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

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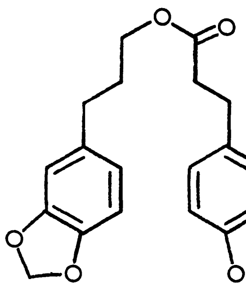
Some esters with two $C_6$-$C_3$ units have been oxidized with thallium (III) trifluoroacetate to afford the corresponding lactones of medium-sized rings, one of which is an 11-membered ring lactone, an 8,8'-secosteganacin-type compound.

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 $^{1}H$ 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 $\delta$5.53, which is shifted to lower magnetic field ($\delta$6.30) on acetylation with $Ac_2O$ - pyridine affording the corresponding acetate (8).[11] Furthermore, when treated with $LiAlH_4$ in THF



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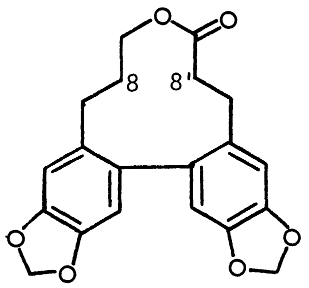

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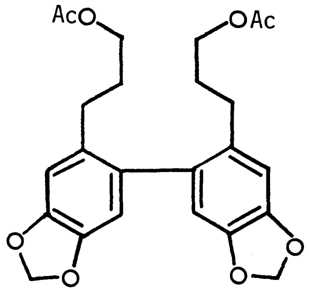

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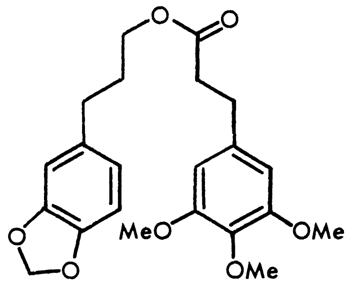

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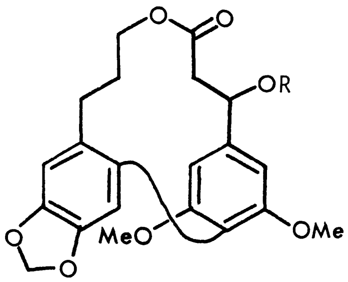
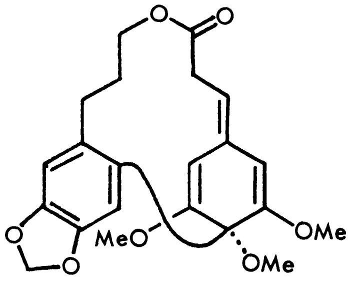


5 R = H ; 7 R = Me
8 R = Ac



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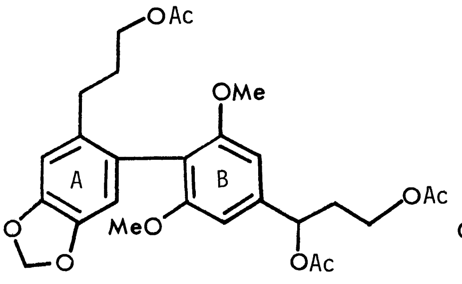

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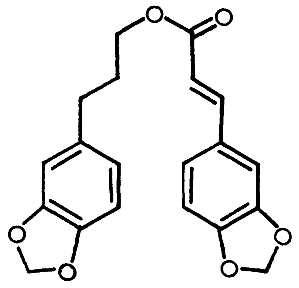

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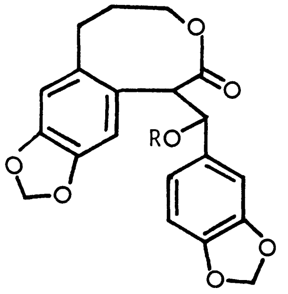

11 R = H
12 R = Ac

(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 $\delta$ 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

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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($M^+$)]; $\nu_{max}$ (Nujol) 1730, 1630, 1605, and 1500 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 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($M^+$)]; $\nu_{max}$ (Nujol) 1720 and 1500 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$1.90(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($M^+$)]; $\nu_{max}$ (film) 1730, 1610, and 1500 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$1.93 (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($M^+$)]; $\nu_{max}$ (film) 1730 and 1580 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$1.90(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($M^+$)]; $\nu_{max}$ (Nujol) 1730, 1605, and 1580 $cm^{-1}$; $^1H$ NMR (pyridine-$d_5$): $\delta$1.22(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($M^+$)]; $\nu_{max}$ (Nujol) 3450, 1720, 1600, 1575, and 1500 $cm^{-1}$; $^1H$ NMR (pyridine-$d_5$): $\delta$1.62(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($M^+$)]; $\nu_{max}$ (Nujol) 1740, 1720, 1600, 1575, and 1500 $cm^{-1}$; $^1H$ NMR (pyridine-$d_5$): $\delta$1.22(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 ($CDCl_3$): $\delta$21.1(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($M^+$)]; $\nu_{max}$ (film) 1730, 1600, and 1575 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$1.87(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($M^+$)]; $\nu_{max}$ (Nujol) 1690, 1630, and 1610 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$1.93(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($M^+$)]; $\nu_{max}$ (nujol) 1730 and 1605 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$1.97(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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