Cyanuric Chloride as a Mild and Active Beckmann Rearrangement Catalyst

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General Methods. Infrared (IR) spectra were recorded on a JASCO FT/IR 460 plus spectrometer. ^1H NMR spectra were measured on a Varian Gemini-2000 spectrometer (300 MHz) at ambient temperature. Data were recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet, m = multiplet), coupling constant (Hz), integration, and assignment. ^{13}C NMR spectra were measured on Varian Gemini-2000 (75 MHz) and VXR 500 (125 MHz) spectrometers. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuteriochloroform at 77.00 ppm). All reaction were carried out under nitrogen. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF254 0.25 mm or silica gel NH_2 F254S 0.25 mm) were used. The products were purified by column chromatography on silica gel (E. Merck Art. 9385). Microanalyses were performed at the Graduate School of Agriculture, Nagoya University. High resolution mass spectral analysis (HRMS) was performed at Chemical Instrument Center, Nagoya University. In experiments that required dry solvents, acetonitrile, nitromethane, toluene, and acetone were purchased from TCI or Wako as the “anhydrous” and stored over 4A molecular sieves. 1,4-Dioxane was freshly distilled from sodium. Other simple chemicals were analytical-grade and obtained commercially.

Representative Procedure for Preparing Ketoximes. To a solution of ketone (30 mmol) and 2.3 equiv of hydroxyamin hydrochloride (69 mmol) in 40 mL of MeOH, 2.5 equiv of sodium acetate trihydrate in 20mL of water was added at room temperature, and the mixture was refluxed for 1 h. After completion of reaction, the mixture was neutralized with saturated aqueous sodium hydrogen carbonate, and diluted with ether. The organic layer was separated, washed successively with brine and dried over anhydrous magnesium sulfate. The solvent was removed *in vacuo*, and the obtained product was purified in good yield by distillation or sublimation under reduced

pressure.

Acetophenone Oxime (entry 1, Table 3): Purchased from TCI, Japan.

***o*-Methoxyacetophenone Oxime (entry 2, Table 3):**¹ IR (film) 3221, 2925, 1599, 1579, 1493, 1460, 1435, 1270, 1246, 1025, 917, 745 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.23 (s, 3H), 3.83 (s, 3H), 6.90–6.97 (m, 2H), 7.28–7.34 (m, 2H), 8.20 (br, 1H).

***m*-Methoxyacetophenone Oxime (entry 3, Table 3):**¹ IR (film) 3250, 3076, 3003, 2938, 2835, 1600, 1579, 1488, 1464, 1454, 1429, 1302, 1231, 1040, 1006, 942, 855, 783, 692 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.29 (s, 3H), 3.84 (s, 3H), 6.91–6.95 (m, 1H), 7.18–7.22 (m, 2H), 7.25–7.33 (m, 1H), 9.07 (br, 1H).

***p*-Methoxyacetophenone Oxime (entry 4, Table 3):**¹ IR (KBr) 3244, 2926, 1607, 1577, 1512, 1311, 1249, 1182, 1024, 922, 837, 822, 599 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.27 (s, 3H), 3.83 (s, 3H), 6.91 (d, *J* = 8.7 Hz, 2H), 7.58 (d, *J* = 8.7 Hz, 2H), 8.90 (br, 1H).

***p*-Fluoroacetophenone Oxime (entry 5, Table 3):** Purchased from Acros Organics.

1-(Benzo[*d*][1,3]dioxol-5-yl)ethanone Oxime (entry 6, Table 3):¹ IR (KBr) 2922, 1735, 1498, 1448, 1302, 1228, 1036, 944, 807 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.24 (s, 3H), 5.99 (s, 3H), 6.81 (d, *J* = 8.1 Hz, 1H), 7.10 (dd, *J* = 1.5, 8.1 Hz, 1H), 7.18 (d, *J* = 1.5 Hz, 1H), 7.46 (s, 1H).

1-(Naphthalen-2-yl)ethanone Oxime (entry 7, Table 3):¹ IR (KBr) 3215, 3053, 2911, 1597, 1503, 1448, 1420, 1384, 1307, 1196, 1132, 1017, 925, 825, 755 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.40 (s, 3H), 7.48–7.51 (m, 3H), 7.83–7.88 (m, 4H), 8.02 (br, 1H).

Isobutyrophenone Oxime (entry 8, Table 3):² a cis- and trans-isomeric mixture (44:56); IR (KBr) 3267, 2968, 2930, 1456, 1384, 1314, 1019, 946, 770, 700 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 1.13 (d, *J* = 6.9 Hz, 3.36 H), 1.21 (d, *J* = 7.2 Hz, 2.64 H), 2.83 (septet, *J* = 6.9 Hz, 0.56 H), 3.60 (septet, *J* = 7.2 Hz, 0.44 H), 7.24–7.45 (m, 5H), 9.30 (br, 0.56 H), 9.65 (br, 0.44 H).

Methyl 4-(Hydroxyimino)-4-phenylbutanoate: (entry 9, Table 3):³ *E/Z* ratio = 90 : 10; IR (film) 3404, 3057, 2952, 1737, 1497, 1439, 1284, 1201, 1174, 937, 762, 696 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) for (*E*)-isomer δ 2.56–2.65 (m, 2H), 3.10–3.16 (m, 2H), 3.66 (s, 3H), 7.57–7.40 (m, 3H), 7.59–7.63 (m, 2H), 8.81 (br, 1H); ¹H NMR (300 MHz, CDCl₃) for (*Z*)-isomer δ 2.57–2.66 (m, 2H), 2.89 (t, *J* = 7.4 Hz, 2H), 3.68 (s, 3H), 7.37–7.45 (m, 3H), 7.60–7.63 (m, 2H).

2-Decanone Oxime (entry 10, Table 3):⁴ *E/Z* ratio = 76 : 24; IR (KBr) 3236, 2925, 2856,

1665, 1465, 1368, 1113, 956, 722 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) for (*E*)-isomer δ 0.86–0.90 (m, 3H), 1.27 (br, 10H), 1.47–1.52 (br, 2H), 1.86 (s, 3H), 2.17 (t, $J = 7.5$ Hz, 2H), 7.60–7.90 (br, 1H); ^1H NMR (300 MHz, CDCl_3) for (*Z*)-isomer δ 0.86–0.90 (m, 3H), 1.27 (br, 10H), 1.87 (s, 3H), 2.36 (t, $J = 7.5$ Hz, 2H), 7.60–7.90 (br, 1H).

Diisopropylketone Oxime (entry 11, Table 3):⁵ IR (KBr) 3312, 2924, 1656, 1462, 1385, 1365, 1117, 1022, 934, 867, 762 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.13 (d, $J = 6.9$ Hz, 6H), 1.16 (d, $J = 6.9$ Hz, 6H), 2.57 (septet, $J = 6.9$ Hz, 1H), 3.21 (septet, $J = 6.9$ Hz, 1H), 9.72 (br, 1H).

Cyclododecaonone Oxime (entry 12, Table 3):⁶ Purchased from Sigma–Aldrich Japan.

Cycloundecaonone Oxime (entry 13, Table 3):⁷ IR (KBr) 2924, 2859, 1637, 1474, 935, 729 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.40–1.48 (m, 12H), 1.62–1.70 (m, 2H), 1.79 (q, $J = 6.3$ Hz, 2H), 2.27–2.36 (m, 4H).

Cyclodecaonone Oxime (entry 14, Table 3):^{7,8} IR (KBr) 3266, 2920, 2861, 1472, 1434, 949, 935 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 1.42–1.59 (m, 10H), 1.71–1.83 (m, 4H), 2.44 (t, $J = 6.6$ Hz, 2H).

Cyclooctaonone Oxime (entry 15, Table 3): Purchased from Sigma–Aldrich Japan.

Cyclohexaonone Oxime (entry 16, Table 3): Purchased from TCI, Japan.

Representative Procedure for the Beckmann Rearrangement of Ketoximes (Table 3).

The mixture of ketoxime (2 mmol) and 5 mol% of cyanuric chloride **9a** (18.41 mg, 0.1 mmol) in 4 mL of dry MeCN was refluxed. After completion of reaction, it was quenched with saturated aqueous sodium hydrogen carbonate. The organic layer was extracted with ethyl acetate, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel to give the corresponding amide in high yield.

Acetanilide (entry 1, Table 3):¹ IR (KBr) 3293, 3155, 1657, 1597, 1555, 1500, 1434, 1369, 1322, 1264, 755, 695 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 2.17 (s, 3H), 7.10 (t, $J = 7.2$ Hz, 1H), 7.26–7.36 (m, 2H), 7.40 (br, 1H), 7.50 (m, 2H).

***o*-Methoxyacetanilide (entry 2, Table 3):**¹ IR (KBr) 3250, 2924, 1654, 1541, 1496, 1458, 1252, 1117, 1025, 750 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 2.20 (s, 3H), 3.88 (s, 3H), 6.87 (dd, $J = 1.8, 8.1$ Hz, 1H), 6.92–7.07 (m, 2H), 7.76 (br, 1H), 8.36 (dd, $J = 1.8, 7.8$ Hz, 1H).

***m*-Methoxyacetanilide (entry 3, Table 3):**¹ IR (KBr) 3257, 2924, 2853, 1664, 1607, 1562, 1494, 1417, 1282, 1155, 1051, 860, 766, 688 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.17 (s, 3H), 3.80 (s, 3H), 6.61 (dd, *J* = 2.1, 8.0 Hz, 1H), 6.96 (d, *J* = 8.1 Hz, 1H), 7.18–7.28 (m, 2H), 7.76 (br, 1H).

***p*-Methoxyacetanilide (entry 4, Table 3):**¹ IR (KBr) 3242, 2924, 2853, 1743, 1647, 1606, 1512, 1246, 1030, 837 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.16 (s, 3H), 3.79 (s, 3H), 6.86 (d, *J* = 9.0 Hz, 2H), 7.07 (brs, 1H), 7.39 (d, *J* = 9.0 Hz, 2H).

***p*-Fluoroacetanilide (entry 5, Table 3):**¹ IR (KBr) 3290, 3071, 2923, 2853, 1662, 1617, 1559, 1507, 1402, 1235, 836 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.17 (s, 3H), 7.01 (d, *J* = 9.0 Hz, 2H), 7.18 (brs, 1H), 7.45 (dd, *J* = 4.8, 9.0 Hz, 2H).

3,4-Methylenedioxyacetanilide (entry 6, Table 3):¹ IR (KBr) 3326, 2923, 1742, 1662, 1546, 1486, 1444, 1238, 1181, 1039, 814 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.15 (s, 3H), 5.95 (s, 2H), 6.74–6.75 (m, 2H), 7.11 (b, 1H), 7.16 (d, *J* = 1.2 Hz, 1H).

***N*-(2-Naphthyl)acetamide (entry 7, Table 3):**¹ IR (KBr) 3283, 1668, 1589, 1561, 1471, 1396, 1351, 1281, 858, 816, 746 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.24 (s, 3H), 7.40–7.46 (m, 3H), 7.76–7.80 (m, 4H), 8.18 (br, 1H).

***N*-Isopropylbenzamide (entry 8, Table 3):**⁹ IR (KBr) 3299, 2971, 1632, 1347, 1289, 1170, 1137, 696 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 1.26 (d, *J* = 6.6 Hz, 6H), 4.28 (m, 1H), 6.11 (br, 1H), 7.38–7.51 (m, 3H), 7.74–7.78 (m, 2H).

***N*-Phenylisobutyramide (entry 8, Table 3):**² IR (KBr) 3433, 3302, 2968, 1661, 1600, 1549, 1442, 1309, 758, 695 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 1.26 (d, *J* = 6.9 Hz, 6H), 2.51 (septet, *J* = 6.9 Hz, 1H), 7.08–7.55 (m, 5H), 7.15 (br, 1H).

Methyl 4-Oxo-4-(phenylamino)butanoate (entry 9, Table 3):¹ IR (KBr) 3360, 2924, 2853, 1724, 1685, 1597, 1543, 1500, 1445, 1404, 1365, 1312, 1244, 1216, 1167, 761, 700 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.67 (t, *J* = 6.6 Hz, 2H), 2.77 (t, *J* = 6.6 Hz, 2H), 3.72 (s, 3H), 7.10–7.52 (m, 5H), 7.55 (brs, 1H).

***N*-Octylacetamide (entry 10, Table 3):**¹ IR (film) 3289, 3088, 2956, 2856, 1652, 1558, 1465, 1438, 1370, 723, 603 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.88 (t, *J* = 6.3 Hz, 3H), 1.27 (br, 10H), 1.44–1.51 (m, 2H), 1.97 (s, 3H), 3.19–3.26 (m, 2H), 5.49 (br, 1H).

***N*-Isopropylisobutyramide (entry 11, Table 3):**¹⁰ IR (KBr) 3297, 2970, 2933, 2873, 1644,

1551, 1366, 1244, 1179, 1096, 699 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.14 (d, $J = 6.9$ Hz, 12H), 2.28 (septet, $J = 6.9$ Hz, 1H), 4.02–4.13 (m, 1H), 5.23 (br, 1H).

Azacyclotridecan-2-one (entry 12, Table 3):¹ IR (film) 3299, 2931, 2854, 1639, 1546, 1448, 1059 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.32 (br, 14H), 1.48–1.51 (m, 2H), 1.64–1.70 (m, 2H), 2.18–2.22 (m, 2H), 3.31 (dd, $J = 6.0, 10.8$ Hz, 2H).

Azacyclododecan-2-one (entry 13, Table 3):¹¹ IR (KBr) 3313, 2926, 1639, 1545, 1466 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.26–1.47 (m, 12H), 1.54–1.74 (m, 4H), 2.20–2.25 (m, 2H).

Azacycloundecan-2-one (entry 14, Table 3):¹² IR (KBr) 3307, 2929, 1638, 1551, 1463, 689 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.32–1.78 (m, 14H), 2.18–2.23 (m, 2H), 3.33 (dd, $J = 5.4, 11.1$ Hz, 2H).

Azacyclononan-2-one (entry 15, Table 3):¹ IR (KBr) 3313, 2927, 1646, 1541, 1447, 1155, 1031, 797, 730 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.56–1.63 (m, 8H), 1.80–1.88 (m, 2H), 2.44 (t, $J = 6.3$ Hz, 2H), 3.35–3.38 (m, 2H), 5.63 (br, 1H).

ϵ -Caprolactam (entry 16, Table 3):¹ IR (KBr) 3211, 3075, 2928, 2856, 1654, 1486, 1438, 1417, 1365, 1198, 1125, 823 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.62–1.80 (m, 6H), 2.47 (t, $J = 5.7$ Hz, 2H), 3.21 (t, $J = 6.3$ Hz, 2H), 6.05 (br, 1H).

Preparation of *O*-2,4,6-Tris(1-phenylethylideneaminoxy)-1,3,5-triazine (5a). To a stirred solution of acetophenone oxime (2.04 g, 15 mmol) and **9a** (922 mg, 5 mmol) in 10 mL of dry MeCN, triethylamine (2.23 mL, 16 mmol) was added at room temperature. After **5a** was precipitated, the white solid was separated by filtration, and washed successively with ether, water and dried under reduced pressure (>90% yield). Mp. 155–156 $^{\circ}\text{C}$; IR (KBr) 2923, 1578, 1552, 1459, 1355, 1105, 1077, 886, 755, 691 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 2.56 (s, 9H), 7.43–7.47 (m, 9H), 7.85 (d, $J = 8.1$ Hz, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 14.8 (3C), 127.3 (6C), 128.6 (6C), 130.8 (3C), 134.8 (3C), 163.4 (3C), 174.5 (3C). Anal. Calcd for $\text{C}_{27}\text{H}_{24}\text{N}_6\text{O}_3$: C, 67.49; H, 5.03; N, 17.49; Found: C, 67.04; H, 4.91; N, 17.23.

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