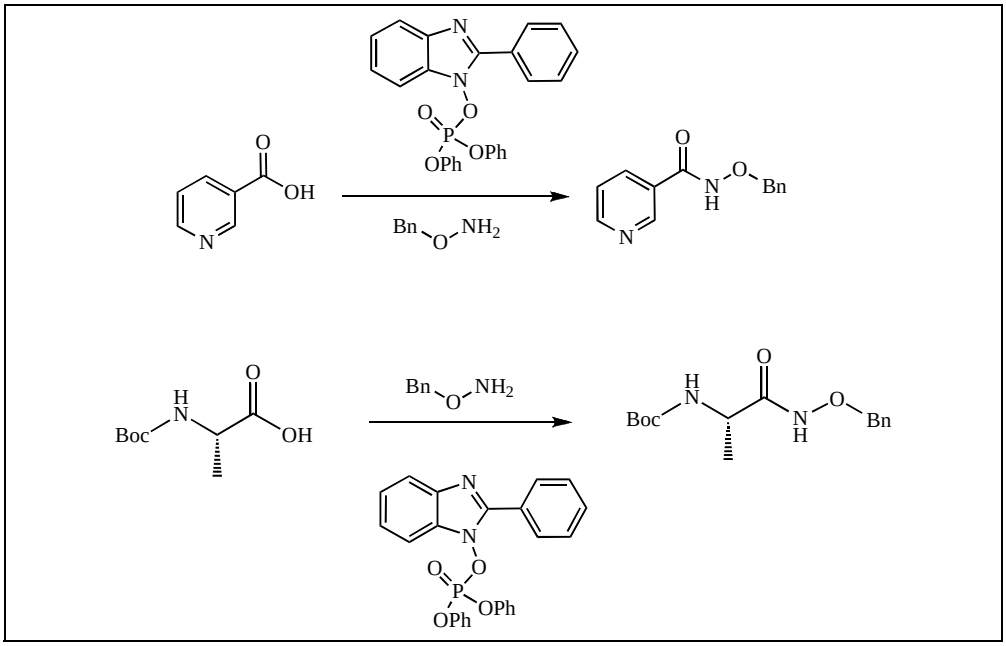
N-[(Diphenoxyphosphoryl)oxy]-2-phenyl-1*H*-benzimidazole as a Versatile Reagent for Synthesis *O*-Alkylhydroxamic Acids

Nagnnath D. Kokare [a, b], Devanand B. Shinde [b] *

[a] Department of Chemical Technology, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad-431004 (MS), India

[b] Wockhardt Research Centre, Aurangabad-431210 (MS), India

Received March 21, 2007



Highly efficient reagent, *N*-[(diphenoxyphosphoryl)oxy]-2-phenyl-1*H*-benzimidazole was synthesized and its applicability was demonstrated for the synthesis of *O*-alkyl hydroxamic acids. The efficiency of the reagent was evaluated through the synthesis of range of *O*-alkyl hydroxamic acids from aromatic carboxylic acids as well as *N*-protected amino acids. The enatiomeric purity of synthesized compounds was measured using chiral HPLC and the degree of racemization that occurred was found to be negligible.

J. Heterocyclic Chem., **45**, 981 (2008).

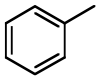
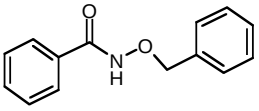
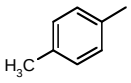
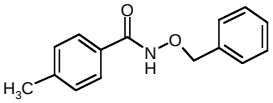
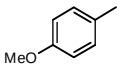
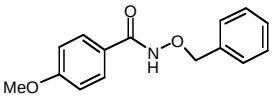
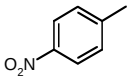
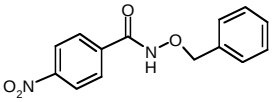
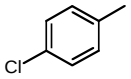
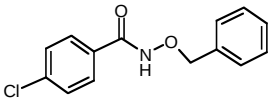
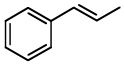
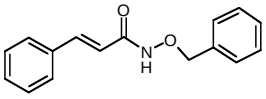
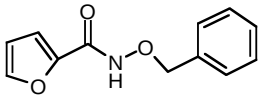
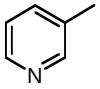
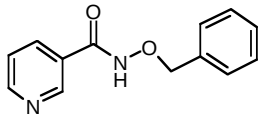
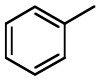
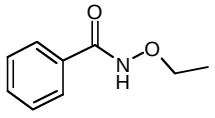
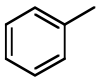
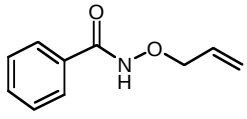
INTRODUCTION

Hydroxamic acid analogues are important targets for the medicinal chemists because of the intrinsic chelating interactions of this functional group with Zn^{++} at the active site of metalloprotiens [1,2]. Also hydroxamic acids are important in many chemotherapeutic agents such as the succinate-based matrix metalloprotienases (MMP) inhibitors [3], the class I/II histone deacetylase (HDAC) inhibitors [4] and iron-containing antibiotics [5]. Literature reveals, the various methods for the preparation of hydroxamic acids starting from carboxylic acids or their derivatives [6] and *N*-acyloxazolidinones [7]. The conversion of ester to hydroxamic acid is generally achieved by two step preparation, firstly salt of hydroxyl amine followed by addition of ester in alcohol solvent [8] or activation of acid using acyl chloride or mixed anhydride and quenching with *O*-protected hydroxyl-amine analogues [9]. Recently, we had developed the coupling reagent *N*-[(diethoxyphosphoryl)oxy]-2-phenyl-1*H*-benzimidazole for synthesis of *O*-alkyl hydroxamic acids from coupling of acid and *O*-alkyl hydroxylamines [10]. Although some of these methods are quite efficient for the preparation substituted hydroxamic acids, these methods suffered from some drawbacks such as instability, toxicity, high volatility of acylating agents like acid chloride or the activated esters, high cost and difficult purification which limit their applications. Hence, the development of a convenient and practical method is important for the efficient preparation of hydroxamic acids from carboxylic acids. In connection with our ongoing research to develop the simple and efficient methods for synthesis of heterocyclic compounds [11], we are gratified to present the simple and efficient method for the synthesis of *O*-alkylhydroxamic acids using reagent *N*-[(diphenoxyphosphoryl)oxy]-2-phenyl-1*H*-benzimidazole.

In previous work, the reagent, *N*-[(diphenoxyphosphoryl)oxy]-2-phenyl-1*H*-benzimidazole was synthesized and its application was demonstrated for the peptide coupling reactions with minimal racemization [11a]. In present article, we had explored the application of reagent for synthesis of the various *O*-alkylhydroxamic acids. The

Table 1

Synthesis of different *O*-alkyl hydroxamic acids using reagent 2.

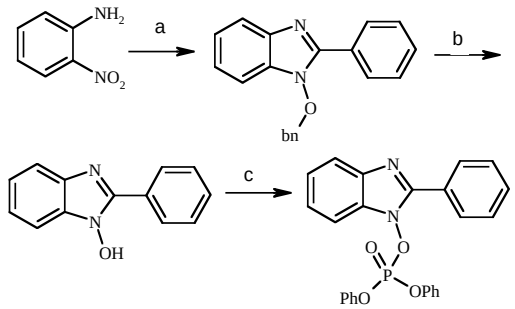
Entry No.	R1	R2	Product (**3a – 3j**)	Reaction time (min)	Yield (%)	Mp °C	
						Found	Reported [Ref.]
1		Bn	 **3a**	50	96	101 -103	102-104 [11]
2		Bn	 **3b**	50	92	126 - 127	128 [13]
3		Bn	 **3c**	45	92	109 - 110	110 -111[11]
4		Bn	 **3d**	30	98	165 - 166	166 -167 [11]
5		Bn	 **3e**	40	95	157 - 158	158[13]
6		Bn	 **3f**	60	87	99 - 100	99 - 100 [11]
7		Bn	 **3g**	50	85	100 - 110	99 - 101[11]
8		Bn	 **3h**	50	91	73 -74	72 - 73 [11]
9		Ethyl	 **3i**	45	88	80 - 81	81 - 82 [11]
10		Allyl	 **3j**	50	93	50 - 51	50 [14]

reagent was synthesized according to the reported procedure [12], which involves synthesis of *N*-hydroxy-benzimidazole (**1**) from the reaction of *ortho*-nitro aniline with benzyl bromide using sodium hydride base. The benzyl deprotection was carried out using 10% Pd/C as catalyst. The coupling reagent *N*-[(diphenoxy-phosphoryl)oxy]-2-phenyl-1*H*-benzimidazole (**2**) was synthesized by treating compound **1** with diphenyl phosphorochloridate and triethylamine base in dichloromethane solvent (Scheme 1).

RESULTS AND DISCUSSION

Initially we focused our efforts on the synthesis of *N*-hydroxy benzamide from benzoic acid and hydroxylamine hydrochloride. To achieve this, although we made different attempts with different variations regarding the solvent, temperature, bases and their equivalents, unfortunately the formation of required compound was not observed. So, we concentrated our efforts on the synthesis of *O*-alkylhydroxamic acids. Interestingly, by using the regent **2**, we were able to synthesize *O*-benzyloxy benzamide in 82% yield in standardized reaction conditions, which includes the use of three equivalent of diisopropylethylamine base and DMF. Also to improve the yield, a new method was developed in which the reagent **2** was synthesized and used *in-situ* for the coupling reaction of carboxylic acid and *O*-alkyl hydroxylamines. The isolated yield of *O*-benzyloxy benzamide was improved up to 96% by using *in-situ* synthesized reagent **2**.

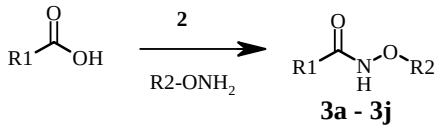
Scheme 1



Synthesis of Reagent

(a) NaH, BnBr, THF, 80 °C, 4 hrs; (b) 10% Pd/C, H_2, methanol, 15 min; (c) $(PhO)_2P(O)Cl$, $(Et)_3N$, dichloromethane, 30 min, 0 °C.

Scheme 2



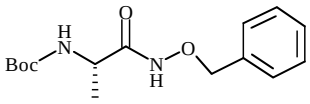
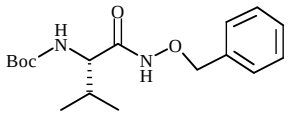
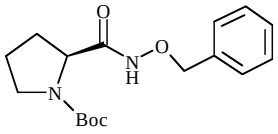
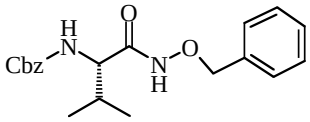
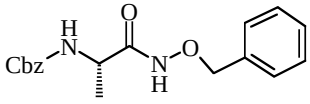
3a - 3j

Synthesis of *O*-alkyl hydroxamic acids

Using the similar reaction conditions, different *O*-alkyl hydroxamic acids (Scheme 2) were synthesized and the results are summarized in Table 1. All synthesized compounds were characterized by mass, IR, and ^{1}H NMR. From the results obtained, the acids with electron withdrawing-substituents like nitro (**3d**) took comparatively less reaction time for the completion of reaction than the acids with the electron-donating like methyl (**3b**) or without the substituents (**3a, 3i,** and **3j**). The reagent 2 shows the superiority over the existing methods regarding the yields and purification method. Especially the 4-nitro *N*-benzyloxy benzamide (**3d**) was isolated with better yield (98%) than the reported methods in the literature (37%) [13]. The easy work up was the more advantageous aspect of this method, which includes only the acid-base treatment and triturating with the suitable solvent to get the pure compound. During the work up, *N*-hydroxy-2-phenylbenzimidazole (**1**) could be easily isolated by acid base treatment and could be *re-used* for synthesis of reagent **2**. To illustrate the efficiency of recovered **1**, *N*-benzyloxybenzamide was synthesized using the reagent synthesized from recovered **1** and that

Table

Synthesis of different *O*-benzyl hydroxamic acids from *N*-protected amino acids.

Entry No	Product	Yield[a] (%)	%ee [b]
1	 **4a**	86	94.7
2	 **4b**	82	91.3
3	 **4c**	93	96.4
4	 **4d**	90	95.5
5	 **4e**	89	91.9

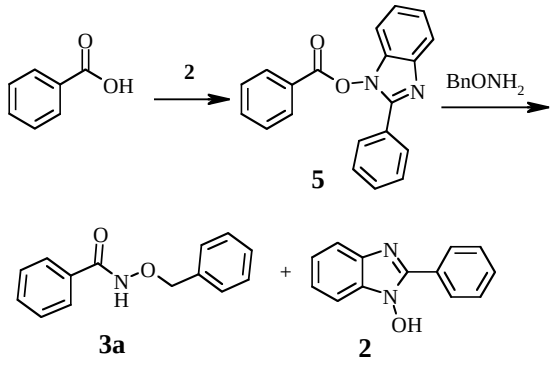
gave the constant better yields (1st recovered **1** - 92% yield, 2nd recovered **1** - 91% yield and 3rd recovered **1** - 91% yield).

The applicability of reagent **2** was also demonstrated for coupling of *O*-benzyl hydroxylamine with *N*-protected amino acids (**4a-4e**). The results obtained are summarized in Table 2. For these reactions, moderate to good yields were obtained and were in the range of 82% to 93%. The extent of racemization occurred was measured using the chiral HPLC. The percentages of enantiomeric excess (ee %) obtained were in the range of 91.3% to 96.4%, which proves the efficiency of coupling reagent **2** for optically active substrates.

The optical rotations of some of the synthesized compounds were measured and compared with the corresponding reported values in literature. In case of (1-Benzyloxycarbamoyl-ethyl) carbamic acid *tert*-butyl ester (**4a**), the reported specific rotation was $[\alpha]_D$ = -58.3° (c = 0.1, $CHCl_3$) [14] and in similar conditions, for our product found -58.2. The observed optical rotation matched well with corresponding reported values in literature and hence supporting for the lower racemization.

The intermediate (**5**) formed from the reaction of benzoic acid and *O*-benzyl hydroxylamine was isolated (Scheme 3) and characterized using mass, IR and ^{1}H NMR spectroscopy. The formation of intermediate **5** suggest the probable mechanism, that firstly benzoic acid reacts with reagent **2** to give the active ester **5** and later with the *O*-benzylhydroxylamine to give the product.

Scheme 3



Probable mechanism and isolation of intermediate **5**.

In conclusion, the reagent **2** was synthesized easily from cheap starting materials and used *in-situ* for synthesis of *O*-alkylhydroxamic acids. The advantages of this coupling reagent are their scalability, higher yields and use of cheap and easily available starting materials for synthesis of reagent. Also minimum racemization occurred during the synthesis of *O*-benzyl protected hydroxamic acids with optical active substrates.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a 400 MHz Varian-Gemini spectrometer and are reported as parts per million (ppm) downfield from a tetramethylsilane internal standard. The following abbreviations are used; singlet (s), doublet (d), triplet (t), quartet (q), multiplate (m) and broad (br). Mass spectra were taken with Micromass - QUATTRO-II of WATER mass spectrometer. HPLC was performed using Zorbax SB-C18 reverse phase column (0.46 X 25 cm) on Shimadzu instrument equipped with an automatic injector with UV-PDA detector. Detection was carried out at 254 nm. The mobile phase consists of 0.05 % TFA and acetonitrile (1:1, V/V). The products were eluted at flow rate of 1 mL/min using isocratic method. Flash column chromatography was performed with 300-400 meshes silica gel and analytical thin layer chromatography was performed on precoated silica gel plates (60F-254) with system (v/v) indicated. Melting points were determined in capillary tubes and are uncorrected.

Synthesis of *N*-[(diphenoxyphosphoryl)oxy]-2-phenyl-1*H*-benzimidazole (2). A solution of *N*-hydroxy-2-phenylbenzimidazole (0.42 g, 0.02 mol) and triethyl amine (0.70 mL, 0.05 mol) was stirred in DCM (2.5 mL) and the diphenyl phosphorochloridate (0.21 mL, 0.024 mol) was added at 0 ° C. The reaction mixture was stirred till the completion of reaction (TLC). Then DCM was evaporated and the residue was stirred with pentane and decanted. The remaining residue was stirred with diethyl ether and decanted three times. The combined diethyl ether was concentrated to give the title compound **2** as a white solid. Yield – 624 mg, (71%); mp 93 - 95 ° C (dec.); IR - (Nujol, cm $^{-1}$) 2930, 1244, 1105, and 1018; ^{1}H NMR ($CDCl_3$) δ 7.2 - 7.4 (m, 13H), 7.6 (d, J=8.0 Hz, 2H), 7.8 (d, J=8.2 Hz, 2H), 8.2 (d, J=8.2 Hz, 2H); EIMS - 443 (M $^+$); Anal. Cald for $C_{25}H_{19}N_2O_4P$: C, 67.87; H, 4.33; N, 6.33. Found: C, 67.81; H, 4.41; N, 6.30.

General procedure for *in-situ* synthesis *O*-alkylhydroxamic acids. A solution of *N*-hydroxy-2-phenylbenzimidazole (0.02 mol) and DIPEA (0.07 mol) was stirred in DMF and the diphenyl phosphorochloridate (0.024 mol) was added with cooling. The reaction mixture was stirred for 10 min and the carboxylic acid (0.016 mol) was added and reaction mixture was stirred for 10 min at 0 °C for active ester formation. Then *O*-alkyl hydroxylamine (0.03 mol) was added and mixture stirred at room temperature till completion of reaction (TLC). Then, saturated aq. NaCl (20 mL) solution was added, and the mixture was extracted with ethyl acetate (15 mL × 2). The organic layer was washed with 2 *N* HCl (15 mL), saturated $NaHCO_3$ (15 mL) and finally water (2 × 20 mL). The organic layer was dried over sodium sulphate, filtered and evaporated to give the corresponding *O*-alkyl hydroxamic acids.

***N*-Benzyloxybenzamide (3a)**. Mp 102 - 104 °C; ^{1}H NMR ($CDCl_3$) δ = 5.01(s, 2H), 7.3 - 7.4 (m, 5H), 7.5(m, 3H), 7.65 (d, J = 8.2 Hz, 2H), 8.87 (br s, 1H); EIMS - 228 (M $^+$); Anal. Cald for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.23; H, 5.64; N, 6.21.

***N*-Benzyloxy-4-methylbenzamide (3b).** Mp 128 - 129 °C; ^{1}H NMR ($CDCl_3$) δ = 2.34(s, 3H), 4.9(s, 2H), 7.3 - 7.4 (m, 7H), 7.65 (d, 2H), 10.2 (br s, 1H); EIMS - 241 (M $^+$); Anal. Cald for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.76; H, 5.96; N, 6.19.

***N*-Benzyloxy-4-methoxybenzamide (3c).** Mp 110 - 111 °C; ^{1}H NMR ($CDCl_3$) δ = 3.8 (s, 3H), 5.0 (s, 2H), 6.82 (d, 2H), 7.35

- 7.4 (m, 5H), 7.65 (d, 2H), 10.15 (br s, 1H); EIMS – 258 (M^+); Anal. Cald for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 69.86; H, 6.11; N, 5.42.

***N*-Benzyloxy-4-nitrobenzamide (3d).** Mp 166 - 167 °C; ^{1}H NMR ($CDCl_3$) δ = 5.1(s, 2H), 7.35 - 7.4 (m, 5H), 7.9 (d, 2H), 8.25 (d, 2H), 10.3 (br s, 1H); EIMS - 273 (M^+); Anal. Cald for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.71; H, 4.48; N, 10.23.

***N*-Benzyloxy-4-chlorobenzamide (3e).** Mp 158 - 159 °C; ^{1}H NMR (DMSO-d_6) δ = 5.0(s, 2H), 7.4 (m, 5H), 7.55 (d, 2H), 7.80 (d, 2H), 11.85 (br s, 1H); EIMS - 262 (M^+); Anal. Cald for $C_{14}H_{12}ClNO_2$: C, 64.25; H, 4.62; N, 5.35. Found: C, 64.19; H, 4.67; N, 5.23.

***N*-Benzyloxy-3-phenylacrylamide (3f).** Mp 99 - 100 °C; ^{1}H NMR ($CDCl_3$) δ = 4.95 (s, 2H), 6.54 (d, *J* =15.0 Hz, 1H), 7.35 (m, 6H), 7.44 (m, 4H), 7.69 (d, *J* =15.0 Hz, 1H), 10.25 (br s, 1H); EIMS - 254 (M^+); Anal. Cald for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 76.01; H, 5.92; N, 5.60.

Furan-2-carboxylic acid benzyloxy-amide (3g). Mp 99 - 101 °C; ^{1}H NMR ($CDCl_3$) δ = 5.0 (s, 2H), 6.46 (m, 1H), 7.16 (m, 1H), 7.4 (m, 6H), 10.35 (br s, 1H); EIMS - 218 (M^+); Anal. Cald for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.71; H, 4.98; N, 6.49.

***N*-Benzyloxy-nicotinamide (3h).** Mp 72 - 73 °C; ^{1}H NMR ($CDCl_3$) δ = 5.02 (s, 2H), 7.35 (m, 6H), 8.12 (d, 1H), 8.65 (d, 1H), 8.92 (s, 1H), 10.2 (br s, 1H); EIMS - 229 (M^+); Anal. Cald for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.45; H, 5.28; N, 12.34.

***N*-Ethoxybenzamide (3i).** Mp 60 - 61 °C; ^{1}H NMR ($CDCl_3$) δ = 1.2(t, 2H), 4.0(t, 3H), 7.45 - 7.5 (m, 3H), 7.7 (d, 2H), 9.8 (br s, 1H); EIMS - 166 (M^+); Anal. Cald for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.80; H, 6.69; N, 8.41.

***N*-Allyloxybenzamide (3j).** Colorless oil; ^{1}H NMR ($CDCl_3$) δ = 4.4(d, 2H), 5.2 - 5.3(m, 2H), 6.1(m, 1H), 7.5(m, 3H), 7.65 (d, 2H), 9.95 (br s, 1H); EIMS - 178 (M^+); Anal. Cald for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.48; H, 6.30; N, 8.93.

Tert-butyl-1-(benzyloxycarbamoyl)ethyl carbamate (4a). Mp 99 - 100 °C; ^{1}H NMR ($CDCl_3$) δ = 1.31(d, *J*=6.8 Hz, 3H), 1.42 (s, 9H), 4.08 (br s, 1H), 4.69(m, 1H), 4.89 (s, 2H), 5.19 (br s, 1H), 7.33 - 7.38 (m, 5H); EIMS - 295 (M^+); Anal. Cald for $C_{15}H_{22}N_2O_4$: C, 61.21; H, 7.53; N, 9.52. Found: C, 61.33; H, 7.51; N, 9.49.

***tert*-Butyl-1-(benzyloxycarbamoyl)-2-methylpropyl carbamate (4b).** Mp 83 - 84 °C; ^{1}H NMR ($CDCl_3$) δ = 0.98 (d, 6H), 1.45 (s, 9H), 2.2(m, 1H), 4.3(dd, 1H), 4.08 (br s, 1H), 4.89 (s, 2H), 5.19 (br s, 1H), 7.33 - 7.38 (m, 5H); EIMS - 323 (M^+); Anal. Cald for $C_{17}H_{26}N_2O_4$: C, 63.33; H, 8.13; N, 8.69. Found: C, 63.41; H, 7.98; N, 8.73.

***tert*-Butyl-2-(benzyloxycarbamoyl)pyrrolidine-1-carboxylate (4c):** Low melting solid; ^{1}H NMR ($CDCl_3$) δ = 1.45 (s, 9H), 1.6-1.8 (m, 4H), 3.35 (t, 2H), 4.29 (t, 1H), 4.89 (s, 2H), 5.19 (br s, 1H), 7.5 (m, 5H); EIMS - 321(M^+); Anal. Cald for $C_{17}H_{24}N_2O_4$: C, 63.73; H, 7.55; N, 8.74. Found: C, 63.58; H, 7.51; N, 8.74.

Benzyl-1-(benzyloxycarbamoyl)-3-methyl butylcarbamate (4d): Oil; ^{1}H NMR ($CDCl_3$) δ = 1.0 (d, 6H), 1.62 (dd, 2H), 1.83 (m, 1H), 4.3(dd, 1H), 4.08 (br s, 1H), 4.89 (s, 2H), 5.2 (s, 2H), 5.19 (br s, 1H), 7.33 - 7.38 (m, 10H); EIMS - 357 (M^+); Anal. Cald for $C_{20}H_{24}N_2O_4$: C, 67.40; H, 6.79; N, 7.86. Found: C, 67.39; H, 6.81; N, 7.89.

Benzyl-1-(benzyloxycarbamoyl)-ethylcarbamate (4e). Mp 121- 122 °C; ^{1}H NMR ($CDCl_3$) δ = 1.32(d, *J*= 6.6 Hz, 3H), 4.1 (br s, 1H), 4.65 (m, 1H), 4.8 (s, 2H), 5.0 (s, 2H), 5.22 (br s, 1H), 7.33 - 7.4 (m, 10H); EIMS - 329 (M^+); Anal. Cald for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.83; H, 6.11; N, 8.54.

Benzoic acid 2-phenyl-benzoimidazol-1-yl ester (5). Mp 234-235 °C; ^{1}H NMR (400 MHz, CDCl3): δ = 7.2 (m, 2H), 7.4(m, Hz, 3H), 7.5-7.7 (m, 7H), 8.2 (d, J = 8.2 Hz, 2H); MS (EI, 70 eV): *m/z* = 315 $[M+H]^+$; Anal. Cald for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.27; H, 4.51; N, 8.90.

Acknowledgement. The authors are thankful to the Head, Department of Chemical Technology, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad- 431004 (MS), India for providing the laboratory facility.

REFERENCES AND NOTES

[1] Jung, M. *Curr. Med. Chem.* **2001**, *8*, 1565.

[2] Brown P. D.; Davidson, A. H.; Gearing, A.; Whittakar, M. Hydroxamic acid matrix metalloproteinase inhibitors. In Matrix Metalloproteinase Inhibitors in Cancer Chemotheraphy; Clendeninn, N, J. *Appelt, K., Eds.; Humana Press: Totowa, NJ*, **2001**; pp –113.

[3] [a] For a review: Whittaker, M.; Floyd, C. D.; Brown, P.; Gearing, A. J. H. *Chem. Rev.* **1999**, *99*, 2735; [b] Caldarelli, M.; Habermann, J.; Ley, S. V. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2049.

[4] [a] Finnin, M. S.; Donigain, J. R.; Cohen, A.; Richon, V. M.; Rifkind, Marks, P.A.; breslow, R.; Pavletich, N. P. *Nature* **1999**, *401*, 188; [b] Miller, T. a.; Witter, D. J.; Belvedere, S. *J. Med. Chem.* **2003**, *46*, 5097; [c] Kim, D. K.; Lee, J. Y.; Kim, J. S.; Ryu, J. H.; Choi, J. Y.; Lee, J. W.; Kim, T. K.; Seo, J. W.; Park, H. J.; Yoo, J.; Park, J. H.; Kim, T. U.; Bang, Y. *J. Med. Chem.* **2003**, *46*, 5745; [d] Lu, Q.; Yang, Y. -T.; Chen, C. –S.; Davis, M.; Byrd, J. C.; Etherton, M. R. *J. Med. Chem.* **2004**, *47*, 467.

[5] [a] Miller, M. *J. Chem. Rev.* **1989**, *89*, 1563; (b) Bergeron, R. J.; Wiegand, J.; McManis, J. S.; Perumal, P. T. *J. Med. Chem.* **1991**, *34*, 3182.

[6] [a] Koshiti, N.; Reddy, G. V.; Jecobs, H.; Gopalan, A. *Synth. Commun.* **2002**, *32*, 3779; [b] Bailen, M. A.; Chinchilla, R.; Dodsworth, D. J.; Najera, C. *Tetrahedron Lett.* **2001**, *42*, 5013; [c] Fray, M. J.; Burslm, M. F.; Dickenson, R. P. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 567; [d] Dankwardt, S. M.; Billedeau, R. J.; lawley, L. K.; Abbot, S. C.; Martin, R, L.; Chan, C. S.; Van Wart, H. E.; Walker, K. A. M. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2513; [e] Nikam, S. S.; Kronberg, B. E.; Johnson, D. R.; Doherty, A. M. *Tetrahedron Lett.* **1995**, *36*, 197; [f] Altenburger, J. M.; Mioskowski, C.; d'Orchymont, H.; Schirlin, D.; Schalk, C.; Tarnus, C. *Tetrahedron Lett.* **1992**, *33*, 5055; [g] Barlaam, B.; Harmon, A.; Maudet, M. *Tetrahedron Lett.* **1998**, *39*, 7865; [h] Ando W.; Tsumaki, H. *Synth. Comm.* **1983**, *13*, 1053; [I] King, F. D.; Pike, S.; Walton D. R. M. *J. Chem. Soc. Chem. Commun.* **1978**, 351.

[7] Sibi, M. P.; Hasegawa, H.; Ghorphade, S. R. *Org. Lett.* **2002**, *4*, 3343.

[8] Hauser, C. R.; Renfrow, W. B. *Organic Synthesis; Wiley: New York*, **1943**, Collect. Vol. II, pp 67.

[9] [a] Burns, C. J.; Groneberg, R. D.; Salvino, J. M.; McGeehan, G.; Condon, S. M.; Morris, R.; Morrissette, M.; Mathew, R.; Darnbrough, S.; Neuenschwander, K.; Scotese, A.; Djuric, S.; Ullrich, J.; Labaudiniere, R. *Angew. Chem. Int. Ed.* **1998**, *37*, 2848; [b] Mori, K.; Koseki, K. *Tetrahedron,* **1988**, *44*, 6013.

[10] Kokare, N. D.; Nagawade, R. R.; Rane, V. P.; Shinde, D. B. *Tetrahedron Lett.* **2007**, *48*, 4437.

[11] [a] Kokare, N. D.; Nagawade, R. R.; Rane, V. P.; Shinde, D. B. *Synthesi*s, **2007**, 766; [b] Bahekar, S. S.; Shinde D. B. *Tetrahedron Lett.* **2004**, *45*, 7999; [c] Bahekar, S. S.; Kotharkar, S. A.; Shinde D. B. *Mendeleev. Commun;* **2004,** 210; [d] Kotharkar, S. A.; Jadhav, M. R.;

Nagawade, R. R.; Bahekar, S. S.; Shinde, D. B. *Lett. in Org. Chem.* **2005**, *2*, 398.

[12] J. M. Gardiner, C. R. Loyns, C. H. Schwalbe, G. C.. Barrett and P. R. Lowe, *Tetrahedron* **1995**, *51*, 4101.

[13] Arnaud, G.; Alessandro, V.; Matteo, Z. *J. Org. Chem.* **2005**, *70*, 6925.

[14] Ramasamy, K.; Olsen, R. K.; Emery, T. *J. Org. Chem.* **1981**, *46*, 5438.

[15] Jeum,- Jong, J.; Young-Dae, P.; Ho-Kyun, K.; Su-dong, C.; Ju-Kyeon, K. *Synth. Commun.* **2005**, *35*, 731.

[16] Alan, R. K.; Nataliya, K.; Boris, V. K. *Synthesis,* **2003**, *18*, 2777.