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Synthesis of some model esters of a constituent of shellac with long chain hydroxy and epoxy fatty acids

G B V SUBRAMANIAN, YOUGESH CHANDER and RAFIA NUZHAT
Department of Chemistry, University of Delhi, Delhi 110 007, India

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Abstract. 10*α*, 10*β*- and 13-esters of dimethyl shellolate have been prepared from the corresponding 10-bromo and 13-iodo derivatives and the potassium salt of *threo*-aleuritic and 16-hydroxy *trans* 9,10-epoxy hexadecanoic acids. The epoxide ring was selectively opened under acid catalysis to give the corresponding *erythro*-glycol, the ester function remaining intact.

Keywords. Halogenated terpenes; model esters; shellac; hexamethyl phosphoramide.

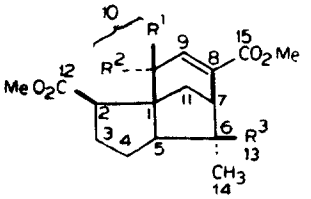
1. Introduction

Attempts have been made to synthesise a number of model esters related to the esters of lac resin (Sukh Dev 1974) aimed at extending to more complex esters including natural esters subsequently. In a previous paper (Subramanian *et al* 1979) the synthesis of some stearate esters of the terpene moiety of shellac was reported. However, attempts to synthesise 10–O–aleuritates were unsuccessful using unprotected aleuritic acid (1). The present paper describes their preparation.

It was felt that a combination of steric factors as well as poorer nucleophilicity of the hydroxy fatty acid moiety were involved as compared to the simple acetylation process (Subramanian *et al* 1977). Among a variety of conditions attempted on the 10-bromo derivative (2), reactions carried out in hexamethyl phosphoramide (HMPA) using the potassium salt of the acids and the halogenated terpenes proved successful in giving the esters. However, the stronger reaction conditions that were necessary led to the formation of a mixture of both the 10*α*- and 10*β*-epimers, necessitating a chromatographic separation. This behaviour was different from the acetylation process where 10*α*-acetates were obtained preferentially. Their separation was successful only in some cases. The products were identified by analytical and spectral data.

Potassium aleuritate and (2) reacted smoothly in HMPA, to give a mixture of 10*α*- and 10*β*-esters. The inference was based on the characteristic and unambiguous n.m.r. signal of the C-10 proton (Subramanian *et al* 1977) in each case

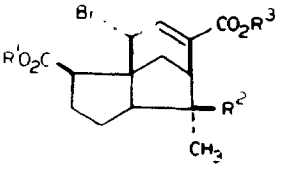
where 10β- was downfield to that of 10α- with a different J value. The separation of this epimeric pair was unsuccessful. The mixture was oxidised with Jones' reagent to give a mixture of the two 10-epimers subsequently esterified to (3) and (4). Column chromatography neatly separated these two and they were characterised by the spectral data. Reaction between the potassium salt of 16-hydroxy *trans* 9,10-epoxy-hexadecanoic acid (Eswaran *et al* 1973) and (2) in HMPA led once again to the formation of both epimers which were readily separated by a column chromatography. Aqueous perchloric acid opened the oxirane ring of both the epimers readily to yield the pure 10α- and 10β- esters of *erythro*-aleuritic acid. Alkaline hydrolysis of these esters gave *erythro*-aleuritic acid as expected.

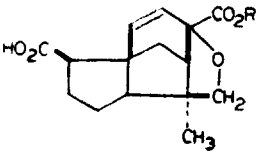


(3) $R^1 = OCO[CH_2]_7CO_2Me$, $R^2 = H$, $R^3 = CH_2OAc$
(4) $R^1 = H$, $R^2 = OCO[CH_2]_7CO_2Me$, $R^3 = CH_2OAc$
(10) $R^1 = OCO[CH_2]_7CH-CH[CH_2]_6OH$, $R^2 = H$, $R^3 = CH_2OAc$

(11) $R^1 = H$, $R^2 = OCO[CH_2]_7CH-CH[CH_2]_6OH$, $R^3 = CH_2OAc$

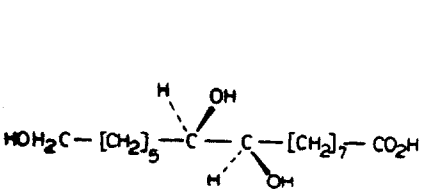
(12) $R^1 = OCO[CH_2]_7CHOHCHOH[CH_2]_6OH$, $R^2 = H$, $R^3 = CH_2OAc$
(13) $R^1 = H$, $R^2 = OCO[CH_2]_7CHOHCHOH[CH_2]_6OH$, $R^3 = CH_2OAc$
(14) $R^1 = OH$, $R^2 = H$, $R^3 = CH_2OCO[CH_2]_7CHOHCHOH[CH_2]_6OH$
(15) $R^1 = OH$, $R^2 = H$, $R^3 = CH_2I$
(16) $R^1 = OH$, $R^2 = H$, $R^3 = Me$
(18) $R^1 = OCO[CH_2]_7CO_2Me$, $R^2 = H$, $R^3 = CO_2Me$

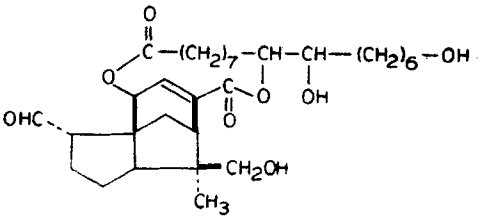




(2) $R^1 = R^3 = Me$, $R^2 = CH_2OAc$
(5) $R^1 = R^3 = Me$, $R^2 = CH_2I$
(6) $R^1 = R^3 = H$, $R^2 = CH_2OAc$
(7) $R^1 = H$, $R^2 = CH_2OAc$, $R^3 = Me$
(17) $R^1 = R^2 = R^3 = Me$

(8) R = H
(9) R = Me





Similarly reaction between (15) (Subramanian *et al* 1980) and potassium aleuritate in HMPA, led to the formation of 13-O-aleuritate (14). This reaction was much slower, required stronger reaction conditions leaving behind unchanged parent compounds. This behaviour contrasts the esterification of the corresponding alcohols where the 13-esters were formed more readily. It was shown by the following results also. (15), on reaction with hydrogen bromide-glacial acetic acid, gave crystalline (5). Treatment with potassium aleuritate in HMPA gave an inseparable mixture of the mono- and di-esters predominated by the 10α- and 10β-esters as shown by n.m.r. spectra. The 10β-esters are representative models for the natural shellac esters (Sukh Dev 1974). In the mass spectrum none of these esters showed the molecular ion peak and the tendency to eliminate the fatty unit was predominant. This was demonstrated by their fragmentation mode which was parallel to that reported (Singh *et al* 1974) for a related ester (18).

For further elaboration of model structures involving more units of both constituents, free C-2 and C-8 carboxy-functions may be required. For example, a low molecular weight ester (19) has been described by Singh *et al* (1978) as a constituent of soft-resin. The acids (6) and (7) were readily prepared from anhydroshellolic acid (8) and its 15-methyl ester (9) respectively by reaction with hydrogen bromide-acetic acid. Unfortunately, these acids formed stable complexes in HMPA and the desired esters could not be prepared.

Ester formation involving 12- and 15-carboxy-functions of the terpene moiety and (9RS, 10RS)-9,10-dihydroxy-16-iodo-hexadecanoate in presence of silver carbonate in acetone solution was reported (Subramanian *et al* 1979). These esters of high purity are obtainable in quantitative yields more easily using the potassium salt of the terpene acids in HMPA.

2. Experimental

Thin layer chromatography (TLC) of the methyl esters was carried out in chloroform–methanol (96 : 4) and of the free acids in toluene–ethylformate–formic acid (5 : 4 : 1) on silica gel plates. Spots were located by spraying with 50% aqueous sulphuric acid followed by charring. Esterifications were carried out in methanolic solution with ethereal diazomethane. Crystallisations were carried out from ethyl acetate-light petroleum (b.p. 60–80°) unless otherwise mentioned. Solvents used in column chromatography are in v/v ratio.

2.1. *Condensation of potassium threo-aleuritate with* 10α-*bromo*-13-*O*-*acetate* (2)

Dimethyl 13-acetoxy-10α-bromocedr-8-ene 12,15-dioate (Subramanian *et al* 1977) (2) (250 mg) and crystalline potassium *threo*-aleuritate (500 mg) were heated in

hexamethyl-phosphoramide (HMPA) (5 ml) at 70° C for 4 hr. The reaction mixture was diluted with ice-cold water and extracted into ethyl acetate. The ethyl acetate extract was washed with dilute hydrochloric acid (1 N) followed by water and dried (anhydrous sodium sulphate). Removal of the solvent gave a gum which appeared to be a mixture of roughly equal amounts of 10β-O-aleuritoyl (12) and 10α-O-aleuritoyl (13) esters based on the signal for the C-10 proton in the n.m.r. spectrum [δ 5·31 (*d*, J 4·5 Hz, CHOCO) for α-isomer and δ 5·68 (*d*, J 2·5 Hz, CHOCO) for β-isomer]. The separation of the two isomers was unsuccessful.

2.2. *Jones' oxidation of the above mixture*

The mixture of 10α- and 10β- aleuritoyl esters (500 mg) in acetone (30 ml) was treated with Jones' reagent (7 ml) [from CrO_3 (2 g) in concentrated sulphuric acid (1·8 ml) and water (6 ml)] at room temperature for 15 hr. The reaction mixture was diluted with ice-cold water and extracted into ethyl acetate, washed with water and dried (Na_2SO_4). Removal of solvent gave a gum which was esterified and column chromatographed over silica gel (12 g). Elution with light petroleum (b.p. 60–80°)–benzene (1 : 1) gave the 10β-epimer (3) (150 mg) as a gum (TLC pure) (Found: C, 62·9; H, 8·0. $C_{29}H_{42}O_{10}$ requires C, 63·2; H, 7·7%), m/e, M^+ not observed, 519, 518, 367, 366, 365, 349, 335, 334 (100%), 317, 289 and 274, ν_{max} (KBr) 1739, 1724 and 1639 cm^{-1}, δ 1·1 (*s*, CMe), 1·2–1·8 (br, CH_2), 2·0 (*s*, OCOMe), 3·6 (*s*, CO_2Me), 3·64 (*s*, CO_2Me), 3·7 (*s*, CO_2Me), 5·7 (*d*, J 2·5 Hz, CHOCO) and 6·45 (*d*, J 2·5 Hz, CH=C). The signal for CH_2OAc (*q*) partially overlapped with the signals for CO_2Me. Further elution with light petroleum (b.p. 60–80°)–benzene (1 : 1) gave the 10α-epimer (4) (120 mg) as a TLC pure gum (Found: C, 63·4; H, 8·0. $C_{29}H_{42}O_{10}$ requires C, 63·2; H, 7·7%), ν_{max} (KBr) 1727–1721 and 1639 cm^{-1}, δ 1·1 (*s*, CMe), 1·20–1·8 (br, CH_2), 2·0 (*s*, OCOMe), 3·6 (*s*, CO_2Me), 3·64 (*s*, CO_2Me), 3·7 (*s*, CO_2Me), 5·3 (*d*, J 4·5 Hz, CHOCO) and 6·7 (*d*, J 4·5 Hz, CH=C). The signal for CH_2OAc (*q*) partially overlapped with the signals for CO_2Me.

2.3. *Condensation of potassium salt of trans-9,10-epoxy-16-hydroxy-hexadecanoic acid with 10α-bromo-13-O-acetate* (2)

The potassium salt was prepared by titrating *trans* 9,10-epoxy-16-hydroxyhexadecanoic acid (Eswaran *et al* 1973) in methanol with methanolic potassium hydroxide, using phenolphthalein as internal indicator.

The 10α-bromo-13-O-acetate (2) (500 mg) and the above potassium salt (750 mg) in HMPA were heated at 70° C for 3 hr. The reaction mixture was diluted with water, extracted into ethyl acetate, washed with dilute hydrochloric acid followed by water and dried. Concentration of the extract gave a gum showing two close moving spots on TLC. Chromatography over silica gel (12 g) and elution with benzene gave the 10β-epimer (10) (150 mg) as a TLC pure gum (Found: C, 65·7; H, 8·5. $C_{35}H_{54}O_{10}$ requires C, 66·2; H, 8·5%), m/e, M^+ not observed, 604, 603, 586, 585, 542, 488, 472, 419, 366, 365, 349, 334 (100%), 333, 332, 318, 317, 306 and 289, ν_{max} (KBr) 1740–1710 and 1637 cm^{-1}, δ 1·13 (*s*, CMe), 1·2–1·8 (br, CH_2), 2·0 (*s*, OCOMe), 3·6 (*s*, CO_2Me), 3·69 (*s*, CO_2Me), 5·68 (*d*, J 2·5 Hz, CHOCO)

and 6·42 (*d*, J 2·5 Hz, CH=C). The signal for C*H*$_2$OAc (*q*) partially overlapped with the signals for CO_2Me.

Further elution with benzene gave the 10*α*-epimer (11) (120 mg) (gum) (TLC) (Found: C, 66·0; H, 8·2. $C_{35}H_{54}O_{10}$ requires C, 66·2; H, 8·5%), ν_{max} (KBr) 1738–1715 and 1640 cm^{-1}, δ 1·12 (*s*, CMe), 1·2–1·82 (br, CH_2), 1·95 (*s*, OCOMe), 3·6 (*s*, CO_2Me), 3·72 (*s*, CO_2Me), 5·35 (*d*, J 4·5 Hz, CHOCO) and 6·75 (*d*, J 4·5 Hz, CH=C). The signal for C*H*$_2$OAc (*q*) partially overlapped with the signals for CO_2Me.

2.4. *Opening of oxirane ring with aqueous perchloric acid*

2.4a. *10β-epimer*: The 10*β*-epimer (10) (50 mg) in dioxan (0·5 ml) was stirred with aqueous perchloric acid (3%, 0·3 ml) at room temperature for 2 hr. The clear solution was diluted with water, extracted into ethyl acetate, washed with water and dried (Na_2SO_4). Removal of the solvent left a gum (TLC pure) (12) (35 mg) (Found: C, 63·9; H, 8·2. $C_{35}H_{56}O_{11}$ requires C, 64·4; H, 8·6%), m/e, M^+ not observed, 603, 602, 542, 365, 349, 335, 334 (100%), 333, 319, 318, 317, 307, 306, 289, 276 and 275, ν_{max} (KBr) 1750–1700 and 1640 cm^{-1}, δ 1·12 (*s*, CMe), 1·2–1·9 (br, CH_2), 2·0 (*s*, OCOMe), 3·6 (*s*, CO_2Me), 3·69 (*s*, CO_2Me), 5·68 (*d*, J 2·5 Hz, CHOCO) and 6·44 (*d*, J 2·5 Hz, CH=C). The signal for C*H*$_2$OAc partially overlapped with the signals for CO_2Me. The opening of the oxirane ring was shown by the complete disappearance of the parent epoxide on TLC.

2.4b. *10α-epimer*: The 10*α*-epimer (11) (50 mg) on similar treatment with perchloric acid in dioxan and work-up gave a TLC pure gum (13) (40 mg) (Found: C, 64·1; H, 8·5. $C_{35}H_{56}O_{11}$ requires C, 64·4; H, 8·6%), ν_{max} (KBr) 1747–1705 and 1640 cm^{-1}, δ 1·13 (*s*, CMe), 1·2–1·8 (br, CH_2), 1·98 (*s*, OCOMe), 3·6 (*s*, CO_2Me), 3·71 (*s*, CO_2Me), 5·35 (*d*, J 4·5 Hz, CHOCO) and 6·74 (*d*, J 4·5 Hz, CH=C). The signal for C*H*$_2$OAc (*q*) partially overlapped with the signals for CO_2Me.

2.5. *Alkaline hydrolysis of the above ester*

The 10*β*-ester (10) (50 mg) was dissolved in dioxan (0·5 ml) and treated with aqueous sodium hydroxide (8%, 1·5 ml) at 25° C for 15 hr. The clear solution was acidified with ice-cold hydrochloric acid when a colourless solid separated out. It was identified as (9RS, 10SR)-9,10,16-trihydroxyhexadecanoic acid (20 mg), m.p. 126° (m.p. 125–26°, Singh *et al* 1967) (m.m.p. and i.r.).

2.6. *Action of hydrogen bromide-glacial acetic acid on dimethyl laccishellolate* (16)

Dimethyl laccishellolate (16) (500 mg) was treated with hydrogen bromide-glacial acetic acid (48%, 9 ml) at 0° C for 5 hr. The excess of reagent was removed by a stream of nitrogen and the residue esterified and crystallised from hot petroleum (b.p. 40–60°) to give dimethyl 10*α*-bromocedr-8-ene-12,15-dioate (17) (350 mg), m.p. 72° (Found: C, 55·3; H, 6·0. $C_{17}H_{23}O_4Br$ requires C, 54·9; H, 6·2%), ν_{max} (KBr) 1709 and 1626 cm^{-1}, δ 0·9 (*s*, CMe), 1·1 (*s*, CMe), 3·66 (*s*, CO_2Me), 3·74 (*s*, CO_2Me), 5·2 (*d*, J 4·5 Hz, CHBr) and 6·8 (*d*, J 4·5 Hz, CH=C).

2.7. *10-O-Aleuritoyl ester of dimethyl laccishellolate*

The above 10α-bromo-derivative (17) (250 mg) and potassium *threo*-aleuritate (500 mg) were heated in HMPA (5 ml) as in the previous cases. Work-up gave a gummy residue (270 mg), as a mixture of dimethyl 10α- and 10β-O-aleuritoyl laccishellolates in the ratio of 5 : 4 (n.m.r.). The C-10 proton appeared at δ 5·4 (*d*, J 4·5 Hz) for α-isomer and 5·75 (*d*, J 2·5 Hz) for β-isomer. Separation of this mixture was unsuccessful.

2.8. *Dimethyl 13-O-aleuritoyl shellolate*

The 13-iodo derivative (Subramanian *et al* 1980) (15) (250 mg) and potassium *threo*-aleuritate (500 mg) in HMPA (5 ml) were kept at 110° for 8 hr. Work-up of the reaction mixture gave a gum which on silica gel column chromatography and elution with 10% light petroleum (b.p. 60–80°)-benzene afforded the unchanged (15) (50 mg) as a gum.

5% Ethyl acetate-benzene gave the 13-O-aleuritate (14) (150 mg) as a TLC pure gum (Found: C, 64·5; H, 8·7. $C_{33}H_{54}O_{10}$ requires C, 64·9; H, 8·8%), m/e, M^+ not observed, 592, 579, 578, 561, 560, 518, 447, 406, 405, 402, 366, 365, 335, 334, 333 and 275 (100%), ν_{max} (KBr) 1740–1700 and 1640 cm^{-1}, δ 1·2 (*s*, CMe), 1·23–1·8 (br, CH_2), 3·7 (*s*, CO_2Me), 3·72 (*s*, CO_2Me), 4·1 (*q*, CH_2OCO), 4·52 (*d*, J 2·5 Hz, CHOH) and 6·63 (*d*, J 2·5 Hz, CH=C).

10% Ethyl acetate-benzene gave *threo*-aleuritic acid (100 mg), m.p. 101°.

2.9. *Action of hydrogen bromide-glacial acetic acid on 13-iodo-derivative* (15)

The 13-iodo- derivative (15) (500 mg) was treated with hydrogen bromide-glacial acetic acid (48%, 9 ml) at 0° for 5 hr. The product was esterified and chromatographed over silica gel (12 g). Elution with light petroleum (b.p. 60–80°)-benzene (1 : 1) gave a gum which on crystallisation from hot petroleum (b.p. 40–60°) yielded dimethyl 10α-bromo-13-iodocedr-8-ene-12, 15-dioate (5) (350 mg), m.p. 91° (Found: C, 41·0; H, 4·1. $C_{17}H_{22}O_4BrI$ requires C, 41·0; H, 4·2%), ν_{max} (KBr) 1710 and 1630 cm^{-1}, δ 1·29 (*s*, CMe), 3·18 (*m*, CH_2I), 3·71 (*s*, CO_2Me), 3·80 (*s*, CO_2Me), 5·35 (*d*, J 4·5 Hz, CHBr) and 6·95 (*d*, J 4·5 Hz, CH=C).

2.10. *Stearoylation of the above 10α-bromo-13-iodo-derivative*

The 10α-bromo-13-iodo-derivative (5) (250 mg) in HMPA was heated with potassium stearate (500 mg) at 110° C for 8 hr. Work-up of the reaction mixture gave (200 mg) as a gum and identified as a 1 : 1 mixture of 10α- and 10β-13-di-O-stearates (n.m.r.). By the mixed anhydride method, the pure β-epimer has earlier been prepared (Subramanian *et al* 1979).

2.11. *Action of hydrogen bromide-glacial acetic acid on*

2.11a. *Methyl anhydroshellolate*: Methyl anhydroshellolate (9) (100 mg) on treatment with hydrogen bromide-glacial acetic acid (48%, 2 ml; 30° C; 15 hr) followed by work-up and crystallisation gave methyl 13-O-acetyl-10α-bromocedr-8-

ene-12-oic-15-oate (7) (80 mg) m.p. 170°. This compound has earlier been obtained (Eswaran *et al* 1973) as a minor product from a similar reaction on dimethyl shellolate.

2.11b. *Anhydroshellolic acid*: Anhydroshellolic acid (Cookson *et al* 1962) (8) (250 mg) on treatment with hydrogen bromide-glacial acetic acid (48%, 4·5 ml) at 30° C for 15 hr gave a product which on crystallisation gave 13-O-acetyl-10*a*-bromocedr-8-ene-12,15-dioic acid (6) (200 mg), m.p. 220° (Found: C, 50·5; H, 5·1. $C_{17}H_{21}O_6Br$ requires C, 50·8; H, 5·2%), ν_{max} (KBr) 1732, 1684 and 1622 cm^{-1}, δ (acetone-d_6) 0·6 (*s*, CMe), 3·18 (*q*, CH_2OAc), 4·5 (*d*, J 4·5 Hz, CHBr) and 6·37 (*d*, J 4·5 Hz, CH=C).

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