Synthetic confirmation for the structure of stipulin†

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A new diprenylated chalcone, stipulin 1 (5',3-di-isopentenyl-2',4',4-trihydroxychalcone) has been characterized from the roots of Dalbergia stipulacea. Synthesis of 8-(2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-6-yl)-2,2-dimethyl-3,4,7,8-tetrahydro-2H,6H-benzo[1,2-b:5,4-b']dipyran-6-one 3 obtained as a final product of the acid catalysed cyclisation of stipulin provided synthetic confirmation for its structure.

A new diprenylated chalcone 5',3-di-isopentenyl-2',4',4-trihydroxychalcone named as stipulin 1 was isolated and characterised from the roots of Dalbergia stipulacea which are used as fish poison. Nuclear prenylation of isoliquiritigenin 2, prepared by condensation of α-resacetophenone with p-hydroxybenzaldehyde, with 2-methyl-but-3-en-2-ol in presence of boron trifluoride etherate under nitrogen atmosphere in dry dioxan medium gave a mixture of compounds none of which resembled stipulin on TLC. Column chromatography of the reaction product yielded 5'-C-prenyl-4,2',4'-trihydroxychalcone 2, isoliquiritigenin and other minor compounds. Treatment of stipulin 1 with formic acid gave a chalcone and flavanone having the structure 1-[7-hydroxy-2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-6-yl]-3-(2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-6-yl)-2-propen-1-one 6, m.p. 199-01°C. Compound 6 on further heating with formic acid isomerised to 8-(4-hydroxyphenyl)-2,2-dimethyl-3,4,7,8-tetrahydro-2H, 6H-benzo[1,2-b:5,4-b']dipyran-6-one 7, m.p. 201-02°C. Nuclear prenylation of 7 with 2-methyl-but-3-en-2-ol and boron trifluoride etherate in nitrogen atmosphere gave 8-[3-(3-methyl-2-butenyl)-4-hydroxyphenyl]-2,2-dimethyl-3, 4, 7, 8-tetrahydro-2H, 6H-benzo[1,2-b:5,4-b']dipyran-6-one 8. Formic acid treatment of 8 on water bath produced the desired flavanone 3 which was found to be identical (TLC and superimposable IR) with that 3 obtained from stipulin, thus providing synthetic confirmation for the structure of stipulin.

Experimental Section

Unless stated otherwise, all melting points are in centigrade scale, uncorrected and were taken on Tempad melting apparatus. UV spectra were recorded on Chemito-2500 spectrophotometer in methanol (λmax values in nm and figures within parentheses refer to logε). IR spectra were recorded on Shimadzu Model-408 spectrophotometer in nujol mull (v max in cm⁻¹). ¹H NMR spectra were recorded on Perkin-Elmer R-32 (90MHz) spectrometer with reference to TMS as internal standard (chemical shift in ppm and J values in Hz). Petroleum ether used has boiling range 60-80°C. Acme silica gel was used for column chromatography and TLC.

2,2-Dimethyl-6-acyl-7-hydroxy-3,4-dihydrobenzopyran 5. 5-C-prenylresacetophenone (4, 2.60g) was heated with formic acid (20mL) on water bath for 45 min. The reaction mixture was poured in cold water (200mL) and usual work up followed by purification by column chromatography gave compound 5; ¹H NMR (CDCl₃): 1.40 (s, 6H, (CH₃)₂C-), 1.88

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1-[7-Hydroxy-2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-6-yl]-3-(4-hydroxyphenyl)-2-propen-1-one

To a solution of 2,2-dimethyl-6-acyl-7-hydroxy-3,4-dihydrobenzopyran (5, 1.80g), and p-hydroxybenzaldehyde (l.60g) in ethanol (30mL) was added 50 %aq. KOH (40mL) and the solution left at room temperature out of contact with air for 4 days. It was then diluted with ice cold water (60mL), ethanol removed and then diluted with dil. HCl and extracted with ether (3x50mL). TLC examination of the ethereal layer showed the presence of compound p-hydroxybenzaldehyde 5 and 6. p-hydroxybenzaldehyde was isolated from the mixture by shaking the ethereal layer with 1%aq. Na2CO3 (3x50mL). Usual work up of the ethereal layer yielded the mixture of 5 and 6, which were separated by column chromatography. Compound 6 crystallized from the chloroform- pet. ether as yellow needles (950mg), m. p. 199-201°C; 1H NMR (CDCl3): 1.30 (s, 6H, (CH3)2-C-C-), 1.82 (t, 2H, -CH2-CH2-Ph), 2.77 (t, 2H, -CH2-Ar), 6.20 (s, 1H, H-3), 6.83 (d, J=8.5Hz, 2H, H-3, H-5), 7.74 (d, J=17Hz, 1H, H6a), 7.77 (d, J=8.5Hz, 2H, H-2, H-6), 7.80 (d, J=17Hz, 1H, H6b), 8.10(s, 1H, H-6'), 12.12 (s, 1H), 13.17 (s, 1H) (both exchangeable with D2O; OH-4, OH-2'); EIMS (m/z, relative
abundance): 324 (M+, 86.6), 269(26.9), 231(15.2), 218(13.7), 205(45.3), 204(16.5), 175(8.0), 150(10.4), 149(100.0), 147(14.2), 120(16.4).

8-(4-Hydroxyphenyl)-2,2-dimethyl-3,4,7,8-tetrahydro-2H,6H-benzo[1,2-b;3,4-b']dipyran-6-one 7. Compound 6 (800mg) was heated with 20mL of formic acid on water bath for 1hr. The reaction mixture was poured over crushed ice and extracted with ether (2×50mL). Usual work up showed it to be a mixture of 6 and 7 which were separated by column chromatography. Compound 7 was crystallized from pet. ether-chloroform as colourless needles (220mg), m.p. 201-02 °; UV: 222.5(4.29), 281.5 (4.22); +AICI 3 222.5, 235.5, 280.5; +NaOAc 220.0, 283.0; +NaOAc/H 3 B0 3 220.0, 281.0; +NaOAc/H 3 B0 3 220.0, 281.0; +NaOMe 221.5, 283.5; 'H NMR (CDCl 3 ) : 1.36 (s, 6H, (CH 3 ) 2 C-C-) , 1.83 (t, 2H, -CH 2 -CHrPh), 2.76 (m, 2H, -CH r CH 2 -Ph), 2.80 (m, 1H), 3.02 (m, I H [H 2 -3] , 5.34 (q, Jtrans=12Hz, Jcis = 4Hz, H-2), 6.37 (s, I H, H-8) , 6.84 (d, J=9Hz, H-5'), 7.20 (m, 2H, H-2', H-6'), 7.69 (s, I H, H-5).

8-(2,2-Dimethyl-3,4-dihydro-2H-1-benzopyran-6-yl)-2,2-dimethyl-3,4,7,8-tetrahydro-2H, 6H-benzo[1,2-b;3,4-b']dipyran-6-one 3. Compound 8 (20mg) was dissolved in formic acid (3.0mL) and heated on water bath for 1hr. Usual work up and purification of the product by column chromatography gave compound 3, a gum (10mg), no colour with ferric chloride. UV: 220.5, 279.5; +AICI 3 279.0; +NaOAc 279.5; +NaOAc/H 3 B0 3 279.0; +NaOMe 280; IR: 1690, 1620, 1570, 1500, 1380, 1350, 1320, 1280, 1265, 1145,1050, 940, 880, 850.0, 810, 740; 'H NMR (CDCl 3 ) : 1.26 (s, 12H, 4xCH 3 ), 1.80 ( t, 4H , 2xmethylene s), 2.75 (m, 4H, 2xbenzylic methylenes), 2.81-3.04 (m, 2H, H r 3) , 5.32(q, Jtrans=12Hz, Jcis = 4Hz, H-2), 6.37 (m, 2H, H-2', H-6'), 7.69 (s, I H, H-5).

This was found to be identical with compound 3 derived from stipulin.

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References
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