249. *Usnic Acid. Part VIII.** C-*Diacetyl Derivatives of Phloroglucinol and* C-*Methylphloroglucinol.*

By F. M. Dean and Alexander Robertson.

By means of boron trifluoride, diacetylphloroglucinol and 2 : 4-diacetyl-6-methylphloroglucinol together with their methyl ethers have been prepared by the *C*-acylation of phloroglucinol, *C*-methylphloroglucinol, and their mono- and di-methyl ethers. This procedure has also been shown to be convenient for the preparation of 2 : 4- and 4 : 6-diacetylresorcinol.

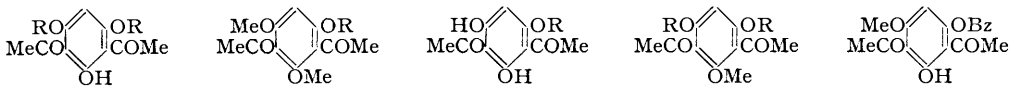
During exploratory studies on the synthesis and degradation of usnic acid and its isomeride usnolic acid it became necessary to examine the preparation and alkylation of diacetylphloroglucinol and its *C*-methyl derivative. Boron trifluoride, under the requisite conditions, has now been found to be a suitable reagent for *C*-acetylation of phloroglucinol derivatives and the method has been extended to the preparation of 2 : 4- and 2 : 6-diacetylresorcinol (cf., *e.g.*, Baker, *J.*, 1934, 71, 1684; Desai and Mavani, *J. Indian Acad. Sci.*, 1949, **29**, *A*, 268; Phillips, Robertson, and Whalley, *J.*, 1952, 4951).

* Part VII, *J.*, 1939, 1594.

As originally prepared by the condensation of phloroglucinol and acetyl chloride with ferric chloride (Nencki, *Ber.*, 1899, **32**, 2417; Goschke and Tambor, *ibid.*, 1912, **45**, 1237) diacetylphloroglucinol is accompanied by triacetylphloroglucinol which, however, is formed in better yield by a Fries reaction on phloroglucinol triacetate (Klarmann, *J. Amer. Chem. Soc.*, 1926, **48**, 2358). Similarly, by the Friedel–Crafts reaction on *O*-dimethylphloroglucinol Tutin and Caton (*J.*, 1910, **97**, 2062) obtained a dimethyl ether of diacetylphloroglucinol which was shown by Gruber and Traub (*Monatsh.*, 1947, **77**, 414) to be the 1 : 5-dimethyl ether which they also prepared in 14% yield from phloracetophenone 2 : 4-dimethyl ether by the Hoesch reaction.

By the boron trifluoride method at room temperature an excellent yield of diacetylphloroglucinol (I; R = H) has been obtained whilst at higher temperatures the product contained some triacetylphloroglucinol which, under the requisite conditions, became the major component. Similarly, phloroglucinol monomethyl ether gave diacetylphloroglucinol 1-methyl ether (III; R = Me) which was not identical with the compound described by Gruber and Traub (*loc. cit.*). It may well be that the compound, m. p. 255—257°, formed by the Hoesch reaction and considered by these authors to be diacetylphloroglucinol 1-methyl ether was unchanged ketimine. *O*-Dimethylphloroglucinol and one molecular proportion of acetylating agent yielded phloracetophenone 2 : 4-dimethyl ether with only traces of phloracetophenone 2 : 6-dimethyl ether, unlike the product from the corresponding Hoesch reaction (Canter, Curd, and Robertson, *J.*, 1931, 1245). With the necessary quantity of acetylating reagent *O*-dimethylphloroglucinol and phloracetophenone 2 : 4-dimethyl ether gave diacetylphloroglucinol 1 : 5-dimethyl ether (I; R = Me) along with a little diacetylphloroglucinol 1-methyl ether (III; R = Me). Under the usual conditions the same mixture was obtained unexpectedly from phloracetophenone 2 : 6-dimethyl ether, implying the migration of an acetyl group. This was supported by the observation that, on treatment with boron trifluoride in a small quantity of acetic acid, phloracetophenone 2 : 6-dimethyl ether gave a little phloracetophenone 2 : 4-dimethyl ether and, possibly, some *O*-dimethylphloroglucinol, a finding which may also explain the difference in the results obtained with the Hoesch and boron trifluoride procedures. Although phloroglucinol diethyl ether gave a mixture of diacetylphloroglucinol 1 : 5-diethyl (I; R = Et) and 1-ethyl ether (III; R = Et), phloracetophenone 2 : 6-diethyl ether was attacked with simultaneous partial dealkylation and only diacetylphloroglucinol 1-ethyl ether could be isolated.

Diacetylphloroglucinol 1 : 3-dimethyl ether (II; R = H) was subsequently prepared and on treatment with free boron trifluoride isomerised completely to diacetylphloroglucinol 1 : 5-dimethyl ether (I; R = Me), whilst with boron trifluoride etherate in the absence of free boron trifluoride the *C*-acetyl group in the *p*-position to the hydroxyl group was eliminated, giving phloracetophenone 2 : 4-dimethyl ether.

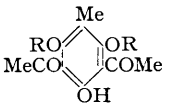


(I) (II) (III) (IV) (V)

The orientation of diacetylphloroglucinol 1-methyl ether (III; R = Me) follows on general grounds from its formation by the controlled methylation of diacetylphloroglucinol which, under somewhat more drastic conditions, gives the 1 : 5-dimethyl ether (I; R = Me) of known orientation. Partial benzylation of diacetylphloroglucinol furnished the 1-benzyl ether (III; R = CH_2Ph), having the expected positive indophenol reaction, and, on methylation followed by debenzylation of the resulting mixed ether (II; R = CH_2Ph), this compound was converted into a dimethyl ether of diacetylphloroglucinol which is isomeric with the known 1 : 5-dimethyl ether (I; R = Me) and is, therefore, diacetylphloroglucinol 1 : 3-dimethyl ether (II; R = H). Similarly, the dibenzyl ether of diacetylphloroglucinol is, by analogy with (I; R = Me), the 1 : 5-dibenzyl derivative (I; R = CH_2Ph) and on methylation gives diacetylphloroglucinol 1 : 5-dibenzyl 3-methyl ether (IV; R = CH_2Ph) which, on debenzylation, furnished diacetylphloroglucinol 3-methyl ether (IV; R = H), forming diacetylphloroglucinol trimethyl ether on methylation. In agree-

ment with the orientations allotted to the monomethyl ethers (III; R = Me) and (IV; R = H) the compound (III; R = Me) gives a positive indophenol reaction whereas (IV; R = H) does not. Further, partial methylation of diacetylphloroglucinol 1-benzyl ether (III; R = CH_2Ph) gave diacetylphloroglucinol 1-benzyl 5-methyl ether (V) which on debenzylation yielded diacetylphloroglucinol 1-methyl ether (III; R = Me).

C-Acetylation of *C*-methylphloroglucinol or of *C*-methyl phloracetophenone by the boron trifluoride method gave 2 : 4-diacetyl-6-methylphloroglucinol (VI; R = H) whilst an excess of the reagents furnished 2 : 4-diacetyl-6-methylphloroglucinol 1 : 5-diacetate (VI; R = Ac) which appears to be identical with the ozonolysis product obtained from decarbousnic acid by Schöpf and Ross (*Annalen*, 1941, **546**, 1).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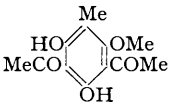
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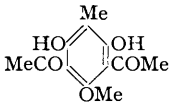
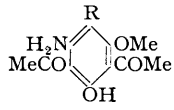

(VIII)


(IX)

Similarly, 2 : 4-diacetyl-6-methylphloroglucinol 1-methyl ether (VII) was obtained from *C*-methylphloroglucinol 2-methyl ether and from *C*-methylphloracetophenone 4-methyl ether and was identical with the product formed by the ozonolysis of usnetol monomethyl ether (Schöpf and Ross, *loc. cit.*), giving *C*-methylphloracetophenone 4-methyl ether on hydrolysis. The isomeride 2 : 4-diacetyl-6-methylphloroglucinol 3-methyl ether (VIII) was obtained from *C*-methylphloracetophenone 6-methyl ether only when the reaction was carried out at above 100° and can be readily distinguished from (VII) by its failure to give a monoketone on hydrolytic decomposition. On the other hand, *C*-methylphloroglucinol 2 : 4-dimethyl ether gave only *C*-methylphloracetophenone 2 : 4-dimethyl ether; a second acetyl group could not be introduced.

In attempts to deacetylate some of the acetates of the diketones with alcoholic ammonia it was found that diacetylphloroglucinol 1-methyl ether gave a nitrogenous derivative which appeared to have the empirical formula $C_{10}H_{10}O_5N{\cdot}OMe$ and to be formed by replacing a carbonyl by an imino-group or a hydroxyl by an amino-group. With a phloroglucinol derivative the latter change is more probable and at present the product is formulated as (IX; R = H). A similar compound, probably (IX; R = Me), was obtained from 2 : 4-diacetyl-6-methylphloroglucinol 1-methyl ether.

Experimental

Except where stated, the light petroleum employed had b. p. 60—80°.

2 : 4- *and* 4 : 6-*Diacetylresorcinol.*—(*a*) A stream of boron trifluoride was led into a mixture of resacetophenone (2 g.), acetic acid (3 ml.), and acetic anhydride (1·4 g.) at 80° for ½ hour, and the mixture kept at 80° for 1 hour, cooled, and diluted with ether. A solution of the resulting yellow product in the minimum volume of hot 80% alcohol was kept at 70° until the colour was discharged and then, on being cooled, gave a colourless crystalline solid (1·8 g.) which was isolated and extracted with hot light petroleum leaving a residue of 4 : 6-diacetylresorcinol. This compound formed colourless prisms (0·9 g.), m. p. 182°, from aqueous alcohol, having a red-brown ferric reaction and a negative 2 : 6-dichloroquinone chloroimide reaction (cf. Gibbs, *Chem. Reviews*, 1927, **3**, 291), and on methylation by the methyl iodide–potassium carbonate method gave the mono- and the di-methyl ether, m. p. 121·5° and 171°, respectively (cf. Eijkmann, Bergema, and Henrard, *Chem. Weekblad*, 1904, **1**, 453).

Evaporation of the light petroleum extract left 2 : 4-diacetylresorcinol, forming colourless needles (0·8 g.), m. p. 85°, from dilute alcohol, which gave an intense red ferric and a mauve 2 : 6-dichloroquinone chloroimide reaction, and a green colour with dilute alkaline hydrogen peroxide.

(*b*) By the interaction of resorcinol dimethyl ether, acetyl chloride, and aluminium chloride Mauthner (*J. pr. Chem.*, 1928, **119**, 311) obtained 4 : 6-resodiacetophenone monomethyl and dimethyl ether. Repetition of this gave the following results. The product from the interaction of resorcinol dimethyl ether (18 g.), acetyl chloride (21 g.), and aluminium chloride (40 g.) in carbon disulphide (30 ml.) at 10° for 1 hour, followed by evaporation of the solvent on the

water-bath, was decomposed with ice and concentrated hydrochloric acid. After being washed with dilute hydrochloric acid, the precipitate was extracted with 2N-sodium hydroxide (100 ml.), and the insoluble residue crystallised from 80% acetic acid, giving the dimethyl ether, m. p. 171°, of 4 : 6-diacetylresorcinol (0·4 g.). The solid from the acidified alkaline extract was digested with hot light petroleum and then crystallised from 80% acetic acid, yielding 4 : 6-diacetylresorcinol (2·3 g.), m. p. 183°. The light petroleum extract contained 4 : 6-diacetylresorcinol monomethyl ether (0·7 g.), m. p. 120°, and a more soluble product which separated from 80% acetic acid in faintly yellow prisms (1·6 g.), m. p. 137°, soluble in aqueous sodium hydrogen carbonate and having a brown-red ferric reaction (Found, in specimen dried in a high vacuum at 80° : C, 61·2; H, 5·4; MeO, 0. $C_{12}H_{12}O_5$ requires C, 61·0; H, 5·1%). This compound appears to be 2 : 4 : 6-*triacetylresorcinol*; it was not attacked by 2N-sodium hydroxide at 100° for 4 hours, reacted with 2 : 4-dinitrophenylhydrazine, and gave a green colour with alkaline hydrogen peroxide. In the purification of the monomethyl ether of 4 : 6-diacetylresorcinol by crystallisation alternately from dilute alcohol and light petroleum a more soluble product, m. p. 109°, was obtained which, since on methylation it gave only the dimethyl ether of 4 : 6-resodiacetophenone, appeared to be a eutectic mixture of 4 : 6-diacetylresorcinol and its monomethyl ether in the ratio approximately 1 : 6. A mixture of the two compounds in this proportion had the same m. p. and mixed m. p. 109°, and was unchanged on repeated recrystallisation from a variety of solvents.

Ethers of 2 : 4-*Diacetylresorcinol.*—(*a*) Methylation of 2 : 4-diacetylresorcinol (2 g.) with methyl sulphate (1·3 g.) and potassium carbonate (1·3 g.) in boiling acetone (100 ml.) for 2 hours gave 2 : 4-*diacetyl*-1-O-*methylresorcinol*, forming large prisms (1·1 g.), m. p. 104°, from light petroleum, which had a deep red ferric reaction (Found, in specimen dried in a high vacuum at 60° : C, 63·7; H, 5·6; OMe, 15·3. $C_{10}H_9O_3{\cdot}OMe$ requires C, 63·5; H, 5·8; OMe, 14·9%). The following alternative preparation served to establish the orientation of this compound : A mixture of 2-hydroxy-4-methoxyacetophenone (3 g.), acetic anhydride (1·6 ml.), and acetic acid (5 ml.) was saturated with boron trifluoride at 50°, kept for 1 hour, and treated with ether (100 ml.). Decomposition of the yellow precipitate with aqueous alcohol gave unchanged ketone but on acidification an N-sodium hydroxide extract of the ethereal filtrate gave 2 : 4-diacetyl-1-*O*-methylresorcinol, m. p. 104° after purification, which did not give a colour with 2 : 6-dichloroquinone chloroimide, a property now found to be common to *o*-hydroxy-aldehydes and -ketones.

Methylation of 2 : 4-diacetyl-1-*O*-methylresorcinol (0·5 g.) with methyl sulphate (0·3 ml.) and potassium carbonate (0·35 g.) in boiling acetone (150 ml.) for 3 hours furnished 2 : 4-*diacetylresorcinol dimethyl ether* which separated from ether and then light petroleum in prisms (0·3 g.), m. p. 60—63°, with a negative ferric reaction [Found : C, 64·7; H, 6·5; OMe, 27·9. $C_{10}H_8O_2(OMe)_2$ requires C, 64·9; H, 6·4; OMe, 27·9%].

(*b*) On being heated under reflux for 8 hours a mixture of 2 : 4-diacetylresorcinol (6 g.), potassium carbonate (6 g.), benzyl bromide (3·8 ml.), and acetone (100 ml.) containing a trace of potassium iodide gave 2 : 4-*diacetyl*-1-O-*benzylresorcinol*, isolated from a benzene solution of the crude product with 2N-sodium hydroxide. Crystallised from benzene–light petroleum, this ether formed colourless prisms (1·8 g.), m. p. 92°, having a deep red ferric reaction (Found, in specimen dried in a high vacuum at 60° : C, 70·7; H, 5·4. $C_{17}H_{16}O_4$ requires C, 70·2; H, 5·7%). After the removal of this compound evaporation of the benzene liquors left 2 : 4-*diacetylresorcinol dibenzyl ether* which separated from benzene–light petroleum and then aqueous alcohol in colourless prisms (3·8 g.), m. p. 128—129°, with a negative ferric reaction (Found, in specimen dried in a high vacuum at 80° : C, 77·3; H, 5·9. $C_{24}H_{22}O_4$ requires C, 77·0; H, 5·9%). Methylation of the monobenzyl ether (0·9 g.) by the methyl iodide–potassium carbonate method yielded 2 : 4-*diacetyl*-1-O-*benzyl*-3-O-*methylresorcinol*, separating from benzene–light petroleum in prisms (0·8 g.), m. p. 101°, with a negative ferric reaction (Found : C, 72·4; H, 6·3; OMe, 10·0. $C_{17}H_{15}O_3{\cdot}OMe$ requires C, 72·5; H, 6·1; OMe, 10·4%).

Phloracetophenone 2 : 4-*Dimethyl Ether.*—(*a*) A solution of phloroglucinol dimethyl ether (5 g.) in ether (10 ml.), containing acetic anhydride (3·5 g.), was saturated with boron trifluoride at 15° and an hour later a yellow solid was isolated by precipitation with water. On decomposition with aqueous alcohol followed by distillation with steam this furnished phloracetophenone 2 : 4-dimethyl ether (3·1 g.), m. p. and mixed m. p. 81°, having a negative indophenol reaction. On crystallisation from alcohol the resinous residue, non-volatile in steam, gave a little phloracetophenone 2 : 6-dimethyl ether.

(*b*) A stream of boron trifluoride was led into phloracetophenone 2 : 6-dimethyl ether (0·5 g.) dissolved in boron trifluoride–ether complex (20 ml.) for 15 min. and next day the mixture was

treated with water (100 ml.). After the removal of the ether with a current of air the solid was decomposed with steam, giving a small amount of phloracetophenone 2 : 4-dimethyl ether, m. p. and mixed m. p. 188°, in the distillate (cf. Canter *et al.*, *loc. cit.*, who give m. p. 185·5°). Crystallised from alcohol, the non-volatile residue gave unchanged phloracetophenone 2 : 6-dimethyl ether (0·3 g.).

(*c*) Interaction of boron fluoride–ether complex (20 ml.), diacetylphloroglucinol 1 : 3-dimethyl ether (0·5 g.), and acetic acid (2 ml.) for 24 hours with isolation of the product in the usual manner gave phloracetophenone 2 : 4-dimethyl ether (0·25 g.), m. p. and mixed m. p. 81·5°.

Phloracetophenone 2 : 4- and 2 : 6-Diethyl Ether.—Interaction of phloroglucinol diethyl ether (Robertson and Subramaniam, *J.*, 1937, 286) (5 g.), methyl cyanide (8 ml.), zinc chloride (5 g.), and excess of hydrogen chloride in ether (200 ml.) at 0° gave a crystalline solid which was isolated next day and dissolved in cold water (150 ml.). The precipitate, which separated almost immediately, was warmed with N-sodium hydroxide (120 ml.) until the evolution of ammonia had ceased and on acidification the resulting solution gave a mixture of the ketones which was crystallised from a little 80% alcohol (yield, 3·2 g.). Extraction of this product with hot light petroleum left a residue of *phloracetophenone 2 : 6-diethyl ether* which separated from dilute alcohol in colourless plates (1·8 g.), m. p. 186—187°, with a negative ferric or indophenol reaction [Found, in specimen dried in a vacuum at 80° : C, 64·1; H, 7·0; OEt, 39·4. $C_8H_6O_2(OEt)_2$ requires C, 64·3; H, 7·2; OEt, 40·2%]. Evaporation of the light petroleum extract left phloracetophenone 2 : 4-diethyl ether (Kostanecki and Tambor, *Ber.*, 1899, **32**, 2263) forming colourless needles (1·1 g.), m. p. 85°, from dilute alcohol, with a plum-red ferric and a blue 2 : 6-dichloroquinone chloroimide reaction.

The isomeric diethyl ethers were methylated by the methyl iodide–potassium carbonate method, giving, respectively, *phloracetophenone 2 : 6-diethyl 4-methyl ether* which formed large plates, m. p. 83°, from light petroleum (Found : C, 65·8; H, 7·7. $C_{13}H_{18}O_4$ requires C, 65·6; H, 7·6%) and *phloracetophenone 2 : 4-diethyl 6-methyl ether* as an oil, b. p. 135°/0·05 mm. (Found : C, 65·6; H, 7·4%).

Diacetylphloroglucinol (I; R = H).—Interaction of phloroglucinol (3 g.), acetic anhydride (5 g.), and excess of boron trifluoride in ether (30 ml.) at 20°, followed an hour later by removal of the solvent with air, gave a boron fluoride complex which was washed with water and dissolved in hot 80% alcohol. On cooling, the solution deposited the diketone in prisms (4 g.), m. p. 168°, after sublimation in a high vacuum or recrystallisation from benzene–light petroleum (Found, in specimen dried in a high vacuum at 80° : C, 57·0; H, 4·8. Calc. for $C_{10}H_{10}O_5$: C, 57·1; H, 4·8%). This compound is soluble in aqueous sodium hydrogen carbonate or benzene and gives an intense red ferric reaction in alcohol. Prepared by the pyridine method, the O-*tribenzoate* separated from benzene in large colourless prisms, m. p. 137°, with a negative ferric reaction (Found : C, 71·5; H, 4·3. $C_{31}H_{22}O_8$ requires C, 71·3; H, 4·3%). The O-*triacetate* was prepared by acetic anhydride–pyridine and to prevent hydrolysis was isolated immediately on decomposition of the excess of anhydride with water. Crystallised from dilute alcohol, the compound formed colourless needles, m. p. 92—93°, with a negative ferric reaction (Found : C, 57·3; H, 4·8. $C_{16}H_{16}O_8$ requires C, 57·1; H, 4·8%). When the aqueous reaction mixture was kept for 24 hours the product consisted of 2 : 4-*diacetylphloroglucinol* 1 : 5-*diacetate* (I; R = Ac) which was also formed by partial hydrolysis of the triacetate (1·7 g.) with pyridine (10 ml.) containing water (0·1 ml.) for 24 hours. This derivative separated from aqueous alcohol in colourless needles, m. p. 116°, with a deep red ferric reaction (Found : C, 57·2; H, 5·1. $C_{14}H_{14}O_7$ requires C, 57·1; H, 4·8%).

2 : 4-*Diacetylphloroglucinol* 1-*Methyl Ether* (III; R = Me).—A mixture of phloroglucinol monomethyl ether (1 g.), acetic acid (2 ml.), acetic anhydride (1·4 g.), and an excess of boron trifluoride were kept for 1 hour at 20° and diluted with excess of ether. On being cooled, a solution of the resulting solid in hot 60% alcohol deposited 2 : 4-*diacetylphloroglucinol* 1-*methyl ether* in needles (1·3 g.), m. p. 106°, unchanged on repeated purification and identical with a specimen prepared from diazomethane and diacetylphloroglucinol in benzene or by methylation of diacetylphloroglucinol (1 g.) with methyl iodide (2 ml.) and potassium acetate (4 g.) in boiling acetone (100 ml.) for 3 hours (Found, in a specimen dried in a high vacuum at 60° : C, 58·8; H, 5·3; OMe, 13·5. $C_{10}H_9O_4$·OMe requires C, 58·9; H, 5·4; OMe, 13·8%). This ether is soluble in aqueous sodium hydrogen carbonate, warm light petroleum, and the usual organic solvents, and gives an intense dark red ferric reaction and a purple colour with 2 : 6-dichloroquinone chloroimide. Prepared by the pyridine method, the *dibenzoate* formed colourless prisms, m. p. 120·5°, from benzene–light petroleum, with a negative ferric reaction (Found : C, 69·7; H, 4·7; OMe, 7·3. $C_{24}H_{17}O_6$·OMe requires C, 69·5; H, 4·7; OMe, 7·2%).

Diacetylphloroglucinol 1-methyl ether (0·5 g.), methyl sulphate (1 ml.), and potassium carbonate (2 g.) in boiling acetone (50 ml.) (2 hours) gave 2 : 4-*diacetylphloroglucinol* 1 : 3 : 5-*trimethyl ether*, prisms (0·5 g.) (from light petroleum), m. p. 110—111°, with a negative ferric reaction [Found : C, 62·2; H, 6·3; OMe, 36·8. $C_{10}H_7O_2(OMe)_3$ requires C, 61·9; H, 6·4; OMe, 36·9%].

Benzylation of diacetylphloroglucinol 1-methyl ether by the potassium carbonate–acetone method yielded 2 : 4-*diacetylphloroglucinol* 3 : 5-*dibenzyl* 1-*methyl ether*, forming plates, m. p. 131°, from benzene–light petroleum (Found : C, 74·1; H, 6·2; OMe, 7·4. $C_{24}H_{21}O_4{\cdot}OMe$ requires C, 74·3; H, 6·0; OMe, 7·9%). Hydrogenolysis of this in methanol with hydrogen and palladium–charcoal regenerated the parent 1-methyl ether.

Diacetylphloroglucinol 1-*Benzyl Ether* (III; R = CH_2Ph).—Diacetylphloroglucinol (4 g.), benzyl bromide (2·7 ml.), potassium carbonate (2·5 g.), a trace of potassium iodide, and acetone (250 ml.) were heated under reflux for 3 hours. The 1-*benzyl ether* crystallised from 90% alcohol in colourless silky needles (2·0 g.), m. p. 127°, with a red ferric reaction and a purple 2 : 6-dichloroquinone chloroimide reaction (Found, in specimen dried in a high vacuum at 80° : C, 68·1; H, 5·5. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%). This was accompanied by unchanged diacetylphloroglucinol (0·2 g.) and an alkali-soluble oil (1·3 g.) which was purified by way of its copper derivative, followed by distillation in a vacuum (b. p. 200°/0·3 mm.) (Found : C, 72·3; H, 5·5%), and had a dark red ferric reaction. Debenzylation of the 1-benzyl ether with hydrogen at 40 lb./sq. in. and palladium–charcoal regenerated diacetylphloroglucinol, m. p. and mixed m. p. 168°.

Methylation of diacetylphloroglucinol 1-benzyl ether (2 g.) with methyl sulphate (1 g.) and potassium carbonate (1 g.) in boiling acetone (100 ml.) for 4 hours gave *diacetylphloroglucinol* 1-*benzyl* 5-*methyl ether* (V), prisms (1·5 g.), m. p. 95°, from benzene–light petroleum, with a blood-red ferric reaction (Found : C, 69·1; H, 5·9; OMe, 9·0. $C_{17}H_{15}O_4{\cdot}OMe$ requires C, 68·8; H, 5·8; OMe, 9·9%). Hydrogenolysis of this gave phlorodiacetophenone 1-methyl ether, m. p. and mixed m. p. 106°.

Treatment of diacetylphloroglucinol 1-benzyl ether (1 g.) with an excess of methyl iodide and potassium carbonate in boiling acetone (60 ml.) for 8 hours gave *diacetylphloroglucinol* 1-*benzyl* 2 : 5-*dimethyl ether* (II; R = CH_2Ph), prisms (1·1 g.), m. p. 84—85°, from light petroleum [Found : C, 69·6; H, 6·3; OMe, 19·4. $C_{17}H_{14}O_3(OMe)_2$ requires C, 69·5; H, 6·2; OMe, 19·0%]. On debenzylation this compound (1 g.) gave *diacetylphloroglucinol* 1 : 3-*dimethyl ether* (II; R = H) which separated from dilute alcohol or light petroleum in prisms (0·6 g.), m. p. 106°, with a deep red ferric reaction [Found : C, 60·5; H, 6·0; OMe, 26·1. $C_{10}H_8O_3(OMe)_2$ requires C, 60·5; H, 5·9; OMe, 26·1%]. Methylation of this furnished diacetylphloroglucinol trimethyl ether, m. p. and mixed m. p. 110°.

Diacetylphloroglucinol 1 : 5-*Dimethyl Ether* (I; R = Me).—Interaction of phloroglucinol dimethyl ether (2 g.) with acetic acid (2 ml.), acetic anhydride (2·4 g.), and an excess of boron trifluoride at 10° for an hour followed by dilution with ether (100 ml.) gave a yellow solid, decomposing with hot 50% alcohol to diacetylphloroglucinol 1 : 5-dimethyl ether which separated from the cooled solution and then crystallised from light petroleum in colourless needles (2 g.), m. p. 128°, with an intense red ferric reaction, readily soluble in the usual organic solvents, and insoluble in aqueous sodium hydrogen carbonate [Found : C, 60·4; H, 5·8; OMe, 25·2. Calc. for $C_{10}H_8O_3(OMe)_2$: C, 60·5; H, 5·9; OMe, 26·1%] (cf. Gruber and Traub, *loc. cit.*). This ether, which had a negative 2 : 6-dichloroquinone chloroimide reaction, was accompanied by a small amount of diacetylphloroglucinol 1-methyl ether, m. p. and mixed m. p. 105°. When phloroglucinol dimethyl ether was replaced by phloracetophenone 2 : 4- or 2 : 6-dimethyl ether and one mol. of acetic anhydride was employed the same products were obtained. The acetate of diacetylphloroglucinol 1 : 5-dimethyl ether had m. p. 152° (Found : C, 59·9; H, 6·0. Calc. for $C_{14}H_{16}O_6$: C, 60·0; H, 5·8%) (cf. Tutin and Caton, *loc. cit.*).

A solution of diacetylphloroglucinol 1 : 3-dimethyl ether (0·5 g.) in ether (20 ml.) containing a little acetic acid was saturated with boron trifluoride and on isolation next day the product was separated into diacetylphloroglucinol 1-methyl ether (less soluble product) (0·05 g.), m. p. and mixed m. p. 105°, and diacetylphloroglucinol 1 : 5-dimethyl ether (0·2 g.), m. p. and mixed m. p. 128°, by fractional crystallisation from dilute alcohol.

Diacetylphloroglucinol 1 : 5-dimethyl ether, m. p. and mixed m. p. 128°, was also prepared by methylation of diacetylphloroglucinol (1 g.) with methyl iodide (2 ml.) and potassium carbonate (2 g.) in boiling acetone (50 ml.) for 2 hours.

Ethylation of diacetylphloroglucinol 1 : 5-dimethyl ether with excess of ethyl iodide by the potassium carbonate–acetone method gave *diacetylphloroglucinol* 3-*ethyl* 1 : 5-*dimethyl ether*,

prisms (from light petroleum), m. p. 96° (Found : C, 63·6; H, 7·0. $C_{14}H_{18}O_5$ requires C, 63·2; H, 6·8%).

Benzylation of diacetylphloroglucinol 1 : 5-dimethyl ether by the usual method for 16 hours gave *diacetylphloroglucinol 3-benzyl 1 : 5-dimethyl ether* which crystallised from light petroleum in thick irregular prisms, m. p. 122° [Found : C, 69·4; H, 6·1; OMe, 18·7. $C_{17}H_{14}O_3(OMe)_2$ requires C, 69·5; H, 6·2; OMe, 19·0%]. Hydrogenolysis of this regenerated the parent dimethyl ether.

Diacetylphloroglucinol 1-Ethyl and 1 : 5-Diethyl Ether.—A solution of phloroglucinol diethyl ether (2 g.) in acetic acid (2 ml.) and acetic anhydride (2·2 g.) was treated with an excess of boron trifluoride at 10—15° for 24 hours. Precipitated with ether (70 ml.) and decomposed with hot dilute alcohol, the yellow product furnished *diacetylphloroglucinol 1 : 5-diethyl ether*, forming irregular prisms (0·8 g.), m. p. 117°, from light petroleum with a red-brown ferric reaction [Found : C, 63·1; H, 4·9; OEt, 33·4. $C_{10}H_8O_3(OEt)_2$ requires C, 63·2; H, 4·9; OEt, 33·8%]. After the separation of the yellow solid the ethereal filtrate was mixed with water, the ether evaporated, and the resulting solid crystallised from light petroleum, giving *diacetylphloroglucinol 1-ethyl ether* in plates (0·4 g.), m. p. 131—131·5°, with a cherry-red ferric and a purple indophenol reaction (Found : C, 60·4; H, 5·9; OEt, 18·6. $C_{10}H_9O_4$·OEt requires C, 60·5; H, 5·9; OEt, 18·9%).

A mixture of ether (5 ml.) and acetic anhydride (0·3 g.) containing a suspension of phloracetophenone 2 : 6-diethyl ether (0·6 g.) was saturated at below 0° with a slow stream of boron trifluoride and immediately treated with ether (100 ml.) and water (100 ml.), with subsequent evaporation of the ether. On decomposition, the resulting complex furnished only diacetylphloroglucinol 1-ethyl ether, m. p. and mixed m. p. 131°.

Methylated with methyl sulphate by the potassium carbonate–acetone method, diacetylphloroglucinol 1-ethyl ether gave *diacetylphloroglucinol 1-ethyl 3 : 5-dimethyl ether* which separated from light petroleum in flat needles, m. p. 63° (Found : C, 63·4; H, 7·1. $C_{14}H_{18}O_5$ requires C, 63·2; H, 6·8%). Similarly diacetylphloroglucinol 1 : 5-diethyl ether gave *diacetylphloroglucinol 1 : 5-diethyl 3-methyl ether*, plates, m. p. 107° (from light petroleum) (Found : C, 64·2; H, 7·0. $C_{15}H_{20}O_5$ requires C, 64·3; H, 7·2%). The isomeride *diacetylphloroglucinol 1 : 3-diethyl 5-methyl ether* was prepared from diacetylphloroglucinol 1-methyl ether with ethyl sulphate or iodide and formed prisms, m. p. 79—80°, from light petroleum (Found : C, 64·2; H, 7·2%).

Diacetylphloroglucinol 1 : 5-Dibenzyl Ether.—Etherification of diacetylphloroglucinol 1-benzyl ether (3 g.) with benzyl bromide (1·3 ml.), potassium carbonate (1·4 g.), and a trace of potassium iodide in boiling acetone (150 ml.) for 8 hours gave the *1 : 5-dibenzyl ether* which separated from dilute alcohol and then light petroleum–benzene in plates (2·9 g.), m. p. 112°, with a brown-red ferric reaction (Found, in specimen dried in a high vacuum at 60° : C, 74·1; H, 6·1. $C_{24}H_{22}O_5$ requires C, 73·9; H, 5·7%). Methylated by the methyl iodide–potassium carbonate method, this compound gave *diacetylphloroglucinol 1 : 5-dibenzyl 3-methyl ether*, prisms, m. p. 93°, from benzene–light petroleum and then dilute alcohol (Found : C, 74·0; H, 6·1. $C_{25}H_{24}O_5$ requires C, 74·2; H, 5·9%). Debenzylation of this gave *diacetylphloroglucinol 3-methyl ether*, crystallising from 40% alcohol in pale fawn, irregular leaflets, m. p. 88°, with a red ferric reaction (Found, in a specimen dried in a high vacuum at 60° : C, 58·5; H, 5·5; OMe, 13·5. $C_{10}H_9O_2$·OMe requires C, 58·9; H, 5·4; OMe, 13·8%). On methylation the 3-methyl ether gave phlorodiacetophenone trimethyl ether, m. p. and mixed m. p. 107°. Ethylation gave phlorodiacetophenone 4 : 6-diethyl 2-methyl ether, m. p. and mixed m. p. 107°. The solid (0·5 g.) obtained by acetylation of diacetylphloroglucinol 3-methyl ether (0·5 g.) with acetic anhydride (6 ml.) and a trace of pyridine was well washed and dried. Crystallised from light petroleum, this gave *diacetylphloroglucinol 1 : 5-diacetate 3-methyl ether* in flat prisms, m. p. 99—100°, with a negative ferric reaction (Found : C, 58·5; H, 5·5; OMe, 8·9. $C_{14}H_{13}O_6$·OMe requires C, 58·4; H, 5·3; OMe, 10·1%).

Triacetylphloroglucinol.—A mixture of phloroglucinol (5 g.), acetic acid (5 ml.), and acetic anhydride (15 g.) was rapidly saturated with boron trifluoride without external cooling. Precipitated with water, the resulting complex was decomposed with hot 80% alcohol, giving *triacetylphloroglucinol* in pale cream-coloured needles (6 g.), m. p. 156°, with an intense dark red ferric reaction and giving an intense green colour with alkaline hydrogen peroxide (Found, in a specimen dried in a high vacuum at 80° : C, 57·1; H, 5·1. $C_{12}H_{12}O_6$ requires C, 57·1; H, 4·8%). Prepared by the methyl sulphate–potassium carbonate method, the *trimethyl ether* crystallised from dilute alcohol in colourless prisms, m. p. 122—124° [Found : C, 61·2; H, 6·1; OMe, 29·2. $C_{12}H_9O_3(OMe)_3$ requires C, 61·2; H, 6·2; OMe, 31·6%].

C-Methylphloracetophenone 4 : 6-Dimethyl Ether.—Interaction of *C*-methylphloroglucinol 2 : 4-dimethyl ether (2 g.) with acetic acid (5 ml.), acetic anhydride (3 g.), and excess of boron trifluoride at 20—30°, followed by decomposition of the product with hot 70% alcohol, gave *C*-methylphloracetophenone 4 : 6-dimethyl ether, forming faintly yellow prisms (1·5 g.), m. p. 145°, from alcohol with a brownish-red ferric and a negative indophenol reaction, identical with an authentic specimen (cf. Curd and Robertson, Part I, *J.*, 1933, 437, who give m. p. 141—142°). Replacement of *C*-methylphloroglucinol 2 : 4-dimethyl ether with the trimethyl ether gave the same product when the reaction was carried out at 20—30° or at 100°.

2 : 4-*Diacetyl-6-methylphloroglucinol.*—A mixture of *C*-methylphloroglucinol (1 g.), acetic acid (10 ml.), acetic anhydride (1·5 g., 2 mol.), and excess of boron trifluoride was kept at room temperature for 20 hours and treated with water. Decomposition of the resulting solid with hot 80% alcohol yielded 2 : 4-diacetyl-6-methylphloroglucinol, forming colourless needles (0·9 g.), m. p. 160°, from dilute alcohol or on sublimation in a high vacuum (Found, in a specimen dried in a high vacuum at 80° : C, 58·8; H, 5·6. Calc. for $C_{11}H_{12}O_5$: C, 58·9; H, 5·4%). With an excess of acetic anhydride the product consisted of 2 : 4-diacetyl-6-methylphloroglucinol 1 : 5-diacetate which separated from light petroleum in needles, m. p. 116°, with an intense red ferric and a negative indophenol reaction (Found : C, 58·2; H, 4·9. Calc. for $C_{15}H_{16}O_7$: C, 58·4; H, 5·2%). The orientation of this compound follows from its production by ozonolysis of decarbousnic acid (cf. Schöpf and Ross., *loc. cit.*).

Methylated by the methyl sulphate–potassium carbonate method in boiling acetone for 2 hours, 2 : 4-diacetyl-6-methylphloroglucinol gave an almost quantitative yield of the *trimethyl ether*, separating from light petroleum (b. p. 40—60°) in colourless prisms, m. p. 66—67°, insoluble in aqueous sodium hydroxide and with a negative ferric reaction [Found : C, 63·1; H, 7·0; OMe, 35·0. $C_{11}H_9O_2(OMe)_3$ requires C, 63·2; H, 6·9; OMe, 35·0%].

Acetylation of 2 : 4-diacetyl-6-methylphloroglucinol (0·5 g. of anhydrous compound) with acetic anhydride (17 ml.) and sodium acetate (3 g.) for 3 days at room temperature gave the triacetate, isolated by evaporation of the filtered reaction mixture and crystallised from dilute methanol as colourless plates (0·5 g.), m. p. 86°, with a negative ferric reaction. The same compound was formed on addition of a drop of pyridine to the diketone (1 g.) in acetic anhydride (10 ml.) followed by water 24 hours later. The mixture was then cooled to 0° and on being agitated gave an almost quantitative yield of the triacetate which, on recrystallisation from dilute alcohol, had m. p. and mixed m. p. 86—87° (Found : C, 58·1; H, 5·1. Calc. for $C_{17}H_{18}O_8$: C, 58·3; H, 5·2%). When the aqueous solution was kept according to Schöpf and Ross (*loc. cit.*) 2 : 4-diacetyl-6-methylphloroglucinol 1 : 5-diacetate was obtained instead and formed colourless needles (1 g.), m. p. and mixed m. p. 116°, from dilute alcohol.

When water (0·4 ml.) was added to a solution of the triacetate (2·5 g.) in pyridine (10 ml.), crystalline 2 : 4-diacetyl-6-methylphloroglucinol 1 : 5-diacetate, m. p. and mixed m. p. 116°, gradually separated. The ready hydrolysis of the triacetate in this manner serves to explain the failure of Schöpf and Ross (*loc. cit.*) to obtain the compound by the pyridine–acetic anhydride method under the conditions employed to isolate the product. Methylation of this diacetate (1·7 g.) with methyl iodide (3 ml.) and potassium carbonate (1·5 g.) in boiling acetone (50 ml.) for 4 hours gave an oil which was dissolved in ether and washed with aqueous sodium hydroxide and then water. The residue left on evaporation of the dried ethereal solution was crystallised from light petroleum, giving 2 : 4-*diacetyl-6-methylphloroglucinol 5-acetate* 1 : 3-*dimethyl ether* in colourless thick leaflets (0·8 g.), m. p. 79—80°, with a negative ferric reaction [Found : C, 59·0; H, 6·1; OMe, 19·9. $C_{13}H_{12}O_4(OMe)_2$ requires C, 58·8; H, 5·9; OMe, 20·2%]. On deacetylation with 10% hydrochloric acid (6 ml.) in alcohol (10 ml.) for 8 hours, this product gave *C*-methylphloracetophenone 4 : 6-dimethyl ether, m. p. 144°, identical with an authentic specimen, a result which serves to orient the parent compound.

2 : 4-*Diacetyl-6-methylphloroglucinol 3-Methyl Ether.*—A mixture of *C*-methylphloracetophenone 6-methyl ether (0·7 g.), acetic acid (5 ml.), acetic anhydride (3 ml.), and excess of boron trifluoride was kept at 80° for 1 hour, and then heated until boron trifluoride effervesced for 20 minutes. On isolation in the usual manner 2 : 4-*diacetyl-6-methylphloroglucinol 3-methyl ether* was extracted from the crude product with hot light petroleum and purified from dilute alcohol, forming large flat needles (0·4 g.), m. p. 94°, with a brownish purple ferric and a negative indophenol reaction (Found : C, 61·0; H, 5·9; OMe, 14·6. $C_{11}H_{11}O_4 \cdot OMe$ requires C, 60·5; H, 5·9; OMe, 13·1%). The residue, insoluble in light petroleum, consisted of a little unchanged *C*-methylphloracetophenone 6-methyl ether. Methylated by the methyl sulphate–potassium carbonate method, 2 : 4-diacetyl-6-methylphloroglucinol 3-methyl ether gave 2 : 4-diacetyl-6-methylphloroglucinol trimethyl ether, m. p. and mixed m. p. 66—67°.

Prepared by the acetic anhydride–pyridine method, 2 : 4-*diacetyl*-6-*methylphloroglucinol* 1 : 5-*diacetate* 3-*methyl ether* formed diamond-shaped plates, m. p. 169°, from dilute alcohol, with a negative ferric reaction (Found in sample dried in high vacuum at 80° : C, 59·9; H, 5·5. $C_{15}H_{15}O_6$·OMe requires C, 59·6; H, 5·6%).

2 : 4-*Diacetyl*-6-*methylphloroglucinol* 1-*Methyl Ether*.—(*a*) A mixture of *C*-methylphloroglucinol 2-methyl ether (2 g.), acetic anhydride (3 ml.), and excess of boron trifluoride in ether (4 ml.) was kept at 20° for 24 hours and treated with water. Decomposition of the yellow solid with hot 80% alcohol gave 2 : 4-diacetyl-6-methylphloroglucinol 1-methyl ether in colourless needles (2·2 g.), m. p. 97°, having a rose-red ferric and a negative indophenol reaction (Found, in a specimen dried at 60° : C, 60·4; H, 6·0; OMe, 13·0. Calc. for $C_{11}H_{11}O_4$·OMe : C, 60·5; H, 5·9; OMe, 13·0%). On methylation with an excess of methyl sulphate (2·3 ml.) and potassium carbonate (0·35 g.) in boiling acetone this compound (0·6 g.) yielded 2 : 4-diacetyl-6-methylphloroglucinol trimethyl ether, m. p. and mixed m. p. 66—67°, and a small amount of an alkali-soluble product which formed elongated prisms, m. p. 59·5—60·5°, from light petroleum or alcohol, with a purple-red ferric reaction, and is provisionally regarded as 2 : 4-diacetyl-6-methylphloroglucinol 1 : 5-dimethyl ether. A small amount of *C*-methylphloracetophenone 4-methyl ether was isolated from the original 80% alcoholic liquors which had m. p. 195°, undepressed on admixture with authentic material, m. p. 197° (Curd and Robertson, *J.*, 1933, 1173).

A slightly improved yield of 2 : 4-diacetyl-6-methylphloroglucinol 1-methyl ether was obtained when *C*-methylphloroglucinol 2-methyl ether was replaced by *C*-methylphloracetophenone 4-methyl ether in the boron trifluoride reaction.

(*b*) Methylation of 2 : 4-diacetyl-6-methylphloroglucinol (1 g.) with methyl iodide or sulphate (1·25 mol.) and potassium carbonate (1 ml.) in boiling acetone (100 ml.) for 6 hours gave the 1-methyl ether which was isolated from the crude reaction product with hot light petroleum and crystallised from dilute alcohol, forming colourless needles (0·6 g.), m. p. 97°. This ether was also prepared from 2 : 4-diacetyl-6-methylphloroglucinol with a slight excess of diazomethane in benzene and subsequent evaporation of the mixture in a vacuum. Attempts to acetylate the ether by the pyridine method failed.

When a solution of 2 : 4-diacetyl-6-methylphloroglucinol 1-methyl ether (0·5 g.) in 2N-sodium hydroxide (25 ml.) was kept at 80° for 20 minutes and acidified, the resulting precipitate consisted of *C*-methylphloracetophenone 4-methyl ether, m. p. 198° after purification from dilute alcohol (Part I, *loc. cit.*), which had a reddish-blue ferric and a purple indophenol reaction, and by the acetic anhydride–pyridine method yielded a *diacetate*, separating from dilute alcohol in colourless needles, m. p. 85°, with a negative ferric reaction (Found : C, 59·9; H, 5·6. $C_{14}H_{16}O_6$ requires C, 60·0; H, 5·7%).

Action of Ammonia on Diacetylphloroglucinol 1-*Methyl Ether*.—On being kept the yellow solution of diacetylphloroglucinol 1-methyl ether in a little ammonia (*d* 0·880) became dark red and deposited a crystalline product. Recrystallised from dilute alcohol, the *substance* formed pale pink leaflets, m. p. 242°, with sintering at 240°, which had a brownish-red ferric and a deep mauve indophenol reaction (Found, in a specimen dried in a high vacuum at 80° : C, 59·3; H, 6·0; N, 6·4; OMe, 13·0. $C_{10}H_{10}O_3N$·OMe requires C, 59·2; H, 5·9; N, 6·3; OMe, 13·5%). With 1% aqueous sodium hydroxide it formed a yellow and in 10% hydrochloric acid a colourless solution. On being boiled the alkaline solution liberated ammonia.

Formed in a similar manner, the *product* from 2 : 4-diacetyl-6-methylphloroglucinol 1-methyl ether separated from dilute alcohol in colourless needles, m. p. 250°, and had the same properties having a dark greenish-blue ferric and a negative indophenol reaction (Found, in a specimen dried in a high vacuum at 80° : C, 60·6; H, 6·5; N, 5·7; OMe, 13·6. $C_{11}H_{12}O_3N$·OMe requires C, 60·8; H, 6·4; N, 5·9; OMe, 13·1%).

UNIVERSITY OF LIVERPOOL. [*Received, December 29th*, 1952.]