# Synthesis of Some 3-Methylbut-2-enylated 1,3,5-Trihydroxyxanthones

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1,3,5-Trihydroxyxanthen-9-one reacts with 2-methylbut-3-en-2-ol in presence of a catalytic amount of $BF_3$-etherate to yield a mixture of 1,3,5-trihydroxy-2,4-bis-(3-methylbut-2-enyl)xanthen-9-one, in poor yield, identical with natural 8-desoxygartanin along with 1,3,5-trihydroxy-4-(3-methylbut-2-enyl)xanthen-9-one (**3**), in good yield, and 1,3,5-trihydroxy-2-(3-methylbut-2-enyl)xanthen-9-one (**4**) in poor yield. Compounds **3** and **4**, the probable biogenetic precursors of 6-desoxyisojacareubin and 6-desoxyjacareubin, have been reported to occur in nature as such but were characterised as their dimethyl ethers. Compounds **3** and **4** on oxidative cyclisation with DDQ gave 6-desoxyisojacareubin and 6-desoxyjacareubin respectively, completely identical with authentic natural samples.

8-Desoxygartanin, isolated from both fruit hulls and ripe fruits of *Garicinia mangostana* Linn.[1] and from the bark and heartwood of *Maclura pomifera*,[2] was assigned the structure (**2**) on the basis of its spectral data and its conversion to a bicyclo-derivative. 6-Desoxyisojacareubin and its possible biogenetic precursor, 1,3,5-trihydroxy-4-(3-methylbut-2-enyl)xanthen-9-one have very recently been isolated[3] from the heartwood of *Pentaphalangium solomonse* Warb. 6-Desoxyjacareubin, a linear isomer of 6-desoxyisojacareubin and its probable biogenetic precursor, 1,3,5-trihydroxy-2-(3-methylbut-2-enyl)xanthen-9-one, were reported[4] to occur in the heartwood of *Calophyllum scriblitifolium*. Both these probable biogenetic precursors were characterised as their dimethyl ethers and their structures were confirmed by comparison with the synthetic samples of the dimethyl ethers, prepared by indirect methods.

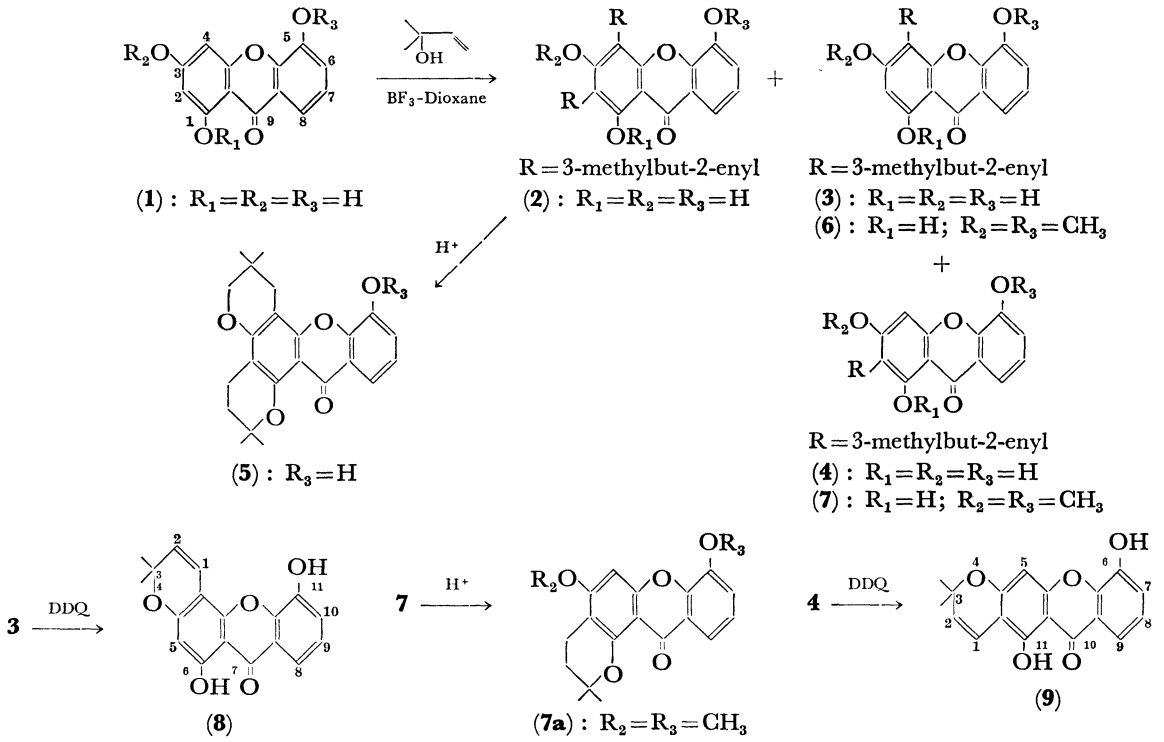
The synthesis of 4-(3-methylbut-2-enyl) and 2-(3-methylbut-2-enyl) derivatives of 1,3,5-trihydroxyxanthen-9-one have now been achieved for the first time with 2-methylbut-3-en-2-ol using catalytic amount of $BF_3$-etherate at room temperature.

1,3,5-Trihydroxyxanthen-9-one (**1**), prepared[5] from anhydrous phloroglucinol and 2,3-dihydroxy benzoic acid in the presence of phosphorous oxychloride and freshly fused zinc chloride, on condensation with 2-methylbut-3-en-2-ol using a catalytic amount of the Lewis acid boron trifluoride etherate in dry dioxane at room temperature gave a semi-solid mass. Thin layer chromatography indicated the formation of a number of products along with a large amount of unreacted xanthone (**1**). The major amount of unreacted xanthone was removed by extracting with 2% aq $Na_2CO_3$. The remaining mixture product on column chromatographic purification gave the following main fractions designated as compounds A, B, C, and D (unreacted xanthone).

Compound A, obtained in 2% yield, gave a green colour with alcoholic ferric chloride. Elemental and spectroscopic data confirmed it to be bis-*C*-(3-methylbut-2-enyl)xanthone. NMR($CDCl_3$) exhibited the resonance signals of two 3-methylbut-2-enyl groups along with the expected signals of other protons (see Experimental). It was established to be 2,4-bis-(3-methylbut-2-enyl) derivative (**2**) because its physical characteristics and spectral data was found to be in complete agreement with the data cited for natural 8-desoxygartanin.[1] On formic acid treatment it gave a bisdihydropyrano derivative (**5**), as indicated by its NMR which showed characteristic multiplets of four methylene protons at the expected chemical shifts (see Experimental) along with the signals for other protons. Other characteristics (mp and UV) were found to be in complete agreement with that of known bicycloderivative,[1] prepared from natural 8-desoxygartanin.

Compound B, obtained in nearly 8% yield, was soluble in dilute aq $Na_2CO_3$ and gave a green colour with alcoholic ferric chloride. Elemental analysis indicated the presence of one 3-methylbut-2-enyl group and its nuclear placement was indicated by the resonance signals shown in its NMR spectrum (see Experimental). It was methylated by using 2 mol of freshly distilled acid free dimethyl sulphate in acetone–potassium carbonate medium to give dimethoxy derivative (**6**) as indicated by its elemental data and confirmed by its NMR spectrum (2×s, $\delta$ 3.8 and 3.88). It gave a green colour with alcoholic ferric chloride. It did not undergo any change on formic acid treatment (indicated by TLC), confirming thereby, beyond doubt, the presence of a 3-methylbut-2-enyl group at 4-position in the dimethyl derivative (**6**) and hence in compound B. Further data was found to be completely identical (mmp; TLC and superimposable IR) with that of an authentic sample of dimethyl ether. Complete identity of these two dimethyl ethers confirmed, beyond doubt, the structure (**3**) for compound B.

Compound C, obtained in 3% yield, gave a green colour with alcoholic ferric chloride, was soluble in dilute aq $Na_2CO_3$. Elemental analysis indicated the entry of one 3-methylbut-2-enyl group into the xanthone nucleus which was confirmed by its NMR spectrum (see Experimental). On methylation with acid free freshly distilled dimethyl sulfate (2 mol) in acetone–potassium carbonate medium it gave a dimethoxy product (**7**), as indicated by its elemental analysis and confirmed by the two methoxyl singlets shown in its NMR spectrum (2×s, $\delta$ 3.98 and 4.12). It gave a positive alcoholic ferric chloride test. Its complete identity (mmp; TLC and co-TLC) with an authentic sample of dimethyl ether confirms the structure (**4**) assigned to compound C. Formic acid treatment yielded a product which did not give any colour change with alcoholic ferric chloride. It clearly in-




dicated the involvement of 1-hydroxyl in cyclisation with the 3-methylbut-2-enyl group, present at the 2-position. Therefore the 3-methylbut-2-enyl group in dimethyl ether and hence in compound C could only be present at the 2-position. This confirms the structure (**4**) for the compound C beyond any doubt.

Compound B (**3**) on oxidative cyclisation with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) in dry toluene afforded a product along with a very minute quantity of unreacted starting material. It was separated by preparative TLC and was identified as an angular mono-chromene as indicated by the two doublets for the olefinic protons shown in NMR (2×d, $\delta$ 5.70 and 6.78). Its structure (**8**), was confirmed by its complete identity (mp; UV; IR) with the natural 6-desoxyisojacareubin. Its formation has also served as an additional proof for the structure (**3**) of compound B.

Similarly, compound C (**4**) on refluxing with DDQ in dry toluene yielded a mixture, from which a chromenoxanthone, as a major product, was separated by preparative TLC. Its NMR spectrum showed two doublets for the olefinic protons of the chromene ring (2×d, $\delta$ 5.72 and 7.02) along with the signals for other protons. The complete agreement of its physical characteristics and spectroscopic data with that of natural 6-desoxyjacareubin[4] confirms its structure (**9**) which again confirms the structure (**4**) of compound C.

## Experimental

Unless otherwise stated, all mps are uncorrected and were taken with a Kofler's mp apparatus; UV spectra were taken in MeOH; IR spectra were recorded using KBr disc and Perkin-Elmer infra-cord spectrophotometer and NMR in $CDCl_3$, $CD_3COCD_3$, $CD_3COCD_3$–$CDCl_3$ using 60 MHz spectrophotometer; silica gel 'Jai' was used for column chromatography and TLC was carried out on silica gel 'Jai' chromatoplates.

*3-Methylbut-2-enylation of 1,3,5-Trihydroxyxanthen-9-one (**1**) with 2-Methylbut-3-en-2-ol.* To a well stirred solution of 1,3,5-trihydroxyxanthen-9-one (**1**, 1 g) in dry dioxane (20 ml) was added boron trifluoride etherate (0.7 ml) and 2-methylbut-3-en-2-ol (0.430 g). The solution was stirred for 4 h at room temperature under anhydrous conditions. Moist ether was added and the ethereal solution stirred for 48 h at room temperature, then washed with water and dried over anhydrous $MgSO_4$. Removal of the solvent gave a solid which was extracted with 2% aq $Na_2CO_3$ to remove the large amount of unreacted xanthone. The remaining mixture was subjected to column chromatography over silica gel and the following three main fractions, designated as compound A, B, C, and D (unreacted xanthone), were obtained.

Compound A crystallised from benzene–petroleum ether mixture as a yellow powder (36 mg); mp 166—167 °C; green colour with alcoholic ferric chloride; $\lambda_{max}$ 244, 261, 322, 375 nm; $\nu_{max}$ 1650 $cm^{-1}$ (>C=O). Found: C, 72.4; H, 6.6%. Calcd for $C_{23}H_{24}O_5$: C, 72.6; H, 6.4%. NMR ($CDCl_3$): $\delta$ 1.68 and 1.80 (2×s, 12H, two $(CH_3)_2C<$), 3.50 (m, 4H, two $-CH_2-$), 5.22 (m, 2H, two $-CH=$), 7.32 (m, 2H, H-6 and H-7), 7.64 (q, $J$=6.5 Hz and 4 Hz, 1H, H-8). This agreed in all respects with the data cited for natural 8-desoxygartanin.[1] Compound A (**2**, 20 mg) in formic acid (1 ml) was heated on a steam bath for 30 min. The resulting pale yellow solution was poured over crushed ice, extracted with EtOAc and then dried and evaporated under reduced pressure. The solid so obtained crystallised from a benzene–hexane mixture as yellow needles (15 mg); mp 258—260 °C; $\lambda_{max}$ 257, 310 nm; NMR ($CDCl_3$): $\delta$ 1.40 and 1.44 (2×s, 12H, two $(CH_3)_2C<$ of pyran rings), 1.84 and 2.82 (2×m, 8H, four $-CH_2-$ of two pyran rings), 7.22 (m, 2H, H-6, and H-7), 7.70 (q, $J$=6.5 Hz and 4 Hz, 1H, H-8). This data was found to be in complete agreement with that of bicyclo-8-desoxygartanin.[1] Thus the structure (**2**), as-

signed to compound A, is fully established.

Compound B crystallised from ethyl acetate–benzene mixture as a yellow fluffy powder (120 mg); mp 199—202 °C soluble in 5% aq $Na_2CO_3$ and giving green colour with alcoholic ferric chloride. $\lambda_{max}$ 245, 285 nm; $\nu_{max}$ 1655 $cm^{-1}$ (>C=O). Found: C, 68.8; H, 5.5%. Calcd for $C_{18}H_{16}O_5$: C, 69.2; H, 5.1%. NMR ($CD_3COCD_3$+$CDCl_3$): $\delta$ 1.66 and 1.74 (2×s, 3H each, $(CH_3)_2C$<, 3.47 (d, $J$= 7.5 Hz, 2H, $-CH_2-$), 3.66 (br s, 1H, 5-OH; exchangeable with $D_2O$), 5.20 (m, 1H, –CH=), 6.22 (s, 1H, H-2), 7.20 (m, 2H, H-6, and H-7), 7.72 (q, $J$=6.5 Hz and 4 Hz, 1H, H-8). An acetone solution of compound B (50 mg in 5 ml) containing freshly distilled acid free dimethyl sulphate (0.030 ml) and freshly ignited $K_2CO_3$ (nearly 200 mg) was refluxed for 4 h. The acetone was removed under reduced pressure, water added and the solid obtained was filtered. This solid was purified by repeated crystallisations from a ethyl acetate–benzene–hexane mixture to yield yellow needles(36 mg); mp 182—184 °C; $\lambda_{max}$ 239, 242, 256, 312, and 368 nm; $\nu_{max}$ 1660 $cm^{-1}$ (>C=O). Found: C, 70.1; H, 6.2%. Calcd for $C_{20}H_{20}O_5$: C, 70.6; H, 5.8%. NMR ($CDCl_3$): $\delta$ 1.62 1.78 (2×s, 6H, $(CH_3)_2C$<), 3.46 (d, $J$=7.5 Hz, 2H, $-CH_2-$), 3.8 and 3.88 (2×s, 3H each, $-OCH_3$ at 3- and 5-positions), 5.2 (m, 2H, H-6 and H-7), 7.68 (q, $J$=6.5 Hz, and 4 Hz, 1H, H-8). It was found to be identical in all respects (mmp; TLC and superimposable IR) with the sample of 1-hydroxy-3,5-dimethoxy-4-(3-methylbut-2-enyl)xanthen-9-one. On formic acid treatment, it did not undergo any change (as indicated by TLC). Thus the structure (**6**) could be assigned to above dimethyl ether and hence the structure (**3**) to compound B.

Compound C crystallised from a ethyl acetate–benzene–petroleum ether mixture as light yellow needles (46 mg); mp 182—184 °C; soluble in 5% aq $Na_2CO_3$; green colour with alcoholic ferric chloride; $\lambda_{max}$ 242, 258, 300 nm; $\nu_{max}$ 1650 $cm^{-1}$ (>C=O). Found: C, 69.4; H, 5.5%. Calcd for $C_{18}H_{16}O_5$: C, 69.2; H, 5.1%. NMR ($CD_3COCD_3$+ $CDCl_3$): $\delta$ 1.78 (m, 6H, $(CH_3)_2C$<), 3.44 (d, $J$=7.5 Hz, 2H, $-CH_2-$), 3.65 (br s, 1H, 5-OH; exchangeable with $D_2O$), 5.24 (m, 1H, –CH=), 6.72 (s, 1H, H-4), 7.28 (m, 2H, H-6, and H-7), 7.94 (q, $J$=6.5 Hz and 4 Hz, 1H, H-8). Its dimethyl ether, prepared as above, crystallised from a ethyl acetate–benzene–petroleum ether mixture as a yellow powder (60%); mp 167—168 °C; insoluble in 5% aq $Na_2CO_3$; positive ferric reaction; $\lambda_{max}$ 245, 258, 308 nm; $\nu_{max}$ 1660 $cm^{-1}$ (>C=O). Found: C, 71.0; H, 5.9%. Calcd for $C_{20}H_{20}O_5$: C, 70.6; H, 5.8%. NMR ($CDCl_3$): $\delta$ 1.80 (m, 6H, $(CH_3)_2C$<), 3.46 (d, $J$=7.5 Hz, 2H, $-CH_2-$), 3.98 and 4.12 (2×s, 3H each, $-OCH_3$ at 3- and 5-positions), 5.35 (m, 1H, –CH=), 6.70 (s, 1H, H-4), 7.36 (m, 2H, H-6 and H-7), 7.92 (q, $J$=6.5 Hz and 4 Hz, 1H, H-8). It was found to be in complete agreement (mmp; TLC; co-TLC) with the sample of 1-hydroxy-3,5-dimethoxy-2-(3-methylbut-2-enyl)xanthen-9-one. This dimethyl ether (2 mg) in formic acid (3 drops) was heated on steam bath for 30 min. After working up as usual, the product obtained gave no colour change with alcoholic ferric chloride. Thus the 3-methylbut-2-enyl group in methyl ether is confirmed to be present at C-2, and involved in cyclisation with the 1-OH. Therefore the structure (**7**) could be assigned to methyl ether and hence the structure (**4**) to compound C. Compound D was recovered starting material (**1**, 878 mg).

*Oxidative Cyclisation of Compound B (**3**) and Compound C (**4**) with DDQ.* *6-Desoxyisojacareubin (**8**)*: A solution of compound B (**3**, 20 mg) in dry toluene (1.5 ml) was refluxed with DDQ (3 mg) for 1 h. It was filtered hot and the residue (colourless hydroquinone) washed with toluene. The removal of solvent under reduced pressure from the filtrate gave a solid mass which was purified by preparative TLC (solvent; ethyl acetate: benzene (1 : 9)). The product, so obtained, crystallised from ethyl acetate–benzene–petroleum ether mixture as a light yellow powder (12 mg); mp 250—251 °C; $\lambda_{max}$ 233, 250, 266, 310 nm; $\nu_{max}$ 1650 $cm^{-1}$ (>C=O). Found: C, 69.3; H, 4.8%. Calcd for $C_{18}H_{14}O_5$: C, 69.6; H, 4.5%. NMR ($CD_3COCD_3$): $\delta$ 1.46 (s, 6H, $(CH_3)_2C$<), 3.60 (br s, 1H, 11 –OH; exchangeable with $D_2O$), 5.70 and 6.78 (2×d, $J$=10 Hz each, 1H each, –CH=CH–), 7.18 (m, 2H, H-9, and H-10), 7.62 (q, $J$=6.5 Hz and 4 Hz, 1H, H-8). This data was found to be in complete agreement with the data cited for natural 6-desoxyisojacareubin.[3]

*6-Desoxyjacareubin (**9**)*: Compound C (**4**, 18 mg) in dry toluene (1.5 ml) was refluxed with DDQ (3 mg) for 1 h. The progress of the reaction was checked with TLC. After working up as above it gave a product, which was purified by preparative TLC (solvent; ethyl acetate: benzene (1 : 9)). The compound, so obtained, crystallised from a ethyl acetate–benzene–petroleum ether mixture as a orange yellow solid (12 mg); mp 212—214 °C; $\lambda_{max}$ 241, 272 sh, 288, 310 sh, 370 nm; $\nu_{max}$ 1650 $cm^{-1}$ (>C=O). Found: C, 69.2; H, 4.9%. Calcd for $C_{18}H_{14}O_5$: C, 69.6; H, 4.5%. NMR($CD_3COCD_3$): $\delta$ 1.47 (s, 6H, $(CH_3)_2C$<), 3.58 (br s, 1H, –OH; exchangeable with $D_2O$), 5.72 and 7.02 (2×d, $J$=10 Hz each, 1H each, –CH=CH–), 7.2 (m, 2H, H-7, and H-8), 7.68 (q, $J$=6.5 Hz and 4 Hz, 1H, H-9). This data agreed completely with the data cited for natural 6-desoxy-jacareubin.[4]

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