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# Synthetic Experiments on the Oxyaldehydes ( II )

( Recived March 20, 1949 )

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## Abstracts

On oxidizing the mixt. of guaethol, formalin, and caustic soda which was allowed to stand at room temp. 1-3 days with m-nitrobenzenesulfonic acid, we obtained 4-oxy-5-ethoxy isophthalaldehyde. Applying the analogous process to various phenols, namely, guajacol, phenol, o-chlorophenol, p-chlorophenol, p-nitrophenol, salicylic acid, and p-oxybenzoic acid, we obtained 4-oxy-5-methoxyisophthalaldehyde, 4-oxy-isophthalaldehyde, 4-oxy-5-chloroisophthalaldehyde and 2-chloro-4-carboxy-6-formyl phenol, 2-oxy-5-chloro isophthalaldehyde and 2-oxy-3-formyl-5-chloro benzoic acid, 2-formyl-4-nitrophenol, 2-oxy-4-formyl benzoic acid, and 4-oxy-3-formyl benzoic acid respectively. o-Nitrophenol gave no condensation product with formalin.  $\alpha$ -Naphthol and  $\beta$ -naphthol gave no definite products.

It was found that the condensation reaction with formalin is prevented when the phenol derivative used has negative group such as nitro or carboxyl, and monoaldehyde is obtained generally. The positions to which aldehyde groups are introduced are *ortho* and *para* positions to a hydroxyl group as in Reimer-Tieman's reaction.

## Introduction

Many aromatic oxyaldehydes are useful, especially for perfumes, and many synthetic methods have been described. Some aromatic oxyaldehydes were obtained from oxyphenyl methyl carbinol derivatives by oxidation using aromatic nitro compounds,<sup>1)</sup> or directly from some phenol derivatives by reaction with formaldehyde and aromatic hydroxyl amines.<sup>2)</sup>

This paper presents the results of reactions among some phenol derivatives, formaldehyde and aromatic nitro compound. As I found in the previous paper<sup>3)</sup> that m-nitrobenzenesulfonic acid was one of the best oxidizing reagents when p-oxybenzylalcohol was oxidized into p-oxybenzaldehyde and that refluxing of 3 hrs. was suitable for the time oxidation reaction, in the present experiment we used

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1) E. P. 399723

2) D. R. P. 105798, E. P. 27236, E. P. 28390

3) Y. Ohtsuka, proceeding of Faculty of Engineering' Keiōgijuku University 2, (1949) 35

m-nitrobenzenesulfonic acid as oxidizing reagent. Phenol, guajacol, graethol, nitrophenols, chlorophenols, oxybenzoic acids, and naphthols were studied as phenol components.

### Experimental Part

#### 1) Guaethol (assisted by Mr. S. Matsuno)

We try two methods. In the former method the condensation process of guaethol with formaldehyde and the oxidation process of condensation product are carried out simultaneously ( Experiment-a ). In the latter the oxidation process is carried out after allowing the condensation mixture to stand several days ( Experiment-b ).

##### a) Experiment ( a )

To a mixture of 5.1 g. of guaethol, 5.1g. of formalin ( 32.5% ) and 13.0cc. of 10% caustic soda, 7.4g. of m-nitrobenzenesulfonic acid sodium salt is added. The resulting solution is heated under the reflux condenser. The temperatures and the durations are shown in table 1. After cooling, the reaction mixture is neutralized with hydrochloric acid, shaken with ether. The ether solution is shaken with aqueous sodium bisulfate solution and the aldehyde is separated by adding sulfuric acid. The aldehyde is obtained in poor yield.

Table 1. Relation between yield and condition of reaction by experiment ( a )

Temp (°C)	40	70		100
Time ( hr )	3	4	17	3
Yield (%)	5.3	11.0	11.0	11.0

##### b) Experiment ( b )

Previously a mixture of 5. lg. of guaethol, 5. lg. of formalin ( 32.5% ), and 13.0cc. of 10% caustic soda is allowed to stand at room temperature 1-3 days, and then added with the mixture of 7. 4g. of m-nitrobenzenesulfonic acid sodium salt and 11.2cc. of 10% caustic soda, and refluxed for 3 hrs. The aldehyde is separated in the same mannar as in experiment ( a )

Table 2. Relation between yield and time of condensation reaction by experiment ( b )

Time of cond. reaction ( hr )	12	36	60	84
Yield ( % )	17.2	28.8	29.2	15.6

This aldehyde is white needle, smelling sweet like vanillin, m.p. 109°C., and gives violet colouration with ferric chlorid, dark red with benzidine, positive test with Tollens' reagent, negative test with Fehling's solution.

Anal. Calcd. for  $C_{10}H_{10}O_4$ : mol. wt., 194.1; C, 61.3; H, 5.14. Found: mol. wt.

(cryoscopic, campher), 198.8; C, 61.6; H, 4.94.

i) The monoxime is obtained from 120 mg. of the dialdehyde and 40 mg. of hydroxylamine hydrochloride in sodium acetate solution. It is recrystallized from water. m.p. 157°C.

Anal. Calcd. for  $C_{10}H_{10}O_4N$ : N, 6.37. Found; N, 6.46.

ii) The dioxime is obtained from 115 mg. of the dialdehyde and 120 mg. of hydroxylamine hydrochloride in sodium acetate solution. It is recrystallized from water. m.p. 172-3°C.

Anal. Calcd. for  $C_{10}H_{10}O_4N_2$ : N, 12.62. Found; N, 12.49.

iii) The phenylhydrazone is obtained from 190 mg. of the dialdehyde and 430 mg. of phenylhydrazine hydrochloride in sodium acetate solution. It is recrystallized from ethanol or methanol as yellow needles. m. p. 199-200°C.

Anal. Calcd. for  $C_{22}H_{22}O_2N_4$ : N, 14.98. Found; N, 14.98.

The structure of this compound is presumed certainly to be 4-oxy-5-ethoxy isophthalaldehyde from the fact that the analyses described previously show two aldehyde groups in it, and that 4-oxy-5-methoxy isophthalaldehyde is obtained from guajacol under the same condition of reaction in the next experiment.

2) Guajacol (assisted by Mr. K. Munakata)

A mixture of 6.2 g. of guajacol (0.05 mol.), 6.9 g. of 32.5% formalin (formaldehyde 0.07 mol.), and 21.7 cc of 10% caustic soda (0.06 mol.) is allowed to stand at 25°C. for 60 hrs, and then added with the mixture of 12.3 g. of *m*-nitrobenzenesulfonic acid sodium salt (0.05 mol.) and 18.7 g. of 10% caustic soda (0.05 mol.), and refluxed for 3 hrs. After neutralizing with hydrochloric acid the reaction mixture is shaken with ether. The separation from the ether solution by bisulphite method yields 2.97 g. (33% of theoretical) of the dialdehyde. This is 4-oxy-5-methoxy-isophthalaldehyde,<sup>4)</sup> m.p. 120°C., giving violet with ferric chloride, deep red with benzidine.

Anal. Calcd. for  $C_9H_8O_4$ : C, 60.0; H, 4.48. Found: C, 59.8; H, 4.55.

Phenylhydrazone, m.p. 188.5°C. yellow needle. Anal. Calcd. for  $C_{21}H_{20}O_2N_4$ : N, 15.56. Found: N, 15.39.

Dioxime, white fiber-like, m.p. 184-6°. Anal. Calcd. for  $C_9H_8O_4N_2$ : N, 13.46, Found: N, 13.47.

3) Phenol (assisted by Mr. K. Munakata)

When phenol is applied as previously described in (2), 4-oxy-isophthalaldehyde is obtained as main product.

5.6 g. of phenol is used. 1.6 g. of the crude aldehyde is separated by bisulphite method. It is added with 24 cc. of petroleum ether, refluxed and filtered while hot,

From the filtrate nothing is obtained, (there is no 2-oxy-isophthalaldehyde). By the sublimation of the residue *p*-oxybenzaldehyde is obtained as white needles, m.p. 115.6°C., in very poor yield, By the recrystallization of the residue 4-oxy-isophthalaldehyde<sup>5)</sup> is obtained as white needles, m.p. 108°C. The yield is 2.58 g. (19.6%

4) J.Koetsche and P.Koetschet. *Helv. chim acta* **13**, (1930) 482

5) *Uswinkel B.* **15**, 2023 (by Reimer-Tiemann synthesis)

of theoretical).

Anal. Calcd. for  $C_8H_6O_3$ : C, 64.0; H, 4.03, Found: C, 63.6; H, 3.97,

#### 4) Nitrophenols

##### a) o-nitrophenol

No condensation product is obtained.

##### b) p-Nitrophenol

The mixture of 5.5 g. of p-nitrophenol, 5.6 g. of formalin, and 15.9 cc. of 10% caustic soda is refluxed for 6 hrs., and then oxidized by 5.8g. of m-nitrobenzenesulfonic acid. The oxyaldehyde is separated in the usual manner and is recrystallized from water. m.p.  $125.5^\circ C$ . The yield is 0.12 g. ( 1.8% of theoretical ).

Anal. Calcd. for  $C_7H_5ON_4$ : N, 7.48. Found: N, 7.36.

The identity of this aldehyde with 2-formyl-4-nitro-phenol is established by analysis and its melting point.<sup>6)</sup> The recovery of the unchanged p-nitrophenol is 88%.

#### ( 5 ) Oxy-benzoic-acid

##### ( a ) Salicylic acid

Applying this process to salicylic acid, 2-oxy-5-formylbenzoic acid is obtained. 6.9g. of salicylic acid is condensed with 6.9 g. of 32.5% formalin at  $25^\circ C$  for 60 hrs., oxidized with 12.3 g. of m-nitrobenzenesulfonic acid sodium salt, and the aldehyde is separated in usual manner. It is recrystallized from water. 0.28 g. of 2-oxy-5-formyl benzoic acid,<sup>7)</sup> needle, m.p.  $246^\circ C$ ., is obtained ( 3.3% of the theory ). This gives slightly yellow colour upon solution in alkali, deep red with ferric chloride, and yellow with benzidine. The recovery of the unchanged salicylic acid is 80%.

Anal. Calcd. for  $C_8H_6O_4$ : C, 57.8; H, 3.64 Found: C, 57.4; H, 3.80.

##### ( b ) p-oxybenzoic acid

The mixture of 5.5 g. of p-oxybenzoic acid, 5.5 g. of formalin and 17.3 cc. of 10 % caustic soda is allowed to stand at  $25^\circ C$ . 60 hrs., and then oxidized with 9.8 g. of m-nitrobenzenesulfonic acid. The crude aldehyde separated in the usual manner is sublimated and then crystallized from water. 0.54 g. of 4-oxy-3-formyl benzoic acid,<sup>8)</sup> prism, m.p.  $242-3^\circ C$ ., is obtained ( 10.8% of the theory ). This gives red with ferric chloride and deep red with benzidine. The recovery of the unchanged p-oxy-benzoic acid is 85%

#### 3 ) Chlorophenols

##### a ) o-Chlorophenols

Franz Hanus has carried out a similar reaction of o-chlorophenol.<sup>9)</sup> He isolated the condensation product of o-chlorophenol with formaldehyde and oxidized it with m-nitrobenzenesulfonic acid, and then obtained 4-oxy-5-chloroisophthalaldehyde and 2-chloro-4-carboxy-6-formyl phenol (presumptive). In our experiment the same

6) v. Miller B. 20, 1929

7) Reimer, Tiemann B. 9, 1271.

8) Reimer, Tiemann B. 10, 1563.

9) Franz Hanus J.prakt. Chem. 158, ( 1941 ) 254-65

aldehydes were obtained.

In our process the mixture of 4.7 g. of o-chlorophenol, 5.1 g. of formalin ( 31.2% ), and 14.4 cc. of 10% caustic soda is allowed to stand at 25° C. for 60 hrs. and oxidized with 8.9 g. of m-nitrobenzenesulphonic acid sodium salt. 0.78 g. of the crude aldehyde is separated from sodium bisulfite layer in the usual manner, and then distilled with steam. From the distillate 0.31 g. of 4-oxy-5-chloro isophthalaldehyde, wite fiber-like, m.p. 127° C., is obtained ( 4.7 % of the theory ).

Anal. Calcd. for  $C_8H_5O_3Cl$ : C, 52.0, H, 2.74. Found; C, 51.8; H, 2.91.

Dioxim m.p. 200°C. Anal. Calcd. for  $C_8H_7O_3N_2Cl$ : N, 13.06. Found: N, 12.98.

When the residue of steam distillation is sublimated fractionally as Hanus carried out, the same compound which he presumed to be 2-chloro-4-carboxy-6-formyl phenol is obtained. m.p. 225°C. The yield is 0.37 g. ( 5.1 % of theoretical ).

Anal. Calcd. for  $C_8H_5O_4Cl$ : C, 47.9; H, 2.51. Found: C, 47.2; H, 2.64.

Semicarbazone m.p. 256.9° C. Anal. Calcd. for  $C_9H_8O_4N_3Cl$ : N, 16.32. Found: N, 16.20.

( b ) p-Chlorophenol

The mixture of 11.3 g. of p-chlorophenol and 185 g. of 31.2% formalin, and 34.8 cc. of 10 % caustic soda is allowed to stand at 25° C. for 60 hrs., and oxidized with 21.6 g. of m-nitrobenzenesulfonic acid sodium salt. 3.1 g. of crude aldehyde obtained are distilled with steam. The distillate gives yellow green fluorescence while hot, and 2-oxy-5-chloro isophthalaldehyde,<sup>10)</sup> fiber like, m.p. 124°C., is crystallized when cooled. This gives yellow precipitate in alkali, red brown coloration with ferric chloride, and deep red with benzidine. The yield is 0.90 g. ( 5.6 % of theoretical ).

Anal. Calcd. for  $C_8H_5O_3Cl$ : C, 52.0; H, 2.73. Found: C, 52.1; H, 2.86.

Dioxim, yellow needles, m.p. 205° C. Anal. Calcd. for  $C_8H_7O_3ClN_2$ : N, 13.06. Found: N, 13.01.

The residue of steam distillation is recrystallized from water, yielding 2-oxy-3-formyl-5-chloro benzoic acid,<sup>11)</sup> which melts at 224°C., gives yellow precipitate in alkali, pink-red colouration with ferric chloride, and red with benzidine. The yield is 2.05g. ( 11.6% of theoretical ).

Anal. Calcd. for  $C_8H_5O_4Cl$ : C, 47.9; H, 2.51. Found. C, 48.6; H, 2.65.

Oxim, m.p. 200°C.. Anal. Calcd. for  $C_8H_6O_4ClN$ : N, 6.50. Found : N, 6.40.

( 7 ) Naphthols.

( a )  $\beta$ -Naphthol

The mixture of 4.3 g. of  $\beta$ -naphthol, 3.8 g. of formalin ( 31.2% ), and 13.0cc. of 10% causti csoda is allowed no snand at 25°C. for 60 hrs. and oxidized with 7.3 g. of m-nitrobenzenesulfonic abid sodium salt. 0.05 g. of the aldehyde obtained is an oily matrial and has not been identified. White needles, m.p. 200°C., is obtained after

10) Alois Zinke, Frrnz Hanus, Erich Ziegler, Franz Speck, Herbert Troger and Erwin Weinhardt. J.Prakt. Chem. 152, ( 1939 ) 126

11) C.A.Bueoler, B.Calvin Bass, Robert B.Derling and Milton E.Lubs J.A.C.S. 62, ( 1940 ) 893

reCRYSTALIZATION of unaldehyde material from benzene, and it is identified as bis-[2-oxy-naphthyl-(1)]-methan by mixed melting.

Though the condensation reactions are carried out in the presence of  $\text{Na}_2\text{CO}_3$ ,  $\text{NaHCO}_3$ , [2-oxy-naphthyl-(1)]-methan is produced always in good yield.

In order to oxidize the presumable oxy-naphthyl methyl carbinol immediately by m-nitrobenzenesulfonic acid, similar process as Experiment (a) of guaethol was tried, but the material obtained from sodium-bisulfite layer was oily and brown.

The main product in this case is also bis-[2-oxy-naphthyl-(1)]-methan.

(b)  $\alpha$ -Naphthol

4.3 g. of  $\alpha$  naphthol is condensed with 3.8 g. of formalin (31.2%), and then oxidized with 5.0g. of m-nitrobenzenesulfonic acid sodium salt. 0.06 g. of brown material is obtained from sodium bisulfite layer which has not been identified.

### Summary

Some phenol derivatives – phenol, guajacol, guaethol, nitrophenols, chlorophenols, oxybenzoic acids, and naphthols – are reacted with formaldehyde and m-nitrobenzene sulfonic acid under several conditions, and oxyaldehydes and some other products are obtained.

Generally in these reactions oxyaldehydes are obtained, but the yield is not very good. When the phenol derivative used has negative group such as nitro or carboxyl, the condensation reaction with formaldehyde is prevented, and so mono-aldehyde is obtained in poor yield. The positions to which aldehyde groups are introduced are *ortho* and *para* positions to a hydroxyl group as in Reimer.–Tiemann's reaction.

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