408. *Experiments on the Synthesis of Rotenone and its Derivatives. Part X.* 6 : 7-*Dimethoxychroman*-4-*one.*

By Harold F. Birch, Alexander Robertson, and T. S. Subramaniam.

By the oxidation of netoric acid Takei and his co-workers (*Ber.*, 1932, **65**, 289) obtained a ketonic product, m. p. 121°, which on the basis of the established structure of the acid (Part VIII, this vol., p. 212) appeared to us to be 6 : 7-dimethoxychroman-3- or -4-one.

The former possibility has been excluded by the synthesis of 6 : 7-dimethoxychroman-4-one, which is identical with the product obtained from netoric acid.

In developing the synthetical evidence for the accepted constitution of netoric acid (this vol., p. 212) the remote possibility was discussed that, since on cyclisation ethyl derrate could give rise to two products, this acid might be a chroman-2-carboxylic acid. The formation of a chroman-4-one with simultaneous elimination of the carboxyl group by oxidation of netoric acid affords additional evidence that the carboxyl group is not attached at the 2-position. Oxidation of a chroman-2-carboxylic acid would not be expected to follow this route and in any case its conversion into a chroman-4-one would normally proceed by way of a chroman-4-one-2-carboxylic acid, which would not readily lose carbon dioxide. On repeating the experiment of Takei and his co-workers, the only substance, in addition to 6 : 7-dimethoxychroman-4-one, which we were able to isolate was unchanged netoric acid.

A synthesis of 5 : 7-*dimethoxychroman*-4-*one* is described.

EXPERIMENTAL.

β-3 : 4-*Dimethoxyphenoxypropionic Acid*.—The following modified preparation of 3 : 4-dimethoxyphenol has been found to be superior to that previously described (J., 1930, 2400; 1932, 1380). Carefully purified 4-aminoveratrole (35 g.), dissolved in water (450 c.c.) and concentrated sulphuric acid (53 c.c.), was diazotised at − 10° and with 16% aqueous sodium nitrite (100 c.c.), and the filtered liquid gradually added to a boiling saturated solution of sodium sulphate (100 c.c.). After cooling, the liquor was decanted from the tarry material and extracted several times with ether, and the residual tar digested with five portions of boiling ether. The crude product left on evaporation of the combined extracts, which had been washed and dried, was purified by being twice distilled in a vacuum, then by recrystallisation from carbon tetrachloride, and finally by distillation in a vacuum. Thus purified, the phenol (13 g.) did not darken on exposure to the air for 3 days.

A solution of sodium β-chloropropionate (prepared from 9·2 g. of the acid and 7 g. of sodium bicarbonate in 12 c.c. of water) was added to 3 : 4-dimethoxyphenol (10 g.), dissolved in 30% aqueous potassium hydroxide (14·5 c.c.), and the mixture heated on the steam-bath for 3 hours, cooled, acidified, and extracted several times with ether. Isolated from the combined ethereal extracts by means of aqueous sodium bicarbonate, the *acid* separated from water (charcoal) as a hydrate in colourless needles (4·3 g.), m. p. 136—137°, soluble in alcohol or hot benzene. On being kept in a high vacuum over phosphoric oxide, this material was dehydrated (Found : C, 58·7; H, 6·2. $C_{11}H_{14}O_5$ requires C, 58·4; H, 6·2%). Unchanged phenol (6·9 g.) was recovered from the ethereal extracts left after the separation of the acid.

6 : 7-*Dimethoxychroman*-4-*one*.—Phosphoric oxide (10 g.) was added to a solution of the foregoing acid (2 g.) in benzene (75 c.c.), and the mixture refluxed for 2½ hours; the reaction was accelerated by constant mechanical agitation. After cooling, the benzene was decanted, the residual oxide dissolved in ice-water, the solution extracted with benzene, and the combined benzene solutions washed with aqueous sodium bicarbonate, aqueous sodium hydroxide, and water, dried, and evaporated. The residual chromanone (1·4 g.) separated from benzene–light petroleum (b. p. 60—80°) in colourless, irregular prisms and from light petroleum (b. p. 80—100°) in slender needles, m. p. 123—124° (Found : C, 63·7; H, 5·8. Calc. for $C_{11}H_{12}O_4$: C, 63·5; H, 5·8%). This compound was identical with a specimen prepared by the oxidation of netoric acid, m. p. and mixed m. p. 123—124° (Takei and co-workers, *loc. cit.*, give m. p. 121°).

Unchanged acid (0·2 g.) was recovered from the aqueous sodium bicarbonate extract.

Of the alternate procedures available for the cyclisation of the phenoxypropionic acid it may be mentioned that treatment of the acid (2 g.) with 95% sulphuric acid at 80° for 3 hours gave a less satisfactory yield of the chromanone (0·8 g.) with no unchanged material, and under the same conditions the use of 85% sulphuric acid gave a yield of 0·5 g. of chromanone. Further, application of Gottesmann's method (*Ber.*, 1933, **66**, 1168) gave a tarry product containing but little chromanone.

Interaction of the chromanone (0·5 g.) and *p*-nitrophenylhydrazine hydrochloride (0·5 g.) in 50% acetic acid (10 c.c.) at 50° gave rise to the *p*-nitrophenylhydrazone, which separated from ethyl acetate in microscopic orange prisms, m. p. 223—224° (Found : N, 12·2. Calc. for $C_{17}H_{17}O_5N_3$: N, 12·2%) (Takei and co-workers, *loc. cit.*, give m. p. 223°).

6 : 7-*Dimethoxy*-3-*veratrylidenechroman*-4-*one*.—A solution of the aforementioned chromanone

(2 g.) and veratraldehyde (1·8 g.) in acetic acid was saturated with hydrogen chloride and in the course of 12 hours a red crystalline product separated. After the addition of excess of ice-water the mixture was boiled for 5 minutes and the resulting *compound* was collected, washed, and recrystallised from alcohol, forming pale yellow plates (1·5 g.), m. p. 156·5—157·5°, which gave a red coloration with concentrated sulphuric acid (Found : C, 67·4; H, 5·4. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·6%).

The analogous *furfurylidene* derivative separated from a mixture of the chromanone (2 g.), freshly distilled furfural (2 g.), alcohol (20 c.c.), and 10% aqueous sodium hydroxide (13·3 c.c.) which had been heated to boiling and then allowed to cool. Recrystallised from alcohol, it formed elongated, flat, canary-yellow prisms (2·5 g.), m. p. 138—139°, which gave a red coloration with sulphuric acid (Found : C, 67·2; H, 4·8. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9%).

Condensation of the chromanone (2 g.) with 2-hydroxy-4-methoxybenzaldehyde (2 g.) in ethyl acetate by means of hydrogen chloride gave rise to 7 : 6′ : 7′-trimethoxychromeno-4′ : 3′ : 2 : 3-benzopyrylium chloride, which is almost insoluble in warm dilute hydrochloric acid. It separated from a warm mixture of equal volumes of alcohol and 12% hydrochloric acid in red needles. Prepared in the usual manner, the *ferrichloride* formed tiny purple prisms, m. p. 256—257° (decomp.), from warm formic acid, sparingly soluble in hot acetic acid (Found : C, 43·9; H, 3·5. $C_{19}H_{17}O_5Cl_4Fe$ requires C, 43·6; H, 3·3%). This pyrylium chloride is closely analogous to the chromenochromanones of the rotenone type (J., 1933, 489).

β-3 : 5-*Dimethoxyphenoxypropionic acid* was prepared from phloroglucinol dimethyl ether (10 g.), dissolved in 30% aqueous potassium hydroxide (14·5 c.c.), and a solution of sodium β-chloropropionate (from 9·2 g. of the acid and 7 g. of sodium bicarbonate in 15 c.c. of water) by the method used for the preparation of β-3 : 4-dimethoxyphenoxypropionic acid. It formed colourless needles (4·1 g.), m. p. 128—129°, from warm water (Found : C, 58·1; H, 6·3. $C_{11}H_{14}O_5$ requires C, 58·4; H, 6·2%). The recovery of unchanged phloroglucinol dimethyl ether was 6·2 g.

5 : 7-*Dimethoxychroman*-4-*one*.—Cyclisation of the foregoing acid (1·45 g.) was effected in boiling benzene (100 c.c.) with phosphoric oxide (6 g.) in the course of 2½ hours. On isolation the resulting *chromanone* separated from light petroleum (b. p. 80—100°) in colourless needles, m. p. 99° (Found : C, 63·5; H, 5·9. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%). Unchanged acid (0·25 g.) was recovered.

The veratrylidene derivative was prepared by the method employed for 6 : 7-dimethoxy-3-furfurylidenechromanone and formed small yellow prisms, m. p. 154—155°, from a little alcohol.

UNIVERSITY OF LIVERPOOL.

[*Received, October* 31*st*, 1936.]