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Synthetic studies on morellin. Part 4: Synthesis of 2,2-dimethyl-12-[3-methylbut-2-enyl]-2*H*,6*H*-pyrano[3,2-b]xanthen-6-one†

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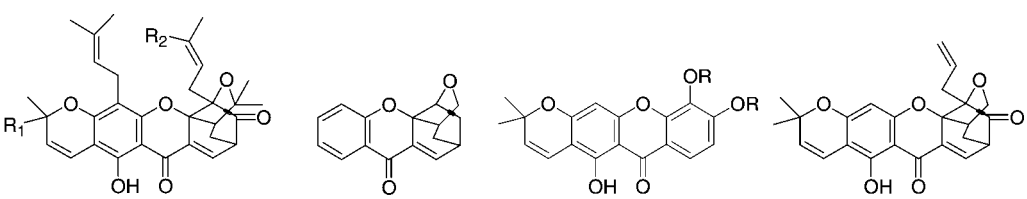
Abstract

A new synthesis of 2,2-dimethyl-12-[3-methylbut-2-enyl]-2*H*,6*H*-pyrano[3,2-b]xanthen-6-one (**7**) is described from 1,3-dihydroxyxanthone and involved the preparation of a linear dihydropyranoxanthone (**26**), its conversion into the pyranoxanthone (**14**) and its prenylated derivative (**31**) followed by a Claisen rearrangement leading to the target substrate (**7**).

Keywords: Morellin, synthetic studies, pyrano[3,2-b]xanthene, Claisen rearrangement.

1. Introduction

The naturally occurring compounds, morellin (**1**),[1] gambogic acid (**2**),[2] and their congeners[3] have a novel nucleus consisting of the 2,4a-ethano-2,3,4,4a-tetrahydroxanthone ring system (**3**). Although preparation[4] of this novel nucleus **3** has been achieved, its conversion into morellin and other related complex xanthones has not been reported so far. Similarly, the heterocyclic bicyclo[2.2.2]octenone structure **5** has been obtained[5] from the substrate **4** through a Claisen rearrangement and an intramolecular Diels–Alder reaction, its elaboration into morellin has not been accomplished. In an effort towards the total synthesis of desoxymorellin (**6**), we have identified[6] pyranoxanthone (**7**) as the key substrate. In order to achieve our target, we have to develop (i) an efficient method for the preparation of the pyranoxanthone (**7**); (ii) its conversion to the dihydro-compound (**9**) through a selective Birch reduction of the methyl ether (**8**); (iii) alkylation of **9** to the diene **10** and finally (iv) conversion of **10** into the hexacyclic compound **11** containing the oxatricyclo[4.3.1.$0^{3,7}$]decan-2-one moiety as indicated in the retrosynthetic (Scheme 1).



1, R_1 = Me; R_2 = CHO
2, R_1 = $Me_2C{=}CHCH_2CH_2$-; R_2 = COOH
6, R_1 = R_2 = Me

3

4 R = $CH_2{=}CHCH_2$-

5

Scheme 1.

† Dedicated to Prof. S. C. Bhattacharyya.
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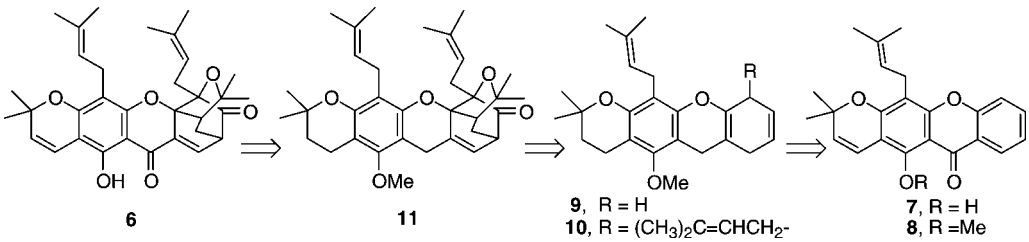
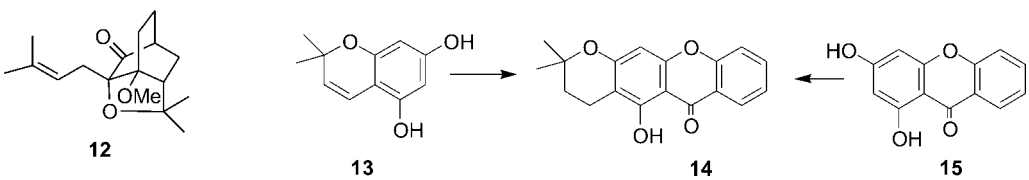


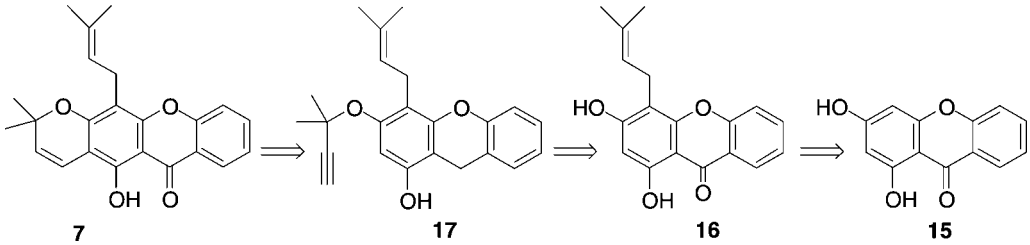
We have earlier developed[6] a general strategy for the construction of oxatricyclo [4.3.1.0^{3,7}]-decan-2-ones, for example, **12** from 1-methoxycyclohexa-1,4-diene. Elaboration of this strategy on the dihydroxanthene (**10**) is expected to afford the compound **11** which can be converted into desoxymorellin (**6**). With this objective, we have now devised an efficient method for the preparation of the pyranoxanthone (**7**) and its methyl ether, morelloxanthone (**8**), and the results are reported in this paper.

Linear pyranoxanthones, for example **14**, are essentially prepared by two methods: the first method involves[7] the condensation of 5,7-dihydroxy-2,2-dimethylchroman (**13**) with suitably substituted *o*-hydroxybenzoic acids followed by dehydration, while the second method[8] deals with an initial nuclear prenylation of 1,3-dihydroxyxanthone (**15**) followed by an oxidative ring closure. Both these methods suffer from several disadvantages such as difficulty in the preparation of starting materials and formation of mixtures of isomeric products in low yield.



Since the prenylxanthone (**7**) has been identified as the key intermediate for the synthesis of desoxymorellin (**6**), an efficient route for its preparation was investigated. Although this compound **7** has been reported earlier,[9,10] we had difficulty in obtaining pure material in reasonable quantities and hence investigated an improved method for its preparation. We envisioned that the pyranoxanthone (**7**) can be obtained from the propargyl ether (**17**), which, in turn, can be prepared by the Mitsunobu reaction[11] of the xanthone (**16**) with 2-methyl-3-butyn-2-ol as shown in the retrosynthesis (Scheme 2). The xanthone **16** can be made from **15**.

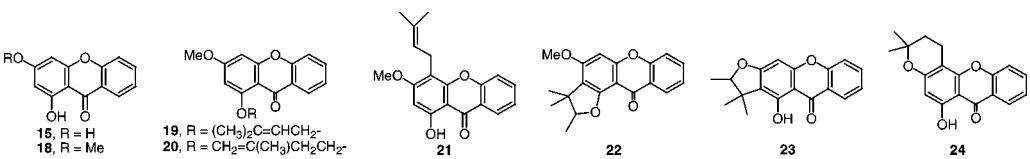
1,3-Dihydroxyxanthone (**15**) was prepared[12] by the condensation of phloroglucinol with salicylic acid in the presence of anhydrous zinc chloride and phosphoryl chloride, and gave the methyl ether (**18**) on treatment with ethereal diazomethane. Heating the methyl ether (**18**) with prenyl bromide and potassium carbonate in dimethylformamide at 85°C for 48 h afforded a mixture of products consisting of 3-methoxy-1-(3-methylbut-2-enyloxy)xanthone **19** (60%) and 3-methoxy-1-(3-methylbut-3-enyloxy)xanthone (**20**) (30%) which were readily separated by column chromatography. The structures of these products were deduced from their ^{1}H NMR spectral data. The xanthone (**19**) showed the presence of two vinyl methyl signals at δ 1.71 and 1.73 as two singlets, while that of **20** had only one vinylmethyl signal at 1.8 and a doublet at 4.59 for the two allylic methylene protons. Claisen rearrangement[13] of the xanthone (**19**) in *N*,*N*-



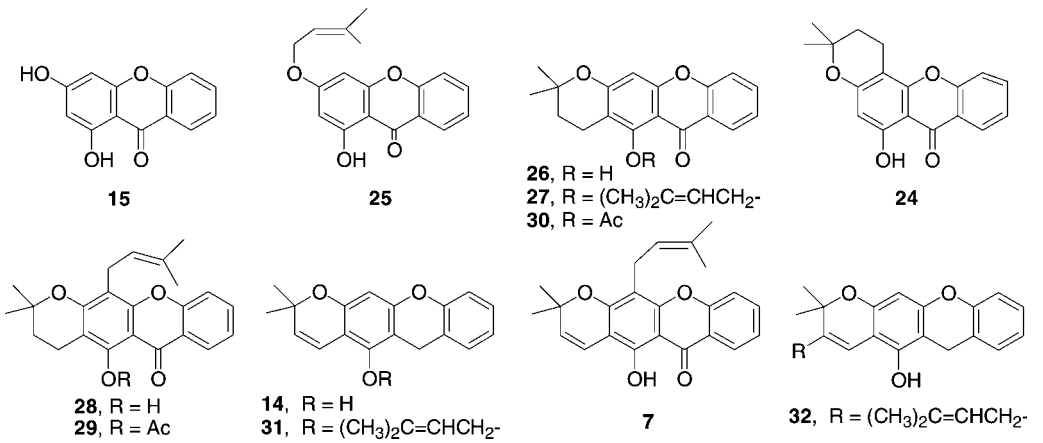
Scheme 2.

dimethylaniline resulted in a mixture of 1-hydroxy-3-methoxy-4-(3-methylbut-2-enyl)xanthone (**21**) (60%) and the furoxanthone (**22**) (30%), besides the starting material (10%). The xanthone (**21**), resulting from a *para* Claisen rearrangement of **19**, showed the presence of the hydroxylmethyl and the carbonyl absorptions at 3320 and 1650 cm^{-1} in its IR spectrum, while the ^1H NMR spectrum showed the presence of two singlets at δ 1.68 and 1.87 due to the two prenyl methyl groups, a doublet at 3.49 (J = 7.6 Hz) for the two methylene protons of the prenyl group, a triplet at 5.23 due to the olefinic proton besides the methoxyl and aromatic protons. On the other hand, the furoxanthone **22** did not show IR absorptions due to the hydroxyl group. The ^1H NMR spectrum of **22** showed the presence of two singlets at δ 1.2 and 1.43 due to the two *gem*-dimethyl protons, a doublet at 1.5 (J = 7 Hz) for the methyl protons situated on the carbon bearing an oxygen substituent and a quartet at δ 4.63 (J = 7 Hz) due to the proton on the carbon bearing the oxygen substituent and the methyl group besides the methoxyl and aromatic protons. The data clearly confirm the structures of the two xanthones (**21** and **22**).

Demethylation of the xanthone **21** was next examined under acidic, basic and neutral conditions.[14] Reaction of **21** with aqueous pyridine at 110°C for 48 h afforded the furoxanthone **22** in 60% yield while the isomeric furoxanthone (**23**) was obtained on reaction of **21** with trimethylsilyl iodide. However, treatment of **21** with hydrobromic acid afforded the angular dihydropyranoxanthone **24**. The structure and mechanism of the products obtained on demethylation of **21** will be discussed elsewhere.[15] Since the dihydroxanthone **16** could not be obtained from **21**, an alternative route for the synthesis of the pyranoxanthone **7** was examined next.



Reaction of **15** with prenyl bromide and potassium carbonate in acetone at 65°C for 6 h afforded the prenyloxyxanthone (**25**) in 80% yield. The ^1H NMR spectrum of **25** showed two singlets at δ 1.81 and 1.86 for the two methyl protons, a doublet at 4.6 for the two methylene protons, a triplet at 5.49 for the olefinic proton and a singlet at 12.84 for the hydrogen-bonded hydroxyl proton besides the six aromatic protons. The xanthone **25**, on heating with a catalytic amount of zinc chloride in dry xylene afforded a 3:2 mixture of the angular and linear dihydropyranoxanthones **24** and **26**, respectively, which is readily separated by chromatography. The structures of these xanthones were deduced from their spectral data. The less polar linear xanthone **26** showed signals at δ 1.42 for the two methyl protons as a singlet, a triplet at 1.84 (J =



6.9 Hz) for the two homobenzylic protons, a singlet at 6.34 for the C-12 aromatic proton, a singlet at 13.18 for the hydrogen-bonded hydroxyl proton besides the aromatic protons. The more polar angular compound **24** was found to be identical with the compound obtained earlier by the demethylation of **21** with HBr. The formation of these two products could be explained on the basis of a heterolytic fission of the prenyloxy bond in **25** under Lewis acid conditions followed by an electrophilic attack of the prenyl cation at C-2 or C-4 and subsequent cyclisation leading to the compounds, **24** and **26**, respectively.

Reaction of the linear xanthone **26** with prenyl bromide and potassium carbonate in DMF at 85°C for 24 h gave the xanthone (**27**) which was subjected to Claisen rearrangement in *N*,*N*-dimethylaniline at 200°C for 8 h affording the hydroxyxanthone **28** in good yield. However, attempted dehydrogenation of **28** or its acetate **29** with DDQ or other reagents did not provide the required product **7** and led only to a complex mixture which was not examined further.

Acetylation of **26** with acetic anhydride and pyridine at 60°C in the presence of a catalytic amount of DMAP gave the acetate **30** in 95% yield. Treatment of the acetate **30** with freshly recrystallized NBS in carbon tetrachloride in the presence of AIBN furnished a bromo compound, which was directly subjected[16] to dehydrobromination with pyridine. The crude product, which showed the presence of bromine, was stirred with tributyltin hydride in dry benzene in the presence of AIBN to yield the pure hydroxyxanthone **14** (overall yield 75% from **30**). The product **14** showed the presence of two doublets at δ5.6 and 6.73 for the C-3 and C-4 olefinic protons confirming that the dehydrogenation of **30** to **14** had occurred.

Reaction of the pyranoxanthone **14** with prenyl bromide and potassium carbonate in DMF afforded the prenylated derivative **31** in good yield. The *O*-prenyl ether (**31**), upon heating in *N*,*N*-dimethylaniline at 200°C for 8 h smoothly underwent a Claisen rearrangement to afford the target xanthone **7**, m.p. 117°C (lit.[9] m.p. 118°C) in 30% yield. The ^{1}H NMR of the xanthone **7** was consistent with the structure and showed the presence of two doublets at δ5.48 and 6.64 for the C-3 and C-4 protons and the absence of the signal at 6.64 for the C-12 aromatic proton. The product **32**, expected from an out-of-ring migration reaction of the substrate, was not present even in trace amounts in the reaction mixture.

2. Conclusion

An efficient method for the synthesis of prenylxanthone **(7)**, and morelloxanthone (**8**), the two important intermediates required for the construction of the complex xanthones, morellin and desoxymorellin, is described.

3. Experimental

M.p.s are uncorrected. IR spectra were recorded as nujol mulls on a Perkin–Elmer model 781 spectrophotometer. ^{1}H NMR spectra were recorded on a JEOL FX-90Q spectrometer in $CDCl_3$ unless otherwise stated. Chemical shifts are reported in ppm using TMS as internal standard. *J* values are given in Hz. Low and high-resolution mass spectra were recorded on a JEOL MS-DX-303 instrument with a built-in direct inlet system. Microanalysis was carried out using a Carlo–Erba 1106 instrument. Analytical and preparative TLC were performed on glass plates coated with Acme silica gel G (containing 13% calcium sulphate binder). Acme silica gel (60–120 mesh) was used for column chromatography.

3.1. *1,3-Dihydroxyxanthen-9-one (**15**)*

A mixture of salicylic acid (12.5 g, 91 mmol), phloroglucinol (126 g, 100 mmol), zinc chloride (31 g, 228 mmol) and phosphoryl chloride (80 ml) was heated at 70°C for 6 h. The reaction mixture was cooled and poured into ice water. The product was filtered, washed with water and dried. The dry powder was subjected to Soxhlet extraction (hexane–ethyl acetate 4:1). Evaporation of the solvent afforded 1,3-dihydroxyxanthone (**15**) (8.26 g, 40%), m. p. 259°C; IR (nujol): ν_{max} 3320, 1650, 1605 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.23 (d, J = 2.2 Hz, 1H, C-2 H), 6.35 (d, J = 2.2 Hz, 1H, C-4 H), 7.2–7.8 (m, 3H), 8.1 (d, J = 8 Hz, 1H, C-8H), 12.8 (s, 1H, OH). Anal. Calc. for $C_{13}H_8O_4$: C, 68.4; H, 3.5%. Found: C, 68.0; H, 3.7%.

3.2. *1-Hydroxy-3-methoxyxanthen-9-one (**18**)*

A cold solution of diazomethane in ether (40 ml), prepared from *N*-methyl-*N*-nitrosourea (7.23 g, 70 mmol), was added slowly to the solution of the hydroxyxanthone (**15**) (8 g, 35 mmol) in ether (40 ml) and allowed to stand at 0°C for 24 h. The excess of diazomethane was destroyed by the careful addition of glacial acetic acid and the organic solvent distilled to yield the methoxyxanthone (**18**) (8.49 g, 100%) as a yellow crystalline solid, m. p. 245°C; IR (nujol): ν_{max} 1650, 1600, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.9 (s, 3H, OMe), 6.35 (d, J = 2.2Hz, 1H, C-2 H), 6.45 (d, J = 2.2 Hz, 1H, C-4 H), 7.4–7.8 (m, 3H), 8.25 (dd, J = 8 and 1.7 Hz, 1H, C-8H), 12.8 (s, 1H, OH). Anal. Calc. for $C_{14}H_{10}O_4$: C, 69.4: H, 4.16%. Found: C, 69.78; H, 4.3%.

3.3. *3-Methoxy-1-(3-methylbut-2-enyloxy)xanthen-9-one (**19**)*

A mixture of the xanthone (**18**) (8 g, 33 mmol), prenyl bromide (9.84 g, 66 mmol), anhydrous potassium carbonate (10 g, 72 mmol) and DMF (70 ml) was heated at 85°C. After an interval of 12 h, a further quantity of prenyl bromide (4.9 g, 33 mmol) and K_2CO_3 (5.46 g, 33 mmol) was added and the temperature maintained at 85°C for 48 h. The reaction mixture was cooled, diluted with water and extracted with ethyl acetate. The organic layer was washed with water, brine, and dried. Removal of the solvent gave a crude product which on purification by column chromatography (hexane–ethyl acetate 17:3) afforded 3-methoxy-1-prenyloxyxanthone (**19**) (6.14 g, 60%)

as a colorless solid, m.p. 107°C; IR (nujol): ν_{max} 1655, 1615, 825 cm^{-1}; UV_{max} [$CHCl_3$] 332, 298, 251 nm (ε, 7750, 15890 and 21630); ^1H NMR ($CDCl_3$): δ 1.71 (s, 3H, Me), 1.73 (s, 3H, Me), 3.79 (s, 3H, OMe), 4.59 (d, J = 7.6 Hz, 2 H, OCH_2), 5.55 (t, J = 7.6 Hz, lH, olefinic proton), 6.25 (d, J = 2.5 Hz, 1H, C-2 H), 6.4 (d, J = 2.5 Hz, 1H, C-4 H), 7.03–7.6 (m, 3H), 8.18 (d, J = 7.7 Hz, 1H, C-8 H). Anal. Calc. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85%. Found: C, 73.23; H, 5.72%.

Further elution yielded 3-methoxy-1-(3-methylbut-3-enyloxy)xanthen-9-one (**20**) (3.07 g, 30%) as a gummy liquid. IR (neat): ν_{max} 1660, 1615, 825 cm^{-1}; UV_{max} [$CHCl_3$] 331, 297, 151 nm (ε, 7230, 14870 and 20860); ^1H NMR ($CDCl_3$) δ 1.87 (s, 3H, Me), 2.72 (t, J = 7.2 Hz, 2 H, allylic CH_2), 3.89 (s, 3H, OMe), 4.2 (t, J = 7.2 Hz, 2H, OCH_2), 4.86 (s, 2H, olefinic protons), 6.33 (d, J = 2.5 Hz, 1H, C-2 H), 6.46 (d, J = 2.5 Hz, 1H, C-4 H), 7.2–7.68 (m, 3H), 8.27 (dd, J = 7.7 Hz, and 1.7 Hz, 1H, C-8 H). Anal. Calc. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85%. Found: C, 73.39; H, 5.76%.

3.4. *1-Hydroxy-3-methoxy-4-(3-methylbut-2-enyl)xanthen-9-one (**21**)*

A solution of the xanthone (**19**) (5.5 g, 17.7 mmol) in *N*,*N*-dimethylaniline (50 ml) was heated at 200°C for 8 h. The reaction mixture was cooled, diluted with $CHCl_3$ and washed with 5N HCl. The organic layer was washed with water and brine, and dried. Removal of the solvent gave a crude mixture, which was purified by chromatography over silica gel. Elution with hexane–ethyl acetate (9:1) afforded the *para* Claisen rearrangement (**21**) (3.3 g, 60%) as a yellow colored solid, m. p. 142°C; IR (nujol): ν_{max} 1650, 1605, 830 cm^{-1}; UV_{max} [$CHCl_3$] 364, 310, 261, 243 nm (ε, 5860, 15000, 28500 and 19900); ^1H NMR ($CDCl_3$): δ 1.68 (s, 3 H, Me), 1.87 (s, 3H, Me), 3.49 (d, J = 7.6 Hz, 2H, CH_2), 3.91 (s, 3H, OMe), 5.23 (t, J = 7.6 Hz, 1H, olefinic proton), 6.39 (s, 1H, C-2 H), 7.24–7.81 (m, 3H), 8.25 (dd, J = 7.7 and 1.7 Hz, 1H, C-8 H), 12.98 (s, 1H, OH). Anal. Calc. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85% Found C, 73.73; H, 5.87%.

Further elution with the same solvent gave 1-hydroxy-3-methoxyxanthone (**18**) (550 mg, 10%) and 2,3-dihydro-4-methoxy-2,3,3-trimethyl-11*H*-furo[2,3-a]xanthen-11-one (**22**) (1.65 g, 35%) as a colorless solid, m. p.149°C; IR (nujol): ν_{max} 1665, 1625, 870 cm^{-1}; UV_{max} [$CHCl_3$] 345, 298, 258 nm (ε, 5660, 14800 and 17600); ^1H NMR ($CDCl_3$) δ 1.2 (s, 3H, Me), 1.43 (s, 3H, Me), 1.5 (d, J = 7 Hz, 3 H, OCHMe), 3.94 (s, 3 H, OMe), 4.63 (q, J = 7 Hz, 1H, OC*H*Me), 6.45 (s, 1H, C-5 H), 7.21–7.72 (m, 3H), 8.3 (dd, J = 7.7 Hz, 1.7 Hz, 1H, C-10 H). Anal. Calc. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85%. Found: C, 73.46; H, 5.70%.

3.5 *2,3-Dihydro-4-methoxy-2,3,3-trimethyl-11H-furo[2,3-a]xanthen-11-one (**22**)*

To a solution of the xanthone **21** (400 mg, 1.29 mmol) in piperidine (4 ml), water (3 ml) was added and refluxed for 48 h. The solvent was removed under reduced pressure, water added and extracted with $CHCl_3$. The organic layer was washed with water, brine and dried. Removal of the solvent gave a crude product, which on column chromatography over silica gel (hexane–ethyl acetate 9:1) afforded the furoxanthone (**22**) (240 mg, 60%).

3.6. *2,3-Dihydro-4-hydroxy-2,3,3-trimethyl-5H-furo[3,2-b]xanthen-5-one (**23**)*

To a solution of the xanthone (**21**) (200 mg, 0.65 mmol) and NaI (96 mg, 0.65 mmol) in CH_3CN (4 ml), was added trimethylsilyl chloride (70 mg, 0.65 mmol) slowly with continu-

ous stirring. The reaction mixture was stirred at room temperature for 30 min, water added and extracted with ether. The ether layer was washed with sodium thiosulfate solution and brine, and dried. Removal of the solvent gave a crude product which on purification by column chromatography over silica gel (hexane–ethyl acetate 9:1) afforded the furoxanthone (**23**) (143 mg, 75%) as a yellow colored solid, m.p. 139°C; IR (nujol): ν_{max} 1655, 1615, 875 cm^{-1}; UV_{max}[$CHCl_3$] 314, 249 nm (ε, 14240 and 21960); ^{1}HNMR ($CDCl_3$) δ1.16 (s, 3H, Me), 1.29 (d, *J* = 6.4 Hz, 3H, CHMe), 1.41 (s, 3H, Me), 4.42 (q, *J* = 6.4 Hz, 1H, OC*H*Me), 6.21 (s, 1H, C-11 H), 7.11–7.6 (m, 3H), 8.1 (dd, *J* = 7.7 and 1.7 Hz, 1H, C-6 H), 12.94 (s, 1H, OH). Anal. Calc. for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44%. Found C, 72.89; H, 5.37%.

3.7. *1,2-Dihydro-3,3-dimethyl-6-hydroxy-3H,6H-pyrano[2,3-c]xanthen-7-one (**24**)*

A solution of the hydroxyxanthone (**21**) (400 mg, 1.29 mmol) in HBr in glacial acetic acid (15 ml, 45% W/V) was refluxed overnight. The solvent was removed under reduced pressure, water added and extracted with ethyl acetate. The organic layer was washed with water, brine, and dried. Removal of the solvent gave a product which on chromatography over silica gel and elution with hexane–ethyl acetate (9:1) afforded the angular dihydropyranoxanthone (**24**) (176 mg, 46%) as a yellow crystalline solid, m.p.188°C; IR (nujol): ν_{max} 1670, 1605, 820 cm^{-1}; UV_{max} [$CHCl_3$] 355, 312, 261, 243 nm (ε, 4500, 14500, 20300 and 20400)); ^{1}H NMR ($CDCl_3$): δ1.40 (s, 6H, 2Me), 1.88 (t, *J* = 6.7 Hz, 2H, CH_2), 2.87 (t, *J* = 6.7 Hz, 2H, CH_2), 6.24 (s, 1H, C-5 H), 7.24–7.78 (m, 3H), 8.26 (dd, *J* = 7.7 and 1.2 Hz, 1H, C-8 H), 12.62 (s, 1H, OH). Anal. Calc. for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44%. Found: C, 73.15; H, 5.58%. A small quantity of 1,3-dihydroxyxanthone (**15**) (67 mg, 23%) was also isolated.

3.8. *1-Hydroxy-3-(3-methylbut-2-enyloxy)xanthen-9-one (**25**)*

A mixture of 1,3-dihydroxyxanthone (**15**) (1.5 g, 6.58 mmol), prenyl bromide (1.96 g, 13.1 mmol) and anhydrous K_2CO_3 (2.18 g, 15.8 mmol) in acetone (15 ml) was refluxed for 6 h. Filtration and distillation of the solvent afforded the crude product which on chromatography over silica gel afforded the 3-prenyloxyxanthone (**25**) (1.56 g, 80%) as a yellow solid, m.p.128°C. IR (nujol): ν_{max} 1660, 1610, 830 cm^{-1}; UV_{max} [$CHCl_3$] 351, 307, 256 nm (ε, 3620, 11500 and 18000); ^{1}H NMR ($CDCl_3$): δ 1.81 (s, 3H, Me), 1.86 (s, 3H, Me), 4.6 (d, *J* = 6.5 Hz, 2H, CH_2), 5.49 (t, *J* = 6.5 Hz, 1H, olefinic proton), 6.35 (d, *J* = 2.4 Hz, 1H, C-2 H), 6.42 (d, *J* = 2.4 Hz, 1H, C-4 H), 7.25–7.78 (m, 3H), 8.23 (dd, *J* = 7.9 and 1.7 Hz, 1H, C-8 H), 12.84 (s, 1H, OH). Anal. Calc. for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44%. Found: C, 72.92; H, 5.51%.

3.9. *3,4-Dihydro-2,2-dimethyl-5-hydroxy-2H,6H-pyrano[3,2-b]xanthen-6-one (**26**)*

To a solution of the xanthone (**25**) (1.5 g, 5.07 mmol) in dry xylene (15 ml), anhydrous $ZnCl_2$ (50 mg) was added and heated at 200°C for 12 h. The reaction mixture was cooled and purified over a silica gel column. It was first eluted with hexane to remove xylene and then with hexane–ethyl acetate (19:1) to afford the linear dihydropyranoxanthone (**26**) (390 mg, 40%) as a yellow crystalline solid, m. p.148°C; IR (nujol): ν_{max} 1650, 1625, 830 cm^{-1}; UV_{max} [$CHCl_3$] 357, 315, 258, 248 nm (ε, 5100, 16300, 19500 and 19400); ^{1}H NMR ($CDCl_3$): δ 1.42 (s, 6H, 2Me), 1.84 (t, *J* = 6.9 Hz, 2H, CH_2), 2.72 (t, *J* = 6.9 Hz, 2H, CH_2), 6.34 (s, 1H, C-12 H), 7.27–7.74 (m, 3H), 8.22 (dd, *J* = 7.9 and 1.7 Hz, 1H, C-7 H), 13.18 (s, 1H, OH). Anal. Calc. for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44%.

Found: C, 73.07; H, 5.48%. Further elution with the same solvent gave the angular dihydropyranoxanthone (**24**) (585 mg, 60%) identical to the sample obtained above.

3.10. *5-Acetyloxy-3,4-dihydro-2,2-dimethyl-2H,6H-pyrano[3,2-b]xanthen-6-one (**30**)*

To a solution of the xanthone (**26**) (360 mg, 1.22 mmol) in pyridine (3 ml) containing DMAP (10 mg), acetic anhydride (125 mg, 1.22 mmol) was added, and let stir at 60° C for 3 h. The solvent was removed under reduced pressure, diluted with water and extracted with ethyl acetate. Removal of the solvent gave a crude product which on chromatography over silica gel (hexane–ethyl acetate 17:3) afforded the acetate **30** (409 mg, 95%) as a colorless solid, m.p. 138° C; IR (nujol): ν_{max} 1760, 1660, 760 cm^{-1}; UV_{max} [$CHCl_3$] 307, 276, 266, 248 nm (ε, 16300, 7600, 6900 and 22600); ^1H NMR ($CDCl_3$): δ 1.37 (s, 6H, 2Me), 1.83 (t, J = 6.9 Hz, 2H, CH_2), 2.51 (s, 3H, O=C-Me), 2.69 (t, J = 6.9 Hz, 2H, CH_2), 6.73 (s, 1H, C-12 H), 7.17–7.68 (m, 3H), 8.2 (dd, J = 7.7 and 1.7 Hz, 1H, C-7 H). Anal. Calc. for $C_{20}H_{18}O_6$: C, 70.99; H, 5.36% Found: C, 70.76; H, 5.43.

3.11. *2,2-Dimethyl-5-hydroxy-2H,6H-pyrano[3,2-b]xanthen-6-one (**14**)*

To a solution of the acetate **30** (375 mg, 1.06 mmol) in CCl_4 (10 ml), freshly recrystallized *N*-bromosuccinimide (296 mg, 1.66 mmol) and AIBN (10 mg) were added and refluxed for 2 h. The reaction mixture was cooled, filtered, and the solvent removed to afford the bromo compound, which was dissolved in pyridine (5 ml) and heated on a water bath under nitrogen atmosphere for 1 h. Pyridine was removed under reduced pressure, water added to the residue and extracted with ethyl acetate. The organic layer was washed with water and brine, and dried. Removal of the solvent gave a crude product, which was dissolved in benzene and refluxed with tri-*n*-butyltin hydride (0.34 ml, 1.27 mmol) and AIBN (10 mg) for 12 h. The organic layer was washed with water and brine, and dried. Removal of the solvent furnished a crude product which on chromatography over silica gel (hexane–ethyl acetate 19:1) afforded the pyranoxanthone **14** (233 mg,); (75% overall yield from **30**) as a yellow crystalline solid, m.p 162° C. IR (nujol): ν_{max} 1650, 1605, 765 cm^{-1}; UV_{max} [$CHCl_3$] 332, 292 nm (ε, 8500 and 28200); ^1H NMR ($CDCl_3$): δ 1.49 (s, 6H, 2Me), 5.6 (d, J = 10.5 Hz, 1H, C-3 H), 6.36 (s, 1H, C-12 H), 6.73 (d, J = 10.5 Hz, 1H, C-4 H), 7.27–7.78 (m, 3H), 8.23 (dd, J = 8 and 1.9 Hz, 1H, C-7 H), 13.15 (s, 1H, OH). HRMS. Calc. for $C_{18}H_{14}O_4$: mass (*m/z*) 294.0892. Found: 294.0890. Anal. Calc. for $C_{18}H_{14}O_4$: 73.4; H, 4.8%. Found: C, 73.25; H, 4.7%.

3.12. *2,2-Dimethyl-5-(3-methylbut-2-enyloxy)-2H,6H-pyrano[3,2-b]-xanthen-6-one (**31**)*

A mixture of the pyranoxanthone (**14**) (210 mg, 0.71 mmol), prenyl bromide (213 mg, 1.42 mmol), anhydrous K_2CO_3 (236 mg, 1.7 mmol) in DMF (3 ml) was heated at 85° C for 12 h. The reaction mixture was cooled, water added and extracted with ethyl acetate. The organic layer was washed with water and brine, and dried. Removal of the solvent yielded a crude product which on purification by chromatography over silica gel and elution with hexane–ethyl acetate (9:1) afforded the prenyloxyxanthone (**31**) (155 mg, 60%) as a yellow solid, m.p.101° C. IR (nujol): ν_{max} 1660, 1610, 755 cm^{-1}; UV_{max} [$CHCl_3$] 347, 316, 273, 245 nm (ε, 5900, 8900, 28500 and 14200); ^1H NMR ($CDCl_3$): δ 1.5 (s, 6H, 2Me), 1.71 (s, 3H, Me), 1.79 (s, 3H, Me), 4.62 (d, J = 7.2 Hz, 2H, CH_2), 5.6 (d, J = 10Hz, 1H, C-3 H), 5.69 (t, 1H), 6.64 (s, 1H, C-12 H), 6.76 (d, J = 10 Hz, 1H, C-4 H), 7.26–7.7 (m, 3H), 8.3 (dd, J = 7.7 and 1.7 Hz, 1H, C-7 H). HRMS: Calc. for $C_{23}H_{22}O_4$: 362.1518. Found: Mass (*m/z*) 362.1423.

3.13. *2.2-Dimethyl-5-hydroxy-12-(3-methylbut-2-enyl)-2H,6H-pyrano[3,2-b]xanthen-6-one (**7**)*

A solution of the above xanthone **31** (120 mg) in *N*,*N*-dimethylaniline (5 ml) was heated at 200° C for 8 h. The reaction mixture was cooled, acidified with 5N HCl and extracted with $CHCl_3$. The organic layer was washed with water and brine, and dried. Removal of the solvent gave the crude product, which on purification by chromatography over silica gel (hexane–ethyl acetate 9:1) afforded the xanthone **7** (100 mg,) as a yellow colored solid, m. p. 117° C; IR (nujol): ν_{max} 1650, 1610, 760 cm^{-1}; UV_{max} [$CHCl_3$] 337, 302, 290, 260, 243 nm (ε, 5910, 21220, 19630, 10380 and 13100); ^1H NMR ($CDCl_3$): δ 1.43 (s, 6H, 2Me), 1.6 (s, 3H, Me), 1.81 (s, 3H, Me), 3.49 (d, J = 7.7 Hz, 2H, CH_2), 5.28 (t, J = 7.7 Hz, 1H, olefinic proton), 5.48 (d, J = 10.5 Hz, 1H, C-3 H), 6.64 (d, J = 10.5 Hz, C-4 H), 7.15–7.66 (m, 3H), 8.13 (d, J = 7.7 Hz, 1H, C-7 H), 13.13 (s, 1H, OH). HRMS: Calc. for $C_{23}H_{22}O_4$: 362.1518. Found: Mass (*m/z*) 362.1406. Anal. Calc. for $C_{23}H_{22}O_4$: C, 76.25; H, 6.0%. Found: C, 76.24; H, 6.1%.

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