[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF DELAWARE]

Some Observations on the Mechanism of Alkaline Permanganate Hydroxylation of Alicyclic Carboxylic Acids

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The steric course of the alkaline permanganate hydroxylation of (α) tertiary carboxylic acids has been examined in the cases of the *endo*- and *exo*norbornanecarboxylic acids. The common reaction product has been identified as norbornane-2-*exo*hydroxy-2-*endo*-carboxylic acid. The norbornane-2-*endo*carboxylic acid underwent hydroxylation almost four times more rapidly than the *exo* isomer, but isocamphenilanic acid (VII) was completely resistant to this reaction. A cyclic Mn^{+5} intermediate formed *via* enolization of a mixed permanganic–carboxylic anhydride is considered as a mechanistic alternative to the course of reaction proposed by Kenyon and Symons.[2b]

Kenyon and Symons[2] have reported that active carboxylic acids, where the α-carbon is the center of asymmetry, are converted to racemic α-hydroxy acids in good yield by potassium permanganate in concentrated alkaline solution. These authors have postulated that for reactions with permanganate the active oxidant is the free hydroxyl radical or the ($\cdot O^-$) radical ion and the product is formed *via* direct attack (with unspecified stereochemical pattern) at the α-carbon by one of these species. They have, furthermore, rejected the possibility that this reaction could involve formation of carbanion character at the α-carbon. We have examined the steric course of this reaction in several alicyclic cases for the purpose of ascertaining the general applicability of the Kenyon and Symons interpretation.

Results and Discussion

When norbornane-2-*endo*carboxylic acid (I) was oxidized under condition very similar to those described by Kenyon and Symons, only a single pure product (III) was recovered in nearly two-thirds the theoretical yield. When the corresponding *exo* isomer II was treated at the same temperature and for the same length of time, the same product (III) was obtained but in much smaller yield (*ca.* 10%). The remainder of the product here was unreacted starting material II. Clearly the *endo* isomer I is more readily oxidized by the alkaline permanganate, but both reactions proceed to product *via* a common intermediate; that is, the product-forming step is common to both reactions.

The structure of III was established by familiar lines of evidence. Oxidation of III with acid chromate yielded only norcamphor. Deformylation, the loss of the elements of formic acid under these conditions, is a characteristic reaction of α-hydroxyacids. An entirely similar reaction, for example, has been reported by Asahina and Ishidate[3] for the preparation of epicamphor from bornane-3-hydroxy-3-carboxylic acid. A boric acid conductivity study also confirmed that the hydroxyl group in (III) was indeed in the α-position (see Experimental).[4]

Proof of the *exo–endo* configurational relationships of the functional groups in III was obtained by reduction with lithium aluminum hydride to the diol IV. The configuration of IV, in turn, was established by tosylation of the primary alcohol function, followed by hydrogenolysis with lithium aluminum hydride in the familiar manner to the tertiary alcohol 2-*exo*hydroxy-2-*endo*methylnorbornane (V). The latter substance was independently synthesized, using the method of Toivonen, *et al.*,[5] for comparison of infrared spectral characteristics and mixed melting point with V. However, repeated attempts at dehydroxylation of V by hydrogenolysis with Raney nickel according to the procedure of Bonner, *et al.*,[6] for aliphatic hydroxy esters failed to regenerate the norbonane-2-*endo*carboxylic acid (I).

The Mechanism of Hydroxylation.—The difference in ease of reaction of the two isomers has been noted above. Somewhat crude rate studies that we have carried out indicate that the *endo*-acid I reacts almost four times faster than the *exo*-acid II. This small magnitude of rate difference can be construed as evidence against a carbonium ion mechanism. One would have expected that a reaction path involving hydride ion abstraction from the norbornane nucleus would be attended by strong anchimeric assistance involving a rate benefit of the order of several hundred or more for *exo*-hydride bond breaking, analogous to what has been often observed in this series for other leaving groups in the *exo* orientation.[7]

On the other hand, a carbanion mechanism, *viz.*, one involving proton abstraction from the α-carbon by base with formation of an enolic intermediate (or the equivalent), is eligible for consideration on the basis of these rate data. Thus, it has been shown[8a] that the α-bromination of carboxylic acids, a common reaction involving the rate-determining formation of enol, also occurs about four to five times more rapidly with I than II and the sole and identical product obtained

(1) (a) Most of the data for this article have been taken from the dissertation of George D. Null, submitted in partial fulfillment of the requirements of the Ph.D. degree at the University of Delaware, June, 1958. (b) Part of the work bring reported here was presented at the 131st Meeting of the American Chemical Society, Miami, Fla., April 10, 1957.

(2) J. Kenyon and M. C. R. Symons, *J. Chem. Soc.*, (a) 2129, (b) 3580 (1953).

(3) Y. Asahina and M. Ishidate, *Ber.*, **66**, 1913 (1933).

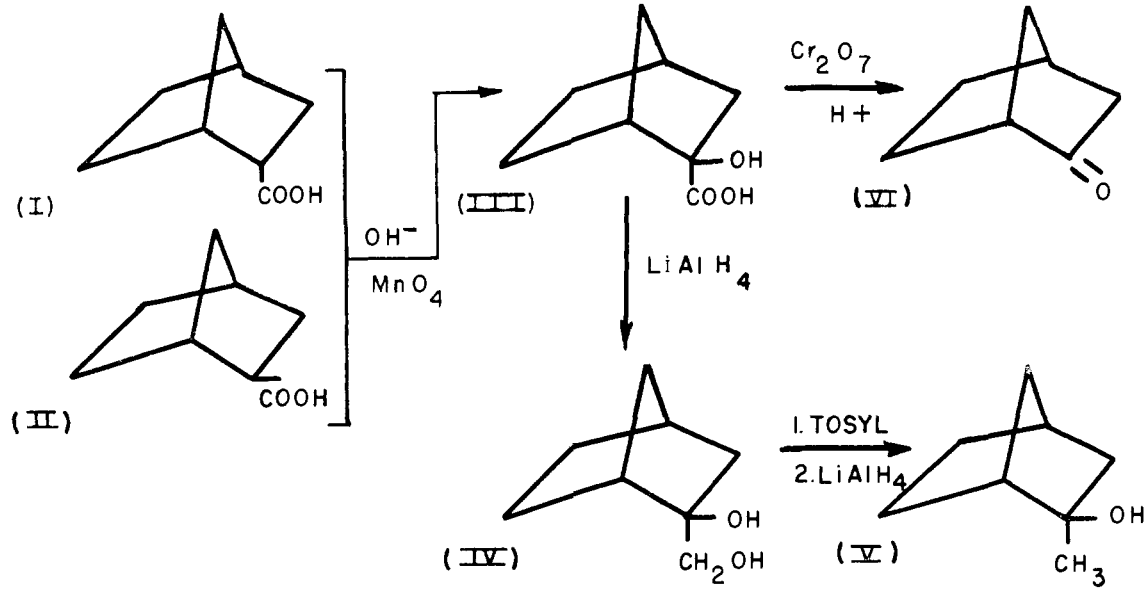
(4) J. Boeseken, *Adv. in Carbohydrate Chem.*, **4**, 189 (1949), has discussed the marked enhancement of the conductivity of boric acid solutions by the presence of α-hydroxyacids.

(5) H. J. Toivonen, K. Siltanen and K. Ojala, *Ann. Acad. Sci. Fenn.*, **AII**, No. 64 (1955).

(6) W. A. Bonner, J. A. Zderic and G. S. Casaletto, THIS JOURNAL, **74**, 5086 (1952).

(7) See, for example, S. Winstein and D. S. Trifan, *ibid.*, **74**, 1147 1154 (1952), and S. Winstein and K. Schreiber, *ibid.*, **74**, 2165, 2171 (1952).

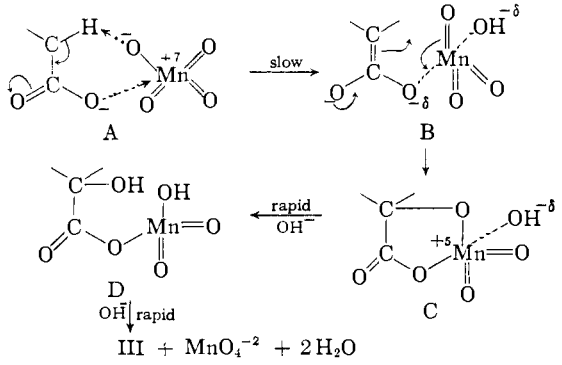
(8) (a) H. Kwart and G. D. Null, *ibid.*, **81**, 2765 (1959); (b) see also W. R. Boehme, *ibid.*, **81**, 2762 (1959).

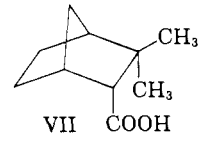


in both cases was analogously proved[8b] to be the *exo*-bromo-*endo*-carboxylate.

The steric preference for reaction of the common enolic intermediate from I and II with an electrophilic reagent approaching from the less hindered *exo* side correlates well with several similar observations by Zimmerman[9] in other alicyclic systems (and does not necessarily imply steric control by neighboring group participation).

Kenyon and Symons[2b] have rejected the carbanion mechanism on the grounds that (*alpha*) optically active carboxylic acids ordinarily fail to racemize in hot concentrated alkaline solution, the hydroxylation reaction conditions. However, the existence of transient enolic intermediates in the reactions of (resolvable) carboxylic acids has been demonstrated previously and there is no prohibition on their formation under conditions where a suitable low energy path is available.[9b] In the bromination of carboxylic acids the enolic intermediate is actually formed *via* abstraction of the more acidic proton of a transient acyl halide or an hydride precursor. Here, an enol derivative of a transient cyclic complex may be the intermediate undergoing hydroxylation. The electron dense center of the carboxylate anion becomes coordinated with the electron deficient Mn^{+7}, while simultaneously or successively a proton is abstracted from the α-carbon, as shown by A → B. An analogous path has been discussed for the assistance to enolization of acetoacetic ester by copper salts.[10] (The dotted lines illustrating the structure B should be understood to indicate some form of coördination other than covalent.) The enolic complex B is transformed by cyclic reduction to the Mn^{+5} complex C which, in turn, experiences rapid hydrolysis and bimolecular attack by hydroxide ion to form the covalent hypomanganate-carboxylic anhydride, D. The latter is, of course, exceedingly unstable to irreversible hydrolysis in the highly basic medium and splits out the product α-hydroxy acid readily. This mechanism implicates base in almost every step and, therefore, is in accord with the observed rate increase with increasing hydroxyl ion concentration. Furthermore, it is in keeping with several similar suggestions of a cyclic intermediate to explain *cis* hydroxylation of olefins in alkaline permanganate.[11] The generally higher yields obtained in this reaction as compared to the permanganate hydroxylation of olefins[11] may perhaps be attributed to the steric accommodation afforded by the possibility of intramolecular electrophilic attack by the permanganate moiety in the mixed anhydride intermediates C and D. The failure which we have experienced in all attempts to make isocamphenilanic acid (VII) undergo reaction under these conditions might also be explained by





(9) (a) See H. E. Zimmerman, *J. Org. Chem.*, **20**, 549 (1955), as well as several other articles which have since appeared from this author's laboratory; (b) H. E. Zimmerman and T. W. Cutshall, THIS JOURNAL, **81**, 4305 (1959).

(10) C. G. Swain, *ibid.*, **72**, 4578 (1950).

(11) See J. Boeseken, *Rec. trav. chim.*, **40**, 553 (1951); **47**, 683 (1928) and K. B. Wiberg and K. A. Saegebarth, THIS JOURNAL, **79**, 2822 (1957) and other references cited in these articles. A. Y. Drummond and W. A. Waters, *J. Chem. Soc.*, 435 (1953), have proposed, however, that the organic compound is oxidized in two successive stages rather than through the cyclic intermediate, but M. C. R. Symons, *ibid.*, 3956 (1953), has contested the basis of their view.

steric factors arising from the requirement for forming a cyclic Mn^{+5} intermediate. Clearly there is no difficulty in forming the enol of VII since bromination occurs quite readily under normal Hell–Volhard–Zelinsky conditions.[8a] The steric hindrance may perhaps be attributed to obstruction in forming the mixed anhydride[12] or to the steric effect of the adjacent methyl groups in shielding the carbanion center from intramolecular attack by the permanganate moiety. The fact that oxidation does not take place at any other position on the ring of VII and that 2-*endo*methylnorbornane is not attacked by permanganate under these conditions emphasizes the important role played by the carboxylic group in the mechanism. However, while the steric selectivity of the reaction is adequately explained by the carbanion mechanism, the free radical path proposed by Kenyon and Symons[2b] is obviously not excluded. A kinetic study directed toward evaluating these alternatives is presently in progress in our laboratories.

Experimental[13]

Norbornanecarboxylic acids I and II were prepared according to procedures previously described by us.[8a]

The Oxidation of I and II.—Fifty grams (0.36 mole) of the *endo*-acid I was mixed with 700 cc. of approximately 6 *M* potassium hydroxide and 90 g. of potassium permanganate. The resulting green mixture was warmed to 65°. After stirring for 3 hr., with no further heating, the reaction mixture was allowed to stand overnight. The excess reagent was discharged with sulfur dioxide and the resulting manganese dioxide was removed by filtration. The slightly yellow filtrate was extracted with diethyl ether, cooled in an ice-bath, slowly acidified with 12 *N* sulfuric acid and finally extracted again with diethyl ether. The ether extracts were dried over sodium sulfate. After removal of the solvent, a white crystalline residue (III) remained which weighed 37.2 g., yield 67%. Upon being twice recrystallized from benzene, the m.p. was 112–114°; *p*-bromophenacyl ester, m.p. 130–131°.

Anal. Calcd. for $C_8H_{12}O_3$: C, 61.49; H, 7.75. Found: C, 61.61; H, 7.76.

When 10 g. (0.07 mole) of the *exo*-acid V was treated with 700 cc. of 9 *M* potassium hydroxide and 22 g. of potassium permanganate under the same conditions as described above for the *endo*-acid I, a yellow oily semi-solid oxidation product resulted. This was subjected to repeated recrystallizations to remove the solid substance from the residual oil. The recrystallized product melted at 108–110° and an admixture of samples from the oxidation of *endo*-I and *exo*-II acids gave no m.p. depression. The infrared spectra of the oxidation products of I and II were identical. The residual oil (about 9 g.) proved to be unreacted *exo*-acid II since it readily formed a *p*-bromophenacyl ester which gave no m.p. depression when mixed with an authentic sample of the same ester of *exo*-acid II. Only about 10% over-all yield of hydroxy acid III could be isolated in these experiments.

The Reaction of the Acid III with Lithium Aluminum Hydride.—Following a procedure similar to that outlined by Wilder and Winston,[14] 7.0 g. (0.18 mole) of lithium aluminum hydride was suspended in 480 cc. of dry diethyl ether, stirred for 0.5 hr., and then treated dropwise with a solution of 30 g. (0.2 mole) of the hydroxy acid III dissolved in 300 cc. of anhydrous diethyl ether. When the addition was completed, refluxing was continued for 2 hr. and then the reaction mixture was allowed to stand overnight. The excess lithium aluminum hydride was decomposed by the cautious addition of water. Subsequent addition of 420 cc. of approximately 10% hydrochloric acid dissolved the precipitate. The layers were separated, the water layer extracted with diethyl ether, the combined extracts washed with water, and dried over anhydrous sodium sulfate. Removal of the solvent left an oil which yielded 14.2 g. of white crystals (IV) when treated with 2,3-dimethylbutane. Recrystallization of this product from 2,3-dimethylbutane, then (90–100°) petroleum ether gave m.p. 101–102°, yield 52%, positive ceric nitrate test.

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.55; H, 9.92. Found: C, 67.68; H, 9.91. The di-*p*-nitrobenzoate was recrystallized twice from ethanol; m.p. 162–163°. *Anal.* Calcd. for $C_{22}H_{20}O_8N_2$: C, 59.99; H, 4.58; N, 6.36. Found: C, 59.70; H, 4.49; N, 6.11.

The Conversion of IV to V.—Using the method of Wilder and Winston,[14] 13.2 g. (0.09 mole) of the diol IV was added to a previously cooled (0°) solution of 19.2 g. (0.1 mole) of toluenesulfonyl chloride in 135 cc. of purified pyridine and placed in a refrigerator at 0° for 40 hr. When the pyridine solution was poured into 300 cc. of ice-cold 6 *N* sulfuric acid, a sticky pink compound separated out. This compound was dissolved in diethyl ether and the water layer extracted several times with ether. The combined extracts were washed with water, dried over anhydrous sodium sulfate and reduced to a volume of approximately 250 cc. This solution of the tosylate was added to a well stirred suspension of 15.6 g. (0.4 mole) of lithium aluminum hydride in 250 cc. of the same solvent. After refluxing the reaction mixture for 20 hr., it was worked up in the usual way to yield 4.8 g. of an oily solid which gave a positive ceric nitrate test. After several sublimations at 24° (1 mm.) this solid melted at 84°. A mixed melting point of this substance with the known alcohol[5] V gave no depression and the infrared spectra of these two compounds proved to be identical, as were the corresponding *p*-nitrobenzoate derivatives. The known alcohol V was prepared by solvolysis of a mixture of two isomeric chlorides (2-*exo*chloro-1-methylnorbornane and 2-*exo*-2-*endo*-methylnorbornane)[15] according to the original method of Toivonen.[5]

The Oxidation of III with Acid Chromate.—When 2.0 g. (0.012 mole) of the hydroxy acid III was mixed with a solution of 1 g. of sodium dichromate in 65 cc. of 1.5 *M* sulfuric acid and refluxed, the orange-brown color of the dichromate was gone within an hour. The reaction mixture was extracted several times with diethyl ether and the combined extracts dried over magnesium sulfate. An oily liquid was obtained upon removal of the ether and gentle warming of this oil yielded a white sublimate (VI) proved to be a carbonyl compound which had a m.p. 91–93°. A portion of the ketone was converted to its corresponding 2,4-dinitrophenylhydrazone, m.p. 129–130°. An admixture of this with the known DNPH of norcamphor gave no melting point depression and the infrared spectra of this derivative and the known were identical.

Attempted Oxidation of 2-*endo*-Methylnorbornane with Alkaline Permanganate.—A variety of experimental conditions was tried; aqueous alkaline solution, the usual condition used with I and II, combined with rapid stirring to effect intimate contact of the reagents; sodium permanganate in *t*-butyl alcohol and sodium *t*-butylate solution containing the same molar equivalent of base as used in the normal reaction with acid I (*vide supra*); potassium permanganate in sodium hydroxide–*t*-butyl alcohol solution of the same concentrations as the normal runs in aqueous solvent. In each case at least 89% of pure hydrocarbon could be recovered unchanged. No other product could be isolated or identified in the crude reaction mixtures before further purification and recovery of the hydrocarbon.

The Preparation of 2-*exo*-Hydroxynorbornane-2-*endo*-methylcarboxylate.—An ether solution of diazomethane was prepared by adding 17.5 g. of N-nitrosomethylurea to an ice-cooled mixture of 52 cc. of 50% KOH and 175 cc. of diethyl ether. After the addition was finished, stirring was continued for 0.5 hr. The ether layer was separated and dried over potassium hydroxide pellets.

Ten grams (0.064 mole) of the hydroxy acid III dissolved in 300 cc. of diethyl ether was added dropwise, during the course of 20 min., to the ice-cooled ether solution of diazomethane. The ether was evaporated on a steam-bath and the oily residue was taken up in ether, washed with sodium carbonate solution, then with water and finally dried over

(12) For a full discussion of steric hindrance in carbonyl reactions see M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., Chap. IV, 1956, p. 201.

(13) All melting and boiling points given are uncorrected.

(14) P. Wilder, Jr., and A. Winston, THIS JOURNAL, **78**, 868 (1956).

(15) A sample of this was very kindly provided by Dr. P. v. R. Schleyer of Princeton, N. J.

magnesium sulfate. Evaporation of the ether left the crude yellow colored ester which was distilled at reduced pressure: b.p. 81° (2.5 mm.), $n^{25}D$ 1.4791, wt. 6.4 g., positive test with ceric nitrate reagent.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.48; H, 8.29. Found: C, 63.10; H, 8.85.

The Attempted Reaction of 2-*exo*Hydroxynorbornane-2-*endo*methylcarboxylate with Raney Nickel.—Using the method of Bonner, *et al.*,[6] 4.9 g. (0.03 mole) of the hydroxy ester, 21 g. of Raney nickel catalyst and 100 cc. of ethanol were placed in a Parr low pressure apparatus and subjected to 20 lb. of hydrogen pressure at a temperature of 60° for 24 hours.

The catalyst was removed by filtration and the filter cake washed with 200 cc. of ethanol. Distillation of the ethanol left a yellow oil which distilled at 76–77° under 1.5 mm. pressure; $n^{25}D$ 1.4789; $n^{25}D$ for known ester, 1.4791; wt. of recovered starting material, 4.0 g.

The Attempted Reaction of Isocamphenilanic Acid with Alkaline Potassium Permanganate.—A solution of 16.8 g. (0.099 mole) of isocamphenilanic acid[16] and 83 g. of potassium hydroxide in 235 cc. of water was mixed with 30 g. of potassium permanganate. This mixture was warmed to 50° and then allowed to stir for 8 hr. while the temperature gradually returned to room temperature (25°). The excess permanganate was decomposed with sulfur dioxide and the solution strongly acidified with 6 *N* sulfuric acid, then extracted several times with diethyl ether. After the ether extracts were dried over magnesium sulfate, the solvent was removed leaving a white crystalline solid. Following several recrystallizations from methanol–water, the compound melted at 117–118°. This acid gave a negative ceric nitrate test and on admixture with a sample of isocamphenilanic acid gave no m.p. depression or change in infrared spectrum; wt. of recovered acid, 14.5 g.

The Measurement[17] of the Conductivity of the Boric Acid Complex with the Hydroxyacid III.

(1) 0.06410 *M* 2-*exo*hydroxynorbornane-2-*endo*carboxylic acid in 0.5 *M* boric acid solution

$$R = \frac{400}{3500} \times 481 = 54.9; \quad L = \frac{C}{R} = \frac{4.25}{549} = 0.0774$$

(2) 0.06410 *M* 2-*exo*hydroxynorbornane-2-*endo*carboxylic acid in water

$$R = \frac{1000}{2500} \times 1134 = 453.6; \quad L = \frac{C}{R} = \frac{4.25}{453.6} = 0.00936$$

(3) 0.5 *M* boric acid solution

$$R = \frac{9000}{1000} \times 1361 = 12{,}249.0; \quad L = \frac{C}{R} = \frac{4.25}{12{,}249.0} = 0.000346$$

extent of complex formation = (*L* for hydroxy acid in 0.5 boric acid) − (*L* for hydroxy acid in water + *L* for 0.5 *M* boric acid)

extent of complex formation = 0.0774 − (0.00936 + 0.000346) = 0.0677

The Relative Rates of Oxidation of I and II.—The analytical procedure involved keeping 5.0-g. samples (0.032 mole) of acid in a solution containing 24.8 g. of KOH, 11.1 g. of $NaMnO_4 \cdot H_2O$ and 70 ml. of water at 24° in a thermostat. Aliquots of 10 ml. were removed at 15-min. intervals, quenched by bubbling in SO_2 until all the MnO_2 had dissolved, acidified and extracted three times with 50-cc. portions of ether. After evaporating the extracts, 50 ml. of standard (0.1007 *N*) $Na_2Cr_2O_7 \cdot H_2O$ in 1 *M* H_2SO_4 was added and the resulting solution refluxed for 45 min. The reaction was cooled with the addition of 50 ml. of water and back titrated with 0.1003 *N* $Na_2S_2O_3$ solution. A small correction was applied to each titer for the amount of oxidation experienced by the unhydroxylated acids I and II, respectively, with the acid chromate standard reagent after 45 min. of reflux. From several determinations the average ratio $k_{endo}/k_{exo} = 3.75$, with an estimated accuracy of about 20%.

NEWARK, DEL.

(16) Prepared according to the procedure given by W. R. Vaughn and R. Perry, Jr., THIS JOURNAL, **74**, 5355 (1952).

(17) The nomenclature and procedure used here is that employed by Boeseken.[4]

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF COLORADO, AND THE SHELL DEVELOPMENT CO.]

Bridged Polycyclic Compounds. X. The Synthesis of *endo* and *exo*-1,2-Dihydrodicyclopentadienes and Related Compounds[1]

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Syntheses of the *endo* (I) and *exo* (II) isomers of 1,2-dihydrodicyclopentadiene have been investigated. The Diels–Alder synthesis from cyclopentadiene and cyclopentene leads to mixtures of both isomers, as well as both dicyclopentadienes. The effect of the severity of reaction conditions upon the composition of the reaction mixture is described, as is the preparation of pure *endo* isomer I. Syntheses of the *endo* and *exo* isomers have been carried out by pyrolysis of the benzoate esters of the *exo*-alcohols X and VIII related to I and II. Analyses were carried out by qualitative infrared measurements on the hydrocarbons and quantitative infrared measurements on their phenyl azide addition products.

As we are interested in a study of addition reactions to the *endo* (I) and *exo* (II) isomers of 1,2-dihydrodicyclopentadiene, it seemed worthwhile to develop a convenient synthesis of each isomer in as high a state of purity as possible.

Bruson and Riener[2] have reported that the Diels–Alder reaction of cyclopentadiene with cyclopentene gives 1,2-dihydrodicyclopentadiene, and it seemed reasonable from the Alder rule[3] that the product might be largely the *endo* isomer I, perhaps contaminated with the *exo* isomer II, as well as with the corresponding dicyclopentadienes III and IV resulting from dimerization of cyclopentadiene. We decided to scrutinize the composition of this mixture and to investigate the effect of reaction conditions upon the *endo*/*exo* ratio, looking toward synthesis of the pure *endo* isomer or of a mixture rich in that isomer. While our work was in progress, Wilder, Culbertson and Youngblood[4] showed that the Bruson–Riener product was in fact largely the *endo* isomer I, although no quantitative analysis was given. The proof of structure of I was carried out by Wilder and his co-workers.[4]

(1) Previous paper in series: S. J. Cristol and R. T. LaLonde, THIS JOURNAL, **81**, 5417 (1959); (a) University of Colorado; (b) Shell Development Co.

(2) H. A. Bruson and T. W. Riener, THIS JOURNAL, **67**, 723 (1945).

(3) K. Alder and G. Stein, *Angew. Chem.*, **50**, 510 (1937).

(4) P. Wilder, Jr., C. F. Culbertson and G. T. Youngblood, THIS JOURNAL, **81**, 655 (1959).