reaction mixture was cooled to give a red-brown oil which was dissolved in about 20 ml. of 95% boiling ethanol. Norite was added and the solution was filtered hot to give a yellow solution which deposited 1.51 g. (87.5% of the theoretical amount) of gray crystals on cooling. After two successive recrystallizations from ethanol (norite), a white product was obtained which melted at 66–67°.

This same procedure was also used for the trimethylene, tetramethylene, *m*-methoxyphenyl and *o*-methoxyphenyl esters, all of which gave oils as crude reaction products.

***p*-Methoxyphenyl Isodehydroacetate.**—Two and five-tenths grams of isodehydroacetyl chloride (0.0134 mole) was melted and poured into a 4" × 1", tared test-tube. One and sixty-six one hundredths grams (0.0134 mole) of *p*-methoxyphenol was added. The mixture was heated under a reflux condenser in an oil-bath at 90–110° for 15 minutes. On cooling a gray-green solid remained. About 20 ml. of 95% ethanol was added and the mixture heated until solution was complete. Norite was then added and the solution was filtered hot. The clear filtrate deposited 2.88 g. (78.6% of the theoretical amount) of white crystals, m.p. 139°, on cooling.

This same procedure also was used for the phenyl, hydroquinone, decamethylene, 2,6-dimethoxyphenyl and β-naphthol esters, all of which gave solids as crude reaction products.

Ultraviolet Absorption Data.—Ultraviolet absorption measurements were made with a Beckman DU photoelectric spectrophotometer using 1.00-cm. silica cells and hydrogen and tungsten discharge lamps as light sources. The esters and anhydride were all measured as solutions in 95% ethanol. The acyl chloride was measured in ether.

LOUISVILLE, KENTUCKY

[CONTRIBUTION FROM THE ROLLIN H. STEVENS MEMORIAL LABORATORY OF THE DETROIT INSTITUTE OF CANCER RESEARCH AND FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

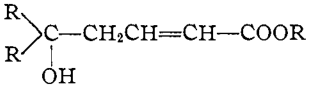
α- and γ-Additions in the Reformatsky Reaction with Methyl γ-Bromocrotonate[1]

BY ANDRE S. DREIDING AND RICHARD J. PRATT

RECEIVED FEBRUARY 11, 1953

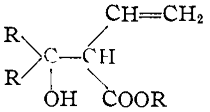
A study of the Reformatsky reaction with methyl γ-bromocrotonate showed that the nature of the product depended on the solvent at the boiling point of which the reaction was performed and on the structure of the carbonyl compound. Thus with cyclohexanone, 4-methylcyclohexanone, β-tetralone and 3,4,5-trimethoxybenzaldehyde, a condensation occurred at the *γ-position* of the bromoester to give γ-substituted crotonic esters ("normal" products, type A) when the reaction was conducted in *boiling benzene. In boiling ether,* the same carbonyl compounds added to the *α-position* of the bromoester to afford α-substituted vinylacetic esters ("abnormal" products, type B). The same Reformatsky reaction with 2-methylcyclohexanone and with α-tetralone yielded predominantly the "normal" products (type A) both in ether and in benzene at their boiling points. With alkali, some of the "normal" Reformatsky esters were saponified to the corresponding unsaturated hydroxyacids, while the "abnormal" esters underwent a reversal of the Reformatsky reaction to give the corresponding carbonyl compound. By suitable dehydrations, hydrogenations and saponifications a number of unsaturated acids were prepared from both the "normal" and "abnormal" Reformatsky esters. Unexpected shifts of the double bonds away from the carboxyl group occurred during the dehydration and saponification of the "normal" esters in the cyclohexanone series. The structures of the products were deduced from their reactions and from their ultraviolet and infrared absorption spectra.

Methyl γ-bromocrotonate has been successfully used in the Reformatsky reaction[2] to give structures of type A which were formed from the attack of the γ-position of the zinc complex of γ-bromocrotonic ester on the respective carbonyl compounds. These esters will be called the "normal" Reformatsky products. It has recently been found[3,4] in a few cases that another product, the "abnormal" Reformatsky ester, may appear which resulted from the reaction of the carbonyl compound with the α-position of γ-bromocrotonic ester.



$$\overset{R}{\underset{R'}{>}}\underset{\overset{|}{OH}}{C}-CH_2CH=CH-COOR$$

A, "normal" Reformatsky ester



$$\overset{R}{\underset{R'}{>}}\underset{\overset{|}{OH}}{C}-\overset{CH=CH_2}{\underset{COOR}{CH}}$$

B, "abnormal" Reformatsky ester

In the present investigation it was found that the temperature at which the reaction is performed or the nature of the solvent and certain structural features of the carbonyl compound influenced the course of the methyl γ-bromocrotonate Reformatsky reaction. With a number of ketones and one aromatic aldehyde, the "normal" Reformatsky esters (A) resulted when the reaction was performed in boiling benzene, while the "abnormal" products (B) predominated in boiling ether. With two ketones, the reaction in both solvents resulted in the "normal" compounds.

When the reaction with methyl γ-bromocrotonate and an excess of cyclohexanone was conducted in refluxing benzene or 1,2-dimethoxyethane the major product was a 30 and 39% yield, respectively, of methyl γ-(1-hydroxycyclohexyl)-crotonate (ester of I)[5] which exhibited an absorption maximum at 211 mμ (ε 16,200), characteristic of α,β-unsaturated acids or esters.[6] In this reaction there was some self-condensation of cyclohexanone to give a 19 and 15% yield (based on methyl γ-bromocrotonate) of a mixture of the known 2-cyclohexenylcyclohexanone and 2-cyclohexylidenecyclohexanone. Evidence for the carbon skeleton of the ester was obtained when hydrogenation, followed by

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(1) A part of this work was supported by institutional grants from the Michigan Cancer Foundation, the American Cancer Society, Inc., and The Kresge Foundation.

(2) For early references see G. Stork, THIS JOURNAL, **69**, 2936 (1947). See also (a) J. W. Cook and R. Philip, *J. Chem. Soc.*, 162 (1948); (b) W. E. Bachmann and A. S. Dreiding, *J. Org. Chem.*, **13**, 317 (1948); (c) J. F. Ahrens and D. A. van Dorp, *Rec. trav. chim.*, **65**, 338 (1946); (d) I. M. Heilbron, E. R. H. Jones and D. G. O'Sullivan, *J. Chem. Soc.*, 866 (1946); (e) J. English, Jr., and J. D. Gregory, THIS JOURNAL, **69**, 2123 (1947); (f) W. E. Bachmann and N. L. Wendler, *ibid.*, **68**, 2582 (1946).

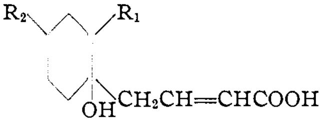
(3) E. R. H. Jones, D. G. O'Sullivan and M. C. Whiting, *J. Chem. Soc.*, 1415 (1949).

(4) J. English, Jr., J. D. Gregory and J. R. Trowbridge, II, THIS JOURNAL, **73**, 615 (1951).

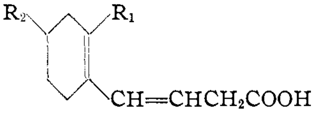
(5) In a similar reaction with cyclohexanone and ethyl γ-iodocrotonate in benzene Fuson, Arnold and Cooke, *ibid.*, **60**, 2272 (1938), isolated ethyl cyclohexylidenecrotonate (ester of VII), as indicated by carbon and hydrogen analysis.

(6) For several references see H. E. Ungnade and I. Ortega, *ibid.*, **73**, 1564 (1951).

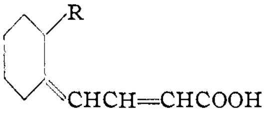
dehydration and saponification yielded crude γ-(1-cyclohexenyl)-butyric acid or a double bond isomer, which was converted into the known γ-cyclohexylbutyric acid by hydrogenation and into the known Δ^9-octalone-1 by a cyclization. Direct saponification of the Reformatsky ester (ester of I) with 6% aqueous methanolic potassium hydroxide at room temperature produced γ-(1-hydroxycyclohexyl)-crotonic acid (I), m.p. 127–128°,[7] in 57% yield. There was no evidence for the formation of cyclohexanone in this alkaline treatment.



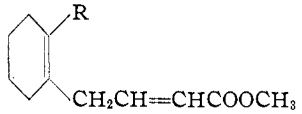
I, $R_1 = R_2 = H$
II, $R_1 = H, R_2 = CH_3$
III, $R_1 = CH_3, R_2 = H$



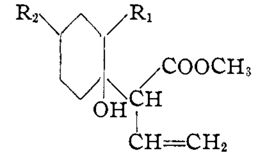
IV, $R_1 = R_2 = H$
V, $R_1 = H, R_2 = CH_3$
VI, $R_1 = R_2\ CH_3, = H$



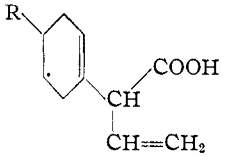
VII, R = H
VIII, R = CH_3



IX, R = H
X, R = CH_3



XI, $R_1 = R_2 = H$
XII, $R_1 = H, R_2 = CH_3$
XIII, $R_1 = CH_3, R_2 = H$



XIV, R = H
XV, R = CH_3

Dehydration of the Reformatsky ester (ester of I) with acetic anhydride and formic acid afforded a crude product with absorption maxima at 212 and 275 mμ (ε 10,960 and 3,670), suggesting that it contained IX and the ester of VII to an approximate extent of 67 and 15%, respectively. Thus in the major portion of the product the new double bond does not appear in conjugation with the α,β-unsaturated ester system but rather in the ring. When this mixture of esters was saponified there resulted two diene acids: γ-(1-cyclohexenyl)-vinylacetic acid (IV), m.p. 61–64°, $\lambda_{\max}^{\text{alc}}$ 234 mμ (ε 23,000) and cyclohexylidenecrotonic acid (VII), m.p. 137–138°, $\lambda_{\max}^{\text{alc}}$ 272 mμ (ε 26,700).[7] The double bonds in these acids were placed on the basis of their absorption spectra, in which respect IV was similar to many trialkyl dienes with an *S-trans* conformation[8] and VII resembled α,β,γ,δ-unsaturated acids.[2b] The absorption spectrum of the crude acid material showed it to contain about 44% of IV and 27% of VII. It might have been expected that the δ,ε-double bond in it would move to the γ,δ-position so as to give a completely conjugated system as in VII. In fact, however, this took place only to a small extent and was overshadowed by the shift of the α,β-double bond away from the carboxyl group and into conjugation with the ring double bond.

When ether was used as the solvent in the same Reformatsky reaction with methyl γ-bromocrotonate and cyclohexanone the main product (60%) was methyl α-(1-hydroxycyclohexyl)-vinylacetate (XI), which showed no absorption maximum in the ultraviolet region above 210 mμ. Its carbon skeleton was established by consecutive hydrogenation, dehydration saponification and again hydrogenation, which yielded the known α-cyclohexylbutyric acid (26%). The isolation of 38% of formaldehyde from an ozonization indicated the presence in XI of a terminal double bond. In contrast to the "normal" Reformatsky ester (ester I), the "abnormal" product (XI) suffered a quantitative cleavage to cyclohexanone under the same mild saponification conditions.[9]

By dehydration of XI with freshly fused zinc chloride in acetic acid, followed by saponification, a double bond was introduced into the ring, rather than into cross-conjugation with the terminal double bond and the carboxyl group. The product was a 50% yield of α-(1-cyclohexenyl)-vinylacetic acid (XIV), which did not exhibit an ultraviolet absorption maximum above 210 mμ. To preclude the possibility of a rearrangement of the carbon skeleton during the dehydration of XI, the diene acid (XIV) was hydrogenated to α-cyclohexylbutyric acid.

It is of interest to compare the infrared absorption spectra of the "normal" (ester of I) and "abnormal" (XI) Reformatsky esters. A peak at 10.3 μ in the former may be due to the two *trans* disposed hydrogens on the double bond (RCH=CHR)[10] and does not appear in the latter. The terminal bond ($RCH=CH_2$) in XI, on the other hand, may be responsible for the absorption bands at 10.8 μ[10a] and near 9.9 or 10.15 μ,[10b] which are not present in the ester of I. These absorption characteristics have been found in this work to serve as distinctive features of the "normal" and "abnormal" Reformatsky esters. The infrared spectra suggest that the "normal" esters have the *trans*-configuration at the double bond.

The behavior of 4-methylcyclohexanone in the Reformatsky reaction with methyl γ-bromocrotonate was entirely analogous to that of cyclohexanone, the "normal" ester (ester of II) being isolated from the reaction in boiling benzene and the "abnormal" product (XII) from boiling ether. These esters were converted to the unsaturated acids II, V and XV, which are described in the experimental section.

With 2-methylcyclohexanone, however, the vinylogous Reformatsky reaction gave predominantly (38–40% yield) the *same* product in boiling ether *and* in boiling benzene. That this was the "normal" ester (ester of III) was shown by saponifica-

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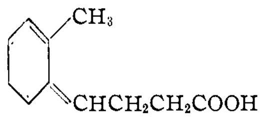
[7] Jones, O'Sullivan and Whiting[3] also condensed cyclohexanone with methyl γ-bromocrotonate and isolated, after dehydration and saponification, two acids, m.p. 64 and 75°, to which structures I and VII, respectively, were assigned. The differences in the melting points of the present and the reported samples of these acids can as yet not be explained.

[8] R. B. Woodward, THIS JOURNAL, **64**, 72 (1942).

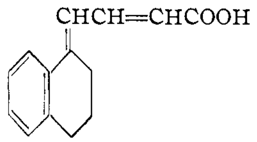
[9] For several examples of the reversal of the Reformatsky reaction see R. L. Shriner in R. Adams, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 14. The conditions mentioned there are more drastic than the ones used in the present case.

[10] (a) D. Barnard, L. Bateman, A. J. Harding, H. P. Koch, N. Sheppard and G. B. B. M. Sutherland, *J. Chem. Soc.*, 915 (1950), (b) H. L. McMurry and V. Thornton, *Anal. Chem.*, **24**, 318 (1952).

tion which converted both samples to γ-(2-methyl-1-hydroxycyclohexyl)-crotonic acid (III), $\lambda_{\max}^{\text{alc}}$ 213 mμ. In the ether reaction, an 11% yield of a lower boiling fraction was observed, which is considered to be the "abnormal" ester (XIII) on the basis of the similarity of its infrared absorption spectrum with that of XI. It is of interest that the diene acid, obtained by dehydration and saponification of the ester of III had an absorption maximum at 243.5 mμ (ε 22,600). By analogy with the previous results, structure VI could be assigned to this acid; however, the increment of its absorption maximum over that of IV and V (10 mμ) is higher than expected[8] for that due to an additional methyl group. According to Woodward's rule,[8] the spectrum would fit better for structure XVI, which might have been the result of a further shift of the double bonds in VI. At present no definite evidence is available on the position of the double bonds in this diene acid.

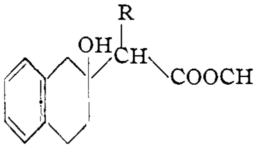


XVI

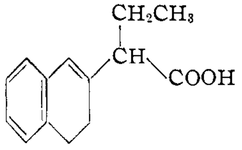


XVII

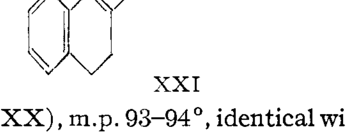
The methyl γ-bromocrotonate Reformatsky reaction with α-tetralone in boiling ether yielded, as with 2-methylcyclohexanone, the "normal" product to give, after dehydration and saponification, a 50% yield of γ-1,2,3,4-tetrahydro-1-naphthylidenecrotonic acid (XVII).[11] With β-tetralone, however, the reaction in boiling ether afforded a 50% yield of the crystalline "abnormal" product, methyl α-(2-hydroxy-1,2,3,4-tetrahydro-2-naphthyl)-vinylacetate (XVIII), which showed absorption bands at 9.99 and 10.87 μ. The product of its catalytic hydrogenation (XIX) did not exhibit these two absorption bands, which confirms the above mentioned conclusion that they may be assigned to the terminal double bond of some "abnormal" Reformatsky esters. Dehydration and saponification of XIX resulted in α-(3,4-dihydro-2-naphthyl)-butyric acid (XX), m.p. 93–94°, identical with a sample prepared by the Reformatsky reaction with β-tetralone and ethyl α-bromobutyrate.[12]



XVIII, R = CH = CH
XIX, R = CH2CH3



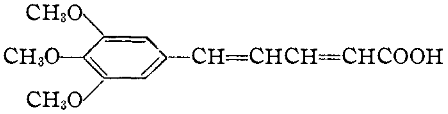
XX



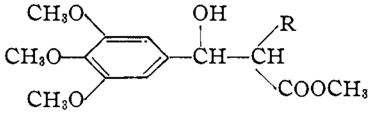
XXI

In benzene, β-tetralone reacted with methyl γ-bromocrotonate and zinc to give a 6% yield of the "abnormal" product (XVIII), which crystallized out of the crude mixture, and about 20% of the oily "normal" ester. A considerable quantity of β-tetralone was recovered. The crude "normal" ester was hydrogenated, dehydrated and hydrolyzed to the previously described γ-(3,4-dihydro-2-naphthyl)-butyric acid (XXI),[2f,12] and the latter was cyclized to the known 4-keto-1,2,3,4,9,10-hexahydrophenanthrene.[2f]

The experience with 3,4,5-trimethoxybenzaldehyde confirmed the previously observed effects. The vinylogous Reformatsky reaction in benzene took the "normal" course, but a dehydration occurred during the reaction or isolation.[13] The product was methyl 3,4,5-trimethoxybenzylidenecrotonate, m.p. 111.5–112.5°, $\lambda_{\max}^{\text{alc}}$ 249, 332 mμ (ε 15,320, 35,100).[14] Hydrogenation of the corresponding acid (XXII) gave the known δ-(3,4,5-trimethoxyphenyl)-valeric acid.



XXII



XXIII, R = CH=CH2
XXIV, R = CH2CH3

In ether, 3,4,5-trimethoxybenzaldehyde underwent the "abnormal" reaction leading to the crystalline methyl β-(3,4,5-trimethoxyphenyl)-β-hydroxy-α-vinylpropionate (XXIII). This ester was hydrogenated to methyl β-(3,4,5-trimethoxyphenyl)-β-hydroxy-α-ethylpropionate (XXIV), identical with a sample from an α-bromobutyrate Reformatsky reaction.

The results of this work suggest that the course of the γ-bromocrotonate Reformatsky reaction is influenced by a steric factor. Apparently the more bulky substituents next to the carbonyl group in α-tetralone and 2-methylcyclohexanone effectively reduced the formation of the "abnormal" Reformatsky ester, which was the only product under the same conditions (boiling ether) with the other, less hindered, carbonyl compounds.

It is not yet clear whether the difference in the reaction course with the latter group of compounds, when conducted in ether and in benzene, is due to the temperature differential at which the reaction occurs, or whether other properties of the solvents play a role. The former possibility appears favored by the fact that the reaction with cyclohexanone in 1,2-dimethoxyethane (b.p. 85°) takes the same course as in benzene. It should be noted in this

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(11) This reaction had been performed previously in a boiling mixture of ether and benzene with the same result.[2f] See also R. C. Gilmore and W. J. Horton, THIS JOURNAL, **73**, 1411 (1951).

(12) W. G. Dauben and R. Teranishi, *J. Org. Chem.*, **16**, 550 (1951), condensed β-tetralone with methyl γ-bromocrotonate and zinc in a mixture of ether and benzene. The acid XXI which was obtained after hydrogenation, dehydration and saponification, could not be purified and may have contained some of the isomer XX.

(13) For a communication announcing the "normal" bromocrotonate Reformatsky reaction with 3,4,5-trimethoxybenzaldehyde see E. C. Horning, M. G. Horning, J. Koo, M. S. Fish, J. A. Parker, G. N. Walker, R. M. Horowitz and G. E. Ullyot, THIS JOURNAL, **72**, 4841 (1950).

(14) This spectrum can be compared with that of methyl γ-(6-methoxy-1,2,3,4-tetrahydro-1-naphthylidene)-crotonate, $\lambda_{\max}^{\text{alc}}$ 248, 343 mμ (ε 12,600, 27,000).[2]

connection that in all previous cases,[2] in which the bromocrotonate Reformatsky reaction had been successfully used for the attachment in high yield of a four carbon acid sidechain at the γ-position, the reaction was run either in benzene or in a mixture of ether and benzene, and the carbonyl compound often had large substituents next to the carbonyl group, while all the condensations in which the "abnormal" reaction had been observed previously were with aldehydes.[3,4]

Acknowledgment.—We are grateful to Dr. J. M. Vandenbelt and Mr. Bruce Scott of Parke, Davis and Co. for the measurements and valuable discussions of most of the ultraviolet and several infrared absorption spectra.

Experimental[15]

Methyl γ-(1-Hydroxycyclohexyl)-crotonate (Ester of I).—A mixture of 13 g. (0.2 mole) of zinc and 19.6 g. (0.2 mole) of cyclohexanone and 9 g. (0.05 mole) of methyl γ-bromocrotonate in 100 cc. of dry benzene was heated gently and the reaction was started by the addition of a few crystals of iodine. When the exothermic reaction subsided after ten minutes, another 9 g. (0.05 mole) of methyl γ-bromocrotonate was added to produce a further exothermic reaction for ten minutes. The reaction mixture was heated with rapid stirring for one hour, cooled and decomposed with dilute acetic acid. The benzene solution was washed well with several portions of 2% aqueous ammonium hydroxide, dried, concentrated and fractionally distilled three times at reduced pressure through a 6-inch Vigreux column. The following fractions were collected: (1) b.p. 69–72° (0.21 mm.), n^{25}D 1.5133, $\lambda_{\max}^{\text{alc}}$ 255 mμ (ε 3,490), no absorption at 2.83 μ in CCl_4, yield 3.33 g.; (2) b.p. 75–93° (0.21 mm.), n^{25}D 1.5120, yield 2.15 g.; and (3) b.p. 96–104° (0.25 mm.), n^{25}D 1.5048, yield 5.94 g.

The first fraction consisted of a mixture of 55% (calculated on the basis of the absorption intensity at 255 mμ) of 2-cyclohexylidenecyclohexanone (reported b.p. 105° at 2 mm., n^{60}D 1.4918,[16] $\lambda_{\max}^{\text{alc}}$ 255 mμ (ε 6,300)[17]) and 45% 2-cyclohexenylcyclohexanone (reported[16] b.p. 142° at 13 mm., n^{60}D 1.5051). When the material of this fraction was converted to the 2,4-dinitrophenylhydrazone, a mixture of a red and an orange derivative was obtained which was difficult to separate. When the mixture of ketones was allowed to stand with methanolic alkali for a few hours, before converting it to the derivative, only the **2,4-dinitrophenylhydrazone of 2-cyclohexenylcyclohexanone** was formed and recrystallized from ethyl acetate as orange needles, m.p. 154.5–155°.

Anal. Calcd. for $C_{18}H_{22}N_4O_4$: C, 60.31; H, 6.19; N, 15.63. Found: C, 60.78; H, 6.14; N, 15.72.

The second fraction may have consisted of a mixture of the first and third fraction and was not investigated.

The third fraction was **methyl γ-(1-hydroxycyclohexyl)-crotonate (ester of I)**, $\lambda_{\max}^{\text{alc}}$ 211 mμ (ε 16,200), $\lambda_{\max}^{CCl_4}$ 2.85, 5.80, 6.02 and 10.3 μ, yield 30%. The hydrogenation of 270 mg. of this ester with 27 mg. of platinum oxide was performed in 8 cc. of acetic acid. After separation of the catalyst, 250 mg. of freshly fused zinc chloride was added and the solution was heated for 30 minutes. Isolation by dilution with water and ether extraction followed by saponification with a 6% solution of potassium hydroxide in 90% aqueous methanol at room temperature yielded an unsaturated acid which may be γ-(1-cyclohexenyl)-butyric acid or a double bond isomer. Hydrogenation with platinum oxide in methanol afforded 120 mg. (52%) of γ-cyclohexylbutyric acid, m.p. 26–28° (reported[18] m.p. 26.5–28.5°), which was converted to the *p*-bromophenacyl ester, m.p. 75–77° (reported[19] 77°).

The γ-(1-cyclohexenyl)-butyric acid, obtained as described above from 6.0 g. of the "normal" Reformatsky ester (ester of I) was cyclized at room temperature for 72 hours in 37 cc. of acetic anhydride and 7 cc. of a 10% solution of zinc chloride in acetic acid. Ether was added and the acidic materials were removed by extraction with 10% sodium hydroxide. Concentration left 1.60 g. (35% from the ester of I) of crude Δ^9-octalone-1, of which an aliquot of 0.30 g. yielded 0.60 g. (91%) of the red 2,4-dinitrophenylhydrazone, m.p. 232–234°. The semicarbazone melted at 237–240° (reported[19] m.p. 242°).

When a Reformatsky reaction with the same quantities of cyclohexanone and methyl γ-bromocrotonate was performed in the same manner, but with 1,2-dimethoxyethane as the solvent, the results were very similar and a 39% yield of methyl γ-(1-hydroxycyclohexyl)-crotonate (ester of I), b.p. 97–108° (0.2 mm.), n^{25}D 1.5008, $\lambda_{\max}^{CCl_4}$ 2.85, 5.81, 6.03 and 10.3 μ, together with a 15% yield of the self-condensation product of cyclohexanone, b.p. 76–83° (0.2 mm.), n^{25}D 1.5130, was isolated. The infrared spectrum of this latter material was identical with fraction 1 from the benzene experiment and indicated the absence of a hydroxyl group.

γ-(1-Hydroxycyclohexyl)-crotonic Acid (I).—A solution of 520 mg. of fraction 3, obtained in the previous experiment (ester of I), and 0.5 g. of potassium hydroxide in 7 cc. of methanol and 1 cc. of water was allowed to stand in a closed vessel for 12 hours. After dilution with water, the neutral material was extracted with ether and yielded only a very small amount of a precipitate with 2,4-dinitrophenylhydrazine reagent. The alkaline solution was acidified to give a colorless clear solution which, after saturation with salt, yielded 220 mg. of a colorless precipitate, m.p. 126–127°. A second crop of 54 mg. with the same melting point was obtained by ether extraction and trituration of the residue with petroleum ether, total yield 57%. Recrystallization from ether–petroleum ether gave **γ-(1-hydroxycyclohexyl crotonic acid (I)** as colorless plates, m.p. 127–128.5°,[7] $\lambda_{\max}^{\text{alc}}$ 211 mμ (ε 13,580), $\lambda_{\max}^{\text{mineral oil}}$ 3.12, 5.92, 6.15 and 10.42 μ, neutral equivalent, calcd. 184, found 183. The acid absorbed 1 mole of hydrogen with platinum oxide in acetic acid.

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76. Found: C, 64.98; H, 8.70.

γ-(1-Cyclohexenyl)-vinylacetic Acid (IV) and Cyclohexylidenecrotonic Acid (VII).—A mixture of 10.5 g. of the ester of I, 30 cc. of 98% formic acid and 20 cc. of acetic anhydride was heated under reflux for three hours in an atmosphere of nitrogen. The formic acid and acetic anhydride were removed at reduced pressure and the residual oil evaporatively distilled at 120° and 1 mm., yield 9.2 g. From the ultraviolet absorption spectrum, $\lambda_{\max}^{\text{alc}}$ 212 and 275 mμ (ε 10,960 and 3,670) it is possible to calculate that the distillate contains approximately 15% of methyl cyclohexylidenecrotonate (ester of VII) and about 67% of methyl γ-(1-cyclohexenyl)-crotonate (IX). These calculations are based on the absorption intensities of the ester of I and VII, and can be considered only very approximate; it is remarkable, however, that there is no indication of even the slightest absorption maximum at 234 mμ, which excludes the presence of an ester with the diene chromophore of IV. The mixture of diene esters was saponified by heating it for three hours in a solution of 4 g. of potassium hydroxide in 30 cc. of methanol and 10 cc. of water. Some of the methanol was removed at reduced pressure and replaced with water. After extraction with ether, acidification of the alkaline solution, and ether isolation, a crude mixture of diene acids was obtained as a sticky solid residue, yield 6.0 g. (68%), $\lambda_{\max}^{\text{alc}}$ 234 and 273 mμ (ε 10,500 and 7,350). Spectrographically, this mixture contained 27% of cyclohexylidenecrotonic acid (VII) and 44% of γ-(1-cyclohexenyl)-vinylacetic acid (IV). After three recrystallizations from petroleum ether, 4.8 g. of the mixture of IV and VII was obtained as colorless needles, m.p. 62–65°. These acids were soluble in petroleum ether at room temperature and crystallized

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[15] The analyses are by Micro-Tech Laboratories, Skokie, Ill. The melting points are not corrected. In the description of the infrared absorption spectra, only those maxima are enumerated which are considered to be significant[10] for the type of compounds examined in this work. Low intensity maxima are not mentioned. The infrared spectra marked* were measured in a Beckmann IR 2, the others in a Baird double beam instrument.

[16] J. Reese, *Ber.*, **75B**, 384 (1942).

[17] H. S. French and L. Wiley, THIS JOURNAL, **71**, 3702 (1949).

[18] T. L. Cairns and R. M. Joyce, *ibid.*, **70**, 1689 (1948).

[19] J. W. Cook and C. A. Lawrence, *J. Chem. Soc.*, 1637 (1935)

readily together at −10°. The early crops were richer in VII and, after fractional crystallization, a pure sample of **cyclohexylidenecrotonic acid** (VII) was isolated and recrystallized from ether–petroleum ether as elongated colorless prisms, m.p. 137–138°,[7] yield 0.3 g., $\lambda_{\max}^{\text{alc}}$ 272 mμ (ε 26,700), $\lambda_{\max}^{\text{CHCl}_3}$ 5.93, 6.08, 10.09, 11.2 and 11.6 μ.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.17; H, 8.68.

The later crops of the petroleum ether crystallizations yielded a sample of **γ-(1-cyclohexenyl)-vinylacetic acid** (**IV**) which was, however, still contaminated with about 18% of VII, m.p. 61–64°, yield 2.0 g., $\lambda_{\max}^{\text{alc}}$ 233.5 and 273 mμ (ε 19,550 and 4,790).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.75; H, 8.72.

With the above information it can be extrapolated that pure IV should absorb light at 233.5 mμ with an intensity of ε 23,800. In contrast to the fully conjugated acid (VII), which decomposed only slowly on standing, the diene acid IV formed a yellow film of oil over the crystals after standing at room temperature for one day. After standing for two weeks, the entire sample had turned into a yellow oil. A sample could be retained in a fair state of purity for three months by storing it at −10° in the dark. When a sample of impure IV was allowed to stand for 25 days, the absorption at 233.5 mμ had decreased from ε 19,550 to 6,410, while the intensity of the maximum at 272 mμ remained unchanged. The mixture of the two acids (m.p. 60–65°, spectrographically 75% IV and 25% VII) was hydrogenated with platinum oxide in methanol to give, after evaporative distillation, a 98% yield of γ-cyclohexylbutyric acid, m.p. 25.5–27° (reported[18] 26.5–28.5°).

Methyl α-(1-Hydroxycyclohexyl)-vinylacetate (XI).—The Reformatsky reaction with 17.9 g. (0.1 mole) of methyl γ-bromocrotonate, 19.6 g. (0.2 mole) of cyclohexanone and 13 g. (0.2 mole) of zinc was run in exactly the same manner as described for the first experiment, except that ether was used as the solvent. In contrast to the reaction in benzene and 1,2-dimethoxyethane, which produced a yellow-brown solution and precipitate, the ether reaction remained colorless and formed a crystalline and colorless precipitate. The colorless crude product was fractionated twice to give 11.9 g. (60%) of **methyl α-(1-hydroxycyclohexyl)-vinylacetate** (**XI**), b.p. 65–71° (0.3 mm.), $n^{25}D$ 1.4796, no ultraviolet maximum above 210 mμ, $\lambda_{\max}^{\text{CCl}_4}$ 2.83, 5.80, 6.10, 9.9, 10.13 and 10.84 μ. A second fraction, b.p. 71–85° (0.2 mm.) (1.76 g.), $n^{25}D$ 1.4925, was also collected, but not investigated.

The conversion of the main product (302 mg. of fraction 1, XI) into 102 mg. (39%) of α-cyclohexylbutyric acid, m.p. 54–56° (reported[20] m.p. 58.5°) was accomplished by the consecutive hydrogenation, dehydration, saponification and again hydrogenation exactly as described above for the ester of I.

The ozonization of 3.0 g. of XI in ethyl acetate at −75° yielded 1.6 g. (38%) of the dimedone derivative of formaldehyde, m.p. 187–189°.

Cleavage of Methyl α-(1-Hydroxycyclohexyl)-vinylacetate (XI) with Alkali.—A solution of 505 mg. of XI and 0.5 g. of potassium hydroxide in 7 cc. of methanol and 1 cc. of water was allowed to stand in a closed vessel at room temperature for 12 hours. After dilution with water, the neutral material was extracted with ether, concentrated and treated with 2,4-dinitrophenylhydrazine reagent. The derivative of cyclohexanone precipitated immediately as a yellow solid, m.p. 157–159° alone and when mixed with an authentic sample, yield 650 mg. (92%). On acidification of the alkaline solution, no precipitate appeared but the odor of crotonic acid was noticeable.

α-(1-Cyclohexenyl)-vinylacetic Acid (XIV).—A solution of 6.0 g. of XI and 6.0 g. of freshly fused zinc chloride in 25 cc. of glacial acetic acid was heated under reflux for 30 minutes, cooled, diluted with water and extracted several times with ether. The ethereal solution was washed with water, dried and concentrated, leaving the crude diene ester. This was saponified by heating it for two hours in a solution of 3 g. of potassium hydroxide in 20 cc. of methanol and 5 cc. of water. Acidification and ether extraction gave 2.4 g. (48%) of crude α-(**1-cyclohexenyl)-vinylacetic acid** (**XIV**), m.p. 89–91°, which was recrystallized from methanol–water or petroleum ether as clusters of colorless needles, m.p. 92–93°, no ultraviolet maximum between 210 and 310 mμ, $\lambda_{\max}^{\text{CHCl}}$ 5.90, 6.10, 9.85, 10.25 and 10.83 μ.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.10; H, 8.51.

This diene acid (XIV) did not decompose on standing as readily as its isomeric acid (IV). Hydrogenation of 228 mg. with platinum oxide in acetic acid gave 141 mg. (60%) of α-cyclohexylbutyric acid, m.p. 55–57° (reported[20] 58.5°). The ozonization of XIV resulted in a low yield of adipic acid, m.p. and mixed m.p. 148–152°.

An authentic sample of α-cyclohexylbutyric acid was prepared by the Reformatsky reaction between 20 g. (0.2 mole) of cyclohexanone, 19.5 g. (0.1 mole) of ethyl α-bromobutyrate and 10 g. (0.15 mole) of zinc in 100 cc. of ether. The product, ethyl α-(1-hydroxycyclohexyl)-butyrate,[21] $n^{25}D$ 1.4739, was collected at 95–96° (0.6 mm.), yield 21 g. Dehydration of 1 g. of this ester with zinc chloride in acetic acid and saponification with methanolic potassium hydroxide, followed by hydrogenation, as described above, yielded, after sublimation, 352 mg. (43%) of α-cyclohexylbutyric acid, m.p. 55–57° (reported[20] 58.5°). This melting point was not depressed on admixture with the samples of this acid obtained from XI and XIV.

The Reformatsky reaction with methyl γ-bromocrotonate and cyclohexanone in a 1:1 mixture of ether and benzene was performed as described above. On distillation, two fractions were collected at 85–95° (0.5 mm.), wt. 10.3 g. and at 95–115° (0.5 mm.), wt. 7.5 g. The second fraction was mostly the "normal" product (ester of I) as was shown by the fact that it gave a 30% yield of γ-(1-hydroxycyclohexyl)-crotonic acid (I) on saponification, m.p. 126–128°. The saponification of the first fraction yielded only cyclohexanone, while dehydration and saponification as described above for the "abnormal" ester (XI) afforded a 35% yield of α-(1-cyclohexenyl)-vinylacetic acid (XIV), m.p. 88–89°.

Reformatsky Reaction with 4-Methylcyclohexanone and Methyl γ-Bromocrotonate. A. In Benzene.—When the reactions, as described above for cyclohexanone, were carried out with 4-methylcyclohexanone, the following products were obtained: **Methyl γ-(4-methyl-1-hydroxycyclohexyl)-crotonate** (**ester of II**), b.p. 115–119° (0.6–0.7 mm.), $n^{25}D$ 1.4902, yield 55%.

γ-(4-Methyl-1-hydroxycyclohexyl)-crotonic acid (**II**), m.p. 187.5–188° from ether–methanol, yield 43%, $\lambda_{\max}^{\text{alc}}$ 212 mμ (ε 13,060), $\lambda_{\max}^{\text{mineral oil}}$ 3.11, 5.91, 6.14 and 10.48 μ (weak peaks also at 10.24 and 10.80 μ). In glacial acetic acid with platinum oxide, 43.6 mg. (0.22 mmole) of II absorbed 0.28 mmole of hydrogen.

Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.37; H, 9.49.

γ-(4-Methyl-1-cyclohexenyl)-vinylacetic acid (V), m.p. 65.5–66.5° from petroleum ether, unstable on standing, yield 29%, $\lambda_{\max}^{\text{alc}}$ 232.5 mμ (ε 26,900), *$\lambda_{\max}^{\text{mineral oil}}$ 5.86, 10.36, 10.82 and 12.82 μ. The fully conjugated acid (corresponding to VII) was not isolated and there was no spectrographic evidence for its occurrence. On catalytic hydrogenation (as above for II), 30.8 mg. (0.171 mmole) of V absorbed 0.339 mmole of hydrogen.

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.26; H, 9.35.

B. In Ether.—The reactions as described above for cyclohexanone gave: **Methyl α-(4-methyl-1-hydroxycyclohexyl)-vinylacetate** (**XII**), b.p. 85–95° (0.3 mm.), $n^{25}D$ 1.4748, yield 59%. Ozonization produced a 55% yield of formaldehyde. Cold methanolic alkali gave a quantitative recovery of 4-methylcyclohexanone as the yellow-orange 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 133–135°. From the alkaline solution a 57% yield of crotonic acid, m.p. 66–69°, was obtained.

α-(4-Methyl-1-cyclohexenyl)-vinylacetic acid (**XV**), m.p. 85–86.5° from petroleum ether, yield 67%, no ultraviolet maximum, $\lambda_{\max}^{\text{mineral oil}}$ 5.9, 6.1, 9.8, 10.6, 11.0, 12.1 μ. With platinum oxide in acetic acid, 42.2 mg. (0.234 mmole) of XVII absorbed 0.444 mmole of hydrogen.

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.10; H, 9.07.

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[20] H. A. Smith, D. M. Alderman and F. W. Nadig, THIS JOURNAL, **67**, 272 (1945).

[21] O. Wallach, *Ann.*, **360**, 26 (1908).

The **p-bromophenacyl ester of XVII** crystallized from methanol as colorless needles, m.p. 86–86.5°.

Anal. Calcd. for $C_{19}H_{21}BrO_3$: C, 60.48; H, 5.61. Found: C, 59.90; H, 5.67.

Reformatsky Reaction with 2-Methylcyclohexanone and Methyl γ-Bromocrotonate. A. In Benzene.—The above described reactions as applied to 2-methylcyclohexanone gave: Methyl γ-(2-methyl-1-hydroxycyclohexyl)-crotonate (ester of III),[2b] b.p. 99–109° (0.5 mm.), n^{25}_{D} 1.5010, yield 40%, $\lambda_{\max}^{CCl_4}$ 2.85, 5.81, 6.03 and 10.1–10.3 μ.

γ-(2-Methyl-1-hydroxycyclohexyl)-crotonic acid (III), m.p. 110–111° from aqueous methanol, yield 42%, $\lambda_{\max}^{alc}$ 213 mμ (ε 14,400), $\lambda_{\max}^{mineral\ oil}$ 3.0, 5.91, 6.07, 10.5 μ. Reduction (as above) of 25.2 mg. (0.127 mmole) of III caused 0.143 mmole of hydrogen to be absorbed.

Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.59; H, 9.27.

Methyl γ-(2-methyl-1-cyclohexenyl)-crotonate (X) and methyl 2-methylcyclohexylidenecrotonate (ester of VIII) were obtained as a mixture by the acetic anhydride and formic acid dehydration of the ester of III, b.p. 85–91° (0.15 mm.), n^{25}_{D} 1.4976, yield 63%, $\lambda_{\max}^{alc}$ 207 and 273 mμ (ε 15,000 and 2,400). The infrared spectrum shows the absence of a hydroxyl group, $\lambda_{\max}^{CCl_4}$ 5.81, 6.05 and 10.19 μ.

γ-(2-Methyl-1-cyclohexenyl)-vinylacetic acid (VI) or **γ-(2-methyl-2-cyclohexenylidene)-butyric acid (XVI)**, m.p. 80–81° from petroleum ether, unstable on standing, yield 35%, $\lambda_{\max}^{alc}$ 243.5 mμ (ε 22,600), $\lambda_{inflection}^{alc}$ 278 mμ (ε 3,850) (thus this sample contains a small amount of 2-methylcyclohexylidenecrotonic acid (VIII), which was not isolated), $\lambda_{\max}^{mineral\ oil}$ 5.88, 10.4, 10.8 and 12.73 μ, neut. equiv., 176 (calcd. 180).

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.15; H, 9.10.

B. In Ether.—In this case, both types of Reformatsky esters were formed, the "normal" one predominating: Methyl γ-(2-methyl-1-hydroxycyclohexyl)-crotonate (ester of III),[2b] b.p. 98–103° (0.2 mm.), n^{25}_{D} 1.4980, yield 38%, $\lambda_{\max}^{CCl_4}$ 2.85, 5.81, 6.03 and 10.1–10.35 μ (the infrared spectrum was identical with the product from benzene).

Methyl α-(2-methyl-1-hydroxycyclohexyl)-vinylacetate (XIII), b.p. 65–86° (0.2 mm.), n^{25}_{D} 1.4750, yield 11%, $\lambda_{\max}^{CCl_4}$ 2.83, 5.80, 6.05, 6.10, 9.85, 10.12 and 10.83 μ. Cold methanolic alkali generated a 74% yield of 2-methylcyclohexanone as the yellow-orange 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 135–137°.

Reformatsky Reaction with α-Tetralone and Methyl γ-Bromocrotonate in Ether.—The crude product from the reaction between 15 g. (0.103 mole) of α-tetralone, 20 g. (0.112 mole) of methyl γ-bromocrotonate, and 10 g. (0.154 mole) of zinc in 100 cc. of ether was dehydrated and saponified, as described above for the ester of I, to give 11 g. (50%) of 1,2,3,4-tetrahydro-1-naphthylidenecrotonic acid (XVII), m.p. 196–197° from carbon tetrachloride (reported[11] m.p. 194–195°, 52% yield from a Reformatsky reaction in a 1:1 mixture of ether and benzene), $\lambda_{\max}^{alc}$ 233.5, 239.5, 247 and 324 mμ (ε 8,100, 8,900, 6,840 and 32,000). Treatment of the sodium salt of XVII with oxalyl chloride and then aniline afforded the **anilide of XVII**, m.p. 159–160° as light yellow plates from ethanol.

Anal. Calcd. for $C_{20}H_{19}NO$: C, 83.01; H, 6.62; N, 4.84. Found: C, 82.55; H, 6.68; N, 5.07.

Reformatsky Reaction with β-Tetralone and Methyl γ-Bromocrotonate. A. In Benzene.—A sample of β-tetralone was obtained by the method of Birch[22] in 80% yield, b.p. 96–98° (1.0 mm.), m.p. 20.4–21°, stable as a white solid at −10° for several months. The crude product (13 g.) from a reaction between 6 g. (0.041 mole) of β-tetralone, 13.8 g. (0.077 mole) of methyl γ-bromocrotonate and 9 g. (0.138 mole) of zinc in 100 cc. of benzene was dissolved in petroleum ether and cooled, when 0.6 g. (6%) of a colorless solid, m.p. 85–87°, precipitated. This was the "abnormal" Reformatsky ester (XVIII), which will be described in the next experiment. From a 1-g. sample of the remaining material, which would not crystallize, approximately 70% of β-tetralone was recovered as the bisulfite adduct. The rest was hydrogenated in the crude state with platinum oxide in methanol, the catalyst was filtered and the solution was concentrated *in vacuo*. The residue was dehydrated by boiling acetic anhydride and formic acid and saponified in methanolic potassium hydroxide to give 85 mg. (12% based on β-tetralone) of γ-(3,4-dihydro-2-naphthyl)-butyric acid (XXI), m.p. 67–69° from petroleum ether (reported[2f] m.p. 70–71°).

Another 1-g. batch of the crude Reformatsky product (containing β-tetralone) was hydrogenated with platinum oxide in methanol and dehydrated by heating with 1.25 g. of potassium acid sulfate at 160° for one hour. Saponification in aqueous methanolic potassium hydroxide, ether extraction of the neutral material, and acidification gave a semisolid acid, which was cyclized by allowing it to stand for twenty-four hours in a solution of 5 cc. of acetic anhydride and 1 cc. of a 5% solution of zinc chloride in acetic acid. After working up as usual[2b] and treating the crude residue with 2,4-dinitrophenylhydrazine reagent, the dark red 2,4-dinitrophenylhydrazone of 4-keto-1,2,3,4,9,10-hexahydrophenanthrene was obtained, m.p. 221–223° from ethyl acetate, undepressed on admixture with an authentic sample, kindly furnished by the late Dr. W. E. Bachmann.[2f]

B. In Ether.—When the Reformatsky reaction with 8 g. (0.055 mole) of β-tetralone, 19.8 g. (0.11 mole) of methyl γ-bromocrotonate, and 9.7 g. (0.15 mole) of zinc was performed in ether, as described above for cyclohexanone, there resulted 18 g. of crude undistilled ester. On cooling its solution in petroleum ether for several days, 6.5 g. (48%) of **methyl α-(2-hydroxy-1,2,3,4-tetrahydro-2-naphthyl)-vinylacetate (XVIII)** precipitated, m.p. 85–87°. Recrystallization from ether–petroleum ether gave a pure sample, m.p. 87.5–88.5°, $\lambda_{\max}^{alc}$ 212 mμ (inflection), 265.5 and 272.5 mμ (ε 9,300, 541 and 565), *$\lambda_{\max}^{mineral\ oil}$ 2.83, 5.84, 6.12, 9.99 and 10.87 μ.

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.20; H, 7.36.

The material from the mother liquor of the above crystallization was evaporatively distilled at 120–150° (0.1 mm.) to give a pale yellow oil (5.0 g., 37%) which exhibited an infrared spectrum almost identical with that of XVIII. It is possible that this oil represents a stereoisomer of XVIII.

Hydrogenation of 502 mg. of the solid "abnormal" Reformatsky ester (XVIII) with platinum oxide (30 mg.) in methanol caused one mole of hydrogen to be absorbed and produced 410 mg. (82%) of colorless crystals, m.p. 54–57°. Recrystallization from aqueous methanol or petroleum ether resulted in a pure sample of **methyl α-(2-hydroxy-1,2,3,4-tetrahydro-2-naphthyl)-butyrate (XIX)**, m.p. 62–63°, $\lambda_{\max}^{alc}$ 212 mμ (inflection), 265.5 and 273 mμ (ε 9,900, 536 and 559), *$\lambda_{\max}^{mineral\ oil}$ 2.85, 5.85 μ (the peaks at 6.12, 9.99 and 10.87 μ were absent in this sample).

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.28; H, 8.19.

The dehydration of 100 mg. of XIX with hot acetic anhydride, followed by saponification afforded 40 mg. (47%) of α-**(3,4-dihydro-2-naphthyl)**-butyric **acid (XX)**, m.p. 90–92°, undepressed on admixture with a sample prepared as described below.

α-(3,4-Dihydro-2-naphthyl)-butyric Acid (XX).—A Reformatsky reaction with 4.5 g. (0.023 mole) of ethyl α-bromobutyrate, 2 g. (0.0136 mole) of β-tetralone and 1.95 g. (0.03 mole) of zinc in 50 cc. of ether afforded 3.79 g. of a dark oil, from which 60% of β-tetralone was recovered as the bisulfite adduct. The crude Reformatsky ester was dehydrated with hot acetic anhydride and formic acid. The residue from the distillation at reduced pressure of the acetic anhydride was saponified with methanolic potassium hydroxide to give, after evaporative distillation, 0.95 g. (32%) of **α-(3,4-dihydro-2-naphthyl)-butyric acid (XX)**, m.p. 93–94° from petroleum ether, $\lambda_{\max}^{alc}$ 213, 218 and 270 mμ (ε 20,300, 20,300 and 13,900).

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 78.01; H, 7.73.

Reformatsky Reaction with 3,4,5-Trimethoxybenzaldehyde and Methyl γ-Bromocrotonate. A. In Benzene.—The reaction between 4.5 g. (0.023 mole) of 3,4,5-trimethoxybenzaldehyde,[23] 10 g. (0.056 mole) of methyl γ-bromocrotonate and 6.6 g. (0.101 mole) of zinc in 80 cc. of ben-

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(22) A. J. Birch, *J. Chem. Soc.*, 430 (1944).

(23) F. Benington and R. D. Morin, THIS JOURNAL, **73**, 1353 (1951).

zene afforded 8 g. of a crude oil, which, on standing, deposited 1.83 g. of solid diene ester (ester of XXIV), m.p. 104–108°. Distillation of the residue at 110–185° (0.25–0.6 mm.) produced a second crop of solid ester, weight 1.1 g., bringing the total yield to 2.93 g. (46%). Recrystallization from ether afforded **methyl 3,4,5-trimethoxybenzylidenecrotonate (ester of XXII)** as colorless prisms, m.p. 111.5–112.5°, $\lambda_{\text{max}}^{\text{alc}}$ 249 and 332 mμ (ε 15,320 and 35,100).[14]

Anal. Calcd. for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.54; H, 6.30.

Saponification of a portion of the diene ester (ester of XXII) gave a quantitative yield of **3,4,5-trimethoxybenzylidenecrotonic acid (XXII)**, m.p. 156–159°, which was recrystallized from benzene as yellow microcrystals, m.p. 162.5–163.0°, $\lambda_{\text{max}}^{\text{alc}}$ 244 and 319 mμ (ε 16,050 and 32,300).[14]

Anal. Calcd. for $C_{14}H_{16}O_5$: C, 63.62; H, 6.10. Found: C, 63.52; H, 6.28.

The diene acid (XXII, 36.8 mg.) absorbed two moles of hydrogen with prereduced platinum oxide in methanol to give 25 mg. (71%) of δ-(3,4,5-trimethoxyphenyl)-valeric acid as colorless plates, m.p. 66–68° (reported,[24] m.p. 69–70°).

B. In Ether.—From a Reformatsky reaction with 5 g. (0.0255 mole) of 3,4,5-trimethoxybenzaldehyde, 13 g. (0.073 mole) of methyl γ-bromocrotonate and 13 g. (0.2 mole) of zinc in 80.0 ml. of dry ether was obtained an oil which, upon cooling, gave 3.03 g. (55%) of **methyl β-(3,4,5-trimethoxyphenyl)-β-hydroxy-α-vinylpropionate (XXIII)** as a light yellow solid, m.p. 82–92°. An analytical sample was obtained as silky cream colored needles, m.p. 102.8–103.4°, from ether.

Anal. Calcd. for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 61.00; H, 7.17.

Hydrogenation of 33.6 mg. of XXIII in absolute methanol with platinum oxide afforded 30.0 mg. (86%) of **methyl β-(3,4,5-trimethoxyphenyl)-β-hydroxy-α-ethylpropionate (XXIV)** as colorless needles from ether and methanol, m.p. 107–108.5°. Admixture with an authentic sample (see below) offered no depression in melting point.

Methyl β-(3,4,5-Trimethoxyphenyl)-β-hydroxy-α-ethylpropionate (XXIV).—A Reformatsky reaction with 3.5 g. (0.0179 mole) of 3,4,5-trimethoxybenzaldehyde, 4.0 g. (0.061 mole) of zinc and 11.2 g. (0.062 mole) of methyl α-bromobutyrate in 40 cc. of dry ether yielded 2.66 g. (50%) of **methyl β-(3,4,5-trimethoxyphenyl)-β-hydroxy-α-ethylpropionate (XXIV)**, m.p. 72–88°. An analytical sample crystallized from ether and methanol, m.p. 109.5–110.5°.

Anal. Calcd. for $C_{15}H_{22}O_6$: C, 60.38; H, 7.43. Found: C, 60.07; H, 7.38.

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[CONTRIBUTION FROM THE ROLLIN H. STEVENS MEMORIAL LABORATORY OF THE DETROIT INSTITUTE OF CANCER RESEARCH]

Reduction of Some Enolizable β-Dicarbonyl Compounds to Unsaturated Alcohols by Lithium Aluminum Hydride. II. β-Diketones[1]

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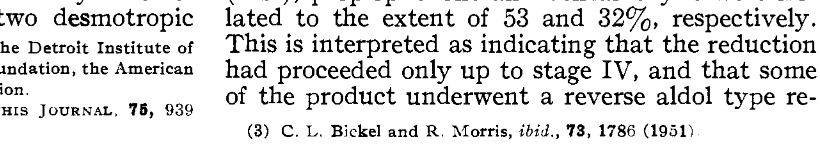
RECEIVED MARCH 23, 1953

In confirmation of the previous observation that enolic β-dicarbonyl compounds are reduced to unsaturated alcohols by lithium aluminum hydride it was found that cyclohexane-1,3-dione and two homologs were converted primarily into 2-cyclohexene-1-ol and the corresponding homologs. The reduction of dibenzoylmethane also resulted in the loss of an oxygen, but the simultaneous saturation of the double bond caused 1,3-diphenylpropane-1-ol to be the major product. That the loss of the oxygen during the lithium aluminum hydride treatment is connected with the enolic nature of the β-dicarbonyl compounds was shown by the reduction of the stable enol and keto forms of 1,1-dibenzoylethane, which yielded 2-methyl-1,3-diphenyl-1-propene-3-ol and 2-methyl-1,3-diphenylpropane-1,3-diol, respectively.

It was recently shown that the lithium aluminum hydride reduction of some enolizable β-keto esters and α-hydroxymethylene ketones yielded mixtures of unsaturated alcohols and 1,3-glycols.[2] The study of this reaction has now been extended to enolizable β-diketones and further evidence on its detailed course has been obtained.

In the previous paper,[2] evidence was cited for the postulate that the diketo portions (I) of the β-dicarbonyl compounds were largely responsible for the formation of 1,3-glycols (II), while the enol forms (III) were converted to unsaturated alcohols (VI). The latter reaction was considered to occur *via* the intermediate enolate salts (IIIa and IV) and the unsaturated carbonyl compound (V). This view receives confirmation from the lithium aluminum hydride reduction in boiling ether of the two desmotropic forms of 1,1-dibenzoylethane. The diketo form (VIIa) afforded a quantitative yield of 2-methyl-1,3-diphenylpropane-1,3-diol (VIIIa, probably mixture of stereoisomers), while the enol form (IXa)[3] was reduced under identical conditions to give a 79% yield of 2-methyl-1,3-diphenyl-1-propene-3-ol (Xa).

When a shorter reaction time was used in the reduction of the enol form of 1,1-dibenzoylethane (IXa), propiophenone and benzaldehyde were isolated to the extent of 53 and 32%, respectively. This is interpreted as indicating that the reduction had proceeded only up to stage IV, and that some of the product underwent a reverse aldol type re-



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(1) This work was supported by grants to the Detroit Institute of Cancer Research from the Michigan Cancer Foundation, the American Cancer Society, Inc., and The Kresge Foundation.

(2) A. S. Dreiding and J. A. Hartman, THIS JOURNAL, **75**, 939 (1953).

(3) C. L. Bickel and R. Morris, *ibid.*, **73**, 1786 (1951).