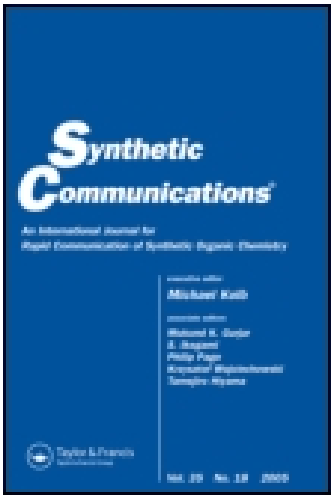

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Facile $AlCl_3$-Promoted Catalytic Beckmann Rearrangement of Ketoximes

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FACILE $AlCl_3$-PROMOTED CATALYTIC BECKMANN REARRANGEMENT OF KETOXIMES

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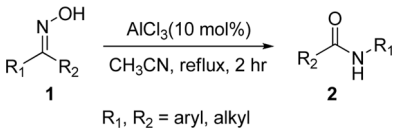
GRAPHICAL ABSTRACT



Abstract *Aluminum chloride, an inexpensive and commercially available Lewis acid traditionally employed for Beckmann rearrangement with stoichiometric amounts, has been now found to smoothly promote the Beckmann rearrangement of various ketoximes to the corresponding amides (up to 99% of yield) with 10 mol% catalyst loading in anhydrous acetonitrile under reflux temperature.*

Keywords Aluminum chloride; Beckmann rearrangement; ketoxime

INTRODUCTION

The Beckmann rearrangement of ketoximes is a fundamental and commonly used organic synthesis tool for the formation of corresponding amides through a Brønsted acid–mediated catalytic cycle.[1] One of the most important industrial applications of this rearrangement reaction is the transformation of cyclohexanone oxime into caprolactam, which is the raw material (monomer) in the production of polymer nylon. The rearrangement, however, requires harsh conditions such as the use of corrosive Brønsted acid, high temperature, and generation of a considerable amount of ammonium sulfate by-product.[2] Hence, over the past half century, extensive efforts have been devoted to the optimization of the catalytic reaction system. Many catalytic systems such as liquid-phase system,[3] vapor-phase system,[4] supercritical water system,[5] and ionic liquid system[6] have been developed so far. Liquid-phase catalytic Beckmann rearrangement under mild conditions has become a topic of current interest because of its advantages such as easy workup and

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industrial practicability. As a consequence, various catalysts such as inorganic catalysts, organocatalysts, and metallic Lewis acid systems were developed. Especially for the metallic Lewis acid, a number of catalytic systems have been reported recently, such as $[RhCl(cod)]_2$,[7] $Yb(OTf)_3$,[8] $Y(OTf)_3$,[9] $Ga(OTf)_3$,[10] $Nd(OTf)_3$,[11] $RuCl_3$,[12] and $HgCl_2$.[13] However, because of drawbacks such as toxicity, high cost, and relatively low catalytic activities (10–50 mol% catalyst loading), these catalysts have not yet been industrially utilized.

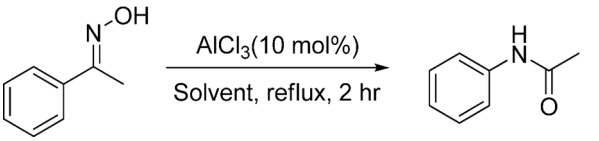
Aluminum chloride ($AlCl_3$)[14] has been widely employed for the Beckmann rearrangement over the past half century; however, stoichiometric amounts or even an excess amount of reagent was needed. In the course of developing a new, practically catalytic Beckmann rearrangement protocol, we found that TsCl,[15] BOPCl,[16] and triphosphazene, 1,3,5-triazo-2,4,6-triphosphorine-2,2,4,4,6,6-chloride (TAPC)[17] can efficiently promote the Beckmann rearrangement with catalytic amounts via a new proposed mechanism. Consequently, we further reasoned that aluminum chloride as partially covalent metal chloride might promote the Beckmann rearrangement as well with catalytic amount via a mechanism similar to that of TsCl or BOPCl. In this communication, we described our preliminary results of the $AlCl_3$-catalyzed Beckmann rearrangement of ketoximes to corresponding amides.

RESULTS AND DISCUSSION

Initially, acetophenone oxime was chosen as the model molecule for the Beckmann rearrangement using 10 mol% of $AlCl_3$ in anhydrous CH_3CN at refluxing temperature. To our amazement, the rearrangement proceeded very smooth, affording acetanilide in 96% yield. Next, a further solvent screening showed that anhydrous acetonitrile gave the optimal result (entries 1–4, Table 1).

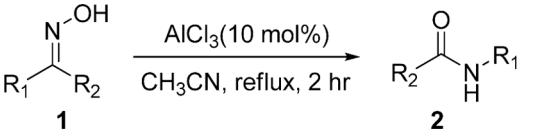
With this encouraging result, we next turned to explore the generality and scope of the $AlCl_3$-promoted Beckmann rearrangement catalytic system. A series of representative ketoximes as substrates were examined under the same conditions, and the results are summarized in Table 2. It is clear that excellent yields were obtained for the rearrangement of all diarylketoneoximes into corresponding amides. For the substituted acetophenone oximes, the rearrangements were generally effective;

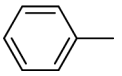
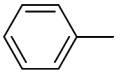
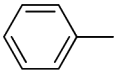
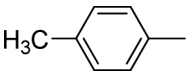
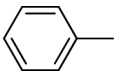
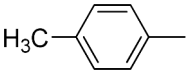
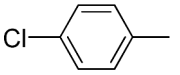
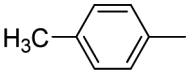
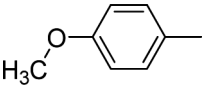
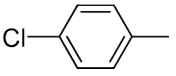
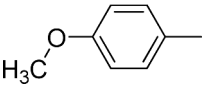
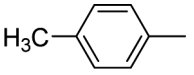
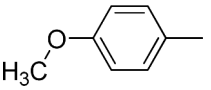
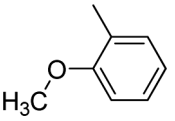
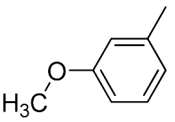
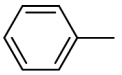
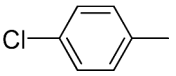
Table 1. Aluminum trichloride (10 mol%)–catalyzed Beckmann rearrangement of acetophenone oxime



Entry	Solvent	Yield (%)
1	THF	Trace
2	Toluene	Trace
3	Dioxane	Trace
4	CH_2Cl_2	Trace
5	CH_3CN	96

Table 2. Scope of $AlCl_3$-catalyzed Beckmann rearrangement

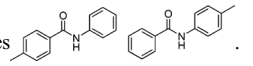


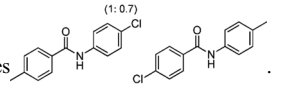
Entry	R^1	R^2	Yield (%)
1(2a)		Me	96
2(2b)			99
3(2c)			99[a]
4(2d)			88[b]
5(2e)			93[c]
6(2f)			99[d]
7(2g)		Me	90
8(2h)		Me	93
9(2i)		Me	20
10(2j)		Me	78
11(2k)		Et	91
12(2l)		Me	60

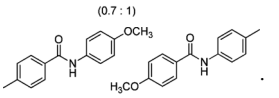
(*Continued*)

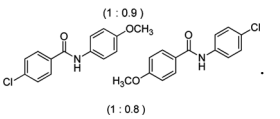
Table 2. Continued

Entry	R^1	R^2	Yield (%)
13(2m)	$(CH_2)_{11}$		76
14(2n)	$(CH_2)_5$		Trace

[a]Overall yield of isomeric mixtures  .

[b]Overall yield of isomeric mixtures  .

[c]Overall yield of isomeric mixtures  .

[d]Overall yield of isomeric mixtures  .

however, the oxime with *ortho*-methoxy dramatically lowered the yield to 20%, and the electron-withdrawing *para*-chloro group decreases the reaction activity (60% yield, entry 12). The Beckmann rearrangement of cyclododecanone oxime using the same condition gave the laurolactam in good yield (76% yield, entry 13). Unfortunately, the rearrangement of cyclohexanone oxime gave only a trace amount of ε-caprolactam.

CONCLUSIONS

In conclusion, we have developed a highly efficient aluminum chloride ($AlCl_3$)–promoted Beckmann rearrangement system in anhydrous acetonitrile under reflux conditions. The procedure offers several advantages including good yields, short reaction times, easily and cheaply obtained catalyst, and simple experimental isolation procedures, which make the new catalytic system a potentially practical procedure for the Beckmann rearrangement.

EXPERIMENTAL

All solvents were distilled under standard procedures prior to use under a nitrogen atmosphere. (For example, CH_3CN was distilled from CaH_2; tetrahydrofuran (THF), dioxane, and toluene were distilled from sodium.) ^1H (400-MHz) chemical shifts are reported in $CDCl_3$, 7.27 ppm, and standards and coupling constants (J) are reported in hertz (Hz). The following abbreviations are used to designate signal multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and br, broad.

General Procedure for $AlCl_3$-Promoted Catalytic Beckmann Rearrangement of Ketoximes

To a solution of ketoxime (2 mmol) in dry CH_3CN (2 mL) under N_2, 2 mL CH_3CN (aluminum trichloride in CH_3CN solvent, 0.1 M/L) were added. The solvent

was refluxed for 2 h. After the reaction course, quenched by the addition of H_2O (10 mL), the organic layer was extracted with ethyl acetate, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The resulting crude product was purified by silica gel column chromatography to give the corresponding amide in good yield.

All known compounds gave NMR spectra that matched data reported in the cited references.[13,15]

N-Phenylacetamide (2a)

Mp 114–115 °C [lit.[13] 114–116 °C]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.59 (brs, 1H), 7.53 (d, $J = 8.0$ Hz, 2H), 7.28 (t, $J = 7.7$ Hz, 2H), 7.09 (t, $J = 7.4$ Hz, 1H), 2.13 (s, 3H).

N-Phenylbenzamide (2b)

Mp 164–165 °C [lit.[18] 164–165 °C]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.03 (brs, 1H), 7.87 (d, $J = 7.3$ Hz, 2H), 7.66 (d, $J = 7.9$ Hz, 2H), 7.54 (t, $J = 7.3$ Hz, 1H), 7.46 (t, $J = 7.5$ Hz, 2H), 7.37 (t, $J = 7.9$ Hz, 2H), 7.16 (t, $J = 7.4$ Hz, 1H).

N-*p*-Tolylbenzamide and 4-Methyl-*N*-phenylbenzamide (2c)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.92–7.73 (m, 6H), 7.65 (d, $J = 7.9$ Hz, 2H), 7.55–7.49 (m, 3H), 7.38 (t, $J = 7.8$ Hz, 2H), 7.32–7.26 (m, 3H), 7.19–7.14 (m, 2H), 2.44 (s, 3H), 2.35 (s, 3H).

4-Chloro-*N*-*p*-tolylbenzamide and *N*-(4-Chlorophenyl)-4-methylbenzamide (2d)

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm): 10.27 (brs, 1H), 10.21 (brs, 1H), 7.98 (d, $J = 8.4$ Hz, 2H), 7.87 (d, $J = 8.0$ Hz, 2H), 7.82 (d, $J = 8.7$ Hz, 2H), 7.64 (d, $J = 8.2$ Hz, 2H), 7.59 (d, $J = 8.4$ Hz, 2H), 7.39 (d, $J = 8.7$ Hz, 2H), 7.33 (d, $J = 7.9$ Hz, Hz, 2H), 7.15 (d, $J = 8.2$ Hz, 2H), 2.38 (s, 3H), 2.27 (s, 3H).

4-Methoxy-*N*-*p*-tolylbenzamide and *N*-(4-Methoxyphenyl)-4-methylbenzamide (2e)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.17 (brs, 1H), 8.16 (brs, 1H), 7.80 (d, $J = 8.4$ Hz, 2H), 7.74 (d, $J = 7.7$ Hz, 2H), 7.53 (d, $J = 6.3$ Hz, 2H), 7.51 (d, $J = 5.1$ Hz, 2H), 7.19 (d, $J = 7.7$ Hz, 2H), 7.11 (d, $J = 7.9$ Hz, 2H), 6.86 (d, $J = 9.6$ Hz, 2H), 6.84 (d, $J = 9.2$ Hz, 2H), 3.85 (s, 3H), 3.78 (s, 3H), 2.38 (s, 3H), 2.32 (s, 3H).

N-(4-Chlorophenyl)-4-methoxybenzamide and 4-Chloro-*N*-(4-methoxyphenyl)benzamide (2f)

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm): 10.22 (brs, 1H), 10.20 (brs, 1H), 7.98 (d, $J = 6.9$ Hz, 2H), 7.96 (d, $J = 6.7$ Hz, 2H), 7.82 (d, $J = 8.4$ Hz, 2H), 7.68

(d, $J = 8.5$ Hz, 2H), 7.58 (d, $J = 8.1$ Hz, 2H), 7.38 (d, $J = 8.4$ Hz, 2H), 7.05 (d, $J = 8.4$ Hz, 2H), 6.92 (d, $J = 8.6$ Hz, 2H), 3.83 (s, 3H), 3.74 (s, 3H).

N-*p*-Tolylacetamide (2g)

Mp 149–150 °C [lit.[13] 149–151 °C]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.28 (brs, 1H), 7.40 (d, $J = 8.2$ Hz, 2H), 7.09 (d, $J = 8.1$ Hz, 2H), 2.30 (s, 3H), 2.12 (s, 3H).

N-(4-Methoxyphenyl)acetamide (2h)

Mp 128–129 °C [lit.[13] 129–130 °C]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.09 (brs, 1H), 7.38 (d, $J = 8.8$ Hz, 2H), 6.81 (d, $J = 8.5$ Hz, 2H), 3.76 (s, 3H), 2.10 (s, 3H).

N-(2-Methoxyphenyl)acetamide (2i)

Mp 85–86 °C [lit.[13] 85–86 °C]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.35 (d, $J = 7.8$ Hz, 1H), 7.79 (brs, 1H), 7.02 (t, $J = 7.4$ Hz, 1H), 6.94 (t, $J = 7.4$ Hz, 1H), 6.86 (d, $J = 8.0$ Hz, 1H), 3.86 (s, 3H), 2.18 (s, 3H).

N-(3-Methoxyphenyl)acetamide (2j)

Mp 81–82 °C [lit.[13] 87–88 °C]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.58 (brs, 1H), 7.28 (s, 1H), 7.16 (t, $J = 8.1$ Hz, 1H), 7.04 (d, $J = 7.9$ Hz, 1H), 6.64 (d, $J = 8.0$ Hz, 1H), 3.73 (s, 3H), 2.13 (s, 3H).

N-Phenylpropionamide (2k)

Mp 106–107 °C [lit.[13] 103–104 °C]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.30 (brs, 1H), 7.55 (d, $J = 7.9$ Hz, 2H), 7.27 (t, $J = 7.7$ Hz, 2H), 7.08 (t, $J = 7.3$ Hz, 1H), 2.37 (q, $J = 7.5$ Hz, 2H), 1.21 (t, $J = 7.6$ Hz, 3H).

N-(4-Chlorophenyl)acetamide (2l)

Mp 180–181 °C [lit.[19] 180 °C]; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm): 10.05 (brs, 1H), 7.60 (d, $J = 8.5$ Hz, 2H), 7.32 (d, $J = 8.5$ Hz, 2H), 2.04 (s, 3H).

Azacyclotridecan-2-one (2m)

Mp 150–151 °C [lit.[20] 143–145 °C]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 6.07 (brs, 1H), 3.26 (dd, $J = 5.7$, 10.5 Hz, 2H), 2.19–2.16 (m, 2H), 1.68–1.62 (m, 2H), 1.55–1.45 (m, 2H), 1.34–1.27 (m, 14H).

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