SHORT PAPER

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Heterogeneous catalysts in the preparation of 2-aryl-1,3-dinitropropanes from β-nitrostyrenes or benzaldehydes†

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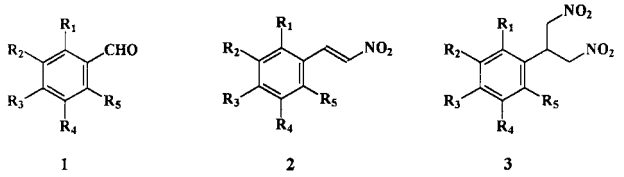
The use of heterogeneous basic catalysts (KF, $NaHCO_3$) in the preparation of 2-Aryl-1,3-dinitropropanes from β-nitrostyrenes or benzaldehydes is described, with one example followed kinetically by HPLC analysis of aliquots of the reaction.

Keywords: heterogeneous catalysts, 2-aryl-1,3-dinitropropanes

The classic preparation of 2-aryl-1,3-dinitropropanes employs the Michael addition of nitromethide anion to β-nitrostyrenes.[1,2] The kinetics of this reaction with a variety of substituted β-nitrostyrenes was studied in DMSO–H_2O mixtures by Bernasconi *et al.*[3] Since β-nitrostyrenes are themselves prepared by condensation of benzaldehydes with nitromethane in the presence of a base,[4] a direct one-pot preparation of 2-aryl-1,3-dinitropropanes from the corresponding benzaldehydes in the presence of excess nitromethane should be feasible. This has been carried out with a series of substituted benzaldehydes that were refluxed in nitromethane in the presence of *n*-butylamine.[5] The yields for this conversion were not high, due to the formation of side products. Also, electron-withdrawing substituents on the aromatic ring led in general to poorer yields of the corresponding 1,3-dinitropropanes. This observation was in contrast with the expectation that these substituents should enhance the reactivity of both the benzaldehyde and the intermediate β-nitrostyrene vis-a-vis the nitromethide anion.

The suggestion that the employed base might be responsible for the observed yields, and the recent report on the use of KF as an alternative catalyst for the Michael addition of nitroalkanes to α,β-unsaturated esters,[6] prompted us to try this weaker base and heterogeneous conditions for the title reaction. In the present report we describe the use of KF and $NaHCO_3$ as heterogeneous catalysts for the preparation of a series of dinitropropanes (**3**) from the corresponding β-nitrostyrenes (**2**). In addition, the two-step conversion of benzaldehyde (**1g**) to the corresponding dinitropropane (**3g**) in the presence of $NaHCO_3$ and excess nitromethane was followed by HPLC analysis of the products in the course of the reaction.



	R_1	R_2	R_3	R_4	R_5
(a)	H	H	H	H	H
(b)	H	O—CH_2—O		H	H
(c)	H	H	Br	H	H
(d)	H	OCH_3	OCH_3	OCH_3	H
(e)	H	OCH_3	OH	H	H
(f)	H	H	$N(CH_3)_2$	H	H
(g)	OCH_3	H	H	OCH_3	H

Scheme 1

Experimental

Melting points were determined with an Electrothermal apparatus, and were not corrected. NMR spectra were recorded on a Bruker AMX 300 spectrometer, employing $CDCl_3$ as solvent and tetramethylsilane as internal reference. The high-resolution mass spectrum of (**3g**) was obtained with a Hewlett Packard 5989A instrument. Chromatographic analyses of reaction mixtures were performed with a Merck-Hitachi HPLC instrument, equipped with an L-6200A Pump, an L-4250 UV-Vis detector, a Lichrospher RP C18 column and a D-2500 chromato-integrator, with the use of a 1:1 mixture of acetonitrile and aqueous H_3PO_4 (1%) as eluent.

All reagents and solvents were purchased from Aldrich, with a purity of 98% or higher. Anhydrous potassium fluoride was used as purchased, without any further drying, being kept in a desiccator.

General preparation of 1-aryl-2-nitroethenes (**2**): A solution of the corresponding benzaldehyde (10 mmol), nitromethane (20 mmol) and *n*-butylamine (1 ml) in glacial acetic acid (10 ml) was refluxed for 1 hour. The 1-aryl-2-nitroethene which separated upon cooling, was filtered and recrystallized in methanol. In this way the following nitroethenes were prepared: 1-phenyl-2-nitroethene (**2a**), 85 % yield, m.p. 545–56 °C, lit.[3] m.p. 56–57 °C; 1-(3,4-methylenedioxyphenyl)-2-nitroethene (**2b**), 87 % yield, m.p. 157–159 °C, lit.[7] m.p. 162 °C 1-(4-bromophenyl)-2-nitroethene (**2c**), 79 % yield, m.p. 155–156 °C; lit.[8] m.p. 156–158 °C 1-(3,4,5-trimethoxyphenyl)-2-nitroethene (**2d**), 84 % yield, m.p. 118–120 °C, lit.[9] m.p. 121–122 °C; 1-(3-methoxy-4-hydroxyphenyl)-2-nitroethene (**2e**), 70% yield, m.p. 162–164 °C, lit.[10] m.p. 160 °C; 1-(4-dimethylaminophenyl)-2-nitroethene (**2f**), 70 % yield, m.p. 181–183 °C, lit.[3] m.p 181 °C; 1-(2,5-dimethoxyphenyl)2-nitroethene (**2g**), 88 % yield, m.p. 116–118 °C, lit.[11] m.p 119–120 °C.

General preparation of 2-Aryl-1,3-dinitropropanes (**3**): A suspension of the 1-aryl-2-nitroethene (3 mmol) and the appropriate base (KF or $NaHCO_3$, 3.6 mmol) in nitromethane (20 ml) was refluxed with vigorous stirring for 0.5–5.5 h. After the reaction was complete, as shown by an analysis of the products by thin-layer chromatography (silica HF-254 (Merck), dichloromethane as eluent), the solvent was removed in a rotary evaporator, the residue extracted with diethyl ether and the ethereal extracts washed with water and dried over anhydrous $MgSO_4$. Evaporation of the solvent followed by flash chromatography of the crude product (silica gel 60G, dichloromethane as eluent) gave the pure dinitropropane. In this way the following 2-aryl-1,3-dinitropropanes were obtained and their identity confirmed by comparison of their ^1H NMR spectra with the data reported in the literature:[5] 2-phenyl-1,3-dinitropropane (**3a**), colourless oil, ^1H NMR ($CDCl_3$) δ 7.4–7.5 (3H, m), 7.2–7.3 (2H, m), 4.77 (4H,d, J = 7.1 Hz), 4.31 (1H,quintet, J = 7.1

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

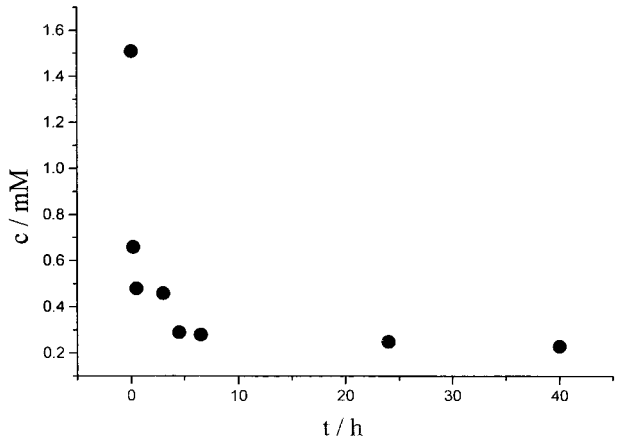
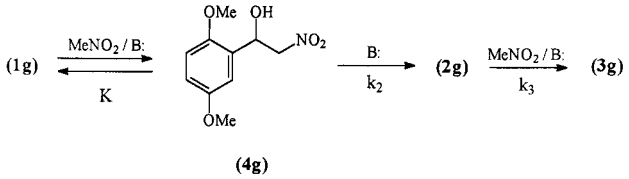


Fig. 1 Variation of the concentrations of benzaldehyde (**1g**) in the first 40 hours of reaction.



Scheme 2

Hz); 2-(3,4-methylenedioxyphenyl)-1,3-dinitropropane (**3b**) m.p. 82–84 °C, lit.[5] m.p. 90 °C. ^{1}H NMR ($CDCl_3$) δ 6.79 (1H, d, *J* = 9 Hz), 6.65–6.75 (2H, m), 5.98 (2H, s), 4.72 (4H, d, *J* = 7.1 Hz) 4.23 (1H, quintet, *J* = 7.1 Hz); 2-(4-bromophenyl)-1,3-dinitropropane (**3c**), m.p. 80–82 °C, ^{1}H NMR ($CDCl_3$) δ 7.53 (2H, d, *J* = 8.4Hz), 7.13 (2H, d, *J* = 8.5 Hz), 4.74 (4H, d, *J* = 7.1 Hz), 4.29 quintet, *J* = 7.1 Hz); 2-(3,4,5-trimethoxyphenyl)-1,3-dinitropropane (**3d**), m.p. 134–136 °C, lit.[5] m.p. 135 °C; ^{1}H NMR ($CDCl_3$) δ 6.40 (2 H, s), 4.77 (4H, d, *J* = 7.1 Hz), 4.25 (1H, quintet, *J* = 7.1 Hz), 3.84 (3H s), 3.86 (6H, s); 2-(3-methoxy-4-hydroxyphenyl)-1,3-dinitropropane (**3e**), m.p. 85–88 °C, lit.[5] m.p. 93 °C. ^{1}H NMR ($CDCl_3$) δ 8.71 (1H, s), 6.82 (1H, d, *J* = 2.1 Hz), 6.80 (1H, d, *J* = 8.1 Hz), 6.70 (1H, dd, *J* = 2.1 Hz, *J'* = 8.1 Hz), 4.90 (4H, d, *J* = 7.1 Hz), 4.20 (1H, quintet, *J* = 7.1 Hz), 3.85 (3H, s) ; 2-(4-dimethylaminophenyl)-1,3-dinitropropane (**3f**), m.p. 108–111 °C, lit.[5] m.p. 112 °C. ^{1}H NMR ($CDCl_3$) δ 7.06 (2H, d, *J* = 8.9 Hz), 6.67 (2H, d, *J* = 8.8 Hz), 4.71 (4H,d, *J* = 7.1 Hz), 4.22 (1H, quintet, *J* = 7.1 Hz), 2.94 (6H, s); 2-(2,5-dimethoxyphenyl)-1,3-dinitropropane (**3g**), m.p. 57–59 °C HRMS (M^+) Calcd for $C_{11}H_{14}N_2O_6$ 270.0852. Found: 270.0857 ^{1}H NMR ($CDCl_3$) δ 6.80–6.90 (2H, m), 6.67–6.74 (1H, m), 4.86 (4H, d, *J* = 7.1 Hz), 4.40 (1H, quintet, *J* = 7.1 Hz), 3.83 (3H, s) and 3.75 (3H, s).

Table 1 gives the yields and reaction times for the two bases employed as catalysts in the case of each product (**3**).

Kinetic measurements: A suspension of 2,5-dimethoxybenzaldehyde (0.5 g, 3.0 mmol), and sodium bicarbonate (0.3 g, 3.6 mmol) in nitromethane (20 ml) was refluxed with vigorous stirring for 300 h. The course of the reaction was followed by HPLC analysis of samples (100 µl) taken at various time intervals, and diluted, after centrifuging for 1 minute, to 10 ml in acetonitrile. All the aromatic components were detected spectrophotometrically at 310 nm. The concentrations of the various species present in solution were estimated by comparison of the obtained peak areas with those of solutions of known concentration of 2,5-dimethoxybenzaldehyde (**1g**), 1-(2,5-dimethoxyphenyl)-2-nitroethene (**2g**) and 2-(2,5-dimethoxyphenyl)-1,3-dinitropropane (**3g**). Errors due to variations in the volume of the samples, or the volume of the reaction mixture, were avoided by the use of naphthalene (0.3 g, 2.35 mmol) added to the reaction mixture as an internal standard.

Results and discussion

The Michael addition of nitromethane to the 1-aryl-2-nitroethenes (**2**) in the presence of KF or $NaHCO_3$ led to the formation of dinitropropanes (**3**) in a rather clean process. The reaction conditions and yields for this conversion are given in Table 1. In general, reactions catalysed by sodium bicarbonate required longer reaction times than those by KF, but the yields tended to be higher.

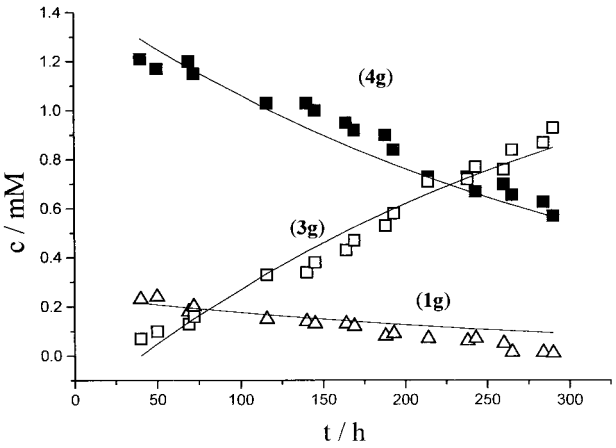


Fig. 2 Variation of the concentrations of the benzaldehyde (**1g**), the intermediate nitroethanol (**4g**) and the dinitropropane (**3g**) with time, after an initial time lag of 40 hours of reaction. The concentrations of (**4g**) were obtained from equation (2). Drawn curves correspond to equations (4), (5) and (6), where $[\mathbf{1g}]_0$ = 1.51 mM, Δt = 40 h, K = 6 and α = 0.0033 h^{-1}.

The direct preparation of 2-phenyl-1,3-dinitropropane by reaction of benzaldehyde and excess nitromethane in the presence of KF or $NaHCO_3$ proved too sluggish to be synthetically useful. This suggested that the first reaction of this two-step process should be much slower than the Michael addition of the nitromethide anion to the intermediate β-nitrostyrene. In order to confirm this, we decided to follow the course of reaction of 2,5-dimethoxybenzaldehyde (**1g**) with excess nitromethane in the presence of $NaHCO_3$.

The process may be described by the sequence shown in Scheme 2.

The concentration of the intermediate 1-(2,5-dimethoxyphenyl)-2-nitroethene (**2g**), which never exceeded 10^{-3} mM during the whole process, was assumed negligible in the kinetic treatment. By contrast, a fairly rapid equilibrium was established in the first 20 hours of reaction between 2,5-dimethoxybenzaldehyde (**1g**) and another species, which was most probably the corresponding 1-(2,5-dimethoxyphenyl)-2-nitroethanol (**4g**). Dehydration of this species to form (**2g**) proceeded slowly.

The variations in concentration for all species intervening in the process are shown in graphs which depict the relatively fast initial decay of (**1g**) in the course of the first 40 hours (Fig. 1) and the slow formation of the dinitropropane (**3g**) in the

Table 1 Yields of 2-aryl-1,3-dinitropropanes (**3**) and reaction times for the reaction of 1-aryl-2-nitroethenes (**2**) with nitromethane in the presence of KF or $NaHCO_3$

Substrate	KF		$NaHCO_3$	
	Reaction time/h	Yield (%)	Reaction time/h	Yield (%)
2a	2.0	45	3.5	65
2b	1.0	40	3.0	75
2c	1.0	35	2.5	55
2d	2.0	45	4.5	52
2e	1.5	48	3.0	51
2f	3.5	58	5.5	93
2g	0.5	70	1.0	65

following 250 hours (Fig. 2). The fact that the intermediate nitroethene (**2g**) never accumulated appreciably in the reaction mixture was an indication that its rate of formation equalled, or was smaller than its rate of disappearance to form the final product. We could thus treat the nitroethene (**2g**) as a relatively unstable intermediate under the reaction conditions, and write equation (1).

$$d[\mathbf{3g}]/d\,t = -\,d[\mathbf{4g}]/dt = k_2'\,[B]\,[\mathbf{4g}] = k_2\,[\mathbf{4g}] \quad (1)$$

This relationship, and equations (2) and (3),

$$[\mathbf{1g}] + [\mathbf{4g}] + [\mathbf{3g}] = [\mathbf{lg}]_0 \quad (2)$$

$$[\mathbf{4g}] / [\mathbf{1g}] = K \quad (3)$$

were used to obtain an expression for the concentration of compounds **1g**, **4g** and **3g** as a function of time t (equations (4), (5) and (6), respectively).

$$[\mathbf{1g}] = [\mathbf{lg}]_0\,[1/(K+1)] \,.\, \exp[-\alpha\,(t-\Delta t)] \quad (4)$$

$$[\mathbf{4g}] = [\mathbf{lg}]_0.\,[K/(K+1)] \,.\, \exp[-\alpha\,(t-\Delta t)] \quad (5)$$

$$[\mathbf{3g}] = [\mathbf{lg}]_0\,\{1 - \exp[-\alpha\,(t-\Delta t)]\} \quad (6)$$

In these equations, $[\mathbf{lg}]_0 = 1.51$ mM was the initial concentration of benzaldehyde **1g**, $\alpha = k_2 \,.\, K / (1 + K)$, and Δt is the time lag of 40 h. The equilibrium constant K incorporated the concentrations of the nitromethane and the basic catalyst B in solution, which remain practically constant throughout the process. The experimental data shown in Fig. 2 are superimposed upon the curves drawn according to equations (4), (5) and (6) for a value of $\alpha = 0.0033\ h^{-1}$ and a pre-equilibrium constant K = 6. From these values we obtain the pseudo-first order rate constant $k_2 = 3.8 \times 10^{-3}\ h^{-1}$.

The above results provide us with a reasonable picture of the whole process, and the effect of the basic catalyst on the yield and outcome of the reactions. The heterogeneous $NaHCO_3$ catalyst acts as a weak base. Because the reaction is carried out in nitromethane, a constant concentration of the nitromethide anion is always present, facilitating the nucleophilic attack of this species on the benzaldehyde (**1g**) and the nitroethene (**2g**). By contrast, base-catalysed dehydration of the intermediate nitroethanol (**4g**) is a difficult process under these heterogeneous conditions, with the result that this step becomes rate-determining.

Stronger bases and homogeneous media tend to accelerate all individual steps. However, side reactions are also facilitated, such as Michael additions of the amine bases, or of the dinitropropane carbanion to the nitroethene intermediate. Both processes are well documented in the literature.[6,12] As a result, the overall reaction, although faster, is less clean, and yields tend to drop because of competing processes leading to side products.

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