Tetrahedron Letters No. 4, pp 331 - 334, 1977. Pergamon Press. Printed in Great Britain.

A MILD, OXIDATIVE NITRO-TO-CARBONYL CONVERSION AND A NEW PROSTAGLANDIN SYNTHON

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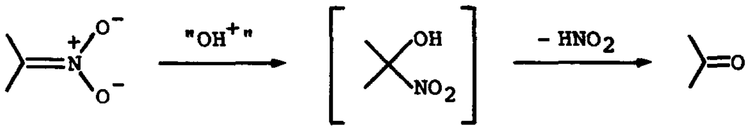
(Received in U.S.A. 5 November 1976; received in U.K. for publication 28 December 1976)

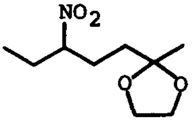
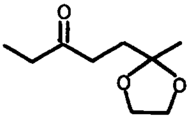
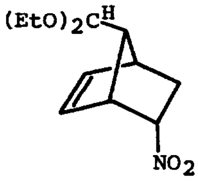
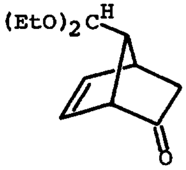
The variety of reactions which the nitro group facilitates has stimulated the search for mild and efficient methods for its transformation into other functionalities, most notably the carbonyl group.[1] The very acidic conditions of the Nef reaction[1a] and the sensitivity of many functional groups to strong oxidizing agents[1b] limited the generality of this conversion until McMurry and co-workers developed a high-yield reductive procedure using aqueous $TiCl_3$,[1c] and an oxidative method using ozone.[1d] We describe here a procedure complementary to these, involving the oxidative cleavage of nitronate anions under very mild conditions using *t*-butyl hydroperoxide and $VO(acac)_2$ as catalyst.

Because of the electronic similarity of nitronates and enols, we considered the use of epoxidizing agents, whose reactions with enols result in the formation of α-hydroxy carbonyl compounds.[2] We expected the analogous α-hydroxy nitro compounds to collapse rapidly to a carbonyl derivative and nitrous acid. Reaction of the anion derived from nitrocyclohexane and potassium *t*-butoxide in benzene with *m*-chloroperbenzoic acid resulted only in rapid destruction of the peracid. Addition of *t*-BuOOH to a benzene solution of the nitronate containing 5 mole% of $VO(acac)_2$[3] was more encouraging, but gave only erratic conversions and moderate yields of cyclohexanone. With the realization that the catalyst was unstable in the presence of the mildly basic nitronate ion and its subsequent addition as a component of the oxidant solution, reproducibly good yields of carbonyl compounds were obtained at room temperature or below. The table on the following page provides some representative examples.



Although this reaction works well for a variety of compounds, the anion derived from 1-nitrocyclooctene[4] reacts with *t*-BuOOH to form 1,2-epoxy-1-nitro-

Catalyzed Oxidation of Nitro Compounds with *t*-BuOK/*t*-BuOOH

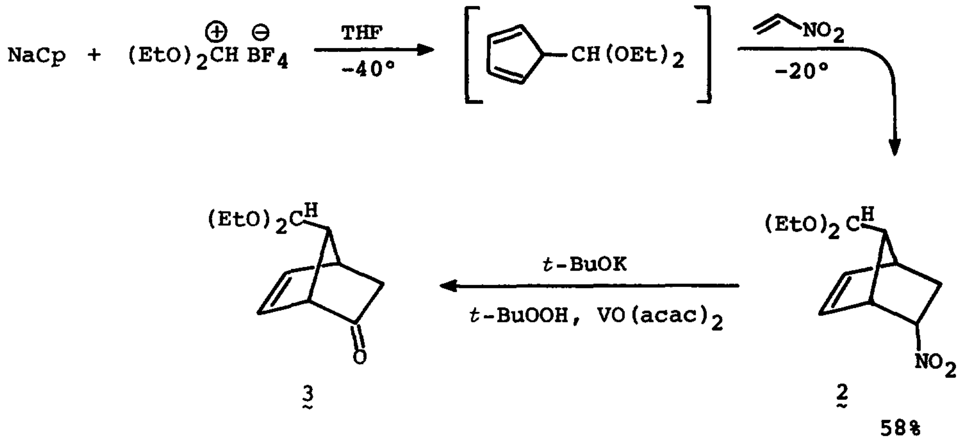
Substrate	*Product*	*Conditions*[a]	*Yield*
Nitrocyclohexane	Cyclohexanone	A	86%[b]
		A	82%[c]
		B	90%[d] 62%[c]
1-Nitrooctane	Octanal	A	45%[b]
5-Nitro-2-heptanone	2,5-Heptanedione	C	60%[b]
Methyl 4-nitrohexanoate	Methyl 4-oxohexanoate	C	20%[b]

(a) Catalyst/temperature: A, $VO(acac)_2$/room temperature; B, $VO(acac)_2$/7°; C, $Mo(CO)_6$/80°; (b) Yield determined by glpc; (c) Isolated yield of purified material; (d) Yield determined by NMR

cyclooctane[5] (mp 36-37°) in 85% yield, in a reaction which is independent of the catalyst.[6] Even when only a small excess of oxidant is used, oxidation of the anion from 1-nitrooctane gives significant amounts of octanoate esters in addition to the desired aldehyde. A more puzzling result was obtained on attempted oxidation of 5-nitroheptan-2-one and methyl 4-nitrohexanoate. In both cases the nitronate anions were inert to the usual oxidation conditions, even in the presence of large excesses of oxidant or catalyst. Although $Mo(CO)_6$[3] was an effective catalyst, in refluxing benzene, the conversions were moderate at best (not more than 60% by glpc).

The general procedure is as follows: A mixture of 1 mmol of the nitro compound and 1.1 equivalents of *t*-BuOK in 2 ml of benzene are stirred for 15 min at room temperature. A solution of 0.3 ml of 90% *t*-BuOOH, 3.5 mg of $VO(acac)_2$, and 0.7 ml of benzene is added over a 15-minute period. After 20 minutes, the mixture is diluted with ether, washed with water and brine, dried and concentrated under reduced pressure to give a product which is further purified as appropriate.

We have used this nitronate oxidation in a synthesis of *anti*-7-(diethoxymethyl)-5-norbornen-2-one (3),[5,8a] as depicted in the scheme below. Alkylation of sodium cyclopentadienide with a diethoxycarbenium salt,[7] followed by Diels-Alder reaction with nitroethylene,[8b] affords the nitronorbornene 2[5] (mp 34-35°). The *syn,endo* stereochemistry of the Diels-Alder adduct 2 has been assigned in analogy to previous work.[8,9] This is a much shorter and more efficient route to the prostaglandin intermediate (3) than a recently reported one leading to the corresponding dimethyl acetal *via* 6-acetoxyfulvene.[8a] By introducing the aldehyde function at the outset as the protected acetal, the selective deprotection and oxidation steps required for the analogous alkoxymethyl synthon[8b,10] can be avoided, as well as the stereochemical difficulties arising in the route based on 6-acetoxyfulvene.[8a]



Acknowledgement: This research was supported by a grant from the National Institutes of Health (no. CA-16616), and by a predoctoral fellowship (to F.R.G.) from the National Science Foundation.

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