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The Thermal Isomerization of *allo*-Ocimene

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The structures of α- and β-pyronene, obtained by the pyrolysis of α-pinene, have been elucidated by Dupont and Dulou,[1] who postulated that these compounds were formed directly from α-pinene by the fission of a bond in the cyclobutane ring. Goldblatt and Palkin[2] have shown, however, that the pyronenes are formed by the recyclization of *allo*-ocimene, one of the principal products obtained in α-pinene pyrolysis. The presence of other hydrocarbons in the *allo*-ocimene pyrolysate was noted by these authors. The purpose of this work has been to identify these other products of *allo*-ocimene pyrolysis.

The method of attack was fractional distillation of the pyrolysate, determination of the physical properties of the individual fractions, and chemical investigation of those fractions which seemed to represent individual components in the highest degree of purity. The ultraviolet absorption spectra were found to be quite useful in this study. Almost every fraction exhibited a maximum absorption in the range from 260–265 millimicrons. The maximum extinction coefficient ($\alpha = E^{g./l.}_{1 cm.}$) for this wave length is plotted in Fig. 1, together with boiling point (at 20 mm.), refractive index, and density, as a function of the weight per cent. of the charge distilled. The absorption characteristics, together with the reactivity toward dienophiles, suggest that the pyrolysis mixture consists largely of conjugated cyclohexadienes, and this has been confirmed by the chemical investigation of the various fractions.

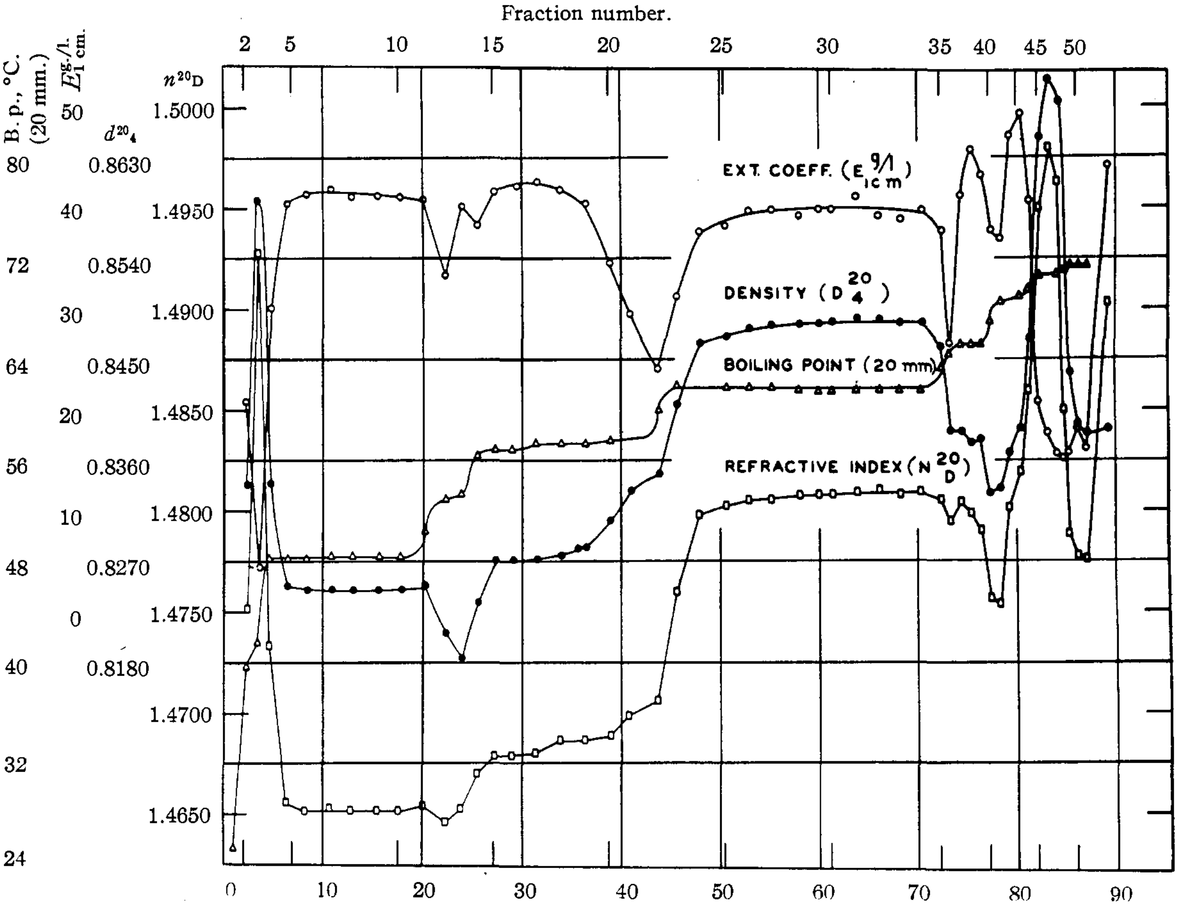

Fig. 1.—Fractional distillation of pyrolysis product from *allo*-ocimene.

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[1] Dupont and Dulou, *Atti X congr. intern.*, **3**, 123-129, 129-139 (1939).

[2] Goldblatt and Palkin, THIS JOURNAL, **66**, 655 (1944).

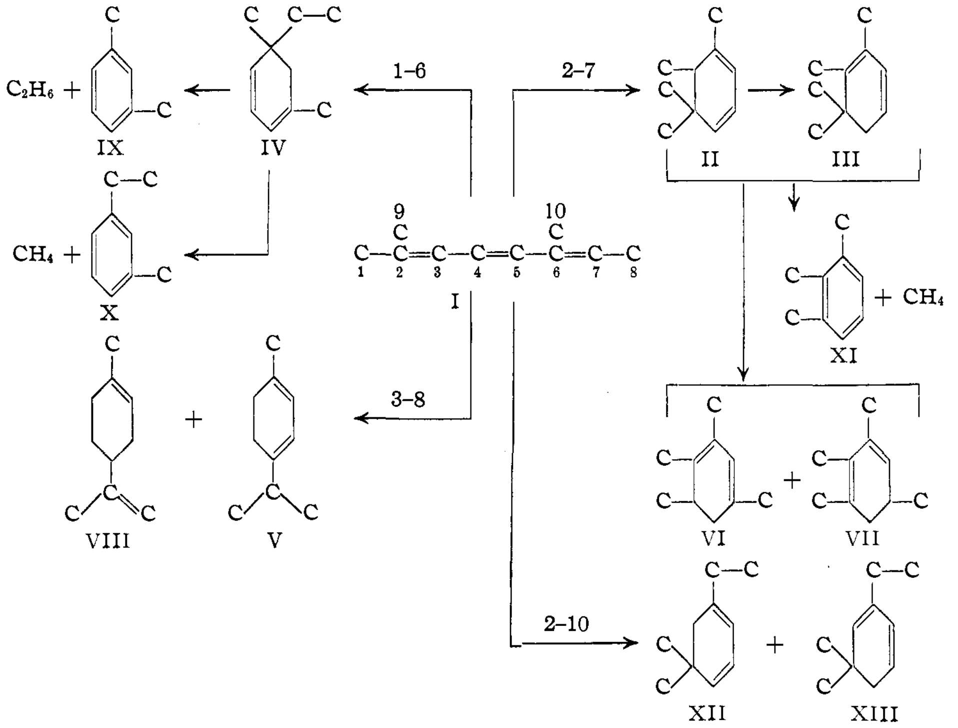

Fig. 2.—*allo*-Ocimene and products of pyrolysis.

In addition to α- and β-pyronene, six other conjugated cyclohexadienes, one non-conjugated terpene, and three aromatic constituents have been identified among the products of pyrolysis of *allo*-ocimene I. The three major constituents are 1,1,2,3-tetramethyl-3,5-cyclohexadiene (α-pyronene, II) (16%), 1,1,2,3-tetramethyl-2,4-cyclohexadiene (β-pyronene, III) (29%), and a new component (19%), which was found to be 1,3-dimethyl-1-ethyl-3,5-cyclohexadiene, IV. The minor constituents identified are α-terpinene, V (4%), 1,2,3,5-tetramethyl-2,4-cyclohexadiene, VI (4%), hemimellitene, XI (3%), 1,2,3,5-tetramethyl-1,3-cyclohexadiene, VII, 1,1-dimethyl-3-ethyl-3,5-cyclohexadiene, XII, and *m*-xylene, IX (1 to 2% each), *m*-ethyltoluene, X, and 1,1-dimethyl-3-ethyl-2,4-cyclohexadiene, XIII (less than 1% each) and dipentene, VIII (trace).

Although the major components can all be accounted for by the direct cyclization of *allo*-ocimene, it is probable that some secondary reaction is involved. It has been shown in this work, for example, that α-pyronene can be converted to β-pyronene by pyrolysis in the liquid phase. Therefore, it seems likely that some, if not all, of the β-pyronene present in the *allo*-ocimene pyrolysate is due to isomerization of α-pyronene.

To account for the minor components it is necessary to postulate some other molecular modification, either before, during, or after cyclization. In the case of α-terpinene, it seems possible that the cyclization of *allo*-ocimene from the 3 to the 8 position has occurred to form the unstable terpene α-phellandrene, which was then converted to α-terpinene by a rearrangement of the double bonds. It is known that α-phellandrene rearranges in the presence of acid catalysts to produce α-terpinene along with γ-terpinene and a diterpene.[3] Figure 2 shows the compounds identified and a possible mechanism of formation from *allo*-ocimene.

The principal reaction used in the study of the structures of the cyclohexadiene components was the Diels–Alder reaction with the dimethyl ester of acetylenedicarboxylic acid. Alder and Rickert[4] found that the adducts of the diethyl ester of acetylenedicarboxylic acid with cyclohexadienes decompose on heating to give ethylene and the diethyl ester of phthalic acid or homologs of these compounds, depending upon the cyclohexadiene used. They treated the diethyl ester with α-terpinene at 160–180°[5] to obtain ethylene and the diethyl ester of 3-methyl-6-isopropylphthalic acid. Dupont and Dulou[1] used the dimethyl ester of acetylenedicarboxylic acid in their study of the pyronenes. With α-pyronene and the dienophile they obtained 2-methyl-2-butene and 3-methylphthalic ester, and with β-pyronene they obtained isobutylene and 3,4-dimethylphthalic ester. They identified the gaseous products through the Raman spectra of the bromides.

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[3] Carter, Smith and Read, *J. Soc. Chem. Ind.*, **44**, 543T–547T (1925); Wallach, *Ann.*, **239**, 44 (1887); **252**, 102 (1889).

[4] Alder and Rickert, *ibid.*, **524**, 184 (1936).

[5] Alder and Rickert, *Ber.*, **70B**, 1364 (1937).

In this work the reaction with the dimethyl ester of acetylenedicarboxylic acid was repeated with the pyronenes and was applied to the identification of α-terpinene and the determination of the structure of the previously unknown cyclohexadienes. The type reaction, using 1,3-dimethyl-1-ethyl-3,5-cyclohexadiene as an example, is illustrated in Fig. 3. The decomposition products obtained with α- and β-pyronenes were the same as those reported by Dupont and Dulou.[1] The isobutylene obtained from β-pyronene was identified by reaction with phenol in the presence of sulfuric acid to give 4-*t*-butylphenol.[6] The dimethyl ester of 3,4-dimethylphthalic acid, m. p. 57.5–58.5°, was identified by conversion to the acid and the anhydride. The melting points reported in the literature for 3,4-dimethylphthalic acid are at variance with each other as well as with the value reported here (m. p. 177–178° with decomposition). de Diesbach and von der Weid[7] reported the compound to melt at 201° whereas Dupont and Dulou[1] reported the melting point to be 150°. Because of this discrepancy the acid was oxidized in a sealed tube with dilute nitric acid to give 1,2,3,4-tetracarboxybenzene which was identified through the tetramethyl ester, m. p. 129–130.5°, which is in agreement with that reported in the literature. Contrary to the findings of Smith and Carlson[8] this ester did not acquire a purple color on long standing under ordinary light. The 3,4-dimethylphthalic acid was also converted to 3,4-dimethylbenzoic acid by heating in a sealed tube at 225–250° with copper powder. The 2-methyl-2-butene obtained from α-pyronene was identified by the physical properties and by its reaction with phenol in the presence of sulfuric acid to form 4-*t*-amylphenol.[6] (2-Methyl-2-butene cannot be distinguished from 2-methyl-1-butene by the phenol reaction alone since the same adduct is obtained with both.) The dimethyl ester of 3-methylphthalic acid, m. p. 43–44°, was identified through the acid and anhydride.

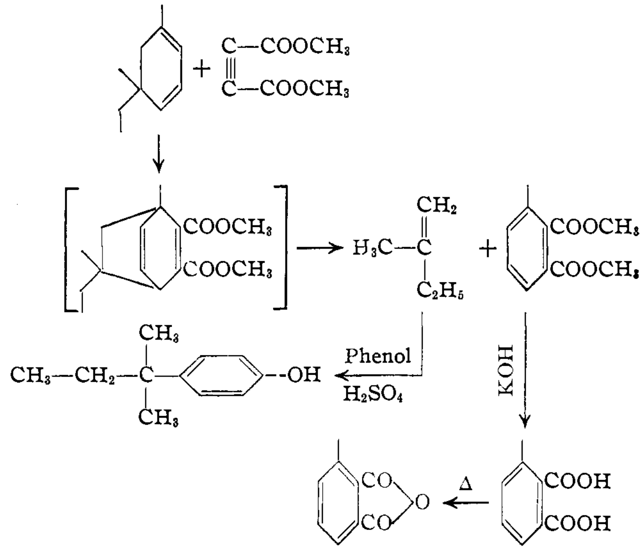

Fig. 3.—Reaction products from 1,3-dimethyl-1-ethyl-3,5-cyclohexadiene and dimethyl acetylenedicarboxylate.

1,3-Dimethyl-1-ethyl-3,5-cyclohexadiene when reacting with the acetylenedicarboxylic ester gave 2-methyl-1-butene, which was identified through the physical constants and the formation of 4-*t*-amylphenol, and the dimethyl ester of 3-methylphthalic acid, identical with the ester obtained from α-pyronene. Only two cyclohexadienes would be expected to yield these products, namely, 1,3-dimethyl-1-ethyl-3,5-cyclohexadiene and 1,2-dimethyl-1-ethyl-2,4-cyclohexadiene. Of these, the former was indicated by dealkanation over platinum to give *m*-xylene.

α-Terpinene was identified through various derivatives with further confirmation through the reaction with dimethyl acetylenedicarboxylate. Ethylene and a dimethyl ester which gave the same acid anhydride (3-methyl-6-isopropylphthalic anhydride) as that obtained by Alder and Rickert,[5] were obtained.

The position of the methyl groups in the two 1,2,3,5-tetramethylcyclohexadienes was established by disproportionation with a palladium–charcoal catalyst or dehydrogenation over a platinum on alumina catalyst to give 1,2,3,5-tetramethylbenzene. Both compounds gave propylene with dimethyl acetylenedicarboxylate, but they gave trimethylphthalic acids (established by oxidation to pentacarboxybenzene) which were not identical. The structure of 1,2,3,5-tetramethyl-1,3-cyclohexadiene was then established by decarboxylation of the trimethylphthalic acid obtained from it with moist copper powder to give 3,4,5-trimethylbenzoic acid. The other trimethylphthalic acid could not be decarboxylated by the procedure used; but since there are only two isomeric trimethylphthalic acids, it must be 3,4,6-trimethylphthalic acid. This, therefore, identifies the other hydrocarbon isomer as 1,2,3,5-tetramethyl-2,4-cyclohexadiene.

1,2,3,5-Tetramethyl-1,3-cyclohexadiene was not obtained in pure form, but occurred in solution with hemimellitene (1,2,3-trimethylbenzene), and was also contaminated with a small amount of dipentene in at least one fraction boiling at 71° (fraction 48). All attempts to separate the diene from the other components in pure form were unsuccessful. The presence of the 1,2,3,5-tetramethylcyclohexadienes in the pyrolysis mixture can be satisfactorily accounted for by postulating a 1,3- rearrangement of one of the geminal methyl groups in α- and/or β-pyronene

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(6) Parker and Goldblatt, *Anal. Chem.*, **21**, 807 (1949).

(7) de Diesbach and von der Weid, *Helv. Chim. Acta*, **10**, 887 (1927).

(8) Smith and Carlson, THIS JOURNAL, **61**, 289-290 (1939).

accompanied by the appropriate redistribution of hydrogen atoms and electrons.

Although no crystalline maleic anhydride or naphthoquinone adducts were obtained from the fractions distilling in the range 50–53°, the ultraviolet absorption spectra and other physical properties indicate the presence of two or more conjugated components in these fractions. By refractionating a composite sample of these fractions at a reflux ratio of 100 to 1 it was possible to get a partial separation and then to establish the presence of the compounds 1,1-dimethyl-3-ethyl-3,5-cyclohexadiene and 1,1-dimethyl-3-ethyl-2,4-cyclohexadiene. Both of these compounds reacted with the dimethyl ester of acetylenedicarboxylic acid to give isobutylene and the dimethyl ester of an ethylphthalic acid. The first yielded the ester of 3-ethylphthalic and the second the ester of 4-ethylphthalic acid. On demethanation over platinum on alumina in an atmosphere of hydrogen both dienes gave *m*-ethyltoluene thus completely establishing the structure of these two components. The presence of the two 1,1-dimethyl-3-ethylcyclohexadienes can be accounted for by cyclization of *allo*-ocimene through the 2 and 10 positions followed by rearrangement of the double bonds to the two possible conjugated positions inside the ring.

Reaction of the hemimellitene-cyclohexadiene mixture with a dienophile, such as maleic anhydride followed by steam distillation, gave about 60% yield of the aromatic constituent, which was identified through the sulfonamide. Two other aromatic components were isolated in a similar fashion. *m*-Xylene, which was indicated by the physical properties, was found in one fraction boiling at 41° (fraction 3) to the extent of about 90%. It was identified through the trinitro derivative. 1-Methyl-3-ethylbenzene was found in an amount of about 10% in a fraction boiling at 60° (fraction 22). It was also identified through the trinitro derivative. The presence of the aromatic components can be readily accounted for by the dealkanation of the three major components. Demethanation of α- and/or β-pyronene would be expected to yield hemimellitene and demethanation and deëthanation of 1,3-dimethyl-1-ethyl-3,5-cyclohexadiene should give *m*-ethyltoluene and *m*-xylene, respectively.

Experimental

Pyrolysis of *allo*-Ocimene.—The *allo*-ocimene was purified by freezing it in a solid carbon dioxide refrigerator and then allowing it to melt slowly. The supernatant liquid was removed continuously with a filter stick until the temperature had increased to about −28°. The residue was then allowed to melt. Three batches so treated were combined to give 1646 g. of material, $n^{26.2}\text{D}$ 1.5410. $d^{25.8}_4$ 0.8043.

This material was then pyrolyzed in the vapor phase using the method and apparatus of Goldblatt and Palkin.[2] The pyrolysis tube was maintained at 443 ± 1° at the center with a throughput of 3.9 g. per minute. The contact time was, therefore, approximately eight seconds. The pyrolysate collected (1409 g.) had the following constants: $n^{25.2}\text{D}$ 1.4763, $d^{25.3}_4$ 0.8317. This was carefully fractionated at 20 mm. pressure in a Podbielniak type column containing six feet of heligrid packing. The distillation was carried out with a reflux ratio of 50:1 and a throughput of about 250 ml. per hour. Distillation temperatures were obtained using an iron–constantan thermocouple and an automatic recording potentiometer. The pressure was maintained to ±0.2 mm. with a triethylene glycol manostat.[9] The refractive index, density, and ultraviolet absorption spectrum in isoöctane were determined for each fraction (Fig. 1).

1,4-Naphthoquinone Adducts.—Several fractions (nos. 8, 12, 17, 19, 22, 28, 36, 38, 40, 43, 47 and 50) which seemed to represent individual components, were treated with 1,4-naphthoquinone. One gram of the quinone was heated for forty-five minutes at 150–155° with an excess of the hydrocarbon (2 ml.). After heating, the excess terpene was removed from the dark opaque mixture by steam distillation and the residue was extracted with ether. The ether solution was dried over anhydrous sodium sulfate, and the ether evaporated. In those cases in which crystals did not form, the residues were dissolved in petroleum ether and allowed to stand until the products crystallized. No crystalline products were obtained with fractions 12, 22, 36, 40 and 50. Fraction 19 gave an adduct identical with that of fraction 17. The crude crystals, when obtained, were pressed on a porous plate to dry. The adducts were purified by recrystallization from petroleum ether and then ethanol. Table I gives the yield of crude material, based on the naphthoquinone, along with melting points of the crude and the recrystallized derivatives. Mixed melting points were taken of those adducts melting close together. It was found that the adduct of fraction 17 depresses the melting point of the adduct of fraction 8, and the adduct of fraction 28 depresses the melting point of the adduct of fraction 38. Carbon and hydrogen analysis of all these compounds showed them to be adducts of isomeric $C_{10}H_{16}$ hydrocarbons.

TABLE I

NAPHTHOQUINONE ADDUCTS OF CYCLOHEXADIENES

Cyclohexadiene			Naphthoquinone adduct		
Compound	Fraction	B. p. (20 mm.), °C.	Yield, %	Melting point, °C. Crude	Melting point, °C. Pure
α-Pyronene	8	48.4	40	88–118	129–130
1,3-Dimethyl-1-ethyl-3,5-cyclohexadiene	17	56.9–57.4	33	101–118	127–128
β-Pyronene	28	61.6	98	90–94	96–97
1,2,3,5-Tetramethyl-2,4-cyclohexadiene	38	65.2	43	89–97	94–95
α-Terpinene	43	68.6–69.0	31	91–97	100-101
1,2,3,5-Tetramethyl-1,3-cyclohexadiene	47	70.8	27	85–93	114–115

Reaction with the Dimethyl Ester of Acetylenedicarboxylic Acid.—The reactions of the terpene fractions with dimethyl acetylenedicarboxylate were carried out in a 50-ml. flask, heated in an oil-bath and fitted by means of a ground glass joint with an air condenser (380 mm. long × 8 mm. o. d.). A 4-mm. (o. d.) tube extended down through the condenser into the flask for the purpose of sweeping out residual gas with air. A side arm at the top of the condenser was connected by means of a glass tube and rubber connections to a water-cooled condenser which was connected at the lower end to a calibrated, ice-cooled, liquid trap. A side arm of the liquid trap was connected to a bottle filled with water which served as a gas trap. The volume of gas liberated was determined by the amount of water displaced.

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[9] Runckel and Oldroyd, *Ind. Eng. Chem., Anal. Ed.*, **18**, 80 (1946).

(A) **Identification and Proof of Structure of α-Pyronene (II).**—Fraction 9, b. p. 48.4° (20 mm.) (5 g.), was heated two and one-half hours with 5.2 g. of dimethyl acetylenedicarboxylate with the temperature of the oil-bath increasing slowly from 100–160°. A vigorous evolution of gas began when the bath temperature had reached 130° and within thirty minutes, 2.1 ml. of liquid had collected in the trap. A total of 2.9 ml. (at 0°) of volatile liquid was collected during the reaction. This liquid was distilled and the center cut ($^3/_4$ of the total) was indicated by the physical constants (b. p. 38.6°, $n^{20.1}\text{D}$ 1.3878[10] to be 2-methyl-2-butene. The olefin was further identified by formation of the 4-*t*-amylphenol derivative.[6] A sample of this volatile degradation product (1.72 g., $n^{20}\text{D}$ 1.3880) was distilled into an absorption tube containing 2.1 ml. of phenol and 0.2 g. of 75% sulfuric acid. This mixture was then heated one hour at 125° and poured into 20 ml. of water. Nearly colorless needles of 4-*t*-amylphenol were obtained (2.74 g., m. p. 83–91°) which after recrystallization twice from petroleum ether melted at 94–96° and did not depress the melting point of the corresponding derivative prepared from an authentic sample of 2-methyl-2-butene.

The non-volatile residue from the thermal decomposition was found to consist chiefly of the dimethyl ester of 3-methylphthalic acid. It was triturated with hexane until crystallization occurred. The crystals were filtered and recrystallized from benzene and hexane to yield 3.9 g. of colorless crystals (m. p. 42–46°). After recrystallization once more from benzene and hexane, and twice from alcohol and water, colorless needles were obtained (m. p. 42.5–44°).

Anal. Calcd. for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.33, 63.11; H, 5.89, 5.80.

Saponification by refluxing with alcohol and potassium hydroxide gave an acid which after recrystallization three times from ethyl acetate, melted at 158°[11] with decomposition.

Anal. Calcd. for $C_9H_8O_4$: C, 60.00; H, 4.47; neutral equivalent, 90.1. Found: C, 59.62, 59.70; H, 4.43, 4.59; neutral equivalent, 91.2.

Further confirmation was obtained by conversion to the anhydride. The acid on heating at 160–170° for fifteen minutes and sublimation at 110–120° and 2–4 mm. pressure gave almost colorless crystals melting at 110–115°. On recrystallization twice from benzene the anhydride was obtained in the form of long colorless needles, m. p. 118–119°. 3-Methylphthalic anhydride was reported by Jurgens[11] to melt at 114–115°.

Anal. Calcd. for $C_9H_6O_3$: C, 66.67; H, 3.73. Found: C, 66.64, 66.43; H, 4.28, 4.33.

(B) **Identification and Proof of Structure of 1,3-Dimethyl-1-ethyl-3,5-cyclohexadiene (IV).**—Fraction 19, b. p. 57.4° (20 mm.) (5.0 g.) was treated with 5.2 g. of dimethyl acetylenedicarboxylate by the method described for fraction 9. The reaction became quite vigorous at 120° (bath temperature) and it was necessary to remove the flask from the bath to reduce the rate of reaction. Two ml. of volatile liquid had distilled over within five minutes, and the flask was heated up to 150° and held at that temperature about 1 hour until no further increase in volume of the volatile fraction was observable. The physical constants indicated this volatile component (3.3 ml. at 0°) to be 2-methyl-1-butene. It was distilled to give two fractions as follows: fraction 1 ($^2/_3$ of total), b. p. 31.2°, $n^{20}\text{D}$ 1.3780; fraction 2, b. p. 31.5°, $n^{20}\text{D}$ 1.3785. 2-Methyl-1-butene has the constants: b. p. 31.0°, $n^{20}\text{D}$ 1.3777.[10] This was further identified by conversion to the phenol derivative.[6] A sample of the low boiling material (1.56 g., $n^{20}\text{D}$ 1.3781, was treated with 2.2 ml. of phenol containing 0.2 g. of 75% sulfuric acid by the procedure described above under the identification and proof of structure of α-pyronene. The 4-*t*-amylphenol (2.60 g., m. p. 82–90°) obtained was recrystallized twice from petroleum ether. It then melted at 94–96° and did not depress the melting point of an authentic sample.

The non-volatile residue from the thermal decomposition was found to consist chiefly of the dimethyl ester of 3-methylphthalic acid. It was cooled on solid carbon dioxide and seeded with the dimethyl ester obtained from α-pyronene to yield a crop of crystals, which after recrystallization from benzene and hexane, weighed 2.6 g. (m. p. 41–43.5°). Recrystallized again from ethanol, the compound melted at 43–44° and did not depress the melting point of the ester obtained from α-pyronene. The acid and anhydride obtained from this ester were also identical with the acid and anhydride obtained from α-pyronene.

The cyclohexadiene (13.6 g.) was hydrogenated by shaking with 25 ml. of acetic acid and 0.10 g. of platinum oxide under a hydrogen pressure of 30 to 20 pounds. Hydrogen absorption had virtually ceased within fifteen minutes, although only 81% of the theoretical amount of hydrogen was absorbed. The catalyst was filtered off and the two liquid phases which separated during the hydrogenation separated. The upper layer was washed with water and dried over calcium chloride (5.24 g., $n^{20}\text{D}$ 1.4458). The acetic acid layer was diluted with 100 ml. of water and the upper phase which separated was removed, washed and dried as before (5.73 g., $n^{20}\text{D}$ 1.4466). The two products were combined. Two batches of material hydrogenated in this way were combined and the composite sample (22.1 g.) washed three times with cold concentrated sulfuric acid and then washed with water and dried over calcium chloride (17.7 g., $n^{20}\text{D}$ 1.4443). This material was distilled through a short Vigreux column and the center cut (10.9 g., b. p. 161–165°, $n^{20}\text{D}$ 1.4412) taken for dehydrogenation. The physical constants of this compound are in good agreement with those reported by Lebedev[12] for 1,3-dimethyl-1-ethylcyclohexane. The center cut was dehydrogenated over a platinum on alumina catalyst at 310–330° by the method of Pines and Ipatieff.[13a] The 10.9 g. of starting material gave 8.2 g. of dehydrogenated product ($n^{20}\text{D}$ 1.4761) and 3720 ml. of gaseous product (at 28°) which was not analyzed. The liquid product was dissolved in 1.5 vols. of pentane and extracted at the temperature of solid carbon dioxide with 2.5 vols. of liquid sulfur dioxide.[13b] The sulfur dioxide layer was evaporated and the residue washed with dilute alkali, then water, and dried over calcium chloride. After drying the liquid (3.4 g., $n^{20}\text{D}$ 1.4977) was distilled through a short Vigreux column. Fraction 1 (1.7 g., b. p. 129–134°, $n^{20}\text{D}$ 1.4962) was nitrated to yield a derivative melting at 182–184° which did not depress the melting point of trinitro-*m*-xylene.

(C) **Identification and Proof of Structure of β-Pyronene (III).**—Fraction 27, b. p. 61.8° (20 mm.) (5.0 g.), was treated as previously described with dimethyl acetylenedicarboxylate. The mixture was heated to 125° and held between 125 and 130° until there was no further evolution of gas (about two hours). The reaction became vigorous at 116° and was almost complete in less than five minutes. No liquid collected in the trap, but 675 ml. of gas was collected. The reaction flask was swept out with 100 ml. of air which was added to the gaseous product.

This gaseous degradation product was then absorbed in liquid phenol, containing sulfuric acid, in a manner similar to that previously described for the other volatile degradation products. This mixture was heated as before to give a good yield of 4-*t*-butylphenol, m. p. 98–100°. Recrystallization from petroleum ether did not alter the melting point. The material did not depress the melting point of an authentic sample. On standing, the residue from the thermal decomposition crystallized. The oily

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[10] Sherrill and Walter, THIS JOURNAL, **58**, 744 (1936).

[11] The melting point of 3-methylphthalic acid is given in the literature variously as 154° (Jurgens, *Ber.*, **40**, 4413 (1907), 154-155° (Dupont and Dulou)[1] and 157° (Weiszberger and Kruber, *Ber.*, **52**, 351 (1919)).

[12] Lebedev, *J. Russ. Phys.-Chem. Soc.*, **45**, 1316; *Chem. Zentr.*, **85**, I, 1406 (1914).

[13] (a) Pines and Ipatieff, THIS JOURNAL, **61**, 1077 (1939); (b) **69**, 1948 (1947).

crystals were pressed on porous plate to dry and recrystallized from hexane to yield 5.5 g. of colorless plates, m. p. 56–57°, which was found to be the dimethyl ester of 3,4-dimethylphthalic acid. After recrystallizing three times from hexane the compound melted at 57.5–58.5°.

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 65.03, 64.85; H, 6.27, 6.36.

Four grams of the dimethyl ester was saponified with potassium hydroxide in alcohol to yield 3.1 g. of the acid (m. p. 158–160° with decomposition). After recrystallizing twice from water, the acid melted at 177–178° with decomposition.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19; neutral equivalent, 97.1. Found: C, 62.09, 62.06; H, 5.31, 5.35; neutral equivalent, 97.9.

Two grams of the acid was heated thirty minutes at 180–185° and sublimed at 115° and 2 mm. pressure to yield 1.7 g. of 3,4-dimethylphthalic anhydride (m. p. 125–127°).

Anal. Calcd. for $C_{10}H_8O_3$: C, 68.18; H, 4.58. Found: C, 68.28, 68.48; H, 4.64, 4.89.

The 3,4-dimethylphthalic anhydride (1.4 g.) was oxidized by heating in a sealed tube at 145–150° for seven hours with 1.5 ml. of fuming nitric acid and 0.75 ml. of water.[14] Cooling the reaction mixture and filtering gave 1.15 g. of crystalline 1,2,3,4-tetracarboxybenzene, m. p. 230–245°. After recrystallization twice from dilute nitric acid the acid melted at 233–245°.

Anal. Calcd. for $C_{10}H_6O_8$: neutral equivalent, 63.5. Found: neutral equivalent, 64.6, 64.1.

The 1,2,3,4-tetracarboxybenzene (0.44 g.) was neutralized in aqueous solution with sodium hydroxide and this solution was treated with 1.5 g. of silver nitrate in water. The silver salt which precipitated was filtered off, dried (1.25 g.), and refluxed in benzene for four hours with an excess of methyl iodide. The benzene solution was filtered and concentrated. On cooling, the tetramethyl ester crystallized out. Recrystallization from methanol gave colorless needles, 0.22 g., m. p. 129–130.5°.

Anal. Calcd. for $C_{14}H_{14}O_8$: C, 54.20; H, 4.55. Found: C, 54.07, 54.08; H, 4.54, 4.61.

3,4-Dimethylphthalic acid (0.5 g.) was thoroughly mixed with an equal weight of copper powder, and the mixture moistened with a few drops of water and sealed in a glass tube. The tube was then placed in a small stainless steel bomb with a few ml. of water and the bomb sealed. The bomb was then heated in a liquid bath at 233–236° (bath temperature) for four hours. The bomb was cooled and opened and the sealed tube cautiously removed and opened. An appreciable gas pressure indicated that decarboxylation had occurred. The residue in the tube was extracted with 10% aqueous sodium hydroxide and the alkaline extract acidified to give 0.33 g. of crystalline material with a neutral equivalent of 130.5. The acid mixture was reprecipitated from alkaline solution and recrystallized twice from ethanol and water to give 0.07 g. of 3,4-dimethylbenzoic acid, m. p. 166–167.[15]

Anal. Calcd. for $C_9H_{10}O_2$: C, 71.98; H, 6.71; neutral equivalent, 150.2. Found: C, 72.18, 72.08; H, 6.89, 6.94; neutral equivalent, 150.6.

(D) Identification and Proof of Structure of 1,2,3,5-Tetramethyl-2,4-cyclohexadiene (VI).—The position of the methyl groups was established by disproportionation to 1,2,3,5-tetramethylbenzene. Fraction 39, b. p. 65.2° (20 mm.) (1.8 g.), was refluxed with 1.5 g. of palladium on charcoal catalyst (5% Pd), for twenty-four hours during which no appreciable amount of gas was evolved. The product was slowly distilled through an unpacked column, 7.5 mm. (i. d.) × 114 mm. long, and separated into seven fractions. The physical constants of the last fraction (0.23 g., b. p. 196°, m. p. −29 to −24°, $n^{20}\mathrm{D}$ 1.5105) indicate the compound to be 1,2,3,5-tetramethylbenzene. The last fraction on nitration gave a nitro derivative, m. p. 183–184°, which did not depress the melting point of the corresponding derivative prepared from an authentic sample of 1,2,3,5-tetramethylbenzene. The position of the double bonds was established by use of dimethyl acetylenedicarboxylate.

Fraction 38, b. p. 65.2° (20 mm.) (5.0 g.) was treated with dimethyl acetylenedicarboxylate. The mixture was heated at 115–120° for two hours to yield 722 ml. of gas but no volatile liquid. This gas was not absorbed readily by phenol and sulfuric acid, and was subsequently identified as propylene. It was completely absorbed by passing five times through 17 ml. of 87% sulfuric acid.[16] This acid solution was diluted to 50 ml. with water and distilled. The first fraction distilling (6 ml.) was salted with potassium carbonate whereupon 1.25 ml. of alcohol, $n^{22.1}\mathrm{D}$ 1.3780, separated. This alcohol (1.1 ml.) was then carefully distilled from calcium oxide to yield 0.71 g. of isopropyl alcohol, 0.91 ml., b. p. 82°, $n^{22.0}\mathrm{D}$ 1.3761, $d^{25.5}{}_4$ 0.7850. The phenyl urethan prepared from the alcohol melted at 87–88.5° and did not depress the melting point of the corresponding derivative prepared from an authentic sample of isopropyl alcohol. The non-volatile residue from the thermal decomposition was found to be the dimethyl ester of 3,4,6-trimethylphthalic acid. It crystallized on stirring, yielding 5.4 g. of colorless crystals, m. p. 48–52°. After recrystallization three times from petroleum ether, this compound melted at 54–55°.

Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.08; H, 6.83. Found: C, 66.06, 66.31; H, 6.84, 6.80.

The ester (5.04 g.) was saponified with potassium hydroxide in alcohol and an aqueous solution of the salt acidified with sulfuric acid to yield 4.23 g. of acid, m. p. 163° with decomposition; m. p. 125–128° after decomposition. Recrystallization of this acid from hot alcohol yielded the anhydride, m. p. 129–130°. The acid is so unstable toward dehydration that precipitation with hydrochloric acid from an aqueous solution of the potassium salt yields the anhydride directly.

Anal. Calcd. for the anhydride, $C_{11}H_{10}O_3$: C, 69.46; H, 5.30; neutral equivalent, 95.1. Found: C, 69.17, 69.19; H, 5.23, 5.27; neutral equivalent, 94.6, 95.0.

The anhydride was oxidized in a sealed tube at 145–150° with nitric acid by the procedure of Freund and Fleischer.[14] The oxidation product which was shown to be pentacarboxybenzene, recrystallized from water and nitric acid and dried *in vacuo* to constant weight, m. p. 235°, with decomposition.

Anal. Calcd. for $C_{11}H_6O_{10}$: C, 44.31; H, 2.03; neutral equivalent, 59.6. Found: C, 44.86, 44.99; H, 2.26, 2.31; neutral equivalent, 60.6.

The acid was converted to the pentamethyl ester by treating the silver salt with methyl iodide. The ester, after recrystallizing several times from methanol, melted at 148–149°.

Anal. Calcd. for $C_{16}H_{16}O_{10}$: C, 52.18; H, 4.38. Found: C, 52.15, 52.37; H, 4.48, 4.53.

(E) Identification of α-Terpinene.—Fraction 43, b. p. 69.0° (20 mm.), was shown to be α-terpinene by the preparation of several derivatives. Heating the terpene with an equivalent amount of maleic anhydride yielded the adduct which after recrystallization several times from petroleum ether, melted at 68-69°. The nitrosite, m. p. 153–154°, was prepared by the method of Macbeth, Smith and West[17] for the preparation of the nitrosite of α-phellandrene. The dihydrochloride prepared by the method of Wallach[18] melted at 51–53°, after recrystallization from petroleum ether and then from methanol.

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[14] Freund and Fleischer, *Ann.*, **411**, 26 (1916).

[15] (a) Fittig and Laubinger, *Ann.*, **151**, 275 (1869); (b) Jacobsen, *Ber.*, **17**, 2374 (1884); (c) Lellmann and Benz, *ibid.*, **24**, 2115 (1891).

[16] Tropsch and Mattox, *Ind. Eng. Chem.*, *Anal. Ed.*, **6**, 404 (1934); Davis and Quiggle, *ibid.*, **2**, 40 (1930).

[17] Macbeth, Smith and West, *J. Chem. Soc.*, 122 (1938).

[18] Wallach, *Ann.*, **350**, 144 (1906).

These melting points are in agreement with those found in the literature.[18,19,20]

The material was further identified by the reaction with the dimethyl ester of acetylenedicarboxylic acid.[5] Five grams of the fraction was heated by the usual procedure with dimethyl acetylenedicarboxylate at 130–160° for 2.5 hours, during which time 510 ml. of ethylene was liberated. The ethylene was identified by preparation of the dibromide. It was brominated by passing it repeatedly through 5 ml. of chloroform containing 1 ml. of bromine until all but 65 ml. had been absorbed. The chloroform solution was distilled and two fractions boiling above 100° were obtained (fraction 1, 1.05 g., $n^{19.4}\text{D}$ 1.5351; and 2, 0.79 g., $n^{19.3}\text{D}$ 1.5368). The material was redistilled and the best fraction further purified by repeatedly freezing, allowing it partly to melt, and removing the supernatant liquid with a filter stick until a small residue remained. This melted at 7–9° ($n^{20.1}\text{D}$ 1.5379) and when mixed with an authentic sample of ethylene bromide (m. p. 10°, $n^{20}\text{D}$ 1.5379), melted at 7–9.5°.

The non-volatile residue from thermal decomposition was distilled *in vacuo* to give 4.8 g. of an ester (b. p. 185–195° (20 mm.), $n^{19.6}\text{D}$ 1.5067) which failed to crystallize. The 4.8 g. was saponified with potassium hydroxide and the aqueous solution acidified with dilute hydrochloric acid to yield a precipitate which, after recrystallization from benzene and petroleum ether, gave 1.5 g. of 3-methyl-6-isopropylphthalic anhydride, m. p. 100–102°. After repeated recrystallization from benzene, the material melted at 102–103°.[5]

Anal. Calcd. for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.33, 70.18; H, 6.16, 5.79.

(F) Identification and Proof of Structure of 1,2,3,5-Tetramethyl-1,3-cyclohexadiene (VII).—The position of the methyl groups in 1,2,3,5-tetramethyl-1,3-cyclohexadiene was established by dehydrogenation to 1,2,3,5-tetramethylbenzene. It was necessary to hydrogenate the diene and extract with liquid sulfur dioxide to remove the aromatic material known to be present before carrying out the dehydrogenation. A composite sample (4.8 g.) of fractions 45 (33%, b. p. 70.6° (20 mm.), $n^{20}\text{D}$ 1.4950) and 47 (67%, b. p. 70.8° (20 mm.), $n^{20}\text{D}$ 1.4963) was hydrogenated in 15 ml. of ethanol containing 0.07 g. of platinum oxide. The hydrogenation (25.5° under a hydrogen pressure of 26 to 24.6 pounds above atmospheric pressure) conducted in a Parr hydrogenator was complete in twenty-five minutes after an absorption of 392 ml. (0.016 mole) of hydrogen. This indicates the presence of 23% diene in the sample. The alcoholic solution was diluted with water and extracted with pentane. The pentane solution was then dried over calcium chloride and extracted with liquid sulfur dioxide to remove the aromatic material. The pentane layer was washed with alkali, with water, and again dried. This solution (25 ml.) was then passed slowly through the platinum on alumina catalyst to dehydrogenate the cycloalkane constituent. The catalyst was maintained at 300–310° and the hydrocarbon mixture put through at an average rate of 0.17 ml. per minute. During the reaction 280 ml. (0.013 mole) of hydrogen (at standard conditions) was evolved. This represents about 50% conversion of the cycloalkane to the corresponding aromatic compound shown to be 1,2,3,5-tetramethylbenzene. The pentane was distilled off and the residue fractionated by distilling from an asbestos-filled micro flask similar to that used by Gettler, Niederl and Benedetti-Pichler.[21] The fractionating column was 60 mm. of 5 mm. (i. d.) tubing. The flask was heated in an oil-bath at 200–220°. A ring of distillate was allowed to climb slowly to the receiver, the flask was then removed from the bath, and the distillate was removed with a capillary pipet. The flask was again immersed and the procedure was repeated until no more distillate could be obtained. The last fraction (0.114 g., $n^{20}\text{D}$ 1.5026) was nitrated with fuming nitric and concentrated sulfuric acids to give almost colorless crystals of 4,6-dinitro-1,2,3,5-tetramethylbenzene, m. p. 182–183°. A mixed melting point with an authentic sample showed no depression.

The position of the double bonds was established by use of the dimethyl ester of acetylenedicarboxylic acid. Fraction 46, b. p. 70.7° (20 mm.), (5.2 g.) with 2.9 g. of dimethyl acetylenedicarboxylate was heated up to 150° and held between 150 and 160° for one and one-half hours during which time 333 ml. of propylene was liberated. The propylene was identified by absorption in 87% sulfuric acid, isolation of the resulting isopropyl alcohol and preparation of the phenylurethan as was described under the description of the identification of 1,2,3,5-tetramethyl-2,4-cyclohexadiene.

The non-volatile portion of the reaction residue was shown to consist largely of the dimethyl ester of 3,4,5-trimethylphthalic acid. It was steam-distilled to remove the aromatic component and the residue which crystallized on cooling was filtered and pressed on a porous plate to yield 3.0 g. of the ester, m. p. 110–115°. After several recrystallizations from benzene, small colorless prisms were obtained, m. p. 117–119°.

Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.08; H, 6.83. Found: C, 65.72, 65.65; H, 6.50, 6.74.

This ester (2.5 g.) was saponified with potassium hydroxide and an aqueous solution of the potassium salt neutralized with hydrochloric acid to yield 2.11 g. of fine crystalline material, m. p. 147–157°. Recrystallization from acetone gave crop 1, m. p. 195° with decomposition (0.6 g.), and crop 2, m. p. 168° with decomposition (0.8 g.). Both crops remelted after decomposition at 182–184°. When mixed, crops 1 and 2 melted at 190° with decomposition and remelted after decomposition at 183–185°. Crop 1, after again recrystallizing from acetone, melted at 211° with decomposition. The acid was heated above 200° and then sublimed *in vacuo*. The anhydride thus obtained after recrystallization from benzene, melted at 183–184°.

Anal. Calcd. for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.11, 69.45; H, 5.20, 5.30.

This anhydride was oxidized with nitric acid by the method described for 1,2,3,5-tetramethyl-2,4-cyclohexadiene. The oxidation product, which was found to be pentacarboxybenzene, after recrystallization twice from water and nitric acid, melted at 235° with decomposition and did not depress the melting point of the corresponding compound described under the identification and proof of structure of 1,2,3,5-tetramethyl-2,4-cyclohexadiene.

Anal. Calcd. for $C_{11}H_6O_{10}$: neutral equivalent, 59.6. Found: neutral equivalent, 61.4.

The pentamethyl ester prepared as before melted at 149–151° after recrystallization from benzene and hexane, and was identical with the pentamethyl ester described previously. The acid obtained from the thermal decomposition product, which was shown to be a trimethylphthalic acid by its oxidation to pentacarboxybenzene, was decarboxylated by heating in a sealed bomb at 235–245° for five hours with an equal weight of copper powder and enough water to wet the mixture. The product obtained by this procedure was found to be 3,4,5-trimethylbenzoic acid, m.p. 220–222°.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37; neutral equivalent, 164.2. Found: C, 73.15, 73.17; H, 7.49, 7.48; neutral equivalent, 163.7, 163.8.

(G) Identification and Proof of Structure of 1,1-Dimethyl-3-ethyl-3,5-cyclohexadiene (XII).—Preliminary work with the material distilling in the range 50–53° (fractions 12, 13, and 14) indicated that it was a gross mixture. Accordingly, these fractions were combined and refractionated at a reflux ratio of 100 to 1 in a semimicro Podbielniak column. 1,1-Dimethyl-3-ethyl-3,5-cyclohexadiene was identified in the higher boiling fractions thus obtained and 1,1-dimethyl-3-ethyl-2,4-cyclohexa-

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(19) Goodway and West, *J. Chem. Soc.*, 702 (1940).

(20) Wallach, *Ann.*, **239**, 35 (1887).

(21) Gettler, Niederl and Benedetti-Pichler, *Mikrochemie*, **11**, 174 (1932), as presented by Morton, "Laboratory Technique in Organic Chemistry," McGraw-Hill Book Company, Inc., New York, N. Y., 1938, p. 74.

diene (XIII) was identified in the lower boiling fractions.

A portion (0.5 g.) of a fraction distilling at 52.0° was treated with dimethyl acetylenedicarboxylate at 130–140°. The gas evolved was identified as isobutylene by formation of 4-*t*-butylphenol. The residue, identified as the dimethyl ester of 3-ethylphthalic acid, melted at 54–55° after two crystallizations from hexane.

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.98, 64.63; H, 6.51, 6.44.

The ester when saponified gave 3-ethylphthalic acid melting at 172° with decomposition.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19; neutral equivalent, 97.1. Found: C, 61.91, 61.72; H, 5.29, 5.24; neutral equivalent, 97.3, 97.9.

The acid when heated above its decomposition point and sublimed *in vacuo* gave 3-ethylphthalic anhydride which, after two recrystallizations from hexane, melted at 101–102°.

Anal. Calcd. for $C_{10}H_8O_3$: C, 68.18; H, 4.58; neutral equivalent, 88.1. Found: C, 68.09, 67.97; H, 4.50, 4.74; neutral equivalent, 88.5, 87.8.

The position of the ethyl group was established by oxidation of the acid to hemimellitic acid. A mixture 0.29 g. of the acid with 1.0 g. of 73% nitric acid was heated in a sealed tube for seven hours at 140°. From this oxidation there was obtained 0.20 g. of large colorless plates. After recrystallizing from water and drying at 105° this acid melted at 190° (with decomposition) and did not depress the melting point of an authentic sample of hemimellitic acid.

Anal. Calcd. for $C_9H_6O_6$: neutral equivalent, 70.0. Found: neutral equivalent, 70.7.

Another portion (1 ml.) of a fraction distilling at 52° was demethanated by mixing it in the vapor phase with hydrogen and passing the mixture through platinum on alumina catalyst at 350°. Most of the demethanated product (0.55 ml., $n^{20}_{\rm D}$ 1.5016) distilled between 161 and 168°. A portion of the distillate oxidized at 145–150° with three times its weight of 73% nitric acid gave a 30% yield of an acid, isophthalic acid, which sublimed above 300° and had a neutral equivalent of 82.9 (theory for isophthalic acid is 83.1). The dimethyl ester prepared by treating the silver salt with methyl iodide and crystallized from 50% aqueous methanol melted at 62–64° and did not depress the melting point of an authentic sample of dimethyl isophthalate.

(H) Identification and Proof of Structure of 1,1-Dimethyl-3-ethyl-2,4-cyclohexadiene (XIII).—A portion (1.0 ml.) of a lower boiling (51°) fraction of the refractionated material was treated with dimethyl acetylenedicarboxylate at 115–150°. The gas evolved was identified as isobutylene by formation of 4-*t*-butylphenol. The residue could not be induced to crystallize. It was saponified and the resulting acid was heated to 170°, distilled *in vacuo*, and crystallized from a little ethyl ether by cooling with solid carbon dioxide. A crystalline material, 0.51 g., melting at 50–70° was thus obtained. On recrystallization from benzene it gave 4-ethylphthalic anhydride, m.p. 76–77°.

Anal. Calcd. for $C_{10}H_8O_3$: C, 68.18; H, 4.58. Found: C, 68.35, 67.94; H, 4.69, 4.61.

4-Ethylphthalic acid was obtained by dissolving the anhydride in hot water to which a small amount of hydrochloric acid had been added. On recrystallization from benzene the acid melted at 133–134°.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19. Found: C, 61.57, 61.55; H, 5.17, 5.38.

The position of the ethyl group was established by oxidation of the anhydride to trimellitic acid. The anhydride, 0.05 g. was oxidized in a sealed tube with 0.25 ml. of 73% nitric acid. There was thus obtained 0.054 g. of an acid which, after recrystallization from acetic acid, melted at 233° and did not depress the melting point of an authentic sample of trimellitic acid.

Anal. Calcd. for $C_9H_6O_6$: neutral equivalent, 70.0. Found: neutral equivalent, 70.2.

(I) Identification of Dipentene.—Addition of a chloroform solution of bromine to a small sample of fraction 48, b.p. 71°, $n^{20}_{\rm D}$ 1.4850, d^{20}_4 0.8530, at dry ice temperature, gave a 9% yield of dipentene tetrabromide, m.p. 125–126°, which did not depress the melting point of an authentic sample.

(J) Identification of Aromatic Components.—The high refractive index and density of fraction 3, b.p. 39.6–41.6° (20 mm.), $n^{20}_{\rm D}$ 1.4929, d^{20}_4 0.8594, suggests it to be largely aromatic in nature. One ml. of this fraction treated with fuming nitric and concentrated sulfuric acids gave a nitro derivative, m. p. 183–185°, which did not depress the melting point of the corresponding derivative of an authentic sample of *m*-xylene.

Fraction 22, 10 ml., b. p. 60° (20 mm.), $n^{20}_{\rm D}$ 1.4707, was heated in an oil-bath with 8 g. of maleic anhydride with the bath temperature increasing from 60 to 105° over a period of fifteen minutes. When the bath temperature had reached 80° a vigorous exothermic reaction occurred with the temperature of the mixture increasing to 175° in one minute. When the reaction temperature had decreased to that of the bath, the mixture was poured into 30 ml. of 20% sodium hydroxide solution and subjected to steam distillation. One ml. of unreacted oil distilled over, b. p. 162°. This oil after drying reacted with fuming nitric and concentrated sulfuric acids to give a derivative, m. p. 88–89°, which did not depress the melting point of the derivative prepared from *m*-ethyltoluene.

As in fraction 3, the physical constants of fractions 44 to 48 indicate the presence of an aromatic component. Fraction 46, 4 ml., b. p. 70.6° (20 mm.), $n^{20}_{\rm D}$ 1.4980, d^{20}_4 0.8701, reacted with 3 g. of maleic anhydride and the mixture was steam-distilled from excess sodium hydroxide to give 2.2 ml. of unreacted oil. This oil was crystallized several times from 30–40% ether on a Dry Ice-bath. After melting, it was dried over calcium chloride and distilled to give $^3/_4$ ml. of distillate (b. p. 176°, $n^{20}_{\rm D}$ 1.5128, d^{20}_4 0.8928). The physical constants indicate the material to be 1,2,3-trimethylbenzene (b. p. 176°, $n^{20}_{\rm D}$ 1.5138, d^{20}_4 0.8947). The sulfonamide was prepared by the method of Huntress and Autenrieth,[22] and after recrystallization from alcohol and water, melted at 194–196°. A mixed melting point with the derivative of an authentic sample of 1,2,3-trimethylbenzene was not depressed.

Pyrolysis of α- and β-Pyronene.—Five grams of α-pyronene, b. p. 154°, in a glass tube was sealed in a stainless steel bomb and heated one and one-half hours at 290–300°. On distillation the product gave 2.6 g. of distillate, b. p. 166–170°. This material reacted with maleic anhydride to give an adduct, m. p. 163–164°, which showed no depression in melting point when mixed with the maleic anhydride adduct of β-pyronene.

β-Pyronene, 5 g., b. p. 167°, when heated in a manner similar to that just described, gave a product, b. p. 165–167°, which consisted chiefly of unchanged β-pyronene.

Acknowledgment.—The authors gratefully acknowledge the assistance of Dorothy M. Oldroyd and Alex C. Burdahl III of the Naval Stores Research Division, who did the fractional distillation of the pyrolysate; the assistance of Robert T. O'Connor and Edwin C. Boudreaux, Jr., who obtained the ultraviolet absorption data, and Lawrence E. Brown who did the carbon–hydrogen microanalyses, all of the Southern Regional Research Laboratory; and that of Dr. C. E. Boord of Ohio State University, who supplied an authentic sample of 1,2,3,5-tetramethylbenzene.

Summary

Twelve components have been identified among the products of thermal isomerization of *allo*-

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[22] Huntress and Autenrieth, THIS JOURNAL, **63**, 3446 (1941).

ocimene. Two of these, α- and β-pyronene, were previously known to occur in the *allo*-ocimene pyrolysate. Two other known terpenes, α-terpinene and dipentene, and three known aromatic compounds, *m*-xylene, *m*-ethyltoluene, and hemimellitene, were also found. In addition, five new hydrocarbons have been found and their structures determined. These are 1,3-dimethyl-1-ethyl-3,5-cyclohexadiene, 1,2,3,5-tetramethyl-2,4-cyclohexadiene, 1,2,3,5-tetramethyl-1,3-cyclohexadiene, 1,1-dimethyl-3-ethyl-3,5-cyclohexadiene and 1,1-dimethyl-3-ethyl-2,4-cyclohexadiene.

The structures were determined by reaction of the cyclohexadienes with the dimethyl ester of acetylenedicarboxylic acid and by dehydrogenation, disproportionation, or dealkanation to give aromatic compounds.

In addition to the new cyclohexadienes, several other new compounds were prepared. These include the naphthoquinone adducts of 1,3-dimethyl-1-ethyl-3,5-cyclohexadiene, of 1,2,3,5-tetramethyl-2,4-cyclohexadiene, of 1,2,3,5-tetramethyl-1,3-cyclohexadiene, and of α-terpinene. Also, the phthalic anhydride homologs, 3,4,5-trimethylphthalic anhydride, 3,4,6-trimethylphthalic anhydride, 3-ethylphthalic anhydride, and 4-ethylphthalic anhydride, their dimethyl esters (except for the dimethyl ester of 4-ethylphthalic acid) and the free acids were obtained. In addition, the dimethyl esters of 3-methylphthalic acid and of 3,4-dimethylphthalic acid have been crystallized and their melting points determined.

NEW ORLEANS, LA. RECEIVED NOVEMBER 25, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE CATHOLIC UNIVERSITY OF AMERICA]

The Molecular Kinetics of Pepsin-Catalyzed Reactions[1]

BY E. J. CASEY AND K. J. LAIDLER

Introduction

Considerable importance attaches to the question of the heats and entropies of reaction and activation associated with reactions catalyzed by enzymes, since the results provide valuable evidence with regard to the detailed mechanisms of these reactions. Very little relevant information exists: about the only systematic studies which enable both heats and entropies of activation to be determined are those of J. A. V. Butler[1a] on reactions catalyzed by trypsin and chymotrypsin, those of H. Neurath, *et al.*,[2] on peptidase and esterase activities of chymotrypsin, and the work in this Laboratory on the urease-catalyzed hydrolysis of urea.[3,4] In the present paper are presented data on the pepsin-catalyzed hydrolysis of two synthetic dipeptides, namely, carbobenzoxy-l-glutamyl-l-tyrosine and its ethyl ester. We have carried out a more detailed investigation than was done by Butler, and are suggesting a new interpretation of his data which brings them into line with those we have obtained.

The results on most of the hydrolytic enzymes may be analyzed in terms of the simple Michaelis–Menten law[5] which may be written in the form

$$v = k_0Kc_ec_s/(1 + Kc_s) \qquad (1)$$

Here v is the rate of reaction, c_e and c_s are the molar concentrations of enzyme and substrate, respectively, K is the equilibrium constant for the *formation* of the enzyme–substrate complex (*i. e.*, the reciprocal of the Michaelis constant, K_m) and k_0 is the specific rate constant for the decomposition of the complex. The equilibrium constant K may be written as

$$K = e^{-\Delta F/RT} = e^{-\Delta S/R}\, e^{-\Delta H/RT} \qquad (2)$$

where ΔF, ΔS and ΔH are the increases in free energy, entropy and heat associated with the formation of the enzyme-substrate complex, R is the gas constant and T the absolute temperature. In the units of liter mole^{-1}, K is invariably greater than unity; ΔF is therefore a negative quantity.

According to Eyring's theory of absolute reaction rates,[6] the rate constant k_0 may be expressed as

$$k_0 = (kT/h)e^{-\Delta F^*/RT} \qquad (3)$$
$$= (kT/h)e^{\Delta S_0^*/R}e^{-\Delta H_0^*/RT} \qquad (4)$$

Combining equations (2), (3), (4) with (1), it may be seen that at low substrate concentrations (when $Kc_s \ll 1$), the rate is equal to

$$v = k_0\,Kc_ec_s \qquad (5)$$
$$= c_ec_s(kT/h)e^{-(\Delta F_0^* + \Delta F)/RT} \qquad (6)$$
$$= c_ec_s(kT/h)\,e^{(\Delta S_0^* + \Delta S)/R}e^{-(\Delta H_0^* + \Delta H)/RT} \qquad (7)$$

At high substrate concentrations, on the other hand, when $Kc_s \gg 1$

$$v = k_0c_e \qquad (8)$$
$$= c_e(kT/h)e^{-\Delta F_0^*/RT} \qquad (9)$$
$$= c_e(kT/h)e^{\Delta S_0^*/R}e^{-\Delta H_0^*/RT} \qquad (10)$$

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(1) Abstracted from part of a dissertation submitted by E. J. Casey to The Catholic University of America in partial fulfillment of the requirements for the degree Doctor of Philosophy in Chemistry, July, 1949.

(1a) J. A. V. Butler, THIS JOURNAL, **63**, 2971 (1941).

(2) S. Kaufman, H. Neurath and G. W. Schwert, *J. Biol. Chem.*, **177**, 793 (1949); *cf.* H. Neurath and E. Elkins-Kaufman, *Federation Proc.*, **8**, 232 (1949).

(3) K. J. Laidler and J. P. Hoare, THIS JOURNAL, **71**, 2699 (1949).

(4) K. J. Laidler and J. P. Hoare, *ibid.*, in the press.

(5) L. Michaelis and M. L. Menten, *Biochem. Z.*, **49**, 333 (1913).

(6) H. Eyring, *J. Chem. Phys.*, **3**, 107 (1935); *cf.* W. F. K. Wynne-Jones and H. Eyring, *ibid.*, **3**, 492 (1935); S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941.