

마이크로웨이브와 CeY Zeolite를 이용한 니트로화합물의 선택적인 환원반응[#]

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Selective Reduction of Nitro Compounds Using CeY Zeolite Under Microwaves

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요약. 포화 그리고 방향족 니트로화합물은 monomode reactor로 CeY zeolite와 formic acid를 사용하여 반응시키면 아민 치환체를 좋은 수율로 선택적으로 환원된다. 이 반응은 몇개의 민감한 작용기를 가진 화합물에 적합하다. 회수한 촉매를 20회 이상 사용 후에도 촉매의 활성을 계속 유지하였다.

주제어: CeY zeolite, 마이크로웨이브, 환원, 니트로 화합물

ABSTRACT. Aliphatic and aromatic nitro compounds were selectively reduced to their corresponding amino derivatives in good yields using formic acid and CeY zeolite under monomode reactor. This system is found to be compatible with several sensitive functionalities. Beside the recycling result showed it had a long catalyst lifetime and could maintain activity even after being used for 20 cycles.

Keywords: CeY zeolite, Monomode reactor, Microwaves, Reduction, Nitro compounds

INTRODUCTION

In recent decade, using an applicable industrial catalyst that is eco-friendly, green and simply recycled in the reaction mixtures has been under attention. Thus, green chemistry has been defined as a set of principles that reduces or eliminates the use or generation of hazardous substances throughout the entire life of chemical materials.¹ If one compares the technology with medical care, Green/Sustainable Chemistry (GSC) focuses on precaution (or prevention) rather than diagnosis and cure.¹ Along this line, Zeolites as a catalyst² which are nontoxic, highly acidic and basic nature, high thermal stability and specific shape selectivity have found more attention.

Rapid and selective reduction of nitro compounds is of importance for the preparation of amino derivatives in organic synthesis, particularly when a molecule has other reducible substituents.³⁻⁷ Numerous new reagents have been developed for the reduction of aromatic nitro compounds,⁸⁻¹⁰ however, little attention has been paid to the reduction of aliphatic nitro

compounds,¹¹⁻¹³ which are traditionally reduced by high pressure.¹⁴ Though the most general methodology for this conversion is catalytic hydrogenation¹⁵ as it is an economical and effective method, particularly in large scale reactions, the reaction has a limited utility in the presence of other reducible functional groups.¹⁶ The selective reduction of nitro group in presence of other reducible functional groups were also achieved using metal based reduction systems.¹⁷ However, the selective reduction of the nitro group in presence of carbonyl group could not easily be attainable under these conditions. In order to overcome these difficulties, zeolite especially CeY as catalysts¹⁸ meet the requirement for organic transformation taking into account their environmental advantage.

Therefore we became interested in a possibility of the selective reduction of nitro groups in presence of other reducible functional groups including carbonyl groups and halides. Herein, we report various nitro compounds are selectively and readily reduced to their corresponding amino derivatives in presence of other functional groups using zeolites and formic acid under microwaves.

Now days MW has been employed not only to decrease reaction times but also to improve yields. MWs constitute a very original procedure for heating materials, clearly different from

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the classical ways. The reduction on reaction times are attributed to be a result of both temperature and pressure effects and supposed specific effects of the radiation, such as improved homogeneity in temperature, a faster temperature rise, and possible modifications of activation parameters ΔH^\ddagger and ΔS^\ddagger .^{19,20} Several reviews have been published covering various aspects of microwave-assisted chemistry.^{21,22}

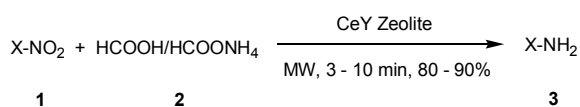
We believe that the time saved by using microwaves is potentially important in traditional organic synthesis but could be of even greater importance in high-speed combinatorial and medicinal chemistry as well as industrial scale production of chemicals. As part of our program aimed at achieving simple and environmentally compatible synthetic methodologies,²³ we wish to report a selective, rapid and mild method of reduction of aliphatic and aromatic nitro compounds to the corresponding amino derivatives using CeY zeolite and formic acid in aqueous media under microwave irradiation (*Scheme 1*). This new system reduced with ease a wide variety of nitro compounds directly to the corresponding amines and many functional groups can be tolerated. When formic acid was replaced by ammonium formate the reduction proceeded effectively and the products were obtained in almost comparable yields.

RESULT AND DISCUSSION

The reduction of nitro group in presence of CeY zeolite and HCOOH or HCOONH₄ was completed within 3 ~ 10 min. TLC and IR monitored the course of the reaction. All the compounds reduced (*Table 1*) by this system were obtained in good yield (80 ~ 92%).

As an initial attempt to find out an optimal reaction condition, a variety of experimental procedures were examined for Nitromethane and Nitroethane (*Table 1*, Entry 1 and 2) by changing reaction medium and conditions (*Tables 2*). Finally, in order to check the possible intervention of specific (non-thermal) MW effects, the results obtained under MW were compared to conventional heating using toluene and DMF as solvent. The reaction, in the case of Entry 1 and 2, has been carried out using preheated oil bath, under the same conditions as under MW (time, temperature, vessel) (*Table 2*). Reactions proceeding with considerable low yields under similar thermal conditions showed there is existence of specific MW effect. The reaction was also tried with or without using CeY zeolite. No desirable conversion to the product showed catalytic effect of CeY zeolite.

These results indicate that CeY zeolite catalyzed using formic acid a versatile reducing system for wide variety of aromatic



Scheme 1

nitro compounds in the presence of other functional groups. The reaction can easily be applicable to a large scale synthesis of aniline compounds as the reaction set-up, sequence and work-up is simple and straightforward. Therefore this procedure does bear a general use for a large scale preparation of aromatic amines specifically in cases where selective, rapid, mild reduction is required.

EXPERIMENTAL

All melting points were taken on a Büchi-Tottoli capillary apparatus and are uncorrected; Microwave dielectric heating was performed in a Smith Creator single mode microwave cavity Personal Chemistry from Biotage GmbH, Germany, and producing continuous irradiation at 2.45 GHz. The reaction vessel was a round-bottomed 100mm DuranTM glass tube with a Schott GL 18 screw cap, provided with Teflon septa as a pressure relief device. All the products were characterized by comparison of their spectral data and mixed m.p. with the reported ones.²⁴ Some of the products such as methylamine, ethylamine and propylamine, could not be checked by TLC and melting points and evaluated by GC. CeY zeolite²⁵ was prepared by metal cation exchange on NaY zeolite according to the known method and activated before use by heating at 550 °C for 4 hrs.

General procedure

A suspension of an appropriate nitro compounds (5 mmol) and CeY zeolite (2 mg) were finely ground with a mortar and pestle. 90% HCOOH (2.5 mL) or ammonium formate (0.5 g) (**2**) was added to this mixture in a Pyrex glass vial, which was placed in a screw capped Teflon vessel. Microwave irradiation was applied for 3 ~ 10 min at 140 °C. After the completion of reaction (TLC analysis), recyclable zeolite was separated by filtration after eluting the product with ethanol under reduced pressure and the residue washed with saturated NaCl solution to remove ammonium formate give pure product in high yield (*Table 2*).

Effect of recycling experiment on yield

After the reaction was completed, the reaction mixture was centrifuged and separated to provide wet solid catalyst in order to reuse the catalyst and to study the catalyst time and stability. To each sample, fresh nitro compound (Entry 1, *Table 1*) and formic acid was added into same amounts as in the initial reaction.

Fig. 1 summarizes the experimental results, which indicate the CeY catalyzed yield of final product was in excess of 90% every 2 h each time. The CeY catalyst maintained sustained activity even after being used for 20 cycles and yield was only slightly decreased.

From the economic point of view, the cost of the catalyst

Table 1. CeY catalyzed reduction of nitro compounds

Entry	X	Reaction time (min)		Product	Isolated Yield (%)	
		HCOOH	HCOONH ₄		HCOOH	HCOONH ₄
1	Nitromethane	6	3	Methylamine	85	78
2	Nitroethane	7	6	Ethylamine	80	73
3	1-Nitropropane	7	5	<i>n</i> -Propylamine	86	68
4	1-Nitrobutane	7	5	<i>n</i> -Butylamine	83	75
5	2-Nitroethyl ethanoate	7	5	2-Aminoethyl ethanoate	88	83
6	1-Nitromethyl butanoate	5	5	1-Aminomethyl butanoate	80	76
7	Nitrobenzene	7	7	Aniline	90	88
8	2,3,4-Nitrophenol	5 - 7	5 - 7	2,3,4-Aminophenol	90	82
9	2,4-Dinitrophenol	10	8	2,4-Diaminophenol	90	85
10	2,3,4-Nitrotoluene	7 - 10	5 - 9	2,3,4-Aminotoluene	91	87
11	1,4-Dinitrobenzene	10	6	1,4-Diaminotoluene	90	82
12	2,3-Dinitrobenzene	9	7	2,3-Phenylenediamine	90	77
13	1,2-Nitronaphthalene	9	5 - 10	1,2-Naphthylamine	90	83
14	2,4-Nitroanisole	5 - 10	8 - 10	2,4-Aminoanisole	90	83
15	2,3,4-Nitroaniline	5 - 10	5 - 10	2,3,4-Phenylenediamine	91	88
16	2,4-Nitrobenzaldehyde	6 - 10	4 - 10	2,4-Aminobenzaldehyde	89	86
17	2,4-Nitroacetophenone	9	6	2,4-Aminoacetophenone	90	84
18	4-Nitrobenzophenone	8	7	4-Aminobenzophenone	90	84
19	4-Nitrobenzamide	9	8	4-Aminobenzamide	90	88
20	4-Nitrophenylacetate	10	5	4-Aminophenylacetate	91	90
21	2,3,4-Nitrobenzoic acid	5 - 8	4 - 9	2,3,4-Aminobenzoic acid	90	86
22	2,3,4-Nitrochlorobenzene	7 - 9	6 - 7	2,3,4-Chloroaniline	90	88
23	2,3,4-Nitrobromobenzene	7 - 9	3 - 6	2,3,4-Bromoaniline	91	85
24	3-Nitroiodobenzene	8	3	3-Iodoaniline	88	79
25	4-Nitrocinnamic acid	9	4	4-Aminocinnamic acid	90	81
26	4-Nitrobenzoxonitrile	10	7	4-Aminobenzonitrile	92	85
27	4-Nitrophenylacetoneitrile	10	8	4-Aminophenylacetoneitrile	91	90
28	4-Nitrophenethylalcohol	10	10	4-Aminophenethylalcohol	90	83
29	3,5-Dinitrosalicylic acid	10	7	3,5-Diaminosalicylic acid	89	85
30	4-Nitroacetanilide	9	5	4-Aminoacetanilide	90	80

Table 2. Comparative study of the reduction of nitro compounds (Entry 1 and 2) using CeY zeolite as catalyst

Entry	Reaction Medium	Zeolite	Reaction conditions	Reaction temperature (°C)	Time (min)	Yield ^a (%)
1	HCOOH	-	MW	120	30	Nil
	HCOONH ₄	-	MW	120	30	Nil
	HCOOH	-	Relux	120	720	Nil
	HCOONH ₄	-	Relux	120	720	Nil
	HCOOH	CeY	MW	120	6	85
	HCOONH ₄	CeY	MW	120	3	78
	HCOOH	CeY	Reflux in Toluene	120	240	52
	HCOOH	CeY	Reflux in DMF	120	260	45
	HCOONH ₄	CeY	Reflux in Toluene	120	300	48
	HCOONH ₄	CeY	Reflux in DMF	120	310	44
2	HCOOH	-	MW	120	30	Nil
	HCOONH ₄	-	MW	120	30	Nil
	HCOOH	-	Reflux	120	720	Nil
	HCOONH ₄	-	Reflux	120	720	Nil
	HCOOH	CeY	MW	120	7	80
	HCOONH ₄	CeY	MW	120	6	73
	HCOOH	CeY	Reflux in Toluene	120	260	46
	HCOOH	CeY	Reflux in DMF	120	300	44
	HCOONH ₄	CeY	Reflux in Toluene	120	375	40
	HCOONH ₄	CeY	Reflux in DMF	120	400	38

^aIsolated yield

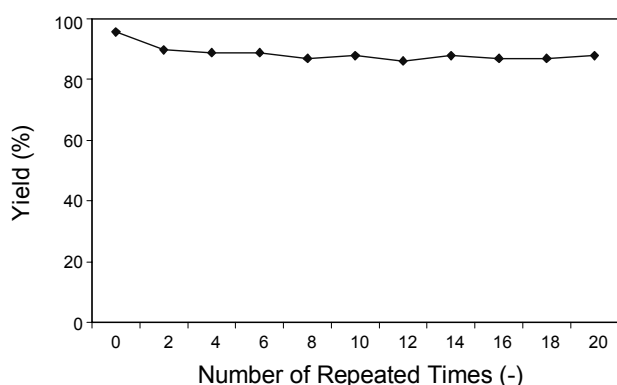


Fig. 1. Effect of repeat use of CeY zeolite on yield.

accounts for a large part of the cost of amine production. Therefore, the stability and sustained activity of the catalyst are of great importance for industrial applications. Therefore, CeY catalyst can contribute much to decreasing the cost of amine production due to its long catalyst life time and good stability as a heterogeneous solid base catalyst.

CONCLUSION

Thus the reduction of nitro compound can be accomplished with CeY zeolite instead of expensive Ni, Pt, Pd *etc.*, without affecting the reduction of any reducible substituents including halogen and carbonyl compounds. The yields were virtually quantitative and analytically pure. Further it has been found that ammonium formate was less effective donor than formic acid with CeY zeolite. The obvious advantages of the proposed method over the previous methods are: (1) selective reduction of nitro compounds in the presence of other reducible groups including carbonyl and halogens, (2) ready availability and easy to operate, (3) rapid reaction, (4) high yields of substituted anilines, (5) avoidance of strong acidic media, (6) required no pressure apparatus and (7) less expensive. This procedure will therefore be of general use especially in cases where rapid, mild and selective reduction is required. Further investigations of other useful applications related to deblocking of protecting groups in peptide synthesis are in progress.

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