20/32 Visking membranes under the conditions used is the same, about 90 hours. At 25°, 2% of the enzyme present in trypsin I autolysates has a 50% escape time of about 10 hr. or about nine times faster than that for trypsin I or II under these conditions. The observation that the concentration of the enzyme with the faster escape rate was about three times higher when dialysis was carried out at 0° indicates that this molecule is considerably less stable at 25° than trypsin. In control experiments, trypsin was found to be stable for 30 hr. at 25° under the same experimental conditions.

It is significant that trypsin I autolysates, identical with those which reveal two enzymatically active components in dialysis experiments through 20/32 Visking membranes at 25°, contain an enzyme that can diffuse through 18/32 Visking membranes at 0°. Trypsin II autolysates which reveal only a single component in dialysis experiments with 20/32 Visking membranes at 25°, with an escape rate identical to that of trypsin, do not contain an enzyme that can dialyze through 18/32 membranes at 0°.

It is of interest to note that Wootton and Hess used the dialysis method of Craig and co-workers for the analysis of acetyltrypsin autolysates and concluded that, under their experimental conditions, an active degradation product of the enzyme does not accumulate in detectable amounts,[18] an observation which has recently been confirmed.[19] When the dialysis experiments of acetyltrypsin autolysates[18] and trypsin autolysates were followed by a determination of enzymatic activity, protein nitrogen, and free amino groups of the dialysates and the material remaining inside 20/32 Visking membranes, the results could be explained on the basis that acetyltrypsin is autolyzed by a cleavage of all susceptible amide bonds of one molecule at a time, while trypsin is autolyzed by an essentially random cleavage of amide bonds of all molecules present. Therefore, trypsin autolysis proceeds under conditions that would allow the accumulation of an enzyme molecule of altered structure, while the autolysis of acetyltrypsin does not.

Craig and co-workers have determined the escape rates of a number of different peptides and proteins through 18/32 and 20/32 Visking membranes and concluded that, as in free diffusion, the molecular weight and shape of the molecules are the major factors which influence the escape rates of these molecules through membranes.[6,20] The data presented are therefore consistent with a difference in size and/or shape between trypsin and the fast moving enzymatic component in autolysates of trypsin I and in autolysates of mixtures of trypsin II and denatured trypsin II. The data also suggest that this fast moving enzymatically active component is considerably less stable than trypsin. This observation assigns a definite function to the amino acid residues of trypsin which are not directly involved in the active site of the enzyme, namely that of stabilizing the active site. Some modifications of this part of the molecule appear to be permissible.

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(18) J. F. Wootton and G. P. Hess, *Biochim. et Biophys. Acta*, **29**, 435 (1958).

(19) I. E. Liener, *ibid.*, **30**, 252 (1958).

(20) L. C. Craig, W. Konigsberg, A. Stracher and T. P. King, in "Symposium on Protein Structure," A. Neuberger, Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, pp. 104–115.

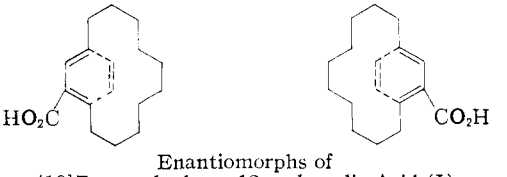
ITHACA, NEW YORK

COMMUNICATIONS TO THE EDITOR

MANY-MEMBERED CARBON RINGS. XXI. RESOLUTION OF [10]PARACYCLOPHANE-12-CARBOXYLIC ACID

Sir:

We wish to report evidence for restricted rotation about carbon–carbon single bonds in the carbocycle [10]paracyclophane. The *o*-carboxylic acid derivative of this hydrocarbon, [10]paracyclophane-12-carboxylic acid (I), has been resolved into pure optical antipodes through its cinchonidine salts. Isolation of enantiomorphs of the acid I thus comprises another cogent example of molecular dissymmetry arising from restricted rotation about single bonds.[1] In this particular instance the position of the *p*-decamethylene bridge must be restricted to regions above or below the faces of the benzene nucleus.



Enantiomorphs of
[10]Paracyclophane-12-carboxylic Acid (I)
(*p*-Decamethylenebenzene-*o*-carboxylic Acid)

The acid I, free of the isomeric [10-*m*]cyclophane-12-carboxylic acid,[2] was synthesized from authentic [10]paracyclophane[3] (n^{27}D 1.5332) *via* a

(1) (a) Lüttringhaus and H. Gralheer, *Ann.*, **557**, 108, 112 (1947); A. Lüttringhaus and G. Eyring, *Angew. Chem.*, **69**, 139 (1957); *Ann.*, **604**, 111 (1957).

(b) D. J. Cram and N. L. Allinger, THIS JOURNAL, **77**, 6289 (1958); D. J. Cram, R. J. Wechter and R. W. Kierstead, *ibid.*, **80**, 3126 (1955).

(2) A. T. Blomquist and F. Jaffe, *ibid.*, **80**, 3405 (1958).

(3) R. E. Stahl, Thesis, Cornell University, Ithaca, N. Y., 1954; D. J. Cram and H. U. Daeniker, THIS JOURNAL, **76**, 2743 (1954).

sequence of three transformations. Chloromethylation[4] of the hydrocarbon gave 12-chloromethyl[10]paracyclophane (73%); b.p. 150–152° (0.7 mm.), $n^{20}D$ 1.5775, m.p. 75–76° (from 30–60° petr. ether at −70°). *Anal.* Calcd. for $C_{17}H_{25}Cl$: C, 77.09; H, 9.55; Cl, 13.39; mol. wt., 265. Found: C, 77.26; H, 9.32; Cl, 13.15; mol. wt., 259 (Rast). Reaction of the chloromethyl compound with sodium 2-nitropropanenitronate[5] produced [10]paracyclophane-12-carboxaldehyde (84%); b.p. 130° (0.15 mm.), $n^{20}D$ 1.5803. *Anal.* Calcd. for $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.76; H, 9.68. This aldehyde showed a typical carbonyl band in the infrared at 5.92 μ and formed a 2,4-dinitrophenylhydrazone derivative, m.p. 202–203°. Finally, neutral permanganate oxidation of the aldehyde in acetone gave the acid I (45%); m.p. 192–193° (from aqueous ethanol). *Anal.* Calcd. for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.56; H, 9.12. Decarboxylation of *I* produced known [10]paracyclophane and bichromic acid oxidation afforded trimellitic acid.

An acetone solution of (±)I and cinchonidine deposited the salt of the (+)acid(−)base which, after recrystallization from acetone, showed m.p. 154–155° and $[\alpha]^{27}D$ + 22±2° (*c*, 10 in $CHCl_3$). *Anal.* Calcd. for $C_{36}H_{46}N_2O_3$: C, 77.93; H, 8.36; N, 5.06. Found: C, 78.15; H, 8.20; N, 5.03. Acidification of this salt with excess 5% hydrochloric acid precipitated pure (+)I; m.p. 160–161°, $[\alpha]^{24}D$ + 80±2° (*c*, 0.77 in $CHCl_3$). *Anal.* Found: C, 78.50; H, 9.25. The combined mother liquor and crystallization filtrates from the isolation of the (+)acid(−)base salt were evaporated to dryness and treated with excess 5% hydrochloric acid. A *rapid* fractional crystallization of this partially racemized acid I from warm ethanol-water gave, as the most soluble fraction, pure (−)I; m.p. 159–160°, $[\alpha]^{28}D$ −82±2° (*c*, 0.96 in $CHCl_3$). *Anal.* Found: C, 78.39; H, 9.31.

Observed changes in the m.p.'s of samples of pure (+) and (−) I on standing at different temperatures for varying lengths of time suggest that the optical antipodes racemize at an appreciable rate in the solid state. For example, (+)I, m.p. 160–161°, showed m.p. 158–162° after standing at −20° for five days. After additional standing for five days at 25° this (+)I had m.p. 155–167°. Complete racemization studies will be made when an adequate quantity of the acid I is at hand.

(4) "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 195.

(5) H. B. Hass and M. L. Bender, THIS JOURNAL, **71**, 1767 (1949).

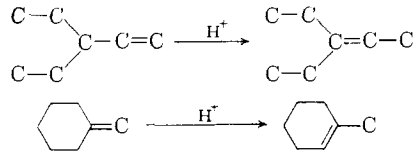
THE BAKER LABORATORY OF CHEMISTRY
CORNELL UNIVERSITY A. T. BLOMQUIST
ITHACA, NEW YORK BRANDES H. SMITH

RECEIVED FEBRUARY 26, 1960

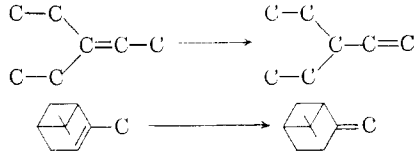
HYDROBORATION AS A CONVENIENT SYNTHETIC ROUTE FOR THE CONTRA-THERMODYNAMIC ISOMERIZATION OF OLEFINS

Sir:

The usual acid catalyzed isomerization of terminal olefins results in a preferential migration of the double bond into the chain or ring, with the final product being predominantly the more thermodynamically stable, most highly substituted olefin.[1]



We wish to report that hydroboration provides a convenient synthetic route from the more stable, highly substituted olefin to the less stable terminal products.



It was demonstrated previously that olefins of all types readily undergo hydroboration to form the corresponding organoborane[2] and that the boron atom readily migrates at temperatures of 100 to 150° from its original internal position in a chain or ring to a less hindered terminal position.[3] In order to achieve the desired contra-thermodynamic transformation from the more stable internal olefin to its less stable terminal isomer, it was necessary to demonstrate that the resulting organoborane could be converted into the desired olefin, *via* the displacement reaction,[4,5] without rearrangement.

Accordingly, 2-methyl-1-butene, 3-methyl-1-butene, 3-ethyl-1-pentene, 3-ethyl-2-pentene, 2,4,4-trimethyl-1-pentene, 2,4,4-trimethyl-2-pentene, and methylenecyclohexane were hydroborated in diglyme at 25° and the reaction products were treated for 3–6 hours with an excess of 1-decene at 160°. In each case the original olefin distilled out of the reaction mixture, with only negligible quantities of isomerized products.

It is noteworthy that even in the case of the organoboranes obtained from the labile, bicyclic systems, α- and β-pinene, displacement regenerates the original olefin without rearrangement. The hydroboration product from α-pinene (oxidizable to isopinocampheol in 90% yield) is isomerized readily to the organoborane from β-pinene (oxidized to *cis*-myrtanol in 70% yield).[6] Displacement of the isomerized product with 1-dodecene permits a simple conversion of α-pinene to β-pinene.

A typical procedure is given: 3-Ethyl-2-pentene, 9.8 g., 100 mmoles, was hydroborated under nitrogen in the usual manner in diglyme with 30 mmoles

(1) B. T. Brooks, *et al.*, ed., "The Chemistry of Petroleum Hydrocarbons," Reinhold Publishing Corp., New York, N. Y., 1955, Vol. 3, pp. 115–127.

(2) H. C. Brown and B. C. Subba Rao, THIS JOURNAL, **81**, 6428 (1959).

(3) H. C. Brown and G. Zweifel, *ibid.*, **82**, 1504 (1960).

(4) R. Köster, *Angew. Chem.*, **68**, 3831 (1956); R. Köster, *Ann.*, **618**, 31 (1958).

(5) H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, **22**, 1136 (1957); H. C. Brown and B. C. Subba Rao, THIS JOURNAL, **81**, 6434 (1959).

(6) R. Dulou and Y. Chrétien-Bessière, *Bull. soc. chim. France*, 1362 (1959), report that the hydroboration of β-pinene, then oxidation, produces *trans*-myrtanol.