An Improved Synthesis of Conjugated Nitroolefins

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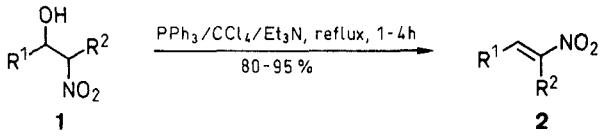
β-Nitro alcohols **1** react with triphenylphosphine/carbon tetrachloride/triethylamine under reflux to give the corresponding nitroolefins **2** in good yields (80–95%). Other groups such as tertiary hydroxyl, ether, halide etc. remain unaffected, and the nitroolefins so produced are exclusively the (*E*)-isomers.

The use of nitroaliphatics in organic synthesis has received resurgent attention during the last decade due to continuous discovery of new efficient methods for converting aliphatic nitro groups into amines, alcohols, ketones[1] etc. In particular, conjugated nitroalkenes, a few of which also occur in nature,[2–5] proved to be versatile synthetic intermediates,[5–7] fungicides[6,8,9] and pharmacologically active substances.[10–13] Alternatively, they are powerful dienophiles in Diels–Alder reactions or readily undergo addition reactions with a variety of nucleophiles.[14]

Usually conjugated nitroolefins are synthesized via elimination of water from β-nitro alcohols formed by the condensation of aldehyde and ketones with nitroalkanes (Henry reaction);[15] although several other approaches are also reported in the literature.[16] Dehydration of β-nitro alcohols is usually carried out by using reagents such as phthalic anhydride,[14,17] dicyclohexylcarbodiimide (DDC),[18] methanesulfonyl chloride,[19] pivaloyl chloride[20,21] etc. More recently Ballini et al reported[22] an efficient chemoselective method for the synthesis of acyclic nitroalkenes using basic alumina with yields ranging from 60–85%. In continuation of our interest in nitroaliphatic compounds[23,24] we were in need of a simple high yielding method for the synthesis of functionalized nitroolefins. We argued that if the hydroxy group of the β-nitro alcohol is transformed into a halide by treating with triphenylphosphine and carbon tetrahalide and simultaneously treated with a suitable base for in situ elimination of the hydrogen halide, it would give conjugated nitroalkenes in a one-pot reaction. This argument has actually been realized and generalized through entry **1a** to entry **1i** (Scheme).

In this procedure the reaction is carried out by refluxing a mixture of β-nitro alcohol, triethylamine and triphenylphosphine in carbon tetrachloride while monitoring the reaction by TLC. After usual workup, the products are purified by chomatography (experimental). It is noteworthy that in our procedure the yields of the products are extremely good (80–90%) and the products are exclusively the (*E*)-isomers and time requirement is relatively low (1–4 h). Other functionalities like isolated double bond, ether, ester etc. are not affected.

When 1-(nitromethyl)cyclohexanol was treated with triphenylphosphine/carbon tetrachloride/triethylamine it was found to remain unaffected even on prolonged exposure (8 h). Similarly **1f** gave **2f** on exposure to this reagent system. The inertness of tertiary hydroxyl groups in **1f** and 1-(nitromethyl)cyclohexanol is indicative of the fact that dehydration of β-nitro alcohols by this method proceeds via halide formation followed by elimination of hydrogen halide. The plausible reason for this selectivity may be due to the fact that tertiary hydroxyl groups are not converted into chlorides with triphenylphosphine/carbon tetrachloride.[25] The (*E*)-geometry of the newly formed double bond was readily assigned on the basis of ^{1}H NMR spectra, the vinylic proton of the (*E*)-isomer appearing at lower field than the corresponding proton of the (*Z*)-isomer because of the strong anisotropic effect of the nitro group.[26] The fully decoupled ^{13}C NMR spectra of **2e** to **2h** recorded at 20 MHz further indicated that these products are not contaminated with the corresponding (*Z*)-isomers.



1 **2**

1, 2	R^1	R^2
a	Ph	H
b	Ph	Me
c	4-$MeOC_6H_4$	Me
d	4-ClC_6H_4	Me
e	$Me_2C{=}CH(CH_2)_2CH(CH_3)CH_2$	Me
f	$Me_2C(OH)(CH_2)_3CH(CH_3)CH_2$	Me
g	$Me(CH_2)_{15}CH_2$	Me
h	Pr	Me
i	$PhCH_2CH_2$	Me

Scheme

In summary, the present method offers a mild and useful alternative to the existing methods for chemoselective synthesis of functionalized conjugated nitroalkenes.

Melting and boiling points are uncorrected. Mass spectra were obtained by EI at 70 eV using a INCOS 50 GC-MS equipment. ^{1}H NMR spectra were recorded in $CDCl_3$ solutions at 60 MHz using TMS as an internal standard. IR spectra were recorded as thin films unless otherwise stated. The β-nitro alcohols were prepared by Henry reaction[15] as a mixture of diastereomers. Products were purified by chromatography or by distillation. Satisfactory microanalyses obtained for all new compounds: C ± 0.1, H ± 0.13, N ± 0.31.

(*E*)-1-Nitro-2-phenylethylene (2a); Typical Procedure:
A solution of **1a** (0.2 g, 1.10 mmol) in CCl_4 (2 mL) was refluxed on a water-bath after mixing with PPh_3 (0.5 g, 1.9 mmol) and a catalytic amount of Et_3N (0.02 mL, 0.14 mmol). The reaction was monitored by TLC. After completion (1 h), the mixture was allowed to cool and anhydr. pentane (5 mL) was added and the stirring continued. The precipitated solid material was filtered and washed with pentane (5 mL). The combined filtrates and the pentane washings were again washed successively with dilute 5% HCl and dried (Na_2SO_4). Re-

moval of solvents in a rotary evaporator yielded a residue which was purified by chromatography on Silica gel G (E. Merck) (eluent: EtOAc; Pet ether 1:10) to afford **2a**; yield 0.18 g (90%); mp 56°C (Lit.[27] mp 56–58°C).

IR: $\nu = 1650, 1520\ cm^{-1}$.

^1H NMR: $\delta = 7.7$ (s, 1H), 7.2 (s, 5H), 2.2 (s, 3H)

MS (m/z) = 149 (M+).

(E)-2-Nitro-3-phenyl-2-propene (**2b**): reaction time 1.5 h; yield: 0.135 g (90%); mp 58°C.

IR: $\nu = 1650, 1525\ cm^{-1}$.

^1H NMR: $\delta = 7.8$ (s, 1H), 7.2 (s, 5H), 2.2 (s, 3H).

MS: (m/z) = 163 (M^+).

(E)-3-[4-Methoxyphenyl]-2-nitro-2-propene (**2c**): reaction time 2 h; yield: 0.19 g (95%); mp 47°C.

IR: $\nu = 1600, 1520\ cm^{-1}$.

^1H NMR: $\delta = 7.3$ (s, 1H), 7.2 (d, $J = 7$ Hz, 2H), 6.8 (d, $J = 7$ Hz, 2H), 3.9 (s, 3H), 2.2 (s, 3H).

MS: (m/z) = 193 (M^+).

(E)-3-[4-Chlorophenyl]-2-nitro-2-propene (**2d**): reaction time 2 h; yield: 0.152 g (95%); mp 68°C.

IR: $\nu = 1650, 1525\ cm^{-1}$.

^1H NMR: $\delta = 7.7$ (s, 1H), 6.9–7.2 (br, 4H), 2.3 (s, 3H).

MS: (m/z) = 197 (M^+).

(E)-5,9-Dimethyl-2-nitrodeca-2,8-diene (**2e**): reaction time 4 h; yield: 0.16 g (80%); oil.

IR: $\nu = 1670, 1600$, and $1525\ cm^{-1}$.

^1H NMR: $\delta = 7.12$ (t, $J = 6.6$ Hz, 1H), 5.1 (t, $J = 6.5$ Hz, 1H), 2.1 (s, 3H), 1.4 (s, 3H), 1.7 (s, 3H), 0.9 (d, $J = 7$ Hz, 3H).

^{13}C NMR ($CDCl_3$): $\delta = 18.7, 20.0, 24.0, 30.0, 32.2, 35.0, 44.0, 48.0, 129.8, 138.1, 140.0, 142.0$.

MS: (m/z) = 212 ($M^+ + 1$).

(E)-9-Hydroxy-5,9-dimethyl-2-nitro-2-decene (**2f**): reaction time 4 h; yield: 0.30 g (60%); oil.

IR: $\nu = 1650, 1520\ cm^{-1}$.

^1H NMR: $\delta = 6.8$ (t, $J = 7$ Hz, 1H), 1.95 (s, 3H), 1.2 (br, 6H), 0.8 (d, $J = 7$ Hz, 3H).

^{13}C NMR ($CDCl_3$): $\delta = 17.0, 24.5, 26.5, 34.5, 34.5, 38.0, 40.0, 42.0, 48.5, 75.0, 140.0, 153.0$.

MS: (m/z) = 229 (M^+).

(E)-2-Nitro-2-eicosene (**2g**): reaction time 3.5 h; yield: 0.18 g (90%), gum.

IR: $\nu = 1670, 1520\ cm^{-1}$.

^1H NMR: $\delta = 7.5$ (t, 1H, $J = 6.5$ Hz, 1H), 2.1 (s, 3H), 1.2 (br, 32H), 0.92 (t, $J = 6.9$ Hz, 3H).

^{13}C NMR ($CDCl_3$): $\delta = 18.5, 27.5, 31.5, 32.5, 32.5, 35.0$ (10 CH_2), 37.0, 38.0, 50.5, 140.0, 141.0.

MS: (m/z) = 325 (M^+).

(E)-2-Nitro-2-hexene (**2h**): Reaction time 3 h; yield: 0.33 g (95%), bp 128–130°C/760 Torr.

IR: $\nu = 1650, 1520\ cm^{-1}$.

^1H NMR: $\delta = 7.6$ (t, $J = 6.5$ Hz, 1H), 2.2 (s, 3H), 1.2 (br, 4H), 0.95 (t, $J = 7$ Hz, 3H).

^{13}C NMR ($CDCl_3$): $\delta = 17.2, 24.0, 26.5, 4.5, 140.0, 140.5$.

MS: (m/z) = 129 (M^+).

(E)-2-Nitro-5-phenyl-2-pentene (**2i**): reaction time 4 h; yield: 0.40 g (80%); bp 164°C/0.35 Torr (Lit.[28] bp 163°C/0.07 Torr).

IR: $\nu = 1670, 1600, 1515\ cm^{-1}$.

^1H NMR: $\delta = 2.08$ (s, 3H), 2.55 (q, 2H, $J = 7.4$ Hz), 7.1–7.4 (m, 6H).

MS: (m/z) = 191 (M^+).

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(1) Seebach, D.; Colvin, E.W.; Lehr, F.; Weller, T. *Chimia* **1979**, 33.
(2) Feuer, H.; Patai, S. *The Chemistry of Nitro and Nitroso Groups*, Parts 1 & 2; Wiley Interscience: New York, 1969/70.
(3) Stermitz, F.R.; Norris, F.A.; Williams, M.C. *J. Am. Chem. Soc.* **1969**, *91*, 4599.
(4) Vrkoc, J. and Ubik, K. *Tetrahedron Lett.* **1974**, 1463.
(5) Soloway, S.B.; Henry, A.C.; Kollmeyer, W.D.; Padgett, J.E.; Roman, S.A.; Tieman, C.H.; Corey, R.A.; Horne, C.A. *Abstracts of Fourth International Congress of Pesticide Chemistry* (IUPAC): Zurich; 1978, 114.
(6) Bousquet, E.W.; Kirby, J.E.; Searle, N.E.; US Patent 2335384 (1943); *Chem. Abstr.* **1944**, *38*, 2834.
(7) Brown, A.W.; Robinson, D.B.W.; Hurtig, H.; Wenner, B.J.; *Can. J. Res.* **1948**, *26D*, 177.
(8) Brian, P.W.; Grove, J.F.; McGowan, J.C. *Nature* **1946**, *158*, 876.
(9) Bocobo, F.C.; Curtis, A.C.; Block, W.D.; Harrell, E.R.; Evans, E.E.; Haines, R.F. *Antibiol. Chemother.* **1956**, *66*, 385.
(10) Schales, O.; Graefe, H.A. *J. Am. Chem. Soc.* **1952**, *74*, 4486.
(11) Dann, O.; Moller, E.F. *Chem. Ber.* **1949**, *82*, 76.
(12) Harker, R.J. US Patent 2889 2436 (1959); *Chem. Abstr.* **1959**, *53*, 17414.
(13) Zee-Cheng, K.; Cheng, C. *J. Med. Chem.* **1969**, *12*, 157.
(14) Ranganathan, D.; Bhusan Rao, C.; Ranganathan, S.; Mehrotra, A.K.; Iyenger, R. *J. Org. Chem.* **1980**, *45*, 1185.
(15) Henry, L. *C.R. Acad. Sci.* **1895**, *120*, 1265.
Wollenberg, R.H.; Miller, S.J. *Tetrahedron Lett.* **1978**, 3219.
(16) Seebach, D.; Beck, A.K.; Mukhopadhyay, T. *Helv. Chim. Acta* **1982**, *65*, 1101.
(17) Buckley, G.D.; Caife, C.W. *J. Chem. Soc.* **1947**, 1471.
(18) Knochel, P.; Seebach, D. *Synthesis* **1982**, 1017.
(19) Melton, J.; McMurry, J.E. *J. Org. Chem.* **1975**, *40*, 2138.
(20) Knochel, P.; Seebach, D. *Tetrahedron Lett.* **1982**, *23*, 3897.
(21) Seebach, D.; Knochel, P. *Helv. Chim. Acta* **1984**, *67*, 261.
(22) Ballini, R.; Catagnani, R.; Petrini, M. *J. Org. Chem.* **1992**, *57*, 2160.
(23) Sarma, B.K.; Barua, N.c. *Tetrahedron* **1993**, *49*, 2253.
(24) Sarma, B.K.; Barua, N.C. *Indian J. Chem., Sect. B* **1993**, *32*, 615.
(25) Single, J.D.; Huang, T.T.S.; Franzus, B. *J. Org. Chem.* **1981**, *46*, 3526.
(26) Ono, N.; Kamimura, A.; Kawai, T.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1987**, 1550.
Hayama, T.; Tomoda, S.; Takeuchi, Y.; Nomura, Y. *Tetrahedron Lett.*, **1982**, *23*, 4733.
Hayama, T.; Tomoda, S.; Takeuchi, Y.; Namoura, Y. *Chem. Lett.*, **1982**, 1109.
(27) David, E. Worrall; *Org. Synth.* **1961**, *1*, 413.
(28) Ballini, R.; Castagnani, R.; Petrini, M.; *J. Org. Chem.* **1992**, *57*, 2160.