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A NEW METABOLITE, ASPERMUTARUBROL, FROM ASPERGILLUS SYDOWI

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A new phenolic metabolite, aspermutarubrol, was isolated from Aspergillus sydowi and bis(5-methyl-2,3-dihydroxyphenyl) ether was assigned to this substance from the spectroscopic evidence and the synthesis of its tetramethyl ether.

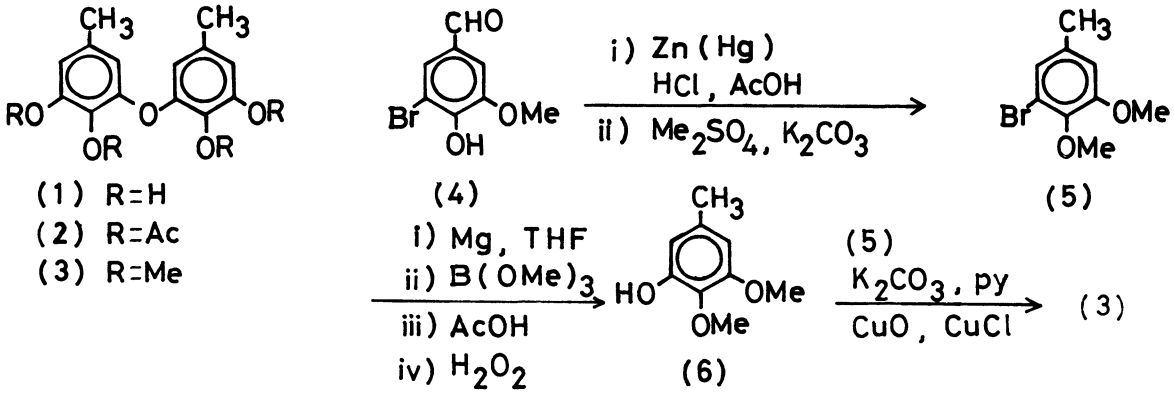
During the course of screening research for plant growth regulators among the metabolites of microorganisms, we have isolated a new phenolic compound from a culture broth of Aspergillus sydowi.[1] This new metabolite, which has no significant plant growth activity but shows antimicrobial activity against A. sydowi itself and gram positive bacteria, was named aspermutarubrol after the nature of turning the culture broth red.

In this communication we report the structure determination of aspermutarubrol (1),[2] $C_{14}H_{14}O_5$, colorless needles from chloroform, mp 148.5-150°, M^+ m/e 262.0828 (calcd. 262.0817), ν_{max} 3320, 1600, 1520, 840 and 820 cm^{-1}, λ_{max}^{EtOH} 229 (ε 13,100), 277 nm (ε 2000), $\lambda_{max}^{EtOH-OH^-}$ 245 (ε 12,300) and 287 nm (ε 4600). It afforded a tetraacetate (2), $C_{22}H_{22}O_9$, M^+ m/e 430.1280 (calcd. 430.1296), oil, on acetylation with acetic anhydride and pyridine (90%). Since the acetate (2) shows no more hydroxyl absorption in the ir spectrum, the oxygen function of (1) is supposed to be four hydroxyl groups and one inactive ether group. Nmr spectra of (1) indicated the presence of the following groups: ^1H nmr (100 MHz, $CDCl_3$-d^6DMSO) 2.20 ($ArCH_3$), 2.5 (broad, OH), 6.35, 6.54 (each d, J=2 Hz, meta coupled aromatic protons) and 7.2 (broad, OH), in the ratio of 3:1:1:1:1, respectively; ^{13}C nmr (25 MHz, CD_3OD) 20.96 (q, CH_3), 111.55, 112.49 (each d, C_4 or C_6), 130.04 (s, C_5), 134.50 (s, C_2), 146.25 and 147.04 ppm (each s, C_1 or C_3). Since the cmr spectrum of (1) shows only seven carbon signals, the molecule has an axis of C_2 symmetry and the $C_7H_7O_2$ units are combined by the ether linkage.[3] Furthermore, in the proton-coupled cmr spectrum the aryl methyl signals appeared as triplets of quartets ($^1J_{C-H}$=125.7 Hz, $^3J_{C-H}$= 4.9 Hz).[4] This indicates the presence of the aryl methyl group flanked by two aromatic protons. The assignment of the other carbon signals (as indicated above)

are based on a combination of off-resonance decoupling and non-decoupling techniques. These data establish the structure (1) for aspermutarubrol. This assignment was confirmed by the synthesis of tetramethyl ether (3).

Clemmensen reduction of the bromide (4), which had been prepared from vanillin by bromination, followed by methylation, gave 3-bromo-4-methyl-1,2-dimethoxybenzene (5) as an oil in 23% yield. The Grignard reagent prepared from the bromide (5) was treated with trimethylborate to give dimethoxyborate. This was then hydrolyzed with acetic acid and oxidized with hydrogen peroxide to give the phenol (6), mp 57-58°, in 69% yield. The phenol (6) was treated with the bromide (5) under the presence of cupric oxide-cuprous chloride and potassium carbonate to give the biphenyl ether (3) as a viscous oil in 42% yield. The spectroscopic and chromatographic data (ir, nmr, ms, glc and tlc) are in accord with those of the corresponding derivatives of natural aspermutarubrol.

The compound (1) in solution is extremely sensitive to air oxidation. The structure of red oxidation products will be the subject of further investigation.



References and Notes

1) Metabolites of A. sydowi; T. Hamasaki, Y. Sato, Y. Hatsuda, M. Tanabe and L.W. Cary, Tetrahedron Letters, 659 (1975), T. Hamasaki, Y. Sato and Y. Hatsuda, Agric. Biol. Chem., 39, 2337 (1975), T. Hamasaki, Y. Sato and Y. Hatsuda, Agric. Biol. Chem., 39, 2341 (1975), T. Hamasaki, K. Nagayama and Y. Hatsuda, Agric. Biol. Chem., 42, 37 (1978).

2) The cultivation of A. sydowi and the isolation and biological activity of (1) will be published eleswhere.

3) In the high-resolution mass spectrum (1) showed the peak corresponding the fragment ion $C_7H_8O_2^+$, m/e 124.0515.

4) The cmr spectrum of 5-methyl-1,2,3-trimethoxybenzene showed following signals: 21.78 ($^1J_{C-H}$=126.9 Hz, $^3J_{C-H}$=4.9 Hz), 55.94 (OMe), 60.77 (OMe), 105.99 (C_4 and C_6), 133.47 (C_5), 135.86 (C_2), 152.96 ppm (C_1 and C_3).

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