Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

A Convenient Two-Step Procedure for the Synthesis of DI-and Trisubstituted α-Nitroalkenes from Tertiary β-Nitro Alcohols

J.C. Ferrand [a], R. Schneider [a], P. Gérardin [a] & B. Loubinoux [a]

[a] LERMAB, Laboratoire de Chimie Organique 4, Université Henri-Poincaré, Nancy-I, Faculté des Sciences, BP 239, 54506, Vandoeuvre-les-Nancy, France

Version of record first published: 23 Aug 2006

To cite this article: J.C. Ferrand, R. Schneider, P. Gérardin & B. Loubinoux (1996): A Convenient Two-Step Procedure for the Synthesis of DI-and Trisubstituted α-Nitroalkenes from Tertiary β-Nitro Alcohols, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 26:23, 4329-4336

To link to this article: http://dx.doi.org/10.1080/00397919608003835

SYNTHETIC COMMUNICATIONS, 26(23), 4329-4336 (1996)

A CONVENIENT TWO-STEP PROCEDURE FOR THE SYNTHESIS OF DI- AND TRISUBSTITUTED α-NITROALKENES FROM TERTIARY β-NITRO ALCOHOLS

J.C. Ferrand, R. Schneider, P. Gérardin, B. Loubinoux*

LERMAB, Laboratoire de Chimie Organique 4, Université Henri-Poincaré, Nancy-I, Faculté des Sciences, BP 239, 54506 Vandoeuvre-les-Nancy (France)

ABSTRACT: Treatment of tertiary β-nitro alcohols **I**, obtained by addition of lithium α-lithionitronates to ketones, with acetic anhydride followed by 1 equivalent of potassium methoxide or *t*-butoxide, according to the nature of R^2, gives α-nitroalkenes **III** in good yields.

Conjugated nitroalkenes are important structural units which can be used as starting materials for many classes of compounds including bioactive compounds.[1]

In the course of our work directed to the synthesis of new fungicides and insecticides, we attempted to prepare several α-nitroalkenes by dehydration of tertiary β-nitro alcohols formed by addition of lithium α-lithionitronates to ketones.[2] This methodology, generally described in the case of secondary β-nitro alcohols, involves interaction between nitroalkanes and aldehydes followed by dehydration or acylation-deacylation processes. Various dehydrating conditions such as dicyclohexylcarbodiimide/copper chloride[3], methanesulfonyl chloride/triethylamine[4], basic

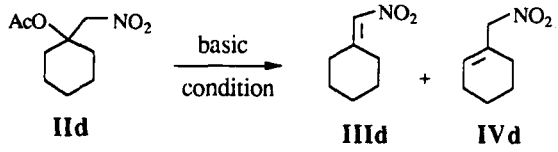
* To whom correspondence should be addressed

alumina[5] and more recently, carbon tetrachloride/triphenyl phosphine/triethylamine[6], have been reported in the literature to effect dehydration of secondary β-nitro alcohols. Methods involving acylation-deacylation processes such as pivaloyl chloride/sodium acetate[7,8], acetic anhydride/sodium acetate[9,10] or phthalic anhydride[11-13] are sometimes described in the case of tertiary β-nitro alcohols, but are limited by their scope of application (nitroalkenes of low boiling point : nitroethylene, 1-nitropropene, 2-nitropropene, 2-methyl-1-nitropropene...)[9,11,12] and their lake of regioselectivity (mixture of isomers)[9,13].

Dehydration of 1-(nitromethyl)cyclohexanol **Id**, used as a representative compound of tertiary β-nitro alcohols, failed with previous procedures. Treatment of **Id** with basic alumina at 40°C, according to Ballini's method[5], afforded a mixture of 1-(nitromethyl)cyclohexene and cyclohexanone. The use of dicyclohexylcarbodiimide[3], methanesulfonyl chloride[4], or carbon tetrachloride/triphenyl phosphine[6], according respectively to Seebach's, McMurry's or Barua's procedures, leaved the starting material unreacted.

In this paper, we report our results concerning the regioselective synthesis of α-nitroalkenes from tertiary β-nitro alcohols. The facile retronitroketolization added to the inertness of the tertiary alcohol function towards the reagents mentioned here above prompted us to acetylate the hydroxyl group to effect its activation. Different conditions were investigated to effect regioselective elimination of acetic acid from 1-(nitromethyl)cyclohexyl acetate **IId**. According to the nature of the base employed, nitromethylenecyclohexane **IIId** and/or 1-nitromethylcyclohexene **IVd** were obtained (Table 1). The use of 1 equivalent of potassium methoxide in MeOH at 0°C permit clean elimination of acetic acid and the α-nitroalkene **IIId** was obtained in good yield. Michael addition of methoxide ion on the α-nitroalkene did not occur if 1 equivalent of base was used and if the reaction time was carefully monitored by TLC (disappearance of the starting nitro acetate).

Table 1.



IId **IIId** **IVd**

Conditions	% of products [a]		
	IId	**IIId**	**IVd**
Et_3N (1eq), CH_2Cl_2, 20°C, 8h	0	0	100
AcONa (2eq), Et_2O, 20°C, 72h	79	21	0
t-BuOK (1eq), *t*-BuOH, 20°C, 10 min	0	76	24
MeONa (1eq), MeOH, 0°C, 8h	80	19	1
MeOK (1eq), MeOH, 0°C, 10 min	2	98	0

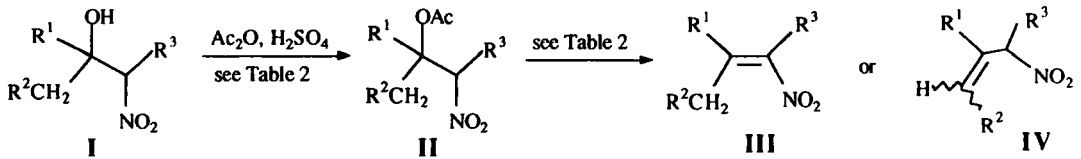
[a] % of products in the crude reaction mixture determined by ^1H NMR

When 1-(1'-nitroethyl)cyclohexyl acetate **IIf** was treated under similar reaction conditions with potassium methoxide, it was found to remain unaffected even on prolonged exposure at room temperature. The use of potassium *t*-butoxide (1 eq.) in *t*-butanol permit, in this case the desired elimination. These results were successfully extended to different tertiary β-nitro alcohols for the synthesis of both dialkyl and trialkyl α-nitroalkenes (Table 2).

Preparation of the allylic isomers **IV**, starting from β-nitro acetates **II**, was also investigated using 3 equivalents of triethylamine. Dialkyl α-nitroalkenes, initially formed in the reaction mixture, isomerize without difficulties to the allylic isomers **IV**. Isomerization of trialkyl α-nitroalkenes is much more difficult and occurs only in the case of cyclic compound **IVf** (Table 2).

In conclusion, we have elaborated simple and efficient synthesis of new α-nitroalkenes and allylic nitrocompounds starting from tertiary β-nitro alcohols.

Table 2.



entry	R1	R2	R3	II		III		IV	
				Condition	Yield (%)	Condition	Yield (%)	Condition	Yield (%)
a	Et	Me	H	5 min, 50°C	89	MeOK/MeOH, 10 min, 0°C	69	20°C, 6h	69
b	n-Pr	Et	H	5 min, 50°C	75	MeOK/MeOH, 10 min, 0°C	60	20°C, 20h	90
c	-(CH2)2-		H	5 min, 50°C	86	MeOK/MeOH, 10 min, 0°C	87	20°C, 4h	87
d	-(CH2)4-		H	5 min, 50°C	96	MeOK/MeOH, 10 min, 0°C	85	20°C, 8h	90
e	n-Pr	Et	Me	2 min, 0°C	82	*t*-BuOK/*t*-BuOH, 30 min , 20°C	90	40°C, 36h	0
f	-(CH2)4-		Me	2 min, 0°C	86	*t*-BuOK/*t*-BuOH, 30 min , 20°C	8	40°C, 36h	91
g	n-Pr	Et	Et	20 min, 50°C	71	*t*-BuOK/*t*-BuOH, 30 min , 20°C	53	40°C, 96h	0
h	-(CH2)4-		Et	20 min, 50°C	81	*t*-BuOK/*t*-BuOH, 30 min , 20°C	64	40°C, 96h	0

Synthetic applications of these new compounds are currently under investigation in our laboratory. Moreover, this method permits the synthesis of more elaborated α-nitroalkenes, which are currently tested as potential fungicides and insecticides.

Experimental section

Commercially available reagents were purchased from Aldrich. NMR spectra were recorded in $CDCl_3$ solutions using TMS as internal standard on a Bruker AM 400. IR spectra were obtained using a Perkin-Elmer 1750 spectrophotometer.

General procedure for the preparation of nitro acetates II. β-Nitro alcohol **I**, prepared according to Seebach's procedure[2] (7 mM), acetic anhydride (857 mg, 8.4 mM) and concentrated sulfuric acid (1 drop) were mixed and reacted at the temperature and for the time indicated in the Table 2. Et_2O (100 ml) and water (25 ml) were added. The organic layer was separated, washed with a 5% sodium bicarbonate solution (25 ml), brine (25 ml), and dried over $MgSO_4$. Removal of solvent gave **II** as yellow oils.

IIa : 2-ethyl-1-nitro-2-butyl acetate. IR (NaCl) : 1738, 1549 and 1375. ^1H NMR (δ) : 0.92 (t, J = 7.3, 6 H), 1.71-1.81 (m, 2 H), 1.93-2.02 (m, 2 H), 2.06 (s, 3 H), 4.93 (s, 2 H).

IIb : 1-nitro-2-propyl-2-pentyl acetate. IR (NaCl) : 1737, 1554 and 1375. ^1H NMR (δ) : 0.95 (t, J = 7.0, 6 H), 1.32-1.40 (m, 4 H), 1.69-1.75 (m, 2 H), 1.91-1.95 (m, 2 H), 2.05 (s, 3 H), 4.94 (s, 2 H).

IIc : 1-(nitromethyl)cyclopentyl acetate. IR (NaCl) : 1741, 1553 and 1374. ^1H NMR (δ) : 1.60-1.92 (m, 8 H), 2.01 (s, 3 H), 4.94 (s, 2 H).

IId : 1-(nitromethyl)cyclohexyl acetate. IR (NaCl) : 1742, 1554 and 1375. ^1H NMR (δ) : 1.20 1.85 (m, 10 H), 2.05 (s, 3 H), 4.92 (s, 2 H).

IIe : 2-nitro-3-propyl-3-hexyl acetate. IR (NaCl) : 1741, 1553 and 1365. ^1H NMR

(δ) : 0.92 (t, J= 7.5, 3 H), 0.93 (t, J = 7.5, 3 H), 1.19-2.15 (m, 8 H), 1.55 (d, J = 7.5, 3 H), 2.05 (s, 3 H), 5.47 (q, J = 7.5, 1 H).

IIf : 1-(1'-nitroethyl)cyclohexyl acetate. IR : (NaCl) : 1737, 1550 and 1365. ^{1}H NMR (δ) : 1.10-1.8 (m, 8 H),1.45 (d, J = 7.5, 3 H), 2.0 (m,1 H), 2.06 (s, 3 H), 2.6 (m, 1 H), 5.61 (q, J = 7.5, 1 H).

IIg : 3-nitro-4-propyl-4-heptyl acetate. IR (NaCl) : 1744, 1553 and 1368. ^{1}H NMR (δ) : 0.82-1.01(m, 9 H), 1.30-1.50 (m, 4 H), 1.70-2.30 (m, 6 H), 2.01 (s, 3 H), 5.18 (dd, J = 11.5, 2.0, 1 H).

IIh : 1-(1'-nitropropyl)cyclohexyl acetate. IR (NaCl) : 1740, 1553 and 1365. ^{1}H NMR (δ) : 0.96 (t, J = 7.5, 3 H), 1.20-1.80 (m, 10 H), 2.06 (s, 3 H), 2.06-2.15 (m, 1 H), 2.55-2.65 (m, 1 H), 5.37 (dd, J = 11.0, 2.0, 1 H).

General procedure for the preparation of disubstituted α-nitroalkenes IIIa-d. To a solution of β-nitro acetate **IIa-d** (3 mM) in MeOH (10 ml) was added dropwise potassium methoxide (3 mM) in 5 ml of MeOH at 0°C. The mixture was stirred for 10 min at 0°C and poured into a separatory funnel. Et_2O (150 ml) and water (50 ml) were added. The organic layer was separated, dried ($MgSO_4$) and concentrated to give **IIIa-d** as yellow oils.

IIIa : 2-ethyl-1-nitrobut-1-ene. IR (NaCl) : 1630, 1522 and 1341. ^{1}H NMR (δ) : 1.10 (t, J = 7.3, 6 H), 2.05-2.20 (m, 4 H), 2.22-2.70 (m, 2 H), 6.85 (s, 1 H).

IIIb : 1-nitro-2-propylpent-1-ene. IR (NaCl) : 1635, 1522 and 1341. ^{1}H NMR (δ) : 0.96 (t, J = 7.3, 3 H), 1.00 (t, J = 7.3, 3 H), 1.47-1.64 (m, 4 H), 2.17 (t, J = 7.4, 2 H), 2.59 (t, J = 7.8, 2 H), 6.90 (s, 1 H).

IIIc : nitromethylenecyclopentane. IR (NaCl) : 1650, 1510 and 1349. ^{1}H NMR (δ) : 1.70-1.85 (m, 4 H), 2.52 (t, J = 7.4, 2 H), 2.98 (t, J = 5.8, 2 H), 6.90 (s, 1 H).

IIId : nitromethylenecyclohexane. IR (NaCl) : 1652, 1514 and 1340. ^{1}H NMR

(δ) : 1.55-1.75 (m, 6 H), 2.23 (t, J = 6.0, 2 H), 2.88 (t, J = 6.0, 2 H), 6.88 (s, 1 H).

General procedure for the preparation of trisubstituted α-nitroalkenes IIIe-h. To a solution of β-nitro acetate **2e-h** (3 mM) in *t*-BuOH (10 ml) was added dropwise potassium *t*-butoxide (3 mM) in 5 ml of *t*-BuOH at 20°C. The mixture was stirred for 30 min at 20°C and poured into a separatory funnel. Et_2O (150 ml) and water (50 ml) were added. The organic layer was separated, dried ($MgSO_4$) and concentrated to give **3e-h** as yellow oils.

IIIe : 2-nitro-3-propylhex-2-ene. IR (NaCl) : 1650, 1521 and 1347. ^1H NMR (δ) : 0.93 (t, J = 7.3, 3 H), 0.96 (t, J = 7.3, 3 H), 1.30-1.55 (m, 4 H), 2.01-2.20 (m, 4 H), 2.15 (s, 3 H).

IIIf : nitroethylenecyclohexane. IR (NaCl) : 1662, 1514 and 1350. ^1H NMR (δ) : 1.18-1.47 (m, 6 H), 2.09-2.40 (m, 4 H), 2.15 (s, 3 H).

IIIg : 3-nitro-4-propylhept-3-ene. IR (NaCl) : 1650, 1520 and 1347. ^1H NMR (δ) : 0.91 (t, J = 7.5, 3 H), 0.96 (t, J = 7.5, 3 H), 1.07 (t, J = 7.5, 3 H), 1.41-1.56 (m, 4 H), 2.0-2.10 (m, 4 H), 2.50 (q, J = 7.5, 2 H).

IIIh : nitropropylenenecyclohexane. IR (NaCl) : 1660, 1515 and 1349. ^1H NMR (δ) : 1.10 (t, J = 7.5, 3 H), 1.50-1.75 (m, 6 H), 2.15-2.30 (m, 4 H), 2.54 (t, J = 7.5, 2 H).

General procedure for the preparation of allylic isomers 4a-d,f. To a solution of β-nitro acetate **II** (3 mM) in CH_2Cl_2 (10 ml) was added Et_3N (9 mM). The mixture was stirred for the time and at the temperature indicated in Table 2. The organic layer was washed with dilute hydrochloric acid (1N), dried over $MgSO_4$ and concentrated to give **IV**. ^1H NMR and IR data of allylic nitrocompounds **IV** are similar to those reported in the literature.[14]

References and notes

1. Seebach, D.; Colvin, E.W.; Lehr, F.; Weller, T. *Chimia*, **1979**, *33*, 1. Barrett, A.G..; MGraboski, G.G. *Chem Rev*, **1986**, *86*, 751. Perekalin, V.V.; Lipina, E.S.; Berestovitskaya, V.M.; Efremov, D.A. "Nitroalkenes". Part 2; Wiley: New York, **1994**.
2. Seebach, D.; Lehr, F. *Angew. Chem.* **1976**, *16*, 540. Lehr, F.; Gonnerman, J.; Seebach, D. *Helv. Chim. Acta.* **1979**, *62*, 2259.
3. Knochel, P.; Seebach, D. *Synthesis.* **1982**, 1017.
4. Melton, J.; Mc Murry, J.E. *J. Org. Chem.* **1975**, *40*, 2138.
5. Ballini, R.; Castagnani, R.; Petrini, M. *J. Org. Chem.* **1992**, *57*, 2160.
6. Saikia, A.K.; Barua, N.C.; Sharma, R.P.; Ghosh, A.C. *Synthesis*, **1994**, 685.
7. Knochel, P.; Seebach, D. *Tetrahedron Lett.* **1982**, *23*, 3897.
8. Seebach, D.; Knochel, P. *Helv. Chim. Acta.* **1984**, *67*, 261.
9. Schechter, H.; Sheperd, J.W. *J. Am. Chem. Soc.* **1954**, *76*, 3617.
10. Zindel, J.; de Meijere, A. *Synthesis*, **1994**, 190.
11. Buckley, G.D.; Scaife, C.W. *J. Chem. Soc.* **1947**, 1471.
12. Ranganathan, D.; Bhusan Rao, C.; Ranganathan, S.; Mehrotra, A.K.; Iyengar, R. *J. Org. Chem.* **1980**, *45*, 1185.
13. Topchiev, A.V.; Alaniya, V.P.; Vagin, M.F. *Dolk. Akad. Nauk. SSR.* **1963**, *151*, 350.
14. Tamura, R.; Sato, M.; Oda, D. *J. Org. Chem.* **1986**, *51*, 4368.

15. We should like to thank CIBA-GEIGY and Mr. Ramos-Tombo for their help.

(Received in the UK 19 March 1996)