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Use Of Selective INEPT Spectroscopy In The Structural Elucidation of a Xanthonolignoid

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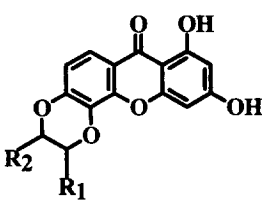
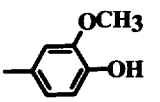
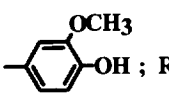
Abstract: Selective INEPT pulse programme was used to determine the orientation of the substituents on the 1,4-dioxane ring of a xanthonolignoid 5′-demethoxycadensin G (**1**). Copyright © 1996 Elsevier Science Ltd

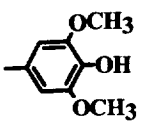
A naturally occurring xanthonolignoid, 5′-demethoxycadensin G, was recently isolated from the plant *Cratoxylum cochinchinese* and its structure was tentatively assigned as (**1**) by comparing its spectral data with that of the known xanthonolignoid cadensin G (**2**).[1] This however is not conclusive evidence for the structure since the spectra of the other isomer (**1a**) may not be significantly different. A persistent problem in the structure elucidation of xanthonolignoids has been the determination of orientation of the substituent groups on the 1,4-dioxane nucleus. Previous reports on the determination of the regiochemistry



(1) R_1 = CH_2OH ; R_2 = 

(1a) R_1 = 

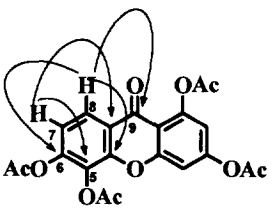
; R_2 = CH_2OH

(2) R_1 = CH_2OH ; R_2 = 

of the ring fusion involved the opening of the dioxane ring by alkaline hydrolysis.[2,3] Since the amount of this natural product (**1**) isolated was quite small, detailed spectroscopic and chemical studies could not be carried out to determine the orientation of the 1,4-dioxane ring. Hence we have synthesized this natural product (**1**) to carry out further NMR studies to determine the orientation of the substituents. We have investigated the suitability of the selective INEPT technique[4] to resolve this problem by inducing polarization transfer across the 1,4-dioxane ring, as this technique has been successfully used in the structural elucidation of coumarinolignans.[5] The application of this technique led us to conclusively prove the orientation of the substituent groups on the 1,4-dioxane ring to be as shown in (**1**).

One-step biomimetic synthesis of the natural xanthonolignoid was achieved by the oxidative coupling of 1,3,5,6-tetrahydroxyxanthone[6] and coniferyl alcohol in the presence of Ag_2O[7] which yielded (**1**) as the only isolable product in 35% yield.[8] The t.l.c, ^1H NMR and ^{13}C NMR spectral data of the synthesized product was found to be identical to those of the natural product (**1**).

A preliminary investigation of the selective INEPT technique was carried out on 1,3,5,6-tetraacetoxyxanthone (**3**) to differentiate between the protons H-7 (δ 7.22) and H-8 (δ 8.13). Observation of the three bond C-H couplings on the aromatic ring was achieved with optimum values for the delays Δ_1 and Δ_2 for J=7Hz. Irradiation of H-7 of (**3**) led to the enhancement of signals due to carbons 5 (δ 132.5) and 8a



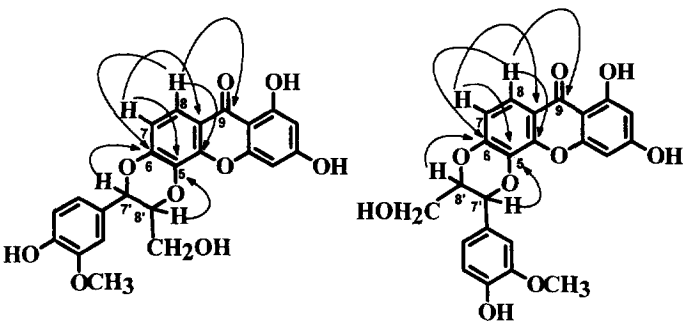
(**3**)

(δ 115.2) indicating that they are coupled through three bonds to H-7. Irradiation of H-8 significantly enhanced the C-6 (δ 150.1), C-4b (δ 147.1) and C-9 (δ 180.8) signals respectively since they are three bonds away from H-8.

The strategies involving the use of selective INEPT technique to differentiate the orientation of the groups on the 1,4-dioxane ring of the xanthonolignoid (**1**) are as shown in diagrams (**1**) and (**1a**).

For the observation of the three bond C-H couplings for the aromatic ring carbon atoms with the aliphatic protons, optimum values for the delays Δ_1 and Δ_2 for 1Hz were determined. Selective irradiation

of the protons at H-7 (δ 7.03) and H-8′ (δ 4.35) resulted in the enhancement of C-5 signal (δ 132.90) in both the cases. This indicates that they are coupled through three bonds to C-5. Similarly when the protons



(1) (1a)

H-8 (δ 7.61) and H-7′ (δ 5.12) were selectively irradiated the C-6 signal at δ 150.30 was enhanced in both the cases since it is three bonds away. Irradiation of H-7 also resulted in the enhancement of signal at C-8a (δ 115.4), whereas irradiation of H-8 resulted in the enhancement of C-4b (δ 147.2) and C-9 (δ 180.8) signals since they are three bonds away.

The above observations of the enhancement of the signals induced in the spectra through the irradiation of the H-7 and H-8′ as well as H-8 and H-7′ allowed us to establish unambiguously that the orientation of the substituent groups on the 1,4-dioxane ring in the xanthonolignoid synthesized is as shown in (**1**). Since this synthetic xanthonolignoid was identical in all respects to that of the natural product, it follows that the orientation of the groups on the 1,4-dioxane ring of the natural product is as shown in (**1**).

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8. Synthesis of Xanthonolignoid : A mixture of 1,3,5,6-tetrahydroxyxanthone (721mg), coniferyl alcohol (500mg) and silver oxide (2.0g) was dissolved in anhydrous benzene (250ml) and distilled acetone (75ml) and stirred in darkness at room temperature for 14hr. Filtration and evaporation of the solvents gave a crude product which was chromatographed on silica gel and eluted with hexane-ethylacetate (1.25:1), yielding the xanthonolignoid (**1**) as the only product as colourless solid (413mg), mp 258-260°C; IR (Nujol) 3400, 1650, 1608, 1523; EIMS: m/z 438 (M^+); ^{1}H NMR (500 MHz, DMSO-d_6): 12.97 (s, 1-OH), 6.40 (d, J=2.1Hz, H-2), 6.22 (d, J=2.1Hz, H-4), 7.03 (d, J=8.8Hz, H-7), 7.61 (d, J=8.8Hz, H-8), 6.92 (d, J=1.9Hz, H-2′), 6.83 (d, J=8Hz, H-5′) 6.91 (dd, J=8.3, 1.8Hz, H-6′) 5.12 (d, J=7.8Hz, H-7′), 4.35 (m, H-8′), 3.44 (m, H-9′), 3.79 (s, 3′-OMe); ^{13}C NMR (125 MHz, DMSO-d_6): 162.9 (C-1), 99.2 (C-2), 166.3 (C-3), 94.9 (C-4), 158.8 (C-4a), 147.2 (C-4b), 132.9 (C-5), 150.3 (C-6), 114.5 (C-7), 117.8 (C-8), 115.4 (C-8a), 180.8 (C-9), 101.73 (C-9a), 126.6 (C-1′), 111.8 (C-2′), 147.7 (C-3′), 147.2 (C-4′), 113.7 (C-5′), 120.6 (C-6′), 76.5 (C-7′), 78.0 (C-8′), 59.8 (C-9′), 55.7 (3′ -OMe).

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