trometer was purchased through a special grant from the American Cancer Society (Massachusetts Division).

Registry No.—1 (R = O), 1224-07-03; 1 (R = OH), 55058-89-4; **2**, 55102-65-3; α isomer **3**, 55102-66-4; β isomer **3**, 55058-90-7; 3β-hydroxyandrost-5-en-17-one-7α,16,16-d_3, 55058-91-8; 3β-hydroxyandrost-5-en-17-one-7β,16,16-d_3, 55102-67-5; 3β-hydroxyandrost-5-en-17-one-7α-d_1, 55058-92-9; 3β-hydroxyandrost-5-en-17-one-7β-d_1, 55102-68-6; 3α,5α-cycloandrost-6-en-17-one-7-d, 55058-93-0.

References and Notes

(1) This is publication No. 1484 of the Cancer Commission of Harvard University. This work was presented in part: Abstracts, 156th National Meeting of the American Chemical Society, Atlantic City, N.J., Sept 1968, No. ORGN 55.

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Interpretation of the Pseudocontact Model for Nuclear Magnetic Shift Reagents. VI. Determination of the Stereoisomeric Relationships of Four Structurally Isomeric Methylbicyclooctenols[1]

M. Robert Willcott, III,*[2] Raymond E. Davis, and Richard W. Holder[3]

Departments of Chemistry, University of Houston, Houston, Texas 77004, University of Texas, Austin, Texas 78712, and Yale University, New Haven, Connecticut 06520

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Assignment of stereochemistry to the four isomeric 5-hydroxy-6-methylbicyclo[2.2.2]oct-2-enes was accomplished by both qualitative and quantitative analyses of lanthanide induced shift (LIS) NMR data. The chemical relationships between these isomers and their epimeric precursors, *endo*- and *exo*-6-methylbicyclo[2.2.2]-oct-2-ene-5-ones, allowed assignment of stereochemical features to these as well. Since some LIS indices could not be assigned accurately, a computer program was designed to use indices of low precision. The combination of auto-assignment (signal assignment by computer) and the ordinary LIS computation distinguished the four isomers by the R-factor ratio test. Statistical analysis shows that the distinction is at the 98% or greater confidence level.

The utility of lanthanide shift reagents for clarification of complex nuclear magnetic resonance spectra (LIS–NMR) and the consequent simplification of structural assignments is well established.[4] Quantitative treatment of the lanthanide-induced chemical shift has led to important decisions about the validity of the pseudocontact model,[5] structure verification,[6] and the statistical basis for the evaluations of the agreement factor.[7] Many examples of the properly judicious application of qualitative techniques for structural resolutions also have appeared.[8] We wish to document a technique of serial addition using europium(III) tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione) [Eu(fod)$_3$] which makes possible a convincing qualitative assignment of stereochemistry to four isomeric methylbicyclooctenols. The same data then are treated quantitatively in a useful extension of the R-factor method to confirm the stereochemical assignments. The good agreement between the two methods contributes to the literature of corroboration which must be constructed before the R-factor method can be trusted in cases where qualitative approaches fail.

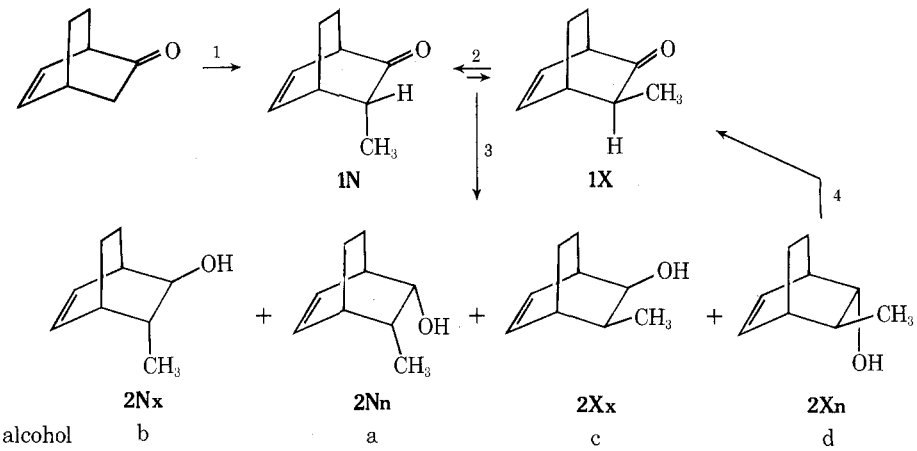
Results

The isomeric ketones *endo*- and *exo*-6-methylbicyclo[2.2.2]oct-2-en-5-one (**1N** and **1X**) and the four isomeric 6-methylbicyclo[2.2.2]oct-2-en-5-ols *endo*-CH$_3$, *endo*-OH (**2Nn**); *endo*-CH$_3$, *exo*-OH (**2Nx**); *exo*-CH$_3$, *exo*-OH (**2Xx**); and *exo*-CH$_3$, *endo*-OH (**2Xn**) were required to identify the thermolysis products in other studies.[10] Scheme I outlines the synthetic procedures used to prepare the required compounds. Prompt work-up of the product of step 1 afforded one of the epimeric ketones (later shown to be **1N**) in pure form. Delayed work-up, or subsequent treatment of **1N** by base, afforded a 65:35 mixture of **1N** and **1X**. Although analytical gas–liquid chromatography (GLC) was adequate to analyze the ketone mixture, all attempts at preparative separation failed.

Reduction of **1N** and the **1N–1X** mixture provided the four isomeric alcohols as shown. These were separated readily and purified by preparative GLC into alcohols a (mp 30–31°), b (mp 67–68°), c (mp 43–44°), and d (mp 82–84°). Jones oxidation of alcohol d, after identification as **2Xn**, afforded ketone **1X** nearly free of epimer **1N**, and proved the only feasible route to this material.

The usual spectroscopic techniques served to confirm the gross structures of compounds **1** and **2** as shown, but except for observation of intramolecular H bonding in alcohols a and d (identifying them[11] as the **2Xn, 2Nn** pair) and notation of the common methyl relationships (**1N**, a + b; **1X**, c + d), definitive stereochemical assignments were not possible. The NMR spectra of alcohols a–d then were run in $CDCl_3$ with both tetramethylsilane (Me_4Si) and $CHCl_3$ internal standards. Each sample was serially treated with successive additions of Eu(fod)$_3$ such that (1) each sample had ca. twice as much Eu(fod)$_3$ as the preceding one, and (2) the final mole ratio of alcohol:Eu(fod)$_3$ was ca. 4:1 (see Experimental Section). NMR spectra were recorded after

Scheme I[a]



[a] Reagents: 1, NaH, CH_3I, glyme; 2, NaH or NaOH; 3, $LiAlH_4$; 4, CrO_3.

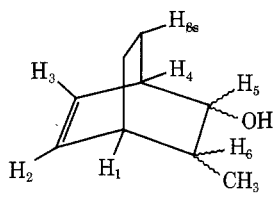
each doping, and decoupling was utilized with the most heavily doped sample to confirm signal assignments. The set of spectra measured for alcohol a is presented as Figure 1; the data for all four alcohols are contained in Table I.

Discussion

Qualitative Approach. The data for each alcohol were plotted as $\Delta\delta$ (LIS shift in parts per million measured from internal Me_4Si or $CHCl_3$) vs. the concentration ratio of alcohol to $Eu(fod)_3$ for each assignable hydrogen. Figure 2 presents the plot for alcohol a. Extrapolation of the shift values to a 1:1 alcohol:$Eu(fod)_3$ molar ratio (line broadening complicates actual measurement of the spectra at this ratio), and selecting the values for the methyl group, H_6, and vinyl protons H_2 and H_3 allows the ready assignment of stereochemistry to the four isomeric alcohols shown in Table II.

These assignments follow from the pattern of extrapolated shifts if the reasonable assumption is made that the Eu atom responsible for the shift perturbations lies spatially

Table I
NMR Chemical Shift Values for Alcohols 2Nn, 2Nx, 2Xx, and 2Xn Doped with Successive Amounts of $Eu(fod)_3$



Alcohol	Ratio alcohol:Eu(fod)$_3$	NMR, δ, ppm							
		H_1	H_2	H_3	H_4	H_5	H_6	H_{8s}	$-CH_3$
2Nn	No doping	2.34	6.56	6.25	2.80	3.96	1.97	*a*	0.88
(a)	64.8:1.0	2.48	6.66	6.42	3.06	4.38	2.16	*a*	1.20
	32.4:1.0	2.64	6.84	6.64	3.34	4.83	2.37	*a*	1.52
	16.2:1.0	2.88	7.12	7.08	3.82	5.60	2.72	*a*	2.12
	8.1:1.0	3.4	7.76	7.76	4.83	7.24	3.4	*a*	3.32
	4.1:1.0	4.44[b]	8.92[b]	9.32[b]	8.84[b]	10.48[b]	4.93[b]	*a*	5.64[b]
2Nx	No doping	2.28	6.30	6.26	2.54	3.30	1.99[c]	1.35[c]	0.93
(b)	61.8:1.0	2.36	6.36	6.32	2.72	3.64	2.20[c]	1.60[c]	1.04
	30.9:1.0	2.44	6.42	6.38	2.90	3.96	2.40	1.84	1.12
	15.4:1.0	2.59	6.52	6.48	3.30	4.64	2.84	2.30	1.33
	7.7:1.0	2.92	6.72	6.71	4.05	5.97	3.70	3.32	1.72
	3.9:1.0	3.56[b]	7.13[b]	7.13[b]	5.64[b]	8.69[b]	5.40[b]	5.30	2.52[b]
2Xn	No doping	2.34	6.80	6.34	2.72	3.40	1.15[c]	*a*	1.12
(d)	62.0:1.0	2.42	6.88	6.46	2.92	3.76	1.45[c]	*a*	1.20
	31.0:1.0	2.52	6.97	6.60	3.16	4.12	1.74[c]	*a*	1.28
	15.5:1.0	2.70	7.16	6.87	3.60	4.82	2.25[c]	*a*	1.46
	7.8:1.0	3.10	7.48	7.48	4.52	6.30	3.46	*a*	1.83
	3.9:1.0	3.85[b]	8.36[b]	8.60[b]	6.24[b]	9.38[b]	5.74[b]	*a*	2.64[b]
2Xx	No doping	2.30	6.61	6.40	2.60	3.88	1.77[c]	*a*	0.97
(c)	68.2:1.0	2.41	6.68	6.46	2.88	4.34	1.96	*a*	1.33
	34.1:1.0	2.54	6.79	6.54	3.22	4.88	2.12	2.77	1.71
	17.1:1.0	2.82	6.98	6.68	3.83	5.92	2.68	3.54	2.41
	8.5:1.0	3.40	7.36	6.95	5.04	7.85	3.56	5.16	3.70
	5.1:1.0	4.04[b]	7.77[b]	7.34[b]	6.41[b]	10.25[b]	4.74[b]	*a*	5.32[b]

[a] Not identified. [b] Identified by double irradiation. [c] Located by extrapolation.

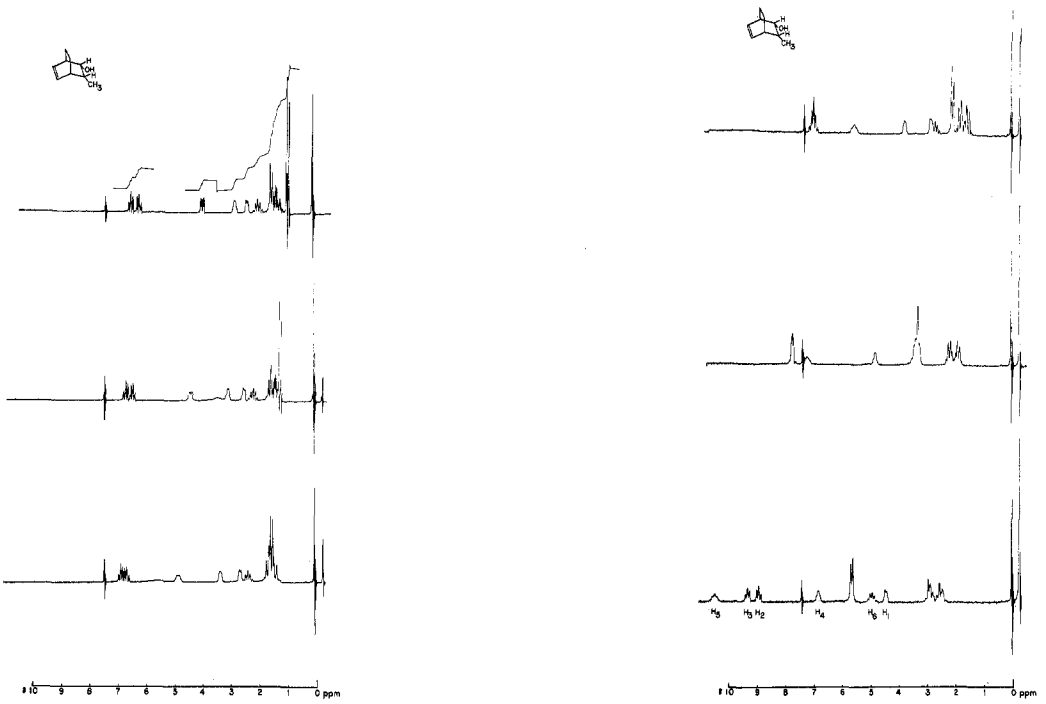
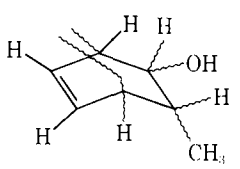


Figure 1. LIS NMR sequence for alcohol a (**2Nn**): a, no $Eu(fod)_3$; b, $Eu(fod)_3$:alcohol = 64.8:1.0; c, 32.4:1.0; d, 16.2:1.0; e, 8.1:1.0; f, 4.1:1.0.

near the oxygen with which it is complexed. Thus the shift magnitudes show that alcohols a and c have OH and CH_3 cis with OH and H_6 trans, alcohols b and d have OH and CH_3 trans with OH and H_6 cis, alcohols a and d have OH endo (near vinyl protons H_2 and H_3), and alcohols b and c have the OH exo (far from the vinyl protons). This pattern, together with the confirming indication from the ir spectra that alcohols a and d are *endo*-OH, and the aforementioned common methyl relationships, completes the stereochemical assignments deduced from the qualitative approach.

Quantitative Approach. For quantitative analysis we have selected to use the more convenient representation of the data in Table I which results from normalizing $\Delta\delta$ for H_5 = 10.0 and forcing the Eu-frequency plot[12] to be linear for each alcohol. These data are contained in Table III.[13] Seven easily assigned resonances, discrete in nearly every experimental spectrum, are shown in partial structure **3** below. The LIS indices for these signals are accurate to 3%.



3

The remaining four resonances, protons 7 and 8 of the ethano bridge, were determined by integration of the spectra and estimation of the possible locations. These four indices are of poor precision (±20%), and cannot be assigned reliably.

We have been investigating local stereochemistry by using partial sets of assigned LIS indices on a routine basis; in this instance we tested four data sets consisting of the seven LIS values for structure **3** vs. each of the four possible geometrical arrangements (**2Nn, 2Nx, 2Xn, 2Xx**). *R* values were obtained for all reasonable locations of the europium relative to the alcohol by a systematic search procedure.[6c] Our experience with the analysis of LIS spectra of

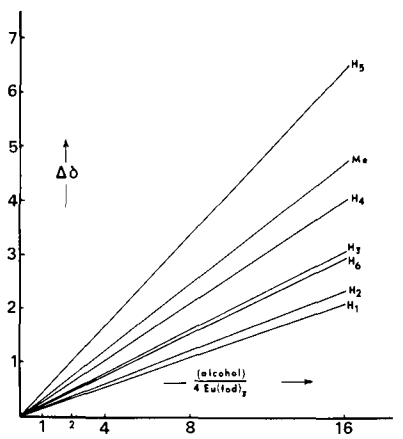


Figure 2. $\Delta\delta$ vs. ratio of added $Eu(fod)_3$ for LIS NMR spectra of alcohol a (**2Nn**).

alcohols led us to select the region in which the C–O–Eu bond angle was 120 ± 20°, the disposition of the europium was away from the steric bulk of the substrate, and the oxygen–europium distance was 2.6 ± 0.4 Å as the "reasonable" locations to investigate. The minimum *R* values obtained in this way for the 16 combinations of data vs. isomer are in Table IV.

Even before applying statistical criteria it is clear that alcohol a accords best with isomer **2Nn** and alcohol d less reliably with isomer **2Xx**. Matching of the two remaining isomers (**2Nx, 2Xn**) with alcohols b and c from *R* factors is not possible at this stage. We were not surprised that isomers **2Nx** and **2Xn** were confused after we realized that the flattened partial structure **3** is enantiomeric for this pair. Note also that an inordinate emphasis is placed on the correct identification of **2Nn**.

A more thorough analysis of the data indicated that inclusion of the poorly determined resonances of the ethano bridge could define all of the structures. We devised a computational feature, auto-assign, to incorporate this additional information. For each lanthanide location during the

Table II
Δδ Extrapolated to 1.0:1.0 Alcohol:Eu(fod)$_3$ Ratio

Alcohol	$-CH_3$	H_6	H_2	H_3	Assignment
a	14.0	8.9	7.0	9.3	**2Nn**
b	4.8	10.2	2.5	2.6	**2Nx**
c	10.8	7.7	2.8	2.5	**2Xx**
d	4.8	13.7	5.1	6.7	**2Xn**

Table III
Chemical Shift Perturbations of Compounds 2

	a	b	c	d
	Assigned Resonances			
H_1	3.22	2.52	2.38	2.73
H_2	3.62	2.61	1.54	1.48
H_3	4.71	3.78	1.61	1.82
H_4	6.18	5.88	5.76	5.97
H_5	10.00	10.00	10.00	10.00
H_6	4.54	7.66	6.30	4.66
CH_3	7.60	2.52	2.95	6.83
	Unassigned Resonances			
H_8	2.3	2.5	7.4	8.0
H_8	2.0	2.0	3.3	4.5
H_7	2.0	2.0	2.2	3.9
H_7	1.7	?	2.2	3.5

systematic search we compute a hypothetical spectrum, match the seven assigned resonances, and select by computer the arrangement of the remaining ethano resonances which produce the lowest overall R factor.[14]

The effect of including the ethano resonances and using auto-assign for the signals due to H_7 and H_8 completes the stereochemical assignments as displayed in Table V. The paired combinations of structure and data omitted from Table V had R factors much larger than those reported in Table IV. The Hamilton statistical tests were carried out as previously described.[7,15] In this testing method, pairwise comparison of four possible structures vs. each data set was made. In this study any one data set points to a single structure, and excludes the other three possibilities. The fact that we found four different structures for the four data set assures the integrity of the PDIGM approach, and encourages the continued use of the LIS method to assess topology.

Conclusions

When all possible stereoisomers of a given set are available it would appear that in many favorable cases qualitative evaluation of NMR data generated by serial additions of a lanthanide shift reagent will allow confident assignment of all stereochemical features. Partial LIS information can be adequate to define the stereochemistry of rigid molecules (such as partial structure **3** vs. **2Nn** and **2Xx** models) even where some members of the stereoisomeric set are absent. Two similar partial sets of experimental data (alcohols b and c) when matched with similar structures (**3**, flattened, makes **2Xn** and **2Nx** enantiomeric) require that less certain LIS indices be introduced to remove the ambiguities.

We are aware that the simplified pseudocontact computational model we have used may be incorrect in several respects. Nevertheless, this interpretation of substrate structure from these LIS data is self-consistent and in complete agreement with the chemical evidence. We will continue to use the pseudocontact model for the interpretation of structure from lanthanide induced shifts until it is shown to give erroneous results.

Table IV
Minimum R Factors for All Structure-Data Pairs. Partial Structure 3

	2Nn	2Nx	2Xn	2Xx
a	4.7	33	38	15.6
b	21.5	5.0	9.0	20.8
c	11.6	5.2	7.8	12.9
d	5.3	30	31	4.1

Table V
Critical Decisions Using Partial Structure 3 and Ethano Bridge Data

	2Nn	2Nx	2Xn	2Xx
a	4.8			
b		6.4	14.0	
c		28	9.2	
d	30.4			5.8

Experimental Section

Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, Ga., and by Alfred Bernhardt Microanalytisches Laboratories, Elbach, West Germany. Melting points were determined on a Thomas-Hoover capillary apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 237 spectrophotometer as dilute solutions in CCl_4. All reported absorptions were corrected with reference to polystyrene bands in the appropriate spectral regions. Nuclear magnetic resonance spectra were obtained on a Jeolco Minimar 100-MHz instrument. Preparative gas-liquid chromatography (GLC) separations were obtained with a Varian Aerograph Model A-90 instrument equipped with a thermal conductivity detector with helium as the carrier gas. Analytical GLC determinations were carried out using a Perkin-Elmer Model 900 gas chromatograph equipped with flame ionization detectors with nitrogen as the carrier gas. Quantitative GLC analyses resulted from automatic integration of peak areas performed by a Hewlett-Packard digital integrator, Model 3370A. The GLC columns utilized are identified as follows: A, 234-ft capillary TCEP; B, 20 ft × 0.375 in., 20% TCEP on 60–80 Chromosorb P; C, 5 ft × 0.125 in., 5% FFAP on 100–120 Chromosorb P (AW, DMCS); D, 20 ft × 0.375 in., 20% FFAP on 60–80 Chromosorb W.

***endo*-6-Methylbicyclo[2.2.2]oct-2-en-5-one (1N).**[16] A well-stirred mixture of 1.94 g (0.081 mol) of oil-free sodium hydride, 285.0 g (2.0 mol) of methyl iodide (washed with sodium bisulfite, dried, and redistilled), and 400 ml of glyme (distilled from lithium aluminum hydride) was heated to 55°. A solution of 4.25 g (0.035 mol) of bicyclo[2.2.2]oct-2-en-5-one[17] in 20 ml of glyme was added in one portion. From time to time 3-μl aliquots were withdrawn and analyzed by GLC (column A, 115°). After 3.0 hr the analysis showed 10.0% 6,6-dimethylbicyclo[2.2.2]oct-2-en-5-one, 74.7% **1N**, 3.7% *exo*-6-methylbicyclo[2.2.2]oct-2-en-5-one (**1X**), and 11.6% unreacted bicyclo[2.2.2]oct-2-en-5-one. The reaction was quenched by adding 100 ml of water and cooling to 25°. The resulting mixture was poured into 200 ml of water and extracted with petroleum ether, and the extracts were washed thoroughly with water. After drying over magnesium sulfate, flash distillation provided 12 g of material, which was concentrated further to 4.66 g by distilling ca. 8 ml of glyme away. Preparative GLC (column B, 170°) was utilized to obtain pure **1N**. The endo configuration was assigned on the basis of the alcohols derived from it by lithium aluminum hydride reduction (vide infra and Discussion). The following spectral properties were observed: ir (CCl_4) 3050, 2950, 2910, 2865, 1740 (C=O), 760 cm^{-1}; NMR ($CDCl_3$) δ 6.2–5.8 (m, 2, vinyl), 3.04 (m, 1), 2.80 (m, 1), 2.1–1.4 (m, 5), 0.99 (d, J = 7.3 Hz, $-CH_3$). Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.83. Found: C, 79.40; H, 8.93.

***endo*-6-Methylbicyclo[2.2.2]oct-2-en-5-one (1N) and *exo*-6-Methylbicyclo[2.2.2]oct-2-en-5-one (1X).** When quenching and work-up of the product mixture from methylation of bicyclo[2.2.2]oct-2-en-5-one was delayed for an additional 3.0 hr, GLC (column A, 115°) showed that isomerization of the kinetic product (**1N**) had occurred to form a 64.6:35.4 mixture of **1N** and epimer

1X. Alternatively, treatment of pure **1N** with sodium hydroxide in methanol provided the same 64.6:35.4 mixture of **1N:1X.** Although capillary GLC was adequate to analyze these two epimers, attempts at preparative resolution failed.[18] Pure **1X** was obtained only from oxidation of an exo-methyl alcohol as described below.

***endo*-6-Methylbicyclo[2.2.2]oct-2-en-*endo*-5-ol (2Nn) and *endo*-6-Methylbicyclo[2.2.2]oct-2-en-*exo*-5-ol (2Nx).** To a well-stirred slurry of 169 mg (4.5 mmol) of lithium aluminum hydride in 35 mg of dry ether, contained in a dry reaction vessel under a nitrogen atmosphere, was added dropwise a solution of 202 mg (1.5 mmol) of **1N** in 12 ml of ether over a 1-hr period. The resulting gray, heterogeneous mixture was stirred for 16 hr and then worked up by successive dropwise additions of 0.169 ml of water, 0.169 ml of 15% sodium hydroxide, and 0.507 ml of water.[19] After a further 1.5 hr of stirring, during which time the solids turned white and granular, the reaction mixture was filtered. The solids were washed with ether, and the combined filtrate was dried over magnesium sulfate, refiltered, and concentrated by flash distillation through a 10-cm Vigreux column to afford 192 mg (93%) of cloudy, colorless oil. Analysis by GLC (column C, 120°) showed the presence of two components in the ratio 69.2:30.8 in the order of their elution times. The two products were separated preparatively by GLC (column D, 135°).

The major, first-eluting, component was a white, waxy solid, mp 30–31°, and was identified as **2Nn** (alcohol a) on the basis of the following spectroscopic properties (see Discussion): ir (CCl_4) 3630 (O–H), 3595 (intramolecular H bond,[11] remains upon dilution), 3050, 2945, 2870, 1615 (C=C), 1060, 715 cm^{-1}; NMR ($CDCl_3$) δ 6.56 (d of d, $J_{12} = J_{23} = 7.8$ Hz, 1, H_2), 6.25 (d of d, $J_{23} = J_{34} = 7.8$ Hz, 1, H_3), 3.96 (d of d, $J_{56} = 8.0$, $J_{45} = 4.0$ Hz, 1, H_5), 2.80 (broad s, 1, H_4), 2.34 (broad s, 1, H_1), 1.97 (m, 1, H_6), 1.60–1.12 (m, 5), 0.88 (d, $J = 7.0$ Hz, 3, $-CH_3$); the NMR run with sequential additions of $Eu(fod)_3$ is summarized in Table I. Anal. Calcd for $C_9H_{14}O$: C, 78.02; H, 10.21. Found: C, 78.09; H, 10.16.

The minor, second-eluting component was also a white, waxy solid, mp 67–68°. It was identified as **2Nx** (alcohol b) on the basis of its spectroscopic characteristics (see Discussion): ir (CCl_4) 3620 (O–H), 3440 (intermolecular H bond), 3040, 2950, 2940, 2910, 2870, 1630 (C=O), 1010, 710 cm^{-1}; NMR ($CDCl_3$) δ 6.4–6.2 (m, 2, H_2 + H_3), 3.30 (broad s, 1, H_5), 2.53 (broad s, 1, H_4), 2.28 (broad s, 1, H_1), 1.96 (s, 1, OH), 2.0–1.0 (m, 5), 0.93 (d, $J = 6.5$ Hz, 3, $-CH_3$); the NMR run with sequential additions of $Eu(fod)_3$ is summarized in Table I. Anal. Calcd for $C_9H_{14}O$: C, 78.02; H, 10.21. Found: C, 77.97; H, 10.26.

***exo*-6-Methylbicyclo[2.2.2]oct-2-en-*endo*-5-ol (2Xn) and *exo*-6-Methylbicyclo[2.2.2]oct-2-en-*exo*-5-ol (2Xx).** Using 708 mg (5.2 mmol) of an equilibrium mixture of **1N:1X** (66.4:33.6, obtained by base-catalyzed epimerization of **1N,** vide supra) and 590 mg (15.6 mmol) of lithium aluminum hydride, the above-described reduction procedure and work-up provided 680 mg (94%) of milky-white semisolid. Analysis by GLC (column C, 120°) showed four components in the ratio 46.0:16.8:20.4:16.8 (order of elution times). All four products were obtained pure by preparative GLC (column D, 135°). The first-eluting component proved to be **2Nn** and the third-eluting component was **2Nx.** The second-eluting component, a white solid, mp 82–84°, was identified as **2Xn** (alcohol d) by the following spectroscopic properties (see Discussion): ir (CCl_4) 3600 (O–H), 3580 (intramolecular H bond,[11] remains upon dilution), 3360 (intermolecular H bond, disappears upon dilution), 3027, 2930, 2860, 1635 (w), 1050, 715 cm^{-1}; NMR ($CDCl_3$) δ 6.80 (d of d, $J_{12} = J_{23} = 7.5$ Hz, 1, H_2), 6.34 (d of d, $J_{23} = J_{34} = 7.5$ Hz, 1, H_3), 3.40 (slightly broadened s, 1, H_5), 2.72 (broad s, 1, H_4) 2.34 (broad s, 1, H_1), 1.8–0.8 (m, 6), 1.12 (s, 3, $-CH_3$, coincident with H_6); the NMR run with sequential additions of $Eu(fod)_3$ is summarized in Table I. Anal. Calcd for $C_9H_{14}O$: C, 78.02; H, 10.21. Found: C, 78.24; H, 10.12.

The fourth-eluting component, a white solid, mp 43–44°, was assigned the structure of the only remaining isomer, **2Xx** (alcohol c), on the basis of its spectroscopic properties (see Discussion): ir (CCl_4) 3610 (O–H), 3450 (intermolecular H bond, disappears upon dilution), 3027, 2930, 2870, 1625 (w), 1020, 705 cm^{-1}; NMR ($CDCl_3$) δ 6.61 (d of d, $J_{12} = J_{23} = 7.5$ Hz, 1, H_2), 6.40 (d of d, $J_{23} = J_{34} = 7.5$ Hz, 1, H_3), 3.88 (d of d, $J_{56} = 8.3$, $J_{45} = 4.0$ Hz, 1, H_5), 2.60 (broad s, 1, H_4), 2.30 (broad s, 1, H_1), 2.0–1.0 (m, 5), 1.67 (s, 1, OH), 0.97 (d, $J = 7.5$ Hz, 3, $-CH_3$); the NMR run with sequential additions of $Eu(fod)_3$ is summarized in Table I. Anal. Calcd for $C_9H_{14}O$: C, 78.02; H, 10.21. Found: C, 78.11; H, 10.12.

***exo*-6-Methylbicyclo[2.2.2]oct-2-en-5-one (IX).** A solution of 47.1 mg (0.34 mmol) of **2Xn** in 30 ml of acetone over 250 mg of sodium sulfate was cooled to −5° in an ice–acetone bath. Jones reagent[20] was added dropwise with stirring until a pale orange color persisted for 5 min. Two drops of 2-propanol was added to discharge the orange color. The reaction solution was filtered and the solids were washed with acetone. The combined filtrates were concentrated by rotatory evaporation to a pale blue-green oil which was taken up in 50 ml of ether, washed once with saturated sodium chloride, and dried over sodium sulfate. Filtration and concentration afforded a yellow oil (35.2 mg) which upon GLC analysis (column A, 95°) proved to be a 75:25 mixture of **1X:2Xn.** Purification by GLC (column B, 140°) provided 12.6 mg (36%) of **1X,** contaminated by <3% **1N** from epimerization under the mild Jones conditions. The structure was assigned by the method of synthesis and the following spectral properties: ir (CCl_4) 3050, 2980, 2960, 1730 (C=O), 1120, 720, 715, 675 cm^{-1}; NMR ($CDCl_3$) δ 6.58 (d of d, J = 7.5 Hz, 1, H_3 or H_2), 3.08 (broad s, 1, H_4 or H_1), 2.76 (broad s, 1, H_1 or H_4), 2.2–0.8 (m, 5), 1.08 (d, $J = 8.0$ Hz, 3, $-CH_3$). Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.83. Found: C, 79.10, H, 8.97.

Reduction of 1X. The stereochemical integrity of the Jones oxidation used to isolate **1X** was demonstrated further by reducing 7.7 mg (0.06 mmol) of **1X** with lithium aluminum hydride according to the procedure described above. Work-up provided an ethereal solution which GLC analysis (column C, 115°) showed to contain only **2Xn** and **2Xx** in the ratio 53:47. No trace of **2Nn** or **2Nx** was present.

Procedure for Measuring $Eu(fod)_3$-Doped NMR Spectra. Using the case of **2Nn** for an example, 32.1 mg (0.232 mmol) of pure **2Nn** was dissolved in the minimum amount of $CDCl_3$, which contained 3% tetramethylsilane and 3% $CHCl_3$ as a double internal standard,[21] and the spectrum was run. Enough $Eu(fod)_3$ was dissolved in a second portion of solvent to ensure a final doping ratio of 4:1 alcohol:$Eu(fod)_3$; in this case 59.3 mg (0.057 mmol) was used. An aliquot of the $Eu(fod)_3$ solution was added to the NMR tube, and the spectrum was run again.[22] The process was repeated, with aliquot sizes calculated so that each doping ratio was twice the preceding one. In this case the ratios were **2Nn**:$Eu(fod)_3$ = 64.8:1.0, 32.4:1.0, 16.2:1.0, 8.1:1.0, and 4.1:1.0. Signal assignments were made on the most highly doped sample with the aid of extensive decoupling experiments, and then each resonance was tracked back as described in the Discussion section using such plots as Figure 2. The data generated for the four alcohols are summarized in Table I.

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Registry No.—**1N,** 53626-33-8; **1X,** 53626-32-7; **2Nn,** 54446-71-8; **2Nx,** 54515-25-2; **2Xn,** 54515-26-3; **2Xx,** 54515-27-4; bicyclo[2.2.2]oct-2-en-5-one, 2220-40-8; $Eu(fod)_3$, 17631-68-4.

References and Notes

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(2) John Simon Guggenheim Memorial Fellow, 1972–1973, University of Houston.
(3) National Science Foundation Graduate Fellow No. 8700-35-45821, 1968–1972. Address comments regarding the synthetic aspects of this work to this author at Chemistry Department, University of New Mexico, Albuquerque, N.Mex. 87131.
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(22) The instrument often needs retuning for each new doping ratio. A delay of several minutes between placing the doped sample in the probe and running the spectrum minimizes the retuning problem.
(23) The program PDIGM includes the autoassign algorithm. Copies of the program are available on request from R.E.D. or M.R.W.

Synthesis and Properties of Some Heterocirculenes[1]

J. H. Dopper and Hans Wynberg*

Department of Organic Chemistry, The University, Zernikelaan, Groningen, The Netherlands

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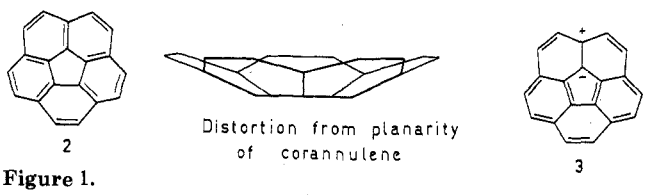
The synthesis of some heterocirculenes is reported. Based on a model study, we recognize two classes of circulenes, namely planar and nonplanar ones. Depending on the ratio of the outer and inner radii, bowl-shaped and corrugated nonplanar circulenes may exist. Attempts to prove that [7]-heterocirculenes belonged to the corrugated type of circulenes failed. The spectral characteristics of heterocirculenes are reported in detail.

Coronene and Corannulene. Coronene (1) is unique in the family of polycyclic aromatic compounds.[2] It has been of interest for many years not only because of its symmetric graphite-like structure but also because its synthesis continues to present a challenge to the ingenuity of the organic chemist. Scholl and Meyer announced in 1932 the first synthesis of **1**.[3a] Since then others have reported improved

1

syntheses of **1**.[3bc] The high symmetry of the coronene molecule is of great value in the interpretation of spectroscopic results and their mathematical treatment. Coronene is an alternant hydrocarbon. According to the Hückel approximation there is no net charge on any atom in the system and the energy levels are symmetrically placed about the value of the α integral.[4] A complete determination of the coronene structure has been obtained by X-ray analysis.[5] It is a completely flat molecule. The carbon–carbon length varies in different parts of the molecule. The central ring and the "spokes" connecting it to the outer edges have bond lengths of 1.43 Å. The outer bonds are of two types measuring 1.41 and 1.38 Å. The planarity of coronene—and its many benzoid homologs—is an obvious consequence of the angular fusion of six benzene rings in the manner indicated (see **1**). When the number of aromatic rings—angularly annulated to form a "coronene"—deviates from six, the possibility of nonplanarity arises. A classical example of this type of molecules is corannulene (**2**), first prepared and studied by Barth and Lawton.[6] It has attracted much interest because despite its coronene-like structure it differs from the latter in two essential features. (a) Corannulene is a nonplanar, highly strained molecule. X-Ray analysis[6] demonstrates that it has a bowl-like shape (Figure 1). (b) Corannulene is a nonalternant hydrocarbon.[4] According



2 3

Figure 1.

to the Hückel theory, the electronic charge on each carbon atom differs in the ground state from one. An attractive way to accommodate this charge separation is found in structure **3**, in which two concentric annulene systems are formed. Both the cyclopentadienyl anion as well as the cyclopentadecaheptaenyl cation obey the well-known Hückel $4n + 2$ rule. SCF–MO calculations carried out by Gleicher[7] support the idea that **3** contributes to the stability of the ground state. However, no experimental data have been presented which substantiate any contribution from **3**.

Results of a Model Study. The structural differences between **1** and **2** (planarity vs. nonplanarity) can be made clearer by the following considerations. It is assumed that there are two circles of fixed diameter both of which are (within moderate limits) flexible. These circles (radii $r1$ and $r2$, $r1 < r2$) are connected by spokes of a constant length a (Figure 2).

The optimal geometry will be determined by the following factors.

(a) If $r1 + a = r2$ then both circles will lie in a common plane (Figure 2a), as in coronene (**1**).

(b) If $r1 + a > r2$ then a likely geometry is one in which

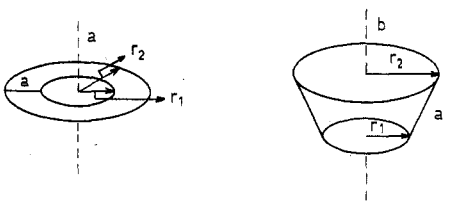


Figure 2.