115. *Anisoxide. Part I.*

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During a re-examination of star aniseed oil (from *Illicium verum*) carried out by one of us in conjunction with Mr. C. B. Radcliffe, M.Sc., in 1932, a new constituent was isolated. We have now studied the reactions of this compound, for which we suggest the name *anisoxide.*

The new compound was isolated from the oil by protracted fractionation with an efficient column and was concentrated in the fraction, b. p. 135—145°/12 mm., which was then heated with sodium–potassium alloy to destroy active oxygenated constituents. Further fractionation afforded a portion, b. p. 138—143°/12 mm., which solidified (m. p. 36—38°). The solid was excessively soluble in the usual organic solvents, but could be recrystallised from ice-cold methyl alcohol, separating in large white cubic crystals, m. p. 41°, having a faint but characteristic odour. It could be distilled unchanged at atmospheric pressure, but on exposure to air rapidly changed to a viscous yellow liquid with production of a pungent odour. The average content of anisoxide in the three specimens of star aniseed oil examined was 0·2%.

Owing to the ease with which anisoxide yields acetaldehyde, persistently low values for carbon were obtained until special precautions were adopted in the analyses. Results agreeing with the formula $C_{14}H_{18}O$ were then obtained and this composition was substantiated by analyses of the hydro-derivatives (below).

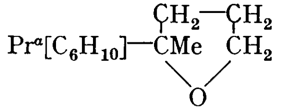
Anisoxide is a cyclic ether, since it is inert towards the usual reagents for alcohols and carbonyl compounds and contains no methoxy- or ethoxy-group. It is highly unsaturated, imparting a deep red colour to tetranitromethane in chloroform solution, but no solid compounds could be obtained with the usual olefinic addenda. The high molecular refraction, $[R_L]_D$ 65·66 (calc. for an aliphatic oxide $C_{14}H_{18}O|_{\overline{5}}^{=}$, 63·96, and for a monocyclic oxide $C_{14}H_{18}O|_{\overline{4}}^{=}$, 62·23), indicates that the oxide contains either conjugated ethylenic linkages or an acetylenic linkage. The presence of conjugated double bonds was proved by (1) the formation of an *addition compound*, $C_{18}H_{20}O_4$, with maleic anhydride, (2) reduction to *dihydroanisoxide*, $C_{14}H_{20}O$, with sodium and alcohol. The dihydro-compound is stable towards further reduction with these reagents and exhibits a smaller exaltation in its molecular refraction.

An attempt to determine the degree of unsaturation by perbenzoic acid titration was frustrated by the slowness of the reaction, only 1·5 atoms of oxygen being absorbed in 300 hours. Energetic catalytic reduction, however, produced *perhydroanisoxide*, $C_{14}H_{26}O$, still containing the oxide ring and giving no colour with tetranitromethane.

Anisoxide afforded 2 mols. of acetic acid on oxidation by the Kuhn–Roth micro-method (chromic anhydride) and one of these is derived from an ethylidene group, since oxidation of anisoxide with moist air at 70° or with dilute ozone in aqueous suspension produces acetaldehyde, which was characterised as aldomedon. The double bond of the ethylidene group is probably conjugated, since dihydroanisoxide does not yield acetaldehyde on oxidation.

In order to determine the nature of the oxide ring, experiments were made with perhydroanisoxide, since anisoxide is resinified by acids and halogens. Perhydroanisoxide was recovered unchanged after treatment with phenylmagnesium bromide at 100°, so the presence of a 1 : 2- or 1 : 3-oxide ring is improbable (Blaise, *Compt. rend.*, 1902, **134**, 553; Grignard, *Bull. Soc. chim.*, 1903, **29**, 944). When perhydroanisoxide was heated with hydrogen bromide in acetic acid, the oxide ring was opened with production of an unstable *dibromide*, $C_{14}H_{26}Br_2$. Digestion with aniline produced an unsaturated *hydrocarbon*, $C_{14}H_{24}$, which was oxidised by ozone to a *ketone*, $C_{11}H_{20}O$, characterised by the preparation of a *semicarbazone*, m. p. 161—162°. Oxidation of this ketone with sodium hypoiodite gave iodoform and it is therefore evident that perhydroanisoxide must be represented by (I) and the ketone $C_{11}H_{20}O$ by (II).

(I.)



$Pr^{a}[C_6H_{10}]—COMe$ (II.)

Anisoxide clearly does not belong to the furan group represented by carlina oxide, perillene, elsholtzione and menthofuran, but is a hydrofuran derivative. In agreement with this, no pyrrole reactions were exhibited by the product obtained by heating anisoxide to 200° with alcoholic ammonia.

Oxidation of anisoxide with potassium permanganate in pyridine solution gave an *acid*, $C_{12}H_{14}O_3$, m. p. 182°, evidently produced by oxidation of the ethylidene group:

$$[C_{11}H_{13}O]\cdot CH\!:\!CHMe \longrightarrow [C_{11}H_{13}O]\cdot CO_2H$$

On further oxidation it afforded first an *acid*, $C_{11}H_{12}O_3$, m. p. 215—216°, and then an *acid*, $C_{11}H_{10}O_4$, m. p. 179·5—180·5°; the latter is a hydroxy-acid, since the *methyl* ester furnished one molecule of methane on reaction with methylmagnesium iodide. Finally, oxidation of dihydroanisoxide with either potassium permanganate or ozone produced a liquid ketone, $C_{14}H_{18}O_2$, characterised by its *semicarbazone*, m. p. 191·5—192·5°. The bearing of these results on the structural problem is reserved for discussion in a subsequent communication.

Takens (*Reichstoffind.*, 1929, **4**, 8) records the presence in fennel oil and star anise oil of a compound, m. p. 21·5°, isomeric with anisoxide. This substance, however, is stated to yield *p*-anol, $CHMe\!:\!CH\cdot C_6H_4\cdot OH$, on distillation at atmospheric pressure and its physical constants are different from those of anisoxide.

The final fraction of star aniseed oil contains, in addition to anisic acid, a small quantity of a paraffin hydrocarbon, $C_{19}H_{40}$, m. p. 45—46°.

EXPERIMENTAL.

Anisoxide.—The pure *oxide* consists of cubic crystals, m. p. 41°, b. p. 140°/11 mm., $d_{4^\circ}^{50^\circ}$ 0·9604, $n_D^{50^\circ}$ 1·5361, $\alpha_D \pm 0^\circ$ (Found: C, 82·8; H, 8·9. $C_{14}H_{18}O$ requires C, 83·2; H, 8·9%). Anisoxide (1·0 g.) and maleic anhydride (0·5 g.) were heated at 170° for ½ hour, and the product washed with alcohol and recrystallised from acetic acid. Microscopic prisms of an *addition compound* decomposing at 280° were obtained (Found: C, 72·1; H, 6·7. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7%).

Reduction of Anisoxide.—(i) *Catalytic.* The oxide (50 g.) in acetic acid (1 l.) and platinum oxide (7·5 g.) were shaken in hydrogen at a pressure of 40 lb. per sq. in., and the catalyst re-activated at intervals by shaking with air. Absorption ceased after 26·5 l. of hydrogen (4·8 mols.) had been absorbed. *Perhydroanisoxide* (49·5 g.), isolated in the usual manner, was a colourless mobile oil, b. p. 120—122°/10 mm., $d_{4^\circ}^{25^\circ}$ 0·8999, $n_D^{25^\circ}$ 1·4656, $[R_L]_D$ 64·66 (calc. for $C_{14}H_{26}O$, 64·10) (Found: C, 79·9; H, 12·6. $C_{14}H_{26}O$ requires C, 80·0; H, 12·4%). Perhydroanisoxide gives no colour with tetranitromethane and does not react with 3 : 5-dinitrobenzoyl chloride.

(ii) *With sodium and alcohol.* Sodium (16·4 g.) was added as rapidly as possible to a boiling solution of anisoxide (10 g.) in ethyl alcohol (75 c.c.), the reaction being completed by heating to 120° and slowly adding more alcohol (100 c.c.). After removal of the alcohol in steam, the oil was extracted with ether, the ether dried and evaporated, and the residue distilled under diminished pressure; *dihydroanisoxide* (9 g.) was obtained as a colourless oil, b. p. 120—122°/10 mm., $d_{4^\circ}^{25^\circ}$ 0·9501, $n_{D}^{25^\circ}$ 1·5073, $[R_L]_D$ 64·00 (calc. for $C_{14}H_{20}|^{=}_{3}O$, 62·69) (Found : C, 82·3, 82·3; H, 10·0, 10·0. $C_{14}H_{20}O$ requires C, 82·4; H, 9·8%).

Oxidation of Anisoxide.—(i) *With air.* Air was aspirated through a suspension of anisoxide (0·5 g.) in water (10 c.c.) at 40—45°. The issuing vapour gave a positive test for acetaldehyde with piperidine and sodium nitroprusside (Rimini, *Z. anal. Chem.*, 1904, **43**, 517) and when it was passed for 8 hours through a solution of 5 : 5-dimethyl*cyclo*hexane-1 : 3-dione (0·6 g. in 10 c.c. of water) a precipitate separated after keeping for 12 hours. The solid had m. p. 140° after recrystallisation from dilute ethyl alcohol (free from acetaldehyde) and did not depress the m. p. (140°) of authentic aldomedon (Neuberg and Reinfurth, *Biochem. Z.*, 1920, **106**, 286).

(ii) *With ozone.* Ozonisation of anisoxide in 70% acetic acid (4 vols.) with 5% ozone for 8 hours at 0°, decomposition of the ozonide with ice-water, and distillation of the liquid furnished acetaldehyde (aldomedon, m. p. and mixed m. p. 140°) and resinous compounds.

(iii) *With chromic anhydride.* Oxidation of anisoxide (13·5 mg.) under the conditions specified by Kuhn and Roth (*Ber.*, 1933, **66**, 274) afforded distillates which neutralised 10·8 and 11·4 ml. of 0·01*N*-sodium hydroxide solution, equivalent to 1·6 and 1·7 mols. of acetic acid respectively.

(iv) *With potassium permanganate.* The same acid (A) was produced when the oxidation was conducted in acetone or water, but the best yields (64%) were obtained in pyridine solution. Potassium permanganate solution (2% : equivalent to 4 atoms of oxygen) was added drop by drop to a mechanically stirred solution of anisoxide in pyridine (30 vols.) at 0°. After 14 hours, the manganese dioxide was removed by filtration and washed with boiling water and the concentrated filtrates were acidified at 0°. The *acid* (A) was purified by conversion into the sodium salt and crystallisation from ligroin, from which it separated in rectangular plates, m. p. 181—182° (Found : C, 69·85; H, 6·7; *M*, by titration, 203. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%; *M*, 206). The *anilide*, prepared by the successive action of thionyl chloride and aniline, crystallised from ligroin in rhombic plates, m. p. 155—156° (Found : C, 75·5; H, 6·8; N, 5·0. $C_{18}H_{19}O_2N$ requires C, 76·6; H, 6·8; N, 5·0%).

Oxidation of the Acid (A).—Aqueous potassium permanganate (2%, 160 c.c.) was slowly added to a stirred solution of the acid A (1·5 g.) in dilute sodium carbonate solution (10 c.c.). After 8 hours the filtered sludge was repeatedly digested with water and the combined washings were concentrated and acidified. The *acid* (B) (yield, 55%) crystallised from dilute acetic acid in long needles, m. p. 215—216° (Found : C, 69·55; H, 5·5. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·2%).

Oxidation of the Acid (B).—Oxidation of the acid B (1·7 g.) in dilute sodium carbonate solution with 2% potassium permanganate solution (190 c.c.) was complete in 10 hours and afforded an *acid* (C), which crystallised from ligroin in clusters of large plates, m. p. 179·5—180·5° (Found : C, 64·0; H, 5·0. $C_{11}H_{10}O_4$ requires C, 64·1; H, 4·8%). The *methyl* ester crystallised from benzene in well-defined plates, m. p. 79—80° (Found : C, 65·7, 65·6; H, 5·7, 5·3. $C_{12}H_{12}O_4$ requires C, 65·5; H, 5·4%). A Zerewitinoff determination showed that the acid (C) contains one hydroxyl group; 0·100 g. of its methyl ester evolved 11·0 c.c. of methane at 15°/758 mm., equivalent to 1·03 atoms of active hydrogen per molecule.

Fission of the Oxide Ring in Perhydroanisoxide.—Perhydroanisoxide (5 c.c.), acetic acid (5 c.c.), and hydrogen bromide–acetic acid (50% ; 5 c.c.) were heated at 100° in a sealed tube for 2 hours and the liquid, which had separated into two layers, was poured into water and extracted with ether. The solution was washed with dilute aqueous sodium carbonate, dried, and evaporated. The residual *dibromide* (Found : Br, 42·9. $C_{14}H_{26}Br_2$ requires Br, 45·2%) was a heavy oil which would not solidify and could not be distilled without decomposition. A mixture of the dibromide (5 g.) and aniline (20 c.c.) was warmed cautiously and, after the exothermal reaction had subsided, was boiled for ½ hour. The mixture was then acidified and distilled in steam, and the colourless oil collected in ether. The *unsaturated hydrocarbon* (2·3 g.) had b. p. 110—112°/10 mm. (Found : C, 87·0; H, 13·2. $C_{14}H_{24}$ requires C, 87·5; H, 12·5%).

Oxidation of the Unsaturated Hydrocarbon, $C_{14}H_{24}$, *with Ozone.*—The hydrocarbon (25 g.) in acetic acid (150 g.), cooled in ice, was ozonised for 8 hours, and the ozonide decomposed by boiling the solution for ½ hour. After most of the acetic acid had been removed by distillation under diminished pressure, the liquid was poured into water, and the neutral products (13 g.) separated from acids (8·5 g.). The acids were esterified with methyl alcohol and distilled, yielding an ester fraction, b. p. 135—140°/5 mm. (5·0 g.; equiv., 214), which was hydrolysed to a mixture of acids (3·0 g.), b. p. 175—190°/10 mm., from which no homogeneous substance could be isolated. Fractionation of the neutral product afforded a *ketone* (1·5 g.), b. p. 102—105°/10 mm. (Found: C, 77·9; H, 10·2. $C_{10}H_{20}O$ requires C, 78·5; H, 11·9%). The new ketone was converted into the *semicarbazone*, which crystallised from methyl alcohol in microscopic prisms, m. p. 161—162° (Found: C, 64·0; H, 10·0; N, 18·6. $C_{12}H_{23}ON_3$ requires C, 64·0; H, 10·0; N, 18·7%). When the ketone was treated with Fuson's reagent (*J. Amer. Chem. Soc.*, 1934, **56**, 1638), iodoform, m. p. and mixed m. p. 119—120°, was produced.

Oxidation of Dihydroanisoxide.—(i) *With potassium permanganate.* The oxide (7·5 g.) in pyridine (75 c.c.) was stirred, and 2% potassium permanganate solution (315 c.c.) added during 10 hours. The manganese dioxide was removed and washed with boiling water. The filtrates were acidified and extracted continuously with ether, and the extract washed with dilute sodium hydroxide solution to remove traces of acids. After removal of the ether, distillation under diminished pressure (10 mm.) afforded the following fractions: (1) 125—135° (2 g.); (2) 135—200° (1 g.). Fraction (1) consisted of dihydroanisoxide, and fraction (2) furnished a *semicarbazone* which separated from benzene–ligroin in small rods, m. p. 191·5—192·5° (Found: C, 65·4; H, 7·2; N, 15·4. $C_{15}H_{21}O_2N_3$ requires C, 65·4; H, 7·6; N, 15·3%). Fraction (2) did not reduce Tollens's reagent and therefore contains a ketone, $C_{14}H_{18}O_2$.

(ii) *With ozone.* Dihydroanisoxide (6 g.) in acetic acid (30 c.c.), cooled in ice, was ozonised for 8 hours, and the ozonide decomposed by boiling for ½ hour. The acid product had b. p. 125—200°/4 mm. (0·2 g.) and the neutral product consisted of dihydroanisoxide, b. p. 123—130°/10 mm. (0·8 g.), and a portion, b. p. 130—160°/10 mm. (0·8 g.), which afforded a semicarbazone, m. p. 191·5—192°, identical with that obtained by method (1).

The Paraffin Hydrocarbon, $C_{19}H_{40}$.—The final fraction, b. p. 160—186°/5 mm., obtained in the distillation of star aniseed oil deposited crystals. These were acidic and after recrystallisation from hot water had m. p. 184° both alone and after admixture with anisic acid. The oily portion of the fraction was washed with alkali and distilled from sodium under diminished pressure. The distillate deposited a wax-like solid, which crystallised from chloroform–methyl alcohol in white flakes, m. p. 45—46° (Found: C, 85·2, 85·2; H, 14·8, 14·8; *M*, cryoscopic in camphor, 264, 266. $C_{19}H_{40}$ requires C, 85·1; H, 14·9%; *M*, 268). The *hydrocarbon* behaves as a saturated compound with tetranitromethane, bromine, and potassium permanganate.

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