obtained on a Beckman IR 33 spectrometer. Mass spectra were obtained on a Hitachi-Perkin-Elmer RMU-6E double focusing mass spectrometer and a Finnigan GC/MS 3200 with a 6100 data system. Ethoxyacetylene was commercially available and also was prepared by bromination of ethyl vinyl ether, dehydrohalogenation with *n*-butylamine, and KOH, respectively.[6]

(Trimethylsilyl)ketene was prepared by a procedure similar to that of Ruden.[4] (Trimethylsiloxy)ketene bis(trimethylsilyl) acetal and methoxyketene bis(trimethylsilyl) acetal were prepared according to a procedure described by Wissner.[7]

Typical Procedure for Reaction of (Trimethylsilyl)ketene with Ketene Bis(trimethylsilyl) Acetal. A 17.5-mmol (2-g) portion of (trimethylsilyl)ketene was added dropwise over 2 h to a stirred solution of 17.5 mmol of ketene bis(trimethylsilyl) acetals at room temperature under a nitrogen atmosphere. After the addition was complete the mixture was stirred until the ketene had been consumed as evidenced by the disappearance of the ketene band in the IR spectrum (24 h). The adduct was vacuum distilled and further purified by VPC.

Trimethyl 2,3-Bis(trimethylsiloxy)-4-(trimethylsilyl)-3-butenoate (3). From a 17.5-mmol (2-g) portion of (trimethylsilyl)ketene, 17.5 mmol (5.12 g) of (trimethylsiloxy)ketene bis(trimethylsilyl) acetal was isolated 6.7 g (94%) of **3**, which distilled at 75–80 °C (0.05 Torr): IR (neat) sharp bands at 2980, 1740 (C=O), 1620 cm^{-1} (C=C); NMR (CCl_4 with $CHCl_3$ as reference) δ 0.15 (s, 9 H), 0.20 (s, 9 H), 0.26 (s, 9 H), 0.30 (s, 9 H), 4.35 (s, 1 H), 4.50 (s, 1 H); mass spectrum, parent peak *m/e* at 406, 407 (M + 1), 408 (M + 2), 409 (M + 3), 391 (M - 15), 292, 221, 147, base peak at *m/e* 73.

Anal. Calcd for $C_{16}H_{38}O_4Si_4$: C, 47.29; H, 9.36. Found: C, 47.01; H, 9.74.

Trimethylsilyl 2-Methoxy-3-(trimethylsiloxy)-4-(trimethylsilyl)-3-butenoate (2). A 17.5-mmol (2.0-g) portion of (trimethylsilyl)ketene and 17.5 mmol (4.1 g) of methoxyketene bis(trimethylsilyl) acetal were reacted to give 5.8 g (95%) of **2**, bp 60–65 °C (0.05 Torr): IR (neat) sharp bands at 2980, 1740 (C=O), 1620 cm^{-1} (C=C); NMR (CCl_4 with $CHCl_3$ as reference) δ 0.15 (s, 9 H), 0.26 (s, 9 H), 0.34 (s, 9 H), 3.95 (s, 3 H), 4.52 (s, 1 H); mass spectrum parent peak *m/e* at 348, 349 (M + 1), 350 (M + 2), 351 (M + 3), 333 (M - 15), 317, 234, 231, 186, 147, base peak at *m/e* 73.

Anal. Calcd for $C_{14}H_{32}O_4Si_3$: C, 48.3; H, 9.20. Found: C, 47.97; H, 9.42.

Acknowledgment. We are grateful to the Robert A. Welch Foundation for support of this work.

(6) Lau, K. S. Y.; Scholser, M. *J. Org. Chem.* **1978**, *43*, 1595.
(7) Wissner A. *J. Org. Chem.* **1979**, *44*, 4617.

Synthesis of (*S*)-β,β,β-Trifluorolactic Acid and (*S*)-α-Methoxy-α-(trifluoromethyl)phenylacetic Acid from (*R*)-Methyl *p*-Tolyl Sulfoxide

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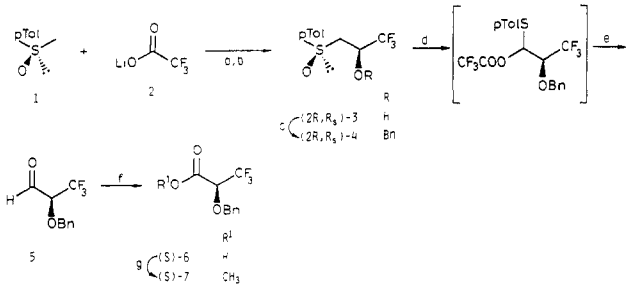
Received December 11, 1989

Selectively fluorinated organic compounds are finding increasing applications in several fields.[1] Fluorinated substances most commonly employed in analytical,[2] biological,[3] and medicinal chemistry[4] contain a single fluorine atom or a trifluoromethyl group. We have already reported the preparation of some chiral and nonracemic monofluorinated products.[5]

In this paper we describe the asymmetric synthesis of two interesting trifluoromethyl-substituted products: the (*S*)-methyl *O*-benzyl-β,β,β-trifluorolactate (**6**) (a compound that has been used in racemic form in medicinal and biological chemistry)[6] and the (*S*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (**10**) (a reagent commonly employed in analytical chemistry).[7]

Scheme I. Synthesis of (*S*)-Methyl *O*-Benzyl-β,β,β-trifluorolactate[a]



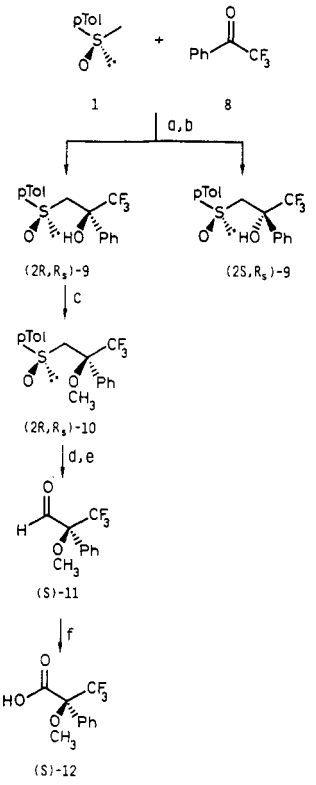
[a] Reagent and conditions: (a) LDA, THF, −78 °C; (b) $NaBH_4$, MeOH, NH_4OH, −40 °C; (c) NaH, BnBr DMF, 0 °C; (d) $(CF_3CO)_2O$, 2,4,6-trimethylpyridine, acetonitrile, 0 °C; (e) $HgCl_2$, H_2O, room temperature; (f) $NaClO_2$, KH_2PO_4, *tert*-butyl alcohol, 2-methyl-2-butene; (g) CH_2N_2, Et_2O, room temperature.

In our synthetic procedure, (2*R*)-1,1,1-trifluoro-3(*R*)-[(4-methylphenyl)sulfinyl]propan-2-ol (**3**), obtained through acylation of the lithium derivative of (*R*)-methyl 4-methylphenyl sulfoxide[8] (**1**) with lithium trifluoroacetate (**2**) and selective reduction of the so-formed trifluorosulfinylpropanone,[9] was *O*-benzylated in high yield by using proper reaction conditions (Scheme I). The so-formed (2*R*,R_S)-(benzyloxy)sulfinyl derivative **4** was treated with trifluoroacetic anhydride and 2,4,6-trimethylpyridine.[10] A clean Pummerer rearrangement occurred and gave an intermediate, (2*R*)-2-(benzyloxy)-1,1,1-trifluoro-3-[(trifluoroacetyl)oxy]-3-[(4-methylphenyl)thio]-propane, which was not isolated but directly hydrolyzed with mercury(II) chloride. (*S*)-*O*-Benzyl-β,β,β-trifluorolactic aldehyde (**5**) was thus produced and directly oxidized with sodium chlorite[11] to the correspondign (*S*)-β,β,β-trifluorolactic acid **6**, which afforded the ester **7** by treatment with diazomethane.

Similarly, the 1,1,1-trifluoro-2-phenyl-3(*R*)-[(4-methylphenyl)sulfinyl]propan-2-ol (**9**) was obtained as a 3:1 mixture of the 2*R*,R_S and 2*S*,R_S diastereoisomers (Scheme II) through hydroxyalkylation of the lithium derivative of (*R*)-methyl *p*-tolyl sulfoxide (**1**) with 1,1,1-trifluoroacetophenone (**8**). Single diastereoisomers were easily obtained

(1) Liebman, J. F., Greenberg, A., Dolbier, W. R., Jr., Eds. *Fluorine Containing Molecules*; VCH Publishers: Weinheim, 1988. Banks, R. E., Ed. *Preparation, Properties and Industrial Applications of Organofluorine Compounds*; Ellis Horwood: Chichester, U.K., 1982.
(2) Wenzel, T. J. *NMR Shift Reagents*; CRC Press: Boca Raton, FL, 1987. Emsley, J. W., Feeney, J., Sutcliffe, L. H., Eds. *Progress in Nuclear Magnetic Resonance Spectroscopy*, Vol. 15; Pergamon Press: Oxford, 1982.
(3) Walker, S. B., Ed. *Fluorine Compounds as Agrochemicals*; Fluorochem Limited: Old Glossop, U.K., 1989. Welch, J. T. *Tetrahedron* **1987**, *43*, 3123.
(4) Sandler, M., Smith, H. J., Eds. *Design of Enzyme Inhibitors as Drugs*; Oxford University Press: Oxford, 1989. Filler, R., Kobayashi, Y., Eds. *Biomedicinal Aspects of Fluorine Chemistry*; Kodansha Ltd.: Tokyo, and Elsevier Biomedical: Amsterdam, 1982.
(5) Bravo, P.; Piovosi, E.; Resnati, G. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1201.
(6) Haydock, D. B.; Mulholland, T. P. C.; Telford, B.; Thorp, J. M.; Wain, J. S. *Eur. J. Med. Chem.* **1984**, *19*, 205. Pogolotti, A., Jr.; Rupley, J. A. *Biochem. Biophys. Res. Commun.* **1973**, *55*, 1214.
(7) Hull, W. E.; Seeholzer, K.; Baumeister, M.; Ugi, I. *Tetrahedron* **1986**, *42*, 547. Ohta, H.; Miyamae, Y.; Kimura, Y. *Chem. Lett.* **1989**, 379. Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512. Sullivan, G. R.; Dale, J. A.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 2143.
(8) Solladiè, G.; Hutt, J.; Girardin, A. *Synthesis* **1987**, 173.
(9) Bravo, P.; Frigerio, M.; Resnati, G. *Synthesis* **1988**, 955.
(10) Sugihara, H.; Tanikaga, R.; Kaji, A. *Synthesis* **1978**, 881.
(11) Ko, K. J.; Frazee, W. J.; Eliel, E. L. *Tetrahedron* **1984**, *40*, 1333.

Scheme II. Synthesis of (*S*)-α-Methoxy-α-(trifluoromethyl)phenylacetic Acid[a]



[a] Reagents and conditions: (a) LDA, THF, −78 °C; (b) chromatographic separation; (c) NaH, CH_3I, DMF, 0 °C; (d) $(CF_3CO)_2O$, 2,4,6-trimethylpyridine, acetonitrile, 0 °C; (e) $CuCl_2$, H_2O, room temperature; (f) $NaClO_2$, KH_2PO_4, *tert*-butyl alcohol, 2-methyl-2-butene.

through flash chromatography. The hydroxyl group of $(2R,R_S)$-**9** was methylated and the sulfinyl residue of the resulting $2R,R_S$ sulfinyl trifluoro ether **10** was removed through a Pummerer rearrangement and successive hydrolyses of the intermediate masked formyl group with copper(II) chloride in basic medium. Oxydation of the resulting (*S*)-α-methoxy-α-(trifluoromethyl)phenylacetic aldehyde **11** gave (*S*)-α-methoxy-α-(trifluoromethyl)-phenylacetic acid (**12**) in optically pure form.

Application of the reaction sequence described above on alcohols $(2S,R_S)$-**3**[9] and $(2S,R_S)$-**9** will furnish (*S*)-**7** and (*S*)-**12**, the enantiomers of the products here described.

The two synthetic sequences reported above show how (*R*)-methyl 4-methylphenyl sulfoxide (**1**) can be used as a synthetic equivalent of a chiral carboxyl group.[12]

Experimental Section

^1H NMR spectra were recorded with a Bruker AC 250 or a Bruker WP 80 spectrometer; $CDCl_3$ was used as solvent and tetramethylsilane as internal standard; δ_H values are in ppm. The same instruments were used for ^{19}F NMR spectra; δ_F values are ppm upfield from $CFCl_3$; C_6F_6 was used as internal standard (δ_F = −162.9) and $CDCl_3$ as solvent. $[\alpha]_D$ values were obtained on a Jasco DIP-181 polarimeter. Melting points are uncorrected and were obtained on a capillary apparatus. TLC were run on silica gel 60 F_{254}; column chromatography was performed with silica gel 60 (60–200 μm, Merck). Solvents were purified as described in ref 5.

(2*R*)-1,1,1-Trifluoro-3(*R*)-[(4-methylphenyl)sulfinyl]-propan-2-ol (3) and $(2S,R_S)$-3. A solution of (*R*)-methyl 4-methylphenyl sulfoxide[8] (**1**) (2.31 g, 15.0 mmol) in dry tetrahydrofuran (20 mL) was added dropwise to a stirred solution of lithium diisopropylamide (16.5 mmol) in the same solvent (20 mL) at −75 °C and under argon. After 5 min a solution of lithium trifluoroacetate (2.70 g, 22.5 mmol) in tetrahydrofuran (30 mL) was added at the same temperature and the resulting mixture was stirred for 20 min. Methanol (30 mL) was added, the temperature was raised to −40 °C and a solution of lithium borohydride (360 mg, 16.5 mmol) in methanol/aqueous ammonia (32%) (9:1, 30 mL) was added dropwise. After stirring 10 min, diluted hydrochloric acid was added until pH 2 was reached, methanol was removed under reduced pressure, and the residue was extracted with ether (3 × 100 mL). The organic layers were combined and dried with anhydrous sodium sulfate. Evaporation under reduced pressure of the solvent and flash chromatography of the residue (*n*-hexane/ethyl acetate/acetic acid 35:20:0.5) afforded the trifluorosulfinylpropanols **3** having the $2R,R_S$ and $2S,R_S$ configuration in 88% yield and in a 7:3 ratio; physical and spectral properties were reported in the literature.[9]

(2*R*)-3-(Benzyloxy)-1,1,1-trifluoro-3(*R*)-[(4-methylphenyl)sulfinyl]propane (4). A solution of the trifluorosulfinyl alcohol $(2R,R_S)$-**3** (2.10 g, 8.32 mmol) in anhydrous DMF (5.0 mL) was added dropwise at 0 °C into a solution of oil-free sodium hydride (398 mg, 16.6 mmol) and benzyl bromide (5.92 mL, 49.8 mmol) in the same solvent (5.0 mL), under argon, and with magnetic stirring. After 3 min, the temperature was lowered to −40 °C, an excess of an aqueous solution of ammonium chloride was added, and the aqueous phase was extracted with ethyl acetate (3 × 200 mL). The collected organic phases were dried with anhydrous sodium sulfate and evaporated under reduced pressure. The oily residue was flash chromatograhed (*n*-hexane/ethyl acetate 3:2) to give crystalline $(2R,R_S)$-(benzyloxy)-trifluorosulphinylpropane **4** in 93% yield and in pure form: $[\alpha]^{20}_D$ +46.6° (*c* 1.00, $CHCl_3$); mp 53–54 °C (diisopropyl ether); ^1H NMR (250 MHz) δ 2.37 (s, 3 H, CH_3Ar), 3.21 (m, 2 H, CH_2S), 4.16 (m, 1 H, CHO), 4.38 and 4.70 (AB system, 2 H, CH_2Ph), 7.1–7.5 (m, 9 H, ArH). Anal. Calcd for $C_{17}H_{17}F_3O_2S$: C, 59.63; H, 5.00. Found: C, 59.84; H, 5.24.

(*S*)-Methyl *O*-Benzyl-β,β,β-trifluorolactate (7). A solution of trifluoroacetic anhydride (0.92 mL, 6.54 mmol) in acetonitrile (4 mL) was added dropwise into a stirred solution of the sulfinyl derivative $(2R,R_S)$-**4** (1.12 g, 3.27 mmol) and 2,4,6-trimethylpyridine (0.86 mL, 6.54 mmol) in the same solvent (20 mL) at 0 °C under argon. After 1 h at room temperature, a solution of mercury(II) chloride (1.22 g, 4.50 mmol) in water (29 mL) was added at 0 °C to the reaction mixture in order to hydrolyze the intermediate geminal trifluoroacetoxy sulfenyl intermediate. Stirring was maintained for 2 h, and the white precipitate was filtered and washed with ethyl acetate (2 × 20 mL). Acetonitrile was removed from the filtrate under reduced pressure, organic products were extracted with ethyl acetate (3 × 100 mL), and the collected organic layers were dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and a part of the resulting oil was flash chromatographed (*n*-hexane/ethyl ether 3:7) to give oily (*S*)-*O*-benzyl-3,3,3-trifluorolactaldehyde (**5**), which showed a marked proclivity for becoming hydrated:[13] ^1H NMR ($CDCl_3$) δ 4.12 (dq, 1 H, CHOBn, $^3J_{H,F}$ = 7.2 Hz, $^3J_{H,H}$ = 1.4 Hz), 9.58 (dq, 1 H, CH=O, $^4J_{H,F}$ = 2.3 Hz). The crude aldehyde **5** was dissolved into *tert*-butyl alcohol (35 mL) and 2-methyl-2-butene (30 mL) to prepare the trifluorolactate **7**. To this solution were added sodium chlorite (2.96 g, 32.7 mmol) and potassium dihydrogen phosphate (3.81 g, 28.0 mmol) dissolved in water (40 mL) dropwise at room temperature and stirring was maintained for 1.5 h. Organic solvents were removed under reduced pressure, the aqueous phase was extracted with ethyl acetate (3 × 200 mL), and the collected organic layers were dried with anhydrous sodium sulfate. The oily residue was flash chromatographed (toluene/ethyl acetate/acetic acid 40:20:1.5) to give 0.61 g (80% yield) of the (*S*)-*O*-benzyl-3,3,3-trifluorolactic acid (**6**). ^1H NMR (90 MHz): 4.34 (q, 1 H, $^3J_{H,F}$ = 6.6 Hz, CHO), 4.80, and 4.84 (AB system, 2 H, CH_2O). A solution of this compound in ethyl ether was treated with a solution of diazomethane in the same solvent at room temperature until the light yellow color did not fade. A drop

(12) Hase, T. A. *Umpoled Synthons*; John Wiley and Sons: New York, 1987.

(13) Lee, A. W. M.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Walker, F. J. *J. Am. Chem. Soc.* **1982**, *104*, 3515.

of acetic acid was added, the solvent was removed under reduced pressure, and the residue was flash chromatographed (*n*-hexane/ethyl ether 8:2) to give 0.62 g (96% yield) of pure (*S*)-methyl *O*-benzyl-3,3,3-trifluorolactate (**7**): $[\alpha]^{20}_D$ +65.1° (*c* 1.00, $CHCl_3$); ^1H NMR (250 MHz) δ 3.83 (s, 3 H, CH_3O), 4.32 (q, $^3J_{H,F}$ = 7 Hz, 1 H, CHO), 4.69 and 4.82 (AB system, 2 H, CH_2Ar), 7.37 (m, 5 H, ArH). [No splitting of any proton signal was observed in the presence of $Eu(hfc)_3$.]; ^{19}F NMR (75 MHz) δ −74.8 (d, *J* = 7.0 Hz). Anal. Calcd for $C_{11}H_{11}F_3O_3$: C, 53.23; H, 4.47. Found: C, 53.41; H, 4.68.

(2*R*)-1,1,1-Trifluoro-2-phenyl-3(*R*)-[(4-methylphenyl)-sulfinyl]propan-2-ol (9) and (2*S*,R_S)-9. A solution of (*R*)-methyl 4-methylphenyl sulfoxide (**1**) (5.78 g, 37.5 mmol) in THF (60 mL) was added dropwise at −78 °C and under argon into a stirred solution of lithium diisopropylamide (41.2 mmol) in the same solvent (45 mL). After 3 min, 2,2,2-trifluoroacetophenone (**8**) (5.8 mL, 41.3 mmol) was added at the same temperature, stirring was continued for 10 min, and then a saturated aqueous solution of ammonium chloride was added. The aqueous phase was separated and extracted with ethyl acetate (3 × 100 mL), and the combined organic layers were dried with sodium sulfate and evaporated under reduced pressure to give a 75:25 mixture of (2*R*,R_S)-**9** and (2*S*,R_S)-**9** in nearly quantitative yields. Single pure diastereoisomers were isolated through flash chromatography (*n*-hexane/ethyl acetate 3:1). **(2*R*,R_S)-9**: R_f (*n*-hexane/ethyl acetate 3:1) 0.35; $[\alpha]^{20}_D$ +125.7° (*c* 1.11, $CHCl_3$); mp 85–87 °C (chloroform); ^1H NMR (90 MHz) δ 2.48 (s, 3 H, CH_3Ar), 3.49 (s, 2 H, CH_2S), 7.2–7.8 (m, 9 H, ArH). Anal. Calcd for $C_{16}H_{15}F_3O_2S$: C, 58.52; H, 4.60. Found: C, 58.80; H, 4.74.

(2*S*,R_S)-9: R_f (*n*-hexane/ethyla cetate 3:1) 0.31; $[\alpha]^{20}_D$ +171.7° (*c* 0.64, $CHCl_3$); mp 76–78 °C (chloroform); ^1H NMR (90 MHz) δ 2.41 (s, 3 H, CH_3Ar), 3.13 and 3.40 (m, 1 H each, CH_2S), 7.2–7.7 (m, 9 H, ArH). Anal. Calcd for $C_{16}H_{15}F_3O_2S$: C,58.52; H, 4.60. Found: C, 58.80; H, 4.74.

(2*R*)-1,1,1-Trifluoro-2-methoxy-2-phenyl-3-[(4-methylphenyl)sulfinyl]propane (10). A procedure similar to the one described above for the preparation of (2*R*,R_S)-**4** was employed in order to methylate the trifluoro sulfinyl alcohol (2*R*,R_S)-**9** and the pure methyl ether (2*R*,R_S)-**10** was obtained in 91% yield: $[\alpha]^{20}_D$ +66.1°; mp 65–67 °C; ^1H NMR (250 MHz) δ 2.40 (s, 3 H, CH_Ar), 3.41 and 3.69 (AB system, 2 H, CH_2S), 3.57 (q, $^5J_{H,F}$ = 1.6 Hz, CH_3O), 7.2–7.6 (m, 9 H, ArH). Anal. Calcd: C, 59.63; H, 5.01. Found: C, 59.81; H, 5.22.

(*S*)-α-Methoxy-α-(trifluoromethyl)phenylacetic Acid (12). The procedure described above for the preparation of (*S*)-*O*-benzyltrifluorolactic acid (**6**) was followed with the difference that copper(II) chloride and potassium carbonate were used to hydrolyze the intermediate geminal trifluoroacetoxy sulfenyl derivative. Starting from (2*R*,R_S)-**10**, the crystalline (−)-(*S*)-**12** was obtained in 76% yield and with physical and spectral properties identical with those of a commercially available sample (Aldrich).[14]

(14) Jeanneret-Gris, G.; Pousaz. *Tetrahedron Lett.* **1990**, *31*, 75.

The Synthesis of 1,1′-Spiroalkane or Fused Annulated 1,2,3,4-Tetrahydroisoquinolines Using a Highly Reactive Formamidine for Metalation–Alkylation

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Received December 22, 1989

We have, on numerous occasions, reported on the use of formamidines in the metalation of the α-carbon of amines and their subsequent alkylation to chiral and achiral amino compounds[1] (Scheme I). In a recent report from this laboratory,[2] we also described a new formamidine, which we felt was considerably more efficient in

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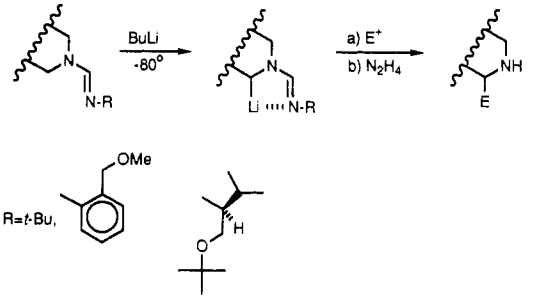
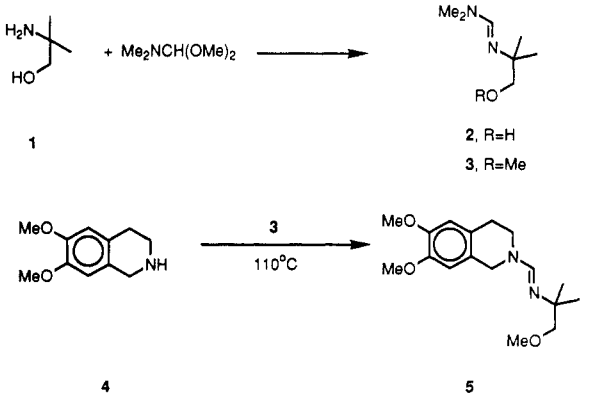
Scheme I



mediating metalation of the α-carbon (Scheme I, R = 2-(methoxymethyl)aniline). Further studies have now uncovered a considerably better formamidine **5** which is readily available and provides the quaternary substitution product in very good yields.

The formamidine in question is that derived from the readily available and inexpensive 2-amino-2-methylpropanol (**1**), which is transformed with dimethylformamide dimethyl acetal into the hydroxy formamidine **2**. Treatment with sodium hydride followed by methyl iodide gave the methyl ether–dimethylformamidine **3** in an overall yield of 72%. The latter may be easily exchanged for most secondary amines, and in the present case we have utilized 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**4**), which, when heated as a 2 M solution in toluene for 40–48 h, gave the isoquinoline formamidine **5** in 80–85% yield.



The present report will now describe how it was possible to prepare either spiroisoquinolines or fused annulated isoquinolines (**9** or **11**, respectively) by the appropriate choice of α,ω-dihaloalkanes. Treatment of the isoquinoline formamidine **5** with LDA in THF at −78 °C gave the red solution of the lithiated intermediate **6**, which, when treated with 4-chloro-1-iodobutane, gave the chloroalkyl derivative **7a** in 93% yield. Similarly, when 5-chloro-1-iodopentane was added to the lithio species, the analogous haloalkyl derivative **7b** was formed in 92% yield. An attempt was made to add a second equivalent of LDA to the reaction without isolation of **7**. It was our intention to generate another carbanion, followed by cyclization to the spiro derivatives **8**. However, a complex mixture of products was obtained, which quickly convinced us that this was not an appropriate route to follow. The haloalkyl derivatives were therefore isolated in the excellent yields mentioned above and were treated with various bases to ascertain the proper reaction conditions necessary for clean deprotonation. It was found that *n*-butyllithium followed by D_2O quench gave little (<5%) deuterium incorporation

(1) Meyers, A. I.; Miller, D. B.; White, F. W. *J. Am. Chem. Soc.* **1988**, *110*, 4778 and earlier references cited.
(2) Gonzalez, M. A.; Meyers, A. I. *Tetrahedron Lett.* **1989**, *30*, 43, 47.