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Structure of the Maleic Anhydride Bis-Adduct of α, p-Dimethylstyrene

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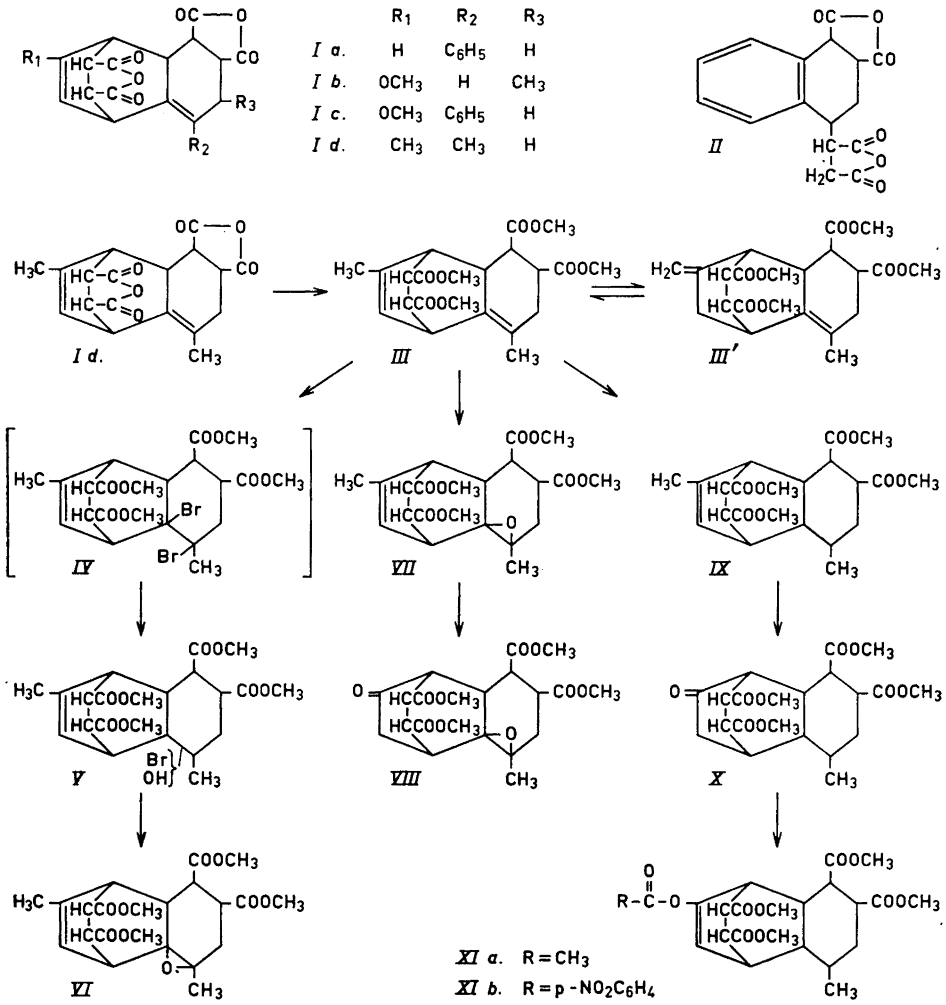
The addition reactions of the maleic anhydride bis-adduct of α,p-dimethylstyrene (Id) have been studied. Employing ozonolysis evidence was found for the existence of methyl-methylene tautomerism illustrated by formulas III and III′.

One of the outstanding features of the maleic anhydride bis-adducts of the type I is their "saturated" character regarding addition reactions. So Wagner-Jauregg [1], the discoverer of the first compound (Ia) of this type, found that it did not add bromine and catalytically activated hydrogen and that it was inert to oxidation with perbenzoic acid as well as with potassium permanganate in acetone solution. Thus, being unable to prove the existence of the two double bonds revealed by the structure Ia, he repudiated it in favor of another one by assuming the second step of addition to proceed by substitution mechanism. Similar observations have been made later by Bruckner *et al.*[2,3] in respect to other bis-adducts (Ib and Ic) of the same type. Although the concept of substitution addition has been recently substantiated by Alder and Schmitz-Josten [4] in the case of one of the two maleic anhydride bis-adducts of styrene (II), the original unsaturated type of formula put forward by Wagner-Jauregg still seems to be valid in other cases.

In a previous paper [5] it was shown, that α,p-dimethylstyrene readily adds two molecules of maleic anhydride to form a bis-adduct, for which the formula Id was established. This bis-adduct, too, revealed a "saturated" character when tested with the double bond reagents mentioned above. Only ozone was added in the amount corresponding to one double bond. When, however, the two anhydride rings were opened by converting the dianhydride to the corresponding tetramethyl ester (III), the rigid structure of the bis-adduct became more flexible allowing also the addition of bromine to one double bond. It was shown that the double bond attacked by both ozone and bromine was the one situated in the side ring (not in the bridged ring). First after the cleavage of this double bond by ozonization the existence of the other one could be demonstrated.



In this paper the addition reactions to the bis-adduct (Id) are further examined. Owing to the easier accessibility by addition reagents and better solubility the tetramethyl ester (III) was used in most experiments. It was prepared by alkaline hydrolysis of the bis-adduct (Id) and methylation of the resulting tetracarboxylic acid by diazomethane. For ascertaining that no change in the position of the double bonds was brought about by the use of strong alkali, the conversion was made in another way also. By methanolysis of the dianhydride and subsequent treatment with diazomethane a monoanhydride dimethyl ester was obtained. This compound, after repetition of the procedure, yielded a tetramethyl ester. It turned out that this ester was identical with the one made by the method including alkaline hydrolysis.

Upon bromination of the tetramethyl ester (III) in carbon tetrachloride solution exactly one molar equivalent of bromine was added. With more bromine the solution turned yellow. It was impossible to isolate the dibromo compound (IV). If, however, the bromination product after evaporation of the solvent was treated with moist methanol, a bromohydrine (V) was obtained. In the formula the mutual orientation of the Br and OH substituents to the double bond is not known. Even the bromohydrine proved rather labile. Upon crystallization from methanol it suffered a loss of one molecule of hydrogen bromide yielding an epoxide (VI). This behaviour is readily understood by considering the tertiary position of the bromine atom in the bromohydrine.

When the tetramethyl ester (III) ($C_{22}H_{28}O_8$) was oxidized with excess of perbenzoic acid in chloroform solution in the cold, exactly one equivalent of active oxygen was consumed and a monoepoxide (VII) ($C_{22}H_{28}O_9$) was the only product that could be isolated (yield 82 %). This epoxide was isomeric but not identical with the one (VI) formed from the bromohydrine by the loss of hydrogen bromide. It proved saturated to bromine and tetranitromethane. So the double bond attacked in both cases must be one and the same and the two epoxides are stereoisomers. When the oxidation was carried out at room temperature, a by-product was isolated along with the epoxide (VII). For this by-product a formula $C_{21}H_{26}O_{10}$ was found by analysis. This same compound could be obtained from the epoxide (VII) by ozonization. The molecular formula of the by-product differs from that of the epoxide by loss of CH_2 and gain of one oxygen atom. For the structure of this compound, see later.

In an attempt to convert the tetramethyl ester (III) into a naphthalene derivative, catalytic hydrogenation formed the first link of the reaction sequence. It was namely intended, after protection of the double bond in the side ring by selective catalytic hydrogenation, to cleave the bicyclo-octene ring system at the other double bond and aromatize the resulting decahydronaphthalene derivative by dehydrogenation. Unfortunately, only the step comprising hydrogenation could be realized. In accordance with earlier statements this adduct also was totally inert to hydrogenation with platinum or palladium catalysts at room temperature and atmospheric or elevated pressure. But when Raney nickel was used as catalyst and the hydrogenation carried out at 105°C and 90 atm. pressure, a dihydro derivative (IV) was readily obtained in a yield of about 70 %. Just as the epoxides this compound, too, proved saturated to bromine and tetranitromethane. All attempts to cleave the bicyclo-octene double bond by oxidation with nitric acid, potassium permanganate or ozone failed. Either unchanged material was recovered or total destruction of the molecule resulted. The only oxidation product that could be isolated was obtained by ozonization. Ozone was consumed very slowly at the temperature of solid carbon dioxide. When an amount of ozone equivalent to two double bonds was passed in, 60 % of the starting material was recovered unchanged. From the reacted material an ozonization product with the molecular formula $C_{21}H_{28}O_9$ was isolated in a yield of 40 %. The formation of this compound from the dihydrotetramethyl ester ($C_{22}H_{30}O_8$) is accordingly exactly analogous with the behaviour of the epoxide (VII) on ozonization. The formation of the ozonization product in both cases may be explained, if a methyl-methylene

tautomerism illustrated by the formulas III and III′ is assumed. On this basis the formulas VIII and X are to be derived for the ozonization product of the epoxide (VII) and dihydrotetramethyl ester (IX), respectively. This assumption is supported by the formation of an acetate (XIa) and *p*-nitrobenzoate (XIb) from the ozonization product (X). In addition, the ozonization product (X) dissolved much faster than the parent compound (IX) in dilute sodium hydroxide solution, as may be expected on the basis of keto-enol tautomerism, for which the formula X offers possibility. Besides, ample analogies for the assumed methyl-methylene tautomerism are to be found in the literature, *e.g.* in the case of some terpenes such as eudesmol [6].

It is to be noted that both of the ozonization products (VIII) and (X) were precipitated by methanol directly after evaporation of the solvent. Accordingly, a so-called "spontaneous decomposition of ozonide" [7] should be involved here.

EXPERIMENTAL

Conversion of the dianhydride (Id) into the tetramethyl ester (III). A suspension of 84 g of the dianhydride (Id) in 840 ml of methanol was refluxed until all was dissolved (20 h). From this solution no crystalline compound could be isolated. It was methylated with an ethereal solution of diazomethane. The bulk of the product, 73.6 g, m.p. 170—185°, crystallized almost immediately. Once recrystallized from acetone the compound was obtained as coarse, colorless crystals, m.p. 192—194°. (Found: C 64.30; H 6.07. Calc. for $C_{20}H_{22}O_7$: C 64.16; H 5.92).

On the basis of the above analysis the product must be a monoanhydride dimethyl ester. Which of the two anhydride rings had opened, remained unsettled. The product was difficultly soluble in methanol, even in hot methanol. It dissolved readily in chloroform. This solution did not decolorize bromine. The product dissolved slowly in dilute sodium hydroxide at room temperature.

The monoanhydride dimethyl ester was converted almost quantitatively into the tetramethyl ester (III) by refluxing for 2 days in methanol and subsequent methylating with ethereal diazomethane.

Bromination of the tetramethyl ester (III). Bromohydrine (V). Epoxide (VI). To a solution of 1.0 g of the tetramethyl ester (III) in 10 ml of carbon tetrachloride was added with stirring 380 mg (equivalent to one double bond) of bromine in 9 ml of carbon tetrachloride while the reaction mixture was cooled in an ice-salt bath. During the addition an amorphous brownish precipitate formed. It was filtered off and discarded. After evaporation of the fuming (HBr) solvent a porous resin remained. Upon trituration with moist methanol it deposited the bromohydrine as white crystals. The yield was 432 mg, m.p. about 130° (decomp.). (Found: C 51.62; H 5.49; Br 15.80. Calc. for $C_{22}H_{29}BrO_9$: C 51.18; H 5.66; Br 15.43.)

Upon attempting to crystallize the above bromohydrine from methanol a clear solution was obtained in the hot, but almost immediately a copious amount of colorless crystals separated. These were filtered and dried. The yield was 300 mg, m.p. 196—199° (without decomp.). The test for unsaturation with bromine in chloroform solution was negative. For this compound an epoxide structure was indicated by the lack of bromine. (Found: C 60.37; H 6.35. Calc. for $C_{22}H_{28}O_9$: C 60.54; H 6.47.)

Oxidation of the tetramethyl ester (III) with perbenzoic acid. Epoxide (VII). To a solution of 18.4 g of the tetramethyl ester (III) in 92 ml of chloroform there was added 6.49 g (1.07 equivalents) of perbenzoic acid in 90 ml of chloroform, while the reaction mixture was stirred and cooled in an ice-salt bath. After standing for 24 h at −12°C the perbenzoic acid content of the solution was determined. It appeared that the consumption of the active oxygen corresponded exactly to one double bond. The solution was diluted with ether and washed first with aqueous bicarbonate, then with water. The solvent was evaporated and the solidified residue crystallized from methanol. The yield of the epoxide, m.p. 169—171°, was 15.7 g (82 %). Once recrystallized from methanol the m.p. was unchanged. (Found: C 60.76; H 6.56. Calc. for $C_{22}H_{28}O_9$: C 60.54; H 6.47.)

In another experiment, where 2 g of the tetramethyl ester (III) were oxidized with excess of perbenzoic acid at room temperature, in addition to the epoxide (VII) 265 mg of a by-product, m.p. 215—230°, was obtained. Upon recrystallization from acetone this compound formed large, rectangular plates, m.p. 231—235°. (Found: C 57.42; H 5.92. Calc. for $C_{21}H_{26}O_{10}$: C 57.53; H 5.98.)

Ozonization of the epoxide (VII). Ozonization product (VIII). 5.0 g of the epoxide (VII) were dissolved in 100 ml of chloroform. Ozonized oxygen containing 5.3 % by volume of ozone was passed through this solution with cooling in dry-ice. After absorption of an amount of ozone equivalent to one double bond the solution was evaporated to dryness at room temperature *in vacuo*. The residue, a porous solid, was dissolved in 50 ml of methanol. After a while white crystals begin to separate, yield 1.77 g, m.p. 207—215°. After recrystallization from acetone the compound was obtained as large, rectangular plates, m.p. 230—235°. From the mother liquor of the first fraction a second crop of crystals, m.p. 225—233°, was obtained. The combined yield of the ozonization product was 41 %. (Found: C 57.50; H 5.96. Calc. for $C_{21}H_{26}O_{10}$: C 57.53; H 5.98.)

The ozonization product (VIII) was proved by mixed melting point determination and infrared absorption spectrum to be identical with the above by-product obtained from the tetramethyl ester (III) by excess of perbenzoic acid at room temperature.

Hydrogenation of the tetramethyl ester (III). Dihydrocompound (IX). 10.0 g of the tetramethyl ester (III) in 300 ml of absolute ethanol was hydrogenated for 36 h at 105° and 90 atm. pressure over 3 g of Raney nickel catalyst. After cooling the catalyst was filtered off and the filtrate concentrated. Large, colorless prisms separated. The yield of the hydrogenation product was 7.45 g (74 %), m.p. 156—158°. From the mother liquor 1.47 g of the unchanged starting material, m.p. 120—122°, was recovered. Once recrystallized from methanol the first compound melted at 158—159°. (Found: C 62.60; H 7.20. Calc. for $C_{22}H_{30}O_8$: C 62.54; H 7.16.)

The dihydrocompound was readily soluble in chloroform. The chloroform solution proved saturated toward bromine and tetranitromethane.

Ozonization of the dihydrocompound (IX). Ozonization product (X). Ozonized oxygen was passed through a solution containing 4.72 g of the dihydrocompound (IX) in 100 ml of chloroform with cooling in dry-ice. From the beginning only about a half of the ozone was absorbed. After absorption of one equivalent the ozonization was interrupted. The solvent was evaporated at room temperature *in vacuo*. The residue, a colorless, viscous liquid, was dissolved in methanol. After a while small, colorless crystals, 1.95 g, m.p. 157 158°, separated. This first fraction was shown to be unchanged starting material by mixed melting point determination. From the mother liquor another compound, 0.96 g, m.p. 185—190°, was obtained. It was recrystallized from methanol to give white leaflets, m.p. 191—193°. (Found: C 59.30; H 6.61. Calc. for $C_{21}H_{28}O_9$: C 59.42; H 6.65.)

The ozonization product, contrary to the starting material, dissolved rather readily in dilute sodium hydroxide at room temperature. It was readily soluble in chloroform. The chloroform solution did not decolorize bromine. The test for double bond with tetranitromethane was also negative. The compound did not form an oxime or a semicarbazone.

The acetate (XIa). A mixture of 200 mg of the ozonization product (X), 100 mg of anhydrous sodium acetate and 1 ml of acetic anhydride was refluxed for 1 h. The reaction product was poured in water and extracted with chloroform. The chloroform solution was washed with aqueous sodium bicarbonate and water and evaporated to dryness. Upon trituration with methanol 159 mg of colorless crystals, m.p. 133—134° separated. (Found: C 58.95; H 6.58. Calc. for $C_{23}H_{33}O_{10}$: C 59.22; H 6.48.)

The p-*nitrobenzoate (XIb).* A mixture of 200 mg of the ozonization product (X) and 120 mg of *p*-nitrobenzoyl chloride in 5 ml of pyridine was refluxed for 1 h. After cooling ether was added. The formed precipitate was brought into solution by means of a few drops of chloroform. After standing for several days 151 mg of yellowish crystals, m.p. 199—205°, separated from the solution. Once recrystallized from a mixture of methanol and acetone small, rectangular plates, m.p. 204—206°, were obtained. (Found: N 2.60. Calc. for $C_{28}H_{31}NO_{12}$: N 2.44.)

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