# *The Selenium Dioxide Oxidation of Substituted Acetophenones*

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It is widely known that the methyl group adjacent to the carbonyl group can conveniently be oxidized to aldehyde group by selenium dioxide. In this way many arylglyoxals (I) have been obtained from substituted acetophenones (II).

ArCOCHO (I) ArCOCH$_3$ (II)

As we came to the need of *o*-nitro- and *o*-acetamino-phenylglyoxal for further synthesis in our study, we carried out the oxidation of *o*-nitro- and *o*-acetamino-acetophenone. It has been reported[1] that the oxidation of *p*-nitro- and *p*-acetamino-acetophenone gives corresponding phenylglyoxal derivatives. We found, however, that the oxidation of the *o*-acetaminoacetophenon did not give *o*-acetaminophenylglyoxal, while that of *o*-nitroacetophenone gave *o*-nitrophenylglyoxal. In the case of the oxidation of *o*-acetaminoacetophenon, its methyl group was oxidized to the carboxylic group, and the product was a mixture of almost equal amount of *o*-acetaminophenylglyoxylic acid (III) and isatin (IV). The presence of (IV) is considered to be the result of deacetylation of (III) and ensuing cyclization. Isatin was, in fact, formed by heating (III) in 10% hydrochloric acid.

(III) reacted with 2,4-dinitrophenylhydrazine, semicarbazide, and thiosemicarbazide to give crystalline products. But they were not the ordinary condensation products (V) at all, though their structures have not been confirmed here.

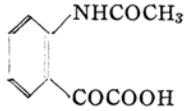
*o*-Nitrophenylglyoxal was also identified by analysis, of its 2,4-dinitrophenylhydrazone and thiosemicarbazone.

*o*-Nitrophenylglyoxal gave the condensation product, *o*-nitrobenzoylacrylic acid (VI), on treatment with malonic acid in acetic acid solution containing a small amount of sulfuric acid, while in pyridine solution, only a small amount of crystals could be obtained, which melted at 233–4°, and had the empirical formula of $C_{15}H_{10}N_2O_6$.

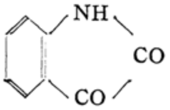
## Experimental

***o*-Nitrophenylglyoxal.**—Fourteen grams of selenium dioxide were dissolved in the mixture of 70 cc. of dioxane and 3 cc. of water with heating. To this warm solution, 19 g. of *o*-nitroacetophenone was added at one time and refluxed for seven hours with constant stirring. After the metallic selenium was filtered off, the most part of dioxane was evaporated, water was added and extracted with ether. After drying over anhydrous sodium salfate, ether was evaporated. From the residue a deep yellow oil distilled at 124-4.5° at a pressure of 3.5 mmHg, yield 13 g. Found: N, 8.24. Calculated for $C_8H_5NO_4$: N, 7.82%.

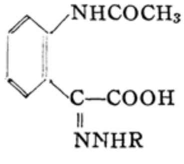
***o*-Nitrophenylglyoxal thiosemicarbazone.**—The thiosemicarbazone was prepared from *o*-nitrophenylglyoxal (1 g.) and thiosemicarbazide (0.6 g ) in dilute ethanol by refluxing for one hour. Recrystallization from ethanol gave light needles, m.p. 172°. Found: N, 22.11. Calculated for $C_9H_8N_4O_3S$: N, 22.2%.



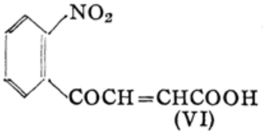
(III)



(IV)



(V)



(VI)

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[1] C. Musante et al., *Gazz. Chim. Ital.*, **81**. 451 (1951). C. A. **46**, 5549 (1952).

**o-Nitrophenylglyoxal 2,4-dinitrophenylhydrazone.**—Small amounts of *o*-nitrophenylglyoxal and 2,4-dinitrophenylhydrazine were heated in ethanol for thirty minutes. Upon recrystallization from ethanol, this hydrazone melted at 186–8°. Found: N, 19.82. Calculated for $C_{14}H_9N_5O_7$: N, 19.6%.

**The oxidation of *o*-acetaminoacetophenone.**—Thirty five grams of *o*-acetaminoacetophenone were oxidized with 22 g. of selenium dioxide in dilute dioxane (120 cc. of dioxane and 4 cc. of water) and extracted with ether in the same way as described above in the case of *o*-nitro derivative. After evaporating ether, a red oily substance remained which soon solidified. This was washed with benzene and added to the aqueous sodium carbonate solution. The insoluble substance was filtered (filtrate A), washed with water and recrystallized from acetone-benzene. The red needles of isatin were obtained., m.p. 200°C. Found: C, 64.88; H, 3.51; N, 10.16. Calculated for $C_8H_5NO_2$: C, 65.3; H, 3.40; N, 9.54%. Filtrate A, when acidfied with hydrochloric acid, gave white crystals. Recrystallization from water gave white needles of *o*-acetaminophenylglyoxylic acid, m.p. 162°C. Found: N, 7.09. Calculated for $C_{10}H_9NO_4$: N, 7.78%.

**The change of *o*-acetaminophenylglyoxylic acid into isatin.** — *o*-Acetaminophenylglyoxylic acid, when heated with 10% hydrochloric acid, went gradually into solution. The hot solution was filtered off from a small amount of insoluble matter and cooled. Red needles were obtained. The mixed melting point with isatin showed no depression.

**The reaction of *o*-nitrophenylglyoxal with malonic acid.**—To a solution of 12 g. of *o*-nitrophenylglyoxal in 24 cc. of gracial acetic acid, 10 g. of malonic acid and 5 drops of concentrated sulfuric acid were added. The mixture was heated at 70°C for thirty minutes and then refluxed for ten minutes, water was then added and extracted several times with saturated sodium carbonate solution. The acidification of the combined water layer with hydrochloric acid gave white crystal accompanied by resinous matter. This was washed with dilute ethanol and recrystallized from dilute ethanol, yield 3 g., m.p. 170°C. Found: C, 53.85; H, 3.48; N, 6.27. Calculated for $C_{10}H_7NO_5$: C, 54.3; H, 3.16; N, 6.33%.

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