# CCCXXVIII.—*The Reactivity of Methyl Groups in Heterocyclic Bases.*

By William Hobson Mills and James Leonard Brierley Smith.

In its characteristic reactivity, the 2-methyl group in quinaldine, α-picoline, and similar heterocyclic bases corresponds in many respects with the methyl group in such compounds as the methyl ketones or nitromethane, or with the methylene group in phenylacetonitrile.

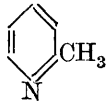
In these substances, it has long been recognised (for example, Henrich, *Ber.*, 1899, **32**, 688) that a marked similarity in constitution exists; the methyl or methylene group is in each case attached to a multivalent element, Y, which is in turn doubly (or trebly) linked to an element of strongly "negative" character, Z, according to a scheme such as $-CH_2 \cdot Y{:}Z$.

It is therefore probable that, as was suggested by Henrich *

* Plancher (*Gazzetta*, 1898, **28**, ii, 417) made a similar suggestion to account for the reactivity of the 2-methyl group in 2-methyl-3 : 3-diethylindolenine.

(compare Vorländer, *Ber.*, 1902, **35**, 4145), the 2-methyl group in the bases of the pyridine and quinoline series owes its reactivity to its being associated, as represented in the Körner-Dewar formula for pyridine, with a $-\dot{C}{:}N-$group, the effect of the $-\dot{C}{:}N-$ on the methyl group in the grouping $CH_3{\cdot}\dot{C}{:}N-$ corresponding with that of the carbonyl group in the grouping $CH_3{\cdot}\dot{C}{:}O$ of the methyl ketones.

If this is true, the possibility of the existence of two chemically distinct forms of α-picoline is indicated, one (I) with a reactive, the other (II) with a non-reactive methyl group. It is scarcely to be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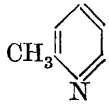
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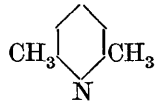
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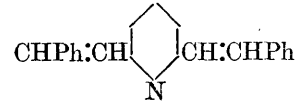
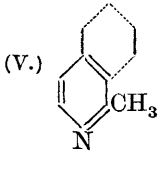

(IV.)

expected that these two forms could be obtained each apart from the other on account of the mobility of the system of linkages existing in the pyridine ring; for example, 2 : 6-dimethylpyridine (III) gives with benzaldehyde and zinc chloride a dibenzylidene derivative (IV) (Schuster, *Ber.*, 1892, **25**, 2398).

If, however, by some means, the mobility of the linkings in the pyridine ring could be diminished, it might be possible to demonstrate a difference of reactivity of the methyl groups attached to the carbon atoms on either side of the nitrogen atom.

There are two obvious methods by which the mobility of the linkages in a ring of this kind can be limited. The first consists in the fusion of the pyridine ring with a benzene ring so as to produce an *iso*quinoline nucleus. The tendency of each of the two six-membered rings to maintain its aromatic character should then fix the linkings in the resulting *iso*quinoline nucleus in positions corresponding with those assumed in Erlenmeyer's naphthalene formula. Marckwald (*Annalen*, 1893, **274**, 331; 1894, **279**, 1) has shown that much experimental evidence exists in favour of this view.

The two isomeric α-picolines fused thus with a benzene ring give 1-methyl*iso*quinoline (V) and 3-methyl*iso*quinoline (VI), respectively. The former compound should contain a reactive, the latter a non-reactive, methyl group.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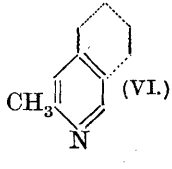
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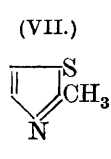
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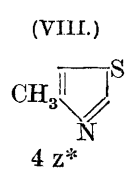

(VIII.)

The second method of fixing the linkages depends on the possibility of replacing a $-C_2H_2-$ group in the pyridine ring by an atom of sulphur. This replacement gives, instead of pyridine bases, bases of the thiazole series, and the resemblance in physical and chemical properties between the compounds of the two series, which Hantzsch has described (*Annalen*, 1889, **250**, 258), is even more striking than that between benzene and thiophen. In place of the two forms of α-picoline we then have 2-methylthiazole (VII) and 4-methylthiazole (VIII), and according to the foregoing considerations the former should contain a reactive, the latter a non-reactive, methyl group.

Investigation of these *iso*quinoline and thiazole derivatives has shown that in fact the properties of a methyl group adjacent to the cyclic nitrogen atom in bases of this type differ in the most marked manner according to the side of the nitrogen atom on which the group is situated.

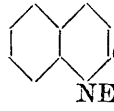
The isomeric 1- and 3-methyl*iso*quinolines were first investigated. Their behaviour towards benzaldehyde was compared and was found to stand in sharp contrast.

When 1-methyl*iso*quinoline was treated with benzaldehyde at 100° in presence of a small quantity of zinc chloride, condensation was found to take place readily; water was seen to separate, and the condensation product, 1-styryl*iso*quinoline, crystallised on cooling.


When 3-methyl*iso*quinoline, on the other hand, was heated with benzaldehyde and zinc chloride under corresponding conditions, no condensation took place even after prolonged heating; there was no separation of water, and the base and the benzaldehyde could both be recovered unchanged.

The reactivity of the methiodides of the two bases was then compared. The reactive character of the 2-methyl group in bases like α-picoline and quinaldine becomes greatly enhanced when the bases are converted into their quaternary salts. For example, α-picoline and quinaldine apparently cannot be made to condense with nitrosodimethylaniline. The alkyliodides of these bases, however, condense with nitrosodimethylaniline with very great ease in alcoholic solution in presence of piperidine to give azomethine derivatives, quinaldine ethiodide for instance giving the compound IX (Kaufmann, *Ber.*, 1912, **45**, 1736):

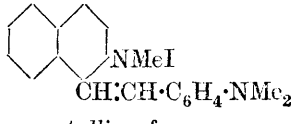
(IX.) 


(X.) 


Again, quinaldine can be made to condense with *p*-dimethylaminobenzaldehyde, as Mr. E. S. Dewing and one of us have found, by heating the two substances together for some hours at 100° with zinc chloride; but quinaldine ethiodide, in presence of a small quantity of piperidine, condenses with this aldehyde even in dilute alcoholic solution, giving *p*-dimethylaminostyryl derivatives, such as the compound (X) obtained from quinaldine ethiodide (König, *J. pr. Chem.*, 1912, [ii], **86**, 172; 1921, [ii], **102**, 63; Barbier, *Bull. Soc. chim.*, 1920, [iv], **27**, 427; Pope and Mills, this vol., p. 946).

On account of the readiness with which these condensations take place and the intense colour of the products, they provide an exceedingly delicate test for the reactivity of a methyl group in bases of the type under consideration. On investigating the methiodides of 1- and 3-methyl*iso*quinoline in this manner, a difference in reactivity was observed which corresponded exactly with that shown by the free bases.

When 1-methyl*iso*quinoline was heated in alcoholic solution with *p*-dimethylaminobenzaldehyde in presence of a small quantity of piperidine, a deep red colour was very rapidly produced and the condensation product to which it was due, 1-p-*dimethylaminostyryl*-iso*quinoline methiodide*,




was easily isolated in crystalline form.

When, however, 3-methyl*iso*quinoline methiodide was treated in the same way, no trace of colour characteristic of a *p*-dimethylaminostyryl dyestuff appeared and no other evidence of the occurrence of condensation could be obtained.

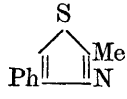
Similarly, a hot alcoholic solution of 1-methyl*iso*quinoline methiodide and nitrosodimethylaniline, on addition of a few drops of piperidine, at once became deep purple, evidently on account of the formation of a dimethylaminoazomethine derivative, whilst in the corresponding mixture in which the 1-methyl methiodide was replaced by the 3-methyl isomeride, there was no development of colour.

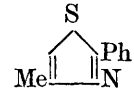
Further, it appears that 1-methyl*iso*quinoline methiodide can undergo a cyanine condensation with quinoline alkyliodides, but

that 3-methyl*iso*quinoline methiodide is unable to take part in such a reaction; for on heating the latter methiodide with an alcoholic solution of quinoline methiodide and sodium hydroxide no colour appeared, but with the former an intense red colour was quickly developed and the solution then showed a double absorption band in the green similar to that which characterises the *iso*cyanines.

After the great contrast in the reactivity of methyl groups in the 1- and 3-positions in *iso*quinoline and its quaternary salts had thus been demonstrated, we proceeded to examine the methyl derivatives of the bases of the thiazole series in a similar manner.

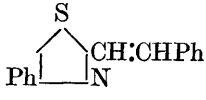
The simple methylthiazoles are somewhat difficult to prepare. Our experiments were therefore carried out with the two isomeric compounds, 4-phenyl-2-methylthiazole (XI) and 2-phenyl-4-methylthiazole (XII), which are readily obtainable by methods described by Hantzsch (*Annalen*, 1889, **250**, 269) and Hubacher (*Annalen*, 1890, **259**, 236):

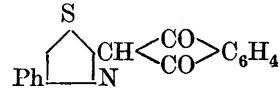
(XI.) 


(XII.) 


The methyl groups in these compounds showed a difference in reactivity which was entirely comparable with that of those in the two methyl*iso*quinolines.

The methyl group in 4-phenyl-2-methylthiazole was even more reactive than that in 1-methyl*iso*quinoline. The free base entered into condensation with benzaldehyde very readily to give 4-phenyl-2-styrylthiazole (XIII); it also condensed with phthalic anhydride to give the thiazole analogue of quinophthalone (XIV).

(XIII.) 


(XIV.) 


The reactivity of the methiodide was still more pronounced. With the greatest facility it gave a *p*-dimethylaminostyryl derivative with *p*-dimethylaminobenzaldehyde, an azomethine derivative with nitrosodimethylaniline, and a dye of the cyanine type with quinoline methiodide and alkali.

In the isomeric base, 2-phenyl-4-methylthiazole (XII), on the other hand, the methyl group, at least so far as reactions of the type of the foregoing are concerned, was found to be completely non-reactive. The free base could not be made to condense with benzaldehyde, and the methiodide appeared to be wholly indifferent towards *p*-dimethylaminobenzaldehyde or nitrosodimethylaniline

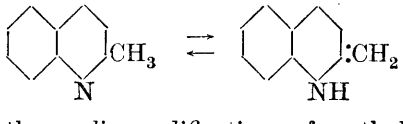
and to be incapable of forming a cyanine dye with quinoline methiodide and alkali.

It is thus perfectly clear that there is a very definite difference in the reactivity of a substituent methyl group adjacent to the nitrogen atom in *iso*quinoline and thiazole bases according as it is situated on one side or the other of the nitrogen.

This would appear to provide evidence of some corresponding difference between the linkings by which the nitrogen atom in *iso*quinoline and thiazole nuclei is attached to the carbon atom on either side of it and thus to support that view of the constitution of the nuclei of these heterocyclic bases, which was used as the basis of the considerations at the beginning of this paper, according to which the atoms are regarded as alternately singly and doubly linked, as in Kekulé's formula for benzene.

It is nevertheless desirable to consider the facts more closely. There is an evident similarity, as has already been stated, between the types of reaction of which the methyl groups in these nitrogenous heterocyclic bases are capable and those which are characteristic of the methyl group in the methyl ketones. It appears, however, to follow, from the work of Lapworth on acetone (T., 1904, **85**, 30) and that of Dimroth (*Ber.*, 1907, **40**, 2404) and K. H. Meyer (*Annalen*, 1911, **379**, 59; **380**, 212, etc.) on the relative activity of keto- and enol-desmotropes, that the distinctive reactivity of the methyl in compounds containing the grouping $CH_3 \cdot CO-$ is dependent on their capability of passing over in a greater or less degree into enolic modifications. It is therefore exceedingly probable that the capacity of the methyl group as such for direct condensation is comparatively slight.

If this is so, then the marked power which quinaldine, for example, possesses of condensing with aldehydes and similar substances must be due to the presence, under the conditions of the reaction, of a small quantity of a reactive tautomeride with which it exists in equilibrium. Such a tautomeride could scarcely be other than the substance XV, the constitution of which corresponds closely



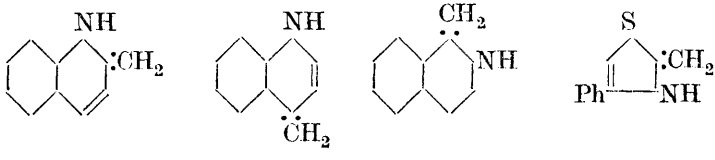
(XV.)

with that of the enolic modifications of methyl ketones. The reactivity assigned to this substance is in harmony with the work of K. H. Meyer (*Ber.*, 1921, **54**, [*B*], 2265, 2268), who has given reasons for attributing great activity to the groupings $NH_2 \cdot \dot{C} : CH_2$ and $NMe_2 \cdot \dot{C} : CH_2$. There is also evidence from analogy to show that there is nothing improbable in the assumption of the limited form-

ation of such a compound from quinaldine, for the occurrence of somewhat similar changes in pyridine and quinoline derivatives is clearly indicated (for example, Marckwald and Meyer, *Ber.*, 1900, **33**, 1885; Fargher and Furness, T., 1915, **107**, 688; compare Tschitschibabin and R. and A. Konowalowa, *Ber.*, 1921, **54**, [*B*], 814), and substitution derivatives of this and analogous compounds exist (for example, Brunner, *Ber.*, 1898, **31**, 1947; Decker and Klauser, *Ber.*, 1904, **37**, 528; Hamilton and Robinson, T., 1916, **109**, 1035; Mills, this vol., p. 457).*

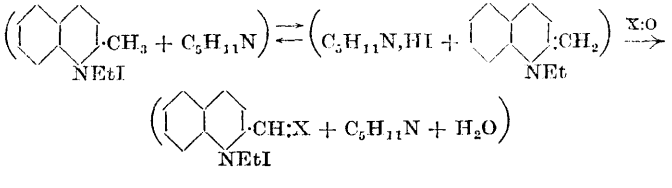
It is therefore possible to consider the difference in reactivity shown by a methyl group in these heterocyclic bases according as it lies on one side or the other of the nitrogen atom not only from the point of view of the nitrogen–carbon linkages, but also from the different but closely related aspect of tautomeric change. The contrast in properties observed in the pairs of isomerides studied may be regarded as indicating that passage into a reactive form is possible when the methyl group is in the one position, but not when it is in the other.

On this view, the reactivity of the methyl groups in quinaldine, lepidine, 1-methyl*iso*quinoline, and 4-phenyl-2-methylthiazole is dependent on a power possessed by these bases of passing over to some extent into forms of the constitutions:

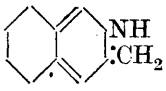


* From this point of view, the reactivity of the methyl group in the quaternary salts of quinaldine and similar bases becomes more readily intelligible. For the various condensations of these substances with compounds of the type X:O (aldehydes, nitroso-compounds, etc.) are brought about in presence of strong bases, such as piperidine—that is to say, under conditions under which a certain amount of the quaternary salt must be converted by removal of the acid into the *N*-alkyl derivative of that compound to which the reactivity of the free base is ascribed.

The condensations of the quaternary salts may thus be supposed to be effected through these methylene bases, which contain the reactive grouping –NAlk·Ċ:$CH_2$, as indicated in the following scheme:



whilst 3-methyl*iso*quinoline and 2-phenyl-4-methylthiazole are non-reactive because they are incapable of corresponding tautomeric changes, for these would involve the formation of compounds of such formulæ as :





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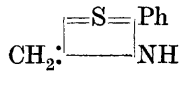
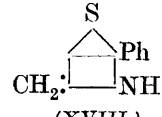
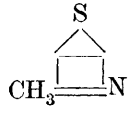



(XVIII.)

From this, the conclusion would be drawn that in compounds with condensed nuclei like quinoline and *iso*quinoline only such changes take place in the heterocyclic ring as are compatible with the retention by the benzenoid ring of its full aromatic character; and also, probably, that bridged modifications such as XIX and XX (the precursors of the forms XVI and XVIII) are not produced to


(XIX.)




(XX.)

any appreciable extent in the intramolecular vibrations of the *iso*quinoline or the thiazole nucleus.

The behaviour of the chloro-derivatives of *iso*quinoline is of interest in this connexion. It seems to be a general rule that when in a methyl compound, R·$CH_3$, the radicle R is of such a nature that the methyl group shows enhanced reactivity, then in the corresponding chloro-compound, RCl, the chlorine also will be unusually reactive.* It would therefore be expected that the chlorine atoms in 1-chloro*iso*quinoline and 3-chloro*iso*quinoline would show a difference of reactivity parallel to that shown by the methyl groups in the two corresponding methyl*iso*quinolines. Experiments of Gabriel and Colman have shown that such a difference does indeed exist.

Whilst 1-chloro*iso*quinoline gives a good yield of *iso*quinoline when heated for three hours with hydriodic acid and red phosphorus at 170—180° (Gabriel and Colman, *Ber.*, 1900, **33**, 986), 3-chloro*iso*quinoline is not reduced under these conditions; for when 1 : 3-dichloro*iso*quinoline is heated with the same reagents at 170° the 1-chlorine atom only is removed and the resulting 3-chloro*iso*quinoline resists further reduction. Complete removal of the chlorine so as to produce *iso*quinoline could only be effected by heating with red phosphorus at 200° (Gabriel, *Ber.*, 1886, **19**, 1655).

* Compare, for example, acetone and acetyl chloride; 2 : 4-dinitrotoluene and 2 : 4-dinitrochlorobenzene; quinaldine and 1-chloroquinoline.

It might be suggested that such reductions are effected through the formation and decomposition of additive products and that the difference in the mobility of the chlorine in the two positions would be accounted for if, as is probable, 1 : 2(or 1 : 4)-additive products of *iso*quinoline are comparatively readily produced whilst 2 : 3-additive products cannot be formed. The unequal mobility of the chlorine atoms seems to us, however, rather to indicate a difference in chemical polarity of the carbon atoms to which they are attached, probably dependent on a difference between the linkings on the two sides of the nitrogen atom such as is indicated in the formula with the alternate single and double bonds.

## EXPERIMENTAL.

### A. *Derivatives of* 1-*Methyl*isoquinoline.

1-*Methyl*isoquinoline.—This base was prepared by the dehydration of ω-acetylaminophenylmethylcarbinol by means of phosphoric oxide in boiling xylene according to the method devised by Pictet and Gams (*Ber.*, 1910, **43**, 2384), the carbinol, in quantities of 3 grams, being dissolved in 50—60 c.c. of hot xylene and boiled gently for twenty minutes with 20—25 grams of phosphoric oxide. The preparation of aminomethylphenylcarbinol (β-hydroxy-β-phenylethylamine) by reduction of benzaldehydecyanohydrin and its acetylation were carried out as described by Wolfheim (*Ber.*, 1914, **47**, 1440).

1-*Styryl*isoquinoline, $C_9H_6N{\cdot}CH{:}CHPh$.—A mixture of 1-methyl-*iso*quinoline with an equimolecular proportion of benzaldehyde and a small amount of the zinc chloride compound of the base was heated in a sealed tube at 100° for twenty hours. Water separated, and the contents of the tube crystallised in long needles on cooling. On recrystallisation from alcohol the *styryl*isoquinoline was obtained in almost colourless needles, which melted at 111° (Found: C = 88·26; H = 5·78. $C_{17}H_{13}N$ requires C = 88·31; H = 5·63 per cent.).

1-*Methyl*isoquinoline *Methiodide*.—This quaternary salt, which has not been previously described, was prepared by heating the base with methyl iodide in a sealed tube at 60° for six hours. It is also formed almost quantitatively when a mixture of the base and methyl iodide is allowed to remain at the ordinary temperature for twenty-four hours. On recrystallisation from absolute alcohol, in which it is readily soluble, the methiodide was obtained in almost colourless needles, melting at 207·5° (Found: I = 44·44. $C_{11}H_{12}NI$ requires I = 44·56 per cent.). The compound is sparingly soluble in cold, easily soluble in hot water.

1-p-*Dimethylaminostyryl*isoquinoline *Methiodide*, $NMe_2 \cdot C_6H_4 \cdot CH{:}CH \cdot C_9H_6N(CH_3)I$.—A solution of 1-methyl*iso*quinoline methiodide (2·2 grams), *p*-dimethylaminobenzaldehyde (1·1 grams), and piperidine (0·3 c.c.) in absolute alcohol (30 c.c.) gave a red colour immediately on heating, and after boiling for three hours red crystals (0·8 gram) separated. These were filtered from the hot solution, and after boiling for four hours more, a further 1·2 grams of crystals were obtained. On recrystallisation from methyl alcohol, the dyestuff was obtained in light red needles with a faint blue reflex. It melted and decomposed at 257°, although the melting point varied with the rate of heating (Found: C = 57·75; H = 5·03; N = 6·78; I = 30·62. $C_{20}H_{21}N_2I$ requires C = 57·69; H = 5·05; N = 6·73; I = 30·53 per cent.). The colour in dilute solution is orange; it is discharged by acidification with mixed acids, but reappears on dilution or addition of alkali.

The dyestuff is a weak photosensitiser; the extra sensitiveness conferred on the gelatino-bromide plate extends approximately to the D line for moderate exposures. Its photo-sensitising action is considerably weaker than that of the isomeric 2-*p*-dimethylaminostyrylquinoline methiodide.

When 1-methyl*iso*quinoline methiodide is heated with nitrosodimethylaniline and piperidine in alcoholic solution, a deep ruby colour is developed. It is therefore to be concluded that condensation takes place with the formation of an azomethine derivative. When the methiodide is heated with alcoholic soda and quinoline methiodide, an intense red colour develops in a few minutes, and the solution shows the double absorption band in the green, characteristic of the *iso*cyanines, whence it appears likely that 1-methyl*iso*quinoline methiodide, like quinaldine methiodide, can undergo the *iso*cyanine condensation. Owing to lack of material, these reactions were not further investigated.

### B. 3-*Methyl*isoquinoline.

3-*Methyl*isoquinoline.—This base was prepared from *o*-cyanophenylacetonitrile according to the method described by Gabriel and Neumann (*Ber.*, 1892, **25**, 3563). By acetylation, treatment with sodium hydroxide and then with sulphuric acid, *o*-cyanophenylacetonitrile is converted into 3-methyl*iso*carbostyril, and from this 3-methyl*iso*quinoline may be obtained, either by converting it into the 1-chloro*iso*quinoline and reducing this with hydriodic acid in sealed tubes, or by distillation with zinc dust in a stream of hydrogen. We found the reduction by zinc dust to be the better method, as it gives practically as good a yield and is much quicker.

3-*Methylisoquinoline and Benzaldehyde.*—This base could not be made to condense with benzaldehyde in the presence of anhydrous zinc chloride.

3-Methyl*iso*quinoline (0·7 gram), benzaldehyde (1·01 grams), and a granule of anhydrous zinc chloride were heated in a sealed tube for forty-four hours at 100°; there was no indication of the formation of water, and the contents of the tube could not be induced to solidify on cooling.

The liquid in the tube was dissolved in ether and extracted several times with dilute sulphuric acid. The separated ethereal solution was found to contain 0·90 gram of benzaldehyde, and on the addition of alkali to the sulphuric acid solution, the unchanged base (0·5 gram) melting at 66° was obtained. This was converted into the picrate, which melted at 197°. (The pure base melts at 66°, and the picrate at 197°.)

3-*Methylisoquinoline Methiodide.*—This compound, which has not been previously described, was obtained by heating the base with methyl iodide in a sealed tube at 50° for four hours. On recrystallisation from absolute alcohol, in which it is easily soluble, the methiodide was obtained in lustrous, golden needles, which melted at 219° (Found: I = 44·49. $C_{11}H_{12}NI$ requires I = 44·56 per cent.). It is easily soluble in hot water or hot dilute alcohol.

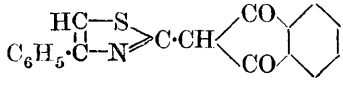
This methiodide could not be made to condense either with *p*-dimethylaminobenzaldehyde or with nitrosodimethylaniline in alcoholic solution in the presence of piperidine, nor would it condense with quinoline methiodide in presence of alcoholic sodium hydroxide solution to give a cyanine dye.

### C. *Derivatives of 4-Phenyl-2-methylthiazole.*

4-*Phenyl-2-styrylthiazole.*—4-Phenyl-2-methylthiazole was prepared from acetamide and phenacyl bromide as described by Hantzsch (*Annalen*, 1889, **250**, 269).

On heating an equimolecular mixture of this base and benzaldehyde with a granule of anhydrous zinc chloride in a sealed tube for thirty-six hours at 100°, water separated, and the contents of the tube crystallised in long needles on cooling. On recrystallisation from absolute alcohol, the substance was obtained in colourless, shining needles, melting at 131·5° (Found: C = 77·20, 77·44; H = 4·94, 5·20. $C_{17}H_{13}NS$ requires C = 77·56; H = 4·95 per cent.).

4-*Phenyl-2-thiazolylphthalonylmethane,*



—4-Phenyl-2-methylthiazole (4 grams), phthalic anhydride (3 grams), and anhydrous zinc chloride (3 grams) were heated in a sealed tube for six hours at 190°. The contents of the tube dissolved readily in concentrated sulphuric acid at 100°, and on pouring this solution into much water, a brown powder was precipitated, which was collected and washed. It was recrystallised from glacial acetic acid, in which it is readily soluble, when the phthalone was obtained in dark brown needles. On recrystallisation of this from absolute alcohol, in which it is sparingly soluble, the dyestuff was obtained in light brown, shining needles, which melted at 257° (Found: N = 4·5. $C_{18}H_{11}O_2NS$ requires N = 4·6 per cent.).

The substance is quite insoluble in caustic soda, and its dilute solution in alcohol dyes silk a faint yellow shade. It is almost insoluble in ether, and it is considerably deeper in colour than the corresponding quinophthalone.

4-*Phenyl*-2-*methylthiazole Methiodide*, $C_{10}H_9NS,CH_3I$.—This methiodide was made by heating the base with methyl iodide in a sealed tube at 80° for twenty-four hours. On recrystallisation from hot water, in which it is easily soluble, the methiodide was obtained in colourless, shining needles, melting at 202°. It is easily soluble in hot absolute or dilute alcohol (Found: I = 40·07. $C_{11}H_{12}NIS$ requires I = 40·07 per cent.).

4-*Phenyl*-2-p-*dimethylaminostyrylthiazole Methiodide*.—On heating a solution of 4-phenyl-2-methylthiazole methiodide (7 grams) and *p*-dimethylaminobenzaldehyde (3·3 grams) in absolute alcohol (80 c.c.) with piperidine (1 c.c.), a red colour developed immediately, and after boiling for forty minutes, red crystals (5 grams) were deposited from the boiling solution, and a further 1 gram separated at the end of the hour. On recrystallisation from methyl alcohol, the dyestuff was obtained in ruby-red crystals with a bluish-green metallic reflex. It melts and decomposes at 243°, but the melting point varies with the rate of heating (Found: C = 53·43; H = 4·90; I = 28·39; S = 7·18. $C_{20}H_{21}N_2IS$ requires C = 53·57; H = 4·69; I = 28·35; S = 7·14 per cent.).

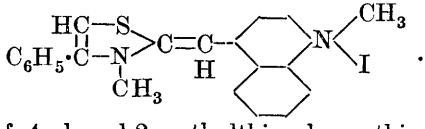
The colour in dilute solution is a deep orange, and is discharged by acids, but reappears on dilution or addition of alkali. The dyestuff is a photosensitiser, and the extra sensitiveness conferred on the gelatino-bromide plate extends to λ 6200, with a maximum at λ 5500 for moderate exposures.

4-*Phenylthiazole*-2-*aldehyde* p-*Dimethylaminoanil Methiodide*.—A solution of 4-phenyl-2-methylthiazole methiodide (5 grams) and nitrosodimethylaniline (2·5 grams) in absolute alcohol (90 c.c.) gave a red colour in the cold on the addition of piperidine (0·15 c.c.), and after boiling for fifteen minutes, bright green crystals (6 grams)

separated from the boiling solution, and about half a gram more was obtained after a further four hours' boiling. On recrystallisation from methyl alcohol, the dyestuff was obtained in red crystals with an intense green metallic reflex. It melted and decomposed at 228°, but the melting point varied somewhat with the rate of heating (Found: C = 50·60; H = 4·58; I = 28·45; S = 7·07. $C_{19}H_{20}N_3IS$ requires C = 50·77; H = 4·46; I = 28·29; S = 7·13 per cent.).

The colour in solution is a deep ruby-red, which is discharged by acids with great ease, but reappears on dilution or addition of alkali.

4-*Phenyl*-3-*methyl*-2-*thiazolenyl*-4-*quinolylmethane Methiodide*,



—A solution of 4-phenyl-2-methylthiazole methiodide (4 grams), quinoline methiodide (7·2 grams), and sodium hydroxide (0·71 gram) in absolute alcohol (80 c.c.) gave an intense red colour on heating, and after boiling for thirty minutes, a semi-crystalline precipitate was formed on cooling. On recrystallisation from methyl alcohol, the cyanine dyestuff was obtained in red crystals with a bluish-green metallic reflex, melting and decomposing at 240° (Found: I = 27·73; S = 6·73. $C_{21}H_{19}N_2IS$ requires I = 27·83; S = 6·99 per cent.).

The colour in solution is a deep orange-red, and is discharged by acidification, but reappears on dilution or addition of alkali. The dyestuff is a photosensitiser, and the extra sensitiveness conferred on the gelatino-bromide plate extends to λ 6000, with a maximum at λ 5300, for moderate exposures.

### D. 2-*Phenyl*-4-*methylthiazole*.

2-*Phenyl*-4-*methylthiazole and Benzaldehyde*.—2-Phenyl-4-methylthiazole was made from thiobenzamide and monochloroacetone, according to the method described by Hubacher (*Annalen*, 1890, **259**, 236), and was found to boil at 282°/762 mm. Hubacher describes it as a liquid: we obtained it in colourless crystals melting at 29·5°.

This base failed to react with the equivalent amount of benzaldehyde in the presence of anhydrous zinc chloride, when heated in a sealed tube for ninety-six hours at 100°. The unchanged base melting at 29° was recovered from the acid aqueous extract of the contents of the tube, and the ethereal extract, on oxidation with potassium permanganate, yielded an amount of benzoic acid

corresponding with 90 per cent. of the benzaldehyde originally taken.

2-*Phenyl*-4-*methylthiazole Methiodide*.—This quaternary salt was obtained in a 70 per cent. yield by heating the base with methyl iodide in a sealed tube for forty-eight hours at 90°.

It is formed with far less readiness than the methiodide of the isomeric 4-phenyl-2-methylthiazole, an almost theoretical yield of which was obtained when the base was heated with methyl iodide for twenty-four hours at 80°. The difference of reactivity towards alkyl iodides of the nitrogen in the two systems, :CMe·N:CPh– and :CPh·N:CMe–, in which the methyl and phenyl groups are interchanged, is noteworthy.

On recrystallisation from hot water, in which it is fairly soluble, the methiodide was obtained as faintly yellow prisms which melted at 192°. It is easily soluble in hot dilute or absolute alcohol (Found : I = 40·16. $C_{11}H_{12}NIS$ requires I = 40·07 per cent.).

When this methiodide (4 grams) and *p*-dimethylaminobenzaldehyde (2 grams) were boiled in absolute alcoholic solution (40 c.c.) with piperidine (0·4 c.c.) for fifteen hours, the solution assumed the brownish-red tinge which is produced when an alcoholic solution of *p*-dimethylaminobenzaldehyde is boiled for a long time with piperidine, but no evidence that any condensation had taken place could be obtained.

On evaporation of the alcohol, a red, semi-crystalline, tarry mass remained, which was well washed with ether and extracted several times with boiling water. In the aqueous solution was found the unchanged methiodide (3·8 grams). In a similar manner, it was proved that, after six hours' boiling of the methiodide and nitrosodimethylaniline with piperidine in alcoholic solution, no condensation had taken place; thus showing a great contrast with the methiodide of 4-phenyl-2-methylthiazole, which gave an 85 per cent. yield of condensation product with nitrosodimethylaniline in the presence of piperidine after boiling the alcoholic solution for only fifteen minutes. No condensation of 2-phenyl-4-methylthiazole methiodide with quinoline methiodide in alcoholic soda solution could be effected.

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