Tetrahedron Letters,Vol.22,No.52,pp 5235-5238,1981 0040-4039/81/525235-04$02.00/0
Printed in Great Britain

A NEW NITRO TO CARBONYL CONVERSION[1]

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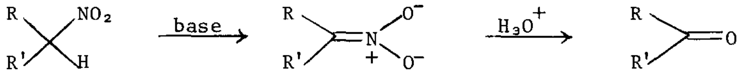
SUMMARY: Nitro compounds are converted into the corresponding carbonyl compounds by treatment with base and MoO_5•Pyr•HMPA.

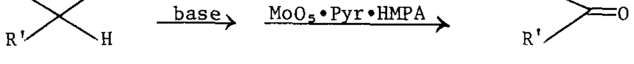
The conversion of a carbon bearing a nitro group and a hydrogen atom into a carbonyl functional group is normally accomplished by use of the Nef reaction (eq 1).[2] By taking


(1)

advantage of the high nucleophilicity of nitronate anions followed by the Nef reaction, the utility of nitroparaffins in preparative organic chemistry is increased. Consequently, the starting nitronate anion is a useful acyl anion equivalent.[3] Unfortunately, the classical Nef reaction works well with only a limited number of systems and this has prompted the development of modified Nef reactions.[4]

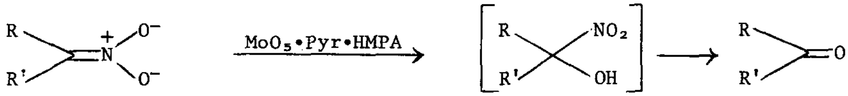
In connection with a recent synthetic investigation, numerous attempts to isolate ketones from functionalized nitro compounds using classical conditions,[1] methanol as solvent,[5a] titanium trichloride,[5b] $VO(acac)_2$,[5c,6] ceric ammonium nitrate,[4a] basic silica gel[5d] and hydrogen peroxide[4b] led to frustration. Consequently, a new method for the preparation of carbonyl compounds from nitroparaffins was developed.

This new conversion is summarized in eq 2. Thus, nitronate anions, generated with


(2)

bases as weak as triethylamine are allowed to react with the pyridine/hexamethylphosphoramide (HMPA) complex of MoO_5[7] to give the corresponding carbonyl compounds (see Table I). A variety of secondary nitro compounds are converted into ketones in good yields. For example, the Diels-Alder adduct of anthracene and ω-nitrostyrene[8] gives a 96% yield of the bridged ketone. Another striking example of possible biological significance[9] is the preparation of ethyl pyruvate in 73% yield. In contrast to these results with secondary nitro compounds, primary nitroparaffins give carboxylic acids as products. Thus, benzoic acid is obtained from α-nitrotoluene in 74% yield and 1-nitropropane yields propionic acid.

The MnO_5 complex has been used to introduce an α-hydroxy substituent into aldehydes, ketones, esters and lactones.[10] In addition, Little recently has converted sulfones into ketones with the same reagent.[11] Consequently, our conversion probably involves the intermediacy of α-nitroalcohols which suffer loss of nitrous acid to give the corresponding aldehyde or ketone (eq 3). Primary nitro compounds give carboxylic acids instead of



(3)

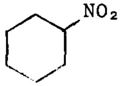
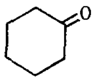
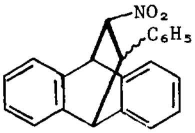
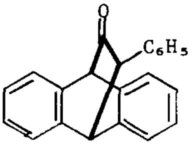
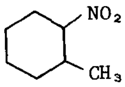
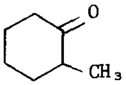
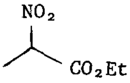
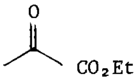
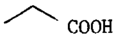
aldehydes because the latter suffer rapid oxidation under the reaction conditions.[12]

Application of this new synthetic method to various total syntheses is planned.

A typical experimental procedure is as follows:

Nitrocyclohexane (0.43 g, 3.3 mmol) in 20 mL of THF was added dropwise over a 5 min period to a solution of diisopropylamine (0.90 mL, 6.7 mmol) and 2.8 mL (6.7 mmol) of n-butyllithium/hexane in 20 mL of THF at -78°C. The molybdenum complex (2.86 g, 6.6 mmol) was added quickly to the nitronate anion solution and the reaction mixture was allowed to warm to room temperature for 3 hours. This was quenched with 40 mL of saturated aqueous sodium sulfite and was extracted twice with ether. The combined ether layers were washed with 5% HCl and brine, dried and concentrated to give, after distillation, 0.28 g (86%) of a colorless liquid having IR and NMR spectra identical with cyclohexanone.

TABLE I. Conversion of Nitro Compounds into Carbonyl Compounds[a]

Nitro Compound	Carbonyl Compound	% Yield[b]
		86 (81)[c]
		96
		85 (40)[d]
		73[c]
		69[c]
$C_6H_5CH_2NO_2$	C_6H_5COOH	74[c]

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[a] All reactions employ lithium diisopropylamide for nitronate anion formation unless *otherwise indicated.*

[b] All yields refer to pure, isolated products and are not optimized.

[c] *Using triethylamine for nitronate anion formation.*

[d] Yield of ketone from the <u>in situ</u> generation of the nitronate anion by the reaction of lithium dimethyl cuprate with 1-nitrocyclohexene (for the addition of cuprates to nitroolefins see S. B. Bowlus, <u>Tetrahedron Lett.</u>, 3591 (1975)).

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3. For example, see D. Seebach, E. W. Colvin, F. Lehr and T. Weller, Chimia, 33, 1 (1979).
4. See reference 3 for an excellent listing of alternative Nef procedures. More recent methods include the following: (a) G. A. Olah and B.G.B. Gupta, Synthesis, 44 (1980). (b) G. A. Olah, M. Arvanaghi, Y. D. Vankar and G.K.S. Prakash, ibid., 662 (1980).
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6. The purity of the tert-butyl hydroperoxide is crucial to the success of this reaction. Commercially available 70% or 90% material gave no reaction and 50% conversion, respectively. Only when 100% pure hydroperoxide was used was cyclohexanone obtained (80% yield) from nitrocyclohexane. This is similar to the results obtained from the epoxidation of olefins using VO(acac)$_2$ and the hydroperoxide where water was found to inhibit the reaction: K. B. Sharpless and R. C. Michaelson, J. Am. Chem. Soc., 95, 6136 (1973).
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9. For a discussion of the enzymatic conversion of nitroparaffins into aldehydes and ketones, see C. Walsh, "Enzymatic Reaction Mechanisms", W. H. Freeman, San Francisco, 1979, p. 396 and N. Duran, A. Faljoni and M. Haun, Rev. Latinoamer. Quim., 11, 119 (1980).
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11. R. D. Little and S. O. Myong, Tetrahedron Lett., 3339 (1980).
12. Benzaldehyde gives a 60% isolated yield of benzoic acid when allowed to stir with one equivalent of MoO$_5$•Pyr•HMPA.

(Received in USA 16 September 1981)