Michael Addition of Secondary Nitroalkanes to β-Substituted α,β-Unsaturated Compounds

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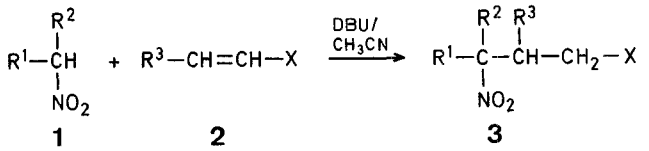
The Michael addition of nitroalkanes is a very important reaction in organic synthesis and has been studied extensively[1]. Various amines[2], alkoxides[1,3], metal fluorides[4], or tetramethylguanidine[5] have been used as catalyst. They are very effective for the reaction of primary nitroalkanes with reactive olefins, but it is rather difficult to bring about the Michael reaction of secondary nitroalkanes **(1)** to β-substituted olefins **(2)**. For example, the reaction of 2-nitropropane with methyl crotonate gives no or only a small amount of product by the conventional procedures using triethylamine or tetramethylguanidine as base[6].

We now present a simple solution of this problem. The use of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base in dipolar aprotic solvents enhances the rate of the Michael reaction greatly. DBU in acetonitrile or dimethylformamide (DMF) is much more effective than other base-solvent systems (Table 1). Secondary nitroalkanes **(1)** undergo the Michael addition with various olefins **(2)** in acetonitrile in the presence of DBU to give the adducts **(3)** in good yields (Table 2).



1 **2** **3**

Preparation of **3** by the conventional procedures is accompanied by some difficulties. For example, only a 6% yield of **3a** is obtained by the procedure using potassium fluoride as a base[4]. Tetraalkylammonium fluorides are generally very effective bases for the Michael addition[7]. However, it takes 5 days to obtain **3b** in 88% yield even when using tetrabutylammonium fluoride[8]. Diethylamine can bring about the reaction of 2-nitropropane with chalcone, but it takes 35 days to obtain **3c** in 96% yield[9].

Thus, the present base-solvent system (DBU/CH_3CN) is much more effective as a catalyst for the Michael reaction of **1** with **2** than other catalysts. However, this catalyst is too strong in some cases and causes polymerization of the olefins. The conventional procedures[2-5] are recommended in such cases.

Table 1. Michael Addition of 2-Nitropropane (**1**; $R^1=R^2=CH_3$) to Methyl Crotonate (**2**; $R^3=CH_3$, $X=COOCH_3$)

Base (equiv)	Solvent	Yield [%] of **3a**[a]
triethylamine (1.0)	acetonitrile	0
tetramethylguanidine (0.1)	acetonitrile	1
tetramethylguanidine (1.0)	acetonitrile	19
DBU (1.0)	acetonitrile	61
DBU (1.0)	dimethylformamide	65
DBU (1.0)	benzene	31

[a] Yield of isolated product; reaction time: 24 h; reaction temperature: room temperature.

Table 2. Michael Addition of Secondary Nitroalkanes **1** to Olefins **2** in Acetonitrile at Room Temperature

Product No.	R^1	R^2	R^3	X	Reaction time [h]	Yield [%][a]	b.p. [°C]/torr or m.p. [°C]	Molecular formula[b] or Lit. Data	I.R. (Nujol) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
3a	CH_3	CH_3	CH_3	$COOCH_3$	24	61	88–90°/1	91–92°/1[4]	1735, 1540, 1375 (neat)	0.97 (d, 3 H, J = 7 Hz); 1.56 (s, 6 H); 2.24 (m, 2 H); 3.65 (m, 1 H); 3.68 (s, 1 H)
3b	CH_3	CH_3	C_6H_5	$COOCH_3$	24	71	71°	70–71°[10]	1730, 1530, 1360	1.50 (d, 6 H, J = 10 Hz); 2.73 (dd, 1 H, J = 15 Hz, 12 Hz); 2.82 (dd, 1 H, J = 15 Hz, 12 Hz); 3.44 (s, 3 H); 3.89 (dd, 1 H, J = 5 Hz, 12 Hz); 7.1–7.4 (m, 5 H)
3c	CH_3	CH_3	C_6H_5	$CO—C_6H_5$	12	95	146.5–148°	146–147°[11]	1710, 1550, 1360	1.52 (s, 3 H); 1.62 (s, 3 H); 3.2–4.2 (m, 3 H); 7.3 (m, 5 H); 7.5 (m, 3 H); 7.9 (m, 2 H)
3d	CH_3	$C_6H_5CH_2$	C_6H_5	$CO—C_6H_5$	12	75	175.5–176°	$C_{24}H_{23}NO_3$ (373.4)	1680, 1530, 1470	1.43 (s, 3 H); 2.60 (d, 1 H, J = 12 Hz); 3.20 (dd, 1 H, J = 16 Hz, 2 Hz); 3.6 (m, 2 H); 4.24 (dd, 1 H, J = 12 Hz, 2 Hz); 6.8–7.8 (m, 15 H)
3e	CH_3	$C_6H_5CH_2$	CH_3	—CN	24	74	104–106°	$C_{13}H_{16}N_2O_3$ (232.3)	2250, 1540, 1360	1.17 (d, 1.5 H, J = 7 Hz); 1.30 (d, 1.5 H, J = 7 Hz); 1.39 (s, 3 H); 2.3 (m, 1 H); 2.7 (m, 2 H); 3.00 (d, 1 H, J = 12 Hz); 3.40 (dd, 1 H, J = 12 Hz, 2 Hz); 6.9–7.4 (m, 5 H)
3f	CH_3	CH_3	C_6H_5	$SO_2—C_6H_5$	24	90	120–122°	$C_{17}H_{19}NO_4S$ (345.1)	1550, 1480, 1290, 1140	1.60 (d, 6 H, J = 8 Hz); 3.4–3.9 (m, 3 H); 7.0–7.6 (m, 10 H)
3g	CH_3	CH_3	CH_3	$SO—C_6H_5$	48	80	oil	$C_{12}H_{15}NO_3S$ (253.3)	1550, 1360, 1060 (neat)	1.0 (m, 1.5 H); 1.2 (m, 1.5 H); 1.40 (s, 3 H); 1.44 (s, 3 H); 1.8 (m, 1 H); 2.6 (m, 2 H); 7.5 (m, 5 H)

[a] Yield of isolated product.

[b] Satisfactory microanalyses obtained: C ±0.17, H ±0.08, N ±0.30.

Methyl 3,4-Dimethyl-4-nitropentanoate (3a); Typical Procedure:
A solution of 2-nitropropane (1.07 g, 12 mmol) and methyl crotonate (1.0 g, 10 mmol) in acetonitrile (5 ml) is mixed with 1,8-diazabicyclo[5.4.0]undec-7-ene (1.52 g, 10 mmol) at room temperature. The resulting solution is kept at room temperature for 24 h, and poured into water (50 ml). The mixture is acidified by dilute hydrochloric acid (pH 2) and extracted with ether (3 × 50 ml). The combined ether extracts are washed with water (100 ml), dried with anhydrous magnesium sulfate, and evaporated in vacuo. The residue is distilled to give **3a**; yield: 1.15 g (61%); b.p. 88–90°C/1 torr (Lit.[4], b.p. 91–92°C/1 torr).

Products **3b–f** are purified by recrystallization and **3g** by column chromatography.

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