

On the Acid-Catalysed Rearrangement of Ozonides*

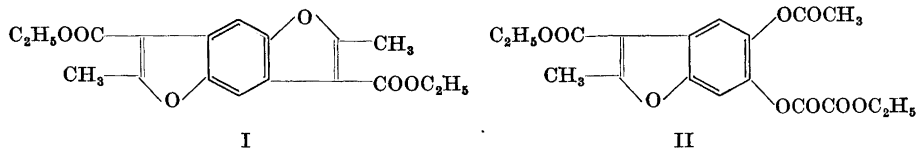
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An acid-catalysed rearrangement of two stable, crystalline ozonides is described. The reaction is intramolecular and the reacting entities are probably the conjugate acids of the ozonides.

It has been reported¹ that suitably substituted benzo [1,2—b:4,5—b'] difurans yield stable, crystalline ozonides. This is also the case with some benzofurans². Criegee's statement³ that stable ozonides often can be obtained from unsaturated five-membered rings is consequently further amplified. Ozonides can, like other peroxy compounds, undergo rearrangements where one of the "peroxidic" oxygen atoms is interposed between two carbon atoms. Undoubtedly such rearrangements often have been confused with anomalous ozonolysis because the net results of the reactions generally are identical. Only in the later years when really pure, stable and monomeric ozonides have become available, such rearrangements have been studied in some detail. Thus, Criegee⁴ has reported on the rearrangement of ozonides from 2,3-disubstituted indenones, while Witkop⁵ described a rearrangement of 2-phenylskatole ozonide.

We wish to describe the acid-catalysed rearrangement of the monozonide and diozonide of diethyl 2,6-dimethylbenzo [1,2—b:4,5—b'] difuran-3,7-dicarboxylate (I).



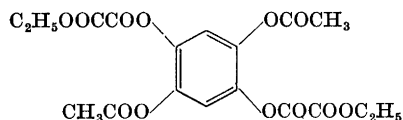
When the ozonides were dissolved in acetic anhydride containing a small amount of perchloric acid, the content of active oxygen disappeared rapidly. From the monozonide ($C_{18}H_{18}O_9$) two products could be isolated. A very small amount of an acid which could not be identified and a substance $C_{18}H_{18}O_9$.

* Presented at the 9. Nordiske Kemikermøde, Aarhus 1956.

The latter contained one O-acetyl group, split off one mole of oxalic acid on alkaline hydrolysis and could be alcoholysed to diethyl oxalate and a substance $C_{12}H_{12}O_5$. The latter could in turn be acetylated to a diacetate $C_{16}H_{16}O_7$. These results are only compatible with the structure II for the rearrangement product $C_{18}H_{18}O_9$.

Also the diozonide ($C_{18}H_{18}O_{12}$) yielded two products; an acid $C_{12}H_{10}O_8$ and a substance $C_{18}H_{18}O_{12}$. The acid gave a dimethyl ester and was identified as 2,5-diacetoxyterephthalic acid. $C_{18}H_{18}O_{12}$ contained two O-acetyl groups and by alkaline hydrolysis split off two moles of oxalic acid. Treatment with sodium acetate in acetic anhydride gave 1,2,4,5-tetracetoxybenzene. Evidently $C_{18}H_{18}O_{12}$ has the structure III.

The rearrangements are isomeric and most probably intramolecular since the same products in approximately the same yields were obtained by rearrangement in propionic anhydride. Further it is likely that the first step in the reaction is an addition of a proton, *i.e.* the reacting entities are the conjugate acids of the ozonides.



III

A semiquantitative experiment shows that with perchloric acid the reaction is very fast at 0°. With sulphuric acid it is somewhat slower but still fast and with hydrogen chloride very slow. The rate of the reaction is apparently dependent on the proton-donating strength of the catalyst. Witkop⁵ has outlined a probable mechanism for the rearrangement of 2-phenylskatole ozonide but did not support it with any special experimental evidence. Especially is the point of protonation arbitrarily chosen. No mechanism will be propounded here (several can be written), but it ought to be mentioned that the point of attack may as well be the ether bridge in the trioxolane ring of an ozonide as the peroxy bridge.

The formation of 2,5-diacetoxyterephthalic acid may be a result of a different course of the rearrangement. In this case the primary product is not an ester but a mixed anhydride of diacetoxyterephthalic acid and ethyl carbonate which is hydrolysed during isolation.

In the experimental part is further described the reduction of the ozonides to the corresponding α -ketoesters.

EXPERIMENTAL

(Melting points are not corrected)

Rearrangement of monozonide. Monozonide (0.90 g) was added in small portions to an ice-cooled mixture of perchloric acid (3 drops, 70%) and acetic anhydride (10 ml). After 30 min the content of active oxygen had disappeared and the mixture was poured into ice-water. A white substance (0.82 g) separated and was recrystallised from petrol ether, m. p. 89–90°. (Found: C 57.4; H 4.7; O-acetyl 11.5. Calc. for $C_{18}H_{18}O_9$ (II): C 57.2; H 4.8; O-acetyl 11.4.) A small amount of the raw product did not dissolve in petrol ether. It was an acid and decomposed at 197–198°.

II (86.7 mg) was boiled with sodium carbonate (10 ml, 2 N) for 60 min in a hydrogen atmosphere. The solution was analysed for oxalic acid. Found: Calcium oxalate dihydrate 30.0 mg. Calc. for $C_{14}H_{13}O_5(OCOCOC_2H_5)$: 33.5 mg. The calcium oxalate was dissolved in dilute hydrochloric acid, extracted with ether and the isolated oxalic acid identified by its X-ray powder diagram.

II (0.98 g) was refluxed with anhydrous ethanol (50 ml) containing hydrogen chloride (3 %) for 60 min). The mixture was evaporated to dryness and extracted with several portions of petrol ether and the extracts concentrated on a water-bath. The residue smelled like an ester and by means of its I.R.-spectrum was identified as diethyl oxalate. From the petrol ether extractions a white substance remained (0.60 g, 98 %). Recrystallised from dilute ethanol, colourless crystals m. p. 182°. (Found: C 61.2; H 5.1. Calc. for $C_{12}H_{12}O_5$: C 61.0; H 5.1.)

$C_{12}H_{12}O_5$ (0.24 g) and acetic anhydride (10 ml) were refluxed for 4 h and poured into ice-water. The separated substance (0.3 g) was recrystallised from benzene. Yellowish crystals, m. p. 158°. (Found: C 60.1; H 5.1; O-acetyl 27.0. Calc. for $C_{16}H_{16}O_7$: C 60.0; H 5.0; two O-acetyl 26.9.)

Rearrangement of diozonide. Diozonide (2.0 g) was rearranged as described for the monozonide. The product was an oil which solidified after two days in a refrigerator. The product (1.2 g) was extracted with hot benzene and the undissolved part (0.4 g) recrystallised from dilute ethanol. Decomp. $> 300^\circ$. (Found: C 50.9; H 3.9. Calc. for $C_{12}H_{10}O_8$: C 51.1; H 3.6.) This substance (0.28 g) was methylated with diazomethane and the product recrystallised from ethanol, m. p. 164–165°. Mixed m. p. with an authentic sample of 2,5-diacetoxyterephthalic acid dimethyl ester was undepressed.

The benzene extract was evaporated and washed with aqueous sodium bicarbonate, the residue being recrystallised from benzene, m. p. 138° (0.6 g). (Found: C 50.7; H 4.3; O-acetyl 20.5. Calc. for $C_{18}H_{18}O_{12}$ (III): C 50.7; H 4.3; two O-acetyl 20.2.)

III (0.23 g), acetic anhydride (10 ml) and sodium acetate (0.5 g) were refluxed for 3 h. Poured into ice-water when a brownish substance separated (0.17 g). Recrystallised from glacial acetic acid (charcoal), m. p. 227–228°. Mixed m. p. with an authentic sample of 1,2,4,5-tetracetoxybenzene was undepressed.

III (268 mg) was hydrolysed with sodium hydroxide and the solution analysed for oxalic acid. Found: calcium oxalate dihydrate 188 mg. Calc for $C_{10}H_8O_4(OCOCOC_2H_5)_2$ 184 mg.

The rearrangements were performed in propionic anhydride and the results were found to be essentially the same as described above.

Reduction of the ozonides. Monozonide (1.8 g) was dissolved in ethyl acetate (100 ml) and a solution of sodium iodide (3 g) in glacial acetic acid (15 ml) was added and the mixture shaken well. After 10 min the liberated iodine was removed with aqueous sodium sulphite. The ethyl acetate was washed with water, dried and concentrated when a dark oil (1.6 g) remained. This crystallised after some time and was recrystallised from dilute ethanol. White crystals, m. p. 99°. Gives a precipitate with 2,4-dinitrophenylhydrazine. (Found: C 59.5; H 5.0. Calc. for $C_{18}H_{18}O_8$: C 59.7; H 5.0.) The substance is regarded as ethyl 2-methyl-3-carbomethoxy-5-acetoxybenzofuranyl-6-glyoxalate (normal reduction product of the monozonide).

Diozonide (1.9 g) in chloroform (100 ml) was chilled to -23° and mixed with sodium iodide (6 g) in glacial acetic acid (30 ml). After 10 min the iodine was removed with aqueous sodium sulphite and the chloroform washed with aqueous sodium bicarbonate, dried and concentrated. A brown oil remained and crystallised in needles (1.4 g). Recrystallised from benzene, m. p. 135°. Positive reaction on carbonyl with 2,4-dinitrophenylhydrazine. (Found: C 54.9; H 4.6; O-acetyl 22.2. Calc. for $C_{18}H_{18}O_{10}$: C 54.8; H 4.6; two O-acetyl 21.8.) The substance is the expected reduction product of the diozonide: Diethyl 1,4-diacetoxybenzene-2,5-diglyoxalate.

One of the authors (E.B.) wishes to express his gratitude to *Fridtjof Nansens Fond* for a grant.

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Received October 14, 1958.

Acta Chem. Scand. **13** (1959) No. 2