Ph). Anal. Calcd for $C_{12}H_{14}O_5S$: C, 53.32; H, 5.22; S, 11.86. Found: C, 53.38; H, 5.29; S, 11.89.

β-Methyl-γ-oxo-γ-phenylbutanoic acid (1b): mp 56–57 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.25 (d, J = 6 Hz, 3 H, β-CH_3), 2.50 (dd, J = 16, 4 Hz, 1 H, α-H), 3.0 (dd, J = 16, 9 Hz, α′-H), 3.8–4.0 (m, 1 H, β-H), 7.48 (t, 2 H, Ph), 7.55 (t, 1 H, Ph), 7.96 (d, J = 6 Hz, 2 H, Ph). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.30. Found: C, 68.68; H, 6.36.

β-Methyl-γ-[4-(methylthio)phenyl]-γ-oxobutanoic acid (1c): mp 70–72 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.23 (d, J = 6 Hz, 3 H, β-CH_3), 2.48 (dd, J = 16, 4 Hz, 1 H, α-H), 2.52 (s, 3 H, SCH_3), 3.0 (dd, J = 16, 9 Hz, 1 H, α′-H), 3.78–3.95 (m, 1 H, β-H), 7.28 (d, J = 6 Hz, 2 H, Ph), 7.90 (d, J = 6 Hz, 2 H, Ph). Anal. Calcd for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92; S, 13.46. Found: C, 60.62; H, 5.91; S, 13.33.

γ-(4-Methoxyphenyl)-β-methyl-γ-oxobutanoic acid (1d): mp 65–67 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.22 (d, J = 6 Hz, 3 H, β-CH_3), 2.48 (dd, J = 16, 4 Hz, 1 H, α-H), 2.98 (dd, J = 16, 9 Hz, 1 H, α′-H), 3.78–3.95 (m, 1 H, β-H), 3.85 (s, 3 H, OCH_3), 6.95 (d, J = 6 Hz, 2 H, Ph), 7.98 (d, J = 6 Hz, 2 H, Ph). Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.93; H, 6.44.

General Preparation of the Lactones 3 and 4. γ-Aryl-β-methyl-γ-oxobutanoic acid (1 mmol) and zinc chloride (1 mmol as 1 M solution in THF) in anhydrous THF (5 mL) was cooled to −78 °C, and a solution of 1.5 M DIBAL-H in toluene (2.4 equiv) was added slowly and stirred at −78 °C for 3 h. The reaction was quenched in 1 N HCl (10 mL), and the reaction products were worked up by extraction with ethyl acetate (2 × 10 mL), dried over Na_2SO_4, and evaporated to give the crude γ-hydroxy acid which was treated as follows. The residue was dissolved in a solution of 0.2% of TFA in dichloromethane (2 mL) (i.e., 4 μL of TFA in 2 mL of CH_2Cl_2) and stirred at room temperature for 2 h. The mixture was evaporated to dryness and purified on column of flash silica gel (230–400 mesh), eluting with dichloromethane to afford the mixture of the desired cis (**3**) and trans (**4**) lactones where the product ratio was determined by ^{1}H NMR (250 MHz).[10] Because the mixtures of cis and trans lactones were not normally separable in pure form by flash chromatography (except in the case of **3b** and **4b**), cis lactones **3** were characterized as a mixture of **3** and **4** in a ratio of 99:1. Also the trans lactones **4** detected by NMR in small amount were identified by their characteristic peaks.[10]

***(RS,SR)*-γ-Hydroxy-β-methyl-γ-[4-(methylsulfonyl)-phenyl]butanoic acid lactone (3a)**: mp 145–146 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.70 (d, J = 6 Hz, 3 H, β-CH_3), 2.40 (dd, J = 16, 4 Hz, 1 H, α-H), 2.88–3.05 (m, 2 H, α′-H and β-H), 3.10 (s, 3 H, SO_2CH_3), 5.70 (d, J = 6 Hz, 1 H, γ-H), 7.50 (d, J = 6 Hz, 2 H, Ph), 8.0 (d, J = 6 Hz, 2 H, Ph). Anal. Calcd for $C_{12}H_{14}O_4S$: C, 56.67; H, 5.55; S, 12.61. Found: C, 56.54; H, 5.77; S, 12.68.

***(RS,SR)*-γ-Hydroxy-β-methyl-γ-phenylbutanoic acid lactone (3b)**:[11] ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.70 (d, J = 6 Hz, 3 H, β-CH_3), 2.35 (dd, J = 16, 4 Hz, 1 H, α-H), 2.78–2.95 (m, 2 H, α′-H and β-H), 5.60 (d, J = 6 Hz, 1 H, γ-H), 7.28 (d, J = 6 Hz, 2 H, Ph), 7.30–7.40 (m, 3 H, Ph). Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.87. Found: C, 74.96; H, 7.02.

***(RS,SR)*-γ-Hydroxy-β-methyl-γ-[4-(methylthio)phenyl]-butanoic acid lactone (3c)**: mp 52–53 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.70 (d, J = 6 Hz, 3 H, β-CH_3), 2.32 (dd, J = 16, 4 Hz, 1 H, α-H), 2.48 (s, 3 H, SCH_3) 2.75–2.95 (m, 2 H, α′-H and β-H), 5.55 (d, J = 6 Hz, 1 H, γ-H), 7.15 (d, J = 6 Hz, 2 H, Ph), 7.25 (d, J = 6 Hz, 2 H, Ph). Anal. Calcd for $C_{12}H_{14}O_2S$: C, 64.83; H, 6.35; S, 14.43. Found: C, 64.65; H, 6.25; S, 14.30.

***(RS,SR)*-γ-Hydroxy-γ-(4-methoxyphenyl)-β-methyl-butanoic acid lactone (3d)**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.70 (d, J = 6 Hz, 3 H, β-CH_3), 2.35 (dd, J = 16, 4 Hz, 1 H, α-H), 2.75–2.95 (m, 2 H, α′-H and β-H), 3.87 (s, 3 H, OCH_3), 5.58 (d, J = 6 Hz, 1 H, γ-H), 6.92 (d, J = 6 Hz, 2 H, Ph), 7.18 (d, J = 6 Hz, 2 H, Ph). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.89; H, 7.12.

4a, 4b,[11] 4c, 4d: ^{1}H NMR (250 MHz, $CDCl_3$) characteristic peaks δ 1.18 (d, J = 6 Hz, 3 H, β-CH_3), 4.95 (d, J = 6 Hz, 1 H, γ-H).

(10) Characteristic signals for cis γ-lactones (*RS,SR* isomers) **3** and trans γ-lactones (*RS,SS* isomers) **4** were determined by simple nuclear Overhauser effect (NOE) studies on both pure lactones isolated, after careful silica gel chromatography of reduction products obtained from treatment of methyl γ-[4-[(*N,N*-dimethylcarbamyl)thio]phenyl]-β-methyl-γ-oxobutanoate with $NaBH_4$.[1] Cis lactone (**3**; X = $SCON(CH_3)_2$) (mp 116–117 °C): ^{1}H NMR (400 MHz, acetone-d_6) δ 0.78 (d, J = 6 Hz, 3 H, β-CH_3), 5.85 (d, J = 6 Hz, 1 H, γ-H). Trans lactone (**4**; X = $SCON(CH_3)_2$) (mp 75–77 °C): ^{1}H NMR (400 MHz, acetone-d_6) δ 1.30 (d, J = 6 Hz, 3 H, β-CH_3), 5.18 (d, J = 8 Hz, 1 H, γ-H).

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Preparation of Unsaturated α-Chloro Acids and Intramolecular [2 + 2] Cycloadditions of the Chloroketenes Derived from Them

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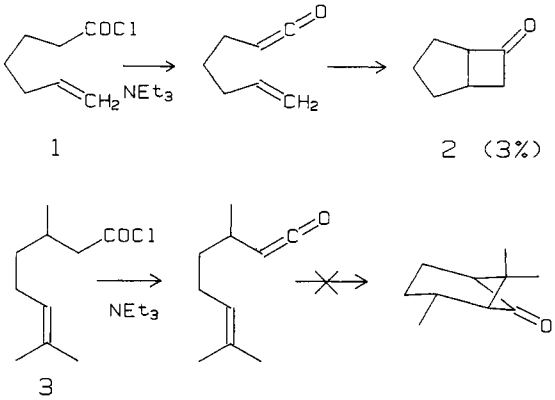
We[2] and others[3] have recently begun to develop the intramolecular [2 + 2] cycloaddition of ketenes to alkenes into a general synthetic method. Although many isolated examples are known,[4] the development of this reaction has been hindered by the limited reactivity of simple alkylketenes. For instance, the ketene prepared by treatment of acid chloride **1** with triethylamine has been reported to provide only a 3% yield of the cycloadduct **2**.[3a] The ketene derived from **3** does not give any cycloadduct.[2a] We chose to examine the intramolecular [2 + 2] cycloadditions of chloroketenes with alkenes,[5] since methylchloroketene is much more reactive in intermolecular [2 + 2] cycloadditions than methylketene.[6]



The preparation of unsaturated chloroketenes required a facile method for the preparation of unsaturated α-chloro acids from the readily available unsaturated acids. This posed two problems. First, the ester enolate or acid di-

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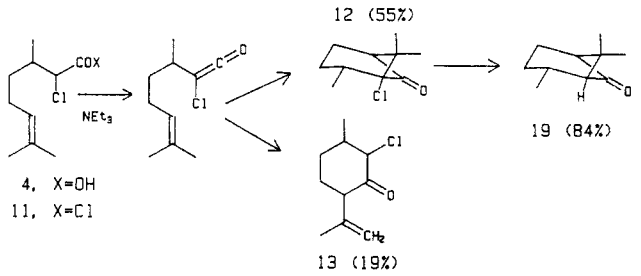
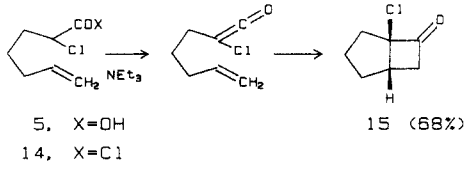
anion[7] had to be chlorinated with a reagent that would not chlorinate the double bond.[8] Second, an α-chloro ester could not be hydrolyzed to an α-chloro acid under basic conditions, since concomitant S_N2 displacement of the chloride would occur. van der Wolf and Pabon reported a multistep, low yield route to unsaturated α-bromo acids via the bromination of unsaturated *tert*-butyl ester enolates with diethyl dibromomalonate and hydrolysis of the *tert*-butyl ester with toluenesulfonic acid in toluene at reflux.[9] However, the stability of reactive double bonds under these conditions is problematic. Rathke and Lindert reported the preparation of α-bromo and α-iodo esters from treatment of the ester enolate with the corresponding halogen.[10] Arnold and Kulenovic reported the halogenation of saturated and unsaturated ester enolates with CCl_4 and CBr_4.[11]

We have found that the preparation of unsaturated α-chloro acids can easily be accomplished in a single step by chlorination of the acid dianion with carbon tetrachloride. The acid was added to 2 equiv of lithium diisopropylamide in 9:1 THF–HMPA at −20 °C, stirred for 2 h, cooled to −78 °C and treated with excess CCl_4. The solution was stirred for 2 h at −78 °C and 1 h at 0 °C and worked up to give the desired α-chloro acid. 2-Chloro-3,7-dimethyl-6-octenoic acid (**4**) (78%), 2-chloro-6-heptenoic acid (**5**) (96%), (*Z*)-2-chloro-6-nonenoic acid (**6**) (79%), (*Z*)-2-chloro-7-decenoic acid (**7**) (75%), (*Z*)-2-chloro-8-undecenoic acid (**8**) (74%), 2-chlorooleic acid (**9**) (97%), and 1-chlorocyclohexanecarboxylic acid (**10**) (84%) were prepared in the indicated yields. As indicated by Arnold and Kulenovic,[11] the trichloromethyl anion does not decompose appreciably to dichlorocarbene during the reaction, since no dichlorocyclopropanes could be detected.

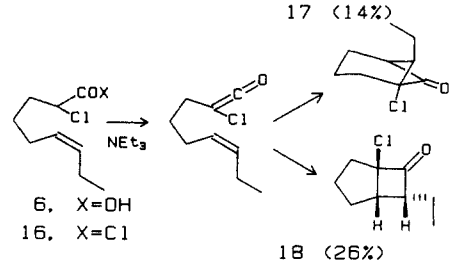
With unsaturated α-chloro acids now readily available, we turned our attention to the preparation of chloroketenes and examination of their intramolecular [2 + 2] cycloaddition reactions. Treatment of **4** with oxalyl chloride



in benzene at reflux gave a quantitative yield of crude acid chloride **11** which was added to excess triethylamine in benzene at reflux. The mixture was heated at reflux for 3 h and worked up to give a 55% yield of the cycloadduct **12** and a 19% yield of the ene adduct **13** as a mixture of diastereomers. In a similar fashion, **5** was converted to acid



chloride **14** which gave the cycloadduct **15** in 68% yield on treatment with triethylamine and **6** was converted to acid chloride **16** which gave cycloadducts **17** and **18** in 14% and 26% yield, respectively.



The intramolecular cycloadditions of unsaturated chloroketenes are, as hoped, much more facile than those of the analogous deschloroketenes. The ketene derived from **14** gives a 68% yield of **15**, while the ketene derived from **1** gives only a 3% yield of **2**.[3a] The ketene derived from **11** gives a 55% yield of **12**, while the ketene derived from **3** does not give any cyclobutanone.[2a]

Treatment of the acid chlorides prepared from **7** and **8** with triethylamine did not give any cyclobutanone containing products as determined by analysis of the NMR and IR spectra. This result suggests that the intramolecular [2 + 2] cycloaddition of unsaturated chloroketenes is restricted to the formation of bicycloheptanones, a result previously observed with other classes of ketenes.[3a] However, 1,2-disubstituted alkenes are the least reactive class of alkenes. This reaction may well be suitable for the formation of bicyclooctanones from reactive alkenes.

The structures of **12**, **15**, **17**, and **18** were assigned based on analysis of their IR and NMR spectra. The cyclobutanone carbonyl appears at a characteristic frequency of 1780–1790 cm^{-1}. The ^1H NMR spectrum of **15** shows the characteristic absorptions for H_1, $H_{7\alpha}$ and $H_{7\beta}$ of a bicyclo[3.2.0]heptan-6-one.[12] The ^1H and ^{13}C NMR spectra of **18** are quite similar to those of **15** except that the carbon spectrum shows the expected shielding for an *endo*-ethyl group and the absorption of H_7 is shifted to higher field in the ^1H NMR spectrum due to conformational changes induced by steric crowding. The coupling constant of 7 Hz between H_1 and H_7 requires that the two hydrogens be cis,[12] indicating that the cycloadditon is stereospecific.

The bicyclo[3.1.1]heptan-6-one skeleton of **12** and **17** was established by the observation that the endo proton on C_3 of these systems is in the shielding cone of the carbonyl group and is shifted upfield to δ 1.3 and 1.05, respectively. No upfield protons are observed in the NMR spectra of the bicyclo[3.2.0]heptan-6-ones **15** and **18**. The stereochemistry of the methyl group in **12** can be established on the basis of the coupling constants of 6.9 and 8.0 Hz between H_2 and the hydrogens on C_3, which indicates that H_2 is pseudoaxial and that the methyl group is in the less hindered endo position. The stereochemistry of **17** was established by the coupling constant of 3.4 Hz between H_5 and H_7. The coupling constant would be 0 Hz in the other diastereomer, in which the dihedral angle between H_5 and H_7 is 90°.

The regiochemistry of these cycloadditions is controlled by electronic effects, as we have observed previously in the intramolecular cycloadditions of vinylketenes and alkoxyketenes.[2] The least substituted, most nucleophilic carbon of the double bond adds to the carbonyl group of

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the ketene, giving rise to bicyclo[3.2.0]heptan-6-ones from terminal alkenes such as **14** and bicyclo[3.1.1]heptan-6-ones from alkenes such as **11** in which the terminal carbon is more highly substituted. 1,2-Disubstituted alkenes such as **16** give rise to mixtures of regioisomers.

We have briefly explored procedures for the dechlorination of **12**. Not surprisingly, zinc and acetic acid failed to reduce this chloroketone. Reduction with $(Bu)_3SnH$ in benzene also failed to reduce **12**. Fortunately, reaction of **12** with $(Bu)_3SnH$ and AIBN in THF at reflux gave an 84% yield of **19**.[13]

In conclusion, we have shown that α-chloro acids can be prepared in high yield in a single step by treatment of an acid dianion with CCl_4. The intramolecular [2 + 2] cycloadditions of the unsaturated chloroketenes prepared from these α-chloro acids provide a versatile route to bicyclo[3.2.0]heptan-6-ones and bicyclo[3.1.1]heptan-6-ones in cases where the cycloaddition of the corresponding deschloroketenes fails.

Experimental Section

Materials and Methods. All reactions were carried out in flame-dried glassware under nitrogen. NMR spectra were recorded on a Varian XL-300 in $CDCl_3$; chemical shifts are reported in δ. Unsaturated acids were either commercially available or were prepared from the commercially available aldehydes by oxidation with silver oxide.

2-Chloro-3,7-dimethyl-6-octenoic Acid (4). Butyllithium (4.8 mL of 2.3 M solution in hexane, 11 mmol) was added to a solution of diisopropylamine (1.31 g, 13 mmol) in 10 mL of dry THF at 0 °C. The solution was stirred at 0 °C for 40 min and cooled to −20 °C. A solution of citronellic acid (0.85 g, 5 mmol) in 10 mL of THF and 2.5 mL of HMPA was added dropwise. The solution was stirred for 2 h at −20 °C and cooled to −78 °C. Carbon tetrachloride (2.41 mL, 25 mmol) in 5 mL of dry THF was added rapidly. The solution was stirred for 2 h at −78 °C and 1 h at 0 °C and quenched with 1 N hydrochloric acid. The aqueous layer was saturated with NaCl and extracted with ether (4 × 50 mL). The combined ether layers were dried and evaporated to give crude **4**. Purification by flash chromatography on silica gel (85:15:0.2 hexane–EtOAc–HOAc) gave 0.8 g (78%) of pure **4** as a 1:1 mixture of stereoisomers: bp 85–90 °C (0.6 torr); ^{1}H NMR 1.02 (d, 0.5 × 3, J = 7.0), 1.08 (d, 0.5 × 3, J = 7.0), 1.2–1.7 (m, 2), 1.62 (br s, 3), 1.68 (br s, 3), 1.85–2.4 (m, 3), 4.25 (d, 0.5 × 1, J = 6.5), 4.39 (d, 0.5 × 1, J = 4.5), 5.1 (br t, 1, J = 6), 9.5 (br s, 1, OH); IR (neat) 1725 cm^{-1}; UV (95% EtOH) λ_{max} 221.5 nm (ϵ 212) (shoulder). Anal. Calcd for $C_{10}H_{17}ClO_2$: C, 58.67; H, 8.32. Found: C, 58.26; H, 8.47.

2-Chloro-6-heptenoic acid (5) (0.78 g) was prepared from 6-heptenoic acid (0.64 g, 5 mmol) as described above for the preparation of **4** in 96% yield: ^{1}H NMR 1.40–1.75 (m, 2), 1.85–2.25 (m, 4), 4.30 (t, 1, J = 7.0), 4.98 (d, 1, J = 11.0), 5.00 (d, 1, J = 17.0), 5.55–5.95 (m, 1); IR (neat) 1723 cm^{-1}. Anal. Calcd for $C_7H_{11}ClO_2$: C, 51.70; H, 6.82. Found: C, 51.62; H, 7.03.

(*Z*)-2-Chloro-6-nonenoic acid (6) (3.00 g) was prepared from (*Z*)-6-nonenoic acid (3.12 g, 20 mmol) as described above for the preparation of **4** in 79% yield: ^{1}H NMR 0.95 (t, 3, J = 7.5), 1.35–1.85 (m, 2), 1.88–2.30 (m, 6), 4.32 (dd, 1, J = 6.5, 6.5), 5.15–5.60 (m, 2); IR (neat) 1725 cm^{-1}; UV (95% EtOH) λ_{max} 214 nm (ϵ 185) (shoulder).

(*Z*)-2-Chloro-7-decenoic acid (7) (1.16 g) was prepared from (*Z*)-7-decenoic acid (1.36 g, 8 mmol) as described above for the preparation of **4** in 75% yield: ^{1}H NMR 0.93 (t, 3, J = 7.0), 1.25–1.75 (m, 4), 1.90–2.30 (m, 6), 4.31 (t, 1, J = 7.0), 5.16–5.60 (m, 2), 10.1 (s, 1); IR (neat) 1725 cm^{-1}. Anal. Calcd for $C_{10}H_{17}ClO_2$: C, 58.68; H, 8.37. Found: C, 58.10; H, 8.46.

(*Z*)-2-Chloro-8-undecenoic acid (8) (1.295 g) was prepared from (*Z*)-8-undecenoic acid (1.47 g, 8 mmol) as described above for the preparation of **4** in 74% yield: ^{1}H NMR 0.95 (t, 3, J = 7.0), 1.20–1.80 (m, 6), 1.80–2.20 (m, 4), 4.30 (t, 1, J = 7.0), 5.16–5.55 (m, 2); IR (neat) 2700–3400, 1725 cm^{-1}. Anal. Calcd for $C_{11}H_{19}ClO_2$: C, 60.41; H, 8.76. Found: C, 60.02; H, 8.74.

2-Chlorooleic acid (9) (1.54 g) was prepared from oleic acid (1.41 g, 5 mmol) as described above for the preparation of **4** in 97% yield: ^{1}H NMR 0.88 (br t, 3, J = 6.5), 1.20–1.60 (m, 20), 1.90–2.20 (m, 4), 4.31 (t, 1, J = 7.0), 5.15–5.55 (m, 2); IR (neat) 2700–3400, 1725 cm^{-1}.

1-Chlorocyclohexanecarboxylic acid (10)[8b] (0.34 g) was prepared from cyclohexanecarboxylic acid (0.32 g, 2.5 mmol) as described above for the preparation of **4** in 84% yield: ^{1}H NMR 0.75–2.20 (m, 10); IR (neat) 2700–3400, 1715 cm^{-1}.

***endo*-1-Chloro-2,2,7-trimethylbicyclo[3.1.1]heptan-6-one (12).** Oxalyl chloride (7.62 g, 60 mmol, 10 equiv) was added dropwise to a cooled solution of acid **4** (1.23 g, 6 mmol) in 12 mL of dry benzene. The solution was heated at reflux for 1 h and cooled to 25 °C. The solvent and excess oxalyl chloride were removed in vacuo to provide the acid chloride **11** in quantitative yield as a 1:1 mixture of stereoisomers: ^{1}H NMR 1.00 (d, 0.5 × 3, J = 7), 1.12 (d, 0.5 × 3, J = 7), 1.25–1.75 (m, 2), 1.62 (br s, 3), 1.70 (br s, 3), 1.90–2.25 (m, 3), 4.47 (d, 0.5 × 1, J = 5.0), 4.64 (d, 0.5 × 1, J = 4.5), 4.95–5.25 (m, 1); IR (neat) 1785 cm^{-1}.

Use of 3–5 equiv of oxalyl chloride instead of 10 equiv gave comparable results.

Crude **11** (1.33 g, 6 mmol) dissolved in 60 mL of dry benzene was added dropwise with stirring to a solution of triethylamine (1.2 g, 12 mmol) in 120 mL of benzene at reflux. The solution was heated at reflux for 3 h and cooled to 25 °C and quenched by the addition of ice water. The organic layer was separated, dried, and evaporated in vacuo to give a red oil. Flash chromatography on silia gel (95:5 hexane–EtOAc) gave 0.61 g (55%) of pure **12** followed by 0.21 g (19%) of **13** as a mixture of diastereomers.

The spectral data for **12** follow: bp 50–55 °C (0.07 torr); ^{1}H NMR 1.07 (d, 3, J = 6.0), 1.16 (s, 3), 1.20 (s, 3), 1.24–1.35 (m, 1), 1.92–2.16 (m, 3), 2.67 (dd, 1, J = 3.0, 3.0, H_5), 2.68 (qdd, 1, J = 6.9, 6.9, 8.0, H_2); ^{13}C NMR 14.2, 20.3, 25.8, 26.2, 28.3, 36.9, 40.6, 61.4, 83.9, 205.0; IR (neat) 1792 cm^{-1}; UV (95% EtOH) λ_{max} 263 nm (ϵ 400). Anal. Calcd for $C_{10}H_{15}ClO$: C, 64.34; H, 8.10. Found: C, 64.36; H, 8.09.

The spectral data for the major diastereomer of **13** follow: ^{1}H NMR 1.05 (d, 3, J = 7), 1.2–2.2 (m, 5), 1.78 (s, 3), 2.7 (m, 1), 3.1 (m, 1), 4.74 (d, 1, J = 6), 4.78 (s, 1), 4.97 (s, 1); IR (neat) 3080, 1730, 1650, 900 cm^{-1}.

(1β,5β)-5-Chlorobicyclo[3.2.0]heptan-6-one (15). Reaction of acid **5** (0.406 g, 2.5 mmol) as described above for the preparation of **11** gave the acid chloride **14** (0.440 g, 96%): ^{1}H NMR 1.45–1.80 (m, 2), 1.90–2.35 (m, 4), 4.56 (dd, 1, J = 5.0, 7.5), 5.03 (d, 1, J = 12.0), 5.05 (d, 1, J = 17.5), 5.55–6.05 (m, 1); IR (neat) 1790 cm^{-1}. Reaction of **14** (0.440 g, 2.4 mmol) with triethylamine as described above for **11** followed by flash chromatography (95:5 hexane–EtOAc) gave 0.233 g (68%) of pure **15**: ^{1}H NMR 1.70–2.18 (m, 5), 2.39 (dd, 1, J 6.4, 12.5, $C_{4\beta}$), 2.60 (dd, 1, J = 5.3, 18.5, $H_{7\alpha}$), 2.93 (ddd, 1, J = 5.3, 10.0, 11.0, H_1), 3.39 (dd, 1, J = 10.0, 18.5, $H_{7\beta}$); ^{13}C NMR 24.6, 31.9, 38.6, 41.0 (CH), 48.3, 82.2, 204.8; IR (neat) 1780 cm^{-1}.

***syn*-1-Chloro-7-ethylbicyclo[3.1.1]heptan-6-one (17) and (1β,5β,7α)-5-Chloro-7-ethylbicyclo[3.2.0]heptan-6-one (18).** Reaction of acid **6** (1.14 g, 6 mmol) as described above for the preparation of **11** gave the acid chloride **16** (1.22 g, 96%): ^{1}H NMR 0.94 (t, 3, J = 7.0), 1.45–1.82 (m, 2), 1.88–2.30 (m, 6), 4.53 (dd, 1, J = 10.0, 6.0), 5.10–5.55 (m, 2); IR (neat) 1790 cm^{-1}. Reaction of **16** (1.22 g, 5.74 mmol) with triethylamine as described above for **11** followed by flash chromatography (95:5 hexane–EtOAc) gave 0.126 g (14%) of **17** followed by 0.234 g (26%) of **18**.

The spectral data for **17** follow: ^{1}H NMR 0.98 (t, 3, J = 7.2), 0.96–1.16 (m, 1, $H_{3\alpha}$), 1.65–1.84 (m, 2), 1.85–1.94 (m, 1), 2.08 (br dd, 1, J = 10.5, 4.5), 2.16–2.24 (m, 1), 2.25–2.31 (m, 1), 2.53 (ddd, 1, J = 13.0, 8.0, 4.5, $H_{2\alpha}$), 2.65 (ddd, 1, J =13.0, 8.0, 8.0, $H_{2\beta}$), 2.92 (dd, 1, J = 3.4, 3.4, H_5); ^{13}C NMR 11.6 (CH_3), 19.4, 22.8, 31.8, 43.2, 46.1 (CH), 57.9(CH), 77.6, 204.5; IR (neat) 1792 cm^{-1}; UV (95% EtOH) λ_{max} 288 nm (ϵ 200).

The spectral data for **18** follow: ^{1}H NMR 1.06 (t, 3, J = 7.0), 1.63–1.85 (m, 4), 2.00–2.14 (m, 2), 2.24 (ddd, 1, J = 7.0, 7.0, 7.0, C_7), 2.27–2.35 (m, 1), 2.61 (ddd, 1, J = 13.0, 11.0, 8.0, $C_{4\beta}$), 3.11 (ddd, 1, J = 7.0, 4.5, 2.0, C_1); ^{13}C NMR 12.0 (CH_3), 15.6, 19.2, 24.0,

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35.4, 43.4 (CH), 54.8 (CH), 75.4, 204.0; IR (neat) 1789 cm^{-1}; UV (95% EtOH) λ_{max} 297 nm (ϵ 37). Anal. Calcd for $C_9H_{13}ClO$: C, 62.61; H, 7.59. Found: C, 62.45; H, 7.79.

***endo*-2,7,7-Trimethylbicyclo[3.1.1]heptan-6-one (19).**[13] A solution of chloro ketone **12** (37 mg, 0.6 mmol), tri-*n*-butyltin hydride (175 mg, 0.6 mmol), and AIBN (5 mg, 0.03 mmol) in 5 mL of dry THF was heated at reflux for 48 h. The solvent was removed in vacuo and the residue was purified by flash chromatography on silica gel (95:5 hexane–EtOAc) to give 25 mg (84%) of pure **19**: ^1H NMR 0.92 (d, 3, J = 7.0), 1.15 (s, 3), 1.18 (s, 3), 1.10–1.35 (m, 1), 1.53–1.63 (m, 1), 1.72 (ddd, 1, J = 7.0, 7.0, 14.0), 1.96–2.20 (m, 1), 2.25 (d, 1, J = 6.7, H_1), 2.44 (br dd, 1, J = 6.7, 6.7, H_5); IR (neat) 1770 cm^{-1}.

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Note Added in Proof: Recent results suggest that the minor cycloadduct obtained from **16** may be the diastereomer of **18** with a β-ethyl group, which could result from epimerization after cyclization, rather than **17**.

Hydroboration. 80. Preparation of (*trans*-2-Phenylcyclopentyl)- and (*trans*-2-Phenylcyclohexyl)boronates of Very High Enantiomeric Purities

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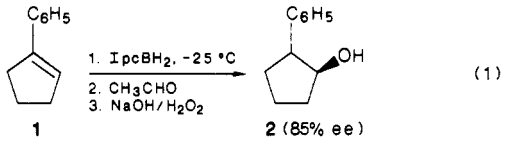
Since the discovery of optically pure monoisopinocampheylborane ($IpcBH_2$),[2] various trans-di- and -trisubstituted olefins of varying structural and steric requirements have been hydroborated to establish the degree of asymmetric induction achievable.[3] The possibility of transferring optically active groups from boron to many other moieties with complete retention of optical activity has led to increased interest in the preparation of borane intermediates of very high enantiomeric purity.[4-6] This study deals with a reexamination of the hydroboration of 1-phenylcyclopentene and 1-phenylcyclohexene and with the preparation of the corresponding boronates of high enantiomeric purity.

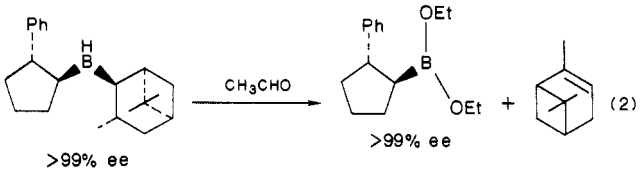
Previously we reported that 1-phenylcyclopentene, upon hydroboration with $IpcBH_2$ (derived from (+)-α-pinene) at −25 °C, followed by oxidation, yields (1*S*,2*R*)-*trans*-2-phenylcyclopentanol.[3] The optical purity of the alcohol, determined by using NMR with chiral shift reagent, was found to be 100%. Recently, a similar experiment gave alcohol of the same rotation. However, capillary GC analysis of the corresponding Mosher (MTPA) ester[7] showed the material to be of only 85% ee (eq 1).



(1)

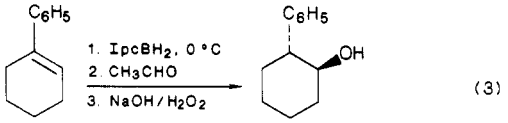
1-Phenylcyclopentene, upon hydroboration with $IpcBH_2$ at −35 °C, followed by treatment with CH_3CHO and alkaline hydrogen peroxide, gave (1*S*,2*R*)-*trans*-2-phenylcyclopentanol in 86% ee. The dialkylborane,[8] isopinocampheyl((1*S*,2*S*)-*trans*-2-phenylcyclopentyl)borane, is a solid and in part crystallizes from the reaction mixture. The crystalline dialkylborane, upon oxidation, yielded (1*S*,2*R*)-*trans*-2-phenylcyclopentanol in 91% ee. The crystalline dialkylborane was dissolved in fresh ethyl ether and the dialkylborane was crystallized at −35 °C. Oxidation of the recrystallized product gave the alcohol in only 95% ee. However, the dialkylborane (91% ee) could be crystallized at 0 °C in ethyl ether to obtain a white crystalline solid, which, upon oxidation, gave (1*S*,2*R*)-*trans*-2-phenylcyclopentanol in >99% ee.

This crystalline dialkylborane (>99% ee), upon treatment with acetaldehyde,[9] yielded the corresponding boronate in >99% ee (eq 2), which could be purified by distillation without loss of activity.



(2)

1-Phenylcyclohexene had also been hydroborated[3] with $IpcBH_2$ [derived from (+)-α-pinene] at 0 °C and the resulting dialkylborane, upon oxidation, yielded (1*S*,2*R*)-*trans*-2-phenylcyclohexanol. The optical purity of the alcohol had been reported to be 88% ee, based on maximum rotation reported earlier.[10] Recently repetition of the experiment gave (1*S*,2*R*)-*trans*-2-phenylcyclohexanol of the same rotation. However, capillary GC analysis of the corresponding Mosher ester showed the material to be ≥97% ee (eq 3). *trans*-2-Phenylcyclohexanol has been shown to be a powerful chiral auxiliary.[11]



(3)

It is evident that capillary GC analysis of the Mosher esters (or other diastereomeric derivatives) provides a far more reliable method for establishing the optical purities than the procedures utilized in the past.

Conclusion

The literature reported values of *trans*-2-phenylcyclopentanol and *trans*-2-phenylcyclohexanol have been corrected. This study makes it possible to obtain *trans*-2-phenylcyclopentyl and *trans*-2-phenylcyclohexylboronates, versatile synthetic intermediates of high optical purities.

Experimental Section

The reaction flasks and other glass equipment were stored in an oven at 150 °C overnight and assembled in a stream of dry

(1) Postdoctoral research associates on Grant GM-10937-23 from the National Institutes of Health. We are indebted to Professor Crhistopher S. Shiner for calling to our attention a discrepancy between the rotation of a sample of optically pure 2-phenylcyclopentanol and the value we had reported.[3]

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(8) Although these dialkylboranes exist in solution as dimers, for convenience, they are referred to as simple dialkylboranes.

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