

Diels-Alder Reaction of α -Phellandrene and Cinnamaldehyde

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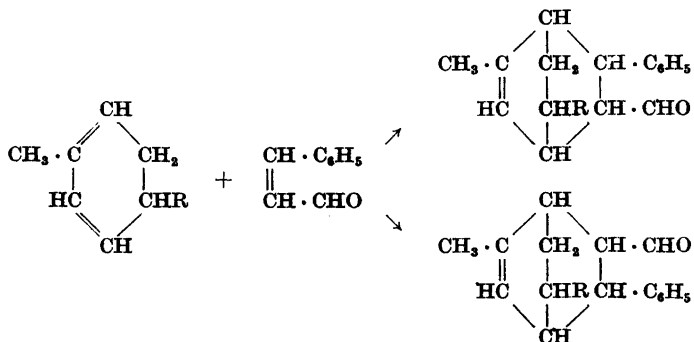
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An adduct of laevorotatory α -phellandrene and cinnamaldehyde has been prepared. The adduct, which is liquid and dextrorotatory seems to consist of one predominating form with at least one other isomeride present. On regenerating the adduct from its phenylhydrazone in methanolic solution the crystalline methyl acetal of the adduct was formed. The adduct of maleic anhydride and α -phellandrene is transformed into a lactonic acid by boiling with water.

Diels-Alder reactions of α -phellandrene have previously been carried out with symmetrical dienophiles such as maleic anhydride and naphthoquinone and with the unsymmetrical dienophiles acrolein and crotonaldehyde; for summary see Northon¹. In the present paper the reaction with cinnamaldehyde is described. The α -phellandrene used was a commercial laevorotatory sample (Eastman) with a specific rotation of -124° . In order to check its reactivity it was treated with maleic anhydride when it readily gave a crystalline adduct as described by Diels and Alder². It was found that this adduct by boiling with water was isomerized to the lactonic acid previously prepared by West³.

The reaction of α -phellandrene with cinnamaldehyde was carried out by heating to 150° . On fractionating the reaction product in a vacuum a crude adduct was obtained which was purified by treatment with sodium hydrogen sulphite. After redistillation the adduct was obtained as an oil with the expected composition $C_{19}H_{24}O$ and with a specific rotation of $+17.8^\circ$.

Theoretically the addition of an unsymmetrical dienophile to one of the optical components of α -phellandrene could give 8 isomeric adducts of two structurally different types as seen from the scheme (R = isopropyl)



In accordance with what has been found by Alder and Stein⁴ the diene synthesis seems also in this case to lead mainly to one product with one other adduct present in small amount. If the adduct was treated with 2,4-dinitrophenylhydrazine two crystalline hydrazones could be isolated, the one being strongly dextrorotatory and the other strongly laevorotatory. With phenylhydrazine one crystalline hydrazone only was isolated and in good yield. It was dextrorotatory and is evidently a derivative of the predominating isomere. An attempt to regenerate the aldehydic adduct from the phenylhydrazone by boiling with a methanolic solution of pyruvic acid led to a new crystalline compound $C_{21}H_{30}O_2$, m. p. 71° , $[\alpha]_D^{20} = +68^\circ$ which was found to be the methyl acetal of the adduct. The acetal on catalytic hydrogenation took up one mole of hydrogen.

From the acetal the adduct itself could only partially be regenerated. Hydrolysis led to a mixture of crystalline acetal and oily adduct, the methoxyl content and rotation of which permitted the calculation of an approximate specific rotation of $+27^\circ$ for the adduct. The oily part of the mixture gave the same dextrorotatory phenylhydrazone from which the acetal had been obtained and the dextrorotatory 2,4-dinitrophenylhydrazone, described above. It is therefore evident that the methyl acetal must be derived from a dextrorotatory component of the adduct.

The crystalline methyl acetal could be obtained directly from the original adduct, although only in poor yield, by heating methanolic solutions containing pyruvic acid, formic acid or 0.02 N hydrochloric acid.

Oxidation of the adduct under mild conditions with hydrogen peroxide gave two monocarboxylic acids. The one was a crystalline compound $C_{19}H_{24}O_2$, m. p. 157° , $[\alpha]_D^{20} = -67^\circ$, and the other an oil with $[\alpha]_D^{20} = +34^\circ$. The acids were boiled with water but no formation of lactones could be detected.

In order to establish the structure and the configuration of the adduct further experimental work will be necessary.

EXPERIMENTAL

α -Phellandrene and maleic anhydride

Optically pure α -phellandrene is rather difficult to obtain as shown by Hancox and Jones⁵ who found the rotation to be $[\alpha]_D^{20} = -177^\circ$. In the present case a commercial (–)- α -phellandrene (Eastman) of $[\alpha]_D^{20} = -124$ was used without further purification. The α -phellandrene and an excess of maleic anhydride on keeping for several days at -5° gave in 38 % yield the adduct described by Diels and Alder². After recrystallization from petroleum ether it had m. p. 126° , $[\alpha]_D^{20} = -10^\circ$ ($c = 3$ in chloroform). The adduct (3 g) was boiled with water (1 l) for one hour and the filtered solution then evaporated on the steam-bath to 200 ml in the course of 24 hours. The lactonic acid which had separated (1.6 g) was recrystallized from a mixture of ethyl acetate and ligroin, m. p. 170° , $[\alpha]_D^{20} = -37^\circ$ ($c = 24$ in chloroform). (Found: C 66.65; H 8.08. Equiv. wt. 250. Calc. for $C_{14}H_{20}O_4$: C 66.70; H 8.05. Equiv. wt. for monobasic acid 252). Treatment of the acid m. p. 170° with an ethereal solution of diazomethane gave the corresponding lactonic ester, which after recrystallization from petrol ether had m. p. 105° . West³ found 104° . $[\alpha]_D^{20} = -18.8^\circ$ (chloroform). (Found: OCH_3 12.51. Calc. for $C_{15}H_{22}O_4$ 11.65).

α -Phellandrene and cinnamaldehyde

The same (-)- α -phellandrene as above (100 g) and cinnamaldehyde (50 g) purified by vacuum fractionation, were heated in sealed tubes for 24 hours at 150°. After removing most of the unreacted α -phellandrene by distillation at 12 mm Hg, the reaction product was fractionated in a high vacuum. The fraction distilling at 114–120°/0.01 mm amounted to about 20 %, based on the quantity of cinnamaldehyde employed in the reaction. The adduct (18 g) was shaken for 2 hours with 25 % sodium hydrogen sulphite (40 ml) and ethanol (20 ml) and the solution then extracted with ether in order to remove impurities. The adduct was regenerated from the bisulphite solution by heating on the steam-bath for 30 min. and was then taken up in ether. The adduct (14 g) distilled at 114–120°/0.01 mm $[\alpha]_D^{20} = +17.8^\circ$ ($c = 3$ in chloroform). (Found: C 84.86; H 9.01; Mol.wt. (camphor) 267; 270. Calc. for $C_{15}H_{24}O$: C 85.07; H 8.96. Mol.wt. 268).

By bromination in ether a liquid bromide was formed which contained 35.87 % Br; calc. for 1 double bond 37.33 %.

The adduct (12 g), in methanol (200 ml) to which 0.4 g platinum oxide had been added, absorbed 1 250 ml hydrogen (1.5 atm.). It was thus apparent that both the double bond and the aldehyde group had been reduced. Calc. for 2 moles of hydrogen; 1 460 ml. The hydrogenated product, after distillation at 152°/0.2 mm, had $[\alpha]_D^{20} = 49^\circ$ ($c = 1$, in chloroform). (Found: C 84.12; H 10.34. Calc. for $C_{15}H_{26}O$: C 83.80; H 10.35).

2,4-Dinitrophenylhydrazones

The phosphoric acid method of Johnson⁶ was used for the preparation of these hydrazones. A solution of 2,4-dinitrophenylhydrazine (5 g) in 85 % phosphoric acid (60 ml) was heated on the steam-bath, diluted with ethanol (40 ml) and filtered. To a solution of the adduct (1 g) in ethanol (20 ml) the calculated amount of the reagent was added. On standing for some hours at room temperature a mixture of red and yellow crystals separated. These were collected by filtration, washed with water and the mixture was crystallized first from glacial acetic acid and then from petrol ether containing 20 % benzene, when red crystals only were obtained, m. p. 191° $[\alpha]_D^{20} = +272^\circ$ ($c = 1.2$, in chloroform). (Found: C 66.95; H 6.59; N 12.65. Calc. for $C_{25}H_{26}O_4N_4$: C 66.95; H 6.30; N 12.95).

In order to isolate the yellow form a fresh portion of the crystal mixture was prepared, dried at room temperature and refluxed with ether when mainly the yellow crystals dissolved. The filtered solution on cooling gave the yellow hydrazone which after recrystallization from glacial acetic acid had m. p. 176°, $[\alpha]_D^{20} = -210^\circ$ ($c = 0.1$ in chloroform). (Found: C 67.24; H 6.40; N 12.38).

Phenylhydrazone

A solution of the adduct (12 g) and phenylhydrazine (3 g, calc. 4.04 g) in methanol (60 ml) was kept at 0° for 4 hours when colourless needles separated in a yield of 40 %. Recrystallized from methanol, m. p. 112°, $[\alpha]_D^{20} = +96^\circ$ ($c = 1$ in ethanol). (Found: C 83.79; H 8.52; N 7.90. Calc. for $C_{25}H_{26}N_2$: C 83.79; H 8.38; N 7.85).

It should be mentioned that a phenylhydrazone with m. p. 124° and $[\alpha]_D^{20} = +151^\circ$ ($c = 1$ in ethanol) was obtained in some cases when the adduct was prepared by heating to 120°. (Found: C 83.49; H 8.37; N 7.97). The two phenylhydrazones gave the same product when treated with a methanolic solution of pyruvic acid.

Oxidation of the adduct

To a vigorously stirred aqueous solution of sodium hydroxide (0.5 N, 100 ml) containing boric acid (0.1 g) and hydrogen peroxide (10 ml 40 %), a solution of the adduct (10 g) in benzene (20 ml) was added dropwise at room temperature. After 3 hours the

mixture was transferred to a separating funnel, and more benzene added. Next day the aqueous layer was acidified with hydrochloric acid and the oil which separated was washed with water. The oil was dissolved in a small quantity of ethanol and water added until turbidity was produced. On keeping in the refrigerator overnight crystals separated (3 g) which on recrystallization from 75 % methanol gave colourless needles with m. p. 157°, $[\alpha]_D^{20} = -67^\circ$ ($c = 1.5$ in chloroform). (Found: C 79.95; H 8.50; Equiv. wt. 281. Calc. for $C_{19}H_{24}O_2$: C 80.24; H 8.51; Equiv. wt. 284.4).

On the addition of water to the mother liquor from the crystals m. p. 157°, an oil deposited which had $[\alpha]_D^{20} = +22^\circ$ ($c = 3.5$ chloroform). (Found: Equiv. wt. 279).

A chromatographic fractionation of this oily acid (1.4 g) was attempted on a column of cellulose, using as an eluant a mixture of ethyl acetate, benzene, *n*-propyl alcohol, water (5:1:2:1). Plotting the optical rotation against fraction number a sharp peak in the curve showed that the dextrorotatory acid was concentrated over a few fractions. From these fractions 1.2 g oily acid were recovered which had $[\alpha]_D^{20} = +34.2^\circ$ ($c = 2.5$ in chloroform).

Phenylhydrazone of the adduct with pyruvic acid

A solution of the phenylhydrazone, m. p. 112° (6 g) and pyruvic acid (4 g) in methanol (60 ml) was refluxed for 3 hours. After cooling water (2 ml) was added and the solution kept in a refrigerator overnight when the methyl acetal of the adduct separated as needles (4.5 g). After recrystallization from 80 % methanol the m. p. was 71°, unchanged on recrystallization from a small volume of benzene. $[\alpha]_D^{20} = +68$ ($c = 2$ in chloroform). (Found: C 80.31; H 9.52; OCH_3 19.10. Calc. for $C_{21}H_{30}O_2$: C 80.21; H 9.61; OCH_3 19.72).

When water was added to the mother liquor the phenylhydrazone of pyruvic acid separated. After purification it had m. p. and mixed m. p. 182°.

Hydrogenation of the acetal, m. p. 71°

Platinum oxide (0.29 g) in glacial acetic acid (30 ml) was shaken in an atmosphere of hydrogen until absorption ceased. After adding the methyl acetal (0.564 g) 34.0 ml hydrogen (960 mm, 19°) were absorbed in the course of 100 min, calc. 34.1 ml. The filtered solution was poured into water, the precipitate taken up in ether and the ethereal solution washed with water and dried. After evaporating the ether the crystalline residue was recrystallized from methanol. M. p. 57–60°, $[\alpha]_D^{20} = +63^\circ$ ($c = 3$ in chloroform). (Found: C 79.39; H 10.19; OCH_3 19.98. Calc. for $C_{21}H_{32}O_2$: C 79.68; H 10.19; OCH_3 19.60).

Hydrazones prepared from the acetal

A solution of the methyl acetal (1 g) and 2,4-dinitrophenylhydrazine (0.75 g) in ethanol (50 ml) was heated to boiling. On adding a few drops of conc. hydrochloric acid a reaction immediately took place and on cooling a red crystalline hydrazone precipitated (1.4 g). The hydrazone after recrystallization from petrol ether containing 20 % benzene, had m. p. 189° and $[\alpha]_D^{20} = +262^\circ$ in chloroform. (Found: C 67.10; H 6.44; N 12.40. Calc. for $C_{25}H_{28}O_4N_4$: C 66.95; H 6.30; N 12.95).

The methyl acetal (4 g) was heated with N hydrochloric acid (100 ml) on a water-bath for 20 hours. On cooling a mixture of oil and crystals deposited. The oil was dissolved in 80 % methanol and the solution, after the addition of phenylhydrazine (1 g), was heated for a short time. When the solution was subsequently kept in a refrigerator colourless crystals separated which had $[\alpha]_D^{20} = +97^\circ$ ($c = 0.6$ in ethanol) and m. p. 112° alone and mixed with the phenylhydrazone of the original adduct.

Preparation of acetal directly from adduct

A solution of the oily adduct (1 g) and pyruvic acid (5 g) in methanol (30 ml) was refluxed for 24 hours. After adding water until turbidity was produced the solution was kept in a refrigerator overnight when a small amount of crystalline material separated which, after recrystallization from petrol ether had m. p. 68–70° and $[\alpha]_D^{20} = +65^\circ$ ($c = 1.1$ in chloroform).

Following the same procedure a small amount of the methyl acetal was also obtained when formic acid was used instead of pyruvic acid. Acetic acid had, however, no effect. On using 0.1 ml 5 N hydrochloric acid instead of pyruvic acid, 0.1 g (10 % yield) of the methyl acetal was obtained. It had m. p. 71° alone and mixed with acetal prepared from the phenylhydrazone.

Hydrolysis of the methyl acetal

A solution of the methyl acetal (1 g) in 75 % methanol (150 ml) to which 1.5 ml N hydrochloric acid had been added, was refluxed for 90 min. The methanol was distilled off, and the oil which separated was taken up in ether. The ethereal solution was washed with water and dried over potassium carbonate. After evaporating the ether the residue was dried in a vacuum over calcium chloride. The methoxyl content of the residue (6.1 %) showed that the acetal had not been completely hydrolysed. As the specific rotation of the residue was found to be +39.7° an approximate specific rotation of +27° could be calculated for the aldehyde corresponding to the acetal.

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