The *sym*-trinitrobenzene derivative formed yellow-orange needles from benzene–alcohol, m. p. 105.6–106.6°.

Anal. Calcd. for $C_{26}H_{19}O_6N_3$: C, 66.52; H, 4.08; N, 8.95. Found: C, 66.37; H, 3.77; N, 9.19.

Summary

The preparation of 1,2,3,4-tetrahydro-4-keto-1-phenyl-2-naphthaleneacetic acid by ring closure of β-benzohydrylglutaric anhydride using aluminum chloride or by direct cyclization of β-benzohydrylglutaric acid using anhydrous hydrogen fluoride is described. The keto group of this keto acid was reduced by the Clemmensen method and the reduced acid cyclized to 1,2,9,10,11,12-hexahydro-2-keto-3,4-benzphenanthrene. By reaction with the appropriate Grignard reagents followed by dehydration and dehydrogenation 2-methyl-3,4-benzphenanthrene and 2-ethyl-3,4-benzphenanthrene were prepared from the above hexahydroketone.

COLUMBUS, OHIO RECEIVED FEBRUARY 26, 1940

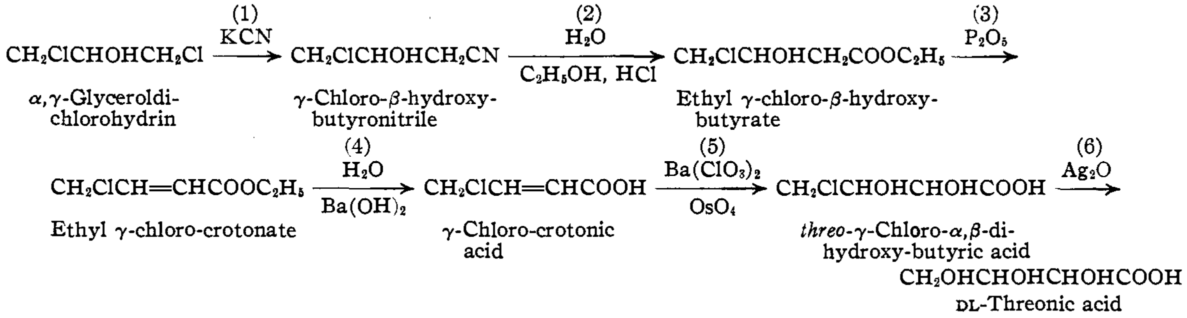
[CONTRIBUTION FROM THE KENT AND GEORGE HERBERT JONES CHEMICAL LABORATORIES, UNIVERSITY OF CHICAGO]

Improvements in the Preparation of DL-Threonic and DL-Erythronic Acids

BY J. W. E. GLATTFELD AND EDWARD RIETZ[1]

The reason for the interest in the two acids mentioned in the title of this article has been recorded several times.[2,3] Briefly, the acids are possible sources of the DL-aldotetroses. These are needed for a proposed study of the saccharinic acid rearrangement of the tetroses which it is hoped to make in these laboratories. Because of the availability of DL-erythronic lactone, definite progress has been made in devising a procedure for its transformation into DL-erythrose.[2] The difficulty of the preparation of DL-threonic acid, however, has prevented corresponding progress with this substance. The main object of the work reported below, therefore, was the simplification and improvement of the known procedure for the preparation of DL-threonic acid.[4] Incidentally, the method of preparation of DL-erythronic lactone was also much improved by the use of vinylacetic acid, an intermediate in the preparation of DL-threonic acid.

DL-Threonic Acid.—The only recorded synthesis of DL-threonic acid is that of Braun.[4b,c]



$$\underset{\alpha,\gamma\text{-Glyceroldichlorohydrin}}{\mathrm{CH_2ClCHOHCH_2Cl}} \xrightarrow{\overset{(1)}{\mathrm{KCN}}} \underset{\gamma\text{-Chloro-}\beta\text{-hydroxybutyronitrile}}{\mathrm{CH_2ClCHOHCH_2CN}} \xrightarrow[\mathrm{C_2H_5OH,\ HCl}]{\overset{(2)}{\mathrm{H_2O}}} \underset{\text{Ethyl }\gamma\text{-chloro-}\beta\text{-hydroxybutyrate}}{\mathrm{CH_2ClCHOHCH_2COOC_2H_5}} \xrightarrow{\overset{(3)}{\mathrm{P_2O_5}}}$$

$$\underset{\text{Ethyl }\gamma\text{-chloro-crotonate}}{\mathrm{CH_2ClCH{=}CHCOOC_2H_5}} \xrightarrow[\mathrm{Ba(OH)_2}]{\overset{(4)}{\mathrm{H_2O}}} \underset{\gamma\text{-Chloro-crotonic acid}}{\mathrm{CH_2ClCH{=}CHCOOH}} \xrightarrow[\mathrm{OsO_4}]{\overset{(5)}{\mathrm{Ba(ClO_3)_2}}} \underset{\textit{threo}\text{-}\gamma\text{-Chloro-}\alpha,\beta\text{-dihydroxy-butyric acid}}{\mathrm{CH_2ClCHOHCHOHCOOH}} \xrightarrow{\overset{(6)}{\mathrm{Ag_2O}}} \underset{\text{DL-Threonic acid}}{\mathrm{CH_2OHCHOHCHOHCOOH}}$$

This process was carried out several times, but great difficulty was experienced at first in inducing the DL-threonic acid sirup to crystallize. The acid is converted into the lactone much more readily, apparently, than Braun's paper[4b] would indicate. To succeed in crystallizing the sirup obtained by concentration of a water solution of the acid, the evaporation must be discontinued before all of the water is removed, that is, while the residue is still a *thin* sirup. If the evaporation is continued at 40° and 2 mm. for four hours after nearly all of the water has been removed, as Braun recommends, the residue will be largely lactone and will not crystallize. That the acid is converted into lactone was demonstrated by the subjection of a sample of crystalline acid to distillation at 3 mm. The distillate, which titration indicated consisted of 87% lactone and 13% free acid, could not be induced to crystallize even when seeded with crystals of DL-threonic acid.

After having succeeded in producing crystalline acid by Braun's procedure, attention was turned

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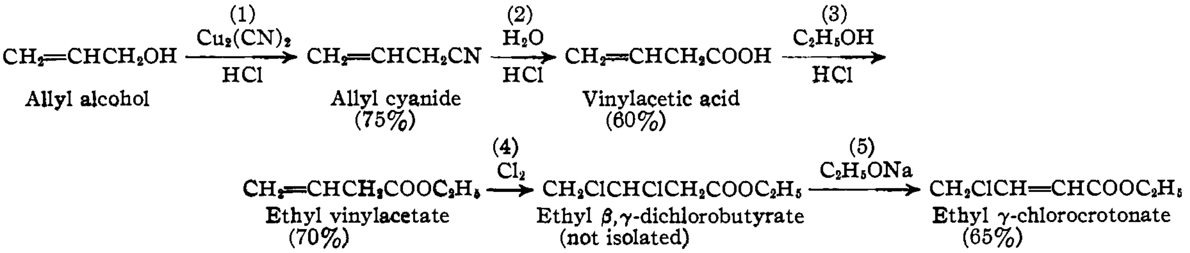
(1) This article is condensed from a dissertation presented by Edward Rietz in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the University of Chicago.

(2) Glattfeld and Kribben, THIS JOURNAL, **61**, 1720 (1939).

(3) Glattfeld and Lee, *ibid.*, **62**, 354 (1940).

(4) Géza Braun, *ibid.*, **52**, (a) 3167, (b) 3176 (1930), (c) **54**, 1133 (1932).

to improvements in the process. These consisted in producing the intermediate, ethyl γ-chlorocrotonate in a 20% yield (calculated from allyl alcohol) by a much simpler method than that used by Braun. The steps involved in the new procedure are

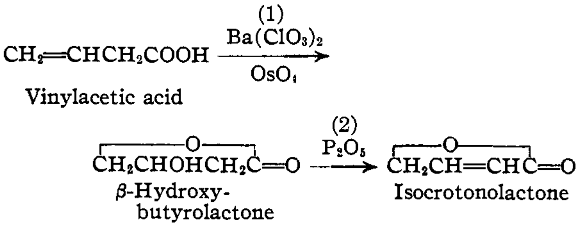


$$\underset{\text{Allyl alcohol}}{CH_2{=}CHCH_2OH} \xrightarrow[HCl]{(1)\ Cu_2(CN)_2} \underset{\substack{\text{Allyl cyanide}\\(75\%)}}{CH_2{=}CHCH_2CN} \xrightarrow[HCl]{(2)\ H_2O} \underset{\substack{\text{Vinylacetic acid}\\(60\%)}}{CH_2{=}CHCH_2COOH} \xrightarrow[HCl]{(3)\ C_2H_5OH}$$

$$\underset{\substack{\text{Ethyl vinylacetate}\\(70\%)}}{CH_2{=}CHCH_2COOC_2H_5} \xrightarrow{(4)\ Cl_2} \underset{\substack{\text{Ethyl } \beta,\gamma\text{-dichlorobutyrate}\\(\text{not isolated})}}{CH_2ClCHClCH_2COOC_2H_5} \xrightarrow{(5)\ C_2H_5ONa} \underset{\substack{\text{Ethyl } \gamma\text{-chlorocrotonate}\\(65\%)}}{CH_2ClCH{=}CHCOOC_2H_5}$$

The feasibility of the procedure was first established by the preparation of the corresponding bromo derivative, which was obtained in 23.4% yield calculated from allyl alcohol. The ester was hydrolyzed to γ-bromocrotonic acid, which in turn was oxidized to *threo*-γ-bromo-α,β-dihydroxybutyric acid. The procedure for the preparation of the bromo ester was then successfully applied to the preparation of the corresponding chloro ester, which in turn was transformed by Braun's procedure (steps 4–6) into DL-threonic acid. This was obtained in 5.3% yield calculated from the allyl alcohol.

DL-Erythronic Acid.—The best source of DL-erythronic acid at present is the lactone of γ-hydroxy-isocrotonic acid, which is obtained by treatment of glycerolmonochlorohydrin with sodium cyanide, followed by hydrolysis of the nitrile so produced.[5] The amount of the unsaturated lactone formed varies greatly, the yield (average 23%) sometimes being as high as 30% and sometimes being almost negligible. It is oxidized to DL-erythronic acid, the lactone of which was obtained by Braun[6] in 75% yield. It was found that vinylacetic acid could be transformed into isocrotonolactone in 21% yield as follows



$$\underset{\text{Vinylacetic acid}}{CH_2{=}CHCH_2COOH} \xrightarrow[OsO_4]{(1)\ Ba(ClO_3)_2}$$

$$\underset{\beta\text{-Hydroxy-butyrolactone}}{CH_2CHOHCH_2C{=}O} \xrightarrow{(2)\ P_2O_5} \underset{\text{Isocrotonolactone}}{CH_2CH{=}CHC{=}O}$$

Although the new procedure does not give the isocrotonolactone in larger yield than the old one at its best, it has definite advantages. It eliminates the uncertainty in the production of the lactone, is less time consuming, avoids the use of sodium cyanide, and permits the use of larger quantities in a run.

A few remarks concerning the oxidation of vinylacetic acid and the dehydration of β-hydroxybutyrolactone should be recorded. When the osmic acid was used in comparatively large amount, the reaction became violent. Furthermore, perfectly pure vinylacetic acid was found to be essential for good results. The pure acid obtained by extraction of the impurities from a solution of the sodium salt gave markedly better yields and required less catalyst than the acid purified by mere fractionation. The dehydration of β-hydroxybutyrolactone has been studied quite extensively in these laboratories. Glattfeld and Stack[7] observed that dehydration occurs (yield of unsaturated lactone 59%) when an absolute alcohol solution of the lactone containing a little sulfuric acid is heated for seventy-five hours in the presence of calcium sulfate. It was found that the use of more vigorous dehydrating agents shortened the time required for dehydration; phosphorus pentoxide was found to be the most satisfactory. By its use yields of the unsaturated lactone as high as 50% were obtained.

Experimental Part

I. Threonic Acid

Allyl Cyanide.—This was prepared in 75% yield (boiling range 115–120° at atmospheric pressure) by heating allyl alcohol and a slight excess of cuprous cyanide and concentrated hydrochloric acid under reflux according to the method of Brekpot.[8]

γ-Bromo-crotononitrile.—Although this material was found to be unsuitable for the preparation of threonic acid, the procedure by which it was prepared is described here because it is new to the literature and because the yield is much higher (55%) than that which the authors obtained by the older method of Lespieau and Brule.[9,10]

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[5] Glattfeld, Leavell, Spieth and Hutton, THIS JOURNAL, **53**, 3164 (1931).

[6] Géza Braun, *ibid.*, **51**, 235, 246 (1929).

[7] Glattfeld and Stack, *ibid.*, **59**, 753 (1937).

[8] Brekpot, *Bull. soc. chim. Belg.*, **39**, 466 (1930).

[9] Lespieau, *Bull. soc. chim.*, [3] **33**, 55 (1905).

[10] Brule, *ibid.*, [4] **5**, 1019 (1909).

One mole (67 g.) of allyl cyanide is dissolved in a mixture of 90 cc. of tertiary butyl alcohol and 450 cc. of medium boiling ligroin. One mole of bromine (160 g.) dissolved in 100 cc. of tertiary butyl alcohol is added dropwise to the vigorously-stirred solution of the nitrile. A mercury seal is used to prevent contact with atmospheric moisture. The temperature is maintained within the range 15–25°. The solution is allowed to stand for fifteen to thirty minutes to ensure complete absorption of the bromine. It is then cooled to 0° and a solution of 23 g. of sodium in the minimum amount of absolute ethyl alcohol necessary to effect solution is added dropwise to the vigorously-stirred solution. The solution is filtered (hood) and the solvent removed under reduced pressure at a maximum temperature of 45°. The residue is fractionated and the fraction boiling at 80–85° at 12 mm. is collected. This weighs 80 g. (55%).

Care is necessary in working with this material. It is a powerful vesicant and lachrymator.

Vinylacetic Acid.—This acid of boiling range 66–69° at 10 mm. was prepared in 60% yield by the hydrolysis of allyl cyanide according to the method of Falaise and Frognier.[11] During the distillation of this compound, a considerable amount of unchanged nitrile is recovered in a carbon dioxide–acetone cooled trap placed between the receiving flask and the pump. When this recovered nitrile is taken into account, the yield of vinylacetic acid approaches 75%.

Ethyl Vinylacetate.—The ester was prepared from vinylacetic acid, ethyl alcohol and hydrogen chloride according to the directions of Falaise and Frognier.[12] The yield of the fraction boiling at 119–124° at atmospheric pressure was 70%.

Ethyl γ-Bromo-crotonate.—The procedures for the preparation of this compound and of ethyl γ-chloro-crotonate are new to the literature and are therefore given in detail.

One fifth of a mole (23 g.) of ethyl vinylacetate is dissolved in 90 cc. of tertiary butyl alcohol, the solution is cooled to 15–25°, and a solution of one-fifth of a mole of bromine (32 g.) in 90 cc. of tertiary butyl alcohol is added dropwise to the well-stirred solution which is contained in a flask equipped with a mercury seal to prevent the access of atmospheric moisture. The solution is then allowed to stand for one-half hour to ensure complete absorption of the bromine, after which it is cooled to 0°. A solution of sodium ethoxide, prepared by the addition of sufficient absolute ethyl alcohol to effect solution of 4 g. of sodium, is added dropwise to the vigorously-stirred solution. The solution is filtered and the solvent removed under reduced pressure at a maximum temperature of 45°. The residue is fractionated and the fraction of boiling range 78–82° at 2 mm. is collected. A yield of 23 g. (60% is obtained. The over-all yield calculated on the basis of the allyl alcohol is 23.4% as compared with Braun's yield of 1.7% calculated on the basis of glycerol.

The material was hydrolyzed and the γ-bromo-crotonic acid was oxidized to *threo*-γ-bromo-α,β-dihydroxybutyric acid as described by Braun. Both compounds melted at the temperature noted by Braun. As the last-named acid is quite difficult to prepare, however, it is not a practical material for the preparation of threonic acid. It was found to be much easier to prepare threonic acid from ethyl γ-chlorocrotonate, the preparation of which is described in the next section.

Ethyl γ-Chloro-crotonate.—Three moles of ethyl vinylacetate (342 g.) is dissolved in 600 cc. of dry carbon tetrachloride, and dry chlorine is passed into the cool (10–20°) well-stirred solution. When the theoretical amount of chlorine (213 g.) has been absorbed (determined by increase in weight of the reaction mixture) the solution is allowed to stand at room temperature for one-half hour to ensure complete absorption of chlorine. The dichloro ester is unstable and loses hydrogen chloride. The mercury seal is not removed, therefore, while the mixture is attaining room temperature. The solution is then cooled to about −5° and a solution of 62 g. of sodium (90% of theory), dissolved in the quantity of absolute alcohol necessary to effect solution, is added dropwise to the vigorously-stirred solution. The temperature is maintained below 0° because of undesirable side reactions which occur at higher temperatures. After the ethoxide has been added, the sodium chloride which has precipitated is removed by filtration or by the use of the centrifuge. Filtration is frequently quite difficult, but the centrifuge has always given a satisfactory separation. The "centrifuging" is best accomplished by the use of four 250-cc. centrifuge tubes, emptying the contents, and repeating the operation until the solid material has been removed from the entire liquid. The solvent is removed under reduced pressure with the water pump, and the residue fractionated. The fraction of boiling range 72–80° at 10 mm. weighs 290 g. (65%).

Threonic Acid.—The procedure for the preparation of threonic acid from this point was essentially that of Braun. Ethyl γ-chloro-crotonate was hydrolyzed to γ-chloro-crotonic acid (78–80°, 60%) which in turn was oxidized to *threo*-γ-chloro-α,β-dihydroxybutyric acid (97–98°, 75%) by means of osmic acid-activated barium chlorate.

Forty-seven grams of *threo*-γ-chloro-α,β-dihydroxybutyric acid was treated according to Braun[4c] and yielded 23 g. of DL-threonic acid, m. p. 98°, 59% yield calculated from the *threo*-γ-chloro-α,β-dihydroxybutyric acid used.

II. Erythronic Acid

While the vinylacetic acid of boiling range 66–69° at 10 mm. is sufficiently pure for the threonic acid synthesis, a higher degree of purity is necessary for the preparation of erythronic acid. This substance was obtained by the procedure of Falaise and Frognier.[13] The pure acid was recovered from the salt in 90% yield and boiled at 71° at 13 mm.

β-Hydroxy-butyrolactone.—Thirty-five grams of pure vinylacetic acid is added to 90 cc. of water containing 25 g. of barium chlorate and 5 cc. of a 0.2% solution of osmium tetroxide. The temperature is kept below 35° by occasional cooling. After one day, an additional 5 cc. of 0.2% osmium tetroxide solution is added. At the end of the third day, the reaction mixture is subjected to distillation under reduced pressure at a maximum temperature of 50°. The lactone is extracted from the residue with absolute

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[11] Falaise and Frognier, *Bull. soc. chim. Belg.*, **42**, 433 (1933).

[12] Falaise and Frognier, *ibid.*, p. 438.

[13] Falaise and Frognier, *ibid.*, p. 436.

alcohol, the solution is filtered free from inorganic material, and subjected to complete distillation under reduced pressure at 40°. The residue is fractionated. The fraction boiling between 135–160° at 2–5 mm. consists chiefly of the hydroxy-lactone. It weighs 14 g. (35%). Fractionation at reduced pressure yields the pure lactone which boils at 145–148° at 2–4 mm.

Preparation of Isocrotonolactone.—Seventy-one grams of phosphorus pentoxide is added, 10 to 20 g. at a time, to a solution of fifty grams of β-hydroxybutyrolactone in 200 cc. of dioxane. The mixture is allowed to stand for an hour (in one experiment the mixture stood overnight without ill effect). The dioxane solution is then decanted into a Claissen flask. The residue is extracted twice with absolute alcohol, the alcohol extracts being added to the dioxane solution. The solvent is removed under reduced pressure (10–15 mm. with water-bath at 70–80°), and the residue is distilled at 7 mm. The boiling range of 22 g. of material obtained in this way was 80–86° (53%).

Anal. Calcd. for $C_4H_4O_2$: H, 4.78; C, 57.1. Found: H, 5.16; C, 57.05.

The lactone was then transformed into DL-erythronic lactone by the procedure of Braun. From 78 g. of the unsaturated lactone of boiling range 82–86° at 7 mm. there was obtained 49 g. of crude DL-erythronic lactone, m. p. 88–90°; a yield of 45%.

Summary

1. New procedures which shorten the time of preparation and increase yields have been devised for the preparation of the following compounds: ethyl γ-bromo-crotonate, ethyl γ-chlorocrotonate, γ-bromo-crotononitrile, β-hydroxy-butyrolactone, and isocrotonolactone.

2. Braun's synthesis of DL-threonic acid has been greatly modified. The over-all yield by the new procedure is 5.3% (calculated from allyl alcohol) as against 2.2% (calculated from glycerol dichlorohydrin) by Braun's procedure.

3. The preparation of β-hydroxy-butyrolactone and isocrotonolactone from vinylacetic acid as reported in this article is a much more dependable process than the procedure in which these substances are made from glycerol monochlorohydrin.

CHICAGO, ILLINOIS RECEIVED JANUARY 26, 1940

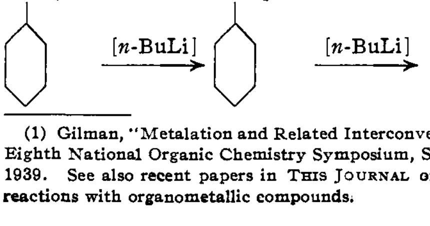
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

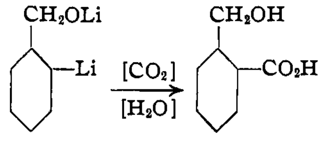
Metalation of Alcohols and Amines

BY HENRY GILMAN, G. E. BROWN, F. J. WEBB AND S. M. SPATZ

Halogen-metal interconversion reactions have been noted in a great variety of reactions, and are of particular interest with polyfunctional compounds.[1] Hydrogen-metal interconversion reactions or metalations are also very common, but because they generally take place at a somewhat slower rate than halogen-metal interconversion reactions there is a greater opportunity for secondary reactions with polyfunctional compounds.

We are now reporting preliminary observations on the metalation of some selected simple alcohols and amines, and will report later on polyfunctional compounds having alcohol and amino groups. Metalation takes place with all the chief types of aromatic alcohols and amines: primary, secondary and tertiary. An illustration is the metalation of benzyl alcohol.





In accordance with the general rules postulated for interconversions with organometallic compounds,[1] metalation occurs *ortho* to the group containing the hetero element. The only exception now known is the metalation of dibenzothiophene by phenylcalcium iodide, where metalation takes place in the 3- and not in the 4-position.[2,3]

Poly-metalation is to be expected with the more reactive organometallic compounds, and was observed earlier in the dibenzofuran series.[4] It may be stated that, in general, halogen-metal interconversions, hydrogen-metal interconversions as well as the numerous other interconver-

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[1] Gilman, "Metalation and Related Interconversion Reactions," Eighth National Organic Chemistry Symposium, St. Louis, Dec. 30, 1939. See also recent papers in THIS JOURNAL on interconversion reactions with organometallic compounds.

[2] Gilman, Jacoby and Pacevitz, *J. Org. Chem.*, **3**, 120 (1938).

[3] Under generally drastic conditions of high temperature and pressure, Houben and co-workers [*Ber.*, **37**, 3978 (1904); **42**, 3729, 4488, 4815 (1909); **46**, 3833 (1913)] have obtained predominantly *para*-amino acids by interaction of carbon dioxide with the complexes derived from various secondary and tertiary amines with Grignard reagents. Under corresponding conditions they did not isolate acidic material from primary aromatic amines.

[4] Gilman and Young, THIS JOURNAL, **56**, 1415 (1934); **57**, 1121 (1935).