



A One Pot, Solvent-Free Synthesis of Acyclic α -Nitro Ketones through the Nitroaldol Reaction

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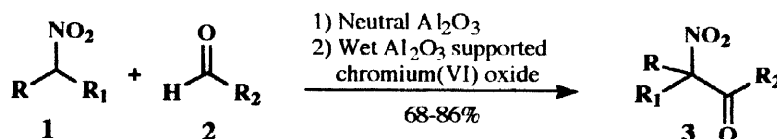
Abstract: Acyclic α -nitro ketones are easily obtained in one pot, through a solvent-free procedure by nitroaldol (Henry) reaction on neutral alumina, then *in situ* oxidation of the nitroalkanol using wet alumina supported chromium(VI) oxide. © 1998 Elsevier Science Ltd. All rights reserved.

Acyclic α -nitro ketones have been widely used¹ as the key building blocks for other functionalities,²⁻¹⁰ or to prepare important natural products.¹¹ Although different methods have been reported for their synthesis,¹²⁻¹⁴ the most widely employed are C-acylation of nitroalkanes,¹⁵ and oxidation of 2-nitroalkanols.¹⁶ However, the latter procedure requires the preparation of the β -nitroalcohol, then its oxidation using an organic solution/suspension of the appropriate oxidant; moreover, strong acidic conditions and/or the help of ultrasound are required.

Environmental and economic pressures are now forcing the chemical community to search for more efficient ways of performing chemical transformations.¹⁷ In this context, we found that the title compounds **3** can be easily prepared, in one pot, through a solvent-free procedure by (Scheme 1) nitroaldol reaction of nitroalkane **1** (2.2 mmol) and aldehyde **2** (2.2 mmol, freshly distilled), on activated¹⁸ neutral alumina (0.6 g, the alumina was added to a mechanically stirred solution of **1** and **2**, at 0 °C, then at room temperature for 20 h). Then, *in situ* addition (0 °C) of wet-alumina supported chromium(VI) oxide [0.88g (8.8 mmol) of CrO₃ and 2.64 g of wet alumina].¹⁹ After standing for additional 20 h, the product was extracted with diethyl ether and passed through a bed of alumina. Evaporation of the organic solvent and flash chromatographic purification afforded the pure α -nitro ketone **3** in good yields (68–86%).

Although the oxidation of nitroalkanols with dry alumina-supported CrO₃ has been already reported to give poor yields of the corresponding α -nitro ketones,^{15g} we found that wet alumina supported chromium(VI) oxide was capable of producing good yields of **3** under mild reaction conditions.

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Scheme 1

Table 1. Preparation of α -Nitro Ketones

entry	R	R ₁	R ₂	Yield (%) of 3 ^a	entry	R	R ₁	R ₂	Yield (%) of 3 ^a
a	CH ₃	H	Ph(CH ₂) ₂	75	i	Br	H	Ph	70
b	CH ₃	H	CH ₃ (CH ₂) ₈	76	j	MeO ₂ C(CH ₂) ₃	H	CH ₃ (CH ₂) ₇	68
c	C ₂ H ₅	H	CH ₃ (CH ₂) ₃	69	k	CH ₃ CO(CH ₂) ₂	H	CH ₃ (CH ₂) ₈	71
d	CH ₃	CH ₃	CH ₃ (CH ₂) ₇	75	l	PhCH ₂	H	CH ₃	70
e	Br	H	CH ₃ (CH ₂) ₈	77	m	CH ₃ (CH ₂) ₃	H	Ph(CH ₂) ₂	86
f	CH ₃	H	α -C ₆ H ₁₁	80	n	CH ₃	H	CH ₃	71
g	CH ₃	H	CH ₃ (CH ₂) ₉	70	o	C ₂ H ₅	H	CH ₃	75
h	PhCH ₂	H	Ph	85					

^aYield of pure, isolated product

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