rotoluenes that is akin to that observed during electrophilic chlorination.[33] Chlorine-atom transfer from either $SnCl_4$ or $SnCl_3$ (eq 14) to the benzylic radical would lead to stannous chloride.[34] Further studies are required to resolve the similar dichotomy that applies to the dimeric products **BB** and **DPM** in eqs 16 and 18, respectively.[18,26,29]

Experimental Section

Materials. Aromatic donors (commercial reagent-grade samples) were used as such or repurified as follows. Hexamethylbenzene (Eastman), durene (Aldrich), and pentamethylbenzene (Aldrich) were recrystallized from ethanol; mesitylene, *p*-xylene, and toluene were redistilled. Naphthalene (Allied), 1-methoxynaphthalene (Aldrich), 1,4-dimethylnaphthalene (Aldrich), anthracene (Aldrich, gold label), 9,10-dimethylanthracene (Aldrich), 9-bromoanthracene (Aldrich), and 2-*tert*-butylanthracene (Aldrich) were used as received. 9-Methylanthracene (Aldrich) was recrystallized from methanol. Stannic chloride (Matheson, Coleman and Bell reagent grade) was redistilled (bp 114 °C) according to standard procedures,[35] and the colorless liquid was stored in a Schlenk flask under an argon atmosphere prior to use. Cyclohexane (Aldrich) was distilled from sodium, and also stored in a Schlenk flask under an argon atmosphere. All subsequent manipulations with $SnCl_4$ were carried out with Schlenk techniques using an all-glass hypodermic syringe equipped with a Teflon (capillary) needle. Glassware was thoroughly dried in a 150 °C oven for at least 2 h and flushed with a stream of argon prior to use.

Determination of the Absorption Spectra and the Formation Constants of the Aromatic EDA Complexes with Stannic Chloride. In a typical experiment, a known amount of aromatic donor was added under an argon atmosphere to 3-mL aliquots of standard stock solutions (different concentrations) of $SnCl_4$ in cyclohexane. The solutions were then placed in a 1-cm quartz cuvette, and the absorbance was measured at the absorption maximum as well as at two other wavelengths close to the absorption maximum. From a plot of $[\text{arene}]/A_{CT}$ against $[SnCl_4]^{-1}$, the slope was estimated as $(K\epsilon_{CT})^{-1}$ and the intercept as ϵ_{CT}^{-1}. All plots were linear with a correlation coefficient of $r > 0.99$. Electronic spectra were recorded on a Hewlett-Packard 8450 diode-array spectrophotometer.

Charge-Transfer Photochemistry of Aromatic EDA Complexes with Stannic Chloride. The photochemical changes accompanying the charge-transfer excitation of the aromatic EDA complexes with stannic chloride were monitored by UV–vis spectroscopy. After a period of time, the reaction mixture was quenched with water, and the resulting extract was analyzed by quantitative gas chromatography using the internal standard method on a Hewlett-Packard 5890 chromatograph with a 12.5-m SE30 (cross-linked methylsilicone) capillary column. GC/MS measurements were carried out on a Hewlett-Packard 5890 chromatograph interfaced to a HP 5970 mass spectrometer (EI, 70 eV). Initially, a cyclohexane solution containing 0.06 M hexamethylbenzene and 0.65 M stannic chloride was irradiated with the focused beam from either a 500-W Osram (HBO-2L2) high-pressure Hg lamp or a 450-W Osram (XBO/OFR) mercury–xenon lamp. The light was passed through an IR water filter and a glass sharp cutoff filter (Corning CS-3 series) to remove light with $\lambda < 350$ nm. The temperature was maintained during the irradiation with the aid of a water bath. The monotonic decrease in the charge-transfer absorption band (Figure 1A) was followed for a 24-h period. The gas chromatography of the photolysate showed that it consisted of pentamethylbenzyl chloride (95% yield) by comparison with that of an authentic sample prepared from hexamethylbenzene and *N*-chlorosuccinimide. A small amount (5%) of decamethyldiphenylmethane,[19] but no decamethylbibenzyl, was observed. Equivalent results were obtained when the same solution was irradiated in a commercial chamber reactor [Rayonet RPR-100, New England Ultraviolet Co.] by utilizing the 3500-A lamps which emitted an approximately Gaussian distribution of light with a half-band width of ±150 Å at 3520 Å. Accordingly, all the aromatic donors in Table II were treated in the chamber reactor by the standard procedures at both the high and low ratios of $[\text{Arene}]/[SnCl_4]$ given in Table I for a 24-h period. The products of side-chain chlorination (designated as **BC**) were independently prepared by the free-radical chlorination of the aromatic donor in carbon tetrachloride with sulfuryl chloride and benzoyl peroxide at 77 °C.[36] The products of nuclear chlorination (designated as **CB**) were either compared with commercial samples, or prepared for the aromatic donor via the ferric chloride-catalyzed chlorination with chlorine in carbon tetrachloride.[37] The bibenzyl dimers (**BB**) were significant only in the CT photochemistry of toluene, *p*-xylene, and mesitylene, and they were prepared by the free-radical dimerization of the aromatic donor with di-*tert*-butyl peroxide.[38] The diphenylmethane dimers (**DPM**)[19] of hexamethylbenzene, pentamethylbenzene, and durene were also available from previous studies.[18,29d,39] In each case, the product comparisons were carried out by GC–MS analysis. The charge-transfer photochemistry of 0.20 M pentamethylbenzene and 0.45 M $SnCl_4$ in dichloromethane afforded pentamethylchlorobenzene (45%) and a mixture of nonamethyldiphenylmethanes (53%), but in the presence of 1.0 M TBA^+Cl^- the yields of these products dropped to 13 and 0%, respectively, and a mixture of tetramethylbenzyl chlorides (33%) and octamethylbibenzyls (49%) was formed.

Stannic bromide (mp 31 °C) formed similar aromatic EDA complexes in cyclohexane (e.g., $h\nu_{CT}$ = 373 and 392 nm for toluene and *p*-xylene). Prolonged irradiation under conditions similar to those described above yielded products of both side-chain and nuclear bromination, but the conversions were too low to warrant further studies.

Acknowledgment. We thank the Swiss National Science Foundation for a fellowship grant to K.B. and the R. A. Welch Foundation for financial support.

Registry No. Mesitylene·Cl_4Sn, 32870-87-4; naphthalene·Cl_4Sn, 35497-38-2; pentamethylbenzene·Cl_4Sn, 32870-85-2; hexamethylbenzene·Cl_4Sn, 32870-84-1; 1,4-dimethoxynaphthalene·Cl_4Sn, 139895-28-6; 1-methoxynaphthalene·Cl_4Sn, 139895-29-7; 9-bromoanthracene·Cl_4Sn, 139913-72-7; anthracene·Cl_4Sn, 35497-39-3; 2-*tert*-butylanthracene·Cl_4Sn, 139895-30-0; 9-methylanthracene·Cl_4Sn, 139895-31-1; 9,10-dimethylanthracene·Cl_4Sn, 139895-32-2; durene·Cl_4Sn, 32870-86-3; *p*-xylene·Cl_4Sn, 139895-33-3; toluene·Cl_4Sn, 36065-04-0.

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Synthesis of Chiral Functionalized *trans*-β-Isopropenyl-γ-(hydroxymethyl)-γ-butyrolactones[1]

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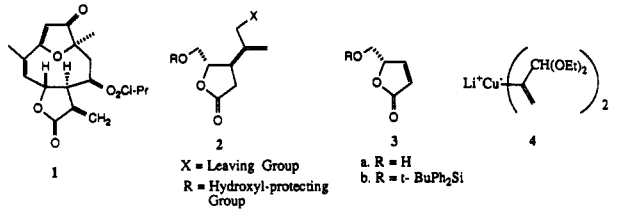
Received November 26, 1991

In connection with studies on the total synthesis of some members of the heliangolide family of sesquiterpenes,[2,3]

(1) Support of this research by a grant (5 R01 CA41688) from the National Institutes of Health is gratefully acknowledged.

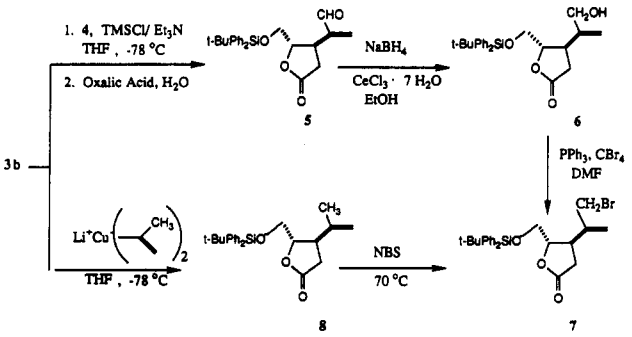
0022-3263/92/1957-2960$03.00/0

including ciliarin (1),[4] the synthesis of γ-lactones such as 2 containing functional groups in both the β and γ substituents became of interest. It was felt that such compounds might serve as synthon equivalents for elaboration of the lower portion of the target natural products. (*S*)-(−)-5-(Hydroxymethyl)-2(5*H*)-furanone (**3a**) is available commercially and has been widely used as a chiral intermediate for the synthesis of a variety of natural products[5] and other biologically important molecules.[6] Although problems associated with the conjugate addition of nucleophilic reagents to hydroxyl-protected derivatives of **3a** have been noted,[3b] examples of stereoselective anti conjugate additions of methyl,[5,7] alkyl,[8] and vinyl[3b] organocuprates to such butenolides are well-documented in the literature. Conjugate additions of organocuprates derived from 3,3-diethoxyisopropenyllithium to cyclic α,β-unsaturated ketones have been reported by several groups.[9] Therefore, with the objective of synthesizing lactones such as **2**, the reaction of lithium bis(3,3-diethoxyisopropenyl)cuprate (**4**) with the *tert*-butyldiphenylsilyl-protected butenolide **3b**[5,10] was explored and some transformations of the conjugate addition product were carried out.



The cuprate reagent **4** was prepared by addition of 2.0 equiv of 2-lithio-3,3-diethoxypropene to the CuBr–Me_2S[11] complex in Me_2S–THF at −78 °C. Reagent **4** was then treated with TMSCl[12] and Et_3N followed by the butenolide **3b** to give the crude acetal of the lactone **5** (Scheme I). Since attempted purification of this acetal by chromatography on silica gel led to its partial hydrolysis, the crude material was subjected directly to hydrolysis with 5% aqueous oxalic acid. Purification of the product by flash chromatography on silica gel gave the aldehydo lactone **5** in 65% overall yield for the two steps. In runs in which the addition of TMSCl/Et_3N was omitted, the yields of **5** were much lower because Michael addition of the enolate resulting from the conjugate addition to unreacted butenolide **3b** and elimination of the *tert*-butyldiphenylsiloxy group were important side reactions.[12] The trans stereochemistry of **5**, which was expected on the basis of previous studies,[3b,5,7,8] was confirmed by decoupling and NOE ^1H NMR experiments. In particular, the magnitude of the trans 4*H*,5*H* coupling constants for the 4-substituted lactone **5** and its derivatives were very similar to those reported by Hanessian and Murry[5] for the corresponding 4-methyl lactone.

Scheme I



The α,β-unsaturated aldehydo lactone **5** was readily transformed into the allylic alcohol **6** and the allylic bromide **7** (Scheme I). Thus, reduction of **5** with $NaBH_4/CeCl_3{\cdot}7H_2O$[13] in absolute ethanol gave alcohol **6** in 95% yield, and reaction of **6** with carbon CBr_4/PPh_3 in DMF[14] afforded the corresponding bromide **7** in 85% yield.

A second route for conversion of butenolide **3b** into allylic bromide **7** was also developed. Conjugate addition of lithium diisopropenylcuprate to butenolide **3b** was carried out according to the procedure developed by Rouessac and co-workers[15] for other γ-substituted α,β-butenolides to produce the lactone **8** in ca. 80% yield (Scheme I). Next, allylic bromination of **8** was attempted using NBS. When this reaction was carried out in the usual manner, by refluxing and/or irradiating a solution of the lactone in CCl_4 containing suspended NBS, the bromo lactone **7** was formed only in very low yield and a considerable amount of decomposition of the starting lactone occurred. However, in a run in which the CCl_4 was inadvertently allowed to evaporate during the reflux period, a somewhat higher yield of bromo lactone **7** was obtained. Thus, an experiment in which 1.0 equiv of lactone was coated on the surface of 5.0 equiv of NBS and the solid was warmed to 70 °C over 6.0 h was attempted. This procedure led to the isolation of the allylic bromide **7** in ca. 30% yield. In addition, approximately 40% of the unreacted lactone **8** was recovered and was available for recycling. The overall yields for the two approaches for the conversion of **3b** into **7** were similar.

Possible synthetic approaches to the heliangolide sesquiterpenes, e.g., ciliarin (1), which involve incorporation of functionalized lactones such as **5** or **7** into the ring

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system of the natural products are under investigation.

Experimental Section

General. Unless otherwise indicated, all reagents and solvents were purchased from Aldrich Chemical Co. or Fisher Scientific Co. and used without further purification. THF and diethyl ether were freshly distilled from sodium/benzophenone ketyl prior to use. Flash chromatography was carried out using E. Merck 60 (250–400 mesh) or Aldrich (support-grade catalyst 951) silica gel. ^{1}H NMR spectra were recorded at 360-MHz using $CDCl_3$ as the solvent and TMS as the internal standard. Infrared (IR) spectra were recorded neat or in $CHCl_3$ solution using 0.1-mm NaCl cells. All air- and moisture-sensitive reactions were conducted under an argon or prepurified nitrogen atmosphere in flame-dried glassware. During workup, all solutions were dried over anhydrous $MgSO_4$, and unless otherwise indicated, solvents were removed in vacuo using a rotary evaporator operated at water aspirator pressure. Ultrasonification was carried out with an 80-W ultrasonic water bath cleaner.

(5*S*,4*R*)-*trans*-5-[(*tert*-Butyldiphenylsiloxy)methyl]-4-(1-formylethenyl)dihydro-2(3*H*)-furanone (5). To a stirred solution of 6.27 g (30 mmol) of 1,1-diethoxy-2-bromo-2-propene in 40 mL of anhydrous ether was added 29.4 mL of *t*-BuLi (1.7 M in pentane) over 15 min at −78 °C under an atmosphere of argon. The reaction mixture was stirred for 2.0 h at −78 °C and added dropwise with stirring over 15 min using a steel cannula to a stirred suspension of 2.57 g (12.5 mmol) of freshly recrystallized CuBr·Me_2S complex[11] in 10 mL of Me_2S and 50 mL of anhydrous THF at −78 °C under argon. The resulting orange-red suspension was stirred at −78 °C for 30 min. Then 3.16 g (31.3 mmol) of Et_3N followed by 2.72 g (30 mmol) of freshly distilled TMSCl in 10 mL of THF was added, and stirring was continued for 15 min. To the mixture was added dropwise with stirring a solution of 3.56 g (10 mmol) of butenolide **3b**[5,10] in 25 mL of THF over 15 min at −78 °C, and stirring was continued at that temperature for 2 h. The temperature of the reaction mixture was allowed to rise to −30 °C, and 50 mL of an ice-cold solution of saturated aqueous NH_4Cl was added slowly with stirring. The mixture was stirred for 15 min and filtered through a pad of Celite, and the THF was removed from the filtrate under reduced pressure. Then, 200 mL of EtOAc was added, the aquoeus layer was separated, and the organic layer was washed with three 25-mL portions of saturated aqueous NH_4Cl until the blue color of the copper complex was removed. The combined aqueous washings were extracted with two 50-mL portions of EtOAc, and the combined organic layers were dried. Removal of the solvent in vacuo gave 5.29 g of the crude diethoxy acetal of the aldehyde **5**. The acetal was hydrolyzed by treatment of the entire batch of crude material with a solution of 5.0 g of oxalic acid in 100 mL of 50% aqueous THF at 25 °C for 4 h. The bulk of the THF was removed in vacuo, and the resulting oily aqueous phase was extracted with two 100-mL portions of EtOAc. The combined organic layers were washed with three 50-mL portions of brine and dried. The solvent was removed, and the residue was subjected to flash chromatography on silica gel. Gradient elution of the column with ether–hexane mixtures (10–80%) gave 0.8 g of the starting butenolide **3b**. Continued elution of the column with pure ether afforded 2.6 g (65%) of the aldehydo lactone **5** as a viscous colorless oil: $[\alpha]^{25}_D$ = +13° (*c* = 1.1, $CHCl_3$); IR (neat) 3080, 3070, 2960, 2950, 2870, 2780, 2705, 1780, 1700, 1635, 1595, 1200, 1140, 970, 885, 850, 800, 770, 735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.56 (s, 1 H), 7.64–7.67 (m, 4 H), 7.35–7.45 (m, 6 H), 6.32 (s, 1 H), 6.14 (s, 1 H), 4.35–4.38 (ddd, *J* = 4.5, 3.4, 2.8 Hz, 1 H), 3.88–3.91 (dd, *J* = 11.2, 3.4 Hz, 1 H), 3.76–3.80 (dd, *J* = 11.2, 2.8 Hz, 1 H), 3.58–3.66 (ddd, *J* = 9.5, 5.6, 4.5 Hz, 1 H), 2.97–3.05 (dd, *J* = 17.9, 9.5 Hz, 1 H), 2.49–2.55 (dd, *J* = 17.9, 5.6 Hz, 1 H), 1.06 (s, 9 H); high-resolution MS *m*/*z* calcd for $C_{20}H_{19}O_4Si$ (M^+ − *t*-Bu) 351.1053; obsd 351.1049.

(5*S*,4*R*)-*trans*-5-[(*tert*-Butyldiphenylsiloxy)methyl]-4-[1-(hydroxymethyl)ethenyl]dihydro-2(3*H*)-furanone (6). A suspension of $NaBH_4$ in 10 mL of absolute EtOH was added dropwise with stirring over 1.0 h to a solution of 2.04 g (5.00 mmol) of the aldehydo lactone **5** and 2.23 g (6.00 mmol) of $CeCl_3·7H_2O$ in 50 mL of EtOH at −20 °C. A saturated aqueous solution of NH_4Cl (50 mL) was then added dropwise with stirring over 15 min. The bulk of the EtOH was removed in vacuo, and the remaining cloudy suspension was diluted with 50 mL of water and extracted with three 100-mL portions of EtOAc. The organic extracts were washed with two 30-mL portions of brine and dried. Removal of the solvent gave 2.0 g (97%) of a viscous, yellow gum that showed one component on TLC (R_f = 0.36, 4:1 ether–hexane). Furanone **6**: IR (film) 3450, 3090, 3050, 2960, 2940, 2870, 1775, 1655, 1585, 1190, 1115, 940, 860, 825, 745, 710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.65–7.67 (m, 4 H), 7.38–7.47 (m, 6 H), 5.17 (s, 1 H), 4.99 (s, 1 H), 4.46–4.49 (ddd, *J* = 5.2, 3.4, 2.8 Hz, 1 H), 4.12 (s, 2 H), 3.89–3.93 (dd, *J* = 11.8, 3.4 Hz, 1 H), 3.72–3.76 (dd, *J* = 11.8, 2.8 Hz, 1 H), 3.20–3.26 (ddd, *J* = 9.0, 6.7, 5.2 Hz, 1 H), 2.86–2.93 (dd, *J* = 17.9, 9.0 Hz, 1 H), 2.51–2.58 (dd, *J* = 17.9, 6.7 Hz, 1 H), 1.06 (s, 9 H); high-resolution MS m/z calcd for $C_{20}H_{21}O_4Si$ (M^+ − *t*-Bu) 353.1209; obsd 353.1199.

(5*S*,4*R*)-*trans*-5-[(*tert*-Butyldiphenylsiloxy)methyl]-4-[1-(bromomethyl)ethenyl]dihydro-2(3*H*)-furanone (7). A. From Hydroxy Lactone 6. To a solution of 0.41 g (1.0 mmol) of the hydroxy lactone **6** in 5.0 mL of DMF was added 0.53 g (2.0 mmol) of PPh_3 and 0.66 g (2.0 mmol) of CBr_4, and the solution was stirred for 48 h at 25 °C. MeOH (1.0 mL) was then added, and stirring was continued for 1.0 h. The bulk of the DMF was removed under reduced pressure, finally at 0.1 mm, while the mixture was warmed to 45 °C. The residue was subjected to flash chromatography on silica gel (40% ether–hexane) to yield 0.4 g (85%) of the bromo lactone **7** as a colorless oil: $[\alpha]^{25}_D$ = +21° (*c* = 1.2, $CHCl_3$); IR ($CHCl_3$) 3170, 3090, 2980, 2950, 2880, 1795, 1650, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.63–7.73 (m, 4 H), 7.36–7.62 (m, 6 H), 5.35 (s, 1 H), 5.08 (s, 1 H), 4.45–4.52 (ddd, *J* = 5.0, 3.4, 2.8 Hz, 1 H), 3.94 (s, 2 H), 3.92–3.88 (dd, *J* = 11.6, 3.4 Hz, 1 H), 3.74–3.82 (dd, *J* = 11.6, 2.8 Hz, 1 H), 3.34–3.45 (m, *J* = 9.4, 6.4, 5.0 Hz, 1 H), 2.95–3.10 (dd, *J* = 17.9, 9.4 Hz, 1 H), 2.47–2.58 (dd, *J* = 17.9, 6.4 Hz), 1.09 (s, 9 H); high-resolution MS *m*/*z* calcd for $C_{20}H_{20}BrO_3Si$ (M − *t*-Bu) 415.0365; obsd 415.0390.

B. Allylic Bromination of the Lactone 8. A solution of 0.73 g (1.9 mmol) of the lactone **8** and 1.64 g (9.25 mmol) of NBS (freshly recrystallized from water and dried) in 50 mL of $CHCl_3$ was placed in a 250-mL round-bottom flask, and the solvent was removed in vacuo using a rotary evaporator. The flask, which contained a thin coating of the lactone deposited on solid NBS, was heated at 70 °C in an oil bath for 6.0 h. After the solution was cooled to room temperature, 100 mL of ether was added and, after thorough mixing, the solid was removed by suction filtration and the solid washed with two 25-mL portions of ether. The ethereal solution was dried, and the solvent was removed. Flash chromatography of the residue using 50% ether–hexane gave 0.25 g (29%) of the bromo lactone **7**. In addition, 0.29 g of the lactone **8** was recovered by further elution of the column.

(5*S*,4*R*)-*trans*-5-[(*tert*-Butyldiphenylsiloxy)methyl]-4-(1-methylethenyl)dihydro-2(3*H*)-furanone (8).[15] To a mixture of 0.16 g (23 mg-atom) of freshly cut Li wire in 20.0 mL of dry ether was subjected to ultrasonication using a water bath while a solution of 1.37 g (11.0 mmol) of freshly distilled 2-bromopropene in 8.00 mL of dry ether was added dropwise with stirring over 20 min at 0–10 °C. The mixture was then subjected to ultrasonication at 0–10 °C until the Li metal completely reacted. The resulting solution was then added with a steel canula with stirring at −78 °C to a solution of 1.08 g (6 mmol) of CuI (freshly recrystallized from a saturated ethereal solution of KI and dried at 100 °C (1.0 Torr)) in 20 mL of ether at −78 °C. The temperature of the mixture was allowed to rise to approximately −30 °C, and after stirring for ca. 25 min, it became greenish-red in color. The mixture was then cooled to −78 °C, and a solution of 1.00 g (2.8 mmol) of the butenolide **3b** in 10 mL of anhydrous ether was added dropwise with stirring over 30 min. Stirring was continued for 1.5 h at −78 °C, and then at −20 °C for 15 min, and then the mixture was quenched with 50 mL of a saturated aqueous NH_4Cl solution. The mixture was then transferred to a continuous extraction apparatus and extracted for 24 h with 100 mL of EtOAc. The resulting EtOAc solution was washed with 50 mL of brine and dried. The solvent was then removed to give an oil, which was subjected to flash chromatography on silica gel. Elution of the column with 20% ether–hexane gave 0.92 g (82%) of lactone **8**: $[\alpha]^{25}_D$ +28° (*c* = 1.0, $CHCl_3$); IR ($CHCl_3$) 3060, 2995, 2930, 2860, 1770, 1645, 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.64–7.67 (m, 4 H), 7.36–7.44 (m, 6 H), 4.83 (s, 1 H), 4.79 (s, 1 H), 4.34–4.37 (ddd, *J* = 5.2, 3.6, 2.8 Hz, 1 H), 3.89–3.92 (dd, *J* = 11.8, 3.6 Hz, 1 H),

3.69-3.73 (dd, J = 11.8, 2.8 Hz, 1 H), 3.12-3.23 (m, J = 9.5, 6.7, 5.2 Hz, 1 H), 2.77-2.85 (dd, J = 18.5, 9.5 Hz, 1 H), 2.43-2.50 (dd, J = 18.5, 6.7 Hz, 1 H), 1.72 (s, 3 H), 1.06 (s, 9 H); high-resolution MS m/z calcd for $C_{20}H_{21}O_3Si$ ($M^+ - t$-Bu) 337.1260; obsd 337.1270.

Acknowledgment. Discussions with David C. Baker and P. C. Raveendranath concerning conjugate additions of organocuprates to α,β-butenolides are gratefully acknowledged, as is the assistance of Ley Hathcock and Russell Timkovich with mass spectral analyses. Grants from the National Science Foundation and the National Institutes of Health for the purchase of high-resolution NMR instrumentation and from the National Institutes of Health for the purchase of a high-resolution mass spectrometer are gratefully acknowledged.

Supplementary Material Available: ^{1}H NMR spectra of compounds 5-8 (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Heteroatom-Facilitated Ortho-Directed Lithiations of 2-Arylimidazoles

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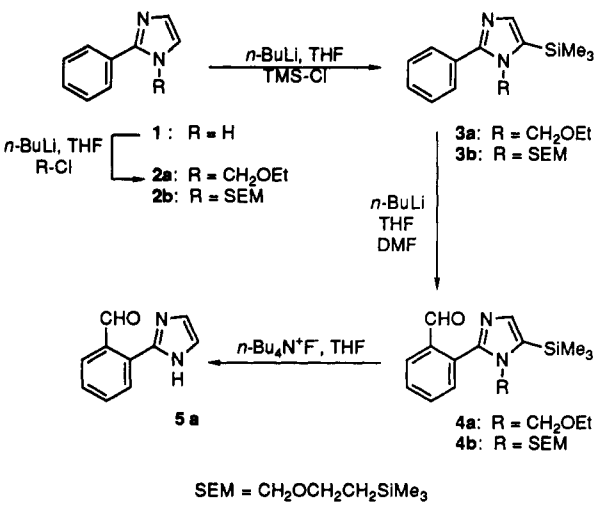
Received January 10, 1992

Over the last two decades, the utility of heteroatom-mediated ortho-metalation of aromatic rings has proven of high value in the synthesis of complex aromatic systems.[1] During the course of work in our laboratories on the preparation of novel fused-tricyclic imidazo[4,5-f]-quinoline immunomodulating agents,[2] we sought to synthesize related nonfused ring systems, such as aryl- and heteroarylimidazoles, which might possess similar activity. To prepare these bicyclic analogues, we decided to investigate the use of the imidazolyl substituent as a potential heteroatom-facilitated, ortho-directing group for the metalation of aromatic compounds. Although precedence existed for the utility of a variety of heterocyclic groups in this context, including for example, oxazolidine, imidazolidine, and benzimidazole,[3] the use of imidazole had not been previously reported.

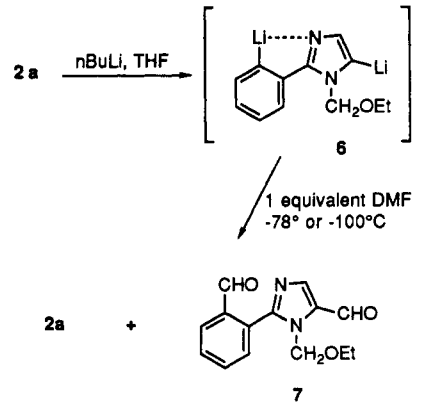
The direct metalation of commercial 2-phenylimidazole (1) using the conditions employed by Houlihan[3b] for the dilithiation of 2-phenylimidazolidine gave complex reaction mixtures. Therefore, compound 1 was reacted initially with n-butyllithium (n-BuLi) and ethoxymethyl chloride or (trimethylsilyl)ethoxymethyl (SEM) chloride in THF to give the N-protected compounds **2a** and **2b** in 51% and 60% yield, respectively (Scheme I).[4]

Scheme I. Metalation of 2-Arylimidazoles



SEM = $CH_2OCH_2CH_2SiMe_3$

Scheme II. Reaction of 2-Phenylimidazole Dianion



Treatment of **2a** or **2b** with 1 equiv of n-BuLi in THF (-78 °C) selectively formed the α-lithiated imidazole intermediate, rather than the ortho-lithiated derivative.[1b] Subsequent reaction of this lithiated intermediate with chlorotrimethylsilane (TMS-Cl) then gave the 5-(trimethylsilyl)-2-phenylimidazoles **3a** and **3b** (52% and 54%, respectively). Since Ganem[5] had previously demonstrated that the TMS moiety can be used as a removable blocking group for metalation sequences, the imidazoles **3a** and **3b** were further reacted.

Reaction of the silylated imidazoles **3a** or **3b** with n-BuLi (THF, -78 °C) then indeed formed the desired ortho-metalated species. Trapping of the lithiated intermediates with DMF yielded the 2-(o-formylphenyl)imidazoles **4a**[6] and **4b**[7] in 73% and 52% yield, respectively.

Desilylation of **4a** was conveniently carried out using tetrabutylammonium fluoride. However, removal of the ethoxymethyl group from the imidazole could only be accomplished in low yield after prolonged refluxing in aqueous 6 M HCl. This result with the ethoxymethyl protecting group was consistent with previous reported findings.[8] In contrast, deblocking of both the SEM and TMS protecting groups on **4b** could be simultaneously

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(6) Compound **4a** was satisfactorily characterized as the hydrochloride salt by NMR, IR, and MS analyses. A satisfactory elemental analysis was obtained for C, H, and N, while the Cl analysis was within 0.53% of theoretical, being outside the normally accepted ±0.4% limit (see the Experimental Section).

(7) Compound **4b** was characterized by NMR and then carried immediately on to the next step without further treatment.

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