Iminium salt-catalyzed liquid-phase Beckmann rearrangement of cyclohexanone oxime

Yusuke Izumi *, Tomokazu Fujita

Department of Applied Chemistry, School of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-01, Japan

Abstract

Alkoxy-methylene-N,N-dimethyliminium salt, a kind of Meerwein salt, effectively catalyzed the liquid-phase Beckmann rearrangement of cyclohexanone oxime to ϵ-caprolactam under mild reaction conditions (50–60°C, atmospheric pressure). The iminium salt was easily prepared in situ either by O-alkylation of N,N-dimethylformamide (DMF) with dimethyl sulfate or by reacting DMF with epichlorohydrin in the presence of a strong acid. The product lactam poisoned the iminium catalyst, though reversibly. In the reaction employing a low concentration of the oxime (0.29 M), turnover of the iminium catalyst derived from heteropolyacid attained 200. A possible mechanism which involves intramolecular migration of the hydroxy group of oxime was proposed.

Keywords: Beckmann rearrangement; Rearrangement; Iminium salt; Cyclohexanone oxime; DMF

1. Introduction

Catalytic rearrangement of oximes into the corresponding lactams without use of stoichiometric amounts of acid promoters has long been an important subject for catalyst researchers, particularly with respect to the commercial production of ϵ-caprolactam in which sulfuric acid is employed as catalyst producing a large amount of ammonium sulfate as a by-product. A great number of heterogeneous catalysts which include silica–alumina [1], supported boron oxide [2–4], faujasite zeolites [5–7], pentasil zeolites [8,9], titanosilicate [10],and supported tantalum oxide [11] have been proposed for the vapor-phase rearrangement of cyclohexanone oxime.

The vapor-phase rearrangement over solid catalysts, however, needs a reaction temperature as high as between 250 and 350°C, thereby lactam selectivity is not sufficiently high, and rapid catalyst deactivation is often caused due to carbon deposit. A liquid-phase catalytic rearrangement process under milder reaction conditions, therefore, appears to be preferable to vapor-phase process, since it not only affords higher lactam selectivity, but it also saves much energy in process operation. Nevertheless no efficient practical catalyst systems for the liquid-phase rearrangement of cyclohexanone oxime have been developed.

One of the authors has previously reported in a rapid communication [12] that the oximes of cyclohexanone, acetaldehyde, and benzaldehyde could be rearranged catalytically (turnover: 2.6–

* Corresponding author.

4.7) in an *N,N*-dimethylformamide (DMF) solution in the presence of an *O*-alkylating agent such as trimethyloxonium tetra-fluoroborate and methyl trifluoromethanesulfonate at 48–65°C. A methoxymethylene-*N,N*-dimethyliminium salt, which can be readily formed from DMF and trimethyloxonium salt [13], was suggested to be the real catalyst species. In addition, another iminium catalyst prepared in situ from DMF, epichlorohydrin, and heteropolyacid gave a high turnover of 43 [12]. A Vilsmeyer complex of $[Me_2N=CHCl]^+SO_4H^-$, which is another type of iminium salt and obtainable by the reaction of DMF with chlorosulfonic acid, has been reported to be able to activate the Beckmann rearrangement, but the equimolar amount of the reagent was required [14]. Recently, a Lewis acid system of $SbCl_5$–$AgSBF_6$ has been reported to catalyze the rearrangement of trimethylsilyl ethers of oximes [15], but the system was not effective for the rearrangement of the ordinary oximes. A transition metal catalyst system of tetrabutylammonium perrhenate(VII) and trifluoromethanesulfonic acid catalyzed the rearrangement, but the turnover of the catalyst was less than 5 [16]. Among these catalysts recently proposed for the liquid-phase Beckmann rearrangement, the iminium salt appears to be the simplest and the most active. The objective of this work was to investigate molecular catalysis of the iminium salt in the rearrangement of cyclohexanone oxime in detail through the optimization of catalyst preparation and reaction conditions, and to propose a possible reaction mechanism.

2. Experimental

2.1. Preparation of iminium salt catalyst

Alkoxy-methylene-*N,N*-dimethyliminium salt (1) is formed by reacting *N,N*-dimethylformamide (DMF) with an *O*-alkylating agent such as trialkyloxonium salts [13] and alkyl esters of strong acids as shown in Scheme 1. Among
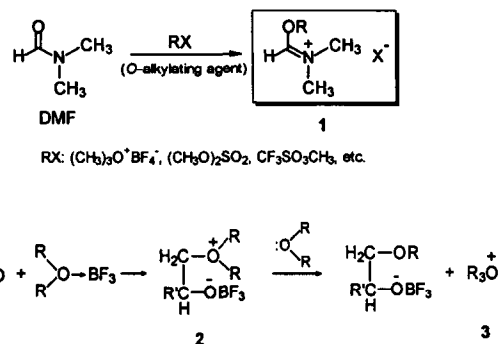
Scheme 1. Formation of iminium salt and trialkyloxonium salt.

these alkylating agents, dimethyl sulfate handles most easily. Alternatively, the iminium salt can be obtained in situ by reacting DMF with epoxide in the presence of a strong acid such as boron trifluoride etherate, because trialkyloxonium cations (2 and 3) are formed from epoxide and a strong acid [17,18]. In the present study, the iminium salt catalyst was prepared in situ according to these two methods.

2.1.1. Catalyst from DMF and dimethyl sulfate

To a Pyrex flask (30 ml) was added by 31.5 mg (0.25 mmol) of dimethyl sulfate and 1.5 ml of anhydrous DMF obtained through distillation with calcium hydride. The reaction mixture was stirred at 60°C for 1 h under a stream of nitrogen to give a DMF solution of iminium salt. The formation of methoxy-methylene-*N,N*-dimethyliminium salt was confirmed by IR and ^{1}H NMR data: 1250 and 1060 cm^{-1} (C–O–C), 1710 cm^{-1} (C=N); $CDCl_3$/TMS, $\delta = 3.73$ (OCH_3), 3.52 and 3.20 ($C=N^+(CH_3)_2$). The reaction between dimethyl sulfate and DMF to form the iminium salt was estimated to be equimolar, since the existence of the equimolar amount of monomethyl sulfate anion was suggested from ^{1}H NMR data ($CDCl_3$/TMS, $\delta = 4.50$ (CH_3OSO_3)).

2.1.2. Catalyst from DMF, epoxide and acid

To a Pyrex flask (30 ml) were added required amounts of acid and epoxide, and 1.5–2.0 ml of anhydrous DMF. The reaction mixture was

stirred at 50°C for 2 h under a stream of nitrogen to give a DMF solution of iminium salt.

2.2. Rearrangement reaction

A DMF solution of cyclohexanone oxime was prepared by adding 0.5 g (4.42 mmol) of the oxime and 10 ml of benzene to 1.0–1.5 ml of DMF in a Pyrex flask (30 ml), followed by azeotropic distillation to remove the water remained in the oxime. The substrate solution thus obtained was mixed with a DMF solution of the iminium salt catalyst, and stirred at 50–60°C for 2 h. At the end of the reaction, the reaction mixture turned yellow to orange. ε-Caprolactam produced was identified by IR and ^{13}C NMR analyses (1660 cm^{-1} (C=O), 3430 cm^{-1} (NH); CDCl$_3$/TMS, δ = 23.9, 36.8, 42.3, 178), and determined by GLC using a Unisole 30T column (2 m). The selectivity to the lactam was more than 99% on the basis of GLC measurements; a trace amount of cyclohexanone was detected.

2.3. Spectrometric observation of reaction process

Methoxy-methylene-N,N-dimethyliminium salt was obtained as a gel-like solid by reacting DMF (1.5 ml) and dimethyl sulfate (1.2 mmol) at 60°C for 5 h, followed by removal of excess DMF through distillation in vacuo. To the gel was added 0.2 ml of choloform and 2.4 mmol of cycohexanone oxime to make a sample solution for IR measurement. The solution was sealed in a flask, then left at room temperature to effect the rearrangement slowly.

3. Results and discussion

3.1. N,N-Dimethylformamide–dimethyl sulfate system

Dimethyl sulfate alone dissolved in benzene, acetonitrile, or 1,2-dichloroethane was inactive

Table 1
Formamides for iminium salt formation [a]

Amide	Oxime conv. (%)	Turnover [b]
N,N-dimethylformamide	35	6.2
N,N-dimethylacetamide	13	2.3
N,N-diisopropylformamide	12	1.7
N-methylformamide	15	2.4
N,N-dimethylthioformamide	13	2.1

[a] Reaction conditions: dimethyl sulfate:oxime = 0.25:4.4 mmol, amide = 3 ml, 60°C, 2 h.
[b] Turnover number per mole of dimethyl sulfate.

for converting cyclohexanone oxime into ε-caprolactam. The iminium salt formed from DMF and dimethyl sulfate was, therefore, responsible for the rearrangement. As shown in Table 1, several amides other than DMF could also be O-alkylated to form active iminium salts, but not so effectively as DMF.

Time dependence of the rearrangement activity is depicted in Fig. 1 for the DMF–$(CH_3O)_2SO_2$ system. The reaction proceeded rapidly within 45 min to give the maximum turnover of 6 on the basis of moles of dimethyl sulfate applied, then the turnover was leveled due to deactivation of catalyst. The activation energy of the reaction was estimated to be 11 kcal mol^{-1} from the experiments performed between 50 and 80°C. Fig. 2 shows first-order dependence of the reaction rate on catalyst concentration. The deviation from the first-order
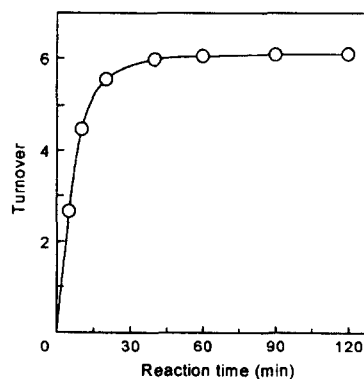

Fig. 1. Time dependence of rearrangement activity (DMF–$(CH_3O)_2SO_2$ system). Dimethyl sulfate:DMF:oxime = 0.25:40:4.4 mmol, 60°C.
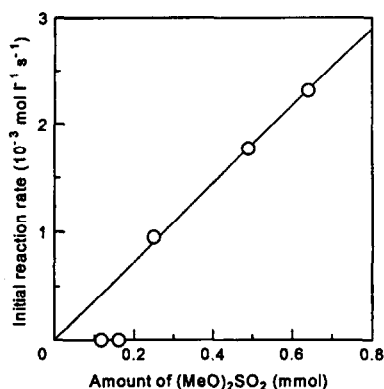
Fig. 2. First order dependence of reaction rate on catalyst concentration (DMF–$(CH_3O)_2SO_2$ system). DMF:oxime = 40:4.4 mmol, 60°C.

dependence observed at lower catalyst concentrations was probably due to deactivation by a trace amount of water remained in the DMF solution or contaminated during the operations. The iminium salt was very susceptible to such basic substances as water, alcohol, and amine.

The catalyst deactivation observed in Fig. 1 was caused not by thermal deterioration of catalyst, but essentially by poisoning with the product ε-caprolactam as depicted in Fig. 3. The turnover was decreased with an increase in the amount of the lactam charged before reaction. The lactam reacted with the iminium salt to form an inactive species, probably reversibly,
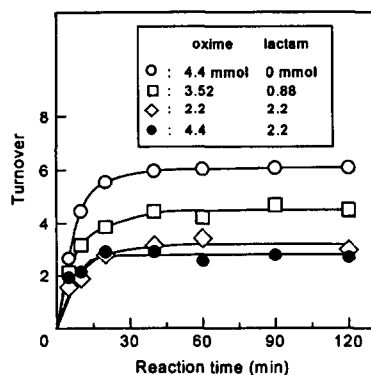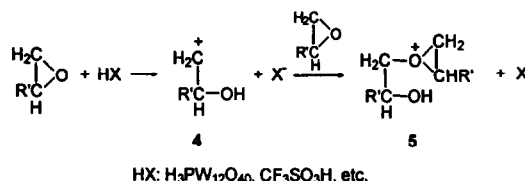

Scheme 2. Formation of O-alkylating agents from epoxide and acid.

because the reaction was not completely retarded even when 2.2 mmol of the lactam was added to 0.25 mmol of catalyst.

3.2. N,N-dimethylformamide–epoxide–acid system

Active iminium salts other than that formed in the DMF–$(CH_3O)_2SO_2$ system could be readily obtained in situ from DMF, epichlorohydrin, and $BF_3 \cdot Et_2O$ according to Scheme 1. We confirmed that active iminium salts could also be prepared when $BF_3 \cdot Et_2O$ was replaced by a strong protonic acid, such as trifluoromethanesulfonic acid or a Keggin-type heteropolyacid. In this case, O-alkylating agents of 4 and 5 were presumably formed according to Scheme 2.

Quite the same tendency of catalyst deactivation in the course of the reaction as noticed in the DMF–$(CH_3O)_2SO_2$ system was also observed in this DMF–epichlorohydrin–acid system.

Fig. 3. Retardation of catalytic activity in the presence of lactam (DMF–$(CH_3O)_2SO_2$ system). Dimethyl sulfate:DMF = 0.25:40 mmol, 60°C.

Table 2
Acid for iminium salt formation

Acid	Oxime conv. (%)	Turnover [a]
$BF_3 \cdot Et_2O$ [b]	81	7.1
CF_3SO_3H [b]	60	5.3
CF_3CO_2H [b]	0	0
$H_3PW_{12}O_{40}$ [c]	78	51
$H_4SiW_{12}O_{40}$ [c]	85	58

[a] Turnover number per mole of acid.
[b] Acid:epichlorohydrin:DMF:CH_3CN:oxime = 0.5:2.5:5:57:4.4 mmol, 50°C, 2 h.
[c] Acid:epichlorohydrin:DMF:cyclohexanone oxime = 0.07:1.3:40:4.4 mmol, 50°C, 2 h.

Table 2 summarizes the results obtained in the DMF–epichlorohydrin–acid system. Incidentally, acid alone without the epoxide did not catalyze the rearrangement in DMF at all. The strong acids effected high activity, but the weaker acid trifluoroacetic acid did not form an active catalyst. Interestingly the Keggin-type heteropolyacid brought about the highest activity, even estimated on the molecular base, not on the proton base. Such high activity of the Keggin-type heteropolyacid is probably due to the unique ability of the heteropoly anion to stabilize a carbenium ion or oxonium ion [19].

Even a small amount of DMF corresponding to only 6 to 10 times (molar basis) of the amount of acid used was enough for adequate formation of the iminium salt. Accordingly, a major part of DMF employed could be replaced by another solvent which dissolved both the iminium salt and the oxime. The effect of solvent on the catalytic efficiency in the DMF–epichlorohydrin–$BF_3 \cdot Et_2O$ system is shown in Table 3. Acetonitrile and 1,2-dichloroethane appeared to be the preferred solvents in the present rearrangement process. Table 4 lists the effect of the sort of epoxide on the catalytic efficiency in the DMF–epichlorohydrin–heteropolyacid system, where triphenyl borate was added as a dehydrating agent to enhance catalyst turnover. The epoxides having electron-withdrawing groups appeared to be more effective.

The deactivation of catalyst was presumably due to reversible poisoning by the product lactam as mentioned above. Accordingly, if the oxime concentration is lowered, the catalyst turnover must increase. Indeed, as shown in Fig. 4, the turnover attained as much as 200 when the oxime concentration was reduced from 1.5 M (the standard condition) to 0.29 M in the DMF–epichlorohydrin–heteropolyacid system.

3.3. Reaction mechanism

The mechanism of the rearrangement reaction was examined with regard to the DMF–$(CH_3O)_2SO_2$ system through the observation of spectral changes in IR absorption of the reaction mixture being left at room temperature. The

Table 4
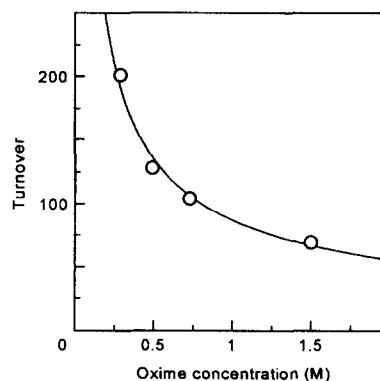Epoxide for iminium salt formation [a]

Epoxide	Oxime conv. (%)	Turnover [b]
none	0	0
epichlorohydrin	53	69
cyclohexene oxide	39	51
1,2-epoxyoctane	42	54
glycidyl phenyl ether	49	64

[a] $H_3PW_{12}O_{40}$:epoxide:DMF:oxime: $(PhO)_3B$ = 0.035:1.3:40:4.4:0.35 mmol, 50°C, 2 h.
[b] Turnover number per mole of acid.

Table 3
Effect of solvent on catalytic activity [a]

Solvent	Oxime conv. (%)	Turnover [b]
dimethylformamide	59	5.3
dimethyl sulfoxide	25	2.4
1,2-dichloroethane	70	6.5
acetonitrile	81	7.1

[a] $BF_3 \cdot Et_2O$:epichlorohydrin:DMF:oxime = 0.5:2.5:5:4.4 mmol, solvent = 3 ml, 50°C, 2 h.
[b] Turnover number per mole of $BF_3 \cdot Et_2O$.

Fig. 4. Dependence of turnover on oxime concentration (DMF–epichlorohydrin–heteropolyacid system). $H_3PW_{12}O_{40}$:epichlorohydrin: DMF:oxime = 0.035:1.3:40:4.4 mmol, $(PhO)_3B$ = 0.1 M, 50°C, 2 h.

spectral changes with time course were illustrated in Fig. 5, together with the reference spectra of the authentic cyclohexanone oxime and ε-caprolactam.

The absorption due to the OH group of the oxime observed at 3600 cm^{-1} decreased as the reaction proceeded. Concomitantly, the absorption at 3430 and 1660–1670 cm^{-1} due to the NH and carbonyl groups of the lactam, respectively, began to increase. In the course of the reaction, the absorption at 1060 and 1250 cm^{-1} due to the C–O–C bond of the iminium catalyst remained almost unchanged. It should be noted that the absorption at 1710 cm^{-1} due to the C=N bond of the iminium once decreased at
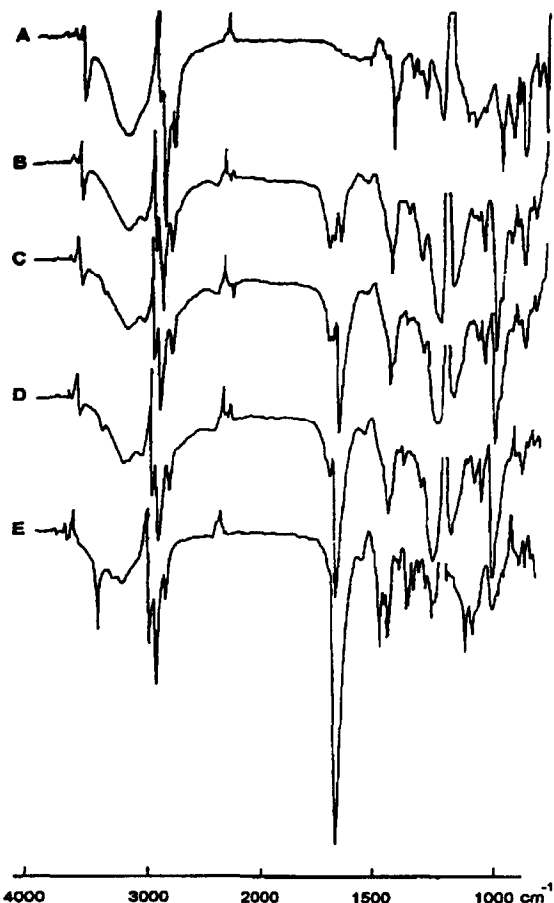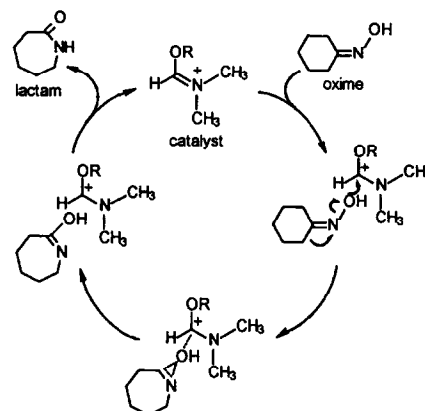

Scheme 3. Possible catalytic cycle.

the initial stage of the reaction forming a new absorption band at 1730 cm^{-1} simultaneously. Eventually this new band disappeared at the end of the reaction. This adsorption observed at 1730 cm^{-1} during the reaction is likely related to an intermediate catalyst species.

On the basis of these spectral changes, a possible mechanism of the rearrangement can be depicted as Scheme 3 which involves intramolecular migration of the hydroxy group of cyclohexanone oxime assisted by a powerful electrophilic property of the iminium cation.

4. Conclusion

Alkoxy-methylene-N,N-dimethyliminium salts, which were readily prepared in situ from common reagents, showed effective molecular catalysis for the liquid-phase Beckmann rearrangement of cyclohexanone oxime to ε-caprolactam under mild reaction conditions. The reversible catalyst deactivation caused by poisoning with the product lactam could be suppressed by the reduction of substrate concentration. Since the iminium catalyst was very susceptible to water, the design of hydrophobic heterogeneous catalyst systems immobilizing this kind of iminium species will lead to the development of a practical liquid-phase rearrangement process in which the problem of catalyst deactiva-

Fig. 5. IR spectral changes of reaction mixture (DMF–(CH$_3$O)$_2$SO$_2$ system). A: cyclohexanone oxime, B: reaction mixture after 0 h, C: after 8 h, D: after 24 h, E: ε-caprolactam.

tion may be overcome, for example, by employing a continuous flow reactor.

Acknowledgements

References

[1] British Petroleum, Br. Pat. 881927 (1961).
[2] BASF, Ger. Pat. 1227028 (1967).
[3] Bayer, Japan Kokai No. 37686 (1978).
[4] S. Sato, K. Urabe and Y. Izumi, J. Catal., 102 (1986) 99; S. Sato, S. Hasebe, H. Sakurai, K. Urabe and Y. Izumi, Appl. Catal., 29 (1987) 107.
[5] P.S. Landis and P.B. Venuto, J. Catal., 6 (1966) 245.
[6] T. Yashima, S. Horie, S. Saito and N. Hara, Nippon Kagaku Kaishi, (1977) 77.
[7] Y. Murakami, Y. Saeki and K. Ito, Nippon Kagaku Kaishi, (1978) 21.
[8] Mobil Oil, US Pat. 4359421 (1982).
[9] H. Sato, N. Ishii, K. Hirose and S. Nakamura, Proc. 7th Int. Zeolite Congr., (1986) 755; H. Sato, K. Hirose, M. Kitamura and Y. Nakamura, Proc. 8th Int. Zeolite Congr., (1989) 1213; H. Sato, A. Sakamoto, K. Hirose and K. Chikaishi, Chem. Lett., (1989) 548; H. Sato and K. Hirose, ibid., (1993) 1765; H. Sato, K. Hirose and Y. Nakamura, ibid., (1993) 1987; H. Sato, S. Shimizu, N. Abe and H. Hirose, ibid., (1994) 59.
[10] A. Thagarah, S. Sivasanker and P. Ratnasamy, J. Catal., 137 (1992) 252; J. Sudhakar Reddy, R. Ravishankar, S. Sivasanker and P. Ratnasamy, Catal. Lett., 17 (1993) 139.
[11] T. Ushikubo and K. Wada, J. Catal., 148 (1994) 138.
[12] Y. Izumi, Chem. Lett., (1990) 2171.
[13] H. Meerwein, P. Borner, O. Fuchs, H.J. Sasse, H. Schrodt and J. Spille, Chem. Ber., 89 (1956) 2060.
[14] M.A. Kira and Y.M. Shaker, Egypt. J. Chem., 16 (1973) 551.
[15] T. Mukaiyama and T. Harada, Chem. Lett., (1991) 1653; T. Harada, T. Ohno, S. Kobayashi and T. Mukaiyama, Synthesis, (1991) 1216.
[16] K. Narasaka, H. Kusama, Y. Yamashita and H. Sato, Chem. Lett., (1993) 489.
[17] G.A. Olah, G.K.S. Prakash and J. Sommer, Superacids, John Wiley & Sons, New York, 1985, p. 185.
[18] H. Meerwein, Org. Synth., Coll. Vol. V, (1973), p. 1080.
[19] Y. Izumi, K. Matsuo and K. Urabe, J. Mol. Catal., 18 (1983) 299.