(13) Melting points were determined on a Fisher-Johns block and are uncorrected. Infrared spectra were obtained of liquid films or carbon tetrachloride solutions as noted on a Perkin-Elmer 457 instrument. NMR spectra were recorded on Varian A-60A or EM-360 spectrometers with Me_4Si as an internal standard. GC data were recorded on a Varian Aerograph A90-P3 instrument with a thermal conductivity detector. Mass spectra were recorded on a Varian MAT CH5 instrument. Elemental analyses were performed by Atlantic Microlabs, Inc., Atlanta, Ga.

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Synthesis of 2-Substituted 4-Oxahomoadamantanes

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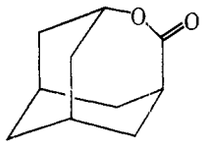
An entry into 2-substituted 4-oxahomoadamantanes has been developed. Treatment of bicyclo[3.3.1]non-6-ene-3-*endo*-methanol with *m*-chloroperbenzoic acid gives 2-*exo*-hydroxy-4-oxahomoadamantane (**8**). Jones oxidation of **8** provides the corresponding ketone, which undergoes reduction with sodium borohydride to give exclusively 2-*endo*-hydroxy-4-oxahomoadamantane. Extensions of this reaction permit the preparation of 2,5-disubstituted and 2,5,5-trisubstituted 4-oxahomoadamantanes. An improved synthesis of 4-oxahomoadamantane is also noted, and its ^{13}C NMR spectrum is reported.

The synthesis, chemistry, and pharmacology of heteroadamantanes and related cage compounds have attracted considerable attention.[2] With the exception of 4-oxahomoadamantan-5-one[3,4] (**1**) and its derivatives,[5] the only substituted 4-oxahomoadamantanes which are known are compounds **2–6**.[6] We now wish to report the stereoselective



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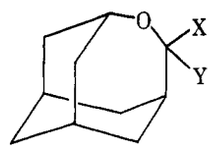
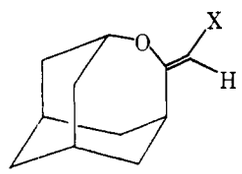


2, X = OH; Y = CH_3
3, X = OH; Y = CH_2Cl
4, X = I; Y = CH_2I



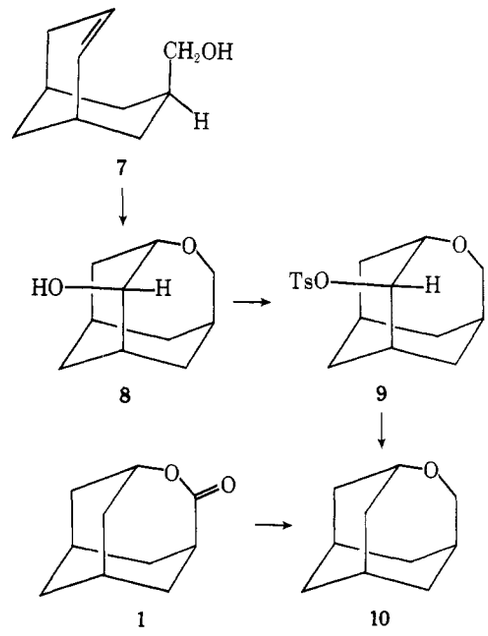
5, X = H
6, X = I

synthesis of both 2-*exo*-hydroxy- and 2-*endo*-hydroxy-4-oxahomoadamantane.[7] Extensions of the reactions employed to prepare these compounds permit the synthesis of 2,5-disubstituted and 2,5,5-trisubstituted 4-oxahomoadamantanes.

Results and Discussion

Treatment of bicyclo[3.3.1]non-6-ene-3-*endo*-methanol[3a,4a] (**7**) with *m*-chloroperbenzoic acid affords 2-*exo*-hydroxy-4-oxahomoadamantane (**8**) in ca. 70% yield. The skeletal framework of **8** follows from its conversion to the known ether,[3a,8] 4-oxahomoadamantane (**10**). Reaction of **8** with *p*-toluenesulfonyl chloride in pyridine gives exo tosylate **9**. Subsequent treatment of **9** with lithium aluminum hydride provides **10**. Owing to some minor discrepancies between the ^1H NMR parameters observed for **10** and those previously reported for this compound,[9] ether **10** was also synthesized by an independent route. Treatment of lactone **1** with boron trifluoride etherate and lithium aluminum hydride provides **10** in 95% yield. The physical and spectral properties of **10** prepared by these independent routes are identical. Moreover, consistent with the presence of a plane of symmetry in **10**, the ^{13}C NMR spectrum of **10** contains only seven signals and three of these signals are twice as intense as the others.[10] Since the reported syntheses of **10** all either proceed in low yield and/or give mixtures of reaction products[3a,8] and since **1** can readily be prepared from commercially available 2-adamantanone[3] (**11**), the route **11** → **1** → **10** appears to be the method of choice for the synthesis of 4-oxahomoadamantane.

The assigned skeletal position and stereochemistry of the hydroxyl substituent in **8** follow in part from its mode of synthesis. Thus, **7** → **8** is rationalized as occurring by initial epoxidation of **7** from the less sterically encumbered face of the carbon–carbon double bond to give **12**, which then undergoes intramolecular nucleophilic attack by the hydroxylic oxygen to provide **8**. In order to firmly establish the stereochemistry at C-2 in **8**, the C-2 epimer of **8** was also prepared. Oxidation of **8** with Jones reagent gives 4-oxahomoadamantan-2-one (**13**), and sodium borohydride reduction of **13** provides 2-*endo*-hydroxy-4-oxahomoadamantane (**14**). In an earlier study we were not able to devise GLC conditions



7

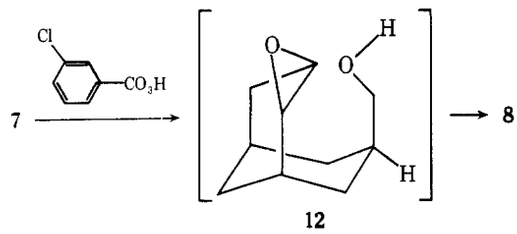
8

9

1

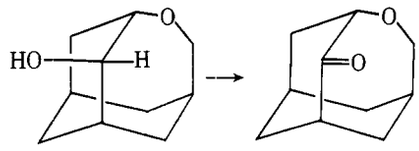
10

0022-3263/78/1943-3179$01.00/0

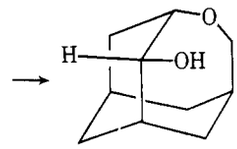


12

for the effective separation of 2-*exo*- and 2-*endo*-hydroxyhomoadamantane.[11] However, apparently due to the significant intramolecular hydrogen bonding present in **14**, epimeric alcohols **8** and **14** could be readily resolved by GLC. Analysis of the crude reaction mixture from **13** → **14** showed that endo



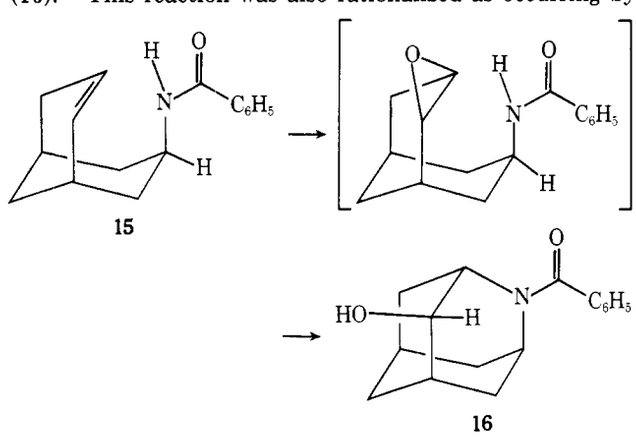
8 **13**



14

alcohol **14** is obtained from this reaction in greater than 99% stereochemical purity. This result is consistent with an examination of molecular models which clearly indicates that attack at the carbonyl carbon in **13** across the face of the seven-membered ring should be significantly impeded by the endo hydrogen at C-5. By contrast, there is no apparent steric hindrance to attack at the carbonyl carbon in **13** across the face of the six-membered ring.

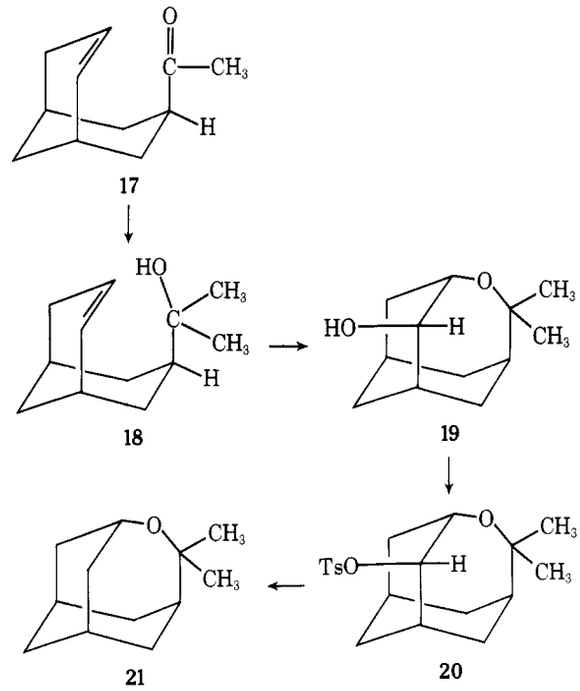
The formation of **8** from **7** parallels the earlier observation by Staas and Spurlock that treatment of bicyclo[3.3.1]non-6-en-3-*endo*-ylbenzamide (**15**) with *m*-chloroperbenzoic gives exclusively 4-*anti*-hydroxy-*N*-benzoyl-2-azaadamantane (**16**).[5a] This reaction was also rationalized as occurring by



15 **16**

spontaneous intramolecular attack on an initially formed epoxide intermediate.[5a] Other reactions of *m*-chloroperbenzoic acid with olefins which have neighboring functional groups are well known.[12]

Since a variety of α-substituted secondary alcohols and α,α-disubstituted tertiary alcohols related to **7** can readily be prepared, the reaction **7** → **8** offers a route for the synthesis of a number of 2,5-disubstituted and 2,5,5-trisubstituted 4-oxahomoadamantanes.[13] In order to illustrate this point, we have prepared 5,5-dimethyl-2-*exo*-hydroxy-4-oxahomoadamantane (**19**). Treatment of ketone **17** with an excess of methyllithium gives tertiary alcohol **18**. Subsequent reaction of **18** with *m*-chloroperbenzoic acid provides **19** in 95% yield.



17 **18** **19** **20** **21**

Consistent with the structure assignment, the ^{1}H NMR spectrum of **19** contains a broad multiplet for the C-2 and C-3 methine protons at δ 3.87–3.67 and two singlets for the constitutionally heterotopic C-5 methyls at δ 1.29 and 1.26. The skeletal framework of **19** was firmly established by its conversion to 5,5-dimethyl-4-oxahomoadamantane (**21**). Reaction of **19** with *p*-toluenesulfonyl chloride in pyridine gives tosylate **20** which is readily reduced with lithium aluminum hydride to provide **21**. The ^{1}H NMR spectrum of **21** shows a sharp singlet at δ 1.25 for the enantiotopic methyls at C-5.

Experimental Section

Melting points were obtained in sealed capillary tubes using a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were obtained on Perkin-Elmer 180 or 337 spectrophotometers. Proton magnetic resonance spectra were recorded with Varian A-60A or Perkin-Elmer R-12B 60-MHz spectrometers and are referenced to an internal standard of tetramethylsilane. Apparent splittings are reported in all cases. Unless noted otherwise, yields were obtained by integration of appropriate signals in the ^{1}H NMR spectrum of the product(s) vs. the signal of a predetermined amount of an added standard (generally chloroform or trichloroethylene) and are regarded as being accurate to ca. ±10%. Elemental analyses were performed by Micro-Analysis, Inc., Wilmington, Del.

2-*exo*-Hydroxy-4-oxahomoadamantane (8). A solution of 85% *m*-chloroperoxybenzoic acid (1.22 g, 6 mmol) in methylene chloride (25 mL) was added dropwise to a stirred solution of bicyclo[3.3.1]-non-6-ene-3-*endo*-methanol[3a,4a] (760 mg, 5 mmol) in methylene chloride (50 mL) which was maintained at 0 °C. The reaction was stirred at room temperature for 36 h, at which time the excess peracid present was destroyed by the addition of 10% aqueous sodium sulfite until a negative starch–iodide test was obtained. The reaction mixture was diluted with methylene chloride (50 mL), washed successively with 5% aqueous sodium bicarbonate (4 × 25 mL) and water (2 × 15 mL), and then dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure gave 605 mg of **8** (72% yield) as a white solid which was homogeneous by GLC analysis (10 ft × 0.25 in DC-550 column; 200 °C). Purification of the product by GLC (above conditions) provided **8**: mp 302–303 °C; NMR δ ($CDCl_3$) 4.14–3.73 (m, 4 H) and 2.51–1.13 (m, 12 H); IR ν (CCl_4) 3635, 3420, 2915, 1460, 1440, 1145, 1100, 1075, 1060, and 1035 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.53; H, 9.41.

2-*exo*-*p*-Toluenesulfonyloxy-4-oxahomoadamantane (9). Purified[14] *p*-toluenesulfonyl chloride (1.2 g, 59 mmol) was added to a solution of **8** (500 mg, 20 mmol) in freshly distilled dry pyridine (15 mL) at 0 °C. The reaction was stirred until a homogeneous solution was obtained, and it was then stored at 5 °C for 24 h. At this point the reaction was quenched by pouring it into a slurry of ice and water (50

mL) and stirring it vigorously for 15 min. A white solid resulted which was suction filtered. The crude tosylate was dissolved in a minimal amount of petroleum ether at room temperature, treated with Darco G-60, and cooled in a dry ice–acetone bath until crystallization was complete. The crystals were collected by suction filtration and dried under vacuum at room temperature to afford 150 mg of **9** (16% yield) as a white powder: NMR δ ($CDCl_3$) 8.35–7.5 (d of d, 4 H, aromatic protons), 4.61 [br s, 1 H, CH(OTs)], 4.26–3.88 (br m, 3 H, –CH–O– and $-CH_2-O-$), and 2.79–0.96 (br m, 14 H; containing a methyl singlet at δ 2.54); IR ν (CCl_4) 2920, 1365, 1190, 1180, 1150, 1100, 1065, and 1000 cm^{-1}.

4-Oxahomoadamantane (10). A. A solution of **9** (150 mg, 0.5 mmol) in anhydrous ether (15 mL) was added dropwise to a stirred suspension of lithium aluminum hydride (90 mg, 2.7 mmol) in anhydrous ether (35 mL) and heated at reflux for 48 h. The reaction mixture was cooled in an ice bath, and the excess lithium aluminum hydride present was destroyed by the dropwise addition of ice-cold water (5 mL). The resulting white suspension was dissolved by the addition of 10% aqueous hydrochloric acid (25 mL). The aqueous layer was separated and extracted with ether (2 × 25 mL). The combined organic layers were washed successively with 5% aqueous sodium bicarbonate (3 × 25 mL) and water (25 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure afforded 70 mg of **10** (ca. quantitative yield) as a white solid which was homogeneous by GLC analysis (10 ft × 0.25 in DC-550 column; 175 °C). Purification by GLC (above conditions) provided **10** as a white solid: mp 271–272 °C (lit.[3a] mp 268–269 °C); ^1H NMR δ ($CDCl_3$) 4.38–4.12 (m, 1 H, –CH–O–), 3.93 (d, J = 2.5 Hz, 2 H, $-CH_2-O-$), and 2.21–1.43 (br m, 13 H); ^{13}C NMR[10] δ ($CDCl_3$) (tentative assignments) 74.3 (C-5), 72.1 (C-3), 37.8 (C-2 and C-11), 37.0 (C-7 and C-10), 35.4 (C-9), 34.4 (C-6), and 26.7 (C-1 and C-8); IR ν (CCl_4) 2915, 2850, 1440, 1255, 1145, 1110, 1065, 995, and 880 cm^{-1}.

B. A solution of lactone **1**[3] (530 mg, 3.2 mmol) and 45% boron trifluoride etherate complex (12 mL) in anhydrous ether (75 mL) was added dropwise to a stirred suspension of lithium aluminum hydride (1.0 g, 26 mmol) in anhydrous ether (100 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 45 min and then at reflux for 2 h. The reaction was then cooled to room temperature, and the excess lithium aluminum hydride present was destroyed by the dropwise addition of 10% aqueous hydrochloric acid (25 mL). The aqueous layer was separated and extracted with ether (2 × 50 mL). The combined organic layers were then washed successively with 5% aqueous sodium bicarbonate (4 × 25 mL) and water (25 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure gave 456 mg of **10** (95% yield) as a white solid. GLC analysis (10 ft × 0.25 in DC-550 column; 175 °C) of this material showed the presence of a single component. Purification of the product by GLC (above conditions) gave a white solid whose physical and spectral properties were identical with those of **10** obtained by procedure A.

4-Oxahomoadamantan-2-one (13). To a stirred solution of **8** (500 mg, 3 mmol) in acetone (30 mL) at 0 °C was added 4 mL of a freshly prepared solution of Jones reagent (2.8 g of chromic anhydride, 4.5 mL of sulfuric acid, and 12 mL of water). The reaction was stirred at 0 °C for 1 h and at room temperature for 3 h, diluted with water (15 mL), and stirred for an additional hour. At this point the reaction mixture was saturated with sodium chloride and extracted with ether (4 × 25 mL). The combined ether extracts were washed successively with saturated aqueous sodium bicarbonate (4 × 15 mL) and water (2 × 15 mL) and dried over anhydrous magnesium sulfate. The solvent was evaporated at reduced pressure, and the residue was sublimed (90 °C at 0.05 mm) to give 370 mg of **13** (74% yield) as a white solid. GLC analysis (10 ft × 0.25 in DC-550 column; 200 °C) showed the presence of a single component. Purification by GLC (above conditions) afforded **13** as a white solid: mp 277–278 °C; NMR δ (CCl_4) 4.12–4.03 (m, 3 H, –CH–O– and $-CH_2-O-$) and 2.68–1.47 (br m, 11 H); IR ν (CCl_4) 2925, 2860, 1726, 1460, 1440, 1280, 1200, 1135, and 1060 cm^{-1}.

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.53; H, 8.57.

2-*endo*-Hydroxy-4-oxahomoadamantane (14). A solution of sodium borohydride (265 mg, 7 mmol) in methanol (10 mL) was added to a stirred solution of **13** (290 mg, 1.7 mmol) in methanol (25 mL) at 0 °C. The reaction was stirred at 0 °C for 45 min and then at room temperature for 45 min, at which point the reaction was quenched by the addition of water (10 mL). The resulting solution was saturated with sodium chloride and extracted with ether (3 × 50 mL), and the combined extracts were dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure provided 275 mg of **14** (96% yield) as a white solid. GLC analysis (10 ft × 0.25 in SE-30 column; 190 °C) indicated a single component. Purification by GLC (above conditions) afforded **14** as a white solid: mp 314–315 °C; NMR δ (CCl_4) 4.18–3.96 (m, 1 H, –CH–O–), 3.90–3.73 (m, 2 H, $-CH_2-O-$), 3.48 [dt, J = 4 and 1 Hz, 1 H, CH(OH)], 2.76 (s, 1 H, OH), and 2.23–1.25 (br m, 11 H); IR ν (CCl_4) 3555, 3400, 2920, 2860, 1445, 1390, 1135, 1105, 1080, and 1050 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.60; H, 9.43.

Oxidation of **14** with Jones reagent by the procedure described for **8** → **13** regenerated **13**.

3-*endo*-Acetylbicyclo[3.3.1]non-6-ene (17). An ethereal solution of methyllithium (80 mL of a 1.65 M solution; ca. 132 mmol) was added dropwise to a vigorously stirred solution of 3-*endo*-carboxybicyclo[3.3.1]non-6-ene[4a] (9.8 g, 59 mmol) in anhydrous ether at 0 °C at such a rate that the temperature of the reaction mixture did not exceed 5 °C. Following this addition, the reaction was stirred at 0 °C for 30 min and at room temperature for 4 h. The reaction was quenched by slowly pouring the reaction mixture into a saturated solution of ammonium chloride. The aqueous layer was separated and extracted with ether (4 × 50 mL). The combined ether layers were washed with 5% aqueous sodium bicarbonate (4 × 50 mL; acidification of the combined basic washes afforded a 300-mg recovery of unreacted starting material) and water (2 × 50 mL) and then dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure provided a yellow liquid. Vacuum distillation of this material gave 7.9 g (84% yield) of ketone **17** as a colorless liquid: bp 70–73 °C (0.5 mm); NMR δ ($CDCl_3$) 5.71–5.18 (br m, 2 H, –CH=CH–) and 2.68–1.28 (br m, 14 H; containing a methyl singlet at δ 2.05); IR ν (CCl_4) 3020, 2925, 2905, 2855, 1704, 1430, 1350, 1210, 1190, 1170, and 1105 cm^{-1}.

The semicarbazone derivative of **17** was prepared according to the procedure outlined by Fieser,[15] mp 209–210 °C.

Anal. Calcd for $C_{12}H_{19}N_3O$: C, 65.13; H, 8.65; N, 18.99. Found: C, 64.89; H, 8.87; N, 18.87.

α,α-Dimethylbicyclo[3.3.1]non-6-ene-3-*endo*-methanol (18). A 2 M ethereal methyllithium solution (5 mL, ca. 10 mmol) was added to a stirred solution of **17** (300 mg, 1.8 mmol) in anhydrous ether (60 mL) at 0 °C at such a rate that the temperature of the reaction mixture did not exceed 5 °C. The reaction mixture was stirred at 0 °C for 2 h and then carefully quenched by the dropwise addition of water (40 mL). The reaction mixture was extracted with ether (3 × 40 mL), and the combined ether extracts were dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure gave 290 mg of **18** (89% yield) as a viscous liquid. The crude product was purified by GLC (10 ft × 0.25 in SE-30 column; 200 °C) which afforded **18** as a colorless oil: NMR δ (CCl_4) 6.03–5.30 (m, 2 H, –CH=CH–) and 2.52–0.94 (br m, 18 H; containing the gem dimethyl singlet at δ 1.09); IR ν (CCl_4) 3625, 3500–3400, 3020, 2935, 2905, 2840, 1380, 1370, 935, 925, and 910 cm^{-1}.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.80; H, 10.97.

2-*exo*-Hydroxy-5,5-dimethyl-4-oxahomoadamantane (19). A solution of 85% *m*-chloroperoxybenzoic acid (625 mg, 3 mmol) in methylene chloride (50 mL) was added dropwise to a stirred solution of **18** (500 mg, 2.8 mmol) in methylene chloride (100 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and at room temperature for 23 h. Workup of the reaction mixture followed the procedure described for **7** → **8**. Evaporation of the solvent at reduced pressure gave 520 mg of **19** (95% yield) as a colorless liquid which solidified on standing. Analysis of the crude reaction mixture by GLC (10 ft × 0.25 in SE-30 column; 225 °C) indicated the presence of a single component. Purification of this material by GLC (above conditions) afforded **19** as a white solid: mp 55.5–57 °C; NMR δ (CCl_4) 3.87–3.67 [m, 2 H, –CH–O– and CH(OH)], 2.86 (s, 1 H, OH), and 2.43–1.10 (br m, 17 H; containing methyl singlets at δ 1.29 and 1.26); IR ν (CCl_4) 3625, 3400, 2910, 1550, 1460, 1445, 1380, 1365, 1145, 1050, and 1035 cm^{-1}.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.40; H, 10.24.

5,5-Dimethyl-4-oxahomoadamantane (21). Purified[14] *p*-toluenesulfonyl chloride (180 mg, 0.9 mmol) was added to a solution of **19** (175 mg, 0.9 mmol) in freshly distilled dry pyridine (4 mL) at 0 °C. The reaction mixture was stirred at 0 °C until a homogeneous solution was obtained, and then it was stored at ca. 5 °C for 3 days. The reaction was quenched by pouring it into a slurry of ice and water (25 mL) and then stirring it vigorously for 30 min. The resulting pale yellow solid was filtered by suction and dried under vacuum at room temperature to provide 100 mg (ca. 30% yield) of **2-*exo*-*p*-toluenesulfonyloxy-5,5-dimethyl-4-oxahomoadamantane (20)** as an off-white powder.

A solution of **20** (100 mg, 0.3 mmol) in anhydrous ether (10 mL) was added dropwise to a stirred suspension of lithium aluminum hydride

(50 mg, 1.3 mmol) in anhydrous ether (50 mL) and heated at reflux for 48 h. Workup of the reaction mixture followed the procedure described for **9** → **10**. Evaporation of the solvent at room temperature afforded 42 mg (81% yield) of **21** as a colorless liquid. Analysis of the crude reaction mixture by GLC (10 ft × 0.25 in DC-550 column; 175 °C) indicated only a single component. Purification by GLC (above conditions) provided pure **21** as an oil: NMR δ (CCl_4) 4.18–3.93 (br s, 1 H, –CH–O–), 2.34–1.43 (br m, 13 H), and 1.25 (s, 6 H, gem dimethyls); IR ν (CCl_4) 2975, 2905, 2850, 1460, 1440, 1385, 1360, 1255, 1215, 1145, 1120, 1095, 1070, and 1050 cm^{-1}.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 80.02; H, 11.08.

Acknowledgment. This work was supported by grants from the Research Corporation and the University of Delaware Research Foundation.

Registry No.—**1**, 21898-84-0; **7**, 21932-99-0; **8**, 66483-52-1; **9**, 66483-53-2; **10**, 21898-86-2; **13**, 66483-54-3; **14**, 66537-45-9; **17**, 66483-55-4; **17** semicarbazone, 66483-56-5; **18**, 28644-53-3; **19**, 66483-57-6; **20**, 66483-58-7; **21**, 66483-59-8; 3-*endo*-carboxybicyclo[3.3.1]non-6-ene, 21932-98-9.

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Insect Antifeedants. 1. Diels–Alder Approach to the Synthesis of Ajugarin I

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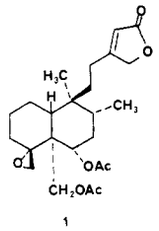
An approach to the synthesis of the antifeedant ajugarin I (**7**) employing a Diels–Alder reaction for the preparation of the decalin position of the molecule is described. Cycloaddition of 2,4-pentadien-1-ol (**5**) and carbomethoxy-*p*-benzoquinone (**6**) affords a mixture of hemiacetals **8** and **9** having the same gross regio- and stereochemistry. The structures of the adducts are determined by spectroscopic means and X-ray crystallography of their reduced transformation products **10** and **11**. Conversion of the initial adduct mixture to a potentially synthetically useful intermediate **31** is accomplished by reductive cleavage of a γ-keto unsaturated acetal, **29**.

Ajugarin I (**1**) isolated from *Ajuga remota* (Labitae) exhibits significant antifeeding activity against African army worms.[1] It is a member of the clerodane class[2] of rearranged diterpenes, many of which have also been shown to act as in-

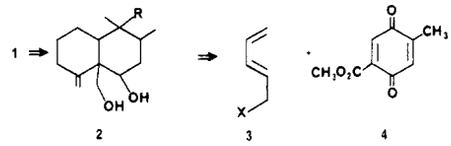


1

sect antifeedants.[3] The structure and activity of ajugarin I were recently described by Nakanishi and associates.

We are presently embarked on a project directed toward the synthesis of ajugarin I and its congeners. In this paper, we report some of the results of a Diels–Alder approach to the construction of the decalin portion of the structure of the natural product.

The placement and the nature of the groups about the periphery of the bicyclic unit of **1** suggested to us the retrosynthetic plan illustrated in brief form in the scheme **1** → **2** → **3** + **4**. As shown, we visualized a rapid and efficient construction of the decalin system by a cycloaddition reaction of suitably substituted diene–dienophile partners. In terms of the specific structural requirements of the Diels–Alder combination, the choice of a 1-heteroalkyl-substituted butadiene **3** and a carboalkoxy-*p*-quinone[4] seemed most appropriate.



2 **3** **4**

Our initial efforts in an experimental realization of this synthetic plan have been focused on the addition of several substituted butadienes to the unsubstituted carbomethoxy-*p*-benzoquinone (**6**).[4] The discussion to follow is concerned with the structural and stereochemical outcome of two of these cycloadditions and with the results of several transformations carried out with the initial Diels–Alder adducts.

The first problem to be faced in the Diels–Alder approach to ajugarin I was the question of orientation in the proposed cycloaddition reaction. Dienes substituted at the 1 position are generally assumed to follow an "ortho" rule in Diels–Alder

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