

loid and ethyl phenylmalonate used in this work. We are also grateful to our colleague R. E. Marker for helpful advice and suggestions.

Experimental

Preparation and Resolution of Methylphenylacetic Acid.—*dl*-Methylphenylacetic acid was prepared in 78% yield by a malonic ester synthesis involving ethyl phenylmalonate and methyl iodide. Physical constants for the racemic acid are b. p. 124–125° (3–4 mm.), n_D^{20} 1.5211, d_4^{20} 1.097. Resolution of the acid was accomplished by three recrystallizations of the strychnine salt from 75% ethyl alcohol.⁷ Decomposition of the strychnine salt with hydrochloric acid yielded a pure acid with $[\alpha]_D^{25}$ 86.1°.

Preparation of *l*-Methylphenylcarbonylisocyanate.—(+)-Methylphenylacetyl chloride was prepared from 9.1 g. of (+)-methylphenylacetic acid and 7.9 g. of thionyl chloride. The excess thionyl chloride was removed by suction. The acid chloride was dissolved in 125 cc. of dry ether, and 11 g. of sodium azide freshly precipitated by addition of acetone to a saturated aqueous solution was added. This mixture was stirred for twenty-four hours at room temperature. The solid was filtered, washed with ether, and ether evaporated from the filtrate using suction only. The residue had the unmistakable isocyanate odor.

Preparation of (–)- α -Phenylethylamine Hydrochloride and its Benzoyl Derivative.—One-third of the above residue was mixed with 25 cc. of concd. hydrochloric acid and stirred vigorously for four hours. The flask became warm and there was a slight evolution of gas. This mixture was then diluted with 100 cc. of water, allowed to

(7) Raper, *J. Chem. Soc.*, **123**, 2558 (1923).

stand, and the resulting precipitate (0.1 g., m. p. 104–113°) filtered off. The aqueous filtrate was extracted with 30 cc. of ether, and this aqueous solution was then evaporated to dryness. The residue had a m. p. of 154–158°. The m. p. of (–)- α -phenylethylamine hydrochloride is 171°,⁸ (+)- α -phenylethylamine hydrochloride 159–160°;⁹ $[\alpha]_D^{24}$ –5° in water.

The crude amine hydrochloride was converted by the Schotten–Baumann reaction to 1.6 g. of white needles of (–)-benzoyl- α -phenylethylamine. One recrystallization from benzene yielded a product of m. p. 120–121°. Marckwald and Meth,⁸ after repeated recrystallization, report 125.5°. Pope and Read,¹⁰ however, report 119.5°. The specific rotation was $[\alpha]_D^{27}$ –39.2° in benzene with c 2.44, l 2, and α –1.91°. Marckwald and Meth⁸ report $[\alpha]_D$ –39.9° in benzene, c = 3.005; Pope and Read,¹⁰ $[\alpha]_D^{20}$ –43.7° in benzene, c 2.4.

Summary

- (+)-Methylphenylacetic acid has a configuration opposite to that of (+)-alanine.
- A semipinacolic deamination rearrangement has been shown to involve a Walden inversion.
- Additional support is given to the conception of a "rearward" attack on the carbon atom in replacement of groups.

STATE COLLEGE, PENNA. RECEIVED FEBRUARY 21, 1939

(8) Marckwald and Meth, *Ber.*, **38**, 801 (1905).

(9) Hunter and Kipping, *J. Chem. Soc.*, **83**, 1147 (1903).

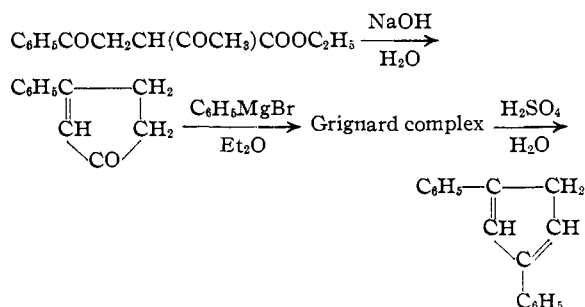
(10) Pope and Read, *ibid.*, **103**, 451 (1913).

[CONTRIBUTION FROM THE UNIVERSITY OF MARYLAND]

Some 1,4-Diaryl-1,3-cyclopentadienes

BY NATHAN L. DRAKE AND JOHN R. ADAMS, JR.¹

Some years ago Borsche and Menz² described a hydrocarbon, C₁₇H₁₄, which they called 1,3-diphenyl-1,3-cyclopentadiene, and synthesized according to the following scheme



(1) From the Doctor's dissertation of J. R. Adams, Jr. This paper was presented at the Milwaukee meeting of the Society, September, 1938.

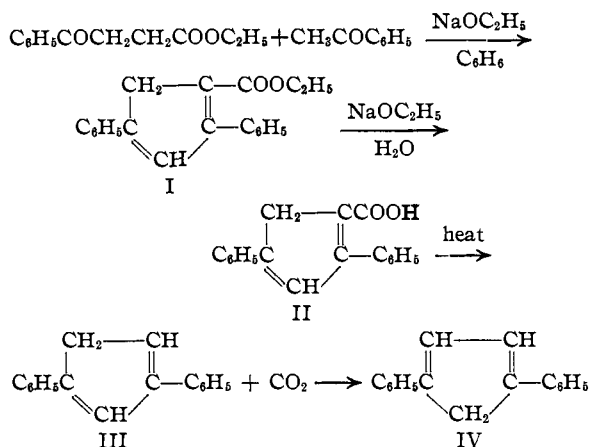
(2) Borsche and Menz, *Ber.*, **41**, 209 (1908).

Borsche and Menz offered no proof of the structure of the diene, apparently assuming that their method of synthesis was in itself sufficient proof.

During a recent study of the condensation of ethyl β -benzoylpropionate with acetophenone in the presence of sodium ethoxide, we obtained this same diene, and it is with this compound, which we have shown beyond all reasonable doubt to be 1,4-diphenyl-1,3-cyclopentadiene, that the present paper deals.

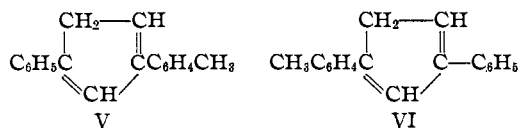
When ethyl β -benzoylpropionate and acetophenone are allowed to react for some time in dry benzene in the presence of two equivalents of sodium ethoxide, and the mixture is cooled, poured into ice water and the layers separated, a crystalline substance separates from the aqueous layer when it is subsequently warmed to about 60°.

Apparently the reactions which have taken place are the following



We have been able to isolate only the acid (II), and the final product (IV). The structure of (IV) follows from the fact that it yields dibenzoylmethane and glyoxal on ozonolysis, and from certain evidence obtained from similar unsymmetrical products.

If (IV) had the same structure as regards its double bonds as (III), then compounds (V) and



(VI) should be isomeric and not identical. These two dienes were made by appropriate reactions and proved to be one and the same substance, indicating that the formula of the diene must be of such a nature that the positions occupied by the aryl groups are equivalent.

Our reasons for assuming a shift of double linkage at some stage of the process *after* hydrolysis to the acid are as follows. The acid (II) can be isolated by acidifying the ice-cold aqueous layer with acetic acid in an ordinary preparation of the diene. The precipitated acid can be recrystallized from benzene, is soluble in aqueous sodium bicarbonate, and its benzene solutions are characterized by an entire lack of the blue fluorescence which appears whenever the diene itself is dissolved in benzene. When (II) is suspended in dilute sodium hydroxide solution and warmed on the steam-bath for about an hour, it is converted practically quantitatively into the diene, whose benzene solutions fluoresce strongly. It seems reasonable to conclude, therefore, that either during or subsequent to the decarboxylation of (II), a shift of double linkage

takes place so that in the final product the unsaturations of the phenyl groups and the double bonds of the diene form a continuous chain of conjugated double linkages.

Both 1-phenyl-4-(*p*)-xenyl-1,3-cyclopentadiene and 1,4-diphenyl-1,3-cyclopentadiene have been prepared by the above method, and by the method of Borsche and Menz; either method of preparation yields the same substance.

Experimental

Preparation of 1,4-Diphenyl-1,3-cyclopentadiene.—Dry sodium ethoxide (from 0.23 g. atom of sodium) was mixed with 200 ml. of dry benzene; 24 g. (0.116 mole) of ethyl β -benzoylpropionate was added, and the mixture shaken occasionally for about ten minutes to complete the solution of the major part of the ethoxide. Acetophenone (14 g.) was then added, the flask stoppered, and allowed to stand for twenty-four hours at 40°. The mixture was next cooled in an ice-bath, poured into a liter of ice water, and shaken well in a separatory funnel. When separation of the benzene layer was complete, the aqueous layer was withdrawn and warmed on the steam-bath to approximately 60°. After several minutes crystals separated, and when no more appeared, the mixture was cooled, the crystals filtered off, and washed well with water. Recrystallized from alcohol or benzene-petroleum ether, the product separates in plates which melt at 158–158.5°.

Anal. Calcd. for $\text{C}_{17}\text{H}_{14}$: C, 93.58; H, 6.48; mol. wt., 218. Found: C, 93.69, 93.64; H, 6.64, 6.60; mol. wt., (from neutralization equivalent of picrate), 214, 218, 212, 216, 220; (by ebullioscopic method in benzene), 231, 222, 227, 211, 207; (by Rast camphor method), 206, 218.

The same compound was prepared by the method of Borsche and Menz.² This compound (m. p. 157.5–158°) when mixed with the one whose synthesis has been described above (m. p. 158–158.5°), melted 157.5–158.0°.

Fluorescence of Solutions of 1,4-Diphenyl-1,3-cyclopentadiene.—Solutions of the diene in benzene, ethanol, methanol, acetic acid, dioxane, acetone, pyridine, and ethyl acetate possess a pronounced purple fluorescence when viewed in ordinary light. No fluorescence is observed, however, if the hydrocarbon is dissolved in carbon tetrachloride, and a drop of two of carbon tetrachloride added to any of the solutions mentioned above causes the fluorescence of the solution to disappear. The hydrocarbon dissolves in concentrated sulfuric acid to give a solution which is red to transmitted light and fluoresces blue. A few milligrams of the substance dissolved in a mixture of a ml. of chloroform and a ml. of glacial acetic acid takes on a yellow color which slowly becomes green when a few drops of concentrated sulfuric acid are added. Cyclopentadiene³ solutions are colored violet by the same treatment.

Picrate of 1,4-Diphenyl-1,3-cyclopentadiene.—Prepared from hot concentrated alcoholic solutions of the diene and picric acid, and crystallized from alcohol containing picric acid, the picrate forms dark purple laths resembling iodine in color, which melt with decomposition at 145–146°.

(3) Afranasiev, *Ind. Eng. Chem., Anal. Ed.*, **8**, 15 (1936).

Anal. Calcd. for $C_{20}H_{20}O_{14}N_6$: C, 51.48; H, 2.98. Found: C, 51.54, 51.25; H, 3.19, 3.02.

The same picrate was prepared from the diene made by the method of Borsche and Menz. This picrate melted with decomposition at 145–146° and showed no depression of decomposition range when mixed with the product prepared from diene made by way of ethyl β -benzoylpropionate and acetophenone.

Trinitrobenzolate of 1,4-Diphenyl-1,3-cyclopentadiene.—Prepared like the picrate above, this substance was recrystallized from alcohol; it forms brick-red plates which melt with decomposition at 151–152°.

Anal. Calcd. for $C_{20}H_{20}O_{12}N_6$: C, 54.04; H, 3.11. Found: C, 53.73, 53.56; H, 3.03, 3.17.

A mixed melting point of this material with the corresponding compound prepared from diene made by the method of Borsche and Menz showed no depression.

1,3-Diphenylcyclopentane.—Hydrogenation of the diene in alcoholic solution in the presence of palladium-charcoal catalyst yielded a product which boiled 140–141° at 3 mm. The product possessed a slight fluorescence due, probably, to presence of the diene. An attempt to remove unsaturated material by means of a sulfuric acid wash yielded a non-fluorescent product, but on redistillation this material became fluorescent; apparently some dehydrogenation took place during the distillation.

Anal. Calcd. for $C_{17}H_{18}$: C, 91.89; H, 8.17. Found: C, 91.95, 92.10; H, 8.39, 8.09.

The physical properties of this cyclopentane are: d^{25}_4 1.0196; n^{25}_D 1.5696; MR calcd., 71.68, obsd., 71.50.

The Anhydride of 1,4-Diphenyl-1,4-endomethylene-2-cyclohexene-5,6-dicarboxylic Acid.—One gram of 1,4-diphenyl-1,3-cyclopentadiene and 0.5 g. of maleic anhydride were dissolved in benzene and the solution warmed on the steam-bath for about an hour. When the benzene solution was cooled, the addition product crystallized; after recrystallization from benzene from which it forms lath-like crystals, the substance melted at 154°.

Anal. Calcd. for $C_{21}H_{18}O_3$: C, 79.75; H, 5.10. Found: C, 79.77, 79.79; H, 5.34, 5.34.

The addition product gives no fluorescence in benzene unless the solution is warmed. In concentrated sulfuric acid it gives the same fluorescence as 1,4-diphenyl-1,3-cyclopentadiene. The fluorescence unquestionably is caused by dissociation of the addition product.

1,3-Diphenyl-4-carboxy-1,3-cyclopentadiene.—This acid was isolated from the aqueous layer of a condensation involving ethyl β -benzoylpropionate, acetophenone, and sodium ethoxide. The aqueous layer obtained in working up the reaction products was not heated, according to the usual practice in preparing the diene, but was cooled in an ice-bath and acidified slowly by means of acetic acid. The flocculent precipitate which resulted from this treatment was concentrated by centrifugation, and separated from the supernatant liquid by decantation. Recrystallization of the product from benzene yielded a compound which crystallized from benzene in fine, colorless needles which melted 157–158°. The oblique extinction of these crystals serves to differentiate them from the other compounds examined.

Anal. Calcd. for $C_{18}H_{14}O_2$: C, 82.44; H, 5.39. Found: C, 82.34, 82.29; H, 5.57, 5.51.

The acid is soluble in dilute sodium hydroxide, in sodium bicarbonate, and in benzene *without fluorescence*. When the acid was warmed in dilute sodium hydroxide for a time on the steam-bath, it was converted practically quantitatively into 1,4-diphenyl-1,3-cyclopentadiene. Recrystallization of the acid from hot alcohol also yields the diene. Diene samples obtained by warming the sodium salt of the acid in dilute alkali and by recrystallization from alcohol were shown by analysis to possess the expected composition.

1-Phenyl-4-(*p*)-tolyl-1,3-cyclopentadiene.—This substance was prepared by a method quite similar to the one described above starting (1) with ethyl β -benzoylpropionate and methyl *p*-tolyl ketone and (2) with ethyl β -*p*-toluylpropionate and acetophenone. The products were identical and a mixed melting point showed no depression.

Anal. Calcd. for $C_{18}H_{16}$: C, 93.06; H, 6.94. Found: C, 92.80, 93.24; H, 7.03, 7.16 (from cpd. prepared as in (1)).

This substance crystallizes from ethyl alcohol in colorless hexagons and melts at 153–153.5°. This diene causes a blue fluorescence of its benzene solutions, and its solution in concd. sulfuric acid fluoresces a dark green and is red to transmitted light.

The Anhydride of 1-Phenyl-4-*p*-tolyl-1,4-endomethylene-2-cyclohexene-5,6-dicarboxylic Acid.—This substance was prepared from diene made by both methods of the preceding paragraph. The product made by method (1) melted at 145.5–146°; that made by method (2) melted at 146–146.5°. A mixture of the two melted at 145.5–146°.

Anal. Calcd. for $C_{22}H_{18}O_3$: C, 79.96; H, 5.49. Found: C, 80.07, 80.04; H, 5.45, 5.67.

Trinitrobenzolate of 1-Phenyl-4-*p*-tolyl-1,3-cyclopentadiene.—This substance was prepared in the usual way using an alcoholic solution of the reactants. The compound possesses a deep carmine color and crystallizes in thin rectangular plates. Whether prepared by method (1) or (2), the compound melts at 145–146° with decomposition.

Anal. Calcd. for $C_{30}H_{22}O_{12}N_6$: C, 54.69; H, 3.37. Found: C, 54.92, 54.75; H, 3.29, 3.52.

1-Phenyl-4-*p*-xenyl-1,3-cyclopentadiene.—The method of preparation of this diene was similar to that used for the other dienes earlier described. The same product resulted regardless of whether the method of Borsche and Menz or our own method of synthesis was employed. This diene crystallizes from benzene in the form of yellow plates which melt at 217–218° with decomposition. Like the other dienes studied, this substance yields fluorescent solutions in organic solvents; its solution in sulfuric acid fluoresces brilliant green, and is red to transmitted light.

Anal. Calcd. for $C_{23}H_{18}$: C, 93.88; H, 6.12. Found: C, 93.49, 94.18; H, 6.28, 6.36.

Attempts to prepare a trinitrobenzolate and a picrate from this diene were unsuccessful. Although solutions of the hydrocarbon and the nitro compound deepened in color when warmed, the color disappeared when the solutions cooled. Evaporation of such a solution to dryness yielded a residue which resembled the picrate of 1,4-diphenyl-1,3-cyclopentadiene in appearance, but which could not be recrystallized.

Ozonolysis of 1,4-Diphenyl-1,3-cyclopentadiene.—The diene (1 g.) dissolved in chloroform, was allowed to react at -30° with an equivalent of ozone (2 moles) made from air. The resulting solution was treated with water and the chloroform removed by distillation. The insoluble residue was separated from the water by decantation, and dissolved in ether. After this ethereal solution had been washed several times with water, the ether was evaporated, and the residue treated with a solution of cupric acetate in absolute alcohol. A yellowish precipitate of the copper derivative of dibenzoylmethane formed immediately, was filtered off, and recrystallized from benzene; yield 45%; m. p. $296-302^{\circ}$ with decomposition (value given in literature: $294-307^{\circ}$ dec.). Dibenzoylmethane liberated from this copper derivative melted at $79-80^{\circ}$. This specimen melted at $79-80^{\circ}$ when mixed with a pure sample of dibenzoylmethane (m. p. $79-80^{\circ}$) prepared synthetically.

Preparation of the *p*-Nitrophenylosazone of Glyoxal.—The ozonide of 1,4-diphenyl-1,3-cyclopentadiene prepared as above was decomposed by adding its solution (chloroform) to a solution of sodium bisulfite; the chloroform was removed by distillation. The aqueous solution was extracted with ether and then treated with 1.4 g. of *p*-nitrophenylhydrazine and 3-4 ml. of glacial acetic acid. When

the mixture was warmed gently a flocculent red precipitate formed. The mixture was centrifuged, and the precipitate washed with water, and recrystallized from pyridine to constant melting range, $306-307^{\circ}$ with decomposition.

Anal. Calcd. for $C_{14}H_{12}O_4N_2$: C, 51.20; H, 3.69. Found: C, 51.30; H, 3.71.

Summary

1. The preparation of three 1,4-diaryl-1,3-cyclopentadienes by the condensation of methyl aryl ketones and β -arylpropionates in the presence of sodium ethoxide has been described.

2. A mechanism for these syntheses has been proposed and one of the intermediates isolated.

3. Several derivatives of these dienes have been described.

4. The structure of the so-called 1,3-diphenyl-1,3-cyclopentadiene of Borsche and Menz has been shown to be that of 1,4-diphenyl-1,3-cyclopentadiene.

COLLEGE PARK, MD.

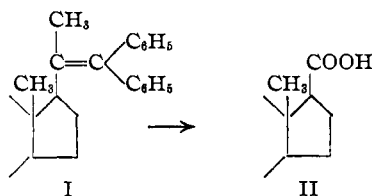
RECEIVED MARCH 16, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXII. etio-Cholanic Acids from the Pregnanediols

BY RUSSELL E. MARKER AND EUGENE L. WITTE

One method of preparation of C_{21} hydroxy steroid derivatives such as occur in the recently isolated cortical hormones involves the use of *etio*-cholanic acid derivatives.¹ The *etio*-cholanic acids have been prepared previously in low yields by the oxidation of the diphenyl derivatives (I) to



the corresponding acids (II),² or in better yield in the case of *etio*-desoxycholic acid³ by three steps involving the condensation of 3,12-diacetoxy-*etio*-cholanyl methyl ketone with benzaldehyde followed by ozonization and oxidation with periodic acid without the isolation of intermediates. In the present work it was found that the 21-benzal derivatives of the isomeric pregnanol-3-one-20

acetates could be oxidized directly with chromic anhydride to give the correspondingly substituted *etio*-cholanic acids in good yield. Since it has been shown previously⁴ that the isomeric pregnanol-3-one-20 compounds can be obtained from the pregnanediols, and since the 21-benzal derivatives are readily prepared from the former compound in good yield, this method makes the conversion of the pregnanediols to the *etio*-cholanic acid a practical one.

The condensation of benzaldehyde with pregnanol-3(α)-one-20 (III) using sodium ethylate takes place very readily at room temperature and gives an excellent yield of the 21-benzal derivative (IV). This product on acetylation formed the acetate which could be oxidized with chromic anhydride in acetic acid to give approximately 70% of the acetate of *etio*-lithocholic acid (V). Hydrolysis gave the free *etio*-lithocholic acid and oxidation of this substance yielded 3-keto-*etio*-cholanic acid. The melting points of these acids are in accord with those of the same acids prepared by Sawlewicz and Reichstein.²

(1) Steiger and Reichstein, *Helv. Chim. Acta*, **20**, 1164 (1937).

(2) Palmer, von Werder, Honigmann and Heyns, *Ber.*, **68**, 1814 (1935); Sawlewicz and Reichstein, *Helv. Chim. Acta*, **20**, 949 (1937); Steiger and Reichstein, *ibid.*, **20**, 1040 (1937).

(3) Hoehn and Mason, *THIS JOURNAL*, **60**, 1493 (1938).

(4) Marker, Kamm and Jones, *THIS JOURNAL*, **59**, 1595 (1937); Marker, Kamm and Witte, *ibid.*, **59**, 1841 (1937).