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THALLIUM (III) TRIFLUOROACETATE OXIDATION OF SOME ESTERS HAVING TWO C_6-C_3 UNITS

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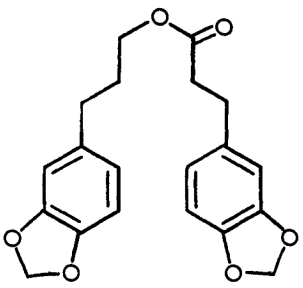
Some esters with two C_6-C_3 units have been oxidized with thallium (III) trifluoroacetate to afford the corresponding lactones of medium-sized rings, one of which is an 11-membered ring lactone, an 8,8'-secosteganacin-type compound.

Thallium (III) trifluoroacetate (TTFA) as an oxidizing agent has been successfully used for biaryl syntheses by Taylor, McKillop, and their co-workers.[1] Interestingly, the synthesis of an isostegane has also been carried out using TTFA,[2] which seems to be superior to $VOCl_3$ or VOF_3 in this case.

From view points of biological and antitumor activities, we have synthesized many different types of neolignan by means of electrochemical oxidation of phenolic compounds.[3] In connection with our synthetic studies of these neolignans, we wish to describe oxidation of some esters having two C_6-C_3 units with TTFA in trifluoroacetic acid, affording some biogenetically plausible compounds (8,8'-secosteganacin-type neolignan and others), although they have not yet been found in nature.

3-(3',4'-Methylenedioxyphenyl)propionic acid reacted with 3-(3',4'-methylenedioxyphenyl)propanol in pyridine containing DCC and catalytic amount of TsOH (room temp., 14 h) to afford the corresponding ester (1)[4] in almost quantitative yield, which was subjected to oxidation with TTFA in trifluoroacetic acid (room temp., 3 min) giving a desirable lactone (2) of an 11-membered ring in 14% yield, whose structure was unambiguously determined on the basis of its spectral data[5] coupled with the following chemical evidence: on reduction with $LiAlH_4$ in Et_2O (room temp., 1 h) followed by acetylation with Ac_2O - pyridine, the lactone (2) was readily converted into a diacetate (3)[6] in almost quantitative yield, whose ^1H NMR spectrum has two sharp singlets assignable to two different types of isolated aromatic protons. This compound was also produced in 69% yield by oxidation of 3-(3',4'-methylenedioxyphenyl)propyl acetate with TTFA in trifluoroacetic acid (room temp., 10 min). Furthermore, 3 was reconverted into the 11-membered ring lactone (2) in ca. 5% yield, when hydrolized with 0.5M MeONa in dioxane followed by oxidation with pyridinium chlorochromate in CH_2Cl_2 (room temp., overnight).

According to essentially the same procedure as described in 1, an ester (4)[7] was synthesized from 3-(3',4',5'-trimethoxyphenyl)propionic acid and 3-(3',4'-methylenedioxyphenyl)propanol in almost quantitative yield. This ester (4) was also oxidized with TTFA in trifluoroacetic acid (room temp., 10 min) to afford a 13-membered ring lactone (5), in 65% yield, via a plausible intermediate (6).[8] When the reaction mixture was quenched with MeOH instead of H_2O, the corresponding lactone (7)[9] with a newly introduced MeO group was obtained in 53% yield. The structure of 5 was elucidated by its spectral data[10] coupled with some chemical evidence. The ^1H NMR spectrum of 5 has a methine triplet at δ5.53, which is shifted to lower magnetic field (δ6.30) on acetylation with Ac_2O - pyridine affording the corresponding acetate (8).[11] Furthermore, when treated with $LiAlH_4$ in THF



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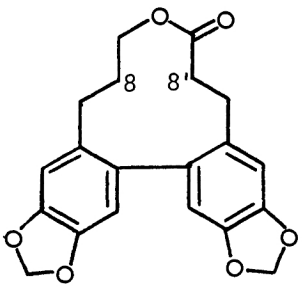

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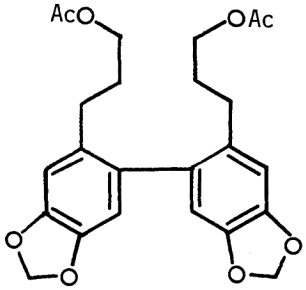

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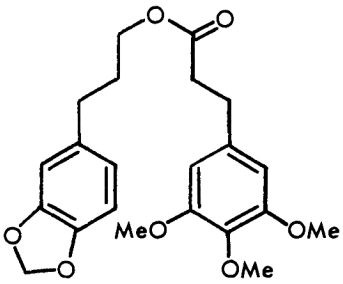

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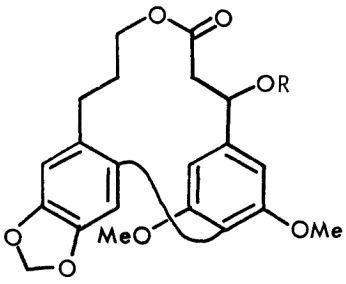
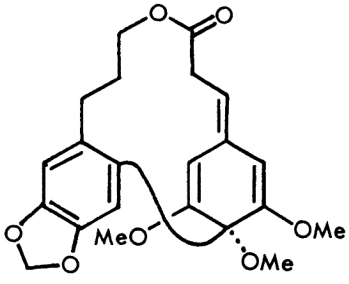


5 R = H ; 7 R = Me
8 R = Ac



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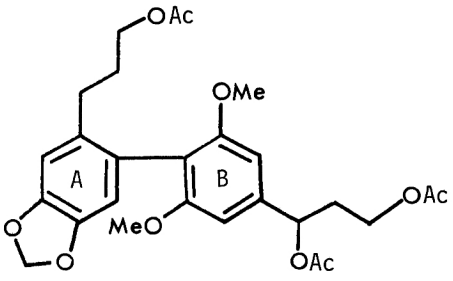

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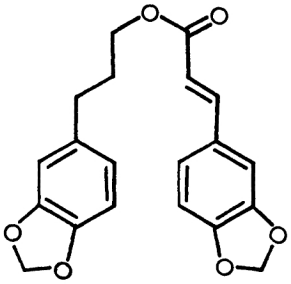
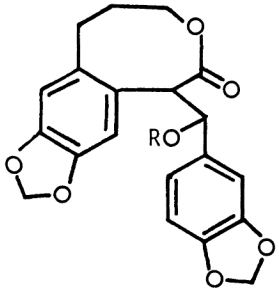


10



11 R = H
12 R = Ac

(room temp., 4 h) and then acetylated with Ac_2O - pyridine, 5 was readily converted into a triacetate (9),[12] whose ^1H NMR spectrum ($CDCl_3$) has two sharp singlets at δ 3.63 and 6.50, suggesting that 5 has the two equivalent MeO groups as well as the two equivalent protons attached to the B ring.

We also made a conjugated ester (10)[13] from 3-(3',4'-methylenedioxyphenyl)propanol and 3,4-methylenedioxycinnamic acid under the similar condition to that of 1. When treated with TTFA in trifluoroacetic acid - CH_2Cl_2 (3 : 5) containing small amount of BF_3·etherate (room temp., 2 min), the ester (10) was converted into an 8-membered ring lactone (11)[14] in 36% yield, which was characterized as its acetate (12).[15] In cases of the two esters derived from 3-(3',4'-methylenedioxyphenyl)allyl alcohol and 3-(3',4'-methylenedioxyphenyl)propionic acid or 3,4-methylenedioxycinnamic acid, however, the reaction mixture was too complex to be separable.

Further synthetic studies on lactones as well as on lactams of medium- and large-sized rings, usig thallium (III) salts, are in progress.

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References

1. A. McKillop, A. G. Turrell, D. W. Young, and E. C. Taylor, J. Am. Chem. Soc., 102, 6504 (1980) and many references cited therein; E. C. Taylor, J. G. Andrade, G. J. H. Rall, and A. McKillop, ibid., 102, 6513 (1980).

2. R. C. Cambie, M. G. Dunlop, P. S. Rutledge, and P. D. Woodgate, Synthetic Commun., 10, 827 (1980).

3. M. Iguchi, A. Nishiyama, H. Eto, and S. Yamamura, Chem. Lett., 1981, 939; ibid., 1979, 1397; M. Iguchi, A. Nishiyama, Y. Terada, and S. Yamamura, Analytical Lett., 12 (A 10), 1079 (1979) and references cited therein.

4. 1: mp 42 - 44 °C; $C_{20}H_{20}O_6$ [m/e 356(M^+)]; ν_{max} (Nujol) 1730, 1630, 1605, and 1500 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.87(2H, m), 2.4-3.0(6H, complex), 3.98(2H, t, J= 6Hz), 5.82(4H, s), and 6.5-6.8(6H, complex).

5. 2: mp 141 °C; $C_{20}H_{18}O_6$ [m/e 354(M^+)]; ν_{max} (Nujol) 1720 and 1500 cm^{-1}; ^1H NMR ($CDCl_3$): δ1.90(2H, m), 2.3-2.7(6H, complex), 3.77(2H, t, J= 6Hz), 5.83(4H, s), 6.37(1H, s), 6.40(1H, s), and 6.67(2H, s).

6. 3 as a syrup: $C_{24}H_{26}O_8$ [m/e 442(M^+)]; ν_{max} (film) 1730, 1610, and 1500 cm^{-1}; ^1H NMR ($CDCl_3$): δ1.93 (6H, s), 1.4-2.0(4H, m), 2.32(4H, br.t, J= 7.5Hz), 3.83(4H, t, J= 6Hz), 5.87(4H, s), 6.48(2H, s), and 6.65(2H, s).

7. 4 as a syrup: $C_{22}H_{26}O_7$ [m/e 402(M^+)]; ν_{max} (film) 1730 and 1580 cm^{-1}; ^1H NMR ($CDCl_3$): δ1.90(2H, m),

2.4-3.0(6H, complex), 3.73(3H, s), 3.77(6H, s), 4.00(2H, t, J= 6Hz), 5.83(2H, s), 6.35(2H, s), and 6.4-6.8(3H, complex).

8. In this case, any amount of an 11-membered ring lactone has not been obtained.

9. 7: mp 207 - 208 °C; $C_{22}H_{24}O_7$ [m/e 400(M^+)]; ν_{max} (Nujol) 1730, 1605, and 1580 cm^{-1}; ^1H NMR (pyridine-d_5): δ1.22(2H, m), 1.9-2.4(2H, m), 2.63(1H, dd, J= 9, 12Hz), 3.02(1H, dd, J= 6, 12Hz), 3.45(3H, s), 3.55(3H, s), 3.62(3H, s), 3.2-3.6(1H, superimposed on MeO signals), 4.38(1H, br.dt, J= 11, 4Hz), 4.68(1H, dd, J= 6, 9Hz), 5.87(2H, s), 6.67(1H, br.s), 6.87(1H, s), 7.08(1H, br.s), and 7.15(1H, s).

10. 5: mp 210 - 212 °C; $C_{21}H_{22}O_7$ [m/e 386(M^+)]; ν_{max} (Nujol) 3450, 1720, 1600, 1575, and 1500 cm^{-1}; ^1H NMR (pyridine-d_5): δ1.62(2H, m), 2.0-2.5(2H, m), 2.84(1H, dd, J= 8, 12Hz), 3.15(1H, dd, J= 6, 12Hz), 3.55(3H, s), 3.62(3H, s), 3.3-3.6(1H, superimposed on MeO signals), 4.30(1H, br.dt, J= 11, 4.5Hz), 5.53(1H, dd, J= 6, 8Hz), 5.85(2H, s), 6.72(1H, br.s), 6.87(1H, s), 7.12(1H, s), and 7.43(1H, br.s).

11. 8: mp 178 - 179 °C; $C_{23}H_{24}O_8$ [m/e 428(M^+)]; ν_{max} (Nujol) 1740, 1720, 1600, 1575, and 1500 cm^{-1}; ^1H NMR (pyridine-d_5): δ1.22(2H, m), 2.15(3H, s), 2.0-2.5(2H, superimposed on AcO signal), 2.79 (1H, dd, J= 9, 12Hz), 3.09(1H, dd, J= 6, 12Hz), 3.53(3H, s), 3.65(3H, s), 3.4-3.7(1H, superimposed on MeO signals), 4.25(1H, br.dt, J= 11, 4.5Hz), 5.88(2H, s), 6.30(1H, dd, J= 6, 9Hz), 6.80(1H, d, J= 1.5Hz), 6.88(1H, s), 7.10(1H, d, J= 1.5Hz), and 7.15(1H, s); ^{13}C NMR ($CDCl_3$): δ21.1(q), 30.0(t), 31.6(t), 44.6(t), 55.7(q), 55.9(q), 63.3(t), 73.2(d), 100.7(t), 101.5(d), 103.8(d), 110.2(d), 110.7(d), 117.1(s), 127.3(s), 133.0(s), 140.2(s), 145.5(s), 146.3(s), 158.0 (s), 158.8(s), 168.3(s), and 169.5(s).

12. 9 as a syrup: $C_{27}H_{32}O_{10}$ [m/e 516(M^+)]; ν_{max} (film) 1730, 1600, and 1575 cm^{-1}; ^1H NMR ($CDCl_3$): δ1.87(3H, s), 2.02(3H, s), 2.07(3H, s), 1.5-2.5(6H, complex), 3.63(6H, s), 3.80(2H, t, J= 6Hz), 4.10(2H, m), 5.65(1H, t, J= 6Hz), 5.85(2H, s), 6.45(1H, s), 6.50(2H, s), and 6.68(1H, s).

13. 10: mp 96 - 98 °C; $C_{20}H_{18}O_6$ [m/e 354(M^+)]; ν_{max} (Nujol) 1690, 1630, and 1610 cm^{-1}; ^1H NMR ($CDCl_3$): δ1.93(2H, br.tt, J= 6, 7.5Hz), 2.62(2H, br.t, J= 7.5Hz), 4.10(2H, t, J= 6Hz), 5.80(2H, s), 5.90 (2H, s), 6.16(1H, d, J= 16.5Hz), 6.5-7.0(6H, complex), and 7.49(1H, d, J= 16.5Hz).

14. Elemental analysis of this compound (11) has not been carried out.

15. 12: mp 235 - 237 °C; $C_{22}H_{20}O_8$ [m/e 412(M^+)]; ν_{max} (nujol) 1730 and 1605 cm^{-1}; ^1H NMR ($CDCl_3$): δ1.97(3H, s), 1.7-2.3(2H, m, overlapped with Me singlet), 2.80(2H, m), 4.50(2H, m), 4.60(1H, d, J= 10.5Hz), 5.77(4H, br.s), 6.40(1H, s), 6.49(1H, d, J= 10.5Hz), 6.56(1H, d, J= 7.5Hz), and 6.7-6.9(3H, complex).

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