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Amberlyst A-27, an Efficient Heterogeneous Catalyst for the Michael Reaction of Nitroalkanes with *β*-Substituted Alkene Acceptors

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The Michael addition of nitroalkanes to electrophilic double bonds provides a convenient method[1,2] for the preparation of a number of useful synthetic intermediates[3,4] since the nitro group can be transformed into various functionalities.[3]

Different organic bases such as tetramethylguanidine,[5−8] potassium fluoride/18-crown-6,[9,10] sodium hydride/18-crown-6,[11] diisopropylamine,[6,12] potassium *tert*-butoxide,[6,11] tri-*n*-butylphosphine,[15] triphenyphosphine,[11,16] 1,8-diazobicyclo[5.4.0]undec-7-ene,[17] and tetrabutylammonium fluoride[11] have been used in homogeneous solutions. Under these conditions, multiple Michael adducts are often formed in significant amounts. This problem is most acute in the case of vinylcarbonyl derivatives.

In recent years there has been a tremendous upsurge of interest in various chemical transformations mediated by heterogeneous catalysts, and the associated literature is extensive.[18−21] Innumerable chemical bonds are broken and new chemical bonds are formed during these catalytic processes, and such events frequently occur without a significant change of the catalyst. Moreover, under heterogeneous catalyst, chemical transformations can occur with better efficiencies, higher purity of the products, and an easier workup.

Different heterogeneous catalysts[22−28] have been employed for the Michael reaction of nitroalkanes, but these methods have important limitations. At first, KF was applied, under an inert atmosphere,[22] but a large excess of nitroalkane (20 times) was necessary. Then, a weakly basic macroreticular resin[24] and various sorts of alumina[23,28] were used as heterogeneous bases. However, these bases have been shown to be effective only with a restricted class of electrophilic olefins such as α,*β*-unsaturated esters[24] or conjugated enones.[23,28] Adsorbing KF on neutral alumina[25] greatly enhances the activity of this basic catalyst, but the yields were low to moderate and an excess of nitroalkane (4−8 times) was required. Aliquat 336 provides[27] a useful catalyst for the title reaction with unsaturated esters, but again, an excess (3−15 times) of nitro compound and the use of ultrasound irradiations were required. Recently, layered zirconium hydrogen phosphate has been reported as a new heterogeneous catalyst,[26] but only one example was described.

The requirement for a large excess of nitroalkane in many of the above-reported methods is a serious drawback, expecially when valuable nitro derivatives are employed.

With the aim to avoid all these limitations, we explored several catalysts, and now, we report a significant improvement on this reaction by using commercial Amberlyst A-27, a macroreticular anionic resin with the [$-N(CH_3)_3^+$] as functional group.

The reaction was performed by adding 8−12 g of Amberlyst A-27 to a mixture of 0.05 mol of nitroalkane **1** and 0.05 mol of alkene **2** at 0 °C, without solvent, and then leaving the reaction at room temperature (see Table 1), followed by extraction with diethyl ether, filtration, evaporation, and purification by flash chromatography, affording the pure adduct **3** in high yield.

Under these conditions both primary and secondary nitroalkanes easily react with a variety of electrophilic alkenes, even those substituted in the *β*-position (entries **l**, **m**, and **q**, Table 1). The yields of products vary from good to excellent, and the reaction was found to be substantially independent of catalyst:starting material ratio.

The results reported in Table 1 refer to the solvent-free reaction; however, different solvents such as THF and Et_2O can be used without a significant change of the yield.

Of special interest is the conjugate addition of nitroalkanes to the 5,6-dihydro-2*H*-pyran-2-one (entry **q**, Table 1), because the nitro group facilitates a variety of carbon−carbon bond-forming processes and offers a wide range of efficient methods for its transformation into other functionalities.[3,4] Thus, further elaborations of the obtained lactone derivative are possible.

Compared with other heterogeneous methods, our procedure offers better yields with a large variety of substrates without the need for an excess of nitroalkane.

Experimental Section

General. All ^{1}H NMR spectra were recorded in $CDCl_3$ at 300 MHz. Chemical shifts are expressed in ppm downfield from TMS as internal standard. All the reactions were monitored

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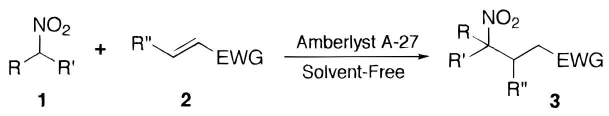
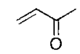
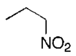
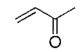
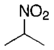
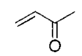
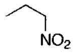
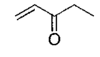
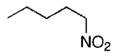
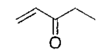
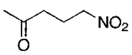
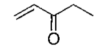
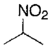
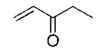
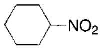
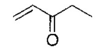
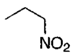
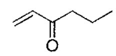
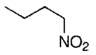
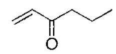
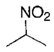
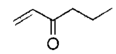
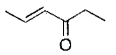
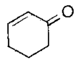
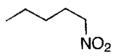
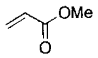
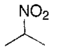
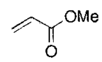
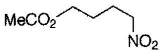
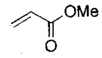
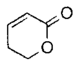
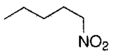
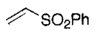
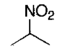
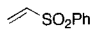
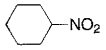
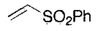
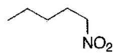
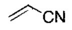
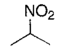
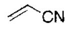
Table 1. Michael Reaction of Nitroalkanes Catalyzed by Amberlyst A-27



entry	Nitroalkane (**1**)	Alkene (**2**)	Yield (%) of (**3**)	Reaction Time (h)
a	$EtNO_2$		76	4
b			90	7
c			75	25
d			77	5
e			84	5
f			75	4
g			70	15
h			65	8
i			85	4
j			86	7
k			85	13
l	$EtNO_2$		75	25
m	$EtNO_2$		93	20
n			75	9
o			80	4
p			85	7
q	$EtNO_2$		55	20
r			65	15
s			80	20
t			70	10
u			60	10
v			75	8

by TLC or GC performed on a Carlo Erba Fractovap 4160 using a capillary column of Duran Glass, stationary phase OV1. The products **3** were purified by flash chromatography[29] on Merck silica gel (0.040–0.063 mm). Amberlyst A-27 was purchased from Carlo Erba Reagenti (also easily available from Fluka and Aldrich).

General Procedure for the Michael Addition of Nitroalkanes to Electrophilic Alkenes. A 100 mL two-necked flask equipped with a mechanical stirrer was charged with the nitro compound **1** (0.05 mol) and cooled with an ice–water bath. After 5 min the alkene **2** (0.05 mol) was added, and the mixture was stirred for 10 min. Amberlyst A-27 (8–10 g) was added, and after being stirred for 15 min, the mixture was left at room temperature for the appropriate time (see Table 1). The Amberlyst was washed with Et_2O (4 × 40 mL), the filtered extract was evaporated, and the crude nitroderivative **3** was purified by flash chromatography (cyclohexane/EtOAc 8:2).

5-Nitrohexan-2-one (entry a): IR (film) 1715, 1545 cm^{-1}; ^1H NMR δ 1.56 (d, 3H, $J = 6.3$ Hz), 1.88–2.32 (t + s, 5H, $J = 6.5$ Hz), 2.4–2.72 (m, 2H), 4.4–4.92 (m, 1H, $J = 6.3$ Hz). Anal. Calcd for $C_6H_{11}NO_3$: C, 49.65; H, 7.64; N, 9.65. Found: C, 49.82; H, 7.78; N, 9.38.

5-Nitroheptan-2-one (entry b): IR (film) 1710, 1545 cm^{-1}; ^1H NMR δ 0.96 (t, 3H, $J = 7.0$ Hz), 2.2 (s, 3H), 1.6–2.85 (m, 6H), 4.4 (t, 1H, $J = 6.0$ Hz). Anal. Calcd for $C_7H_{13}NO_3$: C, 52.82; H, 8.23; N, 8.8. Found: C, 53.04; H, 8.41; N, 8.56.

5-Methyl-5-nitrohexan-2-one (entry c): IR (film) 1715, 1540 cm^{-1}; ^1H NMR δ 1.60 (s, 6H), 2.00–2.60 (m + s, 7H). Anal. Calcd for $C_7H_{13}NO_3$: C, 52.82; H, 8.23; N, 8.8. Found: C, 52.63; H, 8.42; N, 9.01.

6-Nitrooctan-3-one (entry d): IR (film) 1710, 1545 cm^{-1}; ^1H NMR δ 0.95 (t, 3H, $J = 7.4$ Hz), 1.05 (t, 3H, $J = 7.4$ Hz), 1.7–2.18 (m, 4H), 2.38–2.5 (m, 4H), 4.35–4.5 (m, 1H). Anal. Calcd for $C_8H_{15}NO_3$: C, 55.47; H, 8.73; N, 8.09. Found: C, 55.70; H, 8.51; N, 7.95.

6-Nitrodecan-3-one (entry e): IR (film) 1710, 1540 cm^{-1}; ^1H NMR δ 0.88 (t, 3H, J = 7.2 Hz), 1.05 (t, 3H, J = 7.3 Hz), 1.2–1.45 (m, 4H), 1.85–2.15 (m, 4H), 2.38–2.51 (m, 4H), 4.4–4.58 (m, 1H). Anal. Calcd for $C_{10}H_{19}NO_3$: C, 59.68; H, 9.52; N, 6.96. Found: C, 59.88; H, 9.75; N, 6.73.

5-Nitrodecane-2,8-dione (entry f): IR (film) 1700, 1535 cm^{-1}; ^1H NMR δ 1.05 (t, 3H, $J = 7.5$ Hz), 2.0–2.18 (m, 4H), 2.32–2.6 (m + s, 9H), 4.4–4.6 (m, 1H). Anal. Calcd for $C_{10}H_{17}NO_4$: C, 55.8; H, 7.96; N, 6.51. Found: C, 56.1; H, 8.13; N, 6.32.

6-Methyl-6-nitroheptan-3-one (entry g): IR (film) 1710, 1535 cm^{-1}; ^1H NMR δ 1.05 (t, 3H, $J = 7.3$ Hz), 1.58 (s, 6H), 2.12–2.25 (m, 2H), 2.38–2.52 (m, 4H). Anal. Calcd for $C_8H_{15}NO_3$: C, 55.47; H, 8.73; N, 8.09. Found: C, 55.70; H, 8.59; N, 8.22.

1-(1-Nitrocyclohexyl)pentan-3-one (entry h): IR (film) 1710, 1520 cm^{-1}; ^1H NMR δ 1.05 (t, 3H, $J = 7.3$ Hz), 1.25–1.75

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(m, 10H), 2.05−2.2 (m, 2H), 2.31−2.5 (m, 4H). Anal. Calcd for $C_{11}H_{19}NO_3$: C, 61.95; H, 8.98; N, 6.57. Found: C, 62.2; H, 9.12; N, 6.44.

7-Nitrononan-4-one (entry i): IR (film) 1700, 1535 cm^{-1}; ^{1}H NMR δ 0.91 (t, 3H, $J = 7.2$ Hz), 0.95 (t, 3H, $J = 7.3$ Hz), 1.5−2.18 (m, 6H), 2.32−2.48 (m, 4H), 4.35−4.5 (m, 1H). Anal. Calcd for $C_9H_{17}NO_3$: C, 57.73; H, 9.15; N, 7.48. Found: C, 57.89; H, 9.00; N, 7.31.

7-Nitrodecan-4-one (entry j): IR (film) 1700, 1535 cm^{-1}; ^{1}H NMR δ 0.85−1.0 (m, 6H), 1.23−1.43 (m, 2H), 1.5−1.75 (m, 2H), 1.85−2.15 (m, 4H), 2.3−2.5 (m, 4H), 4.45−4.6 (m, 1H). Anal. Calcd for $C_{11}H_{19}NO_3$: C, 59.68; H, 9.52; N, 6.51. Found: C, 59.55; H, 9.35; N, 6.38.

7-Methyl-7-nitrooctan-4-one (entry k): IR (film) 1700, 1535 cm^{-1}; ^{1}H NMR δ 0.85 (t, 3H, $J = 7.4$ Hz), 1.57 (s, 6H), 2.11−2.21 (m, 4H), 2.32−2.44 (m, 4H). Anal. Calcd for $C_9H_{17}NO_3$: C, 57.73; H, 9.15; N, 7.48. Found: C, 57.98; H, 9.32; N, 7.33.

5-Methyl-6-nitroheptan-3-one (entry l): IR (film) 1710, 1540 cm^{-1}; ^{1}H NMR δ 0.9−1.1 (m, 6H), 1.5 (dd, 3H, $J = 2.9$, 6.7 Hz), 2.3−2.7 (m, 4H), 4.5−4.7 (m, 1H). Anal. Calcd for $C_8H_{15}NO_3$: C, 55.47; H, 8.73; N, 8.09. Found C, 55.65; H, 8.54; N, 7.95.

3-(1-Nitroethyl)cyclohexanone (entry m): IR (film) 1710, 1545 cm^{-1}; ^{1}H NMR δ 1.32−2.6 (m, 9H), 1.6 (d, 3H, $J = 6.65$ Hz), 4.36−4.80 (m, 1H). Anal. Calcd for $C_8H_{13}NO_3$: C, 56.13; H, 7.65; N, 8.18. Found: C, 55.97; H, 7.84; N, 7.98.

Methyl 4-nitrooctanoate (entry n): IR (film) 1730, 1545 cm^{-1}; ^{1}H NMR δ 0.9 (t, 3H, $J = 7.3$ Hz), 1.3−1.4 (m, 4H), 1.89−2.44 (m, 6H), 3.69 (s, 3H), 4.47−4.63 (m, 1H). Anal. Calcd for $C_9H_{17}NO_4$: C, 53.19; H, 8.43; N, 6.89. Found: C, 52.97; H, 8.60; N, 7.04.

Methyl 4-methyl-4-nitropentanoate (entry o): IR (film) 1715, 1535 cm^{-1}; ^{1}H NMR δ 1.58 (s, 6H), 2.16−2.39 (m, 4H), 3.69 (s, 3H). Anal. Calcd for $C_7H_{13}NO_4$: C, 40.19; N, 7.23; N, 6.7. Found: C, 39.88; H, 7.45; N, 6.55.

Dimethyl 4-nitropimeloate (entry p): IR (film) 1720, 1535 cm^{-1}; ^{1}H NMR δ 2.0−2.45 (m, 8H), 3.7 (s, 6H), 4.6−4.7 (m, 1H). Anal. Calcd for $C_9H_{15}NO_6$: C, 46.35; H, 6.48; N, 6.01. Found: C, 46.51; H, 6.32; N, 6.2.

4-(1-Nitroethyl)tetrahydropyranone (entry q): IR (film) 1705, 1535 cm^{-1}; ^{1}H NMR δ 1.58 (d, 3H, $J = 6.8$ Hz), 1.6−2.4 (m, 3H), 2.5−2.8 (m, 2H), 4.2−4.35 (m, 1H), 4.4−4.6 (m, 2H). Anal. Calcd for $C_7H_{11}NO_4$: C, 48.55; H, 6.4; N, 8.09. Found: C, 48.66; H, 6.58; N, 7.91.

1-(Phenylsulfonyl)-3-nitroheptane (entry r): IR (film) 1540, 1360, 1135 cm^{-1}; ^{1}H NMR δ 0.88 (t, 3H, $J = 7.4$ Hz), 1.2−1.45 (m, 4H), 1.65−2.1 (m, 2H), 2.2−2.4 (m, 2H), 3.1 (t, 2H, $J = 7.3$ Hz), 4.52−4.7 (m, 1H), 7.55−7.78 (m, 3H), 7.88−7.95 (m, 2H). Anal. Calcd for $C_{13}H_{19}NO_4S$: C, 54.72; H, 6.71; N, 4.91; S, 11.23. Found: C, 54.90; H, 6.54; N, 5.02; S, 11.0.

1-(Phenylsulfonyl)-3-methyl-3-nitrobutane (entry s): IR (film) 1535, 1380, 1165 cm^{-1}; ^{1}H NMR δ 1.6 (s, 6H), 2.3−2.4 (m, 2H), 3.08−3.19 (m, 2H), 7.58−7.73 (m, 3H), 7.58−7.9 (m, 2H). Anal. Calcd for $C_{11}H_{15}NO_4S$: C, 50.56; H, 7.33; N, 5.36; S, 12.27. Found: C, 50.73; H, 7.49; N, 5.2; S, 12.07.

1-(Phenylsulfonyl)-2-(1-nitrocyclohexyl)ethane (entry t): IR (film) 1540, 1380, 1160 cm^{-1}; ^{1}H NMR δ 1.5−1.7 (m, 10H), 2.18−2.47 (m, 2H), 3.0−3.1 (m, 2H), 7.52−7.75 (m, 3H), 7.86−7.96 (m, 2H). Anal. Calcd for $C_{14}H_{19}NO_4S$: C, 56.55; H, 6.44; N, 4.71; S, 10.78. Found: C, 56.38; H, 6.59; N, 4.80; S, 10.90.

4-Nitrooctanenitrile (entry u): IR (film) 2240, 1535 cm^{-1}; ^{1}H NMR δ 0.91 (t, 3H, $J = 6.7$ Hz), 1.2−1.45 (m, 4H), 1.7−2.55 (m, 6H), 4.5−4.7 (m, 1H). Anal. Calcd for $C_8H_{14}N_2O_2$: C, 56.45; H, 8.29; N, 16.46. Found: C, 56.24; H, 8.44; N, 10.32.

4-Methyl-4-nitropentanenitrile (entry v): IR (film) 2220, 1540 cm^{-1}; ^{1}H NMR δ 1.64 (s, 6H), 2.26−2.46 (m, 4H). Anal. Calcd for $C_6H_{10}N_2O_2$: C, 50.69; H, 7.09; N, 19.71. Found: C, 50.90; H, 6.91; N, 19.9.

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