Registry No. 1, 72962-43-7; 2, 80736-41-0; 3, 83-48-7; 5, 93488-33-6; 6, 81481-15-4; 7a, 130200-10-1; 7b, 130200-11-2; 8, 130200-12-3; 9 (isomer 1), 130200-13-4; 9 (isomer 2), 130200-14-5; 10, 130219-71-5; 11, 130200-15-6; 12, 130200-16-7; 13, 130200-17-8; 14, 93488-34-7; 15, 91708-76-8; TsSePh, 68819-94-3; 1-(trimethylsilyl)propyne, 6224-91-5.

A New Synthesis of Primary Aliphatic Amines by N,N-Didebenzylation. Synthesis of a Pirmenol (CI-845) Metabolite

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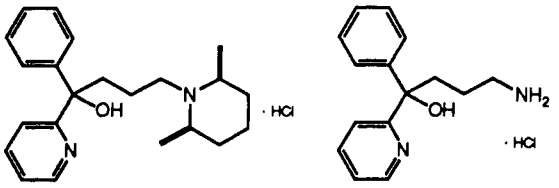
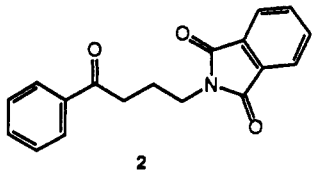
Pirmenol (CI-845) (**1a**) is an antiarrhythmic agent currently in clinical trials.[1] For the synthesis of one of the pirmenol metabolites **1b**, we were unsuccessful in using the Gabriel synthesis[2] to make the primary amine functionality. When we added 2-pyridyllithium to phthalimide **2**, no addition product was isolated. Alternative Gabriel reagents have been developed, but they too have potential drawbacks. They are either amide,[3a,b] phosporamidate,[3c] or sulfonamide[3d,e] derivatives that may interfere with organolithium reagents, or they are reagents[3e,f] requiring undesirable reaction conditions.

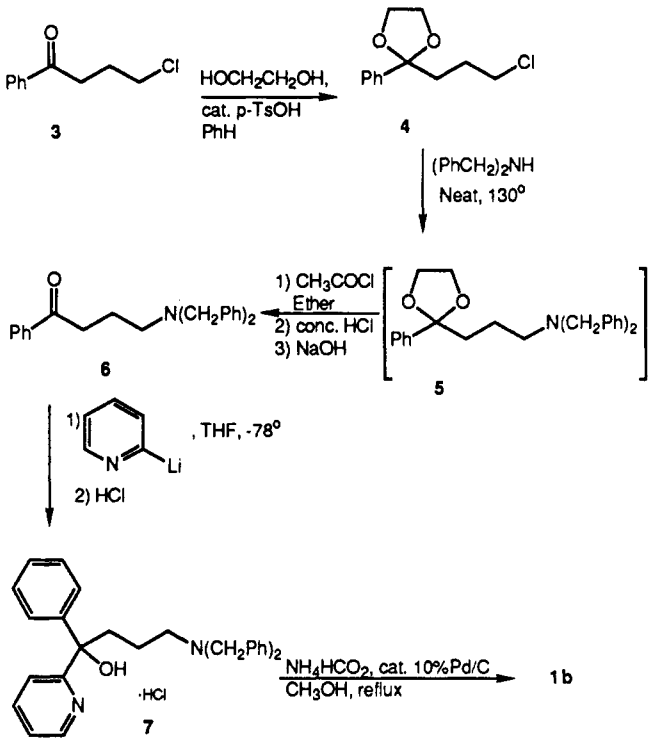




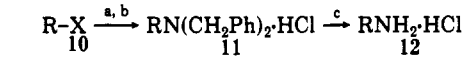
However, we found the dibenzylamino derivative[4] **6** was well suited to our needs. It was easily made using standard conditions, it did not interfere with the 2-pyridyllithium addition, and the dibenzyl groups were easily removed by catalytic transfer hydrogenation (CAT)[5] using ammonium formate in methanol and 10% Pd/C as catalyst.

The synthesis of **1b** is outlined in Scheme I. It was necessary to protect the ketone **3** after two alternate routes failed. The shortest route would have been the addition of 2-pyridyllithium directly to **3**, followed by the use of standard Gabriel chemistry to introduce the primary amino group. However the major product of the addition was **8** (52%) and unreacted starting material (20%). Another possible route was the addition of dibenzylamine to **3**, thereby giving **6** directly. However, experience with the synthesis of pirmenol indicated the major product from this reaction was likely to be cyclopropyl phenyl ketone **9**. Therefore the ketone was protected as the ketal **4**.

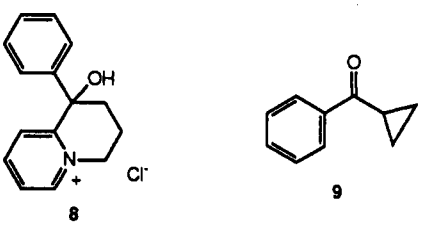
Scheme I. Preparation of Pirmenol Metabolite 1b



Scheme II.[a] General Preparation of Primary Amines[b]



[a] (a) $(PhCH_2)_2NH$, K_2CO_3, diglyme, 140 °C; (b) HCl(g), 2-propanol; (c) NH_4HCO_2, cat. 10% Pd/C, CH_3OH, 65 °C. [b] The reaction conditions used to prepare **1b** were different as described.



High yields were sacrificed for product purity in the ketal formation step (**3** → **4**; 48%) and the 2-pyridyllithium addition step (**6** → **7**; 63%). Nevertheless the overall yield for the five steps was 16%. The high yields obtained for the dibenzylamine addition (**4** → **5**; >85%) and the CAT hydrogenolysis (**7** → **1b**; 63%) encouraged us to investigate this method as an alternative to the Gabriel synthesis.

We set about to convert some simple alkyl halides into primary amines (Scheme II). Examples of these conversions are listed in Table I. The yields of the free bases of **11a-e** were generally in the 85-95% range except for the hindered bromide **10b** (48%). Also, the HCl salt **11b** was difficult to crystallize in good yield, which resulted in the low overall yield for the conversion. However the

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(4) Only two examples of the synthesis of primary amines by *N,N*-didebenzylation have been reported. See: (a) Pawlowski, M.; Grczyca, M. *Pol. J. Chem.* **1981**, *55*(4), 837-41. (Engl.). (b) La Manna, A.; et al. *Farmaco, Ed. Sci.* **1967**, *22*, 667.
(5) For a review, see: Johnstone, R.; Wilby, A. *Chem. Rev.* **1985**, *85*, 129-70.
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(7) Koziara, A.; Osowska-Pacewicka, K.; Zawadzski, S.; Zwierzak, A. *Synthesis* **1985**, 202.

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Table I. Yields of Dibenzylamine Intermediates and Primary Amines

entry	10	% yield of 11	% yield of 12	melting point, °C	
				12	lit.
1	**4**	85[a]	63[b]	133–7[c]	–
2	**a**, $CH_3(CH_2)_7Br$	72	100[d]	197–8	204–6[6]
3	**b**, $CH_3(CH_2)_3CH(CH_2CH_3)CH_2Br$	23	100[d]	glass	–
4	**c**, $PhCH_2CH_2CH_2Br$	78	100[d]	211–3	218–9[7]
5	**d**, $PhCH_2CH_2Br$	68	100[d]	218–21	219–21[7]
6	**e**, m-$CH_3PhOCH_2\overline{CHCH_2O}$	82	100[d]	136–8	–

[a] This is the overall yield for the dibenzylamine addition and the ketal hydrolysis steps (**4** → **6**). [b] This is the yield for the conversion of **7** to **1b**. The hydrogenolysis was done on the free base of **7**. [c] Melting point of the freeze-dried material. [d] The yields are before purification. Approximately 5 mol % of HCO_2NH_4 was present, which was easily removed by crystallization.

epoxide **10e** gave an excellent yield of the corresponding *N,N*-dibenzylamino alcohol **11e**, which upon CAT hydrogenolysis gave the amino alcohol **12e** in excellent yield. The CAT hydrogenolysis method for cleaving *N,N*-dibenzyl groups gave high yields (100%) of the corresponding primary amines before crystallization. Thus the overall yields for the two steps were generally in the 50–80% range. For comparison, the results obtained in the synthesis of the pirmenol metabolite **1b** have been included in Table I (entry 1).

In short, we have described a new and useful alternative to the Gabriel synthesis for making primary aliphatic amines. The method allows reactions to be carried out with the dibenzylamine intermediates that may not work with the corresponding phthalimides. It also makes use of mild deprotection conditions that avoid the high temperatures and strong acid or base, or the strongly nucleophilic hydrazine, required to remove the phthaloyl moiety.

Experimental Section

Melting points were taken with a Thomas Hoover capillary melting point apparatus and are uncorrected. IR spectra were recorded on either a Nicolet MX-1 FTIR or a Mattson Cygnus 100 FTIR. ^1H NMR spectra were recorded on either an IBM WP100SY NMR, a Varian XL200 NMR, or a Bruker AM250 NMR. Chemical shifts are relative to the solvent used: for $CDCl_3$, δ 7.25, and for DMSO-d_6, δ 2.50. MS spectra were recorded on either a Finnigan 4500 mass spectrometer or a VG Analytical 7070E/HF mass spectrometer. HPLC was run on an Alltech C-18 reverse phase column (25 cm × 5 μm) using a pH 2.6 triethylamine–phosphate buffer, methanol, and aceonitrile as mobile phase. GLC were run on a Shimadzu GC-Mini 3 gas chromatograph using a DB-17 Megabore column (15 m), helium carrier gas, and an FID detector.

2-(3-Chloropropyl)-2-phenyl-1,3-dioxolane (4). A stirred mixture of 4-chlorobutyrophenone (300 g, 1.64 mol), ethylene glycol (170 g, 2.7 mol), and *p*-toluenesulfonic acid monohydrate (6.2 g, 0.033 mol) was refluxed in benzene (3.5 L) for 4 days over a Dean Stark trap. The reaction was monitored by GLC, and the heating was stopped when the concentration of ketal reached 78%. The mixture was cooled to 25 °C, washed with 1 M NaOH (500 mL) and saturated NaCl (750 mL), and dried (Na_2SO_4). The mixture was evaporated to an oil, and the oil was crystallized from pentane (330 mL) in three crops to give 179 g (48%; 99.0% pure by GLC) of a white crystalline solid: IR (KBr) 2966, 2890, 1449, 1234, 1027, 911, 759, 706 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 1.68–2.18 (overlapping tt and m, 4 H, propyl C_1 and C_2), 3.48 (t, 2 H, propyl C_3), 3.68–4.15 (2 m, 4 H, C_4 and C_5), 7.35 (m, 5 H, aromatic); MS m/z 227 (M^+). Anal. Calcd for $C_{12}H_{15}ClO_2$: C, 63.58; H, 6.67; Cl, 15.64. Found: C, 63.53; H, 6.68; Cl, 15.94.

4-[Bis(phenylmethyl)amino]-1-phenyl-1-butanone (6). A stirred solution of **4** (179 g, 0.790 mol) in dibenzylamine (475 g, 2.4 mol) was heated under nitrogen at 137 °C for 40 h. The mixture was cooled to 34 °C, and ether (1.1 L) was added with vigorous stirring. The resulting suspension was filtered off and washed with ether (3 × 800 mL). The washings and filtrate were combined, washed with 1 M NaOH (400 mL), water (5 × 300 mL), and saturated NaCl (200 mL), and dried (K_2CO_3). The mixture was evaporated to an oil. The oil was distilled in vacuo (oil bath temperature 195 °C) to remove most of the dibenzylamine (bp 129–134 °C (5 mmHg)). The remaining pot residue (349 g) was dissolved in ether (1.5 L), and the solution was stirred vigorously while 1 equiv of acetyl chloride (15.9 mL) was added to convert the remaining dibenzylamine to dibenzylacetamide. The mixture was stirred for 2.5 h, and then concentrated HCl (40.3 mL) was added dropwise. The resulting precipitate was filtered off, washed with ether, and dried to give 302 g of a white solid. The byproduct dibenzylacetamide remained in ether. The solid was suspended in a two-phase mixture of ether (1.5 L) and 0.5 M HCl (200 mL), and the mixture was stirred at 34 °C for 27 h to hydrolyze the ketal. The suspension was filtered off and washed with ether (6 × 500 mL) to remove glycol. The filter cake was partitioned between ether (1.5 L) and 2 M NaOH (850 mL), and the ether layer was washed with saturated NaCl and dried (K_2CO_3). The ether solution was evaporated to give 229 g (85% for two steps) of a waxy solid containing 95.5% ketone (**6**) and 3.1% ketal (**5**) by GLC. This material was used in the next step without further purification or characterization. A 5-g lot worked up in a slightly different manner was characterized as follows: crystallized from hexane; mp 52–54 °C; IR (KBr) 2795, 1688, 1450, 750, 701 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.93 (overlapping tt, 2 H, C_3), 2.50 (t, 2 H, C_2), 2.93 (t, 2 H, C_4), 3.57 (s, 4 H, benzylic), 7.20–7.55 (m, 13 H, phenyl H on C_3', C_4', C_5' and phenyl H of benzyls), 7.90 (dd, 2 H, phenyl H on C_2' and C_6'); MS m/z 343 (M^+). Anal. Calcd for $C_{24}H_{25}NO$: C, 83.93; H, 7.34; N, 4.08. Found: C, 83.91; H, 7.49; N, 4.07.

(±)-α-[3-[Bis(phenylmethyl)amino]propyl]-2-phenyl-2-pyridinemethanol Hydrochloride (7). To a stirred, −78 °C solution of 2-pyridyllithium (formed in situ by a slow dropwise addition of a solution of 2-bromopyridine (155 g, 0.983 mol) in dry THF (1 L) to a stirred, −78 °C solution of *n*-butyllithium (388 mL of a 2.5 M solution in hexanes) in THF (500 mL) and stirring at −78 °C for 2.5 h) was added dropwise a solution of **6** (291 g, 0.847 mol) in THF (1.8 L) over 1.6 h under nitrogen. The mixture was stirred at −78 °C for 2 h and then allowed to warm to 25 °C overnight. The reaction was quenched with water (45 mL), and the mixture was filtered to remove some insolubles. The filtrate was evaporated to an oil. The oil was dissolved in ether (1 L), and the solution was washed with water (200 mL) and saturated NaCl and dried (K_2CO_3). The solution was evaporated to a solid. The solid was dissolved in hot acetonitrile (780 mL) and allowed to cool. To this solution was added concentrated HCl (65 mL), and the mixture was treated sequentially with CH_3CN (3 × 1 L) and CH_2Cl_2 (3 × 2 L), evaporating to dryness each time. The resulting glass was crystallized from CH_3CN (780 mL) to give 276.3 g (98.4% purity by HPLC) of a solid.

This material was recrystallized from CH_3CN (550 mL) to give 245 g (63%; 99.5% purity by HPLC) of a white crystalline solid. A 142-g lot (100% pure by HPLC assay) worked up in a slightly different manner was characterized as follows: mp 158.5–161.0 °C; IR (KBr) 3294, 2961, 1589, 1447, 750, 698 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz) δ 1.69 (m, 2 H, propyl C_2), 2.08–2.36 (m, 2 H, propyl C_1), 2.80 (m, 2 H, propyl C_3), 4.22 (s, 4 H, benzylic), 6.05 (s, br, 1 H, OH), 7.14–7.82 (m, 18 H, phenyl and pyridyl on C_3, C_4, C_5), 8.50 (d, 1 H, pyridyl C_6), 10.95 (s, br, 1 H, NH); MS m/z 423 (M + 1). Anal. Calcd for $C_{29}H_{30}N_2O$·HCl: C, 75.88; H, 6.81; N, 6.10; Cl, 7.72. Found: C, 75.72; H, 6.77; N, 5.94; Cl, 7.82.

(±)-α-(3-Aminopropyl)-α-phenyl-2-pyridinemethanol Hydrochloride (1b). The hydrochloride salt **7** (244.8 g, 0.5333 mol) was converted to its free base by partitioning between 1 M NaOH

(1 L) and ether (2 L). The ether layer was washed with saturated NaCl (300 mL) and dried (K_2CO_3). Methanol (1 L) was added and the ether evaporated. Additional methanol (1.5 L) was added to the solution followed by Pearlman's catalyst (38 g of 10% Pd/C) and a solution of ammonium formate (149.8 g, 2.38 mol) in water (480 mL). The mixture was refluxed for 1.5 h, cooled, and filtered through Celite. The filtrate was evaporated to an oil, and the oil was partitioned between 1 M NaOH (1 L) and CH_2Cl_2 (1 L). The CH_2Cl_2 layer was washed with saturated NaCl (500 mL), dried (K_2CO_3), and evaporated to an oil; yield 94.7 g (97.9% purity by HPLC). The oil was dissolved in boiling ethyl acetate (1.8 L), and a solution of HCl(g) in 2-propanol (52.3 mL, 0.383 mol of HCl) was added. The solution was cooled, and the white crystalline solid was filtered off; yield 93.2 g (63%). A portion (10.1 g) of this material was freeze-dried from water (40 mL) to give a white amorphous solid: yield 9.8 g (98.9% pure by HPLC); mp 133-137 °C; IR (KBr) 3400, 2950, 1592, 1448, 1001, 702 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz) δ 1.48 (m, 2 H, propyl C_2), 2.42 (m, 2 H, propyl C_1), 2.74 (t, 2 H, propyl C_3), 6.1 (s, 1 H, OH), 7.14-7.89 (m, 8 H, phenyl and pyridyl C_3, C_4, C_5), 8.00 (s, 3 H, NH_3), 8.5 (d, 1 H, pyridyl C_6); MS m/z 242 (M^+). Anal. Calcd for $C_{15}H_{18}N_2O \cdot 1.21HCl \cdot 0.11H_2O$: C, 62.47; H, 6.79; N, 9.71; Cl, 14.87. Found: C, 62.47; H, 6.96; N, 9.75; Cl, 14.89.

Alkylation of Dibenzylamine. A suspension of K_2CO_3 (20 mmol) in a solution of the alkyl halide or epoxide (10.0 mmol) and dibenzylamine (12.0 mmol) in diglyme (10 mL) was heated at 140 °C under nitrogen. After 24 h, the mixture was cooled, and the insolubles were filtered off and washed with ether. The filtrate and washings were evaporated in vacuo (bath temperature 40 °C) to an oil, and the oil was chromatographed on silica gel (100 g) using CH_2Cl_2 as eluent. Fractions containing product were combined and evaporated to give the free base as an oil. The free bases were not characterized.

Hydrochloride Salt Formation. A solution of HCl gas (1 equiv) in dry 2-propanol was added to a solution of the free base in dry 2-propanol or dry ether. The mixture was stored in a freezer (-5 °C) overnight. The resulting crystals were filtered off, washed, and dried. The salts could be recrystallized from 2-propanol. The following HCl salts were prepared in this manner.

***N,N*-Bis(phenylmethyl)octanamine hydrochloride (11a)**: mp 109.5-110.5 °C; IR (KBr) 2926, 1460, 754, 701 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.86 (t, 3 H, CH_3), 1.21 (s, 10 H, C_3 to C_7), 1.92 (m, 2 H, C_2), 2.83 (m, 2 H, C_1), 4.04-4.33 (2 dd, 4 H, benzylic), 7.46 (m, 6 H, phenyl C_3', C_4', C_5'), 7.69 (m, 4 H, phenyl C_2', C_6'), 12.7 (s, 1 H, NH); MS m/z 309 (M^+). Anal. Calcd for $C_{22}H_{31}N \cdot HCl$: C, 76.38; H, 9.32; N, 4.05; Cl, 10.25. Found: C, 76.12; H, 9.34; N, 3.85; Cl, 10.27.

2-Ethyl-*N,N*-bis(phenylmethyl)hexanamine hydrochloride (11b): mp 110-111 °C; IR (KBr) 2929, 1461, 742, 702 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.62 (t, 3 H, C_6), 0.82 (t, 3 H, ethyl C_2), 0.8-1.5 (m, 8 H, C_3, C_4, C_5, ethyl C_1), 1.81 (m, 1 H, C_2), 2.66 (m, 2 H, C_1), 4.06 and 4.60 (m, 2 H + 2 H, benzylic), 7.47 (m, 6 H, phenyl, C_3', C_4', C_5'), 7.70 (m, 4 H, phenyl, C_2', C_6'), 11.6 (s, 1 H, NH); MS m/z 309 (M^+). Anal. Calcd for $C_{22}H_{31}N \cdot HCl$: C, 76.38; H, 9.32; N, 4.05; Cl, 10.25. Found: C, 76.43; H, 9.76; N, 3.94; Cl, 10.30.

***N,N*-Bis(phenylmethyl)benzenepropanamine hydrochloride (11c)**: mp 184.0-186.5 °C; IR (KBr) 2930, 1604, 1455, 1219, 931, 757 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 2.26 (m, 2 H, C_β), 2.56 (t, 2 H), 2.85 (m, 2 H), 4.04 and 4.28 (m, 4 H, benzylic), 7.06 (m, 2 H, phenyl, C_2, C_6), 7.24 (m, 3 H, phenyl, C_3, C_4, C_5), 7.40 (m, 6 H, phenyl, C_3', C_4', C_5'), 7.58 (m, 4 H, phenyl, C_2', C_6') 12.60 (s, 1 H, NH); MS m/z 315 (M^+). Anal. Calcd for $C_{23}H_{25}N \cdot HCl$: C, 78.50; H, 7.45; N, 3.98; Cl, 10.07. Found: C, 78.50; H, 7.49; N, 3.94; Cl, 9.80.

***N,N*-Bis(phenylmethyl)benzeneethanamine hydrochloride (11d)**: mp 205.0-205.5 °C; IR (KBr) 2953, 1458, 750, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.03-3.15 (m, 2 H, C_β), 3.20-3.39 (m, 2 H, C_α), 4.14-4.50 (m, 4 H, benzylic), 7.02-7.07 (m, 2 H, phenyl C_2, C_6), 7.13-7.40 (m, 3 H, phenyl, C_3, C_4, C_5), 7.40-7.60 (m, 6 H, phenyl, C_3', C_4', C_5'), 7.60-7.90 (m, 4 H, phenyl, C_2', C_6'), 13.0 (1 H, NH); MS m/z 302 (M + 1). Anal. Calcd for $C_{22}H_{23}N \cdot HCl$: C, 78.20; H, 7.16; N, 4.15; Cl, 10.49. Found: C, 78.60; H, 7.25; N, 4.26; Cl, 10.71.

1-[Bis(phenylmethyl)amino]-3-(3-methylphenoxy)-2-propanol hydrochloride (11e): mp 144.0-145.2 °C; IR (KBr) 2934, 1604, 1458, 1264, 1053, 753, 702 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.33 (s, 3 H, CH_3), 3-4.5 (baseline, 1 H, OH), 3.07-3.36 (m, 2 H, C_1), 3.72 (t, 1 H, C_2), 3.98-4.12 (m, 2 H, C_3), 4.30-4.62 (m, 4 H, benzylic), 6.62 (d, 1 H, phenyl, C_6'), 6.65 (s, 1 H, phenyl, C_2'), 6.80 (d, 1 H, phenyl, C_4'), 7.17 (t, 1 H, phenyl, C_5'), 7.45-7.59 (m, 6 H, phenyl, C_3'', C_4'', C_5''), 7.59-7.68 (m, 4 H, phenyl, C_2'', C_6''), 12.1 (s, 1 H, NH); MS m/z 362 (M + 1). Anal. Calcd for $C_{24}H_{27}NO_2 \cdot HCl$: C, 72.44; H, 7.09; N, 3.52; Cl, 8.91. Found: C, 72.38; H, 7.23; N, 3.42; Cl, 8.92.

CAT Hydrogenolysis Procedure. A suspension of Pearlman's catalyst (10% Pd/C, 100 mg) in a solution of 11 (2.0 mmol) and HCO_2NH_4 (8.0 mmol) in methanol (10 mL) was refluxed for 2 h. The mixture was allowed to cool, and the suspension was filtered through Celite. The filtrate was evaporated to a white solid which was free of organic impurities by 200-MHz ^1H NMR and MS analyses. The solids did contain approximately 5-10 mol % of HCO_2NH_4. Therefore samples for melting point and elemental analysis were first crystallized from CH_3CN. The following amines were prepared in this manner:

1-Octanamine hydrochloride (12a): mp 197-198 °C; IR (KBr) 2931, 1595, 1517, 1469, 1152, 724 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz) δ 0.87 (t, 3 H, CH_3), 1.26 (s, 10 H, C_3 to C_7), 1.54 (m, 2 H, C_2), 2.74 (t, 2 H, C_1), 7.8 (s, 3 H, NH_3); MS m/z 130 (M + 1). Anal. Calcd for $C_8H_{19}N \cdot HCl \cdot 0.04H_2O$: C, 57.75; H, 12.14; N, 8.42; Cl, 21.31. Found: C, 57.75; H, 12.12; N, 8.20; Cl, 20.99.

2-Ethyl-1-hexanamine hydrochloride (12b): mp (glass); IR (KBr) 3455, 2960, 1617, 1507, 1466, 1558, 668, 468 cm^{-1}; ^1H NMR (DMSO-d_6, 250 MHz) δ 0.83 (t, 3 H, C_6), 0.88 (t, 2 H, ethyl C_2), 1.25-1.45 (m, 9 H, C_3, C_4, C_5, ethyl C_1), 1.58 (m, 1 H, C_2), 2.66 (m, 2 H, C_1), 8.13 (s, 3 H, NH_3); MS m/z 129 (M^+). Anal. Calcd for $C_8H_{19}N \cdot HCl \cdot 0.18H_2O$: C, 56.87; H, 12.15; N, 8.29; Cl, 20.98. Found: C, 56.86; H, 12.17; N, 7.95; Cl, 20.47.

Benzenepropanamine hydrochloride (12c): mp 211-213 °C; IR (KBr) 3448, 2998, 1603, 1487, 1473, 749, 698 cm^{-1}; ^1H NMR (DMSO-d_6, 250 MHz) δ 1.86 (m, 2 H, C_β), 2.65 (t, 2 H), 2.76 (t, 2 H), 7.25 (m, 5 H, phenyl), 8.05 (s, 3 H, NH_3); MS m/z 135 (M^+). Anal. Calcd for $C_9H_{13}N \cdot HCl$: C, 62.97; H, 8.22; N, 8.16; Cl, 20.65. Found: C, 62.85; H, 8.22; N, 7.92; Cl, 20.17.

Benzeneethanamine hydrochloride (12d): mp 218-221 °C; IR (KBr) 3027, 2990, 1466, 1144, 940, 752, 744, 695 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz) δ 2.91 (m, 2 H, C_β), 3.02 (m, 2 H, C_α), 7.31 (m, 5 H, phenyl), 8.03 (s, 3 H, NH_3); MS m/z 122 (M + 1). Anal. Calcd for $C_8H_{11}N \cdot HCl \cdot 0.13H_2O$: C, 60.06; H, 7.72; N, 8.75; Cl, 22.16. Found: C, 60.31; H, 7.65; N, 8.74; Cl, 21.81.

1-Amino-3-(3-methylphenoxy)-2-propanol hydrochloride (12e): mp 136-138 °C; IR (KBr) 3403, 3010, 1595, 1494, 1267, 1058, 775 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz) δ 2.28 (s, 3 H, CH_3), 2.81 and 3.01 (2 dd, 2 H, C_3), 3.4 (s, 1 H, OH), 3.94 (d, 2 H, C_1), 4.05 (m, 1 H, C_2), 6.76 (m, 3 H, C_2', C_4', C_6'), 7.18 (t, 1 H, C_5'), 7.9 (s, 3 H, NH_3); MS m/z 182 (M + 1). Anal. Calcd for $C_{10}H_{15}NO_2 \cdot HCl$: C, 55.17; H, 7.41; N, 6.43; Cl, 16.29. Found: C, 55.19; H, 7.48; N, 6.20; Cl, 16.12.

Hypervalent Iodine in Synthesis. 4. Oxidative Coupling of Isopropylidene 5-Alkylmalonates Using (Diacetoxyiodo)benzene

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Oxidative coupling of electron-rich intermediates has emerged in recent years as an efficient method for the formation of carbon-carbon bonds. Various methods which have been used for a variety of enolate and carbanion dimerizations include electrochemical procedures and the oxidants silver oxide,[1] cupric chloride,[2] cupric

(1) Ito, Y.; Konoike, T.; Saegusa, T. *J. Am. Chem. Soc.* **1975**, *97*, 649.

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