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GENERATION OF SPIRODIENONES RELATED TO GILMICOLIN AND MYCORRHIZIN A

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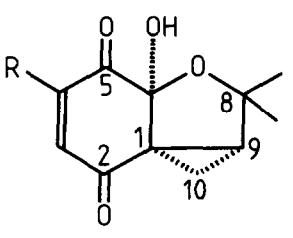
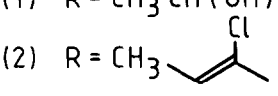
Summary: Treatment of 2,2-dimethyl-3-iodochroman-5-ols (6) and (7) with KOH supported on Al_2O_3 gives acid-sensitive spirodienones (8) and (9); the possible biosynthetic significance of this model reaction is considered.

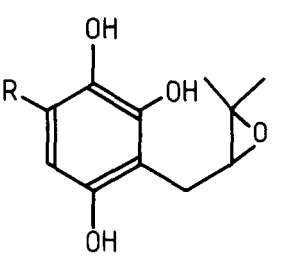
Tamm and his collaborators[1] have proposed that metabolites of the fungus *Gilmaniella humicola* Barron including gilmicolin (1) and mycorrhizin A (2)[2] are formed from a biosynthetic intermediate of the type (3). The co-occurrence of mycorrhizinol (4) suggests that the cyclopropane rings of (1) and (2) may be formed through an intermediate phenolic chroman-3-ol, similar to (4), by conversion of the 3-hydroxyl group to an effective leaving group and subsequent internal C-alkylation. We now report the generation of spirodienones related to (1) and (2) by a route based on these biosynthetic ideas.



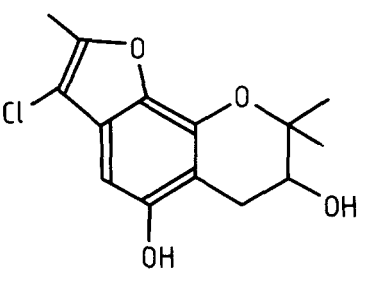
(1) R = $CH_3CH(OH)CH_2$–



(2) R = CH_3



(3)



(4)

Direct prenylation of orcinol with 2-methylbut-3-en-2-ol in aqueous formic acid[3] at 80° gave a 2 : 3 mixture of 2-prenyl- and 4-prenylorcinol which was separated by flash chromatography on silica[4] with 15% ethyl acetate - light petroleum. The more symmetrical 2-prenylorcinol (5) (15% yield), m.p. 76-77° (Found: *m/e* 192. C, 75.2; H, 8.6. $C_{12}H_{16}O_2$ requires M, 192; C, 75.0; H, 8.4%) was distinguished from the 4-prenyl isomer (22%), m.p. 63-64°, by the greater simplicity of its ^{13}C NMR spectrum. 2-Prenylorcinol ($CDCl_3$): δ 17.88, 22.30, 25.81, 122.11, 134.98 (prenyl chain); 21.07 (5-CH_3); 109.17 (C4

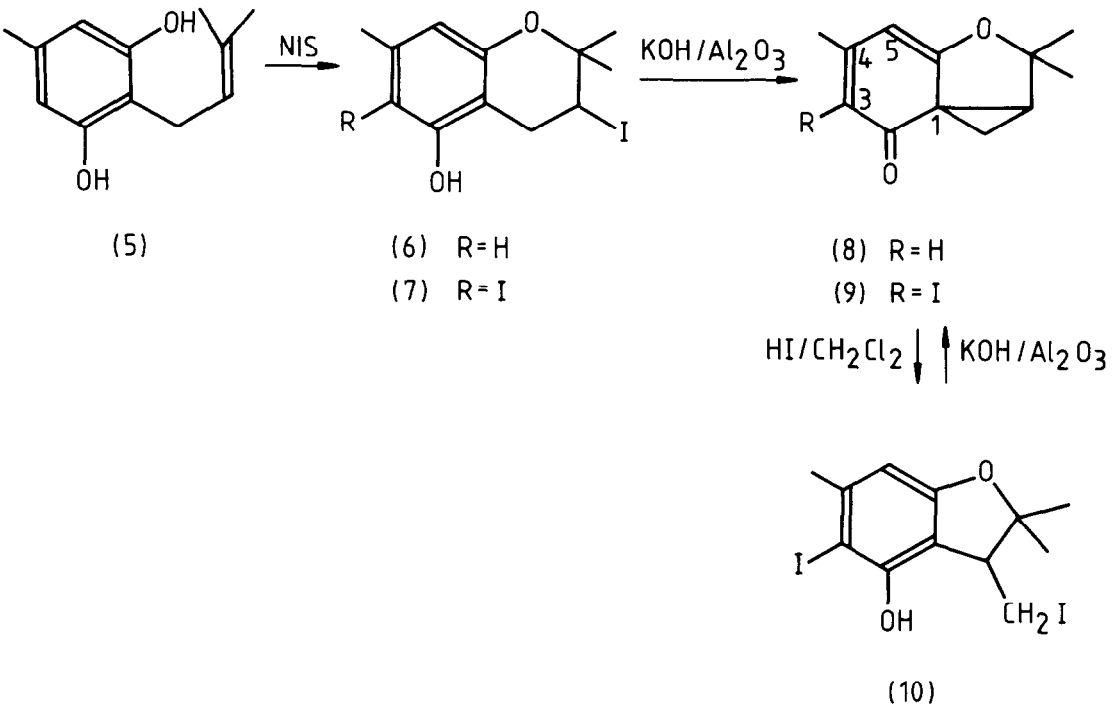
and C6), 110.79 (C2), 137.58 (C5), 154.87 (C1 and C3). 4-Prenylorcinol ($CDCl_3$): δ 17.88, 25.16, 25.75, 122.56, 133.22 (prenyl chain); 19.96 (5-CH_3); 101.23 (C2), 109.95 (C6), 118.40 (C4), 138.75 (C5), 154.22, 155.14 (C1, C3).

Iodocyclization[5] of (5) with one equivalent of N-iodosuccinimide (NIS) in dichloromethane at 30° for 1 h afforded a mixture of the 3-iodochromanol (6), m.p. 86-87° (34%) and the 3,6-diiodochromanol (7), m.p. 139-140° (15%), but the reaction was capricious and the chromatographic separation was tedious. However the use of *two* equivalents of NIS at 0° for 24 h readily gave the 3,6-diiodochromanol (7) alone in 50% yield (Found: *m/e* 444. C, 32.1; H, 3.1%. $C_{12}H_{14}O_2I_2$ requires M, 444; C, 32.5; H, 3.2%). IR and ^1H NMR spectra of these 3-iodochromanols were consistent with those of compounds previously reported.[5]

Slow passage of a solution of (7) (120 mg) in dichloromethane (50 ml) through a column of KOH supported on alumina[6,7] (3 g) gave a yellow solution containing the spirodienone (9). Crude (9) was obtained on evaporation and sublimation of the residue at 55°/0.25 mm Hg as a yellow glass (58 mg) which showed the following properties: *m/e* 316 ($C_{12}H_{13}O_2I$, 34%), 301 (M-CH_3, 100), 189 (M-I, 11), 174 (M-I, CH_3, 37). IR ($CHCl_3$) 1660s, 1630s, 1590m cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$) δ 1.40, 1.47 (CMe_2); 2.42 s (=CMe); an AMX system due to the cyclopropane ring, 1.75 dd, J 5.9, 3.1 Hz and 2.00 dd, J 7.5, 3.1 Hz (CH_2), 2.98 dd, 7.5, 5.9 Hz (CH); 5.65 s (H5). λ_{max} (CH_2Cl_2) 395 nm (ε >5000).

Solutions in dichloromethane were stable for several days at 0°, but were very sensitive to traces of acid (see below).

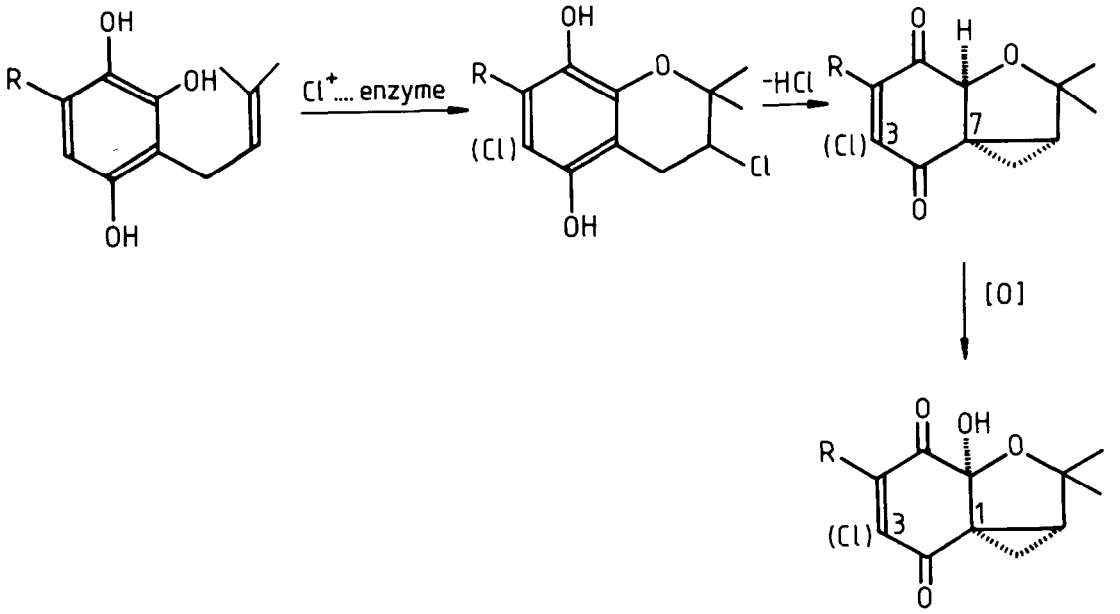
Allylic coupling was evident in the ^1H NMR spectrum of the spirodienone (8) ($J_{H3 - 4CH_3}$ = 1.3 Hz) obtained from the less readily available (6). The absence of this coupling in the spectrum of (9) confirms the location of the iodine substituent at C3. Other spectroscopic properties of (8) were similar to those of (9) but the ultraviolet absorption maximum of (8) was shifted to 375 nm.



(5) (6) R=H (7) R=I (8) R=H (9) R=I (10)

Addition of HI in dichloromethane to a yellow solution of spirodienone (9) decolourized it immediately, but did not regenerate (7). Evaporation of the solution gave instead an oil formulated as the iodomethyl compound (10) on the basis of the following spectra. MS: *m/e* 317 (M - I, 42%), 190 (M - I_2, 100), 175 (M - I_2, CH_3, 63). IR (film) 3380 (OH), 1614, 1598 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$) δ 1.47 s and 1.58 s (CMe_2); 2.22 s ($ArCH_3$); 3.23 t, 9 Hz and 3.56 dd, 9, 2 Hz ($-CH_AH_BI$); 3.85 dd, 9, 2 Hz ($C\underline{H}-CH_2I$); 5.57, br s (OH); 6.19 s (ArH). Slow passage of a dichloromethane solution of (10) through a KOH/alumina column regenerated the spirodienone (9), as shown by UV and NMR spectroscopy.

These model experiments offer some promise for the synthesis of metabolites (1) and (2), but the sequence above may also have more direct biosynthetic significance. The isolation of many chlorine-containing substances from *G. humicola* suggests the possibility of the following pathway for the biosynthesis of metabolites with the tricyclo[4.4.0.0.^{1,9}]-7-oxadecane skeleton. At least two such compounds bear additional chlorine at C3.^{1,2,8}



REFERENCES

1. K. K. Chexal, C. Tamm, J. Clardy, and K. Hirotsu, *Helv. Chim. Acta*, 62, 1129 (1979).

2. J. Trofast and B. Wickberg, *Tetrahedron*, 33, 875 (1977).

3. L. Jurd, K. Stevens, and G. Manners, *Tetrahedron Lett.*, 2275 (1971).

4. W. C. Still, M. Kahn, and M. Abhijit, *J. Org. Chem.*, 43, 2923 (1978).

5. A. Bongini, G. Cardillo, M. Orena, G. Porzi, and S. Sandri, *Tetrahedron Lett.*, 2545 (1979).

6. R. Baird and S. Winstein, *J. Am. Chem. Soc.*, 79, 4238 (1957).

7. J. Castello and G. A. Fletcher, *J. Chem. Soc.*, 3245 (1956).

8. P. Bollinger and T. Zardin-Tartaglia, *Helv. Chim. Acta*, 59, 1809 (1976).

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