

REDUCTION OF ORGANIC COMPOUNDS WITH THIOUREA DIOXIDE. I.

REDUCTION OF KETONES TO SECONDARY ALCOHOLS

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Thiourea dioxide (1) (formamidine-sulphinic acid) which is easily prepared by the oxidation of thiourea with hydrogen peroxide has been known to be a reducing agent capable of reducing many kinds of metallic ions to metals. In recent years thiourea dioxide has been used as a bleaching agent in the production of synthetic fibers, but there have been only two reports (2) concerning the reduction of organic compounds by this reagent. Gore briefly reported that aromatic nitro, azoxy, azo, and hydrazo compounds were reduced to the amines and quinones to hydroquinones but ketones were not reduced.

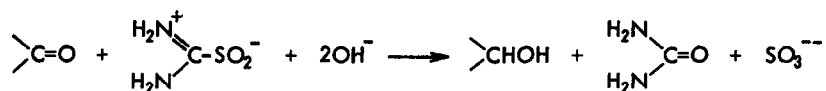
We have studied in detail the action of thiourea dioxide on a variety of ketones and found that it is a convenient and economical reducing agent for obtaining secondary alcohols from corresponding ketones. Aliphatic, alicyclic, aromatic, and heteroaromatic ketones can be easily reduced with this reagent in good yield using an aqueous ethanolic solution in the presence of caustic alkali.

A typical experiment is as follows: To a solution of 1.80 g (0.01 mole) of fluorenone in 30 ml of ethanol, 0.02 mole of sodium hydroxide in 20 ml of water and 1.08 g (0.01 mole) of thiourea dioxide were added under stirring and the mixture was heated for two hours at 90° on a water bath. After removal of ethanol by distillation, the aqueous solution was extracted with ether and the extract was concentrated to remove the solvent. The crude product was dissolved in benzene and chromatographed on silica gel (80 g). Unreacted fluorenone 0.05 g (2.8%) was recovered from the first fraction eluted and fluorenol 1.74 g (95.6%) was obtained from the next fraction. When thiourea dioxide was used in a half molar amount with respect to fluorenone, the yield was reduced to 47.8% and unchanged ketone was recovered.

Generally, reduction of ketones were carried out successfully with 1.0 to 3.0 molar amounts of

thiourea dioxide using sodium hydroxide in twice molar amounts to that of the reducing agent. From the reaction mixture, almost theoretical amounts of sodium sulphite and urea were obtained.

Considering these results, this reaction is presumed to be in the following scheme.



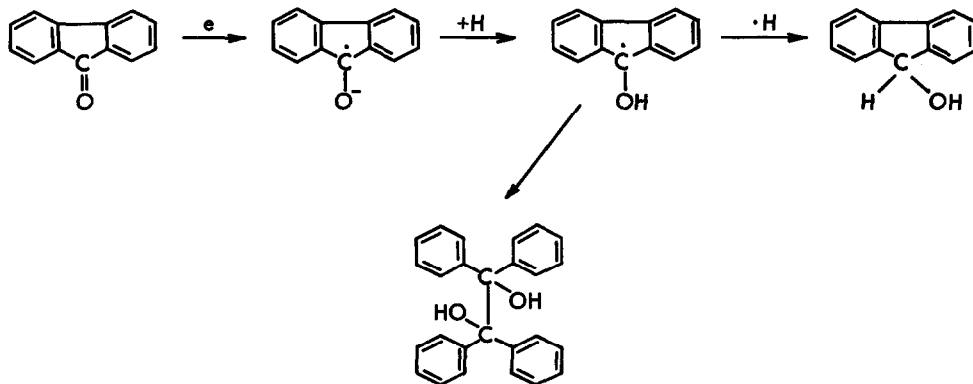
The reducing power of thiourea dioxide was not affected by excess of alkali, but the reduction of fluorenone with thiourea dioxide and sodium hydroxide in a molar ratio of 1 : 1 did not give a satisfactory yield of the alcohol, but afforded a dimer, [9,9'-bifluorenone]-9,9'-diol, as a by-product in yield 36%.

Reduction of ketones which are easily decomposed by alkali occasionally resulted in the formation of by-products. For example, the reduction of benzoylacetone resulted in partial cleavage of its side chain to give phenylmethyl carbinol. The reduction of aliphatic ketones, methylonyl ketone or di-n-propyl ketone for example proceeded at a noticeably slower rate and the reaction gave a poor yield of the alcohol owing to decomposition of the reducing agent in the reaction mixture. However, when more reducing agent was employed, and the addition of the reagent divided into several portions, the yield of the secondary alcohol was markedly increased.

The results of the reduction of ketones were summarized in Table.

In the course of the reduction of fluorenone, it becomes clear from ESR studies and from the reaction products obtained that the reaction proceeded through a radical reaction path. ESR studies on the reduction of fluorenone in alkaline solution showed the presence of the corresponding anion radical, $g = 2.0033$, $a^{\text{H}} = 3.3\text{G}$ (2H), $a^{\text{H}} = 2.6\text{G}$ (2H), $a^{\text{H}} = 0.7\text{G}$ (2H), and $a^{\text{H}} = 0.4\text{G}$ (2H). This ESR spectrum was identical with that obtained on reduction with Rongalit ($\text{NaHSO}_2 \cdot \text{CH}_2\text{O} \cdot 2\text{H}_2\text{O}$).

Considering these results, the reduction may possibly be explainable in terms of a one electron transfer reduction and the mechanism of formation of the secondary alcohol and the dimer is presumed to take place in the following way



Table

| Ketone | Reaction time (hr) | Molar ratio (thiourea dioxide to ketone) | Yield (%) |
|-----------------------------------|--------------------|--|-----------|
| Fluorenone | 2 | 1.0 | 95.6 |
| Benzophenone | 6 | 1.8 | 100.0 |
| Desoxybenzoin | 6 | 1.8 | 99.0 |
| Acetophenone | 6 | 1.8 | *94.4 |
| Propiophenone | 6 | 1.8 | *93.3 |
| Dibenzylketone | 2 | 1.8 | 96.7 |
| Benzylmethylketone | 6 | 1.8 | *97.3 |
| 3-Benzoylpyridine | 6 | 1.8 | 100.0 |
| β -Acetonaphthone | 6 | 2.4 | 91.1 |
| α -Methylaminoacetophenone | 2 | 3.0 | 78.0 |
| Cyclohexanone | 6 | 1.8 | 80.9 |
| Methylnonylketone | 7 | 2.4 | *74.2 |
| Di-n-propylketone | 6 | 2.4 | *75.5 |

* Yields were determined by quantitative gas chromatography.

a) All reduction were done in dilute alcohol solution at 90° .

b) Sodium hydroxide was used in twice molar amount of thiourea dioxide.

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