# Chemistry

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1964

SovietRxiv

## Abstract

## Full Text

*Chemistry*

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# STEREOCHEMISTRY OF THE OXIDATION OF GEOMETRIC ISOMERS OF 13-METHYL-7-ACETOXY-$\Delta^{4(12)}$-DODECAHYDROPHENANTHRENE-1,2-DICARBOXYLIC ACID AND THEIR DERIVATIVES

*(Presented by Academician B. A. Kazanskii, 19 III 1964)*

As has already been noted earlier, oxidation of the double bond with peracetic acid in cyclic compounds containing the system of $\Delta^4$-cyclohexene-cis-1,2-dicarboxylic acid proceeds stereoselectively from the side opposite to the carboxyl groups (1). In contrast to this, in the oxidation of the corresponding anhydrides the reaction proceeds less stereospecifically, with formation in a number of cases of both isomeric epoxides (2). For the simplest monocyclic anhydrides, in which the boat conformation of the six-membered ring is more preferred, epoxy anhydrides are formed with a cis arrangement of the anhydride and oxide rings (3,4).

[Displayed chemical reaction schemes]

In this connection, it was of interest to elucidate the stereochemistry of the oxidation of isomeric 7-substituted 13-methyl-$\Delta^{4(12)}$-dodecahydrophenanthrene-1,2-dicarboxylic acids and their anhydrides, previously obtained on the basis of the diene condensation of vinylcyclohexenes of type (I) with maleic anhydride (5,6). It could be assumed that, in the case of such compounds, owing to the peculiarities of their spatial structure, the stereochemistry of epoxidation would be influenced not only by the polar and steric effects of the carboxyl groups or by the conformational features of the $\Delta^4$-cyclohexene ring, but also by the steric effect of the axial angular group at $C_{13}$, as occurs in steroid compounds. For this purpose, using the 7-acetoxy derivatives as examples, we studied the oxidation both of the isomeric acids themselves (IVa, b) and their diesters (Va, b), as well as of the corresponding anhydrides (II) and (III).

It proved that oxidation of the isomeric acids (IVa, Va) and their diesters (IVb, Vb) proceeds stereospecifically and leads to the isomeric $\alpha$-epoxides (VIa, b) and (VIIa, b), the configuration of which follows from the fact that

upon saponification they readily give the corresponding oxy-$\gamma$-lactone acids (VIII) and (IX). This result shows that, in the oxidation of acids and esters reaction scheme with compounds (I)-(XIII), showing epoxidation and related transformations; substituents include $X = O, OAc$, and a cyclic acetal group; $R = H$ or $CH_3$

Figure 1: reaction scheme with compounds (I)-(XIII), showing epoxidation and related transformations; substituents include $X = O, OAc$, and a cyclic acetal group; $R = H$ or $CH_3$

of the dodecahydrophenanthrene series, the principal factors determining

the stereochemistry of the epoxidation reaction are the electronic and steric effects of the carboxyl groups; their influence, leading to oxidation from the side of the molecule opposite to them, is considerably greater than the spatial influence of the axial methyl group adjacent to the double bond.

Further investigation showed that epoxidation of the isomeric anhydrides (II) and (III) also proceeds stereospecifically; however, the spatial direction of the reaction in these cases is opposite to the stereochemistry of the oxidation of the dicarboxylic acids and their esters. It was found that the epoxy anhydrides (X) and (XI) formed in this process are different from the corresponding epoxy anhydrides (XII) and (XIII), obtained from the $\alpha$-epoxy acids (VIa) and (VIIa), and, consequently, must have a cis arrangement of the oxide and anhydride rings.

Thus, the results of epoxidation of the isomeric anhydrides (II) and (III) show that in this reaction, as in the case of anhydrides of the simplest $\Delta^4$-cyclohexene-cis-1,2-dicarboxylic acids ($^{3,4}$), oxidation occurs from the side of the anhydride ring and does not depend on the shielding-

···of the influence of the axial angular group. Consideration of molecular models shows that such stereochemistry of the oxidation of anhydrides of $o$-dicarboxylic acids of the dodecahydrophenanthrene series is not connected with the boat-shaped conformation possible for them of the cyclohexene ring, but apparently depends on other, more subtle conformational features of such polycyclic systems, which favor the formation of reactive conformations with less shielding of the $\beta$-region.

## Experimental Part

### Oxidation of isomeric 13-methyl-7-acetoxy-$\Delta^{4(12)}$-dodecahydrophenanthrene-1,2-dicarboxylic acids, their diesters and anhydrides

To a suspension, cooled to 0°, of 500 mg of the substance to be oxidized in 30 ml of chloroform, 0.3 ml of 90% peracetic acid is added; the mixture is stirred for 2 h at 0° and kept for 12 h at room temperature. The solvent is distilled off in vacuo, ether is added to the residue, and the product formed is filtered off and recrystallized from a suitable solvent. In this way were obtained: $\alpha$-oxy acid (VIa)—m.p. 266-268°; diester (VIb)—m.p. 149-150° (from methanol)

Found, %: C 64.01; H 7.48

$C_{21}H_{30}O_7$. Calculated, %: C 63.94; H 7.64

On acid saponification of the acid oxide (VIa) and subsequent treatment with diazomethane, $\gamma$-lacto ester (VIII) was isolated, m.p. 236-237° (from methanol), $\nu$ (in chloroform) 1776, 1738 $cm^{-1}$.

Found, %: C 63.00; H 7.46

$C_{20}H_{28}O_7$. Calculated, %: C 63.14; H 7.42

$\alpha$-Oxy acid (VIIa)—m.p. 212-215°; diester (VIIb)—m.p. 135-136° (from aqueous acetone)

Found, %: C 64.13; H 7.81

$C_{21}H_{30}O_7$. Calculated, %: C 63.94; H 7.64

Acid saponification of the acid oxide and subsequent treatment with diazomethane leads to dioxy-$\gamma$-lacto ester (IX), m.p. 213-214° (from acetone), $\nu$ (in chloroform) 1773, 1733 $cm^{-1}$

Found, %: C 63.80; H 7.73

$C_{18}H_{26}O_6$. Calculated, %: C 63.88; H 7.74

$\beta$-Epoxyanhydride (X)—m.p. 215-216° (from benzene)

Found, %: C 65.47; H 7.01

$C_{19}H_{24}O_6$. Calculated, %: C 65.50; H 6.94

$\beta$-Epoxyanhydride (XI)—m.p. 209-210° (from benzene)

Found, %: C 65.55; H 6.97

Preparation of $\alpha$-epoxyanhydrides (XII) and (XIII). A mixture of 500 mg of the corresponding $\alpha$-oxy acid, 10 ml of pyridine, and 5 ml of acetic anhydride is left overnight at room temperature. The volatile products are distilled off in vacuo, ether is added, and the product obtained is filtered off.

$\alpha$-Epoxyanhydride (XII)—m.p. 186-187° (from benzene)

Found, %: C 65.52; H 7.14

$C_{19}H_{24}O_6$. Calculated, %: C 65.50; H 6.94

$\alpha$-Epoxyanhydride (XIII)—m.p. 176–177° (from benzene)

Found, %: C 65.45; H 6.98

It has been established that oxidation with peracetic acid of isomeric 13-methyl-7-acetoxy-$\Delta^{4(12)}$-dodecahydrophenanthrene-1,2-dicarboxylic acids and their esters leads to $\alpha$-oxides, whereas oxidation of the corresponding anhydrides gives isomeric $\beta$-epoxy anhydrides having a *cis* arrangement of the oxide and anhydride rings. It has been shown that the stereochemistry of these reactions does not depend on the steric effect of the axial angular methyl group.

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Received
17 III 1964

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*Note: Figure translations are in progress. See original paper for figures.*