added to suppress ionization. Sodium chloride was added to keep the concentration of anions constant (at 0.40 *M* for *N*,*N*-dimethylethylene diamine and *N*,*N*-dimethyl-1,3-propanediamine, and at 0.17 *M* for *N*,*N*-dimethyl-1,4-butanediamine and *N*,*N*-dimethyl-1,5-pentanediamine). The chemical shift of 75% neutralized methylamine was found to be unaffected by the addition of 0.5 *M* sodium chloride. All plots of chemical shift *vs.* number of equivalent of acid added for monoamines were linear.

Determinations of pK_a.—Standard aqueous solutions of the diamines were titrated potentiometrically at 35 ± 1° with standard perchloric acid using a Beckman Research pH meter, Model 101900. About 15 pH readings were taken in the range 0.2–0.8 mol of acid per mole of diamine and another 15 in the range 1.2–1.8 mol of acid per mole of diamine. The pH was taken as $-\log a_{H^+}$, and the Davies equation[8] (which becomes eq 5 at 35°) was

$$\log f = -0.52Z^2\left(\frac{\sqrt{\mu}}{1+\sqrt{\mu}} - 0.2\mu\right) \qquad (5)$$

used to calculate ionic activity coefficients. Each of the possible pairs of pH values, one from the first and one from the second part of the titration, was used to calculate a value of pK_1 and pK_2, and the results obtained in a given titration were averaged.[9] Considering that the values of pK_1 depend largely on the pH's measured with around 0.5 mol of acid per mole of diamine, and the values of pK_2 depend largely on pH's measured with about 1.5 mol of acid per mole of diamine, the average ionic strengths at which the values of pK_1 were obtained ranged from about 0.014 to 0.19 *M* and those at which pK_2 were obtained ranged from about 0.023 to 0.23 *M*. For each amine the concentration of amine and titrating acid were varied so that the ionic strength at which each p*K* was determined varied by at least threefold. In no case was any trend noticed in the thermodynamic pK_a values, the overall average values of which are listed with their standard deviations in Table III.

The values of f_m and f_d used in the plots according to eq 1 were calculated from the concentration acidity constants at the appropriate ionics trength which was calculated from the thermodynamic constants and the Davies equation.

Registry No.—$Me_2N(CH_2)_2NH_2$, 108-00-9; $Me_2N(CH_2)_3NH_2$, 109-55-7; $Me_2N(CH_2)_4NH_2$, 3529-10-0; $Me_2N(CH_2)_5NH_2$, 3209-46-9.

Acknowledgment.—We wish to thank Kenneth W. Narducy for the computer calculation of the p*K* values reported here.

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[8] C. W. Davies, *J. Chem. Soc.*, 2093 (1938).

[9] *Cf.* D. J. MacDonald, *J. Org. Chem.*, **33**, 4559 (1968).

Bicyclo[3.1.0]hexane Conformation. The Crystal Structure of *N-exo*-6-Bicyclo[3.1.0]hexyl-*p*-bromosulfonamide

MARVIN F. GROSTIC,* DAVID J. DUCHAMP, AND CONNIE G. CHIDESTER

The Research Laboratories, The Upjohn Company, Kalamazoo, Michigan 49001

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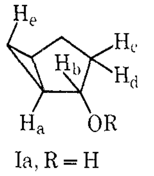
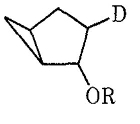
The crystal structure of the *p*-bromosulfonamide of 6-aminobicyclo[3.1.0]hexane has been determined by single-crystal X-ray diffraction. This structure shows the boat conformation as previously indicated by nuclear magnetic resonance studies.

A nuclear magnetic resonance (nmr) study of compounds I and II indicated that the bicyclo[3.1.0]hexane system was in the boat conformation.[1] This



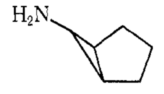
Ia, R = H
b, R = CH_3



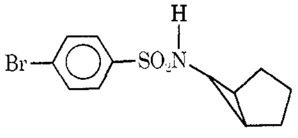
IIa, R = H
b, R = CH_3

conformation explained the unique doublet at τ 6.27 (*J* = 5.1 cps) in the nmr spectrum of compounds Ia and Ib resulting from the splitting of the absorption of the *cis* C-2 hydrogen (H_b in I) by the *cis* C-3 hydrogen (H_c in I). This was verified by the synthesis of IIb and the presence of a singlet at τ 5.88 in its nmr spectrum. Other nmr studies have also confirmed this boat conformation for the bicyclo[3.1.0]hexane system.[2-6]

The synthesis of 6-aminobicyclo[3.1.0]hexane (III)[7] offered an opportunity to prepare a heavy atom derivative for X-ray crystallographic studies as an



III



IV

independent method of testing the conformation of bicyclo[3.1.0]hexanes. The *p*-bromosulfonamide IV was prepared according to the Hinsberg reaction.[8]

Results and Discussion

Crystallographic Measurements.—The structure of the *p*-bromosulfonamide IV was determined by single-crystal X-ray diffraction using the heavy-atom method. Details of the structure analysis, final atomic coordinates (Table I), and thermal parameters (Table I) are given in the Experimental Section.

Figure 1 is a plot of the X-ray data of the molecule with the hydrogens placed in their calculated rather than observed coordinates. As this figure indicates, the bicyclo[3.1.0]hexane system is in the boat conformation. The four ring atoms, C(8), C(9), C(11), and C(12) are all coplanar with the C(7) and C(10) atoms lying

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[1] P. K. Freeman, M. F. Grostic, and F. A. Raymond, *J. Org. Chem.*, **30**, 771 (1965).

[2] M. S. Bergqvist and T. Norin, *Ark. Kemi*, **22**, 137 (1964).

[3] K. Tori, *Chem. Pharm. Bull.*, **12**, 1439 (1964).

[4] H. E. Smith, J. C. D. Brand, E. H. Massay, and L. J. Durham, *J. Org. Chem.*, **31**, 690 (1966).

[5] A. Diefferbacker and W. von Philipsborn, *Helv. Chem. Acta*, **49**, 897 (1966).

[6] S. Winstein, E. C. Friedrich, R. Baker, and Y. Lin, *Tetrahedron, Suppl.*, **8**, II, 621 (1966).

[7] The authors wish to thank Dr. Jacob Szmuszkovicz, The Upjohn Co., for this compound.

[8] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 5th ed, Wiley, New York, N. Y., 1964, p 119.

TABLE I

FINAL ATOMIC COORDINATES AND THERMAL PARAMETERS FOR COMPOUND IV[a]

	X	Y	Z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Br	40107 (7)	100785 (16)	23354 (5)	1270 (8)	5119 (40)	645 (4)	−415 (34)	713 (9)	351 (21)
S	−559 (14)	26460 (30)	14252 (8)	913 (15)	3190 (63)	272 (5)	727 (59)	405 (14)	164 (35)
O(1)	−4059 (37)	20261 (70)	6541 (21)	1245 (47)	3557 (180)	287 (15)	1208 (160)	422 (43)	5 (85)
O(2)	3760 (38)	10208 (76)	20194 (22)	1264 (49)	3447 (168)	353 (17)	1102 (161)	454 (47)	817 (92)
N	−11926 (42)	37601 (96)	14816 (24)	915 (49)	4481 (222)	250 (17)	370 (190)	367 (48)	−73 (109)
C(1)	10774 (47)	46545 (104)	16599 (28)	794 (51)	3505 (257)	257 (20)	736 (209)	504 (54)	200 (122)
C(2)	20189 (54)	47736 (109)	24028 (31)	1022 (61)	3880 (285)	280 (22)	611 (254)	350 (60)	608 (142)
C(3)	29015 (54)	63911 (127)	26012 (34)	867 (62)	4736 (300)	340 (25)	547 (247)	398 (66)	746 (151)
C(4)	28208 (55)	78771 (112)	20593 (37)	941 (62)	3501 (273)	529 (30)	189 (237)	928 (75)	−196 (153)
C(5)	18900 (58)	77747 (110)	13166 (33)	1128 (69)	3366 (274)	325 (24)	695 (249)	422 (66)	437 (142)
C(6)	10254 (54)	61469 (124)	11271 (31)	1000 (64)	4307 (284)	240 (21)	846 (239)	342 (62)	396 (137)
C(7)	−18372 (48)	55544 (103)	9545 (32)	679 (50)	3118 (262)	344 (23)	162 (188)	300 (55)	−316 (121)
C(8)	−27724 (60)	49382 (111)	1664 (36)	1309 (72)	2298 (235)	435 (26)	670 (262)	157 (71)	−218 (150)
C(9)	−31130 (79)	65908 (145)	−4627 (43)	2270 (123)	5116 (369)	477 (35)	2542 (376)	931 (110)	44 (188)
C(10)	−33738 (73)	87061 (139)	−1488 (44)	1576 (93)	4351 (313)	689 (40)	1764 (314)	1126 (104)	895 (197)
C(11)	−37478 (62)	79528 (153)	4422 (43)	1078 (76)	6945 (453)	607 (36)	2007 (322)	633 (85)	−838 (205)
C(12)	−31569 (59)	57497 (138)	7311 (39)	924 (65)	5546 (380)	539 (32)	582 (265)	763 (77)	464 (176)

	X	Y	Z		X	Y	Z
H(1)	2046 (51)	3723 (98)	2707 (30)	H(8)	−3439 (49)	4886 (91)	991 (30)
H(2)	3587 (49)	6087 (99)	3151 (29)	H(9)	−4773 (50)	7527 (99)	83 (31)
H(3)	1790 (49)	8854 (99)	977 (29)	H(10)	−3952 (49)	8918 (99)	692 (31)
H(4)	494 (51)	6316 (99)	666 (30)	H(11)	−2841 (50)	9354 (95)	−106 (30)
H(5)	−1003 (49)	4081 (96)	1941 (31)	H(12)	−4255 (51)	9788 (89)	−701 (31)
H(6)	−1290 (48)	6982 (95)	1101 (30)	H(13)	−3836 (52)	5895 (99)	−987 (31)
H(7)	−2662 (51)	3686 (99)	69 (30)	H(14)	−2629 (54)	6440 (99)	−720 (30)

[a] × 10^4 for hydrogens, × 10^5 for other atoms. Standard deviations in the last digit are given in parentheses following each parameter.

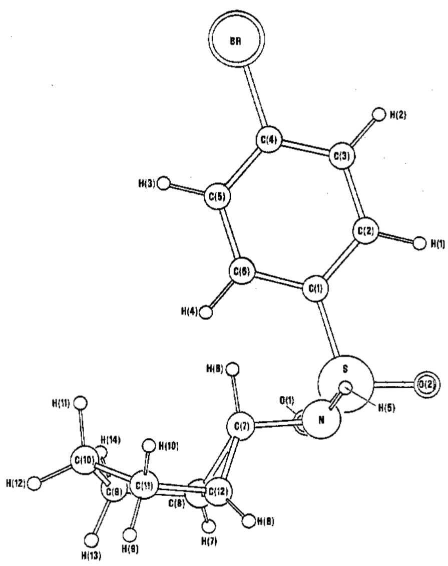

Figure 1.—Plot of compound IV molecule.

above the plane determined by these four ring atoms. Table II lists the best plane calculations from the X-ray data and clearly shows that C(7) and C(10) are on the same side of the determined plane.

TABLE II

BEST PLANE CALCULATIONS FOR CRYSTALLINE COMPOUND IV

Atom	Deviation, Å	Wt
C(8)	0.0000	1.00
C(9)	0.0000	1.00
C(10)	−0.4125	0.0
C(11)	0.0000	1.00
C(12)	0.0000	1.00
C(7)	−1.1974	0.0

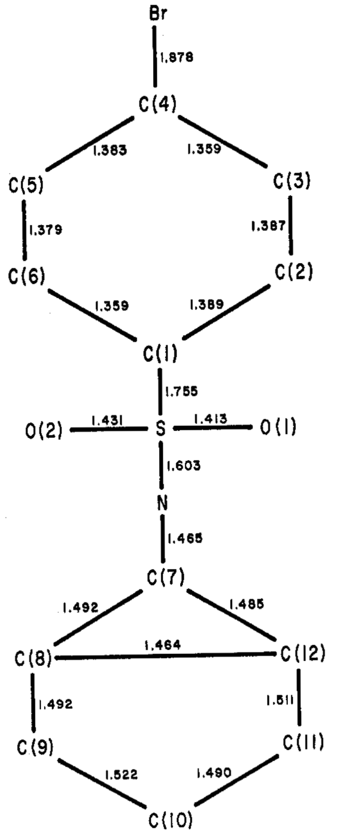

Figure 2.—Observed bond lengths for compound IV.

Figures 2 and 3 show the observed bond lengths and angles for compound IV. These values are within expected values for a compound of this type. Standard deviations are estimated to be 0.01 Å for C–C bonds and 1.0° for C–C–C angles.

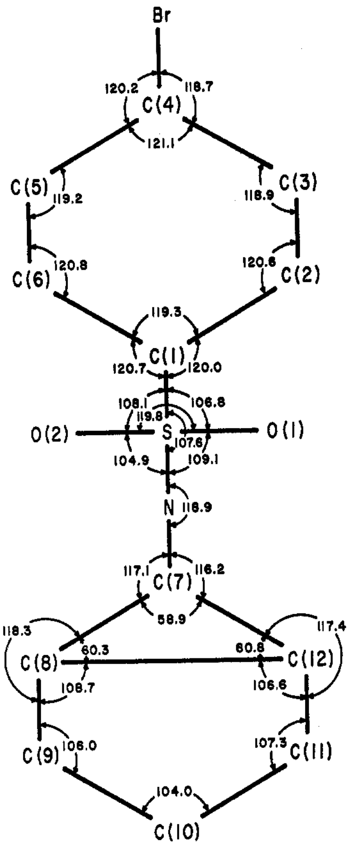

Figure 3.—Observed angles for compound IV.

The dihedral angle calculations were of particular interest in this molecule. Since, in the nmr study of compounds I and II, the dihedral angles were estimated from the coupling constants, it was hoped that the X-ray results would be similar. Figures 4a and 4b show this to be true. Since the hydrogen positions determined in X-ray refinement with heavy atoms present are poor, calculated hydrogen positions (assuming standard geometry) were used in X-ray dihedral angle calculations. The estimated dihedral angles from nmr studies of I were about 20° for the H_b-C-C-H_c angle and about 100° for the H_b-C-C-H_d angle. These correspond to the X-ray results of 26.5 and 95.3°, respectively (Figure 4a), or 26.9 and 94.8° (Figure 4b). Likewise, the H_a-C-C-H_b angle was estimated at about 80° and found by X-ray to be 75.7° [H(7), C(8), C(9), H(14)] and 74.7° [H(8), C(12), C(11), H(10)].

Experimental Section

***N-exo*-6-Bicyclo[3.1.0]hexyl-*p*-bromosulfonamide.**—A mixture of 480 mg of *p*-bromosulfonyl chloride and 360 mg of *exo*-6-aminobicyclo[3.1.0]hexane in 10 ml of dry benzene was allowed to stand for 1 hr at room temperature. The solution was filtered and the filtrate was evaporated. The residue was recrystallized from dilute ethanol and analyzed by infrared and mass spectrometry. Crystals suitable for the X-ray analysis were obtained by crystallization from an acetone–Skellysolve B mixture.

Crystallographic Measurements.—*N-exo*-6-Bicyclo[3.1.0]hexyl-*p*-bromosulfonamide (IV) crystallizes in the monoclinic space group $P2_1/c$ as evidenced by systematic absences of $h0l$ for l odd and $0k0$ for k odd. The unit cell constants are a = 12.31 (±0.02), b = 6.10 (±0.01), and c = 19.45 (±0.03) Å, β = 116.8° (±0.2°). The calculated volume is 1460 Å^3; the calculated density is 1.437 g/cm^3 assuming four molecules per unit cell.

Complete three-dimensional intensity data were measured using a General Electric diffractometer with an Electronics and

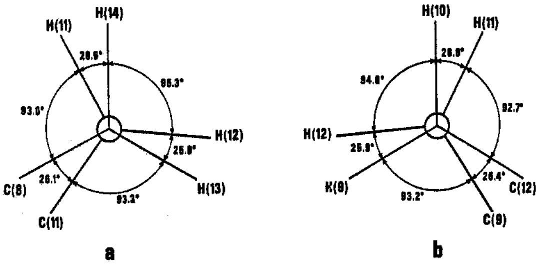

Figure 4.—(a) Dihedral angles along the C(9) (front) and C(10) (back) bond. (b) Dihedral angles along the C(11) (front) and C(10) (back) bond.

Alloys full circle orienter and Datex automation. The crystal was coated by dipping in colloidion. The θ–2θ scan technique with nickel-filtered copper radiation and a scintillation counter were used. The crystal showed significant change during data collection as evidenced by the intensities of the reflections 5,0,2; 0,0,10; and 0,4,0 which were measured periodically during data collection. $I_{\text{final}}/I_{\text{initial}}$ was 0.76.

Background counts were taken on either side of each peak and averaged, scaled, and subtracted from the cumulative scan count to give the observed intensity for each reflection. If the observed intensity so obtained was negative, it was set equal to zero and assigned zero weight in subsequent calculations. Observed intensities were corrected for Lorenz and polarization effects in the usual way. Intensities were then corrected for crystal deterioration. An absorption correction was applied using the method of Busing and Levy.[9] The linear absorption coefficient is 60.1 cm^{-1} for copper K_α radiation. Each intensity was assigned a standard deviation according to[10]

$$\sigma^2(I) = \sigma^2 \text{ counting} + (0.03)I^2$$

The data were placed on an approximate absolute scale by Wilson statistics. Through all the corrections described above, the assigned standard deviation for each observed intensity was scaled by propagation of error to give a standard deviation for that corrected intensity. The final set of data consisted of 2183 reflections of which 119 were assigned zero weight.

Derivation of a trial structure proceeded by the heavy atom method. Positions for the bromine and sulfur atoms were derived from analysis of a three-dimensional sharpened Patterson map. Structure factors calculated using these two atoms were used to phase a three-dimensional electron density map. From this map positions for the remaining 15 atoms were easily derived.

The structural parameters and the scale factor were refined by multiple-matrix least squares. The function minimized was $\Sigma\omega(|F_0|^2 - |F_c|^2)^2$. The initial weighting function was the Hughes I/F_0 type. Scattering factors are those of the "International Tables for X-Ray Crystallography."[11] Several cycles of least squares with isotropic temperature factors were followed by several cycles of least squares with anisotropic thermal parameters according to the expression

$$\exp[-(h^2B_{11} + k^2B_{22} + l^2B_{33} + hkB_{12} + hlB_{13} + klB_{23})]$$

A difference Fourier was then calculated to locate hydrogen atoms. Predicted positions for all hydrogen atoms were also calculated to aid in interpretation of the difference map. All hydrogens were found at positions very close to the calculated positions. No extraneous peaks were observed. Hydrogen coordinates were included in the refinement; all hydrogen atoms were assigned an isotropic temperature factor of 3.5 which was not refined. For the refinements the weighting scheme used was

$$\sqrt{\omega} = \frac{1}{\sigma(F_0{}^2)}$$

where $\sigma(F_0{}^2)$ was the one assigned at data reduction time and subsequently scaled.

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[9] W. R. Busing and H. A. Levy, *Acta Crystallogr.*, **10**, 180 (1957).

[10] S. W. Peterson and H. A. Levy, *ibid.*, **10**, 70 (1957).

[11] "International Tables for X-Ray Crystallography," Vol. III, Kynoch Press, Birmingham, England, 1959.

A correction for secondary extinction was applied according to the equation[12]

$$(F_c*)^2 = \frac{F_c^2}{1 + g\beta F_c^2}$$

The parameter, g, was refined in the least squares. With the hydrogen atoms and secondary extinction factor included, the refinement was continued until shifts in all positional and thermal parameters were less than $^1/_3$ standard deviations. The final R for these refinements was 0.076. The

$$\text{weighted } R = \left\{\frac{\Sigma\omega(|F_0|^2 - |F_c|^2)^2]}{\Sigma\omega|F_0|^4}\right\}^{1/2} = 0.13$$

and the standard deviation of fit =

$$\left\{\frac{\Sigma\omega(|F_0|^2 - |F_c|^2)^2}{m - s}\right\}^{1/2} = 1.90$$

The standard deviation of fit is expected to be 1.0 if the refinement has converged and if the weighting scheme and structural model are adequate.

The final parameters are listed in Table I. The final value of the secondary extinction parameter, g, is 1.041 × 10^{-5}. A table of observed and calculated structure factors has been deposited with the National Auxiliary Publication Service.[13] All calculations were done on the IBM 360 computer using programs of the CRYM system written by one of the authors (D. J. Duchamp).

Registry No.—IV, 31128-90-2.

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[12] A. C. Larson, *Acta Crystallogr.*, **23**, 664 (1967).

[13] Listings of structure factors will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Reprint Department, ACS Publications, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to author, title of article, volume, and page number. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

Conformation and Reactivity in the *cis,trans*-2,6-Cyclodecadienyl System[1,2]

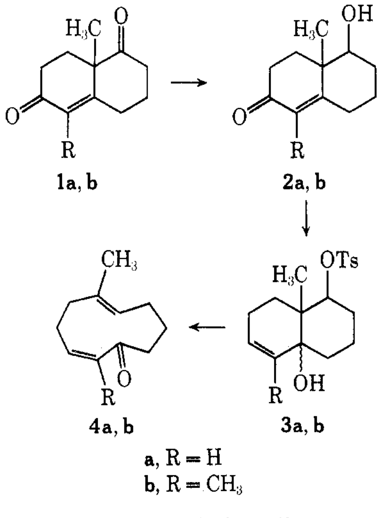
P. S. WHARTON* AND M. D. BAIRD

Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706

Received February 23, 1971

6-Methyl- and 2,6-dimethyl-*cis,trans*-2,6-cyclodecadienones (**4a** and **4b**) were synthesized by fragmentation of octalin diol monotosylates. They exhibit the properties of twisted α,β-unsaturated ketones. 2,6-Dimethyl-*cis,trans*-2,6-cyclodecadienyl methyl ether exists in two conformations in carbon disulfide (70:30 at −62°). Solvolysis of the corresponding *p*-nitrobenzoate (**5** PNB) in buffered acetic acid at 30° yielded exclusively *trans*-bicyclo[5.3.0] products, and it is tentatively concluded that participation of the C-6,7 double bond contributes significantly to the solvolytic rate.

Ten-membered rings have been of unusual interest with respect to the stereochemisty of transannular reactions.[3] The following study of the *cis,trans*-2,6-cyclodecadienyl system, originally undertaken with thoughts of sesquiterpene synthesis, is exemplary.



6-Methyl-*cis,trans*-2,6-cyclodecadienone (4a) was prepared by fragmenting hydroxy tosylate **3a** with potassium *tert*-butoxide in *tert*-butyl alcohol.[4] Cyclodecadienone **4a** was obtained in 20% overall yield from ketol **2a**[5] by conversion of the ketol to a crystalline tosylate which was then subjected to epoxidation, hydrazine reduction, and fragmentation, without isolation of intermediates.[6] Dienone **4a**, obtained by this method, exhibits the properties of a twisted α,β-unsaturated ketone. The ultraviolet maximum at 228 nm in ethanol is of low intensity, ε 4680.[7] The relative nmr shifts of the α and β hydrogens are reversed from normal, with the β hydrogen at τ 4.4 at higher field than the α hydrogen at τ 3.8.[7] The stereochemistry of the double bonds of **4a** must be cis-2 (unchanged during the reaction, with the vinyl hydrogens showing a coupling constant of 11.5 Hz[7]) and trans-6 (determined by the geometrical constraint of the fragmentation step[8]).

2,6-Dimethyl-*cis,trans*-2,6-cyclodecadienone (4b) was then synthesized, without further study of **4a.** It was prepared in 64% overall yield by the procedure already described but starting from ketol **2b**.[9] The new dienone differs from **4a** solely by the presence of a methyl group at C-2, but this additional methyl group greatly facilitated analysis of a reaction described later

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[1] This investigation was supported by Public Health Service Research Grants GM 14133 and GM 16338 from the Division of General Medical Sciences, U. S. Public Health Service.

[2] This article is abstracted from the Ph.D. thesis of M. D. B., University of Wisconsin, 1969. The research was carried out in part at Wesleyan University.

[3] For a survey of transannular reactions in medium-sized rings see A. C. Cope, M. M. Martin, and M. A. McKervey, *Quart. Rev., Chem. Soc.*, **20**, 119 (1966).

[4] Under similar conditions formation of another 2,6-cyclodecadienone by fragmentation–elimination has been demonstrated by M. Iguchi and A. Nishiyama, *Tetrahedron Lett.*, 4295 (1969).

[5] C. B. C. Boyce and J. S. Whitehurst, *J. Chem. Soc.*, 2680 (1960).

[6] This sequence is superior to that originally used to prepare 6-methyl-*trans*-5-cyclodecenone, which unnecessarily involved benzoylation of ketol **2a** and subsequent saponification; see P. S. Wharton, *J. Org. Chem.*, **26**, 4781 (1961).

[7] *cis*-2-Cyclodecenone exhibits a uv maximum at 227 nm in ethanol with ε 3500 and nmr chemical shifts for the α and β protons at τ 3.67 and 4.23, respectively, $J_{2,3}$ = 11.9 Hz. For further comparison the following constants are also noted: *cis*- and *trans*-2-cycloundecenones, $J_{2,3}$ = 12.1 and 16.7 Hz, respectively; *cis*- and *trans*-2-cyclododecenones, $J_{2,3}$ = 11.6 and 15.9 Hz, respectively. See M. Regitz and J. Ruter, *Chem. Ber.*, **102**, 3877 (1969).

[8] P. S. Wharton and G. A. Hiegel, *J. Org. Chem.*, **30**, 3254 (1965), and references cited therein.

[9] V. F. Kucherov and I. A. Gurvich, *Zh. Obshch. Chim.*, **31**, 796 (1961); *J. Gen. Chem. USSR*, **31**, 731 (1961).