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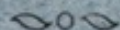
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THE ABSORPTION SPECTRA
OF SOME SUBSTITUTED
PYRAZINES AND THEIR SALTS

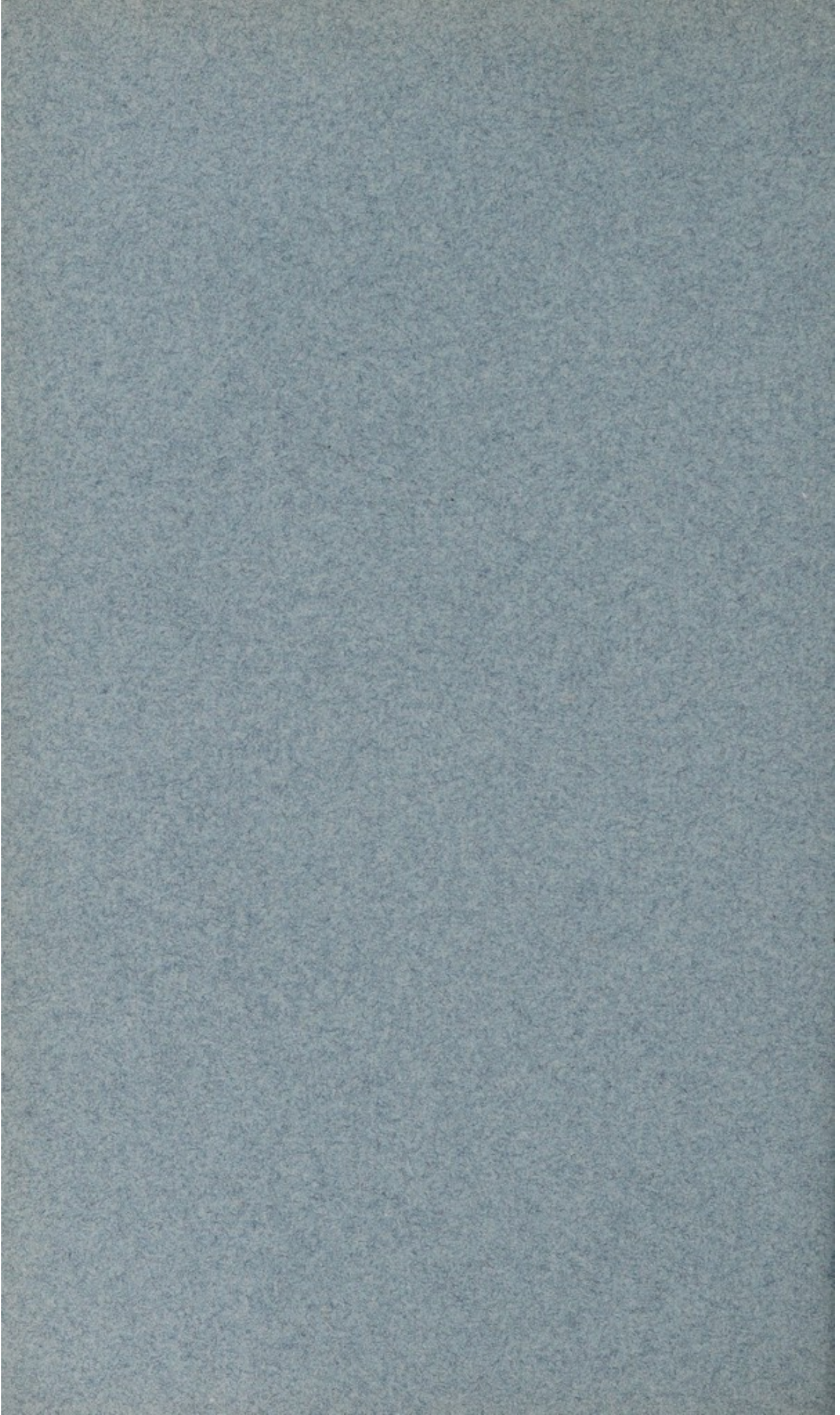
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CCLVIII.—*The Absorption Spectra of Some Substituted Pyrazines and their Salts.*

By FRANK TUTIN and FREDERIC WILLIAM CATON.

IN the preceding paper, the preparation of 2: 5- and 2: 6-diphenylpyrazine, *pp'*-dimethoxy-2: 5- and -2: 6-diphenylpyrazine, and *mm'pp'*-tetramethoxy-2: 5- and -2: 6-diphenylpyrazine is described. During the course of this work, certain remarkable colour changes were observed on treating these bases with acids, which suggested to us that a fuller investigation of the subject might lead to interesting results. Thus, whilst the hydrochloride of 2: 6-diphenylpyrazine appeared colourless, the corresponding salts of the analogous *pp'*-dimethoxy- and *mm'pp'*-tetramethoxy-bases were bright yellow and orange-coloured respectively. Furthermore, on adding sulphuric acid to a chloroform solution of *pp'*-dimethoxy-2: 5-diphenylpyrazine, a yellow liquid which exhibited an intense, green fluorescence was first produced, whilst on the addition of an excess of the acid a very deep violet-coloured solution resulted.

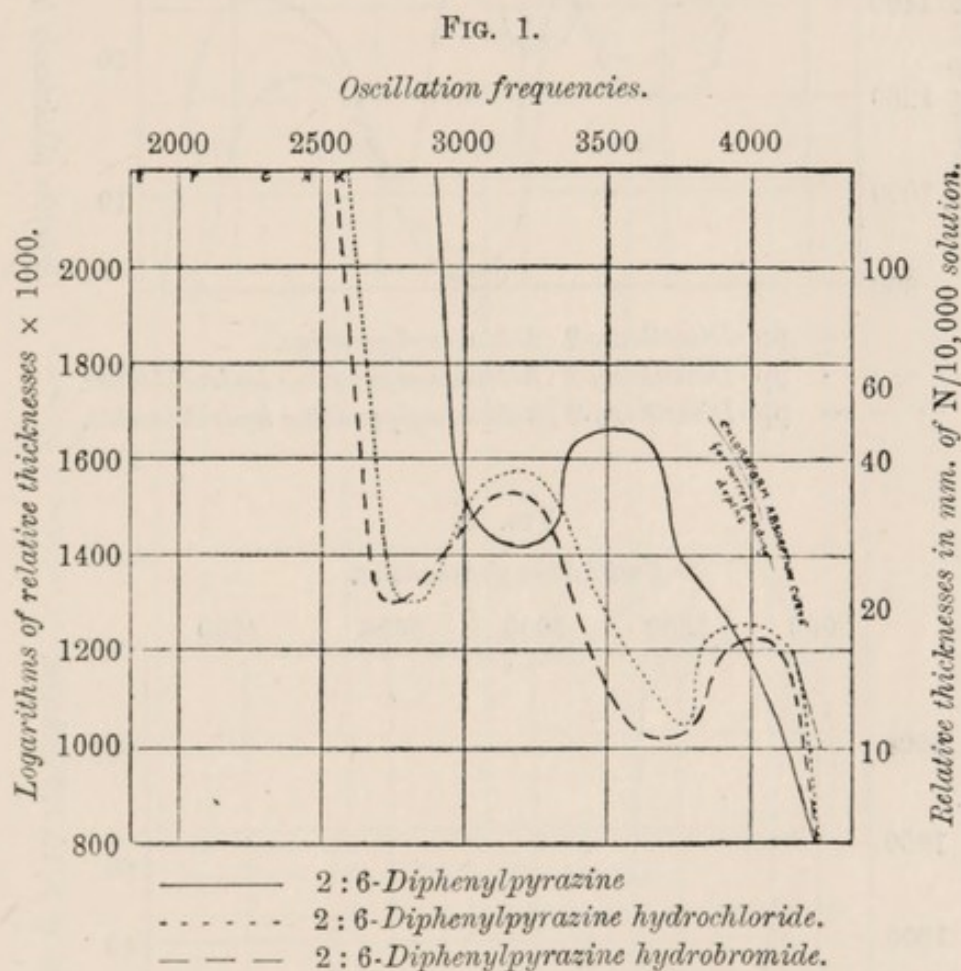
The further investigation of the bases in question rendered it evident that pyrazine derivatives, which have hitherto been stated to be monoacidic bases, in reality yield two series of salts, the di-acid salts being in all cases much more highly coloured than the corresponding derivatives containing but one equivalent of acid. The depth of colour of corresponding salts of analogous bases was found to increase with the accumulation of methoxyl groups, and to be somewhat greater in compounds of the 2: 5-series than in the corresponding members of the 2: 6-series.

The colours of the salts obtained will be seen on reference to the following table:

Base.	Mono-hydrochloride.	Mono-hydrobromide.	Monosulphate.	Dihydrochloride.	Dihydrobromide.	Disulphate.
2:5-Diphenylpyrazine.	Very pale yellow solution.	Pale yellow solution.	(?)	Bright yellow solution.	Golden-yellow crystals.	Yellow crystals.
2:6-Diphenylpyrazine.	Practically colourless crystals.	Pale yellow crystals.	Colourless crystals.	Yellow solution.	(?)	Yellow solution.
<i>pp'</i> -Dimethoxy-2:5-diphenylpyrazine.	Bright yellow crystals.	Orange-coloured crystals.	Yellow crystals.	(?)	Deep violet solution, or deep violet solid (HBr and solid base).	Crystals resembling potassium permanganate
<i>pp'</i> -Dimethoxy-2:6-diphenylpyrazine.	Yellow crystals.	Deep yellow crystals.	Pale yellow crystals.	(Could not be formed.)	Deep violet solid (HBr and solid base).	Violet-coloured solution.
<i>mm'</i> <i>pp'</i> -Tetramethoxy-2:5-diphenylpyrazine.	—	—	Orange-red crystals.	—	—	Deep blue solution, or black crystals with metallic lustre
<i>mm'</i> <i>pp'</i> -Tetramethoxy-2:6-diphenylpyrazine.	Deep yellow crystals.	Orange-coloured crystals.	Yellow crystals.	(Could not be formed.)	Bluish-black solid (HBr and solid base).	Deep blue solution.

In order therefore to throw some light on the nature of these colour changes, some of the above-mentioned bases and certain of their salts have been examined spectroscopically in chloroform solution. This solvent was chosen as both the bases and their salts are sufficiently soluble in it, and, although it has a certain amount of general absorption in the extreme ultra-violet region of the spectrum, it was thought that it would not interfere appreciably with the results. Moreover, the salts of the pyrazines have much less tendency to hydrolyse when dissolved in chloroform than in alcoholic solution.*

The curves obtained from 2:6-diphenylpyrazine, *pp'*-dimethoxy-



2:6-diphenylpyrazine, and *mm'**pp'*-tetramethoxy-2:6-diphenylpyrazine are shown in Figs. 1, 2, and 3 respectively. From these it is seen that each of the bases shows absorption in the ultra-violet part of the spectrum, and that salt-formation is accompanied by a considerable shift of the bands towards the red end, thus accounting for the development of colour on treatment with acids. In the case of 2:6-diphenylpyrazine hydrochloride, which is practically colourless, the absorption bands still lie within the ultra-violet

* Even when employing chloroform as a solvent for the salts it was necessary to have a certain excess of the respective acid in the solution.

FIG. 2.

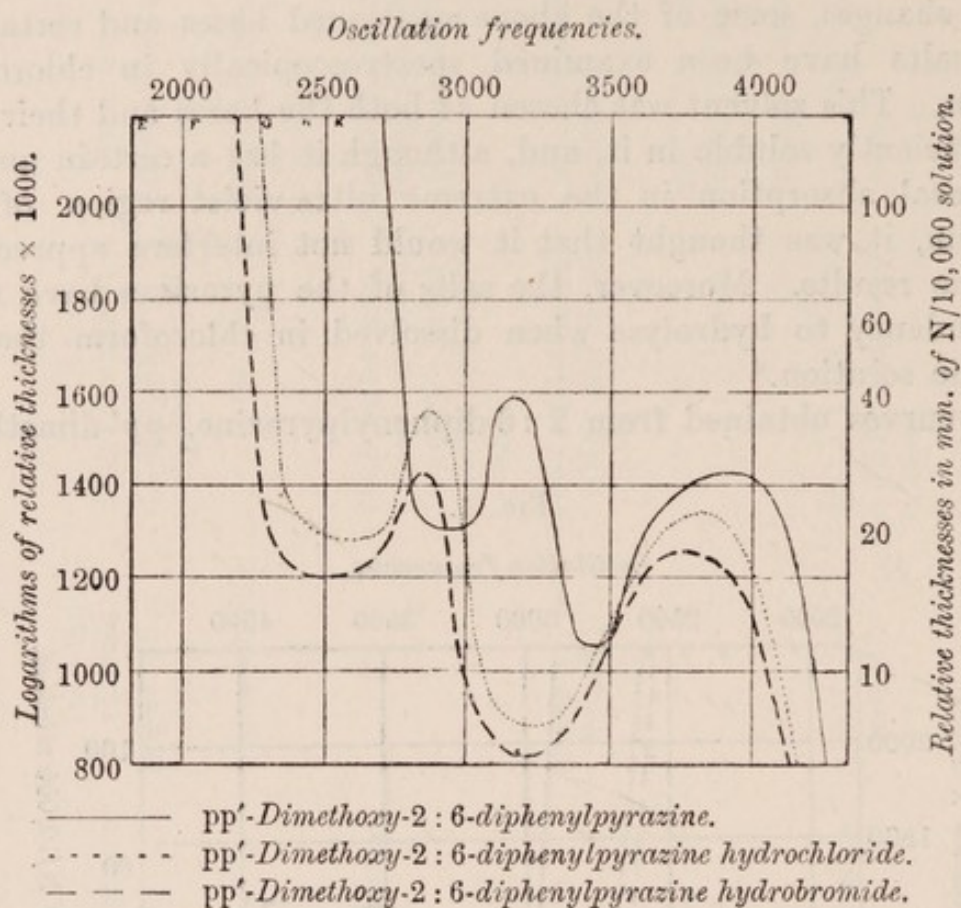
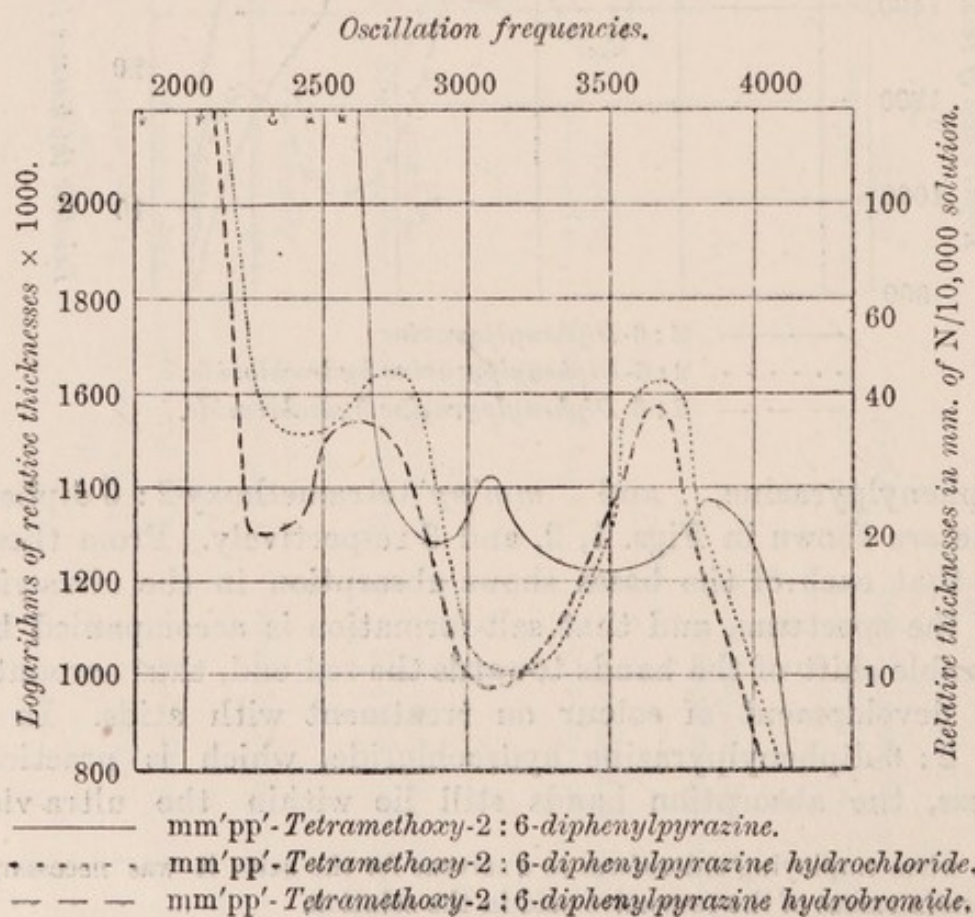
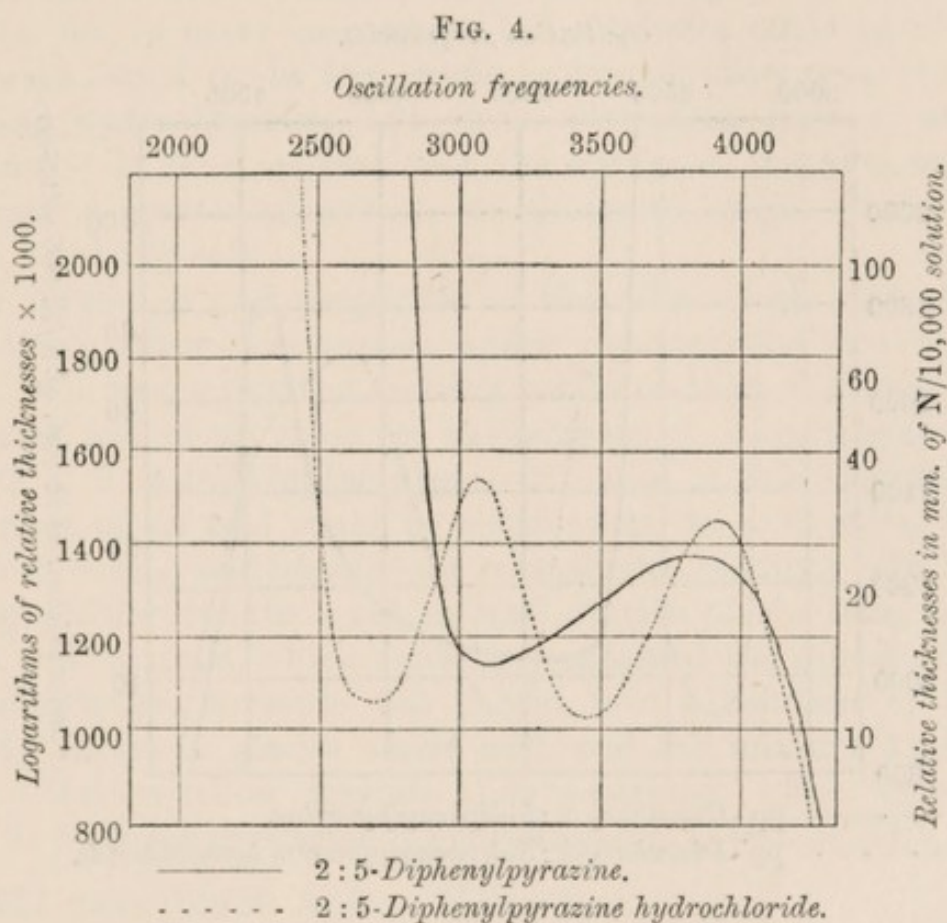


FIG. 3.



region, but one band shown by the corresponding hydrobromide just extends into the visible part of the spectrum, thus explaining the pale yellow colour of the salt in question. The shift of the absorption bands towards the red end of the spectrum caused by the substitution of hydrobromic for hydrochloric acid is not nearly so great as that caused by the conversion of the base into its hydrochloride, thus indicating that the alteration in position of the bands in the latter case must be due chiefly to salt-formation, and only in a minor degree to the weight or nature of the acid radicle attached.

The di- and tetra-methoxy-bases of the 2:6-series, and all of the salts show two absorption bands, but in the case of 2:6-diphenyl-

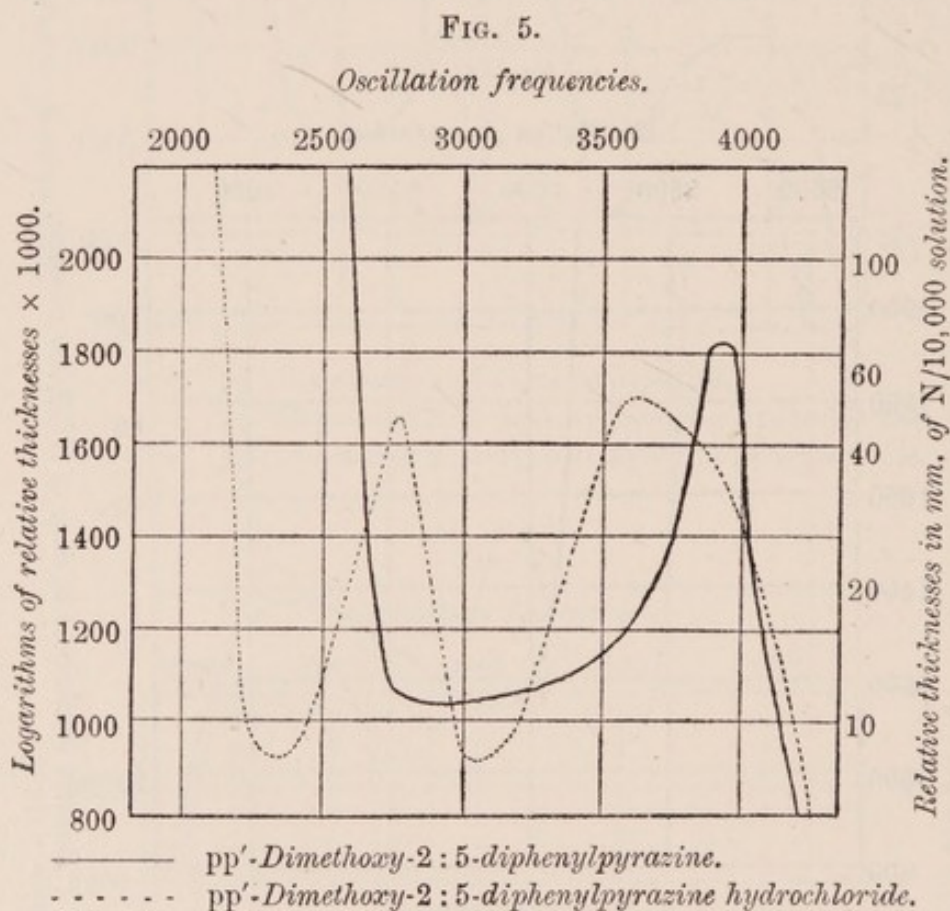


pyrazine only one band is seen. Nevertheless, it is considered most probable that the absorption of all three 2:6-substituted bases is, in reality, similar, the second absorption band of the last-mentioned base being lost owing to the absorption shown by the chloroform which was used as a solvent.

The curves yielded by 2:5-diphenylpyrazine and its monohydrochloride, and by *pp'*-dimethoxy-2:5-diphenylpyrazine and the corresponding salt of this base, are shown in Figs. 4 and 5 respectively. It will be observed in the case of these 2:5-substituted bases that the curves show only one absorption band, whilst two such are exhibited by the curves obtained from the salts. One possible

explanation of this is that the second absorption band of the 2:5-substituted bases has been lost owing to the absorption caused by the chloroform, just as is thought likely to be the case with 2:6-diphenylpyrazine, as already mentioned. On the other hand, the fact that the band shown by the 2:5-substituted bases is much broader than either of the bands in any of the other curves obtained would suggest that in the bases of the 2:5-series the two absorption bands may have become merged into one.

Certain general conclusions may be drawn from the absorption curves given, namely, the following: (1) The similarity of the



curves given by the bases and their salts, particularly in the 2:6-series, indicates that no change other than the rearrangement of valencies necessitated by the change $N^{III} \rightarrow N^V$ occurs on treating the bases in question with acids. (2) That salt-formation causes an increased persistency of the bands, together with a very large shift towards the red end of the spectrum. This result is similar to, but very much greater than, that which has previously been observed in the case of pyridine and its homologues (Hartley, *Trans.*, 1885, **47**, 685; Baker and Baly, *ibid.*, 1907, **91**, 1122; and Purvis, *Proc. Camb. Phil. Soc.*, 1908, **14**, 436). (3) The introduction of methoxyl groups causes a shift of the absorption bands towards the red end of the spectrum—an effect which has several times pre-

viously been noted by other workers. (4) The position of the substituent groups in the pyrazine nucleus affects the position of the absorption bands shown by the bases and their salts, the bands shown by the 2:5-substituted compounds being nearer the red end of the spectrum than those shown by their 2:6-substituted isomerides (compare Purvis, *loc. cit.*).

The absorption curves given also appear to indicate that the weight of the acid radicle present in a given salt had an effect on the position of the bands, the hydrobromides being more deeply coloured than the corresponding hydrochlorides. It would appear premature, however, to consider this conclusion as proved, without considerable further evidence obtained by the study of a variety of salts, for, in every case where the sulphates could be obtained, they were found to be less deeply coloured than even the corresponding hydrochlorides, but their absorption spectra were not examined. It thus appears that the nature of the acid employed may have a greater effect than its molecular weight on the colour of the resulting salt.

The formation and properties of the salts which were obtained from the pyrazine derivatives under consideration are described below. In most cases the melting points of these derivatives were indefinite, and of no value for the purpose of characterisation.

Salts of 2:5-Diphenylpyrazine.—No salt of this base with one equivalent of an acid could be obtained in the solid state, but the *dihydrobromide* and *disulphate* crystallised readily. On passing hydrogen chloride into a chloroform solution of the base, a yellow liquid was obtained, which doubtless contained the *dihydrochloride*.

Dry hydrogen bromide was passed into a solution of 2:5-diphenylpyrazine in glacial acetic acid, and the mixture kept a few hours. Golden-yellow crystals then separated, which were found to be 2:5-diphenylpyrazine dihydrobromide, $C_4H_2N_2(C_6H_5)_2 \cdot 2HBr$:

0.1527 gave 0.1435 AgBr. $HBr = 40.5$.

$C_{16}H_{12}N_2 \cdot 2HBr$ requires $HBr = 41.1$ per cent.

This salt was readily dissociated by water, alcohol, or moist air. On heating it with ethyl acetate, it dissolved and partly dissociated, and, on cooling the solution, a mixture of dihydrobromide and base separated, but no monohydrobromide was obtained.

2:5-Diphenylpyrazine *disulphate*, $C_4H_2N_2(C_6H_5)_2 \cdot 2H_2SO_4$, resulted on the addition of concentrated sulphuric acid to a solution of the respective base in ethyl acetate or glacial acetic acid; the monosulphate could not be obtained. 2:5-Diphenylpyrazine disulphate forms yellow plates, which, when exposed to moist air, readily dissociate, yielding the colourless base:

0.2417 gave 0.2570 BaSO_4 . $\text{H}_2\text{SO}_4 = 44.7$.

$\text{C}_{16}\text{H}_{12}\text{N}_2 \cdot 2\text{H}_2\text{SO}_4$ requires $\text{H}_2\text{SO}_4 = 45.8$ per cent.

Although the result of this analysis is not in very close agreement with the theoretical figures, owing to the readiness with which the salt dissociates, it nevertheless proves conclusively that the salt has the formula indicated above.

Salts of 2: 6-Diphenylpyrazine.—The monohydrochloride of this base is described in the preceding paper (p. 2501). It is a practically colourless, crystalline solid. The *monohydrobromide*, however, is pale yellow, whilst the *monosulphate* is quite colourless. The *dihydrochloride* and *disulphate* were obtained in the form of solutions, both of which were yellow, but no positive indication of the formation of a dihydrobromide could be obtained.

2: 6-Diphenylpyrazine monohydrobromide, $\text{C}_4\text{H}_2\text{N}_2(\text{C}_6\text{H}_5)_2 \cdot \text{HBr}$, separated in pale yellow needles on passing hydrogen bromide into a solution of the respective base in a mixture of ethyl acetate and alcohol. Like the previously described salts, it readily dissociated:

0.1408 gave 0.0840 AgBr . $\text{HBr} = 25.7$.

$\text{C}_{16}\text{H}_{12}\text{N}_2 \cdot \text{HBr}$ requires $\text{HBr} = 25.9$ per cent.

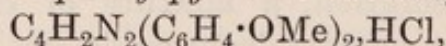
2: 6-Diphenylpyrazine monosulphate, $\text{C}_4\text{H}_2\text{N}_2(\text{C}_6\text{H}_5)_2 \cdot \text{H}_2\text{SO}_4$, crystallised in quite colourless needles on adding concentrated sulphuric acid to a solution of 2: 6-diphenylpyrazine in glacial acetic acid:

0.1316 gave 0.0934 BaSO_4 . $\text{H}_2\text{SO}_4 = 29.8$.

$\text{C}_{16}\text{H}_{12}\text{N}_2 \cdot \text{H}_2\text{SO}_4$ requires $\text{H}_2\text{SO}_4 = 29.7$ per cent.

Salts of pp'-Dimethoxy-2: 5-diphenylpyrazine.—The *monohydrochloride*, *monohydrobromide*, and *monosulphate* of pp'-dimethoxy-2: 5-diphenylpyrazine crystallised readily, and the *disulphate* was also obtained in crystals, although it was very unstable. A solution of the *dihydrobromide* was obtained as a deep violet-coloured liquid by saturating a solution of pp'-dimethoxy-2: 5-diphenylpyrazine in glacial acetic acid with hydrogen bromide; and this salt also appeared to be formed on passing dry hydrogen bromide over the solid base. No positive evidence of the formation of a dihydrochloride could be obtained.

pp'-Dimethoxy-2: 5-diphenylpyrazine monohydrochloride,



was formed by saturating a warm solution of the pyrazine derivative in glacial acetic acid with hydrogen chloride. On cooling, the salt separated in bright yellow needles:

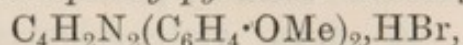
0.3191 gave 0.1374 AgCl . $\text{HCl} = 10.9$.

$\text{C}_{18}\text{H}_{16}\text{O}_2\text{N}_2 \cdot \text{HCl}$ requires $\text{HCl} = 11.1$ per cent.

This salt dissociated much more readily than the corresponding

derivative of the 2:6-substituted base, and, when dissolved in chloroform, exhibits an intense green fluorescence.

pp'-Dimethoxy-2:5-diphenylpyrazine monohydrobromide,



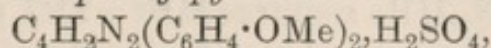
was prepared in a manner similar to the salt last described. It formed orange-coloured needles:

0.2781 gave 0.1373 AgBr. $\text{HBr} = 21.3$.

$\text{C}_{18}\text{H}_{16}\text{O}_2\text{N}_2\cdot\text{HBr}$ requires $\text{HBr} = 21.7$ per cent.

pp'-Dimethoxy-2:5-diphenylpyrazine monohydrobromide, like the corresponding hydrochloride, is fluorescent in chloroform solution.

pp'-Dimethoxy-2:5-diphenylpyrazine monosulphate,



separated in yellow needles on adding sulphuric acid to a warm solution of the respective base in glacial acetic acid, and cooling the mixture. It dissociates readily, and, like the last-mentioned two salts, is fluorescent in chloroform solution:

0.2700 gave 0.1581 BaSO_4 . $\text{H}_2\text{SO}_4 = 24.6$.

$\text{C}_{18}\text{H}_{16}\text{O}_2\text{N}_2\cdot\text{H}_2\text{SO}_4$ requires $\text{H}_2\text{SO}_4 = 25.1$ per cent.

When to a solution of *pp'*-dimethoxy-2:5-diphenylpyrazine in chloroform, concentrated sulphuric acid was added, a yellow solution of the monosulphate was first formed, which exhibited a brilliant green fluorescence, but on introducing an excess of the acid the base was dissolved by the latter, yielding an intensely violet-coloured liquid below the chloroform. Sufficient ethyl acetate was then added to render the mixture homogeneous, and the liquid kept a few hours, when *pp'*-dimethoxy-2:5-diphenylpyrazine disulphate, $\text{C}_4\text{H}_2\text{N}_2(\text{C}_6\text{H}_4\cdot\text{OMe})_2\cdot 2\text{H}_2\text{SO}_4$, separated in small prisms, resembling in colour crystals of potassium permanganate. This disulphate is very unstable; it dissociates in ordinary air, yielding the yellow monosulphate, and, if the air be unusually damp, complete dissociation ensues. The dissociated mixture may, however, be successively reconverted into the yellow monosulphate and the deep violet-coloured disulphate by desiccation:

0.1224 gave 0.1200 BaSO_4 . $\text{H}_2\text{SO}_4 = 41.1$.

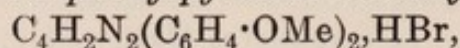
$\text{C}_{18}\text{H}_{16}\text{O}_2\text{N}_2\cdot 2\text{H}_2\text{SO}_4$ requires $\text{H}_2\text{SO}_4 = 40.2$ per cent.

This disulphate dissociated so readily that it could not be washed with any solvent, and it is owing to this fact that the analysis indicated a somewhat high percentage of sulphuric acid.

Salts of pp'-Dimethoxy-2:6-diphenylpyrazine.—This base readily yielded a crystalline monohydrochloride, monohydrobromide, and monosulphate, the first of which has been described in the preceding

paper (p. 2506). No indication of the formation of a dihydrochloride could be obtained, but the *dihydrobromide* was obtained as a very deep violet-coloured solid by passing dry hydrogen bromide over the solid base. A deep violet-coloured solution of the *disulphate* in concentrated sulphuric acid was formed, but this salt could not be crystallised.

pp'-Dimethoxy-2: 6-diphenylpyrazine monohydrobromide,



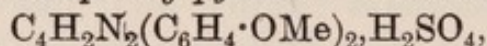
crystallised in deep yellow needles on the addition of a little concentrated hydrobromic acid to a solution of the base in a mixture of ethyl acetate and alcohol:

0.1685 gave 0.0832 AgBr. $\text{HBr} = 21.3$.

$\text{C}_{18}\text{H}_{16}\text{O}_2\text{N}_2\cdot\text{HBr}$ requires $\text{HBr} = 21.7$ per cent.

This salt is not fluorescent, thus differing from its 2: 5-substituted isomeride.

pp'-Dimethoxy-2: 6-diphenylpyrazine monosulphate,



was obtained on adding concentrated sulphuric acid to a solution of the respective base in ethyl acetate. It was not fluorescent, and formed pale yellow needles, which dissociated fairly readily:

0.2635 gave 0.1549 BaSO_4 . $\text{H}_2\text{SO}_4 = 24.7$.

$\text{C}_{18}\text{H}_{16}\text{O}_2\text{N}_2\cdot\text{H}_2\text{SO}_4$ requires $\text{H}_2\text{SO}_4 = 25.1$ per cent.

Salts of mm'pp'-Tetramethoxy-2: 5-diphenylpyrazine.—The amount of this base available was very small, and therefore only its behaviour towards sulphuric acid was investigated. It was markedly more basic than the previously mentioned bases. When treated with a small amount of sulphuric acid in glacial acetic acid solution, it yielded *mm'pp'-tetramethoxy-2: 5-diphenylpyrazine monosulphate*, $\text{C}_6\text{H}_3(\text{OMe})_2\cdot\text{C}_4\text{H}_2\text{N}_2\cdot\text{C}_6\text{H}_3(\text{OMe})_2\cdot\text{H}_2\text{SO}_4$, which formed orange-red needles. If, however, the solution contained any excess of sulphuric acid, the orange-coloured crystals of the monosulphate soon gave place to small, jet-black prisms of the corresponding *disulphate*, $\text{C}_6\text{H}_3(\text{OMe})_2\cdot\text{C}_4\text{H}_2\text{N}_2\cdot\text{C}_6\text{H}_3(\text{OMe})_2\cdot 2\text{H}_2\text{SO}_4$. These crystals possessed a brilliant metallic lustre, and were permanent in the air, although they were dissociated fairly readily by alcohol. A dilute solution of *mm'pp'-tetramethoxy-2: 5-diphenylpyrazine disulphate* in concentrated sulphuric acid had an intensely blue colour. The amount of these salts was not sufficient for analysis.

Salts of mm'pp'-Tetramethoxy-2: 6-diphenylpyrazine.—This base readily yielded a crystalline monohydrochloride, monohydrobromide, and monosulphate, but no di-acid salt of it could be crystallised. No evidence of the existence of a dihydrochloride could be obtained, but a compound of a bluish-black colour with a bronze lustre, which

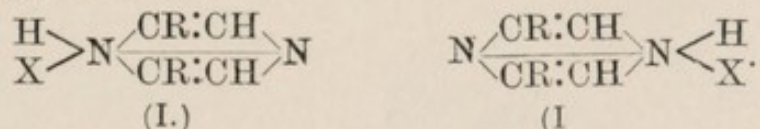
was doubtless the *dihydrobromide*, was obtained by passing dry hydrogen bromide over the crystalline base. A deep blue-coloured solution of the *disulphate* in concentrated sulphuric acid was also obtained.

mm'pp'-Tetramethoxy-2: 6-diphenylpyrazine monohydrochloride has been described in the preceding paper (p. 2511). It is deep yellow, and does not dissociate so readily as the previously described hydrochlorides.

mm'pp'-Tetramethoxy-2: 6-diphenylpyrazine monohydrobromide, $C_6H_3(OMe)_2 \cdot C_4H_2N_2 \cdot C_6H_3(OMe)_2 \cdot HBr$, was obtained in orange-coloured needles on passing hydrogen bromide into a solution of the respective base in warm ethyl acetate. The amount of product available was small, and it was not analysed.

mm'pp'-Tetramethoxy-2: 6-diphenylpyrazine monosulphate, $C_6H_3(OMe)_2 \cdot C_4H_2N_2 \cdot C_6H_3(OMe)_2 \cdot H_2SO_4$, was prepared by adding concentrated sulphuric acid to a solution of the respective base in ethyl acetate. It formed yellow needles, which were stable in the air, but were dissociated by alcohol or water.

Two series of isomeric mono-acid salts of the 2: 6-substituted pyrazines are possible, which would be represented respectively by the following formulæ:



Throughout the course of this work, however, no indication of the presence of isomerides was observed, and it is therefore probable that the acid attaches itself to one of the nitrogen atoms more readily than to the other. If this be the case, the mono-acidic salts of the 2: 6-substituted pyrazines are probably represented by formula II. Furthermore, the fact that no di-acid salt of the last-mentioned bases could be crystallised may be due to these salts being difficult of formation, owing to steric hindrance, but it is quite likely that it is due only to their being more soluble than their 2: 5-substituted isomerides.

In conclusion, the authors wish to acknowledge their indebtedness to Dr. J. T. Hewitt, who kindly placed at their disposal the spectroscope with which the curves given in this paper were obtained.

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