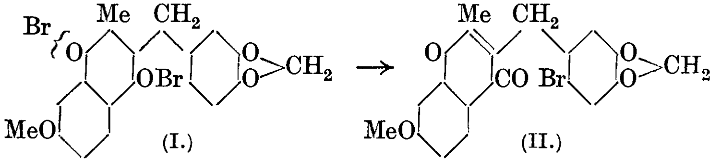
CXXXVIII.—*Synthesis of 7-Methoxy-3-(6′-bromohomopiperonyl)-2-methyl-1 : 4-benzopyrone.*

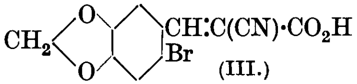
By WILSON BAKER.

BAKER and ROBINSON (J., 1925, **127**, 1426) recently described the dibromide of 7-methoxy-3-homopiperonyl-2-methyl-1 : 4-benzopyrone (I), and showed that it was transformed by boiling with alcohol into a monobromo-substitution product of the original pyrone, which was formulated as the 6-bromohomopiperonyl derivative (II).


(I.) (II.)

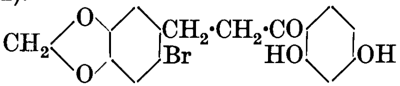
As some theoretical conclusions were drawn from this reaction, it has been considered advisable to establish definitely the constitution of the monobromo-derivative. The compound (II) has therefore been synthesised. It is identical in all respects with the product obtained from the dibromide, the original formula being thus confirmed.

The synthesis was first attempted from 6-bromopiperonal by a series of reactions analogous to those used for the preparation of 7-methoxy-3-homopiperonyl-2-methyl-1 : 4-benzopyrone (Baker and Robinson, *loc. cit.*), but this was found impracticable. 6-Bromopiperonal could not be induced to condense with an alkaline, aqueous solution of sodium cyanoacetate, but it condensed readily with ethyl cyanoacetate in presence of piperidine, and the resulting ester was hydrolysed to 6-*bromopiperonylidenecyanoacetic acid* (III). This acid on reduction with sodium amalgam in aqueous solution gave, however, α-cyano-β-piperonylpropionic acid, the bromine atom being eliminated.


(III.)


(IV.)

The *nitrile* (IV) was therefore prepared by bromination of β-piperonylpropionitrile, the position of the bromine atom being established by the fact that on hydrolysis it gave the corresponding acid, m. p. 139—140°, described by Weinstein (*Annalen*, 1885, **227**, 43). The position of the bromine atom in Weinstein's acid was not known at the time, but it was prepared by the oxidation of the acid $CH_2O_2{:}C_6H_2Br{\cdot}CH_2{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CO_2H$, and its formation was accompanied by the production of a bromopiperonal, m. p. 129°, and a bromopiperonylic acid, m. p. 204°, both of which have since been shown to be 6-bromo-derivatives. It follows that the bromopiperonylpropionic acid was also the 6-derivative. By condensation with resorcinol under the conditions of the Hoesch synthesis β-6-*bromopiperonylpropionitrile* gave 6′-*bromohomopiperonylresacetophenone* (V), which by acetylation with acetic anhydride in presence of sodium acetate, followed by hydrolysis and methylation, gave the chromone (II).



(V.)

EXPERIMENTAL.

6-*Bromopiperonylidenecyanoacetic Acid* (III).—6-Bromopiperonal (10 g.), ethyl cyanoacetate (10 c.c.), alcohol (50 c.c.), and piperidine (10 drops) were heated for 10 minutes. The yellow crystals, m. p. 131°, obtained were identical with the product prepared by Bechert (*J. pr. Chem.*, 1894, **50**, 19) by brominating piperonylidenecyanoacetic ester, which has since been shown by Piccinini (*Atti R. Accad. Sci. Torino*, 1905, **40**, 463) to be the 6-bromo-derivative. By hydrolysis with a slight excess of alcoholic sodium hydroxide for 5 minutes, dilution, extraction with ether, and acidification, the acid was precipitated. It crystallised from much alcohol in bright yellow, lustrous needles, which melted on rapid heating at about 300° (decomp.) (Found : C, 44·7 ; H, 2·3 ; N, 4·9 ; Br, 27·1. $C_{11}H_6O_4NBr$ requires C, 44·6 ; H, 2·0 ; N, 4·7 ; Br, 27·0%). It gives a yellow solution in concentrated sulphuric acid.

β-6-*Bromopiperonylpropionitrile* (IV).—A mixture of β-piperonylpropionitrile (25 g.), glacial acetic acid (500 c.c.), and bromine (25 g.) was kept for ½ hour, heated for 5 minutes, and poured into water. The product crystallised from alcohol in colourless needles, m. p. 81° (Found : C, 47·4 ; H, 3·4 ; N, 5·7 ; Br, 31·8. $C_{10}H_8O_2NBr$ requires C, 47·3 ; H, 3·2 ; N, 5·5 ; Br, 31·5%). The reaction mixture must not stand for longer, as owing to the action of hydrogen bromide and acetic acid β-6-*bromopiperonylpropionamide* separates. This crystallises from alcohol in colourless, lustrous needles, m. p. 151° (Found : C, 44·3 ; H, 3·9 ; N, 5·4 ; Br, 29·6. $C_{10}H_{10}O_3NBr$ requires C, 44·1 ; H, 3·7 ; N, 5·2 ; Br, 29·4%). β-6-Bromopiperonylpropionic acid crystallises from chloroform in colourless prisms, m. p. 139—140° (Found : Br, 29·4. Calc., Br, 29·3%) (compare Weinstein, *loc. cit.*). In concentrated sulphuric acid, these substances, compound (V), and 6-bromopiperonal give cherry-red solutions, which soon darken, turn brown, and finally brownish-green. In the last case, the final colour is more brown.

6'-*Bromohomopiperonylresacetophenone* (V).—β-6-Bromopiperonylpropionitrile (10 g.), resorcinol (20 g.), anhydrous ether (200 c.c.), and powdered zinc chloride (10 g.) were saturated with anhydrous hydrogen chloride, and again after 24 hours. After standing, the solid ketimine was washed with ether and hydrolysed by heating with water for 2 hours. The ketone was dissolved in aqueous sodium hydroxide, the solution extracted with ether, and the product precipitated by carbon dioxide (yield 4 g.). It crystallises from slightly diluted acetic acid in pale brown prisms, m. p. 163° (Found : C, 52·3; H, 3·5; Br, 21·6. $C_{16}H_{13}O_5Br$ requires C, 52·6; H, 3·6; Br, 21·9%).

7-*Methoxy*-3-(6'-*bromohomopiperonyl*) - 2 - *methyl*-1 : 4 - *benzopyrone* (II).—The above ketone (2 g.), anhydrous sodium acetate (2 g.), and acetic anhydride (20 c.c.) were heated at 180° for 36 hours. Treatment with water gave a dark, uncrystallisable oil, which was hydrolysed with dilute alcoholic sodium hydroxide. The phenolic compound was methylated at 60° with methyl sulphate and aqueous potassium hydroxide; a solid (1·4 g.) then separated which by crystallisation from alcohol (200 c.c.) (charcoal) formed bunches of pale brown prisms, m. p. 206—207°. The melting point was not depressed on admixture with a specimen of the bromo-derivative prepared from the dibromide (I). Further, its reaction with sulphuric acid was identical with that given by the compound prepared from (I). The cherry-red solution rapidly became somewhat purple and darker, then light grey, and finally bright olive-green, the changes occupying about 3 minutes at the ordinary temperature.

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