

Zeolite as Base Catalyst: Nitroaldolic Condensation

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In this work we have studied the activity and selectivity of alkaline Y and X zeolites to promote the nitroaldolic condensation of aromatic aldehydes with nitroalkanes affording nitroalkenes. The reaction is promoted by the intrinsic basicity of the zeolites, which increases with an increase of both the aluminium content in the framework and the radius of the counter cation. Indeed, high yields and selectivities were obtained carrying out the reactions over CsNaX zeolite. The nature of the reactants, in particular, nitroalkanes, affects the yield and shape selectivity effect was observed. © 2000 Academic Press

Key Words: CsNaX zeolite; base catalyst; nitroaldolic condensation; nitroalkene.

1. INTRODUCTION

The use of heterogeneous catalysts in the production of petrochemicals as well as fine chemicals represents one of the most successful lines of research in catalysis. In addition to the known advantages they may replace dangerous, corrosive, or toxic catalysts in some cases. It is possible to say that they are potential environmentally friendly catalysts (1).

Solid acids are widely used to obtain selective processes that minimise the waste production. Indeed, the use of zeolites as main catalysts in the petrochemical cracking reactions and in oil processing, some of the largest processes among the industrial chemical ones, represents a case of particular importance (2, 3).

The studies of solid basic catalysts are not so extensive, probably because most of the reactions of industrial interest are catalysed by acids and in addition the generation of basic sites often requires high-temperature pretreatment and catalyst deactivation may easily occur (3). Anionic clays (hydrotalcite-like), metal oxides, and cationic zeolites are the most used solids with basic properties. Zeolites are crystalline microporous metal oxides that could combine the activity due to the basic sites and the geometrical constraints introduced by the molecular sieve. Zeolites with

basic properties can be obtained by alkali metals impregnation (strong basic sites) or by alkali metal cation exchange (weak basic sites). The alkali metal cations compensate the negative charge of the framework due to aluminium being tetrahedrally coordinated. The appearance of the positive and negative charge generates the acidobasic character of the zeolites. Indeed, it has been shown that alkaline faujasite has basic properties (3–5). Alkaline Y and X zeolites have been used to catalyse Knoevenagel and aldol condensations, alkylation reactions, dehydrocyclization of *n*-alkanes, and hydrogenation–dehydrogenation reactions (3).

In this work, we have studied the activity and selectivity of alkaline Y and X zeolites, to promote the nitroaldolic condensation of aromatic aldehydes with nitroalkanes. The nature of the sites involved in the reaction and shape-selective effects have been studied.

Unsaturated nitrocompounds are important precursors of a large variety of target molecules and possess biological activity representative of insecticides (6), fungicides (7), and pharmacologically active substances (8). They are powerful dienophiles in the Diels–Alder reaction and readily undergo addition reactions with many different nucleofiles. Due to the easy conversion of the nitro group into a variety of diverse functionalities, nitroalkenes are quite versatile compounds in synthetic organic chemistry (9). The most versatile synthesis of nitroolefins involves the Henry condensation reaction of a carbonyl compound with a nitroalkane, followed by dehydration of the β -nitroalcohol formed. The Henry reaction is routinely accomplished under mildly basic conditions (10) and several reagents have been used for the dehydration step (11).

In view of the increased interest in the catalysis of organic reactions by inorganic materials, different procedures to obtain conjugated nitroalkenes catalysed by oxide, clay, or mesoporous hybrid material have been reported, starting from β -nitroalcohols (12) or directly from carbonyl compounds (13).

Our interest in the use of heterogeneous catalysts for fine chemicals preparation (14) has prompted us to explore the potential of zeolites in the nitroaldolic condensation.

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TABLE 1
Main Structural Characteristics and Chemical Composition of the Catalysts
(mmol/100 g of Hydrated Zeolite)

Catalyst	Surface area ^a (m ² g ⁻¹)	Si/Al ratio ^b	Na (mmol)	Li (mmol)	K (mmol)	Cs (mmol)
HY (HSZ 330)	460 ± 10	3.0	—	—	—	—
NaY (HSZ 320)	570 ± 10	2.8	290	—	—	—
LiNaY	n.d. ^c	2.8	173	128	—	—
KNaY	n.d.	2.8	73	—	210	—
RbNaY	n.d.	2.8	69	—	—	—
CsNaY	n.d.	2.8	98	—	—	147
NaX (13X)	350 ± 10	1.23	441	—	—	—
CsNaX	320 ± 10	1.23	253	—	—	134

^a Measured by N₂ physisorption following the BET procedure.

^b Data obtained from the furnishing.

^c Not determined.

2. EXPERIMENTAL

2.1. Materials

Y-HSZ 320, 330, and 13X zeolites were purchased from Tosoh Corp. and Fluka AG, Switzerland, respectively.

NaX and NaY zeolites were exchanged by lithium, potassium, and cesium in a 1 M solution of the corresponding metal chloride at 80°C for 60 min, using a liquid-to-solid ratio of 10 (4). The samples were filtered, washed free of chlorides, and dried at 773 K. The chemical composition of the resulting materials showed that a partial substitution of the sodium atoms occurred, as expected for a single cation-exchange treatment. The main characteristics of the catalysts used are summarised in Table 1. Surface measurements were obtained on a high-speed surface area analyzer 2200 Micrometrics apparatus following the BET procedure (15).

2.2. Reaction Procedure

The reaction was carried out in a round-bottomed flask fitted with a condenser; aldehyde (10 mmol), nitroalkane (40 mmol), and zeolite (1 g) were heated at reflux (16) in an oil bath at 140°C under stirring for 24 h unless otherwise stated. After cooling to room temperature, the catalyst was filtered and washed with dichloromethane; the filtrate was analysed by gas chromatography-mass spectrometry (GC-MS) (HP5890 Series 2 coupled to HP5971A mass selective detector at 70 eV). The products were isolated by silica gel chromatography with hexane/ethyl acetate as an eluant and were characterised by ¹H-NMR, GC-MS, and m.p.

The yield and selectivity were determined on the basis of the aldehyde fed by GC analysis on a capillary column using the internal standard method and by silica gel chromatography.

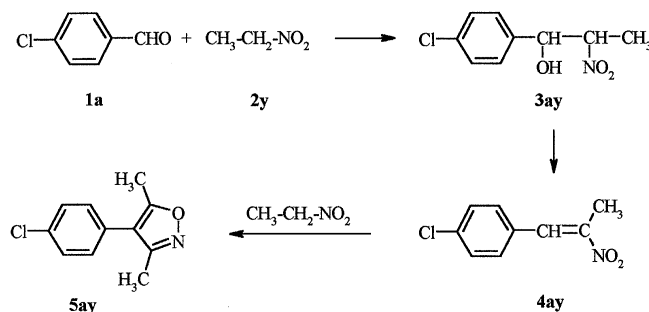
Deactivation of the catalyst could occur, probably due to the neutralisation of basic sites by carboxylic acid formed by the oxidation of aldehyde, which occurs when the reaction is carried out in the presence of air; hence, the reaction is better under an inert atmosphere.

The model reaction of 4-chlorobenzaldehyde and nitroethane was monitored between 1 and 23 h. Samples were taken periodically, the catalyst was filtered and washed with dichloromethane, and the course of the reaction was followed by gas-liquid chromatography using 1,3,5-tri-*tert*-butylbenzene as the internal standard added to the reaction.

The ¹H-NMR analyses of the products were carried out with a Bruker AC300 or AMX400 spectrometer in CDCl₃ with TMS as the internal standard. Chemical shifts are reported in δ (ppm) and are referenced to TMS. The chemical structures of the products obtained in the model reaction are presented in Scheme 1.

2.3. Spectroscopic-Spectrometry Data of the Reaction Products

(*E*)-1-(4-Chlorophenyl)-2-nitropropene (**4ay**). ¹H-NMR: 7.95 (m, 1H, Ar-CH=C), 7.36 (d, 2H, *J*=8.6 Hz, ArH, $\frac{1}{2}$ *para* system), 7.29 (d, 2H, *J*=8.6 Hz, ArH, $\frac{1}{2}$ *para*



SCHEME 1

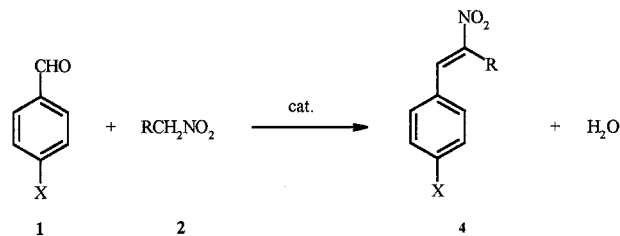
system), 2.35 (d, 3H, $J=1.1$ Hz, CH₃). MS: 199 ($M+2$, 3), 197 (M^+ , 8), 116 (50), 115 (100).

1-(4-Chlorophenyl)-2-nitropropan-1-ol (3ay). ¹H-NMR (400 MHz): 7.35 (m, 4H, ArH), 5.38 (d, 0.4 × 1H, $J=3.6$ Hz, CHOH), 5.02 (d, 0.6 × 1H, $J=8.8$ Hz, CHOH), 4.72 (qd, 0.6 × 1H, $J=8.8$ and 6.8 Hz, CHCH₃), 4.66 (qd, 0.4 × 1H, $J=6.8$ and 3.6 Hz, CHCH₃), 2.8 (br s, 1H, OH), 1.49 (d, 0.4 × 3H, $J=6.8$ Hz, CH₃), 1.32 (d, 0.6 × 3H, $J=6.8$ Hz, CH₃). MS: 215 (M^+ , 2), 170 (10), 168 (30), 143 (23), 141 (79), 111 (26), 77 (100).

3,5-Dimethyl-4-(4-chlorophenyl)-isoxazole (5ay). ¹H-NMR: 7.41 (d, 2H, $J=8.5$ Hz, ArH, $\frac{1}{2}$ *para* system), 7.18 (d, 2H, $J=8.5$ Hz, ArH, $\frac{1}{2}$ *para* system), 2.39 (s, 3H, CH₃), 2.25 (s, 3H, CH₃). MS: 209 ($M+2$, 15), 207 (M^+ , 47), 140 (26), 138 (80), 103 (100).

2.4. Scanning Electron Microscopy

Particles of zeolite CsNaX were arranged in spherical clusters with an average diameter of about 2–3 μm. SEM investigations revealed the clusters had a fine structure made of platelike single crystals with an average diameter of about 1 μm (see micrograph in Fig. 1). As confirmed by SEM images of NaX and CsNaX zeolites, the morphology and crystal size of the catalyst remained unchanged after cation exchange. NaY (HSZ 320) zeolite SEM images showed a uniform distribution of polyhedral crystals of small size (≤ 0.5 μm) (17).



SCHEME 2

3. RESULTS AND DISCUSSION

3.1. Catalyst Effect on Nitroaldolic Condensation

The nitroalkenes **4** are the products obtained by the condensation of benzaldehyde **1** and nitroalkane **2** (Scheme 2).

It is known that under basic catalysis the reaction starts with the formation of the anion of nitroalkane followed by its attack on the carbonyl group of the aldehyde.

When the model reaction between 4-chlorobenzaldehyde **1a** and nitroethane **2y** was carried out using the acid zeolite HSZ 330, the nitroalkene **4ay** was obtained in moderate yield, probably via carbonyl group activation (18) (Table 2, entry 1). On the contrary, the employment of HSZ 320, a cationic NaY zeolite, gave the product **4ay** in good yield (62%).

Aiming at promoting a base-catalysed process, alkali cation-exchanged Y and X zeolites were examined (Table 2).

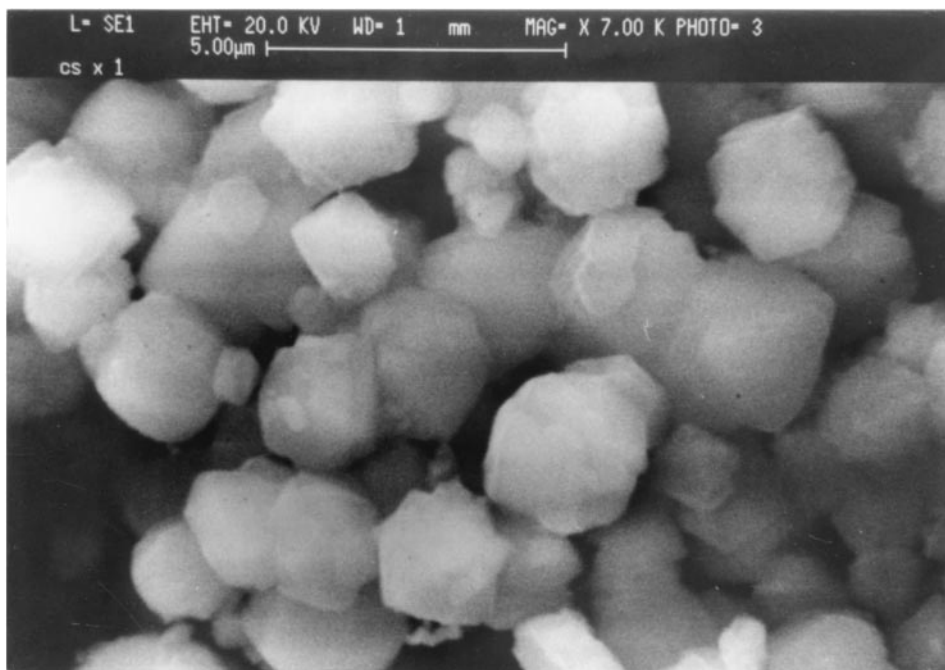
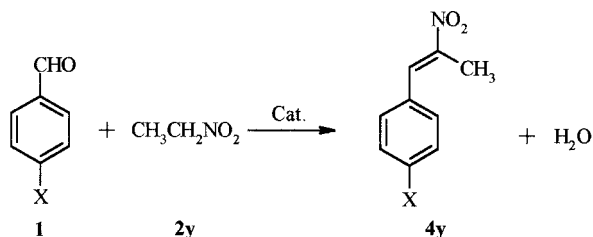


FIG. 1. Scanning electron micrograph (SEM) of the CsNaX catalyst.

TABLE 2

Reaction of Benzaldehydes with Nitroethane in the Presence of Different Catalysts



Entry	Aldehyde	X	Catalyst	Product	Yield (%)	Select. (%)
1	1a	Cl	HY	4ay	36	63
2	1a	Cl	NaY	4ay	62	79
3	1a	Cl	LiNaY	4ay	50	67
4	1a	Cl	KNaY	4ay	57	74
5	1a	Cl	RbNaY	4ay	63	78
6	1a	Cl	CsNaY	4ay	65	81
7	1a	Cl	NaX	4ay	74	92
8	1a	Cl	CsNaX	4ay	80	91
9	1b	H	CsNaX	4by	68	90
10	1c	OCH ₃	CsNaX	4cy	65	90
11	1d	NO ₂	CsNaX	4dy	86	93

In good accordance with the results reported for Knoevenagel condensation by Corma *et al.* (4), the reactivity increases from lithium to cesium and from Y to X zeolites. The basic strength of alkali ion-exchanged zeolites follows the order $\text{Li} < \text{Na} < \text{K} < \text{Cs}$ because the average oxygen charge increases with an increasing ionic radius of the exchanged cation (5). Further, increasing the aluminium content of the zeolite strengthens the basic character and this accounts for the higher activity of X than Y zeolites.

Indeed, high yield (80%) and selectivity (91%) were observed carrying out the reaction over CsNaX zeolite as the catalyst (Table 2, entry 8). These results are in agreement with the observation that the intrinsic basicity of zeolites with the same crystalline structure, in our case a faujasite-type structure, depends on the chemical composition, *i.e.*, on the Si/Al ratio and type of counter cation (5). As seen from SEM images the NaX and CsNaX catalyst have similar crystal dimensions. This enables us to correlate the activity with the basicity of the zeolite catalyst, excluding a reaction control by the internal diffusion. These data are in accordance with the statement that in an exchanged CsNaX catalyst most of the basic sites are able to abstract protons with $\text{p}K_a$ around 10 (4).

The model reaction between **1a** and **2y** in the presence of the CsNaX zeolite was monitored between 1 and 23 h (Fig. 2). It is interesting to observe that the diattack by-product **5ay** is formed at the beginning of the reaction and the amount did not increase in the time.

3.2. Mechanism

The reaction mechanisms occurring on the surfaces are suggested to be essentially the same as that in homogeneous basic conditions (3). Indeed, the intermediacy of 2-nitroalkanol, which suffers loss of water to give the corresponding nitroalkene, was evidenced using half the amount of the CsNaX catalyst. In that case 1-(4-chlorophenyl)-2-nitropropanol (**3ay**, Scheme 1) could be isolated as the main product.

3.3. Influence of the Nature of the Reactant

The condensation was carried out using different aromatic aldehydes and the results from Table 2 show that the

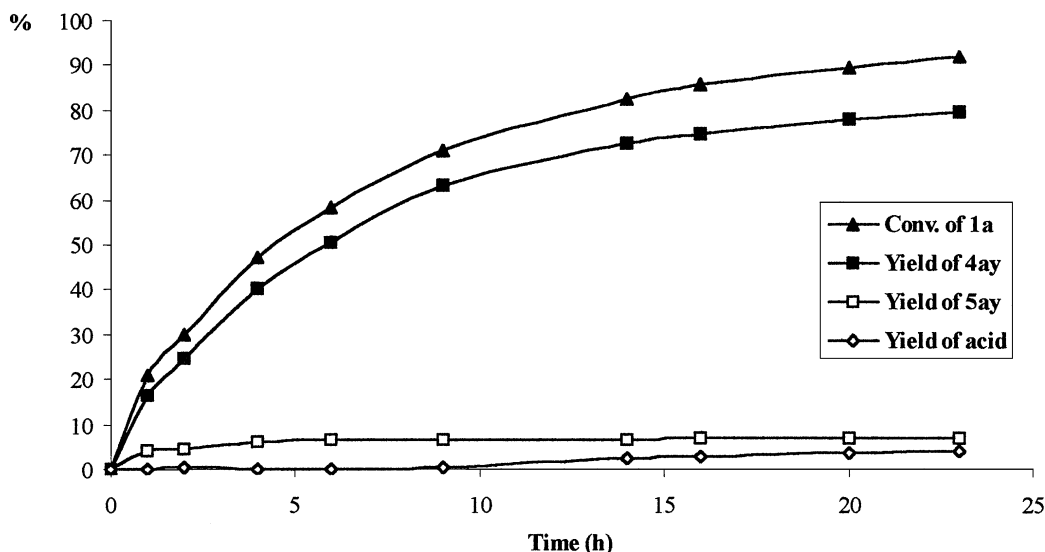
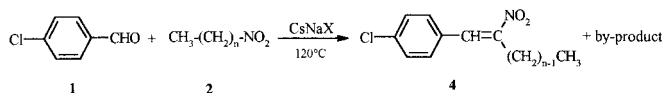


FIG. 2. Condensation between **1a** and **2y** on the CsNaX catalyst.

TABLE 3

Effect of Nitroalkane Chain Length



Entry	Nitroalkane	<i>n</i>	Product	Yield (%) 4	Yield (%) By-product
1	2x	0	4ax	30	54 ^a
2	2y	1	4ay	56	8 ^b
3	2z	2	4az	81	3 ^b
4	2u	3	4au	92	—
5	2v	5	4av	23	—
6	2w	8	4aw	15	—

^aMichael addition product.

^bIsoxazole derivative.

presence of an electron acceptor group on the aromatic ring of benzaldehyde increases the yield; meanwhile, the presence of an electron donor group decreases the yield (Table 2, entries 8–11). In all the cases the isomer *E* was obtained and isolated (19).

The effect of the nitroalkane chain length was investigated (Table 3). It should be noted that nitromethane has a particular reactivity, as already observed by other authors (10), probably due to the presence of only one carbon atom and to its small dimension.

From the data reported in Table 3, it can be observed that the carbon chain length (*n* value) markedly affects the reactivity. Indeed, the yield increases with increasing the carbon atom number of nitroalkane from 2 to 4 (*n* = 1–3) and then decreases for longer chains. These results remind one of a shape-selectivity effect reported for the acylation of aromatic substrates catalysed by acid zeolites, even if the reagent chain length was higher (20, 21).

Since nitroalkane is used in excess as a reagent solvent (4 equiv), the Michael addition of a second molecule of reagent on the nitroalkene formed could be expected.

It is noteworthy to observe that a cyclic by-product (22), due to Michael addition, is formed in a small amount using nitroethane and decreases rapidly with the chain length increasing. The Michael addition producing bulky products is suppressed due to the small space of the cavities where the basic sites are located. The minimisation of Michael addition by shape selectivity of alkali ion-exchanged zeolites was reported in the literature (23) in the reaction of benzaldehyde with ethyl cyanoacetate.

Attempts to recycle showed that the catalyst recovered after dichloromethane washing had been reused directly three times, giving the product **4ay** with unchanged high selectivity and a modest lowering of yield.

CONCLUSIONS

Alkali metal cation-exchanged *X* and *Y* zeolites, in particular CsNaX, are active and selective catalysts for the condensation of benzaldehydes and nitroalkanes. The activity of the zeolites increases with an increase of the aluminium content in the framework and increase in the radius of the counter cation. Indeed, the zeolite cages are microreactors, the walls of which are the basic sites whose strength and number can be controlled by selecting the chemical composition.

The activity of substituted benzaldehydes shows the influence of electronic effects. Regarding the nitroalkanes, steric factors play an important role, showing that the combined effect of basicity and shape selectivity have to be considered in this heterogeneous nitroaldolic condensation.

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REFERENCES

- (a) Sheldon, R. A., *Chem. Ind. (London)* 12 (1997). (b) Clark, J. H., and Macquarrie, D. J., *Chem. Soc. Rev.* 303 (1996). (c) Hölderich, W. F., in "Comprehensive Supramolecular Chemistry" (J. L. Atwood *et al.*, Eds.), Vol. 7, p. 671. Pergamon Press, Oxford, 1996. (d) Cusumano, J. A., *CHEMTECH Aug.* 482 (1982).
- Hölderich, W., Hesse, M., and Naumann, F., *Angew. Chem. Int. Ed. Engl.* 27, 227 (1988).
- Hattori, H., *Chem. Rev.* 95, 537 (1995).
- Corma, A., Fornés, V., Martín-Aranda, R. M., García, H., and Primo, J., *Appl. Catal.* 59, 237 (1990).
- Barthomeuf, D., *Catal. Rev.* 521 (1996).
- (a) Bousquet, E. W., Kirby, J. E., and Searle, N. E., U.S. Patent 2,335,384, 1943; *Chem. Abstr.* 38, 2834 (1944). (b) Brown, A. W. A., Robinson, D. B. W., Hurtig, H., and Wenner, B. J., *Can. J. Res.* 26D, 177 (1948).
- (a) Brian, P. W., Grove, J. F., and McGowan, J. C., *Nature* 158, 876 (1946). (b) McGowan, J. C., Brian, P. W., and Hemming, H. G., *Ann. Appl. Biol.* 35, 25 (1948). (c) Bocobo, F. C., Curtis, A. C., Block, W. D., Harrell, E. R., Evans, E. E., and Haines, R. F., *Antibiol. Chemother.* 6, 385 (1956).
- (a) Schales, O., and Graefe, H. A., *J. Am. Chem. Soc.* 74, 4486 (1952). (b) Dann, O., and Moller, E. F., *Chem. Ber.* 82, 76 (1949). (c) Harker, R. J., U.S. Patent 2,889,246, 1959; *Chem. Abstr.* 53, 17414i (1959). (d) Zee-Cheng, K., and Cheng, C., *J. Med. Chem.* 12, 157 (1969).
- (a) Barret, A. G. M., and Graboski, G. G., *Chem. Rev.* 86, 751 (1986). (b) Kabalka, G., and Varma, R. S., *Org. Prep. Proc. Int.* 19, 283 (1987). (c) Barret, A. G. M., *Chem. Soc. Rev.* 20, 95 (1991). (d) Ballini, R., Bosica, G., and Schaafstra, R., *Liebigs Ann.* 1235 (1994). (e) Ballini, R., Bosica, G., and Rafaiiani, G., *Helv. Chim. Acta* 78, 879 (1995). (f) Fioravanti, S., Pellacani, L., Stabile, S., Tardella, P. A., and Ballini, R., *Tetrahedron* 54, 6169 (1998).

10. (a) Rosini, G., in "Comprehensive Organic Synthesis" (B. M. Trost, Ed.), Vol. 2, p. 321. Pergamon Press, Oxford, 1991. (b) Bauer, H. H., and Urbas, L., "The Chemistry of the Nitro and Nitroso Group" (H. Feuer, Ed.), Part 2, p. 75. Wiley Interscience, New York, 1970.
11. (a) Ranganathan, D., Rao, C. B., Ranganathan, S., Mehrotra, A., and Iyengar, R., *J. Org. Chem.* **45**, 1185 (1980). (b) Knochel, P., and Seebach, D., *Synthesis* 1017 (1982). (c) Knochel, P., and Seebach, D., *Tetrahedron Lett.* **23**, 3897 (1982). (d) Saikia, A. K., Barua, N. C., Sharma, R. P., and Ghosh, A. C., *Synthesis* 685 (1994).
12. Ballini, R., Castagnani, R., and Petrini, M., *J. Org. Chem.* **57**, 2160 (1992).
13. (a) Rosini, G., Ballini, R., Petrini, M., and Sorrenti, P., *Synthesis* 515 (1985). (b) Bandgar, B. P., Zirange, M. B., and Wadgaonkar, P. P., *Synlett* 149 (1996). (c) Kantam, M. L., and Sreekanth, P., *Catal. Lett.* **57**, 227 (1999).
14. (a) Bigi, F., Frullanti, B., Maggi, R., Sartori, G., and Zambonin, E., *J. Org. Chem.* **64**, 1004 (1999). (b) Ballabeni, M., Ballini, R., Bigi, F., Maggi, R., Parrini, M., Predieri, G., and Sartori, G., *J. Org. Chem.* **64**, 1029 (1999). (c) Bigi, F., Chesini, L., Maggi, R., and Sartori, G., *J. Org. Chem.* **64**, 1033 (1999).
15. Brunauer, S., Emmett, P. H., and Teller, E., *J. Am. Chem. Soc.* **60**, 309 (1938).
16. In preliminary experiments carried out at rt no product could be detected.
17. Unpublished results from our laboratory.
18. Climent, M. J., Corma, A., Garcia, H., and Primo, J., *J. Catal.* **130**, 138 (1991).
19. The E geometry was readily assigned on the basis of $^1\text{H-NMR}$ spectra: Ono, N., Kamimura, A., Kawai, T., and Kaji, A., *J. Chem. Soc. Chem. Commun.* 1550 (1987).
20. (a) Chiche, B., Finiels, A., Gauthier, C., and Geneste, P., *J. Org. Chem.* **51**, 2128 (1986).
21. The different reactivities of nitroalkanes could be ascribable to shape-selectivity effect, even if not rationalised, because they show similar pK_a values. See: Shorter, J., "The Chemistry of Functional Groups: The Chemistry of Amino, Nitroso, Nitro and Related Groups" (S. Patai, Ed.), Part 1, Chap. 11, p. 479. John Wiley & Sons, Chichester, 1996.
22. 3,5-Dimethyl-4-(4-chlorophenyl)isoxazole and 3,5-diethyl-4-(4-chlorophenyl)isoxazole were formed as by-products. For isoxazole formation from 1,3-dinitroderivatives, see: (a) Heim, F., *Chem. Ber.* 2016 (1911). (b) Meisenheimer, J., and Weibezahn, K., *Chem. Ber.* 3195 (1921).
23. Corma, A., and Martín-Aranda, R. M., *J. Catal.* **130**, 130 (1991).