Reaction of Carbanions Derived From α,β-Unsaturated Nitro Compounds With Electrophiles to Give α-Substituted Products

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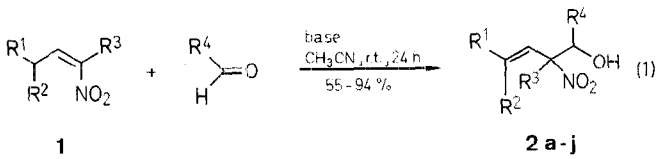
The reaction of α,β-unsaturated nitro compounds with aldehydes or electron deficient olefins, in the presence of a base provides a simple method for the preparation of α-substituted allylic nitro compounds. The initially formed allylic carbanion reacts regioselectively at the position α to the nitro group. The products formed, γ,δ-unsaturated β-nitro alcohols **2** and δ,ε-unsaturated γ-nitro ketones, esters, nitriles, and sulfones **3**, can serve as useful synthetic intermediates.

The reaction of α-heterosubstituted allylic carbanions with electrophiles provides difficult problems of regiochemistry, α- vs. γ-alkylation, and many studies have been done on this subject.[1] However, there are few reports on the reaction of carbanions derived from allylic nitro compounds with electrophiles,[2] for it is rather difficult to prepare allylic nitro compounds by conventional methods.[3] As the nitro group at the allylic position is readily replaced by various nucleophiles, such as active methyene compounds,[4] enolates,[5] amines,[6] sulfinates,[7] thiolates,[8] and lithium dialkylcuprates,[9] the reaction of allylic nitro compounds with electrophiles is of much interest in organic synthesis.

In this paper we wish to report a simple method for the preparation of α-substituted allylic nitro compounds **2** and **3**, by the hydroxyalkylation of α,-unsaturated nitro compounds **1** and by the Michael addition of compounds **1** to electron deficient olefins. The new method is shown in eq 1 and 2. Treatment of α,β-unsaturated nitro compounds **1** with base results in the formation of allylic carbanions, which react with aldehydes or electron deficient olefins regioselectively at the position α to the nitro group. The reaction with aldehydes was carried out by stirring a mixture of **1** with the aldehyde and base (0.1 equiv) in acetonitrile at room temperature for ca. 24 h. The choice of base is important for this reaction. Triethylamine, ethyldiisopropylamine, or 1,4-diazabicyclo[2,2,2]octane (DABCO) was used, depending on the reactivity of the nitroolefin and aldehyde involved. When R^3 is hydrogen, various aldehydes react with **1**, but when R^3 is not hydrogen, the aldehydes are limited to formaldehyde. The results are summarized in Table 1.



1 **2 a-j**

base = $(C_2H_5)_3N$, i-$C_3H_7N(C_2H_5)_2$, 1,4-diazabicyclo [2.2.0] octane (DABCO)

Table 1. Hydroxyalkylation of α,β-Unsaturated Nitro Compounds **1**[a]

R^1	R^2	R^3	R^4	Base	Product	Yield (%)
H	H	CH_3	H	$(C_2H_5)_3N$	**2a**	80
H	H	C_2H_5	H	$(C_2H_5)_3N$	**2b**	77
H	H	n-C_7H_{15}	H	$(C_2H_5)_3N$	**2c**	78
H	H	$(CH_2)_2CO_2CH_3$	H	$(C_2H_5)_3N$	**2d**	60
n-C_4H_9	H	CH_3	H	$(C_2H_5)_3N$	**2e**	94
$CH_2C_6H_5$	H	CH_3	H	$(C_2H_5)_3N$	**2f**	82
n-C_4H_9	H	C_2H_5	H	$(C_2H_5)_3N$	**2g**	77
CH_3	CH_3	H	C_2H_5	DABCO	**2h**	58
CH_3	H	H	C_2H_5	DABCO	**2i**	55
H	$-(CH_2)_3-$		H	$(i$-$C_3H_7)_2N(C_2H_5)$	**2j**	65

[a] The reaction was carried out at room temperature for 24 h.

Table 2. Michael Addition of α,β-Unsaturated Nitro Compounds **1**

R^1	R^2	R^3	Y	Product	Yield (%)
H	H	CH_3	$COCH_3$	**3a**	71
H	H	CH_3	CO_2CH_3	**3b**	63
H	H	CH_3	CN	**3c**	72
H	H	CH_3	$SO_2C_6H_5$	**3d**	66
CH_3	CH_3	H	$COCH_3$	**3e**	65
CH_3	H	CH_3	CO_2CH_3	**3f**	71
n-C_6H_{13}	H	CH_3	CO_2CH_3	**3g**	56[b]

[a] The reaction was carried out at room temperature for 24 h.
[b] Reaction time 3 d.

The Michael addition of allylic nitro compounds to electron deficient olefins, such as α,β-unsaturated ketones, esters, nitriles and sulfones was carried out by stirring a mixture of **1** with the electron deficient olefin and tetramethylguanidine (0.1 equiv) at room temperature for about 24 h. The adducts **3** were obtained

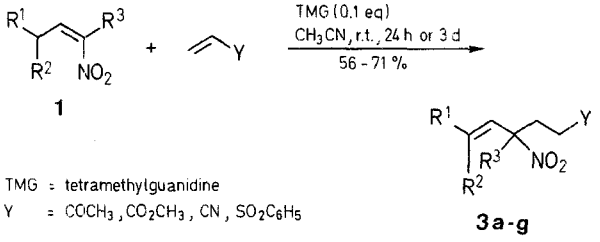


Table 3. Spectral Data for α-Substituted Alkylic Nitro Compounds **2** and **3**

Compound	Molecular Formula[a]	b.p. (°C)/torr	IR (neat)[b] ν (cm⁻¹)	^{1}H-NMR ($CDCl_3$/TMS)[c] δ (ppm)
2a	$C_5H_9NO_3$ (131.2)	110/1	3350, 1530, 1330	1.68 (s, 3H); 2.80 (br t, 1H); 3.7–4.2 (m, 2H); 5.34 (d, 1H, J = 17 Hz); 5.36 (d, 1H, J = 10 Hz); 6.06 (dd, 1H, J = 17 Hz, 10 Hz)
2b	$C_6H_{11}NO_3$ (145.2)	115/1	3300, 1530, 1330	0.92 (t, 3H, J = 8 Hz); 2.12 (q, 2H, J = 8 Hz); 2.54 (br t, 1H); 4.10 (m, 2H); 5.36 (d, 1H, J = 17 Hz); 5.49 (d, 1H, J = 10 Hz); 6.20 (dd, 1H, J = 17 Hz, 10 Hz)
2c	$C_{11}H_{21}NO_3$ (215.3)	120/0.2	3300, 1530, 1350	0.94 (t, 3H, J = 8 Hz); 1.1–1.5 (m, 10H); 1.9–2.1 (m, 2H); 3.0 (br t, 1H); 4.10 (m, 2H); 5.38 (d, 1H, J = 17 Hz); 5.50 (d, 1H, J = 10 Hz); 6.22 (dd, 1H, J = 17 Hz, 10 Hz)
2d	$C_8H_{13}NO_5$ (203.2)	130/1	3400, 1700, 1530, 1350	2.42 (m, 5H); 3.68 (s, 3H); 4.04 (m, 2H); 5.32 (d, 1H, J = 17 Hz); 5.44 (d, 1H, J = 10 Hz); 6.06 (dd, 1H, J = 17 Hz, 10 Hz)
2e	$C_9H_{17}NO_3$ (187.3)	140/1	3400, 1540, 1350	0.88 (t, 3H, J = 8 Hz); 1.2–1.5 (m, 4H); 1.64 (s, 3H); 2.0–2.2 (m, 2H); 2.60 (br s, 1H); 3.70 (d, 1H, J = 12 Hz); 4.12 (d, 1H, J = 12 Hz); 5.86–5.90 (m, 2H)
2f	$C_{11}H_{15}NO_3$ (209.3)	110/0.2	3400, 1530, 1350	1.72 (s, 3H); 2.7 (br s, 1H); 3.46 (d, 2H, J = 8 Hz); 3.8 (d, 1H, J = 12 Hz); 4.2 (d, 1H, J = 12 Hz); 5.9–6.1 (m, 2H); 7.3 (m, 5H)
2g	$C_{10}H_{19}NO_3$ (201.3)	110/0.2	3400, 1540, 1350	0.94 (t, 3H, J = 8 Hz); 0.96 (t, 3H, J = 8 Hz); 1.2–1.7 (m, 4H); 2.0–2.3 (m, 4H); 3.2 (br s, 1H); 4.10 (s, 1H); 4.12 (s, 1H); 5.8–5.9 (m, 2H)
2h	$C_8H_{15}NO_3$ (173.2)	130/1	3400, 1530, 1350	0.99 (t, 3H, J = 8 Hz); 1.3–1.7 (m, 2H); 1.80 (s, 6H); 2.92 (br s, 1H); 3.9–4.2 (m, 1H); 5.0–5.5 (m, 2H)
2i	$C_7H_{13}NO_3$ (159.2)	120/1	3400, 1540, 1350	1.0 (t, 3H, J = 8 Hz); 1.5 (m, 2H); 1.88 (d, 3H, J = 8 Hz); 2.8 (br s, 1H); 4.2–4.5 (m, 2H); 5.5 (m, 1H); 6.0 (m, 1H)
2j	$C_7H_{11}NO_3$ (157.2)	120/1	3400, 1530, 1360	1.5–2.1 (m, 4H); 2.4 (m, 2H); 3.6 (br s, 1H); 3.86 (s, 2H); 6.0 (m, 2H)
3a	$C_8H_{13}NO_3$ (171.2)	150/1	1700, 1530, 1360	1.61 (s, 3H); 2.08 (s, 3H), 2.12–2.48 (m, 4H), 5.12 (d, 1H, J = 17 Hz), 5.22 (d, 1H, J = 10 Hz); 6.12 (dd, 1H, J = 17 Hz, 10 Hz)

Table 3. (Continued)

Compound	Molecular Formula[a]	b.p. (°C)/torr	IR (neat)[b] ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[c] δ (ppm)
3b	$C_8H_{13}NO_4$ (187.2)	150/1	1720, 1535, 1370	1.64 (s, 3H); 2.26 (m, 4H); 3.60 (s, 3H); 5.24 (d, 1H, J = 17 Hz); 5.26 (d, 1H, J = 10 Hz); 6.12 (dd, 1H, J = 17 Hz, 10 Hz)
3c	$C_7H_{10}N_2O_2$ (154.2)	135/1	2100, 1530, 1370	1.68 (s, 3H); 2.4 (m, 4H); 5.30 (d, 1H, J = 17 Hz); 5.34 (d, 1H, J = 10 Hz); 6.14 (dd, 1H, J = 17 Hz, 10 Hz)
3d	$C_{10}H_{15}NSO_4$ (213.3)	oil[d]	1530, 1340, 1280, 1140	1.62 (s, 3H); 2.4 (m, 2H); 3.1 (m, 2H); 5.32 (d, 1H, J = 17 Hz); 5.40 (d, 1H, J = 10 H); 6.08 (dd, 1H, J = 17 Hz, 10 Hz); 7.6–8.0 (m, 5H)
3e	$C_9H_{15}NO_3$ (185.3)	140/1	1700, 1540, 1340	1.78 (s, 3H); 1.80 (s, 3H); 2.15 (s, 3H); 2.22–2.69 (m, 4H); 5.20 (m, 1H); 5.30 (d, 1H)
3f	$C_9H_{15}NO_4$ (201.3)	150/1	1720, 1540, 1350	1.64 (s, 3H); 1.78 (d, 3H, J = 5 Hz); 2.2–2.5 (m, 4H); 3.70 (s, 3H); 5.8–5.9 (m, 2H)
3g	$C_{14}H_{25}NO_5$ (271.4)	140/0.2	1720, 1540, 1350	0.90 (t, 3H, J = 7 Hz); 1.2–1.6 (m, 8H); 1.68 (s, 3H); 2.1–2.4 (m, 6H); 3.70 (s, 3H); 5.8–5.9 (m, 2H)

[a] Satisfactory microanalyses obtained: C ± 0.32, H ± 0.26, N ± 0.28.
[b] Recorded on a Hitachi 215 spectrophotometer.
[c] Recorded on a JEOL Ps-100 spectrometer.
[d] Not distilled.

in good yields. The results are summarized in Table 2. Here again the choice of base is very important. Stronger bases caused polymerization of olefins and bases weaker than tetramethylguanidine gave poor yields.

Since α,β-unsaturated nitro compounds are readily prepared by dehydration of β-nitro alcohols,[3] and since the nitro group of **2** and **3** can be converted into various groups, the method described in reactions 1 and 2 could prove to be quite useful in organic synthesis.

Hydroxyalkylation of α,β-Unsaturated Nitro Compounds; General Procedure:
A solution of α,β-unsaturated nitro compound (**1**; 10 mmol), the appropriate aldehyde (10 mmol; in the case of formaldehyde, a 37% solution), and base (1 mmol) in acetonitrile (10 ml) is stirred at room temperature for 24 h. The reaction mixture is poured into water (50 ml) containing 1 normal hydrochloric acid (10 ml), and extracted with ethyl acetate (3 × 50 ml). The extracts are washed with water (50 ml) and dried with anhydrous magnesium sulfate. The solvent is removed under reduced pressure, and the residue is distilled of subjected to column chromatography (silica gel, hexane/ethyl acetate as eluent) to give γ,δ-unsaturated β-nitro alcohols **2** (Tables 1 and 3).

Michael Addition of α,β-Unsaturated Nitro Compounds; General Procedure:
A solution of **1** (10 mmol), the appropriate electron deficient olefin (13 mmol), and tetramethylguanidine (1 mmol) in acetonitrile (10 ml) is stirred at room temperature for 24 h (3 d for **3 g**. The reaction mixture is worked-up in the same way as in the preparation of **2** to give δ,ε-unsaturated γ-nitro ketones, esters, nitriles, and sulfones **3** after purification by column chromatography (silica gel, hexane/ethyl acetate as eluent (Tables 2 and 3).

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