184. *The Mobility of Groups containing Sulphur. Part V.*

By David T. Gibson.

In Part IV (J., 1937, 1509) it was shown that the introduction of a thioalkyl (or thioaryl) group into a reactive methylene compound is influenced by the character of the various groups R. :

$$\underset{\text{(Dextro-.)}}{R{\cdot}SO_2{\cdot}SR'} + CH_2R''R''' \xrightarrow{\text{alkali}} \underset{\text{(Lævo-.)}}{R{\cdot}SO_2Na} + SR'{\cdot}CHR''R'''$$

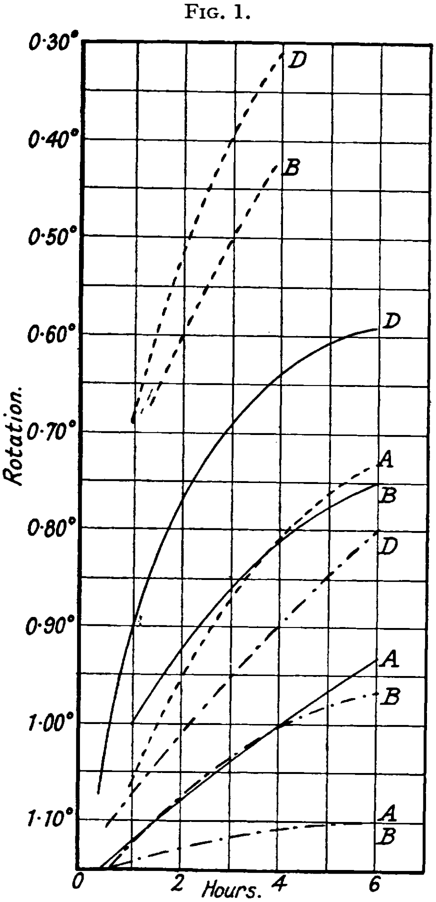
The effect of the group SR′ has now been further examined, the reaction being followed polarimetrically as before, and it is shown that the conjugation of the lone pair of electrons on the entering sulphur atom with the double bond of the (enolised) substitution product, *e.g.*, $R{-}\ddot{S}{-}C(CO{\cdot}CH_3){=}C(OH){\cdot}CH_3$, acts as a favouring, but not essential, factor in the reaction.

It has been shown (McClelland, J., 1929, 1590; Cohen and Smiles, J., 1930, 406; Arndt and Martius, *Annalen*, 1932, **499**, 257; Arndt, Martin, and Partington, J., 1935, 602) that in cyclic systems the free valency electrons of sulphur may be considered as a source of electrons tending to increase the negative character of carbonyl oxygen and thus favouring enolisation, with the consequent development of conjugation between the lone pair of the sulphur atom and the ethylene bond. A similar effect obtains with non-cyclic systems, for acetonyl alkyl sulphides, but not sulphones, yield cyanohydrins (Delisle, *Annalen*, 1890, **260**, 252) and react with alkyl nitrate (Arndt and Rose, J., 1935, 4).

Now, since Arndt and Eistert (*Ber.*, 1936, **59**, 2385) have suggested that the driving force in the Claisen condensation is the tendency to develop a conjugated system, it seemed possible that the introduction of thioaryl (or thioalkyl) groups into compounds containing reactive methylene groups (Brooker and Smiles, J., 1926, 1723) would be also facilitated by the tendency for the system $R{-}\ddot{S}{-}C(CO{\cdot}CH_3){=}CR{\cdot}OH$ to be formed. On the other hand, Hauser and Renfrow (*J. Amer. Chem. Soc.*, 1937, **59**, 1823) have effected condensation with an ester in which a conjugated intermediate product cannot easily be imagined, and bissulphonylmethanes, where conjugation is impossible (Arndt and Martius, *loc. cit.*, p. 236), have been shown to be substituted with velocity comparable with that of enolisable compounds (Part IV; Gibson, J., 1937, 1509); moreover, cyano-derivatives, which do not enolise extensively (Arndt, Scholz, and Frobel, *Annalen*, 1935, **521**, 111), are among the most rapidly substituted (Fig. 6).

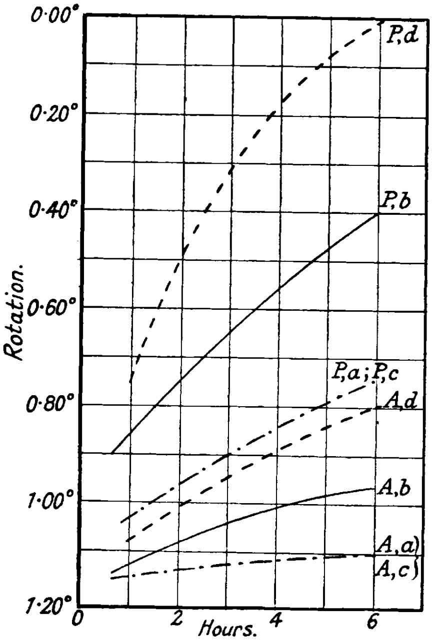
Further, Brooker and Smiles (*loc. cit.*) showed that a second thioaryl substituent enters deoxybenzoin (I) so much more rapidly than the first that they were unable to isolate (II); *i.e.*, a substituent may enter even if it involves the ***disappearance*** of conjugation (cf. McClelland and Longwell, J., 1923, **123**, 3312). By using a milder alkaline medium, (II) has now been isolated (Expt. 1), whereas stronger alkali affords (III). Fig. 1 illustrates the effect of p_H on the rates of reaction of deoxybenzoin with various compounds in presence of sodium propionate, acetate, or formate (decreasing alkalinity) (Expt. 4).

Fig. 1.



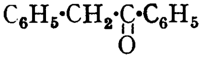
– – – – – – Sodium *propionate.*
———— *Sodium acetate.*
— · — · — · *Sodium formate.*
A. *Bis(ethylsulphonyl)methane.*
B. *Ethyl acetoacetate.*
D. p-*Toluenesulphonylacetone.*

Fig. 2.

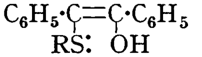


a. Bis(ethylsulphonyl)methane.
b. Ethyl acetoacetate.
c. Methylacetylacetone.
d. p-*Toluenesulphonylacetone.*

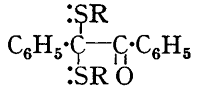
Solvent { *P. Pyridine.* *A. Alcohol.* }


$C_6H_5{\cdot}CH_2{\cdot}\underset{O}{\underset{\|}{C}}{\cdot}C_6H_5$

(I; not conjugated.)


$C_6H_5{\cdot}\underset{RS:}{\underset{|}{C}}{=}\underset{OH}{\underset{|}{C}}{\cdot}C_6H_5$

(II; conjugated.)

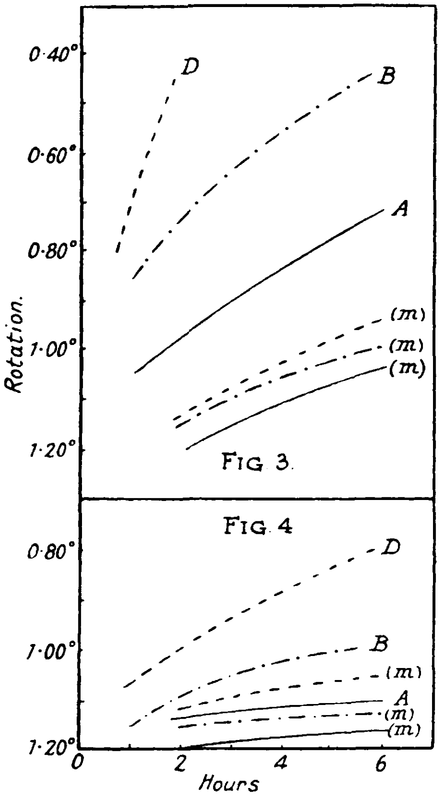

$C_6H_5{\cdot}\overset{:SR}{\underset{:SR}{C}}{-}\underset{O}{\underset{\|}{C}}{\cdot}C_6H_5$

(III; not conjugated.)

Finally, attempts to transfer a thioaryl group from a substituted bis-sulphonylmethane to acetylacetone were unsuccessful (Expt. 2); and the thioalkyl- (or thioaryl-) sulphonylacetones did not give colour reactions with ferric chloride.

Nevertheless, the following considerations indicate that a " Konjugations-bestreben " effect, though secondary, is perceptible. Methylene derivatives which undergo the Smiles–

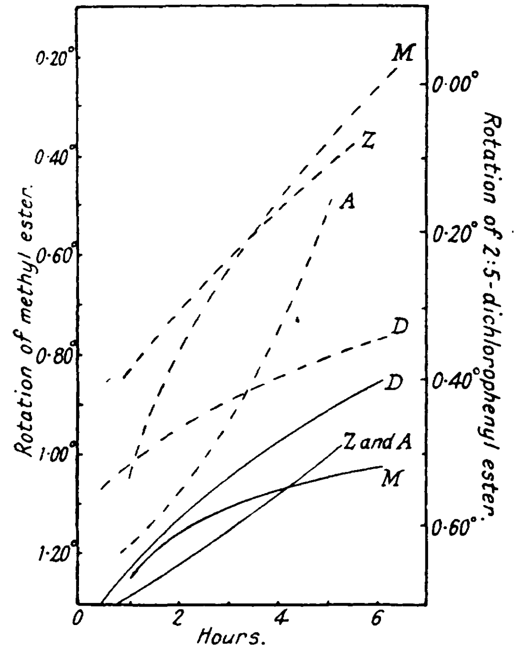
Brooker substitution may be divided into four types: (*a*) bis(ethylsulphonyl)methane, (*b*) ethyl acetoacetate, (*c*) ethyl methylacetoacetate, (*d*) phenylsulphonylacetone; in these, the possibility of conjugation by thioarylation may be regarded as respectively (*a*) nil, (*b*) increased, (*c*) eliminated, (*d*) introduced. Now, since pyridine is a solvent which favours enolisation (Meyer, *Ber.*, 1912, **45**, 2843), it may be expected that, if rates of substitution in alcohol and in pyridine are compared, type (*d*) will show the greatest increase and types (*a*) and (*c*) the least (Expt. 3) (see Fig. 2). It is somewhat surprising, however, that even with methylacetylacetone, one of the most enolised of alkylated keto-enol compounds, there is some increase with pyridine. The several curves, omitted for clarity, are practically coincident with those of bis(ethylsulphonyl)methane. Again, since the monomethylated derivatives corresponding to (*a*), (*b*), and (*d*) on thioarylation lose the hydrogen necessary for enolisation, it is evident that, if comparison be made between the rates of thioalkylation of (*a*), (*b*), (*d*) and of their respective methyl derivatives, the difference will be least between (*a*) and its methyl derivative, since with both conjugation is nil; it will be greater between (*b*) (increasing conjugation) and its methyl derivative (eliminated); and greatest between (*d*) (conjugation introduced) and its methyl derivative (nil). The differences will be more pronounced in pyridine (Fig. 3) than in alcohol (Fig. 4).



D- - - - p-*Toluenesulphonylacetone.*
B—·—·— *Acetoacetic ester.*
A———— *Bis*(*ethylsulphonyl*)*methane.*
(m) *Methylated compounds,* >CHMe.

FIG. 3. *Pyridine solution.*
FIG. 4. *Alcoholic solution.*

FIG. 5.



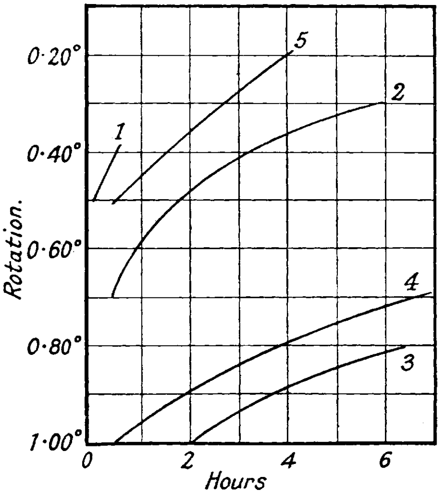
- - *With* 2 : 5-*dichlorophenyl camphorthiolsulphonate.*
—— *With methyl camphorthiolsulphonate.*

Z. Dibenzoylmethane.
M. Ethyl malonate.
A. Bis(*ethylsulphonyl*)*methane.*
D. p-*Toluenesulphonylacetone.*

Lastly, comparison may be made between two thiosulphonic esters, *viz.*, methyl and 2 : 5-dichlorophenyl camphorthiolsulphonates. The rates of reaction in acetone (Expt. 5) show that the group S·$C_6H_3Cl_2$ always enters more rapidly than ·SMe even when the possibility of conjugation is absent, but it will be observed (Fig. 5) that this superiority is least marked with *p*-toluenesulphonylacetone, with which substitution connotes the development of conjugation. In view of the relative strengths of acetic and dichlorobenzoic acids, it is to be expected that a conjugated system will be formed by MeS• more readily than by $C_6H_3Cl_2$•S•. In Fig. 6 are collected several curves relating to substances supplementary to the previous paper (Part IV, *loc. cit.*). In this connexion, it is particularly significant for the idea of optimum activation that, whereas all the related disubstituted methanes undergo reaction, neither *p*-toluenesulphonyl-α-cyanoacetone nor *p*-toluenesulphonyl-α-cyanoacetic ester shows any reaction (Expt. 6).

The possibility of a more general method of exploring this reaction is opened up by the observation that, whereas Connor's mercuric chloride test for active methylene (*J. Amer. Chem. Soc.*, 1936, **58**, 1132, 1387) is given by the *p*-toluenesulphonyl derivatives of nitromethane, acetamide, acetonitrile, and methylacetone, and also by ethyl phenylsulphonylbutyrate and malononitrile, yet it is negative with the substituted derivatives phenylthiobis(ethylsulphonyl)methane, phenylsulphonyl-α-methylthioacetone, 2 : 5-dichlorophenylthioacetylacetone, tris(ethylsulphonyl)-methane, and also *p*-toluenesulphonyl-α-cyanoacetone.

FIG. 6.



1. *Malononitrile.*
2. *Toluenesulphonylnitromethane.*
3. *Cyanoacetamide.*
4. *Benzoylacetic ester.*
5. *Chlorophenylsulphonylacetonitrile.*

EXPERIMENTAL.

Expt. 1.—Brooker and Smiles, using sodium ethoxide, found that deoxybenzoin reacted so readily with disulphoxides that the mono-substitution product could not be isolated, only the di-derivative being obtained. With chloroanisyl disulphoxide, in presence of sodium acetate, however, the mono-chloroanisylthiodeoxybenzoin, m. p. 100°, has now been obtained. It was converted by 2 : 5 dichlorophenyl disulphoxide and sodium ethoxide into the di-derivative, m.p. 170°, described by Brooker and Smiles.

Expt. 2.—Acetylacetone and 2 : 5-dichlorophenylthiobis(arylsulphonyl)methanes in alcohol with sodium acetate gave no trace of 2 : 5-dichlorophenylthioacetylacetone.

Expt. 3.—Solutions contained each reactant N/20 in aqueous alcohol (1 : 4) or aqueous pyridine (1 : 4) with sodium formate.

Expt. 4.—N/20-Solutions in 95% alcohol were used, containing severally sodium propionate, acetate, or formate.

Expt. 5.—N/20-Solutions were used in 85% acetone, with sodium acetate; with sodium formate there was practically no reaction at all. In 80% pyridine, reaction goes easily with sodium formate, but the differences are masked by solvent effect. In acetone, the rotation of methyl camphorthiolsulphonate changes from + 1·30° to — 0·50°, and that of the dichlorophenyl ester from + 0·65° to — 0·50°.

Expt. 6.—*p*-Toluenesulphonylnitromethane (Arndt and Rose, J., 1935, 8) is very conveniently (contrast Troger and Nolte, *J. pr. Chem.*, 1920, **101**, 143) obtained by warming (undistilled) bromonitromethane and sodium *p*-toluenesulphinate for a short time in alcohol. *p*-Toluenesulphonyl-cyanoacetone and -cyanoacetic ester, prepared as Arndt, Scholz, and Frobel suggested, are conveniently freed from less acidic products by extraction with sodium formate solution instead of bicarbonate; these were tested for reaction in 95% alcohol with sodium acetate.

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