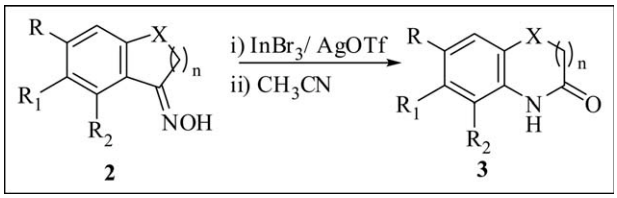
$InBr_3$- and AgOTf-Catalyzed Beckmann Rearrangement of (*E*)-Benzoheterocyclic Oximes

Vishnu K. Tandon,* Anoop K. Awasthi, Hardesh K. Maurya, and Pushyamitra Mishra

Department of Chemistry, University of Lucknow, Lucknow 226 007, India
*E-mail: vishnutandon@yahoo.co.in

Received October 29, 2009
DOI 10.1002/jhet.438
Published online 7 December 2011 in Wiley Online Library (wileyonlinelibrary.com).



Beckmann rearrangement of (*E*)-4-chromanone oxime, (*E*)-5-oximino-3,4-dihydro-1(2*H*)-benzoxepines, and (*E*)-5-oximino-3,4-dihydro-1(2*H*)-benzothiepine are catalyzed by $InBr_3$ and AgOTf in refluxing acetonitrile resulting in the formation of pharmaceutically active heterocycles benzoxazepin-4-one, 5-oxo-benzoxazocines, and 5-oxo-benzothiazocine derivative, respectively, in excellent yield.

J. Heterocyclic Chem., **49**, 424 (2012).

INTRODUCTION

Beckmann rearrangement involving the transformation of ketoximes into amides is a fundamental reaction in organic synthesis and has led to numerous applications due to the ease with which nitrogen can be inserted into carbon chains starting from prepared ketones [1]. Generally, strong Bronstead/Lewis acids ranging from stoichiometric to catalytic amounts are used to accomplish the Beckmann rearrangement. Development of this important rearrangement promoted by a catalytic amount of active species has been strongly desired during the last decade. In recent years, new reagents such as BF_3. Et_2O [2], super critical water [3], and metaboric acid [4] have been deployed for the synthesis of lactams by Beckmann rearrangement. Ketoximes undergo Beckmann rearrangement by use of chlorosulphonic acid in presence of toluene with high selectivity [5]. Yang and coworkers have reported Beckmann rearrangement of ketoximes by use of an effective and green catalyst, sulfamic acid [6]. Ketoximes undergo Beckmann rearrangement under very mild condition in presence of 2,4,6-trichloro[1,3,5]-triazene in DMF at room temperature to form amides [7]. Silica-supported MoO_3 has been used as a catalyst for the Beckmann rearrangement of oximes into amides [8]. Zhu *et al*. have used BOP-Cl(*tris*(2-oxo-3-oxazolidinyl)phosphinic chloride, the first organophosphorous catalyst, for the conversion of ketoximes into amides by Beckmann rearrangement [9]. Dai and coworkers have used Grignard reagent for the first time to induce Beckmann rearrangement directly without any additional protic agents for the synthesis of 2-aryl-1-benzazocines [10].

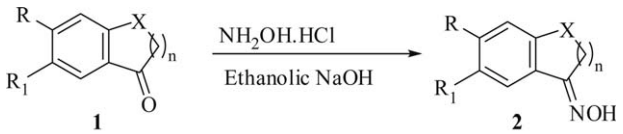
RESULTS AND DISCUSSION

As part of our research program to study indium bromide and silver triflate for synthesis of different industrially and biologically important heterocycles [11] and indium chloride [12] catalyzed Beckmann rearrangement of α-tetralone oxime, we became interested in the synthesis of analogs of oxazine and oxazepine [11].

We have studied indium bromide, a economical catalyst better than indium chloride and silver triflate combination of reagents, for the synthesis of 2,3-dihydrobenzo[*b*][1,4]oxazepin-4(5*H*)-one (**3a**), 3,4-dihydro-2H-benzo[*b*][1,4]oxazocin-5(6*H*)-ones (**3b–e**), and 3,4-dihydro-2*H*-benzo[*b*][1,4]thiazocin-5(6*H*)-one (**3f**) from corresponding oximes (**2a–f**), [13], which is more stable stereoisomer than Z-oximes [14]. The (*E*)-oximes **2** used for the Beckmann rearrangement were synthesized from corresponding ketones by reaction with $NH_2OH.HCl$ in ethanolic NaOH (Scheme 1) [15]. The oximes were characterized by their IR, ^1H NMR, and elemental analytical data (Table 1). (*E*)-5-oximino-3,4-dihydro-1(2*H*)-benzoxepin (**2b**; $X = O$, $n = 3$, $R_1{=}R_2{=}H$) in IR spectrum exhibited OH band at 3244 cm^{-1}. In ^1H NMR spectra, a multiplet for two protons at C-3 appeared at δ 2.00; a multiplet at δ 2.85 appeared for 4-CH_2; a triplet for OCH_2 appeared at δ 4.25; a multiplet at δ 7.6 appeared for 4-phenyl-H. The elemental analytical data for C, H, and N obtained for **2b** were within ±0.25 range.

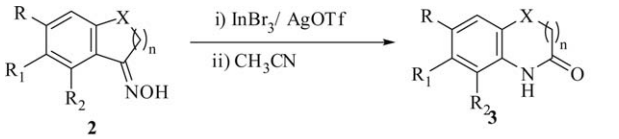
Our efforts to study Beckmann rearrangement of (*E*)-oximes **2** using $InBr_3$ resulted in very poor yield of lactam **3** (5–15%). However, we were successful in carrying out Beckmann rearrangement of (*E*)-oximes **2**

Scheme 1



(**a**) X=O, n=2, R=R_1=H
(**b**) X=O, n=3, R=R_1=H
(**c**) X=O, n=3, R=H, R_1=Me
(**d**) X=O, n=3, R=R_1=Me
(**e**) X=O, n=3, R=H, R_1=OMe
(**f**) X=S, n=3, R=R_1=H

Scheme 2



(**a**) X=O, n=2, R=R_1=R_2=H
(**b**) X=O, n=3, R=R_1=R_2=H
(**c**) X=O, n=3, R=R_2=H, R_1=Me
(**d**) X=O, n=3, R=R_1=Me, R_2=H
(**e**) X=O, n=3, R=R2=H, R_1=OMe
(**f**) X=S, n=3, R=R_1=R_2=H
(**g**) X=O, n=3, R=R_2=Me, R_1=H
(**h**) X=CH_2, n=2, R=R_1=H
(**i**) X=CH_2, n=1 R=R_1=H

derived from cyclic ketones **1** with $InBr_3$ and AgOTf in good to excellent yield (Scheme 2).

Thus, the reaction of (*E*)-oxime derivatives **2** on reaction with a mixture of $InBr_3$ and AgOTf as catalyst resulted in the formation of rearranged cyclic amide 2,3-dihydrobenzo[*b*][1,4]oxazepin-4(5*H*)-one (**3a**), 3,4-dihydro-2*H*-benzo[*b*][1,4]oxazocin-5(6*H*)-ones (**3b-e**), 3,4-

Table 1

Physical and spectral data of heterocyclic (*E*)-oximes **2a–f** [15].

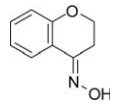
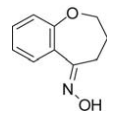
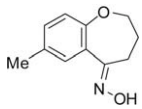
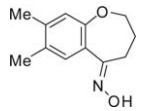
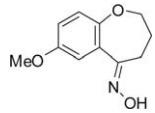
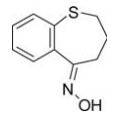
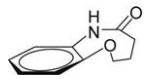
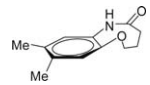
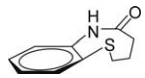
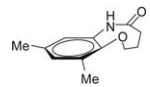
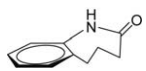
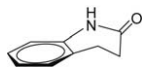
2	Compound	Yields	Mp (°C)	Physical/spectral data
a		81%	140	(*E*)-4-Chromanone oxime (2a): Colorless solid; crystallized from aq. EtOH; colorless crystals [16].
b		86%	94	(*E*)-5-Oximino-3,4-dihydro-1(2*H*)-benzoxepine (2b): Colorless solid; crystallized from aq. EtOH; colorless crystals [17]; IR (KBr): 512, 656, 750, 826, 972, 1050, 1126, 1203, 1285, 1491, 1606, 2367, 2952, 3244 cm^{-1}; ^1H NMR: δ 2.00 (m, 2H, 3-CH_2), 2.85 (m, 2H, 4-CH_2), 4.25 (t, 2H, OCH_2), 7.6 (m, 4H, phenyl-H); Anal. Calcd. for $C_{10}H_{11}NO_2$ (177): C, 67.78; H, 6.26; N, 7.90; Found: C, 67.58; H, 6.22; N, 7.86.
c		84%	73	(*E*)-7-Methyl-5-oximino-3,4-dihydro-1(2*H*)-benzoxepine (2c): Crystallized from benzene–Hexane; pale yellow crystals [18]; IR (KBr): 461, 511, 587, 655, 748, 825, 859, 886, 959, 1055, 1079, 1125, 1202, 1236, 1284, 1320, 1378, 1412, 1454, 1491, 1605, 2363, 2952, 3244 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.79 (bh, 1H, OH), 2.01 (m, 2H, CH_2), 2.31 (s, 3H, CH_3), 2.92 (t, 2H, CH_2), 4.14 (t, 2H, OCH_2), 6.88 (d, 1H, phenyl-H), 7.08 (m, 1H, phenyl-H), 7.28 (d, 1H, phenyl-H); Anal. Calcd. for $C_{11}H_{13}NO_2$ (191): C, 69.09; H, 6.85; N, 7.32; Found: C, 68.79; H, 6.75; N, 7.21.
d		88%	110	(*E*)-7,8-Dimethyl-5-oximino-3,4-dihydro-1(2*H*)-benzoxepine (2d): Crystallized from benzene–Hexane; dark yellow crystals [19].
e		85%	86	(*E*)-7-Methoxy-5-Oximino-3,4-dihydro-1(2*H*)-benzoxepine (2e): Crystallized from benzene–Hexane; pale yellow crystals [20]; IR (KBr): 512, 588, 749, 826, 969, 1056, 1205, 1283, 1380, 1492, 1606, 2953, 3230 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.80 (m, 2H, CH_2), 2.82 (m, 2H, CH_2), 3.68 (s, 3H, OCH_3), 3.98 (t, 2H, CH_2), 6.85 (m, 3H, phenyl-H)); Anal. Calcd. for $C_{11}H_{13}NO_3$ (207): C, 63.76; H, 6.32; N, 6.76; Found: C, 63.64; H, 6.29; N, 6.73.
f		87%	98	(*E*)-5-Oximino-3,4-dihydro-1(2*H*)-benzothiepine (2f): Crystallized from benzene-Hexane; brown crystals [21]; IR (KBr): 466, 539, 634, 754, 904, 960, 8035, 1087, 1150, 1244, 1300, 1351, 1440, 1586, 1628, 1721, 1853, 2368, 2923, 3062, 3250 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.16 (m, 2H, CH_2), 2.89–3.01 (m, 4H, CH_2), 7.17–7.51 (m, 4H, phenyl-H), 8.63 (bh, 1H, OH)); Anal. Calcd. for $C_{10}H_{11}NOS$ (193): C, 62.15; H, 5.74; N, 7.25; S, 16.59; Found: C, 61.86; H, 5.71; N, 7.23; S, 16.55.

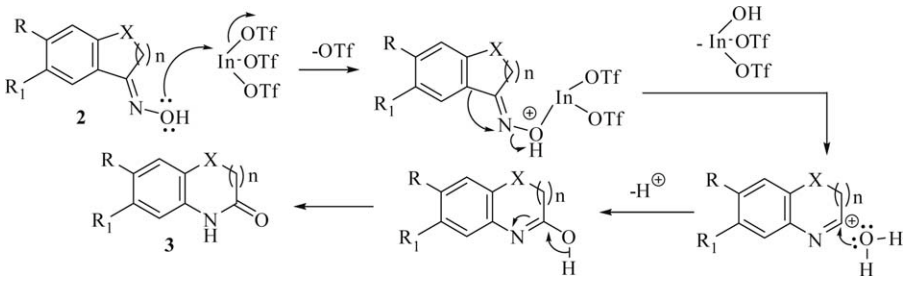
Table 2

Physical and spectral data of lactam **3a-i** synthesized by Beckmann rearrangement of heterocyclic (*E*)-oxime **2** [22].[a]

3	Compound	Yields	Mp (°C)	Physical/spectral data
a		85%	124–126	2,3-Dihydro-1,5-Benzoxazepin-4-one (3a): Colorless solid; crystallized with $CHCl_3$/Hexane [23], IR (KBr): 571, 646, 684, 720, 840, 948, 1034, 1067, 1099, 1173, 1218, 1231, 1284, 1350, 1399, 1432, 1441, 1591, 1653, 2950, 3051, 3176, 3283, 3421 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.80 (bS, 1H, NH), 2.72 (t, 2H, $J = 6$ Hz, CH_2), 4.25 (t, 2H, $J = 6$ Hz, OCH_2), 7.00–7.09 (m, 3H, phenyl-H), 7.79 (m, 1H, phenyl-H); ^{13}C NMR ($CDCl_3$): δ 37, 70, 115, 120, 121, 127, 128, 154, 172; Anal. Calcd. for $C_9H_9NO_2$ (163): C, 66.25; H, 5.56; N, 8.58; Found: C, 66.04; H, 5.52; N, 8.51.
b		81%	148	5-Oxo-2,3,4,5-tetrahydro-6*H*-1,6-benzoxazocine (3b): Colorless solid; crystallized from benzene, colorless crystals [17]; IR (KBr): 586, 635, 673, 764, 807, 870, 897, 934, 1004, 1058, 1090, 1183, 1208, 1241, 1285, 1352, 1399, 1439, 1438, 1597, 1663, 2957, 3057, 3186, 3292, 3428 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.76 (bS, 1H, NH), 2.03 (m, 2H, CH_2), 2.37 (t, 2H, $J = 6$ Hz, CH_2), 4.26 (t, 2H, $J = 6$ Hz, OCH_2), 7.09–7.26 (m, 3H, phenyl-H), 7.69 (m, 1H, phenyl-H); ^{13}C NMR ($CDCl_3$): δ 26, 31, 75, 115, 120, 121, 127, 129, 155, 173; Anal. Calcd. for $C_{10}H_{11}NO_2$ (177): C, 67.78; H, 6.26; N, 7.90; Found: C, 67.69; H, 6.23; N, 7.84.
c		75%	141	5-Oxo-8-methyl-2,3,4,5-tetrahydro-6*H*-1,6-benzoxazocine (3c): Colorless solid; crystallized from benzene [17] IR (KBr): 670, 773, 816, 871, 897, 935, 1008, 1056, 1080, 1126, 1166, 1190, 1222, 1290, 1318, 1352, 1394, 1442, 1509, 1591, 1667, 2364, 2945, 3230, 3423 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.89 (bs, 1H, NH), 2.01 (m, 2H, CH_2), 2.25 (s, 3H, CH_3), 2.36 (m, 2H, CH_2), 4.19 (t, 2H, $J = 6$ Hz, OCH_2), 6.91 (s, 1H, phenyl-H), 7.03 (s, 1H, phenyl-H), 7.96 (s, 1H, phenyl-H); ^{13}C NMR ($CDCl_3$): δ 21, 26, 31, 75, 115, 120, 127, 128, 135, 155, 176; Anal. Calcd. for $C_{11}H_{13}NO_2$ (191): C, 69.09; H, 6.85; N, 7.32; Found: C, 68.88; H, 6.81; N, 7.29.
d		88%	194	5-Oxo-8,9-dimethyl-2,3,4,5-tetrahydro-6*H*-1,6-benzoxazocine (3d): Colorless solid; crystallized from Hexane, colorless crystals [24]; IR (KBr): 468, 563, 680, 768, 819, 890, 1000, 1071, 1150, 1246, 1313, 1396, 1442, 1656, 3043, 3174 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.71 (s, 1H, NH), 2.02 (m, 2H, CH_2), 2.24 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 2.32 (m, 2H, CH_2), 4.19 (t, 2H, $J = 6$ Hz, OCH_2), 7.05 (s, 1H, phenyl-H), 7.35 (s, 1H, phenyl-H); ^{13}C NMR ($CDCl_3$): δ 19, 20, 26, 31, 75, 120, 123, 124, 132, 139, 148, 176; Anal. Calcd. for $C_{12}H_{15}NO_2$ (205): C, 70.22; H, 7.37; N, 6.82; Found: C, 69.98; H, 7.34; N, 6.78.
e		84%	135	5-Oxo-8-methoxy-2,3,4,5-tetrahyro-6*H*-1,6-benzoxazocine (3e): Colorless solid, crystallized from $CHCl_3$-Hexane; colorless crystals; IR (KBr): 564, 613, 675, 718, 774, 811, 863, 932, 1011, 1037, 1059, 1088, 1186, 1210, 1247, 1286, 1312, 1352, 1402, 1440, 1458, 1508, 1595, 1670, 2366, 2957, 3240, 3429 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.62 (s, 1H, NH exchangeable with D_2O shake), 2.01 (m, 2H, CH_2) 2.37 (t, 2H, $J = 6$ Hz, CH_2), 3.78 (s, 3H, OCH_3), 4.16 (t, 2H, $J = 6$ Hz, OCH_2), 6.59 (d, 1H, phenyl-H), 6.80 (m, 2H, phenyl-H), 7.09 (d, 1H, phenyl-H)); ^{13}C NMR ($CDCl_3$): δ 26, 31, 55, 75, 110, 114, 115, 127, 150, 155, 176; Anal. Calcd. for $C_{11}H_{13}NO_3$ (207): C, 63.76; H, 6.32; N, 6.76; Found: C, 63.58; H, 6.28; N, 6.71.
f		86%	176	5-Oxo-2,3,4,5-tetrahydro-6*H*-1,6-benzothiazocine (3f): Brown color solid; crystallized from Hexane; brown crystals [25] IR (KBr): 487, 517, 557, 628, 694, 753, 875, 954, 1026, 1136, 1185, 1235, 1314, 1333, 1444, 1472, 1586, 1661, 2365, 2930, 3046, 3172 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.25 (s, 1H, NH), 1.88 (m, 2H, CH_2), 2.15 (m, 2H, CH_2), 2.84 (m, 2H, SCH_2), 7.07–7.81 (m, 4H, phenyl-H)); ^{13}C NMR ($CDCl_3$): δ 28, 32, 34, 125, 126, 131, 132 (2C), 148, 172; Anal. Calcd. for $C_{10}H_{11}NOS$ (193): C, 62.15; H, 5.74; N, 7.25; S, 16.59; Found: C, 61.92; H, 5.71; N, 7.22; S, 16.54.
g		80%	212	5-Oxo-7,9-dimethyl-2,3,4,5-tetrahydro-6*H*-1,6-benzoxazocine (3g): Colorless solid; crystallized from Hexane; colorless crystals [26]; IR (KBr): 467, 512, 563, 601, 625, 679, 767, 819, 889, 1000, 1070, 1149, 1182, 1245, 1271, 1313, 1396, 1442, 1495, 1657, 2368, 2954, 3043, 3174 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.71 (s, 1H, NH), 2.04 (m, 2H, CH_2), 2.24 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 2.32 (m, 2H, CH_2), 4.19 (m, 2H, OCH_2), 6.81 (d, 2H, phenyl-H); ^{13}C NMR ($CDCl_3$): δ 18, 20, 26, 31, 75, 121, 126, 127, 133, 137, 155, 176; MS (m/z): 206 (M^++1); Anal. Calcd. for $C_{12}H_{15}NO_2$ (205): C, 70.22; H, 7.37; N, 6.82; Found: C, 70.10; H, 7.33; N, 6.79.
h		89%	141	4,5-dihydro-1*H*-benzo[*b*]azepin-2(3*H*)-one (3h): Colorless solid; crystallized from $CHCl_3$/Hexane; colorless crystals [27]; IR (KBr); 595, 632, 682, 763, 786, 817, 863, 915, 946, 980, 1020, 1054, 1110, 1156, 1254, 1292, 1327, 1385, 1439, 1490, 1600, 1664, 2365, 2866, 2930, 2975, 3062, 3192 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.84 (s, 1H, NH), 2.25 (m, 2H, CH_2), 2.38 (t, 2H, $J = 7$ Hz, CH_2), 2.83 (t, 2H, $J = 7$ Hz, CH_2), 7.00–7.28 (m, 4H, phenyl-H), 8.13 (bs, 1H, N=C—OH), ^{13}C NMR ($CDCl_3$): δ 22, 35, 38, 126 (2C), 127, 128, 136 (2C), 172; Anal. Calcd. for $C_{10}H_{11}NO$ (161): C, 74.51; H, 6.88; N, 8.69; Found: C, 74.48; H, 6.82; N, 8.60.
i		87%	166	3,4-dihydroquinolin-2(1*H*)-one (3i): Colorless solid; crystallized from Benzene/Hexane; colorless crystals [28]; IR (KBr): 566, 613, 680, 748, 815, 867, 914, 1033, 1114, 1200, 1245, 1281, 1341, 1385, 1434, 1492, 1593, 1684, 1796, 1905, 2366, 2737, 3093, 3195 cm^{-1}; ^1H NMR ($CDCl_3$); δ 1.67 (s, 1H, NH), 2.64 (t, 2H, $J = 7$ Hz, CH_2), 2.97 (t, 2H, $J = 7$ Hz, CH_2), 6.77–7.26 (m, 4H, phenyl-H), 8.38 (bs, 1H, N=C—OH); ^{13}C NMR ($CDCl_3$): δ 26, 30, 120, 125, 126, 128, 136, 137, 171; Anal. Calcd. for C_9H_9NO (147): C, 73.45; H, 6.16; N, 9.52; Found: C, 73.38; H, 6.12; N, 9.48.

[a] Stereo stable configuration of lactam is prepared by Chem 3D ultra 10.

Scheme 3



dihydro-2*H*-benzo[*b*][1,4]thiazocin-5(6*H*)-one (**3f**), 4,5-dihydro-1*H*-benzo[*b*]azepin-2(3*H*)-one (**3g**), and 3,4-dihydroquinolin-2(1*H*)-one (**3h**) in excellent yields (Scheme 2, Table 2) [22].

Compound **3e** in IR spectrum exhibited C=O band at 1670 cm^{-1} and NH at 3240 cm^{-1}. In ^1H NMR spectra, a singlet at δ 1.62 exchangeable with D_2O appeared for NH, a multiplet at δ 2.01 for CH_2 appeared for 2-protons at C-4. A triplet at 2.37 for 2-protons of CH_2 appeared for C-3 and a singlet at δ 3.78 for 3-protons appeared for OMe, a triplet at 4.16 for 2-protons of OCH_2 and two doublets and multiplet for aromatic protons appeared between δ 6.59 and 7.09.

The Beckmann rearrangement reaction of (*E*)-keto oximes **2** in presence of $InBr_3$/AgOTf is regioselective leading to formation of lactam **3** exclusively. This became evident by independent synthesis of lactam **3b** from ketone **1b** [29]. In presence of AgOTf, indium bromide is converted into indium triflate, the triflate ion being a better leaving group than bromide ion increases the rate of the reaction. It is essential to use silvertriflate as the triflate anion is weakly coordinating, it is useful as a halide abstraction reagent. The role of Ag^+ is to facilitate the acceleration of the rate of reaction as AgBr is precipitated as side product.

The plausible mechanism of formation of lactam 3 from (*E*)-ketoxime 2 is exhibited in Scheme 3.

The new route to synthesis of these pharmaceutically active heterocycles and reactivity of other metal triflates are being further explored. In summary, we have demonstrated $InBr_3$- and AgOTf-catalyzed Beckmann rearrangement of cyclic-(*E*)-oximes **2** resulting in the formation of rearranged cyclic amides **3** in excellent yields.

Acknowledgments. A.K.A. thanks C.S.T. [CST/SERPD/2001], Lucknow, India, for Junior Research Fellowship, and H.K.M. acknowledges UGC, New Delhi, India, for assessment of Senior Research Fellowship.

REFERENCES AND NOTES

[1] Gawley, R. E. Org react 1988, 35, 1, and references cited here.

[2] Anilkumar, R.; Chandrasekhar, S. Tetrahedron Lett 2000, 41, 5427.

[3] Buero, M.; Ikeshoji, T.; Liew, C. C.; Terakura, K.; Parrinello, M. J Am Chem Soc 2004, 126, 6280.

[4] Chandrasekhar, S.; Gopalaiah, K. Tetrahedron Lett 2002, 43, 2455.

[5] Li, D.; Shi, F.; Guo, S.; Deng, Y. Tetrahedron Lett 2005, 46, 671.

[6] Wang, B.; Gu, Y.; Luo, C.; Yang, T.; Yang, L.; Suo, J. Tetrahedron Lett 2004, 45, 3369.

[7] Luca, L. D.; Giacomelli, G.; Porcheddu, A. J Org Chem 2000, 67, 6272.

[8] Dongare, M. K.; Bhagwat, V. V.; Ramana, C. V.; Gurjar, M. K. Tetrahedron Lett 2004, 45, 4759.

[9] Zhu, M.; Cha, C.; Deng, W. P.; Shi, X. X. Tetrahedron Lett 2006, 47, 4861.

[10] Ma, Z.; Dai, S.; Yu, D. Tetrahedron Lett 2006, 47, 4721.

[11] Tandon, V. K.; Maurya, H. K. Heterocycle 2009, 77, 611.

[12] Barman, D. C.; Thakur, A. J.; Prajapati, D.; Sandhu, J. S. Chem Lett 2000, 1196.

[13] Cordero-Vargas, A.; Quiclet-Sire, B.; Zard, S. Z. Bioorg Med Chem 2006, 14, 6165.

[14] Perreira, M.; Kim, E. J.; Thomas, C. Z.; Hanover, J. A. Bioorg Med Chem 2006, 14, 837 and reference 7 cited therein.

[15] General method for the synthesis of Oximes (**2**): A suspension of ketone **1** (0.02 mol) and $NH_2OH.HCl$ (1.4 g, 0.02 mol) in 15 mL of 50% aq. EtOH and NaOH (0.8 g, 0.02 mol) was refluxed for 1 h. Oximes **2** were obtained as solid on cooling and crystallized from suitable solvent.

[16] Powell, S. G. J Am Chem Soc 1923, 45, 2708.

[17] Tandon, V. K.; Khanna, J. M.; Anand, N.; Srimal, R. C.; Prasad, C. R.; Kar, K. Indian J Chem 1975, 13, 1.

[18] Fontaine, G. Ann Chim (Paris) 1968, 3, 179.

[19] Fontaine, G.; Maitte, P. Compt Rend 1964, 258, 4583.

[20] Tandon, V. K.; Chandra, A.; Dua, P. R.; Srimal, R. C. Arch Pharm 1993, 326, 221.

[21] Mohrbacher, R. J.; Carson, E. L. U.S. Pat. 3,243,439 (1966); Chem Abstr 1966, 64, 19623b.

[22] General procedure for the Beckmann rearrangement of oximes (**2**) to lactams (**3**): A mixture of oxime **2** (10 mmol), $InBr_3$ (1.5 mmol), AgOTf (4.5 mmol), and acetonitrile (20 mL) was refluxed under nitrogen at 90°C for 2h. After removal of the solvent, the semisolid compound was dissolved in CH_2Cl_2 (20 mL), extracted with water (3 × 10 mL), brine (10 mL) and dried over Na_2SO_4 to afford semisolid which was crystallized with suitable solvent.

[23] Huckle, D.; Lockhart, I. M.; Wright, M. J Chem Soc 1965, 1137.

[24] Badilescu, I. I. Rev Roum Chim 1975, 20, 1077.

[25] Mohrbacher, R. J. U.S. Pat. 3,311,615 (1967); Chem Abstr 1967, 67, 43830w.

[26] Huckle, D.; Lockhart, I. M.; Webb, N. E. J Chem Soc 1971, 2252.

[27] Chen, W. Y.; Gilman, N. W. J Heterocycl Chem 1983, 20, 663.

[28] Canoria, L.; Rodriguez, J. G. J Heterocycl Chem 1985, 22, 1511.

[29] De Sousa, A. L.; Pilli, R. A. Org Lett 2005, 7, 1617.