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On the Mechanism of Acid Promoted Ring Opening of a Pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-Spiroannulated Oxetane[1]

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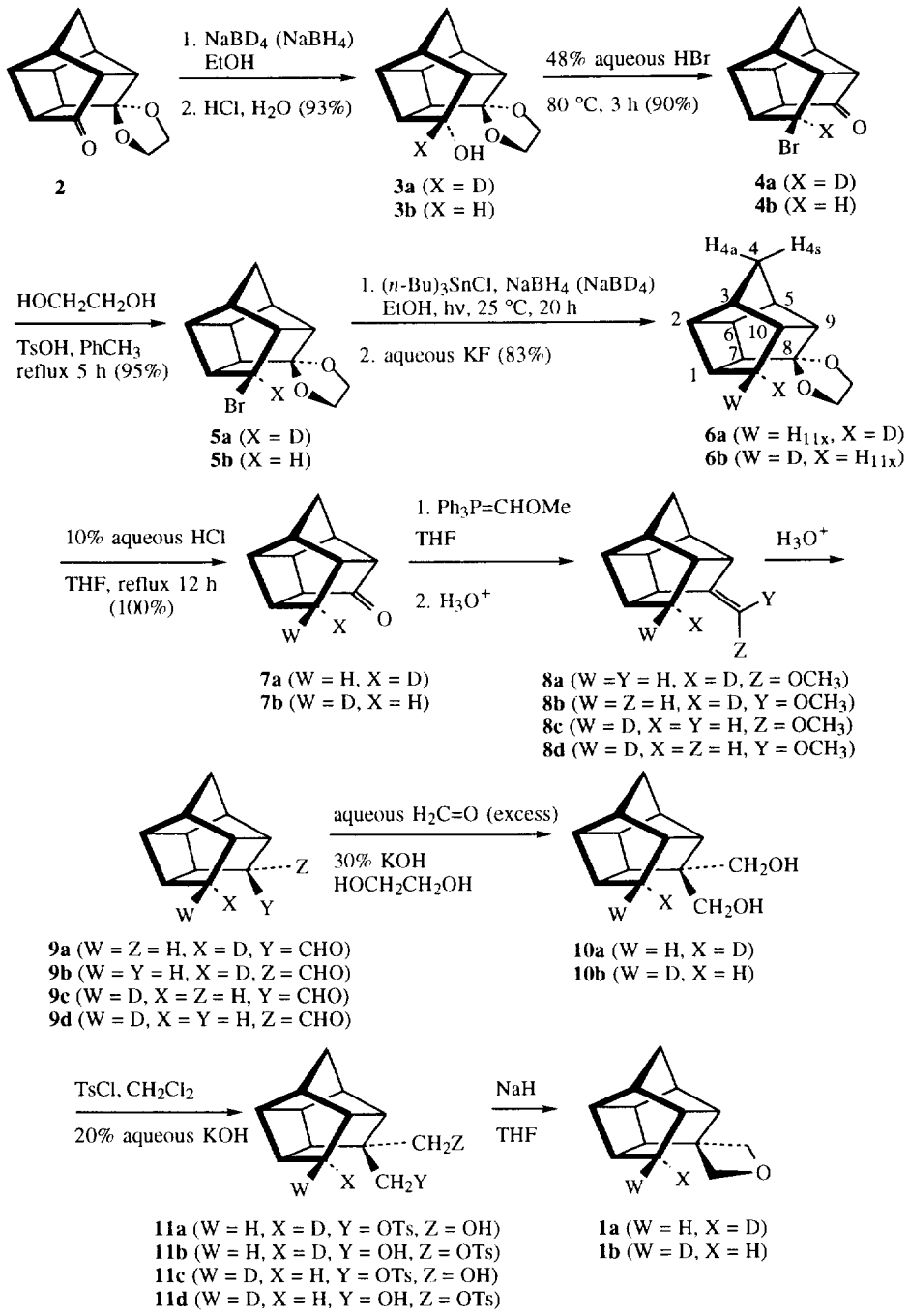
Abstract: Specifically deuterated cage-spiroannulated oxetanes **1a** and **1b** each undergo ring opening with concomitant skeletal rearrangement when heated with glacial HOAc in the presence of a catalytic amount of concentrated H_2SO_4. The fate of the deuterium atom in each substrate, as determined via analysis of the NMR spectra of the rearrangement products, establishes unequivocally that a key step in this process proceeds via highly stereoselective intramolecular 1,5-hydride transfer. Copyright © 1996 Elsevier Science Ltd

Substituted pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecanes ("PCUs") are of considerable current interest as a new class of energetic materials[2] and as intermediates for the synthesis of complex natural products and molecular clefts.[3] In addition, interest has been expressed in the use of oxetane-derived polymers as binders in solid gun propellants and as key components of cast-cured explosives.[4] In this context, it was of interest to incorporate an energetic polycyclic "cage" hydrocarbon unit, e. g., PCU, into an oxetane by spiroannulating the cage compound onto the 3-position of the oxetane moiety, thereby increasing the total energy content of the resulting oxetane relative to the parent (unsubstituted) compound. We now report details of the synthesis of two novel, specifically deuterated, cage-spiroannulated oxetanes (**1a** and **1b**) and their respective subsequent acid promoted ring openings.

Synthesis of 1a and 1b. The method that was used to synthesize **1a** and **1b** is shown in Scheme 1. We elected to introduce deuterium into the molecule at C(11) via $NaBD_4$ promoted reduction of the readily available PCU-8,11-dione mono(ethylene acetal), **2**.[5] Reduction of the carbonyl group in **2**, performed by using either $NaBD_4$ or $NaBH_4$, proceeds stereoselectively to afford **3a** and **3b**, respectively, in high yield. Isomerization of the C(11)-X bond in **3a** and in **3b** was performed via the three-step sequence shown in Scheme 1. Application of this procedure afforded **6a** [which contains an *endo* C(11)-D bond] and **6b** [which contains an *exo* C(11)-D bond], respectively. The structure of **6a** was confirmed via analysis of its ^1H and ^{13}C NMR spectra (*vide infra*). Interestingly, we infer from this result that $(n\text{-Bu})_3SnH$ promoted reduction of the *exo*-C(11)-Br bond in **5a** proceeds with retention of configuration. The remaining steps in the reaction sequence that leads to the formation of specifically deuterated spiro-oxetanes **1a** and **1b** (Scheme 1) follow standard procedures (see the Experimental Section).

Scheme 1



2

3a (X = D)
3b (X = H)

4a (X = D)
4b (X = H)

5a (X = D)
5b (X = H)

6a (W = H_{11x}, X = D)
6b (W = D, X = H_{11x})

7a (W = H, X = D)
7b (W = D, X = H)

8a (W =Y = H, X = D, Z = OCH_3)
8b (W = Z = H, X = D, Y = OCH_3)
8c (W = D, X = Y = H, Z = OCH_3)
8d (W = D, X = Z = H, Y = OCH_3)

9a (W = Z = H, X = D, Y = CHO)
9b (W = Y = H, X = D, Z = CHO)
9c (W = D, X = Z = H, Y = CHO)
9d (W = D, X = Y = H, Z = CHO)

10a (W = H, X = D)
10b (W = D, X = H)

11a (W = H, X = D, Y = OTs, Z = OH)
11b (W = H, X = D, Y = OH, Z = OTs)
11c (W = D, X = H, Y = OTs, Z = OH)
11d (W = D, X = H, Y = OH, Z = OTs)

1a (W = H, X = D)
1b (W = D, X = H)

Analysis of the ^1H and ^{13}C NMR Spectra of 6a. The presence of the *endo*-11-deuterium atom in **6a** serves to simplify the spectrum by removing the signals that are due to H(*endo*-11) in the parent (unlabeled) compound. A further consequence of this specific deuterium atom substitution is that the ^1H and ^{13}C resonances which are associated with the H(*exo*-11) and C(11), respectively, can be assigned unambiguously in the parent compound.

The quaternary carbon atom, C(8), appears as a singlet at δ 116.6 in the off-resonance decoupled ^{13}C NMR spectrum of **6a**. The remaining ^{13}C resonances in **6a** were determined via analysis of the results of a two-dimensional proton-decoupled (but not deuterium-decoupled) INADEQUATE experiment,[6] which was performed for ^{13}C signals in the region δ 26-48 (spectral width 1695 Hz). The NMR experiments are described in detail in the Experimental Section. Chemical shift assignments for the polycyclic ring ^1H and ^{13}C resonances in **6a** are summarized in Table 1. The ethylene acetal ^1H resonances (i.e., -OC*H*$_2$C*H*$_2$O-) appear as a centrosymmetric AA'BB' pattern at δ 3.6-3.9; the corresponding ^{13}C chemical shifts occur at δ 62.4 and 65.2.

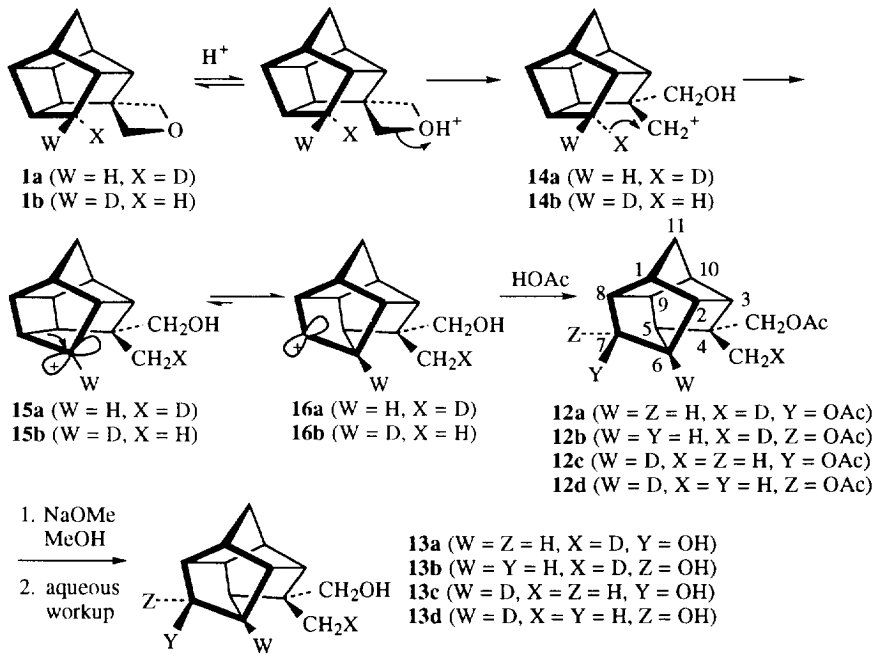
Table 1. ^1H and ^{13}C Chemical Shift Assignments in **6a**.

Position	^1H Chemical Shift (δ, ppm)	^{13}C Chemical Shift (δ, ppm)	Comments
1	2.66	35.74 (d)	
2	2.50	41.69 (d)	
3	2.22	47.34 (d)	
4	1.19 (H4a) 1.63 (H4s)	35.05 (t)	Assigned via nOe study;[7] see the Experimental Section.
5	2.36	44.13 (d)	
6	2.50	39.60 (d)	
7	2.25	40.02 (d)	
8	- -	116.64 (s)	
9	1.98	47.60 (d)	
10	2.38	42.79 (d)	
11	1.08 [H(11x)] 2.08 [H(11n)]	28.84 (dt)	H(11x): dt, J = 4.1, 12.0 Hz; H(11n): d, J = 12.0 Hz; C(11): $^1J_{CD}$ = 20.9 Hz, due to coupling with D(11n).

Acid Promoted Ring Opening of Spiro-oxetanes 1a and 1b. Previously,[1] we reported that a solution of (nondeuterated) **1** in glacial HOAc, when heated in the presence of a catalytic amount of concentrated H_2SO_4, afforded rearranged cage diacetates, i. e., nondeuterated analogs of **12a/12c** and **12b/12d** (Scheme 2; ratio **12a/12c** [*exo*-C(7)-OAc] : **12b/12d** [*endo*-C(7)-OAc] = 4 : 1). Unequivocal verification of the structure of these products was secured via X-ray crystallographic methods; thus, the crystal structures of (nondeuterated) **12a/12c** and of **13b/13d** (formed via base promoted hydrolysis of nondeuterated **12b/12d**) were obtained.[1]

It was suggested that these products are formed via the mechanism shown in Scheme 2, a key step of which involves intramolecular 1,5-hydride shift in (nondeuterated) carbocationic intermediate, **14a/14b**, to produce **15a/15b**. In an effort to garner experimental evidence to further elucidate the nature of this transformation, we have studied the acid promoted ring opening of **1a** [which contains an *exo* C(11)-D bond] and of **1b** [which contains an *endo* C(11)-D bond]. The question regarding the intramolecularity of the conversion of **14a/14b** to **15a/15b** then can be addressed by determining the fate of the deuterium label concomitant with acid promoted ring opening of **1a** and **1b**, respectively.

Scheme 2



1a (W = H, X = D)
1b (W = D, X = H)

14a (W = H, X = D)
14b (W = D, X = H)

15a (W = H, X = D)
15b (W = D, X = H)

16a (W = H, X = D)
16b (W = D, X = H)

12a (W = Z = H, X = D, Y = OAc)
12b (W = Y = H, X = D, Z = OAc)
12c (W = D, X = Z = H, Y = OAc)
12d (W = D, X = Y = H, Z = OAc)

13a (W = Z = H, X = D, Y = OH)
13b (W = Y = H, X = D, Z = OH)
13c (W = D, X = Z = H, Y = OH)
13d (W = D, X = Y = H, Z = OH)

In our hands, acid promoted rearrangement of **1a** afforded an inseparable 4:1 mixture of **12a** and **12b**. Saponification of this mixture afforded a mixture of diols **13a** and **13b**, which could be separated by column chromatography. In this manner, isomerically pure **13b**, mp 136-138 °C, could be obtained.

Next, the fate of the deuterium label in **1a** concomitant with its acid promoted rearrangement to **12b** was assessed via analysis of the ^{1}H and ^{13}C NMR spectra of **13b** (formed via saponification of a primary rearrangement product, **12b**). Thus, integration of the broadened resonance signal at δ 1.05 [due to the *endo* methyl group at C(4) in **13b**] reveals the presence of only two protons, thereby suggesting that this "methyl group" is, in reality, a CH_2D group. This conclusion is reinforced by the fact that a signal at δ 18.9 in the proton noise-decoupled ^{13}C NMR spectrum of **13b** appears as a triplet, J = 19.2 Hz (due to $^{1}J_{CD}$ coupling). This result suggests that acid promoted rearrangement of **1a** to **12b** proceeds via intramolecular 1,5-hydride transfer of *endo*-C(11)-D in a manner that is consistent with the mechanistic step shown in Scheme 2 by which cationic intermediate **14a** proceeds to **15a**.

In order to obtain independent verification of the foregoing conclusion, the corresponding acid promoted rearrangement of **1b** was studied. Thus, acid promoted rearrangement of **1b** once again produced an inseparable 4:1 mixture of **12c** and **12d**. Saponification of this mixture afforded a mixture of diols **13c** and **13d**, which could be separated by column chromatography. In this manner, isomerically pure **13d** could be obtained.

As in the case of the corresponding reaction of **1a** (vide supra), the fate of the deuterium label in **1b** concomitant with its acid promoted rearrangement to **12d** was assessed via analysis of the ^1H and ^{13}C NMR spectra of **13d** (formed via saponification of a primary rearrangement product, **12d**). Thus, integration of the resonance signal at δ 1.05 [sharp singlet, due to the *endo* methyl group at C(4) in **13d**] reveals the presence of three equivalent CH_3 group protons. In addition, a signal at δ 50.6 in the proton noise-decoupled ^{13}C NMR spectrum of **13b** appears as a triplet, J = 20.0 Hz (due to $^1J_{CD}$ coupling). Taken together with the corresponding results obtained for acid promoted rearrangement of **1a** (*vide supra*), this result suggests that acid promoted rearrangement of **1a/1b** to **12b/12d** proceeds via highly stereoselective intramolecular 1,5-hydride transfer of *endo* C(11)-D(H) in a manner that is consistent with the mechanistic step shown in Scheme 2 by which cationic intermediate **14a/14b** proceeds to **15a/15b**. The fact that intramolecular 1,5-hydride shifts have been reported to accompany cationic rearrangements in a wide variety of systems has been noted previously.[1]

Summary and Conclusions. Specifically deuterated cage-spiroannulated oxetanes **1a** and **1b** have been synthesized via the method shown in Scheme 1. Acid promoted rearrangement of each oxetane proceeds via ring opening with concomitant skeletal rearrangement. The fate of the deuterium atom in each substrate was assessed by analysis of the ^1H and ^{13}C NMR spectra of a diol (**13b** and **13d**, respectively), which was isolated by careful column chromatographic separation of the mixture of diols that resulted via saponification the rearrangement products [(**12a** + **12b**) and (**12c** + **12d**), respectively]. The results of the NMR spectral analyses support the mechanism shown in Scheme 2 and suggest that a key step in this process proceeds via highly stereoselective intramolecular 1,5-hydride transfer.

Experimental Section

Melting points are uncorrected. Elemental microanalyses were performed by personnel at Galbraith Laboratories, Knoxville, TN and at M-H-W Laboratories, Phoenix, AZ on non-deuterium containing analogs of the new compounds whose syntheses are reported herein. Detailed procedures for the synthesis and acid promoted rearrangement of (specifically deuterated) **1a** are given below.

***exo*-11-Deuterio-*endo*-11-hydroxypentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8-one ethylene ketal (3a).** A solution of **2**[5] (1.006 g, 4.60 mmol) in EtOH (10 mL) was cooled to 0 °C by application of an external ice-water bath. To this cooled solution was added dropwise with stirring a cold solution of $NaBD_4$ (410 mg, 9.76 mmol) in water (2.0 mL) during 10 minutes. After the addition of the reducing agent had been completed, the reaction mixture was stirred at 0 °C for 2 h, at which time the cold bath was removed. The continuously stirred reaction mixture was allowed to warm gradually to room temperature during 2 h, at which time the cold bath was re-installed, and the reaction was quenched via dropwise addition of 3% aqueous HCl (10 mL) to the stirred, cold reaction mixture. The reaction mixture was transferred into a separatory funnel and then was extracted with CH_2Cl_2 (3 x 20 mL). The combined extracts were washed with brine (20 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated *in vacuo*. Compound **3a** (0.951 g, 93 %), was thereby obtained as a colorless oil; IR (neat) 3421 (m), 2955 (s), 2862 (m), 1332 (s), 1139 (s), 1059 (s), 919 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.08 (*AB*, J_{AB} = 10.6 Hz, 1 H), 1.56 (*AB*, J_{AB} = 10.8 Hz, 1 H), 2.05-2.71 (m, 8 H), 3.65-4.15 (m, 4 H), 5.28 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 34.8 (t), 38.6 (d), 38.8 (d), 39.0 (d), 39.7 (d), 43.3 (d), 44.4 (d), 46.5

(d), 46.9 (d), 62.8 (t), 65.3 (t), 71.7 (d), 115.5 (s). This material was used as obtained in the next synthetic step, without additional purification.

***exo*-11-Bromo-*endo*-11-deuteriopentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8-one (4a).** A mixture of **3a** (951 mg, 4.30 mmol) and 48% aqueous HBr (20 mL, excess) was heated at 80 °C for 3 h and then was allowed to cool gradually to room temperature. The reaction mixture was poured into ice-water (20 mL), and the resulting aqueous suspension was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the filtrate was concentrated *in vacuo*. The residue, a brown oil was purified by column chromatography on silica gel by using a 5-10 % EtOAc-hexane gradient elution scheme. Pure **4a** (929 mg, 90 %) was thereby obtained as a colorless microcrystalline solid: mp 82.5-83.5 (lit.[5] mp 84.5-85.3 °C); IR (KBr) 2967 (m), 2942 (m), 2929 (m), 2854 (w), 1733 cm^{-1} (s); ^{1}H NMR ($CDCl_3$) δ 1.63 (*AB*, J_{AB} = 11.06 Hz, 1 H), 1.89 (*AB*, J_{AB} = 10.4 Hz, 1 H), 2.30-2.40 (m, 1 H), 2.50-2.62 (m, 1 H), 2.70-2.79 (m, 2 H), 2.86-2.98 (m, 1 H), 3.04-3.17 (m, 2 H), 3.20-3.28 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 35.8 (d), 36.5 (t), 42.9 (d), 44.0 (d), 45.2 (d), 46.6 (d), 47.6 (d), 53.5 (d), 54.2 (s), 56.2 (d), 216.1 (s).

***exo*-11-Bromo-*endo*-11-deuteriopentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8-one ethylene ketal (5a).** A mixture of **4a** (2.40 g, 9.99 mmol), ethylene glycol (634 mg, 10.2 mmol), and *p*-toluenesulfonic acid (TsOH, 33 mg, catalytic amount) in $PhCH_3$ (20 mL) was placed in a 50 mL three-neck round bottom flask which had been fitted with a reflux condenser and a Dean-Stark apparatus. The reaction mixture was refluxed for 5 h, during which time water was removed by azeotropic distillation. The reaction mixture was allowed to cool gradually to room temperature and then quenched by addition of ice cold 10% aqueous Na_2CO_3 (50 mL). The resulting aqueous suspension was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified via column chromatography on silica gel by eluting with 3% EtOAc-hexane. Pure **5a** (2.69 g, 95%) was thereby obtained as a colorless oil; IR (neat) 2969 (s), 2869 (m), 1332 (m), 1106 (s), 1086 (s), 1032 (s), 939 (m), 686 (w), 653 cm^{-1} (w); ^{1}H NMR ($CDCl_3$) δ 1.34 (*AB*, J_{AB} = 10.9 Hz, 1 H), 1.70 (*AB*, J_{AB} = 11.0 Hz, 1 H), 2.01-2.15 (m, 1 H), 2.27-2.45 (m, 1 H), 2.45-2.68 (m, 3 H), 2.68-2.96 (m, 2 H), 2.96- 3.14 (m, 1 H), 3.65-4.05 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 34.3 (t), 38.7 (d), 41.0 (d), 42.0 (d), 44.4 (d), 45.3 (d), 46.8 (d), 49.7 (d), 51.4 (d), 57.3 (s), 62.9 (t), 65.5 (t), 115.1 (s); Anal. Calcd. for $C_{13}H_{15}BrO_2$: C, 55.12; H, 5.30; Found: C, 54.94; H, 5.13.

***endo*-11-Deuteriopentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8-one ethylene ketal (6a).** A solution of **5a** (136 mg, 0.48 mmol) and Bu_3SnCl (48 mg, 0.15 mmol) in dry EtOH (15 mL) under argon was cooled to 0 °C via application of an external ice water bath. To this cooled solution was added dropwise with stirring a solution of $NaBH_4$ (20 mg, 0.053 mmol) in dry EtOH (3 mL). After the addition of the reducing agent had been completed, the external cold bath was removed, and the reaction mixture was irradiated under argon with a 250 W tungsten filament lamp for 20 h. The reaction was quenched via addition of saturated aqueous KF (10 mL), and the resulting mixture was stirred overnight at room temperature. The quenched reaction mixture was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the filtrate was concentrated *in vacuo*. The residue, a milky, white oil, was purified via column chromatography on silica gel by eluting first with hexane and then with 4% EtOAc-hexane. Pure **6a** (82 mg, 83%) was thereby obtained as a colorless oil; IR (neat) 2962 (s), 2949 (s), 2862 (m), 1332 (m), 1106 (s), 1086 (m), 1032 (m), 945 (w), 933 cm^{-1} (w); ^{1}H NMR ($CDCl_3$) δ 1.00 (br s, 1 H), 1.19 (*AB*, J_{AB} = 11.9 Hz, 1 H), 1.62 (*AB*, J_{AB} = 10.6 Hz, 1 H), 1.91-2.04 (m, 1 H), 2.17-2.72 (m, 4 H), 3.61-3.93 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 28.6 (d), 35.1 (t), 35.7 (d), 39.6 (d), 40.0 (d), 41.7 (d), 42.7 (d), 44.2 (d), 47.4 (d), 47.6 (d), 62.5 (t), 65.3 (t), 116.7 (s). Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90; Found: C, 76.55; H, 8.00.

***endo*-11-Deuteriopentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8-one (7a).**[8] To a solution of **6a** (180 mg, 0.88 mmol) in THF (5 mL) was added 10% aqueous HCl (2 mL, excess), and the resulting mixture was refluxed with stirring for 12 h. The reaction mixture was allowed to cool to ambient temperature and then was concentrated *in vacuo*. The residue was extracted with CH_2Cl_2 (3 x 40 mL). The combined organic extracts were washed with water (20 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated *in vacuo*. The residue, a colorless oil, was purified via column chromatography on silica gel by eluting with 5% EtOAc-hexane, thereby affording pure **7a** (147 mg, 100%) as a colorless, waxy solid: mp 195.5-197.0 °C [lit. mp 191-192 °C (subl.)[8a]; 204-205 °C (sealed tube)[8c]]; IR (KBr) 2967 (m), 2928 (m), 1740 cm^{-1} (s); ^{1}H NMR ($CDCl_3$) δ 1.38 (s, 1 H), 1.50 (*AB*, J_{AB} = 10.3 Hz, 1 H), 1.84 (*AB*, J_{AB} = 10.8 Hz, 1 H), 2.22-2.38 (m, 1 H), 2.42-2.60 (m, 2 H), 2.61-2.82 (m, 2 H), 2.82-3.02 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 30.6 (d), 36.6 (d), 37.5 (t), 39.3 (d),

43.1 (d), 43.6 (d), 44.3 (d), 48.1 (d), 48.4 (d), 52.7 (d), 221.0 (s); mass spectrum (70 eV), *m/z* (relative intensity) 161 (molecular ion, 67.4), 96 (100.0), 95 (47.3), 83 (48.3), 82 (9.0).

(*Z*)- and (*E*)-*endo*-11-Deuterio-8-(methoxymethylene)pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecanes (8a and 8b). A suspension of $CH_3OCH_2PPh_3^+$ Cl^- (5.3 g, 15 mmol) in dry THF (40 mL) under argon was cooled to 0 °C via application of an external ice-water bath. To this cooled suspension was added with stirring a 2.5 M solution of *n*-BuLi in hexane (7.5 mL, 15 mmol). The resulting deep orange-colored mixture was stirred under argon at 0 °C for 0.5 h, at which time a solution of **7** (600 mg, 3.73 mmol) in dry THF (5 mL) was added dropwise with stirring during 6 minutes. The resulting mixture was stirred at 0 °C under argon for 1 h. The external cold bath was removed; the reaction mixture was allowed to warm gradually to ambient temperature and then was stirred at that temperature for 4 h. The reaction mixture was transferred into a separatory funnel and then was washed with water (3 x 30 mL). The organic layer was dried (MgSO4) and filtered, and the filtrate was concentrated *in vacuo*. The residue, a yellow semi-solid, was further purified via flash column chromatography on silica gel by eluting with hexane. Compounds **8a** and **8b** (obtained as a mixture of isomers, 504 mg, 72%) was thereby obtained as a colorless oil: bp 95-96 °C (2.0 mm Hg); IR (neat) 2961 (s), 2941 (s), 2890 (m), 2857 (m), 1695 (m), 1217 (m), 1114 cm^{-1} (m); ^{1}H NMR ($CDCl_3$) δ 1.08 (br s, 1 H), 1.26 (*AB*, J_{AB} = 9.5 Hz, 1 H), 1.62-1.74 (m, 1 H), 2.13-2.70 (m, 7 H), 3.02-3.12 (m, 0.6 H), 3.20-3.34 (m, 0.4 H), 3.50, 3.51 (2 s, total 3 H), 5.73, 5.77 (2 s, ratio 1.2:1, total 1 H) ; ^{13}C NMR ($CDCl_3$) δ 29.5 (d), 29.6 (d), 34.7 (t), 34.9 (t), 36.1 (d), 38.0 (d), 38.8 (d), 39.4 (d), 42.7 (d), 42.8 (d), 43.0 (d), 43.1 (d), 44.0 (d), 45.0 (d), 46.3 (d), 46.4 (d), 46.6 (d), 46.7 (d), 59.3 (2 C, q), 122.8 (s), 123.1 (s), 136.0 (d), 136.3 (d). Anal. Calcd for $C_{13}H_{16}O$: C, 83.20; H, 8.42. Found: C, 82.94; H, 8.57.

***endo*-11-Deuterio-8-formylpentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecanes (9a and 9b).** A mixture of **8a** and **8b** (504 mg, 2.68 mmol) was dissolved in THF (7 mL). Water (7 mL) was added, and argon was bubbled through the reaction mixture for 0.5 h to purge dissolved oxygen. Concentrated aqueous HCl (1.2 mL) was added, and the resulting mixture was stirred under argon at ambient temperature overnight. The reaction was quenched by pouring it carefully with stirring into 5% aqueous $NaHCO_3$ (50 mL). The resulting aqueous suspension was extracted with Et_2O (3 x 30 mL). The combined organic layers were washed sequentially with water (20 mL) and brine (20 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated *in vacuo*. A mixture of **9a** and **9b** (392 mg, 84%) was thereby obtained as a colorless oil; IR (neat) 2962 (s), 2935 (s), 2799 (m), 2696 (w), 1708 (s), 1055 cm^{-1} (w); ^{1}H NMR ($CDCl_3$) δ 1.06 (br s, 1 H), 1.17 (*AB*, J_{AB} = 10.5 Hz, 1 H), 1.67 (*AB*, J_{AB} = 10.5 Hz, 1 H), 2.05-2.90 (m, 8 H), 2.90-3.15 (m, 1 H), 9.51, 9.99 (2 s, ratio 1:4, total 1 H); ^{13}C NMR ($CDCl_3$) δ 27.2 (d), 30.0 (d), 33.6 (t), 34.2 (t), 35.5 (d), 35.8 (d), 36.1 (d), 37.1 (d), 41.3 (d), 41.6 (d), 41.8 (d), 42.1 (d), 42.4 (d), 42.7 (d), 43.0 (d), 44.0 (d), 45.8 (d), 46.0 (d), 46.3 (d), 51.9 (d), 55.3 (d), 204.1 (d), 204.7 (d).

The mixture of **9a** and **9b** thereby obtained was further characterized by converting it into the corresponding mixture of 2,4-dinitrophenylhydrazones. Thus, to a mixture of 2,4-dinitrophenylhydrazine (400 mg, 2.0 mmol) and water (3 mL) in a small Erlenmeyer flask was added concentrated H_2SO_4 (2.0 mL) dropwise with stirring. Ethanol (10 mL) was added, and the resulting clear solution was added slowly to a solution of **9a** and **9b** (200 mg, 1.1 mmol) in EtOH (10 mL). The resulting mixture was allowed to stand at ambient temperature for 1 h. The reaction mixture was cooled to induce crystallization and then filtered. The residue was recrystallized from EtOH-CH_2Cl_2, thereby affording a mixture of the the 2,4-dinitrophenylhydrazone derivatives of **9a** and **9b** (340 mg, 85%) as an orange microcrystalline solid: mp 171-172 °C; ^{1}H NMR ($CDCl_3$) δ 0.85-1.82 (m, 4 H), 2.25-2.52 (m, 4 H), 2.60-2.80 (m, 4 H), 3.00-3.30 (m, 1 H), 2.82-7.97 (m, 2 H), 8.25-8.35 (m, 1 H), 9.16-9.18 (m, 1 H), 11.00 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 29.7 (t), 29.9 (t), 34.2 (t), 34.3 (t), 36.0 (d), 36.1 (d), 38.8 (d), 41.0 (d), 41.3 (d), 41.5 (d), 42.1 (d), 42.2 (d), 44.5 (d), 44.8 (d), 45.1 (d), 46.3 (d), 46.5 (d), 46.8 (d), 116.4 (d), 116.5 (d), 123.4 (d), 123.5 (d), 128.6 (s), 129.98 (d), 130.0 (d), 137.6 (s), 145.1 (s), 152.4 (d), 154.5 (d). Anal. Calcd for $C_{18}H_{18}N_4O_4$: C, 61.01; H, 5.12. Found: C, 60.68; H, 5.46.

***endo*-11-Deuterio-8,8-bis(hydroxymethyl)pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (10a).** A mixture of **9a** and **9b** (392 mg, 2.24 mmol), ethylene glycol (2.5 mL), and 37% aqueous formaldehyde (1.5 mL, excess) under argon was cooled to 0 °C via application of an external ice-water bath. To this cooled mixture was added with stirring 50% aqueous KOH (1.5 mL, excess). The external cold bath was removed, and the reaction mixture was refluxed under argon for 6 h. The reaction mixture was allowed to cool to ambient temperature. Water (40 mL) was added, and the resulting aqueous suspension was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were washed sequentially with water (2 x 20 mL) and brine (20 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated *in vacuo*. The residue, a brown solid, was

recrystallized from $CHCl_3$, thereby affording **10a** (336 mg, 72%) as a colorless microcrystalline solid: mp 111-112 °C; IR (KBr) 3296 (s), 2954 (s), 2941 (s), 2870 (m), 2857 (m), 1010 (m), 997 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.04 (br s, 1 H), 1.19 (*AB*, J_{AB} = 10.4 Hz, 1 H), 1.61 (A*B*, J_{AB} = 10.4 Hz, 1 H), 2.05-2.26 (m, 3 H), 2.26-2.65 (m, 6 H), 2.65-2.78 (m, 1 H), 3.20 (d, *J* = 10.5 Hz, 1 H), 3.39 (d, *J* = 10.6 Hz, 1 H), 5.88 (d, *J* = 11.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 29.6 (d), 33.3 (t), 36.0 (d), 39.5 (d), 41.5 (d), 41.8 (d), 42.1 (d), 43.8 (d), 44.5 (d), 47.1 (d), 50.2 (s), 66.4 (t), 70.3 (t). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.92; H, 8.98; Found: C, 75.69; H, 8.80.

***endo*-11-Deuterio-8,8-bis(hydroxymethyl)pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane monotosylates (11a and 11b).** To a solution of **10a** (200 mg, 0.97 mmol) in CH_2Cl_2 (7 mL) was added 20% aqueous NaOH (7 mL). The resulting suspension was stirred vigorously, and TsCl (240 mg, 1.26 mmol) was added in small portions during 4 h. The progress of the reaction was monitored via tlc analysis of aliquots that were withdrawn periodically. The reaction mixture was stirred at ambient temperature for 24 h and then was transferred into a separatory funnel. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were washed with water (2 x 20 mL), dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The oily residue was purified via column chromatography on silica gel by using a 10-15% EtOAc-hexane gradient elution scheme. A mixture of **11a** and **11b** (266 mg, 75%) was thereby obtained as a colorless, viscous oil; IR (neat) 3535 (m), 2954 (s), 2877 (m), 1592 (w), 1352 (m), 1172 (m), 1094 (m), 1023 (m), 952 (m), 933 (m), 849 (m), 836 (m), 810 (m), 726 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 0.95, 1.06 (2 br s, total 0.5 H), 1.15 (*AB*, J_{AB} = 10.4 Hz, 1 H), 1.60 (A*B*, J_{AB} = 10.4 H, 1 H), 1.77 (s, 1 H), 2.02-2.84 (m, which includes a singlet at δ 2.44, total 11 H), 3.05 (d, *J* = 11.2 Hz, 1 H), 3.26 (d, *J* = 11.1 Hz, 1 H), 3.48 (d, *J* = 9.2 Hz, 0.5 H); ^{13}C NMR ($CDCl_3$) δ 21.6 (2 C, q), 29.2 (d), 29.2 (d), 33.0 (t), 33.1 (t), 35.9 (d), 36.1 (d), 38.4 (d), 39.0 (d), 41.3 (d), 41.5 (d), 41.6 (d), 41.8 (d), 43.4 (d), 43.9 (d), 44.2 (d), 47.1 (d), 48.5 (s), 49.9 (s), 63.1 (t), 65.9 (t), 71.7 (t), 75.0 (t), 127.79 (d), 127.82 (d), 129.8 (d), 129.9 (d), 132.6 (s), 132.8 (s), 144.7 (s), 144.8 (s). Anal. Calcd for $C_{20}H_{24}O_4S$: C, 66.64; H, 6.71. Found: C, 66.19; H, 6.85.

2,3,4,5,5a,5b-Hexahydrospiro[1,2,4-ethanylylidene-1*H*-cyclobuta[*cd*]pentalene-5(1a*H*),3'-oxetane (1a). A suspension of NaH (197 mg, 4.9 mmol) in dry THF (10 mL) under argon was cooled to 0 °C via application of an external ice-water bath. To this cooled suspension was added with stirring a solution of **11a** and **11b** (266 mg, 0.74 mmol) in dry THF (5 mL). The external cold bath was removed, and the reaction mixture was stirred at ambient temperature under argon for 3 days. Methanol (3 mL) was added to decompose unreacted NaH. The resulting mixture was transferred into a separatory funnel and then washed with water (2 x 20 mL). The organic layer was dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified via column chromatography on silica gel by eluting with 4% EtOAc-hexane, thereby affording **1a** (57 mg, 41%) as a colorless waxy solid. Repeated sublimation of this material afforded analytically pure **1a**: mp 102-103 °C; IR (KBr) 2941 (s), 2928 (s), 2851 (s), 1449 (w), 1288 (w), 1249 (w), 978 (m), 946 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 0.99 (br s, 1 H), 1.19 (*AB*, J_{AB} = 10.4 Hz, 1 H), 1.63 (A*B*, J_{AB} = 10.4 Hz, 1 H), 2.04-2.12 (m, 1 H), 2.12-2.22 (m, 1 H), 2.28-2.60 (m, 4 H), 2.60-2.75 (m, 1 H), 2.75-2.87 (m, 1 H), 4.26 (q, *J* = 5.5 Hz, 2 H), 4.55 (*AB*, J_{AB} = 6.1 Hz, 1 H), 4.73 (A*B*, J_{AB} = 6.1 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 28.5 (d), 34.7 (t), 35.7 (d), 41.4 (d), 41.8 (d), 42.0 (d), 43.5 (d), 43.6 (d), 46.4 (d), 47.0 (s), 50.3 (d), 77.9 (t), 83.6 (t). Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.86; H, 8.62.

***exo*-4-Acetoxymethyl-*endo*-4-deuteriomethyl-7-acetoxypentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecanes (12a and 12b).** To a solution of **1a** (57 mg, 0.30 mmol) in glacial HOAc (6 mL) was added concentrated H_2SO_4 (5 drops, catalytic amount), and the resulting mixture was refluxed for 12 h. The reaction mixture was allowed to cool gradually to ambient temperature and then was concentrated *in vacuo*. Methylene chloride (40 mL) was added to the residue, and the resulting mixture was washed sequentially with saturated aqueous $NaHCO_3$ (2 x 10 mL), water (20 mL), and brine (20 mL). The organic layer was dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*, thereby affording a colorless oil (70 mg). Careful integration of the ^1H NMR spectrum of the product thereby obtained indicated it was a mixture of **12a** and **12b** (ratio **12a**:**12b** = 4:1); IR (neat) 2965 (m), 2867 (w), 1735 (s), 1368 (w), 1237 (s), 1032 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 0.96 (br s, 2 H), 1.37 (s, 2 H), 1.73-1.88 (m, 2 H), 2.00 (s, 3 H), 2.03 (s, 3 H), 2.05-2.32 (m, 4 H), 2.33-2.58 (m, 2 H), 3.95, 4.03 (2 s, total 2 H), 4.80, 4.90 (2 s, total 2 H). This mixture of **12a** and **12b** was used as obtained in the next synthetic step, without further purification or characterization.

***exo*-4-Hydroxymethyl-*endo*-4-deuteriomethyl-7-hydroxypentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecanes (13a and 13b).** To a solution of NaOMe (60 mg, 1.1 mmol) in MeOH (8 mL) was added with stirring a solution of **12a** and **12b** (70 mg, 0.1 mmol, *vide supra*) in MeOH (2 mL). The resulting mixture was stirred at