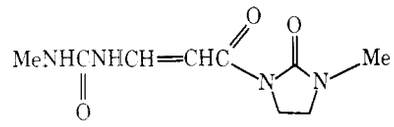
reaction 1 were tried which did not yield the expected products. These were **1a** plus urea, *N*-methylthiourea, or *S*-benzylisothiourea, 1-methyluracil plus **2a**, and 1-methylcytosine plus **4**.

The fact that the type of reaction discussed here occurs only under conditions where enolate anion formation has been observed[2,5] strongly suggests that the mechanism involves this intermediate, with the reactive center being at C-1 or C-3. On the other hand, the former possibility apparently is ruled out by the fact that no reaction product, e.g., A, was obtained



A

corresponding to attack of 4 on C-1 of the enolate (**3b**; Y = H, Z = 1-methylimidazolidone-3) prepared from 3-(β-chloroethyl)-1-methyluracil plus TMAH in Me_2SO.[5]

Experimental Section

^1H NMR spectra were obtained on a Varian A-60A spectrometer at room temperature using tetramethylsilane or sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) as internal standards. A Cary 14 spectrophotometer was used to obtain UV spectra. Mass spectra were obtained on a Varian M-66 mass spectrometer at an ionizing potential of 70 eV, an ionizing current of 30 μA, a resolution of ~1200, and with perfluorokerosene as a standard.

Thin-layer chromatography was performed on Analtech silica gel G thin-layer plates containing fluorescent indicator (Analtech, Inc., Newark, Del.). Preparative chromatography (dry column) was performed on silica gel Woelm (ICN, Cleveland, Ohio). The progress of such chromatography was monitored by TLC. High-pressure liquid chromatography (LC) was performed using a Waters ALC 202 liquid chromatograph with a Corasil I column (Waters Associates, Inc., Framingham, Mass.), 4 ft × 0.125 in.

Melting points are corrected.

Reaction of 1,3-Diethyluracil (1b) with 1,3-Dimethylurea (2a). Compounds **1b** (80 mg, 0.48 mmol) and **2a** (40 mg, 0.46 mmol) were dissolved in 2.5 mL of Me_2SO and 2.5 mL of 0.1 N TMAH (0.25 mmol) in Me_2SO was added. After 1 h the reaction mixture was treated with 200 μL of glacial acetic acid and it was desalted by passing the mixture through 3 g of silica gel. The silica gel was washed with 25 mL of AcOEt to elute all UV-containing materials. The solvents were evaporated in vacuo and the residue was dissolved in 10 mL of absolute EtOH. The UV spectrum indicated 79% of the original chromophore was present. LC analysis with 5% EtOH in *n*-hexane showed 51% conversion to **1a**.

Repetition of the above experiment, at the same dilution, using 1 mL of 0.1 N TMAH (0.10 mmol) gave 84% of the original chromophore. LC analysis showed this mixture contained 48% of **1a**.

Reactions of 1,3-Dimethyluracil (1a), 1,3-Diethyluracil (1b), and 1,3-Dimethylthymine with *N*-Methylurea (4). Compounds **1b** (80 mg, 0.48 mmol) and **4** (40 mg, 0.54 mmol) were combined and treated with 5 mL of 0.1 N TMAH (0.50 mmol) in Me_2SO. After 1 h the reaction mixture was treated with 0.2 mL of glacial acetic acid and it was desalted as described above. The residue, after evaporation of Me_2SO and AcOEt, was dissolved in absolute EtOH. UV indicated 80% retention of the chromophore and LC showed that the material was a mixture of 22% **1b**, 35% 3-methyluracil, and 42% 1-methyluracil. The ethanol was evaporated and the residue was dissolved in 1 N NaOH and extracted with $CHCl_3$. The $CHCl_3$ layer contained the starting material. Neutralization of the basic aqueous layer, followed by evaporation, afforded a mixture of the two monomethyluracils. This was confirmed by ^1H NMR.

When **1a** was subjected to the same reaction conditions, 96% conversion to 1- and 3-methyluracils was observed. With 0.3 equiv of base, only 15% of a mixture of the two isomers was obtained in 1 h.

When 1,3-dimethylthymine was subjected to the same reaction conditions as **1b** for 1 h, complete conversion to a mixture of 1- and 3-methylthymine was observed. The two isomers were obtained in a ratio of 38:62, but which one was more abundant is not known.

Reaction of 1,3-Dimethyluracil (1a) with Acetamidine (5). 4-Hydroxy-2-methylpyrimidine (7). Compounds **1a** (210 mg, 1.50 mmol) and **5** hydrochloride (160 mg, 1.69 mmol) were dissolved in 10 mL of Me_2SO. TMAH was added in two portions (280 mg, 1.54 mmol each) and the reaction mixture was shaken vigorously. After 2 h, TLC indicated some starting material was still present. An additional 90 mg (0.77 mmol) of TMAH was added and the reaction mixture was stirred at room temperature for 24 h. It then was desalted on 10 g of silica gel and the solvents were evaporated in vacuo. The residue was dissolved in 10 mL of $CHCl_3$ and extracted with 2 × 10 mL of H_2O. The $CHCl_3$ layer contained 60 mg (29%) of **1a**. UV analysis of the aqueous extracts indicated that 36% of **7** was present. The material was chromatographed on an anion-exchange column [Rexyn AG 1(OH^-)]. After washing the column with water, the UV-absorbing material was released from the column by acidification with HCl. Evaporation afforded a solid which had mp 260–265 °C and gave a positive test with silver nitrate. This solid was dissolved in absolute EtOH and $NaHCO_3$ was added until CO_2 evolution ceased. The solid was removed by filtration and the filtrate was evaporated in vacuo. The residue was recrystallized from MeOH to give pure **7**: mp 211–213 °C (lit.[4] mp 212.5–213 °C); ^1H NMR (D_2O) δ 2.77 (s, 3, CH_3), 6.72 (d, 1, J = 8 Hz, H-5), and 7.55 (d, 1, J = 8 Hz, H-6); M^+· 110 (98).

Reaction of 1,3-Dimethyluracil (1a) with *N,N*-Dimethylguanidine (6). 2-(Dimethylamino)-4-hydroxypyrimidine (8). Compounds **1a** (210 mg, 1.50 mmol) and **6** hydrochloride (250 mg, 2.00 mmol) were dissolved in 10 mL of Me_2SO and 660 mg (3.65 mmol) of TMAH was added. The reaction mixture was stirred at room temperature. After 7 days the reaction mixture was desalted on 10 g of silica gel. The residue obtained after evaporation of solvents was dissolved in 10 mL of $CHCl_3$ and extracted with 3 × 10 mL of H_2O. The $CHCl_3$ layer afforded 60 mg (26%) of **1a**. The aqueous extracts were concentrated in vacuo to 10 mL and poured on to an anion-exchange column [Rexyn AG 1(OH^-)]. The initial washes with water afforded ~13% more **1a**. Acidification with HCl caused the release of the remaining UV-absorbing material, λ_{max} (0.1 N HCl) 262 nm and λ_{max} (0.1 N NaOH) 280 nm. Evaporation afforded 110 mg (41%) of **8** as the hydrochloride, which was dissolved in absolute EtOH and treated with aqueous $NaHCO_3$ until CO_2 evolution ceased. The solution was concentrated in vacuo and filtered to remove NaCl. The filtrate was evaporated in vacuo and the residue was crystallized from water to give pure **8**: mp 175–177 °C (lit.[6] mp 175.5–176.5 °C); ^1H NMR ($CDCl_3$) δ 3.19 (s, 6, CH_3), 5.69 (d, 1, J = 6.5 Hz, H-5) and 7.72 (d, 1, J = 6.5 Hz, H-6); M^+· 139 (100).

Registry No.—**1a**, 874-14-6; **1b**, 22390-04-1; **2a**, 96-31-1; **4**, 598-50-5; **5** HCl, 124-42-5; **6** HCl, 22583-29-5; **7**, 19875-04-8; **8**, 1635-28-5; **8** HCl, 66575-45-9; 1,3-dimethylthymine, 4401-71-2; 3-methyluracil, 608-34-4; 1-methyluracil, 614-77-0.

References and Notes

(1) The authors are indebted to two anonymous donors for their generosity in providing partial support for this investigation. Additional support was provided by a Biomedical Sciences Support Grant from the General Research Support Branch, Division of Research Resources, Bureau of Health Professions Education and Manpower Training, National Institutes of Health.
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A New Convenient Synthesis of Bridgehead Substituted Norbornenes[1]

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Bridgehead substituted norbornenes, while being simple compounds in appearance, are synthesized only with difficulty. To date the syntheses of these compounds have involved a Wagner–Meerwein type rearrangement step. For example, the bridgehead methoxycarbonylnorbornene (**4**; Scheme I) has been prepared from *exo*-2-bromo-*endo*-2-methoxycarbonylnorbornane.[2] The bridgehead chloronorbornene has

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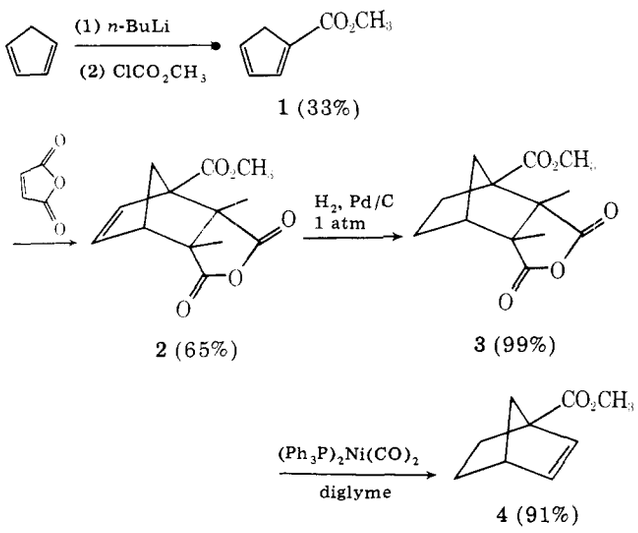
Scheme I



been prepared from 2,2-dichloronorbornane by a similar rearrangement.[3]

Because many substituents may not be stable under the acidic conditions of the rearrangement and because the synthesis of disubstituted compounds is complicated by scrambling during the rearrangement, a more general route was sought. It was desired that the position of the substituent be fixed early in the scheme, leading unambiguously to the desired product. This was accomplished in our approach as outlined in Scheme I.

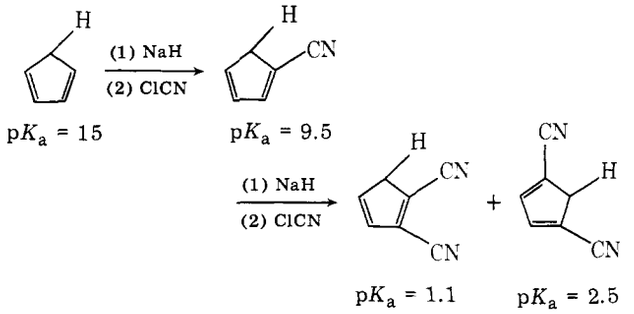
To this end, the oxidative bisdecarboxylation scheme published by Trost and Chen[4] was used. Substituted succinic anhydrides can be oxidatively bisdecarboxylated using $(Ph_3P)_2Ni(CO)_2$ in diglyme at reflux. This procedure has been used recently by other workers to synthesize bicyclic compounds prepared only with difficulty by other routes.[5]

The synthesis of 1-methoxycarbonylcyclopentadiene (1) was based on the work of Thiele[6] and Peters.[7] It was found to be more convenient to lithiate cyclopentadiene using *n*-BuLi than to form the sodium, potassium, or other metal salt. The cyclopentadienyllithium was acylated with methyl chloroformate to form 1 (shown in Scheme I). However, when an electron-withdrawing group was attached to the cyclopentadiene ring, the pK_a of the system decreased precipitously, favoring the formation of diacylated cyclopentadiene. In a study by Webster[8] on the related cyanation of cyclopentadiene, the dramatic effect shown in Scheme II was observed. Precautions such as low reaction temperatures and rapid addition of the acylating agent improved the yield somewhat, but this step still remained the lowest (33%) yielding step of the entire synthetic scheme.

After workup, 1 existed mostly as the Diels–Alder dimer and was distilled into a receiver at −78 °C to form the monomeric species. This diene reacted readily with maleic anhydride in diethyl ether solution at 25 °C to form the Diels–Alder adduct 2 as a white solid[9] in 40% yield. A significant amount of dimerized 1 was also formed, which was recovered, redistilled to form the monomer, and reacted again with maleic anhydride to increase the overall yield of product 2 from 1 to 65%.

The anhydride 2 was hydrogenated at 1 atm H_2 pressure over Pd/C catalyst to form the saturated anhydride 3 in quantitative yield. The saturated anhydride 3 was then oxidatively decarboxylated using freshly prepared $(Ph_3P)_2Ni(CO)_2$ in anhydrous diglyme at reflux. In previous reports,[4,5] 1 equiv of the Ni complex was used; however, it was found that only catalytic amounts are necessary. When 0.2 equiv was used, the reaction proceeded at about the same rate as when

Scheme II



1.0 equiv was used and the workup was easier. The extent of reaction was followed by collecting the effluent gases (CO and CO_2), and the reaction was terminated when 1 equiv of each was collected. Although the reaction was done at an elevated temperature (diglyme at reflux), yields of 85–91% were attained. The ester 4 was isolated as an oily liquid with a pleasant fruity odor.

The overall yield for the sequence was 20% from cyclopentadiene (59% from 1). This yield is comparable with that of Wilt et al.[2e] for their preparation of 4, but the route described here is shorter and more generally applicable. It should be possible to use any C(1)-substituted cyclopentadiene with the same sequence to produce a variety of bridgehead substituted norbornenes.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. All boiling points are uncorrected. Elemental analyzes were performed on an F & M Model 185 C, H, and N analyzer at the University of Kansas. Infrared spectra were recorded on a Beckman IR-33 spectrophotometer. Proton nuclear magnetic resonance spectra were recorded on a Varian EM-360 spectrometer, using tetramethylsilane (Me_4Si) as an internal standard. Mass spectra were determined on a Varian-Atlas CH-5 electron impact mass spectrometer. Solvents and reagents were routinely distilled or recrystallized prior to use. Reactions were routinely performed in a dry nitrogen atmosphere.

1-Methoxycarbonylcyclopenta-1,3-diene (1). To 600 mL of anhydrous THF (freshly distilled from $LiAlH_4$) was added 33.0 g (0.50 mol) of freshly cracked cyclopentadiene. This mixture was cooled to −78 °C (dry ice/EtOH), and 342 mL (0.50 mol) of 1.46 M *n*-BuLi/hexane was slowly added (the temperature was maintained below −50 °C). After the addtion was complete, the solution was allowed to slowly warm to 25 °C and was stirred for 1 h. It was then recooled to −78 °C, and 47.3 g (38.6 mL, 0.50 mol) of $ClCO_2CH_3$ was added at such a rate that the reaction mixture remained below −50 °C. After the addition was complete (10 min), the solution was allowed to warm to 25 °C and was stirred for 10 min. The red solution was poured into 1 L of water. The layers were separated, and the aqueous layer was washed with Et_2O (2 × 200 mL). The combined organic layers were washed with water (5 × 500 mL) and saturated brine and dried ($MgSO_4$) at 0 °C for 1 h.

The solvent was removed in vacuo, and the red oily residue was distilled through a 10 cm Vigreux column and collected at −78 °C. A clear oily liquid was collected (20.60 g, 33%); bp 60–62 °C (5 mm); IR (liquid film) 1715 (C=O), 1590 (olefin), 1090 (C–O), and 675 (olefin) cm^{-1}; NMR ($CDCl_3$) δ 7.27 (m, 1, C**H**=CCO_2CH_3), 6.50 (m, 2, C=CH), 3.72 (s, 3, $-OCH_3$), and 3.23 (m, 2, $-CH_2-$).

1-Methoxycarbonylbicyclo[2.2.1]hept-5-ene-*endo,endo*-2,3-dicarboxylic Anhydride (2). This Diels–Alder adduct was made by dissolving 24.50 g (0.250 mol) of recrystallized maleic anhydride in Et_2O and adding 26.72 g (0.216 mol) of 1. This mixture was stirred for 10 min and allowed to sit at 25 °C overnight to crystallize. The resultant white solid was recrystallized from EtOAc to yield 18.49 g (39%) of a white solid: mp 149–150 °C (lit.[7b] mp 150 °C); IR (2% in KBr) 3010 (olefin), 1860 and 1765 (anhydride C=O), 1720 (ester C=O), 1065 (C–O), and 715 (olefin) cm^{-1}; NMR ($CDCl_3$) δ 6.43 (m, 2, C=CH), 4.17–3.70 (m, 2, H-2 and H-3), 3.90 (s, 3, $-OCH_3$), 3.62 (m, 1, H-4), and 2.00 (m, 2, $-CH_2-$); mass spectrum (70 eV), *m/e* (relative intensity) 222 (M^+, 0.6), 124 (71), 93 (23), 91 (16), 79 (16), 65 (23), 59 (16), 32 (29), and 28 (100). Anal. Calcd for $C_{11}H_{10}O_5$: C, 59.46; H, 4.50. Found: C, 59.26; H, 4.48.

1-Methoxycarbonylbicyclo[2.2.1]heptane-*endo,endo*-2,3-dicarboxylic Anhydride (3). To a 500-mL round-bottom flask was added 9.50 g (0.0428 mol) of **2** and 250 mL of dry EtOAc. The flask was purged with dry N_2 and stirred to affect solution, and then 0.95 g of 5% Pd/C was added. The mixture was hydrogenated at 1 atm pressure. After 30 min the calculated amount of H_2 was consumed. The mixture was filtered, the solvent volume was reduced by 70% in vacuo, and the product was allowed to crystallize. A total of 9.46 g (99%) of large white crystals, mp 157–158 °C, was recovered: IR (2% in KBr) 1865 and 1800 (anhydride C=O), 1730 (ester C=O), and 1080 (C–O) cm^{-1}; NMR ($CDCl_3$) δ 4.07–3.37 (m, 2, H-2 and H-3), 3.78 (s, 3, $-OCH_3$), 2.90 (m, 1, H-4), 2.15–1.50 (m, 6, $-CH_2-$); mass spectrum (70 eV), *m/e* (relative intensity) 224 (M^+, 0.1), 193 (16), 152 (25), 124 (100), 93 (18), 91 (9), 79 (16), 65 (11), 59 (16), and 28 (20). Anal. Calcd for $C_{11}H_{12}O_5$: C, 58.93; H, 5.36. Found: C, 58.88; H, 5.33.

1-Methoxycarbonylbicyclo[2.2.1]hept-2-ene (4). To a 250-mL round-bottom flask attached to a gas collection apparatus was added 9.45 g (0.042 mol) of **3**, 5.39 g (0.008 mol) of freshly prepared $(Ph_3P)_2Ni(CO)_2$,[10] and 75 mL of anhydrous diglyme (freshly distilled from sodium). The stirred solution was heated at reflux and the effluent gas collected. The reaction mixture turned from yellow to brown to black as the heating was continued. After 6 h, 1880 mL of gas (1 equiv each of CO and CO_2) had been collected. The diglyme was removed in vacuo through a short-path apparatus, codistilling the product [bp 40 °C (2.5 mm)]. Then 2-(2-ethoxyethoxy)ethanol (2 × 25 mL) was added and distilled to dryness [bp 51 °C (0.02 mm)]. The combined distillates were poured into 800 mL of water and extracted with pentane[11] (4 × 100 mL). The combined pentane layers were washed with water (4 × 75 mL) and then with saturated brine and dried ($MgSO_4$).

The pentane was removed in vacuo to yield 5.82 g (91%) of a clear oil with a fruity odor: IR (liquid film) 3080 (olefin), 1740 (C=O), 1575 (olefin), 1110 (C–O), and 705 (olefin) cm^{-1}; NMR ($CDCl_3$) δ 6.10 (m, 2, C=CH), 3.72 (s, 3, $-OCH_3$), 2.92 (m, 1, H-4), and 2.20–0.92 (m, 6, $-CH_2-$); mass spectrum (70 eV), *m/e* (relative intensity) 152 (M^+, 8), 124 (100), 121 (11), 96 (28), 79 (25), 77 (14), 64 (25), 59 (21), 39 (14), 32 (42), 31 (55), 29 (22), and 28 (55).

Registry No.—**1**, 35730-27-9; **2**, 66483-32-7; **3**, 66551-63-1; **4**, 15023-46-8; cyclopentadiene, 542-92-7; maleic anhydride, 108-31-6; $ClCO_2CH_3$, 79-22-1.

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(9) If the Diels–Alder reaction is run at higher temperatures, a significant amount of 5-methoxycarbonylbicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic anhydride was formed due to the presence of the tautomeric 2-methoxycarbonylcyclopenta-1,3-diene.
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Heterogeneous Reactions. 5. The Anti Orientation of Elimination for the Dehydrobromination of *meso*- and *dl*-2,3-Dibromobutane and (*E*)- and (*Z*)-2-Bromobut-2-ene with Solid Potassium *tert*-butoxide

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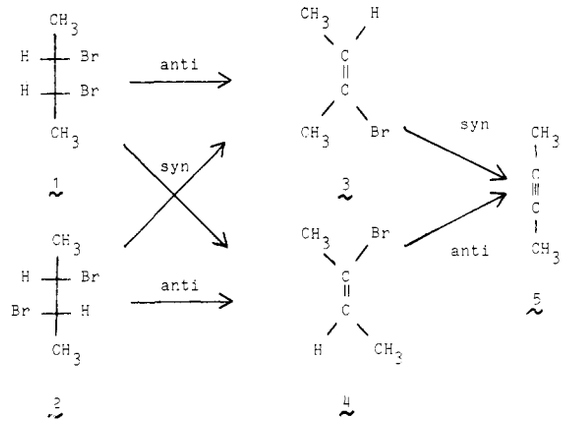
One of the most important stereochemical features of bimolecular base promoted β-elimination reactions is the relative orientation of the leaving groups. An important factor which is associated with the E2 reaction is the transition state stabilization derived from the partially developed double bond, and in order to maximize this stabilization the leaving groups must be periplanar. The periplanar requirement may be satisfied with the dihedral angle between these two groups being either 0° (syn) or 180° (anti).[1] In systems where both carbon centers involved in the elimination are chiral, a specific relative orientation of the leaving groups for diastereomeric reactants will dictate a different product selection (for example see Scheme I). In most solution reactions involving the dehydrohalogenation of alkyl halides the stereochemistry of the elimination has been shown to be predominantly anti-periplanar.[2-5]

Scheme I



We have recently reported a heterogeneous reaction system which has proven to be very efficient for effecting the base-promoted dehydrohalogenation of alkyl halides.[6] This heterogeneous reaction system utilizes solid phase alkoxide bases and vapor phase alkyl halides. Since the conditions of the heterogeneous reaction system are quite different from the more common solution reactions, it is important to determine the stereochemical requirement for these dehydrohalogenations. In fact, a syn elimination involving the simultaneous stabilization of the leaving groups by the anion and cation of the solid base is an attractive possibility under heterogeneous conditions.

The dehydrobromination of the diastereomeric *meso*-2,3-dibromobutane (**1**) and *dl*-2,3-dibromobutane (**2**) and the determination of any stereochemical selection from the analysis of the resulting (**E**)-2-bromobut-2-ene (**3**) and (**Z**)-2-bromobut-2-ene (**4**) provides a system which allows an examination of the syn vs. anti selection under heterogeneous conditions. These results yield a useful comparison with similar solution reactions.[2-5] Subsequent reaction of both **3** and **4** is also possible to yield but-2-yne (**5**). These reactions involve the elimination of a second molecule of HBr and provide a system which compares the syn vs. anti elimination of vinyl halides.[7,8]

Results and Discussion

Samples of **1** and **2** were prepared via the bromination of (**E**)- and (**Z**)-but-2-ene, respectively. The resulting dibromides were shown to have an isomeric purity of greater than 95% by ^1H NMR.[9] The *meso* and *dl* diastereomers, **1** and **2**, were reacted separately with solid potassium *tert*-butoxide at 100 °C according to methods which have been previously described.[6,11] The products of the dehydrobromination reaction for each isomer were analyzed by gas chromatography. Reactions for the preparation of **3** and **4**, according to the method of Bordwell and Landis, were not totally stereospecific.[3] The reactions yielded **3** which was found to be contaminated with 9% **4** and **4** which was found to be contaminated with 3% **3**.

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