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SULFONATION OF SUBSTITUTED ACETOPHENONES

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Until recently (1), very few reports have appeared in the literature on the direct sulfonation of ketones in which the reaction products have been isolated and identified (2–6). Hence, the reaction of dioxane sulfur trioxide with several ketones of singular structure has been studied.

α-Chloroacetophenone reacts with dioxane sulfur trioxide to give α-chloroacetophenone-α-sulfonic acid in good yield. Similarly α-fluoroacetophenone, *m*-diacetylbenzene, and *p*-diacetylbenzene were converted by this reagent to α-fluoroacetophenone-α-sulfonic acid, *m*-diacetylbenzene-α,α′-disulfonic acid, and *p*-diacetylbenzene-α,α′-disulfonic acid respectively.

The structures of the sulfonic acids obtained from the diacetylbenzenes were established by comparing their S-benzylthiuronium salts with authentic samples. Authentic samples of the sulfonic acids were synthesized by a Strecker reaction on the corresponding α,α′-dibromoketones. The structures of the sulfonic acids obtained from the phenacyl halides were established by oxidation (7) to benzoic acid and by the preparation and analysis of S-benzylthiuronium salts. Furthermore, aqueous sodium hydroxide cleaved (1) the sulfonation products obtained from α-chloro- and α-fluoroacetophenone to benzoic acid and an unidentified sulfur-containing material. An attempt to synthesize α-chloroacetophenone-α-sulfonic acid by the chlorination of acetophenone-α-sulfonic acid resulted in decomposition.

o-Diacetylbenzene with the sulfur trioxide complexes of dioxane and pyridine (8), and dibenzoylmethane with the former reagent, gave green colorations but no identifiable sulfonates. In the latter case, hydrolysis of the reaction mixture gave back dibenzoylmethane. An attempt to prepare a salt of the postulated intermediate enol sulfate with triethylamine did not succeed.

When ethyl *p*-acetyl-α-toluate was added to dioxane sulfur trioxide, a disulfonic acid was obtained. Alkaline permanganate oxidation of the sodium sulfonate gave terephthalic acid, and the S-benzylthiuronium derivative analyzed correctly for the disulfonate. An attempt to prepare *p*-$(ClCH_2CO)C_6H_4CHBrCO_2Et$, by chloroacetylating the bromoester, for use in a contemplated Strecker synthesis of the corresponding sulfonate, was unsuccessful.

EXPERIMENTAL

m-Diacetylbenzene. This material, prepared according to published procedures (9, 10), had b.p. 150–155° (15 mm.); its *oxime* melted at 200–203°, lit. (10) m.p. 204°. For sulfonation, 15 g. (0.093 mole) of *m*-diacetylbenzene, dissolved in ethylene chloride, was added to the freshly prepared sulfonating agent (0.2 mole) (11). After stirring the reaction mixture for five hours at 5°, it was poured into ice-cold water. The two layers were separated, and the organic layer was washed with water while the aqueous layer was washed with ethylene chloride. The washings were combined with their respective layers. After drying over

Drierite, the solvent was distilled from the organic layer, leaving only a trace of residue. The water layer was neutralized with sodium carbonate and evaporated to dryness. The residue was extracted with hot 70% aqueous ethanol. The crystals, formed on cooling the extract, were filtered and dried. The mother liquor was decolorized with Norit and evaporated to to a small volume; more crystals were obtained. After recrystallizing from 70% aqueous ethanol, 20 g. (58.7% yield) of disodium *m*-diacetylbenzene-α,α'-disulfonate (I) was obtained.

Anal. Calc'd for $C_{10}H_8Na_2O_8S_2$: Na, 12.56. Found: Na, 12.52, 12.58.

The *S-benzylthiuronium salt* of I crystallized with difficulty and had m.p. 140–141°.

Anal. Calc'd for $C_{26}H_{30}N_4O_8S_4$: N, 8.56. Found: N, 8.7.

A sample of I was oxidized with alkaline permanganate to *isophthalic acid*; *p-bromophenacyl ester*, m.p. 186°, lit. (12) m.p. 186°.

The *S-benzylthiuronium salt* of an authentic sample of *m*-diacetylbenzene-α,α'-disulfonic acid, prepared by a Strecker reaction on α,α'-dibromo-*m*-diacetylbenzene (13), melted at 140–141°. No melting point depression was observed when it was mixed with the S-benzylthiuronium salt of I.

p-Diacetylbenzene. This compound was prepared in the same manner as its *meta* isomer. *p*-Diacetylbenzene (15 g., 0.093 mole) dissolved in ethylene chloride was added to 0.2 mole of dioxane sulfur trioxide. The reaction temperature was not allowed to rise above 25°. Disodium *p*-diacetylbenzene-α,α'-disulfonate (II) (18 g., 53% yield) was isolated.

Anal. Calc'd for $C_{10}H_8Na_2O_8S_2$: Na, 12.56. Found: Na, 12.51.

Alkaline permanganate oxidation of II gave *terephthalic acid* which was confirmed by preparing its *p-bromophenacyl ester*, m.p. 225°; lit. (12) m.p. 225°.

The *S-benzylthiuronium salt* of II had m.p. 180.5–181°.

Anal. Calc'd for $C_{26}H_{30}N_4O_8S_4$: N, 8.56. Found: N, 8.49.

The *S-benzylthiuronium derivative* of an authentic sample of *p*-diacetylbenzene-α,α'-disulfonic acid (10) had m.p. 180.5–181°. A mixture m.p. with the corresponding derivative of II showed no depression.

α-Chloroacetophenone. Treatment of α-chloroacetophenone (18.4 g., 0.12 mole) with 0.12 mole of freshly prepared dioxane sulfur trioxide reagent gave 28 g. (77% yield) of barium α-chloroacetophenone-α-sulfonate (III) after working up the product.

Anal. Calc'd for $C_{16}H_{12}BaCl_2O_8S_2$: Ba, 22.73. Found: Ba, 22.50.

The *S-benzylthiuronium salt* of III melted at 119–120°.

Anal. Calc'd for $C_{14}H_{17}ClN_2O_4S_2$: N, 6.98. Found: N, 6.97.

Sodium acetophenone-α-sulfonate (14) was chlorinated (15), and the resulting material was neutralized with sodium hydroxide solution and evaporated to dryness. The residue was extracted with 95% aqueous ethanol, and the extract was evaporated to dryness. Attempts to purify the residue with ethanol-water mixtures were unsuccessful, and it failed to form an S-benzylthiuronium derivative.

α-Fluoroacetophenone. α-Fluoroacetophenone (16) (41.4 g., 0.30 mole) was added to 0.30 mole of dioxane sulfur trioxide reagent. Barium α-fluoroacetophenone-α-sulfonate (37.3 g., 45.9% yield) was isolated (IV).

Anal. Calc'd for $C_{16}H_{12}BaF_2O_8S_2$: Ba, 24.04. Found: Ba, 23.80.

The *S-benzylthiuronium derivative* of IV had m.p. 128.5–129.5°.

Anal. Calc'd for $C_{14}H_{17}FN_2O_4S_2$: N, 7.29. Found: N, 7.46.

o-Diacetylbenzene. o-Diethylbenzene (17) (34 g., 0.253 mole) was placed in a three-neck, 1-l., round-bottom flask equipped with a stirrer, reflux condenser, and a thermometer and containing 40 g. (0.253 mole) of potassium permanganate, 75 g. (0.29 mole) of magnesium nitrate hexahydrate, and 750 ml. of water. The reaction mixture was heated at 60–70° for six hours. About 14 g. of unreacted diethylbenzene was recovered, and very little of the desired material was obtained.

In each of six additional runs 40.3 g. (0.3-mole portions) of *o*-diethylbenzene was used with 126.4 g. (0.8-mole portions) of potassium permanganate. Magnesium nitrate hexahydrate was used to keep the mixture neutral, and the temperature was kept at 60–70° for eight hours. The *o*-diacetylbenzene fractions were combined and vacuum-distilled, and a total of 18.3 g. of pale yellow liquid, b.p. 107–109° (1 mm.), was obtained. This liquid crystallized when it was placed in an ice-water bath, and the solid melted at 38–39°; lit. (18), m.p. 38–39°. There was also recovered 142.5 g. of *o*-diethylbenzene and 20.1 g. of *o*-ethylacetophenone.

To the dioxane sulfur trioxide reagent (0.13 mole), 10 g. (0.062 mole) of *o*-diacetylbenzene was added over a period of two hours at 5°. The mixture became dark on addition, and it was stirred for three more hours at 5°. The mixture was then poured into ice-cold water, and the water layer was separated from the organic layer. The aqueous layer was neutralized with sodium carbonate and then evaporated to dryness. The residue was extracted with a 75% ethanol-water mixture, but no crystals were formed on chilling the extract. Evaporating the solution to a smaller volume yielded only inorganic material, and removal of ethylene chloride from the dried organic layer left an insignificant amount of unreacted *o*-diacetylbenzene.

Dibenzolymethane. Dibenzoylmethane (19) (7.85 g., 0.035 mole) was added to 0.035 mole of dioxane sulfur trioxide. No sulfonate was isolated, and 5.5 g. of original dibenzoylmethane was recovered.

In a similar run triethylamine (0.035 mole), freshly distilled and dried over calcium hydride, was added to the reaction mixture. In this case, the reaction mixture was not poured into water, but an attempt was made to isolate and purify the product directly from the mixture; however, no identifiable product was isolated.

Ethyl p-acetyl-α-toluate. Ethyl *p*-acetyl-α-toluate (20) (2.54 g., 0.0127 mole) was added to 0.026 mole of dioxane sulfur trioxide. Three g. of sodium sulfonate (V) was obtained.

Anal. Calc'd for $C_{12}H_{12}Na_2O_9S_2$: Na, 11.2. Found: Na, 10.9.

Alkaline permanganate oxidation of V gave *terephthalic acid* which was confirmed by preparing its *p*-bromophenacyl ester.

The *S-benzylthiuronium salt* of V melted at 196–196.5°.

Anal. Calc'd for $C_{28}H_{34}N_4O_9S_4$: N, 8.02. Found: N, 8.06.

SUMMARY

1. Several substituted acetophenones have been directly sulfonated with dioxane sulfur trioxide to give α-ketosulfonates in fair yields.

2. *o*-Diacetylbenzene and dibenzoylmethane react with dioxane sulfur trioxide; however, identifiable ketosulfonates were not isolated. Dibenzoylmethane presumably formed the enol sulfate.

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