Oxidiation of Isomeric Pyridylcarbinols with Pyridinium Chlorochromate

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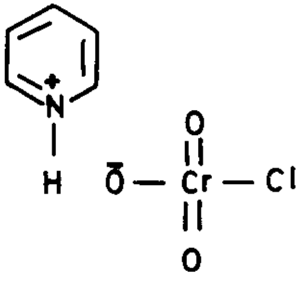
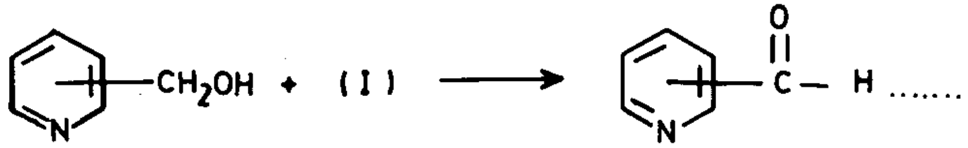
Summary: Oxidation of the three isomeric pyridylcarbinols with pyridinium chlorochromate has been studied. In each case moderate yield of the respective pyridine aldehyde was obtained. The reaction is of significant importance for preparation of isomeric pyridine aldehydes since they are not further oxidised to the corresponding carboxylic acids.

Since aldehydes are easily oxidized to the corresponding carboxylic acids, the preparation of the former by oxidation of primary alcohols always requires the use of relatively mild oxidants. Some of the important reagents employed for this purpose include chromium trioxide in glacial acetic acid [1], chromium trioxide-pyridine complex [2,3], potassium dichromate [4], potassium permanganate [5], lead tetraacetate [6,7], dimethylsulphoxide [8] and N-bromosuccinimide [9]. Recently pyridinium chlorochromate (I) has also emerged [10] as a useful reagent for oxidizing primary and secondary alcohols to the respective carbonyl compounds. As far as oxidation of isomeric pyridylcarbinols to respective aldehydes is concerned not much work has so far been reported. The only report available in the literature in this respect is about the oxidation of isomeric pyridylcarbinols with lead tetraacetate [11]. In view of the usefulness of (I) for oxidation of various primary alcohols to yield the corresponding aldehydes and difficulties involved in preparaton of oxidation sensitive isomeric pyridine aldehyes by other methods, we have studied the oxidation of isomeric pyridylcarbinols with pyridinium chlorochromate. In this article we wish to report the results of these studies.



(I)

As a result of present investigations, 2-pyridylcarbinol, 3-pyridylcarbinol and 4-pyridylcarbinol were successfully oxidized to the corresponding aldehydes in moderate yields. The general oxldation reaction for these substrates is represented by Equation 1. The reaction in general was found to be convenient and rapid. In addition, in each case no trace of pyridine carboxylic acid was obtained indicating the usefulness of the reaction to obtain pyridine aldehyde. The aldehydes obtained as the reaction products were identified on the basis of their boiling points, some chemical tests of aldehydes, comparitive tlc against authentic samples, their IR spectra and preparation of phenyl hydrazone and 2,4-dinitrophenyl hydrazone derivatives. In Table 1 are summarized the %



(1)

Table-1: Oxidation of Isomeric Pyridylcarbinols with Pyridinium Chlorochromate

Carbinol	Oxidation Product	% Yield	Boiling Point (obs.)°C	(lit.)°C	Phenyl hydrazone M.P (obs.)°C	(lit.)°C	2,4-Dinitrophenyl hydrazone M.P. (obs.)°C	(lit.)°C
2-Pyridyl-carbinol	Pyridine-2-aldehyde	40.2	38/7mm	62-63/14mm[a]	181	182[c]	237	237[c]
3-Pyridyl-carbinol	Pyridine 3-aldehyde	46.5	62/5mm	97-99/26mm[b]	159	159[c]	258	259[c]
4-Pyridyl-carbinol	Pyridine-4-aldehyde	45.5	63/9mm	82-83/16mm[b]	177	178[c]	282	283[c]

(a) Reference 13d (b) Reference 13a (c) Reference 15

yields and the boiling points of the isomeric pyridine aldehydes obtained as a result of oxidation. The melting points of their derivatives are also included in the Table. Each aldehyde responded positive to the Fehling's solution and Tollen's reagent tests for aldehydes. Furthermore, the IR spectrum (neat) of each isomeric pyridine aldehyde displayed a strong C=O strecting absorption at 1700 cm^{-1} and an aldehydic C-H streching absorption at 2740 cm^{-1}.

Experimental

Reagents and Substrates

Pyridine-2-carboxylic acid, pyridine-3-carboxylic acid, pyridine-4-carboxylic acid, pyridine, hydrochloric acid, lithium aluminum hydride and absolute ethanol were obtained from E.Merck. Chromium trioxide was supplied by May & Baker. All chemicals were used without further purification. Pyridinium chlorochromate was prepared by the method for Corey and Suggs [10]. Isomeric pyridylcarbinols were prepared from the corresponding ethyl pyridylcarboxylates by reduction as given below.

Isomeric ethyl pyridylcarboxylates were prepared from the corresponding carboxylic acids by the same method as reported [12] for the preparation of ethyl 3-pyridylcarboxylate from pyridine-3-carboxylic acid. The esters were obtained in yields of about 75% and were characterized on the basis of their boiling points; ethyl 2-pyridylcarboxylate b.p. (obs.) 242-243°, b.p.(lit.) [13a] 243°; ethyl 3-pyridylcarboxylate b.p.(obs.) 223-224°, b.p.(lit.) [13a] 222-224°; ethyl 4-pyridylcarboxylate b.p.(obs.) 219-220°, b.p.(lit.) [13b] 219-220°.

3-Pyridylcarbinol and 4-pyridylcarbinol were prepared by reduction of the corresponding ethyl pyridylcarboxylate with lithium aluminum hydride by the method reported [14] for preparation of 3-pyridylcarbinol. 3-Pyridylcarbinol was purified by vacuum distillation at 92-3°/8 mm b.p.(lit.) [13c] 142-143°, picrate m.p. (obs.) 162°, m.p. (lit.) [13c] 162-3°. 4-Pyridylcarbinol was purified by azeotropic distillation with benzene, m.p.(obs.) 56°, m.p.(lit.) [13c] 57-60°, picrate m.p.(obs.) 156-7°, m.p.(lit.) [13c] 157-8° 2-Pyridylcarbinol was prepared by reduction of ethyl 2-pyridylcarboxylate with lithium aluminium hydride by the method of Micovic et al. [11]. 2-Pyridycarbinol was obtained in good yield, b.p.(obs.) 110-112°/16 mm b.p.(lit.) [13c] 112-113° /16 mm, picrate m.p. (obs.) 158°, m.p.(lit.) [13c] 159°.

Oxidation of Pyridylcarbinols

Pyridinium chlorochromate (0.75 mole) was suspended in an excess of chloroform (80 ml) in a 250-ml three necked round bottom flask fitted with a reflux condenser, a mechanical stirrer and a dropping funnel containing a solution of the respective pyridylcarbinol (0.5 mole) in chloroform (30 ml). The solution of pyridylcarbinol was then added slowly over a period of about twenty minutes to the reaction flask containing the thoroughly stirred suspension of pyridinium chlorochromate. In each case the reaction started vigorously in the begining but subsided later. After addition of the alcohol was complete, the reaction mixture was refluxed for three hours. The reaction mixture was then allowed to cool to room temperature and filtered. The black residue left sticking to the walls of the flask was then washed with diethyl ether (2x30 ml). The filtrate and ethereal washings were combined and the solvents removed. In each case yellowish green oil was obtained which was subjected to vacuum distillation to yield the respective pyridine aldehyde.

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