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^{13}C NMR SPECTROSCOPY OF CYCLOPENTENPOLIOLS

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Abstract—The ^{13}C NMR spectral parameters of eleven cyclopentenpoliols are discussed. Chemical shift criteria to distinguish isomeric 3' and 4' monodeoxy *eucommiols* have been clearly established.

Although many ^{1}H NMR studies on cyclopentane and cyclopentene poliols have already been reported[1] and further examples were recently cited in a review,[2] only a few detailed accounts of the ^{13}C NMR spectral characteristics of similar compounds so far appeared,[3] and particularly none dealing with cyclopentenpoliols.

Since a certain number of derivatives of eucommiol **4**[4] (Δ^3 *series*) and isoeucommiol **11**[5] (Δ^4 *series*)[6] have been prepared by our laboratory, we have studied their ^{13}C NMR spectra in the hope that application of these results will contribute to the structural analysis in this sector.

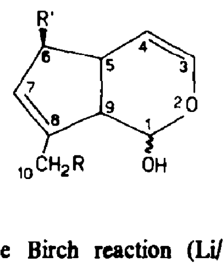
The spectra were completely assigned with the aid of ^{1}H-off-resonance (SFORD) and GATED decoupled spectra, together with NOE considerations and application of known chemical shift rules (α, β, γ effects of CH_3, CH_2OH, OH) and reciprocal comparison between compounds. Helpful was also the comparison of spectra of isoeucommiol series with those of related $\Delta^{7,8}$ unsatured parent iridoid glucosides.[7,8] The ^{13}C NMR chemical shifts of compounds **1**→**11** are listed in Table 1.

PREPARATION OF CYCLOPENTENPOLIOLS

In two previous papers we reported the structures of eucommiol **4**, tetraacetyleucommiol **5** and bisdeoxyeucommiol **6**[4] and of isoeucommiol **11**.[5]

The preparation of the remaining compounds was achieved by univocal one step reactions. The assignment of their structures was based chiefly on the ^{1}H NMR analysis data (Table 2) also in comparison with those of parent compounds.

In particular compounds **1** and **9** were prepared by $NaBH_4$ reduction of **A** and **B**, aglycones respectively of 6,10-bisdeoxyaucubin[5] and of bartsioside.[9] The reaction led to the expected reductive opening of hemiacetalic (dialdehydic) function of dihydropyrane ring with obtaining of cyclopentenpoliols **1** and **9**, in accordance with the formation of **11** from aucubigenin **C**.[5]



A R = R' = H
B R = OH, R' = H
C R = R' = OH

The Birch reaction (Li/NH_3) on isoeucommiol **11** afforded, by selective hydrogenolysis of allylic alcoholic functions, mainly bisdeoxyisoeucommiol **7** and minor amounts of monodeoxyisoeucommiol **8**.

Analogous reaction (Li/NH_3) on **4** gave, besides known bisdeoxyeucommiol **6**,[4] a mixture of both possible monodeoxyeucommiols **2**(22%) and **3**(30%). The assignments of the correct structures to these isomeric compounds, which could result a complex task by ^{1}H NMR approach, was easily and unequivocally achieved by the analysis of ^{13}C NMR data (*vide infra*).

RESULTS AND DISCUSSION

Δ^3 *Series*

The introduction of an OH substituent at C-1 (**1**–**2**) in β configuration induces a large downfield shift (+46.77 ppm) of this carbon as well as smaller deshieldings for the β carbons (+9.57 ppm, C-2; +8.69 ppm, C-5) and upfield shifts for the γ carbons (−2.83 ppm, C-3; −2.15 ppm, C-4; −2.75 ppm, C-2').[10] Similar effects of OH-1 are observed in **3** (+46.71 ppm), **4** (+46.48 ppm) and **6** (+46.80 ppm).

The comparison of the pair **6**–**4** shows that the replacement of both vinylic Me groups by hydroxymethyl functions causes the deshielding (β effect) of the quaternary olefinic C-3 (+7.08 ppm) and C-4 (+6.34 ppm) and the shieldings (γ effect) of both allylic C-2 (−3.11 ppm) and C-5 (−3.56 ppm) carbons.

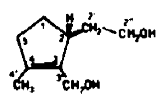
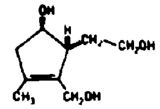
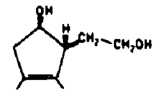
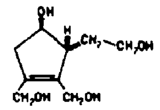
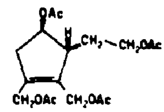
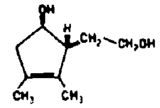
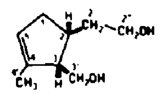
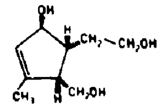
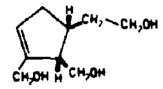
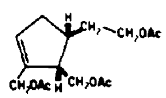
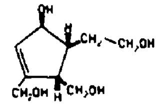
As regards the correct assignment of the two quaternary sp^2 carbons of compounds **4**, **5** and **6** which exhibit similar chemical shift values, they have been discriminated each other on the basis of their different splitting diagrams observed in "Gated decoupled" spectra. The expanded multiplet at lower field shows a major complexity due to additive geminal coupling with the allylic methylene protons at C-5. The other multiplet to slightly higher field results less complex because of two bond C–H coupling with the unique proton at C-2. Thus the olefinic signal at lower field must be attributed to C-4 and the other one at C-3. Easier is obviously the assignment of these carbons in the other compounds of the series.

The sp^2 carbons of he Δ^4 *series* are on the contrary easily distinguishable because of their different signal intensity in PND (lack of NOE) and multiplicity in SFORD spectra.

The difficult task of an unambiguous differentiation of the isomeric allylic monodeoxyeucommiols **2** and **3**—obtained together with **6** by Li/NH_3 reduction of **4** at selected temperature value (Experimental)—was easily resolved considering the shift variations induced, with respect to parent compounds **4** and **6**, on olefinic C-3 and C-4 and alternatively on allylic C-2 and C-5 by the introduction of an OH function at C-3' or C-4'.

In fact the olefinic C-3 and C-4 of **2** show, with respect to **6**, deshielding values (+6.50 and +1.76 ppm)

Table 1. ^{13}C NMR Assignments

	C-1	C-2	C-3	C-4	C-5	C-2'	C-2"	C-3'	C-4'
 **1**	28.82 t	43.27 d	139.36 s	136.53 s	37.41 t	36.34 t	61.34 t	56.45 t	13.98 q
 **2**	75.59 d	52.84 d	136.53 s	134.38 s	46.10 t	33.59 t	61.04 t	56.65 t	13.86 q
 **3**	75.53 d	56.28 d	131.68 s	138.08 s	42.11 t	33.05 t	60.97 t	12.16 q	58.45 t
 **4**	75.30 d	52.93 d	137.11 s	138.96 s	42.19 t	33.11 t	60.84 t	56.17 t	57.91 t
 **5**	77.06 d	51.16 d	135.25 s	135.65 s	40.44 t	29.58 t	62.30 t	58.48 t	59.88 t
 **6**	75.62 d	56.04 d	130.03 s	132.62 s	45.75 t	33.29 t	61.06 t	12.09 q	13.77 q
 **7**	38.04 t	38.69 d	52.44 d	142.00 s	127.24 d	33.32 t	62.13 t	60.64 t	15.55 q
 **8**	82.32 d	48.50 d	52.06 d	144.98 s	129.99 d	31.28 t	62.16 t	59.76 t	15.36 q
 **9**	37.52 t	39.08 d	49.23 d	144.76 s	129.50 d	33.05 t	62.03 t	60.57* t	61.05* t
 **10**	37.02 t	38.99 d	46.28 d	143.47 s	130.79 d	29.31 t	63.69 t	62.88* t	62.30* t
 **11**	81.84 d	48.55 d	48.74 d	147.26 s	130.77 d	31.07 t	62.02 t	60.17* t	60.36* t

rather similar to those (+5.46 and +1.65 ppm) observed for C-4 and C-3 of isomer 3. The parallel comparison of 2 and 3 with 4 evidentiates analogous shift differences: +4.58 and +0.58 ppm for C-4 and C-3 of 2 and +5.43 and +0.88 ppm for C-3 and C-4 of 3.

These crossed shift correlations indicate unequivocally that the vynilic Me group must be linked at C-3 in 3 and at C-4 in 2.

The alternative criterion of comparing the shift variations of allylic C-2 and C-5 carbons of 2 and 3 with those of 4 and 6 respectively, leads to identical conclusions. It is interesting to note the near identical shift values observed for C-2 in the pairs 2-4 (52.84, 52.93 ppm) and 3-6 (56.28, 56.04 ppm) and for C-5 in the reverse couples 2-6 (46.10, 45.75 ppm) and 3-4 (42.11, 42.19 ppm).

As regards the correct assignment of the signals relative to three CH_2OH groups, the comparison 4-6 shows that the saturated C-2" must be the most deshielded one. Further comparison of 1, 2 and 3 with 4 allows an easy discrimination between the allylic C-3' and C-4', the latter always resonating at lower field.

Δ^4 *Series*

Pure effects of the OH replacement at C-1 may be inferred from pairs of compounds such 7-8 and 9-11: (a) +44.28 and +44.32 ppm for C-1 (α effect), (b) +9.81 and +9.47 ppm for C-2 (β effect).

Other significant chemical shift changes are observed in the same pairs for the olefinic C-5 (+2.75 and +1.27 ppm, β effect) and C-4 (+2.98 and +2.50 ppm, γ effect), for allylic C-3 (−0.38 and −0.49 ppm, γ effect) and for C-2' (−2.04 and −1.98 ppm, γ effect).

In this series the C-1 carbon is allylic and always more deshielded than in corresponding terms of Δ^3 *series* (e.g. 1-7, 2-8 and 4-11).

In the isoeucommiol series the discrimination between the CH_2OH signals seems to be less easy than in the eucommiol one. Comparison of spectral data of **7**, **8**, **9** and **11** would indicate that also in these compounds the C-2″ is the most deshielded of the three hydroxymethyl carbons, and resonates always in a very narrow range (62.02–62.16 ppm). The assignment of C-3′ in **7** and **8** is consequently definited, while some uncertainty remains for the discrimination of C-3′ and C-4′ in **9** and **11**, although the reported tentative assignments seem to be preferred.

The crossed comparison between corresponding compounds of the two series allows to outline the different deshielding values caused by the shift of the double bond from Δ^3 to Δ^4 on the C-1 carbon, now in allylic position, according to its methylene (+9.22 ppm, **1–7**) or hydroxymethyne situation (+6.73 ppm, **2–8** and +6.54 ppm, **4–11**).

The same change $C\text{-}3(sp^2) \rightarrow C\text{-}3(sp^3)$ induces the upfield shift of C-2 (−4.58 ppm, −4.34 ppm and −4.38 ppm respectively in the three above pairs) and, on the contrary, the downfield shift of C-3′ (+4.19, +3.11 and +4.00 ppm), although both carbons have lost the allylic position.

The double bond shift is the reason also for the deshielding of olefinic C-4 (+5.47, +10.60 and +8.30 ppm) and for the shielding of C-2′(−3.02, −2.31 and −2.04 ppm).

The acetylation of OH functions induces (pairs **4–5** and **9–10**) the expected small downfield shift of primary hydroxymethyl (+1.46, −2.31 ppm) and secondary hydroxymethine carbons (+1.76 ppm).

Replacing OH functions by acetoxy groups causes, as expected, a decreasing of the deshielding effects on β carbons in the two series:

(a) Δ^3 *series*: on C-2 (−1.77 ppm), on C-5 (−1.75 ppm), on C-2′ (−3.53 ppm), on C-3 (−1.86 ppm) and on C-4 (−3.31 ppm)

(b) Δ^4 *series*: on C-2′ (−3.74 ppm), on C-3 (−2.95 ppm) and on C-4 (−1.29 ppm).

The substituent effects observed (OH, CH_3, CH_2OH). induce additive shift increments which could be used to predict chemical shift parameters of known or unknown analogous compounds.

We have also registered the ^1H NMR spectra of all compounds above discussed which also allow to obtain interesting correlations. As the detailed analysis of these data would require a long discussion which is beyond the aim of this work, we report the only bare data (Table 2) for the benefit of other workers in the field.

EXPERIMENTAL

Silica gel (140–230 Mesh, Merck) used for column chromatography was washed several times with hot water, then dried and activated at 120° for 12 hr. Silica gel plates 60 F_{254}(Merck) were used in tlc. Spray reagent: 2 N H_2SO_4, heating at 120°.

^1H NMR spectra were taken with a Perkin–Elmer R-32 (90 MHz) using HDO as internal standard at 4.70 ppm for D_2O solns and TMS as internal standard for $CDCl_3$ solns. The ^{13}C NMR spectra were recorded with Varian CFT-20 (20 MHz) and Bruker WH-90 (22.63 MHz) spectrometers, using dioxane as internal standard (67.4 ppm from TMS) for D_2O solns and TMS as internal standard for $CDCl_3$ solns.

Compounds **1**, **2**, **3**, **7**, **8** and **9** gave satisfactory elemental analysis.

$NaBH_4$ *Reduction of the aglycone of* 6,10-*bisdeoxyaucubin, poliol* (**1**). Crude aglycone of 6,10-bisdeoxyaucubin (130 mg)[5] dissolved in 40% EtOH (10 ml) was treated with $NaBH_4$ (300 mg, ~10 times molar excess) for 1 hr at room temp. After this period $NaBH_4$ excess was decomposed by bubbling CO_2 until pH ≃ 7, and then the clarified soln was evaporated *in vacuo* and diluted with water (10 ml) then decolorizing charcoal (1 g) was added and the suspension stratified on a gooch funnel (2 cm dia). The charcoal layer was washed with H_2O (0.5 l) then eluted with MeOH (0.5 l) affording a residue (120 mg) which chromatographed on silica gel (9 g) in benzene–MeOH (7:3) gave pure **1** as an oil.

Li/NH_3 *Reduction of* **4**, *monodeoxyeucommiols* (**2**) *and* (**3**). To eucommiol **4** (0.6 g) dissolved in abs. EtOH (3 ml) was added liquid ammonia (150 ml) and then, with stirring, Li (0.4 g) in small pieces over a period of 4 hr, keeping the temp at −50°. The blue final soln was decolorized with abs EtOH (1 ml) and left overnight to allow the ammonia to evaporate. Removal of volatile liquids was completed at reduced pressure. The residue was dissolved in water (100 ml) and neutralized with 6 N HCl. The water soln was treated with decolorizing charcoal (10 g) and the resulting suspension stratified on a gooch funnel (8 cm dia), washed with water (2 l) and then eluted with MeOH (0.3 l). Evaporation *in vacuo* of MeOH soln gave an amorphous residue (0.45 g) which chromatographed on silica gel (25 g) in $CHCl_3$–MeOH (9:1) gave successively **3** (30 mg, $R_f = 0.32$) and **2** (15 mg, $R_f = 0.27$) as oils, together with **6** (50 mg) and unaffected **4** (290 mg). **3**$[\alpha]_D^{25} = -53°$ (MeOH, $c = 0.15$). **2**$[\alpha]_D^{25} = -74$ (MeOH, $c = 0.11$).

Li/NH_3 *Reduction of* **11**, *poliols* (**7**) *and* (**8**). To isoeucommiol **11** (300 mg) dissolved in liquid ammonia (300 ml) was added Li in small pieces (1.5 g) over a period of 4 hr, keeping the temp at −40°. The soln, worked up as described for **2** and **3**, gave a residue (240 mg) which chromatographed on silica gel (20 g) in EtOAc–MeOH (9:1) afforded **7** (120 mg, $R_f = 0.45$), **8** (30 mg, $R_f = 0.38$) and unaffected **11** (40 mg, $R_f = 0.25$).

$NaBH_4$ *Reduction of bartsiogenin, poliol* (**9**). Crude bartsiogenin[9] (100 mg) dissolved in water (5 ml) was treated with $NaBH_4$ (200 mg, ~10 times molar excess) and worked up as previously described for **1**. The final residue (70 mg) chromatographed on silica gel (6 g) in EtOAc–MeOH (9:1) afforded pure **9** (45 mg) as an oil.

Triacetate (**10**). Compound **9** (50 mg) was treated with anhyd pyridine (0.3 ml) and Ac_2O (0.6 ml) for 1 hr at room temp, then MeOH (3 ml) was added and the soln left for 20 m. Evaporation *in vacuo* gave a residue (60 mg) which chromatographed on silica gel (5 g) in $CHCl_3$–Et_2O (8:2) afforded pure **10** (45 mg) as an oil.

The preparation of the remaining compounds was carried out according to known procedures: **4**[4], **5**[4], **6**[4], **11**.[5]

REFERENCES

[1] G. Wolczunowicz, F. G. Cocu and Th. Posternak, *Helv. Chim. Acta* **53**, 2275 (1970); F. G. Cocu, G. Wolczunowicz, L. Bors and Th. Posternak, *Ibid.* **53**, 739 (1970).

[2] H. Booth, *Progress in* NMR *Spectroscopy* (Edited by J. W. Emsley, J. Feeney and L. H. Sutcliffe), p. 215–216. Pergamon Press, Oxford (1969), and refs. therein.

[3] R. G. S. Ritchie, N. Cyr, B. Korsch, H. J. Koch and A. S. Perlin, *Can. J. Chem.* **53**, 1424 (1975); R. Hanselaer and P. De Clercq, *Org. Magn. Reson.* **13**, 376 (1980).

[4] A. Bianco, C. Iavarone and C. Trogolo, *Tetrahedron* **30**, 4117 (1974).

[5] A. Bianco, M. Guiso, C. Iavarone, P. Passacantilli and C. Trogolo, *Ibid.* **33**, 851 (1977).

[6] In order to simplify the comparison of ^1H and ^{13}C NMR data, we maintained for **11** and related compounds (Δ^4 *series*) the IUPAC numbering used for eucommiol **4** and derivatives (Δ^3 *series*).

[7] A. Bianco, C. Bonini, M. Guiso, C. Iavarone and C. Trogolo, *Gazz. Chim. Ital.* **108**, 17 (1978).

[8] Our unpublished data of bartsioside and linaride.

[9] A. Bianco, M. Guiso, C. Iavarone and C. Trogolo, *Gazz. Chim. Ital.* **106**, 725 (1976).

[10] The corresponding effects in the pair cyclopentane/cyclopentanol are +48.00 ppm, +9.7 ppm and −1.9 ppm. E. Breitmaier and W. Voelter ^{13}C NMR *Spectroscopy*, pp. 122, 140. Verlag Chemie (1974).

Table 2. ^{1}H NMR Assignments

Δ^3series	2H-C(1) H-C(1)	H-C(2)	2H-C(5)	2H-C$^{2'}$	2H-C$^{2''}$	CH$_2$OH-3	CH$_2$OH-4	CH$_3$-3	CH$_3$-4
1 (D_2O)	2.1-1.7 cm	2.77 bsg	2.20 bsg	2.1-1.1 cm	3.62 t J=7.0	4.14 dd J_{AB}=12.0			1.70 bs
2 (D_2O)	4.18^c	2.7-2.5^b	2.80 bdd 2.20 bd $J_{5\alpha,5\beta}$ = 17.0 $J_{5\alpha,1\alpha}$ = 6.0	2.1-1.2 cm	3.70 t J=7.0	4.20 dd J_{AB}=12.0			1.72 bs
3 (D_2O)	4.16 bs	2.46 bd	2.80 bd 2.20 bd $J_{5\alpha,5\beta}$ = 18.0 $J_{5\alpha,1\alpha}$ = 6.0 $J_{5\beta,1\alpha}$ = 2.5	2.0-1.1 cm	3.67 t J=7.0		4.16 bs	1.67 bs	
4$^{(4)}$ (D_2O)	4.24 bs	2.72^b am	2.90 bdd 2.32 bd $J_{5\alpha,5\beta}$ = 18.0	2.1-1.2 cm	3.71 t J=7.0	4.24 bs	4.24 bs		
5$^{(4)}$ ($CDCl_3$)	5.08 Se	2.88^b am	2.92 bdd 2.39 bd $J_{5\alpha,5\beta}$ = 18.0 $J_{5\alpha,1\alpha}$ = 6.0 $J_{5\beta,1\alpha}$ = 2.5	2.1-1.2 cm	4.13 t J=7.0	4.72 bs	4.72 bs		
6$^{(4)}$ (D_2O)	4.12 se	2.40 bd	2.70 bdd 2.14 bd $J_{5\alpha,5\beta}$ = 17.0 $J_{5\alpha,1\alpha}$ = 6.0 $J_{5\beta,1\alpha}$ = 2.5	2.0-1.2 cm	3.67 t J=7.0			1.63 bs	1.63 bs

Δ^4series	2H-C(1) H-C(1)	H-C(2)	H-C(3)	H-C(5)	2H-C$^{2'}$	2H-C$^{2''}$	CH$_2$OH-3	CH$_2$OH-4	CH$_3$-4
7 (D$_2$O)	2.5-1.9	2.5-1.9	2.48 bsg	5.66 bs	2.1-1.7 cm	3.68 t J=7.0	3.74 d J=5.0		1.78 bs
8 (D$_2$O)	4.56 bd	2.6-2.1 cm	2.70 bsg	5.56 bs	2.1-1.9 cm	3.76 t J=7.0	3.72 d		1.80 bs
9 (D$_2$O)	2.6-2.0	2.6-2.0	2.67 bsg	5.84 bs	2.0-1.4 cm	3.68 t J=7.0	3.70 d	4.20 bs	
10 (CDCl$_3$)	3.0-2.1	3.0-2.1	2.80 bsg	5.84 bs	2.0-1.5 cm	4.14 t J=7.0	4.5-3.9 o	4.68 bs	
11$^{(5)}$ (D$_2$O)	4.60 d	2.3-1.7	2.85 bs	5.80 bs	2.3-1.7	3.75 t J=6.6	3.71 d J=4.0	4.24 bs	

(a) most of the assignments have been checked by spin decoupling experiments

(b) hidden by Hα-5 proton

(c) covered by C$\underline{H}_2$OH-3 signals

Chemical shifts (δ) in ppm, coupling constants (J) in Hz; bd=broad doublet, bdd= broad doublet of doublets, bs=broad singlet, bsg=broad signal, cm=complex multiplet, d=doublet, dd=doublet of doublets, o=octet, se=sextet, t=triplet.