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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 used[1] 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 activated[18] 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 CrO_3 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 CrO_3 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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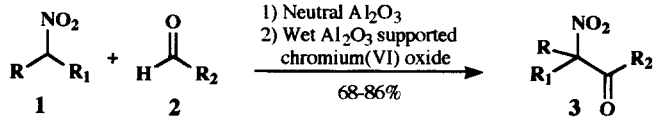

Scheme 1

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	$MeO_2C(CH_2)_3$	H	$CH_3(CH_2)_7$	68
c	C_2H_5	H	$CH_3(CH_2)_3$	69	k	$CH_3CO(CH_2)_2$	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	c-C_6H_{11}	80	n	CH_3	H	CH_3	71
g	CH_3	H	$CH_3(CH_2)_9$	70	o	C_2H_5	H	CH_3	75
h	$PhCH_2$	H	Ph	85					

[a]Yield of pure, isolated product

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