255. *Selenium Dioxide, a New Oxidising Agent. Part I. Its Reaction with Aldehydes and Ketones.*

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IT has long been known that selenium dioxide, selenious and selenic acids and selenites are readily reduced to selenium by a variety of substances, but no previous systematic study of their oxidising properties appears to have been made. Recently, when the work to be described in the first three parts of this series was complete, the use of selenious and selenic acids for the oxidation of methylbenzanthrones and allied compounds to the corresponding aldehydes was reported (I. G. Farb. A.G., B.P. 1931, 347,743). Lauro (*Ind. Engin. Chem.*, *Anal. Sec.*, 1931, **3**, No. 4, 401) has described the advantageous use of selenium instead of copper as the catalyst in the Kjeldahl determination of nitrogen.

Selenium dioxide is readily recovered either by burning, or by oxidising the precipitated selenium with nitric acid and subliming the product. The latter method is more convenient in the laboratory.

1. *Methylglyoxal.*—Selenium dioxide (400 g.) and acetone (2 l.) were heated under reflux for 3—4 hours, carefully during the initial stage when the reaction was exothermic. The yellow liquid product was decanted, the black residue washed with acetone, and the whole liquid fractionated. The pale yellow distillate, b. p. 56·5°, was an azeotropic mixture of acetone containing about 1% of methylglyoxal and could be conveniently used as the initial material for further preparation of methylglyoxal. 1600 C.c. were recovered up to 80° and the residual liquid was fractionated under reduced pressure. The higher-boiling fraction condensed to a bright yellow, mobile liquid, which quickly set exothermically and became paler. The lower-boiling fractions, which contained a greater proportion of water, simply became viscous. [According to Harries and Turk (*Ber.*, 1905, **38**, 1630), the jelly is a polymeride of methylglyoxal.] The evolution of heat accompanying this polymerisation has not

previously been reported, possibly because hitherto this compound has not been readily prepared in quantity. Depolymerisation is effected by distillation. The yield of methylglyoxal (containing a little water), b. p. 54—70°/50 mm., was more than 50 g. The bisphenylhydrazone prepared from it had m. p. 145° (Found : C, 71·5; H, 6·1; N, 22·5. Calc. : C, 71·7; H, 6·0; N, 22·3%), and the dioxime had m. p. 154° (Found : N, 27·7. Calc. : N, 27·5%). The mother-liquors from the latter preparation when rendered ammoniacal gave the nickel salt of methylglyoxime (Found : Ni, 22·3. Calc. : Ni, 22·5%).

A fraction of methylglyoxal, b. p. 54°/10 mm., was redistilled from calcium chloride (Found: C, 44·1; H, 6·3. Calc. for $CH_3{\cdot}CO{\cdot}CHO$: C, 50·0; H, 5·6%); the presence of approximately $\frac{1}{2}H_2O$ is thus indicated (compare Meisenheimer, *Ber.*, 1912, **45**, 2635; Fischer and Taube, *Ber.*, 1924, **57**, 1502; 1926, **59**, 857; Fischer, Feldman, and Dangschat, *Ber.*, 1929, **62**, 854).

When a mixture of acetone with a little water was added to selenium dioxide in the cold, the reddish colour due to the liberation of selenium developed more rapidly than was the case when ordinary dry acetone was used, indicating that selenious acid and not selenium dioxide was the active oxidising agent. This was tested as follows : A Pyrex glass apparatus was heated to softening in a current of dry air and cooled. Pure, freshly sublimed selenium dioxide was placed in one limb of the apparatus, and pure dry acetone (Timmermans, *Sci. Proc. Roy. Dublin Soc.*, 1912, **13**, 330) distilled on to anhydrous copper sulphate in the other. The two limbs were separated by a tap and the selenium dioxide limb communicated with a side arm containing phosphoric oxide. This limb was evacuated and sealed, and the dioxide sublimed through a narrow constriction. In this way, selenium dioxide containing no appreciable quantity of selenious acid was obtained. The tap was now opened, and the acetone distilled on to the dioxide by cooling the latter. The faint red colour due to the formation of selenium appeared in approximately the same time (about 4 mins.) as that required for its appearance when ordinary pure acetone was used. A second experiment gave the same result. It is probable, therefore, that selenium dioxide itself, as well as selenious acid, can take a definite stoicheiometric part in these reactions.

Yields almost 60% of the theoretical (calculated from the weight of selenium dioxide) of methylglyoxal containing only a few units % of water have been obtained by using "recovered" acetone initially. The amounts of methylglyoxal formed were estimated by Friedemann's method (*J. Biol. Chem.*, 1927, **73**, 331), and the results showed that practically 100% of the oxygen from the selenium dioxide is utilised in the formation of methylglyoxal according to the equation $SeO_2 + CH_3{\cdot}CO{\cdot}CH_3 = CH_3{\cdot}CO{\cdot}CHO + Se + H_2O$. Loss occurs in the isolation of the methylglyoxal owing to decomposition on distillation. If distillation is carried past the temperature mentioned above, a small quantity of oil accompanied by free selenium is obtained. This was shown to be a very unstable selenium compound which breaks down on heating, giving some methylglyoxal. The formation of such unstable selenium compounds is one source of loss in these oxidations.

Methylglyoxal itself is readily oxidised by selenium dioxide, yielding principally carbon dioxide and carbon monoxide together with small quantities of formaldehyde and glyoxylic acid. In the above preparation of methylglyoxal it is essential to have a large excess of acetone present to act as a diluent, otherwise only poor yields of methylglyoxal are obtained, owing to its further oxidation.

Phenylglyoxal.—Acetophenone (220 g.) and selenium dioxide (100 g.) were refluxed for 2 hours and the product, when cold, was extracted thoroughly with boiling water. The extract on cooling deposited white crystals (phenylglyoxal hydrate) contaminated by a little selenium. The whole was therefore extracted with ether; from the dried extract, phenylglyoxal, b. p. 96—97°/25 mm., was obtained. This gave a phenylhydrazone, m. p. 153° (Found : N, 18·0. Calc. : N, 17·8%), and a disemicarbazone, m. p. 143° (Found : N, 34·0. Calc. : N, 33·9%). Crystals of phenylglyoxal hydrate, obtained by boiling with water, were recrystallised from rectified spirit; m. p. 91° (Found : C, 63·0; H, 5·7. Calc. : C, 63·2; H, 5·6%). A yield of over 50%, calculated on the selenium dioxide, was obtained.

The above method can be modified by steam-distilling the product and fractionally extracting it with ether; the excess of acetophenone, containing a little phenylglyoxal, can thus be recovered.

Diacetyl and Ethylglyoxal.—In order to determine whether there is a preferential attack on the methyl of the methylene group adjacent to the carbonyl group in an aliphatic ketone, the reaction with methyl ethyl ketone was studied.

Methyl ethyl ketone (450 c.c.) and selenium dioxide (112 g.) were refluxed, carefully at first, until the precipitated selenium had coagulated. The liquid was decanted, the selenium washed with 50 c.c. of the pure ketone, and the united liquids submitted to distillation from a steam-bath; 250 c.c. (the excess of methyl ethyl ketone containing some diketone) were obtained. The residual liquid, filtered from some selenium, gave 110 g., b. p. 76—145° mm., containing 61·5 g. of diacetyl and ethylglyoxal (estimated by precipitating the nickel salts of the mixed dioximes). Several grams of ethylglyoxal were isolated by further fractionation in a vacuum, and this gave a bisphenylhydrazone, m. p. and mixed m. p. 116° (Found : N, 21·3. Calc.: N, 21·1%), a monosemicarbazone, m. p. 236—237°, and a nickel salt of its dioxime (Found : Ni, 20·0. Calc.: Ni, 20·3%). The yield of ethylglyoxal of 80% purity was 22%, calculated on the weight of selenium dioxide. The product contained water.

Only a fraction of 1 g. of diacetyl of reasonable purity was isolated. This gave a dioxime, m. p. and mixed m. p. 240° (Found : N, 24·3. Calc.: N, 24·1%), and a bisphenylhydrazone, m. p. 237° (Found : N, 21·4. Calc.: N, 21·1%).

The above indicates that ethylglyoxal is preferentially formed in this oxidation. It is, however, impossible to be certain of this without further experiments, for it was necessary to refractionate the diacetyl four times at a stage where one sufficed to give pure derivatives with ethylglyoxal, and a little decomposition occurs each time.

Methylethylglyoxal.—Diethyl ketone (250 c.c.) and selenium dioxide (112 g.) were refluxed for 2 hours, carefully in the initial stage. The liquid was then distilled, 221 c.c., b. p. 100—115°, being collected. As the b. p. of diethyl ketone falls within the boiling range of methylethylglyoxal, no attempt was made to separate the diketone. This, however, was shown to be the principal product by precipitating the nickel salt of its dioxime, m. p. 280° after recrystallisation from rectified spirit (Found : Ni, 17·9. Calc.: Ni, 18·0%).

Phenylmethylglyoxal.—Selenium dioxide (56 g., dissolved in rectified spirit, 300 c.c., to reduce the vigour of the reaction) and propiophenone (67 g.) were refluxed over-night and then steam-distilled until the distillate no longer reduced ammoniacal silver nitrate. The first fraction, principally alcohol, was freed from this by redistillation, and the residue added to the second milky fraction, which was then well cooled and fractionally extracted with ether. Fairly pure propiophenone (19 g.), b. p. 205—212°, was obtained first, and then, sodium chloride having been added to the aqueous liquid, phenylmethylglyoxal, b. p. 120—125°/23 mm. This gave a monoxime, m. p. 165° (Found : N, 8·7. Calc.: N, 8·6%), and the nickel salt of the dioxime, m. p. 238° (decomp.) (Found : Ni, 12·5. Calc.: Ni, 12·6%). The yield of product of 90% purity (the remainder being principally water) was 50%, calculated on the selenium dioxide used.

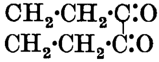
cyclo*Hexane*-1 : 2-*dione*.—Selenium dioxide (56 g.), dissolved in rectified spirit (300 c.c., preferably recovered from a previous experiment) was added to *cyclo*hexanone (50 g.) at 70—80° during 2 hours, and the whole refluxed for 2 hours. As much of the liquid as possible was distilled from a steam-bath, the remainder decanted from the selenium, this washed with ether, and the combined washings and liquid freed from ether and distilled under reduced pressure, selenium present both in solution and in combination thus being removed; 40 g. of oil (*cyclo*hexanone and *cyclo*hexane-1 : 2-dione) and water were thus obtained. A solution of the oil in 200 c.c. of ether was extracted consecutively with three equal volumes of ice-cold 10% caustic potash solution, the total of which was equivalent to 1½ times that necessary to react with all the oil, assumed to be pure dione in the mono-enolic state. The potash extract was shaken once with ether (which removed 9 g. of *cyclo*hexanone), acidified with ice-cold hydrochloric acid, and saturated with sodium chloride. Ether then extracted an oil which gave 11 g. of a very pale green liquid (*cyclo*hexane-1 : 2-dione), b. p. 96—97°/25 mm., and 2 g. of a dark red fraction (contaminated dione), b. p. up to 140°/25 mm., on distillation (Found : C, 64·0; H, 7·1. Calc. : C, 64·3; H, 7·2%). The dione gave a bisphenylhydrazone, m. p. 152° (Found : N, 19·5. Calc. : N, 19·2%), a dioxime, decomp. 185—190° (Found : N, 19·6. Calc. : N, 19·5%), and its nickel salt (Found : Ni, 17·1. Calc. : Ni, 17·2%), and a phenylurethane, m. p. 121°. These derivatives were compared (mixed m. p.) with specimens prepared from the dione made by Wallach's method (*Annalen*, 1924, **437**, 174). Wallach's statement (*loc. cit.*) that the dione is a solid, m. p. 39—40°, could not be confirmed. When either of the specimens of dione was exposed to the air for some months, crystals of adipic acid were formed, m. p. 148° (Found : C, 49·1; H, 6·9. Calc. : C, 49·3; H, 6·8%).

The formation of adipic acid, which was also found in the higher-boiling 2 g.-fraction in the preparation, indicates that the continued oxidation of the dione with selenium dioxide breaks down the *cyclo*hexane ring and does not give an aromatic ring.

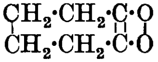
A yield of pure dione of 35%, calculated on the selenium dioxide used, was obtained.

The preparation of this simple 1 : 2-cyclic diketone offered an opportunity of determining whether an additional ring, involving the two ketonic oxygen atoms, is present.

(I.)



$$\begin{array}{l}CH_2\cdot CH_2\cdot C{:}O\\ CH_2\cdot CH_2\cdot C{:}O\end{array}$$



$$\begin{array}{l}CH_2\cdot CH_2\cdot C\cdot O\\ CH_2\cdot CH_2\cdot C\cdot O\end{array}$$

(II.)

Dr. S. Sugden kindly measured the parachor of this dione (M, 112·1), and the result shows that the ketonic (or enolic) structure is correct.

t	21°	26°	34°	42·5°	52·5°	
γ	44·22	43·59	42·36	41·26	39·63	
D......	1·1187	1·1130	1·1060	1·0976	1·0881	
$[P]$ ...	258·5	258·5	258·6	258·6	258·4	Mean, 258·5

Calculated for (I), $[P]$ = 258·1. Calculated for (II), $[P]$ = 246·5.

Experiments on bromine addition showed that the freshly distilled dione was chiefly the diketo-compound, the quantity of enol present gradually increasing until after 2 months an equilibrium mixture containing nearly 40% of enol had been formed.

cyclo*Pentane*-1 : 2-*dione*.—Selenium dioxide (56 g.) in rectified spirit (300 c.c.) was added to *cyclo*pentanone (42 g.) in hot rectified spirit (200 c.c.) during 2 hours. After 2 hours' refluxing, the more volatile liquid was distilled from a steam-bath and the residual liquid was decanted and extracted with hot water. The extract, which contained no selenium, indicating that reduction of the dioxide was complete, was saturated with sodium chloride, and ether then removed 8 g. of a yellow oil, from which 2·5 g. of *cyclo*pentane-1 : 2-dione, b. p. 124—126°/35 mm., were obtained in a similar manner to that employed for the extraction of the corresponding *cyclo*hexanedione. It would not solidify, even on strong cooling and long standing (Dieckmann, *Ber.*, 1897, **30**, 1471; 1902, **35**, 3208, describes the pentanedione as a crystalline mass, m. p. 55—60°) and gave the following derivatives : dioxime, m. p. 208° (Found : N, 22·0. Calc. : N, 21·9%), disemicarbazone, decomp. 245—250° (Found : N, 39·6. Calc. : N, 39·6%), bisphenylhydrazone, m. p. 145° (Found : N, 20·4. Calc. : N, 20·2%). The yield was only 7%, and as all the dioxide was used, it is probable that the dione was itself oxidised by selenium dioxide at the temperature of the reaction.

Buchu-camphor (*Diosphenol*).—Selenium dioxide (21 g.) in rectified spirit (200 c.c.) was refluxed over-night with 38 g. of menthone. The liquid was then decanted, and steam-distilled after addition of 36 g. of sodium carbonate (this is necessary to prevent the selenium remaining in the decanted liquid, probably in unstable combination, from being carried over into the distillate). Ether extracted from the distillate a yellow oil (30 g.), which was redissolved in a little ether and shaken with aqueous caustic soda. Addition of hydrochloric acid to the soda extract precipitated a yellow oil, which set to a white crystalline mass. This solid and the acid solution were extracted with ether, and slow evaporation of the dried extract gave 1·8 g. of pure white crystalline buchu-camphor, m. p. 82° (Found : C, 71·3; H, 9·6. Calc. : C, 71·4; H, 9·6%). It gave a phenylurethane, m. p. 112—113° (Found : C, 71·0; H, 7·3. Calc. : C, 71·0; H, 7·4%), and a disemicarbazone, m. p. 268° (Found : C, 54·7; H, 7·0. Calc. : C, 54·9; H, 7·1%).

Owing to the small yield (15%) of buchu-camphor, the brown liquid remaining after the distillation was tested and found to contain, unreduced, nearly two-thirds of the original selenium dioxide; this indicates that a solvent of higher b. p. than ethyl alcohol might be used with advantage.

Glyoxal.—A methylene group adjacent to the carbonyl group of an aldehyde is readily oxidised to carbonyl by selenium dioxide. After initial difficulties, due to the properties of glyoxal, it has been shown that the reaction $CH_3 \cdot CHO + SeO_2 = (CHO)_2 + H_2O + Se$ proceeds almost quantitatively.

(a) *Pressure bottle method.* A well-cooled mixture of selenium dioxide (28 g.) and acetaldehyde (100 c.c.) was warmed in a pressure bottle for 6 hours. (There is a considerable danger of explosion if the temperature exceeds 60—80°, gaseous products including carbon dioxide and monoxide being formed.) When cool, the product was decanted from the selenium, which was washed with acetaldehyde, and the united liquids were distilled until the temperature reached 80°. An aqueous extract of the remaining liquid (some paraldehyde had been formed) was acidified with hydrochloric acid, boiled, and freed from a trace of unreduced selenium dioxide by means of sulphur dioxide. An aliquot part of the filtered liquid was neutralised with sodium carbonate, and an excess of acetic acid and phenylhydrazine added; glyoxalbisphenylhydrazone (Found: N, 23·7. Calc.: N, 23·5%) was precipitated almost quantitatively (m. p. 173° after recrystallisation from methyl alcohol): 1 part in 1000 can be estimated in this way (compare Curtius, *J. pr. Chem.*, 1917, **95**, 212). The wide range of m. p.'s reported for this compound, 169° to 177° (Fischer, *Ber.*, 1884, **17**, 575; Pickel, *Annalen*, 1885, **232**, 228; Oddo and Cusmano, *Gazzetta*, 1911, **41**, ii, 246; Curtius, *loc. cit.*; Neuberg, *Ber.*, 1908, **41**, 960), is probably due to the presence of stereoisomerides. Glyoxime, m. p. 177°, also was prepared from the aqueous extract.

If mineral acid is present, aqueous solutions of glyoxal polymerise rapidly, giving the inert hexaglycol hydrate (Schiff, *Annalen*, 1874, **172**, 1). The estimation of the glyoxal present is therefore best carried out immediately the unreduced selenium dioxide has been removed. The yield is nearly 90%, calculated on the weight of selenium dioxide.

The above experiment was more conveniently carried out in an autoclave for 2 hours at 80°. The excess of acetaldehyde was then removed by distillation, a slight excess of the calculated quantity of sodium bisulphite added to the remaining sticky liquid, and the bisulphite compound collected after standing over-night. The product, which was pinkish owing to the presence of a trace of selenium, was recrystallised from alcohol–water. Yield, about 90%.

(b) *Tube method.* Acetaldehyde vapour was passed over a thin layer of selenium dioxide (5 g.) in a sloping hard-glass tube (about 3 cm. diam. and 30 cm. long), the temperature being gradually raised to 230°. (The selenium formed in the reduction is the "vitreous" variety, which is liquid above 220°, and unless the temperature is raised sufficiently high to melt the selenium each particle of dioxide becomes coated with selenium, which prevents further access of the acetaldehyde vapour.) The selenium produced slowly melted and trickled down the tube. Some dioxide which condensed in the cooler part of the tube was reduced by reheating. The glyoxal mostly remained in the tube, only a little passing into the condenser and the receiver with the acetaldehyde vapour. Monomeric glyoxal, which probably polymerised to the reactive trimeric form almost at once, was visible as a greenish vapour surrounding the selenium. The tube and the distillate, after removal of the excess of acetaldehyde, were extracted with hot water and the identity of the product and the yield (80—90%) were determined in the manner previously described. The slightly impure glyoxalbisphenylhydrazone obtained melted at 166—167°.

When acetaldehyde or even the higher-boiling paraldehyde was simply refluxed for a prolonged period with selenium dioxide, reduction of this was not complete; *e.g.*, after 6 hours' refluxing, paraldehyde reduced only 40% of the dioxide present.

Methylglyoxal.—Selenium dioxide (55 g.) and propaldehyde (100 g.) were refluxed for 4 hours and the product was extracted with ether. After standing over-night with calcium chloride, to dry and to coagulate a small amount of selenium which had separated, the ether was removed, and the residual liquid distilled in a vacuum, 6·5 g. of methylglyoxal, b. p. 46°/25 mm., being obtained, and also 5 g. of a dark yellowish-brown fraction, boiling a few degrees higher; this proved to be methylgloxal containing unstable evil-smelling selenium compounds which decomposed on further distillation, yielding more methylglyoxal. A yield of 30% of pure methylglyoxal (except for approximately $\frac{1}{2}H_2O$), calculated on the selenium dioxide, was obtained.

Ethylglyoxal.—Selenium dioxide (110 g.) and *n*-butaldehyde (250 g.) were refluxed for 4 hours and after 12 hours ether was added and the resulting liquid filtered. The selenium recovered here was 80% of the theoretical weight, the rest being recovered at later stages. The liquid obtained from the dried extract was fractionated and some difficulty was experienced in separating the ethylglyoxal from the excess of butaldehyde; 10 g., b. p. 45—60°/10 mm., of pure (except for H_2O) ethylglyoxal, which showed a spontaneous exothermic polymerisation to a jelly similar to that of methylglyoxal, though not so pronounced, were finally obtained along with several less pure fractions. The total yield of ethylglyoxal, containing water and a few units % of *n*-butaldehyde, was about 45%. This gave a bisphenylhydrazone, m. p. 115—116° (Found :

N, 21·4. Calc.: N, 21·1%), and a disemicarbazone, m. p. 226—227° (decomp.) (Found: N, 41·6. Calc.: N, 41·6%).

Phenylglyoxal.—Selenium dioxide (100 g.) and phenylacetaldehyde (220 g.) were refluxed for 2 hours. From the cooled product, phenylglyoxal (yield, 35%) was extracted with boiling water in the manner already described.

A New Test for Lævulose.—A preliminary study showed that of the sugars lævulose, glucose, lactose, and maltose, only lævulose gave a precipitate of red selenium when boiled with selenium dioxide in acid solution. With sucrose, prolonged boiling was necessary to give the red precipitate. These reactions are sufficiently sensitive to serve as convenient tests.

The selenium in all these experiments was precipitated in the red amorphous state and then coagulated, giving finally almost black porous lumps of the "vitreous" modification. This is not its general behaviour (compare Saunders, *J. Physical Chem.*, 1900, 4, 424).

Discussion.

These experiments show that selenium dioxide has a specific oxidising action on aldehydes and ketones of various types, whereby 1 : 2-diketones and aldoketones are conveniently obtained in quantity. Test-tube experiments have shown that, although ketones which do not contain a methylene group, *e.g.*, benzophenone, are oxidised by selenium dioxide, the reaction takes place only on strong heating and more or less complete oxidation then occurs. Compounds which contain a methylene group, activated by proximity to a negative group, appear to be specifically oxidised at reasonably low temperatures (compare Imperial Chemical Industries, Ltd., and Riley, B.P., 1931, 354,798; I. G. Farbenind. A.G., *loc. cit.*).

These researches were instigated by a study of the tendency of the selenite ion to enter the co-ordinated cobalt complex (Riley, J., 1928, 2985). The relative ease with which large yields of selenitopentamminocobaltic chloride were obtained indicated that the selenite ion might possibly possess a tendency also to act specifically with organic compounds, for the cyanide and nitrite ions also readily form complex ions and also react readily at low temperatures with organic compounds.

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