mixture was poured into H_2O (30 mL) and extracted with AcOEt (15 mL × 3). The extract was washed with saturated NaCl and dried over $MgSO_4$. Removal of the solvent in vacuo left a solid which was chromatographed on a silica gel flash column with CH_2Cl/EtOH = 20/1 to give the 5,7-diene (entry 1) (193 mg, 84%) as a pale yellow powder: mp 164–165 °C; IR (KBr) 3350, 2995, 2905, 1395, 1380, 1170, 1110, 1080, 1065, 855 cm^{-1}; ^1H-NMR ($CDCl_3$), δ 0.61 (3 H, s), 1.02 (3 H, s), 1.22 (3 H, d, J = 7.2 Hz), 1.24 (6 H, s), 3.00 (1 H, d, J = 3.6 Hz), 3.20–3.38 (1 H, br), 3.32 (1 H, d, J = 3.6 Hz), 3.44–3.56 (1 H, m), 3.78–3.92 (2 H, m), 5.32–5.40 (1 H, m), 5.68 (1 H, brd, J = 5.7 Hz); MS m/z 416 (M^+), 68 (100); UV (EtOH) λ_{max} 289, 278, 267 nm. The other 5,7-dienes shown in Table I are known compounds and have the following melting points: entry 2, 148–149.5 °C;[5] entry 3, 186.5–187.5 °C;[5] entry 4, 112–113 °C; entry 5, 118–119 °C;[7] entry 6, 169 °C;[8] entry 7, 120.5–121.5 °C. The physical and spectral properties agree with the literature data.[5-8]

Acknowledgment. We thank to Dr. Masatomo Hamana, Professor Emeritus of Kyushu University for his encouragement.

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N,O-Bis(phenoxycarbonyl)hydroxylamine: A New Reagent for the Direct Synthesis of Substituted *N*-Hydroxyureas

Andrew O. Stewart* and Dee W. Brooks

Immunosciences Research Area, Department 47K, Abbott Laboratories, Abbott Park, Illinois 60064

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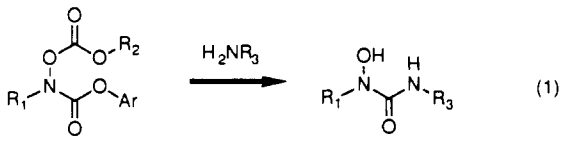
A series of potent, selective, orally active inhibitors of the enzyme 5-lipoxygenase has been investigated which contain the *N*-hydroxyurea as a necessary component for biological activity.[1] Inhibitors of 5-lipoxygenase represent a promising new therapy for a variety of disorders involving leukotriene mediators.[2] One objective in this pharmaceutical discovery research was to devise efficient synthetic methods for the preparation of substituted *N*-hydroxyureas.[3]

A common method for the preparation of *N*-hydroxyureas has been the treatment of hydroxylamines with an isocyanate or potassium cyanate. The hydroxylamines themselves can be obtained from acid-catalyzed reduction of the corresponding oxime using borane pyridine.[4]

Alternatively, Miller has demonstrated that O-substituted hydroxamates can be alkylated with alcohols using the Mitsunobu reaction (Scheme I).[5,6] *N*-(Benzyloxycarbonyl)hydroxylamine derivatives or the commercially available *N,O*-bis(*tert*-butyloxycarbonyl)hydroxylamine gave high yields of the adducts **5** under these conditions (Scheme I). These alkylated products require *deprotection* to give the hydroxylamine **6** which can then be treated with an isocyante to provide the requisite *N*-hydroxyureas. Both of the above methods typically require acidic conditions or hydrogenolysis and the intermediacy of a hydroxylamine. We required a method utilizing a suitably protected hydroxylamine that could be alkylated by the Mitsunobu reaction and could also be deprotected under nonacidic conditions without hydrogenolysis.

After examining derivatives of hydroxylamine and several commercially available chloroformates we reasoned that *N*-(phenoxycarbonyl)hydroxylamines of the general formula **1** should, on treatment with an amine, directly give the corresponding *N*-hydroxyurea **2** (eq 1). This was



(1)

1 **2**

based on the well-known conversion of phenylcarbonates to *O*-carbamoyl derivatives,[7] the preparation of *N,N'*-disubstituted ureas by both the aminolysis of phenylcarbamates[8,9] and the consecutive addition of amines to bis(4-nitrophenyl)carbonate,[10] as well as the reported conversion of diphenyl cyanocarboimidates to *N*-cyano-*N,N'*-disubstituted guanidines by stepwise addition of amines.[11] Adaptation of a literature procedure for preparation of *N,O*-bis(benzyloxycarbonyl)hydroxylamine,[12] but substituting phenyl chloroformate, gave crystalline *N,O*-bis(phenoxycarbonyl)hydroxylamine (**1a**) (Scheme II). This stable crystalline material reacted smoothly with a variety of alcohols in the Mitsunobu reaction (triphenylphoshine/diisopropyl azodicarboxylate[13]/THF) (Scheme III). After chromatography (silica gel) these adducts **8** were treated with ammonia in various solvents. Under these conditions, the carbonate is rapidly cleaved to give the *N*-hydroxyphenylurethane **10** which can be isolated.[14] Prolonged exposure to ammonia converts the intermediate *N*-hydroxyphenylurethanes **10** to the desired *N*-hydroxyureas **11**.

Good yields were obtained in the alkylation of the hydroxylamine derivative **1a** with several alcohols (Table I).

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(4) (a) Summers, J. B.; Gunn, B. P.; Martin, J. G.; Martin M. B.; Mazdiyasni, H.; Stewart, A. O.; Young, P. R.; Bouska, J. B.; Goetze, A. M.; Dyer, R. D.; Brooks, D. W.; Carter, G. W. *J. Med. Chem.* **1988**, *31*, 1960. (b) Kawase, M.; Kikugawa, Y. *J. Chem. Soc., Perkin Trans. 1* **1979**, 643.
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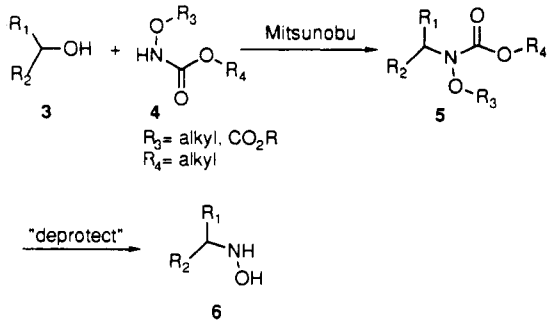
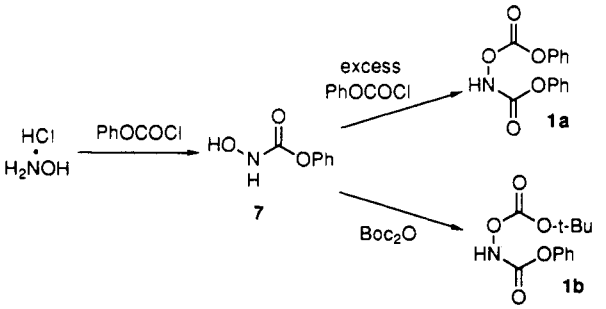
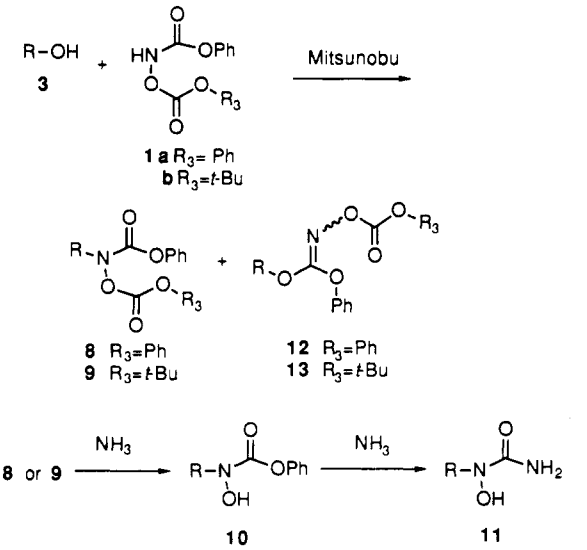
Scheme I



Scheme II



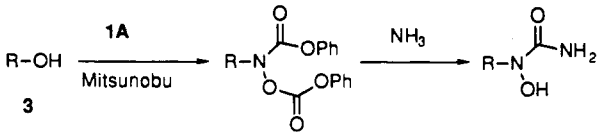
Scheme III

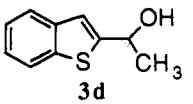
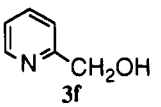


Miller reported that competitive O-alkylation is usually suppressed by *N*-(alkoxycarbonyl)hydroxylamine derivatives,[5a] and we have found that the *N*-(phenoxycarbonyl)hydroxylamine **1a** also gives primarily N-alkylated **8** (Scheme III). However, due to hindered rotation of the *N*,*O*-bis(phenoxycarbonyl)-alkylated hydroxylamines, signals in the proton NMR appear broad, making small amounts of O-alkylated **12** material difficult to detect. Entry 4 was unique in that significant amounts of O-alkylated material were observed. Reaction of alcohol **3d** with **1a** followed by chromatography gave an 85% yield of alkylated material which consisted of a 3:1 ratio of N-alkylated **8d** to O-alkylated **12d** products.[15] Chromatographic separation was difficult, and the phenoxyhydroximates **12d** were not stable once isolated. A 48% yield of the desired purified N-alkylated product was achieved. Participation by sulfur might explain the different reactivity of this alcohol. The key feature of reagent **1a** is the *N*-(hydroxyphenyl)carbamate, which acts as a masked *N*-hydroxyurea. It does not require special deprotection and reacylation. The protecting group on oxygen can be any acyl or alkoxycarbonyl group that is cleaved in the subsequent ammonia treatment. A variety of analogous reagents can be envisioned. For example, O-acylation of *N*-(phenoxycarbonyl)hydroxylamine[16] (**7**) with di-*tert*-butyl dicarbonate provided the *N*-(phenoxycarbonyl)-*O*-(*tert*-butoxycarbonyl)hydroxylamine (**1b**) (Scheme II). Reaction of **1b** with alcohol **3d** gave an 82% yield of alkylated material. In this case a 7:1 ratio of N-alkylated **9d** to O-alkylated **13d** material was obtained. The *tert*-butyl O-alkylated hydroximate derivatives **13d** were more stable than the phenoxy analogs **12d** but still decomposed on standing at room temperature after isolation. Treatment of the N-alkylated adduct **9d** with ammonia gave the desired *N*-hydroxyurea **11d** in 75% yield.

The rate of conversion **8a–f** to ureas **11a–f** by ammonia varied depending on the structure of **8**. The cleavage of the carbonate in all solvents, even aqueous ammonium hydroxide, occurred within minutes at room temperature. The conversion of the *N*-(hydroxyphenyl)carbamate to *N*-hydroxyurea was much slower and often required use of anhydrous ammonia in alcoholic solvent at room temperature in order to go to completion within 24 h. A large excess of ammonia in concentrations varying from 3% to 50% in methanol or 2-methyl-2-propanol was used at room temperature, in sealed vessels where necessary, to obtain

Table I. Reaction of *N*,*O*-Bis(phenoxycarbonyl)hydroxylamine with Alcohols and Conversion to *N*-Hydroxyureas



entry	alcohol 3	carbamate 8[a] (%)	*N*-hydroxyurea 11[a] (%)
1	$PhCH_2OH$ **3a**	**8a** (92)	**11a** (71)
2	PhCHOHCH$_3$ **3b**	**8b** (79)	**11b** (61)
3	$PhCH_2CH_2OH$ **3c**	**8c** (95)	**11c** (73)
4	 **3d**	**8d** (48)[b]	**11d** (56)
5	*t*-$BuCH_2CH_2OH$ **3e**	**8e** (92)	**11e** (68)
6	 **3f**	**8f** (93)	**11f** (54)

[a] Yield of isolated purified material. [b] Combined yield of *N*- and *O*-alkylated material was 85%.

(15) Structures **12d** and **13d** were tentatively assigned based on ^{1}H NMR; the chemical shift for the methine adjacent to the benzo[*b*]-thiophene is further downfield for the *O*-alklated products (**12d**, **13d**) than the N-alkylated products (**8a**, **9a**). For a more detailed discussion of N- vs O-alkylation of hydroxamates see reference 5.

(16) (a) Oesper, R. E.; Broker, W. *J. Am. Chem. Soc.* **1925**, *47*, 2606. (b) Steinberg, G. M.; Bolger, J. *J. Org. Chem.* **1956**, *21*, 660.

better yields. In a typical procedure, the Mitsunobu product 8 was dissolved in 2-methyl-2-propanol, this was cooled, liquid ammonia was condensed into the reaction vessel, and it was sealed.[17] After being stirred at room temperature, the reaction was recooled and opened and the ammonia allowed to evaporate. Chromatography of the residue to remove phenol and urea gave pure *N*-hydroxyurea.

N,O-Bis(phenoxycarbonyl)hydroxylamine can be readily prepared on large scale. This stable crystalline solid can be alkylated with alcohols to give adducts that can be converted directly to *N*-hydroxyureas by treatment with ammonia. This sequence does not require deprotection and reacylation, avoids in situ generation of the corresponding hydroxylamine, and is compatible with acid-sensitive functionality.

Experimental Section

Melting points were determined in open capillaries and are uncorrected. ^{1}H NMR spectra were measured at 300 MHz in DMSO-d_6 unless specified otherwise. Analytical TLC analysis was performed on Merck F254 silica gel. Silica gel (Merck, 230–400 mesh ASTM) was used for flash column chromatography. Products were visualized by UV light. THF was distilled from benzophenone/sodium. Diisopropyl azodicarboxylate and triphenylphosphine were obtained from Aldrich Chemical Co. and used without further purification.

***N,O*-Bis(phenoxycarbonyl)hydroxylamine (1a).** To a 0 °C stirred $NaHCO_3$ (143 g, 1.70 mol) solution (1 L, H_2O) in a 4-L Erlenmeyer flask was added H_2NOH·HCl (58.76 g, 0.85 mol). After foaming had subsided the reaction mixture was stirred for 0.5 h. Phenyl chloroformate (400 g, 2.55 mol) was poured directly into the vigorously stirred cold reaction mixture, rapidly followed by addition of more $NaHCO_3$ (214.5 g, 2.55 mol) solution (2.0 L, H_2O). The reaction mixture was stirred 0.5 h at 0 °C, the ice bath removed, and the reaction stirred 2 h at rt. The resulting suspension was filtered, and the white solid was washed with water. The resulting wet solid was suspended in hexanes (800 mL), refiltered, and collected; the suspension in hexanes and filtration was repeated two more times (to remove excess phenyl chloroformate). The resulting solid was dissolved in ether (800 mL), washed with brine, dried ($MgSO_4$), and concentrated to afford 200 g of the hydroxylamine derivative as a white solid. This material was dissolved in 450 mL of ether with heating, and hexanes were added (500 mL) with continued heating until some cloudiness developed. Seed crystals were added, and the product began to crystallize (precipitate). As solid formed, more hexanes were added (to a total volume of 1.8 L) and the flask allowed to stand overnight at rt. The mixture was then cooled to 5 °C and the white solid collected, washed with hexanes, and dried to afford 175 g (75%) of white crystalline **1a**: mp 80–82 °C; ^{1}H NMR δ 7.16–7.54 (m, 10 H), 12.30 (1 H, bs). Anal. Calcd for $C_{14}H_{11}NO_5$: C, 61.54; H, 4.06; N, 5.13. Found: C, 61.50; H, 4.14; N, 5.13.

***N*-(Phenoxycarbonyl)hydroxylamine (7).** To a 0 °C stirred $NaHCO_3$ (121 g, 1.43 mol) solution (700 mL H_2O) in a 2-L three-necked flask equipped with an overhead stirrer was added H_2NOH·HCl (55.1 g, 0.8 mol). After foaming had subsided the reaction mixture was stirred for 0.5 h. CH_2Cl_2 (500 mL) was added followed by the addition of phenyl chloroformate (100 g, 0.64 mol), and the reaction mixture was stirred for 0.5 h at 0 °C and 2 h at rt. The reaction mixture was diluted with H_2O, CH_2Cl_2, and enough ethyl acetate to make the organic layer homogeneous. The organic layer was separated, washed with brine, dried ($MgSO_4$), and concentrated to give 78 g (80%) of a white solid: mp 104–105 °C (EtOAc/hexanes); ^{1}H NMR δ 7.10 (m, 2 H), 7.22 (m, 1 H), 7.40 (m, 2 H), 9.08 (bs, 1 H), 10.31 (bs, 1 H). Anal. Calcd for $C_7H_7NO_3$: C, 54.9; H, 4.61; N, 9.15. Found: C, 55.17; H, 4.35; N, 9.22.

***N*-(Phenoxycarbonyl)-*O*-(*tert*-butyloxycarbonyl)hydroxylamine (1b).** A solution of *N*-(phenoxycarbonyl)-hydroxylamine (7) (12.22 g, 0.08 mol) and di-*tert*-butyl dicarbonate (17.44 g, 0.08 mol) in THF (75 mL) was vigorously stirred at rt, and a solution of 1 N NaOH (80 mL) was added dropwise. The reaction was stirred 2 h at rt. The reaction was diluted with 200 mL of ether and 100 mL of brine. The organic layer was washed with additional brine, dried ($MgSO_4$), and concentrated. The last traces of solvent were removed under high vacuum and the resulting residue solidified to give 18.74 g (93%) of a white solid. Recrystallization from ether/hexane gave a first crop of 13 g of large plates: mp 62–64 °C; ^{1}H NMR δ 1.48 (s, 9 H), 7.11–7.18 (m, 2 H), 7.24–7.31 (m, 1 H), 7.39–7.47 (m, 2 H), 11.83 (1 H, bs). Anal. Calcd for $C_{12}H_{15}NO_5$: C, 56.91; H, 5.97; N, 5.53. Found: C, 56.80; H, 5.94; N, 5.52.

***N,O*-Bis(phenoxycarbonyl)-*N*-benzylhydroxylamine (8a).** To a 0 °C stirred THF (40 mL) solution of benzyl alcohol (**3a**) (1.08 g, 10.0 mmol), **1a** (3.0 g, 11.0 mmol), and triphenylphosphine (3.14 g, 12.0 mmol) was slowly added dropwise a THF solution (10 mL) of diisopropyl azodicarboxylate (2.43 g, 12.0 mmol). After the addition the reaction mixture was concentrated. Purification by flash column chromatography (silica gel, eluting with 25% Et_2O/hexanes) gave 3.35 g (92%) of a white solid: mp 116–118 °C (Et_2O/hexanes); ^{1}H NMR ($CDCl_3$) δ 5.01 (s, 2 H), 7.08–7.51 (m, 15 H); IR ($CDCl_3$) 1805, 1735, 1490, 1190 cm^{-1}; MS (DCI-NH_3) *m/e* 381 (M + NH_4)$^+$, 232. Anal. Calcd for $C_{21}H_{17}NO_5$: C, 69.41; H, 4.72; N, 3.82. Found: C, 69.68; H, 4.56; N, 3.88.

***N*-Benzyl-*N*-hydroxyurea (11a).** In a screw-top vessel with a Teflon O-ring was placed the hydroxylamine **8a** (0.67 g, 1.85 mmol) and 2-methyl-2-propanol (3 mL). Liquid NH_3 (2 mL) was condensed using a cold finger (dry ice/acetone) into the cooled (−78 °C) reaction vessel. The vessel was sealed, the ice bath was removed, and the reaction mixture was allowed to stir at rt for 2 h. The reaction mixture was then placed in the refrigerator overnight. The vessel was then recooled to −78 °C and opened. The ice bath was removed, the reaction mixture was allowed to come to rt, and the NH_3 was allowed to evaporate. The reaction mixture was diluted with hexanes and evaporated to dryness. The residue was purified by flash column chromatography (silica gel, eluting with 5% MeOH/CH_2Cl_2) to give 0.24 g (78%) of a white solid: mp 142–144 °C (EtOAc/hexanes); ^{1}H NMR δ 4.52 (s, 2 H), 6.35 (bs, 2 H), 7.20–7.35 (m, 5 H), 9.35 (s, 1 H); IR (KBr) 3400, 3280, 1745, 1455, 1210 cm^{-1}; MS (DCI-NH_3) *m/e* 184 (M + NH_4)$^+$, 167 (M + H)$^+$, 149. Anal. Calcd for $C_8H_{10}N_2O_2$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.49; H, 6.16; N, 16.61.

***N,O*-Bis(phenoxycarbonyl)-*N*-(1-phenylethyl)hyroxylamine (8b).** Compound **5b** was prepared as described for **5a** from *sec*-phenethyl alcohol (**3b**) (1.0 g, 8.18 mmol), **1a** (2.45 g, 9.00 mmol), triphenylphosphine (2.46 g, 9.40 mmol), and diisopropyl azodicarboxylate (1.90 g, 9.40 mmol) in THF (60 mL). Purification by flash column chromatography (silica gel, eluting with 10% EtOAc/hexanes) gave 2.43 g (79%) of a thick oil: ^{1}H NMR δ 1.71 (bd, J = 6 Hz, 3 H), 5.65 (bq, J = 6 Hz, 1 H), 7.0–7.58 (m, 15 H); IR ($CDCl_3$) 1805, 1730, 1490, 1215, 1190 cm^{-1}; MS (DCI-NH_3) *m/e* 395 (M + NH_4)$^+$, 378 (M + H)$^+$, 291. Anal. Calcd for $C_{22}H_{19}NO_5$: C, 70.02; H, 5.07; N, 3.71. Found: C, 69.78; H, 5.07; N, 3.82.

***N*-(1-Phenylethyl)-*N*-hydroxyurea (11b).** Compound **11b** was prepared as described for **11a** from **8b** (1.38 g, 3.66 mmol), using MeOH (10 mL) (instead of 2-methyl-2-propanol) and NH_3 (10 mL). Purification by flash column (silica gel, eluting with 5% MeOH/CH_2Cl_2) gave 0.40 g (61%) of a white solid: mp 133–134 °C (EtOAc/hexanes); ^{1}H NMR δ 1.40 (d, J = 6 Hz, 3 H), 5.30 (q, J = 6 Hz, 1 H), 6.28 (bs, 2 H), 7.18–7.37 (m, 5 H), 9.05 (s, 1 H); IR (KBr) 3480, 3288, 3080, 2800, 1650, 1570, 1470 cm^{-1}; MS (DCI-NH_3) *m/e* 361 (2M + H)$^+$, 198 (M + NH_4)$^+$, 181 (M + 1)$^+$, 165. Anal. Calcd for $C_{19}H_{12}N_2O_2$: C, 59.99; H, 6.71; N, 15.55. Found: C, 59.97; H, 6.81; N, 15.41.

***N,O*-Bis(phenoxycarbonyl)-*N*-(2-phenylethyl)hydroxylamine (8c).** Compound **8c** was prepared as described for **8a** from phenethyl alcohol (**3c**) (1.0 g, 8.18 mmol), **1a** (2.45 g, 9.00 mmol), triphenylphosphine (2.46 g, 9.40 mmol), and diisopropyl azodicarboxylate (1.90 g, 9.40 mmol) in THF (60 mL). Purification by flash column chromatography (silica gel, eluting with 15% EtOAc/hexanes) gave 2.90 g (94%) of a thick oil: ^{1}H

(17) Caution: it was pointed out by one of the reviewers that the mixture of frozen 2-methyl-2-propanol and liquid NH_3 in a sealed reaction vessel could generate high pressure upon warming, and caution should be used on a large scale. Replacing 2-methyl-2-propanol with methanol did give similar yields on most substrates. Substituting aqueous ammonium hydroxide for anhydrous ammonia also gave similar yields in most cases but reaction times were much longer.

NMR δ 3.04 (t, J = 7 Hz, 2 H), 4.13 (t, J = 7 Hz, 2 H), 6.98 (m, 2 H), 7.22–7.55 (m, 13 H); IR ($CDCl_3$) 1805, 1740, 1490, 1230, 1185 cm^{-1}; MS (DCI-NH_3) m/e 395 $(M + NH_4)^+$, 378 $(M + H)^+$, 259, 232. Anal. Calcd for $C_{24}H_{19}NO_5$: C, 70.02; H, 5.07, N, 3.71. Found: C, 70.00; H, 4.87; N, 3.62.

N-(2-Phenylethyl)-N-hydroxyurea (11c). Compound **11c** was prepared as described for **11a** from **8c** (0.65 g, 1.72 mmol) in 2-methyl-2-propanol (5 mL) and NH_3 (5 mL). Purification by flash column (silica gel, eluting with 5% MeOH/CH_2Cl_2) gave 0.23 g (75%) of a white solid: mp 135–136 °C (EtOAc/hexanes); ^1H NMR δ 2.80 (t, J = 7 Hz, 2 H), 3.53 (t, J = 7 Hz, 2 H), 6.31 (bs, 2 H), 7.33–7.55 (m, 5 H), 9.35 (s, 1 H); IR (KBr) 3455, 3190, 1655, 1625, 1575, 1480 cm^{-1}; MS (DCI-NH_3) m/e 198 $(M + NH_4)^+$, 181 $(M + H)^+$, 165. Anal. Calcd for $C_9H_{12}N_2O_2$: C, 59.99; H, 6.71; N, 15.55. Found: C, 60.14; H, 6.70; N, 15.44.

N,O-Bis(phenoxycarbonyl)-N-(1-benzo[b]thien-2-ylethyl)hydroxylamine (8d). Compound **8d** was prepared as described for **8a** from 2-(hydroxyethyl)benzo[b]thiophene (**3d**) (0.5 g, 2.81 mmol), **1a** (0.843 g, 3.09 mmol), triphenylphosphine (0.85 g, 3.24 mmol), and diisopropyl azodicarboxylate (0.65 g, 3.21 mmol) in THF (20 mL). Purification by flash column chromatography (silica gel, eluting with 10% EtOAc/hexanes) gave 1.04 g (85%) of a thick oil that contained N-alkylated **8d** and a E/Z mixture of O-alkylated hydroximates **12d** (an approximately 3:1 **8d** to **12d** ratio by ^1H NMR). A second chromatography gave a small amount of pure **12d**, which was prone to decomposition after isolation. A combustion analysis could not be obtained, and the compound would even rapidly transform in DMSO-d_6. A ^1H NMR of the E/Z mixture could be obtained in $CDCl_3$: ^1H NMR ($CDCl_3$) δ 1.86 (d, J = 7 Hz, 1.5 H), 1.87 (d, J = 7 Hz, 1.5 H), 6.21 (m, 1 H), 6.65 (bs, 1 H); 6.97 (bm, 1 H), 7.13–7.57 (m, 13 H). The second chromatography also gave some mixed fractions and 0.58 g (48%) of **8d** as a thick oil: ^1H NMR ($CDCl_3$) δ 1.89 (d, J = 7 Hz, 3 H), 5.92 (q, J = 6 Hz, 1 H), 6.85–7.54 (m, 13 H), 7.73–7.88 (m, 2 H); MS (DCI-NH_3) m/e 451 $(M + NH_4)^+$, 296, 202, 161. Anal. Calcd for $C_{24}H_{19}NO_5S$: C, 66.5; H, 4.42; N, 3.23. Found: C, 66.78; H, 4.37; N, 2.95.

O-(tert-Butyloxycarbonyl)-N-(phenoxycarbonyl)-N-(1-benzo[b]thien-2-ylethyl)hydroxylamine (9d). Compound **9d** was prepared as described for **8a** from 2-(hydroxyethyl)benzo[b]thiophene (**3d**) (0.25 g, 1.4 mmol), **1b** (0.37 g, 1.47 mmol), triphenylphosphine (0.41 g, 1.55 mmol), and diisopropyl azodicarboxylate (0.31 g, 1.53 mmol) in THF (25 mL). Purification by flash column chromatography (silica gel, eluting with 10% EtOAc/hexanes) gave 0.48 g (82%) of a thick oil that contained N-alkylated **9d** and a E/Z mixture of O-alkylated hydroximates **13d** (>7:1, **9d** to **13d** ratio by ^1H NMR). A second chromatography gave 0.042 g of pure **13d**. This material was prone to decomposition after isolation, and a combustion analysis could not be obtained: ^1H NMR ($CDCl_3$) δ 1.35 (bm, 9 H), 1.82 (d, J = 7 Hz, 1.5 H), 1.83 (d, J = 7 Hz, 1.5 H), 6.15 (m, 1 H), 6.57 (bs, 1 H), 7.08–7.53 (m, 9 H); MS m/e 431 $(M + NH_4)^+$, 202, 161. The second chromatography also gave some mixed fractions and 0.29 g (50%) of **9d** as a thick oil: ^1H NMR ($CDCl_3$) δ 1.25–1.65 (bm, 9 H), 1.81 (bm, 3 H), 5.84 (q, J = 7 Hz, 1 H), 7.10–7.54 (m, 8 H), 7.70–7.84 (m, 2 H); MS (DCI-NH_3) m/e 431 $(M + NH_4)^+$, 331, 202, 161. Anal. Calcd for $C_{22}H_{23}NO_5S$: C, 63.91; H, 5.61; N, 3.39. Found: C, 64.01; H, 5.60; N, 3.20.

N-(1-Benzo[b]thien-2-ylethyl)-N-hyroxyurea (11d). Compound **11d** was prepared as described for **11a** from **8d** (0.43 g, 0.99 mmol) in 2-methyl-2-propanol (2 mL) and NH_3 (2 mL). Purification by flash column (silica gel, eluting with 5% MeOH/CH_2Cl_2) gave 0.131 g (56%) of a white solid: mp 158–160 °C (EtOAc/hexanes); ^1H NMR δ 1.51 (d, J = 7 Hz, 3 H), 5.57 (q, J = 7 Hz, 1 H), 6.44 (bs, 2 H), 7.24–7.37 (m, 3 H), 7.76 (m, 1 H), 7.89 (m, 1 H), 9.23 (s, 1 H); IR (KBr) 3460, 3180, 1655, 1520, 1470 cm^{-1}; MS (DCI-NH_3) m/e 254 $(M + NH_4)^+$, 237 $(M + H)^+$, 219, 161. Anal. Calcd for $C_{11}H_{12}N_2O_2S$: C, 55.92; H, 5.12; N, 11.86. Found: C, 55.93; H, 4.96; N, 11.74. Treatment of **9d** (0.21 g, 0.51 mmol) in 2-methyl-2-propanol (4 mL) and NH_3 (1 mL) for 24 h, followed by workup as described for **8d**, gave 0.09 g (75%) of **11d**.

N,O-Bis(phenoxycarbonyl)-N-(3,3-dimethyl-1-butyl)-hydroxylamine (8e). Compound **8e** was prepared as described for **8a** from 3,3-dimethyl-1-butanol (**3e**) (0.5 g, 4.89 mmol), **1a** (1.40 g, 5.13 mmol), triphenylphosphine (1.41 g, 5.38 mmol), and diisopropyl azodicarboxylate (1.08 g, 5.34 mmol) in THF (60 mL). Purification by flash column chromatography (silica gel, eluting with 10% EtOAc/hexanes) gave 1.65 g of a thick oil that after high vacuum solidified on standing to give 1.60 g (92%) of a white solid: mp 73–75 °C; ^1H NMR δ 0.97 (s, 9 H), 1.65 (m, 2 H), 3.86 (m, 2 H), 7.14–7.54 (m, 10 H); IR ($CDCl_3$) 1800, 1735, 1490, 1230, 1175 cm^{-1}; MS (DCI-NH_3) m/e 375 $(M + NH_4)^+$, 358 $(M + H)^+$, 239, 222. Anal. Calcd for $C_{20}H_{23}NO_5$: C, 67.21; H, 6.49; N, 3.92. Found: C, 67.13; H, 6.44; N, 3.97.

N-(3,3-Dimethyl-1-1-butyl)-N-hydroxyurea (11e). Compound **11e** was prepared as described for **11a** from **8e** (0.52 g, 1.46 mmol) in 2-methyl-2-propanol (2 mL) and NH_3 (2 mL). Purification by flash column (silica gel, eluting with 5% MeOH/CH_2Cl_2) gave 0.16 g (68%) of a white solid: mp 87–89 °C (EtOAc/hexanes); ^1H NMR δ 0.88 (s, 9 H), 1.41 (m, 2 H), 3.32 (m, 2 H), 6.17 (bs, 2 H), 9.11 (s, 1 H); IR (KBr) 3490, 3270, 3200, 2875, 1635, 1580, 1480 cm^{-1}; MS (DCI-NH_3) m/e 195 $(M + NH_4)^+$, 178 $(M + 1)^+$, 162. Anal. Calcd for $C_7H_{16}N_2O_2$: C, 52.48; H, 10.07; N, 17.48. Found: C, 52.41; H, 10.05; N, 17.51.

N,O-Bis(phenoxycarbonyl)-N-[(2-pyridyl)methyl]-hydroxylamine (8f). Compound **8f** was prepared as described for **8a** from 2-pyridylcarbinol (**3f**) (0.5 g, 4.58 mmol), **1a** (1.31 g, 4.80 mmol), triphenylphosphine (1.32 g, 5.03 mmol), and diisopropyl azodicarboxylate (1.02 g, 5.04 mmol) in THF (60 mL). Purification by flash column chromatography (silica gel, eluting with 4% acetone/hexanes) gave 1.69 g of a thick oil that after high vacuum solidified to give 1.50 g (90%) of a white solid: mp 103–107 °C dec; ^1H NMR δ 5.24 (s, 2 H), 7.12–7.55 (m, 12 H), 7.88 (m, 1 H), 8.65 (m, 1 H); IR ($CDCl_3$) 1810, 1750, 1590, 1490, 1190 cm^{-1}; MS (DCI-NH_3) m/e 365 $(M + H)^+$, 232, 135. Anal. Calcd for $C_{20}H_{16}N_2O_5$: C, 65.93; H, 4.43; N, 7.69. Found: C, 66.03; H, 4.65; N, 7.79.

N-[(2-Pyridyl)methyl]-N-hydroxyurea (11f). Compound **11f** (0.55 g, 1.51 mmol) was dissolved in 3% NH_3 in MeOH (15 mL) and allowed to stir overnight at rt. The reaction was then concentrated, and purification by flash column (silica gel, eluting with 7% MeOH/CH_2Cl_2) gave 0.135 g (54%) of a white solid: mp 158–159 °C dec (EtOAc); ^1H NMR δ 4.65 (s, 2 H), 6.46 (bs, 2 H), 7.22–7.36 (m, 2 H), 7.76 (m, 1 H), 8.49 (m, 1 H), 9.48 (s, 1 H); IR (KBr) 3405, 3330, 2670, 1695, 1645, 1415 cm^{-1}; MS (DCI-NH_3) m/e 168 $(M + H)^+$, 152. Anal. Calcd for $C_7H_9N_3O_2$: C, 50.30; H, 5.43; N, 25.14. Found: C, 50.40; 5.43; N, 24.86.

Electrohalogenation of Propargyl Acetates and Amides To Form the 1,1-Dibromo-2-oxo Functionality and a Facile Synthesis of Furaneol

Tsutomu Inokuchi, Sigeaki Matsumoto, Michihiro Tsuji, and Sigeru Torii*

Department of Applied Chemistry, Faculty of Engineering, Okayama University, Okayama 700, Japan

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Oxidation of acetylenic bonds with metallic peroxides offers a practical access to 1,2-diketones.[1] Alternative promising approaches to this functionality reported in the literature involve π-complexation of alkynes with mercury(II) ion followed by oxidation with Mo(VI) or W(VI) peroxo complexes.[2] However, the undesired carbon–carbon bond cleavage of the 1,2-dicarbonyl framework is a drawback to this method which occurs as a result of overoxidation.[3] In addition, hazardous mercury(II) acetate

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