CHEMISTRY LETTERS, pp. 1091-1094, 1977. Published by the Chemical Society of Japan

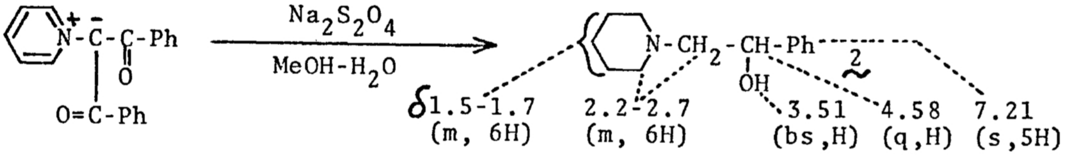
REDUCTION OF PYRIDINIUM AND CARBONYL COMPOUNDS BY REFLUXING SODIUM DITHIONITE SOLUTIONS

Hiroshi MINATO,* Shinichi FUJIE, Kentaro OKUMA, and Michio KOBAYASHI
Department of Chemistry, Tokyo Metropolitan University, Setagaya, Tokyo 158

Sodium dithionite in refluxing MeOH-H_2O was found to be an effective reducing agent for converting pyridinium ions to piperidines and carbonyl compounds to alcohols, respectively.

Reduction of N-alkylpyridinium salts with an aqueous solution of sodium dithionite (1) is a standard method for preparation of 1,4-dihydropyridine derivatives.[1] We wish to report that reduction of N-alkylpyridinium compounds with 1 in refluxing MeOH-H_2O yields the corresponding piperidines and that of carbonyl compounds under the same conditions yields the corresponding alcohols.

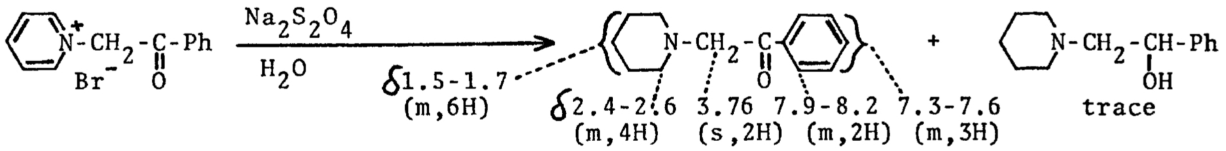
After pyridinium dibenzoylmethylide (7.0 mmol) was reduced in a refluxing mixture of MeOH (150 ml) and H_2O (300 ml) containing 1 (85 mmol) and Na_2CO_3(150 mmol) under nitrogen for 15 hrs, the solution was concentrated under reduced pressure, and the aqeuous solution obtained was extracted with CH_2Cl_2. When the CH_2Cl_2 extracts were evaporated, white solids were obtained, which were recrystallized from CCl_4-hexane; yield, 72%; mp 68.0-70.5°.



The product was identified as N-(2-hydroxy-2-phenylethyl)piperidine (2) by its C,H,N analysis (Calcd for $C_{13}H_{19}ON$: C, 76.05; H, 9.33; N, 6.82. Found: C, 75.37; H, 9.39; N, 6.68) and the comparison of its NMR spectrum and melting point with those of an authentic sample (prepared from styrene oxide and piperidine by using the method of Emerson[2]).

Clearly both the pyridinium ring and the carbonyl group were reduced. Since it appears that one benzoyl group had been lost before the reduction took place and the presence of two benzoyl groups is not necessary, N-phenacylpyridinium bromide was treated under the same conditions; the same product, **2**, was isolated in a 47% yield.

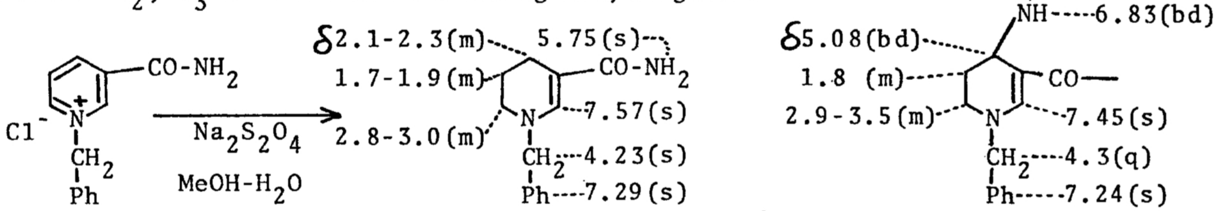
When N-phenacylpyridinium bromide was reduced in H_2O alone (450 ml) without any MeOH as a co-solvent under the same conditions, the main product was N-phenacylpiperidine (64%) with only a trace amount of **2**. N-Phenacylpiperidine is insoluble in hot water. The above results show that, as the pyridinium ions were reduced, the product formed was removed from the reducing aqueous solution and only the pyridinium ring was selectively hydrogenated with the carbonyl function remaining unreduced.



Thus the reduction with **1** in water is a good method for selective reduction of the pyridinium compounds containing carbonyl groups which should be kept unreduced.

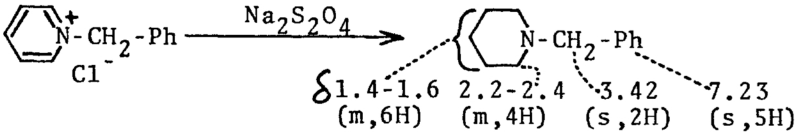
The above results also point out that the rate of reduction of pyridinium ions is greater than that of carbonyl groups.

When 1-benzylnicotinamide chloride was reduced under the same conditions, the product found was 1-benzyl-1,4,5,6-tetrahydronicotinamide (yellow oil; yield, 12%). The structure assignment is based on its NMR spectrum. We recently reported that, when the trimer formed by base-catalyzed cyclization of 1-benzylnicotinamide chloride was hydrogenated by H_2/Raney-Ni, its 1,4,5,6-tetrahydro product was formed with its C_2, C_3 double bond remaining unhydrogenated.[3]



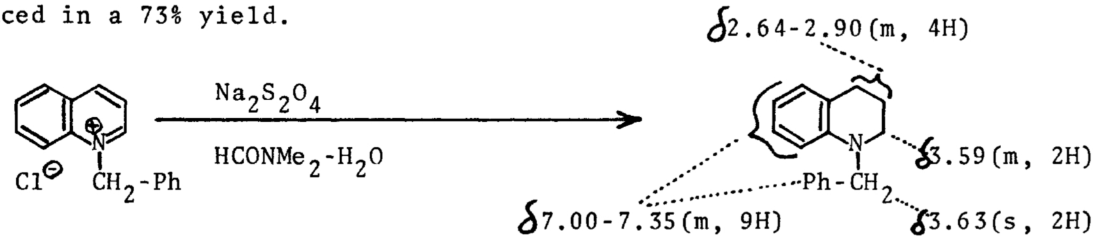
(Product of the reduction of trimer[3])

When N-benzylpyridinium chloride was reduced under the same conditions, the product isolated was N-benzylpiperidine(37%).

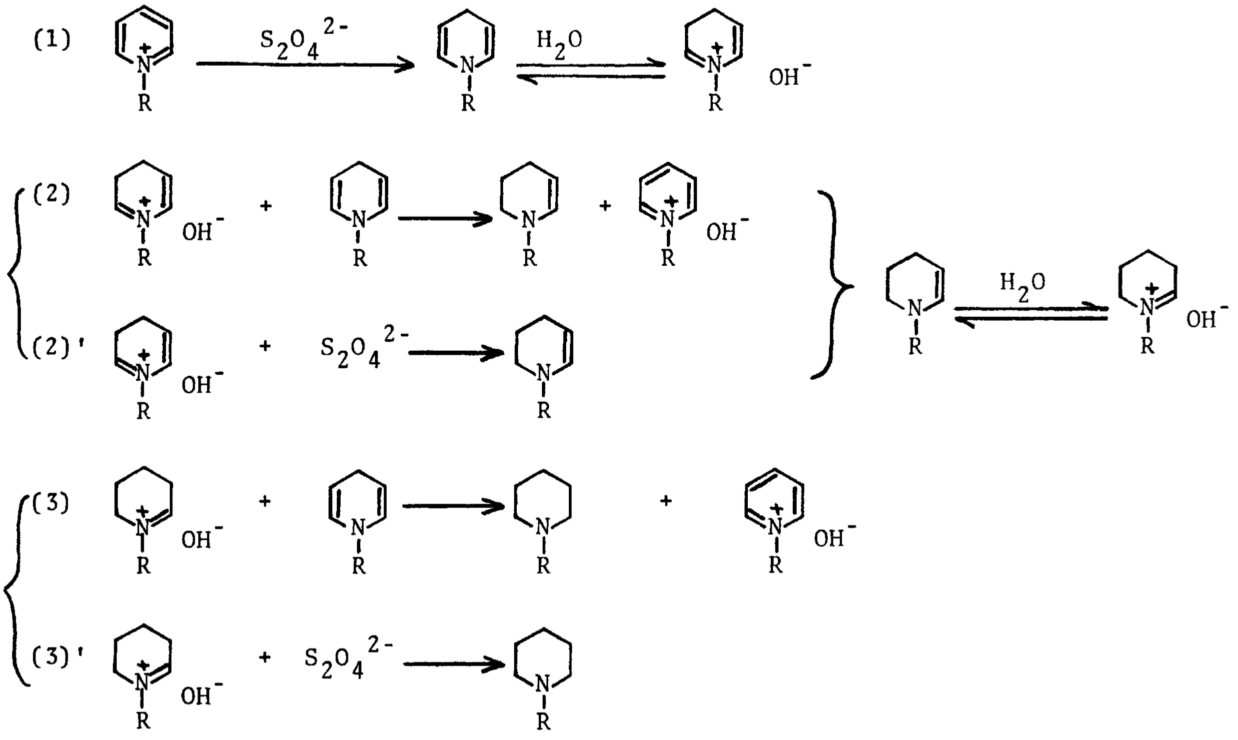


The comparison of the reductions of these two N-benzylpyridinium salts shows that when 3-carbamoyl groups are present on pyridinium rings, the C_2, C_3 double bonds remain unhydrogenated.

When N-benzylquinolinium chloride (4.5 mmol) was reduced in a refluxing mixture of N,N-dimethylformamide (90 ml) and water (90 ml) containing **1** (86 mmol) and $NaHCO_3$(160 mmol) under nitrogen for 2 hrs, N-benzyl-1,2,3,4-tetrahydroquinoline was produced in a 73% yield.



As to the mechanism of this reduction,[4] the reaction sequences shown below are plausible.



The occurrence of Step (1) is probably certain since the reduction of pyridinium salts with **1** is a standard method for preparation of 1,4-dihydropyridines.[1] Since 1,4-dihydropyridines reduce pyridinium ions very rapidly at room temperature,[5] Step (2) is a plausible process. In an attempt to elucidate the mechanism of this reduction, 1-benzyl-1,4-dihydronicotinamide[6] (14 mmol) was treated in a refluxing mixture of MeOH (150 ml) and H_2O (300 ml) containing Na_2CO_3 (150 mmol) under nitrogen for 5 hrs.[7] No reaction took place, and 1-benzyl-1,4-dihydronicotinamide was recovered. Thus, Steps (2) and (3) are eliminated. The experimental results obtained so far indicate that this reduction proceeds probably by Steps (1), (2)', and (3)'.

Carbonyl compounds containing no pyridinium groups were also found to be reduced by **1**. Thus, benzophenone was converted to benzhydrol in 96% yield (mp 66.5-68.0°; its NMR spectrum was identical with that of an authentic sample). Benzaldehyde was reduced to benzyl alcohol (23%), and acetophenone was reduced to 1-phenylethanol (10%).

This reduction method cannot be applied to esters or amides. When methyl benzoate was treated, benzoic acid (84%) was the product. The results described above for 1-benzylnicotinamide chloride show that amide carbonyl groups cannot be reduced by **1**.

Recently, deVries, van Bergen, and Kellogg reported that aldehydes and ketones are reduced by **1** in refluxing H_2O-$HCONMe_2$.[8] Their yields are good, but under their conditions, **1** must be added in portions since "a batch of the reagent loses most of its reducing properties after one hour."[8] It appears that the best conditions for the reduction with **1** are yet to be established and further work is necessary for complete understanding of this powerful and inexpensive reducing agent.

1. D. Mauzerall and F. H. Westheimer, J. Am. Chem. Soc., 77, 2261 (1955).
2. W. S. Emerson, ibid., 67, 516 (1945).
3. Y. Ohnishi, H. Minato, K. Okuma, and M. Kobayashi, Chem. Lett., 525 (1977).
4. We thank a referee for his helpful suggestions.
5. H. Minato, T. Ito, and M. Kobayashi, Chem. Lett., 13 (1977).
6. This was used because it is more stable than 1-alkyl-1,4-dihydropyridines.
7. Separate experiments have shown that 2 hr refluxing in a MeOH-H_2O mixture is enough for the reduction of pyridinium ring, whereas longer refluxing is necessary for R-CO-R.
8. J. G. de Vries, T. J. van Bergen, and R. M. Kellogg, Synthesis, 246 (1977).

(Received July 13, 1977)