[CONTRIBUTION FROM THE CHEMICAL INSTITUTE, FACULTY OF SCIENCE, UNIVERSITY OF ZAGREB]

REACTION OF $\alpha,\gamma,\delta,\zeta$-TETRAKETONES WITH SELENIUM DIOXIDE. POLYOXO COMPOUNDS. V.

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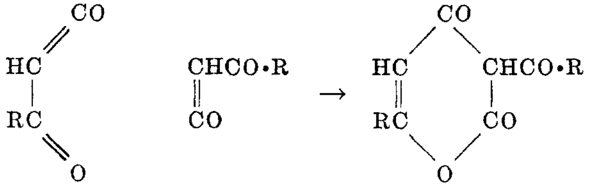
$\alpha,\gamma,\delta,\zeta$-Tetraketones (I), easily obtained by the condensation of diethyl oxalate with two moles of a methyl ketone (1), were readily oxidized with lead tetraacetate in glacial acetic acid at room temperature to dehydroacetic acids (IV), and not, as would be expected, to acetoxy derivatives (2).

A mechanism for this reaction is proposed (2), following which the dienolic form of the tetraketone (II) undergoes an oxidative fission with lead tetraacetate, giving two moles of acyl ketene (III) and this is then converted by diene condensation to the dehydroacetic acid (IV).

I $R{\cdot}COCH_2COCOCH_2CO{\cdot}R$
II $R{\cdot}COCH{:}C(OH)C(OH){:}CHCO{\cdot}R$
III $R{\cdot}COCH{:}CO \;+\; OC{:}CHCO{\cdot}R$



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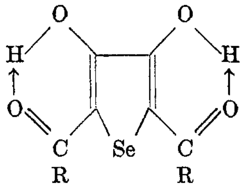

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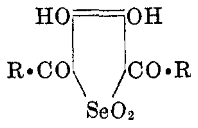

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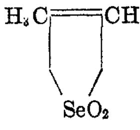

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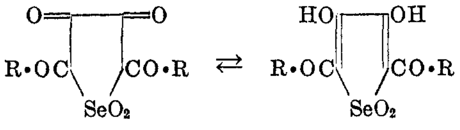

VIII IX

a. R = C_6H_5
b. R = p-C_6H_4Cl
c. R = p-$C_6H_4OCH_3$
d. R = α-Naphthyl
e. R = β-Naphthyl
f. R = Isobutyl
g. R = OC_2H_5

In the attempt to obtain compounds with a greater number of vicinal carbonyl groups, we oxidized 1,6-diphenyl-1,3,4,6-hexanetetrone (Ia) with selenium dioxide in dioxane. An intensely orange-colored, well crystallized reaction product was obtained in a 30% yield, having the empirical formula $C_{18}H_{12}O_4Se$. From this formula it is evident that two hydrogen atoms of 1,6-diphenyl-1,3,4,6-hexanetetrone (Ia) were substituted by a selenium atom. This new compound melts at 165°, and gives a dark brown color with an ethanolic ferric chloride solution. It was subjected to various procedures, *e.g.* it was refluxed for 12 hours with concentrated hydrochloric acid; refluxed for 24 hours with one mole of selenium dioxide in isoamyl alcohol; dissolved in *N* NaOH and refluxed for several hours, or the same alkaline solution was left at room temperature for several days. All these procedures left the compound unchanged. With an ethereal solution of diazomethane the compound $C_{18}H_{12}O_4Se$ gave a well crystallized dimethyl ether, which remained unchanged when treated with 30% hydrogen peroxide following the procedure usually employed for the preparation of selenoxides (3). With acetic anhydride and traces of sulfuric acid the compound $C_{18}H_{12}O_4Se$ gave a diacetate. Both the dimethyl ether and the diacetate show no color reaction with an ethanolic ferric chloride solution, and can be converted by hydrolysis to the starting material (Va).

The diacetate and the dimethyl ether of $C_{18}H_{12}O_4Se$ gave bis-2,4-dinitrophenylhydrazones with 2,4-dinitrophenylhydrazine, which indicates the presence of two enolic and two carbonyl groups in the compound $C_{18}H_{12}O_4Se$ (Va). Furthermore, the bis-mercaptol derivative was prepared from the dimethyl ether of $C_{18}H_{12}O_4Se$ with 1,2-ethanedithiol. An ethanolic solution of Va forms red precipitates with aqueous solutions of *e.g.*, copper, nickel, cobalt, and uranium salts, also if these are very diluted. It is evident that the enolic and carbonyl groups of $C_{18}H_{12}O_4Se$ are in such positions as to be able to form chelates.

The experimental facts given above do not contradict our assumption that the compound $C_{18}H_{12}O_4Se$ is 2,5-dibenzoyl-3,4-dihydroxyselenophene (Va). To confirm this, we prepared the dichloro derivative of the above mentioned dimethyl ether of Va with chlorine at 0°. This dichloro derivative, when treated with potassium iodide liberated iodine, and could be titrated as a selenide dihalide (4, 5). Refluxing with zinc dust in tetrachloromethane yielded the original dimethyl ether of Va. Slow decomposition of the dichloro derivative took place on standing at room temperature in a vacuum desiccator. From the decomposition products only the original dimethyl ether of Va could be isolated in a 71% yield, and therefore it is not probable that this compound contains the structural unit $—SeCH_2—$ as the selenide dihalides of such compounds readily decompose to selenide monohalides and alkyl halides (6–8).

All these data confirm the conclusion that the selenium of the compound obtained by oxidation of Ia with selenium dioxide is divalent, that it is part of a selenide linkage, and that the selenide is aromatic of character. Furthermore, the dimethoxy derivative of the original selenium-containing compound Va, oxidized in glacial acetic acid with CrO_3 yielded 1.85 moles of benzoic acid, which is also in accordance with the formula Va.

Our suggestion for the mechanism of this reaction is that 1,4-addition of selenium dioxide takes place on the conjugated diene of the dienolic form (II).

The thus formed cyclic selenone (VI) would represent the first stage of this reaction, which is analogous to the formation of 3,4-dimethylselenacyclopent-3-ene-1,1-dioxide (VII) from 2,3-dimethylbutadiene-1,3 and selenium dioxide (9).

During the oxidation of 1,3,4,6-tetraketones with selenium dioxide, the cyclic selenone (VI) containing the enediol system can be dehydrogenated to the dehydro derivative (VIII or IX). It can also be assumed that the enediol system of the cyclic selenone (VI) can reduce a second molecule of selenone to the selenophene (V). Moreover, similarly to the formation of diphenyl selenide and diphenyl sulfide by the heating of diphenyl sulfone with selenium or sulfur respectively (10), it can be assumed that the cyclic selenone (VI) can be converted to the selenophene (V) with the selenium formed from the selenium dioxide oxidation taking place in the side reactions. In connection with the elucidation of this reaction mechanism, a solution of 1,6-diphenyl-1,3,4,6-hexanetetrone (Ia) in dioxane was refluxed for 24 hours with selenium. From the reaction mixture only the pure starting material was isolated, in 86% yields, and it is therefore highly improbable that the selenium formed in the side reactions could react with the tetraketones I to form the selenium-containing compounds V.

Following the same procedure as given for the oxidation of 1,6-diphenyl-1,3,4,6-hexanetetrone, we also oxidized 1,6-di-(*p*-chlorophenyl)-1,3,4,6-hexanetetrone (Ib) and obtained the compound $C_{18}H_{10}Cl_2O_4Se$ (Vb), which also shows that two hydrogen atoms were substituted with selenium. In the same manner 1,6-di-(*p*-methoxyphenyl)-1,3,4,6-hexanetetrone (Ic), 1,6-di(α-naphthyl)-1,3,4,6-hexanetetrone (Id), 1,6-di-(β-naphthyl)-1,3,4,6-hexanetetrone (Ie), 2,11-dimethyl-4,6,7,9-dodecanetetrone (If), and diethyl 3,4-diketoadipate (Ig) gave, on oxidation with selenium dioxide in dioxane, poor yields of analogous, selenium-containing compounds (Table I). All these compounds are orange-colored crystals, which gave a dark brown color with ferric chloride.

The compounds Ib–e have similar properties as Ia, but the aliphatic selenium-containing compounds If–g are not nearly as stable; *e.g.* after being refluxed for a

TABLE I

OXIDATION PRODUCTS OF α,γ,δ,ζ-TETRAKETONES WITH SeO_2

Formula	Starting Material	Ref.	Yield, %	M.P., °C.	Crystallized from[a]	Analyses			
						Calc'd		Found	
						C	H	C	H
$C_{18}H_{10}Cl_2O_4Se$ (Vb)	Ib	(12)	46	160–161	A	49.12	2.29	49.45	2.61
$C_{20}H_{16}O_6Se$ (Vc)	Ic	(13)	11	117	B	55.69	3.74	56.16	3.94
$C_{26}H_{16}O_4Se$ (Vd)	Id	(12)	37	265	C	66.25	3.42	66.02	3.86
$C_{26}H_{16}O_4Se$ (Ve)	Ie	(12)	20	195	A	66.25	3.42	65.94	3.49
$C_{14}H_{20}O_4Se$ (Vf)	If	(12)	24	176	D	50.76	6.09	50.99	5.82
$C_{10}H_{12}O_6Se$ (Vg)	Ig		8	195	E	39.10	3.94	38.95	3.67

[a] Solvent is designated by capital letter: A, benzene-petroleum ether; B, dichloromethane; C, aqueous acetone; D, acetone; E, dichloromethane-petroleum ether.

few minutes with N NaOH they are converted to selenium-free compounds. The constitution of these aliphatic tetraketones If–g will be the subject of further investigations.

EXPERIMENTAL

All melting points are uncorrected.

2,5-Dibenzoyl-3,4-dihydroxyselenophene (Va). Pure 1,6-diphenyl-1,3,4,6-hexanetetrone prepared according to Brömme and Claisen (1) (Ia, 3 g., 0.01 mole) was refluxed for 24 hours with a suspension of SeO_2 (2.4 g., 0.022 mole) in dioxane (30 ml.). After the first half hour of refluxing selenium began to separate, and after 24 hours 0.75 g. (0.0095 gram-atom) of selenium was collected. The filtrate was evaporated under reduced pressure, the residue dissolved in chloroform, and the solution washed with water. After evaporating the solvent, the residual substance was dissolved in a small quantity of hot benzene, from which, after cooling, 1 g., (29%) of crystals separated, showing the m.p. 163–165°, and a deep red mother liquor remained. Recrystallization from acetone yielded bright orange prisms, m.p. 165°. The substance could be sublimed at 140–160°/0.02 mm.

Anal. Calc'd for $C_{18}H_{12}O_4Se$ (371.24): C, 58.23; H, 3.26; Se, 21.27.

Found: C, 58.27, 58.43; H, 3.09, 3.21; Se, 21.28 (11).

2,5-Dibenzoyl-3,4-dimethoxyselenophene. The finely powdered 2,5-dibenzoyl-3,4-dihydroxyselenophene (Va, 0.5 g.) was treated with an ethereal solution of diazomethane, and left at room temperature for 12 hours. The ether then was evaporated, and the residual red-brown oil was dissolved in ether, and filtered through a column of Al_2O_3 (10 g., activity IV according to Brockmann). After eluting the column with benzene, 0.43 g. (86%) of pale crystals were obtained, m.p. 77–80°. After repeated recrystallization from benzene-petroleum ether, yellow prisms of 2,5-dibenzoyl-3,4-dimethoxyselenophene (0.25 g., 50%) remained, m.p. 87°.

Anal. Calc'd for $C_{20}H_{16}O_4Se$ (399.29): C, 60.16; H, 4.04; OCH_3, 15.54.

Found: C, 60.40; H, 4.11; OCH_3, 16.46; Mol. wt. (Pregl-Roth), 392, 402.

To a solution of the above mentioned dimethoxy derivative (0.2 g.) in glacial acetic acid (2 ml.), 48% hydrobromic acid (0.5 ml.) was added. After refluxing for an hour, the reaction mixture was diluted with water (25 ml.). An orange-colored precipitate separated (0.96 g.), which after recrystallization from benzene gave orange needles, yield 0.69 g. (45%), m.p. 165°; mixture m.p. with $C_{18}H_{12}O_4Se$ (Va), 165°.

Bis-2,4-dinitrophenylhydrazone of 2,5-dibenzoyl-3,4-dimethoxyselenophene. To a solution of 2,5-dibenzoyl-3,4-dimethoxyselenophene (0.2 g.) in methanol (10 ml.), a methanolic solution of 2,4-dinitrophenylhydrazine was added (16 ml. of a solution of 2.5 g. of 2,4-dinitrophenylhydrazine in 100 ml. of methanol and 4 ml. of concentrated hydrochloric acid). After the mixture was left at room temperature for 24 hours, the red prisms were collected, yield 0.47 g. (99%), m.p. 252°. They were recrystallized from dioxane, m.p. 262°.

Anal. Calc'd for $C_{32}H_{24}N_8O_{10}Se$ (759.54): C, 50.60; H, 3.19.

Found: C, 50.66; H, 3.30.

Bis-mercaptol derivative of 2,5-dibenzoyl-3,4-dimethoxyselenophene. 2,5-Dibenzoyl-3,4-dimethoxyselenophene (0.85 g.) and ethanedithiol (1 ml.) were dissolved in a 3% solution of anhydrous hydrochloric acid in dioxane (10 ml.). After standing at room temperature for two weeks, the reaction mixture was evaporated to dryness *in vacuo*, and the residue was dissolved in benzene. From this benzene solution colorless needles of the bis-mercaptol derivative of 2,5-dibenzoyl-3,4-dimethoxyselenophene were obtained by precipitation with petroleum ether. Yield, 1.05 g. (87%), m.p. 170°. The compound was recrystallized from benzene-petroleum ether, m.p. 172°. (The analytical sample was melted in a high vacuum before analysis.)

Anal. Calc'd for $C_{24}H_{24}O_2S_4Se$ (551.63): C, 52.25; H, 4.39.

Found: C, 52.28; H, 4.30.

Preparation of the bis-mercaptol derivative of 2,5-dibenzoyl-3,4-dihydroxyselenophene

(Va) in the same manner as given above failed, and only high yields of the starting material were recovered.

2,5-Dibenzoyl-3,4-dimethoxyselenophene dichloride. Chlorine was passed through a solution of the above mentioned dimethoxy derivative (0.5 g.) in tetrachloromethane (10 ml.) during 15 minutes at 0°. Lemon-yellow needles of 2,5-dibenzoyl-3,4-dimethoxyselenophene dichloride separated at once, yield 0.49 g. (82%), m.p. 69° (decomp.).

Anal. Calc'd for $C_{20}H_{16}Cl_2O_4Se$ (470.20): C, 51.08; H, 3.43.
Found: C, 51.27; H, 3.53.

This dichloro derivative (0.100 g.) was titrated with $N/50$ $Na_2S_2O_3$ according to McCullough, Campbell, and Krilanovich (5). Mol. weight, calc'd: 470. Found: 462.

A solution of the dichloro derivative of 2,5-dibenzoyl-3,4-dimethoxyselenophene (0.2 g.) in tetrachloromethane (10 ml.) was treated with zinc dust (0.24 g.), and the mixture was refluxed for 4 hours. After proceeding in the usual manner, a yellow oil was obtained, which crystallized at once on the addition of petroleum ether. Yield 0.12 g. (73%) of yellow crystals of 2,5-dibenzoyl-3,4-dimethoxyselenophene, m.p. 87°.

The *dichloro derivative* of 2,5-dibenzoyl-3,4-dimethoxyselenophene decomposes spontaneously in a vacuum desiccator into a viscous oil from which 2,5-dibenzoyl-3,4-dimethoxyselenophene, m.p. 87°, can be recovered in a 71% yield. (Confirmed by analysis and mixture m.p.)

Oxidation of 2,5-dibenzoyl-3,4-dimethoxyselenophene with CrO_3. To a solution of 2,5-dibenzoyl-3,4-dimethoxyselenophene (0.3 g., 0.0007 mole) in glacial acetic acid (5 ml.) at 60°, a solution of CrO_3 in 75% acetic acid was added (3 ml.), containing 0.5 g. CrO_3 per ml. The oxidation was carried out at 60°, and was complete after an hour. The reaction mixture was cooled, diluted with water (100 ml.), and extracted with ether. From the ethereal extracts benzoic acid could be isolated; yield after sublimation 0.15 g. (91%, 1.85 moles), m.p. 121°.

2,5-Dibenzoyl-3,4-diacetoxyselenophene. A mixture of 2,5-dibenzoyl-3,4-dihydroxyselenophene (Va, 0.5 g.) and acetic anhydride (3 ml.) was heated with traces of concentrated sulfuric acid on a steam-bath for an hour. By that time the reaction mixture was liquid. The excess acetic anhydride was evaporated to dryness under reduced pressure, the residue cooled to 0°, and water (20–30 ml.) was added. After standing for a short time at 0°, the crystals were collected and dried, yield 0.5 g. (82%), m.p. 118°. Recrystallization from aqueous acetone gave white needles of 2,5-dibenzoyl-3,4-diacetoxyselenophene, constant m.p. 135°.

Anal. Calc'd for $C_{22}H_{16}O_6Se$ (455.31): C, 58.03; H, 3.54.
Found: C, 58.24; H, 3.62.

Bis-2,4-dinitrophenylhydrazone of 2,5-dibenzoyl-3,4-diacetoxyselenophene. To a solution of 2,5-dibenzoyl-3,4-diacetoxyselenophene (0.2 g.) in the minimum quantity of methanol, a methanolic solution of 2,4-dinitrophenylhydrazine was added (8 ml. of the same solution as used for the preparation of the 2,4-dinitrophenylhydrazone of the dimethoxy derivative of Va). After the mixture was left at room temperature for 48 hours, the red crystals which had gradually separated were collected, yield 0.4 g. (100%), m.p. 208°. These were recrystallized from dioxane, m.p. 253°.

Anal. Calc'd for $C_{34}H_{24}N_8O_{12}Se$ (815.56): C, 50.07; H, 2.97.
Found: C, 49.97; H, 3.20.

Reaction of $C_{14}H_{20}O_4Se$ (Vf) with diluted NaOH. To a solution of $C_{14}H_{20}O_4Se$ (Vf, 330 mg., 0.001 mole) obtained by the oxidation of 2,11-dimethyl-4,6,7,9-dodecanetetrone with SeO_2 (Table I), in methanol (10 ml.), N NaOH (4.4 ml., 0.004 mole) was added and the mixture was left at room temperature for an hour. The reaction mixture was then acidified to Congo Red with concentrated hydrochloric acid, and selenium (48 mg., 61%) was filtered off. From the mother liquor red crystals (100 mg.) of a selenium-free compound, soluble in petroleum ether, were isolated.

The compound $C_{10}H_{12}O_5Se$ (Vg) reacted similarly to Vf on treatment with diluted NaOH.

SUMMARY

Oxidation of $\alpha,\gamma,\delta,\zeta$-tetraketones (Ia–g) with selenium dioxide gave poor yields of crystalline, orange-colored selenium-containing compounds (Va–g).

A description of experimental data is given, which support our suggestion that the selenium-containing compounds Va–e are 2,5-diacyl-3,4-dihydroxyselenophenes.

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REFERENCES

(1) Brömme and Claisen, *Ber.*, **21,** 1134 (1888).
(2) Balenović, *Rec. trav. chim.*, **67,** 282 (1948); *Experientia*, **2,** 406 (1946).
(3) Rheinbolt and Giesbrecht, *J. Am. Chem. Soc.*, **69,** 644 (1947).
(4) McCullough, *J. Am. Chem. Soc.*, **64,** 2672 (1942).
(5) McCullough, Campbell, and Krilanovich, *Ind. Eng. Chem., Anal. Ed.*, **18,** 638 (1946).
(6) Behagel and Hofmann, *Ber.*, **72,** 697 (1939).
(7) Edwards, Gaythwaite, Kenyon, and Phillips, *J. Chem. Soc.*, 2293 (1928).
(8) Campbell, Walker, and Coppinger, *Chem. Revs.*, **50,** 279 (1952).
(9) Backer and Strating, *Rec trav. chim.*, **53,** 1113 (1934).
(10) Krafft and Vorster, *Ber.*, **26,** 2813 (1893).
(11) Drew and Porter, *J. Chem. Soc.*, 2092 (1929).
(12) Keglević, Malnar, and Tomljenović, *Arhiv kem.*, (in press).
(13) Widman and Virgin, *Ber.*, **42,** 2803 (1909).