

atom and possibly a shift of a hydrogen with the corresponding opening of a double bond, the free energy decreases are, respectively, 60,200, 57,980 and 50,730 calories.

These changes indicate that, in the crystal at any rate, the bond energies are distinctly affected by their position in the compound.

Summary

1. The heat capacities of adenine, hypoxanthine, guanine, xanthine, uric acid, allantoin

and alloxan have been determined over the temperature range 90 to 298.1°K.

2. From the heat capacities and an empirical extrapolation formula, the entropies at 298.1°K. have been calculated.

3. Using the entropies in conjunction with other data accurate free energies have been calculated for these compounds.

4. Some interesting relations between the free energies have been pointed out.

PASADENA, CALIF.

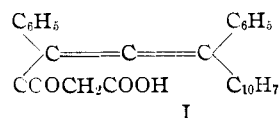
RECEIVED APRIL 2, 1935

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

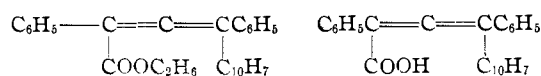
The Resolution of an Allenic Compound

BY E. P. KOHLER, J. T. WALKER AND M. TISHLER

For reasons too well known to require exposition it has long been desirable to know whether allenic compounds, in which at least one of the hydrogen atoms on each of the terminal carbon atoms of allene has been replaced by a substituent, can be obtained in optically active forms. The matter now seems to be definitely settled because Mills¹ has recently announced the formation of an optically active allene by an asymmetric degradation and we are able to report the production of optical opposites by the resolution of the acid



The reasons which ultimately led to the preparation of this acid for resolution and which justify its use for this purpose may be stated briefly as follows. Lapworth and Wechsler² in one of the earliest of the many attempts to prepare an allenic compound suitable for resolution³ heated diphenyl naphthyl butyrophenone with phosphorus pentachloride and treated the mixture of products with alcohol and pyridine. They thus obtained a crystalline ester, and, by subsequent hydrolysis, a crystalline acid, to which with certain reservations they ascribed the allenic formulas



(1) Mills and Maitland, *Nature*, **135**, 994 (1935).

(2) Lapworth and Wechsler, *J. Chem. Soc.*, **97**, 38 (1910).

(3) For the most important references, see Preudenberg, "Stereochemie," p. 804.

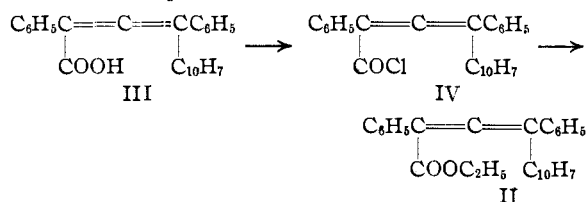
As these compounds can be obtained without great difficulty from material with which we are familiar we decided to employ them in our work.

In view of the reservations of Lapworth and Wechsler it was necessary at the outset to establish the allenic formulas with certainty. We began with the ester because it is easier to manipulate and we secured evidence that is conclusive. The composition, molecular weight and ethoxyl content are all in complete agreement with the formula. Oxidation of the ester with permanganate results in phenyl naphthyl ketone and an oil which is hydrolyzed to phenyl glyoxylic acid. On catalytic hydrogenation the ester adds two atoms of hydrogen rapidly—forming an intermediate reduction product which still reduces permanganate—and then less rapidly two more atoms of hydrogen to form a saturated ester. This evidence is conclusive because the ability to add four atoms of hydrogen excludes the possibility of any form of ring compound and the oxidation products show that the substituents are in their appointed places.

The acid has peculiar chemical and physical properties but its structure is as certain as that of the ester. It liberates a mole of gas from methylmagnesium iodide in the cold and it forms a silver salt from which ethyl iodide regenerates the ester. Although properly constituted, the acid does not lend itself to attempts at resolution because its salts appear to have no power to crystallize. As the esters crystallize well, the preparation of diastereomers by ester interchange with an optically

active alcohol offered one way out of the difficulty but the results of preliminary experiments in this direction were not encouraging. We therefore decided on a more radical alteration and, as a means to this end, prepared the acid chloride.

The acid chloride, like the esters and the acid itself, is a comparatively inactive substance. In the presence of pyridine, however, it reacts both with hydroxyl and with amino compounds and the formation of the allenic ester in the reaction with alcohol proves that there is no alteration of structure in the sequence



Once the acid chloride was available the way was open for transforming the acid into a great variety of substances more suitable for resolution. We selected the glycolic acid derivative because it could be prepared by a reaction which we knew to be free from irregularity and because we anticipated both that it would be more soluble and that it would have more crystallizing power than the allenic acid itself. It proved to be admirably adapted for resolution. It was easily purified because it crystallizes well and its resolution by means of the brucine salt presented no unusual difficulties. The acid, which melts at 195°, is a racemate or racemic mixture of two optical opposites which melt at 145–146° and which in ethyl acetate have the rotation $[\alpha]_D 29.5^\circ$.

Experimental Part

The Ethyl Ester of α,γ -Diphenyl- γ -naphthylallene Carboxylic Acid, II.—The ester was obtained by the sequence of reactions employed by Lapworth and Wechsler, by esterification of the acid through the silver salt and by boiling the acid chloride with alcohol and pyridine. All preparations had the physical properties described by the previous authors.

Anal. Calcd. for $\text{C}_{28}\text{H}_{22}\text{O}_2$: C, 86.2; H, 5.6; OC_2H_5 , 11.5; mol. wt., 390. Found: C, 86.3; H, 5.9; OC_2H_5 , 11.4; mol. wt., 408.

Owing to the stability of the ester in acid media it was difficult to get consistent results in the ethoxyl determinations but reliable values were finally obtained by keeping solutions in acetic anhydride containing trichloroacetic acid for three hours at the ordinary temperature before adding hydrogen iodide and proceeding in the usual manner.

Oxidation.—The ester was oxidized at the ordinary temperature with permanganate in acetone, employing 6

g. of oxidizer for 2 g. of substance. The product, isolated in the usual manner, was an oil. This oil when treated with methyl alcoholic sodium hydroxide was partially converted into the sodium salt of phenylglyoxylic acid—identified in the form of its phenylhydrazone. The residual unhydrolyzable oil solidified when treated with ether and petroleum ether, yielding 0.8 g. of phenyl naphthyl ketone.

Hydrogenation: Ethyl α,γ -Diphenyl- γ -naphthylbutyrate, $\text{C}_6\text{H}_5\text{CH}(\text{COOC}_2\text{H}_5)\text{CH}_2\text{CH}(\text{C}_6\text{H}_5)\text{C}_{10}\text{H}_7$.—The hydrogenation of the ester with Adams platinum oxide as catalyst was slow and uncertain, the catalyst evidently being poisoned with great rapidity. With palladium hydroxide precipitated on calcium carbonate as catalyst the hydrogenation proceeded rapidly and smoothly. Thus a solution of 6 g. of the ester in 25 cc. of ethyl acetate absorbed hydrogen at the rate of 225 cc. per hour until one double bond had been saturated. The rate then dropped to 80 cc. until a total of 750 cc. had been absorbed. The resulting solution no longer reduced permanganate. When it was freed from catalyst and concentrated it deposited a solid which was recrystallized from ether–petroleum ether. It separated in small prisms and melted at 124–125°.

Anal. Calcd. for $\text{C}_{28}\text{H}_{26}\text{O}_2$: C, 85.3; H, 6.6; OC_2H_5 , 11.4. Found: C, 85.2; H, 6.5; OC_2H_5 , 11.0.

An attempt to isolate a partially hydrogenated ester was unsuccessful, the product being an oil. It was established, however, that the power to reduce permanganate is retained until four atoms of hydrogen have been absorbed.

α,γ -Diphenyl- γ -naphthylbutyric Acid, $\text{C}_6\text{H}_5\text{CH}(\text{COOH})\text{CH}_2\text{CH}(\text{C}_6\text{H}_5)\text{C}_{10}\text{H}_7$.—As additional evidence that the reduction product, and therefore also the substance reduced, is an open-chain compound, it was hydrolyzed with bases. The resulting acid crystallized from ether–petroleum ether in small prisms and it melted at 147°.

Anal. Calcd. for $\text{C}_{28}\text{H}_{22}\text{O}_2$: C, 85.3; H, 6.0. Found: C, 85.5; H, 6.2.

α,γ -Diphenyl- γ -naphthylallene Carboxylic Acid, III.—The peculiar properties of the acid that is obtained by hydrolyzing the ester (II) with bases have been described by Lapworth and Wechsler. As the acid is not extracted from its ethereal solution by bicarbonates but is extracted by caustic alkalies it is easily freed from both acidic and neutral impurities. Acids rapidly isomerize it to a crotono lactone but it is surprisingly stable in the presence of bases—it was recovered intact after it had been boiled for five hours with 10% alcoholic sodium hydroxide.

Esterification.—The acid was converted into a silver salt by cautiously treating its cold solution in alkali with dilute nitric acid until a faint permanent precipitate was formed and then adding excess of silver nitrate. The salt was amorphous. It was thoroughly dried *in vacuo*, then suspended in ether and boiled for four hours with excess of ethyl iodide. The sole product was the ester from which the acid had been obtained.

The Acid Chloride, IV.—Thionyl chloride isomerizes the allenic acid to a crotono lactone but, fortunately, it is possible to convert it in large part into the chloride by employing phosphorus pentachloride. Our procedure was as follows. To a suspension of 16 g. of the acid in hot benzene was added 9 g. of phosphorus pentachloride.

When the vigorous reaction subsided the mixture was boiled until evolution of hydrogen chloride ceased. A slight excess of the pentachloride was removed and the yellow solution was heated to 100° under diminished pressure until all of the solvent and the oxychloride were removed. The residue was dissolved in a small quantity of absolute ether and the solution was cautiously diluted with petroleum ether which precipitated a small quantity of amorphous polymer. This was removed by filtration and the solution was set aside for crystallization, or, better after pure chloride was available, inoculated. The first crop was 13.5 g. and an additional 2 g. of less pure chloride was obtained from the mother liquor. The chloride crystallizes well in colorless prisms and it melts at 122°.

Anal. Calcd. for $C_{26}H_{17}OCl$: C, 82.0; H, 4.5. Found: C, 81.5; H, 4.5.

The chloride is comparatively inactive. It is perfectly stable in the air and it is scarcely affected by boiling alcohol. Alcoholic solutions of alkalis, however, rapidly hydrolyze it to the salts of the allenic acid and it also reacts readily with ammonia and with amines in ethereal solution. The reaction with hydroxyl compounds was examined with care. The most satisfactory results were obtained by employing pyridine as a condensing agent and operating in benzene or in absolute ether. In this manner the chloride was easily converted into the original ethyl ester (II) and into a methyl ester which crystallized in prisms, melted at 110° and was identified by comparison with a sample prepared by way of the silver salt.

Anal. Calcd. for $C_{27}H_{20}O_2$: C, 86.2; H, 5.3. Found: C, 85.9; H, 5.3.

The Glycolic Acid Ester of the Allenic Acid, I.—A solution of 4.0 g. of the acid chloride and 1.5 g. of glycolic acid in absolute ether was treated with 10 cc. of dry pyridine and then boiled for two hours. The pyridine was then removed with dilute acid and the product was extracted from the ethereal solution with sodium bicarbonate. The bicarbonate solution, on acidification, deposited 3.3 g. of a crystalline acid which after recrystallization from ether-petroleum ether, melted at 195°.

Anal. Calcd. for $C_{28}H_{20}O_4$: C, 79.9; H, 4.8. Found: C, 79.8; H, 4.8.

The ester acid is readily soluble in acetone and in ether, moderately soluble in hot benzene. It crystallizes from benzene in very small needles. As a preliminary to reso-

lution 1 g. of the acid was treated with an equivalent quantity of each of the following alkaloids: strychnine, quinine, cinchonine, cinchonidine, quinidine and brucine. The last alone gave a solid product.

Resolution: The Dextro Acid, I.—A solution of 4.7 g. of the acid and 5.2 g. of brucine in 60 cc. of dry methyl alcohol was boiled for an hour during which time it deposited a quantity of a solid salt. The suspension was filtered while hot and the salt was washed with methyl alcohol. It weighed 4.0 g. and it melted at 145°. The melting point was not changed by three recrystallizations from a mixture of acetone and methyl alcohol from which the salt separated in small transparent prisms.

The acid was liberated by shaking a suspension of the salt in ether three times with 10% hydrochloric acid. The ethereal layer was washed and shaken with bicarbonate. From the bicarbonate solution precipitated an oil that was converted into a solid by treatment with ether-petroleum ether. The solid melted at 145–146° and its rotation in ethyl acetate was $[\alpha]_D +29.5^\circ$. Neither the melting point nor the rotation was changed by two recrystallizations from ether-petroleum ether.

Anal. Calcd. for $C_{28}H_{20}O_4$: C, 79.9; H, 4.8. Found: C, 79.9; H, 4.8.

The Levo Acid.—The mother liquor from which the salt of the dextro acid had been removed was allowed to cool. It deposited first an oil and then a small quantity of the dextro salt. It was set aside for twenty-four hours, then filtered. The filtrate was evaporated and the residue was treated like the salt of the dextro acid. The ether-petroleum ether solution that was obtained in this manner first deposited some of the *d,l* acid melting at 195° and then an acid melting at 144–146°. Owing to a mishap, the quantity of this acid was too small for further purification. The melting point and the rotation in ethyl acetate— $[\alpha]_D -28.4^\circ$ —show that it was practically pure levo acid.

Anal. Calcd. for $C_{28}H_{20}O_4$: C, 79.9; H, 4.8. Found: C, 80.0; H, 4.9.

A mixture of equal weights of the *d* and *l* acids melted at 195°.

Summary

This paper contains a description of a successful resolution of an allenic acid.

CAMBRIDGE, MASS.

RECEIVED AUGUST 5, 1935