

Deuterium and the Octant Rule for Ketones. Syntheses and Circular Dichroism Data of Chiral 4-Deuterioadamantan-2-ones

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The syntheses of optically active (1*R*)-4(e)-deuterioadamantan-2-one (5), (1*R*)-4(a)-deuterioadamantan-2-one (18), and the (1*S*)-4,4-dideuterioadamantan-2-one (21) are described. To achieve this goal we developed a new general route for chiral adamantanones. From the circular dichroism data of 5, 18, and 21 in isoctane we must conclude that deuterium as a substituent β to the carbonyl behaves in a dissignate manner.

Numerous examples of asymmetric molecules owing their chirality to deuterium substitution are known.^{1,2} Detailed and exact information about the influence of deuterium on the $n\pi^*$ Cotton effects of chiral ketones is lacking, however. The data Djerassi published³ on (*R*)-3-deuteriocyclopentanone has limited use because of the lack of conformational integrity of the cyclopentane system: the Cotton effect of (*R*)-3-deuteriocyclopentanone reflects either the influence of deuterium by itself or this influence in combination with that of chiral conformations⁴ of the cyclopentanone ring system.

As is well known, an exact knowledge of the conformation of the molecule is essential for useful interpretation of Cotton effects data. In the case of chirality due to deuterium it is clear that minor conformational ambiguities may swamp the small deuterium effects. The choice of the rigid adamantane framework for an examination of the influence of deuterium substitution on the $n\pi^*$ carbonyl Cotton effect is evident in light of Snetzke's earlier contributions.^{5,11,12}

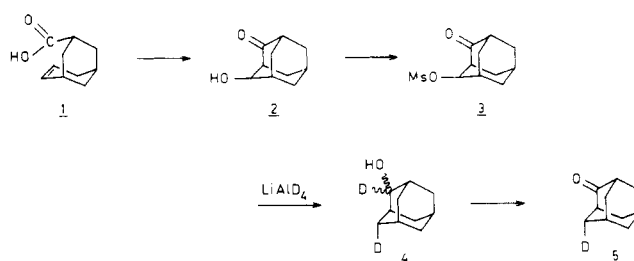
This paper reports the details of the syntheses and circular dichroism data of (1*R*)-4(e)-deuterioadamantan-2-one (5),⁶ the (1*R*)-4(a)-deuterioadamantan-2-one (18), and the (1*S*)-4,4-dideuterioadamantan-2-one (21).⁷

Synthesis. The starting material in our synthesis was the *endo*-bicyclo[3.3.1]non-6-en-3-carboxylic acid⁸ (1). Resolution of this acid was achieved using (+)-dehydroabietylamine. The diastereomeric salts could be separated by fractional crystallization from 96% ethanol. Decomposition of the salt $[\alpha]_{578} + 77.8^\circ$ gave an optically active acid (+)-(1), $[\alpha]_{578} + 130.7^\circ$.

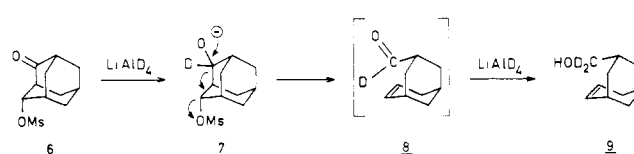
In a separate experiment optically active acid 1, $[\alpha]_{578} + 115.9^\circ$, was converted to a mixture of diastereomeric amides using the acid chloride⁹ of 1 and optically pure (-)- α -phenylethylamine, $[\alpha]_{\text{D}} - 39^\circ$ (neat). Analytical separation of these amides by high-pressure liquid chromatography was possible and an enantiomeric excess of $77 \pm 3\%$ was established for the acid 1, $[\alpha]_{578} + 115.9^\circ$. The extrapolated absolute rotation of acid 1 would be $[\alpha]_{578} + 151 \pm 6^\circ$ (it must be realized that extrapolation of optical rotations, itself dependent on concentration, cannot give entirely exact data). The acid 1 with $[\alpha]_{578} + 126.4^\circ$ used in our further work has an optical purity of $84 \pm 3\%$. This is extrapolated from the value of the absolute rotation (with its inherent failings).

The acid 1 could be transformed readily to an epimeric mixture of 4-hydroxyadamantan-2-ones by treatment with acetic anhydride and boron trifluoride etherate in benzene.¹⁰ The optical purity of the 4(a)- and 4(e)-hydroxyadamantan-2-ones (2 and 10) was almost identical to that of acid 1, as could be verified on the CD data of 2 and 10.¹¹ The only previous synthesis of optically active 4-hydroxyadamantan-2-ones was elegantly achieved by Snetzke using the laborious and low yield route starting with Meerwein's ester.^{11,12} Our new route as described above proceeds in an overall yield of 84% starting with acid 1 as compared to 30% of the old route starting with 2-carboxyadamantan-4,8-dion. The 4(a)-hydroxyadamantan-2-one (2) was isolated from the mixture and

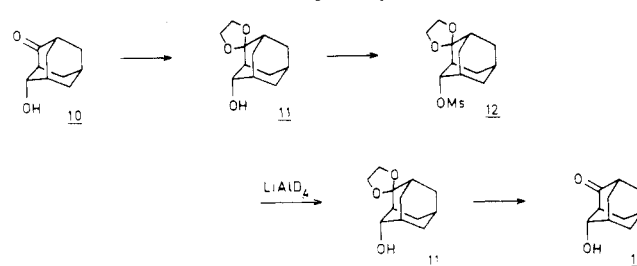
Scheme I. Synthesis of 4(e)-Deuterioadamantan-2-one (5)



Scheme II. Ring Opening of 6



Scheme III. Attempted Synthesis of 18



treated with methanesulfonyl chloride in dry pyridine to give the 4(a)-methylsulfonyloxyadamantan-2-one (3)⁸ (Scheme I). Reduction of this ketone 3 with 5 equiv of lithium aluminum deuteride in dry ether furnished the alcohols 4 which were oxidized to the 4(e)-deuterioadamantan-2-one (5) (deuterium equatorial >95%). This percentage of equatorial deuterium was established by ¹H NMR analysis of the separated sets of axial and equatorial hydrogens, a separation which was induced through addition of Eu(fod)₃ in chloroform-*d*.¹⁴

To synthesize the epimeric 4(a)-deuterioadamantan-2-one (18) we first tried a route as described above via the 4(e)-methylsulfonyloxyadamantan-2-one (6). The reduction of this compound resulted in ring opening of the adamantane system⁸ (as shown in Scheme II) giving the 3-hydroxydideuteriomethylbicyclo[3.3.1]non-6-ene 9, among other products. To circumvent this ring opening we tried a route via the ethylene ketal of 4(e)-methylsulfonyloxyadamantan-2-one (12) (see Scheme III). Reduction of this ketal 12 with lithium aluminum deuteride almost exclusively attacks the sulfur atom giving the 4(e)-hydroxyadamantan-2-one (10), after hydrolysis of the ketal.

For the successful preparation of 4(a)-deuterioadamantan-2-one (18) we introduced deuterium at the equatorial

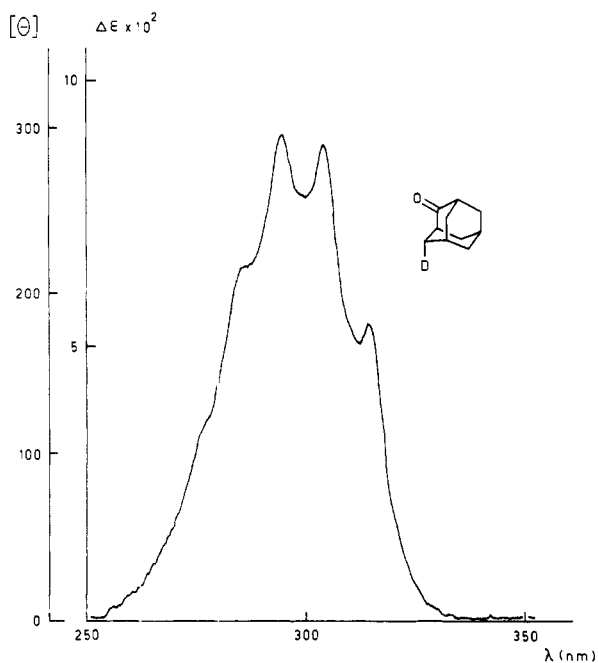
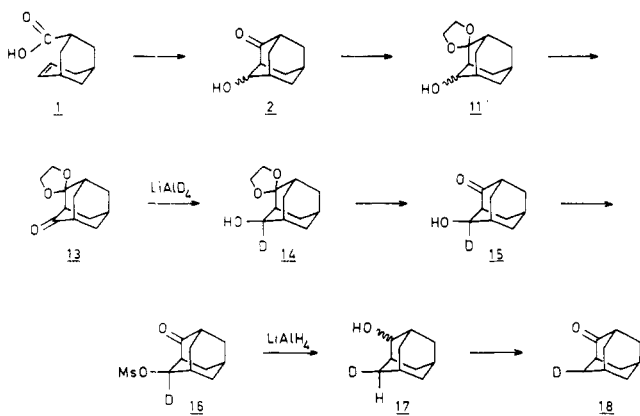
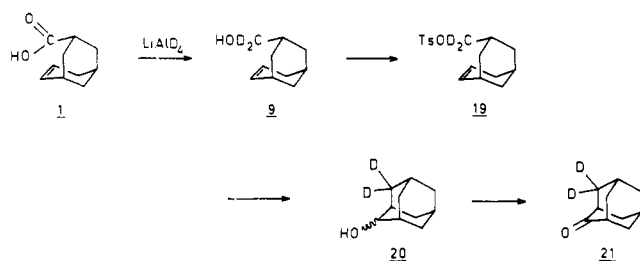


Figure 1. Circular dichroism spectrum of 4(e)-deuterioadamantan-2-one in isoctane (one scan).

Scheme IV. Synthesis of 4(a)-Deuterioadamantan-2-one (18)



Scheme V. Synthesis of 4,4-Dideuterioadamantan-2-one (21)



position in the 4(a)-hydroxyadamantan-2-one as shown in Scheme IV. The epimeric mixture of optically active 4-hydroxyadamantan-2-ones (2 and 10) was subsequently ketalized with ethylene glycol, oxidized with chromic acid, reduced with lithium aluminum deuteride, and hydrolyzed. The highly stereoselective formation of the axial epimer of 14 over the equatorial one (as determined from the integration of the peaks of both epimers of the 4-hydroxy-4-deuterioadamantan-2-ones, separated using HPLC) reflects steric control of the reducing agent by the ketal group.^{8,15} The 4(a)-hydroxy-4(e)-deuterioadamantan-2-one (15) was now transformed to the 4(a)-deuterioadamantan-2-one (18) in exactly the same manner as described above for the 4(e)-deuterioadamantan-

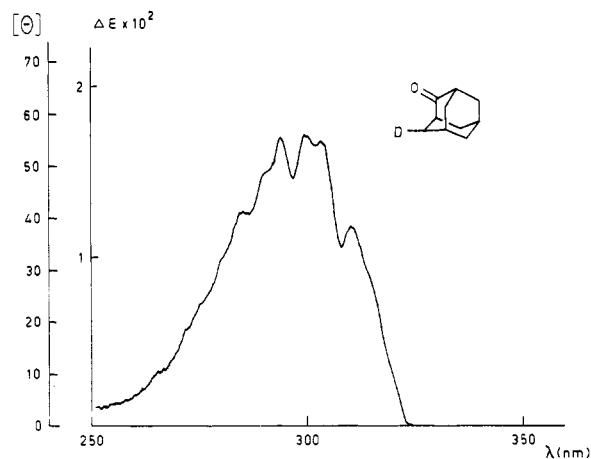


Figure 2. Circular dichroism spectrum of 4(a)-deuterioadamantan-2-one in isoctane (one scan).

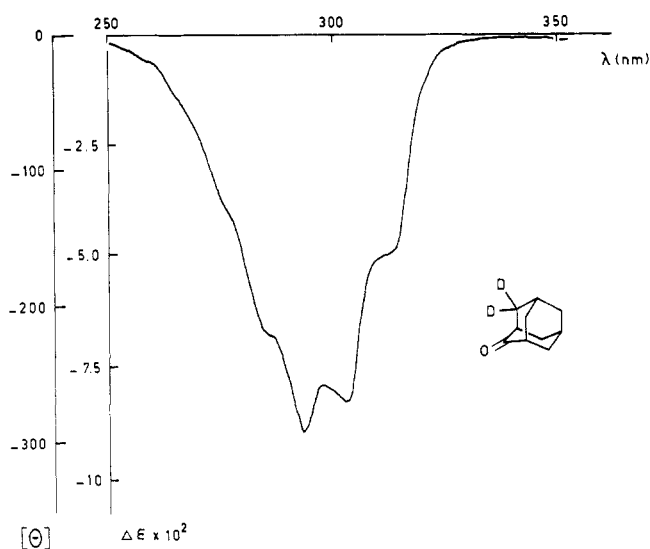


Figure 3. Circular dichroism spectrum of 4,4-dideuterioadamantan-2-one in isoctane (one scan).

2-one (5) except that lithium aluminum hydride was used as reducing agent instead of the lithium aluminum deuteride. The percentage of axial deuterium was established as described above¹⁴ (deuterium axial >95%).

The 4,4-dideuterioadamantan-2-one (21) was prepared as shown in Scheme V.⁷ The unsaturated carbinol 9 was prepared by lithium aluminum deuteride reduction of the carboxylic acid 1. Reaction of this alcohol 9 with *p*-toluenesulfonyl chloride in dry pyridine yielded the corresponding tosylate (19). In the solvolysis of this compound (19) two reactions occur:¹⁶ a direct conversion to the desired alcohol 20, and the formation of its tosylate via internal return. Hydrolysis of the latter in boiling 96% ethanol then furnished alcohol 20 in excellent yield. The 4,4-dideuterioadamantan-2-one (21) was obtained by oxidation with chromic acid in acetone.

Results

The absolute configuration of the *endo*-bicyclo[3.3.1]non-6-en-3-carboxylic acid (1), $[\alpha]_{578} +130.7^\circ$, could be assigned as (3*S*) on the basis of its transformation to the (1*S*)-4,4-dimethyladamantan-2-one.^{7,13} The assignment (3*R*) for acid 1 correlated also with the absolute configurations that could be expected for the 4(a)- and 4(e)-hydroxyadamantan-2-ones (2 and 10). Through the known chemical correlations it is clear that the absolute configurations of all of the compounds discussed in this paper are now established. The molecules as

Table I. Rotations and Deuterium Content of 5, 18, and 21

Compd ^b	Specific rotation ^a at λ , nm				% deuterium
	578	546	436	365	
5 (0.39)	[+2.7°]	[+3.2°]	[+8.4°]	[+22.7°]	97
18 (0.48)		[+1.1°]	[+2.4°]	[+5.2°]	96
21 (0.53)	[-3.4°]	[-4.0°]	[-8.3°]	[-20.4°]	98

^a Rotations are taken in isoctane. For the precision of the data see Discussion. Note solvent effect for 21, $[\alpha]_{578} -2.8^\circ$ (ethanol).
^b Concentration in parentheses.

drawn in this paper depict these absolute configurations (for nomenclature see Experimental Section).¹⁷

The 4(e)-deuterioadamantan-2-one (5) with an absolute configuration,⁵ which can be described as (1*R*), showed a positive Cotton effect for the $n\pi^*$ transition. A positive Cotton effect is also observed for the (1*R*)-4(a)-deuterioadamantan-2-one (18) while the (1*S*)-4,4-dideuterioadamantan-2-one (21) showed a negative Cotton effect. Table I lists the rotations of 5, 18, and 21 at four different wavelengths together with the percentages of deuterium incorporated.

Since the optical purities of the starting material 1 and of the 4-hydroxyadamantan-2-ones (2 and 10) are known as $84 \pm 3\%$, we assume that the optical purity of these deuterated adamantanes is in the order of 84% (see Discussion). To our knowledge direct determination of the optical purity of a ketone, which optical activity is solely due to deuterium substitution, has never been realized. Nevertheless we prepared the diastereomeric cyclic thioketals of 21 using enantiomerically pure (*S*)-(+)-butane-2,3-thiol in order to test the limit of our recently developed ¹³C method for enantiomeric excess determination.¹⁸ No separation of signals was observed. Thus the enantiomeric excess of these ketones is based upon that of the precursors.

The CD data of the three deuterated adamantane-2-ones are depicted above. The $n-\pi^*$ transition shows a surprisingly strong Cotton effect with $\Delta\epsilon$ of +0.090 at 295 nm in isoctane for the 4(e)-deuterioadamantan-2-one (5). The 4(a)-deuterioadamantan-2-one (18) exhibits a weaker Cotton effect with $\Delta\epsilon$ of +0.017 at 294 nm in isoctane, while the 4,4-dideuterioadamantan-2-one (21) gives a value of $\Delta\epsilon$ of -0.088 in the same solvent at the same wavelength.

Discussion

The CD data of the epimeric ketones 5 and 18 show that deuterium as perturber in the β equatorial position in a cyclohexanone system has much more influence on the $n\pi^*$ transition than deuterium in the β axial position has. This is generally observed for chiral perturbers β to the carbonyl chromophore in a cyclohexanone system.¹⁹

The CD spectrum of the 4(e)-deuterioadamantan-2-one (5) could be a composite of two superimposed spectra namely that of the 4(e)-deuterioadamantan-2-one (5) (>95%) and of its epimer 18 (<5%). An estimate of 1% of the magnitude of possible error introduced into the spectrum of 5 by the presence of 5% of the 4(a)-deuterioadamantan-2-one (18) can be made from the CD data knowing that the percentage axial deuterium is also >95%. For the 4(a)-deuterioadamantan-2-one (18), this error is in the order of 25%. In addition to the possible error given above, and the fact that deuterium is not 100% incorporated (see Table I), there remains the possibility of some optical fractionation of the intermediates and final products during purification.²⁰ For the dideuterio compound 21 optical fractionation and the fact that 98% deuterium is incorporated are possible errors.

An octant projection of 5 and 18 places deuterium in both compounds in the (-) back octant.²¹ For each of the compounds a positive Cotton effect is observed for the $n\pi^*$ tran-

sition. For the 4,4-dideuterioadamantan-2-one (21) the two deuterium atoms are in the (+) back octant but 21 shows a negative Cotton effect in the CD spectrum.

We therefore conclude that deuterium behaves dissignate according to the nomenclature of Kirk and Klyne²² (anti-octant in the old nomenclature). The reason for this behavior might be sought in the low refractivity of deuterium compared to that of hydrogen²³ and/or in the fact that the C-D bond length is shorter than the C-H bond length.²⁴

Experimental Section

General. Melting points were determined on a Mettler FP₂ apparatus. Infrared spectra were recorded on a Unicam SP200 infrared spectrophotometer. ¹H-NMR spectra were recorded on a Varian A60 instrument or a Varian XL-100 using tetramethylsilane as an internal standard. Mass spectra (M) were obtained on a AEI MS 902 instrument; only the parent peak is given. Gas liquid chromatography was carried out on all compounds on a Varian aerograph 1400 apparatus showing no difference in retention times for the deuterated and analogous undeuterated compounds. Optical activity was measured on a Perkin-Elmer 241 polarimeter using 10-cm cells. Circular dichroism was measured on a Cary 60 apparatus in a 1-cm cell. Both measurements were done at room temperature (20–22 °C). High-pressure liquid chromatography was carried out on a Waters LC Model 6000 A and a Prep 500 apparatus.

(3*R*)-endo-Bicyclo[3.3.1]non-6-en-3-carboxylic Acid (1). The racemic compound was synthesized as described by Faulkner and McKervey.^{8b} The racemic acid 1 (50 g) and (+)-dehydroabietylamine (86 g) were heated under reflux for 2 h in 1100 mL of 96% ethanol. The hot solution was cooled very slowly to room temperature. The salt, $[\alpha]_{578} +77.8^\circ$ (*c* 0.5 96% ethanol), obtained after nine crystallizations, was decomposed with 10% hydrochloric acid and the *endo*-bicyclo[3.3.1]non-6-en-3-carboxylic acid was extracted into ether (3 × 75 mL). The combined ether layers were treated with 2 N aqueous sodium hydroxide and the alkaline layer was acidified with 2 N hydrochloric acid, extracted with ether (3 × 50 mL), dried, and evaporated giving the (+)-*endo*-bicyclo[3.3.1]non-6-en-3-carboxylic acid (1) as a white crystalline compound, $[\alpha]_{578} +130.7^\circ$ (*c* 0.5, 96% ethanol). Spectral and physical data are identical with published values.^{8a,b} To a solution of acid 1 (50 mg, $[\alpha]_{578} +115.9^\circ$, *c* 1.0 in 96% ethanol) in benzene oxalyl chloride (400 mg) was added. After stirring for 15 min the solvent and the excess of oxalyl chloride were evaporated. The acid chloride of 1 was then dissolved in ether and placed in an ice bath.

Adding optically pure (-)- α -phenylethylamine, $[\alpha]_D -39^\circ$ (4 equiv), in ether gave a white precipitate. After being stirred for 1 h, the mixture was washed with 1 N hydrochloric acid, 10% aqueous sodium hydroxide, and water. The solution was dried and the solvent evaporated, giving a white solid (80 mg). This solid could be separated into diastereoisomers using HPLC, stainless steel column, i.d. 1/8 in., packed with Lichrosorb Si 60, 5 μ with hexane/methylene chloride as eluent.

The ratio of diastereomers was determined by integration of the peak areas (Spectra-Physics Autolab system I in line with HPLC) and found to be 8.85:1.15 (77%). Both peaks were separate and their identity was established by collecting and identifying the two amide fractions: IR (Nujol) 3400 (NH), 1640, 1540 (C=O); NMR (CDCl₃) δ 5.78 (5 H), 5–6 (3 H), 1.2–2.7 (14 H including doublet CH₃ at δ 1.37, *J* = 7 Hz); *m/e* 269.

(1*R*)-4(e)- and (1*R*)-4(a)-Hydroxyadamantan-2-one (10 and 2). A solution of (+)-*endo*-bicyclo[3.3.1]non-6-en-3-carboxylic acid (1) (1.39 g, $[\alpha]_{578} +125.6^\circ$, *c* 1.0, 96% EtOH), acetic anhydride (8 g), and distilled boron trifluoride etherate (2.4 g) in dry benzene (25 mL) was stirred at room temperature for 1 h. After cooling, cold water was added, the benzene was evaporated, and the solution was made alkaline with 10% aqueous sodium hydroxide. The mixture was heated to reflux for 1 h in order to hydrolyze the initially formed acetates. After cooling, the mixture was extracted with chloroform (4 × 50 mL) and the extract was washed with water and dried. Evaporation gave a white solid (1.1 g) of 4(e)- and 4(a)-hydroxyadamantan-2-one (10 and 2). The epimers were separated using a Waters Prep 500 apparatus, with a Preppak-500/silica cartridge at a flow rate of 250 mL/min. Elution with hexane-acetone (4:1) gave 4(e)-hydroxyadamantan-2-one (10) (yield 0.2 g (15%); $[\alpha]_{578} +5.0^\circ$ (*c* 0.54, dioxane)) and 4(a)-hydroxyadamantan-2-one (2) (yield 0.9 g (69%); $[\alpha]_{578} -15.6^\circ$ (*c* 0.48, dioxane)). All spectra data including the chiroptical properties were identical with the literature.^{11,12}

(1*R*)-4(a)-Methylsulfonyloxyadamantan-2-one (3). 4(a)-

Methylsulfonyloxadamantan-2-one (3) was synthesized from 2, $[\alpha]_{578} -15.6^\circ$, as described⁸ ($[\alpha]_{578} -3.7^\circ$ (*c* 0.45, dioxane)).

(1R)-4-Deuterioadamantan-2-deuterio-2-ol (4). A solution of 4(a)-methylsulfonyloxadamantan-2-one (3) (0.24 g, $[\alpha]_{578} -3.8^\circ$, *c* 0.4, dioxane) in ether was added dropwise to a stirred slurry of lithium aluminum deuteride (0.4 g) in ether at 0 °C. After stirring at room temperature for 30 min, the suspension was heated under reflux for 1 h. The cooled suspension was treated with ice water and the aqueous layer was extracted with ether (3 × 25 mL). The combined ether layers were washed with water and dried. Evaporation gave a white solid (0.14 g). Crystallization from hexane at -40 °C gave the 4-deuterioadamantan-2-deuterio-2-ol (4): yield 0.12 g (78%); mp 257–260 °C; IR (Nujol) 3300 (OH), 2100, 2140 cm^{-1} (CD); NMR (CDCl_3) no signal at δ 3.85; *m/e* 154.

(1R)-4(e)-Deuterioadamantan-2-one (5). 4-Deuterioadamantan-2-deuterio-2-ol (4) (0.10 g) in acetone (20 mL) was treated with Jones reagent²⁵ with stirring until the first permanent red color appeared. Propan-2-ol was added to remove the excess of Jones reagent. After evaporation of acetone, water was added. Successive extraction with ether (3 × 25 mL), drying, and evaporation gave a white solid. Purification was done using HPLC on a 30-cm stainless steel column, o.d. 1/4 in. packed with Lichrosorb Si 60, 5 μ with hexane/ CH_2Cl_2 , 1:1 as eluent. Sublimation at 120 °C (20 mm) afforded the 4(e)-deuterioadamantan-2-one (5): yield 0.06 g (60%); $[\alpha]_{578} +2.7^\circ$ (*c* 0.37, isooctane); mp 254–256 °C; IR (Nujol) 1720 (C=O), 2320, 2160 cm^{-1} (CD); NMR (CDCl_3) δ 2.65–2.45 (2 H), 2.30–1.70 (12 H); *m/e* 151.

Determination of the Percentage of Axial and Equatorial Deuterium. To the 4-deuterioadamantan-2-ones in deuteriochloroform a solution of tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium (3 g in 3 mL of CDCl_3) was added until complete separation of the signals for the nonequivalent protons of the adamantanone system was obtained in the ^1H NMR spectrum. The percentage of axial and equatorial deuterium β to the carbonyl could be determined from the integration of the peak areas of these protons. The experimental data for the integration of the peak areas of the protons α and β axial, β equatorial, γ , and δ to the carbonyl were respectively for compound 5 46-93-73-47-47 and for compound 18 41-65-85-41-42 (arbitrary units).

These data and the percentages of deuterium incorporated in both compounds (see Table I) allow a reliable estimate of >95% equatorial deuterium for 5 and >95% axial deuterium for 18 to be made.

(1S)-4,4-Ethylendioxadadamantan-2-one (13). A solution of 2 and 10 (1.1 g) prepared as described above and ethylene glycol (2 g) in anhydrous benzene containing 10 mg of *p*-toluenesulfonic acid was heated for 16 h using a Dean-Stark water separator. Ether was added and the mixture was extracted with aqueous sodium hydrogencarbonate and water. After drying the etheral extract and evaporating the solvent, the residue was treated with Jones reagent²⁵ as described above for 5. The 4,4-ethylendioxadadamantan-2-one (13) was chromatographed over alumina (Merck, Aluminum oxide 90 active, neutral). Elution with hexane/ether 3:1 gave a colorless oil: yield 0.81 g (66%); $[\alpha]_{578} -9.2^\circ$ (*c* 0.55, hexane); IR (liquid) 1710, 1730 (C=O), 1110 cm^{-1} (COC); NMR (CDCl_3) δ 3.97 (4 H), 2.65–2.40 (2 H), 2.4–1.7 (10 H); *m/e* 208. Anal. Calcd for $\text{C}_{12}\text{H}_{16}\text{O}_3$: C, 69.21; H, 7.74. Found: C, 69.04; H, 7.84.

(1R)-4(a)-Hydroxy-4(e)-deuterioadamantan-2-one (15). A solution of 4,4-ethylendioxadadamantan-2-one (13) (0.62 g) ($[\alpha]_{578} -9.2^\circ$, *c* 0.55, hexane) in anhydrous ether (20 mL) was added dropwise to a slurry of lithium aluminum deuteride (0.7 g) in anhydrous ether (25 mL). After stirring under reflux for 30 min the cooled mixture was treated as described for 4. Hydrolysis of the acetal could be achieved through boiling the acetal alcohol 14 (0.61 g) in 10% aqueous acetone with a few drops of concentrated hydrochloric acid. After evaporation of the acetone, water was added and the aqueous layer was extracted with chloroform (3 × 30 mL). The combined chloroform layers were washed with saturated sodium hydrogencarbonate and dried. Evaporation gave the 4(a)-hydroxy-4(e)-deuterioadamantan-2-one (0.38 g). After chromatography under the same conditions as for 2 pure 15 could be obtained: yield 0.32 g (57%); $[\alpha]_{578} -10.8^\circ$ (*c* 0.32, dioxane); mp 214–218 °C; IR (Nujol) 3460 (OH), 2050, 2120 cm^{-1} (CD); NMR (CDCl_3) no signal at δ 4.25; *m/e* 167.

(1R)-4(a)-Methylsulfonyloxy-4(e)-deuterioadamantan-2-one (16). Starting with 4(a)-hydroxy-4(e)-deuterioadamantan-2-one (15) prepared above 4(a)-methylsulfonyloxy-4(e)-deuterioadamantan-2-one (16) was synthesized according to the procedure described by Faulkner and McKervey.^{9b} The *dl* ketone melted at 109–111 °C; we found for 16; mp 88–89 °C; $[\alpha]_{578} -1.6^\circ$ (*c* 0.32, dioxane); NMR (CDCl_3) no signal at δ 5.22; *m/e* 245.

(1R)-4-Deuterioadamantan-2-ol (17). A solution of 4(e)-deuterio-4(a)-methylsulfonyloxadamantan-2-one (16) (0.15 g, $[\alpha]_{578}$

-1.6° , *c* 0.32, dioxane) was treated with lithium aluminum hydride (0.13 g) exactly as described for 4. Crystallization from hexane at -40 °C afforded the 4-deuterioadamantan-2-ol (17): yield 0.08 g (85%); IR (KBr disk) 3280 (OH), 2100, 2200 cm^{-1} (CD); NMR (CDCl_3) signal at δ 3.85 (HCOH); *m/e* 153.

(1R)-4(a)-Deuterioadamantan-2-one (18). 4-Deuterioadamantan-2-ol (17) (0.08 g) was treated with Jones reagent as described above for the (1S)-4(e)-deuterioadamantan-2-one (5). Purification by HPLC and sublimation afforded the 4(a)-deuterioadamantan-2-one (18) (same conditions as for 5): yield 0.05 g (63%); mp 250–253 °C; $[\alpha]_{546} +1.2 \pm 0.4^\circ$ (*c* 0.48, isooctane); IR (KBr disk) 1725 (C=O), 2100, 2180 cm^{-1} (CD); NMR (CDCl_3) δ 2.65–2.45 (2 H), 2.30–1.70 (11 H); *m/e* 151.

(3R)-3-Hydroxydideuteriomethylbicyclo[3.3.1]non-6-ene (9). A solution of *endo*-bicyclo[3.3.1]non-6-en-3-carboxylic acid (1) (1.9 g, $[\alpha]_{578} +126.4^\circ$, *c* 0.5, 96% ethanol) in ether (100 mL) was added dropwise to a stirred slurry of lithium aluminum deuteride (3.8 g) in ether (20 mL). The mixture was then heated under reflux for 2 h. After treatment of the cooled extract with water, the aqueous layer was extracted with ether (4 × 50 mL). The combined ether layers were washed with water and dried. Evaporation gave 1.64 g of a yellow oil. After short-path distillation at 170 °C (20 mm) the 3-hydroxydideuteriomethylbicyclo[3.3.1]non-6-ene (9) was obtained as a colorless oil: yield 1.52 g (87%); $[\alpha]_{578} +185.5^\circ$ (*c* 1.0, 96% ethanol); IR (liquid) 3400 (OH), 1645 (C=C), 2100, 2200 cm^{-1} (CD); NMR (CDCl_3) δ 5.5–6.0 (2 H, vinyl protons), 1.3–2.5 (11 H), no doublet at δ 3.57; *m/e* 154. Anal. Calcd for $\text{C}_{10}\text{H}_{14}\text{D}_2\text{O}$: C, 77.86; H, 9.15; D, 2.61. Found: C, 77.12; H, 9.13; D, 2.60.

(1S)-4,4-Dideuterioadamantan-2-ol (20). 9 (1.28 g) was added to a stirred solution of *p*-toluenesulfonyl chloride (1.58 g) in dry pyridine (100 mL) at 0 °C. The mixture was kept at 8 °C for 48 h and then was poured into cold water and extracted with ether (3 × 50 mL). The extract was washed successively with 10% hydrochloric acid, saturated aqueous sodium hydrogencarbonate, and water and dried. Evaporation gave an oil (19) which was immediately dissolved in 96% ethanol (100 mL) and heated under reflux overnight. After evaporation of the solvent water was added and extraction with ether (3 × 50 mL) gave (after drying and evaporation) a white compound. Crystallization from hexane gave 4,4-dideuterioadamantan-2-ol (20): yield 0.74 g (59%); $[\alpha]_{578} +0.7^\circ$ (*c* 2.0, 96% ethanol); mp 258–260 °C; IR (KBr disk) 3250 (OH), 2205, 2100 cm^{-1} (CD); *m/e* 154. Anal. Calcd for $\text{C}_{10}\text{H}_{14}\text{D}_2\text{O}$: C, 77.86; H, 9.15; D, 2.62. Found: C, 77.75; H, 9.18; D, 2.62.

(1S)-4,4-Dideuterioadamantan-2-one (21). 4,4-Dideuterioadamantan-2-ol (20) (0.55 g) in acetone (25 mL) was treated with Jones reagent²⁵ exactly as described above for (+)-4(e)-deuterioadamantan-2-one (5). Purification through sublimation afforded the (-)-4,4-dideuterioadamantan-2-one (21): yield 0.52 g (94%); $[\alpha]_{578} -2.8^\circ$ (*c* 1.0, 96% ethanol); mp 251–253 °C; IR (KBr disk) 1720 (C=O), 2100, 2200 cm^{-1} (CD); NMR (CDCl_3) δ 2.65–2.45 (2 H), 2.30–1.70 (10 H); *m/e* 152. Anal. Calcd for $\text{C}_{10}\text{H}_{12}\text{D}_2\text{O}$: C, 78.90; H, 7.95; D, 2.65. Found: C, 79.08; H, 8.06; D, 2.65.

Registry No.—(+)-1, 64889-20-9; (3R)-1, 64937-51-5; (3R)-1 dehydroabietylamine salt, 64998-10-3; (3R)-1 acid chloride, 64937-52-6; (3R)-1 (-)- α -phenylethylamide derivative, 65404-82-2; (3S)-1 (-)- α -phenylethylamide derivative, 65450-99-9; (1R)-2, 27863-77-0; (1R)-3, 65437-67-4; (1R)-4 isomer 1, 65404-83-3; (1R)-4 isomer 2, 65437-69-6; (1R)-5, 65437-68-5; (3R)-9, 65404-84-4; (1R)-10, 27863-78-1; (1S)-13, 65404-85-5; 14, 65404-86-6; (1R)-15, 65404-87-7; (1R)-16, 65404-88-8; 17, 65404-89-9; (1R)-18, 65404-90-2; 19, 65404-91-3; 20, 65404-92-4; (1S)-21, 65494-21-5; (+)-dehydroabietylamine, 1446-61-3; (-)-2-phenylethylamine, 2627-86-3.

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- After this work had been completed and during the preparation of this manuscript D. A. Lightner, T. C. Chang, and J. Horwitz, *Tetrahedron Lett.*, 3019 (1977), reported the synthesis by the old laborious route¹¹ of the chiral 4(e)-deuterioadamantan-2-one. In a short communication we previously announced the preparation of the dideuterio compound 21.⁷ Although the spectral data Lightner reports for the chiral 4(e)-deuterioadamantan-2-one agrees well with our data,²⁰ we suggest that the assignment of the absolute

configuration as reported by Lightner is in error. Thus the molecule as represented by Lightner in his figure has the configuration (1*R*) and not (1*S*) as stated in the text.

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Kinetics and Mechanisms of the Thermal Decomposition of Triphenyl-1,2-dioxetane

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Triphenyl-1,2-dioxethane (**1**) was prepared and the kinetics of thermolysis in benzene and methanol were studied in order to more clearly define stepwise vs. concerted reaction paths in dioxethane decompositions. Activation parameters in benzene are $E_a = 23.3 \pm 0.3$ kcal/mol, $\log A = 12.04 \pm 0.19$, $\Delta H^\ddagger = 22.6 \pm .3$ kcal/mol, $\Delta S^\ddagger = -5.6 \pm 0.9$ eu, and in methanol $E_a = 23.3 \pm 0.5$ kcal/mol, $\log A = 12.07 \pm 0.34$, $\Delta H^\ddagger = 22.6 \pm 0.5$ kcal/mol, $\Delta S^\ddagger = -5.5 \pm 1.5$ eu. Activation parameters were calculated for **1**, based on stepwise O-O and C-C initiated bond ruptures of the dioxetane ring. The calculated values for the O-O process are $E_a = 25.1$ kcal/mol, $\log A = 12.8$, $\Delta H^\ddagger = 24.4$ kcal/mol, $\Delta S^\ddagger = -1.86$ eu, and for the C-C process $E_a = 35.2$ kcal/mol, $\log A = 13.9$, $\Delta H^\ddagger = 34.5$ kcal/mol, $\Delta S^\ddagger = +3.2$ eu. Considering the experimental activation parameters for **1** in comparison to calculated activation parameters, based on the O-O stepwise process and in comparison to experimental activation parameters for other dioxetanes, the O-O stepwise process appears most reasonable for **1**. The lack of any significant solvent effect in proceeding from benzene to methanol is also consistent with a stepwise thermolysis of **1**.

The formation of excited state molecules in the thermolysis of dioxetanes has attracted the interest of chemists in recent years.¹ Two mechanisms have been suggested for the thermolysis of these four-ring peroxides, namely, a concerted mechanism and a stepwise process initiated with peroxide bond rupture. These two mechanisms may represent the two ends of a mechanistic sequence, where the stepwise process merges into the concerted mode as the lifetimes of the stepwise biradical species decrease.

Of the simply substituted dioxetanes that we have studied to date, it appears that the kinetic data could be most readily accommodated by a stepwise thermolysis mechanism.² For example, observed experimental activation parameters are in good agreement with those calculated based on a stepwise process. The progressive replacement of methyl groups by up to two phenyl groups caused little or no change in the activation parameters. In addition, the predominance of triplet excited state carbonyl products relative to excited state singlets can be explained in a conventional manner without violating spin conservation.^{2b}

These data suggest that we have been viewing dioxetanes that undergo decomposition at the stepwise end of the mechanistic spectrum. Dioxetanes of this type, with simple alkyl substitution or with up to two phenyl substituents,

produce predominantly triplets in low to moderate efficiency.^{2d} We are now interested to proceed toward the concerted end of this potential mechanistic spectrum. Some of the questions that arise in this survey are: (i) what type of substitution on the dioxetane ring is required to promote a concerted process; (ii) how large a change in activation parameters will be observed over the entire stepwise to concerted reaction spectrum; (iii) and how will efficiencies and electronic states of the carbonyl products vary over the mechanistic spectrum?

One of our approaches in an attempt to proceed to the concerted end of the mechanistic spectrum is to progressively place phenyl substituents on the dioxetane ring.² We now report our kinetic results with the most highly phenyl substituted dioxetane prepared to date, i.e., triphenyl-1,2-dioxetane. Kinetic studies were made in benzene and methanol solvent. The latter solvent was used to provide the most favorable conditions for a concerted process.^{2a}

Results

Triphenyl-1,2-dioxetane (**1**) was prepared by standard procedures from triphenylethylene. Numerous attempts were made to purify **1** by recrystallization and chromatography. Occasionally, **1** would partially survive silica gel column