

# Kinetics of Sodium Borohydride Reduction of Substituted 4-Methylthioacetophenones : Evidence for Steric Enhancement of Resonance

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The rates of reduction of a number of substituted 4-methylthioacetophenones by sodium borohydride in isopropanol medium have been studied. The observed values of 3-methyl and 3-halogeno-4-methylthioacetophenones record significant deviation from the values calculated on the basis of additivity principle. The observed rate constants are lower than the predicted values. This indicates that the mesomeric interaction between the methylthio and acetyl groups is enhanced when there is a substituent, *ortho* to the methylthio group. In the case of 3-halogeno compounds, the percentage of enhancement increased as the bulk of the halogen increases. The expected steric inhibition of resonance is observed in the case of 3,5-dimethyl-4-methylthioacetophenone.

FOLLOWING the discovery of steric enhancement of resonance by Baliah and Uma<sup>1</sup> several studies by Baliah and Kanagasabapathy<sup>2</sup>, Krishna Pillay and Kanagavel<sup>3</sup>, Jayanthi<sup>4</sup>, Baliah and Theymoli<sup>5,6</sup> and recently Ganapathy and Ramanujam<sup>7</sup> provided additional support to this phenomenon. The present study of the sodium borohydride reduction of substituted 4-methylthioacetophenones also substantiates the phenomenon without any reservation.

## Experimental

The substituted 4-methylthioacetophenones were prepared by known procedures. The solvent isopropanol was distilled over quick lime and allowed to stand over sodium borohydride overnight. It was then distilled using a fractionating column. AnalaR sodium borohydride (B.D.H.) was used. Double distilled water was used for the kinetic measurements.

Sodium borohydride in isopropanol was prepared by adding excess of sodium borohydride to isopropanol and allowing to stand for a few days with intermittent shaking. It was filtered and kept in a brown bottle. Sodium borohydride was estimated by the method described by Bowden and Hardy<sup>8</sup>.

Solutions of known concentration of sodium borohydride in isopropanol and of acetophenone were prepared and kept in a thermostat maintained at 30°. Equal volumes of each solution were mixed and aliquots were withdrawn at suitable intervals and poured into a stoppered conical flask containing sodium hydroxide (0.1 M) and a known excess of standard potassium iodate, with constant shaking. After a few min, 10 ml potassium iodide (5% solution) was added, followed by immediate addition of 5 ml sulphuric acid (1 M). The contents of the flask were diluted with water and the liberated

iodine was titrated against sodium thiosulphate using starch as indicator. The rate constants were calculated using the second order rate equation.

## Results and Discussion

The mechanism and rates of reaction of a number of ketones and aldehydes with sodium borohydride in isopropanol have been investigated by Brown *et al*<sup>9-11</sup>. The reaction follows second-order kinetics, the transfer of the first hydrogen atom of borohydride ion to the carbonyl carbon being slow and hence the rate-determining step. In the present study, reduction of nine acetophenones has been carried out and the data are shown in Table 1. The

TABLE 1—RATES OF REDUCTION OF SUBSTITUTED ACETOPHENONES WITH SODIUM BOROHYDRIDE IN ISOPROPANOL, AT 30°

Acetophenone	$k \times 10^4 \text{ l mole}^{-1} \text{ sec}^{-1}$	
	Found	Calcd.
Unsubstituted	13.19	—
4-Methylthio-	8.23	—
3-Methyl-	4.46	—
3-Chloro-	161.00	—
3-Bromo-	187.70	—
3-Methyl-4-methylthio-	2.03	2.78
3-Chloro-4-methylthio-	45.52	<sup>a</sup> 100.46
3-Bromo-4-methylthio-	49.93	117.10
3,5-Dimethyl-4-methylthio-	7.48	—

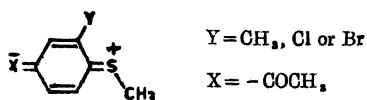
rate constants for polysubstituted acetophenones could be calculated using the relation

$$k_{xy} = \frac{k_x k_y}{k_u}$$

where  $k_x$  and  $k_y$  are rate constants of the mono-substituted acetophenones and  $k_u$  that of the

un substituted acetophenone. The calculated values are also given in the Table.

*p*-Methylthioacetophenone undergoes reduction at a slower rate when compared to acetophenone because of the mesomeric interaction between the *para* substituents. However, the rate of reduction of 3-methyl-4-methylthioacetophenone is still lower. The rate observed ( $2.03 \times 10^{-4}$  l mole $^{-1}$  sec $^{-1}$ ) is significantly low, compared to the value ( $2.78 \times 10^{-4}$  l mole $^{-1}$  sec $^{-1}$ ) calculated on the basis of the additivity principle. This proves that mesomeric interaction is higher in this compound which is not solely due to the methyl group. The  $-\text{CH}_3$  of the  $-\text{SCH}_3$  group occupies a position away from the *ortho* substituent as shown below :



Such a preferred orientation restricts the free rotation of the  $-\text{SCH}_3$  group, thereby increasing the probability of its attaining planarity with the benzene ring. There can, therefore, be an enhanced resonance interaction of the methylthio group with the aromatic ring resulting in the enhancement of resonance.

If a single substituent *ortho* to  $-\text{SCH}_3$  group enhances its resonance interaction, the two *ortho* substituents should prevent the  $-\text{SCH}_3$  group from attaining planarity with the ring and hinder conju-

gation. Such a steric inhibition is observed in 3,5-dimethyl-4-methylthioacetophenone. Indeed, this type of bulk effect of the 3-substituent is observed in the reaction of N,N-dimethylanilines with allyl bromide $^{1,2}$ .

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