311. *The Mobility of Groups containing a Sulphur Atom. Part IV.*

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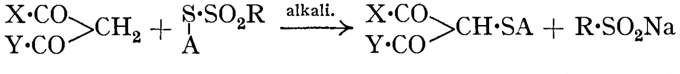
The use of thiolsulphonic esters to introduce thioalkyl (or thioaryl) groups into compounds containing a reactive methylene group has been studied polarimetrically to determine the effect of alkalinity, the ester group, the thiolsulphonic group, and the groups activating the methylene group. The effect of the last is the most complicated, involving enolisation, an optimum degree of activation, and pseudo-reversibility of the reaction.

The reaction discovered by Brooker and Smiles (J., 1926, 1723)



$$\begin{matrix}X\cdot CO\\ Y\cdot CO\end{matrix}\!\!>CH_2 + \begin{matrix}S\cdot SO_2R\\ |\\ A\end{matrix} \xrightarrow{\text{alkali.}} \begin{matrix}X\cdot CO\\ Y\cdot CO\end{matrix}\!\!>CH\cdot SA + R\cdot SO_2Na$$

and extended to sulphonyl derivatives (Gibson, J., 1931, 2637) has now been explored in detail by taking advantage of the change in rotation of the solution when *d*-camphorthiolsulphonic esters are used (cf. Gibson and Loudon, this vol., p. 487).

The exchange of sulphonyl groups between sulphinates and thiolsulphonic esters showed that the sulphonyl group is a potential anion; consequently, the remainder of the molecule (SA) must be capable of functioning transiently as a cation, and so the above reaction may be regarded as the combination of this cation with the methylene anion. This view is supported by the observations that the reaction is favoured (1) by increasing alkalinity; (2) by a strongly negative entering group A, which increases the acceptor tendency of the group SA; (3) by use of thiolsulphonic esters which liberate a relatively strong sulphinic acid

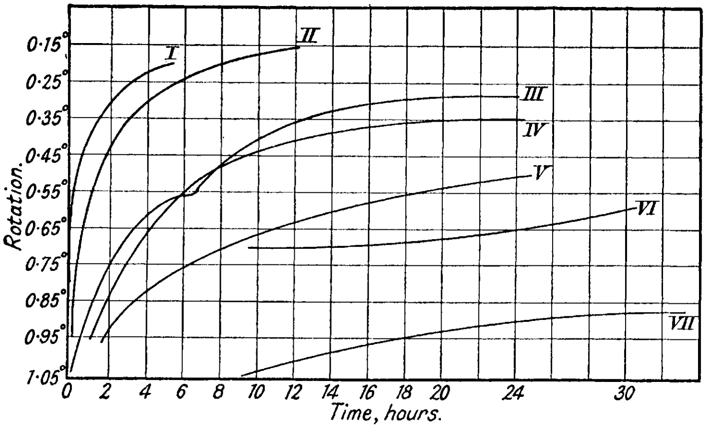
$$(C_6H_3Cl_2\cdot SO_2\cdot S\cdot C_6H_3Cl_2 > C_6H_4Cl\cdot SO_2\cdot S\cdot C_6H_3Cl_2 > C_6H_4Me\cdot SO_2\cdot S\cdot C_6H_3Cl_2).$$

It may be noted that, whereas benzenesulphonyl chloride was found to effect chlorination (J., 1931, 2641), it has now been found that the alkylsulphonyl chlorides may be very advantageously used to introduce an alkylsulphonyl group into reactive methylene compounds.

The effect of the group X, Y, carbonyl, or sulphonyl is more complicated, and evidence has been obtained for the existence of at least three factors, *viz.*, (1) enolisation, (2) pseudo-reversibility, (3) optimum activation, though it is not yet certain to what extent they are connected.

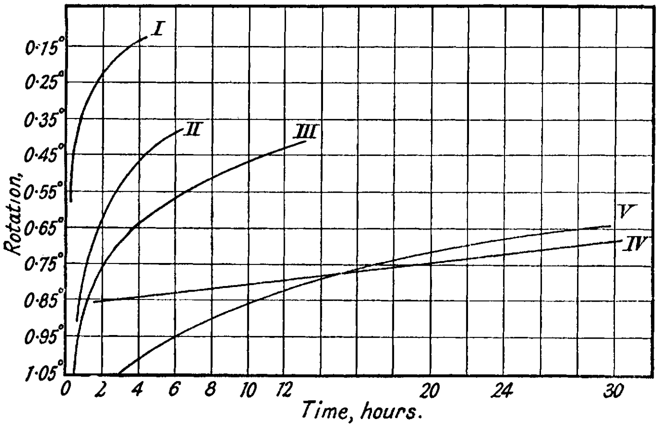
(1) If the compounds examined are arranged according to rate of reaction with methyl *d*-camphorthiolsulphonate, consistent effects of the groups X and Y are only observed when separate comparison is made between (*a*) those which enolise and (*b*) those which, according to Arndt and Martius (*Annalen*, 1932, **499**, 228), do not enolise. It will be seen from Figs. 1 and 2 that the order for (*a*) is approximately $CN > CH_3{\cdot}CO > C_6H_5{\cdot}CO > CO_2C_2H_5 > C_6H_5$, and for (*b*) $CN > C_6H_5{\cdot}CO > CH_3{\cdot}CO > CO_2C_2H_5 > R{\cdot}SO_2 > C_6H_5$.

FIG. 1.



I. *Phenacyl cyanide.*
II. *Ethyl cyanoacetate.*
III. *Acetylacetone.*
IV. *Benzoylacetone.*
V. *Ethyl acetoacetate.*
VI. *Dibenzoylmethane.*
VII. *Ethyl malonate.*

FIG. 2.



I. *Phenylsulphonylacetonitrile.*
II. *Phenylsulphonylacetophenone.*
III. p-*Tolylsulphonylacetone.*
IV. *Ethyl* p-*tolylsulphonylacetate.*
V. *Bisethylsulphonylmethane.*

The position of C_6H_5 in each series is inferred from the behaviour of deoxybenzoin (slight reaction in 2—4 days) and of benzylmethylsulphone (no reaction).

The fact that the rate in the two series is of the same order, however, indicates that extent or ease of enolisation is not a necessary condition of reaction. It is significant, and in agreement with the reaction hypothesis advanced above, that none of the phenolic enol–keto-compounds (phloroglucinol, naphthol, or hydroxyquinoline) which gave positive results (Brooker and Smiles, *loc. cit.*) showed any reaction under the present milder conditions.

(2) Two molecular proportions of methyl camphorthiolsulphonate to each molecule

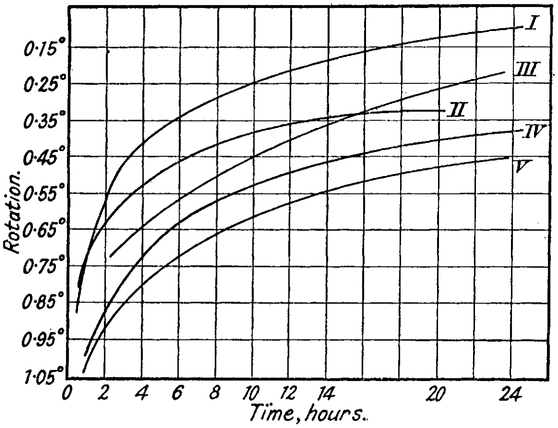
of keto-methylene compound were used to detect, if possible, mono- or di-substitution, for with the former, reaction should come to a standstill at 50%. In fact, with the majority of compounds it ceased at a point in the range 40—70%. Specific tests showed that this appearance of incomplete reaction is not due to side reactions such as (1) oxidation of camphorsulphinic acid to the sulphonic acid, (2) hydrolytic decomposition of the methylene compound $R{\cdot}CO{\cdot}CH_2 \vdots CO{\cdot}CH_3$, or (3) exchange of sulphonyl radicals, for this only occurs with alkylthioacetonylsulphones, and then much too slowly to affect the present results; or (4) to a true reversibility of substitution; but probably to a pseudo-reversibility :

$$R{\cdot}SO_2{\cdot}SR + R{\cdot}S{\cdot}CHXY \xrightarrow{H_2O} R{\cdot}SO_2{\cdot}OH + CH_2XY + R{\cdot}S{\cdot}S{\cdot}R$$

(cf. the exchange of alkylthio-groups; J., 1932, 1822).

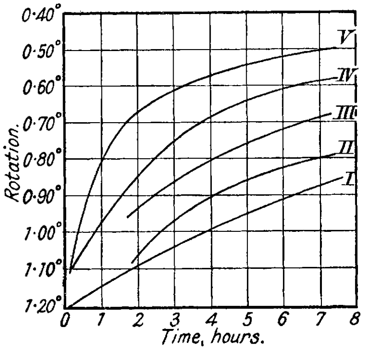
(3) Further, a certain optimum activation of the methylene group is to be expected, for if it is too acidic, the anion >CH′ will be a poor donor; whereas if it is too weakly acidic, no hydrogen ion will separate. Confirmation of this was obtained in the observation that, whereas dibenzoylmethane and bisphenylsulphonylmethane both undergo reaction, none was observed with corresponding mono- or tri-derivatives. Failure in case of the latter pair was not due to trisubstituted methanes *per se*, for both ethyl methylmalonate and αα′-bisphenylsulphonylethane react—though slowly. Again, in Figs. 3 and 4 it will be observed that, among the sulphonylacetones and bissulphonylmethanes, increasing acidic strength of the group $R{\cdot}SO_2$ corresponds with increasing reactivity except in the case of the very strongest—2 : 5-dichlorophenylsulphonyl- being definitely less reactive than 4-chlorophenylsulphonyl-acetone (Fig. 3, II). In this connection, too, it is noteworthy that the series (*a*) and (*b*) above do not at all correspond with the " Reihenfolge der acidifizierenden Wirkung " given by Arndt (*loc. cit.*, p. 241).

FIG. 3.



I. 4-*Chlorophenylsulphonylacetone.*
II. 2 : 5-*Dichlorophenylsulphonylacetone.*
III. p-*Tolylsulphonylacetone.*
IV. *Methylsulphonylacetone.*
V. 4-*Methoxy*-m-*tolylsulphonylacetone.*

FIG. 4.



I. *Bisethylsulphonylmethane.*
II. *Phenylsulphonylmethylsulphonylmethane.*
III. *Bis*-p-*tolylsulphonylmethane.*
IV. *Bisphenylsulphonylmethane.*
V. *Bis*-4-*chlorophenylsulphonylmethane.*

Certain reactions were examined in connection with hypotheses subsequently discarded : dimethyldihydroresorcinol (reaction just perceptible in 24 hours), *p*-tolylsulphonylacetamide (much slower than ethyl ester), di-*p*-toluoylmethane (slightly but definitely slower than dibenzoylmethane). No reaction was observed with phenylacetonitrile, with ketonic or enolic dibenzoylethane, or with ethyl phenylacetate.

EXPERIMENTAL.

The reaction was investigated by mixing equal volumes of *N*/10-methyl *d*-camphorthiolsulphonate + sodium acetate in alcohol–water (95 : 5) and an *N*/20-solution of the methylene compound in absolute alcohol. Thus the reactants were in the ratio 2 : 1, and the possibility of disubstitution could be detected. Measurement was made at 20° with mercury green light in 2-dm. tubes. The measurements with 2 : 5-dichlorophenyl esters were made in alcohol–pyridine solution (3 : 1). In the former series, the observed rotation changed from + 1·20° to − 0·20°, in the latter from + 0·60° to − 0·10°.

Methyl *d*-camphorthiolsulphonate is conveniently prepared by adding powdered *d*-camphorsulphonyl chloride gradually to an equal weight of sodium sulphide crystals dissolved in an equal weight of water, and shaking after each addition till the precipitated sulphur has redissolved; the solution is then treated with methyl sulphate (1 mol.), with cooling, and after standing overnight is freed from methyl sulphide and excess of methyl sulphate by brief steam-distillation. The residual oil soon crystallises, and is conveniently purified from ether. The methyl *r*-camphorthiolsulphonate, m. p. 50°, is so much more soluble that even if camphor of inferior optical quality is used, the final product is pure, although the yield naturally suffers.

(1) *The effect of alkali.* Solutions of methyl *d*-camphorthiolsulphonate are (optically) stable to dissolved sodium acetate. Stronger alkali accelerates the Brooker–Smiles reaction, but rapidly decomposes the methyl thiolsulphonate. The use of several mols. of sodium acetate makes no difference.

(2) *The effect of the group* SA. The following are the times (in hours) for reaction at 20° in alcohol–pyridine (3 : 1) with sodium acetate; concentration *N*/25 :

	Camphorthiolsulphonate.	
	Methyl.	Dichlorophenyl.
Acetylacetone	6	2
Acetoacetic ester	4	1
Methylsulphonylacetone	6½	4
Ethyl malonate	20 (50% reacted)	20 (full
Bisethylsulphonylmethane	24	7

The times for 50% reaction (in hours) in *N*/20-solution in alcohol–pyridine (1 : 1) with acetylacetone were : SMe, 6; SPh, 2; $S{\cdot}C_6H_3Cl_2$, *ca.* $\frac{1}{6}$ (as soon as observation could be taken).

(3) *The effect of the group* $R{\cdot}SO_2$. A series of esters $R{\cdot}SO_2{\cdot}S{\cdot}C_6H_3Cl_2$ reacted with acetylacetone in presence of lacmoid and sodium acetate. The indicator colour changed to acid in 5 mins. for R = 2 : 5-dichlorophenyl, in 30 mins. for R = 4-chlorophenyl, and in 3—5 hrs. for R = *p*-tolyl or *d*-camphoryl.

The Introduction of Alkylsulphonyl Groups.—An excess of alkylsulphonyl chloride was added to a cold alkaline solution of the reactive methylene compound. After removal of any unchanged material with acetic acid, the required compound separated on acidification with hydrochloric acid. In this manner from $CH_2(SO_2X)(SO_2Y)$, methylsulphonyl chloride gave $CH(SO_2X)(SO_2Y)(SO_2Me)$ in the following cases : X = Ph, Y = *p*-tolyl; X = Ph, Y = Et (J., 1931, 2683); X = *p*-tolyl, Y = Me; X = Ph, Y = Me (J., 1932, 1825). From phenylsulphonylacetophenone, it gave *(phenylsulphonyl)(methylsulphonyl)benzoylmethane*, m. p. 166° (Found : S, 18·2; *M*, 358. $C_{14}H_{14}O_5S_2$ requires S, 18·9%; *M*, 338).

d-Camphorsulphonyl chloride with bisethylsulphonylmethane gave *camphorsulphonylbisethylsulphonylmethane*, m. p. 213° (Found : *M*, 419. $C_{15}H_{26}O_7S_3$ requires *M*, 414). Benzenesulphonyl chloride with methylsulphonylacetone gave diphenyldisulphone; and with bisethylsulphonylmethane, bisethylsulphonyldichloromethane, m. p. 98° (incorrectly reported as the monochloro-derivative, J., 1931, 2642).

Similarly attempts to obtain trisulphonylmethanes with benzenesulphonyl fluoride or β-naphthalenesulphonyl iodide were unsuccessful.

The Incompleteness of Reaction.—(1) The rotation of the solutions changed from positive towards zero, coming to a standstill but never reverting as would have happened if sulphinate had been undergoing oxidation.

(2) Solutions of ethyl acetoacetate and of ethyl toluenesulphonylacetate (selected as giving the flattest curves) were kept for 48 hours with sodium acetate. Thereafter, reaction with methyl camphorthiolsulphonate was exactly the same as with fresh solutions.

(3) A solution of sodium camphorsulphinate with, severally, (i) phenylsulphonyl-α-methylthioacetone, (ii) 4-methoxy-*m*-tolylsulphonyl-α-methylthioacetone, and (iii) methylsulphonylethylsulphonylphenylthiomethane, showed no change.

(4) The exchange of sulphonyl radical takes several days at 60° (Gibson and Loudon, *loc. cit.*).

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