Synthesis of 2-Nitroalkanols on Alumina Surfaces without Solvent: A Simple, Mild and Convenient Method

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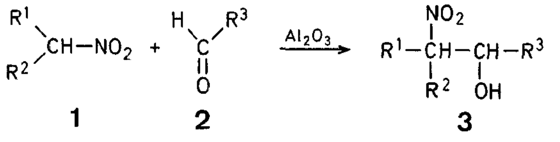
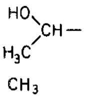
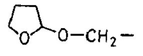
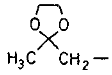
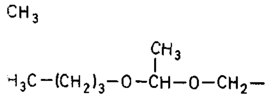
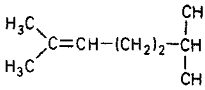
The nitroaldol addition (Henry reaction)[1] yielding 2-nitroalkanols is one of the classical C—C bond forming processes. 2-Nitroalkanols are useful intermediates for the synthesis of nitroalkenes, 2-aminoalcohols and α-nitroketones[2-5].

Several methods to obtain 2-nitroalkanols have been developed, however, these procedures often are disadvantageous. The yields are not always good and mixtures of products are sometimes obtained. A major reason for this is based on the propensity of aliphatic nitro compounds to undergo oxygen alkylation in preference to carbon alkylation. Recently, this problem has been overcome by using silyl nitronates in the fluoride ion-catalyzed reaction with carbonyl compounds[6] or by the addition of α,α-doubly metallated nitroalkanes to aldehydes at −90°C[7,8]. However, these procedures require expensive reagents and are technically too cumbersome to be suitable for large scale preparations.

We report here a mild, simple, and convenient new heterogeneous method for an effective synthesis of 2-nitroalkanols **3a-k** from nitroalkanes **1** and aldehydes **2** on an alumina surface in the absence of a solvent. The starting compounds **1** and **2** are completely adsorbed by vigorous stirring with a sufficient amount of alumina. After standing for 24 h at room temperature, the products **3** are isolated in high yields (Table) by washing with dichloromethane, filtration of the organic extracts, and evaporation of the solvent under reduced pressure.

Alumina has long been used as a catalyst and reagent in organic synthesis[9-13]. Our procedure works well on a gram scale using commercial Carlo Erba RS chromatographic alumina (activity I according to Brockmann). Good results are obtained also with substrates which are acid or base sensitive. We think the practical advantages of chromatographic alumina for effecting the very mild preparation of polyfunctional and labile 2-nitroalkanols will increase the applications of this heterogeneous reagent in organic synthesis.



3	R^1	R^2	R^3
a	C_2H_5	H	CH_3
b	CH_3	H	C_2H_5
c	$H_3COOC-CH_2-CH_2-$	H	C_2H_5
d	 $HO(H_3C)CH-$	H	$i\text{-}C_3H_7$
e	CH_3	H	$c\text{-}C_6H_{11}$
f		H	$n\text{-}C_6H_{13}$
g		H	$n\text{-}C_6H_{13}$
h	CH_3	H	$C_6H_5-CH_2-CH_2-$
i	CH_3	CH_3	$C_6H_5-CH_2-CH_2-$
j	 $H_3C-(CH_2)_3-O-CH(CH_3)-O-CH_2-$	H	$C_6H_5-CH_2-CH_2-$
k	CH_3	H	 $(H_3C)_2C=CH-(CH_2)_2-CH(CH_3)-CH_2-$

2-Nitroalkanols 3a-k; General Procedure:

A 100 ml two necked flask equipped with a mechanical stirrer is charged with a nitro compound **1** (0.05 mol) and cooled with an ice-water bath. An aldehyde **2** (0.05 mol) is added and the mixture stirred for 2-3 min. Chromatographic alumina (Carlo Erba RS, activity I according to Brockmann; 10 g) is added and stirring is continued for 1 h at room temperature. After standing for 23 h, the alumina is washed with dichloromethane (3 x 40 ml). The filtered extract is evaporated at reduced pressure to give crude 2-nitroalkanols **3**. At temperatures below 80°C unreacted nitro compound **1** and aldehyde **2** are distilled

Table. Synthesis of 2-Nitroalkanols **3a-k**

3	Yield[a] [%]	b.p. [°C]/torr	Molecular formula[b] or Lit. b.p. [°C]/torr	I.R. (film) [cm⁻¹][c]		¹H-N.M.R. ($CDCl_3$/TMS_{int})[d] δ [ppm]
				ν_{OH}	ν_{NO_2}	
a	80	60°/0.5	100°/10[14]	3400	1550	1.0 (t, 3H, J=7.5 Hz); 1.3 (dd, 3H, J=6.0 Hz); 1.8-2.1 (m, 2H); 3.0 (s, 1H); 3.9–4.6 (m, 2H)
b	71	80°/3.8	90-96°/8[15]	3450	1550	1.1 (t, 3H, J=7.5 Hz); 1.4-1.7 (m, 5H); 2.7 (s, 1H); 3.8-4.7 (m, 2H)
c	84	110-112°/1.2	$C_8H_{15}NO_5$ (205.2)	3460	1540	1.02 (t, 3H, J=7.5 Hz); 1.40-1.80 (m, 2H); 2.05-2.70 (m, 4H); 3.65-4.20 (m+s, 4H); 4.40-4.75 (m, 1H)
d	69	68-70°/3.5	$C_7H_{15}NO_4$ (177.2)	3400	1550	0.80-1.50 (m, 10H); 4.20-4.70 (m, 3H)
e	75	90-92°/0.6	$C_9H_{17}NO_3$ (187.2)	3440	1550	0.81-2.40 (m+d, 14H); 3.60-4.05 (m, 1H); 4.50-4.85 (m, 1H)
f	86	oil[e]	$C_{13}H_{25}NO_5$ (275.3)	3420	1550	0.90 (t, 3H, J=6.0 Hz); 1.10-2.15 (m, 14H); 3.68-4.32 (m, 5H); 4.45-4.90 (m, 1H); 5.05-5.30 (m, 1H)
g	86	oil[e]	$C_{13}H_{25}NO_5$ (275.3)	3450	1550	0.87 (t, 3H, J=6.0 Hz); 1.2-1.6 (m, 13H); 2.35-2.85 (m, 2H); 3.85-4.1 (m, 5H); 4.5-4.8 (m, 1H)
h	71	145°/0.9	$C_{11}H_{15}NO_3$ (209.2)	3450	1550	1.5 (dd, 3H, J=7.5 Hz); 1.7-1.9 (m, 2H); 2.7-2.9 (m, 2H); 3.9-4.6 (m, 2H); 7.1-7.3 (m, 5H)
i	69	oil[e]	$C_{12}H_{17}NO_3$ (223.3)	3450	1550	(s+s, 6H); 1.7-1.9 (m, 2H); 2.7-2.9 (m, 2H); 3.9-4.3 (m, 1H); 7.1-7.3 (m, 5H)
j	82	oil[e]	$C_{17}H_{27}NO_5$ (325.4)	3420	1550	0.92 (t, 3H, J=6.75 Hz); 1.10-2.10 (m+d, 9H); 2.55-3.10 (m, 2H); 3.20-3.70 (m, 2H); 3.80-4.25 (m, 3H); 4.40-4.85 (m, 2H); 7.23 (m, 5H)
k	78	oil[e]	$C_{12}H_{23}NO_3$ (229.3)	3450	1550	0.75-2.45 (m, 19H); 3.80-4.80 (m, 2H); 4.95-5.30 (m, 1H)

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[a] Yield of pure, isolated product.

[b] Satisfactory microanalyses obtained: C ±0.12, H ±0.13, N ±0.14 (Hewlett-Packard Model 185, C,H,N-Analyzer).

[c] Recorded on a Perkin-Elmer 297 spectrometer.

[d] Recorded at 90 MHz using a Varian EM 390 spectrometer.

[e] Isolated and purified by distillation of unreacted starting materials under reduced pressure from the reaction mixture.

off. Then, the temperature is carefully raised to reach the b.p. of the 2-nitroalkanol **3**. (*Caution!* Overheating may cause thermal decomposition of products **3**).

Performing the reaction under a nitrogen atmosphere or stirring the solid reaction mixture for a longer period of time does not improve the yield.

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