One-Pot Synthesis of 1,3-Dinitroalkanes under Heterogeneous Catalysis

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Received 19 April 2004

Abstract: Reaction of aldehydes with an excess of nitromethane in the presence of basic alumina as solid catalyst allows the one pot preparation of 1,3-dinitroalkanes. The synthesis proceeds through the nitroaldol reaction of nitromethane, which acts both as nucleophile and as solvent, to the aldehydes with the formation of β-nitroalkanols as intermediates that convert to nitroalkenes. Further nucleophilic behavior of the nitromethane produces the in situ conjugate addition of its carbanion to the formed nitroalkenes giving the one-pot synthesis of the title compounds. The catalyst shows general applicability with aliphatic, aromatic and heteroaromatic aldehydes.

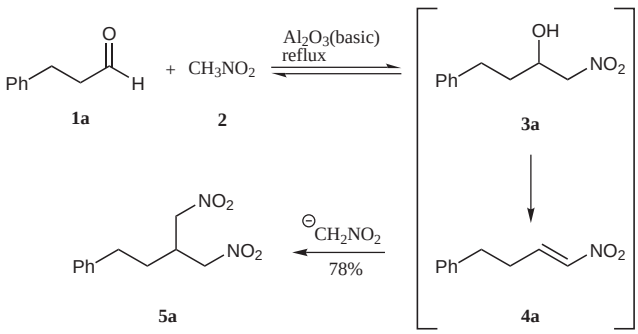
Key words: 1,3-dinitroalkanes, Michael additions, heterogeneous catalysis, alumina, one-pot

The use of nitro compounds as reactive intermediates in organic synthesis has attracted the interest of many researches in recent years.[1] Both the activating effect of the nitro group, and its facile transformation into various functional groups have extended the importance of the these compounds in the synthesis of complex molecules.[2] In this context, 1,3-dinitro compounds are of great interest because they could be used as precursors of a variety of (i) 1,3-difuntionalized molecules, (ii) heterocycles,[3] (iii) carbohydrate derivatives,[4] and (iv) potentially active energetic materials.[5]

The synthesis of complex molecules is traditionally performed by a sequence of separate reaction steps, each step requiring its own conditions, reagents, solvent, and catalyst. After each reaction is completed, the solvent and the waste products are removed and discarded, and the intermediate product is separated and purified. Now environmental and economical pressures are forcing the chemical community to search for more efficient ways of performing chemical transformations.[6] These new issues can be addressed by the development of new synthetic methods that, bringing together small and simple components, generate complex structures in one-pot, much the same way as nature does.[7]

These considerations are driving our efforts in developing new methodologies for the preparation of important targets[8] and now we wish to report the one-pot synthesis of the title compounds.

The standard procedures, for the preparation of 1,3-dinitro compounds, proceed through the conjugate addition (Michael reaction) of nitroalkanes to pre-prepared nitroalkenes,[3,4,9] but, it is well known that the synthesis of nitroolefins are often intricate and proceeds in poor yields due to their high reactivity and easy conversion into dimeric or polymeric derivatives; moreover the synthesis of the latter compounds needs two more steps [(i) nitroaldol reaction and (ii) dehydration] starting from aldehydes and aliphatic nitro compounds.[10] Although some attempts for the one-pot synthesis of the title compounds, from aldehydes and nitroalkanes, have been already reported,[11–14] two of these seems limited to aromatic and heteroaromatic aldehydes,[11,12] while the other ones give very poor yields[13] and/or reported just one example.[14] Based on our previous experience on the use of basic alumina for the generation of new C–C bond starting from nitroalkanes,[15] we planned the one pot synthesis of the title compounds by using basic alumina as solid catalyst. As model reaction we tested the reaction of hydrocinnamaldehydes **1a** with nitromethane **2** (Scheme 1), in the presence of basic alumina and, as reported in the experimental part, we found that the production of the 1,3-dinitroalkane **5a** (Scheme 1) can be obtained by using a large excess of **2** and under reflux temperature.

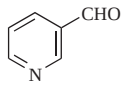
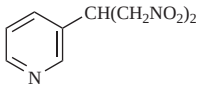
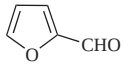
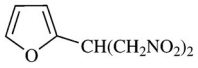


Scheme 1

The reaction proceeds through the nitroaldol reaction of the nitromethane **2**, which acts both as nucleophile and as solvent, with the aldehyde **1a**, with the formation of the β-nitroalkanol **3a** as intermediate, that converts to the nitroalkene **4a**. Further nucleophilic behavior of the nitromethane produces the conjugate addition of its carbanion to the electron-poor alkene **4a** giving the one-pot synthesis of **5a**. It is important to point out that the equilibrium conversion (**1a** + **2**) → **3a** and the successive generation of the nitroalkene **4a**, are both strongly helped by the in situ trapping of **4a** with nitromethane, avoiding any possible decomposition of the formed conjugated ni-

SYNTHESIS 2004, No. 12, pp 1938–1940
Advanced online publication: 21.07.2004
DOI: 10.1055/s-2004-829160; Art ID: Z07604SS

Table 1 Dinitro Compounds **5a–k** Prepared

Entry	Aldehyde **1**	Product **5**	Yield (%)[a]	Time (h)
a	$Ph(CH_2)_2CHO$	$Ph(CH_2)_2CH(CH_2NO_2)_2$	78	3.5
b	$(CH_3)_2CHCHO$	$(CH_3)_2CHCH(CH_2NO_2)_2$	62	3.5
c	$CH_3(CH_2)_4CHO$	$CH_3(CH_2)_4CH(CH_2NO_2)_2$	65	3.5
d	$CH_3(CH_2)_2CHO$	$CH_3(CH_2)_2CH(CH_2NO_2)_2$	68	3.5
e	$CH_3(CH_2)_7CHO$	$CH_3(CH_2)_7CH(CH_2NO_2)_2$	69	3.5
f	*p*-$O_2NC_6H_4CHO$	*p*-$O_2NC_6H_4CH(CH_2NO_2)_2$	60	4
g	PhCHO	$PhCH(CH_2NO_2)_2$	71	4
h	*p*-$F_3CC_6H_4CHO$	*p*-$F_3CC_6H_4CH(CH_2NO_2)_2$	72	3.5
i	*p*-$MeOC_6H_4CHO$	*p*-$MeOC_6H_4CH(CH_2NO_2)_2$	74	4.5
j			60	5
k			70	3

[a] Yield of pure, isolated products.

troolefin. A number of different aldehydes were then chosen to assess the scope of the method (Table 1). This synthesis is the sum of three different steps and gives good yields (60–78%) with aliphatic, aromatic and heteroaromatic aldehydes (Table 1).

It is important to stress that the use of heterogeneous catalysis avoids any aqueous work up since the catalyst can be simply removed by filtration, washed with EtOAc and the obtained filtrate was concentrated under vacuum giving the crude product **5** that was directly submitted to flash chromatography. Moreover, under our mild conditions other functionalities such as ethers, trifluoromethyl, and heterocycles can be preserved. It is noteworthy that trinitro derivative **5f** could also be obtained.

In conclusion, we have reported the first, general, mild, heterogeneous one-pot procedure for the synthesis of 1,3-dinitroalkanes. It is noteworthy that the catalyst shows general applicability with aliphatic, aromatic, and heteroaromatic aldehydes.

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or CD_3COCD_3 (see Table 2) at 200 MHz and 50 MHz, respectively, on Varian Gemini 200 spectrometer. Chemical shift are expressed in ppm downfield from TMS. Mass spectra were recorded with a non-polar capillary column, utilizing electron impact (EI) at an ionizing energy of 70 eV. Elemental analyses were performed using a C, H Analyzer Model 185 from Hewlett-Packard. All the reactions were monitored by TLC and/or gas chromatography analysis, performed on Hewlett-Packard 5890 series II using a capillary column (0.32 mm × 25 m).

One-Pot Preparation of Dinitro Compounds 5; General Procedure

To a stirred solution of aldehyde **1** (2 mmol) in nitromethane **2** (2.258 g, 2 mL, 37 mmol), basic alumina (Fluka, activity I, according to Brockmann; 1 g) was added at r.t. and the resulted mixture was refluxed for the appropiate time (see Table 1). After completion of the reaction the solid catalyst was removed by filtration and washed with EtOAc (3 × 40 mL). The filtrate was concentrated under vacuum and the crude product was purified by flash chromatography (cyclohexane–EtOAc) to give the pure compound **5**.

Table 2 Spectroscopic Data of Dinitro Compounds **5a–k**

Compound	IR (KBr)[a] (cm^{-1})	^1H NMR (200 MHz, $CDCl_3$):[b] δ (ppm), *J* (Hz)	^{13}C NMR (75 MHz, $CDCl_3$):[b] δ (ppm), *J* (Hz)	EI–MS (70 eV): *m/z*
5a	1382, 1557, 1602, 3028	1.78–1.86 (m, 2 H), 2.72–2.79 (m, 2 H), 2.84–2.98 (m, 1 H), 4.52 (dd, *J* = 13.7, 5.2 Hz, 2 H), 4.63 (dd, *J* = 13.4, 6.4 Hz, 2 H), 7.15–7.35 (m, 5 H)	30.8, 32.7, 35.6, 76.0, 127.0, 128.5, 129.1, 139.8	30, 65, 77, 91 (100), 104, 117, 129, 145, 177, 238
5b	1378, 1553	0.98 (d, *J* = 6.6 Hz, 6 H), 1.75–1.96 (m, 1 H), 2.76–2.94 (m, 1 H), 4.52 (d, *J* = 6.2 Hz, 4 H)	19.3, 28.1, 41.9, 74.8	30, 41 (100), 55, 69, 83
5c	1380, 1551	0.84 (t, *J* = 6.7 Hz, 3 H), 1.21–1.50 (m, 8 H), 2.77–2.96 (m, 1 H), 4.41–4.62 (m, 4 H)	14.0, 22.4, 26.1, 29.1, 31.5, 36.2, 76.2	29, 39, 41 (100), 55, 69, 81, 95, 109
5d	1381, 1553	0.89–0.97 (m, 3 H), 1.36–1.48 (m, 4 H), 2.82–2.97 (m, 1 H), 4.50 (dd, *J* = 13.5, 5.5 Hz, 2 H), 4.63 (dd, *J* = 13.4, 6.7 Hz, 2 H)	13.9, 19.7, 31.3, 36.0, 76.2	30, 41, 55 (100), 67, 83
5e	1380, 1433, 1467, 1556	0.87 (t, *J* = 6.6 Hz, 3 H), 1.25–1.45 (m, 14 H), 2.87–2.93 (m, 1 H), 4.50 (dd, *J* = 13.6, 5.5 Hz, 2 H), 4.63 (dd, *J* = 13.2, 6.6 Hz, 2 H)	14.2, 22.8, 26.4, 29.1, 29.2, 29.3, 31.9, 36.2, 76.1	29, 41 (100), 55, 67, 81, 95, 109, 137, 164, 199
5f	1380, 1552	4.57–4.68 (m, 1 H), 5.10–5.26 (m, 4 H), 7.81 (d, *J* = 8.7 Hz, 2 H), 8.27 (d, *J* = 8.7 Hz, 2 H)	42.5, 77.1, 124.9, 130.5, 144.5, 148.9	30, 39, 50, 63, 77, 89, 104, 115 (100), 116, 132, 148, 161, 178, 208

Table 2 Spectroscopic Data of Dinitro Compounds **5a**–**k** (continued)

Compound	IR (KBr)[a] (cm^{-1})	^1H NMR (200 MHz, $CDCl_3$):[b] δ (ppm), *J* (Hz)	^{13}C NMR (75 MHz, $CDCl_3$):[b] δ (ppm), *J* (Hz)	EI–MS (70 eV): *m/z*
5g	1376, 1560, 1654, 3034	4.22–4.33 (m, 1 H), 4.69–4.82 (m, 4 H), 7.17–7.20 (m, 2 H), 7.22–7.38 (m, 3 H)	42.0, 77.0, 127.6, 129.3, 129.7, 134.5	30, 39, 51, 65, 77, 91, 105, 117 (100), 133, 163, 210
5h	1380, 1552	4.32–4.46 (m, 1 H), 4.72–4.88 (m, 4 H), 7.38 (d, *J* = 8.2 Hz, 2 H), 7.65 (d, *J* = 8.2 Hz, 2 H)	41.6, 76.5, 126.7, 126.8, 126.9, 127.0, 128.2, 138.4	30, 39, 51, 63, 77, 91, 103, 117, 133, 151, 165 (100), 173, 185, 201, 212, 231, 259
5i	1379, 1543, 1615	3.78 (s, 3 H), 4.21–4.29 (m, 1 H), 4.71 (d, *J* = 1.8 Hz, 2 H), 4.75 (d, *J* =1 .8 Hz, 2 H), 6.87 (d, *J* = 8.8 Hz, 2 H), 7.14 (d, *J* = 8.8 Hz, 2 H)	41.3, 55.4, 77.1, 115.0, 126.0, 128.7, 160.1	30, 39, 51, 65, 77, 91, 103, 121, 133 (100), 147, 164, 193, 240
5j	1376, 1560, 1654, 3034	4.40–4.59 (m, 1 H), 5.01–5.27 (m, 4 H), 7.40 (dd, *J* = 7.7, 4.8 Hz, 1 H), 7.92 (dt, *J* = 8.1, 2.0 Hz, 1 H), 8.55 (dd, *J* = 4.7, 1.5 Hz, 1 H), 8.70 (d, *J* = 2.1 Hz, 1 H)	40.5, 77.1, 124.6, 132.6, 135.9, 150.6, 150.7	30, 39, 51, 65, 78, 91, 106, 118 (100), 134, 211
5k	1377, 1563	4.37–4.54 (m, 1 H), 4.81 (d, *J* = 7.0 Hz, 4 H), 6.28–6.31 (m, 1 H), 6.33–6.39 (m, 1 H), 7.41 (t, *J* = 0.73 Hz, 1 H)	36.0, 74.7, 109.0, 111.0, 143.6, 147.3	30, 39, 55, 65, 79 (100), 94, 107, 153, 200

[a] IR for the compounds **5i**, **5j** and **5k** were performed in nujol.
[b] ^1H and ^{13}C NMR for the compounds **5f** and **5j** were recorded in CD_3COCD_3.

Acknowledgment

The work was carried out in the framework of the National Project 'Il Mezzo Acquoso nelle Applicazioni Sintetiche dei Nitrocomposti Alifatici' supported by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Rome, Italy.

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