

INFLUENCE OF THE SULPHUR ATOM ON OPTICAL ROTATORY POWER.

By P. P. Shukla.

Apart from compounds owing their optical activity to an asymmetric sulphur atom, there are those in which the activity due to asymmetric carbon is influenced by a sulphur atom comprised in their constitution. Mercaptanyl and sulphonyl derivatives of some active compounds are instances of this latter class, along with cystine and its derivatives. Among such compounds the estimation of this influence has not been made, and the present paper describes attempts to achieve this purpose.

Aryl derivatives of imino and bisiminocamphor were found by Forster, B. K. Singh and their collaborators to possess very high rotatory power (*J.C.S.*, 1909, **95**, 942; 1919, **115**, 586 and 889, 980 and 1599; 1921, **119**, 789 and 1971). The thio-derivatives of this class should therefore be convenient for the purpose indicated above, as it might be expected that considerable differences in rotation would be observable, and that some definite effect might be traceable to the sulphur atom.

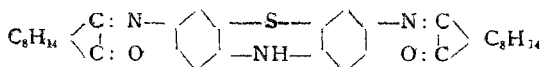
Hilditch (*J.C.S.*, 1908, **93**, 1618) has studied the influence of bi-, quadri and hexavalent sulphur on optical rotation. His work differs from the present inquiry, however, because he examined the rotatory power possessed by various sulphuryl derivatives of an optically active substance and then compared the effect produced by the sulphur atom in its different valencies; whereas my purpose has been to investigate the rotatory power of some thio-imino-compounds in all of which the sulphur is bivalent. On comparing this with the rotatory power of similar derivatives not containing sulphur, it was invariably found that the sulphur atom had a depressing effect on the rotatory power, but the depression varied considerably in magnitude, as illustrated by the following examples:

Compound	[M] in chloroform	Depression
<i>p p'</i> -Diphenylenebisiminocamphor	5472° or 5433°	
<i>p p'</i> -Thiodiphenylenebisiminocamphor	4848	624° or 585
<i>p p'</i> -Dithiophenylenebisiminocamphor	4460	3
<i>p p'</i> -Ditolylenebisiminocamphor	3929 or 4007	
<i>p p'</i> -Thioditolylenebisiminocamphor	2201	1728 or 1806

This depression may be caused by breaking the series of conjugated linkages, these being essential for producing that exaltation of rotatory power which reaches the maximum in 1 : 4-naphthylenebisiminocamphor with $[M]_D^{20} 13,416^\circ$ (Singh and Singh, *J.C.S.*, 1920, 117, 1599). On the other hand, the sulphur atom being associated with unsaturated valency, this might have had an exaltatory influence on rotatory power. The work of Hilditch made this a reasonable expectation. He found that a bivalent sulphur atom has a great influence on rotation, and states that most remarkable effect of all is the change observed when two bivalent sulphur atoms are conjugated, as seen from the following examples :—

<i>L</i> -Amyl alcohol, $C_5H_{11}OH$	$[M]_D$	—	4.58° .
Di- <i>L</i> -amyl sulphide, $(C_5H_{11})_2S$	„	+	42.67 .
Di- <i>L</i> -amyl disulphide, $(C_5H_{11})_2S_2$	„	+	149.40 .

Thus in the case of the iminocamphors, the depression produced by breaking the continuity of conjugated linkages is not outweighed by any exaltation due to a sulphur atom rich in residual affinity. This explanation of the depression observed on bringing sulphur into the active camphor molecule could be tested in a simple manner. If the introduction of sulphur does not involve a breakage in the continuity of conjugated linkages the optical effect should be enhanced. Thus, *pp'*-thiodiphenylaminebisiminocamphor, preserves the continuity



of conjugated linkages, and comparison with the unthionated compound prepared by B. K. Singh, M. Singh and J. Lal (*J.C.S.*, 1921, 119, 1971) should establish the above point. Unfortunately, however, all attempts to prepare this compound failed. In spite of repeated efforts, *pp'*-diaminodiphenylamine could not be condensed with camphorquinone.

This failure is not a solitary example. *pp'*-Dithiolutidine is another compound which did not undergo condensation even on heating it with camphorquinone at about 200° . Nevertheless, from all these attempts at condensation, successful or otherwise, some facts which seem to deserve record have emerged. Firstly, the presence of anhydrous sodium sulphate is found to facilitate condensation in all cases. Thus *pp'*-thiolutidine and camphorquinone do not

appear to react when an alcoholic solution is refluxed during 12 hours, but in presence of anhydrous sodium sulphate condensation is complete in seven hours. Secondly, the readiness with which various diamines undergo condensation appears to diminish in proceeding from the unthionated amine to the monothionated, and thence to the dithionated. Thus benzidine and camphorquinone are condensed when refluxed for six hours in alcoholic solution (Forster and Spinner, *J.C.S.*, 1919, 115, 889) whilst thioaniline requires seven hours' refluxing with anhydrous sodium sulphate, and *pp'*-dithioaniline requires 24 hours. Similarly, tolidine hydrochloride and sodium acetate give the condensation product during four hours on a water-bath (Singh, Singh and Lal, *J.C.S.*, 1921, 119, 1971) whilst thio-*p*-toluidine requires not less than seven hours' refluxing in alcoholic solution with anhydrous sodium sulphate; dithio-*p*-toluidine in similar conditions does not react during one hundred hours.

EXPERIMENTAL.

Preparation of the thio-bases required for condensation with camphorquinone presented unexpected difficulties. Although such bases, e.g., thioaniline have been known for many years, the experimental details controlling their preparation are often omitted, or stated in a manner which renders but scanty assistance to subsequent workers.

Thioaniline was first obtained by Merz and Weith (*Ber* 1871, 4, 364) by heating aniline and sulphur together at 170-180°, hydrogen sulphide being liberated and a large proportion of ill-defined, resinous material produced; they found that adding litharge reduced the reaction-temperature to between 150° and 160°. On repeating these experiments it was found that extracting thioaniline from the dark green, resinous melt presented much difficulty. Merz and Weith first removed the unchanged aniline and then precipitated fractionally the hydrochloric acid extract; this procedure was followed, but the preponderating amount of sticky material precipitated along with a small quantity of thioaniline could not be avoided, and the crude thioaniline soon became green by oxidation. It was finally purified by dissolving in ether-alcohol, carefully adding dilute sulphuric acid and neutralizing the precipitated sulphate with caustic soda. About one gram of purified thioaniline resulted from 50 grams of aniline, and it is noteworthy that Merz and Weith did not state their yield. It seemed possible that a catalyst might control the reaction in one direction only; but whilst iodine is the most successful of all catalysts employed in preparing thiodiphenylamine from diphenylamine and sulphur, its application in the present case was not fruitful. Thus, although it reduced the reaction-temperature to 140°, as indicated by

the liberation of hydrogen sulphide at that temperature, it did not prevent the formation of much resinous by-product.

An entirely different procedure for obtaining thioaniline was next investigated. *p*-chloronitrobenzene in action with sodium or potassium sulphide gives dinitrodiphenyl sulphide, and this on reduction should yield thioaniline. The process is not new, nor is it so simple as might appear; it has been studied by several workers who find, that along with dinitrodiphenyl disulphide there are produced according to the conditions of the experiment the following compounds:—*p*-nitrothiophenol (m.p. 77°): 4:4'-*p*-dichloroazoxybenzene (m.p. 155°): 4-nitro-4'-aminophenyl sulphide (m.p. 143°): *p*-nitrophenyl sulphoxide (m.p. 119°): 4:4'-dinitrodiphenyl disulphide (m.p. 180.5°) and the *p*-nitrophenyl ether of *p*-azophenylmercaptan (m.p. 164°).

Experiments were therefore made to determine the conditions most suitable for the preparation of dinitrodiphenyl disulphide by this process, when it soon appeared that the procedure of Nietzki and Bothof (*Ber.*, 1894, 27, 3261) is the most promising. A concentrated aqueous solution of sodium sulphide is poured into an alcoholic solution of *p*-chloronitrobenzene, and the mixture refluxed on a water-bath during seven hours. The results indicate, firstly, that with molecular proportions only one-half the *p*-chloronitrobenzene reacts, the remainder being recovered unchanged; nevertheless, diminishing the proportion of sodium sulphide still further reduces the yield. Secondly, that commercial sodium sulphide containing a considerable amount of hydrosulphide, generates *p*-nitrophenyl mercaptan which is oxidised in air to *pp*'-dinitrodiphenyl disulphide.

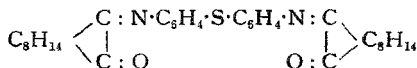
Kehrmann and Bauer's procedure (*Ber.*, 1896, 29, 2364) on the other hand eliminates the effect of heat. Results by this method indicate that the yield of mixed dichloroazoxybenzene, dinitrodiphenyl sulphide and *p*-nitro-*p*'-aminodiphenyl sulphide decreases, while that of dinitrodiphenyl disulphide increases with an increasing proportion of sodium sulphide, so that using a large excess, nearly six molecular proportions, only the disulphide is produced. When sodium sulphide is replaced by the hydrosulphide the principal product is dinitrodiphenyl disulphide again, as might be expected.

A still simpler reaction would be that of finely powdered *p*-chloronitrobenzene with alkali sulphide in aqueous solution. With potassium sulphide the action starts slowly and appears to be controllable, but after shaking the cold mixture during half-an-hour considerable heat was liberated suddenly, and the solution became dark red. After further shaking for three hours and remaining overnight, unchanged

p-chloronitrobenzene was filtered and the aqueous solution acidified, when a pale yellow solid was precipitated. This crystallised from much alcohol in large, thin, magnificent needles, sometimes three inches in length; it is the *p*-nitrophenyl ether of *p*-azophenylmercaptan, m.p. 164°.

Dinitrodiphenyl sulphide is reduced with zinc dust and acetic acid, excess of metal being dissolved in hydrochloric acid and the product treated with excess of caustic soda. When ether is used to extract thioaniline an emulsion is formed and is difficult to break; chloroform was therefore substituted. Evaporation of the solvent leaves a dirty green solid crystallisable from dilute alcohol, which deposits slender needles, m.p. 105°.

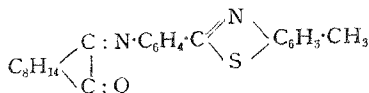
Thiodiphenylenebisiminocamphor,



Thioaniline thus obtained is condensed with two molecular proportions of camphorquinone by heating in alcoholic solution with anhydrous sodium sulphate. The purified product crystallises from benzene in spherical aggregates of small needles, m.p. 215° (Found: S, 6.32. $\text{C}_{22}\text{H}_{36}\text{O}_2\text{N}_2\text{S}$ requires S, 6.25 per cent.). A solution of 0.1320 gram in 25 c.c. of chloroform gave $\alpha_D 5.8^\circ$, whence $[\alpha]_D 947^\circ$ and $[\text{M}]_D 4848^\circ$.

Dehydrothiitoluidine and Primuline.

These two compounds were first prepared by A. G. Green (*J.C.S.*, 1889, 55, 228) by heating together at 175° *p*-toluidine (2 mols.) and sulphur (4 atoms); a modification due to Fierz-David was followed in preparing the compounds. After removing unchanged *p*-toluidine the melt was extracted with alcohol (93 per cent.), in which the crude dehydrothiitoluidine dissolves. It was purified by a lengthy process of crystallisation, first from ordinary alcohol and then from amyl alcohol, and crystallised from the latter in minute, faint yellow needles, m.p. 192°. The residue consists largely of primuline, and although this is stated to be insoluble in almost all organic media, extraction with these is not a satisfactory method for isolating the compound, which was first freed from some associated dehydrothiitoluidine with boiling, dilute hydrochloric acid: this left primuline as a pale brown, amorphous powder, melting above 275°, soluble in pyridine, westron, aniline and nitrobenzene, but not crystallising from any of these.

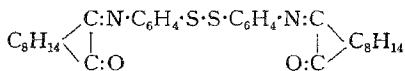
Methylbenzothiazolbenzenyliminocamphor,

Dehydrothiolutidine condenses with camphorquinone when molecular proportions are heated in alcohol during 12 hours, but the action occurs more readily in amyl alcohol. The product crystallises from benzene in small, ill-defined aggregates, m.p. 182° (Found: S, 8.33. $\text{C}_{24}\text{H}_{24}\text{ON}_2\text{S}$, requires S, 8.25 per cent.) A solution, of 0.1164 gram in 25 c.c of chloroform gave $\alpha_D 2.63^\circ$, whence $[\alpha]_D 564.8^\circ$ and $[\text{M}]_D 2756^\circ$. When heated with camphorquinone in pyridine solution, primuline does not appear to undergo condensation.

Dithioaniline

This compound was originally prepared by Merz and Weith (*loc. cit.*) but after some preliminary experiments I prepared it by reducing dinitrodiphenyl disulphide obtained according to the slightly modified procedure of Wohlfahrt (*J. pr. Chem.*, 1902, **66** [2], 551). This gave a 50 per cent. yield of dinitrodiphenyl disulphide, which was purified by repeated crystallisation from motor-benzol and melted at 182°. Blanksma (*Rec. Trav. Chim.*, 1900, **19**, 111) gives the m.p. 170°, unchanged by recrystallisation, although when prepared from *p*-nitrophenyl mercaptan it melts at 180°, as recorded by Willgerodt, Bamberger and Kraus, Kehrman and Bauer. In these experiments, also with alcohol, I have repeatedly obtained the compound with higher m.p., together with *pp'*-dinitrodiphenyl sulphide and *p*-nitro-*p'*-aminophenyl sulphide. Blanksma states that the crystals explode to a fine powder at 134°, but I found the substance to melt at 182° without previous explosion, although, as the temperature falls, it solidifies at 145° and finally explodes at 100°.

Leuckart (*J. pr. Chem.*, 1890, **41** [2], 199) states that when *pp'*-dinitrodiphenyl disulphide is reduced with zinc dust and acetic acid, *p*-nitrothiophenol is formed, whilst zinc and sulphuric acid give *pp'*-diaminodiphenyl disulphide. These results were not confirmed, dinitrodiphenyl disulphide being repeatedly recovered unchanged from such attempts at reduction. The *pp'*-diaminodiphenyl disulphide was finally obtained, however, by dissolving the dinitro-compound in boiling glacial acetic acid and carefully adding the calculated amount of freshly prepared stannous chloride solution. Dithioaniline thus obtained crystallised from dilute alcohol in slender, yellow needles, m.p. 85°.

pp'-Dithiodiphenylenebisiminocamphor,

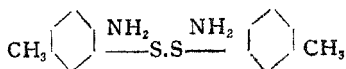
Dithioaniline (4 g.) and camphorquinone (7 g.) were dissolved in 25 c.c. of 99 per cent. alcohol and refluxed during 12 hours, the product being washed twice with boiling alcohol and crystallised from benzene in which it is freely soluble. Small aggregates of yellow needles were deposited, and these became orange at 160°, red at 195°, softening at 200° and melting at 201-202° (Found: S, 11.54. $\text{C}_{32}\text{H}_{36}\text{O}_2\text{N}_2\text{S}_2$ requires S, 11.76 per cent.). A solution of 0.0732 gram in 25 c.c. of chloroform gave α_D 2.4°, whence $[\alpha]_D$, 820° and $[\text{M}]_D$, 4460°.

pp'-Thiitoluidine and *pp'*-Dithiitoluidine.

pp'-Thiitoluidine was first obtained by Merz and Weith (*loc. cit.*) employing a method resembling that used for thioaniline; to free the substance from resinous by-products a long and tedious process has to be pursued, and consequently the yields are bad. Their method was therefore modified with the fortunate result that *pp'*-thiitoluidine was obtained in good yield with only a small quantity of *pp'*-dithiitoluidine as by-product and no resin.

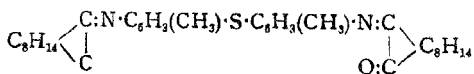
p-Toluidine (107 g.), sulphur (32 g. of powder, not flowers) and anhydrous sodium carbonate (9.5 g.) were intimately mixed, and heated in a round bottom flask surrounded by oil at 140°. On adding a pinch of litharge no change occurred at once, but after a short interval at that temperature gentle frothing was noticed and became brisk. Litharge (112 g.) was then added in amounts sufficient to maintain frothing during about an hour and a half, the temperature being controlled to that mentioned. When most of the litharge had been added the frothing diminished, and ceased when all was entered. The cold melt was a dark green, viscous resin, and was extracted with 600 c.c. of 94 per cent. boiling alcohol. The extract was filtered hot, freed from alcohol by distillation, then rendered alkaline with caustic soda (5 c.c. of 10 per cent.) and steamed, yielding about 50 grams of *p*-toluidine. The black, oily residue in the distillation-flask solidified on cooling, and was extracted with 300 c.c. of hot, dilute hydrochloric acid (1:4), the hot-filtered extract being evaporated on the water-bath. The first crop (thin yellow needles, 30 g.) of hydrochloride gave almost pure *p*-thiitoluidine, m.p. 103° when basified with ammonia; yield, 15 grams. The acid extract on further concentration gave a second crop (brownish yellow crystals, 10 g.) which was dissolved in warm water and reprecipitated with hydrochloric acid; the thin, yellow needles (7 g.) when basified with ammonia gave a yellowish base (3.5 g.) melting at 74°.

As the high-melting base (103°) dissolved in ether-alcohol does not give a precipitate with dilute sulphuric acid, the low melting base was dissolved in ether-alcohol and treated with dilute sulphuric acid until precipitation ceased. The precipitate was filtered, washed with ether-alcohol and recrystallised from hot water, which deposited thin, white needles. The base liberated from this product by ammonia crystallised from dilute alcohol in small, pale green needles, m.p. 89° (Found: S, 22.19, C₁₄H₁₆S₂ requires S, 23.19 per cent.). It was thus identical with the dithiitoluidine synthesised by Jacobsen and Ney (*Ber.*, 1889, **27**, 908) and shown to have the constitution.



The other base crystallised from dilute alcohol in slender, yellowish-green needles, m.p. 104°, and has been identified as 4-diaminotolyl sulphide (3) or di(6-amino-3-methylphenyl) sulphide. It appears to have been erroneously stated by Purgotti (*Gazetta*, 1890, **20**, 32) as giving *o*-ditolyl sulphide with nitrous acid in alcohol. This probably arose from the fact that the boiling-points of *o*- and *m*-ditolyl sulphides are approximate, while at that time *m*-ditolyl sulphide not been made. *o*-Ditolyl sulphide, which Purgotti stated to boil at 284–286°, was later (*Ber.*, 1895, **28**, 1674; 1906, **39**, 3595) shown to have m.p. 64° and b. p. 175° (16 mm.). *m*-Tolyl sulphide appears to have the same b. p., 174° under 12 mm. pressure (*Ber.*, 1906, **39**, 3595). When the above base (m.p. 104°) was treated with ethyl nitrite in alcohol there was produced a yellowish oil boiling at 175° (15 mm.) and remaining liquid after many days in the ice-chest; I therefore believe this to be *m*-tolyl sulphide.

*pp*¹-Thioditolylenebisiminocamphor.



Thio-*p*-toluidine (2 g.) and camphorquinone (3.3 g.) dissolved in 90 per cent. alcohol were refluxed with anhydrous sodium sulphate during seven hours, it having been found that without the salt condensation does not take place in 12 hours. On evaporating the filtered solution, yellowish crystals separated and were recrystallised from motor-benzol in small, indefinite orange groups, m.p. 216° (Found: S, 5.90. C₃₄H₄₀O₂N₂S requires S, 5.90 per cent.). A solution of 0.1360 gram in 25 c.c. of chloroform gave α_D^{25} 2.25°, whence $[\alpha]_D^{25}$ 407.6° and $[\text{M}]_D^{25}$ 2201°.

Dithio-*p*-toluidine (2.5 g.) and camphorquinone (3.5 g.) were similarly treated during 100 hours, and from the resinous mass left on evaporating alcohol the camphorquinone was removed by steam. On rubbing this residue with petroleum (b.p. 60–80°) there remained a small quantity of dark brown powder melting at 216°. This product was also obtained by heating dithiotoluidine sulphate (1.5 g.) intimately mixed with camphorquinone (1.5 g.) and anhydrous sodium acetate (3 g.) in a long test-tube fitted with a condenser and surrounded by oil at 200°; the dark sticky mass remaining after treating the cold melt with water was washed with alcohol and petroleum, when the dark brown powder was left. This is not the condensation product as it does not give camphorquinone with boiling dilute or concentrated hydrochloric acid; moreover, it is not produced from the base alone when this is exposed to the temperature stated.

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