CCCII.—*Derivatives of 2-Phenyl-6-methyl-4-pyrone. The Non-resolution of 2-Phenyl-6-methyl-4-pyrone d-α-Bromocamphor-π-sulphonate.*

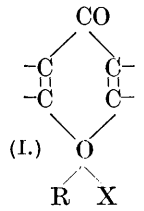
By CHARLES STANLEY GIBSON and JOHN LIONEL SIMONSEN.

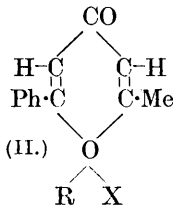
IN a note published some years ago (P., 1913, **29**, 159), Levy, Holmyard, and Ruhemann described briefly some experiments on the attempted resolution of the relatively stable 2-phenyl-6-methyl-4-pyrone *d*-α-bromocamphor-π-sulphonate into its diastereoisomerides. Subsequently Dr. Levy continued these experiments in this department, but, finding himself unable to devote the necessary time to the work, he suggested that we should complete the investigation.

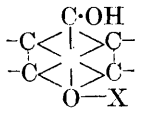
At the time of publication of the above note, the authors held the view that the salts of the 4-pyrones were true oxonium salts represented by the general formula (I), where R = H and X = acid radicals, and in this case it is obvious that in derivatives such as (II), which are asymmetrical, resolution of the salt into its diastereoisomerides is to be anticipated.

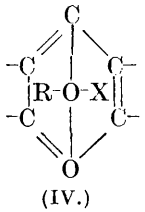
Since Collie and Tickle (J., 1899, **75**, 710) first described the salts of dimethylpyrone and ascribed to them formula (I), the constitution of these salts has been the subject of much discussion. Werner (*Ber.*, 1901, **34**, 3309) suggested the centric formula (III), whilst Collie (J., 1904, **85**, 971) adopted a bridged formula (IV). The

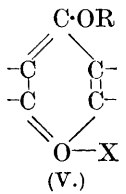
important experiments of Baeyer (*Ber.*, 1910, **43**, 2337) appeared to show beyond question that the correct formulation of the salts was (V). In 1914, Boon, Wilson, and Heilbron (J., **105**, 2176; compare Baly, Collie, and Watson, J., 1909, **95**, 144), from a study of the absorption spectra of a number of arylidene-pyrones and their salts, suggested that although the salts of dimethylpyrone were best represented by the bridged structure (IV), the salts of the arylidene-bases were true oxonium salts (I).

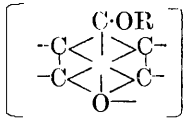












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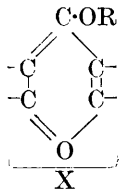

Hantzsch (*Ber.*, 1919, **52**, 1535, 1544), from a comparison of the absorption spectra of the pyrones, thiopyrones, and their salts, concluded that the true salts were co-ordination compounds of the general formula (VI), which is identical with that (III) suggested by Werner (*loc. cit.*). This view was apparently accepted by Arndt, Scholz, and Nachtwey (*Ber.*, 1924, **57**, 1903). The bridged formula of Collie would, however, appear still to have adherents (compare Drew, this vol., p. 518).

The divergent views on the constitution of the salts of the 4-pyrones enhance the importance of a careful repetition of Levy, Holmyard, and Ruhemann's experiments, since if the resolution of 2-phenyl-6-methyl-4-pyrone *d*-α-bromocamphor-π-sulphonate could be effected, it would lend support to a bridged formulation of these salts, as it would be difficult to account for optical isomerism in the case of co-ordinated compounds. We have therefore subjected the pure salt to a prolonged and careful systematic examination. Seventeen fractional crystallisations from pure dry acetone were carried out, but the optical rotatory powers of the six final fractions, when dissolved in pure ethyl alcohol, were all identical, and no sign of resolution was observed. In so far as one is justified in drawing conclusions from negative results, therefore, our experi-

ments would appear to support the co-ordination formulation of these salts.

As it seemed to us possible that a methylated compound might more readily lend itself to resolution, we prepared the *methylmethosulphate* and the *methiodide* of 2-phenyl-6-methyl-4-pyrone. These compounds were, however, found to be unsuitable, being readily hydrolysed.

It has been suggested by Boon, Wilson, and Heilbron (*loc. cit.*) that the salts of the arylidene-pyrones are true oxonium salts (see, however, Heilbron, Barnes, and Morton, J., 1923, **123**, 2564); we therefore prepared *2-phenyl-6-piperonylidenemethyl-4-pyrone*, but this colourless substance yields such intensely coloured salts that the stereochemical investigation of the d-α-*bromocamphor-π-sulphonate* has so far been found to be impossible with the equipment at present available. When the piperonylidene derivative is treated with bromine in chloroform solution a yellow crystalline solid, m. p. 155—157°, is obtained; this was not analysed but probably consisted of the dibromo-derivative (compare Boon, Wilson, and Heilbron, *loc. cit.*). On crystallisation from acetone, hydrogen bromide was eliminated and an ochreous crystalline solid, m. p. 222°, separated. Analysis showed this to be the *monobromopiperonylidene-pyrone* but the position of the bromine atom was not determined.

EXPERIMENTAL.

2-Phenyl-6-methyl-4-pyrone.—The pyrone was prepared by the method of Ruhemann (J., 1908, **93**, 431), except that finely powdered sodamide was used in place of dry sodium ethoxide and the reaction mixture was mechanically stirred during the condensation. By these modifications of the original process the yield was somewhat improved.

The *hydrochloride* was readily obtained by the saturation of an ethereal solution of the pyrone with hydrogen chloride at 0° (Levy, Holmyard, and Ruhemann, *loc. cit.*). The crude salt melted somewhat indefinitely at 161°, and crystallised from a large volume of acetone in fine, glistening prisms, which softened at 105° and melted to a red oil at 165°. It was very readily soluble in water and alcohol, only sparingly soluble in acetone, and insoluble in ether, benzene, and light petroleum (Found: C, 64·7; H, 4·9; HCl, 16·2. $C_{12}H_{11}O_2Cl$ requires C, 64·7; H, 4·9; HCl, 16·4%).

Perchlorate. A warm solution of the pyrone (1 g.) in dilute alcohol (3 c.c.) was treated with an excess of a dilute aqueous solution of perchloric acid. The *perchlorate* separated immediately as an oil which rapidly solidified. It crystallised from dilute alcohol or from much hot water in fine needles, which softened at 135—

137° and melted at 145—147° (Found : C, 61·0, 61·6; H, 4·6; $HClO_4$, by titration, 21·4. $C_{24}H_{21}O_8Cl$ requires C, 61·0; H, 4·5; $HClO_4$, 21·3%).

Sulphate. The pyrone, dissolved in the minimum quantity of methyl alcohol, was treated with the requisite amount of 0·1*N*-sulphuric acid, and the clear solution evaporated to dryness under diminished pressure at room temperature. The crystalline residue after trituration with a little cold acetone had m. p. 165°. It separated from much acetone in iridescent glistening prisms, m. p. 168—169°. It was very soluble in water and methyl alcohol, but insoluble in benzene and ethyl acetate (Found : C, 50·4; H, 4·5. $C_{12}H_{12}O_6S$ requires C, 50·7; H, 4·2%).

Methylmethosulphate. The pyrone, dissolved in the minimum quantity of benzene, was mixed with the calculated amount of freshly distilled methyl sulphate. On standing, the solution, which developed a pink colour, gradually deposited the methylmethosulphate in fine, long needles. After remaining for 48 hours, the crystals were collected, washed with benzene, and dried in a vacuum, m. p. 140—143° with slight previous softening (Found : C, 53·0; H, 5·0. $C_{14}H_{16}O_6S$ requires C, 53·8; H, 5·1%). The *methylmethosulphate* could not be purified by recrystallisation. It was very soluble in water, and in methyl and ethyl alcohols, but insoluble in benzene, ethyl acetate, and light petroleum; it dissolved in a large volume of hot dry acetone, but underwent decomposition. The first fraction which separated on cooling softened at 120° and had m. p. 140—142°, analysis showing it to be a mixture of the methylmethosulphate and the sulphate (Found : C, 51·3; H, 4·9. Calc. for $C_{12}H_{12}O_6S$: C, 50·7; H, 4·2%. Calc. for $C_{14}H_{16}O_6S$: C, 53·8; H, 5·1%). The presence of the sulphate in the solution was confirmed by concentration, whereupon the pure sulphate crystallised in prisms, m. p. 167° (Found : C, 50·2; H, 4·4%). When an aqueous solution of the methylmethosulphate (m. p. 140—143°) was treated with a dilute solution of perchloric acid, the pyrone perchlorate, m. p. 145—147°, was obtained (Found : C, 60·4; H, 4·4; Cl, 7·5. Calc. : C, 61·0; H, 4·5; Cl, 7·5%). The methylmethosulphate did not react with silver *d*-α-bromocamphor-π-sulphonate in alcoholic solution.

Methiodide. When the methylmethosulphate, dissolved in water, was treated with an excess of a dilute solution of potassium iodide, and placed in the ice-chest, the *methiodide* gradually separated. The crystals, which were generally discoloured, decomposed at 105° and were somewhat unstable. Purification was best effected by solution in cold acetone and precipitation by careful addition of light petroleum; colourless needles were deposited, the decom-

position point being unchanged. On keeping, the crystals rapidly become discoloured owing to the liberation of iodine. This compound was analysed by Dr. Levy (Found: C, 47·3; H, 4·1. $C_{13}H_{13}O_2I$ requires C, 47·6; H, 4·0%). The methiodide cannot be prepared by the direct action of methyl iodide on the pyrone; when heated under diminished pressure it decomposed with liberation of methyl iodide and regeneration of the pyrone. The pyrone was also formed when the methiodide was shaken in aqueous solution with either silver oxide or lead oxide. On treatment of an alcoholic solution of the methiodide with perchloric acid, the perchlorate of the pyrone was formed.

2-Phenyl-6-methyl-4-pyrone d-*α-Bromocamphor-π-sulphonate.*—We have prepared this salt by two methods, the second method being preferred for the preparation in quantity, since the pyrone hydrochloride can be more effectively purified than the pyrone itself. (i) The pyrone, dissolved in the minimum quantity of alcohol, was mixed with the requisite amount of a standard aqueous solution of *d*-α-bromocamphor-π-sulphonic acid. When the solution was evaporated to dryness under diminished pressure at room temperature, the salt remained as a crystalline solid. It was recrystallised from acetone and obtained in colourless prisms, m. p. 153—154°.

(ii) The pyrone hydrochloride (10 g.) in alcohol (125 c.c.) was mixed with a solution of silver *d*-α-bromocamphor-π-sulphonate * (18·5 g.) in alcohol (100 c.c.), both solutions being slightly warmed. Silver chloride separated immediately, and after standing for some hours the solution was filtered, and the solvent removed at 30° under diminished pressure, a colourless salt remaining. This was systematically recrystallised from acetone, and after seventeen crystallisations six fractions were obtained. The optical rotatory powers, determined in all cases in absolute ethyl alcohol at 20° ($c = 0{\cdot}400$, $l = 4$), were: $[\alpha]_{5461}$ +83·05°, 82·7°, 82·6°, 82·5°, 82·35°, 82·2°. The salt crystallised from acetone in colourless prisms, softening at 153°, m. p. 157—158° (Found: C, 52·9; H, 5·2. Calc.: C, 53·1; H, 5·0%).

2-Phenyl-6-piperonylidenemethyl-4-pyrone.—To a mixture of 2-phenyl-6-methyl-4-pyrone (1·6 g.) and piperonal (1·5 g.) in alcohol (5 c.c.), a drop of concentrated potassium hydroxide solution was added. A deep red colour developed, and on standing a crystalline solid (1·4 g.) separated. The *piperonylidene* derivative crystallised from acetone, in which it was somewhat sparingly soluble, in colour-

* This salt does not appear to have been analysed previously. It crystallised from alcohol with one molecule of water of crystallisation (Found: C, 27·3; H, 3·6; Ag, 24·6. $C_{10}H_{14}O_4SBrAg,H_2O$ requires C, 27·5; H, 3·7; Ag, 24·8%).

less, soft needles, m. p. 194° (Found : C, 75·4; H, 4·5. $C_{20}H_{14}O_4$ requires C, 75·4; H, 4·4%). It dissolved in concentrated hydrochloric acid, yielding a deep red solution, the salt being decomposed by addition of water. The *perchlorate*, prepared by the addition of perchloric acid to an acetone solution of the pyrone, crystallised in terra-cotta needles, decomp. 143°. Owing to its exploding just above the m. p., the compound could not be analysed. The salt dissociated somewhat readily and could only be recrystallised in the presence of perchloric acid.

For the preparation of the d-*α-bromocamphor-π-sulphonate*, the piperonylidene derivative (0·4852 g.) was dissolved in hot acetone (90 c.c.), and an aqueous solution of the acid (0·475 g.) added. The orange-coloured solution was evaporated to dryness under diminished pressure at room temperature, and an orange, crystalline solid remained. This was recrystallised from much dry acetone, from which it separated in soft orange prisms, m. p. 205—206° with slight previous softening (Found : C, 57·2; H, 4·7. $C_{30}H_{29}O_8BrS$ requires C, 57·2; H, 4·6%).

When a chloroform solution of the piperonylidene derivative of the pyrone was treated with an equivalent quantity (1 mol.) of bromine, a bright red solid separated. This rapidly redissolved, and on stirring a yellow crystalline solid was deposited. This had m. p. 155—157°, but unfortunately it was not analysed. On recrystallisation from acetone, in which it was sparingly soluble, it apparently underwent decomposition with loss of hydrogen bromide, and the *monobromo*-derivative separated in ochreous plates, decomp. 222°. The quantity available was insufficient for the determination of the position of the bromine atom (Found : Br, 19·9. $C_{20}H_{13}O_4Br$ requires Br, 20·1%).

We wish to acknowledge the assistance of Dr. J. H. Nutland who prepared some of the pyrone used in these experiments and carried out some of the analyses. A grant from the Government Grant Committee of the Royal Society, which has covered the greater portion of the cost of this investigation, is also gratefully acknowledged.

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