of pyridine hydrochloride was heated at 210° for 2 hr. The reaction was cooled and poured onto ice water to produce a crude precipitate. After several recrystallizations of the solid from alcohol-water, 100 mg. of crystalline material was obtained, which was identical to III (melting point and mixed melting point).

2-Hydroxy-6-methylacetophenone (XVIII) *and the corresponding hydrazone* (XIX). A mixture of 1 g. of 2-methoxy-6-methylacetophenone (XVII) and 7 g. of pyridine hydrochloride was heated under nitrogen at 210–215° for 90 min. The deep red mixture was cooled and water was added. The aqueous solution was extracted with ether and the ether layer was extracted with 1N sodium hydroxide solution. The basic extract was acidified and extracted with ether. Distillation of the ether gave 400 mg. of XVIII, which showed hydroxyl and carbonyl (1667 cm.$^{-1}$) absorption in the infrared.

To 300 mg. of XVIII dissolved in ethanol, 2 ml. of hydrazine (95+%) and a drop of glacial acetic acid were added. After 3 hr. at reflux temperature, the solvent and excess hydrazine were removed to give a residue, which was dissolved in 100 ml. of boiling *n*-heptane. Upon cooling 120 mg. of white needles, m.p. 139–141° were obtained. A mixture melting point with V from the Fries reaction showed no depression; the infrared spectra of V and XIX were identical.

Acknowledgment. We wish to thank Mr. Walter Musliner for the preparation of some of the intermediates.

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[CONTRIBUTION FROM THE MIAMI VALLEY LABORATORIES, PROCTER & GAMBLE CO.]

Thermal Isomerization of Hydroborated Olefins

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Received March 30, 1961

The effects of chain length and hydroxyl substituents on the extent and direction of boron migration along a hydrocarbon chain were studied by thermal isomerization, oxidation, and hydrolysis of hydroborated 11-tricosene and oleyl alcohol. Boron migration along the long chains in the trialkylborane derived from the unsubstituted 11-tricosene is complete, and oxidation gives good yields of 1-tricosanol. Migration along the long chains in the trialkylborane derived from the terminally substituted oleyl alcohol proceeds in both directions. Migration in one direction gives, after oxidation and hydrolysis, 1,18-octadecanediol, while migration in the other direction, toward the original hydroxyl group, does not go beyond the 4- position, possibly due to coordination with the oxygen atom in a 6-membered ring. Oxygenated functional groups, such as in free alcohols and ketones, appear to be capable of inhibiting boron migration.

Brown and Subba Rao discovered that, in the presence of ethers, olefins of wide structural variety react with diborane at room temperature to yield trialkylboranes.[1] Products thus formed from terminal olefins may be oxidized and hydrolyzed to primary alcohols, providing a convenient anti-Markownikoff hydration. Trialkylboranes from internal olefins may be thermally isomerized to the corresponding 1-alkylboranes,[2] which then yield primary alcohols on oxidation.

In the present study, the effect of a hydroxyl substituent, and of the chain length on the extent and direction of boron atom migration along a hydrocarbon chain was investigated.

Hydroxy-substituted olefin. A recent publication by Fore and Bickford[3] described the successive hydroboration, attempted isomerization, and oxidation of methyl oleate. They found that oxidation of heat-treated and nonheat-treated boranes of methyl oleate yielded the same products, namely 1 : 1 mixtures of 9- and 10-hydroxystearic acids (after saponification of the ester).

An unsaturated alcohol was used for the present study because the alcohol group undergoes no net change in the procedures employed. Oleyl alcohol was chosen to ascertain the direction and extent of boron migration in terminally hydroxy-substituted long-chain compounds.

Oleyl alcohol was hydroborated and esterified by diborane to give a cross-linked, polymeric tris(tristearylborane) borate. Oxidation and hydrolysis gave a mixture of the isomeric 1,9- and 1,10-octadecanediols identical to that produced by epoxidation and reduction of oleyl acetate. Working with methyl oleate, Fore and Bickford[3] had already demonstrated that the hydroboration was nonselective as to the 9- and 10- positions.

Thermal isomerization (four hours at 160°) before oxidation and hydrolysis of hydroborated oleyl alcohol led to 10–13% yields of the 1,18-isomer in the octadecanediol product. This isomer was isolated by urea adduction of the isomeric diacetates and identified by elemental analyses, hydroxyl value, and infrared analysis, the last showing no secondary alcohol absorption.

The diols from the unadducted fraction of the diacetates did not contain 1,2-diols (negative periodate tests) and were different, on the basis of mixed melting point determinations, from the previously mentioned mixture of 1,9- and 1,10-diols and also the 1,6- and 1,7-diol mixture obtained

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[1] H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, **22**, 1136 (1957).

[2] H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, **22**, 1137 (1957).

[3] S. P. Fore and W. G. Bickford, *J. Org. Chem.*, **24**, 920 (1959).

by epoxidation and reduction of petroselinic (6-octadecenoic) acid. Oxidation of the diols from the unadducted fraction of the diacetates with chromium trioxide gave, in 58% yield, a mixture of ketostearic acids, shown by x-ray powder diffraction comparison with an authentic sample to be predominantly 4-ketostearic acid. The absence of decarboxylation during heating justifies the assumption that no 3-ketostearic acid was present in this mixture which melted sharply and differently from the corresponding derivative obtained by chromium trioxide oxidation of the 1,9- and 1,10-diol mixture. The diol made from 4-ketostearic acid did not depress the melting point of the unadducted diols. On the basis of the above information, the 1,4-diol, with a small quantity of the 1,5-diol, is the most likely isomer resulting from boron migration toward the original hydroxyl group.

Identification of both 1,18- and 1,4-octadecanediol isomers showed that thermally-induced migration of the boron atoms had proceeded in both directions from the original point of attachment of the boron atoms. According to Brown,[2] terminal boranes are more stable than internal boranes. Those boron atoms which move toward the hydroxyl group, however, do not closely approach the 1-position. It is possible that they are "trapped" in the 4-position by coordination with the electron pair of oxygen in a six-membered ring. Such coordination is suggested by Abel's[4] findings that O-B coordination exists within the borate ester group. If the boron atoms are trapped at C-4, they never reach the 1-, 2-, or 3- positions.

Brown[5] observed that a four-hour isomerization period provided only a 40% yield of 1-tetradecanol from a sample of mixed tetradecenes, and an eighteen-hour period was needed to yield 70% of the same product. In view of this, hydroborated oleyl alcohol was isomerized for twenty hours in an attempt to obtain higher yields of 1,18-diol. No appreciable change in yield resulted.

Unsubstituted olefin. To determine whether the length of an unsubstituted chain influences the extent of boron migration, 11-tricosene ($C_{23}H_{46}$) was hydroborated and isomerized for four hours at 188°. Oxidation gave a mixture of tricosanols (64% yield) shown to contain 80% *n*-tricosyl alcohol by urea adduction and infrared analysis. The remarkable ease with which the boron atom migrates along eleven carbon atoms in hydroborated 11-tricosene demonstrates that chain length is not responsible for the failure of all the boron atoms to reach the end positions in the oleyl alcohol example.

It was found that certain oxygen-containing functional groups are capable of inhibiting boron atom migration.[6] When alcohols or ketones are added to hydroborated trioleyl borate before heating, the oxidized and hydrolyzed product is identical in melting point to the diols resulting from direct oxidation of the hydroborated ester, and no 1,18-diol is formed. This suggests that complex formation between the boron atom and the oxygen atom of the inhibiting molecule may be responsible for the inhibition of migration. The oxygen atoms in ketones and free alcohols would be expected to make these agents stronger Lewis bases than do those in borate esters because of "back coordination"[4] of the latter within the borate ester group. Since the ketone can be recovered unchanged by distillation, chemical reaction with the borane is not responsible for the inhibition exhibited by this functional group.

The above results parallel those obtained by Fore and Bickford,[3] who found identical products from heat-treated and nonheat-treated hydroborated methyl oleate.

Thus, a hydroxyl (or borate) group at the end of the chain may trap part of the boron atoms and prevent migration to that end of the chain. Atoms which are successful in migrating to the end of the chain reach that end which is farthest from the hetero substituent.

EXPERIMENTAL

General. All manipulations of diborane and trialkylboranes described below were carried out in a nitrogen atmosphere. Diborane generation and the procedures for hydroboration and oxidation were essentially those previously described by Brown.[1] Diborane was generated by the addition of a bis-2-ethoxyethyl solution of sodium borohydride to boron trifluoride etherate and carried into the reactor with a slow stream of nitrogen. In some experiments, the olefin and sodium borohydride were placed in the reactor and diborane was generated *in situ* by the addition of boron trifluoride etherate. Exhaust gases were passed through an acetone wash-bottle to trap any unchanged diborane. Detailed procedures for several representative runs are given below.

Hydroboration and oxidation of oleyl alcohol with internally generated diborane. Oleyl alcohol, 81.0 g. (0.3 mole), and sodium borohydride, 8.62 g. (0.23 mole), were mixed with 150 ml. of bis-2-ethoxyethyl ether and placed in a flask equipped with dropping funnel, stirrer, and nitrogen inlet. (A separate experiment showed that, under these conditions, the reaction of oleyl alcohol with sodium borohydride to form the tetraalkoxy borate was only 0.2% complete in 7 hr., as measured by hydrogen evolution.[7]) After the apparatus was thoroughly flushed with nitrogen, boron trifluoride etherate, 22.0 g. (0.15 mole), in 50 ml. of the same solvent was added dropwise over a 2-hr. period. The maximum temperature reached was 43°. After an additional 2 hr. of stirring, during which a gelatinous solid appeared,

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(4) E. W. Abel, W. Gerrard, M. F. Lappert, and R. Shafferman, *J. Chem. Soc.*, 2895 (1958).

(5) H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **81**, 6434 (1959).

(6) Certain amines have been reported to interfere with boron isomerization from an internal to a terminal position: S. A. Leone and A. A. Hinckley, *A.C.S. Abstracts of Papers*, Cleveland, Ohio, April 1960, Division of Organic Chemistry, p. 60.

(7) Methanol reacts rapidly with sodium borohydride to form hydrogen and $NaB(OCH_3)_4$: H. I. Schlesinger and H. C. Brown, U. S. Patent **2,461,661**, February 15, 1949.

10 ml. of water was slowly added to destroy residual diborane. Then, 14.4 g. of sodium hydroxide in 100 ml. of water was added, followed by 37.4 g. of 30% hydrogen peroxide. When the exothermic oxidation was completed, the contents of the flask were mixed with 300 ml. of water. The organic layer was separated and later combined with benzene extracts of the water solution. The benzene was then removed by atmospheric distillation and the bis-2-ethoxyethyl ether removed under vacuum. There remained 79.4 g. of a yellow oil which solidified on cooling. Recrystallization from benzene gave the crystalline C_{18}-diols, 31.4 g., 36.5% yield, m.p. 64.5–65.5°.

Anal. Calcd. for $C_{18}H_{38}O_2$: C, 75.5; H, 13.4; hydroxyl value, 391. Found: C, 75.5; H, 13.1; hydroxyl value, 382.

The oil which remained was shown by infrared analysis and hydroxyl value determinations to be oleyl alcohol.

Hydroboration, isomerization, and oxidation of oleyl alcohol, external generation. Oleyl alcohol, 20.2 g. (0.075 mole), was dissolved in 175 ml. of bis-2-ethoxyethyl ether and treated with diborane generated externally by the addition of sodium borohydride, 5.7 g. (0.15 mole), in bis-2-ethoxyethyl ether (150 ml.) to 34.2 g. (0.24 mole) of boron trifluoride etherate. Solid formation was evident when half the diborane had been generated, and the contents completely solidified when generation was complete. This gelatinous solid was heated at 160° for 4 hr. prior to oxidation and hydrolysis as described previously. Recrystallization from petroleum ether gave 10.6 g. of the C_{18}-diol and 6.6 g. of oleyl alcohol. Ten grams of the diol was refluxed for 10 min. with 100 ml. of pyridine and 37 ml. of acetic anhydride to give the diacetate. The crude product, extracted with ether, was dissolved in 120 ml. of acetone, cooled to 0°, mixed with 3.4 g. of urea (0.3 g./g. of sample) and stirred for 2 hr. The urea and adduct were removed by filtration and added to water (100 ml.). The acetone solution was adducted as before until no water-insoluble product was obtained. The diacetate, 1.7 g., m.p. 57–58°, was recrystallized from ethanol.

Anal. Calcd. for $C_{22}H_{42}O_4$: C, 71.3; H, 11.4. Found: C, 71.0; H, 11.5.

Saponification with alcoholic potassium hydroxide gave 1.35 g. of 1,18-octadecanediol, m.p. 91.5–93.5° (lit.,[8] m.p., 92°).

Anal. Calcd. for $C_{18}H_{38}O_2$: C, 75.5; H, 13.4; hydroxyl value, 391. Found: C, 74.9; H, 13.1; hydroxyl value, 405.

Infrared analysis showed only primary alcohol groups. This corresponds to a 13.5% yield of this isomer. Other runs which employed longer isomerization periods (up to 70 hr.) and/or higher temperature (188°) gave 10–13% yields of 1,18-diol.

Oxidation of unadducted diols. Saponification of the unadducted fraction of the diacetates from the 4-hr. isomerization experiment followed by recrystallization of the resultant diols gave 4.5 g. of product, m.p. 60.5–63.0°. Chromium trioxide, 5.18 g., was dissolved in 66 ml. of acetic acid and 3.5 ml. of water and added to the diol (dissolved in glacial acetic acid) over a 2-hr. period while maintaining the temperature at 32–35°. The solution was stirred at 35–40° for an additional hour; then it was added to water (500 ml.). Ether extraction gave 2.7 g., 58% yield, of the crude ketostearic acids. Recrystallization from ether gave 0.8 g. of product, m.p. 92–93.5°.

Anal. Calcd. for $C_{18}H_{34}O_3$: C, 72.5; H, 11.4. Found: C, 72.5; H, 11.4.

Comparison of this product with 4-ketostearic acid by X-ray powder diffraction showed that the major component was the 4- isomer. Another isomer was present in small quantity (10%), and it is assumed, by the narrow melting point range of the ketostearic acids, to be the 5- isomer.

Preparation of 1,9- and 1,10-octadecanediol mixture. Oleyl alcohol, 53.7 g. (0.2 mole), was converted to the acetate by refluxing for 10 min. with a solution of 260 ml. of pyridine and 100 ml. of acetic anhydride. Dilution with water, followed by ether extraction gave the crude, liquid oleyl acetate (60 g.). Thirty grams was dissolved in 50 ml. of methylene dichloride and added dropwise to a solution of 23.2 g. of 40% peracetic acid and 5.6 g. of anhydrous sodium acetate dissolved in 100 ml. of methylene dichloride, contained in a 500-ml. flask equipped with mechanical stirrer and thermometer. Temperature was maintained at 35° during the 1.5-hr. addition and the stirring continued for 1 hr. after addition was completed. The solution was added to water and the bottom product layer dried with magnesium sulfate before removal of methylene dichloride using a Rinco evaporator. The crude epoxy acetate, 30.1 g., was dissolved in diethyl ether (100 ml.) and added to 7.0 g. (0.18 mole) of lithium aluminum hydride in 200 ml. of ether for reduction to the octadecanediol mixture. Recrystallization from ether gave 15.3 g. (53% yield based on oleyl alcohol) of crystals, melting point and mixture melting point with the diols obtained by hydroboration and oxidation of oleyl alcohol, 64.5–65.5°. Oxidation with chromium trioxide gave a mixture of ketostearic acids, m.p. 66.5–68°, in good agreement with the same mixture prepared by Fore and Bickford.[3]

Preparation of 1,6- and 1,7-octadecanediol mixture. Methyl petroselinate was epoxidized and reduced as described above to give a mixture of 1,6- and 1,7-octadecanediols, m.p. 70.5–71.0 from diethyl ether.

Preparation of 4-ketostearic acid and 1,4-octadecanediol. This is an adaptation of a procedure originally described by Newman.[9] At −80°, an ethereal solution of tetradecylmagnesium bromide, prepared from 5.98 g. (0.25 g.-atom) of magnesium and 55.4 g. (0.2 mole) of tetradecyl bromide, was added dropwise to a stirred solution of succinic anhydride, 4.0 g. (0.04 mole), in mixed ether-pyridine (80% by weight ether, 465 ml.). The addition required 3 hr. and stirring was continued an additional 2 hr. The mixture was kept at −80° overnight, then hydrolyzed at room temperature. Recrystallization from diethyl ether gave the keto acid, m.p. 91–93.5° (lit.,[10] m.p. 96.5–97.1°). Reduction with lithium aluminum hydride gave the 1,4-diol, m.p. 62.0° from diethyl ether. No melting point depressions were observed when the above products were compared with the diols from the unadducted fraction of the diacetates obtained from the successive hydroboration, isomerization. and oxidation of oleyl alcohol.

Preparation of trioleyl borate (I). Although the preparation, of trioleyl borate is not described in this reference, the procedure is that used by Dupire[11] to prepare other borates. Oleyl alcohol, 81.0 g. (0.3 mole), boron trioxide, 8.0 g. (0.11 mole), and 100 ml. of benzene were placed in a 250-ml., three necked flask. The flask was fitted with Soxhlet extractor, condenser, and thermometer. Anhydrous copper sulfate powder, 24.0 g., was placed in the thimble and the mixture refluxed for 24 hr. Benzene was then removed by distillation at atmospheric pressure and the remaining liquid heated to 280° at less than 1.0-mm. pressure with a rapid nitrogen stream bubbling through the oil. No distillate was obtained, and since the oleyl alcohol being used originally boiled at 169–189° (4.0 mm), it was assumed that it had all been converted to the borate ester. Infrared analysis showed no hydroxyl groups. This viscous, yellow oil was not further purified. Exposure to the atmosphere caused immediate hydrolysis, as evidenced by a film of solid boric acid which deposits on the surface. All handling was therefore done under dry nitrogen.

Hydroboration, isomerization, and oxidation of I. Trioleyl borate, 21.2 g. (0.26 mole), was hydroborated with diborane

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(8) A. Franke and O. Liebermann, *Monatsh.*, **43**, 589 (1923).

(9) M. S. Newman and W. T. Booth, Jr., *J. Am. Chem. Soc.*, **67**, 154 (1945).

(10) R. Calderon *et al.*, *J. Am. Oil Chemists' Soc.*, **37**, 132 (1960).

(11) A. Dupire, *Compt. rend.*, **202**, 2086 (1936).

generated by the addition of 5.7 g. (0.15 mole) of sodium borohydride in 150 ml. of bis-2-ethoxyethyl ether to 34.2 g. of boron trifluoride etherate (0.24 mole). Hydroborated trioleyl borate forms a glass-like, stiff gel with bis-2-ethoxyethyl ether. This unusual, clear gel is so stiff that it can easily be cut and chipped and the entrapped solvent imparts sufficient resiliency so that these chips actually bounce. They slowly fuse together on long standing and the solvent can be removed by strong heating under vacuum to give a glass-like product. Pieces of this glass also fuse together on long standing and are slowly oxidized and hydrolyzed by contact with the air.

Since this cross-linked polymer could be neither distilled nor crystallized, it could not be purified for analysis. In physical appearance, the polymers resulting from the hydroboration of both oleyl alcohol and trioleyl borate are indistinguishable.

This gel (in bis-2-ethoxyethyl ether) was heated to 160° for 20 hr., then oxidized and hydrolyzed as previously described to give 5.8 g. of C_{18}-diols, and 11.4 g. of oleyl alcohol which had not been hydroborated. Urea adduction of the diacetates showed that 13% of the diol was the 1,18-isomer.

Hydroboration, isomerization, and oxidation of I *in presence of other functional groups.* Another portion of I, 21.2 g. (0.26 mole), was hydroborated as before, but, prior to heating, oleyl alcohol, 18.7 g. (0.07 mole), was added. The solution was then refluxed for 20 hr. and oxidized to give 10.95 g. of C_{18}-diols and 21.6 g. of oleyl alcohol. Urea adduction gave a small quantity of an oil and none of the 1,18-diacetate. The same result was obtained when 2-undecanone was added prior to heating. The ketone was recovered unchanged by distillation.

In all these oleyl alcohol and trioleyl borate experiments, diol yields were quite difficult to reproduce because the polymer solidified the bis-2-ethoxyethyl ether medium, entrapping unchanged molecules and preventing further reactions with diborane. Final yields of diol therefore depend on such variables as the rate of diborane addition and the success with which the solid is broken up to permit further reaction.

Hydroboration, isomerization, and oxidation of 11-tricosene. The olefin,[12] 96.8 g. (0.3 mole), and 2.84 g. (0.075 mole) of sodium borohydride were dissolved in 200 ml. of bis-2-ethoxyethyl ether in a flask. Diborane was generated *in situ* by the slow addition of 7.55 g. (0.053 mole) of boron trifluoride etherate in 50 ml. of the same solvent. After this addition was complete, the solution was heated for 4 hr. at 185–190°. Oxidation gave the tricosanols, 65.5 g. 64% yield, m.p. 64.2–66.8° after recrystallization from ethanol.

Anal. Calcd. for $C_{23}H_{48}O$: C, 81.1; H, 14.2. Found: C, 81.2; H, 14.1.

The acetates were prepared, and repeated urea adductions showed that 80% of the product could be adducted. Saponification and recrystallization from ethanol gave *n*-tricosyl alcohol, m.p. 73.5–74.5°.[13] This product contained no secondary alcohol, as shown by infrared.

In another run, a 69-hr. heating period was employed and the yield of *n*-tricosyl alcohol, as determined by urea adduction, was 82%.

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(12) Research Division, Armour and Co., Chicago, Ill. By oxidative cleavage with periodate-permanganate, Dr. D. F. Kuemmel of our Laboratories showed that essentially all the unsaturation in this sample resides in the mid-chain position.

(13) Lit. melting point the same; P. A. Levene and F. A. Taylor, *J. Biol. Chem.*, 59, 905 (1924).

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, THE UPJOHN CO.]

The Neutral Solvolysis of the Aspirin Anion in Aqueous and Mixed Solvents

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Received March 14, 1961

Aspirin anion is hydrolyzed in ethanol-water to ethyl acetate, acetic acid, and salicylic acid, whereas the mixed anhydride of aspirin and acetic acid does not yield ethyl acetate under similar conditions. This further implicates ethanol in the rate determining step as previously postulated on kinetic evidence. The rate of acetic acid formation remains relatively invariant with increasing alcohol content of the media although the rate of ethyl acetate formation increases. A mechanism is proposed that rationalizes existing evidence on aspirin anion solvolysis.

There is good evidence that the mechanism of hydrolysis of the anion of acetylsalicylic acid in neutral solution, as proposed by several workers[1–3] in one form or another, is by an intramolecular attack of carboxylate ion on the carbonyl carbon of ester producing either (a) an anhydride intermediate which is subsequently rapidly hydrolyzed to salicylate and acetate or (b) a tetrahedral intermediate whose further reaction leads to products.[1,3] The former pathway has strong arguments in its favor. They have been well stated and summarized by Bender.[4] This pathway is stereochemically attractive, acetate ion is indeed a catalyst for the hydrolysis of a number of phenylacetates with a high probability of an anhydride intermediate,[5–7] and hydrolysis of aspirin anion in O^{18} labeled water should yield an expected lesser fraction of O^{18} in the final salicylate product if the intermediate anhydride cleaves as expected with nucleophile (water) attack on the acetyl carbonyl carbon of

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(1) J. D. Chanley, E. M. Gindler, and H. Sobotka, *J. Am. Chem. Soc.*, 74, 4347 (1952).

(2) D. Davidson and L. Auerbach, *J. Am. Chem. Soc.*, 75, 5984 (1953).

(3) E. R. Garrett, *J. Am. Chem. Soc.*, 79, 3401 (1957).

(4) M. L. Bender, *Chem. Revs.*, 60, 53 (1960).

(5) M. L. Bender and B. W. Turnquest, *J. Am. Chem. Soc.*, 79, 1656 (1957).

(6) T. C. Bruice and R. Lapinski, *J. Am. Chem. Soc.*, 80, 2265 (1958).

(7) M. L. Bender and M. C. Neveu, *J. Am. Chem. Soc.*, 80, 5388 (1958).