

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY, DETROIT 2, MICH.]

Conformational Analysis. XII. The Bicyclo[5.3.0]decanes^{1,2}

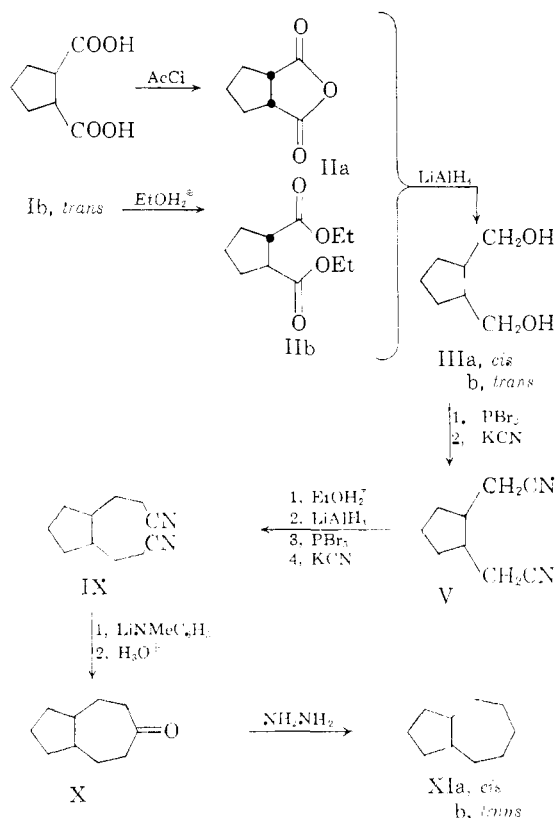
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The *cis* and *trans* isomers of the bicyclo[5.3.0]decanes (perhydroazulenes) have been prepared and equilibrated at various elevated temperatures by heating with palladium catalyst. The *trans* predominates slightly at equilibrium, $K_{535} = 1.5$. For the reaction *cis*- \rightleftharpoons *trans*-perhydroazulene, the calculated thermodynamic quantities are: $\Delta H_{535} = 0.3 \pm 0.2$ kcal./mole, and $\Delta S_{535} = 0.3 \pm 0.4$ e.u.

Because of the occurrence of the perhydroazulene ring system in a variety of natural products,³ the relative stability of the *cis* and *trans* isomers is of some interest. Previous work with the decalins⁴ and hydrindanes⁵ has shown that the thermodynamic quantities for such isomerizations can be obtained by equilibrating the isomers at various elevated temperatures. It is usually possible to obtain ΔH and ΔS for the reaction with an accuracy that is comparable to that which can be obtained by the more laborious calorimetric methods.⁶ The failure of the equilibration method in the case of the bicyclo[5.2.0]nonane system because of the facility of hydrogenolytic ring cleavage was also noted.⁷

The present work was directed at obtaining the thermodynamic quantities for the perhydroazulene system by means of this equilibration technique. The preparation of the two perhydroazulenes has been reported previously,⁸ but the synthesis used in the present work was somewhat different and is outlined on the flowsheet. The *cis* and *trans* isomers of 1,2-cyclopentanedicarboxylic acid, the former as the anhydride and the latter as the diester, were used as starting materials. These acids were twice chain extended *via* the alcohols, halides and nitriles, and yielded the stereoisomerically pure nitriles IX. The latter were ring closed and converted to the ketones X by the Thorpe-Ziegler method.⁷ Wolff-Kishner reduction⁹ of the ketones gave the pure isomers of perhydroazulenes XI. The physical constants of the compounds had the following values; *cis*: b.p. 196.5° (746 mm.), $n_D^{25} 1.4744$, $d_4^{25} 0.8940$; *trans*: b.p. 190.5° (746 mm.), $n_D^{25} 1.4717$, $d_4^{25} 0.8816$. From these constants the conformational rule¹⁰ indicates



that the *trans* is of lower heat content, and this is correct.

The equilibration of the *cis*- and *trans*-perhydroazulenes was carried out by heating small samples in sealed tubes with a palladium-on-carbon catalyst. Equilibrium was approached from both sides at several temperatures over the range 494–576°K. The method of choice for analysis of equilibrated hydrocarbon mixtures is vapor phase chromatography.⁴ Unfortunately all of the many columns tried proved to be unsuited for the present separation. The analysis was therefore carried out by the less accurate infrared method. Using synthetic mixtures it was found that an accuracy of about $\pm 2\%$ in the *cis/trans* ratio was possible.

When an analysis such as the present one is carried out by the infrared method, there is always the possibility that decomposition products are present, and these may lead to incorrect analytical values. It was found that a band at 12.8 μ appeared and steadily increased when either of the isomers was treated under equilibration conditions. This band

(1) Paper XI. N. L. Allinger, J. Allinger, L. A. Freiberg, R. Czaja and N. A. LeBel, *J. Am. Chem. Soc.*, **82**, 5876 (1960).

(2) This research was supported in part by a grant from the Research Corporation and in part by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of these funds.

(3) For example, see Elsevier's "Encyclopedia of Organic Chemistry," edited by E. Josephy and F. Radt, Vol. 12A, Series III, Elsevier Publisher Co., Inc., New York, N. Y., 1948, p. 420.

(4) (a) N. L. Allinger and J. L. Coke, *J. Am. Chem. Soc.*, **81**, 4080 (1959); (b) *J. Org. Chem.*, *in press*.

(5) N. L. Allinger and J. L. Coke, *J. Am. Chem. Soc.*, **82**, 2553 (1960).

(6) For more detailed calorimetric data on the decalin system see (a) J. P. McCullough, H. L. Finke, J. F. Messerly, S. S. Todd, T. C. Kincheloe and G. Waddington, *J. Phys. Chem.*, **61**, 1105 (1957); (b) W. G. Dauben, O. Rohr, A. Labbauf and F. D. Rossini, *ibid.*, **64**, 283 (1960); (c) T. Miyazawa and K. S. Pitzer, *J. Am. Chem. Soc.*, **80**, 60 (1958). For the hydrindane system, see C. C. Browne and F. D. Rossini, *J. Phys. Chem.*, **64**, 927 (1960).

(7) N. L. Allinger, M. Nakazaki and V. Zalkow, *J. Am. Chem. Soc.*, **81**, 4074 (1959).

(8) F. Sorm and M. Romanuk, *Coll. Czech. Chem. Comm.*, **22**, 779 (1957).

(9) Huang-Minton, *J. Am. Chem. Soc.*, **68**, 2487 (1946).

(10) N. L. Allinger, *ibid.*, **79**, 3443 (1957).

continued to increase in intensity after equilibrium was reached, and yet no further change in the *cis/trans* ratio occurred. As long as only this ratio was used it was clear that the analysis would not be affected by this impurity.

From the *cis/trans* ratios at different temperatures a plot of $\ln K$ vs. $1/T$ was made. The intercept and slope of the least squares line drawn through the experimental points,⁴ gave for the liquid phase isomerization *cis* \rightleftharpoons *trans*-perhydroazulene: $\Delta H_{535} = -0.3 \pm 0.2$ kcal./mole, and $\Delta S_{535} = 0.3 \pm 0.4$ e.u. The small magnitude of these values is noteworthy, and indicates that when substituted perhydroazulenes are considered, the relative stabilities will probably be altered considerably depending on the types and arrangements of the substituents.

The entropy of the *trans* isomer might have been expected to be larger than that of the *cis* by $R \ln 2 = 1.4$ e.u., since it is *dl* while the *cis* is *meso*. The *cis* is probably a little more flexible though, and it appears that the effects just about cancel. The small difference in enthalpy is as expected. The conformations of the cycloheptane molecule have been examined theoretically,¹¹ and it was found that almost any dihedral angle is available with very little change in enthalpy or, in other words, both isomers are unstrained. The enthalpy difference between the isomers should therefore be much smaller than that found in the hydrindane case (1.07 kcal.).⁵

Experimental

Diethyl *trans*-1,2-Cyclopentanedicarboxylate (IIb).—Pimelic acid was converted to diethyl α, α' -dibromopimelate,¹² b.p. 172–177° (5 mm.). This compound gave 1-cyano-1,2-dicarbethoxycyclopentane¹³ upon treatment with sodium cyanide, and hydrolysis¹² of this material furnished *trans*-1,2-cyclopentanedicarboxylic acid, m.p. 161–162°. Esterification by the azeotropic method gave IIb, b.p. 114–115° (5 mm.), n_D^{20} 1.4421 (reported¹³ b.p. 133° (17 mm.), n_D^{20} 1.4451).

***cis*-1,2-Cyclopentanedicarboxylic Acid Anhydride (IIa).**—The *trans*-diacid Ib was converted to the *cis*-anhydride^{12b} with acetyl chloride, yield 71%, b.p. 117–120° (3 mm.), m.p. 73–74°; reported^{12b} m.p. 73.5–74°.

***cis*-1,2-Bis-(hydroxymethyl)-cyclopentane (IIIa).**—Reduction of anhydride IIa with lithium aluminum hydride gave the diol, yield 85%, b.p. 99–102° (0.1 mm.), n_D^{20} 1.4810; reported¹³ b.p. 103° (0.15 mm.), n_D^{20} 1.4840.

***cis*-1,2-Bis-(bromomethyl)-cyclopentane (IVa).**—Diol IIIa was converted to the dibromide by adding 0.18 mole dropwise with stirring during 2 hours to 0.18 mole of phosphorus tribromide cooled in an ice-salt-bath. The mixture was allowed to warm to room temperature, and was then heated at 80° overnight. The reaction mixture was poured onto ice and the mixture was extracted with methylene chloride. The combined extracts were washed with dilute sodium carbonate solution and dried with anhydrous calcium chloride. The solvent was evaporated and the dibromide was distilled, b.p. 109–110° (4 mm.), n_D^{20} 1.5392, yield 70%.

Anal. Calcd. for $C_7H_{12}Br_2$: C, 32.83; H, 4.72. Found: C, 33.17; H, 4.71.

***cis*-1,2-Bis-(cyanomethyl)-cyclopentane (Va).**—A solution containing 17 g. of dibromide IVa and 9.2 g. of potassium cyanide in 100 ml. of 75% ethanol was heated under reflux for 15 hours. After 50 ml. of alcohol was distilled, the residue was diluted with cold water and extracted with

ether. The ether layer was separated, washed with saturated sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the product was distilled; yield 62%, b.p. 125° (0.75 mm.), n_D^{20} 1.4759.

Anal. Calcd. for $C_9H_{12}N_2$: C, 72.94; H, 8.16. Found: C, 72.70; H, 7.06.

***cis*-1,2-Bis-(carbethoxymethyl)-cyclopentane (VIa).**—Dinitrile Va, 27 g., was heated in a refluxing solution containing 64 ml. of concd. sulfuric acid in 165 ml. of 95% ethanol for 15 hours. The cooled mixture was poured into water and the resulting mixture was extracted with ether. The ether phase was washed with dilute sodium bicarbonate solution and water, and was dried. The ether was removed and the diester was distilled; b.p. 142–150° (5 mm.), yield 34 g. (77%). The analytical sample distilled, n_D^{20} 1.4518.

Anal. Calcd. for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.46; H, 8.77.

***cis*-1,2-Bis-(β -hydroxyethyl)-cyclopentane (VIIa).**—Thirty-four grams of diester VIa in 170 ml. of ether was added during 2 hours to a stirred suspension of 15 g. of lithium aluminum hydride in 500 ml. of ether. The reaction mixture was heated under reflux overnight, and 25 g. of ethyl acetate was then added. The mixture was acidified with dilute hydrochloric acid and the resulting solution was continuously extracted with ether for 25 hours. The ether was evaporated and the diol was distilled; wt. 16 g. (71%), b.p. 157–162° (5 mm.), n_D^{20} 1.4837.

Anal. Calcd. for $C_9H_{18}O_2$: C, 68.31; H, 11.47. Found: C, 68.40; H, 11.38.

***cis*-1,2-Bis-(β -cyanoethyl)-cyclopentane (IXa).**—Diol VIIa was converted to the dibromide by the method used to convert IIIa to IVa. Distillation furnished VIIIa, b.p. 117–120° (1.8 mm.). This material was converted to the dinitrile by the method used to convert IVa to Va. Distillation gave the product in 52% over-all yield, b.p. 142–144° (0.5 mm.), n_D^{20} 1.4770.

Anal. Calcd. for $C_{11}H_{16}N_2$: C, 74.95; H, 9.15. Found: C, 74.82; H, 9.44.

***cis*-Bicyclo[5.3.0]decanone-4 (Xa).**—To a stirred suspension of 3.5 g. of lithium in 2.5 l. of dry ether under nitrogen in a high dilution apparatus¹⁴ was added 39 g. of bromobenzene during 2.5 hours. After 0.5 hour, 34 g. of *N*-methyl-aniline was added during 20 minutes. Dinitrile IXa, 8.8 g., in 1 l. of dry ether was added over a period of 48 hours. The cooled mixture was decomposed by dropwise addition of 150 ml. of 3.3 *N* hydrochloric acid. The resulting mixture was vigorously stirred 0.5 hour at 25° to hydrolyze the imine. The water layer was separated and extracted with ether, and the solvent was evaporated from the combined organic layers under vacuum. The organic residue was heated under reflux with 200 ml. of 33% sulfuric acid for 24 hours, during which time the ketone was steam distilled and collected. The water from the steam distillation was returned automatically to the distillation flask by a device adapted from a continuous extractor. This procedure kept the concentration of the acid constant. The product was then taken up in ether, and the ether phase was washed and dried. The ether was evaporated through a small column and the residue was treated with a solution prepared by dissolving 4 g. of semicarbazide hydrochloride and 6 g. of sodium acetate in 50 ml. of 40% ethanol. The solution was warmed, then cooled, and the crude semicarbazone was collected, m.p. 177–179°, wt. 6.1 g. (58%). Four recrystallizations of this material from aqueous alcohol gave fluffy needles, m.p. 182–184°, reported¹⁵ m.p. 185°.

***cis*-Bicyclo[5.3.0]decane (XIa).**¹⁶—Five grams of the purified semicarbazone of ketone Xa was heated under reflux for 1.5 hours with 3.3 g. of 95% hydrazine and 4.5 g. of potassium hydroxide in 25 ml. of diethylene glycol. Water and excess hydrazine were then allowed to distil until the temperature of the mixture reached 185°. The distillate was saved and the residue was heated under reflux

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(12) (a) R. C. Fuson, C. L. Fleming, P. F. Warfield and D. E. Wolf, *J. Org. Chem.*, **10**, 121 (1945); (b) R. C. Fuson and W. Cole, *J. Am. Chem. Soc.*, **60**, 1237 (1938).

(13) L. N. Owen and A. G. Peto, *J. Chem. Soc.*, 2382 (1955).

(14) R. Huisgen, W. Rapp, I. Ugi, H. Walz and I. Glogger, *Ann.*, **586**, 52 (1954).

(15) F. Sorm and J. Fajkos, *Coll. Czech. Chem. Comm.*, **12**, 81 (1947).

(16) We are indebted to Professor F. Sorm for supplying us with a small sample of this compound for our preliminary studies.

until nitrogen evolution ceased (8 hours). The reaction mixture was cooled, diluted with water, and the hydrocarbon was steam distilled. The combined distillates were extracted with pure pentane. The combined pentane solutions were washed and dried, and the pentane was removed by fractional distillation. After distillation the hydrocarbon had b.p. 196.5°, n_D^{20} 1.4744, d_4^{20} 0.8940, yield 2.3 g. (70%). Gas phase chromatography showed the compound was substantially better than 99% pure; reported⁸ n_D^{20} 1.4761, d_4^{20} 0.8833.

Anal. Calcd. for C_9H_{16} : C, 87.10; H, 12.90. Found: C, 86.83; H, 12.66.

trans-1,2-Bis-(hydroxymethyl)-cyclopentane (IIIb).—Diester IIb was reduced with lithium aluminum hydride to the diol, b.p. 128–130° (2.5 mm.), n_D^{20} 1.4773 (reported¹³ b.p. 147° (11 mm.), n_D^{20} 1.4760).

trans-1,2-Bis-(bromomethyl)-cyclopentane (IVb).—Diol IIIb was converted to the dibromide in a manner similar to that described for the preparation of IVa; yield 66%, b.p. 75–77° (1.3 mm.), n_D^{20} 1.5336.

Anal. Calcd. for $C_7H_{12}Br_2$: C, 32.83; H, 4.72. Found: C, 32.88; H, 4.63.

trans-1,2-Bis-(cyanomethyl)-cyclopentane (Vb) was prepared from dibromide IVb as described for the preparation of Va from IVa; yield 65%, b.p. 120–121° (0.75 mm.), n_D^{20} 1.4708.

Anal. Calcd. for $C_9H_{12}N_2$: C, 72.94; H, 8.16. Found: C, 72.75; H, 7.86.

trans-1,2-Bis-(carbethoxymethyl)-cyclopentane (VIb).—Nitrile Vb was converted to the ester as described for the conversion of Va to Via. The yield was 65%, b.p. 99–118° (0.8–1.7 mm.), n_D^{20} 1.4477.

Anal. Calcd. for $C_{13}H_{22}O_4$: C, 64.44; H, 9.16. Found: C, 64.42; H, 8.87.

trans-1,2-Bis-(β -cyanoethyl)-cyclopentane (IXb).—Diester VIb was reduced to the diol with lithium aluminum hydride as described for the preparation of VIIa; the crude product was converted to the dinitrile as described for the preparation of IXa. The dinitrile was distilled; b.p. 147–148° (0.75 mm.), n_D^{20} 1.4715, over-all yield 40%.

Anal. Calcd. for $C_{11}H_{16}N_2$: C, 74.95; H, 9.15. Found: C, 74.70; H, 9.35.

trans-Bicyclo[5.3.0]decanone-4 (Xb).—The cyclization of IXb, the hydrolysis and the decarboxylation all paralleled the conversion of IXa to Xa. The semicarbazone of Xb was isolated in 48% yield, m.p. 170–175° (reported¹⁵ m.p. 178°).

trans-Bicyclo[5.3.0]decane (XIb).—The hydrocarbon was prepared from the ketone Xb as described for preparation of the *cis* isomer XIa; b.p. 190.5° (746 mm.), n_D^{20} 1.4717, d_4^{20} 0.8816; reported⁸ n_D^{20} 1.4751, d_4^{20} 0.8794. Gas chromatography showed the hydrocarbon was better than 99% pure.

Anal. Calcd. for $C_{10}H_{18}$: C, 86.99; H, 13.12. Found: C, 86.71; H, 13.42.

Equilibration Studies.—A 100-mg. sample of the hydrocarbon to be equilibrated together with 20 mg. of 10% palladium-on-carbon was sealed in a tube with a total volume of about 0.2 ml. or less. The tube was heated in an iron pipe in a furnace at the desired temperature $\pm 1.5^\circ$. At the end of the heating period, the equilibration was quenched by plunging the iron pipe into an ice-bath. The catalyst was centrifuged to the bottom, the tube was opened and the sample was withdrawn.

Vapor phase chromatography on the following columns failed to separate the isomeric perhydroazulenes: squalene on florex; tricresyl phosphate, silicone grease, tricyanoethylation product of glycerol and γ -methyl- γ -nitropimelonitrile, all on firebrick. The analysis was therefore carried out by the infrared method. Synthetic mixtures could be analyzed to $\pm 1\%$ by using bands at 10.14 μ (*cis*) and 11.05 μ (*trans*). The data are summarized in Table I.

TABLE I

DATA FOR THE REACTION *cis*- \rightleftharpoons -*trans*-DECAHYDROAZULENE

T, °K.	Starting isomer	% <i>trans</i> /% <i>cis</i>	K _e
494	<i>trans</i>	59.4/37.8	1.71
511	<i>cis</i>	59.6/36.3	1.67
532	<i>cis</i>	55.6/36.9	1.507
	<i>trans</i>	56.8/37.5	1.515
548	<i>cis</i>	57.5/36.8	1.563
	<i>trans</i>	58.1/38.1	1.525
576	<i>cis</i>	53.4/35.6	1.500
	<i>trans</i>	56.9/37.8	1.505

[CONTRIBUTION FROM THE LYMAN LABORATORY, HARVARD UNIVERSITY, CAMBRIDGE 38, MASS.]

The Nuclear Magnetic Resonance Spectra of the 10-Methyldecalols-2

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The high-resolution n.m.r. spectra of the four isomers of 10-methyldecalol-2 were studied. The data show that the ring configuration greatly affects the resonance position of the angular methyl hydrogens and that there is also a smaller effect due to the hydroxyl group being either *cis* or *trans* to the methyl group. Comparisons are made with similar data in the literature. In addition, the spectra from the 2-hydrogens are discussed and a method of identification for molecules of unknown hydroxyl conformation is examined.

The high-resolution n.m.r. spectra of the four possible isomers of 10-methyldecalol-2 were obtained at 60 Mc./s. Single recordings of these spectra are reproduced in Fig. 1. The samples were dissolved in degassed CS_2 and the usual spinning technique was employed. Frequency shifts were measured relative to internal hexamethyldisiloxane and the data are presented so that a positive shift from the standard signifies that the peak lies to *low* field.¹ The peak separations were calibrated by the use of audio sidebands from a variable frequency oscillator whose frequency was monitored by a cycle counter. The field was swept upfield and downfield on alternate calibrations in order to

minimize the effect due to drift. Four calibrations were made for each spectrum and the standard deviations for the peak positions relative to the standard were less than 0.2 c./s. or 0.003 p.p.m. for the methyl peaks and less than 0.5 c./s. or 0.008 p.p.m. for the 2-hydrogen peaks.

Angular Methyl Groups.—The chemical shifts in p.p.m. to low field relative to internal hexamethyldisiloxane for the methyl groups in the four isomers of 10-methyldecalol-2 are listed in Table I along with data from the literature for 10-methyl-*cis*-decalin² and five steroid molecules^{2,3} approximately

(2) J. A. Pople, W. G. Schneider and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, pp. 291–292.

(3) J. N. Shoolery and M. T. Rogers, *J. Am. Chem. Soc.*, **80**, 5121 (1958).

(1) The reversal of sign from the usual convention is so chosen to avoid the continual repetition of minus signs.