Preparation of Methyl Carbamates from Primary Alkyl- and Arylcarboxamides Using Hypervalent Iodine[1]

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A series of 14 primary alkyl- and arylcarboxamides were treated with $PhI(OAc)_2$ in KOH–CH_3OH at 5–10 °C to give the corresponding methyl carbamates in good to excellent yields. These conditions avoid the use of elemental bromine or heavy metal reagents ($Pb(OAc)_4$, AgOAc, $Hg(OAc)_2$), while taking advantage of the commercial availability of $PhI(OAc)_2$. The methyl carbamates are easily purified via column chromatography on silica gel. The isolated yields of the carbamates ranged from 72% for methyl *N*-cyclopropylcarbamate to 97% for methyl *N*-phenylcarbamate.

The Hofmann rearrangement converts primary carboxamides to amines using aqueous NaOH and Br_2.[2] Methods involving reagents such as $Pb(OAc)_4$,[3a] benzyltrimethylammonium tribromide in aqueous NaOH,[4] and NBS with $Hg(OAc)_2$ or AgOAc in DMF[5] have also been reported. In recent years, iodine(III) reagents have been used to perform the same conversions under acidic conditions. Iodine(III) reagents normally employed are $PhI(OCOCF_3)_2$,[6] PhIO–HCO_2H,[7] and PhI(OTs)OH,[8] which lead to high yields of the corresponding ammonium salts. Analytical and synthetic usefulness have been recently demonstrated in peptide sequencing[9] and *retro-inverso* peptide synthesis.[10]

Convenient rearrangements of aliphatic carboxamides using $PhI(OCOCF_3)_2$, PhIO–HCO_2H, and PhI(OTs)OH are carried out with isolation of the amines as the corresponding ammonium salts in high yields. However, some of these reagents demonstrate only modest stability. Loudon et al.[6b] have specifically noted that $PhI(OCOCF_3)_2$ should be freshly prepared and stored in a refrigerated, dark container under an inert atmosphere to avoid yellowing of the reagent which renders it ineffective in the Hofmann rearrangement. PhIO also decomposes at room temperature, undergoing disproportionation to give $PhIO_2$ and PhI.[11] The methods using PhI(OTs)OH reported by Koser et al.[8] are particularly convenient since the reagent is stable at room temperatures and the ammonium tosylate salts tend to crystallize from the reaction upon cooling. Reactions involving aryl carboxamides using these iodine(III) reagents give complex mixtures of products due to further oxidation of the initially formed aryl amine by the iodine(III) reagents.[6a,c,7a,8a,9]

Three exceptions involving arylcarboxamides have been noted in the literature. Tscherniac[12] reported the conversion of phthalimide to anthranilic acid using PhIO in aqueous KOH. Baumgarten and Smith[13] treated benzamide and cinnamide with $PhI(OAc)_2$ (diacetoxyiodobenzene, DAIB) in refluxing *tert*-butyl alcohol using triethylamine, tin(IV) chloride, or di-*n*-butyltin dilaurate as catalysts to give the corresponding *t*-butyl carbamates. Finally, Swaminathan and Venkatasubramanian[14] reported rearrangement of benzamide in acetic acid with DAIB leading to the formation of acetanilide. However, the nonreproducibility of the reaction by others has been the subject of controversy.[6b]

Our research was prompted by the desire to develop a general Hofmann rearrangement method to include arylcarboxamides while avoiding the use of Br_2, the use of heavy metals (Ag^5, Hg^5, Pb^3), and reflux conditions[13] and taking advantage of DAIB, which is stable and commercially available or is easily prepared by the method of Sharefkin and Saltzman.[15] Our method uses DAIB in methanolic KOH at 5–10 °C to generate methyl carbamates in good yields from the corresponding primary carboxamides.

Results and Discussion

Moriarty et al.[16] have recently reported the use of DAIB in methanolic KOH for the preparation of synthetically

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(1) Presented in part at the 203rd National meeting of the American Chemical Society, San Francisco, CA, 1992; ORGN 60.

(2) Wallis, E. S.; Lane, J. F. *Org. React.* **1946**, *3*, 267.

(3) (a) Baumgarten, H. E.; Smith, H. L.; Staklis, A. *J. Org. Chem.* **1975**, *40*, 3554. (b) Acott, B.; Beckwith, A. L. J.; Hassanali, A. *Austr. J. Chem* **1968**, *21*, 197. (c) Acott, B.; Beckwith, A. L. J.; Hassanali, A. *Austr. J. Chem.* **1968**, *21*, 185. Acott, B.; Beckwith, A. L. J. *J. Chem. Soc., Chem. Commun.* **1965**, 161.

(4) Kajigaeshi, S.; Asano, K.; Fujasaki, S.; Kakinami, T.; Okamoto, T. *Chem. Lett.* **1989**, 463.

(5) Jew, S.-S.; Park, H. G.; Park, H.-J.; Park, M.-S.; Cho, Y.-S. *Tetrahedron Lett.* **1990**, *31*, 1559.

(6) (a) Radhakrishna, A. S.; Parham, M. E.; Riggs, R. M.; Loudon, G. M. *J. Org. Chem.* **1979**, *44*, 1746. (b) Loudon, G. M.; Radhakrishna, A. S.; Almond, M. R.; Blodgett, J. K.; Boutin, R. H. *J. Org. Chem.* **1984**, *49*, 4272. (c) Loudon, G. M.; Boutin, R. H. *J. Org. Chem.* **1984**, *49*, 4277. (d) Almond, M. R.; Stimmel, J. B.; Thompson, A. E.; Loudon, G. M. *Org. Synth.* **1988**, *67*, 132. (e) Tamura, M.; Jacyno, J.; Stammer, C. H. *Tetrahedron Lett.* **1986**, *27*, 5435.

(7) (a) Radhakrishna, A. S.; Rao, C. D.; Varma, R. K.; Sing, B. B.; Bhatnagar, S. P. *Synthesis* **1983**, 538. (b) Wasielewki, C.; Topolski, M.; Dembkowski, M. *J. Pract. Chem.* **1989**, *331*, 507.

(8) (a) Lazbin, I. M.; Koser, G. F. *J. Org. Chem.* **1986**, *51*, 2669. (b) Vasudervan, A.; Koser, G. F. *J. Org. Chem.* **1988**, *53*, 5158. (c) Moriarty, R. M.; Khoshrowshahi, J. S.; Awasthi, A. K.; Penmasta, R. *Synth. Commun.* **1988**, *18*, 1179.

(9) Loudon, G. M.; Parham, M. E. *Tetrahedron Lett.* **1978**, 437.

(10) (a) Waki, M.; Kitajima, Y.; Izumiya, N. *Synthesis* **1981**, 266. (b) Pallai, P.; Goodman, M. *J. Chem. Soc., Chem. Commun.* **1982**, 280. (c) Squadrini, F.; Verdini, A. S.; Viscomi, G. C. *Gazz. Chim. Ital.* **1984**, *114*, 25. (d) Fuller, W. D.; Goodman, M.; Verlander, M. S. *J. Am. Chem. Soc.* **1985**, *107*, 5821. (d) Shimihigashi, Y.; Kodama, H.; Waki, M.; Costa, T. *Chem. Lett.* **1989**, 1821.

(11) Banks, D. F. *Chem. Rev.* **1966**, *66*, 243.

(12) Tscherniac, J. *Chem. Ber.* **1903**, *36*, 218.

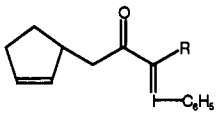
(13) Smith, H. L. Ph. D. Thesis, University of Nebraska, Lincoln, NE, 1970.

(14) Swaminathan, K.; Venkatasubramanian, N. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1161.

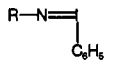
(15) Sharefkin, J. G.; Saltzman, H. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. *5*, p 660.

0022-3263/93/1958-2478$04.00/0

useful β-carbonyl iodonium ylides **1a–c** from the corresponding β-carbonyl compounds. Interestingly, Yamada et al.,[17] Abramovitch et al.,[18] and Mansuy et al.[19] found that the treatment of aryl- or alkylsulfonamides and trifluoroacetamide with DAIB under basic conditions led to the formation of isolable iminoiodinanes **2a–c**.



1a. R = CO_2CH_3
b. R = $SO_2C_6H_5$
c. R = NO_2



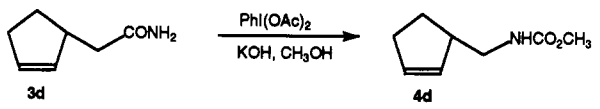
2a. R = p-CH_3-$C_6H_4SO_2$
b. R = CH_3SO_2
c. R = CF_3CO

When DAIB was added to a cold (5–10 °C) solution of carboxamide **3d** in methanolic KOH the solid DAIB dissolved in about 5 min giving a pale yellow solution. The reaction was checked after about 1 h by thin-layer chromatography (TLC) which revealed the complete disappearance of the starting amide. Work up of the reaction afforded methyl carbamate **4d** (Scheme I).

Our best results were obtained by the addition of DAIB (1 equiv) in one portion to a chilled (5–10 °C), stirred solution of the **3d** (1 equiv) and KOH (2.5 equiv) in methanol. Upon dissolution of the DAIB the reaction was stirred for 15 min, followed by removal of the ice bath and warming to room temperature. Completion of the reaction was evidenced by TLC, and then the methanol was removed in vacuo followed by partition of the residue (dichloromethane–water) and subsequent purification by flash column chromatography on silica gel to afford methyl carbamate **4d** in 88% isolated yield. A series of alkylcarboxamides **3a,b** and alkenylcarboxamides **3c–g** containing remote olefinic sites were similarly converted to the corresponding methyl carbamates **4a–g** in good yields (Table I).

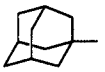
Since arylcarboxamides were not suitable for reaction under acidic conditions we decided to investigate their compatibility under basic conditions. When benzamide, **3h**, was treated with DAIB in methanolic KOH, the corresponding carbamate **4h** was obtained in 97% isolated yield. Several other arylcarboxamides were similarly subjected to the same conditions including the binaphthylcarboxamide **3i** and the heteroaromatic carboxamides **3j–l**, all of which afforded good yields of the corresponding methyl carbamates **4i–l** (Table II). (*E*)-Cinnamide (**3m**) was converted to the known methyl (*E*)-*N*-(2-phenylethenyl)carbamate (**4m**) in 82% isolated yield. Examination of the crude reaction mixture by TLC and ^1H NMR revealed only one product formed. Since the Hofmann rearrangement using iodine(III) reagents has been shown to proceed with retention of configuration at a migrating chiral center,[6b,13] we were curious as to whether (*Z*)-cinnamide would give the expected methyl (*Z*)-*N*-(2-phenylethenyl)carbamate. (*Z*)-cinnamic acid was prepared from (*E*)-cinnamic acid using a three-step synthesis described by Galamb et al.[20] The (*Z*)-cinnamic acid was converted to the amide and purified by flash column chromatography affording **3n** in 62% yield. The vinyl proton coupling constants of the two isomers (**3m** and **3n**) were compared and found to differ as expected for *Z–E* isomers, J_{ab} = 15.8 Hz (**3m**) and J_{ab} = 12.6 Hz (**3n**), respectively. The obtained values were in agreement with the literature values.[21,22] Reaction of **3n** under the described conditions led to the isolation of the expected (*Z*)-carbamate **4n** in 76% yield as a colorless oil. Monitoring of the reaction by TLC and ^1H NMR of the crude reaction showed no evidence of the (*E*)-isomer **3m**. ^1H

Scheme I



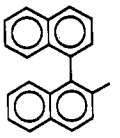
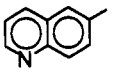
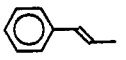
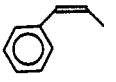
3d **4d**

Table I. Reactions of Alkyl Carboxamides with $PhI(OAc)_2$ in Methanolic KOH

$RCONH_2$	R	$RNHCO_2CH_3$	yield,[a] %
3a		**4a**	72
3b		**4b**	78
3c		**4c**	83
3d		**4d**	88
3e		**4e**	90
3f		**4f**	89
3g		**4g**	90

[a] Isolated yields after flash column chromatography (silica gel).

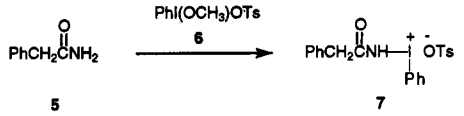
Table II. Reactions of Aryl Carboxamides with $PhI(OAc)_2$ in Methanolic KOH

$ArCONH_2$	Ar	$ArNHCO_2CH_3$	yield,[a] %
3h		**4h**	97
3i	 (±)	**4i**	91
3j		**4j**	86
3k		**4k**	82
3l		**4l**	91
3m		**4m**	82
3n		**4n**	70

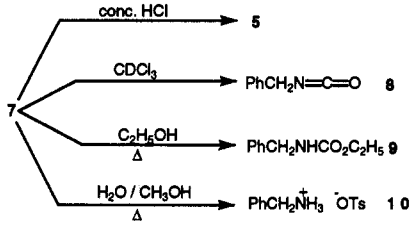
[a] Isolated yields after flash column chromatography (silica gel).

(16) (a) Moriarty, R. M.; Prakash, O.; Vaid, R. K.; Zhao, L. *J. Am. Chem. Soc.* **1989**, *111*, 6443. (b) Guo, L. Ph. D. Thesis, University of Illinois at Chicago, Chicago, IL, 1991.
(17) Yamada, Y.; Yamamoto, T.; Okawara, M. *Chem. Lett.* **1975**, 361.
(18) Abramovitch, R. A.; Bailey, T. D.; Takaya, T.; Uma, V. *J. Org. Chem.* **1974**, *39*, 340.
(19) Mansuy, D.; Mahy, J. P.; Dureault, A.; Bedi, G.; Battioni, P. *J. Chem. Soc., Chem. Commun.* **1984**, 1161.
(20) Galamb, V.; Alper, H. *Tetrahedron Lett.* **1983**, *24*, 2965–2968.
(21) Sasaki, S.-I. *Handbook of Proton-NMR Spectra and Data*; Academic Press: Tokyo, 1986; Vol. 7, p 151.
(22) Glover, S. A.; Goosen, A. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1348.

Scheme II



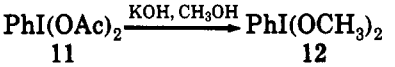
Scheme III. Decomposition of N-Phenyliodonio-α-Phenylacetamide Tosylate



NMR comparison of the carbamates **4m** and **4n** revealed the vinyl coupling constants to be J_{ab} = 14.5 Hz (**4m**) and J_{ab} = 9.4 Hz (**4n**) which are in agreement with the literature values.[23,24]

Mechanistically, the reaction probably follows a path similar to the classic Hofmann rearrangement. Koser et al.[25] and Loudon et al.[6] have proposed and supported such a mechanism in their studies. Koser et al.[25] treated phenylacetamide (**5**) with methoxy(tosyloxy)iodobenzene **6** and isolated the *N*-(phenyliodonio)carboxamide tosylate salt **7** (Scheme II). They further demonstrated (Scheme III) that under varying reaction conditions reversion to give **5** occurred or rearrange to give isocyanate **8**, ethyl carbamate **9**, or the benzylammonium tosylate salt **10**. A similar mechanism is envisioned under basic conditions. Addition of DAIB **11** to methanolic KOH leads to the formation of $PhI(OCH_3)_2$ **12** (Scheme IV).[26] Reaction of

Scheme IV

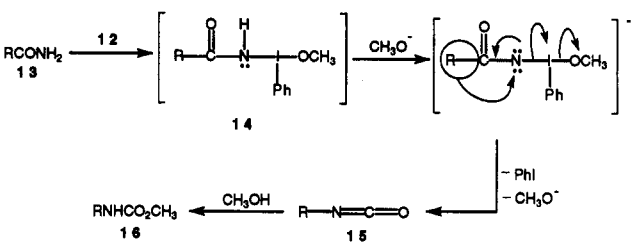


the amide **13** with **12** leads to the probable formation of the *N*-(phenyliodonio) intermediate **14** (Scheme V). Rearrangement of **14** leads to the formation of an isocyanate **15** as similarly illustrated in Scheme III. Under acidic conditions the isocyanate is rapidly hydrolyzed to the amine, which in the case of arylamines is further oxidized. Under the basic conditions (KOH–methanol) the free amine is not generated, but rather the isocyanate is trapped by the solvent affording the carbamate **16**.

Experimental Section

All melting points were obtained on a Thomas-Hoover capillary melting point apparatus and are uncorrected. NMR spectra were obtained using either an IBM WP-200SY (200 MHz) or a Bruker AM-400 (400 MHz) in $CDCl_3$ with tetramethylsilane as the internal standard, unless otherwise noted. Infrared spectra were recorded on an IBM System 9000 FT-IR. Mass spectra were obtained either on a Finnigan MAT 112/S (EI) or a Finnigan MAT-90 (CI, HRMS). Elemental analyses were performed by Midwest MicroLabs, Indianapolis, IN. Flash column chromatography was performed using E. Merck 60 (70–230 mesh) silica

Scheme V



gel with hexane–ethyl acetate as the eluents unless otherwise noted. Diacetoxyiodobenzene (DAIB) was prepared by the method of Sharefkin and Saltzman[25] and was used without further purification. All solvents and reagents used for the rearrangement reactions were commercial ACS reagent grade and were used as received. Benzamide (**3h**) and nicotinamide (**3k**) were obtained from Aldrich and used as received.

General Procedure for the Preparation of Carboxamides. Carboxamides **3a**,[27] **c**,[28] **d**,[29] **j**,[30] **l**,[31] **m**[21,32] were prepared from the commercially available carboxylic acids by conversion to the acid chloride as described by Callant et al.[33] followed by treatment with NH_3 as described by Moriarty et al.[8c] 1-Adamantanecarboxamide[34] (**3b**) was prepared from the corresponding acid chloride (Aldrich) and NH_3 as previously described. 3-Cyclohexenecarboxamide (**3e**) was prepared as described by Loudon et al.[6c] The obtained amides matched physical data as described in the literature. Carboxamides **3f**, **g**, **i**, and **n** were prepared as follows.

4-Cycloheptenecarboxamide (3f). 4-Cycloheptenecarboxylic acid[35] (5.00g, 35.7 mmol) was converted to the amide as described in the general procedure. Recrystallization from acetone afforded **3f** (4.36g, 88%) as large white plates: mp 175.5–176.5 °C; IR (Nujol) 3339 (NH), 3173 (NH), 1632 (C=O) cm^{-1}; ^1H NMR δ 5.80 (dt, J = 4.9, 2.1 Hz, 2 H), 5.47 (br s, 2 H, NH_2), 2.60–1.40 (m, 9 H); ^{13}C NMR (DMSO-d_6) 177.8 (C=O), 131.6, 47.8, 29.7, 26.6; MS (EI, 70eV) m/z (rel intensity) 139 (M^+, 100), 96 (22), 95 (48), 91 (18). Anal. Calcd for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 68.72; H, 9.20; N, 9.93.

4-Cyclooctenecarboxamide (3g). 4-Cyclooctenecarboxylic acid[35a] (7.00g, 45.5 mmol) was converted to the acid chloride as described by Erman and Kretchmar,[36] followed by treatment with NH_3 as described in the general procedure. Recrystallization from acetone afforded **3g** (2.23g, 32%) as pale yellow crystals: mp 200–201.5 °C (lit.[35a] mp 201–202 °C); IR (KBr) 3350 (NH), 3173 (NH), 1659 (C=O) cm^{-1}; ^1H NMR δ 5.70 (dt, J = 10.6, 7.7 Hz, 1 H), 5.65 (dt, J = 10.5, 6.6 Hz, 1 H), 5.35 (br s, 2 H, NH_2), 2.5–1.2 (m, 11 H); ^{13}C NMR: 178.8 (C=O), 129.9, 129.8, 43.6, 32.0, 29.8, 27.5, 25.4, 24.0; MS (EI, 70eV) m/z (rel intensity) 153 (M^+, 47), 109 (54).

1,1′-Binaphthyl-2-carboxamide (3i). 1,1′-Binaphthyl-2-carboxylic acid[37] (3.00 g, 10.0 mmol) was converted to the amide as described in the general procedure. Recrystallization from 2-propanol afforded **3i** (2.00g, 72%) as a fine white crystalline solid: mp 207–208 °C; IR (Nujol) 3273 (NH), 3163 (NH), 1649 (C=O) cm^{-1}; ^1H NMR (acetone-d_6) δ 8.20–7.10 (m, 13 H, aromatic), 5.30 (br s, 1 H, NH), 5.20 (br s, 1 H, NH); ^{13}C NMR (DMSO-d_6) 170.3 (C=O), 135.8, 135.5, 134.3, 133.0, 132.9, 132.4, 132.2, 127.9, 127.7, 126.5, 126.3, 126.2, 126.0, 125.9, 125.6, 125.2, 124.4; MS (EI, 70eV) m/z (rel intensity) 297 (M^+, 100), 253 (55),

(23) Zhang, Z.; Pan, Y.; Hu, H.; Kao, T. *Synthesis* **1991**, 539.
(24) Brettle, R.; Mosedale, A. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2185.
(25) Lazbin, I. M.; Koser, G. F. *J. Org. Chem.* **1987**, *52*, 476.
(26) (a) Schardt, B. C.; Hill, C. L. *Inorg. Chem.* **1983**, *22*, 1563. (b) Moriarty, R. M.; Prakash, O. *Acc. Chem. Res.* **1986**, *19*, 244.
(27) Schlatter, M. J. *J. Am. Chem. Soc.* **1941**, 1733.
(28) Paul, R.; Tchelitcheff, S. *Bull. Chem. Soc. Fr.* **1949**, 470.
(29) Clive, D. L. J.; Singh, A.; Wong, C. K.; Kiel, W. A.; Menchen, S. M. *J. Org. Chem.* **1980**, *45*, 2120.
(30) Brode, W. R.; Bremer, C. *J. Am. Chem. Soc.* **1934**, *56*, 993.
(31) Einhorn, A.; Fiebelman, R. *Liebigs. Ann. Chem.* **1908**, *361*, 153.
(32) Posner, T. *Chem. Ber.* **1905**, *38*, 2316.
(33) Callant, P.; De Wilde, H.; Vanderwalle, M. *Tetrahedron* **1981**, *37*, 2079.
(34) Stetter, H.; Wulff, K. *Chem. Ber.* **1962**, *95*, 2302.
(35) (a) Stork, G.; Landesman, H. K. *J. Am. Chem. Soc.* **1956**, *78*, 5129. (b) Murray, D. F.; Baum, M. W.; Jones, M. J., Jr. *J. Org. Chem.* **1986**, *51*, 1.
(36) Erman, W. F.; Kretchmar, H. C. *J. Org. Chem.* **1968**, *33*, 1545.
(37) Wilson, J. M.; Cram, D. J. *J. Org. Chem.* **1984**, *49*, 4930.

252 (47). Anal. Calcd for $C_{21}H_{15}NO$: C, 84.82; N, 5.08; N, 4.71. Found: C, 84.62, H, 5.09; N, 4.82.

(*Z*)-Cinnamide (3n). (*Z*)-Cinnamic acid[20] (1.00g, 6.75 mmol) was converted to the amide as described in the general procedure. The crude amide was purified by flash column chromatography (3:20:77 methanol–ethyl acetate–chloroform) to afford **3n** (0.62g, 62%) as a white solid:[22] mp 85–85.5 °C; IR (KBr) 3229 (NH), 3155 (NH), 1666 (C=O); ^{1}H NMR δ 7.45–7.26 (m, 5 H, Ar), 6.82 (d, J = 12.6 Hz, 1 H), 6.08 (br s, 1 H, NH), 5.96 (d, J = 12.6 Hz, 1 H), 5.82 (br s, 1 H, NH); ^{13}C NMR 169.1 (C=O), 137.5, 134.8, 129.9, 128.7, 128.4, 123.8; (EI, 70eV) m/z (rel intensity) 147 (M^+, 34), 146 (84), 131 (43), 130 (16), 103 (100), 102 (42). Anal. Calcd for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.27; H, 6.09; N, 9.58.

General Procedure for Preparation of Substituted Methyl Carbamates. To a stirred solution of potassium hydroxide (2.5 equiv) in methanol (50 mL) was added the carboxamide (1 equiv). The mixture was stirred at room temperature until a homogeneous solution was obtained followed by cooling to 5–10 °C in an ice–water bath. The diacetoxyiodobenzene (1 equiv) was added in one portion and dissolved within 5 min to give a clear yellow solution. The reaction was stirred at ice-bath temperature for 15 min followed by warming to room temperature while stirring for an additional 45 min. Upon completion of the reaction (TLC) the methanol was removed in vacuo and the yellow residue was partitioned between water (100 mL) and CH_2Cl_2 (50 mL). The CH_2Cl_2 was separated, and the water layer was extracted with CH_2Cl_2 (2 × 50 mL). The CH_2Cl_2 extracts were combined, washed with water (1 × 50 mL) and brine (1 × 50 mL), dried over anhydrous $MgSO_4$, and filtered. The CH_2Cl_2 was removed in vacuo to give the crude carbamate which was purified by flash column chromatography (two column volumes of hexane to remove iodobenzene, followed by elution with 80/20 hexanes–ethyl acetate) to afford the pure final product.

Methyl *N*-Cyclopropylcarbamate (4a). Cyclopropanecarboxamide (**3a**) (2.00 g, 23.5 mmol) afforded **4a** (2.08 g, 72%) as a clear colorless oil: bp_{12} 95–96 °C (lit.[38] bp_{11} 84–85 °C); IR (neat) 3323 (NH), 3092, 3013, 2955, 1707 (C=O) cm^{-1}; ^{1}H NMR δ 5.29 (br s, 1 H, NH), 3.56 (br s, 3 H, OCH_3), 2.47 (m, 1 H), 0.60 (m, 2 H), 0.42 (m, 2 H); ^{13}C NMR 157.7 (C=O), 51.7 (OCH_3), 22.8, 6.5.

Methyl *N*-(1-Adamantyl)carbamate (4b). 1-Adamantanecarboxamide (**3b**) (1.00 g, 5.79 mmol) afforded **4b** (0.944g, 78%) as white crystals: mp 117–119 °C (lit.[34] mp 120 °C); IR (KBr) 3271 (NH), 1722 (C=O) cm^{-1}; ^{1}H NMR: δ 4.50 (br s, 1 H, NH), 3.60 (s, 3 H, OCH_3), 2.05 (br s, 3 H), 1.90 (br s, 6 H), 1.65 (br s, 6 H); ^{13}C NMR: 155.1 (C=O), 51.0 (OCH_3), 50.6, 42.0, 36.4, 29.6; MS (EI, 70eV) 209 (M^+, 35), 152 (100), 120 (68).

Methyl *N*-(3-Butenyl)carbamate (4c). 4-Pentene-1-carboxamide (**3c**) (4.00 g, 40.4 mmol) afforded **4c** (4.37 g, 83%) as a colorless oil: $bp_{0.1}$ 35–37 °C; IR (neat) 3339 (NH), 3078, 2947, 1705 (C=O) cm^{-1}; ^{1}H NMR δ 5.57 (m, 1 H), 5.10 (m, 2 H), 4.73 (br s, 1 H, NH), 3.58 (s, 3 H, OCH_3), 3.20 (m, 2 H) 2.35 (m, 2 H); ^{13}C NMR 156.9 (C=O), 135, 116, 51.7 (OCH_3) 40.2, 34.0. Anal. Calcd for $C_6H_{11}NO_2$: C, 55.79; H, 8.58; N, 10.84. Found: C, 55.83; H, 8.42; N, 10.47.

Methyl *N*-[(2-Cyclopentenyl)methyl]carbamate (4d). 2-Cyclopenteneacetamide (**3d**) (2.00 g, 16.0 mmol) afforded **4d** (2.15 g, 88%) as a clear colorless oil: $bp_{0.30}$ 69–70 °C; IR (neat) 3335 (NH), 1703 (C=O) cm^{-1}; ^{1}H NMR δ 5.70 (dt, J = 5.7, 2.1 Hz, 1 H), 5.50 (dt, J = 5.6, 2.1 Hz, 1 H), 5.10 (br s, 1 H, NH), 3.52 (s, 3 H, OCH_3), 3.00 (m, 2 H), 2.77 (br s, 1 H), 2.20 (m, 2 H), 1.90 (m, 1 H), 1.40 (m, 1 H); ^{13}C NMR 157.1 (C=O), 132.3, 131.6, 51.5 (OCH_3), 45.7, 45.1, 31.6, 26.7. Anal. Calcd for $C_8H_{13}NO_3$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.65; H, 8.42; N, 8.97.

Methyl *N*-(3-Cyclohexenyl)carbamate (4e). 3-Cyclohexene-1-carboxamide (**3e**) (0.50 g, 3.99 mmol) afforded **4e** (0.56g, 90%) as a white solid: mp 38–39 °C; IR (KBr) 3333 (NH), 1695 (C=O) cm^{-1}; ^{1}H NMR: δ 5.70 (m, 1 H) 5.60 (m, 1 H), 4.70 (br s, 1 H, NH), 3.70 (br s, 3 H, OCH_3); ^{13}C NMR 156.3 (C=O) 126.7, 124.2, 51.6 (OCH_3) 46.0, 31.7, 28.2, 23.4; MS (EI, 70 eV) m/z (rel intensity) 155 (M^+, 11), 108 (11), 102 (28), 101 (100). Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.71; H, 8.34; N, 9.14.

Methyl *N*-(4-Cycloheptenyl)carbamate (4f). 4-Cycloheptene-1-carboxamide (**3f**) (0.341 g, 2.45 mmol) afforded **4f** (0.369 g, 89%) as a white solid: mp 84–85 °C; IR ($CDCl_3$, film) 3289 (NH), 1709 (C=O) cm^{-1}; ^{1}H NMR δ 5.80 (m, 2 H), 4.76 (br s, 1 H, NH), 3.75 (br s, 1 H), 3.65 (s, 3 H, OCH_3); ^{13}C NMR: 155.9 (C=O), 131.7, 53.6, 51.8 (OCH_3), 33.4, 24.2; MS (EI, 70eV) m/z (rel intensity) 169 (M^+, 10), 154 (11), 94 (89), 79 (100). Anal. Calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.98; N, 8.28. Found: C, 63.75; H, 8.98; N, 8.25.

Methyl *N*-(4-Cyclooctenyl)carbamate (4g). 4-Cyclooctene-1-carboxamide (**3g**) (1.00 g, 6.53 mmol) afforded **4g** (1.08 g, 90%) as a white crystalline solid: mp 55–56.5 °C; IR ($CDCl_3$ film) 3329 (NH), 1701 (C=O) cm^{-1}; ^{1}H NMR δ 5.66 (m, 2 H), 4.79 (br s, 1 H, NH), 3.63 (s, 3 H, OCH_3), 2.80–1.60 (m, 11 H); ^{13}C NMR 156.0 (C=O), 130.0, 129.6, 51.6 (OCH_3), 50.9, 35.2, 34.5, 26.8, 26.7, 23.2; MS (EI, 70 eV) m/z (rel intensity) 183 (M^+, 11), 128 (68), 108 (47), 101 (100). Anal. Calcd for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35; N, 7.64. Found: C, 65.37; H, 9.43; N, 7.48.

Methyl *N*-Phenylcarbamate (4h). Benzamide (**3h**) (1.00 g, 8.26 mmol) afforded **4h** (1.21 g, 97%) as colorless crystals: mp 47–48 °C (lit.[39] mp 48–49 °C); IR (KBr) 3304 (NH), 1709 (C=O); ^{1}H NMR δ 7.50–6.9 (m, 5 H, Ar), 6.70 (br s, 1 H, NH), 3.76 (s, 3 H, OCH_3); ^{13}C NMR 154.2 (C=O), 128.8, 123.3, 118.9, 52.0 (OCH_3).

Methyl *N*-[2-(1,1′-Binaphthyl)]carbamate (4i). 2-(1,1′-Binaphthyl)carboxamide (**3i**) (1.00 g, 3.05 mmol) afforded **4i** (1.00 g, 91%) as a white crystalline solid: mp 125–126 °C; IR (KBr) 3416 (NH), 1743 (C=O) cm^{-1}; ^{1}H NMR δ 8.50 (d, J = 8.1 Hz, 1 H), 8.10 (q, J = 7.7 Hz, 3 H), 7.90 (d, J = 8.1 Hz, 1 H), 7.70 (t, J = 7.3 Hz, 1 H), 7.55 (t, J = 7.6 Hz, 1 H), 7.45 (d, J = 6.9 Hz, 1 H), 7.40 (t, J = 7.2 Hz, 1 H), 7.30 (m, 2 H), 7.20 (t, J = 8.1 Hz, 1 H), 7.10 (d, J = 7.6 Hz, 1 H), 6.32 (s, 1 H, NH), 3.57 (s, 3 H, OCH_3); ^{13}C NMR 153.9 (C=O), 134.0, 133.9, 133.3, 132.9, 132.4, 130.3, 129.0, 128.9, 128.8, 128.5, 127.8, 126.8, 126.5, 126.4, 125.9, 125.5, 124.5, 119.1, 52.1 (OCH_3); MS (EI, 70 eV) m/z (rel intensity) 327 (M^+, 40), 267 (18), 202 (100). Anal. Calcd for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.71; H, 5.35; N, 4.31.

Methyl *N*-(2-Pyridyl)carbamate (4j). 2-Pyridinecarboxamide (**3j**) (1.07 g, 7.0 mmol) afforded **4j** (1.14 g, 86%) as a white crystaline solid: mp 128–129 °C (lit.[40] mp 131–132 °C); IR (KBr) 3200 (NH), 2950, 1736 (C=O) cm^{-1}; ^{1}H NMR δ 9.50 (s, 1 H, NH), 8.35 (d, J = 4.3 Hz, 1 H), 8.05 (d, J = 8.3 Hz, 1 H), 7.70 (dt, J = 1.3, 7.1 Hz, 1 H), 7.0 (m, 1 H), 3.83 (s, 3 H, OCH_3); ^{13}C NMR 154.4 (C=O), 152.5, 147.5, 130.5, 118.5, 112.5, 52.3 (OCH_3); MS (EI, 70eV) m/z (rel intensity) 152 (M^+, 100), 121 (57), 120 (60).

Methyl *N*-(3-Pyridyl)carbamate (4k). Nicotinamide (**3k**) (1.00 g, 6.57 mmol) afforded **4k** (1.03 g, 82%) as a white crystalline solid: mp 117–118 °C (lit.[40] mp 120–121 °C); IR (KBr) 3430 (NH), 1726 (C=O) cm^{-1}; ^{1}H NMR δ 9.23 (br s, 1 H, NH), 8.50 (d, J = 2.3 Hz, 1 H), 8.35 (d, J = 4.1 Hz, 1 H), 8.10 (br s, 1 H), 7.25 (m, 1 H), 3.74 (s, 3 H, OCH_3); ^{13}C NMR 154.5 (C=O), 143.5, 139.9, 135.8, 126.0, 123.7, 52.3 (OCH_3); MS (EI, 70 eV) m/z (rel intensity) 152 (M^+, 100), 120 (22), 107 (65), 93 (17).

Methyl *N*-(6-Quinolyl)carbamate (4l). 6–Quinolinecarboxamide (**3l**) (1.00 g, 5.80 mmol) afforded **4l** (1.06 g, 91%) as a white crystalline solid: mp 184–185 °C; IR (KBr) 3233 (NH), 1724 (C=O) cm^{-1}; ^{1}H NMR δ 8.82 (dd, J = 1.5, 4.2 Hz, 1 H), 8.09 (d, J = 6.7 Hz, 2 H), 8.03 (d, J = 9.4 Hz, 1 H), 7.53 (dd, J = 9.0, 2.4 Hz, 1 H), 7.37 (q, J = 4.2 Hz, 1 H), 7.12 (br s, 1 H, NH), 3.83 (s, 3 H, OCH_3); ^{13}C NMR 153.8 (C=O), 148.2, 144.6, 136.9, 134.9, 129.4, 128.4, 122.2, 120.9, 113.4, 51.5 (OCH_3); MS (EI, 70 eV) m/z (rel intensity) 202 (M^+, 100), 170 (51), 116 (52). Anal. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.34; H, 4.98; N, 13.35. Found: C, 64.92; H, 4.96; N, 13.47.

Methyl (*E*)-*N*-(2-Phenylethenyl)carbamate (4m). (*E*)-Cinnamide (**3m**) (0.50 g, 3.4 mmol) afforded **4m** (0.49 g, 82%) as white flakes: mp 120–121 °C (lit.[23,41] mp 119 °C); IR ($CDCl_3$ film) 3308 (NH), 1724 (C=O) cm^{-1}; ^{1}H NMR δ 7.30–7.20 (m, 6

(38) Lipp, P.; Buchremer, J. Seeles, H. *Liebigs. Ann. Chem.* **1932**, *499*, 1.

(39) George, D. K.; Moore, D. H.; Brian, W. P.; Garman, J. A. *J. Agric. Food Chem.* **1953**, *2*, 356.

(40) Shriner, R. L.; Child, R. G. *J. Am. Chem. Soc.* **1952**, *74*, 549.

(41) Kyorin Pharmaceutical Co., Br. Patent 953 716; *Chem. Abstr.* **1964**, *61*, 4379g.

H, including one vinyl), 6.68 (br s, 1 H, NH), 6.00 (d, J = 14.5 Hz, 1 H), 3.73 (s, 3 H, OCH_3); ^{13}C NMR 154.1 (C=O), 136.2, 128.6, 126.3, 125.3, 124.1, 110.8, 52.7 (OCH_3); MS (CI) 178 (M^+, 100), 177 (20), 146 (17).

Methyl (*Z*)-*N*-(2-Phenylethenyl)carbamate (4n). (*Z*)-Cinnamide (**3n**) (0.50 g, 3.4 mmol) afforded **4n**[24] (0.42 g, 76%) as a colorless oil: IR (neat) 3327 (NH), 1740 (C=O) cm^{-1}; ^1H NMR δ 7.37–7.19 (m, 5 H, Ar), 6.96 (br s, 1 H, NH), 6.70 (dd, J = 9.4, 11.5 Hz, 1 H), 5.63 (d, J = 9.4 Hz, 1 H), 3.73 (s, 3 H, OCH_3); ^{13}C NMR 154.3 (C=O), 135.6, 128.9, 128.7, 126.8, 123.3, 108.0, 52.6 (OCH_3); MS (EI, 70 eV) m/z (rel intensity) 177 (M^+, 76), 145 (45), 118 (40), 117 (54), 91 (100); HRMS calcd for $C_{10}H_{11}NO_2$ m/z 177.0789 (M^+), found 177.0787 (M^+).

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