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Selective Nitroaldol Condensations over Heterogeneous Catalysts in the Presence of Supercritical Carbon Dioxide

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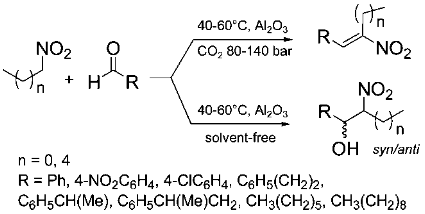
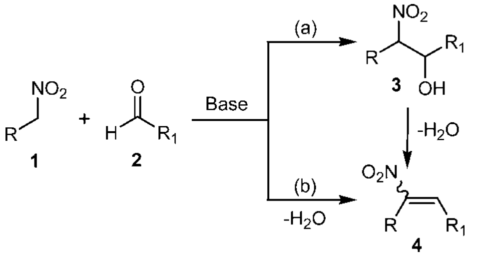


At 40−60 °C, in the presence of heterogeneous catalysts based on Al_2O_3, supercritical carbon dioxide not only acts as a good solvent for the reaction of aromatic and aliphatic aldehydes with 1-nitroalkanes but, most importantly, it also allows the selectivity to be tuned between the competitive formation of β-nitroalcohols and nitroalkenes (from the Henry reaction and the nitroaldol condensation, respectively). In particular, when the pressure (and the density) of the supercritical phase is enhanced from 80 to 140 bar, the nitroalkene's selectivity increases, on average, from ~60 to >90%. Experiments show that, in the same pressure range, a steep increase of the concentration profiles of reactant aldehydes takes place. By contrast, under solvent-free conditions, the reaction usually proceeds with a higher conversion, but nitroalkanols are the major products.

Introduction

The reaction of nitroalkanes with carbonyl derivatives is among the key synthetic tools for the construction of carbon−carbon bonds in organic chemistry.[1] The reaction is typically carried out under basic conditions, to allow the formation of β-nitroalkanols. However, when primary nitroalkanes (**1**) are involved, two competitive processes may occur (Scheme 1): the formation of (i) nitroalkanols (**3**, path a) through the so-called nitroaldol−Henry reaction and of (ii) conjugated nitroalkenes (**4**, path b) via the nitroaldol condensation.

SCHEME 1



Both products **3** and **4** are of great synthetic interest. β-Nitroalcohols undergo a variety of chemical transformations for the synthesis of β-aminoalkanols, α-hydroxyketones, α-nitroketones, and other synthetic intermediates,[1,2] while nitroalkenes are good Michael acceptors and dienophiles in Diels−Alder reactions,[3] as well as versatile starting materials to prepare different functionalities.[1c,3,4] Compounds **4** are also recognized for their biological activity.[5]

In the most classical arrangement, the nitroaldol reactions are performed under homogeneous conditions, in the presence

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(1) (a) Rosini, G. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1999; Vol. 1. (b) Luzzio, F. A. *Tetrahedron* **2001**, *57*, 915–945. (c) Ono, N. In *The Nitro Group in Organic Synthesis*; Feuer, H., Ed.; Wiley-VCH: New York, 2001.

(2) Ballini, R.; Bosica, G.; Fiorini, D.; Palmieri, A. *Tetrahedron* **2005**, *61*, 8971–8993.

(3) (a) Kabalka, G. W.; Guindi, L. H. M.; Varma, R. S. *Tetrahedron* **1990**, *46*, 7443–7457. (b) Barret, A. G. M. *Chem. Soc. Rev.* **1991**, *20*, 95–127. (c) Barrett, A. G. M.; Graboski, G. G. *Chem. Rev.* **1986**, *86*, 751–762. (d) Perekalin, V. V.; Lipina, E. S.; Berestovitskaya, V. M.; Efremov, D. A. *Nitroalkenes*; John Wiley & Sons: Chichester, UK, 1994.

(4) Ballini, R.; Bosica, G. *Synthesis* **1994**, 723–726.

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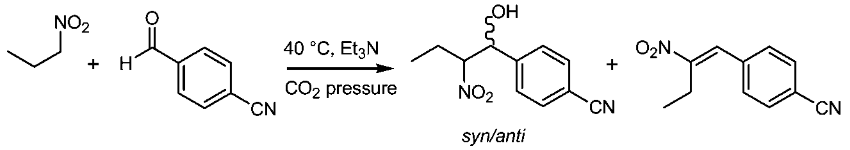
SCHEME 2



of a base catalyst in an organic solvent. Alternatively, heterogeneous catalysts have been introduced which allow for solvent-free synthesis.[6] Whatever the methodology, the selective formation of β-nitroalkanols or of conjugate nitroalkenes very often requires a careful choice of reaction parameters (temperature, reaction time, basic strength of catalyst, etc.). Particularly, the preparation of nitroalkenes, which usually needs stronger conditions,[1,4] implies multistep procedures.

As a part of our research program on eco-friendly carbon−carbon bond forming methodologies,[7] we decided to investigate the activity and, most of all, the selectivity of nitroaldol reactions/condensations in the presence of supercritical carbon dioxide as the solvent. This is a largely unexplored area: to the best of our knowledge, only one recent paper has been reported on the reaction of *p*-cyanobenzaldehyde with 1-nitropropane carried out at 40 °C, under different CO_2 pressures, including the subcritical state (Scheme 2).[8]

The use of supercritical CO_2 ($scCO_2$) was claimed to induce a dramatic shift of the stereoselectivity of the Henry reaction, with respect to the *syn/anti* ratio usually observed in more conventional conditions (solventless, toluene, or MeCN as solvents). All tests were referred to a homogeneous catalyst such as Et_3N.[9] Supercritical CO_2, however, due to the low viscosity (η) and the high diffusivity (D) (0.01−0.03 mPa·s and ~0.07 $\times$ 10^{-6} m^2 s^{-1}, respectively),[10] is very efficient at penetrating meso- and microporous structures which are typical of the conventional supports used in the heterogeneous catalysis. Mostly for this reason, the use of $scCO_2$ as a solvent/carrier is reported to improve the mass transfer (and the reaction rate/selectivity) of a variety of different processes, including alkylations,[10,11] etherifications and esterifications,[12] hydrogenations and hydroformylations,[13,14] and oxidations[15] catalyzed by zeolites, supported acids, and metals immobilized on organic/inorganic matrixes such as Deloxan, Amberlyst, alumina, and silica. It should be noted here that basic Al_2O_3 as such or mixed with KF is a convenient heterogeneous catalyst also for nitroaldol reactions.[16]

These observations in conjunction with our interest for green synthetic methods using $scCO_2$[17] have inspired the present work. We wish to report here that, in the presence of heterogeneous catalysts, preferably based on or supported on basic Al_2O_3, the reaction of aromatic and aliphatic aldehydes with both nitroethane and 1-nitrohexane takes place efficiently in dense carbon dioxide; even more intriguingly, the process is extremely selective toward the formation of the corresponding nitroalkenes (**4**; Scheme 1, path b). This study also provides good evidence that the reaction selectivity is tuned by the CO_2 pressure, and that the overall reaction outcome is strictly related to the trend of the solubility of aldehydes in the supercritical medium.

Results

Aromatic Aldehydes. Initial experiments were carried out using both benzaldehyde (**2a**) and 4-nitrobenzaldehyde (**2b**) as model substrates. The relative amounts of reactants and of the catalyst were chosen according to procedures already described by us.[2] A mixture of the aldehyde (**2a**: 152 μL, 1.5 mmol, or **2b**: 0.23 g, 1.5 mmol), RCH_2NO_2 (**1a**: R = CH_3, 130 μL, 1.8 mmol, or **1b**: R = $CH_3(CH_2)_4$, 260 μL, 1.8 mmol), and commercial basic Al_2O_3 (0.3−0.45 g) was charged in a 30 mL autoclave, which was then loaded with CO_2 at 100 bar. The reactor was electrically heated at the desired temperature (40 or 60 °C), and the mixture was kept under magnetic stirring. After 18 h, the autoclave was cooled to rt and slowly purged (1 h). The mixture was then analyzed by ^{1}H NMR, which showed products from both the Henry reaction and the nitroaldol condensation (Scheme 3).[18]

The same reactions were also performed under solvent-free conditions (*solFC*) in a conventional 5 mL glass reactor thermostatted by an oil bath.

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(5) (a) Brown, A. W. A.; Robinson, D. B. W.; Hurtig, H.; Wenner, B. J. *Can. J. Res.* **1948**, *26D*, 177–187. (b) Bousquet, E. W.; Kirby, J. E.; Searle, N. E. U.S. Patent 2,335,384, 1943, *38*, 2834; *Chem. Abstr.* 1944, *38*, 2834. (c) Brian, P. W.; Grove, J. F.; McGowan, J. C. *Nature* **1946**, *158*, 876–877. (d) McGowan, J. C.; Brian, P. W.; Hemming, H. G. *Ann. Appl. Biol.* **1948**, *35*, 25–36. (e) Bocobo, F. C.; Curtis, A. C.; Block, W. D.; Harrel, E. R.; Evans, E. E.; Haines, R. F. *Antibiot. Chemother.* **1956**, *6*, 385–390. (f) Schales, O.; Graefe, H. A. *J. Am. Chem. Soc.* **1952**, *74*, 4486–4490. (g) Dann, O.; Moller, F. F. *Chem. Ber.* **1949**, *82*, 76–92. (h) Karker, R. J. U.S. Patent 2,889,246, 1959; *Chem. Abstr.* 1959, *53*, 17414i. (i) Zee-Cheng, K.; Cheng, C. *J. Med. Chem.* **1969**, *12*, 157–161.

(6) Ballini, R.; Palmieri, A. *Curr. Org. Chem.* **2006**, *10*, 2145–2169.

(7) Project "*Ecofriendly organic syntheses mediated by new catalytic systems*" funded by MUR (Italian Ministry of Unversity and Research); grant # 2006031724_002.

(8) (a) Parratt, A. J.; Adams, D. J.; Clifford, A. A.; Rayner, C. M. *J. Chem. Soc., Chem. Commun.* **2004**, 2720–2721. (b) Rayner, C. M. *Org. Process Res. Dev.* **2007**, *11*, 121–132.

(9) Et_3N is very soluble in $scCO_2$: Jessop, P. G.; Hsiao, Y.; Ikariya, T.; Noiory, R. *J. Am. Chem. Soc.* **1996**, *118*, 344–355.

(10) (a) Gross, T.; Chen, L.; Lüdemann, H.-D. In *Supercritical Fluids as Solvents and Reaction Media*; Brunner, G., Ed.; Elsevier: Amsterdam, 2004; Chapter 2.1. (b) Baiker, A. *Chem. Rev.* **1999**, *99*, 453–473.

(11) Hitzler, M. G.; Smail, F. R.; Ross, S. K.; Poliakoff, M. *Chem. Commun.* **1998**, 359–360.

(12) (a) Gray, W. K.; Smail, F. R.; Hitzler, M. G.; Ross, S. K.; Poliakoff, M. *J. Am. Chem. Soc.* **1999**, *121*, 10711–10718. (b) Vieville, C.; Mouloungui, Z.; Gaset, A. *Ind. Eng. Chem. Res.* **1993**, *32*, 2065–2068.

(13) Hyde, J. R.; Licence, P.; Carter, D.; Poliakoff, M. *Appl. Catal. A* **2001**, *222*, 119–131.

(14) (a) Tadd, A. R.; Marteel, A.; Manson, M. R.; Davies, J. A.; Abraham, M. A. *Ind. Eng. Chem. Res.* **2002**, *41*, 4514–4522. (b) Marteel, A. E.; Tack, T. T.; Bektesevic, S.; Davies, J. A.; Manson, M. R.; Abraham, M. A. *Environ. Sci. Technol.* **2003**, *37*, 5424–5431.

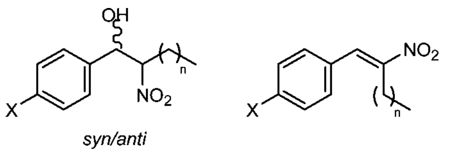
(15) Fan, L.; Watanabe, T.; Fujimoto, K. *Appl. Catal.* **1997**, *158*, L41−L46.

(16) Ballini, R.; Bosica, G.; Forconi, P. *Tetrahedron* **1996**, *52*, 1677–1684.

(17) (a) DeSimone, J.; Selva, M.; Tundo, P. *J. Org. Chem.* **2001**, *66*, 4047–4049. (b) Selva, M.; Tundo, P.; Perosa, A. *Tetrahedron Lett.* **2002**, *43*, 1217–1219. (c) Loris, A.; Perosa, A.; Selva, M.; Tundo, P. *J. Org. Chem.* **2003**, *68*, 4046–4051. (d) Selva, M.; Tundo, P.; Perosa, A.; Dall'Acqua, F. *J. Org. Chem.* **2005**, *70*, 2771–2777. (e) Tundo, P.; Loris, A.; Selva, M. *Green Chem.* **2007**, *9*, 777–779. (f) Maggi, R.; Bertolotti, C.; Orlandini, E.; Oro, C.; Sartori, G.; Selva, M. *Tetrahedron Lett.* **2007**, *48*, 2131–2134.

(18) Although many methods for the preparation of nitroalkenes are known, they generally produce (*E*)-nitroalkenes which are difficult to convert into the corresponding *Z*-isomers. At most, mixtures of the *E*- and *Z*-products are obtained, where (*Z*)-olefins are always minor products (see ref 3 and: (a) Knochel, P.; Seebach, D. *Synthesis* **1982**, 1017–1018. (b) Ono, N.; Kamimura, A.; Kawai, T.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1987**, 1550–1551. (c) Stanetty, P.; Kremslehner, M. *Tetrahedron Lett.* **1998**, *39*, 811–812. (d) Fioravanti, S.; Pellacani, L.; Tardella, P. A.; Vergari, M. C. *Org. Lett.* **2008**, *10*, 1449–1451. In Scheme 3, (*E*)-nitroolefins are indicated (characterization data are reported in Supporting Information).

SCHEME 3



X = H, n = 0:	**3a**	**4a**
X = H, n = 4:	**3a'**	**4a'**
X = NO2, n = 0:	**3b**	**4b**
X = NO2, n = 4:	**3b'**	**4b'**

Results are reported in Table 1.

Three main aspects were recognized from the analysis of Table 1: (i) At both 40 and 60 °C, conversions of both aldehydes (**2a**,**b**) were usually lower in supercritical CO_2 with respect to the solvent-free conditions (compare entries 1−2, 3−4, 5−6, 7−8, and 9−10). This difference substantially disappeared for reactions of 4-nitrobenzaldehyde at 60 °C that showed rather similar conversions (76−77%) regardless of the medium and of the nature of the nitroalkane (**1a** or **1b**) used (entries 11−14). On average, conversions were higher at 60 °C than at 40 °C.[19] (ii) Compound **2b** was more reactive than **2a**. Under the same conditions, the conversion of benzaldehyde was 1.5−3 times lower than that of 4-nitrobenzaldehyde (compare entries 1−4 to 9−12, and 7−8 to 13−14). (iii) The reaction selectivity (*S*%) toward nitroalkenes **4a**,**b′** was increased considerably when experiments were run under CO_2 pressure rather than in solvent-free conditions. Remarkable cases were observed for both aldehydes; for example, in the reaction of benzaldehyde, *S*% for compounds **4a**,**a′** went from 49 to 79% and from 55 to 92%, respectively (entries 3−4 and 7−8). Likewise, at comparable high conversions of 4-nitrobenzaldehyde (76−77%), the reaction selectivity (*S*% for compounds **4b**,**b′**) increased from 39 to 86% and from 36 to 62%, respectively (entries 11−12 and 13−14).

To continue the investigation, experimental conditions were set according to these preliminary results. In particular, to reach reasonably high conversions, a temperature of 60 °C[20] and the use of 1-nitroethane as the nucleophile were chosen. Other possible effects of supercritical CO_2 on the reaction selectivity were then analyzed.

Effect of CO_2 Pressure on Reactivity and Solubility of Aromatic Aldehydes. Supercritical carbon dioxide is often described as a tunable solvent;[21] in fact, its solvating ability is strictly related to its physicochemical properties (density and viscosity), which can be widely adjusted through small variations of pressure and temperature. For example, at 35 °C, the density and viscosity of CO_2 practically triple (d: from 0.28 to 0.81 g/mL, η: from 0.022 to 0.075 mPa·s) when the pressure is increased from 75 to 150 bar.[22]

Bearing this in mind, two sets of experiments were devised: (i) in the first, the reactions of aldehydes **2a**,**b** with nitroethane catalyzed by basic Al_2O_3 were examined at 60 °C in $scCO_2$ by varying the pressure of the supercritical phase over the range of 80−150 bar ($d_{CO_2} = 0.19−0.56$ g/mL); (ii) in the second, operating at the same temperature (60 °C) and within the same pressure interval, the concentration of both compounds **2a**,**b** in $scCO_2$ was measured. In particular, reactions were performed according to the procedure defined in Table 1. Concentration measurements were carried out in a 90 mL stainless steel autoclave equipped with a calibrated loop and needle valves for sample withdrawals; the reactor was loaded with the aldehyde (**2a**: 2.5 g; **2b**: 1.0 g) and CO_2 at 80 to 150 bar.[23]

The relatively low boiling point of nitroethane (114−115 °C) did not allow reproducible measures of its concentration in the supercritical medium. However, the visual inspection of mixtures of nitroethane/$scCO_2$[24] revealed that homogeneous solutions occurred at $P \geq 90$ bar.

Figures 1 and 2 report the result for benzaldedyde and 4-nitrobenzaldehyde, respectively. For a convenient comparison, each figure displays on a single plot the trend of aldehyde conversion and reaction selectivity (*S*% for nitroalkenes **4a**,**b′**) (black and red profiles) and of the molar concentration of aldehydes **2a**,**b** in $scCO_2$ (blue profile) versus the pressure of the supercritical phase. Data of reactions carried out under solvent-free conditions ($P_{CO_2} = 0$) are also indicated.

Results of Figures 1 and 2 confirmed the data of Table 1. For both reactions, the increase of the CO_2 pressure had opposite effects on the conversion of aldehydes and on the selectivity: the first (conversion) always dropped, while the formation of products **4a**,**b** became more and more favored.

This was particularly manifest for benzaldehyde (Figure 1); as the pressure was increased from 80 to 140 bar, the substrate conversion decreased from 55 to 25% (black curve). At the same time, the selectivity of the nitroaldol condensation (compound **4a**) was dramatically improved from 50 to 92% (red curve).[25] It should be noted that, in the same pressure range, the molar concentration of benzaldehyde dissolved in $scCO_2$ increased by nearly 11-fold (blue curve), and at 140 bar, it approximated the experimental limit value (0.26 M).[23]

In the case of 4-nitrobenzaldehyde (**2b**, Figure 2), the increase of the CO_2 pressure resulted in modest variations of both conversion and selectivity, which were reduced and enhanced, respectively, from 76 to 50%, and from 81 to 88% (black and red curves).[25] Under solvent-free conditions, however, the selectivity for **4b** was only 39% (see also entry 11, Table 1). The molar concentration of aldehyde **2b** in $scCO_2$ was also augmented by the increase of pressure (up to 3.3×10^{-2} M at 150 bar), though it remained well below the expected maximum limit of 7.5×10^{-2} M.[23]

This trend of reactivity/selectivity was corroborated by additional experiments in which 4-chlorobenzaldehyde (**2c**) was

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(19) A number of organic reactions including condensations and dehydrative condensation processes can be catalyzed/promoted by Al_2O_3, and very different catalyst loadings are reported; see, for example: Kabalka, G. W.; Pagni, R. M. *Tetrahedron* **1997**, *53*, 7999–8065. In this work, Al_2O_3 was used in a two-fold weight excess with respect to aldehydes to allow sufficiently fast reactions. However, in a single reaction of benzaldehyde and nitroethane carried out under the conditions of entry 6 in Table 1, Al_2O_3 was reduced to 1/3 of its original amount (weight ratio Al_2O_3:**2a** = 0.67); the nitroaldol condensation proceeded albeit with a lower conversion (28% after 18 h; *S*% = 82). This indicates that Al_2O_3 can be referred to as a catalyst.

(20) For the same reason, the reaction of 4-nitrobenzaldehyde with 1-nitrohexane was performed only at 60 °C (entries 13 and 14, Table 1).

(21) *Chemical Synthesis Using Supercritical Fluids*; Jessop, P. G., Leitner, W., Eds.;Wiley-VCH: Weinheim, Germany,1999; Chapter 1.

(22) http://webbook.nist.gov.

(23) Concentration measurements in $scCO_2$ were carried out through gravimetric analyses which required rather large amounts (1−2.5 g) of aldehydes (details are in the Experimental Section). For this reason, the autoclave (90 mL) used for these tests was bigger than that used for reactivity experiments. Under such conditions, if both compounds **2a**,**b** were completely dissolved in the supercritical phase, then the maximum expected molar concentrations would have been 0.26 and 0.075 mol/L for benzaldehyde and 4-nitrobenzaldehyde, respectively.

(24) Both the top and the bottom of the autoclave were equipped with sapphire windows, by which the content of the reactor could be examined at any given pressure.

(25) Since no measures were made between 0 and 80 bar, dotted lines indicated both conversion and selectivity trends.

TABLE 1. Reactions of Aldehydes 2a,b with Both 1-Nitroethane and 1-Nitrohexane in the Presence of Basic Al_2O_3 and $scCO_2$[a]

entry	aldehyde	RCH_2NO_2[b]	T (°C)	P_{CO_2} (bar)[c]	conv (%)[d]	products (%) 3[e]	4	sel (%)[f]
1	**2a**: X = H	**1a**: R = Me	40	0	38	20	18	48
2	**2a**: X = H	**1a**: R = Me	40	100	16	5	11	69
3	**2a**: X = H	**1a**: R = Me	60	0	55	28	27	49
4	**2a**: X = H	**1a**: R = Me	60	100	42	9	33	79
5	**2a**: X = H	**1b**: R = n-C_5H_{11}	40	0	34	17	17	50
6	**2a**: X = H	**1b**: R = n-C_5H_{11}	40	100	5	2	3	60
7	**2a**: X = H	**1b**: R = n-C_5H_{11}	60	0	42	19	23	55
8	**2a**: X = H	**1b**: R = n-C_5H_{11}	60	100	25	3	23	92
9	**2b**: X = NO_2	**1a**: R = Me	40	0	82	72	10	14
10	**2b**: X = NO_2	**1a**: R = Me	40	100	47	17	30	64
11	**2b**: X = NO_2	**1a**: R = Me	60	0	76	45	30	39
12	**2b**: X = NO_2	**1a**: R = Me	60	100	77	11	66	86
13	**2b**: X = NO_2	**1b**: R = n-C_5H_{11}	60	0	76	49	27	36
14	**2b**: X = NO_2	**1b**: R = n-C_5H_{11}	60	100	76	29	47	62

[a] All reactions were carried out for 18 h in the presence of basic Al_2O_3 as a catalyst (the weight ratio of Al_2O_3:aldehyde was 2). Each experiment was repeated twice; the values for conversions, selectivities, and yields were the average of two runs that did not differ more than 5−7%. [b] The molar ratio of **1a**,**b**:**2a**,**b** was 1.2. [c] Odd entries (1, 3, 5, 7, 9, 11, and 13): reactions carried out under solvent-free conditions. [d] The conversion was referred to the aldehyde; it was determined by ^1H NMR. [e] Total amounts of *syn/anti* isomers (determined by ^1H NMR). [f] Selectivity (%) toward the formation of nitroalkenes **4a**,**b′**. This was calculated by the following expression: sel (%) = [**4**/(**3** + **4**)] × 100, where the amounts of compounds **3** (total of *syn/anti* isomers) and **4** were estimated from ^1H NMR spectra.

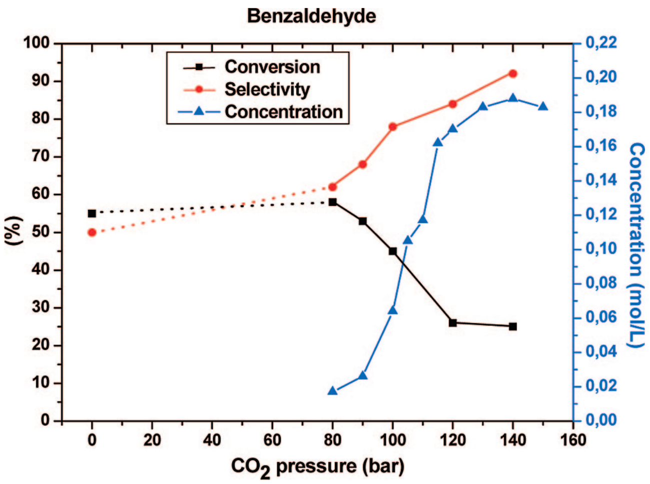


FIGURE 1. Left ordinate: the effect of CO_2 pressure on the conversion of benzaldehyde and on the selectivity (S% for compound **4a**) of the reaction of **2a** with nitroethane (black and red curves) at 60 °C. Right ordinate: molar concentration of benzaldehyde in $scCO_2$ at different pressures and at 60 °C (blue curve).

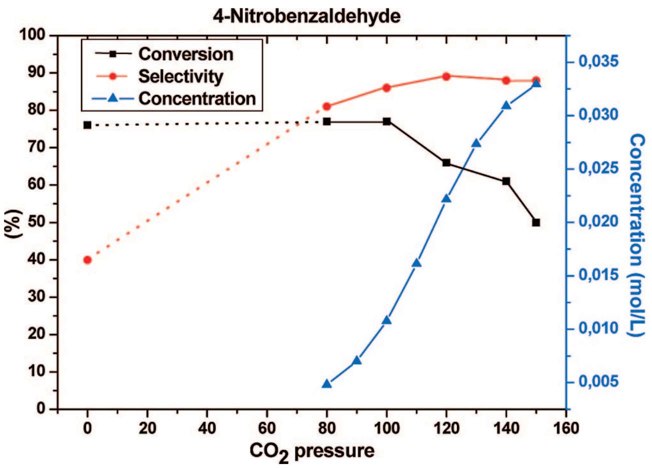


FIGURE 2. Left ordinate: the effect of CO_2 pressure on the conversion of 4-nitrobenzaldehyde and on the selectivity (S% for compound **4b**) of the reaction of **2b** with nitroethane (black and red curves) at 60 °C. Right ordinate: molar concentration of 4-nitrobenzaldehyde in $scCO_2$ at different pressures and at 60 °C (blue curve).

set to react under the conditions of Figures 1 and 2 (**2c**: 0.21 g, 1.5 mmol; nitroethane: 130 μL, 1.8 mmol; basic Al_2O_3: 0.42 g; T = 60 °C, t = 18 h; CO_2: 80−140 bar). Results are reported in Figure 3.

The behavior was rather similar to that of benzaldehyde; in the range of 80−140 bar, the conversion of **2c** dropped from 56 to 13%, while the selectivity for **4c** [4-ClC_6H_4CH=$C(NO_2)CH_3$: E-isomer[18]] increased from 65 to 91%.[25] The concentration of 4-chlorobenzaldehyde in the supercritical phase was not measured; though, at 60 °C, mixtures of **2c**/$scCO_2$ gave homogeneous solutions at $P \geq 120$ bar.[24]

In all cases, NMR analyses showed that the diastereomeric excess (de, *anti*) in the formation of nitroaldol isomers of compounds **2a**−**c** was not substantially affected by the CO_2 pressure; de varied from ~30 to ~40% on going from 80 to 140 bar. Under solvent-free conditions, it was only slightly higher (45%).

Aliphatic Aldehydes. In the presence of basic Al_2O_3 as a catalyst, the reactions of nitroethane with 3-phenylpropionaldehyde (**2d**), 2-phenylpropionaldehyde (**2e**), 3-phenylbutyraldehyde (**2f**), n-decylaldehyde (**2g**), and n-heptylaldehyde (**2h**) were investigated under the conditions of Table 1. Some preliminary experiments showed that aliphatic aldehydes were more reactive than aromatic ones. For this reason, a complete set of reactivity data of compounds **2d**−**h** was gathered only at 40 °C. A mixture of aldehyde (1.5 mmol), $CH_3CH_2NO_2$ (1.8 mmol), and basic Al_2O_3 (the weight ratio of Al_2O_3:**2** was 2) was charged in a 30 mL autoclave, which was then loaded with CO_2 at 100 bar. After 18 h at 40 °C, the autoclave was cooled to room temperature and slowly purged (1 h). The reaction mixture was analyzed by ^1H NMR.

The same reactions were also performed under solvent-free conditions (solFC) in a conventional 5 mL glass reactor thermostatted by an oil bath.

The Henry reaction and the nitroaldol condensation were the sole observed processes for all substrates **2d**−**h** (Scheme 4). Nitroalkenes (**4d**−**h**) were obtained as E-isomers.[18]

Results are reported in Table 2. In the table, the selectivity (%) was expressed toward the formation of nitroalkenes **4d**−**h**.

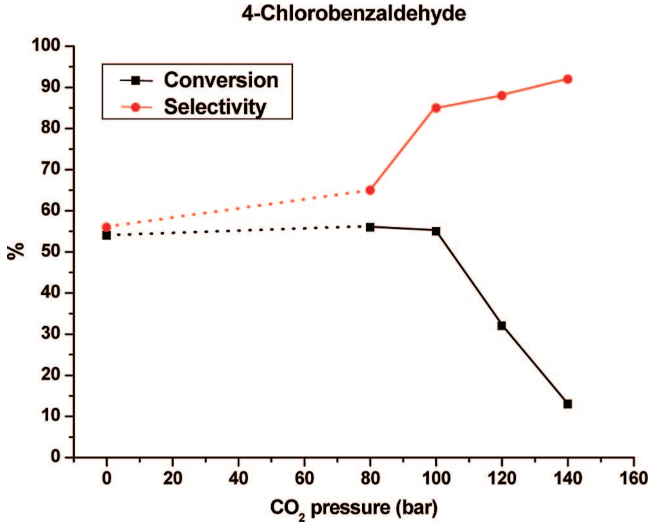
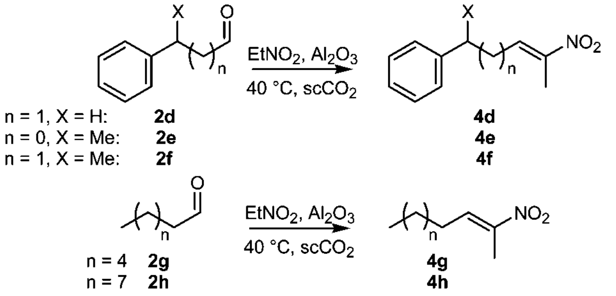


FIGURE 3. The effect of CO_2 pressure on the conversion of 4-chlorobenzaldehyde (**2c**) and on the selectivity (*S*% for compound **4c**) in the reaction with nitroethane at 60 °C.

SCHEME 4. Aliphatic Aldehydes Used in the Reaction with Nitroethane and Basic Al_2O_3



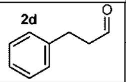
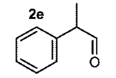
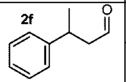
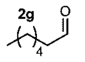
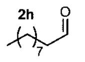
The presence of dense CO_2 had the same twofold effect observed for aromatic aldehydes. The conversion of aliphatic aldehydes was generally lower (44–60%) in the supercritical medium with respect to solvent-free conditions (85–93%). By contrast, the selectivity for products **4d**–**h** was much higher in CO_2 (84–97%) than in its absence (30–74%) (compare entries 2, 4, 6, 8, and 10 to 1, 3, 5, 7, and 9).

The effects of the CO_2 pressure were further investigated by studying the reactions of 3-phenylpropanal (**2d**) and *n*-heptylaldehyde (**2g**) with nitroethane at 40 °C in the range of 70–120 bar (d_{CO_2} = 0.19–0.72 g/mL). In the same pressure interval, also the concentration of **2d** (2.5 g) in $scCO_2$ was measured through the procedure described above for aromatic aldehydes.

Figures 4 and 5 report the result for compounds **2d** and **2g**, respectively. The trend of aldehyde conversion and reaction selectivity (*S*% for nitroalkenes **4a** and **4g**) (black and red curves) and of the molar concentration of **2d** in $scCO_2$ (blue profile) are shown against the pressure of the supercritical phase. Data of reactions carried out under solvent-free conditions (P_{CO_2} = 0) are also indicated.

The reaction conversion and the selectivity (*S*% for products **4d**–**g**) were decreased and enhanced, respectively, by the increase of the CO_2 pressure, in a fashion that closely resembled the behavior reported in Figures 1–3.[24] However, Figures 4 and 5 displayed that sharp variations of both reaction parameters (conversion and selectivity) occurred in the pressure range of 80–100 bar (d_{CO_2} = 0.28–0.62 g/mL at 40 °C), which was, on average, 10–20 bar below the corresponding interval observed for aromatic aldehydes (90–120 bar, d_{CO_2} = 0.23–0.44 g/mL at 60 °C; Figures 1 and 3). In addition, the concentration profile of 3-phenylpropionaldehyde in $scCO_2$ (blue curve, 40 °C, Figure 4) appeared shifted by nearly 20 bar with respect to that obtained for benzaldehyde (blue curve, 60 °C, Figure 1). At 120 bar, the concentration limit value of **2d** was reached (0.21 M).[22]

TABLE 2. Reactions of Aldehydes 2d–h with 1-Nitroethane in the Presence of Basic Al_2O_3 and $scCO_2$[a]

Entry	Aldehyde	P_{CO_2} (bar)[b]	Conv.'n (%)[d]	Nitroalkene 4, (%)[e]	Selectivity (%)[f]
1		0	93	35	38
2		100	59	51	86
3		0	90	27	30
4		100	48	44	91
5		0	90	52	58
6		100	45	41	90
7		0	92	31	34
8		100	45	38	84
9		0	85	63	74
10		100	44	42	97

[a] All reactions were carried out for 18 h at 40 °C, in the presence of basic Al_2O_3 as a catalyst (the weight ratio of Al_2O_3:aldehyde was 2). Entries 1–6 and 8–10: experiments were repeated twice; the values for conversions, nitroalkene amount, and selectivity were the average of two runs that did not differ more than 5–7%. Entries 7–9: experiments were run once. The molar ratio of nitroethane:**2d**–**h** was 1.2. [b] Odd entries (1, 3, 5, 7, and 9): reactions carried out under solvent-free conditions. [d] The conversion referred to the aldehyde; it was determined by ^1H NMR. [e] Amounts of nitroalkenes **4d**–**h** (determined by ^1H NMR). [f] Selectivity (%) toward the formation of nitroalkenes **4d**–**h**. This was calculated by the following expression: sel (%) = [**4**/(**3** + **4**)] × 100, where quantities of compounds **3** (total of *syn/anti* nitroaldol isomers) and **4** were estimated from ^1H NMR spectra.

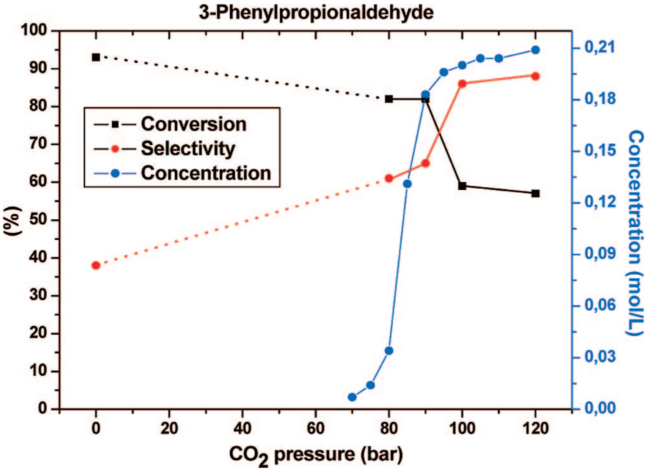


FIGURE 4. Left ordinate: the effect of CO_2 pressure on the conversion of 3-phenylpropionaldehyde (**2d**) and on the selectivity (*S*% for compound **4d**) in the reaction with nitroethane (black and red curves) at 40 °C. Right ordinate: molar concentration of **2d** in $scCO_2$ at different pressures and at 40 °C (blue curve).

Different Catalysts. The reactions of nitroethane with benzaldehyde (**2a**), 4-nitrobenzaldehyde (**2b**), and 3-phenylpropionaldehyde (**2d**) were explored also in the presence of three different Al_2O_3-based catalysts such as KF supported on basic

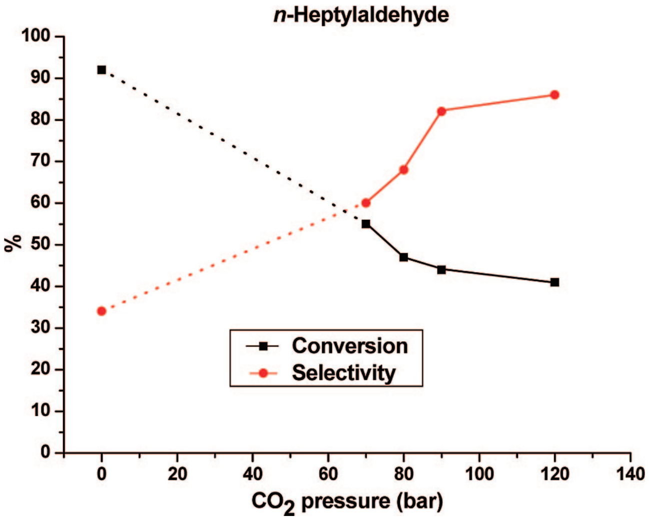


FIGURE 5. The effect of CO_2 pressure on the conversion of *n*-heptylaldehyde (**2g**) and on the selectivity (*S*% for compound **4g**) in the reaction with nitroethane at 40 °C.

Al_2O_3, neutral Al_2O_3, and acid Al_2O_3 (details on these catalytic systems are reported in the Experimental Section). Reaction conditions were those of Table 1 for compounds **2a**,**b** and of Table 2 for compound **2d** (**2**: 1.5 mmol; nitroethane: 1.8 mmol; catalyst: **2** in a 2 weight ratio; Table 1: 60 °C; Table 2: 40 °C). All aldehydes were set to react for 18 h, under solvent-free conditions and in $scCO_2$ at 100 bar (30 mL autoclave).

Results are reported in Figure 6A−C for the case of **2a**, **2b**, and **2c**, respectively. For each catalyst, the reaction conversions observed under solFC and in supercritical CO_2 are shown by red and green bars, respectively. The corresponding selectivities toward nitroalkenes **4a**, **4b**, and **4d** are indicated with gray and blue columns. Figure 6A−C also displays data of reactions catalyzed by basic alumina (Tables 1 and 2).

The following aspects emerged from this investigation:

(i) Conversion. Regardless of conditions, different catalysts did not considerably affect the conversions of aromatic aldehydes, which ranged from 30 to 50% and from 60 to 75% for benzaldehyde and 4-nitrobenzaldehyde, respectively (Figure 6A,B, red and green bars). An exception was the reaction of **2a** over acid alumina that proceeded to a very low extent in $scCO_2$ (∼10%, Figure 6A).

By contrast, the conversion of 3-phenylpropanal (on average, higher than for aromatic substrates) showed modest variations in the absence of solvent (80−95%; Figure 6C, red bars), while it significantly changed in the supercritical phase, from a maximum of 87% on KF/Al_2O_3 to only 22% on acidic Al_2O_3 (green bars).

(ii) Selectivity. The selectivity (*S*%) for nitroalkenes **4** was always better in $scCO_2$ than under solvent-free conditions (compare blue vs gray bars). Nonetheless, especially for aromatic substrates, it decreased rather constantly from basic to neutral and acid catalysts; in this sequence, *S*% dropped from 80 to ∼20%, and from 86 to 54% for benzaldehyde and 4-nitrobenzaldehyde, respectively (Figure 6A,B, blue bars). In the case of 3-phenylpropanal, in dense CO_2, a sharp decrease of the selectivity was observed only over acid alumina (27%, Figure 6C).

Although far from being exhaustive, this analysis suggested that basic catalysts offered the best compromise between conversion and selectivity; especially for reactions performed in the supercritical medium, basic Al_2O_3 appeared more suitable for aromatic aldehydes, while KF/Al_2O_3 for 3-phenylpropanal.

Reaction conditions were not optimized; other possible effects such as the amount of catalysts, the reaction time, the temperature, etc. were not investigated. However, to further substantiate the results, some of the products reported on Tables 1 and 2 and Figure 6 were isolated and their yields (*Y*, %) were calculated. In particular, nitroalkenes **4a**,**b** and **4d** were purified by FCC (eluant: petroleum ether/ethyl acetate in 4:1 v/v) after the reaction of the corresponding aldehydes over basic Al_2O_3 and KF/Al_2O_3.[27]

In addition, two more experiments were carried out with both 2-phenylpropionaldehyde and 3-phenylbutyraldehyde (**2e** and **2f**, respectively), which were set to react under the conditions of Figure 6C (40 °C, KF/Al_2O_3 catalyst). Products **4e** and **4f** were isolated accordingly.

Yields (*Y*, %) of compounds **4a**,**b** and **4d**−**f** are reported in Table 3.

Within limits of the experimental errors, the isolated yields of products **4** were in good agreement with values of conversions and selectivities determined by the ^1H NMR analyses of reactions of Table 3.

Discussion

Reactivity of Aromatic and Aliphatic Aldehydes. In both $scCO_2$ and under solvent-free conditions, the results of reactions catalyzed by basic Al_2O_3 (Tables 1 and 2 and Figures 1−5) indicate that aliphatic aldehydes have similar reactivity (Tables 2 and 3) and are, on average, more reactive than aromatic ones. Moreover, the conversion of 4-nitrobenzaldehyde is higher than that of benzaldehyde. This trend is substantially confirmed also by Table 3 and Figure 6, which compare the reactivity of compounds **2a**−**g** over different Al_2O_3-based catalysts, and by the results reported by Akutu et al.[28] for the nitroaldol reaction carried out over a variety of solid base catalysts (MgO, CaO, KF/Al_2O_3, etc.).

This behavior is possibly explained by factors affecting the reactivity of the carbonyl carbon, such as (i) the higher steric hindrance expected for aromatic aldehydes with respect to aliphatic ones and (ii) the general increase of the −CO electrophilic character induced by electron-withdrawing substituents (i.e., the NO_2 group). To our knowledge, these aspects have not been further detailed in the literature, for both the Henry reaction and the nitroaldol condensation.

Effects of the CO_2 Pressure on the Reaction Outcome. In the supercritical phase, most of the CO_2 properties are affected by its pressure. In particular, the density, which at a reduced temperature (T_r) of 1.1, increases by around 80% when the reduced pressure (P_r) is augmented from 1 to 3.[29] Accordingly, a sharp enhancement of the solubility of organic compounds in CO_2 is usually observed in the proximity and above the critical point. This behavior may offer an explanation for the trend of

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[26] Figure 6A,B: Experiments were repeated twice for the four sets of catalysts. Figure 6C: Experiments were repeated twice except for acid Al_2O_3 that was run once. For duplicate reactions, the values for conversions and selectivity were the average of two runs that did not differ more than 5−7%.

[27] Products **4a**,**b** and **4d** were purified by FCC (details are in the Experimental Section).

[28] (a) Akutu, A.; Kabashima, H.; Seki, T.; Hattori, H. *Appl. Catal. A* **2003**, *247*, 65–74. (b) Hattori, H. *J. Jpn. Petr. Inst.* **2004**, *47*, 67–81.

[29] Lucien, F. P.; Foster, N. R. In *Chemical Synthesis Using Supercritical Fluids*; Jessop, P. G., Leitner, W., Eds.; Wiley-VCH: New York, 1999; Chapter 1.2, pp 39–53 $T_r = T/T_c$; T_c = critical temperature = 31.1 °C; $P_r = P/P_c$; P_c = critical pressure = 73.8 bar.

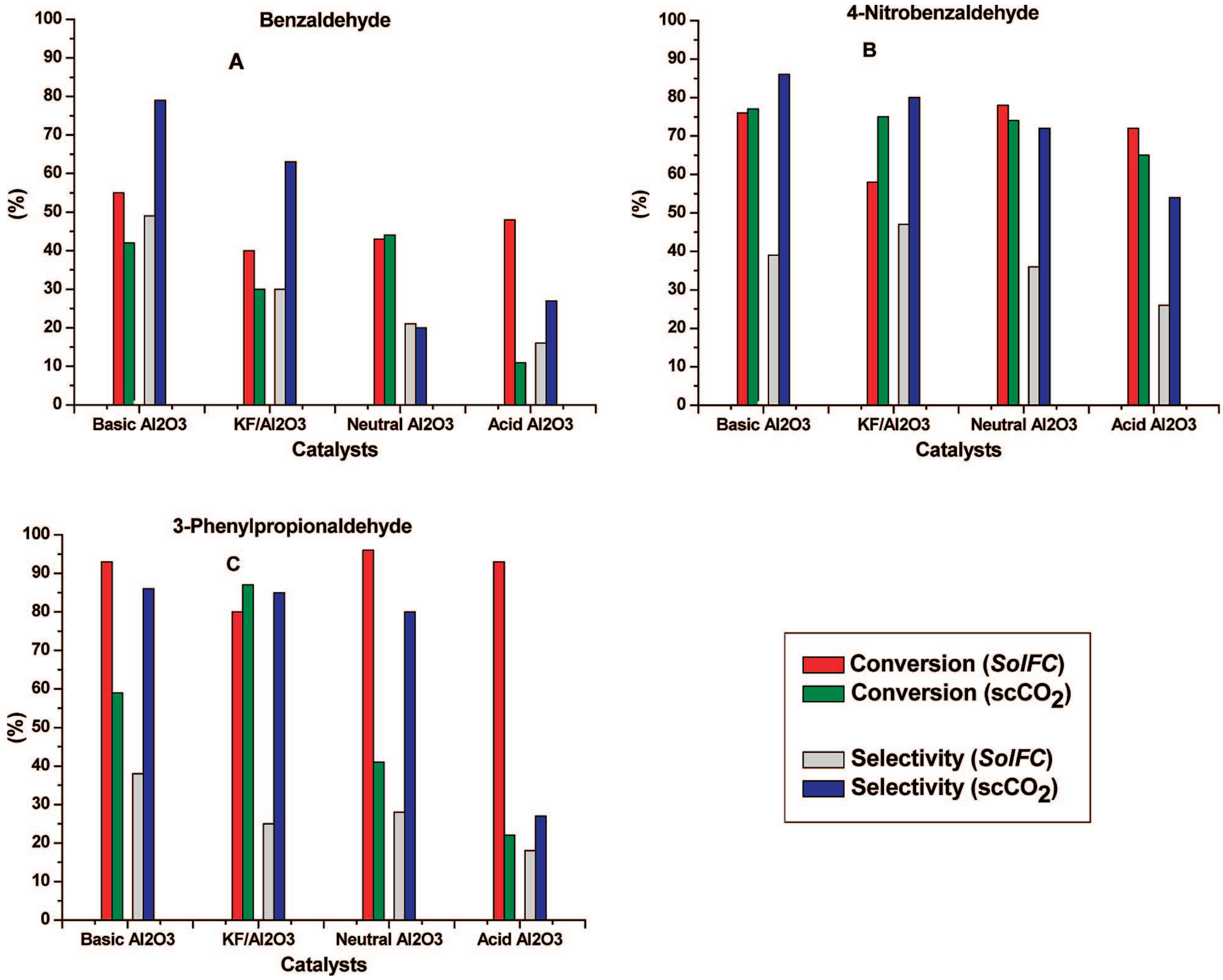

FIGURE 6. The reaction of nitroethane with (A) benzaldehyde, (B) 4-nitrobenzaldehyde, (C) 3-phenylpropionaldehyde in the presence of four different catalysts.[26]

conversions shown by Figures 1−5. Although in this investigation, the equipment used for the reactivity tests and the concentration measures is not strictly comparable (see Experimental Section), it is incontrovertible that, when the operating pressure is increased (from 70 to 140 bar), the steep rise observed in the solubility profiles of aldehydes in $scCO_2$ (Figures 1 and 4, blue curves) closely mirrors the drop of the corresponding conversions (black curves). In other words, if the concentration of reagents in the supercritical phase increases,[30] then they are plausibly desorbed/removed from the catalytic surface, so that the reaction rate is reduced. A similar negative effect of the pressure was observed by others and by us in the investigation of Diels−Alder cycloadditions and of nucleophilic displacements, carried out in dense CO_2 in the presence of silica-supported catalysts.[17c,31] It should be noted, however, that also for the homogeneously catalyzed reaction of 4-cyanobenzaldehyde with 1-nitropropane (Scheme 2) a decrease of the reaction rate was induced by high pressures (≥120 bar).[8] Hence, under these conditions, the liquid-like density of CO_2 does not completely rule out a "conventional" dilution effect.

The above reasoning also clarifies why the maximum solubility of 3-phenylpropionaldehyde (**2d**) in $scCO_2$ (Figure 4, *plateau* of the blue profile) appears shifted to lower pressures (~110 bar) with respect to the corresponding point for benzaldehyde (**2a**: ~140 bar, Figure 1). The trend cannot be ascribed to the different polarity of the substrates,[32] but it is rather due to the tunable density of CO_2. In fact, concentration measures for compounds **2a** and **2d** were performed at 60 and 40 °C, where the supercritical phase reaches comparable densities (and solvating power as well) in the range of 0.56−0.67 g/mL at pressures of 140 and 110 bar, respectively.

Another situation occurs for 4-nitrobenzaldehyde (**2b**, Figure 2), whose low solubility in $scCO_2$ plausibly comes from the combined effects of two properties: the higher polarity of **2b** with respect to **2a** and **2d** and, most of all, the low vapor pressure of **2b** (mp 103−106 °C).[25] This latter property is only partially balanced by the increase of the density of CO_2 up to 150 bar ($d_{CO_2} = 0.6$ g/mL, at 60 °C). In fact, concentration measures reported for 2-nitrobenzaldehyde in supercritical CO_2 claim that a complete miscibility of this substrate is reached only at d_{CO_2} of 0.9 g/mL (25 °C, 175 bar).[33]

The tunable features of CO_2 are likely to account for the high selectivity observed in the formation of nitroalkenes **4**.

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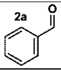
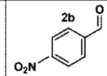
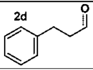
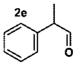
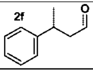
[30] Nitroethane is assumed to be completely dissolved at $P \geq 90$ bar (see Results).

[31] (a) Weinstein, R. D.; Renslo, A. R.; Danheiser, R. L.; Tester, J. W. *J. Phys. Chem. B* **1999**, *103*, 2878–2887.

[32] The dielectric constants (ε) of benzaldehyde and of cinnamaldehyde are 17.85 and 17.72, respectively (*CRC Handbook of Chemistry and Physics*, 75th ed.; Lide, D. P., Ed.; CRC Press: Boca Raton, FL, 1994);ε is not available for 3-phenylpropionaldehyde (**2d**); however, the structure similarity between **2d** (hydroxycinnamaldehyde) and cinnamaldehyde strongly suggests that the two compounds should have also a comparable permittivity.

TABLE 3. Isolated Yields of Nitroalkenes **4a**,**b** and **4d**−**f**[a]

Entry	Aldehyde	P_{CO2} (bar)	Catalyst[b]	T (°C)	Conv.'n (%)[c]	Products, 4	
						Sel. (%)[d]	Isolated Yield (Y, %)[e]
1	 2a	100	Basic Al_2O_3	60	42	79	51
2	 2b	100	Basic Al_2O_3	60	76	86	66
3	 2d	100	KF/Al_2O_3	40	87	85	72
4	 2e	100	KF/Al_2O_3	40	88	81	67
5	 2f	100	KF/Al_2O_3	40	86	80	63

[a] All reactions were carried out for 18 h at 60 and 40 °C in $scCO_2$ (100 bar). Each experiment was repeated twice; the values for conversions, selectivity, and isolated yields were the average of two runs that did not differ more than 5−7%. [b] The weight ratio of catalyst:aldehyde was 2. The molar ratio of nitroethane:**2** was 1.2. [c] The conversion referred to the aldehyde, and it was determined by ^1H NMR. [d] Selectivity (%) toward the formation of nitroalkenes **4a**,**b** and **4d**−**f** was calculated as reported in Table 2. [e] Isolated yields of compounds **4** were obtained after their purification by FCC.

This result is not necessarily associated with the trend of the concentration of reactants in the supercritical phase. In fact, the reactions of 4-nitrobenzaldehyde are selective even though the substrate possesses a limited solubility in $scCO_2$ over the whole range of pressures explored here (Table 1 and Figure 2). A plausible hypothesis for the selectivity control should consider other peculiar aspects of CO_2: (i) Above the critical point ($P_c = 74$ bar, $T_c = 31$ °C), the so-called *clustering* or local density enhancement gives rise to special solvation effects not ordinarily found in conventional liquid mixtures.[10b] Accordingly, a modest variation of pressure alters both the solutes/solvent and the transition states/solvent interactions that may affect the product distribution. In this respect, a different partitioning of nitroaldol/nitroalkene products between $scCO_2$ and the catalyst is expected; the more polar Henry product (nitroaldol) is likely to reside over the Al_2O_3 surface (rather than in the supercritical solvent), where the dehydration takes place. (ii) The high diffusivity (D) of $scCO_2$ not only favors the mass transfer of reagents over solid catalysts[10] but it also helps the desorption of products and co-products such as water that, in the present case, is generated by the nitroaldol condensation (Scheme 1).[34] The CO_2-mediated removal of water from the catalyst pores has been reported as a crucial factor for addressing the selectivity of oxidation reactions carried out in $scCO_2$ over Pd supported on Al_2O_3.[35] (iii) Thanks to its weak acidity, carbon dioxide is an excellent probe to characterize heterogeneous base catalysts.[36] In particular, under the conditions investigated here for nitroaldol reactions, CO_2 is certainly chemisorbed over the basic sites of solid Al_2O_3. Although this acid−base interaction is expected to modify or even to poison, to some extent, the catalytic surface,[24] it may also alter the reaction pathways in favor of nitroalkene products.

Activity of Different Catalysts. In supercritical CO_2, basic Al_2O_3 and KF/Al_2O_3 show better catalytic performances than neutral and, particularly, acid aluminas (Figure 6 and Table 3). This is ascribed to the different modes of reactant activation: in the first step of the reaction, basic catalysts efficiently generate stable nitronate carbanions from nitroalkanes,[1] while neutral/acid systems allow only a modest enhancement of the electrophilic character of aldehydic carbonyls.

Conclusions

In the current literature, the large number of publications involving both the Henry reaction and the strictly related nitroaldol condensation proves how these transformations continue to attract interest in several fields of organic synthesis. Although these reactions are often studied separately, a new frontier of this chemistry lies, in our view, in the study of innovative and possibly more eco-compatible conditions, able to modulate the selectivity between the two processes. After the pioneering paper reporting on the Henry reaction performed in $scCO_2$,[8] this work represents the first extensive investigation in this area. In particular, the emerging original aspect is that, in the presence of heterogeneous catalysts, supercritical CO_2 can not only act as a green solvent for the reaction of both aromatic and aliphatic aldehydes with 1-nitroalkanes but also shift the selectivity (up to 97%) toward the formation of nitroalkenes (from the nitroaldol condensation). On the other hand, under solvent-free conditions, nitroaldols (from the Henry reaction) are the major products. This result is achieved by the combination of the tunable properties of CO_2 and the nature of the catalysts used. Among the tested aluminas, basic systems perform better than neutral and acid ones; however, only if the pressure (and the density) of the supercritical phase is increased from 80 to 140 bar, then the nitroalkene's selectivity increases, on average, from ~60 to more than 90%. Several effects, such as the local density enhancement, the high diffusivity, and the weak acidic character of the supercritical phase, are likely to account for this behavior.

Experimental Section

SAFETY WARNING: Operators of high-pressure equipment should take proper precautions to minimize the risks of personal injury.[37]

Reactions Carried out in an Autoclave. In a typical experiment, a stainless-steel 30 mL reactor equipped with sapphire windows on both top and bottom apertures, a pressure gauge, two inlet and purge valves, and a thermocouple was charged with nitroethane (**1a**, 130 μL, 1.8 mmol), an aldehyde (**2a**−**h**, 1.5 mmol), and the catalyst (basic, neutral, or acid Al_2O_3 as well as KF on Al_2O_3: the weight ratio of catalyst:aldehyde was 2). The autoclave was then pressurized with CO_2 (SFC/SFE grade) at approximately 60 bar by using an automatic syringe pump (ISCO model 260 D), and it was electrically heated at the desired temperature (40 or 60 °C). The reaction mixture was magnetically stirred. The final pressure (80−140 bar; see Tables 1−3 and Figures 1−6) was reached by

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(33) Dandge, D. K.; Heller, J. P.; Wilson, K. V. *Ind. Eng. Chem. Prod. Res. Dev.* **1985**, *24*, 162–166.

(34) It should be noted that water has a limited, but not negligible, solubility in $scCO_2$: Toews, K. L.; Shroll, R. M.; Wai, C. M. *Anal. Chem.* **1995**, *67*, 4040–4043. Plausibly, the maximum amount of water produced by the nitroaldol condensation is completely dissolved in CO_2.

(35) (a) Caravati, M.; Grunwaldt, J.-D.; Baiker, A. *Phys. Chem. Chem. Phys.* **2005**, *7*, 278–285. (b) Caravati, M.; Grunwaldt, J.-D.; Baiker, A. *Appl. Catal. A* **2006**, *298*, 50–56.

(36) Hattori, H. *Chem. Rev.* **1995**, *95*, 537–550.

(37) Jessop, P. G.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996**, *118*, 344–355.

slowly adding the remaining CO_2 to the reactor. Then, the reaction was allowed to proceed for 18 h. After cooling to rt, CO_2 was slowly vented by bubbling it into diethyl ether (5 mL) cooled at 0 °C. The content of the cell was washed with additional ether (5 mL), and the catalyst was filtered. The solvent of the combined ethereal solutions was removed in vacuo, and finally, the residues were analyzed by ^1H NMR.

The same procedure was also used by replacing 1-nitroethane with 1-nitrohexane (**1b**, 260 μL, 1.8 mmol; see Table 1).

Reactions Carried out under Solvent-Free Conditions. The reactions of 1-nitroethane with aldehydes **2a**−**h** were also carried out under solvent-free conditions, by adjusting a procedure previously reported by us:[2] a 5 mL test tube was charged with 1-nitroethane (**1a**, 130 μL, 1.8 mmol), an aldehyde (**2a**−**h**, 1.5 mmol), and the catalyst (basic, neutral, or acid Al_2O_3 as well as KF on Al_2O_3: the weight ratio of catalyst:aldehyde was 2). The reaction mixture was then magnetically stirred and heated at 40 or 60 °C in an oil bath for 18 h. After cooling to rt, the catalyst was filtered and washed with diethyl ether (5 mL). The solvent of the clear solution was removed in vacuo, and finally, the residue was analyzed by ^1H NMR.

Characterization and Isolation of Products. The formation of nitroaldols **3a**−**h** and nitroalkenes **4a**−**h** was confirmed by the ^1H NMR spectra of reaction mixtures. The spectroscopic data were in good agreement with those reported in the literature.[38]

In the case of reactions of nitroethane with aldehydes **1a**,**b** (entries 4 and 12, Table 1), **1d** (entry 2, Table 2), and **1e**,**f** (Figure 6c), carried out in $scCO_2$, the corresponding nitroalkenes **4a**,**b** and **4d**−**f** were also isolated. At the end of each experiment, the resulting reaction mixtures were purified by FCC on silica gel using an eluant solution of petroleum ether/ethyl acetate (4:1 v/v). Isolated yields of compounds **4a**, **4b**, **4d**, **4e**, and **4f** were 51 (0.12 g), 66 (0.21 g), 72 (0.21 g), 67 (0.19 g), and 63% (0.19 g), respectively. The ^1H NMR and GC/MS spectra of pure nitroalkenes are reported below. A $^{13}C\{^1H\}$ NMR spectrum was recorded for the new compound **4f**.

(*E*)-2-Nitro-1-phenylpropene, 4a:[39] ^1H NMR ($CDCl_3$) δ 8.11 (1H, s), 7.47 (5H, m), 2.48 (3H, s); MS (EI), *m/z* (relative int) 163 (M^+, 8%), 146 (9), 117 ($M^+ - NO_2$, 42), 116 (30), 115 ($M^+ - 2H - NO_2$, 100), 105 (32), 91 (42), 77 (14), 65 (17), 51 (24).

(*E*)-2-Nitro-1-(4-nitro)phenylpropene, 4b:[40] ^1H NMR ($CDCl_3$) δ 8.31 (d, 2H, $J = 8.5$ Hz), 7.59 (d, 2H, $J = 8.5$ Hz), 8.09 (br s, 1H), 2.46 (d, 3H, $J_{H-H} = 1.0$ Hz); MS (EI), *m/z* (relative int) 208 (M^+, 5%), 161 ($M^+ - NO_2 - H$, 19), 132 (20), 115 ($M^+ - 2NO_2$, 42), 115 ($M^+ - H - 2NO_2$, 100), 63 (22).

(*E*)-2-Nitro-5-phenyl-2-pentene, 4d:[41] ^1H NMR ($CDCl_3$) δ 7.33−7.14 (m, 7H), 2.82 (t, 2H, $J_{H-H} = 7.5$ Hz), 2.55 (q, 2H, $J = 7.7$ Hz), 2.05 (s, 3H); MS (EI), *m/z* (relative int) 191 (M^+, <1%), 144 ($M^+ - NO_2 - H$, 10), 91 [$M^+ - CH_2CHC(CH_3)NO_2$, 100], 65 (10).

(*E*)-2-Nitro-4-phenyl-2-pentene, 4e:[42] ^1H NMR ($CDCl_3$) δ 7.36−7.22 (m, 6H), 3.71 (dq, 1H, $J = 6.9$ Hz, $J' = 10.3$ Hz), 2.23 (d, 3H, $J_{H-H} = 1.0$ Hz), 1.47 (d, 3H, $J_{H-H} = 6.9$ Hz); MS (EI), *m/z* (relative int) 191 (M^+, 5%), 145 ($M^+ - NO_2$, 12), 144 ($M^+ - NO_2 - H$, 13), 130 ($M^+ - NO_2 - Me$, 26), 129 (58), 105 [$M^+ - CHC(CH_3)NO_2$, 100], 91 (25), 77 (53), 51 (37).

(*E*)-2-Nitro-5-phenyl-2-hexene, 4f: ^1H NMR ($CDCl_3$) δ 7.33−7.17 (m, 5H), 7.08 (t, 1H, $J = 7.95$ Hz), 2.95 (m, 1H, $J_{H-H} = 7.0$ Hz), 2.50 (m, 2H), 2.04 (d, 3H, $J_{H-H} = 0.9$ Hz), 1.34 (d, 3H, $J_{H-H} = 7.0$ Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 148.3, 145.1, 134.2, 128.6, 126.7, 126.6, 39.3, 36.8, 21.5, 12.4; MS (EI), *m/z* (relative int) 205 (M^+, <1%), 105 [$M^+ - CH_2CHC(CH_3)NO_2$, 100], 91 (5), 77 (56), 51 (8). Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.26; H, 7.33; N, 6.85.

Concentration of Benzaldehyde (2a), 4-Nitrobenzaldehyde (2b), and 3-Phenylpropionaldehyde (2d) in $scCO_2$: Figures 1, 2, and 4. In a typical experiment, the aldehyde (**2a**: 2.5 g, 23.6 mmol; **2b**: 1.0 g, 6.6 mmol; **2d**: 2.5 g, 18.7 mmol) was charged in a 90 mL stainless-steel autoclave, which was heated at 40 °C (for **2d**) or at 60 °C (for **2a**,**b**) and brought to the desired pressure of CO_2 in the range of 80−150 bar (see also ref 21). The mixture was kept under stirring at 750 rpm. After 30 min, the agitation was stopped, and an aliquot of the mixture was withdrawn through a stainless-steel calibrated loop of 1.12 mL fitted to the autoclave head. The loop was vented into diethyl ether (5 mL) and washed thoroughly with additional ether (5 mL). The solvent of the combined ethereal solutions was removed in vacuo, and the amount of the liquid or solid residue of **2** was determined gravimetrically. The measure was repeated twice for each of the chosen pressures.

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Supporting Information Available: ^1H NMR for **4a**, **4b**, **4d**, **4e**, and **4f** in $CDCl_3$ and ^{13}C NMR spectra of the new compound **4f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[38] (a) Bulbule, V. J.; Deshpande, V. H.; Velu, S.; Sudalai, A.; Sivasankar, S.; Sathe, V. T. *Tetrahedron* **1999**, *55*, 9325–9332. (b) Dumez, E.; Faure, R.; Dulcere, J.-P. *Eur. J. Org. Chem.* **2001**, *13*, 2577–2588. (c) Ballini, R.; Bosica, G.; Marcantoni, E.; Vita, P.; Bartoli, G. *J. Org. Chem.* **2000**, *65*, 5854–5857. (d) Mourad, M. S.; Varma, R. S.; Kabalka, G. W. *J. Org. Chem.* **1985**, *50*, 133–135. (e) Tokunaga, Y.; Ihara, M.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1* **1997**, 207–210. (f) Ono, N.; Maruyama, K. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 4470–4472.

[39] McAnda, A. F.; Roberts, K. D.; Smallridge, A. J.; Ten, A.; Trewhella, M. A. *J. Chem. Soc., Perkin Trans. 1* **1998**, 501–504.

[40] (a) Ballini, R.; Bigi, F.; Gogni, E.; Maggi, R.; Sartori, G. *J. Catal.* **2000**, *191*, 348–343. (b) Caldarelli, M.; Habermann, J.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1999**, 107–110.

[41] Ballini, R.; Castagnani, R.; Petrini, M. *J. Org. Chem.* **1992**, *57*, 2160–2162.

[42] Chounan, Y.; Ono, Y.; Nishii, S.; Kitahara, H.; Ito, S.; Yamamoto, Y. *Tetrahedron* **2000**, *56*, 2821–2831.