Detailed Assignment of $^1$H and $^{13}$C NMR Data of Lychnopholide and Centratherin

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Abstract: As part of our research work on the isolation and identification of natural products, mainly sesquiterpene lactones, we have recently undertaken a detailed study of $^1$H and $^{13}$C NMR data, using 2D-NMR modern techniques, of several heliangolide lactones. The continuous evolution of NMR equipment accompanied by the development of new techniques has made it possible to reduce mistaken interpretations and uncertain assignments occasionally found in the earlier literature. In this report, we describe the total assignment of $^1$H and $^{13}$C NMR data of lychnopholide and centratherin, two trypanocidal sesquiterpene lactones that appear recurrently in many plant extracts studied in our laboratory. Both structures are closely related to the sesquiterpene lactones 15-deoxygoyazensolide and Goyazensolide. NMR spectra were recorded on Bruker Avance DRX500 or DRX400 equipment. An unequivocal assignment of all chemical shifts (both for $^1$H and $^{13}$C) and a measurement of most scalar coupling constants ($^1$H) for both structures were achieved through analysis of COSY, HMOC, HMBC and J-resolved spectra. Relative stereochemistry was determined by analysis of coupling constants comparison with values found through molecular mechanics computer programs, and also by NOE experiments. We have also demonstrated in both cases that the position of the ester group on the medium sized ring can be determined by HMBC, which makes X-ray analysis for this purpose no longer necessary.

As part of our research work on the isolation and identification of natural products, mainly sesquiterpene lactones, we have recently undertaken a detailed study of $^1$H and $^{13}$C NMR data, using 2D-NMR modern techniques, of several heliangolide lactones. The continuous evolution of NMR equipment accompanied by the development of new techniques has made it possible to reduce mistaken interpretations and uncertain assignments occasionally found in the earlier literature. In this report, we describe the total assignment of $^1$H and $^{13}$C NMR data of lychnopholide (1) and centratherin (2), two trypanocidal sesquiterpene lactones which appear recurrently in many plant extracts studied in our laboratory. Both structures are closely related to the sesquiterpene lactones 15-deoxygoyazensolide (3) and Goyazensolide (4).

NMR spectra were obtained on a 11.7 Tesla Bruker Avance DRX500 equipment (500.13 MHz for $^1$H and 125.76 MHz for $^{13}$C) using a probehead of 5mm (BBI 1H-BB) and on a 9.39 Tesla Bruker Avance DRX400 equipment (400.13 MHz for $^1$H and 100.62 MHz for $^{13}$C) using a probehead of 5mm (DUL 13C-1). A 30° pulse (P1) was used, during 8.5 µs for $^1$H and 14.25 µs for $^{13}$C; for $^1$H d1=1 s and ns=16 and for $^{13}$C d1=2 s and ns=2048. All samples were prepared at a concentration of 18-25 mg/mL in CDCl$_3$ with TMS as internal reference and were analyzed at 300 K.
For both compounds (1 and 2) the use of HHCOSY and J-resolved experiments allowed an unequivocal assignment of all hydrogen chemical shifts and a measurement of most scalar coupling constants. Most carbon chemical shifts could be assigned with information from HMQC spectra. For quaternary carbons, comparison of experimental data with calculated spectra was enough for most cases. However, a few ambiguities, including some mentioned in previous papers,\textsuperscript{3,4} required information from the HMBC spectra to be cleared up.

As already demonstrated for 15-deoxygoyazensolide, the stereochemistry of hydrogens 9\textalpha and 9\textbeta can be determined by comparing \(J_{\text{vic}}\) values with calculated data and confirmed by NOE experiments.

The stereochemistry of these molecules (confirmed by X-ray analysis for compound 2)\textsuperscript{10} is also confirmed by NOE experiments. HMBC spectra again confirmed the relative positions of the ester groups (position 8) and lactone rings (12-6 lactonization), as opposed to the first structure proposed for this class of lactones.\textsuperscript{1,2} We have thus confirmed that the positions of the ester groups (position 8) and lactone rings (12-6 lactonization), as opposed to the first structure proposed for this class of lactones.\textsuperscript{1,2} We have thus confirmed that the
easily available HMBC spectra can render X-ray analysis to determine the relative positions of the ester and lactone in these sesquiterpenes no longer necessary.

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References
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