Tetrahedron Letters,Vol.23,No.44,pp 4567-4568,1982 0040-4039/82/444567-02$03.00/0
Printed in Great Britain

SYNTHESIS OF COLLETOCHLORIN D

Kau-Ming Chen and Madeleine M. Joullié*

Department of Chemistry, University of Pennsylvania
Philadelphia, Pennsylvania 19104

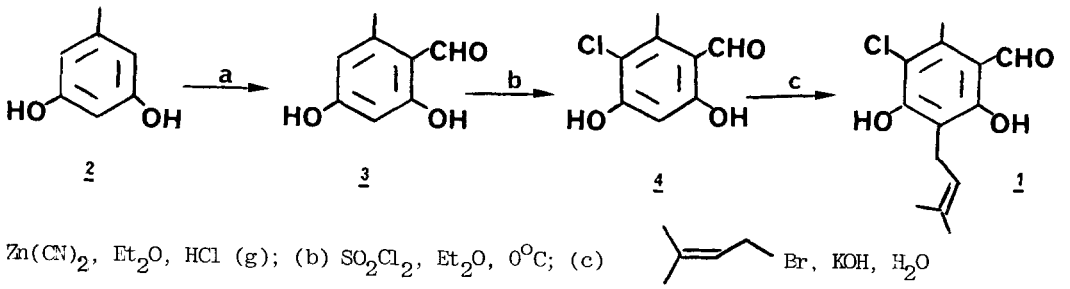
Abstract: An efficient three-step synthesis of Colletochlorin D from orcinol has been achieved.

Colletotrichum nicotianae is the causal fungus of the tobacco disease known as anthracnose.[1] Investigations of the culture filtrates of this fungal strain afforded several compounds containing a 5-chloroorsellinaldehyde moiety and different side chains. These natural prenylated phenols have been named colletochlorins[2] A[3], B, C[3], and D[4]. The syntheses of colletochlorins A and B have been described recently.[5] We had previously attempted the synthesis of colletochlorin D (1) via a multistep route from orcinol (2) but had been unable to demethylate both intermediate protected phenol groups employed in this route.[6] We have now devised a three-step synthesis of 1 from 2. An important feature of the present synthesis is the elimination of protection and deprotection protocols. Our approach may be regarded as a simple, general route to other natural products containing a 5-chloro-orsellinaldehyde (4) unit. The synthesis of 1 is described in the Scheme.

Orcinol (2) is formylated under Gattermann conditions[7] with zinc cyanide in dry ether and anhydrous hydrogen chloride to afford aldehyde 3 mp 178°-180°C, in yields varying from 76-85%.[8]

Chlorination of 3 with sulfuryl chloride in ether[9] at 0° affords a mixture which can be separated by column chromatography on silica gel (ethyl acetate: hexane, 1:5) to yield pure 4[10] as a white solid, mp 168°-170°C, lit[5] mp 130-132°C. Alkylation of 4 with 1-bromo-3-methyl-2-butene in 10% aqueous potassium hydroxide at 0°C,[11] yielded 1 (29%).

Preparative tlc on silica gel plates (ether:petroleum ether, 1:10) afforded pure 1 (25% yield).[12] Colletochlorin D is obtained as white needles by recrystallization from ether-hexane, mp 142-144°C, lit[4] mp 140°-142°C.



(a) $Zn(CN)_2$, Et_2O, HCl (g); (b) SO_2Cl_2, Et_2O, 0°C; (c) Br, KOH, H_2O

REFERENCES AND NOTES

1. F. A. Wolf and J. M. Flowers, Jr., Tobacco Science, 93 (1957).

2. Y. Kosuge, A. Suzuki, S. Hirata, and S. Tamura, Agr. Biol. Chem., 37, 455 (1973).

3. Y. Kosuge, A. Suzuki, and S. Tamura, Agr. Biol. Chem., 38, 1265 (1974).

4. Y. Kosuge, A. Suzuki, and S. Tamura, Agr. Biol. Chem., 38, 1553 (1974).

5. K. Mori, and K. Sato, Tetrahedron, 38, 1221 (1982).

6. A. E. Guthrie, J. E. Semple, and M. M. Joullié, J. Org. Chem., 47, 2369 (1982).

7. W. E. Truce, "Organic Reactions", Vol. IX, R. Adams, ed., John Wiley & Sons, 1957, p. 37.

8. IR (KBr) 3100, 1650, 1600, 1490, 1300, 1260, 1220, 1160, 870, 830, 740, and 720 cm^{-1}; ^1H NMR (C_2D_6CO) δ2.54 (s, 3H, CH_3), 6.30 (d, 1H, =CH), 6.18 (d, 1H, =CH), 9.60 (br,s, 1H, 4-OH), 10.10 (s, 1H, CHO), 12.50 (br s, 1H, 2-OH).

9. J. A. Elix and S. Norfolk, Aust. J. Chem., 28, 1113 (1975).

10. IR (KBr) 3000, 1650, 1600, 1420, 1380, 1260, 1220, 840, 760, and 725 cm^{-1}; ^1H NMR (C_2D_6CO) δ2.65 (s, 3H, CH_3), 6.40 (s, 1H, =CH), 9.70 (br s, 1H, 4.0 H), 10.20 (s, 1H, CHO), 12.52 (br.s, 1H, 2-OH); high resolution mass spectrum, elemental composition of M calcd. for $C_8H_7O_3Cl$: 186.00835, found: 186.0079. Although there is a discrepancy between our melting point and that reported in the literature, we are certain of the purity of product 3.

11. T. Meikle and R. Stevens, J. Chem. Soc., Perkin I, 1303 (1978).

12. IR (KBr) 3200, 1650, 1280, 1170, 1100, 905, 795 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.69 (s, 3H, ), 1.79 (s, 3H, ), 2.60 (s, 3H, Ar-CH_3), 3.39 (d, 2H, J = 7.1 Hz, Ar-CH_2), 5.22 (t, 1H, ), 6.41 (br.s, 1H, 4-OH), 10.14 (s, 1H, CHO), 12.69 (s, 1H, 2-OH); high resolution mass spectrum, elemental composition of M calcd for $C_{13}H_{15}O_3Cl$: 254.07097, found: 254.0671.

(Received in USA 16 August 1982)