with an averge deviation from the mean of 0.003 and a probable error of 0.001. The sharp singlet at 4.07 ppm in the NMR spectrum of methyl 3,5-dinitrobenzoate prepared from D_2O undergoes a similar transformation, in this case giving 0.060 of the intensity of the aromatic peaks. For both products this leads to the conclusion that they are 94% deuterated in their methyl groups.

The deuterium content of the water was determined by following the procedure described above up to the countercurrent extraction. The reaction mixture was then acidified with a small volume of strong acid in D_2O. From this solution 2.5 mL of water was distilled, bp 102–110 °C, contaminated with a little DMSO. The deuterium content of this water was found to be 97%.[25] This is not thought to be significantly different from the 94% deuteration of the two products.

Diazomethane shows a very broad, low-intensity absorption in the visible and near-ultraviolet, with an ill-defined maximum, λ_{max}, somewhere between 350 and 400 nm and a maximum extinction coefficient of around 6. This is the band which is responsible for its yellow color. In determining rate constants it was necessary to monitor the diazomethane concentration at a wavelength somewhat above λ_{max}, in order to avoid interference from UV-absorbing substances which build up with time in these reaction mixtures; 410 nm was used.

Registry No.—Diazomethane, 334-88-3; phenol, 108-95-2.

References and Notes

(1) (a) This work was supported, in large part, and publication costs assisted by the National Science Foundation through Grants CHE76-01181 and GP-31360X to the University of Minnesota. (b) M. M. Kreevoy was a guest of the Physical Chemistry Laboratory, Oxford, while he was preparing this paper. He wishes to thank the members of that laboratory, particularly Dr. W. J. Albery, for their warm hospitality.
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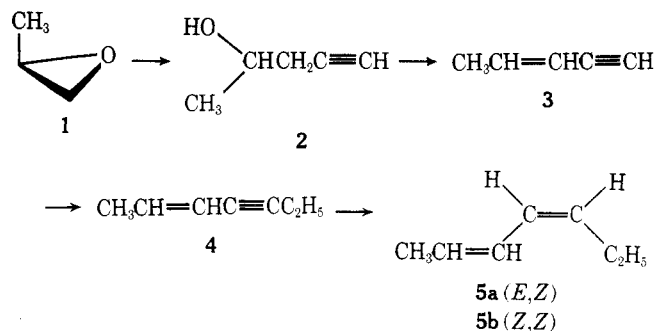## A Convenient Synthesis of (E,Z)- and (Z,Z)-6-Deuterio-2,4-heptadiene

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The successful elucidation of the mechanistic details of any reaction depends initially upon the reliability of available

Scheme I

synthetic procedures. This is especially obvious when the specific introduction of an isotopic label is desired.

For the detailed investigation of the rearrangement chemistry of 2,4-heptadiene, we required the 6-deuterio analogue (10). In this note we present the conceptually simple yet operationally challenging synthesis of this specifically labeled hydrocarbon.

Results and Discussion

Our approach to the synthesis of (E,Z)-6-deuterio-2,4-heptadiene (10a) involved the intermediate preparation of 6-deuterio-2-hepten-4-yne (9). Preliminary results (Scheme I) indicated this to be a rational approach: ethynylation of propylene oxide (1),[3] followed by tosylation of the resulting alcohol (2) and base-catalyzed elimination gave a 55:45 mixture of the known[4] (E)- and (Z)-3-penten-1-ynes (3); alkylation of 3 with ethyl bromide, followed by catalytic hydrogenation over freshly prepared Lindlar catalyst[5,6] or, alternatively, hydralumination[6,7] with diisobutylaluminum hydride in hexane and subsequent hydrolysis gave (E,Z)- and (Z,Z)-2,4-heptadiene (5) in 29% isolated yield based on 3-penten-1-yne (3), or 7.4% based on starting propylene oxide (1).
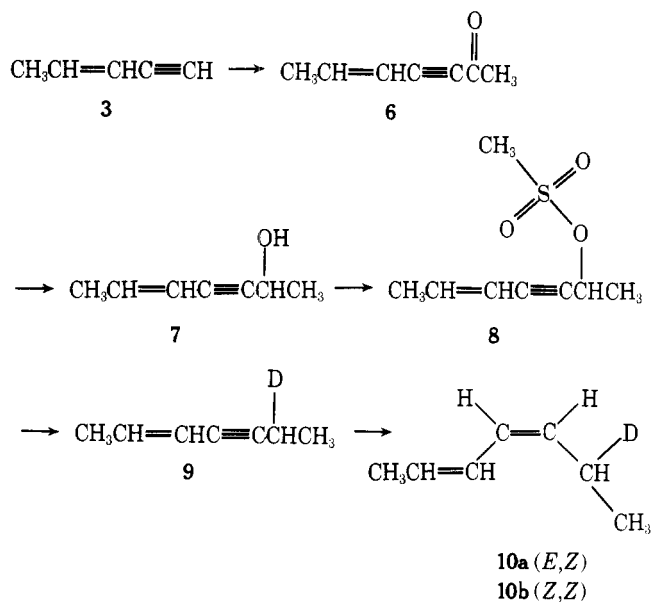
Careful gas chromatographic monitoring of the hydralumination reaction revealed a significant difference in the rates of reaction for the individual 2-hepten-4-yne diastereomers. The hydralumination of the E diastereomer of 4 is so much more rapid than the corresponding addition to the Z diastereomer that early hydrolysis of the reaction mixture constitutes a highly stereoselective synthesis of (E,Z)-2,4-heptadiene (5a). If the bulky diisobutylaluminum group adds preferentially to C-4 of 4,[8] it should encounter less steric hindrance when adding to the E diastereomer; however, the exact regiochemistry of this addition has not yet been determined.[16]

In order to utilize this synthetic sequence for the preparation of 10, the starting 6-deuterio-2-hepten-4-yne (9) was secured through the reaction of acetic anhydride with the Grignard reagent from 3-penten-1-yne (3),[9] diisobutylaluminum hydride reduction of the resulting 2-hepten-4-yn-6-one (6),[10] mesylation,[11] and lithium aluminum deuteride reduction[12] as depicted in Scheme II. Hydrogenation of the labeled enyne 9 over freshly prepared Lindlar catalyst[5] in scrupulously dried cyclohexane afforded the title compound (10) in 25% yield based on starting 3-penten-1-yne (3). The product was obtained as a mixture of E,Z and Z,Z diastereomers which could be separated by preparative gas chromatography. Mass spectrometric analysis revealed the product to be >98% d_1.

Experimental Section

^{1}H NMR spectra were obtained on a Varian T-60 instrument. Infrared spectra were recorded on a Beckman IR-20 spectrophotometer. Mass spectra were secured on a Finnigan 1015D quadrupole mass spectrometer with a variable leak inlet, an ion source temperature of 55 °C, an ionization potential of 70 eV, and, for chemical ionization spectra, a reagent gas pressure of 1.0 Torr. Analytical and preparative

Scheme II

$$CH_3CH = CHC \equiv CH \longrightarrow CH_3CH = CHC \equiv C\overset{\overset{\displaystyle O}{\|}}{C}CH_3$$

3   6

$$\longrightarrow CH_3CH = CHC \equiv C\overset{\overset{\displaystyle OH}{|}}{C}HCH_3 \longrightarrow CH_3CH = CHC \equiv C\overset{\overset{\displaystyle O=S=O}{|}}{C}HCH_3$$

7   8

$$\longrightarrow CH_3CH = CHC \equiv C\overset{\overset{\displaystyle D}{|}}{C}HCH_3 \longrightarrow$$

9

10a (*E,Z*)
10b (*Z,Z*)

gas chromatographic separations were achieved on a Varian Model A90-P instrument using the following columns: A, 6.0 m × 6 mm 20% Carbowax 20M on Chromosorb W aluminum column; B, 7.6 m × 6 mm 20% β,β'-oxydipropionitrile on Chromosorb P copper column; C, 7.6 m × 6 mm 20% Carbowax 20M on Chromosorb W copper column; D, 4.6 m × 6 mm 10% SE-30 on Chromosorb W aluminum column; E, 1.5 m × 6 mm 30% saturated AgNO$_3$ in glycerol on Firebrick copper column.

Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

2-Hepten-4-yne (4).[13] Ammonia (350 mL) was condensed in a 1-L, three-neck round-bottom flask fitted with a mechanical stirrer and dry ice condenser. After 0.2 g of Fe(NO$_3$)$_3$ and 10.5 g (450 mmol) of Na pellets had been added over 30 min, the gas inlet tube was replaced with an addition funnel. After all the Na had reacted, 15.0 g (230 mmol) of 3-penten-1-yne (3) was added with stirring. After 3 h, 48 mL (650 mmol) of ethyl bromide was added. The reaction mixture was stirred and allowed to warm to room temperature over 8 h. After cooling to 0 °C, 50 mL of H$_2$O in 75 mL of ethyl ether was added with stirring. The ethereal layer was removed, combined with the ether extracts of the neutralized aqueous phase, dried (MgSO$_4$), filtered, and distilled (bp 100–105 °C) to give 12.4 g (58%) of 4. Analytically pure samples of 4 were secured through preparative gas chromatography using column A at 75 °C: IR (CHCl$_3$) ν_{CH} 2990–2860, $\nu_{C\equiv C}$ 2220, $\nu_{C=C}$ 1640 cm^{-1}; methane chemical ionization mass spectral fragmentations for [M + H]$^+$ *m/e* 95, [M]$^+$ 94, [M − CH$_3$]$^+$ 79; ^{1}H NMR (cis isomer, CDCl$_3$) δ 1.10 (methyl, t, *J* = 7 Hz, 3 H), 1.89 (methyl, d, *J* = 7 Hz, 3 H), 2.30 (methylene, q, *J* = 7 Hz, 2 H), 5.40 (C-3 vinyl, d of m, J_1 = 12 Hz, J_2 = 2 Hz, 1 H), 5.7 (C-2 vinyl, d of q, J_1 = 12 Hz, J_2 = 7 Hz, 1 H); ^{1}H NMR (trans isomer, CDCl$_3$) δ 1.08 (methyl, t, *J* = 7 Hz, 3 H), 1.85 (methyl, d, *J* = 7 Hz, 3 H), 2.30 (methylene, q, *J* = 7 Hz, 2 H), 5.45 (C-3 vinyl, d of m, J_1 = 16 Hz, J_2 = 2 Hz, 1 H), 6.0 (C-2 vinyl, d of q, J_1 = 16 Hz, J_2 = 7 Hz, 1 H).

2-Hepten-4-yn-6-one (6). Freshly prepared 1-propylmagnesium chloride (19.5 mmol) in 45 mL of ether contained in a 500-mL three-neck round-bottom flask with a dry ice condenser was treated with 3-penten-1-yne (3, 13.6 mmol) at −78 °C with mechanical stirring under dry nitrogen. After warming to 25 °C over 8 h, the reaction mixture was cooled to −78 °C, treated with 30 mL of freshly distilled acetic anhydride in 20 mL of anhydrous ether with stirring under dry nitrogen, allowed to stir for 2 h at −78 °C, warmed to 25 °C, heated at reflux for 2 h, and quenched through the addition of 35 mL of H$_2$O at 0 °C. This mixture was stirred and allowed to warm to 25 °C over 8 h. The product (6) was isolated in 70% yield after extraction into ether (3 × 15 mL), washing with saturated NaHCO$_3$ (2 × 15 mL) and H$_2$O (1 × 20 mL), drying (MgSO$_4$), filtering, and distilling [bp 75–80 °C (18 mm)] through a Teflon spinning-band distillation column. Analytical samples were collected from column D operated at 127 °C: IR (cis isomer, CHCl$_3$) ν_{CH} 3030–2900, $\nu_{C\equiv C}$ 2180, $\nu_{C=O}$ 1662 cm^{-1}; IR (trans isomer, CHCl$_3$) ν_{CH} 3050–2920 cm^{-1}, $\nu_{C\equiv C}$ 2210, $\nu_{C=O}$ 1675, $\nu_{C=C}$ 1640, and $\nu_{C=CH}$ 965 and 985 cm^{-1}; electron impact mass spectrum (70 eV) [M]$^+$ *m/e* 108, [M − CH$_3$]$^+$ 93, [M − CH$_3$ − CO]$^+$ 65; ^{1}H NMR (cis isomer, CDCl$_3$) δ 1.90 (methyl, br d, *J* = 7 Hz, 3 H), 2.35 (methyl, s, 3 H), 5.55 (C-3 vinyl, d of m, J_1 = 11 Hz, J_2 = 2 Hz,

1 H), 6.2 (C-2 vinyl, d of q, J_1 = 11 Hz, J_2 = 7 Hz, 1 H); ^{1}H NMR (trans isomer, CDCl$_3$) δ 1.85 (methyl, br d, *J* = 7 Hz, 3 H), 2.38 (methyl, s, 3 H), 5.60 (C-3 vinyl, d of m, J_1 = 16 Hz, J_2 = 2 Hz, 1 H), 6.4 (C-2 vinyl, d of q, J_1 = 16 Hz, J_2 = 7 Hz, 1 H).

Anal. Calcd for C$_7$H$_8$O: C, 77.75; H, 7.46. Found: C, 77.67; H, 7.53.

2-Hepten-4-yn-6-ol (7). In a 1-L three-neck round-bottom flask fitted with a reflux condenser, gas inlet tube, and a dropping funnel was placed 30.0 g (280 mmol) of 2-hepten-4-yn-6-one (6) in 50 mL of anhydrous ether. At 0 °C 440 mL (370 mmol) of 20% diisobutylaluminum hydride in hexane was added slowly with stirring under dry nitrogen. After the initial vigorous reaction had subsided, the reaction mixture was heated at reflux for 5 h. The reaction was quenched by adding the mixture to a slurry of 300 g of ice in 100 mL of H$_2$O and 150 mL of ether. The product was isolated in 71% yield after extraction (3 × 35 mL), washing with H$_2$O (3 × 55 mL), drying (MgSO$_4$), filtering, and distilling [bp 60–75 °C (7 mm)]. Analytical samples were obtained by preparative separations on column A operated at 130 °C: IR (cis isomer, CCl$_4$) ν_{OH} 3630–3120, ν_{CH} 3040–2860, $\nu_{C\equiv C}$ 2225, $\nu_{C=C}$ 1645, ν_{CO} 1090 and 1065, ν_{C-CH} 715 cm^{-1}; IR (trans isomer, CCl$_4$) same as for the cis isomer except $\nu_{C\equiv C}$ 2210, ν_{C-CH} 940 cm^{-1}; methane chemical ionization mass spectral fragmentations for [M + H]$^+$ *m/e* 111, [M + M − H$_2$O]$^+$ 93; ^{1}H NMR (cis isomer, CDCl$_3$) δ 1.50 (methyl, d, *J* = 6 Hz, 3 H), 1.88 (methyl, d of d, J_1 = 7 Hz, J_2 = 2 Hz, 3 H), 1.98 (hydroxyl, s, 1 H), 4.70 (methine, br q, *J* = 6 Hz, 1 H), 5.45 (C-3 vinyl, d of m, J_1 = 11 Hz, J_2 = 2 Hz, 1 H), 6.0 (C-2 vinyl, d of q, J_1 = 11 Hz, J_2 = 7 Hz, 1 H); ^{1}H NMR (trans isomer, CDCl$_3$) δ 1.42 (methyl, d, *J* = 6 Hz, 3 H), 1.75 (methyl, d of d, J_1 = 7 Hz, J_2 = 2 Hz, 3 H), 1.80 (hydroxyl, s, 1 H), 4.60 (methine, br q, *J* = 6 Hz, 1 H), 5.45 (C-3 vinyl, d of m, J_1 = 16 Hz, J_2 = 2 Hz, 1 H), and 6.2 (C-2 vinyl, d of q, J_1 = 16 Hz, J_2 = 7 Hz, 1 H).

Anal. Calcd for C$_7$H$_{10}$O: C, 76.33; H, 9.15. Found: C, 76.56; H, 9.24.

6-Deuterio-2-hepten-4-yne (9). The mesylate of 2-hepten-4-yn-6-ol (7) was prepared by the method of Crossland and Servis.[11] To a 100-mL three-neck round-bottom flask fitted with a reflux condenser, dropping funnel, and gas inlet tube was added 2.00 g (18.2 mmol) of 2-hepten-4-yn-6-ol (7), 50 mL of anhydrous ether, and 2.80 g (27.3 mmol) of freshly distilled triethylamine. A solution of 3.13 g (2.73 mmol) of freshly distilled methanesulfonyl chloride in 10 mL of ether was added over 10 min at 0 °C with stirring under dry nitrogen. After stirring an additional 2 h at 0 °C, the reaction mixture was slurried with 0.5 g of MgSO$_4$, filtered, and concentrated under vacuum at 25 °C: ^{1}H NMR (CDCl$_3$) δ 3.00 (mesylate methyl, s, 3 H).

The mesylate was found to be thermally unstable and did not hold up well to the usual mesylate purification procedure;[11] however, the concentrated reaction mixture was entirely satisfactory for the reduction.

In a 250-mL three-neck round-bottom flask fitted with an addition funnel, reflux condenser, and gas inlet tube was placed 0.900 g (21.4 mmol) of lithium aluminum deuteride and 40 mL of anhydrous ether. The crude mesylate from 7 was dissolved in 10 mL of ether and added slowly to the reaction vessel with stirring under dry nitrogen at 0 °C. The reaction mixture was stirred for 5 h as it was allowed to warm to 25 °C, whereupon it was again cooled to 0 °C and then quenched with 50 mL of H$_2$O. After stirring for 30 min, the mixture was filtered and washed with 10% HCl (1 × 30 mL at 0 °C), saturated NaHCO$_3$ (2 × 30 mL at 0 °C), and saturated NaCl (2 × 30 mL). After drying (MgSO$_4$) and filtering, the product was isolated in 50% yield by distillation. Analytical samples were secured from GLC column C operated at 75 °C. The product was chromatographically identical with the unlabeled material which was prepared from the anion of 3-penten-1-yne (3) with ethyl bromide or the lithium aluminum hydride reduction of the mesylate of 2 hepten-4-yn-6-ol (7). Electron impact mass spectrometric analysis revealed the product to be 98% d$_1$ and 2% d$_0$. The NMR spectrum of 9 differs from the unlabeled material (4) in that the δ 1.10 and 1.08 methyl triplets are reduced to broader doublets and the δ 2.30 methylene quartets exhibit a 50% reduction in peak area (from 2 H to 1 H).

2,4-Heptadiene (5). To a 50-mL three-neck round-bottom flask equipped with a reflux condenser, dropping funnel, and gas inlet tube was added 1.03 g (11.1 mmol) of 2-hepten-4-yne (4) followed by 14.4 mL (12.2 mmol) of 20% diisobutylaluminum hydride in hexane with magnetic stirring under dry nitrogen at 0 °C. After the vigorous reaction had subsided, the ice bath was replaced with an oil bath and the reaction was heated at 50 °C for 5 h. The resulting mixture was poured over a mixture of 15 mL of ether, 5 g of crushed ice, and 10 mL of H$_2$O. The product was isolated in 50% yield after extraction into ether (3 × 5 mL), drying (Na$_2$SO$_4$), filtering, and distilling (bp 106–109 °C). Analytical samples were collected from GLC column C operated

at 105 °C. (The individual diene diastereomers could be isolated using a combination of columns B and E.) The isolated 2,4-heptadiene was identical in all respects with authentic material (Chemical Samples Co.) except in isomer distribution. By NMR spectral analysis and independent synthesis,[14] the product was found to be a mixture of *E,Z* and *Z,Z* diastereomers.

6-Deuterio-2,4-heptadiene (10). In a 250-mL three-neck round-bottom flask fitted with a dry ice condenser, dropping funnel and gas inlet tube was placed 70 mL of dry cyclohexane, 0.5 mL of freshly distilled quinoline, and 50 mg of Lindlar catalyst. Hydrogen gas was flushed through the flask held at 0 °C in an ice bath with vigorous stirring for several minutes before 1.00 g (10.5 mmol) of 6-deuterio-2-hepten-4-yne (9) was added. The reaction mixture was stirred under a positive pressure of hydrogen for 8 h as it was allowed to slowly warm from 0 to 25 °C. It was then filtered with the aid of Celite and preparatively separated from the solvent on GLC column C at 105 °C to give a mixture of *E,Z* and *Z,Z* diastereomers.[15] Electron impact mass spectrometric analysis showed the product to be 98% d_1 and 2% d_0.

Registry No.—(*E*)-3, 2004-69-5; (*Z*)-3, 1574-40-9; (*E*)-4, 63640-74-4; (*Z*)-4, 63640-75-5; **5a**, 54354-36-8; **5b**, 31357-25-2; (*E*)-6, 63640-76-6; (*Z*)-6, 63640-77-7; (*E*)-7, 63640-78-8; (*Z*)-7, 63640-79-9; (*E*)-8, 63640-80-2; (*Z*)-8, 63640-81-3; (*E*)-9, 63640-82-4; (*Z*)-9, 63640-83-5; **10a**, 63640-84-6; **10b**, 63640-85-7; ethyl bromide, 74-96-4; propyl chloride, 540-54-5.

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(16) **Note Added in Proof.** Deuterium labeling experiments confirm that the diisobutylaluminum group does indeed add to C-4 of **4**.[14]

Synthesis of *exo*-(7-Bicyclo[4.1.0]heptyl)oxirane and *exo*-7-Vinylbicyclo[4.1.0]heptane

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Although during the last few years many vinylcyclopropane and cyclopropyl oxirane derivatives have been prepared and their rearrangement investigated,[1] the relatively simple (7-bicyclo[4.1.0]heptyl)oxirane (5) still seems to be unknown and the synthesis of 7-vinylbicyclo[4.1.0]heptane (6) has been reported only recently.[2] In connection with another project, ethyl *exo*-(7-bicyclo[4.1.0]heptyl)glyoxylate (1) was synthesized in our laboratory.[3] This α-keto ester containing the bi-

cyclo[4.1.0]heptyl moiety attached to a bifunctional two-carbon unit is a suitable starting material for the desired cyclopropane derivatives.

Reduction of the glyoxylate 1 with LiAlH₄ gave the diol 2, a potential common precursor of both compounds 5 and 6. According to the method of Corey and Winter,[4] the diol 2 was treated with thiocarbonyldiimidazole in refluxing toluene to convert it into the cyclic thionocarbonate 3, which was converted to the desired olefin 6 by treatment with an excess of trimethyl phosphite at 110 °C.
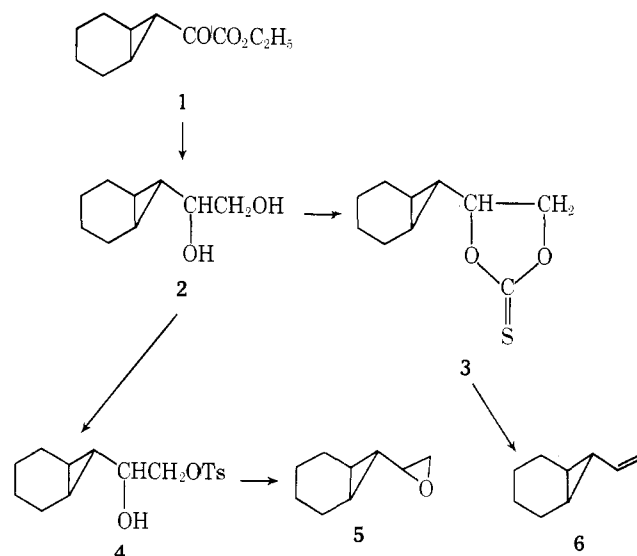
The exo nature of the compounds all along the reaction sequence was proven by the oxidative conversion of both the diol 2 and the olefin 6 into the known *exo*-bicyclo[4.1.0]heptane-7-carboxylic acid.[5,10] In contrast with this result, in the direct vinylcyclopropanation of cyclohexene with vinyldiazomethane[2] a mixture of the exo and endo isomers was obtained, with the unusual preferential formation of the more congested endo isomer.

Epoxidation of the 7-vinylnorcarane 6 with *m*-chloroperbenzoic acid, a potential route to oxirane 5, gave a complex product mixture. Systems having contiguous cyclopropane and epoxide rings are known to be rather unstable and the participation of the cyclopropane ring in developing neighboring carbocation centers is generally accepted to explain the formation of secondary products such as diols, esters, etc., instead of the desired aldehydes.[6] The synthesis of oxirane 5 has been accomplished in rather high yields by the selective tosylation of the diol 2, followed by elimination of tosic acid from the monotosylate 4 under basic conditions.

Experimental Section[7]

***exo*-(7-Bicyclo[4.1.0]heptyl)ethane-1,2-diol (2).**[8] To a magnetically stirred slurry of LiAlH₄ (6.0 g, 0.16 mol) in dry THF (100 mL) a solution of 1[3] (3.2 g, 16 mmol) in THF (100 mL) was added dropwise at room temperature. After the addition was completed, the mixture was heated at reflux for 3.5 h, excess LiAlH₄ was destroyed by cautious addition of water (20 mL), followed by NaOH (10% solution, 10 mL), and the THF was removed. The residue was diluted with saturated NaCL solution and extracted with CHCl₃. On evaporation, the dried CHCl₃ extract gave 2.3 g (90%) of semisolid, crude diol 2. The analytical sample, crystallized from hexane–pentane (3:2), melted at 52–54 °C: IR (CHCl₃) 3400 (br), 3500 cm⁻¹; NMR δ 0.35–1.0 (m, 3 H, cyclopropyl), 1.0–2.3 (m, 8 H, cyclohexane CH₂), 2.8–3.8 (m, 3 H, –CHOHCH₂OH); mass spectrum *m/e* 138(M⁺ − H₂O).

Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.50; H, 10.36.

Monotosylation of Diol 2. To an ice-cold solution of diol 2 (0.22 g, 1.46 mmol) in dry pyridine (7 mL) was added *p*-TsCl (0.3 g, 1.58 mmol). The mixture was kept in the refrigerator for 16 h, then 5% NaHCO₃ solution (15 mL) was added, followed by EtOAc (15 mL). The mixture was stirred for a few minutes, the phases were separated,