$CeCl_3·7H_2O$–NaI/SiO_2 promoted Beckmann rearrangement (under solvent-free and microwave irradiation)

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$CeCl_3·7H_2O$–NaI/SiO_2 system promoted Beckmann rearrangement of a variety of aldoximes and ketoximes was efficiently conducted under solvent-free and microwave irradiation conditions. This protocol afforded an alternative method for the preparation of amides by Beckmann rearrangement with advantages of short reaction time, high yield, no pollution, simple operation and easy work-up.

Keywords: Beckmann rearrangement, microwave irradiation, $CeCl_3·7H_2O$–NaI, solvent-free

The Beckmann rearrangement is a very important reaction in organic synthesis and in the chemical industry.[1] The conventional Beckmann rearrangement usually requires the use of strong Bronsted or Lewis acids, *i.e.* concentrated sulfuric acid, phosphorus pentachloride in diethyl ether, and hydrogen chloride in acetic anhydride, which always cause environmental problems because of the difficulty in separation.[2] Recently, SiO_2 supported catalysts such as SiO_2 supported sulfuric acid[3] and MoO_3[4] have been reported, which have efficiently resolved the separation problem and therefore eliminated the pollution caused by using catalysts. In addition, Beckmann rearrangement has also been conducted under solvent-free[5] and microwave irradiation conditions.[6] This avoided the use of volatile organic solvents, and the reaction was significantly accelerated.

The $CeCl_3·7H_2O$–NaI system has become an attractive candidate as a water tolerant Lewis acid promoter in organic synthesis. $CeCl_3·7H_2O$ and NaI are cheap, nontoxic, and stable compounds, and therefore the protocols based on their uses represent an environmentally benign alternative to current chemical processes using water intolerant Lewis acids. Recently, $CeCl_3·7H_2O$–NaI system has been used to promote the intramolecular addition reactions of 7-hydroxy-1,3-dienes,[7] cleavage of aliphatic and aromatic *tert*-butyl ethers,[8] alkylation of activated quinoline and isoquinoline,[9] tetrahydropyranylation of hydroxy groups,[10] stereoselective Julia olefination of cyclopropyl carbinol,[11] heteroatom nucleophilic addition to electron-poor alkenes,[12] stereoselective aldol coupling of α,β-acetylenic ketones,[13] chemoselective iodination of alcohols,[14] indole addition to carbonyl compounds,[15] stereoselective synthesis of 2,4-disubstituted chiral tetrahydroquinolines,[16] allylation reactions of aldehydes,[17] *etc*. The earlier applications of the $CeCl_3·7H_2O$–NaI system have been reviewed by Bartoli and coworkers.[18]

To expand the application of $CeCl_3·7H_2O$–NaI system in organic synthesis and continue the development of SiO_2 supported catalysts, we report a $CeCl_3·7H_2O$–NaI/SiO_2 promoted expeditious and environmentally benign method for Beckmann rearrangement under solvent-free and microwave irradiation.

Results and discussion

Initially, benzophenone oxime was selected as a model substrate and the reaction was carried out using $CeCl_3·7H_2O$ as promoter under solvent-free and microwave irradiation. It was found that oxime was mainly hydrolysed to the corresponding ketone while the amide was generated as just a minor product. Furthermore, when one equivalent of $CeCl_3·7H_2O$ was used, the substrate was hydrolysed to produce the ketone completely in very high selectivity. Therefore, this protocol is possibly a good alternative for the deprotection of carbonyl compounds (entry 1, Table 1). Then the Beckmann rearrangement was attempted using $CeCl_3·7H_2O$–NaI system, but the rearrangement product was obtained in low yield (entry 2, Table 1). In further studies, $CeCl_3·7H_2O$–NaI system dispersed on silica gel was prepared by simple mixing of both reagents in acetonitrile, followed by complete removal of the solvent.[19] Fortunately, it was found that $CeCl_3·7H_2O$–NaI/SiO_2 promoted the reaction of benzophenone oxime chemoselectively to give the desired rearrangement product in excellent yield under solvent-free and microwave irradiation (entry 3, Table 1). The amount of $CeCl_3·7H_2O$–NaI/SiO_2 used in the reaction was optimised. It was found that the amount of $CeCl_3·7H_2O$ and NaI was decisive for completion of Beckmann rearrangement. Among the different ratios, the optimal molar ratio for benzophenone oxime, $CeCl_3·7H_2O$, and NaI was 1: 1.25: 1. In addition, the product could be readily separated by extraction, and the $CeCl_3·7H_2O$–NaI/SiO_2 could be recovered by filtration.

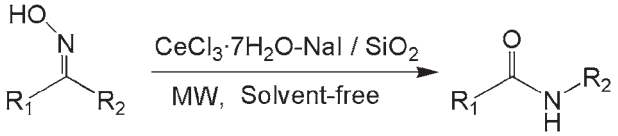
The role of the sodium iodide is established in the reaction, one possibility is to enhance the activity of cerium trichloride as Lewis acid [20] (Eqn (1)). It is probable that a halide-exchange reaction between $CeCl_3·7H_2O$ and NaI occurred during the preparation of $CeCl_3·7H_2O$–NaI/SiO_2, which is responsible for the enhancement of activity of system.

$$CeCl_3 + nNaI \rightarrow CeCl_{(3-n)}I_n + nNaCl \qquad (1)$$

Silica gel has an important role in the reaction, and its presence is found to be essential for the high efficacy of the reaction. A reasonable explanation may be that the silica gel is mildly acidic and may interact favourably with $CeCl_3$ at its surface. The oxime probably coordinates at a vacant coordination site of Ce metal, which subsequently promotes the reaction.

The generality, scope and efficiency of this method were explored using a variety of representative oximes as substrates (Scheme 1). The results are summarised in Table 2.

The Beckmann rearrangements of aromatic ketoximes proceeded effectively to afford the corresponding amides in good to excellent yields (entries 6–16, Table 2), compared to aliphatic oximes, which afforded slightly lower yields



R_1=alkyl,aryl,heterocyclyl

R_2=alkyl,aryl,H

Scheme 1

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Table 1 The effect of different promoter on the conversion and selectivity of benzophenone oxime[a]

Entry	Promoter	Amount (mmol)	Conversion (%)	Selectivity (%)	
				Amide	Ketone
1	$CeCl_3{\cdot}7H_2O$	0.1	63	60	40
		0.2	65	30	70
		0.5	72	40	60
		1	85	None	99
2	$CeCl_3{\cdot}7H_2O$-NaI	1: 0.8	60	48	52
		1: 1	70	60	40
		1.25: 1	74	70	30
		1.25: 1.25	76	72	28
3	$CeCl_3{\cdot}7H_2O$-NaI/SiO_2	1: 0.8/0.56 g	76	99	None
		1: 1/0.56 g	89	99	None
		1.25: 1/0.56 g	91	99	None
		1.25: 1.25/0.56 g	90	99	None

[a]Reaction condition: benzophenone oxime (1 mmol), microwave power (450 W), reaction time (4 min).

and needed a longer time (entries 1–5, Table 2). Considering the configuration of substrates, we presume that the π–π conjugated structures in the aryl oxime increase the activity of hydroxy and favours the reactions. In the case of unsymmetrical ketoximes the reactions were selective and only one amide was produced for each substrate. It was observed that the rates as well as yields of reactions were dependent on the substituents on the aryl rings. Electron donating groups such as MeO and Me on the aromatic rings enhanced the rates of the reactions compared to the electron withdrawing ones such as halo and nitro. Both sterically less and more hindered oximes were successfully converted into amides. In the present method, as shown in Table 2, aromatic aldoximes were also converted into the corresponding amides in good yields (entries 17–20, Table 2). Furthermore, aldoximes only gave the primary amides. It was also interesting to note that sensitive furfuraldoxime was also converted into corresponding amide without any difficulty. The Beckmann rearrangement was generally suggested to proceed through *anti*-migration, wherein, the Z-forms of oximes were expected to give the corresponding amides.[21]

In conclusion, we have developed an efficient method for Beckmann rearrangement using $CeCl_3{\cdot}7H_2O$–NaI/SiO_2 as promoter under solvent-free and microwave irradiation, which offers a simple and expeditious technique for amides. This protocol has advantage of generality, simplicity, recyclability, high yield, and no pollution.

Experimental

General procedure for Beckmann rearrangement

Silica gel (0.56 g) was added to the mixture of $CeCl_3{\cdot}7H_2O$ (0.47 g, 1.25 mmol) and NaI (0.15 g, 1 mmol) in acetonitrile (5 ml), and the mixture was stirred overnight at room temperature. Then the acetonitrile was removed by evaporation under reduced pressure. To the resulting solid, oxime (1 mmol) was added. The mixture was ground with a pestle in an agate mortar at room temperature until a fine powder was obtained. The powder was subjected to a microwave irradiation at 450 W of output power for the appropriate time as indicated in Table 2. After completion of the reaction, the mixture was extracted with 2 × 5 ml of acetone and the combined extract was evaporated off the solvent to give the product. Typical example: N-(*p*-methoxyphenyl)acetamide (entry 7, Table 2): ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.16 (s, 3H), 3.81 (s, 3H), 6.87 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 8.2 Hz, 2H), 7.89 (br s, NH). ^{13}C (100 MHz, $CDCl_3$): δ 24.2, 55.5, 114.1, 122.2, 131.3, 156.5, 168.9.

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Table 2 $CeCl_3{\cdot}7H_2O$–NaI/SiO_2 promoted Beckmann rearrangement under solvent-free and microwave irradiation[a]

Entry	R_1	R_2	Time/min	Yield/%[b]	M.p. or b.p. (lit.)
1	CH_3	CH_3	6	85	200–202 (204–206)[22]
2	CH_3	CH_3CH_2	6	72	95–97/10 mmHg (90–92/8 mmHg)[22]
3	CH_3	$(CH_3)_2CHCH_2$	6	75	217–219 (221)[23]
4	$(CH_2)_5$		6	75	70–73 (68–71)[22]
5	$(CH_2)_4$		6	82	40–42 (38–40)[22]
6	CH_3	C_6H_5	3	87	111–112 (113–115)[22]
7	CH_3	*p*-$CH_3OC_6H_4$	3	87	126–127 (128–130)[22]
8	CH_3	*p*-HOC_6H_4	8	82	173–174 (168–172)[22]
9	C_6H_5	C_6H_5	4	91	160–162 (161–163)[24]
10	C_6H_5	*p*-$CH_3OC_6H_4$	3	86	150–151 (152–153)[24]
11	C_6H_5	*p*-$CH_3C_6H_4$	4	85	158–160 (157–159)[25]
12	C_6H_5	*o*-$CH_3C_6H_4$	4	89	141–142 (144–145)[26]
13	C_6H_5	*o*-ClC_6H_4	8	80	103–104 (101–102)[27]
14	C_6H_5	*p*-ClC_6H_4	8	75	194–195 (190–192)[25]
15	C_6H_5	*p*-BrC_6H_4	8	76	198–199 (197)[28]
16	C_6H_5	*p*-$O_2NC_6H_4$	8	72	195–196 (197–198)[24]
17	C_6H_5	H	6	81	126–127 (125–128)[22]
18	*o*-HOC_6H_4	H	6	79	142–145 (140–144)[22]
19	*p*-$CH_3OC_6H_4$	H	4	80	168–170 (164–167)[22]
20		H	4	75	137–138 (140–142)[29]

[a]All substrates were synthesised according to known literature procedures. All products were characterised by comparison of their melting points, IR, and ^{1}H NMR spectra with those of authentic samples.
[b]All yields refer to isolated products except entries 1–3, which were determined by GC.

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