CHEMISTRY LETTERS, pp. 523 - 526, 1985. © 1985 The Chemical Society of Japan

REDUCTION OF NITRO ALKENES BY A MODEL OF NAD(P)H(1)

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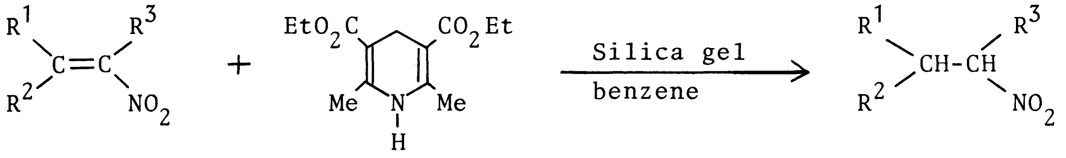
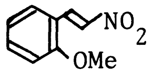
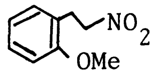
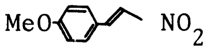
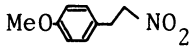
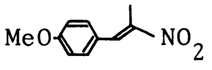
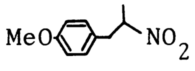
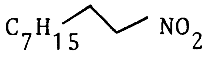
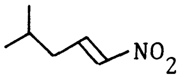
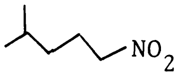
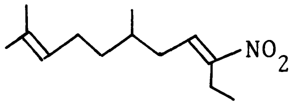
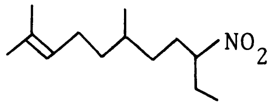
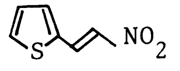
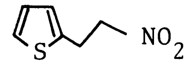
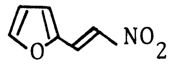
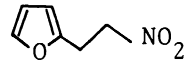
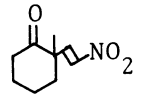
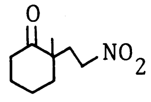
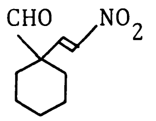
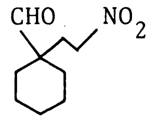
Carbon-carbon double bonds in α,β-unsaturated nitro compounds are reduced smoothly into the corresponding nitro alkanes by a model of NAD(P)H in benzene in the presence of silica gel. Other functional groups are inert under the reaction conditions.

The usefulness of nitro alkanes as synthetic intermediates has increased in recent years mainly because of the facility of nitro group to be converted into other functional groups such as carbonyl(2) and amino groups.(3) The carbon-carbon bond formation *via* carbanions stabilized by an adjacent nitro group is also important in synthetic organic chemistry. A widely used method for the synthesis of nitro alkanes involves reduction of α,β-unsaturated nitro compounds.(4) Although several methods for the reduction of nitro olefins have been reported, some of them accompany the formation of dimeric products and all of them have limited chemoselectivity: use of $NaBH_4$ or $LiAlH_4$ causes the reduction of halide and carbonyl groups. On the other hand, nitro olefins are smoothly reduced in enzymatic systems by NAD(P)H.(5) However, the substrate reactive in enzymatic systems are limited mainly because of the specificity exerted by biological systems. The insolubility of nitro olefins in aqueous solutions is another problem. For these reasons, we have attempted to develop a new system of reduction in which a carbon-carbon double bond in a nitro alkene is reduced smoothly and selectively. The use of NAD(P)H model system(6,8) in place of an enzymatic one may provide a powerful reducing system. The mimetic reduction has no specificity on substrate and can be run in organic solvents. In fact, we found that Hantzsch ester (HEH), an NAD(P)H model, reduces various nitro olefins in excellent to good yields in the presence of silica gel(7) in benzene. Examples are summarized in Table 1.



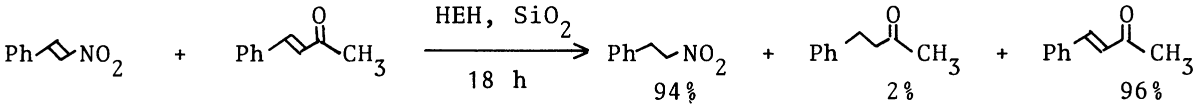
HEH

Table 1. Reduction of nitro alkenes to nitro alkanes[a)]

Entry	Nitro alkene	Nitro alkane	Yield/%[b)]
1			96 (100)[c)]
2			94
3			90
4			87 (100)[c)]
5			100
6			97
7			87
8			88
9			93
10			93
11			100
12			55[d)]

a) Reaction Conditions: [substrate]= 1.0 mmol, [HEH]= 1.1 mmol, [silica gel]= 100 mg; 20 h at 60 °C in benzene (4 ml) under an argon atmosphere in the dark.
b) Isolated yield. c) Numbers in parentheses are yields determined on GLPC.
d) The starting material was so unstable that it could not be purified enough and decomposed during the reaction.

Aliphatic and aromatic nitro alkenes were reduced smoothly neither accompanying reduction of nitro group nor dimerization of olefins. Other functional groups such as esters and ethers were inert under the reaction conditions. The chemoselectivity of the present reduction system is remarkable: only a carbon-carbon double bond conjugated with a nitro group was reduced, while other carbon-carbon double bonds remained practically inert (entry 8). Olefinic functions in α,β-unsaturated esters and nitriles were not affected. Although olefinic double bonds in α,β-unsaturated ketones are known to be reduced easily,[8)] the chemoselectivity of the present reduction is remerkable even for substrates of this kind: an equimolar mixture of β-nitrostyrene and *trans*-4-phenyl-3-butene-2-one was subjected to the reduction with 1.1 equivalent moles of HEH. After 18 hours, it was found that the nitrostyrene was reduced to 2-phenyl-1-nitroethane in 94% yield, while the enone was reduced only in 2 % yield and 96% of the unreacted enone was recovered.



A carbonyl group is usually sensitive to the reduction with NAD(P)H or its models. However, it is not reduced by HEH when silica gel exists in the reaction mixture. Thus, nitro alkenes that have a ketone (entry 11) or an aldehyde (entry 12) functional group in the same molecule were reduced to the corresponding saturated nitro compounds in which carbonyl groups remained unchanged. Although the run in entry 12 gave the product in relatively low yield, this was due to the instability of the starting material. With any other reducing method so far attempted, we did not obtain the corresponding nitro alkane.

The role of silica gel in the reduction is not clear now, but it is obvious that the selectivity is exerted because silica gel promotes, does not retard, the reduction: nitro alkenes are not reduced in the absence of silica gel. This behavior of silica gel is interesting and noteworthy in comparison with the role of silica gel in the reduction by $LiAlH_4$.[9)] In the latter case, silica gel deactivates the metal hydride to enhance the selectivity of reduction.

We believe that the present method has a synthetic utility since HEH is easy to be synthesized[10)] and stable against light and air. Applications of the present reduction to the synthesis of natural products are now under investigation.

For a typical experiment, a mixture of β-nitrostyrene (149 mg, 1 mmol), HEH (1.1 mmol) and silica gel (100 mg) in 4 ml of benzene was heated at 60 °C. After 20 hours, the benzene was evaporated and the residue was subjected to a column chromatography on silica gel with hexane as an eluent, giving 2-phenyl-1-nitroethane (146 mg) in 96% yield.

We wish to thank Prof. Kaoru Fujii of our institute for generous supply of nitro ketone and nitro aldehyde.

References

1) NAD(P)$^+$-NAD(P)H Model. Part 56.
2) E. Keinan and Y. Mazur, J. Am. Chem. Soc., 99, 3861 (1977); M.R. Galobarbes and H.W. Pinnick, Tetrahedron Lett., 22, 5235 (1981).
3) J.E. Baldwin, S.B. Harber, C. Hoskins, and L. Kruce, J. Org. Chem., 42, 1239 (1977).
4) Reduction of nitro alkenes; E.P. Kohler and N.L. Drake, J. Am. Chem. Soc., 45, 1281 (1923); R.T. Gilsdorf and F.F. Nord, J. Am. Chem. Soc., 74, 1837 (1952); H. Shechter, D.E. Ley, and E.B. Roberson Jr., *ibid.*, 78, 4984 (1956); A.I. Meyers and J.C. Sircar, J. Org. Chem., 32, 4134 (1967); A.K. Sinababu and R.T.Borchardt, Tetrahedron Lett., 24, 227 (1983); see also Ref. 6. Reduction of nitro alkenes to alkenes has been reported; N. Ono, S. Kawai, K. Tanaka, and A. Kaji, Tetrahedron Lett., 1979, 1733.
5) P.D. Show, Biochemistry, 6, 2253 (1967).
6) Reduction of nitrostyrene by N-benzyl-1,4-dihydronicotinamide/acetic acid was reported. However, the yield of 2-phenyl-1-nitroethane was unsatisfactory therein.
K. Wallenfels, W. Ertel, A. Hockendorf, J. Rieser, and K.H. Uberschar, Naturwissenschaften, 62, 459 (1975).
7) Silica gel was purchased from Nakarai Chem. Co.Ltd., (Silica gel 60, 35-70 mesh).
8) Recentry we reported the reduction of α,β-unsaturated carbonyl compounds by HEH/silica gel ; K. Nakamura, M. Fujii, A. Ohno, and S. Oka, Tetrahedron Lett., 25, 3985 (1984).
9) Y. Kamitori, M. Hojo, R. Masuda, T. Inoue, and T. Izumi, Tetrahedron Lett., 23, 4585 (1982).
10) A. Singer and S.M. McElvain, Org. Synth., Coll. Vol. 2, 214 (1943).

(Received January 25, 1985)