Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
Tetrahedron 61 (2005) 4015–4021

Nitroaldol-reaction of aldehydes in the presence of non-activated Mg:Al 2:1 hydrotalcite; a possible new mechanism for the formation of 2-aryl-1,3-dinitropropanes

Agnieszka Cwik,[a] Aliz Fuchs,[b] Zoltán Hell[a,*] and Jean-Marc Clacens[c]

[a]*Department of Organic Chemical Technology, Budapest University of Technology and Economics, H-1521 Budapest, Hungary*
[b]*Research Group for Organic Chemical Technology, Hungarian Academy of Sciences, H-1521 Budapest, Hungary*
[c]*Institut de Recherches sur la Catalyse, 2, Avenue Albert Einstein, 69626 Villeurbanne Cédex, France*

Received 27 August 2004; revised 2 February 2005; accepted 18 February 2005

Abstract—Commercially available, non-activated 2:1 Mg:Al hydrotalcite catalyzes the nitroaldol reaction between a variety of aromatic and aliphatic aldehydes and simple nitroalkanes such as nitromethane and nitroethane. A new mechanism is proposed for the formation of the 1,3-dinitropropanes. The *threo*/*erythro* diastereoselectivity of the nitroethane-adducts was determined by ^{1}H NMR spectroscopy and was found to range from 50:50 to 70:30. The substituents of the aromatic aldehydes influenced the isomer ratio.

1. Introduction

The Henry reaction, which is also known as nitroaldol addition, is a fundamental reaction in organic chemistry.[1] The 2-nitroalkanols formed are an important class of compounds often used as key intermediates in the synthesis of numerous products. They are particularly versatile intermediates for the synthesis of nitroalkenes, 2-amino-alcohols and 2-nitro-ketones. They are also useful intermediates in the synthesis of valuable pharmaceuticals and pharmaceutical intermediates such as (*S*)-propanolol,[2] or (*S*)-(−)-pindolol,[3] antibiotics (e.g., ezomycin,[4] tunicamycin[5]), natural products such as the sex pheromone of the Douglas Fir Tussock moth[6] or cyclopeptide alkaloids.[7] Moreover, 2-nitroalkanol derivatives are important as fungicides.[8] Due to their versatility, a considerable amount of work about their synthesis has been reported.

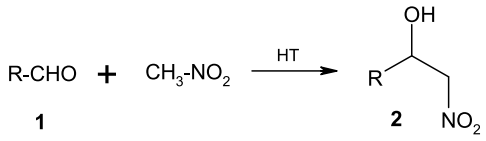
Several organic and inorganic catalysts have been described in the literature for the preparation of 2-nitroalcohols from nitroalkane and carbonyl derivatives. These include alkali metal hydroxides, alkaline earth oxides, carbonates, bicarbonates, alkoxides, quaternary ammonium salts. Both protic and aprotic solvents and solvent-free conditions have been used. The development of new catalysts for the Henry reaction needs to avoid competitive reactions such as aldol condensation, epimerization of stereogenic centers created during the reaction, the Cannizzaro reaction, the Tishchenko reaction, and the Nef-type reaction. Moreover, 2-nitro-alcohols may be dehydrated to the nitroalkenes that readily polymerize. Since the Henry reaction creates stereogenic centers in the products, considerable effort has also been directed toward the development of enantioselective versions.[9,10] A lot of various new catalysts have recently been developed, like Amberlyst A-21,[11] benzyltrimethyl-ammonium hydroxide,[12] rhodium complex,[13] proaza-phosphatranes,[14] Mg–Al–O–*t*Bu hydrotalcite,[15] heterobimetallic complexes with lanthanide BINOL system,[16] or guanidines.[17]

Nevertheless, the development of new catalyst and procedure of the Henry reaction has been constantly in focus, because of the need to reduce the amount of toxic waste materials and byproducts, to develop new asymmetric catalyst, and to use less toxic, 'green' promoters.

Nowadays, the use and design of environmental-friendly solid acid and solid base catalysts has become an important research target. These materials have a lot of useful properties, for example, high versatility, easy treatment and work-up, mild experimental conditions, high yield and selectivity, they are inexpensive and often reusable. Hydrotalcites (HT), the anionic layered double hydroxides (LDHs) have potential application as

Keywords: Hydrotalcite; Henry reaction; 1,3-Dinitropropanes; Mechanism; Diastereoselectivity.
* Corresponding author. Tel.: +36 1 463 1414; fax: +36 1 463 3648; e-mail: zhell@mail.bme.hu

0040–4020/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.02.055



Scheme 1.

Table 1. Effect of solvent on the reaction between 3-nitrobenzaldehyde **1f** and nitromethane using non-activated Mg:Al 2:1 HT

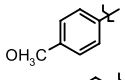
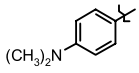
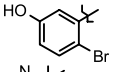
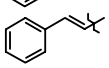
Entry	Solvent	Temperature (°C)	Time (h)	Conversion (%)[a]
1	Ethanol	20	1	46
2	Tetrahydrofuran	20	1	40
3	Nitromethane	20	1	65
4	Nitromethane	20	3.5	75
5	Nitromethane	20	5	95

[a] Determined by ^{1}H NMR, based on the starting aldehyde.

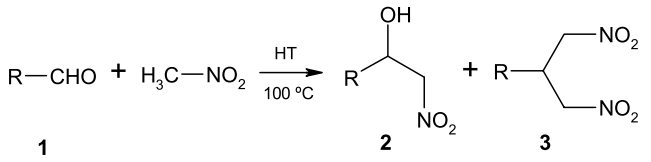
adsorbents, anion-exchangers and basic catalysts. These materials can be described by the formula $[M(II)_{(1-x)}M(III)_x(OH)_2]^{x+}(A^{m-}_{x/m})nH_2O$, where M(II) is a divalent ion like Mg, Cu, Ni, Co, Mn, Zn; M(III) is a trivalent ion like Al, Fe, Cr, Ga; A is the compensating anion like OH^-, Cl^-, NO_3^-, CO_3^{2-}, SO_4^{2-} and x is in the range of 0.1–0.33, closely resembles that of brucite, $Mg(OH)_2$. In HT a number of the divalent cations are replaced by trivalent cations, resulting in positively charged layers. Charge-balancing anions and water molecules are situated in the interlayers.[18] Numerous studies on their structure,[19] physical properties[20] and their catalytic activity have been reported, for example, in Michael addition,[21] Knoevenagel condensation,[22] or Meerwein–Ponndorf–Verley reduction.[23]

In this paper, we present the development of an eco-friendly, simple and convenient, catalytic diastereoselective method for the synthesis of 2-nitroalkanols from nitroalkanes and aldehydes, catalyzed by commercially available Mg:Al 2:1 hydrotalcite. Our research target was to

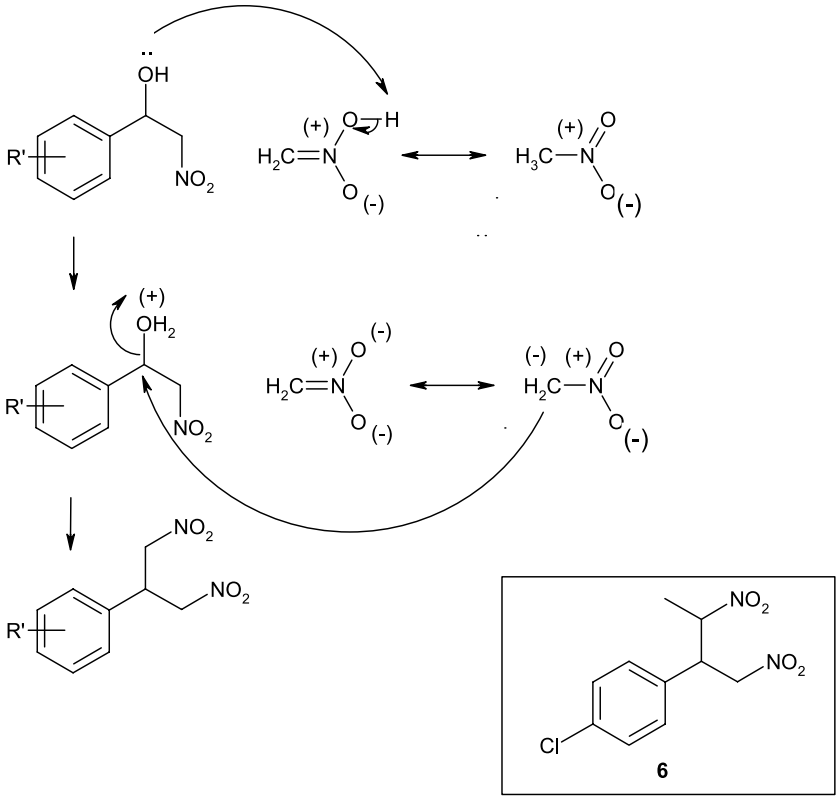
Table 2. Henry reaction between various aldehydes and nitromethane using Mg:Al 2:1 HT

2	R	Temperature (°C)	Time (h)	Conversion[a] (%)[b]
2a[27]		20	5	80 (74)[b]
2b		20	5	100 (91)[b]
2c		20	5	100 (95)[b]
2d		20	5	30
		100	5	8
2e[28]		20	5	70 (62)[b]
2f[29]		20	5	100 (95)[b] (94)[c]
2g[30]		20	5	60 (54)[b]
2h[15]		20	5	86 (80)[b]
2i[31]		20	5	43
2j[29]		20	5	8
		20	10	8
2k		20	5	47
2l[27]		20	5	100 (94)[b]
2m[30]		20	5	10
2n[32]		20	5	52
2o[32]	CH_3	20	5	(67)[b]
2p[27]	CH_3–CH_2	20	5	(90)[b]
2q[32]	$(CH_3)_3$–C	20	5	40

[a] Determined by ^{1}H NMR, based on the starting aldehyde.
[b] Isolated yield in parenthesis.
[c] Isolated yield after third cycle.



Scheme 2.



Scheme 3.

investigate the catalytic activity of this type of hydrotalcite, which does not need inert atmosphere, can be easily handled and does not require high-temperature pretreatment or long procedures like rehydration to be activated.

2. Results and discussion

Based on the data provided by the manufacturer the commercial Mg:Al 2:1 hydrotalcite (HAS-type) has the molecular formula $[Mg_4Al_2(OH)_{12}]CO_3$, its specific surface (BET) is 80 m^2/g, and the pH of its 5% suspension (filtered) is 8.6. The elemental analysis of the product dried at 110 °C for 2 h gave Al_2O_3 20.5%, MgO 33.8%, CO_2 11.0%, $Cl^- < 0.1\%$, $SO_4^{2-} < 0.1\%$, $Na^+ < 0.5\%$.

To our best knowledge until now only patents had published the use of these materials as catalysts for some polymerisation reactions.[24,25] Recently we described the synthesis of 4-hydroxyaryl piperidinols from bis-Mannich bases using this catalyst.[26]

First, we examined the reaction of 3-nitrobenzaldehyde and nitromethane (Scheme 1) in the presence of the catalyst (6 mol%).

The reaction was carried out at room temperature in ethanol, tetrahydrofuran, and nitromethane (Table 1). In the first two cases (entries 1, 2), the conversions were rather similar. Not surprisingly the use of nitromethane as solvent (20 mol equiv) gave the best results. Increasing the reaction time led to significant increase in the conversion (see entries 4 and 5). Without HT no reaction was observed.

We investigated the reactivity of a variety of aldehydes under the same reaction conditions as for **1f**, and the appropriate 2-nitroalcohols **2** were generally obtained in good to excellent yield. The results are summarized in Table 2. Compounds **2b**,**c**,**d**,**k** have not been described in the literature yet. Their structures were confirmed by their spectroscopic data and elemental analysis (see Section 4). The derivatives of benzaldehydes bearing electron-withdrawing groups **1b**,**c**,**f** and pyridine-2-carbaldehyde **1 l** were more reactive, giving 100% conversion, than those with electron-donating groups **1d**,**g**,**i**,**j**. Especially with salicylaldehyde **1d** and *p*-dimethylaminobenzaldehyde **1j** the conversions were very low, even after modification of the reaction conditions like reaction temperature, or reaction time, respectively.

Reaction of salicylaldehyde **1d** with nitromethane in the presence of HT at 100 °C for 5 h gave a reaction mixture of the nitroalcohol and an unknown product in a ratio of 3:1. This was separated by column chromatography, using

dichloromethane as eluent, yielding a dark yellow solid. The mass spectrometry showed that the new product was the 1,3-dinitro-compound **3a**. The ^{1}H and ^{13}C NMR spectra also confirmed this structure. Repetition of this reaction in boiling toluene with 1 equiv of nitromethane gave the same product mixture.

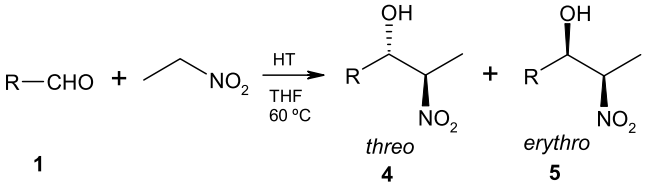
Some related 1,3-dinitro-compounds have already been described in the literature.[33–36] The mechanism of their formation was assumed to be a three-step base-catalysed reaction as follows: (1) nitroaldol addition to form the nitroalcohol; (2) dehydration of this to give the corresponding nitrostyrene; (3) Michael-addition of nitromethane to the nitrostyrene.[33,35] However, during our synthesis we could not isolate the nitrostyrene or even detect its formation. This is in good agreement with the statements in the literature that hydrotalcites are usually unable to induce dehydration in aldol-type reactions, and with the results reported by Choudary et al.[15,39] for the Henry reaction (Scheme 2).

When the pure Henry-product **2h** was heated in boiling toluene in the presence of HT, no formation of the appropriate nitrostyrene was detected, the starting material could be recovered.

In addition, reacting the pure 3,β-dinitro-styrene (prepared by the traditional NaOH/methanol method) with nitromethane in the presence of HT in boiling nitromethane, the conversion was quite slow, we observed the total consumption of the styrene only after 3 h boiling.

If the formation of the 1,3-dinitro-compound had occurred via the nitrostyrene and the formation of this latter had been so slow, we should have detected the formation of the nitrostyrene either by TLC of the reaction mixture or by NMR. This means that in the case of HT, another mechanism for the formation of the 1,3-dinitro-compounds should be supposed. Since nitromethane has a tautomeric *aci* form (Scheme 3) this could protonate the Henry-product, this protonation would be followed by the loss of water and the cation thus formed would be attacked by the anion of nitromethane. Scheme 3 shows this supposed reaction pathway. For the verification of this hypothesis we reacted **2h** with nitroethane at 100 °C for 5 h. ^{1}H NMR investigation of the crude reaction product showed the presence of the appropriate dinitro compound **6** (ca. 30%, Scheme 3) and no nitrostyrene. The reaction was quite slow but this can be explained with the lower pK_a value of nitroethane than nitromethane (8.456 and 10.211 at 25 °C, respectively[37]).

When nitroethane was used, the nitroaldol addition of various aldehydes (Scheme 4) in THF as solvent at 60 °C in the presence of catalytic amount of Mg:Al HT (2:1) (6 mol%) gave the corresponding nitroalcohols in good yields within 6.5 h (Table 3).



Scheme 4.

The reaction can be applied both to aromatic and aliphatic aldehydes. The highest diastereoselectivity was obtained with *ortho*-substituted aldehydes **1b**,**c**,**d** and with pyridine-2-carbaldehyde **1h**. The *threo*/*erythro* diastereoselectivity was determined by ^{1}H NMR spectroscopy. In their ^{1}H NMR spectra the extent of vicinal coupling constants of the products between the α-N–C–H and the α-O–C–H verify the formation of isomers. In the case of *threo* isomers $J=7$–9 Hz, and *erythro* isomers $J=3.2$–4 Hz.[38] In some cases we obtained an excess of the *erythro*-isomer. It is interesting to note the significant difference in the diastereoselectivity for *ortho*-chlorobenzaldehyde with nitroethane compared with the data reported by Bulbule et al.,[38] where 100% *threo* isomer was obtained.

In these reactions none of the appropriate 1,3-dinitro compounds were observed. This can be explained with the lower reaction temperature and the use of THF as solvent, since in this case a small excess of nitroethane was used. In the experiments with nitromethane the 1,3-dinitro compounds were not observed if a solvent other than nitromethane was used.

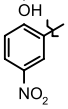
The catalyst was recovered from the reaction mixture by simple filtration, washed with nitromethane and treated at 120 °C for 1 h. This could be successfully reused under the above-reported conditions. These results show that Mg:Al 2:1 hydrotalcite was reusable for three cycles without loss of activity (Table 2, **2f**).

Table 3. Reaction of nitromethane and aldehydes with Mg:Al 2:1 HT at 100 °C

3	R	Conversion (%)	Time (h)	Yield of **3** (%)[a]
3a		30	5	10
3b		70	5	20
3c		100	5	20

[a] Determined by ^{1}H NMR.

Table 4. Diastereoselective synthesis of 2-nitroalcohols catalysed by Mg:Al 2:1 HT

4	R	Temperature (°C)	Conversion[a] (%)[b]	*Erythro–threo*[c] (%)
4a[38]		60	62	40:60
4b[38]		60	86	66:34
4c		60	85	70:30
4d		60	32	70:30
4e		60	57	30:70
4f[38]		60	(81)[b]	50:50
4g[31]		60	60	45:55
4h[40]		60	100 (95)[b]	65:35
4i[41]	CH_3	20	(64)[b]	47:53
4j[42]	CH_3–CH_2	60	(92)[b]	48:52

[a] Determined by ^{1}H NMR, based on the starting aldehyde.
[b] Isolated yield in parenthesis.
[c] Calculated by ^{1}H NMR.

3. Conclusion

In summary, we have shown that commercially available non-activated Mg:Al 2:1 hydrotalcite is a highly efficient basic catalyst for the Henry reaction. In the reaction with nitromethane at room temperature we obtained only 2-nitroalcohols in good to excellent yields. By increasing the temperature to 100 °C 1,3-dinitro compounds were obtained. The advantages of our method developed are the following: the reaction is eco-friendly since it minimises harmful reagents; the experimental and work-up procedure is very simple; the catalyst does not require any complicated pre-treatment and is recyclable, and this method realises a new application for the commercial HT product.

4. Experimental

4.1. General

Commercially available starting materials were used without further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avanche 300 (300 MHz) and Bruker Avance DRX-500 (500 MHz) spectrometer using TMS as internal standard. Melting points were determined on Gallenkamp apparatus and were uncorrected. IR spectra were recorded on a Perkin–Elmer Model 1600 instrument. TLC was performed on Merck Kieselgel plates (60 F_{254}) with an eluent: hexane–acetone 4:1. Column chromatography was carried out on Merck Kieselgel 60–240 mesh using dichloromethane as eluent. The spectral and physical data of the known compounds were identical with those reported in the literature (for references see Tables 2 and 4). The new compounds gave satisfactory elemental analysis.

4.2. Characterization of hydrotalcite

The Mg:Al 2:1 hydrotalcite was the commercially product of Süd-Chemie AG, München (HSA-type). The catalyst was dried at 120 °C for 1 h before use.

The presence of the pure hydrotalcite structure was confirmed by XRD pattern, and by thermogravimetry. The XRD pattern of the HT sample exhibits the characteristic reflections corresponding to a ordered-crystalline layered structure (Fig. 1).[16] From the (003) reflection ($2\Theta = 11.46°$) we calculated the 7.72 Å basal interlayer spacing. Correspondingly, from the (110) reflection ($2\Theta = 60.41°$) the brucite-like layer thickness is 3.06 Å.

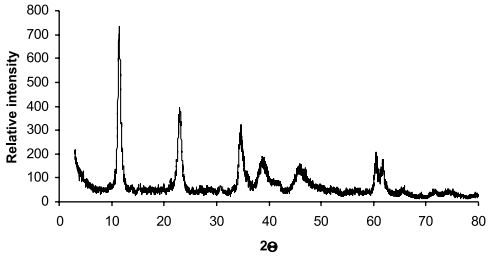


Figure 1.

X-ray diffraction (XRD) pattern was recorded on Philips PW 1050/81 instrument with Cu Kα_1 radiation (λ = 1.54184 Å) equipped with EVA Diffract-AT (Siemens Socabim) software. The samples were step-scanned in steps of 0.02° (2Θ) in the range from 3 to 70°. Thermogravimetric measurements (TG) were performed using Setaram Labsys TG equipment (Setaram, France) with 10.9 mg test material at a heating rate of 10 K min^{-1} in the temperature range 20–700 °C in nitrogen atmosphere. The

parameters obtained corresponded to those reported in the literature.[15]

4.3. General procedure for the Henry reaction of nitromethane and various aldehydes

A mixture of the aldehyde (5 mmol) and hydrotalcite (0.13 g) in nitromethane (5.6 ml, 0.1 mol) was stirred at room temperature for 5 h. The catalyst was filtered off and washed with nitromethane (3 ml). The filtrate was evaporated, and the residue, if necessary, was washed with saturated aq $NaHSO_3$ (2×10 ml). The organic phase was dried over anhydrous $MgSO_4$ and concentrated to give the corresponding nitroalcohol derivative. The known products were characterized by comparing the ^1H NMR and melting point data with those reported in the literature (for references see Table 2).

4.4. Spectral data of the new compounds

4.4.1. 1-(2-Chlorophenyl)-2-nitro-ethanol (2b). 0.92 g (91%), yellow oil, IR (neat): 1377, 1555, 3530 ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.35 (1H, br s, OH), 4.43 (1H, dd, $J_1=2$ Hz, $J_2=9$ Hz, CH_2), 4.64 (1H, dd, $J_1=2$ Hz, $J_2=11.5$ Hz, CH_2), 5.81 (1H, d, $J=9.5$ Hz, *CH*OH), 7.26–7.39 (3H, m, Ph), 7.62–7.63 (1H, m, Ph). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 71.2, 86.3, 127.9, 128.5, 130.7, 131.1, 132.7, 136.5. MS (EI): *m/z* (%) 201 (M^+, 5), 185 (7), 183 (21), 156 (8), 154 (24), 143 (100), 141 (33), 110 (26). $C_8H_8NO_3Cl$. Anal. Calcd C 47.64, H 6.95, N 3.98. Found C 47.86, H 7.06, N 4.07.

4.4.2. 1-(2-Bromophenyl)-2-nitro-ethanol (2c). 1.17 g (95%), yellow oil, IR (neat): 1368, 1550, 3511 ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.12 (1H, br s, OH), 4.45 (1H, dd, $J_1=3.5$ Hz, $J_2=9.5$ Hz, CH_2), 4.67 (1H, dd, $J_1=2.5$ Hz, $J_2=11.5$ Hz, CH_2), 5.81 (1H, d, $J=9.5$ Hz, *CH*OH), 7.21–7.26 (1H, m, Ph), 7.38–7.41 (1H, m, Ph), 7.56–7.61 (1H, m, Ph), 7.65–7.68 (1H, m, Ph). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 71.4, 87.2, 128.1, 128.8, 130.9, 131.4, 132.9, 137.1. MS (EI): *m/z* (%) 246 (M^+, 2), 230 (8), 228 (7), 200 (6), 198 (6), 185 (14), 183 (14), 156 (100). $C_8H_8NO_3Br$. Anal. Calcd C 38.95, H 3.25, N 5.68. Found C 39.09, H 3.41, N 5.73.

4.4.3. 1-(2-Hydroxyphenyl)-2-nitro-ethanol (2d). 0.27 g (30%), yellow oil, IR (neat): 1382, 1558, 3528 ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.31 (1H, s, OH), 4.61 (1H, dd, $J_1=3$ Hz, $J_2=10.5$ Hz, CH_2), 4.76 (1H, dd, $J_1=3$ Hz, $J_2=10$ Hz, CH_2), 5.61 (1H, d, $J=9.5$ Hz, *CH*OH), 6.98–7.04 (2H, m, Ph), 7.5–7.57 (2H, m, Ph), 11.02 (1H, s, Ph*OH*). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 70.9, 84.5, 127.4, 128.4, 128.9, 130.6, 131.1, 135.4. MS (EI): *m/z* (%) 183 (M^+, 2), 165 (7), 136 (15), 123 (100), 93 (10). $C_8H_9NO_4$. Anal. Calcd C 52.46, H 7.65, N 4.92. Found C 52.63, H 7.78, N 5.06.

4.4.4. 1-(2-Hydroxy-5-bromophenyl)-2-nitro-ethanol (2k). 0.66 g (47%), yellow oil, IR (neat): 1382, 1557, 3518 ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.61 (1H, br s, OH), 4.59 (1H, dd, $J_1=3$ Hz, $J_2=10.5$ Hz, CH_2), 4.71 (1H, dd, $J_1=3$ Hz, $J_2=10$ Hz, CH_2), 5.59 (1H, d, $J=10$ Hz, *CH*OH), 6.69 (1H, d, $J=9$ Hz, Ph), 7.32–7.36 (1H, m, Ph), 7.65–7.69 (1H, d, $J=2$ Hz, Ph), 10.93 (1H, s, Ph*OH*). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 71.2, 88.1, 127.8, 128.5, 130.1, 130.8, 132.9, 136.4. MS (EI): *m/z* (%) 279 (M^+, 5), 261 (6), 232 (15), 214 (21), 172 (36). $C_8H_8NO_4Br$. Anal. Calcd C 36.64, H 5.34, N 3.05. Found C 36.87, H 5.29, N 3.16.

4.5. General procedure for the reaction of nitroethane and various aldehydes

A mixture of the aldehyde (5 mmol) and nitroethane (6 mmol) with hydrotalcite (0.13 g) in THF (10 ml) was stirred at 60 °C for 6.5 h. Then the catalyst was filtered off and washed with THF (3 ml). The filtrate was evaporated, and the residue, if necessary, was washed with saturated aq $NaHSO_3$ (2×10 ml). The organic phase was dried over anhydrous $MgSO_4$ and concentrated to give the corresponding nitroalcohol derivative. The *threo*/*erythro* diastereoselectivity of the products was determined by ^1H NMR spectroscopy based on the vicinal coupling constants of the products between the α-N–C–H and the α-O–C–H (see Table 4). The known products were characterized by comparing the ^1H NMR and melting points data with those reported in the literature (for references see Table 4).

4.6. Spectral data of the new compounds

4.6.1. 1-(2-Bromophenyl)-2-nitro-propan-1-ol (4c). 1.11 g (85%), yellow oil, IR (neat): 1372, 1548, 3520 ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.45 (3H, d, $J=6.6$ Hz, CH_3), 1.47 (3H, d, $J=6.3$ Hz, CH_3), 3.23 (1H, br s, OH), 4.9 (1H, m, *CH*CH_3), 5.6 (1H, d, $J=8.4$ Hz, *threo-CH*OH), 5.81 (1H, d, $J=4.4$ Hz, *erythro-CH*OH), 7.28–7.64 (3H, m, Ph), 7.9 (1H, m, Ph). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 16.1, 72.5, 73.9, 84.0, 88.3, 127.2, 128.2, 130.3, 132.1, 133.3, 137.5. MS (EI): *m/z* (%) 260 (M^+, 2), 243 (21), 213 (15), 196 (100), 186 (29), 155 (44). $C_9H_{10}NO_3Br$. Anal. Calcd C 41.54, H 3.80, N 5.38. Found C 41.82, H 3.95, N 5.56.

4.6.2. 1-(2-Fluorophenyl)-2-nitro-propan-1-ol (4d). 0.32 g (32%), yellow oil, IR (neat): 1366, 1540, 3540 ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.38 (3H, d, $J=6.9$ Hz, CH_3), 1.47 (3H, d, $J=6.9$ Hz, CH_3), 3.97 (1H, m, OH), 4.84 (1H, m, *CH*CH_3), 5.42 (1H, d, $J=9.1$ Hz, *threo-CH*OH), 5.74 (1H, d, $J=3.3$ Hz, *erythro-CH*OH), 7.11–7.61 (3H, m, Ph), 7.85 (1H, m, Ph). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 16.3, 73.1, 74.6, 87.8, 88.9, 128.2, 128.9, 131.4, 131.7, 133.1, 137.8. MS (EI): *m/z* (%) 199 (M^+, 5), 181 (20), 152 (100), 134 (38), 125 (28), 95 (10). $C_9H_{10}NO_3F$. Anal. Calcd C 54.27, H 5.03, N 7.04. Found C 54.49, H 5.26, N 6.96.

4.6.3. 1-(3-Hydroxyphenyl)-2-nitro-propan-1-ol (4e). 0.56 g (57%), yellow oil, IR (neat): 1352, 1522, 3532 ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.31 (3H, d, $J=6.6$ Hz, CH_3), 1.48 (3H, d, $J=6.6$ Hz, CH_3), 3.49 (1H, m, OH), 4.71 (1H, m, *CH*CH_3), 4.95 (1H, d, $J=9$ Hz, *threo-CH*OH), 5.34 (1H, d, $J=3.6$ Hz, *erythro-CH*OH), 6.77–7.12 (4H, m, Ph). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 16.4, 73.3, 75.3, 87.6, 88.2, 122.1, 124.1, 130.4, 131.8, 133.4, 137.5. MS (EI): *m/z* (%) 197 (M^+, 2), 179 (5), 132 (15), 123 (68), 121 (100), 105 (15), 93 (10). $C_9H_{11}NO_4$. Anal. Calcd C 54.82, H 5.58, N 7.11. Found C 54.99, H 5.72, N 7.38.

4.7. General procedure for the synthesis of 1,3-dinitro compounds

A mixture of the aldehyde (5 mmol) and hydrotalcite (0.13 g) in nitromethane (5.6 ml, 0.1 mol) was stirred at 100 °C for 5 h. Then the catalyst was filtered off and washed with nitromethane (3 ml). The solvent was evaporated, the residue was purified by column chromatography (eluent: dichloromethane) to give the new compounds.

4.7.1. 2-(2-Hydroxyphenyl)-1,3-dinitro-propane (3a). 0.34 g (30%), dark yellow oil, IR (neat): 1380, 1556, 3482 ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.37–4.45 (1H, m, CH), 4.83–4.88 (4H, m, CH_2), 5.91 (1H, br s, OH), 6.73 (1H, d, $J=7.8$ Hz, Ph), 6.85–6.90 (1H, m, Ph), 7.10–7.19 (2H, m, Ph). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 40.3, 76.6, 111.9, 125.2, 128.1, 131.5, 132.0, 154.4. MS (EI): *m/z* (%) 226 (M^+, 10), 210 (12), 192 (15), 162 (5), 150 (29), 149 (83), 117 (6), 77 (20), 60 (4). $C_9H_{10}N_2O_5$. Anal. Calcd C 47.79, H 4.42, N 12.39. Found C 47.25, H 4.11, N 12.09.

4.7.2. 2-(4-Chlorophenyl)-1,3-dinitro-propane (3b). 0.86 g (70%), yellow oil, IR (neat): 1374, 1548 ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.30–4.35 (1H, m, CH), 4.74–4.78 (4H, m, CH_2), 7.18 (2H, d, $J=6.3$ Hz, Ph), 7.35 (2H, d, $J=8.4$ Hz, Ph). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 41.2, 76.6, 128.8, 129.9, 130.3, 135.3. MS (EI): *m/z* (%) 244 (M^+, 15), 197 (30), 151 (38), 137 (41), 125 (27), 115 (100), 112 (10), 89 (16), 77 (22). $C_9H_9N_2O_4Cl$. Anal. Calcd C 44.17, H 3.68, N 11.45. Found C 43.87, H 3.32, N 11.09.

4.7.3. 2-(3-Nitrophenyl)-1,3-dinitro-propane (3c). 1.28 g (100%), dark yellow oil, IR (neat): 1365, 1584 ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.52–4.55 (1H, m, CH), 4.89–4.93 (4H, m, CH_2), 7.62–7.66 (1H, m, Ph), 7.76–7.79 (1H, m, Ph), 8.17–8.20 (1H, m, Ph), 8.20–8.24 (1H, s, Ph). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 40.8, 77.3, 124.4, 128.6, 130.4, 134.8, 137.5, 148.79. $C_9H_9N_3O_6$. Anal. Calcd C 42.35, H 3.53, N 16.47. Found C 42.02, H 3.23, N 16.11.

Acknowledgements

The financial support of the Hungarian Scientific Research Fund (OTKA T-037757) is gratefully acknowledged. This publication was prepared within the framework of the Hungarian-French intergovernmental scientific and technological cooperation, TéT project No. F-8/02.

References and notes

1. Luzzio, F. A. *Tetrahedron* **2001**, *57*, 915.
2. Sasai, H.; Itoh, N.; Suzuki, T.; Shibasaki, M. *Tetrahedron Lett.* **1993**, *34*, 855.
3. Sasai, H.; Yamada, Y. M. A.; Suzuki, T.; Shibasaki, M. *Tetrahedron* **1994**, *50*, 12313.
4. Sakanaka, O.; Ohmorti, T.; Kazaki, S.; Suami, T.; Ishii, T.; Ohba, S.; Saito, Y. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1753.
5. Suami, T.; Sasai, H.; Matsuno, K. *Chem. Lett.* **1983**, 819.
6. Ballini, R. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1419.
7. Heffner, R. J.; Jiang, J.; Jouillié, M. M. *J. Am. Chem. Soc.* **1992**, *114*, 10181.
8. Mikite, G.; Jakucs, K.; Darvas, F.; Lopata, A. *Pestic. Sci.* **1982**, *13*, 557.
9. Risgaard, T.; Gothelf, K. V.; Jorgersen, K. A. *Org. Biomol. Chem.* **2003**, *1*, 153.
10. Evans, D. A.; Seidel, D.; Rueping, M.; Lam, H. W.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2003**, *125*, 12692.
11. Ballini, R.; Bosica, G.; Forconi, P. *Tetrahedron* **1996**, *52*, 1677.
12. Bulbule, V. J.; Jnaneshwara, G. K.; Deshmukh, R. R.; Borate, H. B.; Deshpande, V. H. *Synth. Commun.* **2001**, *31*, 3623.
13. Kiyooka, S. I.; Tsutsui, T.; Maeda, H.; Kaneko, Y.; Isobe, K. *Tetrahedron Lett.* **1995**, *36*, 6531.
14. Kisanga, P. B.; Verkade, J. G. *J. Org. Chem.* **1999**, *64*, 4298.
15. Choudary, B. M.; Kantam, M. L.; Kavita, B. *J. Mol. Catal. A* **2001**, *169*, 193.
16. Sasai, H.; Suzuki, T.; Arai, S.; Shibasaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 4418.
17. Chinchilla, R.; Najera, C.; Sánchez-Agulló, P. *Tetrahedron: Asymmetry* **1994**, *5*, 1393.
18. Cavani, F.; Trifiro, F.; Vaccari, A. *Catal. Today* **1991**, *11*, 173.
19. Reichle, W. T. *Chemtech* **1986**, *1*, 58.
20. Tichit, D.; Lhouty, M. H.; Guida, A.; Chiche, B. H.; Figueras, F.; Auroux, A.; Bartalini, D.; Garrone, E. *J. Catal.* **1995**, *151*, 50.
21. Choudary, B. M.; Kantam, M. L.; Reddy, Ch. R. V.; Rao, K. K.; Figueras, F. *J. Mol. Catal. A* **1999**, *146*, 279.
22. Choudary, B. M.; Kantam, M. L.; Kavita, B.; Reddy, Ch. K.; Rao, K. K.; Figueras, F. *Tetrahedron Lett.* **1998**, *39*, 3555.
23. Kumbhar, P. S.; Sanchez-Valente, J.; Lopez, J.; Figueras, F. *Chem. Commun.* **1998**, 535.
24. Staeuber, H.; Voerckel, V.; Wiegner, J.-P. PCT Int. Appl. 2003, Pat. Appl. No. WO 2002-US18991.
25. Takushima, T.; Takamoto, Y.; Tenra, T.; Miyaji, N. Jpn. Kokai Tokkyo Koho 1999, Pat. Appl. No. Jp. 1997-300161.
26. Cwik, A.; Fuchs, A.; Hell, Z.; Clacens, J.-M. *J. Mol. Catal. A* **2004**, *219*, 377.
27. Meyers, A. I.; Sircar, J. C. *J. Org. Chem.* **1967**, *32*, 413.
28. Kamlet, 1938, US 2151517.
29. Boileau, J. *Bull. Soc. Chim. Fr.* **1953**, 1007.
30. Youn, S. W.; Kim, Y. H. *Synth. Lett.* **2000**, *6*, 880.
31. Bailey, K. *Tetrahedron* **1972**, *28*, 3981.
32. Lucet, D.; Sabelle, S.; Kostelitz, O.; Le Gall, T.; Mioskowski, Ch. *Eur. J. Org. Chem.* **1999**, *10*, 2583.
33. Lambert, A.; Lowe, A. *J. Chem. Soc.* **1947**, 1517.
34. Alcantara, M. D.; Escribano, F. C.; Gomez-Sanchez, A.; Dianez, M. J.; Estrada, M. B.; Castro, A. L.; Perez-Garrido, S. *Synthesis* **1996**, *1*, 64.
35. Niazimbetova, Z. I.; Evans, D. H.; Liable-Sands, L. M.; Rheingold, A. L. *J. Electrochem. Soc.* **2000**, *147*, 256.
36. Ferro, A.; Rezende, M. C.; Sepulveda-Boza, S.; Reyes-Parada, M.; Cassels, B. K. *J. Chem. Res.* **2001**, *7*, 294.
37. Turnbull, D.; Maron, S. H. *J. Am. Chem. Soc.* **1943**, *65*, 212.
38. Bulbule, V. J.; Deshpande, V. H.; Velu, S.; Sudalai, A.; Sivasankar, S.; Sathe, V. T. *Tetrahedron* **1999**, *55*, 9325.
39. Choudary, B. M.; Kantam, M. L.; Reddy, Ch. V.; Rao, K. K.; Figueras, F. *Green Chem.* **1999**, 187.
40. Hunt, R. G.; Reid, S. T. *J. Chem. Soc. Perkin Trans. 1* **1977**, *22*, 2462.
41. Chen, Q.; Wang, T.; Zhang, Y.; Wang, Q.; Ma, J. *Synth. Commun.* **2002**, *32*, 1031.
42. Rosini, G.; Ballini, R.; Sorrenti, P. *Synthesis* **1983**, *12*, 1014.