STUDIES ON MOLECULAR-REARRANGEMENTS OF α-GLYCOLS. IV. INFLUENCE OF SUBSTITUENTS ON A PINACONE IN ITS REACTIVITY. REDUCTION OF DI-*p*-METHOXY-BENZOPHENONE.

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When trisubstituted α-glycols are treated with dehydrating agent, the influence of substituents can be seen chiefly in the mode of molecular rearrangement, and the reaction products are ketones or aldehydes.(1) $\alpha\alpha$-Dimethyl-β-acetyl glycol, $(CH_3)_2C(OH).CH(OH).COCH_3$, is the only instance known in which a trisubstituted α-glycol undergoes simultaneously molecular rearrangement and dissociation into ketone and carbinol by the action of rearranging agents.(2) The author has attributed the dissociation of this glycol to the presence of unstable linkage in the molecule between α and β carbon atoms. If it be so, aromatic pinacones are quite possible to give simultaneous reaction of rearrangement and dissociation under the same conditions, because they bear close resemblance to hexa-aryl ethanes with respect to the negativities of substituents and are assumed to have unstable linkages between the two adjacent carbon atoms in chain, owing to their strongly positive polarities. In fact, all known aromatic pinacones split into corresponding ketones and carbinols at their melting points, and particularly in the case of tetra-*p*-bromobenzopinacone, it is reported that pinacoline rearrangement and dissociation into ketone and carbinol take place simultaneously by the action of acetyl chloride.(3) Under the same conditions, not a single case of dissociation has been reported with other aromatic pinacones with highly negative groups such as diphenyl, fluoryl or xanthyl.(4)

For the purpose of drawing some conclusion on the influence of negative substituents upon the reactivities of pinacones by collecting a series of new data, tetra-*p*-methoxybenzopinacone is first studied, because it contains anisyl radical which is regarded the most negative organic radical, and yet all that we can find in literature about it, is

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(1) $$RR'C(OH).CHR''(OH) \rightarrow \begin{cases} RR'R''C.CHO & \text{(Semihydrobenzoin rearrangement).} \\ RR'CH.CO.R'' & \text{(Vinyl dehydration).} \\ RCO.CHR'R'' & \text{(Semipinacoline rearrangement).} \end{cases}$$

(2) Migita, this Bulletin, **4** (1929), 225–234.

(3) Montagne, *Rec. trav. chim.*, **43** (1924), 126–142.

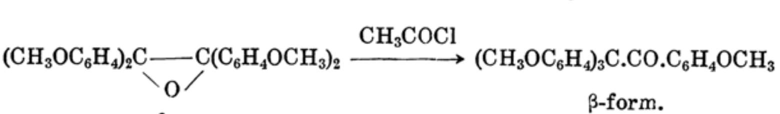
(4) Gomberg and Bachmann, *J. Am. Chem. Soc.*, **49** (1927), 236–257.

the following few lines with a proviso "unpublished" that anisyl pinacone, $(CH_3OC_6H_4)_2C(OH).C(C_6H_4OCH_3)_2(OH)$, melts at 182°C. and remelts at 117–118°C., if the melting point is remeasured after one hour with the same sample.(1)

Reduction of Di-*p*-Methoxybenzophenone. In order to prepare the pinacone in question, the reduction of di-*p*-methoxy-benzophenone was tried by the following methods, which are usually employed for this purpose, namely, reductions by zinc dust and acetic acid, by absolute alcohol under direct sunlight, and by binary mixture of magnesium and its iodide in ether-benzene solution.

According to the authors(2) the third method seems most suitable for preparation of pinacones with highly negative substituents, for it gives not only very satisfactory yields (75–100%) on many aromatic ketones, but also it enables us to reduce ketones such as dibiphenylyl ketone, fluorenone, and xanthone, of which reduction to corresponding pinacones has been proved unsuccessful by other methods. However, in the case of dimethoxy-benzophenone, the reaction did not proceed smoothly and resulted in formation of a tarry matter, though the reaction was carried out under various conditions.

As the above method had proved unsuccessful, reduction by hot glacial acetic acid and zinc dust was tried. The reaction product, however, was not the expected pinacone, but the corresponding pinacoline, the rearrangement product of the pinacone. A similar case has been reported in reduction of *p*-methoxy-benzophenone.(3) Supposing that this pinacoline formation was due to heating the reaction mixture, the reduction was repeated at room temperature by using the same reducing agents. But the product was not again the pinacone but the pinacoline. That this pinacoline is of β-form, and not of α-form with oxide-ring, was proved by its stability toward acetyl chloride, for the latter should be easily converted to the former by this treatment.



$$(CH_3OC_6H_4)_2\underbrace{C\text{——}C}_{O}(C_6H_4OCH_3)_2 \xrightarrow{CH_3COCl} (CH_3OC_6H_4)_3C.CO.C_6H_4OCH_3$$

α-form. β-form.

Lastly tetramethoxy-benzopinacone was obtained by reducing the ketone under direct sunlight with absolute alcohol in a sealed tube. This pinacone decomposes on melting, usually into dianisyl ketone and

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(1) Bouvet, *Bull. soc. chim.*, **[4]**, **15** (1915), 209.

(2) Gomberg and Bachmann, *J. Am. Chem. Soc.*, **49** (1927), 236–257.

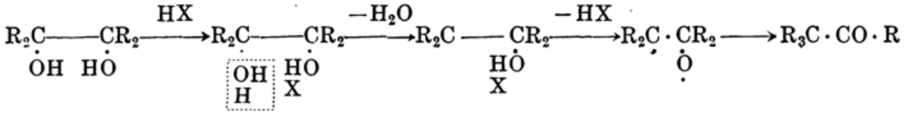
(3) Tiffeneau and Orékhoff, *Bull. soc. chim.*, **37** (1925), 430.

dianisyl carbinol. Facility of rearrangement is one of the characteristics of this pinacone, and slightly warmed acetic acid is sufficient to convert it to the pinacoline. Though a close experiment was carried out in order to know if this pinacone undergoes dissociation as well as rearrangement by the action of acetyl chloride, no dissociation products were detected.

On the Facility of Rearrangement of Pinacones. (a) *Effect of Highly Negative Substituents.* The effect of negative substituents upon the reactivities of pinacones can be seen clearly in the reduction of benzophenone and its methoxy-derivatives by zinc dust and acetic acid (See the following table).

Reducing agent / Ketone	Zinc dust and acetic acid	
	At room temperature	At higher temperature
$CH_3OC_6H_4.CO.C_6H_4OCH_3$	Pinacoline	Pinacoline
$CH_3OC_6H_4.CO.C_6H_5$	Pinacone(2)	Pinacoline(1)
$C_6H_5.CO.C_6H_5$		Pinacone(3)

In dimethoxy-benzophenone, pinacoline formation from ketone takes place even at room temperature, and in the case of methoxy-benzophenone at high temperature, while in benzophenone, pinacoline formation is not observed under these conditions. In order to convert benzopinacone into the pinacoline by the action of acetic acid, it is necessary to heat it in a sealed tube, at 180–200°C. Thus we can see a marked increase of reactivity of the pinacone caused by successive introductions of methoxy-radical into the benzophenone molecule; which will be easily explained from the mechanism of pinacoline rearrangement discussed in foregoing papers. According to the author's interpretation,(4) the first stage of the pinacoline rearrangement is the attraction between one of the hydroxyl groups of the pinacone and the hydrogen ion of the acid, and the reaction proceeds in the following manner.



$$\underset{\dot{\mathrm{O}}\mathrm{H}}{\mathrm{R_2C}}-\!\!-\underset{\mathrm{H}\dot{\mathrm{O}}}{\mathrm{CR_2}}\xrightarrow{\mathrm{HX}}\underset{\boxed{\substack{\mathrm{OH}\\ \mathrm{H}}}}{\mathrm{R_2C}}-\!\!-\underset{\substack{\mathrm{H}\dot{\mathrm{O}}\\ \mathrm{X}}}{\mathrm{CR_2}}\xrightarrow{-\mathrm{H_2O}}\mathrm{R_2C}-\!\!-\underset{\substack{\mathrm{H}\dot{\mathrm{O}}\\ \mathrm{X}}}{\mathrm{CR_2}}\xrightarrow{-\mathrm{HX}}\mathrm{R_2C}\cdot\underset{\dot{\mathrm{O}}}{\mathrm{CR_2}}\longrightarrow\mathrm{R_3C}\cdot\mathrm{CO}\cdot\mathrm{R}$$

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(1) Tiffeneau and Orékhoff, *Bull. soc. chim.*, **37** (1925), 430.
(2) Bachmann and Moser, *J. Am. Chem. Soc.*, **54** (1932), 1126.
(3) Zagumenni, *Ber.*, **14** (1881), 1402.
(4) Migita, this Bulletin, **3** (1928), 312.

Evidently, the attraction between hydrogen ion and the hydroxyl group is stronger, according as the negativity of the latter is larger; then it follows naturally from the theory of induced alternate polarity that pinacones with highly negative substituents should undergo rearrangement with great facility. And in the case of tetramethoxy-benzopinacone, owing to the extreme negativity of anisyl radical, its hydroxyl groups may be supposed to have so strongly negative polarity as the rearrangement takes place even by the action of a weak organic acid at ordinary temperature.

(b) *Function of a Small Quantity of Iodine in Pinacoline Rearrangement.* Gomberg and Bachmann⁽¹⁾ reported that a crystal or two of iodine in hot acetic acid is sufficient to convert a number of aromatic pinacones, including benzopinacone, to the pinacolines. The function of iodine in this case is supposed either to increase the negativity of oxygen atom of hydroxyl groups by attracting its hydrogen atom, or to produce hydroiodic acid by reacting with acetic acid, which behaves as rearranging agent. Then, in the case of pinacones with extremely negative groups the rearrangement can occur by the action of acetic acid even in the absence of iodine, as seen in the case of tetramethoxy- and dimethoxy-benzopinacones. Besides these, sym. di-*p*-methoxy-di-*p*-ethoxy-benzopinacone, sym. di-*p*-methoxy-di-*p*-phenyl-benzopinacone and sym. di-*p*-anisyl-di-β-naphthyl glycol may be cited in illustration, which will be described in other papers.

Experimental Part.

p-Anisic Acid. M. p. 182°C. Behrens⁽²⁾ describes that it crystallises in needles of straight extinction and of negative character, but the crystals must be chiefly of oblique extinction, since they belong to monoclinic system and the face most developed is (110).⁽³⁾ This was confirmed by actual observation.

Di-p-Methoxy-Benzophenone. This ketone was prepared from *p*-anisole and anisoyl chloride.⁽⁴⁾ It crystallises from alcohol in plates or needles with oblique extinction, melts at 143°C., and is difficultly soluble in ligroin and ether, and readily in acetone and chloroform. In concentrated sulphuric acid it dissolves with yellow colouration, which was reported to be red in literature.⁽⁴⁾

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(1) Loc. cit.

(2) Behrens-Kley, "Organische Mikrochemische Analyse," p. 79.

(3) Groth, "Chemische Krystallographie" IV, p. 504.

(4) Schnackenberg and Scholl, *Ber.*, **36** (1903), 654.

Reduction of Di-p-Methoxybenzophenone.

Reduction by Zinc-Dust and Acetic Acid. (a) *At High Temperature.* To a boiling solution of 2.4 gr. of the ketone in 15 c.c. of acetic acid, 6.5 gr. of zinc dust were added in portions. The solution, assuming light greenish tint, was kept gently boiling for 3 hours. Excess of zinc dust was filtered hot from solution and washed thrice with hot glacial acetic acid. The filtrate and washings were poured into water. Slightly greenish precipitates were gathered and purified from alcohol. It forms slender needles with straight extinction and of negative character, melting at 140–141°C. with slight decomposition and solidified in a glassy mass. It is readily soluble in acetone and chloroform, sparingly in ether and hot ligroin, and moderately in alcohol. It dissolves in concentrated sulphuric acid with intense mixed colours of green, blue and violet which changed to purple on standing.

Analysis. Subst. = 0.1613; CO_2 = 0.4549; H_2O = 0.0884 gr.
Found: C = 76.9; H = 6.14%.
Calc. for $C_{30}H_{28}O_5$ (tetramethoxybenzopinacoline): C = 76.9; H = 5.98%.

Action of Acetyl Chloride. In order to determine whether this pinacoline is of α- or β-form, it was treated with acetyl chloride in benzene solution as in the manner described later. The purified product was proved to be unchanged pinacoline. Thereby it is shown that the pinacoline is of β-form.

Hydrolysis. After boiling 0.5 gr. of this pinacoline with alcoholic potash for 12 hours, the product was poured into water, and the filtered solution was acidified with hydrochloric acid. Separated acid was recrystallized from hot water and was easily identified as *p*-anisic acid.

(b) *At Room Temperature.* Two grams of the ketone were dissolved in sufficient glacial acetic acid to keep it in solution at room temperature and an excess of zinc dust was added to the solution. After allowing the mixture to stand at room temperature (20–30°C.) for four days, the solution, filtered from unchanged zinc dust, and poured into a large quantity of water. Yellowish precipitates were washed with cold ether and then recrystallised from alcohol. The product crystallises in colourless fine needles which melt at 141°C. and dissolve in concentrated sulphuric acid with mixed colours of intense green, blue and purple. It was identified as tetra-*p*-methoxy-benzopinacoline by mixed melting point test.

Reduction by Absolute Alcohol under Direct Sunlight. Four grams of dianisyl ketone and 20 c.c. of absolute alcohol were sealed in a tube and exposed in sunlight. In the first two days, the change of the crystalline appearance in the tube was observed and the solution assumed yellowish tint. After a week, the tube was opened and granular crystals were filtered off from the solution smelling richly of acetaldehyde. The crystals were treated with hot 95% alcohol repeatedly to remove unchanged dianisyl ketone, until the residue, obtained by evaporation of the alcoholic solution, gives with concentrated sulphuric acid intense blue coloration, free from yellow tint produced when the ketone is present. This procedure accompanies considerable loss of pinacone, but we can obtain the pinacone with reliable melting point only in this way. The product crystallises from a quantity of alcohol in white microscopic prisms with straight extinction and of positive character. It decomposes at melting point which is 176°C. when the temperature of the bath is slowly raised, and 181°C. when heated quickly. It remelts, after solidification, at 123–125°C., while 117–118°C. is given by Bouvet.(1) It dissolves in concentrated sulphuric acid imparting to the solution mixed colours of intense blue and violet.

Anal.: Subst. = 0.1118; CO_2 = 0.3028; H_2O = 0.0636 gr.
Found: C = 73.8; H = 6.34%.
Calc. for $C_{30}H_{30}O_6$ (tetramethoxybenzopinacone): C = 73.9; H = 6.18%.

Reduction by Gomberg's Binary Mixture. To a boiling suspension of 1 gr. of magnesium in the solvent consisting of 15 c.c. of absolute ether and 20 c.c. of benzene, 1 gr. of iodine was added and the content was kept briskly boiling until practically colourless solution was obtained (about for one hour). The solution of magnesium iodide was cooled, to which 1 gr. of di-*p*-methoxy-benzophenone dissolved in 10 c.c. of warm benzene was added, and the content was shaken. During this process, heat was evolved and the solution became opaque and assumed brownish-red colour. The solution was gradually clarified and coloured deep red, while magnesium was coated with sticky substance, presumably owing to the formation of complex between the ketone and magnesium iodide. The content was shaken with repeated additions of fresh magnesium but every time it was coated immediately. When the reaction mixture was shaken for ten hours with a great excess of magnesium (a hundred times of theoretical amount), or heated to boiling to complete the reaction with efficient condenser of which upper end was stoppered, the solution was coloured dark and magnesium was uncoated. On hydrolysis, brown rosinous matter was obtained which gave yellowish-brown amorphous substance (about 0.1 gr.) when purified from alcohol. The product, however, was not the pinacone nor the pinacoline in question, since it dissolves in concentrated sulphuric acid with reddish-brown colouration.

Some Reactions of Tetramethoxybenzopinacone.

Analytical Procedure. Separation of the pinacone, and its rearrangement and decomposition products in the presence of one another,

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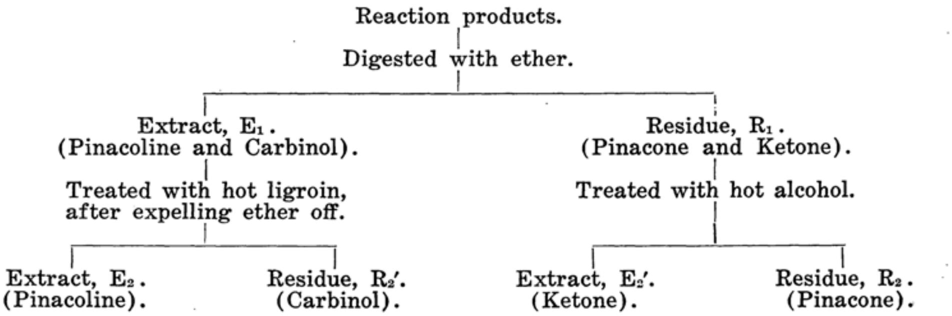
(1) Loc. cit.

which is indispensable in the study of reactions of tetramethoxybenzopinacone, was effected by the following scheme:



Of course, complete separation is attained by no means in this way, but it is not difficult to obtain a pure compound by further recrystallisation. For their identification, besides melting point and mixed melting point test, the colour reaction with concentrated sulphuric acid proved of good service.

Decomposition at Melting Point. 0.2 Gr. of the pinacone was heated at 185°C. for one hour, the cooled mass was powdered and analysed after the above process. The same white crystalline substance was obtained both from R_1 and E_2 which was identified as dimethoxybenzophenone. Repeated recrystallization of R_2', a semi-solid, from chloroform and ligroin, did not succeed in isolation of a compound with definite melting point. But it can be assumed to be dimethoxybenzohydrol by its behaviour toward solvents and by red colouration produced when dissolved in concentrated sulphuric acid.

Rearrangement of the Pinacone. (a) *Action of Hot Glacial Acetic Acid.* 0.1 Gr. of the sample was heated with 2 c.c. of glacial acetic acid at 100°C. for ten minutes, the content was poured into water and analysed. Tetramethoxybenzopinacoline, which melts at 140°C. with slight decomposition and solidifies in a glassy mass was obtained.

(b) *Action of Acetyl Chloride.* Two grams of the pinacone was dissolved in a mixture of 50 c.c. of dry benzene, 20 c.c. of acetyl chloride and 10 c.c. of glacial acetic acid, and was gently boiled for eight hours. After distilling the benzene off, the content was treated in the same way as in the last case. Tetramethoxybenzopinacoline was the only product isolated, dianisyl ketone and dianisyl carbinol being not detected.

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