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Stereoselective preparation of (*E*)-ε-nitro-β,γ-unsaturated methyl esters: Amberlyst A 27, using microwave, as superior catalyst for the 1,6-conjugate addition of nitroalkanes to methyl 1,3-butadiene-1-carboxylate

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Abstract—1,6-Conjugate addition of nitroalkanes to methyl 1,3-butadiene-1-carboxylate, performed with Amberlyst A 27, using microwaves and in the absence of any solvent, allows the prevalent formation of the β,γ-unsaturated adduct, over the α,β-unsaturated one. The products were exclusively obtained as (*E*)-isomers. © 2001 Elsevier Science Ltd. All rights reserved.

Nitroalkanes have been demonstrated to be highly versatile building blocks for the preparation of natural products.[1] For a projected synthesis of natural substances, we required a large amount of ε-nitro-β,γ-unsaturated methyl esters. Although these molecules can be obtained by reaction of nitronate anions reaction with (π-allyl)cobalt complexes produced from the acylation of 1,3-dienes by acetylcobalt tetracarbonyl[2] or by 1,6-conjugate addition of nitroalkanes,[3] we found these published routes unsatisfactory. In fact these methods suffer from important disadvantages such as complex reaction conditions, low yields and/or very long reaction time (12 days) and modest generality.

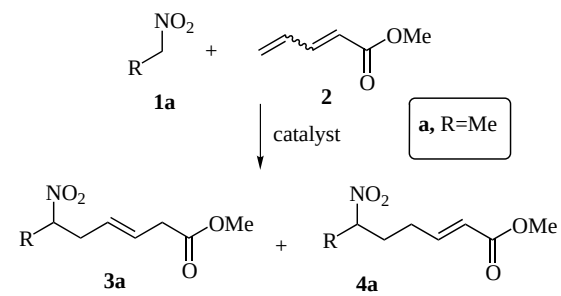
It is well documented that 1,6-conjugate addition may produce both α,β- and β,γ-unsaturated adducts,[4] the latter resulting from kinetic protonation[4b] of the enolate formed in the 1,6-addition reaction.

Based on our previous experience on the Michael addition of aliphatic nitro compounds to electron poor alkenes,[5] we looked for the more efficient catalytic conditions in order to improve the preparation of the β,γ-unsaturated derivatives by 1,6-conjugate addition of a nitroalkane **1** to 1,3-butadiene-1-carboxylate **2**. We chose the addition of nitroethane **1a** to **2** (commercially available as *cis*+*trans* mixture), as model reaction (Scheme 1), in the presence of different catalysts, under homogeneous or heterogeneous conditions.

The results, summarized in Table 1, show that the best goal, in terms of yields, selectivity towards the β,γ-unsaturated adduct, minimization of the by-products, was achieved with Amberlyst A 27, using microwave (500 W),[6] in the absence of any solvent and in a very short reaction time (7 min).[7]

Application of this procedure with different nitroalkanes was then investigated and we found that all the products **3** were exclusively obtained as (*E*)-isomers in satisfactory yields (Table 2), even with functionalized nitrocompounds.[8]

If nitromethane is employed as starting material, the predominance of the double addition was observed (62% of **5**, Scheme 2).



Scheme 1.

Keywords: nitroalkanes; conjugate addition; microwave; catalysis; stereoselective.

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Table 1. 1,6-Conjugate addition of nitroethane (R = Me) **1a** to methyl 1,3-butadiene-1-carboxylate **2**

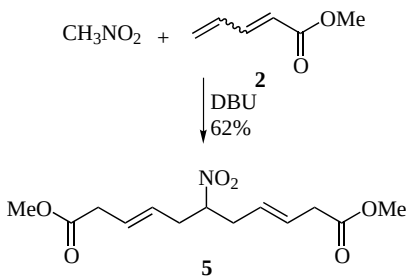
Catalyst (mol)	Solvent	Reaction time	Yield (%)[a] of **3a**	Yield (%)[a] of **4a**	Starting material (%)[a]	Other[b] (%)[a]	Temperature (°C)
DBU (1)	CH_3CN	2 days	6	40	0	54	−20 to rt
NaOH 0.1 M (1)	H_2O/CTACl	12 days	0	21	12	67	0 to rt
NaOH 0.1 M (1)	H_2O	2 days	40	6	32	12	0 to rt
DMAP (1)	CH_2Cl_2	2 days	0	0	100	0	0 to rt
TMG[c] (1)	THF	12 h	35	7	44	14	rt
PPh_3 (0.1)	THF	12 h	0	0	70	30	0 to rt
Amberlyst A 27 (mw 500 W)	Neat	7 min	85	10	0	5	–
Al_2O_3 (basic) (mw 500 W)	Neat	10 min	0	0	100	0	–
HPP[d] (1)	THF	2 days	15	30	15	40	rt
Amberlyst A 27	Neat	2 days	38	4	53	5	rt

[a] Determined by GC.
[b] By-products due to polyadditions, polymerization, etc.
[c] Tetramethylguanidine.
[d] Hexahydro pyrimido pyrimidin.

Table 2. Conjugate addition of nitroalkanes to 1,3-butadiene-1-carboxylate with Amberlyst A 27-microwave

	R	Yield (%)[a] of **3**
a	CH_3	70
b	CH_3CH_2	62
c	$CH_3(CH_2)_5$	68
d	$MeOCO(CH_2)_2$	75
e	$CH_3(CH_2)_2$	55
f	$CH_3CO(CH_2)_2$	55
g	$PhCH_2$	60
h	$CH_3(CH_2)_3$	56

[a] Yield of pure, isolated product.



Scheme 2.

In order to confirm the result obtained with DBU (high prevalence of the α,β-unsaturated adduct), we treated compound **3a** with DBU (1 equiv.) in CH_3CN and under these basic conditions **3a** converts to **4a** (conversion >90%).

In conclusion, the present letter provides the first general method for the formation of the title compounds by 1,6-conjugate addition of nitroalkanes to methyl 1,3-butadiene-1-carboxylate. Moreover, the absence of any solvent and the short reaction time make this procedure an attractive way for the selective preparation of the title compounds.

Acknowledgements

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7. **Typical procedure**: Nitroethane **1a** (0.45 g, 6 mmol) and Amberlyst A 27 (700 mg) were amalgamated in a 25 ml Pyrex flask, then the diene **2** (*cis*+*trans* mixture, 0.56 g, 5 mmol) was added and the mixture was placed at 500 W in a domestic oven, with the temperature monitored at 70°C. The mixture was then irradiated for 7 min and, after cooling, was extracted with Et_2O and the catalyst was filtered off. Evaporation of the solvent, followed by flash chromatography of the mixture produced 0.79 g (70%) of the pure compound **3a**. IR: $\nu = 1738$, 1545 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.51$ (d, 3H, $J = 6.7$ Hz), 2.4–2.5 (m, 1H), 2.6–2.7 (m, 1H), 3.03 (dd, 2H, $J = 7.0$, 0.9 Hz), 3.66 (s, 3H), 4.5–4.6 (m, 1H), 5.44 (dtt, 1H, $J = 15.3$, 7.0, 1.2 Hz), 5.68 (dtt, 1H, $J = 15.3$, 7.0, 1.2 Hz); ^{13}C NMR ($CDCl_3$): $\delta = 19.11$, 38.07, 38.39, 52.39, 83.25, 127.59, 127.66, 172.26; EIMS (70 eV) m/z 156, 140, 99, 81 (100), 67, 59, 41.
8. Selected analytical data for the compounds **3c**,**d**,**f**,**g**:
   3c: IR: $\nu = 1738$, 1555 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 0.88$ (t, 3H, $J = 6.5$ Hz), 1.2–1.4 (m, 6H), 1.6–1.8 (m, 1H), 1.9–2.0 (m, 1H), 2.4–2.5 (m, 1H), 2.6–2.7 (m, 1H), 3.04 (d, 2H, $J = 6.8$ Hz), 3.68 (s, 3H), 4.4–4.6 (m, 1H), 5.46 (dt, 1H, $J = 15.3$, 6.9 Hz), 5.69 (dt, 1H, $J = 15.3$, 6.8 Hz); ^{13}C NMR ($CDCl_3$): $\delta = 14.36$, 22.79, 25.85, 31.56, 33.75, 37.22, 38.08, 52.37, 88.77, 127.33, 127.80, 172.27; EIMS (70 eV) m/z 212, 196, 113, 95, 81 (100), 67, 55, 41.
   3d: IR: $\nu = 1738$, 1549 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.1$–2.7 (m, 6H), 3.05 (d, 2H, $J = 6.9$ Hz), 3.68 (s, 3H), 3.69 (s, 3H), 4.5–4.7 (m, 1H), 5.47 (dt, 1H, $J = 15.3$, 7.0 Hz), 5.71 (dt, 1H, $J = 15.3$, 6.8 Hz); ^{13}C NMR ($CDCl_3$): $\delta = 22.84$, 28.50, 30.34, 33.75, 37.21, 38.04, 52.41, 87.42, 127.25, 127.82, 172.16, 172.75; EIMS (70 eV) m/z 228 (M+1), 196, 180, 149, 121, 93, 79 (100), 59, 41.
   3f: IR: $\nu = 1738$, 1712, 1548 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.0$–2.2 (m, 5H), 2.4–2.7 (m, 4H), 3.01 (dd, 2H, $J = 7.0$, 1.3 Hz), 3.64 (s, 3H), 4.5–4.6 (m, 1H), 5.43 (dtt, 1H, $J = 15.3$, 7.0, 1.2 Hz), 5.66 (dtt, $J = 15.3$, 7.0, 1.2 Hz); ^{13}C NMR ($CDCl_3$): $\delta = 27.33$, 30.54, 37.30, 38.04, 39.40, 52.38, 87.60, 127.39, 127.67, 172.19, 206.84; EIMS (70 eV) m/z 243 (M^+), 242, 211, 187, 127, 115 (100), 59, 43.
   3g: IR: $\nu = 1738$, 1552 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.4$–2.5 (m, 1H), 2.6–2.7 (m, 1H), 3.0–3.1 (m, 2H), 3.2–3.3 (m, 2H), 3.66 (s, 3H), 4.7–4.8 (m, 1H), 5.46 (dt, 1H, $J = 15.3$, 7.3 Hz), 5.68 (dt, 1H, $J = 15.3$, 7.9 Hz), 7.1–7.3 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta = 33.92$, 36.72, 38.08, 52.40, 89.63, 127.48, 127.79, 127.93, 129.04, 129.44, 135.79, 172.24; EIMS (70 eV) m/z 243 (M^+), 216, 142, 129, 91 (100), 71, 59.