

from acetone to give 7 $\beta$ -methylhydrocortisone acetate, m.p. 193–196°. An analytical sample had m.p. 198–200°,  $[\alpha]_D +121^\circ$  (acetone),  $\lambda_{\text{max}}^{\text{ole}}$  245 m $\mu$ ,  $a_M$  16,425.

*Anal.* Calcd. for C<sub>24</sub>H<sub>44</sub>O<sub>6</sub>: C, 68.87; H, 8.19. Found: C, 69.05; H, 8.30. KALAMAZOO, MICH.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY]

## The Relative Stabilities of *cis* and *trans* Isomers. V. The Bicyclo[5.2.0]nonanes. An Extension of the Conformational Rule<sup>1,2</sup>

BY NORMAN L. ALLINGER, MASAO NAKAZAKI AND VERA ZALKOW

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Pure *cis*- and *trans*-bicyclo[5.2.0]nonane have been prepared by unequivocal methods. The equilibrium between the isomers could not be established by heating with palladium catalyst, apparently because of the ease of rupture of the four-membered ring under these conditions. Application of the conformational rule led to the conclusion that the heat contents of the isomers are similar, that of the *trans* isomer probably being somewhat lower.

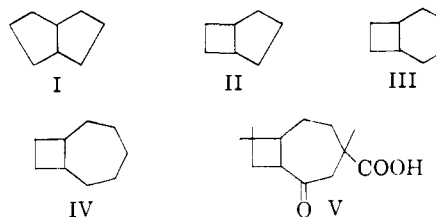
### Introduction

Fused ring systems of the decalin and hydrindane types have been examined with respect to the relative stabilities of *cis* and *trans* ring junctures in considerable detail while systems containing larger rings, although well known in other respects, have not been studied previously in this regard.

It seems clear that a simple decalin system is more stable<sup>3</sup> in the *trans* form and this case is well understood in terms of conformational analysis.<sup>4</sup> The available evidence indicates that in the hydrindane system the heat contents are more nearly equal than in the decalins, and for some substituted hydrindanes the *cis* isomer is more stable.<sup>4</sup> The six-membered ring in hydrindane would have a lower energy if the attached groups were equatorial, but in opposition to this effect, a five-membered ring tends to be more nearly planar than does a six.<sup>5</sup> Since it is energetically more economical to decrease a dihedral angle between an axial and an equatorial bond in a six-membered ring than between two equatorial bonds,<sup>6</sup> this strain energy is greater in the *trans*-hydrindane than in the *cis* and just about cancels the tendency for the six-membered ring to prefer equatorial substituents.

When two five-membered rings are fused together (I), the *cis* isomer appears to be of lower free energy,<sup>7</sup> and the four-membered ring must be even more nearly planar than the five.<sup>8</sup> When a second ring is fused to a cyclobutane ring in the 1,2-position, it is clear that if the second ring is sufficiently small the *cis* isomer will be of lower heat content, while if the second ring is sufficiently large, the *trans* isomer will be so favored. Since

it appears to be more stable in the *cis* form, it appears certain that the same will be true for II. In going up the homologous series of compounds II, III, IV and so on, it cannot be unambiguously predicted where the crossover point will be. As



soon as the second ring contains seven atoms (IV) the 1,2-*trans*-(di-pseudoequatorial) positions in this ring are on the average closer together than the corresponding *cis* positions, and therefore it might be predicted that the *trans* isomer of IV will have the more negative heat content. It probably also will have the more negative entropy,<sup>4a,9</sup> and a prediction as to the relative free energies would seem hazardous. Barton and his co-workers<sup>10</sup> have, however, made a tentative assignment of *cis* and *trans* ring junctures of V on the basis of stability. The bicyclo[5.2.0]nonane ring system (IV) appears to have been found in nature only when part of a larger ring system such as the lunicolchicines.<sup>11</sup>

### Discussion

The system chosen for study in the present work was the parent hydrocarbon IV. The introduction of a carbonyl adjacent to the ring juncture would have facilitated isomerization, but would also have

- (1) Paper IV, THIS JOURNAL, **81**, 232 (1959).
- (2) This work was supported by a Frederick Gardner Cottrell grant from The Research Corporation.
- (3) Throughout this paper the expression "stable" refers exclusively to free energy, and not to enthalpy.
- (4) For a summary of the evidence and references, see (a) N. L. Allinger, *J. Org. Chem.*, **21**, 915 (1956); (b) W. G. Dauben and K. S. Pitzer, in "Steric Effects in Organic Chemistry," Ed. M. S. Newman, John Wiley and Sons, Inc., New York, N. Y., 1956, p. 3.
- (5) (a) C. G. LeFèvre and R. J. W. LeFèvre, *Rev. of Pure and Applied Chem.*, **5**, 303 (1955); (b) E. L. Eliel and C. Pillar, THIS JOURNAL, **77**, 3600 (1955).
- (6) Reference 4b, p. 37.
- (7) (a) J. W. Barrett and R. P. Linstead, *J. Chem. Soc.*, 436 (1935); (b) L. N. Owen and A. G. Peto, *ibid.*, 2383 (1955).
- (8) G. W. Rathjens, Jr., N. Freeman, W. D. Gwinn and K. S. Pitzer, THIS JOURNAL, **75**, 5634 (1953).

- (9) This is more likely true in this case than with the decalins. The decalin case was discussed previously (ref. 1a), and subsequently the *cis* isomer was found to have the more positive entropy (T. Miyazawa and K. S. Pitzer, THIS JOURNAL, **80**, 60 (1958), and J. Coke, unpublished results), contrary to earlier work (G. S. Parks and J. A. Hatton, *ibid.*, **71**, 2773 (1949)). With the bicyclo[5.2.0]nonanes the excess entropy of the *cis* form should be due to a greater flexibility, while both of the decalins are now known to be rather rigid, and the entropy difference is due mainly to a difference in symmetry. It has been shown (H. G. Derx, *Rec. trav. chim.*, **41**, 312 (1922)) that the *cis*-cycloheptane-1,2-diol forms a more stable boric acid complex than does the *trans* isomer, but the difference seems small, and the extension to the present case seems uncertain.
- (10) D. H. R. Barton, T. Bruun and A. S. Lindsey, *J. Chem. Soc.*, 2210 (1952).
- (11) P. D. Gardner, R. L. Brandon and G. R. Haynes, THIS JOURNAL, **79**, 6334 (1957), and references cited.

led to undesirable complicating effects.<sup>12</sup> With a hydrocarbon equilibration usually can be brought about by heating with palladium (hydrogenation-dehydrogenation),<sup>13</sup> or with an acid such as sulfuric acid<sup>14</sup> or aluminum chloride<sup>15</sup> (carbonium ion). Alternatively, at least a qualitative enthalpy of isomerization might be obtained from the physical constants by application of the conformational rule.<sup>16</sup>

The preparations of pure samples of *cis*- and *trans*-IV are outlined on the flow sheet. The *cis* and *trans* isomers of 1,2-dicarboxycyclobutane (IV) are well known and their structures have been firmly established.<sup>17</sup> The *trans*-ester and the *cis*-anhydride were separately reduced with lithium aluminum hydride to the corresponding alcohols, a procedure which is known to give no epimerization.<sup>18</sup> The alcohols were converted to the bromides VIII with phosphorus tribromide. The shortest feasible route to a derivative of the acid desired for closure to the seven-membered ring from bromide VIII was the malonic ester synthesis. Although a reaction with two molecules of malonic ester was desired, it was clear that a ring closure

reaction leading to diester XV would be an important side reaction. It was found that the *trans* isomer would react with two moles of malonic ester, implying as expected a relatively high free energy in the *trans*-bicyclo[3.2.0]heptane ring system. With this isomer the yield of tetraester was good, the ratio of tetraester XII to cyclized diester XV formed being about 6. The *cis* isomer, on the other hand, ring closed quite readily. Under the same reaction conditions used for the *trans* isomer, the corresponding product ratio was less than 0.2.

This result was anticipated, and a more laborious but more fruitful approach to the *cis*-tetraester was employed for practical synthesis, and this involved first extending the chain with potassium cyanide, next a hydrolysis to give acid XI, and then repetition of the steps leading from the acid to the alcohol, bromide and finally to the desired homologous dinitrile XXII. This *cis*-nitrile now was subjected to a Ziegler high dilution ring closure<sup>19</sup> which gave the iminonitrile. After hydrolysis and decarboxylation, the *cis*-ketone XIXa was obtained in an over-all yield of 72% from the nitrile. Wolff-Kishner reduction<sup>20</sup> gave *cis*-bicyclo[5.2.0]nonane (IVa).

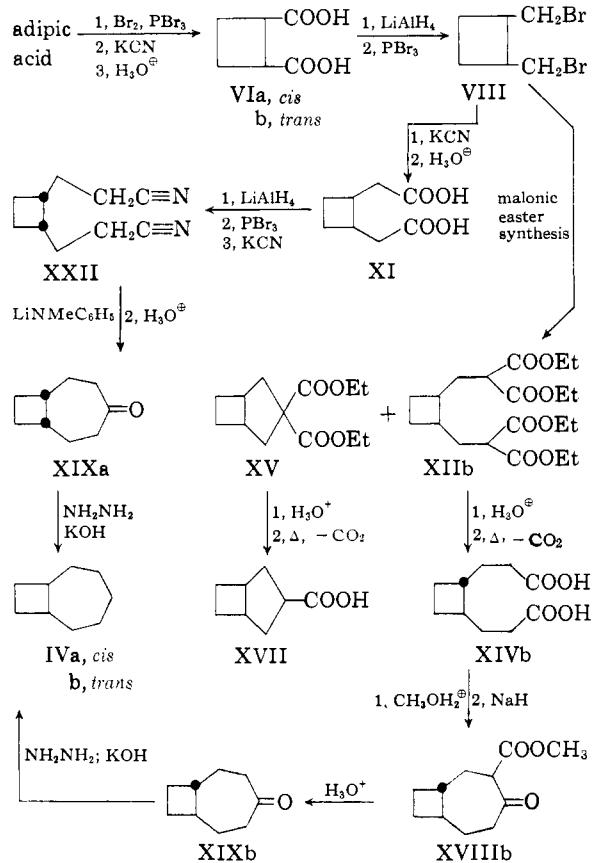
The *trans* intermediate of use for further synthesis was tetraester XIIb. After saponification and decarboxylation, diacid XIVb was obtained. This acid was esterified, and the ester was ring closed with sodium hydride in a modified Dieckmann reaction.<sup>21</sup> In this way keto ester XVIIIb was obtained in 51% yield. Hydrolysis and decarboxylation of the keto ester gave the ketone XIXb, which was reduced to the *trans* hydrocarbon by the Wolff-Kishner method.<sup>20</sup>

## Results

The most simple and straightforward way to try to determine the relative stability of the bicyclo[5.2.0]nonanes appeared to be by epimerization with palladium and measurement of the isomer ratio at equilibrium. However, that some difficulty might be experienced in practice was indicated by the known ease of hydrogenolytic<sup>22</sup> and thermal<sup>23</sup> rupture of the cyclobutane ring.

It was found that the *cis* and *trans* isomers of IV were easily separable by gas chromatography using tricresyl phosphate on firebrick as the adsorbent. The retention time of the *cis* was longer, reflecting the difference in the boiling points.

Isomerization experiments were carried out in sealed tubes with palladium-on-charcoal catalyst. The times and temperatures used to equilibrate hydrindane (237° for 30 hours), or decalin (250° for 48 hours) left either isomer of IV virtually unchanged. This resistance to equilibration is interpreted as due to the reluctance of a carbon atom in the four-membered ring to assume a planar configuration (I strain)<sup>24</sup> as is presumably<sup>25</sup> necessary



(12) (a) P. A. Robins and J. Walker, *J. Chem. Soc.*, 1789 (1955); (b) W. Klyne, *Experientia*, **12**, 119 (1956).

(13) W. E. Bachmann and A. S. Dreiding, *THIS JOURNAL*, **72**, 1323 (1950).

(14) A. K. Roebuck and B. L. Evering, *ibid.*, **75**, 1631 (1953).

(15) G. Chiurdoglu and J. L. Jaminet, *Bull. soc. chim. Belges*, **62**, 448 (1953).

(16) N. L. Allinger, *THIS JOURNAL*, **79**, 3443 (1957).

(17) W. H. Perkin, Jr., *J. Chem. Soc.*, 572 (1894).

(18) D. S. Noyce and D. B. Denney, *THIS JOURNAL*, **72**, 5743 (1950).

(19) K. Ziegler, H. Eberle and H. Ohlinger, *Ann.*, **504**, 94 (1933).

(20) Huang-Minlon, *THIS JOURNAL*, **68**, 2487 (1946).

(21) F. F. Blicke, J. Azuara, N. J. Doorenbos and E. B. Hotelling, *ibid.*, **75**, 5418 (1953).

(22) R. Willstätter and J. Bruce, *Ber.*, **40**, 4456 (1907).

(23) C. T. Genaux, F. Kern and W. D. Walters, *THIS JOURNAL*, **75**, 6196 (1953).

(24) H. C. Brown, R. S. Fletcher and R. B. Johanneson, *ibid.*, **73**, 212 (1951).

(25) The relative rates of catalytic deuterium exchange on hydro-

for isomerization. When the isomerization was attempted with either isomer under more strenuous conditions, for example 315° for 84 hours, it was found by gas chromatography that a considerable amount of lower boiling material was formed, but none of the other isomer was observed. The same result was obtained under conditions where most of the starting material was recovered unchanged.

Because of the known tendency for aluminum chloride to cause rearrangement<sup>26</sup> even in the rather stable decalin systems, together with the fact that generation of a carbonium ion at the bridgehead in IV would also be subject to a considerable amount of I-strain, the acid-catalyzed isomerization did not appear promising and was not investigated.

A qualitative method of determining relative enthalpy differences is by use of the conformational rule, which states that a pair of (liquid) *cis-trans* isomers which do not differ in dipole moment have enthalpies inversely related to their molecular volumes.<sup>16</sup> The pertinent physical properties of the hydrocarbons (IV) were as follows: *cis*, b.p. 165.4° (760 mm.),  $n_D^{25}$  1.4664,  $d_4^{25}$  0.8638; *trans*, b. p. 162.8° (760 mm.),  $n_D^{25}$  1.4662,  $d_4^{25}$  0.8628. The *cis* isomer therefore has the higher values for its physical constants, and the conformational rule predicts that it also has a higher heat content. The differences in physical properties appear to be quite small, however, except for the boiling points. Unfortunately, the boiling point seems to be the least dependable of the physical properties.<sup>1,27</sup> The enthalpy and entropy differences appear to be small and work in opposite directions and therefore it is not possible to make even a qualitative estimate of the relative free energies of the isomeric hydrocarbons.

Since the enthalpy difference concluded to exist above rests directly on the assumed applicability of the conformational rule to the system at hand, the desirability of examining further the limitations of the rule was indicated. It appeared worthwhile to ask whether or not it might be possible to use this rule in a quantitative way, and a test case was provided by the six *cis-trans* isomers of the 1,2-, the 1,3- and the 1,4-dimethylcyclohexanes.<sup>23</sup> If the enthalpies of these compounds are plotted against their molar volumes, it is seen that the points lie within experimental error of a straight line (Fig. 1).

It was noted that 1,1-dimethylcyclohexane would, if plotted on this graph, have an energy about 0.6 kcal. below the line.<sup>23</sup> Ethylcyclohexane would fall above the line by about this amount.<sup>23</sup> It therefore seemed likely that the "branched chain effect," which serves to lower the enthalpy of branched relative to normal compounds, did not affect the

carbons were found to be cycloheptane > cyclopentane > cyclohexane (R. L. Burwell, Jr., B. K. C. Shim and H. C. Rowlinson, *THIS JOURNAL*, **79**, 5142 (1957)).

(26) W. G. Dauben, J. B. Rogan and E. J. Blanz, Jr., *ibid.*, **76**, 6381 (1954), and references cited therein.

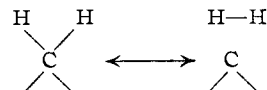
(27) (a) E. L. Eliel and R. G. Haber, *J. Org. Chem.*, **23**, 2041 (1958); (b) W. Hückel and A. Hubele, *Ann.*, **613**, 27 (1958).

(28) American Petroleum Institute, "Physical and Thermodynamic Properties of Hydrocarbons and Related Compounds," National Bureau of Standards.

molar volume. The indicated empirical correction was made for 1,1-dimethylcyclohexane, and for ethylcyclohexane, and these values are also included in Fig. 1.

A test of the conformational rule against some open chain compounds appeared to be both possible and desirable. If a plot is made of the relative heat contents against the molar volumes for the octanes<sup>23</sup> (omitting one which is a solid) little correlation is apparent (Fig. 2). If chain branching affects the energy, but not the molar volume, as is indicated above, this branching effect would have to be taken into account. It has been shown that for some simple paraffins the energy lowering attributed to chain branching can be semi-quantitatively accounted for as being due to electron correlation, or intramolecular dispersion forces,<sup>29</sup> but accurate calculations by this method are tedious for large molecules.

Another suggestion which has been made<sup>30</sup> to account for the increased stability of branched chains is to attribute slightly different values to the exchange integrals between atoms separated by one atom, depending on the atoms involved.<sup>31</sup> In other language, resonance forms of the type



are more important when non-bonded forms involve bonding between two atoms of the same kind (H-H or C-C) rather than two different atoms.

To quantitatively apply either or both of these ideas (to the first approximation) the same method can be used. Since for isomers the change in branching in going from one to another changes both the H-C-H and C-C-C bond arrangements by the same number, the importance of each of the effects mentioned can be taken as proportional to only the number of pairs of hydrogen atoms (paired in all possible ways) attached to the same carbon atom and summed over the molecule. An empirical quantity, 0.6 kcal./mole, is assigned to each of these hydrogen pairs, and hence a "corrected" enthalpy is obtained for a compound by adding to its observed enthalpy 0.6 times the number of these hydrogen pairs it contains.

There are always three hydrogen pairs per CH<sub>3</sub>-group, one per CH<sub>2</sub>- group, and zero for tertiary and quaternary carbons. When these numbers are summed, the total for *n*-octane is (2×3) + (6×1) = 12, and for a methyl heptane (3×3) + (5×1) = 14. With 2,3-dimethylhexane and 2,2-dimethylhexane, respectively, the numbers are 14 and 15, and so on. When these numbers, multiplied by 0.6 kcal./mole, are added to the observed enthalpies, these "corrected" enthalpies for the octanes are related to the molecular volumes as shown in Fig. 3. The correlation is now considerably improved, only one of the 17 points clearly falls further from the least squares line than can be attributed to the

(29) K. S. Pitzer and E. Catalano, *THIS JOURNAL*, **75**, 4844 (1956).

(30) G. E. K. Branch and M. Calvin, "The Theory of Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1941, p. 274.

(31) The overlap between such non-adjacent atoms is known to be appreciable (R. S. Mulliken, *Record of Chemical Progress*, **13**, 67 (1952)).

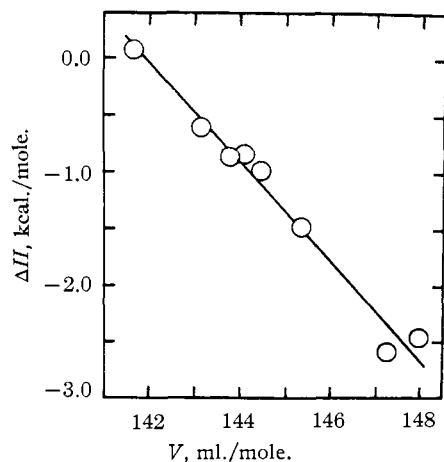


Fig. 1.—The relationship between the "corrected" heat content and molar volume for the dimethylcyclohexanes in the liquid phase at 25°.

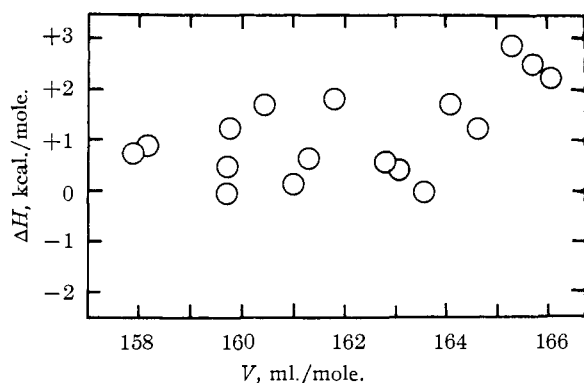


Fig. 2.—The relationship between the heat content and molar volume for the octanes in the liquid phase at 25°.

probable experimental error in the combustion measurements.

The conformational rule previously has been limited to *cis-trans* isomers, since they are of necessity of equal branching. It is now possible to take branching into account and to compare more distantly related compounds, and in at least a semi-quantitative way.

In considering the applicability of the conformational rule to the present case, it would seem prudent to examine the geometry of the system in more detail. The previously discussed examples which contain six-membered rings and open chains are somewhat ideal in that they are in nicely staggered conformations and have very close to tetrahedral angles for all bonds, and there is no strain. If an attempt is made to include, for example, propylcyclopentane in the plot with the dimethylcyclohexanes, it is found that it has far too large a heat content, and presumably this is because the known ring strain of the five-membered ring is not reflected in the molar volume. If the strain is kept constant a more satisfactory comparison is possible. Thus the various dimethylcyclopentanes yield a plot similar to Fig. 1, although the fit is not quite as good in this case.

In the two compounds of present interest (IV) the strain inherent in the cyclobutane ring must be

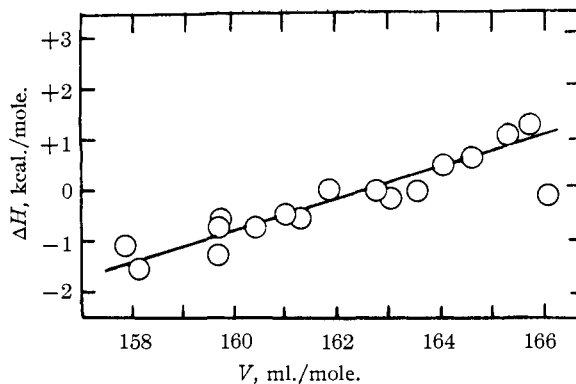


Fig. 3.—The relationship between the "corrected" heat content and molar volume for the octanes in the liquid phase at 25°.

nearly the same. There are insufficient data available on rings containing more than six members from which to draw quantitative conclusions, but in the one known case where a test of the rule was made in a seven-membered ring the predictions were qualitatively correct.<sup>1</sup> The tentative application of the rule to the hydrocarbons IV has therefore been made, and the conclusion is that probably the heat contents of the isomers are similar with that of the *trans* isomer being lower.

### Experimental<sup>32</sup>

**Cyclobutane-1,2-dicarboxylic Acids.**<sup>33</sup>—Adipic acid was converted to diethyl  $\alpha,\alpha$ -dibromoadipate, b.p. 122° (7 mm.), by the Hell-Volhard-Zelinsky method.<sup>34</sup> Treatment of the bromoester with potassium cyanide gave semi-solid dimethyl-1-cyano-1,2-cyclobutanedicarboxylic acid<sup>17</sup> in 72% yield, b.p. 117–122° (0.7 mm.). This material was subjected to acid hydrolysis, and the resulting crude tricarboxylic acid was extracted for 24 hours with ether in a continuous extraction apparatus. Thermal decarboxylation furnished the crude stereoisomeric mixture of cyclobutane-1,2-dicarboxylic acids.

***trans*-1,2-Cyclobutanedicarboxylic Acid (VIb).**—The crude acid mixture was esterified by the azeotropic method with ethanol, benzenesulfonic acid and benzene, and the ester was epimerized by treatment with sodium ethoxide. The *trans*-ester so obtained had b.p. 98–100° (3 mm.),  $n_D^{25}$  1.4369. Acid hydrolysis of the *trans*-ester gave the acid, which was crystallized from ether, m.p. 127–128.5° (reported<sup>17</sup> m.p. 130.5–131.0°). The mixture melting point with the *cis* isomer was 106–129°.

***trans*-1,2-Bis-(hydroxymethyl)-cyclobutane (VIIb).**—Reduction of the *trans*-ester was carried out with lithium aluminum hydride following the procedure of Blomquist and Verdol.<sup>35</sup> After decomposition of the reaction product with water the mixture was acidified with dilute hydrochloric acid, and the resulting solution was continuously extracted with ether. Distillation yielded a colorless viscous liquid, b.p. 111–114° (3 mm.),  $n_D^{25}$  1.4716; literature<sup>35</sup>  $n_D^{25}$  1.4736 for a sample of unspecified stereochemistry.

*Anal.* Calcd. for  $C_6H_{12}O_2$ : C, 62.03; H, 10.41. Found: C, 61.99; H, 10.87.

The di- $\alpha$ -naphthylurethan, prepared in the usual way, was recrystallized from ethanol, m.p. 141.5–142.5°. The mixture melting point with the *cis* isomer (m.p. 145.5–147.0°) was 135–140°.

*Anal.* Calcd. for  $C_{28}H_{26}N_2O_4$ : C, 73.92; H, 5.77. Found: C, 74.02; H, 5.86.

(32) Microanalyses by Miss M. A. DaRooge.

(33) E. R. Buchman, A. O. Reims, T. Skei and M. J. Schlatter, *THIS JOURNAL*, **64**, 2696 (1942).

(34) P. C. Guha and D. K. Sankaran, "Organic Syntheses," Coll. Vol. 11f, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 623.

(35) A. T. Blomquist and J. A. Verdol, *THIS JOURNAL*, **77**, 1806 (1955).

*trans*-1,2-Bis-(bromomethyl)-cyclobutane (VIIIb).<sup>35</sup>—To 61 g. of phosphorus tribromide cooled to  $-10^{\circ}$  was added with stirring 26.4 g. of VIIIb in 25 ml. of benzene. The solution next was allowed to warm to room temperature for a total of 2 hours, and then was heated to  $70^{\circ}$  for an additional 18 hours. The mixture now was poured onto ice, and the product was extracted with ethylene dichloride. The organic phase was separated, washed in turn with dilute sodium carbonate and water, and dried over calcium chloride. After removal of the drying agent and evaporation of the solvent the dibromide was distilled, b.p.  $76.5\text{--}79^{\circ}$  (3 mm.),  $n_D^{25}$  1.5320, wt. 44.2 g. (80%).

*Anal.* Calcd. for  $C_6H_{10}Br_2$ : Br, 66.06. Found: Br, 65.85.

*trans*-1,2-Bis-(cyanomethyl)-cyclobutane (IXb).—A mixture of 4.5 g. of sodium cyanide and 10.0 g. of bromide VIIIb in 75 ml. of 80% ethanol was heated under reflux for 10 hr. The ethanol was removed by distillation and the residue was poured onto ice. The resulting mixture was extracted with ether, and the ether extracts were separated, washed with water and saturated sodium chloride solution and dried over magnesium sulfate. After evaporation of the solvent the product was distilled, b.p.  $136\text{--}138^{\circ}$  (3 mm.),  $n_D^{25}$  1.4615, wt. 4.1 g. (74%).

*Anal.* Calcd. for  $C_8H_{10}N_2$ : C, 71.57; H, 7.51. Found: C, 71.58; H, 7.57.

*trans*-1,2-Bis-(carboethoxymethyl)-cyclobutane (Xb).—A mixture of 3.8 g. of *trans*-dicyanide, 25 ml. of 95% ethanol and 10 ml. of concd. sulfuric acid was boiled for 6 hr. and to the cooled reaction mixture 200 g. of crushed ice was added. The ester was isolated by extracting with ether, washing the extracts with water and sodium carbonate solution, and drying with magnesium sulfate. After evaporation of the ether the ester was distilled, b.p.  $122^{\circ}$  (3 mm.),  $n_D^{25}$  1.4417, wt. 5.0 g. (80%).

*Anal.* Calcd. for  $C_{12}H_{20}O_4$ : C, 63.13; H, 8.83. Found: C, 63.22; H, 9.00.

*trans*-1,2-Bis-(carboxymethyl)-cyclobutane (XIb).—The acid was obtained by hydrolyzing the ester with methanolic potassium hydroxide. Dilution of the reaction mixture with water and acidification yielded a solid which was recrystallized from water, m.p.  $124\text{--}125.5^{\circ}$ . A mixture melting point with the *cis* isomer (m.p.  $174.5\text{--}176.5^{\circ}$ ) was  $119\text{--}155^{\circ}$ .

*Anal.* Calcd. for  $C_8H_{12}O_4$ : C, 55.80; H, 7.03. Found: C, 55.75; H, 7.28.

The *trans*-1,2-Bis-( $\beta,\beta$ -dicarboethoxyethyl)-cyclobutane (XIIb).—To a hot solution prepared from 5.1 g. of sodium and 125 ml. of absolute ethanol was added 194 g. of freshly distilled diethyl malonate. A solution of 24.3 g. of bromide VIIIb in 25 ml. of absolute ethanol then was added dropwise during 3 hours to the refluxing malonic ester solution. Heating and stirring was continued for an additional 14 hours, and the ethanol was removed by distillation. The residue was poured onto 200 g. of ice and the solution was extracted with ether. The extracts were washed and dried and the ether was removed. Distillation furnished, after a forerun of unreacted malonic ester, 5.0 g., b.p.  $59\text{--}130^{\circ}$  (0.7 mm.), and 28.4 g. (71%) of crude XIIb, b.p.  $130\text{--}173^{\circ}$  (0.4 mm.). For analysis a sample of this high boiling fraction was redistilled, b.p.  $175^{\circ}$  (0.3 mm.),  $n_D^{25}$  1.4526.

*Anal.* Calcd. for  $C_{20}H_{32}O_8$ : C, 59.98; H, 8.06. Found: C, 59.99; H, 8.18.

*trans*-1,2-Bis-( $\beta$ -carboethoxyethyl)-cyclobutane (XIIIb).—The mixture of 64.9 g. of above-mentioned tetraester, 120 ml. of 6 *N* hydrochloric acid and 55 ml. of acetic acid was heated under reflux for 11 hours. The solution was evaporated to dryness and the semi-solid residue was decarboxylated by heating at  $180^{\circ}$ . The resulting semi-solid was esterified in 90% yield as described for the preparation of VIb with the substitution of methanol for ethanol. The ester had  $n_D^{25}$  1.4489, b.p.  $107\text{--}110^{\circ}$  (0.8 mm.).

*Anal.* Calcd. for  $C_{12}H_{20}O_4$ : C, 63.16; H, 8.77. Found: C, 63.03; H, 8.75.

*trans*-1,2-Bis-( $\beta$ -carboxyethyl)-cyclobutane (XIVb).—Saponification of a sample of ester XIIIb with alcoholic potassium hydroxide as described for the preparation of XIb furnished the acid, which after two recrystallizations from a large volume of water gave plates, m.p.  $64\text{--}65^{\circ}$ .

*Anal.* Calcd. for  $C_{10}H_{18}O_4$ : C, 59.98; H, 8.06. Found: C, 59.76; H, 7.95.

*trans*-4,4-Dicarboethoxybicyclo[3.2.0]heptane (XVb).—The low boiling fractions from the preparation of ester XIIb were combined from two runs and redistilled to give a 16% yield (based on bromide) of ester XVb, b.p.  $100\text{--}105^{\circ}$  (0.8 mm.),  $n_D^{25}$  1.4594.

*Anal.* Calcd. for  $C_{12}H_{20}O_4$ : C, 64.97; H, 8.39. Found: C, 65.15; H, 8.17.

*trans*-4,4-Dicarboxybicyclo[3.2.0]heptane (XVIb).—A solution prepared from 4.5 g. of ester XVb, 5 g. of potassium hydroxide and 30 ml. of 50% methanol was heated under reflux for 19 hours. The solution was evaporated almost to dryness, and the precipitated salt was dissolved by addition of water. Acidification of the solution precipitated the desired acid, which was recrystallized from water to yield 3.0 g. (87%) of crystals, m.p.  $182^{\circ}$  dec.

*Anal.* Calcd. for  $C_9H_{12}O_4$ : C, 58.68; H, 6.57. Found: C, 58.82; H, 6.64.

*trans*-4-Carboxybicyclo[3.2.0]heptane (XVIIb).—The malonic acid XVIb was decarboxylated by heating at  $185^{\circ}$  for 1 hour. The resulting pale yellow liquid was distilled at 4 mm., b.p.  $116\text{--}118^{\circ}$ ,  $n_D^{25}$  1.4834.

*Anal.* Calcd. for  $C_8H_{12}O_2$ : C, 68.54; H, 8.63. Found: C, 68.50; H, 8.65.

The anilide was recrystallized from aqueous ethanol, m.p.  $135\text{--}137^{\circ}$ . The mixture m.p. with the *cis*-anilide (m.p.  $134\text{--}135^{\circ}$ ) was  $127\text{--}132^{\circ}$ .

*Anal.* Calcd. for  $C_{16}H_{17}NO$ : C, 78.10; H, 7.98. Found: C, 77.80; H, 7.88.

5-Carbomethoxy-*trans*-bicyclo[5.2.0]nonanone-4 (XVIII).

—Ester XIIIb was cyclized by the modified Dieckmann method.<sup>21</sup> The ester, 18.3 g., dissolved in one liter of dry xylene was added over a period of 54 hours (*via* a Hershberg dropping funnel) to a stirred, refluxing mixture of 4.8 g. of sodium hydride, 3 l. of dry xylene, 12 g. of 6 mm. glass beads, and about 2 ml. of absolute methanol under a nitrogen atmosphere in a high dilution apparatus.<sup>36</sup> Refluxing and stirring were continued 1 hour after the addition of ester was complete; the reaction flask was cooled to room temperature and finally in ice. Twelve grams of glacial acetic acid was added dropwise over a period of 0.5 hour to the cold stirred reaction mixture, and this was followed by the dropwise addition of 50 ml. of water. The reaction mixture was filtered, the xylene solution was washed with water, dried, and the solvent was removed. The residue was distilled and 8 g. (51%) of product, b.p.  $128\text{--}135^{\circ}$  (3.5 mm.),  $n_D^{25}$  1.4754, was obtained. The infrared absorption curve showed bands at 5.70 and 5.85  $\mu$ .

*Anal.* Calcd. for  $C_{11}H_{16}O_3$ : C, 67.35; H, 8.16. Found: 67.29; H, 8.01.

*trans*-Bicyclo[5.2.0]nonanone-4 (XIXb).—Keto-ester XVIII, 7.8 g., was heated under reflux for 2 hours with a solution prepared from 100 ml. of water and 35 ml. of concd. sulfuric acid. Water, 100 ml., was added and the ketone was steam distilled slowly from the reaction mixture. The water layer was separated from the organic layer and was extracted with ether 6 times. The combined organic layer and ether extracts were washed once with water and then dried over anhydrous calcium chloride. The ether was removed by distillation through a small column, and 4 g. (73%) of ketone, b.p.  $118\text{--}120^{\circ}$  (54 mm.),  $n_D^{25}$  1.4796, was obtained by distillation. The infrared spectrum showed a single carbonyl band at 5.83  $\mu$ .

*Anal.* Calcd. for  $C_9H_{14}O$ : C, 78.26; H, 10.14. Found: C, 78.37; H, 10.28.

The semicarbazone recrystallized from ethanol-water as fluffy needles, m.p.  $156\text{--}157^{\circ}$ .

*Anal.* Calcd. for  $C_{10}H_{17}N_3O$ : C, 61.54; H, 8.72. Found: C, 61.31; H, 8.99.

*trans*-Bicyclo[5.2.0]nonane (IVb).—The Wolff-Kishner reduction of the ketone was carried out according to the modification of Huang-Minlon.<sup>20</sup> Potassium hydroxide, 3.74 g., was swirled and heated with 2.75 g. of hydrazine hydrate in 15 ml. of diethylene glycol until dissolved. *trans*-Bicyclo[5.2.0]nonanone-4, 3.1 g., was added to the

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

diethylene glycol solution, and the mixture was heated under reflux for 1.5 hours. Excess hydrazine and water then were allowed to distil until the temperature of the reaction mixture reached 185°. The distillate was saved and refluxing was continued until nitrogen evolution ceased (about 8 hours).

The reaction mixture was cooled so that water could be added, and the hydrocarbon was steam distilled. The combined distillates were extracted with pure pentane 6 times. The pentane solutions were combined, washed once with water, and dried over anhydrous magnesium sulfate. The pentane was removed by fractionation and the hydrocarbon was distilled twice, b.p. 154–157° uncorr.,  $n_D^{25}$  1.4662. Gas analysis showed that the compound was substantially better than 99% pure.

*Anal.* Calcd. for  $C_9H_{16}$ : C, 87.10; H, 12.90. Found: C, 87.19; H, 12.71.

**Anhydride of *cis*-1,2-dicarboxycyclobutane** was prepared according to Buchman's procedure.<sup>17</sup> The yield from adipic acid was 55–60%, b.p. 97–100° (0.05 mm.). This material was recrystallized from benzene, m.p. 76–78°. This recrystallized anhydride was used in the following syntheses.

***cis*-1,2-Dicarboxycyclobutane (VIa).**—The *cis*-anhydride was hydrolyzed by boiling with water. The acid was recrystallized from ether–benzene, m.p. 136.5–138°, literature m.p. 139.5–140°.

***cis*-1,2-Bis-(hydroxymethyl)-cyclobutane (VIIa).**—The reduction was carried out on the anhydride in a manner similar to that described for the preparation of diol VIIb, yield 90%, b.p. 111–113° (2.7 mm.),  $n_D^{25}$  1.4730.

*Anal.* Calcd. for  $C_6H_{12}O_2$ : C, 62.03; H, 10.41. Found: C, 61.55; H, 10.29.

**The di- $\alpha$ -naphthylurethan** was recrystallized from ethanol, m.p. 145.5–147°, literature m.p. 135–136.5°.

*Anal.* Calcd. for  $C_{23}H_{26}N_2O_4$ : C, 73.92; H, 5.77. Found: C, 73.73; H, 5.76.

***cis*-1,2-Bis-(bromomethyl)-cyclobutane (VIIIa).**—The bromide was prepared by essentially the same method described for compound VIIIb, yield 71%, b.p. 92° (4.5 mm.).

*Anal.* Calcd. for  $C_8H_{10}Br_2$ : Br, 66.06. Found: Br, 65.51.

***cis*-1,2-Bis-(cyanomethyl)-cyclobutane (IXa).**—The bromide VIIIa was converted to the nitrile as described for the preparation of IXb; yield 67%, b.p. 139–145° (2 mm.),  $n_D^{25}$  1.4688.

*Anal.* Calcd. for  $C_8H_{10}N_2$ : C, 71.57; H, 7.51. Found: C, 71.70; H, 7.55.

***cis*-1,2-Bis-(carboxymethyl)-cyclobutane (XIa).**—The nitrile IXa was first converted to the ester as described for the preparation of Xb. The crude ester was distilled, b.p. 114–120° (1.2 mm.), yield 67%. The ester was hydrolyzed as described for the preparation of XIb. The acid was recrystallized from water three times, m.p. 174.5–176.5°, yield 64%. For analysis a sample again was recrystallized from water, needles, m.p. 178–178.5°. The mixture m.p. with the *trans* isomer (m.p. 124–125.5°) was 119–155°.

*Anal.* Calcd. for  $C_8H_{12}O_4$ : C, 55.80; H, 7.03. Found: C, 55.65; H, 6.89.

***cis*-1,2-Bis-(carboethoxymethyl)-cyclobutane (Xa).**—Acid XIa was esterified as described for the preparation of the ester of VIb, except that toluene was substituted for benzene. The product, obtained in nearly quantitative yield, had b.p. 116–120° (1.5 mm.),  $n_D^{25}$  1.4463.

*Anal.* Calcd. for  $C_{12}H_{20}O_4$ : C, 63.13; H, 8.83. Found: C, 62.90; H, 9.01.

***cis*-1,2-( $\beta$ -Hydroxyethyl)-cyclobutane (XX).**—The lithium aluminum hydride reduction of ester Xa was carried out as described for the preparation of VIIb. The product, isolated as previously described, was distilled, b.p. 138–140° (1 mm.), yield 93%,  $n_D^{25}$  1.4810.

*Anal.* Calcd. for  $C_8H_{16}O_2$ : C, 66.62; H, 11.18. Found: C, 66.47; H, 11.14.

**The di- $\alpha$ -naphthylurethan** was recrystallized from ethanol, m.p. 144.5–145.5°.

*Anal.* Calcd. for  $C_{30}H_{30}N_2O_4$ : C, 74.66; H, 6.27. Found: C, 74.11; H, 6.67.

***cis*-1,2-Bis-( $\beta$ -bromoethyl)-cyclobutane (XXI).**—A mixture containing 240 g. of 48% hydrobromic acid, 62 g. of

concd. sulfuric acid and 68 g. of diol XX was refluxed for 4 hours. After cooling, the dark colored lower layer was separated, and the upper layer was extracted with chloroform. The crude dibromide and the chloroform extract were combined and washed successively with concentrated sulfuric acid, water, 5% sodium carbonate solution, and water. After drying the solution over calcium chloride, the chloroform was removed on a steam-bath. The residue was distilled, b.p. 111–113° (1.2 mm.), wt. 101 g. (80%),  $n_D^{25}$  1.5267.

*Anal.* Calcd. for  $C_8H_{14}Br_2$ : C, 35.58; H, 5.22; Br, 59.20. Found: C, 35.75; H, 5.25; Br, 59.20.

***cis*-1,2-Bis-( $\beta$ -cyanoethyl)-cyclobutane (XXII).**—The bromide was converted to the nitrile by the method used to convert bromide VIIIb to nitrile IXb. Distillation of the product gave an 81% yield, b.p. 165–170° (1.5 mm.),  $n_D^{25}$  1.4724.

*Anal.* Calcd. for  $C_{10}H_{14}N_2$ : C, 74.03; H, 8.70. Found: C, 73.94, 74.08; H, 8.87, 8.69.

***cis*-1,2-Bis-( $\beta$ -carboethoxyethyl)-cyclobutane.**—The nitrile XXII was converted to the ester as described for preparation of ester (XI); yield 79%, b.p. 132–137° (0.7 mm.),  $n_D^{25}$  1.4518.

*Anal.* Calcd. for  $C_{14}H_{24}O_4$ : C, 65.60; H, 9.44. Found: C, 65.57; H, 9.37.

***cis*-1,2-Bis-( $\beta$ -carboxyethyl)-cyclobutane (XXIII).**—A sample of the above ester was converted to the acid as described for the conversion of Xb to XIb. After two recrystallizations from water the acid was obtained as plates, m.p. 135–136°.

*Anal.* Calcd. for  $C_{10}H_{16}O_4$ : C, 59.98; H, 8.06. Found: C, 59.88; H, 7.89.

**Malonic Ester Synthesis with *cis*-1,2-Bis-(bromomethyl)-cyclobutane.**—The malonic ester synthesis with 30.0 g. of bromide VIIIa was carried out as described for the *trans* isomer VIIIb. Distillation gave recovered malonic ester, then two fractions, (1) wt. 30 g., b.p. 57–101° (0.8 mm.); (2) wt. 6.7 g., b.p. 101–174° (0.2 mm.).

***cis*-4,4-Dicarboethoxybicyclo[3.2.0]heptane (XVa).**—Fraction I of the above distillation was redistilled, b.p. 110–120° (3 mm.), wt. 25 g. (84%). A center cut, b.p. 115°, was used for analysis,  $n_D^{25}$  1.4646.

*Anal.* Calcd. for  $C_{12}H_{20}O_4$ : C, 64.97; H, 8.39. Found: C, 64.87; H, 8.53.

***cis*-4,4-Dicarboxybicyclo[3.2.0]heptane (XVIa).**—Twenty-five grams of diester XVa was heated under reflux for 7 hours with 110 ml. of 8 N hydrochloric acid. The two-phase mixture then was steam distilled and yielded 8 g. of volatile material. The dark homogeneous residue was concentrated under vacuum and the solid which crystallized out during this process was collected, wt. 11 g. An analytical sample was recrystallized from water, prisms, m.p. 174° dec.

*Anal.* Calcd. for  $C_9H_{12}O_4$ : C, 58.68; H, 6.57. Found: C, 58.93; H, 6.42.

**4-Carboxy-*cis*-bicyclo[3.2.0]heptane (XVIIa).**—Nine grams of acid XVIa was decarboxylated at 185°. The product was distilled, wt. 5.0 g., b.p. 118–121° (3.5 mm.),  $n_D^{25}$  1.4813.

*Anal.* Calcd. for  $C_8H_{12}O_2$ : C, 68.54; H, 8.63. Found: C, 68.32; H, 8.41.

**The anilide,** recrystallized from ethanol–water, gave two fractions of crystals which are considered to be epimeric at position 4; soluble fraction, recrystallized from 50% ethanol, m.p. 134–135°.

*Anal.* Calcd. for  $C_{14}H_{17}NO$ : C, 78.10; H, 7.98. Found: C, 77.84; H, 8.18.

The other fraction, slightly soluble in 50% ethanol, recrystallized from 95% ethanol, m.p. 186–187°.

*Anal.* Calcd. for  $C_{14}H_{17}NO$ : C, 78.10; H, 7.98. Found: C, 77.89; H, 8.18.

The two anilides showed a mixture melting point of 129–135°.

***cis*-Bicyclo[5.2.0]nonanone-4 (XIXa).**—To a stirred, refluxing mixture of 2.5 liters of dry ether and 3.5 g. of lithium metal under a nitrogen atmosphere in a high dilution apparatus,<sup>36</sup> was added 39 g. of bromobenzene over a period of 2.5 hours. N-Methylaniline, 34 g., then was added over a period of 20 minutes, next 8.1 g. of *cis*-1,2-bis-( $\beta$ -cyanoethyl)-

cyclobutane (XXII) in one liter of dry ether over a period of 48 hours. The reaction mixture was cooled to room temperature and decomposed by the addition of 100 ml. of 2 *N* hydrochloric acid and 50 ml. of 6 *N* hydrochloric acid. Stirring at room temperature next was continued 0.5 hour to hydrolyze the imine.

The water layer was separated, extracted once with ether, and discarded. The volatile material from the combined organic layers was distilled under vacuum and the residue was heated under reflux with 200 ml. of 33% sulfuric acid for 3 hours. The ketone was steam distilled out of the reaction mixture over a period of 24 hours. The distillate was extracted 5 times with ether and the ether extracts were combined, washed with water, and dried over magnesium sulfate. The solvent was removed by fractionation, and the ketone was distilled, b.p. 100–104° (35–40 mm.),  $n_D^{25}$  1.4876, yield 5.0 g. (72%).

*Anal.* Calcd. for  $C_9H_{14}O$ : C, 78.26; H, 10.14. Found: C, 78.14; H, 10.04.

The semicarbazone, recrystallized from ethanol-water, gave fluffy needles, m.p. 178–179°. Mixture melting point with the semicarbazone of the *trans* isomer was depressed.

*Anal.* Calcd. for  $C_{10}H_{17}N_3O$ : C, 61.54; H, 8.72. Found: C, 61.27; H, 8.77.

*cis*-Bicyclo[5.2.0]nonane (IVa).—The Wolff-Kishner reduction of ketone XIXa was carried out as described for the preparation of the *trans* isomer XIXb. The product was distilled twice,  $n_D^{25}$  1.4662, b.p. 152–155° uncorr. Gas chromatography showed the compound was substantially better than 99% pure.

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

**Equilibration Studies with the Bicyclo[5.2.0]nonanes.**—One of the pure isomeric hydrocarbons, in the amount of 100–200 mg., was heated in a small sealed tube with *ca.* 20 mg. of 10% palladium-on-carbon. The results of the equilibration experiment then were determined by vapor phase chromatography. A 10-foot column of tricresyl phosphate on firebrick was used for the separation.

At 133°, where the retention times were 62 and 50 minutes, respectively, for the *cis*- and *trans*-hydrindane, the corresponding times for IV *cis* and *trans* were 69 and 63 minutes.

When the equilibration was carried out with IVb for 48 hours at 250°, the vapor phase analysis showed only a single peak corresponding to the starting isomer. The *cis* isomer IVa showed several % reaction under these conditions, but IVb was absent. At 315° considerable reaction took place with both isomers. From the *trans* isomer of IV (retention time 66 minutes) there was obtained a mixture which showed on vapor phase analysis two principal peaks in a 1:1 ratio with retention times of 65 and 55 minutes. From the *cis* isomer similarly there was obtained a 1:1 mixture with retention times of 70 and 55 minutes. In each case four minor components were detected, with retention times of less than 56 minutes and in total amount less than 5% of the mixture. In no case was any of the isomerized compound detected.

DETROIT, MICH.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WAYNE STATE UNIVERSITY]

## The Relative Stabilities of *cis* and *trans* Isomers. VI. The Decalins<sup>1,2</sup>

BY NORMAN L. ALLINGER AND JAMES L. COKE

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The equilibrium constant for the reaction *cis*-decalin  $\rightleftharpoons$  *trans*-decalin has been measured in the liquid phase under a pressure of hydrogen over the temperature range 531–641°K. From the data the thermodynamic quantities for the isomerization under these conditions were calculated as  $\Delta H^{685} = -2.72 \pm 0.20$  kcal./mole, and  $\Delta S^{685} = -0.55 \pm 0.30$  e.u. The feasibility of this general method for measuring the thermodynamic constants for such a reaction has been established.

### Introduction

The relative stabilities of *cis* and *trans* junctures in fused ring systems are of fundamental importance in organic chemistry, and qualitative equilibrium data as well as a few approximate heats of combustion for some simple cases have been available<sup>3</sup> for many years. More recently, with the development of the principles of conformational analysis,<sup>4</sup> a better understanding of these stabilities has been achieved, and a more quantitative knowledge of such systems has become desirable. Such a knowledge of complex systems as are commonly found in nature, for example in the steroids and terpenes, has been and will continue to be a great help in understanding much of the chemistry of these compounds. Conformational analysis enables predictions to be made only with respect to the heat contents of various structures. In order to gain a quantitative understanding of the stabilities of such ring junctures, it is necessary that

both the heats and entropies of isomerization be determined for a variety of simple systems. The almost total absence of entropy data for fused ring systems has led usually to the neglect of entropies of isomerization.<sup>5</sup> That this neglect may lead to incorrect conclusions has been pointed out previously.<sup>6</sup>

The thermodynamic functions of an organic compound may be obtained from the heat of combustion together with either spectral or heat capacity measurements. Both methods commonly are used, and they are quite generally applicable and quite accurate though rather laborious. In the present case the real interest lies not in the entropy and heat content of each isomer, but rather in the difference between these quantities for the two isomers. Such differences may in principle be determined from measurements of the equilibrium constant between the isomers as a function of temperature. There appears to be only one earlier attempt in the literature to obtain the thermodynamic quantities from the isomerization of a fused ring system in this way.<sup>7</sup>

The objectives of the present work were both to

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