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Received May 26, 1978

The hydrogenation of 1-alkyl-3-acylpyridinium salts in methanol in the presence of 10% palladium-charcoal/disodium hydrogen phosphate-sodium dihydrogenphosphate suspension leads to the corresponding tetrahydropyridines. This represents an improvement over the Wenkert method.

J. Heterocyclic Chem., 15, 1509 (1978)

It has been shown by Wenkert (1) that β -acylpyridines and their *N*-alkyl salts are reduced to 3-acyl-2-piperidineins on palladium catalyzed hydrogenation in the presence of triethylamine, the vinylogous amide system being stable under these conditions.

This method has proved to be very useful in alkaloid synthesis (2). However, in some cases hydrogenation of 1-alkyl-3-acylpyridinium salts under these conditions leads to low yields or anomalous results (3,4). It appears that this is probably due to the presence of an acidic proton on the substituent in the 2 or 4 position of the pyridine ring, e.g. 1 or 5. The removal of this proton by triethylamine gives the new conjugated system 3 or 7 which is subsequently completely reduced (3,4). Furthermore, the basicity of the medium favours side reactions such as the transformation 9 \rightarrow 11 (5) involving neighbouring group participation. Reduction in alkaline medium was considered necessary for the existence of the vinylogous amide group which is inert to hydrogenation (1).

Having encountered the aforementioned difficulties (4, 5), we looked for a modification of the Wenkert method. We observed that the hydrogenation could be carried out in methanol solution in the presence of a 10% palladium-charcoal/disodium hydrogenphosphate-sodium dihydrogenphosphate suspension. These conditions are efficient in preventing the protonation of the vinylogous amide group and its subsequent hydrogenation.

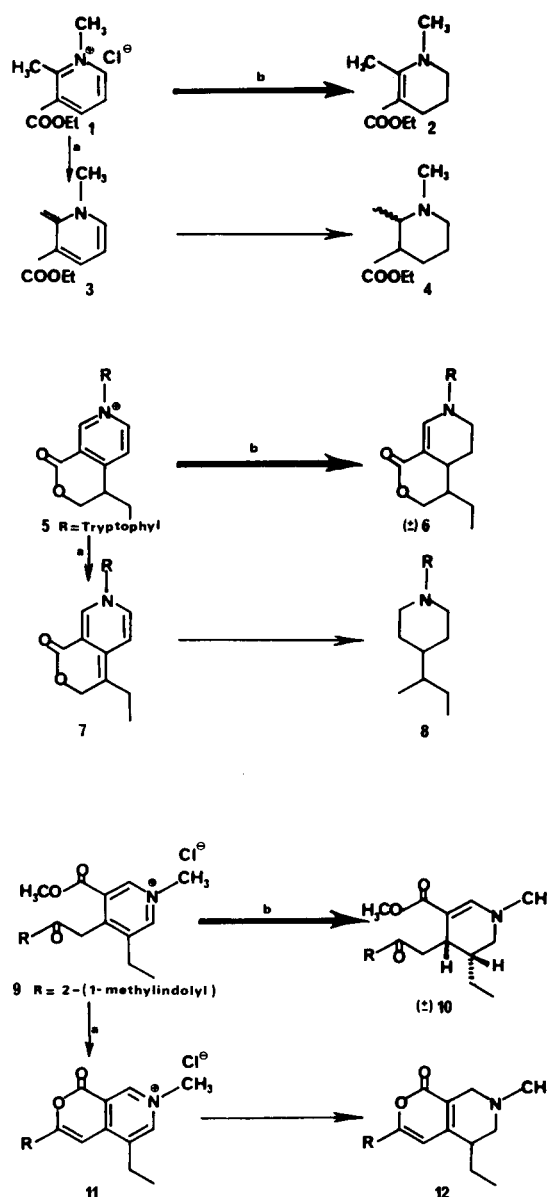
In this manner the hydrogenation of 1 leads to 2 as the major product although it is impossible to prevent the formation of a small amount of the piperidine 4 which was reported to be the exclusive product under the Wenkert conditions (3).

Other examples in the total synthesis of indole alkaloids have proved the efficiency of this modification of a general method: the intermediate 6 (4) (Y 60%) and 10 (Y 30%) have been synthesized with the prevention of side reactions (compound 12) or by-product formation (compound 8).

EXPERIMENTAL

Tetrahydropyridine (2).

2-Methyl nicotinate methiodide was converted into its methochloride 1 by means of silver chloride. A suspension of 1 (108



a: 10% palladium-charcoal, triethylamine, methanol, hydrogen¹

b: 10% palladium-charcoal, methanol, Na₂HPO₄ + NaH₂PO₄ suspension, hydrogen

mg.), pulverized disodium hydrogenphosphate (216 mg.) and sodium dihydrogenphosphate (84 mg.) and 10% palladium-charcoal (50 mg.) in methanol (12 ml.) was hydrogenated at room temperature and atmospheric pressure for 15 hours. The catalyst and the salts are then filtered and the filtrate evaporated to dryness. Purification on preparative tlc afforded **2** (15 mg.), oil; ms: 183 (M^+ , 57%), 154 (53%), 138 (100%), 110 (100%); ir (chloroform): ν cm^{-1} 1665, 1565; uv (ethanol): λ max $m\mu$ (ϵ) 298 (26,100); ^1H nmr (deuteriochloroform): (TMS $\delta = 0$ ppm) NCH_3 2.9 singlet, $-\text{N}-\text{C}-\text{CH}_3$ 2.36 broad singlet.

A small amount of **4** (**3**) (5 mg.) can also be isolated from the tlc.

REFERENCES AND NOTES

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