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OXIDATION OF ACTIVE METHYLENES BY DIMETHYL SULFOXIDE: A NEW NINHYDRIN SYNTHESIS

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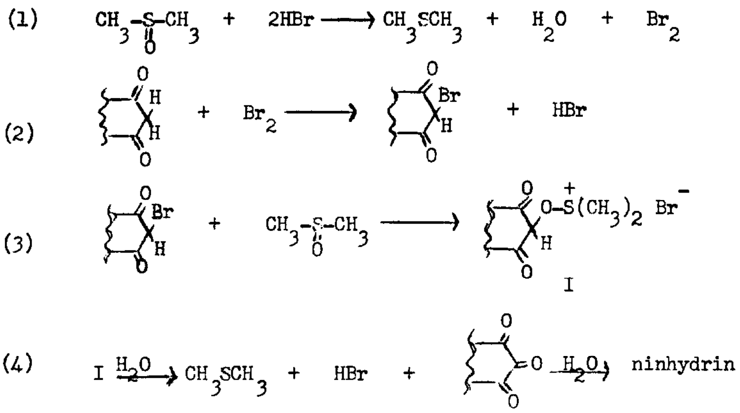
In recent years dimethyl sulfoxide per se, or in combination with activating electrophiles has been applied extensively in the oxidative conversion of alkyl halides, tosylates, chloroformates and alcohols to the corresponding carbonyl compounds (2). We wish to report an analogous oxidation of certain activated methylene moieties.

As part of a search for a convenient synthesis of ninhydrin, the Kornblum oxidation (3) of 2-bromo-1,3-indanedione (4) was attempted and the desired product was obtained in 36% yield. Subsequently bromination of 1,3-indanedione in dimethyl sulfoxide with molecular bromine proved to be a more direct and superior method for the preparation of ninhydrin (5). It was found that this reaction proceeded quite well when as little as 0.25 mole of bromine was employed per mole of dione. This observation suggested that bromine was regenerated by the dimethyl sulfoxide oxidation of hydrogen bromide (6) which, in turn, resulted from a. the initial bromination of 1,3-indanedione and b. the collapse of the dimethylalkoxysulfonium bromide (I) - the postulated intermediate for the Kornblum reaction (2). Thus the intriguing possibility presented itself that the oxidation of 1,3-indanedione to ninhydrin could be effected by dimethyl sulfoxide in the presence of catalytic amounts of hydrogen bromide as shown in the following sequence of events:



A solution consisting of 29.2 g. (0.20 mole) 1,3-indanedione, 3.2 g. (0.04 mole) of anhydrous hydrogen bromide and 62.4 g. (0.80 mole) of dimethyl sulfoxide was heated at 70°-90° until all of the resulting dimethyl sulfide had distilled out from the reaction mixture. The excess dimethyl sulfoxide was removed under reduced pressure and the residue was heated for one hour at 100° C. with 200 ml. of 0.3N hydrochloric acid. The acidic solution was decolorized, concentrated and cooled; upon filtration, ninhydrin was obtained in a yield of 80-82% theory.

While the above conditions are optimal for the preparation of ninhydrin the oxidation proceeded quite well at hydrogen bromide to dione ratios, as low as 1:10. Aqueous hydrobromic acid could be employed in place of the anhydrous variety (10 g. of 1,3-indanedione in 100 ml. of dimethyl sulfoxide reacted, as above, with 48% hydrobromic acid - at a molar ratio of acid to dione of 1:2 - was converted to ninhydrin in a yield of 66%). Inert solvents (toluene, ethyl acetate) were acceptable as replacement for that portion of the dimethyl sulfoxide which served as reaction solvent. Other alkyl sulfoxides could be used as oxidants, but the yields of ninhydrin were lower than those obtained with dimethyl sulfoxide.

Preliminary results on the extension of the hydrogen bromide catalyzed dimethyl sulfoxide oxidation to other molecules possessing active methylene groups are summarized in Table I.

TABLE 1

Starting Material	Oxidation Product	Yield %
peri-1,3-Naphthidenedione (7)	peri-1,2,3-Naphthidenetrione (8)	38
1,3-Benz[f]-Indanedione (9)	1,2,3-Benz[f]-Indanetrione Hydrate (10)	88
Desoxybenzoin	Benzil	95
Dibenzoylmethane	1,3-Diphenyl-1,2,3-Propanetrione	12
Diphenylmethane	Benzophenone (11)	15
Acetophenone	Phenylglyoxal (12)	10
2-Picoline	2-Pyridine Carboxaldehyde (11)	3

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4. The methods given for the synthesis of 2-bromo-1,3-indanedione by C. L. Arcus and G. C. Barrett, *J. Chem. Soc.*, 2098 (1960) were found to yield mixtures containing large amounts of 2,2-dibromo-1,3-indanedione. The desired monobromo derivative, m.p. 121-122°, was prepared by the selective bromination of 1,3-indanedione with copper (II) bromide in accordance with a general procedure described by L. C. King and G. K. Ostrum, *J. Org. Chem.*, **29**, 3459 (1964).
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9. The dione was prepared via the Claisen condensation between ethyl acetate and ethyl-2,3-naphthalenedicarboxylate followed by hydrolysis and decarboxylation in gl. acetic acid. The brown solid, m.p. 225-227° (ethanol) was characterized by elemental anaylsis and I. R. spectrum.
10. The yellow trione hydrate, m.p. 296-298° (benzene) was charcterized by elemental analysis and I. R. spectrum.
11. Isolated as hydrazone.
12. Isolated, after reaction with o-phenylenediamine, as 2-phenylquinoxaline.