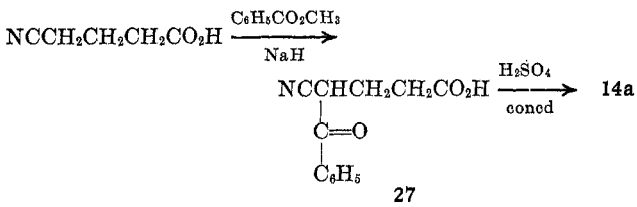
SCHEME II



for alkylations and carbonyl addition condensations involving **1a–c**, presumably because dianion formation was incomplete with this reagent.[32]

The present dianion route to α-substituted derivatives of **1a–c** permits the synthesis of a variety of such compounds in a single operation under mild conditions. Condensation at the carbanion site of dianions **2a–c** followed by hydrolysis of the imide function also offers a facile two-step method for the preparation of certain acyclic compounds, *e.g.*, the synthesis of 2-alkylglutaric and 4-aroylbutyric acids *via* dianion **2a**. Even in reactions where yields were low the dianion method may still be perferred over more circuitous procedures because of its greater convenience and the ease with which the water soluble heterocyclic precursors to dianions **2a–c** can be separated from the desired products.

(32) See J. F. Wolfe, G. B. Trimitsis, and C. R. Hauser, *Can. J. Chem.*, **43**, 2561 (1968).

Registry No.—**3b**, 19450-21-6; **3c**, 24866-78-2; **3e**, 24866-79-3; **3f**, 24866-80-6; **3g**, 24866-81-7; **3h**, 24866-82-8; **3i**, 24866-83-9; **4**, 24866-84-0; **5**, 24866-85-1; **6**, 19450-22-7; **7**, 24929-21-3; **8**, 24866-87-3; **9**, 24866-88-4; **10**, 24866-89-5; **12**, 24866-90-8; **13**, 24866-91-9; **14a**, 24866-92-0; **14b**, 19450-23-8; **14c**, 24866-94-2; **16a**, 24866-95-3; **16b**, 24866-96-4; **16c**, 24866-97-5; **16d**, 24866-98-6; **16e**, 24866-99-7; **17**, 24867-00-3; **18**, 24929-22-4; **20**, 24867-01-4; **21**, 24867-02-5; **27**, 24867-03-6; 2-(*p*-chlorobenzyl)glutaric acid, 24867-04-7.

Acknowledgment.—We are pleased to acknowledge the National Science Foundation for providing funds to aid in the purchase of the Perkin-Elmer Hitachi RMU-6E mass spectrometer used in this research. We also wish to thank Dr. John G. Dillard for obtaining the mass spectral data and Dr. Harold M. Bell for helpful discussions concerning this work.

Optically Active Adamantanes *via* Microbiological Hydroxylation. Absolute Configuration and the "Anti-octant" Effect of the Axial 3-Methyl Group of Cyclohexanone[1]

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Oxygenation of *N*-benzoyl-4β,*N*-dimethyl-1-adamantanamine (**3**) with *Sporotrichum sulfurescens* (ATCC 7159) gave *N*-benzoyl-4β,*N*-dimethyl-1-adamantanamine-4,7-diol (**5**) and (1*S*)-*N*-benzoyl-4β,*N*-dimethyl-1-adamantanamine-4,6α-diol (**6**). Oxygenation of the epimeric substrate, *N*-benzoyl-4α,*N*-dimethyl-1-adamantanamine (**4**), gave (1*R*)-*N*-benzoyl-6α,*N*-dimethyl-1-adamantanamine-4α-ol (**11**). Diol **6** readily formed a cyclic sulfite ester (**7**), proving the 1,3 diaxial relationship of the two hydroxyl groups and also establishing the relative configuration of the methyl substituent in all compounds. Nmr established that diol **6** was substituted at the 4,6 positions. Optical activity was demonstrated by circular dichroism (CD) spectra of ketones **8** and **12**, derived from **6** and **11**, respectively. The absolute configuration of the optically active molecules was assigned on the basis of the CD curve of (1*R*)-*N*-benzoyl-*N*-methyl-6-methylene-1-adamantanamine-4-one (**9**), derived from **8**. The two series of products were correlated by reduction of **9** to a mixture of **12** and its epimer, **10**. Ketone **12**, which contains an axial 3-methyl cyclohexanone system, demonstrates a weak "anti-octant" effect for this system in its CD spectrum.

Part A

Optically active adamantanones have been prepared[2] in order to test the effects of certain substituents on the octant rule.[3] Other optically active adamantanes have been prepared[4] in order to assess the effect of distance upon the optical rotatory power of various functional groups in chiral molecules.[5] In every case, resolution was achieved by the classical method of fractional crystallization of the appropriate carboxylic acid salt. We have recently found that optically active products may be obtained from the microbiological oxygenation of either achiral molecules[6] or racemic mixtures of chiral molecules[7] by the mold *Sporotrichum sulfurescens* (ATCC 7159). We have also found that the same microorganism gives good yields of hydroxylated products when *N*-acyl-1-adamantanamines are used as substrates.[8] The possibility of preparing an optically active adamantane by a microbial reaction therefore was of interest, since this would provide an alternate route to such molecules and would also further test the ability of the microbial reagent to achieve stereoselective reactions. The hydroxylation of the

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(1) Stereochemistry of Microbiological Hydroxylation. Part V.

(2) (a) W. S. Briggs, M. Suchý, and C. Djerassi, *Tetrahedron Lett.*, 1097 (1968); (b) G. Snatzke and G. Eckhardt, *Chem. Ber.*, **101**, 2010 (1968); (c) G. Snatzke and G. Eckhardt, *Tetrahedron*, **24**, 4543 (1968).

(3) W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne, and C. Djerassi, *J. Amer. Chem. Soc.*, **83**, 4013 (1961).

(4) (a) H. Hamil and M. A. McKervey, *Chem. Commun.*, 864 (1969); (b) J. Applequist, P. Rivers, and D. E. Applequist, *J. Amer. Chem. Soc.*, **91**, 5705 (1969).

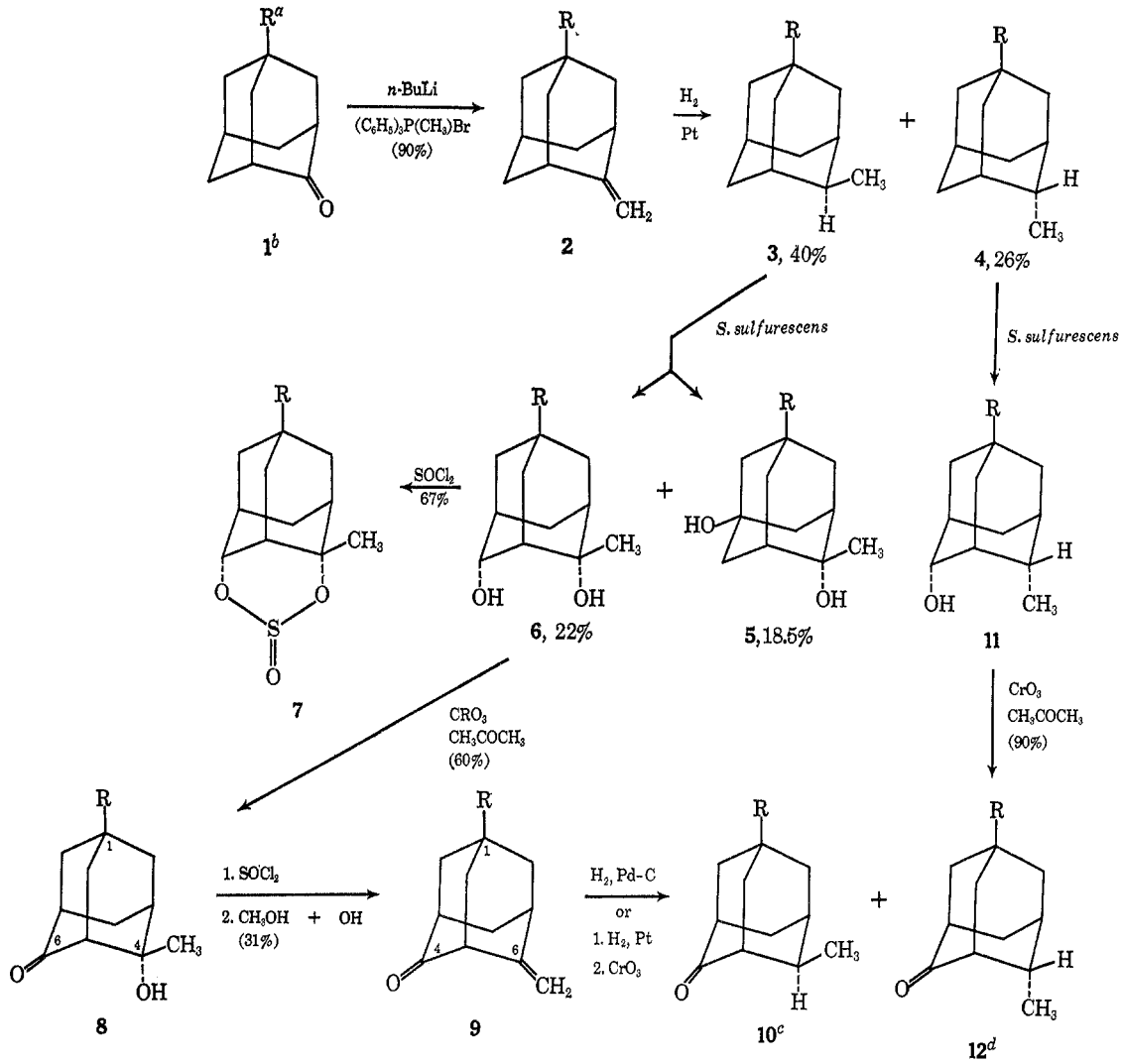
(5) R. C. Fort, Jr., and P. von R. Schleyer, *Chem. Rev.*, **64**, 277 (1964).

(6) G. S. Fonken, M. E. Herr, H. C. Murray, and L. M. Reineke, *J. Org. Chem.*, **33**, 3182 (1968).

(7) R. A. Johnson, H. C. Murray, L. M. Reineke, and G. S. Fonken, *ibid.*, **34**, 2279 (1969), and references cited therein.

(8) M. E. Herr, R. A. Johnson, H. C. Murray, L. M. Reineke, and G. S. Fonken, *ibid.*, **33**, 3201 (1968).

SCHEME I



[a] R = $-N(CH_3)COC_6H_5$ in all compounds. [b] Reference 8. [c] Not isolated. [d] 58% from 9.

epimeric *N*-benzoyl-4,*N*-dimethyl-1-adamantanamines (**3** and **4**) by *S. sulfurescens* and further chemical modifications of the products are outlined in Scheme I.

The stereoselective nature of the hydroxylations of **3** and **4** was demonstrated by the circular dichroism (CD) curves of ketones **8–10**, **12**,[9] all of which demonstrated significant carbonyl n → π* Cotton effects (see Table I). The absolute configuration of this series of compounds has been assigned on the basis of the CD curve of ketomethylene **9**, which shows a positive n → π* Cotton effect. The rotational characteristics of β,γ-unsaturated ketones, such as **9**, are critically dependent upon the relative disposition of double bond and carbonyl group.[10] However, for suitable orientations, the double bond perturber alone determines the sign of the carbonyl n → π* Cotton effect and absolute configurations can be assigned on the basis of the octant rule.[10] An excellent model for the present determination is cholest-5-en-3-one, which is known to give an n → π* Cotton curve consistent with the octant rule[11] and which has the same disposition of ketone and

TABLE I

CIRCULAR DICHROISM DATA FOR ADAMANTANES[a]

Compd	CD maxima (mμ) and molecular ellipticity ([θ], deg cm² decimol⁻¹)
8	307.5 (1540), 298 (2300), 290 (2200)
9	314 (6570), 303 (9290), 295 (7930)
12 (from **3**)	313.5 (−210), 303 (−310), 294 (−220)
12 (from **4**)	314 (−220), 303 (−310), 294 (−230)
10 and **12**[b] (mixture)	310 (420), 300 (600), 292 (570)
2(e)-methyladamantan-4-one[c]	310 (1750), 300 (2570), 292.5 (2310)
2(a)-methyladamantan-4-one[d]	313 (−230), 303 (−310), 294 (−230), 284i (−110)

[a] All CD spectra were obtained on a Cary 60-CD spectropolarimeter in dioxane using 1- or 5-cm pathlength cells and a concentration of about 0.5 mg/ml. [b] A mixture, estimated from the nmr spectrum to be approximately 2:3 in **10** and **12**. [c] Reference 2c. The solvent is dioxane. [d] Reference 13. The solvent is dioxane.

(9) We are indebted to Professor W. Klyne, Westfield College, for bringing to our attention the possibility that ketonic derivatives, such as **8**, would be more likely to have measurable optical rotation in their CD spectra than would compounds **6** or **11**. CD spectra of the latter, necessarily carried out on dilute solutions due to the strong absorbance of the benzamide chromophore, demonstrated no measurable optical activity. Other optically active adamantanes have also shown extremely low optical rotation.[4]

(10) A. Moscowitz, K. Mislow, M. A. W. Glass, and C. Djerassi, *J. Amer. Chem. Soc.*, **84**, 1945 (1962).

(11) R. Grinter, S. F. Mason, and G. W. Vane, *Trans. Faraday Soc.*, **60**, 285 (1964).

methylene as does **9**. Both cholest-5-en-3-one and **9** give positive n → π* Cotton effects with almost identical fine structure and molar ellipticity maxima, $[\theta]_{296m\mu}$ = +9750 for the former and $[\theta]_{303m\mu}$ = +9300 for **9**. This establishes the absolute configuration of **9** as (1*R*)-*N*-benzoyl-*N*-methyl-6-methylene-1-adamantanamin-4-one and of the other optically active adamantanes as shown in Scheme I. The close agreement of the Cotton effect magnitudes of **9** and cholest-5-en-3-one and the sharp melting points observed suggest that the optical purity of the compounds in the present study is very high.

The stereochemical correlations outlined in Scheme I also enabled us to consider the question of the existence of an "anti-octant" effect for an axial 3-methyl group of cyclohexanone. This question was raised by the results of Pao and Santry in their development of a self-consistent field molecular orbital (SCF MO) approach to the calculation of optical rotatory strengths, and their signs, for methyl cyclohexanones.[12] Their results were generally consistent with those expressed by the octant rule[3] except for their prediction that the sign of rotation for an axial 3 substituent on the cyclohexanone ring should be opposite and approximately equal in magnitude to that predicted by the octant rule.[12]

Ketones **8** and **10** show positive Cotton effects (Table I), consistent with the octant rule. However, ketone **12** shows a weak, negative Cotton effect, consistent in sign but having an intensity of about one-tenth that predicted by the SCF MO theory or of that observed for the equatorial 3-methyl derivative, (1*R*)-2-methyladamantan-4-one.[2c] Subsequent to the completion of this work, the preparation and CD spectra of both enantiomers of 2-methyladamantan-4-one having the methyl substituent in the axial configuration were reported.[13] Our results are in excellent agreement with those reported (see Table I) and confirm the abnormal contribution of an axial 3-methyl group to the CD spectrum of cyclohexanones. It therefore appears that, except for magnitude, the "anti-octant" effect shown by the various axial 3 perturbers, which have been examined to the present,[14] is a consequence of the position rather than of the nature of the perturber.

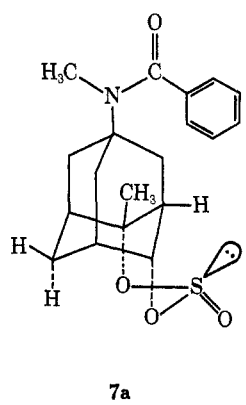
Part B

Interest in the stereochemistry of microbiological hydroxylation has led us to prepare as substrates the epimeric *N*-benzoyl-4,*N*-dimethyl-1-adamantanamines, **3** and **4**. Both are achiral compounds, but substitution at any position other than C-4 or C-7 is sufficient to introduce chirality into either molecule. This fact, combined with our previous experience with the hydroxylation of *N*-acyl-1-adamantanamines by *S. sulfurescens*,[8] held promise for the use of **3** and **4** as oxygenation substrates. If optically active products could be obtained in this manner, they would be of potential value for the study of substituent effects on the optical rotation of inherently symmetric chromophores, such as the carbonyl group. We here describe in greater detail the structural and stereochemical relationships of the products and their modifications; the optical properties of these having been summarized in Part A.

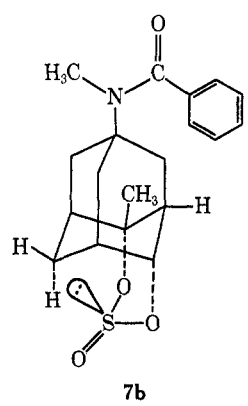
The two substrate molecules, **3** and **4**, were obtained from the reduction of the olefin **2**, which was formed in excellent yield from ketone **1**.[8] Chromatographic analyses of the reduction mixture indicated roughly equivalent amounts of the two 4-methyl derivatives; however separation of the two was extremely difficult and resulted in the lower and unequal yields shown in Scheme I.

Oxygenation of **3** with *S. sulfurescens* gave two diols, **5** and **6**, as products. One of these (**5**) failed to undergo chromic acid oxidation[15] and therefore must have two tertiary hydroxyl groups. One hydroxyl group must be at C-4 (nmr shows a singlet for the C-4 methyl group) and the other is tentatively assigned to the C-7 bridgehead position. The second diol (**6**) contained one secondary hydroxyl group, which could be oxidized to a ketone (**8**) by chromic acid. A singlet for the methyl signal in the nmr spectrum of **6** placed the tertiary hydroxyl group at the C-4 position. The two hydroxyl groups in **6** were shown to have a 1,3-diaxial relationship by the formation of the cyclic sulfite ester **7** from **6**. Only at positions C-2 ar C-6 can hydroxyl groups be placed so that they would be in a 1,3-diaxial relationship with a C-4 alcohol. The nmr spectrum (100 Mc) of **7** in deuteriobenzene showed a triplet (δ 3.92 $J \simeq 4$ Hz) for the secondary carbinol proton, which collapsed to a doublet (δ 3.95) upon irradiation of the C-5 proton. Only a C-6 carbinol proton has two adjacent protons capable of producing the observed triplet splitting. The possibility that the cyclic sulfite ester was formed from a 2,4-diol is thereby eliminated. Also, as a consequence of these observations, the stereochemistry of the methyl group in **6** can be assigned a cis configuration with respect to the *N*-methylbenzamido group. The stereochemistry of the methyl group in all molecules which have been chemically related to **6** is therefore also established.

The nmr spectrum of cyclic sulfite ester **7** is deserving of further comment. The signal for the C-5 proton at δ 3.39 at first appears extremely far downfield until the structure of the product is examined in detail. Two conformations, **7a** and **7b**, are possible for the sulfite



7a



7b

ester portion of the molecule; however examination of molecular models suggests that conformation **7b** will be

(12) Y. H. Pao and D. P. Santry, *J. Amer. Chem. Soc.*, **88**, 4157 (1966).

(13) G. Snatzke, B. Ehrig, and H. Klein, *Tetrahedron*, **25**, 5601 (1969).

(14) Snatzke and Eckhardt have previously prepared 4-chloro-, 4-bromo-, 4-iodo-, 4-azido-, and 4-carboxyadamantan-2-ones in which the 4 substituent is in an axial 3 position with respect to the cyclohexanone ring.[2b] They found that these groups also have signs of rotation opposite to those expected from the octant rule.[2c]

(15) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

highly unfavorable from consideration of steric interactions. Conformation **7a** is much more favorable and in this conformation it can be seen that considerable deshielding of the C-5 proton will occur due to the proximity of either the oxygen or the electron pair (presumably the latter) on the sulfur atom.

Oxygenation of substrate **4** gave a monohydroxylated product (**11**) in low yield. Oxidation of **11** with chromic acid gave ketone **12**, showing that the hydroxyl group of **11** was secondary. The position of the hydroxyl group was determined in the following way. Dehydration of keto alcohol **8** by treatment with thionyl chloride followed by methanolic potassium hydroxide provided the ketomethylene compound **9**. Reduction of the methylene group gave a mixture of two methyl ketones from which one could be isolated in pure form. This ketone was identical to ketone **12**, establishing that the hydroxyl group of **11** was at the C-6 position. Additionally, the identity of the two ketones establishes the relative configurations of the methyl groups in the reduction products obtained from **9**. The configuration of the hydroxyl group in **11** is presumed to be trans with respect to the benzamido group, since hydroxylation to give such an orientation of functional groups has been found to occur almost exclusively in a number of alicyclic benzamides.[16] In fact, whereas hydroxylation at the methyl substituted C-4 carbon is the one feature common to both products obtained from **3**, oxygenation at C-4 in **4** is apparently blocked by the trans methyl group at this position.

The chemical conversion of ketone **8** into ketone **12** was also necessary in order to allow assignment of absolute configurations to all of the optically active compounds obtained. It was not clear what effect the axial (with respect to the cyclohexanone ring) hydroxyl group might have on the sign of rotation in the CD curve of **8** nor was it certain that hydroxylation of the two substrates would necessarily give products of the same enantiomeric series. However, negative Cotton effects for samples of **12** obtained from both series of compounds demonstrated that the same enantiomeric form was being dealt with throughout.

Experimental Section

***N*-Benzoyl-*N*-methyl-4-methylene-1-adamantanamine (2).**—A solution of 100 ml of 1.6 *M* *n*-butyllithium in hexane was added with stirring under a nitrogen atmosphere, to a mixture of 57.3 g (0.16 mol) of methyl triphenylphosphonium bromide in 500 ml of benzene. While continuing to stir under nitrogen and maintaining the temperature at 50°, a solution of 45.4 g of *N*-benzoyl-*N*-methyl-1-adamantanamine-4-one[8] in 150 ml of benzene was added during 30 min. The mixture was heated at 60–70° for 2 hr, allowed to stand at room temperature overnight, and stirred with 300 ml of water for 2 hr, and the layers were separated. The organic layer was concentrated under reduced pressure to 200 ml and filtered. The filtrate was chromatographed over a 1200-g silica gel column which has been prepared with cyclohexane–ethyl acetate (1:1). The column was eluted in 600-ml fractions with the same solvent mixture. The residues from fractions 2–5 were recrystallized from methylene chloride–hexane to give 40 g of product: mp 94–96°; ir (Nujol) 1630, 1380, 1285, 1070, 900, 804, 728, 704 cm^{-1}; nmr ($CDCl_3$) δ 4.56 (s, 2, C=H_2), 2.79 (s, 3, N–CH_3).

Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.01; H, 8.31; N, 4.88.

***N*-Benzoyl-4β,*N*- and -4α,*N*-dimethyl-1-adamantanamine (3, 4, Respectively).**—A mixture of 25.0 g of **2**, 250 ml of methanol, and 1.0 g of platinum oxide catalyst prepared under nitrogen was shaken with hydrogen (54.5 psig) for 1 hr. The catalyst was removed by filtration through Celite and the filtrate was concentrated to dryness under reduced pressure. The solid residue was separated into its two component isomers by three chromatographs over a silica gel column, 100 g of silica gel per gram of substrate. The solvent system for elution was 10% ethyl acetate in Skellysolve B hydrocarbons and the cuts were 100 ml each. After each chromatograph, the residues were examined by silica gel tlc; the residues containing the individual isomers were pooled and those containing mixtures were rechromatographed. Recrystallization of the less polar isomer from Skellysolve B gave 10.30 g of product **3**: mp 69–71°; ir (Nujol) 1630, 1380, 1068, 1062, 1023, 803, 732, 706 cm^{-1}; nmr ($CDCl_3$) δ 2.82 (s, 3, NCH_3), 1.10 (d, 3, J = 6 Hz, $CHCH_3$).

Anal. Calcd for $C_{19}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94. Found: C, 80.50; H, 8.94; N, 4.94.

The more polar isomer was recrystallized from Skellysolve B to give 7.19 g of product **4**: mp 94–97°; ir (Nujol) 1620, 1378, 1078, 1060, 1023, 803, 730, 706 cm^{-1}; nmr ($CDCl_3$) δ 2.83 (s, 3, NCH_3), 1.07 (d, 3, J = 6 Hz, $CHCH_3$).

Anal. Calcd for $C_{19}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94. Found: C, 80.20; H, 8.93; N, 4.98.

Biotransformation Process.—The culture used in these experiments was *Sporotrichum sulfurescens* v. Beyma (ATCC 7159). The process has been described previously,[17] with the exception that we have now added a dispersing agent Ultrawet DS-30 (2.5 ml/l.) to the fermentations.

Isolation of Products from the Microbiological Oxygenations.—The general procedure was to extract the fermentation beers with methylene chloride and evaporate to dryness to give a crude extract residue, which was processed for pure products as described in the experiments below.

Bioconversion of *N*-Benzoyl-4β,*N*-dimethyl-1-adamantanamine (3) to *N*-Benzoyl-4β,*N*-dimethyl-1-adamantanamine-4,7-diol (5) and (1*S*)-*N*-Benzoyl-4β,*N*-dimethyl-1-adamantanamine-4,6α-diol (6).—The extract residue from a 2.0 g fermentation of **3** was chromatographed over 200 g of Florisil, eluting with 4 l. of solvent Skellysolve B containing increasing proportions of acetone from 0 to 50%, and collecting fractions of 60 ml each. The residues were examined by tlc and fractions 36–42 (0.73 g) were combined (pool A) and fractions 45–50 (0.63 g) were combined (pool B).

Pool A was recrystallized from methylene chloride–ether to give 0.49 g of **6**: mp 175–178°; ir (Nujol) 3300 (OH), 1610 cm^{-1} (amide); nmr ($CDCl_3$) δ 4.06 (m, 1, CHOH), 2.83 (s, 3, NCH_3), 1.45 (s, 3, $COHCH_3$).

Anal. Calcd for $C_{19}H_{25}NO_3$: C, 72.35; H, 7.99; N, 4.44. Found: C, 71.93; H, 7.96; N, 4.27.

Pool B was recrystallized from methanol–benzene to give 0.41 g of **5**: mp 221–223°; ir (Nujol) 3400 (OH), 1650 cm^{-1} (amide); nmr (DMF-d_7) δ 2.88 (s, 3, NCH_3), 1.40 (s, 3, $COHCH_3$).

Anal. Calcd for $C_{19}H_{25}NO_3$: C, 72.35; H, 7.99; N, 4.44. Found: C, 71.95; H, 7.90; N, 4.65.

Bioconversion of *N*-Benzoyl-4α,*N*-dimethyl-1-adamantanamine (4) to (1*R*)-*N*-Benzoyl-6α,*N*-dimethyl-1-adamantanamin-4α-ol (11).—The extract residue from a 2.0-g conversion was subjected to gradient chromatography over 150 g of Florisil eluting in fractions of 85 ml each with 4 l. of solvent Skellysolve B plus increasing proportions of acetone from 0 to 25%. Examinations of the fraction residues by tlc resulted in the pooling of fractions 31–34; this residue (120 mg) was recrystallized from methylene chloride–ether; yield of **4** was 70 mg: mp 181–182°; ir (Nujol) 3500 (OH), 1600 cm^{-1} (amide); nmr ($CDCl_3$) δ 2.83 (s, 3, NCH_3), 1.02 (d, 3, J = 6 Hz, $CHCH_3$).

Anal. Calcd for $C_{19}H_{25}NO_2$: C, 76.22; H, 8.42; N, 4.68. Found: C, 76.33; H, 8.21; N, 4.71.

(1*R*)-*N*-Benzoyl-6α,*N*-dimethyl-1-adamantanamine-4-one (12).—(1*R*)-*N*-Benzoyl-6α,*N*-dimethyl-1-adamantanamin-4α-ol (**11**) (13 mg) in acetone was oxidized by the Jones method and the product was recrystallized from dioxane–water to give **12**: mp 136–137°; ir (Nujol) 1740 (C=O), 1625 cm^{-1} (amide).

Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80. Found: C, 76.47; H, 7.98.

(1*R*)-*N*-Benzoyl-4β,*N*-dimethyl-1-adamantanamine-4,6α-diol Cyclic Sulfite (7).—A mixture of 100 mg of **6** and 1.0 ml of thionyl

(16) R. A. Johnson, M. E. Herr, H. C. Murray, and G. S. Fonken, *J. Org. Chem.*, **33**, 3217 (1968); *ibid.*, **35**, 622 (1970).

(17) R. A. Johnson, M. E. Herr, H. C. Murray, and G. S. Fonken, *ibid.*, **33**, 3187 (1968).

chloride was allowed to stand for 20 min and the excess reagent was removed under reduced pressure. The residue was chromatographed over 20 g of Florisil, gradient elution with Skellysolve B–acetone, to give 80 mg of product **7**. Recrystallization from ether–Skellysolve B gave the analytical sample: mp 152–154°; nmr (benzene-d_6) δ 3.87 (t, 1, J = 6 Hz, $\begin{matrix}CH\\CH\end{matrix}>CHOS$), 3.38 (m, 1, $O{=}S<\begin{matrix}OCH\\OC\end{matrix}>CHCH_2$), 1.87 (s, 3, NCH_3), 1.13 (s, 3, $OCCH_3$) (see Discussion for spectrum at 100 Mc).

Anal. Calcd for $C_{19}H_{23}NO_4S$: C, 63.13; H, 6.41; S, 8.87. Found: C, 63.28; H, 6.41; S, 8.89.

(1*R*)*N*-Benzoyl-*N*,4β-dimethyl-1-adamantanamin-4-ol-6-one (8).—Compound **6** (140 mg) in acetone was oxidized by the Jones method and the crude was recrystallized from aqueous acetone to give **8**: mp 179–182°; ir (Nujol) 3500 (OH), 1725 (C=O), 1620 cm^{-1} (amide); nmr ($CDCl_3$) δ 2.84 (s, 3, NCH_3), 1.55 (s, 3, $COHCH_3$).

Anal. Calcd for $C_{19}H_{23}NO_3$: C, 72.81; H, 7.40. Found: C, 72.88; H, 7.40.

(1*R*)-*N*-Benzoyl-*N*-methyl-6-methylene-1-adamantanamin-4-one (9).—Compound **8** (0.900 g) and 10.0 ml of thionyl chloride was warmed on a steam bath for 5 min and the excess reagent was removed under reduced pressure. The residue was triturated with water to give 0.72 g of solid. The nmr spectrum of this material indicated a mixture of about $^2/_3$ methylene-C-6 and about $^1/_3$ chloro compound; so it was taken up in 12 ml of methanol and 5.0 ml of 10% aqueous potassium hydroxide solution and heated at reflux for 3 hr. Dilution with water and concentrating gave a crude solid product which was recrystallized from acetone–water: yield of **9**, 0.26 g; mp 162–163°; ir (Nujol) 1730 (C=O), 1625 cm^{-1} (amide); nmr ($CDCl_3$) δ 4.75 (m, 2, $C{=}CH_2$), 2.84 (s, 3, NCH_3).

Anal. Calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 76.78; H, 7.62; N, 4.76.

(1*R*)-*N*-Benzoyl-6α,*N*-dimethyl-1-adamantanamine-4-one (12) and the 6β-Methyl Isomer (10).—A mixture of 155 mg of **9**, 25 ml of methanol, and 40 mg of 10% palladium on carbon was shaken with hydrogen (35 psig) for 110 min. The catalyst was removed by filtration and the residue from the filtrate was examined by nmr. The spectrum indicated a mixture of two parts of **10** to three parts of **12**. We were unable to separate the two isomers by chromatography, but pure **12** (90 mg) was obtained by direct crystallization from methanol–water: mp 138–139°; ir (Nujol) identical with **12** prepared by oxidation as described above and the mixture melting point was not depressed; nmr ($CDCl_3$) δ 2.85 (s, 3, NCH_3), 0.97 (d, 3, J = 7 Hz, $CHCH_3$). The filtrate residue from **12** was rich in **10** and melted at 83–112°, but we were unable to obtain this compound pure.

Registry No.—**2**, 25934-87-6; **3**, 25934-88-7; **4**, 25934-89-8; **5**, 25934-70-1; **6**, 25934-91-2; **7**, 25934-92-3; **8**, 25934-93-4; **9**, 25934-94-5; **11**, 25934-95-6; **12**, 25934-96-7.

Reactive Intermediates in the Anodic Oxidation of Cycloalkanecarboxylic Acids[1,2]

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Anodic oxidations of a series of α-deuteriocycloalkanecarboxylic acids (I-*n*-*d*) in aqueous solution and at carbon anodes produce mixtures containing bicycloalkanes, cycloalkene, cycloalkanol, cycloalkyl cycloalkanecarboxylate, and bicycloalkyl. The extents of internal hydrogen rearrangement accompanying the formation of alkene and alcohol products have been measured by nmr techniques. The alcohols are formed from intermediates that have undergone more hydrogen shifts than are the alkenes, with the maximum difference being found for the cyclooctane derivatives. Thermal decompositions of *tert*-butyl cyclooctaneperoxycarboxylate (II and II-*d*) and of dicyclooctylmercury in aqueous solvents produced, presumably from cyclooctyl radical intermediates, cyclooctane, cyclooctene, and cyclooctanol. The α-D peroxy ester (II-*d*) gave cyclooctene without detectable rearrangement of the deuterium label. The interpretation of these data has focused on the nature of the intermediates from which most products are formed in the electrolyses. We conclude that alcohol formation is not a dependable indication of a cationic process in aqueous solution, but still cationic rather than radical pathways account for most (if not all) of the cycloalkene, cycloalkanol, and bicycloalkane products obtained from these anodic oxidations.

Part A

The Kolbe electrolysis of salts of carboxylic acids has been known for over 100 years, and the process has been usefully employed for the synthesis of radical coupling products.[3] Renewed interest in these electrolyses has been spurred recently, however, by observations of products presumed to be formed from cationic rather than radical intermediates.[4] Although these reactions appear quite unpromising for general synthetic applications, they do appear to be reasonably convenient sources of high energy, probably poorly solvated, cationic intermediates of theoretical interest. We have investigated the anodic oxidation of a series

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