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Tetrahedron Letters 49 (2008) 2407–2409
Tetrahedron Letters

Nor-dehydrodeguelin and nor-dehydrorotenone, C_{22} coumaronochromones from *Lonchocarpus nicou*

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Received 5 December 2007; revised 8 February 2008; accepted 12 February 2008
Available online 14 February 2008

Abstract

Lonchocarpus nicou roots lipophile extract yielded, among isoflavonoids, two coumaronochromones isomers. Spectroscopic analysis assigned the structure of nor-dehydrodeguelin to the former and (−)-nor-dehydrorotenone to the latter, the two products only differing by the cyclization of the C_5 side chain. Biogenetically, the two compounds could be considered as resulting either from cyclization of the corresponding 2′-hydroxyisoflavones and/or from oxidative ring-B contraction of the dehydrorotenoids parents.

Keywords: Fabaceae; Millettieae; *Lonchocarpus nicou*; Coumaronochromones; nor-Dehydrodeguelin; nor-Dehydrorotenone

The chemical investigation of nonpolar metabolites from *Lonchocarpus nicou* roots, a tropical liana of the Fabaceae family,[1–3] afforded a series of thirty prenylated isoflavonoids mainly based upon rotenone and deguelin structures.[4] All the phytochemicals were identified to rotenoids, dehydrorotenoids, as well as products resulting from either a ring-B extension (13-*homo*-13-oxadehydrorotenoids) or a ring-C cleavage (*seco*-rotenoids).[5] Further multistep chromatographic treatment of the lipophile extract[4,5] yielded two extra isomers **1** (4 mg) and **2** (5 mg) closely related to the known dehydrodeguelin (**3**) and (−)-dehydrorotenone (**4**). The structure of the newly reported compounds in the plant kingdom was established as coumaronochromones by spectroscopic evidence including UV, MS as well as NMR.

Compound **1** was isolated as a white amorphous powder, $[\alpha]_D^{21}$ ±0 (*c* 0.003, $CHCl_3$). It exhibited a UV spectrum with bands at λ_{max} (MeOH): 251, 293 and 330 nm, respectively. The molecular formula $C_{22}H_{18}O_6$ was deduced from HREIMS (found: 378.1093; calcd: 378.1103). The 14 double-bond equivalents from the molecular formula matched the recorded ^{13}C NMR data (Table 1) for 17 sp^2 C atoms (174 ppm > δ > 95 ppm) along with five aliphatic carbons (78 ppm > δ > 28 ppm). Eight degrees of insaturation corresponded to two tetrasubstituted aromatic rings as shown by the four ^1H NMR signals in the shift range 8.2–6.9 ppm. One ring was 1,2,3,4-tetrasubstituted (AM system at δ 8.15 ppm and δ 6.94 ppm and *ortho*-coupling of 8.7 Hz); the other ring was 1,2,4,5-tetrasubstituted consequently to two singlets integrating for one proton each at δ 7.65 and 7.11 ppm. The further three degrees of insaturation were consistent with one highfield keto group (δ 173.7 ppm) and one 1,2-disubstituted double bond revealed by two doublets at δ 6.93 ppm and 5.80 ppm for two cis-coupled protons ($J = 10.0$ Hz). In the ^1H NMR spectrum, the broadening of only both doublets at δ 5.80 ppm (ethylenic H) and δ 6.94 ppm (aromatic H) was suitable for long range coupling ($J < 1$ Hz) between the two nuclei. Thus, the above-mentioned ethylenic bond must be firstly located on the 1,2,3,4-tetrasubstituted aromatic ring at the *meta* position (C-8) with respect to H-6 (δ 6.94 ppm) and secondly included in a condensed supplementary ring, to agree with the *anti* relationship between the two nuclei.[6] Finally,

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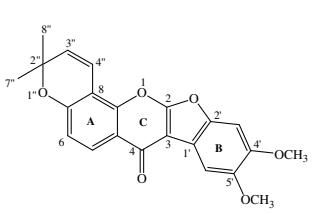
doi:10.1016/j.tetlet.2008.02.063

Table 1
^{1}H (400 MHz) and ^{13}C (100 MHz) NMR data for coumaronochromones **1** and **2** in $CDCl_3$ (δ ppm; J Hz)

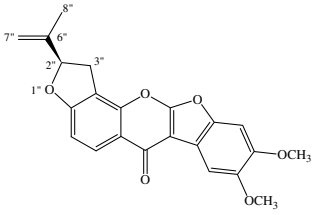
	1				**2**		
H/C	^{13}C	^{1}H	HMBC	H/C	^{13}C	^{1}H	HMBC
2	164.1			2	164.1		
3	99.5			3	99.5		
4	173.7			4	173.8		
5	126.5	8.15 d (8.7)	C-4, C-7, C-9	5	128.0	8.24 d (8.6)	C-4, C-7, C-9
6	115.1	6.94 br d (8.7)	C-8, C-9, C-10	6	108.3	6.98 d (8.6)	C-8, C-9, C-10
7	157.2			7	164.8		
8	109.7			8	113.8		
9	149.3			9	150.5		
10	117.5			10	118.0		
1′	115.1			1′	115.1		
2′	143.5			2′	143.5		
3′	95.8	7.11 s	C-1′, C-5′	3′	95.8	7.11 s	C-1′, C-5′
4′	148.0[a]			4′	148.0[a]		
5′	147.9[a]			5′	147.9[a]		
6′	103.6	7.65 s	C-3, C-2′, C-3′, C-4′	6′	103.6	7.66 s	C-3, C-2′, C-3′, C-4′
2″	77.8			2″	87.9	5.45 br t (8.9)	C-7″, C-8″
3″	131.2	5.80 d (10.0)	C-8	3″	31.7	3.65 dd (15.9; 9.8)	C-7, C-9, C-6″
						3.31 dd (15.9; 7.9)	C-7, C-9, C-6″
4″	114.8	6.93 br d (10.0)	C-2″	6″	142.8		
7″	28.2	1.52 s	C-3″	7″	113.1	5.16 br s	C-2″, C-8″
						5.00 br s	C-2″, C-8″
8″	28.2	1.52 s	C-3″	8″	17.1	1.83 br s	C-2″, C-7″
OCH_3	56.6	4.00 s	C-4′ or C-5′	OCH_3	56.6	4.00 s	C-4′ or C-5′
	56.5	3.96 s	C-4′ or C-5′		56.5	3.96 s	C-4′ or C-5′

[a] Values with the same superscript in one column may be interchanged.

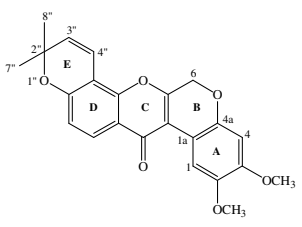
the remaining three unprotonated insaturations, the two further heterocycles and one π-bond were deduced as follows. In the 1,2,3,4-tetrasubstituted aromatic ring, deshielding of H-5 (δ 8.15 ppm) was due to electron-withdrawing substituent consistent in an *ortho*-CO group (C-4: δ 173.7 ppm); inversely, the proton at δ 6.94 ppm (H-6) was shielded by two conjugated electron-donating OR substituents. The substitution pattern of this benzene ring was corroborated by HMBC cross-peaks analysis, which furthermore pointed out O- and C-substituents. The proton at δ 8.15 ppm (H-5) exhibited three large connectivities induced by ^{3}J couplings with quaternary O-bonded carbons: C-4 (δ 173.7 ppm), C-7 (δ 157.2 ppm) and C-9 (δ 149.3 ppm). On the same ring, the proton at δ 6.94 ppm (H-6) showed two cross-peaks with quaternary C-linked carbons: C-8 (δ 109.7 ppm) and C-10 (δ 117.5 ppm) due to ^{3}J couplings and a connectivity involved by ^{4}J coupling with the above-mentioned oxy C-9. All these findings evidenced a 2,4-di-O- and 3-C-substituted benzoyl moiety condensed with the reported 1,2-disubstituted π-bond belonging to a cyclized C_5H_8 chain. Identified with a *gem*-dimethylpyran, it was characterized in the ^{13}C NMR by the signals highlighting 2 equiv methyls (δ 28.2 ppm), two methines (C-3″: δ 131.2 ppm and C-4″: δ 114.8 ppm) and a lowfield quaternary sp^3 C (C-2″: δ 77.8 ppm). Thus, ring closure of the heterocycle would occur at either the *ortho* or the *para* position with respect to the keto group. Although neither C-7 (δ 157.2 ppm) nor C-9 (δ 149.3 ppm) displayed any connectivity with H-4″ (δ 6.93 ppm) in the HMBC spectrum, cyclization would occur at C-7 to support the above-mentioned *anti* periplanar H-6 and H-4″. Furthermore, the combination of the shielded 4-keto group (δ 173.7 ppm) and the *ortho*-oxygen with two quaternary sp^2 carbons (C-2: δ 164.1 ppm and C-3: δ 99.5 ppm) is suitable for an O-bonded C-atom β-conjugated to the carbonyl for the former and for a C-linked carbon β-conjugated to an oxygen for the latter. Hence, the partial structure $C_{14}H_{10}O_3$ issued from the above results was a 2,3-disubstituted 2′,2′-dimethylpyrano(5′,6′:8,7)chromone.



1



2



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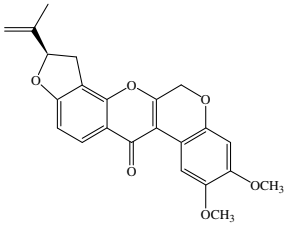

4

Finally, the remaining $C_8H_8O_3$ moiety, linked twice with the 2,3-disubstituted chromone, corresponded to five double bond equivalents. It was constituted by the next 1,2,4,5-tetrasubstituted benzene bearing three oxygen atoms as shown by the downfield quaternary C signals (C-2′: δ 143.5 ppm, C-4′,5′: δ 148.0 and 147.9 ppm). Two heteroatoms belonged to methoxy groups (δ 56.6 and 56.5 ppm) in the *ortho* positions since the third was linked to the chromone part along with the last and highfield *ortho* quaternary C (C-1′: δ 115.1 ppm). This result was fully supported by the HMBC map for the *para*-oriented H (H-3′: δ 7.11 ppm and H-6′: δ 7.65 ppm). The 3′-proton exhibited one ^3J cross-peak with C-1′ and one more with C-5′ close to C-4′. Conversely, H-6′ showed one ^4J connectivity with C-3′ (δ 95.8 ppm) and two ^3J cross-peaks with C-2′ (δ 143.5 ppm) and C-3 (δ 99.5 ppm). To conclude, the complete structure for this new C_{22} isoflavonoid was 4′,5′-dimethoxycoumarono-2″,2″-dimethylpyrano(5″,6″:8,7)-chromone for which the trivial name nor-dehydrodeguelin was assigned because it was closely related to the C_{23} rotenoid dehydrodeguelin (**3**).[4,7]

With a slightly more polar chromatographic behaviour and $[\alpha]_D^{21}$ −53 (*c* 0.003, $CHCl_3$), compound **2** was also isolated as a white amorphous powder. It showed a UV spectrum with bands at λ_{max} (MeOH): 257, 289 and 323 sh nm, respectively. The HREIMS of the molecular ion (found: 378.1093; calcd: 378.1103) evidenced the same molecular formula $C_{22}H_{18}O_6$ as **1**. Comparison of the ^{1}H and ^{13}C NMR data for both compounds (Table 1) showed that the major difference between them was only cyclization of the C_5H_8 side chain. The six-membered ring in **1** was replaced by a five-membered ring likely condensed to the chromone moiety in **2**. This result was suggested in the ^{1}H NMR by three sets of signals integrating for one proton each at δ 5.45 ppm (H-2″), δ 3.65 ppm (H-3″$_a$) and δ 3.31 ppm (H-3″$_b$) in agreement with an oxymethine vicinal to an endocyclic methylene with two nonequivalent protons ($J_{gem} = 15.9$ Hz). The resulting C_2 chain belonged to a 2-substituted 2,3-dihydrofuran 4,5-condensed with the chromone part. Finally, three broad singlets accounting for one methyl (H-8″: δ 1.83 ppm) and one olefinic methylene (H-7″$_a$: δ 5.16 ppm; H-7″$_b$: δ 5.00 ppm) identified the 2-substituent to an isopropenyl side chain. The ^{13}C NMR spectrum supported this partial structure grouping two olefinic C (C-6″: δ 142.8 ppm and C-7″: δ 113.1 ppm) and three aliphatic nuclei (C-2″: δ 87.9 ppm, C-3″: δ 31.7 ppm and C-8″: δ 17.1 ppm). On the basis of the above evidence, the newly reported compound **2** in *L. nicou* was established to be 4′,5′-dimethoxycoumarono-2″-isopropenyl-2″,3″-dihydrofurano(4″,5″:8,7)chromone for which the trivial name (−)-nor-dehydrorotenone was proposed because it was related to (−)-dehydrorotenone (**4**).[4,7] It was previously reported as a by-product (3% yield) resulting from the photooxidative conversion of (−)-dehydrorotenone into (−)-6-oxodehydrorotenone (25% yield).[8,9]

The coumaronochromones are generally reported to co-occur with the structurally analogous 2′-hydroxyisoflavones[10–16] and, although not yet proven, it is likely that the latter group could be the biosynthetic precursor of the former group.[8,10,17] Indeed, 2′-hydroxyisoflavones may be converted into the corresponding coumaronochromones using a variety of oxidative reagents.[13,14,16,17] As none of the 2′-hydroxyisoflavones was detected in the *L. nicou* sample, the coumaronochromones within this species might also be issued from the dehydrorotenoids parents by oxidative ring-B contraction.

Acknowledgements

The authors are grateful to *Région Limousin* for supporting a part of this work (Grant No. 2002-1716) as well as to Dr. J.-M. Marbouty (Université de Limoges) for his help in correcting the English language.

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