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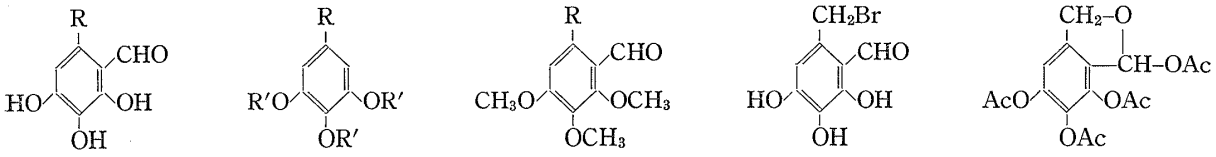
Syntheses of Fomecins A and B, Antibiotics produced by the Basidiomycete *Fomes juniperinus*

Fomecins A and B, phenolic antibiotics produced by the basidiomycete *Fomes juniperinus* SCHRENK, were synthesized starting from gallic acid.

Keywords——synthesis; fomecin A; fomecin B; antibiotic; phenol; *Fomes juniperinus*; basidiomycete

Fomecins A and B, isolated from the culture liquid of the basidiomycete *Fomes juniperinus* SCHRENK, have been characterized as 6-hydroxymethyl-2,3,4-trihydroxybenzaldehyde (**1**) and 3,4,5-trihydroxyphthalaldehyde (**2**), respectively.[1] They show weak but rather broad antibacterial activities and antiviral activities.[1a] Chemical characteristics of such polyhydric phenols, combined with their biological activities, led us to undertake the syntheses of these two antibiotics.

3,4,5-Trimethoxybenzylalcohol (**3**), prepared from gallic acid (**4**) by a known procedure,[2] reacted with dichloromethyl methyl ether in CH_2Cl_2 at 0° (1 hr) with $TiCl_4$ as a catalyst to give 6-chloromethyl-2,3,4-trimethoxybenzaldehyde (**5**) (58%); mp 86°; MS *m/e*: 246 (M+2), 244 (M^+), 209 (M−35); IR (Nujol) 1673 cm^{-1} (CHO); NMR ($CDCl_3$, 60 MHz) δ: 10.45 (s, CHO), 6.95 (s, Ar), 5.05 (s, CH_2Cl), 4.02, 3.97, 3.90 (s, OCH_3). SeO_2 oxidation of **5** in dioxane (reflux, 2 hr) afforded 3,4,5-trimethoxyphthalaldehyde (**6**), mp 97—99°, in 56% yield, which was treated with BBr_3 (−70~20°, 18 hr) in CH_2Cl_2 to give **2**. The conversion of **5** into **2** was also accomplished as follows. Reaction of **5** with $AgNO_3$ in MeOH gave methyl ether (**7**), mp 77°, (92%). Treatment of **7** with BBr_3 in CH_2Cl_2 provided 6-bromomethyl-2,3,4-trihydroxybenzaldehyde (**8**), mp *ca.* 150° (dec.), in 85% yield: MS *m/e*: 248 (M+2), 246 (M^+), 167 (M−79), 166 (M−80); IR (KBr) 1630 cm^{-1} (CHO); NMR (DMSO-d_6) δ: 10.28 (s, CHO), 6.60 (s, Ar), 4.98 (s, CH_2Br). Oxidation of **8** with SeO_2 in dioxane gave **2** in 27% yield; mp *ca.* 230° (dec.); MS *m/e*: 182 (M^+), 154 (M−28), 153 (M−29); UV (EtOH) 264, 287, 343 nm; IR (KBr) 1681, 1627 cm^{-1} (CHO); NMR (acetone-d_6) δ: 12.65 (s, OH), 10.82 (s, CHO), 10.07 (s, CHO), 9.27, 8.87 (s, OH), 7.20 (s, Ar). Melting points and the UV, IR, and NMR spectral data of **2** were consistent with those of fomecin B reported by McMorris and Anchel.[1b,3]



1: R=CH_2OH **3**: R=CH_2OH, R′=CH_3 **5**: R=CH_2Cl **8** **9**
2: R=CHO **4**: R=COOH, R′=H **6**: R=CHO
7: R=CH_2OCH_3

Chart 1

Several attempts to hydrolyze **8** were unsuccessful. However, catalytic hydrogenation of **2** in ethanol under 3 atm hydrogen in the presence of platinum oxide afforded **1** (8%) which was separated from the starting material by countercurrent distribution; mp 160° (dec.);

1) *a*) M. Anchel, A. Hervey, and W.J. Robbins, *Proc. Nat. Acad. Sci.*, **38**, 655 (1952); *b*) T.C. McMorris and M. Anchel, *Can. J. Chem.*, **42**, 1595 (1964).
2) S. Goodwin and B. Witkop, *J. Am. Chem. Soc.*, **79**, 179 (1957).
3) A total synthesis of fomecin B has just been reported: S.M. Al-Mousawi, R.J.S. Green, and J.F.W. McOmie, *Bull. Soc. Chim. Belg.*, **88**, 883 (1979).

MS *m/e*: 184 (M^+), 167 (M−17), 166 (M−18); UV (EtOH) 242, 305 nm; IR (KBr) 1637 cm^{-1} (CHO); NMR (DMSO-d_6) δ: 10.11 (s, CHO), 6.50 (s, Ar), 4.65 (s, CH_2O). **1** was identified by mp, UV, IR, NMR, and MS with an authentic sample of fomecin A. On acetylation, **1** gave the tetraacetate (**9**), mp 134°, which was identical to that derived from natural fomecin A.

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