Facile Procedure for the Synthesis of *N*-Aryl-*N*-hydroxy Carbamates

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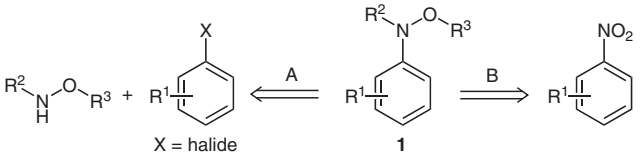
Abstract: An efficient one-pot procedure for the zinc-mediated reduction of nitroarenes in the presence of chloroformates leading to the corresponding N,O-bisprotected hydroxylamine is described. Reactions proceed smoothly under ambient conditions in THF–water mixtures in good to excellent yield (34–81%). Solvolysis of the bisprotected hydroxylamines with sodium methoxide at room temperature provides access to synthetically versatile *N*-aryl-*N*-hydroxy carbamates in excellent yields (89–97%).

Key words: hydroxylamine, carbamate, zinc-mediated reduction

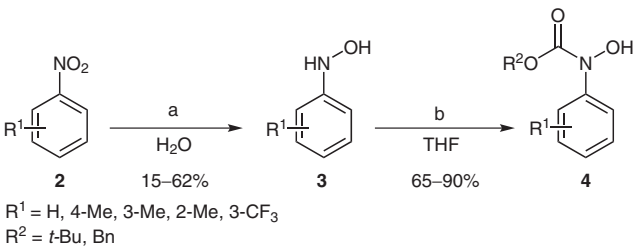
N-Aryl hydroxylamines are a significant class of compounds that are key building blocks in the synthesis of natural products and biologically active compounds.[1] Diverse applications in the preparation of heterocycles,[2–5] nitrones,[6] rearrangement precursors,[7] electophilic aminating agents,[8] amino acid derivatives,[9,10] and a number of pharmaceutical applications[11] make improved methods to access this functionality important.

As part of a program to develop novel hydroxylamine-based reactions and reagents[12] we were interested in N-protected-*N*-aryl hydroxylamines **1**. We recently reported both copper- and palladium-catalyzed[13,14] methods to access this motif (disconnection A; Scheme 1). An alternative and arguably more economical route to access this functionality involves zinc-mediated reduction of nitroarenes (disconnection B; Scheme 1). Traditional methods for disconnection B involves partial reduction of nitroarenes,[15] which requires strict conditions to prevent overreduction and careful workup to isolate the hydroxylamine product. Existing procedures for this reduction include catalytic transfer hydrogenation[16] and metal-mediated reductions[17] which can also be promoted using ultrasound.[18]



Scheme 1 Disconnective strategies for *N*-aryl hydroxylamines

In our hands, zinc-mediated reduction of nitroarenes **2** in aqueous ammonium chloride gave the corresponding *N*-aryl hydroxylamines **3** in low to moderate yields (15–62%), mainly due to overreduction, difficulties in isolation and solubility issues (Scheme 2). Subsequent carbamate protection of the hydroxylamine nitrogen typically resulted in a mixture of mono- and bisprotected hydroxylamine (**4** and **5**), revealing a similar nucleophilicity of the two heteroatoms. Protection at lower temperature (–78 °C) allowed for selective synthesis of *N*-aryl-*N*-hydroxy carbamates **4** in good yield (65–90%). This two-step procedure allowed access to a range of *N*-aryl hydroxylamines **4**; however, the methodology suffered from disappointing yields and the necessity for column chromatography after each step. We therefore investigated a more efficient approach to the desired *N*-aryl-*N*-hydroxy carbamates.



Scheme 2 *Reagents and conditions*: a) Zn (2 equiv), NH_4Cl (1 equiv); b) $ClCO_2R^2$ (1.1 equiv), Et_3N (2 equiv) or $(Boc)_2O$ (1.1 equiv), –78 °C.

We envisaged performing the reduction in the presence of a reactive chloroformate could prevent overreduction by trapping the *N*-aryl hydroxylamine intermediate. In addition, liberation of hydrochloric acid during the reaction could also lead to activation of the zinc powder, improving the overall efficiency of the process. Good precedent pointing towards the success of this approach came from the preparation of biologically active *N*,*O*-bisacetyl hydroxylamines using indium- or zinc-mediated[19,20] reductions in the presence of acetic anhydride.

Reaction of chloroformates with water is typically slow; we therefore employed a mixture of THF–water, as the reaction medium at 0 °C. Initially reacting 2.1 equivalents of benzylchloroformate in the presence of zinc powder (4 equiv) and NH_4Cl (1.1 equiv, Scheme 3). The results obtained under these conditions are outlined in Table 1. Pleasingly, this improved the overall efficiency of the

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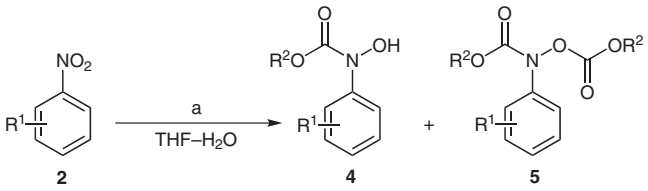
reaction and allowed direct access to protected *N*-aryl hydroxylamines **4** with improved overall yields (entries 1–3). However, control over the mono- and bisprotected products (which were readily separable by chromatography) was limited. Methyl chloroformate was an equally effective substrate, once again delivering the desired hydroxylamine products (entries 4–6). Interestingly, altering the electronics of the aromatic ring tended to alter the product distribution between the mono- and bisprotected products **4** and **5**. For example, introduction of an electron-donating substituent on the starting aromatic tended to lead preferentially to the bisprotected aryl hydroxylamine **5** (entries 2, 5, and 6). Use of the less electrophilic $(Boc)_2O$ to intercept the hydroxylamine intermediate was less successful (entry 7), the major product isolated being over reduced *N*-Boc aniline (45%). Attempts to improve this yield by modification of the reaction conditions were not fruitful.



R^1 = H, 4-Me, 3-Me, 2-Me, 4-CN
R^2 = Me, Bn, Ph, *t*-Bu

Scheme 3 *Reagents and conditions*: a) Zn (4 equiv), NH_4Cl (1.1 equiv), $ClCO_2R^2$ (2.1 equiv), 0 °C.

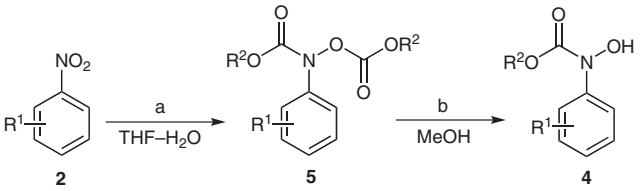
Table 1 Reduction of Nitroarenes in the Presence of Chloroformates[a]

Entry	R^1	R^2	Yield (%)[b]	
			4	**5**
1	H	Bn	31	33
2	4-Me	Bn	14	44[c]
3	4-NC	Bn	23	26
4	H	Me	21	49
5	2-Me	Me	9	53
6	3-Me	Me	9	62
7	H	*t*-Bu	14	16

[a] All reactions were carried out on a 10 mmol scale.
[b] Isolated yield.
[c] Based on ^{1}H NMR, product contaminated with benzyl alcohol.

In an attempt to create a uniform product distribution we increased the amount of chloroformate used to three equivalents (Scheme 4). This resulted in significantly improved yields of the bisprotected hydroxylamine **5** (34–81%, Table 2; entries 1–11).[21] The reaction was tolerant of both electron-withdrawing and electron-donating substituents on the starting nitroarene, providing efficient access to the products. Reactions with phenyl chloroformate were sluggish compared to other chloroformates and resulted in an inseparable mixture of compounds, however, treatment of the crude reaction mixture directly with sodium methoxide in methanol provided access to phenyl *N*-hydroxy carbamates in moderate yields (entries 12 and 13).

Selective hydrolysis of the bisprotected hydroxylamines **5** was carried out with sodium methoxide in methanol at room temperature and provided the *N*-hydroxy carbamates **4** in excellent yields (89–97%, Table 2).[22]



R^1 = H, 4-Me, 3-Me, 2-Me, 3-CF_3, 4-CN, 4-I
R^2 = Me, Bn, Ph

Scheme 4 *Reagents and conditions*: a) Zn (4 equiv), NH_4Cl (1.1 equiv), $ClCO_2R^2$ (3 equiv), 0 °C; b) NaOMe (1 equiv), r.t.

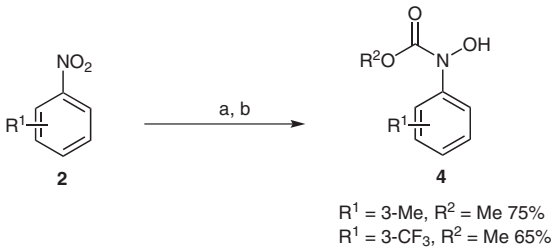
Table 2 Reduction and Hydrolysis of Nitroarenes[a]

Entry	R^1	R^2	Yield (%)[b]	
			5	**4**
1	H	Bn	81	91
2	4-Me	Bn	72	92[c]
3	4-NC	Bn	45	89[c]
4	3-F_3C	Bn	79	93[c]
5	H	Me	76	96
6	2-Me	Me	73	94
7	3-Me	Me	81	96
8	4-Me	Me	78	97
9	3-F_3C	Me	68	93
10	4-I	Me	71	95
11	4-NC	Me	34	93
12	H	Ph	–	35[d]
13	4-Me	Ph	–	41[d]

[a] All reactions were carried out on a 10 mmol scale.
[b] Isolated yield.
[c] Based on ^{1}H NMR, product contaminated with benzyl alcohol.
[d] After direct hydrolysis.

Attempts to develop a one-pot procedure by addition of KOH (3 equiv) to the crude reaction mixture directly after reduction failed due to the precipitation of zinc salts leading to purification difficulties. However, it was possible to avoid purification of the intermediate and combine the two synthetic steps. After reduction and bisprotection the

organic layer was washed with sodium bicarbonate solution, brine and the solvent removed under reduced pressure. Dissolving the crude reaction mixture in methanol and adding sodium methoxide (1 equiv) gave the mono-protected *N*-aryl hydroxylamine **4** in good overall yield (65–75%, Scheme 5), providing a simple and convenient method with which to access this versatile functionality.



Scheme 5 *Reagents and conditions*: a) Zn (2 equiv), NH_4Cl (1.1 equiv), $ClCO_2R^2$ (3 equiv), THF–H_2O, 0 °C; b) NaOMe (1 equiv), MeOH, r.t.

In conclusion, we have developed a simple and efficient method for the conversion of nitroarenes to synthetically versatile *N*-aryl-*N*-hydroxy carbamates by a two-step protocol without the need for purification of intermediates. Specific advantages of this method over existing literature procedures include increased yields, simple and convenient reaction conditions, reduction in overall reaction time, a single purification procedure, and the avoidance of hazardous or precious metals within the transformation. Application of this methodology in the preparation of arrays of druglike molecules is currently under way.

General Procedure for the Reduction Nitroarenes to N,O-Bisprotected *N*-Aryl Hydroxylamines

To a solution of nitroarene (10 mmol) in THF–H_2O (60 mL, 2:1) was added NH_4Cl (11 mmol), and the mixture was cooled to 0 °C. The chloroformate (30 mmol) was added via syringe, and after 5 min Zn powder (40 mmol) was added in one portion. After 2 h the phases were separated and the organic layer diluted with Et_2O (60 mL), washed with sat. $NaHCO_3$ (2 × 50 mL), H_2O (50 mL), and brine (50 mL). The organic layer was dried over $MgSO_4$ and the solvent removed under reduced pressure. Purification by column chromatography on SiO_2 (EtOAc–PE, 1:5 to 1:3) gave the bisprotected hydroxylamine **5** (34–81%).

General Procedure for the Solvolysis of N,O-Bisprotected *N*-Aryl Hydroxylamines

Sodium methoxide (1.0 equiv) was added in one portion to a solution of N,O-bisprotected *N*-aryl hydroxylamine (1.0 mmol) in MeOH (5 mL), and the mixture was stirred at r.t. for 2–4 h. The reaction mixture was reduced, dissolved in Et_2O (30 mL), and washed with sat. NH_4Cl solution (20 mL), H_2O (20 mL), and brine (20 mL). The organic layer was dried over $MgSO_4$ and the solvent removed under reduced pressure. Purification by column chromatography on SiO_2 (EtOAc–PE, 1:3 to 1:1) gave the *N*-aryl-*N*-hydroxy carbamate **4** (89–97%).

Acknowledgment

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References and Notes

(1) Schmidt, A. *Science of Synthesis*, Vol. 31b; Ramsden, C. A., Ed.; Thieme: Stuttgart, **2007**, 1739.
(2) For the preparation of indoles, see: Blechert, S. *Tetrahedron Lett.* **1984**, *25*, 1547.
(3) For the preparation of isoxazolidines, see: Imran, M.; Khan, S. A.; Siddiqui, N. *Ind. J. Pharm. Sci.* **2004**, *66*, 377.
(4) For the preparation of oxadiazolidinones, see: Gopalsamy, A.; Kincaid, S. L.; Ellingboe, J. W.; Groeling, T. M.; Antrilli, T. M.; Krishnamurthy, G.; Aulaugh, A.; Friedrichs, G. S.; Crandall, D. L. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 3477.
(5) For the preparation of aziridines, see: Murugan, E.; Siva, A. *Synthesis* **2005**, 2022.
(6) For the preparation of nitrones, see: (a) Evans, D. A.; Song, H.-J.; Fandrick, K. R. *Org. Lett.* **2006**, *8*, 3351. (b) Chatterjee, A.; Bhattacharya, P. K. *J. Org. Chem.* **2006**, *71*, 345. (c) Young, I. S.; Williams, J. L.; Kerr, M. A. *Org. Lett.* **2005**, *7*, 953.
(7) For applications in [3,3]-sigmatropic rearrangements, see: (a) Porzelle, A.; Woodrow, M. D.; Tomkinson, N. C. O. *Eur. J. Org. Chem.* **2008**, 5135. (b) Lobo, A. M.; Prabhakar, S. *Pure Appl. Chem.* **1997**, *69*, 547.
(8) Srivastava, R. S.; Khan, M. A.; Nicholas, K. M. *J. Am. Chem. Soc.* **2005**, *127*, 7278.
(9) For the preparation of β-amino acids, see: Fuller, A. A.; Chen, B.; Minter, A. R.; Mapp, A. K. *J. Am. Chem. Soc.* **2005**, *127*, 5376.
(10) For the preparation of β-amino alcohols, see: Aschwanden, P.; Kværnø, L.; Geisser, R. W.; Kleinbeck, F.; Carreira, E. M. *Org. Lett.* **2005**, *7*, 5741; and references cited therein.
(11) Johansson, W.; Parkinson, G. N.; Denny, W. A.; Neidel, S. *J. Med. Chem.* **2003**, *46*, 4009.
(12) (a) Beshara, C. S.; Hall, A.; Jenkins, R. L.; Jones, K. L.; Jones, T. C.; Killeen, N. M.; Taylor, P. H.; Thomas, S. P.; Tomkinson, N. C. O. *Org. Lett.* **2005**, *7*, 5729. (b) Beshara, C. S.; Hall, A.; Jenkins, R. L.; Jones, T. C.; Parry, R. T.; Thomas, S. P.; Tomkinson, N. C. O. *Chem. Commun.* **2005**, 1478. (c) Hall, A.; Jones, K. L.; Jones, T. C.; Killeen, N. M.; Porzig, R.; Taylor, P. H.; Yau, S. C.; Tomkinson, N. C. O. *Synlett* **2006**, 3435. (d) Hall, A.; Huguet, E. P.; Jones, K. L.; Jones, T. C.; Killeen, N. M.; Yau, S. C.; Tomkinson, N. C. O. *Synlett* **2007**, 293. (e) Jones, T. C.; Tomkinson, N. C. O. *Org. Synth.* **2007**, *84*, 233. (f) Knowles, D. A.; Mathews, C. J.; Tomkinson, N. C. O. *Synlett* **2008**, 2769.
(13) Jones, K. L.; Porzelle, A.; Hall, A.; Woodrow, M. D.; Tomkinson, N. C. O. *Org. Lett.* **2008**, *10*, 797.
(14) Porzelle, A.; Woodrow, M. D.; Tomkinson, N. C. O. *Org. Lett.* **2009**, *11*, 233.
(15) Kamm, O. *Org. Synth., Coll. Vol. I* **1941**, 445.
(16) (a) Ayyanger, N. R.; Brahme, K. C.; Kalkote, U. R.; Srinivasan, K. V. *Synthesis* **1984**, 938. (b) Entwistle, I. D.; Gilkerson, T.; Johnstone, R. A. W.; Telford, R. P. *Tetrahedron* **1978**, *34*, 213. (c) Rondestvedt, C. S. Jr.; Johnson, T. A. *Synthesis* **1977**, 850.
(17) For example: (a) Ren, P.-D.; Pan, X.-W.; Jin, Q.-H.; Yao, Z.-P. *Synth. Commun.* **1997**, *27*, 3497. (b) Ren, P.-D.; Dong, T.; Wu, S. *Synth. Commun.* **1997**, *27*, 1547. (c) Bartra, M.; Romea, P.; Urpí, F.; Vilarrasa, J. *Tetrahedron* **1990**, *46*, 587. (d) Yanada, K.; Yamaguchi, H.; Meguri, H.;

Uchida, S. *J. Chem. Soc., Chem. Commun.* **1986**, 1655. (e) Uchida, S.; Yanada, K.; Yamaguchi, H.; Meguri, H. *Chem. Lett.* **1986**, 1069.

(18) Shi, Q. X.; Lu, R. W.; Jin, K.; Zhang, Z. X.; Zhao, D. F. *Chem. Lett.* **2006**, *35*, 226.

(19) Kin, B. H.; Cheong, J. W.; Han, R.; Jun, Y. M.; Baik, W.; Lee, B. M. *Synth. Commun.* **2001**, *31*, 3577.

(20) Kin, B. H.; Jun, Y. M.; Suh, S. W.; Baik, W.; Lee, B. M. *J. Chem. Res., Synop.* **1998**, 46.

(21) **Spectroscopic Data for New Compounds**

Benzyl *N*-Phenyl-*N*-(benzoxycarbonyloxy) Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.45 (m, 2 H), 7.40–7.26 (m, 13 H), 5.26 (s, 2 H), 5.22 (s, 2 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.2, 153.4, 139.4, 135.4, 134.1, 129.1, 129.0, 128.8, 128.7, 128.6, 128.5, 128.4, 128.0, 127.7, 124.0, 71.6, 68.6. HRMS: m/z calcd for $[M + H]^+$ $C_{22}H_{19}NO_5Na$: 400.1161; found: 400.1167.

Benzyl *N*-4-Tolyl-*N*-(benzoxycarbonyloxy) Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.29 (m, 12 H), 7.18 (d, 2 H, J = 8.0 Hz), 5.27 (s, 2 H), 5.24 (s, 2 H), 2.25 (s, 3 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.7, 153.0, 140.7, 136.0, 135.5, 134.5, 129.7, 129.0, 128.8, 128.7, 128.6, 128.4, 122.0, 70.9, 67.2, 20.9. HRMS: m/z calcd for $[M + H]^+$ $C_{23}H_{22}NO_5$: 392.1498; found: 392.1497.

Benzyl *N*-4-Cyano-*N*-(benzoxycarbonyloxy) Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65–7.58 (m, 4 H), 7.39–7.31 (m, 10 H), 5.28 (s, 2 H), 5.27 (s, 2 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 153.6, 151.9, 143.0, 134.7, 133.7, 133.0, 129.3, 128.8, 128.7, 128.6, 128.2, 120.1, 118.4, 109.1, 72.3, 69.2. HRMS: m/z calcd for $[M + NH_4]^+$ $C_{23}H_{22}N_3O_5$: 420.1559; found: 420.1570.

Benzyl *N*-3-Trifluoromethylphenyl-*N*-(benzoxycarbonyloxy) Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (br s, 1 H), 7.66–7.64 (m, 1 H), 7.50–7.49 (m, 2 H), 7.39–7.30 (m, 10 H), 5.27 (s, 2 H), 5.26 (s, 2 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 153.9, 152.7, 140.0, 135.0, 133.9, 131.8 (q, CF_3, J = 42 Hz), 129.6, 129.1, 128.8, 128.7, 128.6, 128.5, 128.1, 125.6, 123.6, 123.6, 119.5, 72.0, 69.0. HRMS: m/z calcd for $[M + NH_4]^+$ $C_{23}H_{22}F_3N_2O_5$: 463.1481; found: 463.1472.

Methyl *N*-2-Tolyl-*N*-(methoxycarbonyloxy) Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 (d, 1 H, J = 7.8 Hz), 7.29–7.24 (m, 3 H), 3.88 (s, 3 H), 3.82 (s, 3 H), 2.37 (s, 3 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.8, 154.8, 137.8, 137.4, 131.1, 129.5, 128.5, 126.7, 56.2, 54.0, 17.16. HRMS: m/z calcd for $[M + H]^+$ $C_{11}H_{14}NO_5$: 240.0872; found: 240.0867.

Methyl *N*-3-Tolyl-*N*-(methoxycarbonyloxy) Carbamate

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.28 (m, 3 H), 7.15 (d, 1 H, J = 7.0 Hz), 3.94 (s, 3 H), 3.87 (s, 3 H), 2.39 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.7, 154.1, 139.2, 139.1, 128.9, 128.8, 125.1, 121.5, 56.4, 54.0, 21.5. HRMS: m/z calcd for $[M + H]^+$ $C_{11}H_{14}NO_5$: 240.0872; found: 240.0863.

Methyl *N*-4-Tolyl-*N*-(methoxycarbonyloxy) Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (d, 2 H, J = 8.1 Hz), 7.19 (d, 2 H, J = 8.1 Hz), 3.90 (s, 3 H), 3.83 (s, 3 H), 2.36 (s, 3 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.8, 154.3, 138.4, 136.8, 129.7, 125.1, 56.3, 53.9, 21.1. HRMS: m/z calcd for $[M + H]^+$ $C_{11}H_{11}NO_5$: 240.0866; found: 240.0868.

Methyl *N*-3-Trifluoromethylphenyl-*N*-(methoxycarbonyloxy) Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (s, 1 H), 7.68–7.66 (m, 1 H), 7.54–7.52 (m, 2 H), 3.96 (s, 3 H), 3.89 (s, 3 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.4, 153.4, 139.9, 131.4 (q, CF_3, J = 32 Hz), 129.5, 125.9, 123.8, 121.4, 119.6, 56.7, 54.2. HRMS: m/z calcd for $[M + H]^+$ $C_{11}H_{11}NO_5F_3$: 294.0589; found: 294.0589.

Methyl *N*-4-Iodophenyl-*N*-(methoxycarbonyloxy) Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, 2 H, J = 4.8 Hz), 7.14 (d, 2 H, J = 4.8 Hz), 3.84 (s, 3 H), 3.77 (s, 3 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.5, 153.5, 139.1, 138.1, 125.2, 92.3, 56.6, 54.2. HRMS: m/z calcd for $[M + H]^+$ $C_{10}H_{11}NO_5{}^{127}I$: 351.9682; found: 351.9675.

Methyl *N*-4-Cyanophenyl-*N*-(methoxycarbonyloxy) Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, 2 H, J = 8.1 Hz), 7.58 (d, 2 H, J = 7.0 Hz), 3.94 (s, 3 H), 3.88 (s, 3 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.1, 152.5, 143.0, 133.0, 120.3, 118.3, 109.2, 57.0, 54.4. HRMS: m/z calcd for $[M + NH_4]^+$ $C_{11}H_{14}N_3O_5$: 268.0928; found: 268.0931.

(22) **Phenyl *N*-Phenyl-*N*-hydroxy Carbamate**

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (br s, 1 H), 7.54 (d, 2 H, J = 7.8 Hz), 7.40–7.35 (m, 4 H), 7.26–7.22 (m, 2 H), 7.14 (d, 2 H, J = 7.8 Hz). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 153.7, 150.7, 140.2, 129.5, 128.8, 126.5, 126.0, 122.5, 121.5. HRMS: m/z calcd for $[M + H]^+$ $C_{13}H_{12}NO_3$: 230.0812; found: 230.0812.

Phenyl *N*-4-Tolyl-*N*-hydroxy Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (br s, 1 H), 7.41–7.33 (m, 4 H), 7.25–7.21 (m, 1 H), 7.19–7.11 (m, 4 H), 2.36 (s, 3 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 153.8, 150.8, 137.7, 136.7, 129.5, 129.4, 125.9, 123.0, 121.5, 21.0. HRMS: m/z calcd for $[M + NH_4]^+$ $C_{14}H_{17}N_2O_3$: 261.1239; found: 261.1230.

Benzyl *N*-4-Tolyl-*N*-hydroxy Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.30 (m, 7 H), 7.15 (d, 2 H, J = 8.2 Hz), 5.21 (s, 2 H), 2.23 (s, 3 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 155.6, 140.8, 138.4, 135.8, 129.2, 128.6, 128.1, 127.1, 122.7, 68.3, 21.0. HRMS: m/z calcd for $[M + H]^+$ $C_{15}H_{16}NO_3$: 258.1125; found: 258.1126.

Benzyl *N*-4-Cyano-*N*-hydroxy Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, 2 H, J = 9.0 Hz), 7.58 (d, 2 H, J = 9.0 Hz), 7.43–7.33 (m, 5 H), 5.30 (s, 2 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.2, 144.7, 134.9, 132.7, 128.98, 128.4, 119.4, 118.8, 107.0 69.1. HRMS: m/z calcd for $[M + NH_4]^+$ $C_{15}H_{16}N_3O_3$: 286.1192; found: 286.1194.

Benzyl *N*-3-Trifluoromethylphenyl-*N*-hydroxy Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (br s, 1 H), 7.56–7.55 (m, 1 H), 7.31–7.29 (m, 2 H), 7.21–7.13 (m, 5 H), 5.10 (s, 2 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 155.0, 141.4, 135.0, 131.0 (q, J = 32 Hz, CF_3), 129.1, 128.7, 128.7, 128.2, 127.8, 127.1, 124.2, 118.1, 69.0. HRMS: m/z calcd for $[M + NH_4]^+$ $C_{15}H_{16}FN_2O_3$: 329.1108; found: 329.1110.

Methyl *N*-2-Tolyl-*N*-hydroxy Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.0 (br s, 1 H), 7.36–7.33 (m, 1 H), 7.28–7.22 (m, 3 H), 3.75 (s, 3 H), 2.34 (s, 3 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 157.5, 139.5, 136.2, 130.9, 128.9, 127.5, 126.6, 53.8, 17.6. HRMS: m/z calcd for $[M + Na]^+$ $C_9H_{11}NO_3Na$: 204.0631; found: 204.0634.

Methyl *N*-3-Tolyl-*N*-hydroxy Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.2 (br s, 1 H), 7.33–7.28 (m, 3 H), 7.06 (d, 2 H, J = 6.6 Hz), 3.84 (s, 3 H), 2.40 (s, 3 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 156.4, 140.9, 138.5, 128.4, 126.9, 123.1, 119.7, 53.7, 21.5. HRMS: m/z calcd for $[M]^+$ $C_9H_{11}NO_3$: 181.0739; found: 181.0735.

Methyl *N*-4-Tolyl-*N*-hydroxy Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.34 (s, 3 H), 3.77 (s, 3 H), 7.15 (d, 2 H, J = 8.2 Hz), 7.33 (d, 2 H, J = 8.2 Hz), 8.55 (br s, 1 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 156.4, 138.4, 136.2, 129.2, 122.8, 53.7, 21.0. HRMS: m/z calcd for [M +

Na]$^+$ $C_9H_{11}NO_3Na$: 204.0631; found: 204.0629.

Methyl *N*-3-Trifluoromethylphenyl-*N*-hydroxy Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (s, 1 H), 7.71 (d, 1 H, J = 8.0 Hz), 7.49–7.41 (m, 2 H), 7.20 (br s, 1 H), 3.89 (s, 3 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 155.7, 141.3, 131.1 (q, CF_3, J = 32 Hz), 129.1, 129.1, 124.1, 122.0, 117.9, 54.0. HRMS: m/z calcd for [M]$^+$ $C_9H_8F_3NO_3$: 235.0456; found: 235.0453.

Methyl *N*-4-Iodophenyl-*N*-hydroxy Carbamate

^{1}H NMR (400 MHz, MeOD): δ = 7.65 (d, 2 H, J = 7.0 Hz), 7.25 (d, 2 H, J = 7.0 Hz), 3.83 (s, 3 H). ^{13}C NMR (62.5 MHz, MeOD): δ = 156.9, 143.5, 138.6, 123.6, 89.0, 53.8. HRMS: m/z calcd for [M + H]$^+$ $C_8H_8INO_3$: 292.9549; found: 292.9550.

Methyl *N*-4-Cyanophenyl-*N*-hydroxy Carbamate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, 2 H, J = 7.0 Hz), 7.60 (d, 2 H, J = 7.0 Hz), 3.90 (s, 3 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.6, 144.3, 132.8, 119.3, 118.7, 107.3, 54.3. HRMS: m/z calcd for [M + Na]$^+$ $C_9H_8N_2O_3Na$: 215.0427; found: 215.0427.