they appear to be formed by hydrolysis of the corresponding acetates when the solution is made basic during the workup in order to isolate the basic reaction products. All the acetates 2, 4 , 6 and 8 can be easily and quantitatively transformed into the corresponding primary alcohols by basic hydrolysis. The product 2 from lepidine is less hydrolyzed during the workup, due to the lower solubility in aqueus solution compared with the corresponding pyridine derivatives.

The typical reaction procedure is exemplified by the reaction of lepidine.

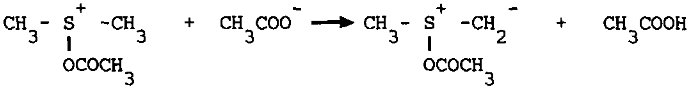
A solution of 10 mmol of lepidine in 28 ml of DMSO, 20 ml of Ac_2O and 7 ml of AcOH was warmed for 24 hrs at 120°C. The mixture is then poured in water, made basic and extracted with CH_2Cl_2. Distillation gives large amount of $CH_3S\text{-}CH_2OCOCH_3$ (90°C / 5 mBar) and at 160-180°C / 5 mBar the products 1 and 2. These last were isolated by flash chromatography (silica gel, 230-400 Mesh, hexane-ethyl acetate 55:45).

The spectral data (NMR, MS, IR) of all the new compounds 1-9 are in accord with the structures assigned.

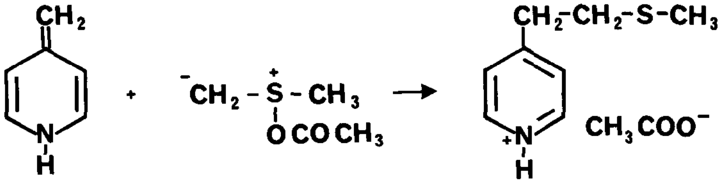
Preliminary results indicate that alkyl heterocycles in the diazine series give similar results so that the reaction appears to be of general character with heteroaromatic bases.

As concerns the mechanism of the reactions, it clearly appears that the reaction involves the benzylic type C-H bonds, leading accordingly to monosubstitution with the isopropyl group, disubstitution with the ethyl group and trisubstitution with the methyl group.

The reaction of the activated pyridine with the ylid intermediate arising from the acetoxysulfonium salt (eq. 8) could be the key step leading to the monosubstitution (eq. 9)

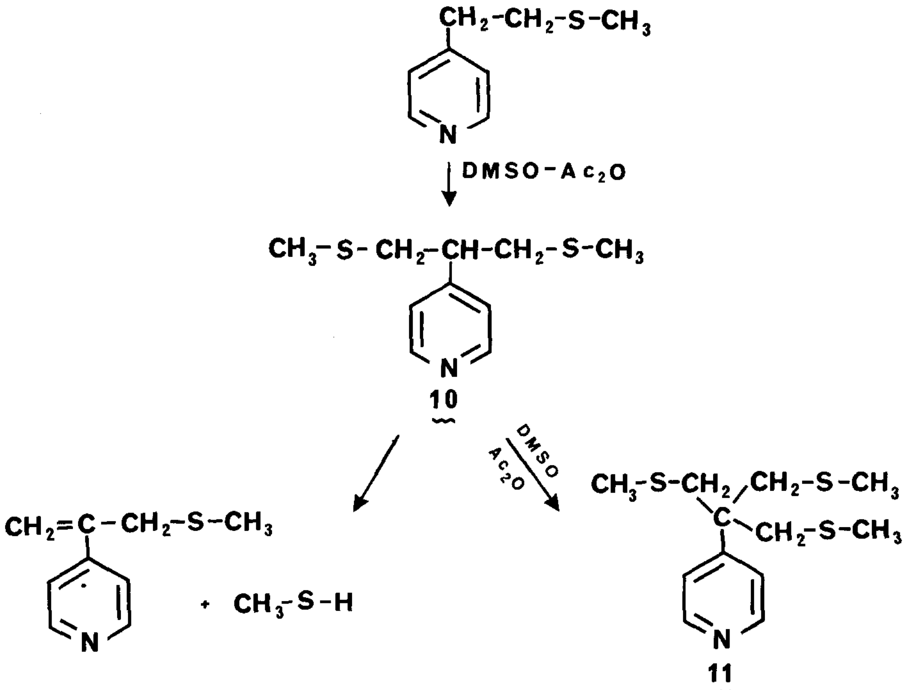


$$CH_3\text{-}\underset{\underset{OCOCH_3}{|}}{\overset{+}{S}}\text{-}CH_3 + CH_3COO^- \longrightarrow CH_3\text{-}\underset{\underset{OCOCH_3}{|}}{\overset{+}{S}}\text{-}CH_2^- + CH_3COOH \qquad (8)$$



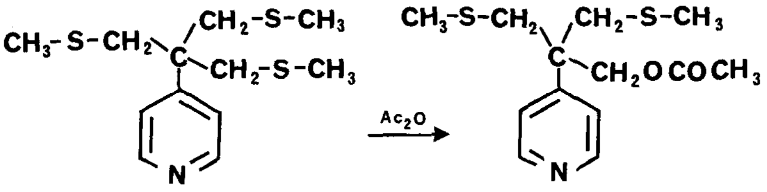
(9)

A further similar substitution would give the compound 10, which can either lose CH_3SH, generating the reaction product 3 and the analogous derivative with lepidine 1 or give the trisubstituted product 11 according to the Scheme 1



Scheme I

The acetates 2, 4, 6 and 8 would arise from the reaction of thioethers with Ac_2O (eq. 10)



(10)

References

1- E. Vismara, F. Fontana and F. Minisci, Gazz. Chim. It. 1987, 117, 135

2- J.G. Moffatt "Oxidation" , Ed. R.L. Augustine, M. Dekker Inc., New York, vol.2, pg 44 (1971).

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