Tetrahedron Letters,Vol.28,No.44,pp 5361-5364,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

THE NEF REACTION ON TRIALKYLSILYL NITRONATES PROMOTED BY m-CHLOROPERBENZOIC ACID. AN EFFICIENT ROUTE TO α-ALKOXYKETONES FROM NITROALKANES[1].

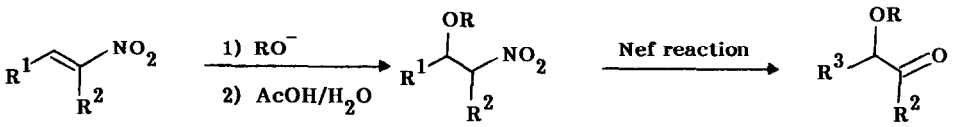
J.M. Aizpurua, M. Oiarbide and C. Palomo*

Departamento de Química Orgánica. Facultad de Ciencias Químicas. P.O. 1072.

Universidad del País Vasco. 20080 San Sebastián. Spain.

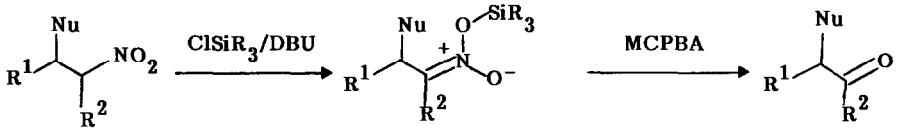
Abstract: Treatment of a nitroalkene with nucleophiles, followed by silylation of the resulting nitroalkane and subsequent treatment with m-chloroperbenzoic acid, provides α-functionalized carbonyl compounds in good yields.

Nitrocompounds are versatile substrates in organic synthesis for carbon-carbon bond formation, and the nitro group can be transformed into a diverse array of functionality[2], most notably, the carbonyl group[2,3]. In the course of a variety of projects being carried out in our laboratory, we required an efficient mild method for the preparation of α-alkoxyketones. An examination of the literature revealed that few methods are available for the preparation of α-alkoxyketones in a straightforward manner[4]. Several groups have demonstrated that conjugate addition of nucleophiles to nitroalkenes followed by an appropriate nitro group functionality provides a useful synthetic strategy for organic synthesis[5]. We expected, therefore, that Michael type addition[6] on a nitroalkene 1 followed by the Nef reaction on the resulting nitroalkane 2 allowed the formation of the α-alkoxyketones 3 .



1 2 3

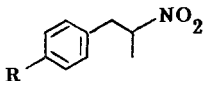
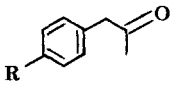
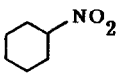
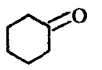
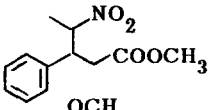
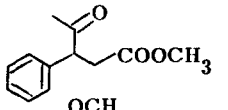
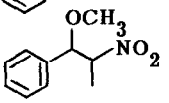
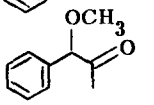
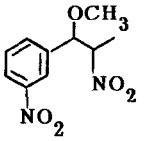
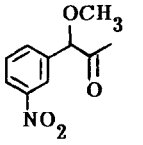
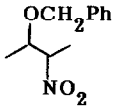
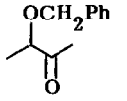
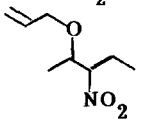
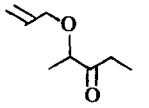
The recent paper by Hwu and Wang[7] on the preparation of such compounds has prompted us to report our own related results on this field. Since the Nef reaction often involves either strongly acidic or strongly basic conditions[3], we have first decided to develop another method for the oxidative cleavage of nitronate anions under mild conditions. It is well known that trialkylsilyl enol ethers readily undergo α-hydroxyalkylation by means of m-chloroperbenzoic acid (MCPBA) under extremely mild conditions[8]. We reasoned that trialkylsilyl nitronates 4 upon treatment with MCPBA, could act in a similar fashion affording the expected carbonyl compounds 3 .



2 4 3

Our finding is that treatment of a trialkylsilyl nitronate derived from a secondary nitroalkane with MCPBA in nearly equimolar amounts afforded the corresponding ketone in very high yield. The following example is representative: 1-methoxy-1-phenyl-2-nitropropane (0.97g, 5mmol) in dichloromethane (15ml), 1,8-diazabicyclo(5.4.0)undec-7-ene (DBU) (0.90ml, 6mmol) and trimethylchlorosilane (1.27ml, 10mmol) were consecutively mixed with stirring for 30min at 0ºC. Then, a solution of MCPBA (1.21g, 7mmol) in dichloromethane (15ml) was slowly dropped on the mixture at the same temperature. The initial slightly yellow solution turned green and after 30min at room temperature, the reaction mixture was washed with 1M Na_2SO_3 (30ml), 1M HCl (30ml) , sat. $NaHCO_3$ (20ml) and finally, with water (30ml). Evaporation of the solvent and distillation of the crude product afforded pure 1-methoxy-1-phenylacetone (0.80g, 95%), (b.p: 110-112ºC/0.8torr). ^{1}H-NMR (CCl_4) δ ppm: 1.78 (s, 3H, CH_3) , 3.21 (s, 3H, OCH_3), 4.90 (s, 1H, CH), 7.42 (s, 5H, arom.). Some experimental results are summarized in Table 1 to illustrate the efficiency of the present method. It is interesting to note that under the conditions reported, several functional groups were not affected by MCPBA, specially the double bond in 2k.

Table 1. Oxidative cleavage of trialkylsilyl nitronates by means of MCPBA.

	Nitrocompound [a]	Ketone [b]	Yield (%) [c]
a	 R = H		92
b	R = Cl		98
c	R = CH_3		99
d	R = OCH_3		97
e	R = CN		95
e			95
g			70
h			95
i			73
j			91
k			81

a) Compounds **a-e** were prepared by the method described by A. Bhattacharjya, H. Mukhopadhyay, and S.C. Pakrashi, Synthesis , 686 (1985). Compound **g** was prepared by the method described by N. Ono, A. Kamimura and A. Kaji, Synthesis, 226 (1984). Compounds **2 h-k** were prepared treating the corresponding nitroalkene (20mmol) with sodium alkoxide (30mmol) in 1,2-dimethoxyethane (20ml), overnight at room temperature.

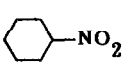
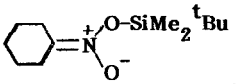
b) All products exhibited physical and spectral characteristics in accordance with the assigned structures.

c) Isolated yields, the purity of products was confirmed by glc and tlc analysis.

The silylation step was crucial for obtaining the desired carbonyl compounds. Bartlett[9] has reported that the nitronate anion derived from nitrocyclohexane and potassium t-butoxide, upon treatment with MCPBA did not lead to the formation of cyclohexanone. Similarly, we have found that in the absence of either trimethylchlorosilane or DBU, no reaction took place between MCPBA and nitrocompounds. It is important to note that, after several organic bases examined for introducing trialkylsilyl groups in nitroalkanes, DBU was found to be the most efficient for this purpose[10]. For example, the use of triethylamine

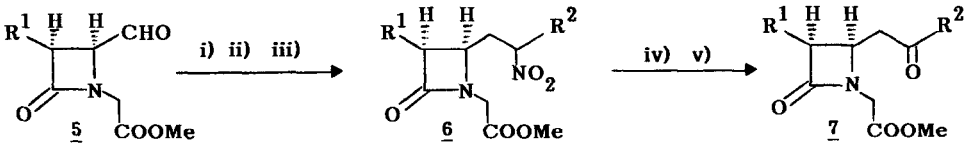
instead of DBU did not lead to the formation of α-substituted trimethylsilyl nitronates, as expected by the observations of Sharma and Torsell[11]. Likewise, 4-(N,N-dimethylamino)pyridine (DMAP)[12], 1,4-diazabicyclo(2.2.6)octane (DABCO)[13] and diisopropylethylamine (DIPEA)[14], which are known as useful bases for introducing the t-butyldimethylsilyl moiety in alcohols, proved to be inefficient for the preparation of trialkylsilyl nitronates[15a] and, therefore, for the preparation of ketones following the present method[15b]. The effectiveness of DBU is well demonstrated by the preparation of a few representative hindered silyl nitronates (Table 2).

Table 2. Preparation of trialkylsilyl nitronates.

Nitrocompound	Product [a]		Yield (%) [b]	b.p.(ºC/torr) [c]
$(CH_3)_2CH\text{-}NO_2$	$(CH_3)_2C{=}N^{+}(O\text{-}R)O^{-}$	R= $SiMe_2{}^tBu$	90	130-133/5
		R= Si^iPr_3	84	115-120/0.2
		R= $SiMePh_2$	96	____ [d]
			95	150/0.01
$CH_3CH_2CH_2\text{-}NO_2$	$CH_3CH_2CH{=}N^{+}(O\text{-}SiMe_2{}^tBu)O^{-}$		90	50/0.15

a) None of these products was formed by using either Et_3N , DMAP, DABCO or DIPEA.
b) Isolated yields. c) Reported boiling points are those observed during Kugelröhr distillation.
d) Decomposition observed during distillation.

On the other hand, attempts to apply this method to α-unsubstituted nitroalkanes failed, and only a mixture of the starting nitroalkane and the corresponding α-dichloronitroalkane was obtained instead of the expected aldehydes[16]. Further application of the present procedure is illustrated by the preparation of acetonyl as well as phenacyl azetidin-2-ones, which are considered as intermediates in the synthesis of bicyclic β-lactams[17].



i) $R^2CH_2NO_2/{}^tBuOK/THF$ **ii)** $MeSO_2Cl/NEt_3/CH_2Cl_2$ **iii)** $NaH_4B/EtOH/Dioxane$ **iv)** $ClSiMe_3$/ **DBU v) MCPBA** (0 - 20ºC) **or** O_3 (-78ºC).

Selected pysical data : 7 (R^1: Phthalimido group , R^2: Ph) : m.p: 127.8ºC ; ^{1}H-NMR δ ($CDCl_3$) : 8.00--7.20 (m,9H,arom.), 6.13 (d, J=3Hz, 1H, CH), 4.66-4.47 (m, 1H, CH), 4.27 (s, 1H, CH), 4.17 (s, 1H, CH), 3.73-3.40 (m, 2H, CH), 3.58 (s, 3H, CH).

In conclusion, from the results reported here, the method can be readily extended to other synthetic purposes and presents a new application of MCPBA in organic synthesis.[18] Further investigations are in current progress in our laboratory.

REFERENCES AND NOTES

1.- Reagents and Synthetic Methods 65. For part 64, see F.P. Cossío, C. López, C. Palomo, **Tetrahedron**, (in press). The present work has been supported by Departamento de Investigación del Gobierno Vasco (Eusko Jaurlaritzako Hezkuntza Saila). A grant from Eusko Jaurlaritza to M.O. is gratefully acknowledged.

2.- a) D. Seebach, E.W. Colvin, F. Lehr, T. Weller, **Chimia**, 33, 1 (1979); b) A.G.M. Barret, G.G. Graboski, **Chem. Rev.**, 86, 751 (1986); c) "The Chemistry of the Nitro and Nitroso Groups", Part 1. H. Feuer Ed. John Wiley. New York , 1969.

3.- a) W.E. Noland, **Chem. Rev.** 55, 137 (1955); b) G.A. Olah, B.G. Gupta, **Synthesis**, 44 (1980) ; c) K. Stelion, M.A. Poupart, **J.Org.Chem.**, 50, 4971 (1985) and references cited; d) R.S. Varma, M. Varma, G.W. Kabalka, **Tetrahedron Lett.** 26, 3777 (1985); e) M.S. Mourad, R.S. Varma, G.W. Kabalka, **Synthesis**, 654 (1985); f) P.S. Vankar, R. Rathore, S. Chandrasekaran, **Synth. Commun.** 17, 195 (1987), and references cited.

4.- R.S. Varma, G.W. Kabalka, **Synth. Commun.** 15, 443 (1985) and references cited therein.

5.- a) E.J. Corey, H. Estreicher, **J.Am.Chem.Soc.**, 100, 6294 (1978); b) A.G.M. Barrett , G.G. Graboski, M.A. Russell, **J.Org.Chem.** 51, 1012 (1986) and references cited; c) N. Ono, A. Kaji, **Synthesis**, 693 (1986).

6.- H.H. Baer, L. Urbas, in "The Chemistry of the Nitro and Nitroso Groups". Part 2. H. Feuer Ed. John Wiley, New York, 1970. p.178.

7.- J.Ru Hwu, N. Wang, **J.Chem.Soc.Chem.Commun.** 427 (1987).

8.- a) A.G. Brook, D.A. Macrae, **J.Organomet.Chem.** 77, C 19 (1974); b) G.M. Rubottom, H.A. Vasquez, D.R. Pellegrina **Tetrahedron Lett.** 4319 (1974); c) A. Hassner, R.H. Reuss, H.W. Pinnick, **J.Org.Chem.** 40, 3427 (1985); d) S.J. Pennanen, **Tetrahedron Lett.** 657 (1980).

9.- P.A.Bartlett, F.R. Green III, T.R. Webb, **Tetrahedron Lett.** 331 (1977).

10.- a) J.M. Aizpurua, C. Palomo, **Tetrahedron Lett.** 26, 475 (1985); b) S. Kim, H. Chang, **Bull.Chem.Soc. Jpn.** 58, 369 (1985).

11.- S.C. Sharma, K. Torsell, **Acta. Chem. Scand.** 333, 379 (1979).

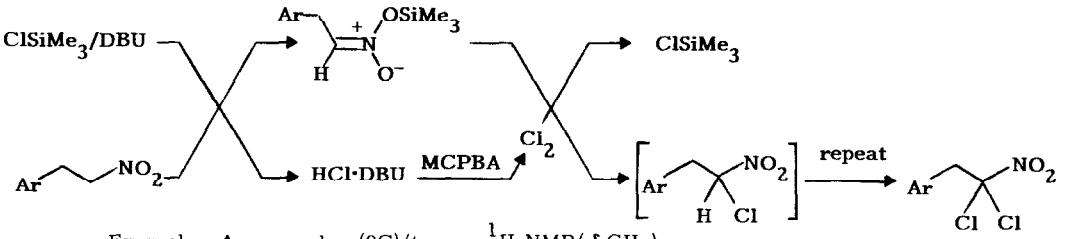
12.- S.K. Chaudhary, O. Hernandez, **Tetrahedron Lett**, 99 (1979).

13.- G.H. Hakimelahi, Z.A. Proba, K.K. Ogilvie, **Tetrahedron Lett**, 22, 5243 (1981).

14.- L. Lombardo, **Tetrahedron Lett**, 25, 227 (1984).

15.- a) For applications of trialkylsilyl nitronates, see ref. 2a and W.P. Weber, in "Silicon Reagents for Organic Synthesis", Springer-Verlag, Berlin (1983); b) For example, 3-phenyl-2-nitropropane upon treatment with Et_3N and $ClSiMe_3$ followed by addition of MCPBA did not lead to the formation of the expected ketone.

16.- For primary nitroalkanes, we assume a reaction sequence as indicated below:



Example	Ar	b.p.(ºC)/torr	^{1}H-NMR(δ CH_2)
a :	C_6H_5-	95-8/2	3.80
b :	4-ClC_6H_4-	135-40/1	3.82
c :	4-$CH_3C_6H_4$-	120-5/1	3.81

17. P.M.W. Foxton, R.C. Mearman, C.E. Newall, P. Ward, **Tetrahedron Lett.** 22, 2497 (1981), see also F.P. Cossío, I. Ganboa, J.M. García, B. Lecea, C. Palomo, **Tetrahedron Lett.** 28, 1945 (1987).

18.- For applications of MCPBA, see the Technical Information Bulletin AL-116 from the Aldrich Chemical Company and Fieser and Fieser's "Reagents for Organic Synthesis" , vol.12; M. Fieser, John Wiley and sons, New York, 1986, p. 118 and references cited therein.

(Received in UK 30 June 1987)