Electronic Supporting Information

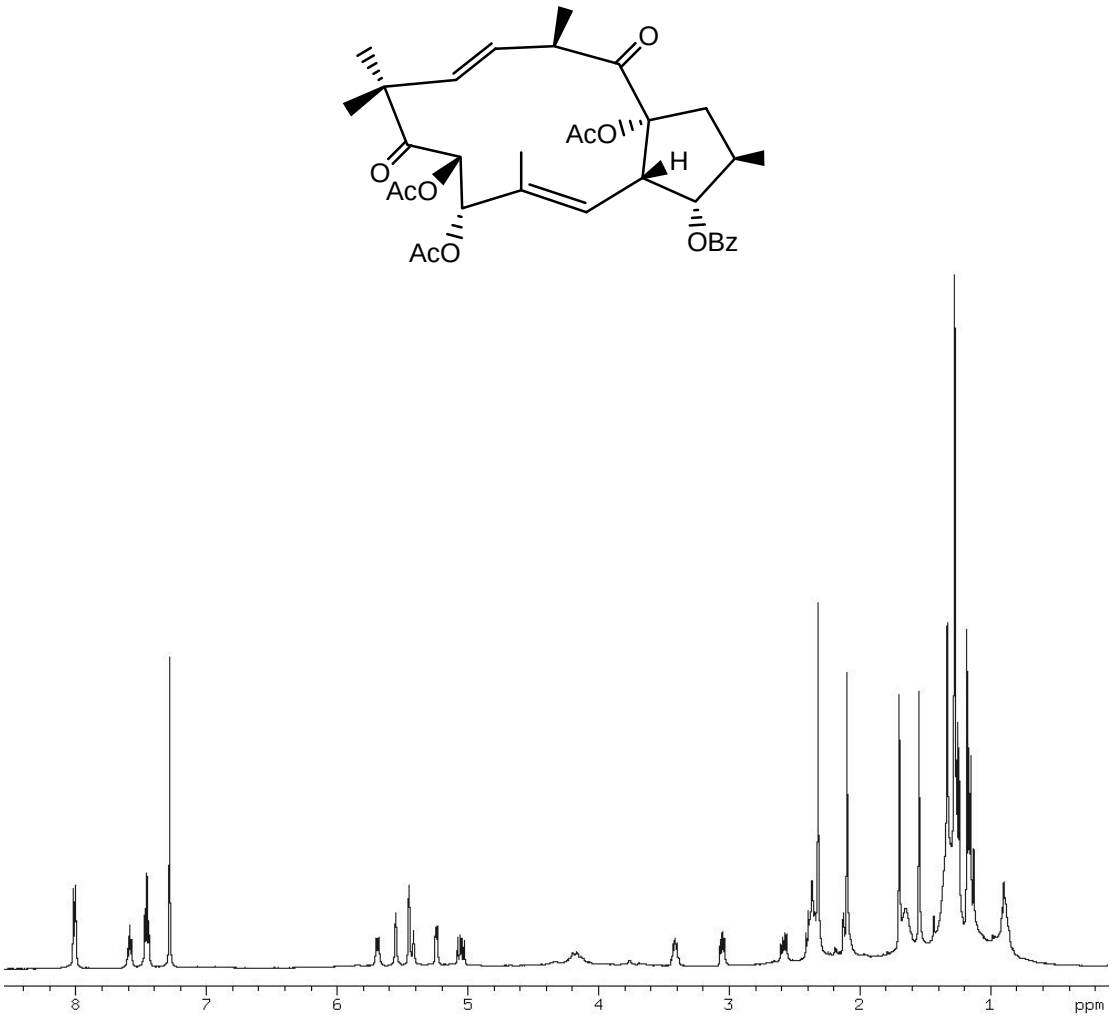
Discovery of New Series of Jatrophane and Lathyrane Diterpenes as Potent and Specific P-Glycoprotein Modulators†

Elisa Barile,[a] Marianna Borriello,[b] Attilio Di Pietro,[c] Agnès Doreau,[c] Caterina Fattorusso,[b] Ernesto Fattorusso,[b] and Virginia Lanzotti*[a]

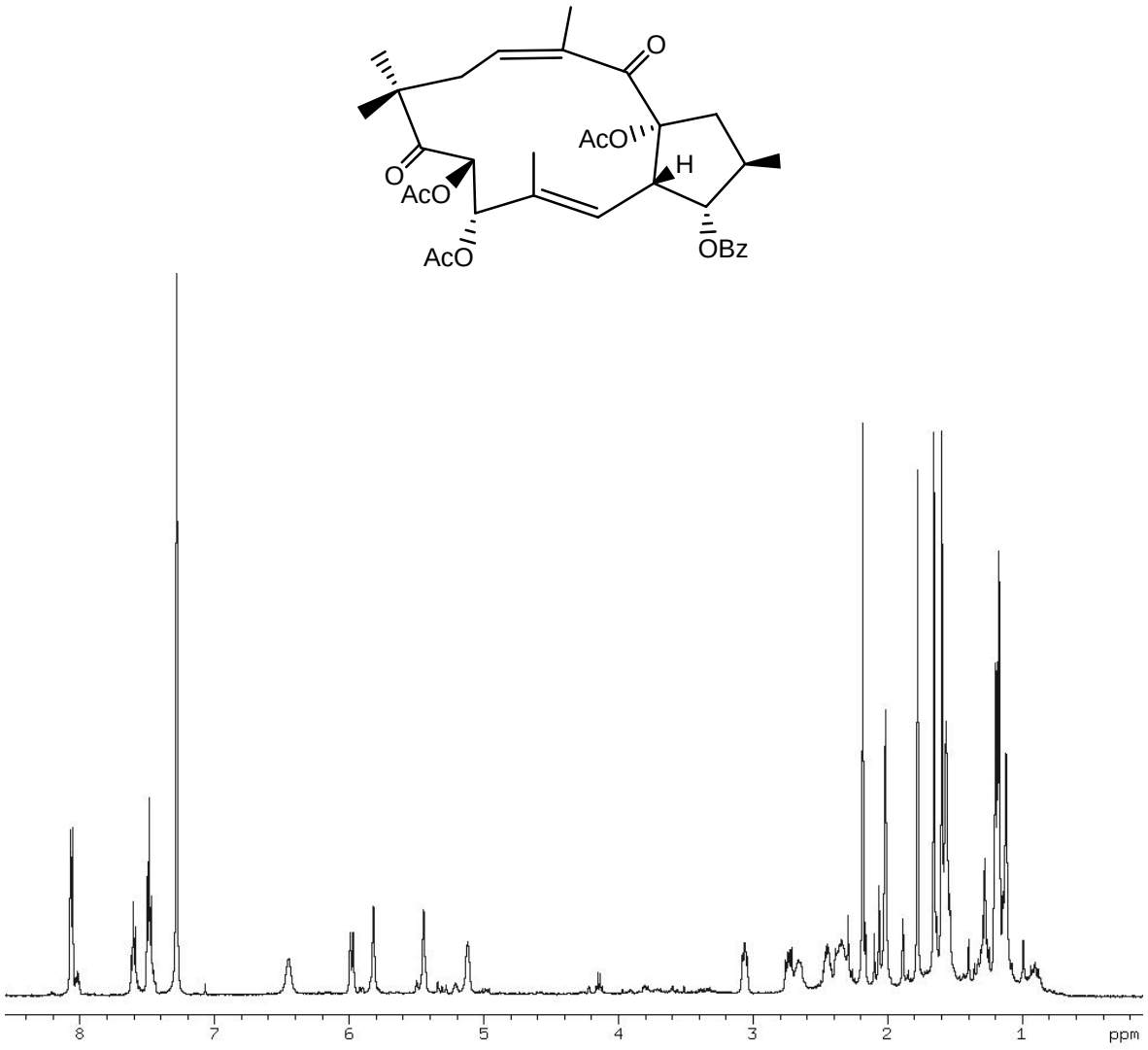
[a]*DISTAAM, Università degli Studi del Molise, Via F. De Sanctis, I-86100 Campobasso, Italy. E-mail: lanzotti@unimol.it ; Phone: +39 874 404649; Fax: +39 874 404652*
[b]*Dipartimento di Chimica delle Sostanze Naturali, Università di Napoli Federico II, Via D. Montesano 49, I-80131 Napoli, Italy*
[c]*Institut de Biologie et Chimie des Proteines, UMR5086 CNRS/Université Lyon1 et IFR128 BioSciences Gerland-Lyon Sud, Passage du Vercors 7, 69367 Lyon Cedex 07, France*

†^{1}H NMR spectra for compounds **1**–**8**, purity criteria for isolated compounds, and minimum energy conformations obtained for each stereoisomers of **1**.

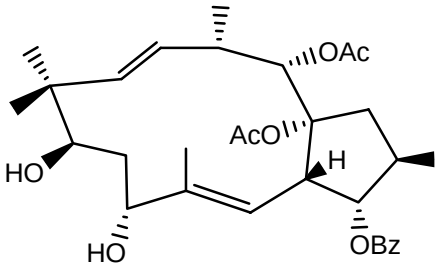
Contents

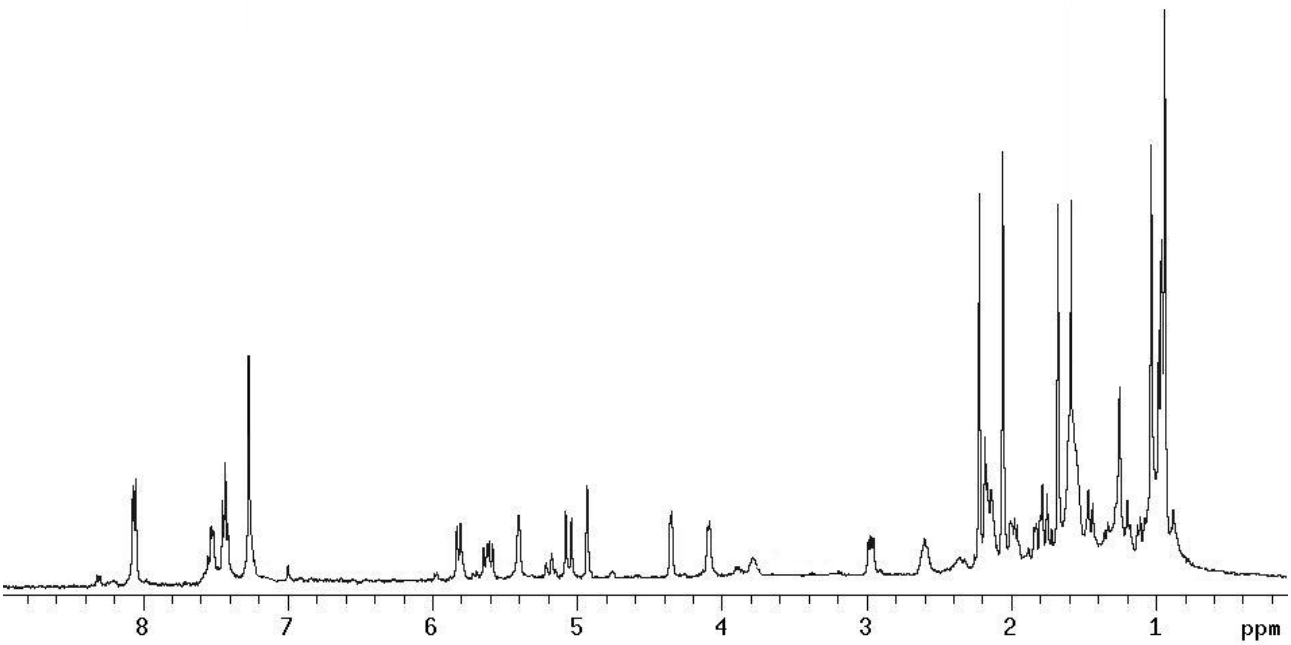


Spectrum S1.
^{1}H NMR spectrum of compound **1** (500 MHz, solvent $CDCl_3$)

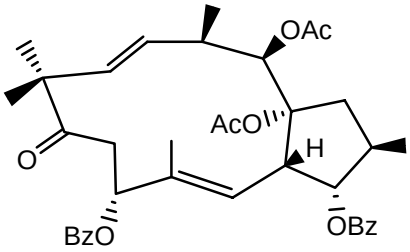


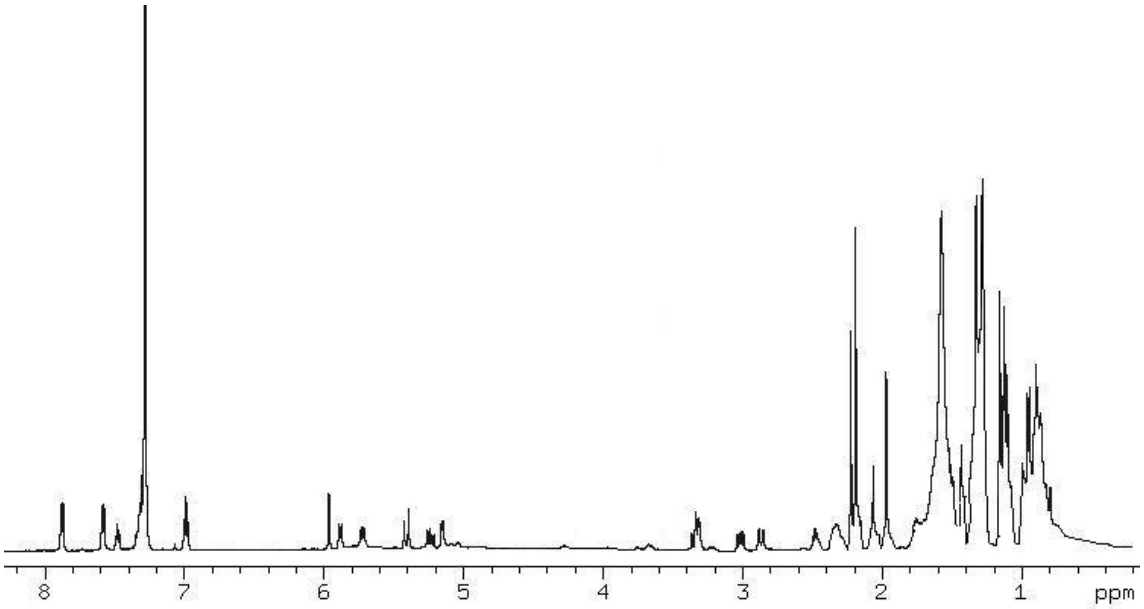
Spectrum S2.
^{1}H NMR spectrum of compound **2** (500 MHz, solvent $CDCl_3$)



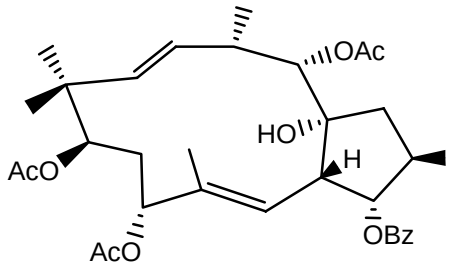


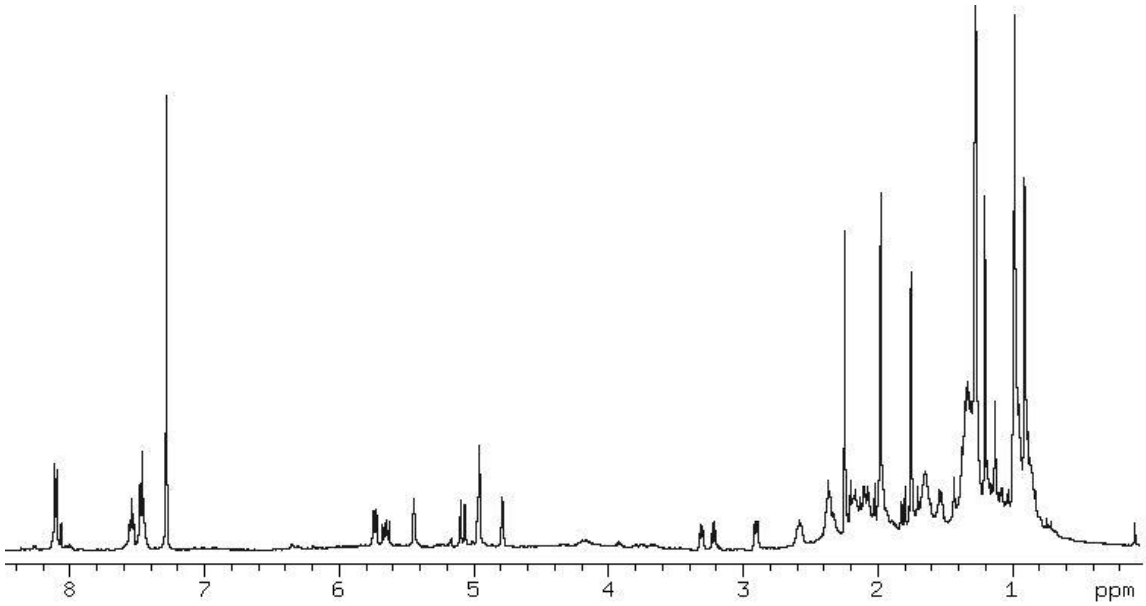
Spectrum S3.
^{1}H NMR spectrum of compound **3** (500 MHz, solvent $CDCl_3$)



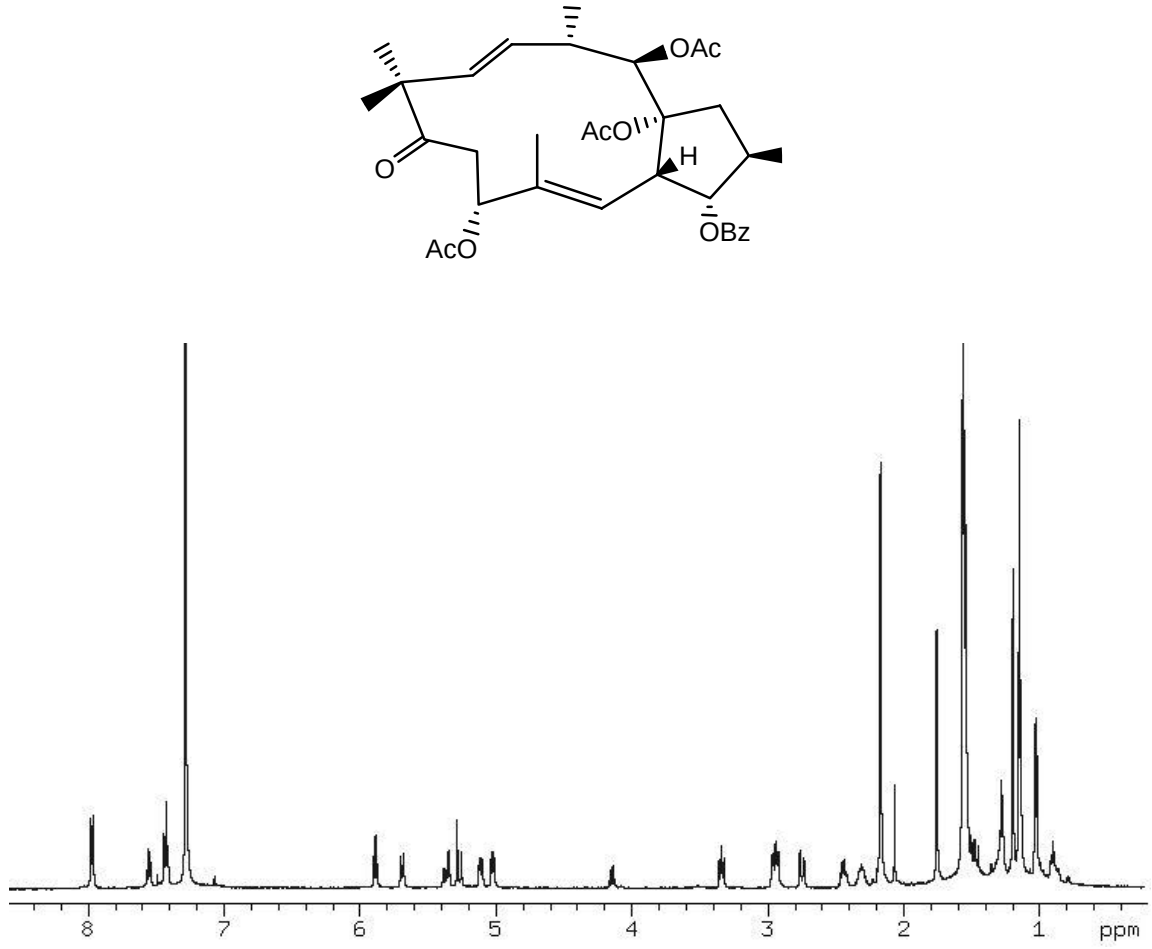


Spectrum S4.
^{1}H NMR spectrum of compound **4** (500 MHz, solvent $CDCl_3$)

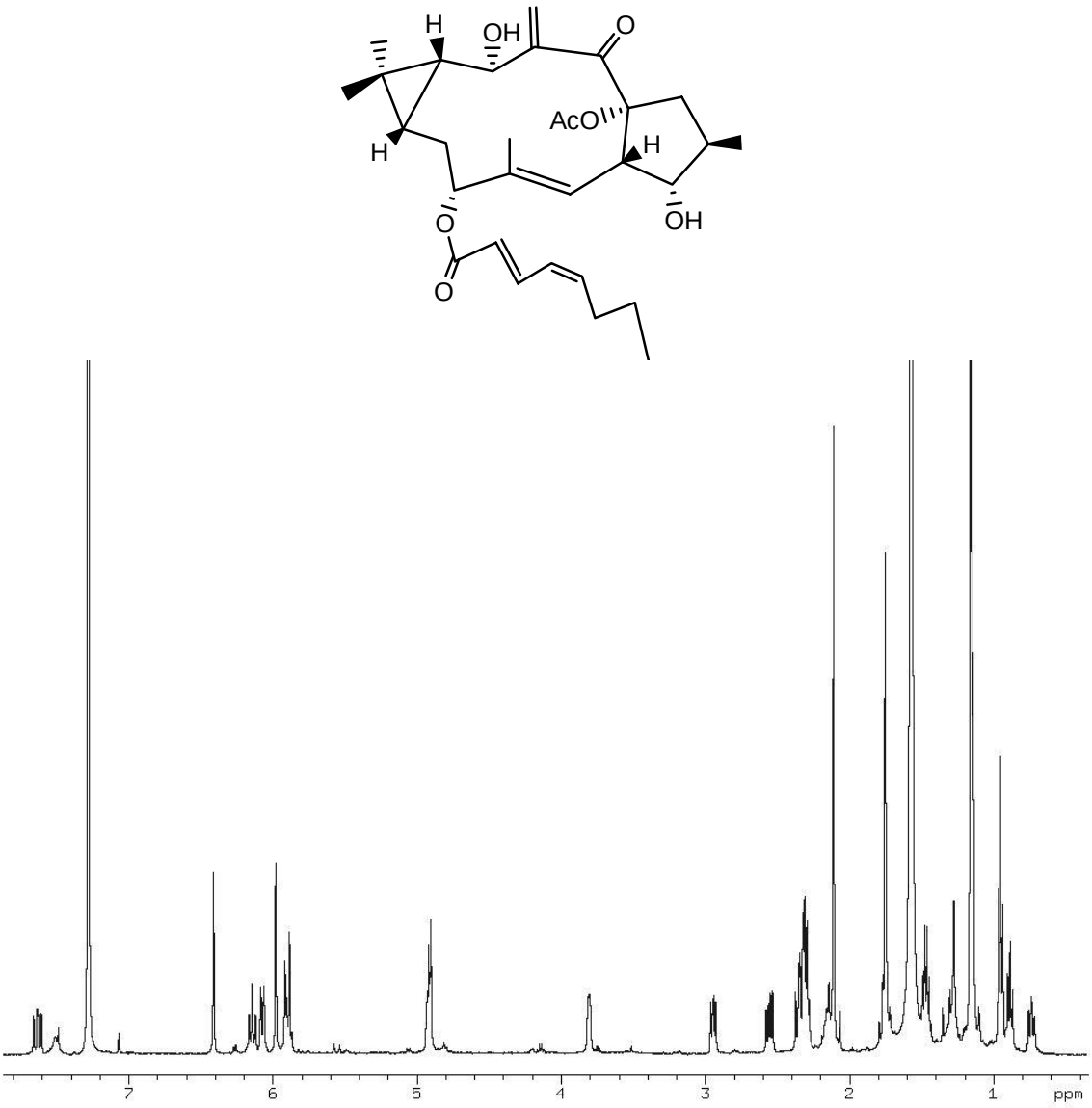




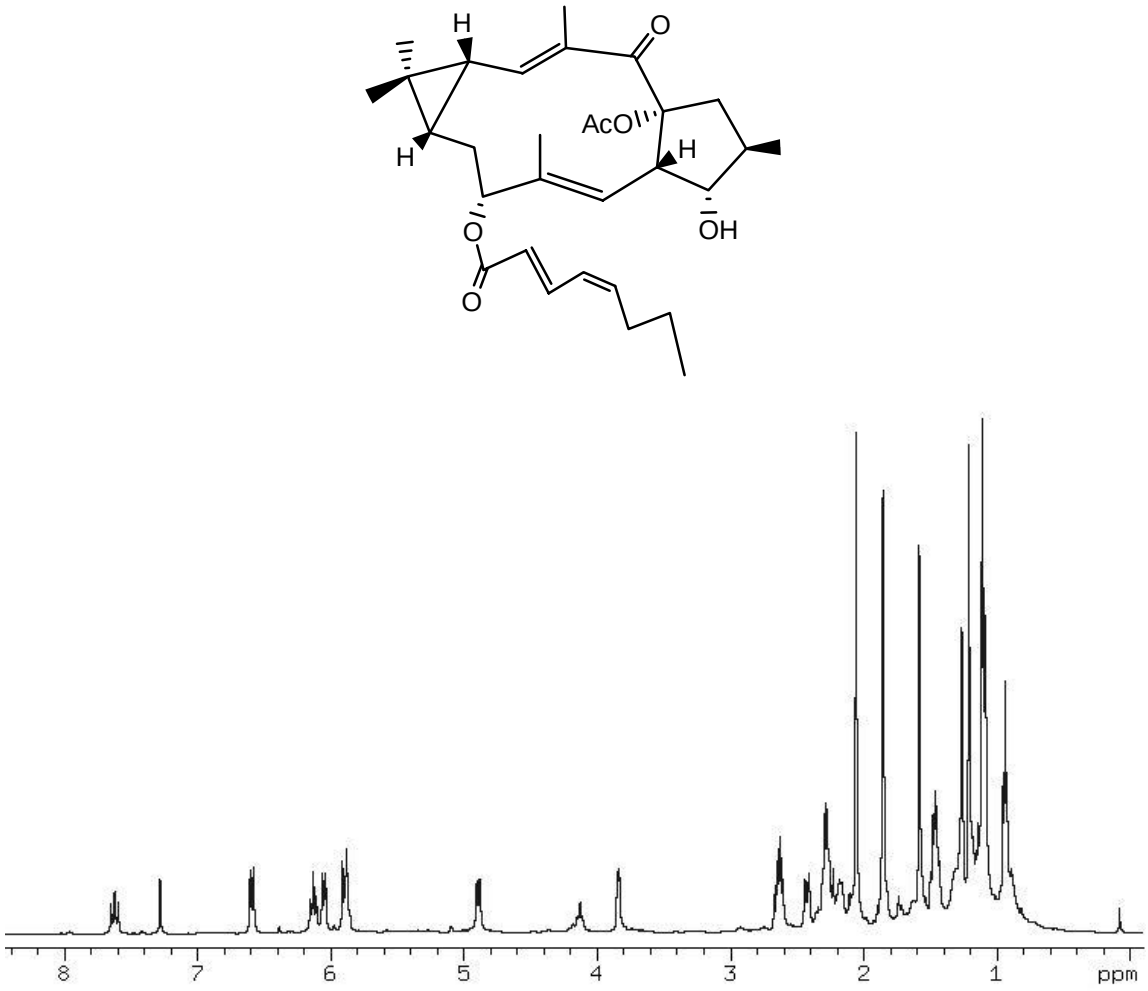
Spectrum S5.
^{1}H NMR spectrum of compound **5** (500 MHz, solvent $CDCl_3$)



Spectrum S6.
^{1}H NMR spectrum of compound **6** (500 MHz, solvent $CDCl_3$)



Spectrum S7.
^{1}H NMR spectrum of compound **7** (500 MHz, solvent $CDCl_3$)



Spectrum S8.
^{1}H NMR spectrum of compound **8** (500 MHz, solvent $CDCl_3$)

Purity criteria for target compounds. The degree of purity of tested compounds was over 95% as indicated by the appearance of a single peak using two different HPLC eluent systems. Retention times (R_t) are expressed in minutes.

Euphoscopin M (**1**): Hexane/EtOAc 75:25 with R_t 54.6. CH_2Cl_2/EtOAc 8:2 with R_t 36.4.

Euphoscopin N (**2**): Hexane/EtOAc 75:25 with R_t 27.9. CH_2Cl_2/EtOAc 8:2 with R_t 18.6.

Euphoscopin C (**4**): Hexane/EtOAc 85:15 with R_t 75.0. CH_2Cl_2/EtOAc 9:1 with R_t 50.0.

Euphornin (**5**): Hexane/EtOAc 75:25 with R_t 59.4. CH_2Cl_2/EtOAc 8:2 with R_t 39.6.

Epieuphoscopin B (**6**): Hexane/EtOAc 8:2 with R_t 24.0. CH_2Cl_2/EtOAc 85:15 with R_t 16.1.

Euphohelioscopin A (**8**): Hexane/EtOAc 75:25 with R_t 42.0. CH_2Cl_2/EtOAc 8:2 with R_t 28.2.

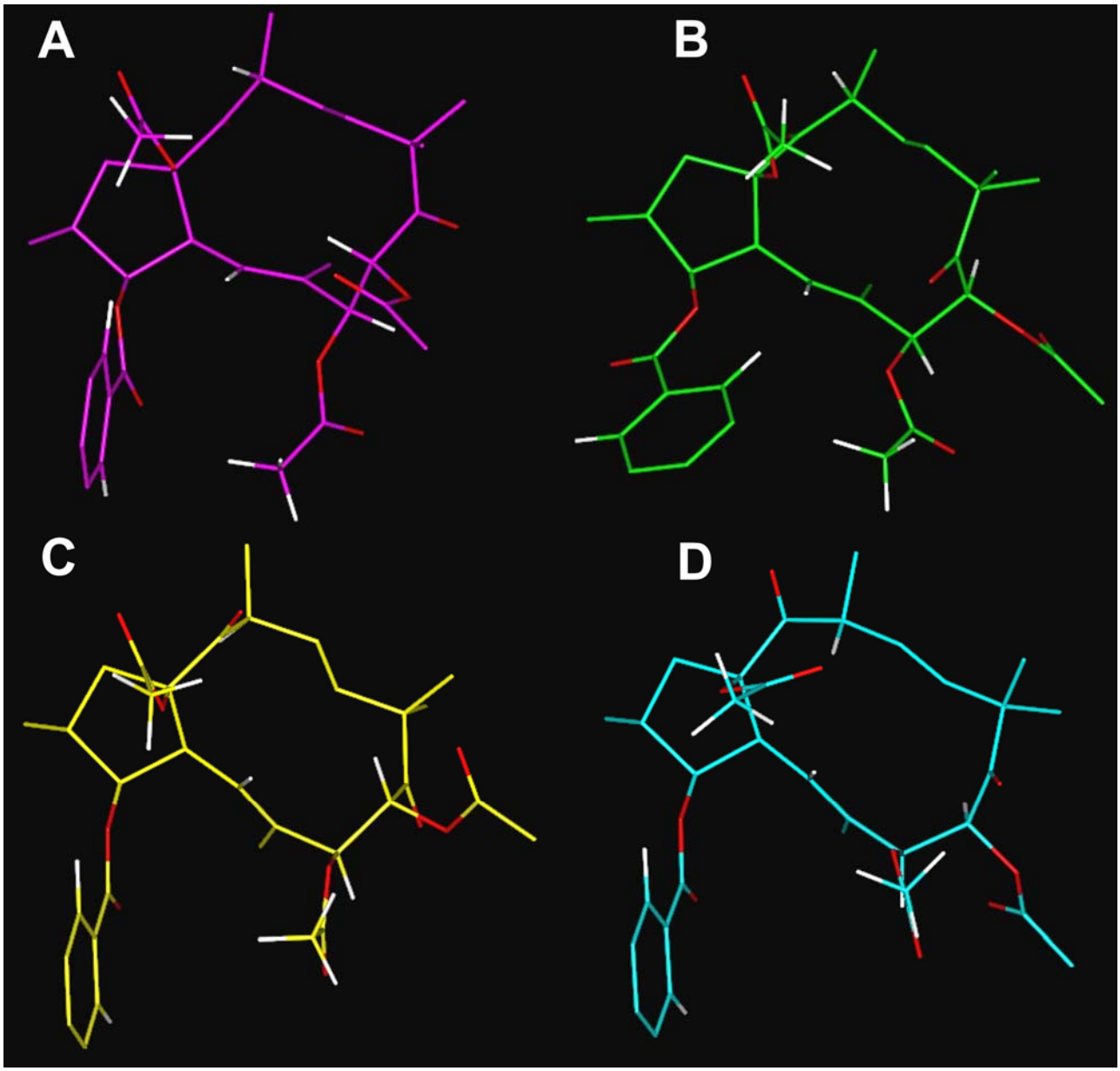


Figure S1.

A-D. Fully optimized AM1 conformers of the possible four steroisomers of euphoscopin M (**1**) at C-8 and C-13 atoms**: A)** 8*R*,13*R*; **B)** 8*S*,13*R*; **C:** 8*R*,13*S* ; **D** 8*S*,13*S* . Atoms are coloured by atom type; hydrogens atoms, with the exceptions of those useful for NMR discussion, are omitted for clarity of presentation.

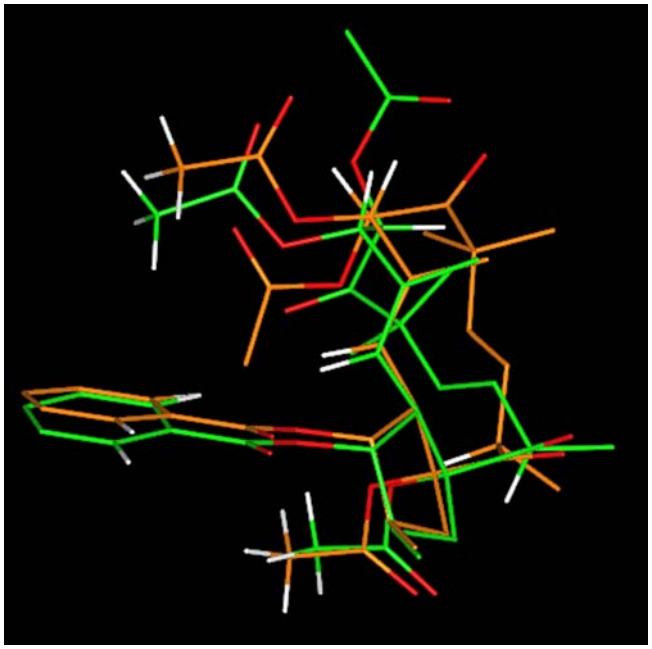


Figure S2.

Superimposition of two low energy conformers of 8*S*,13*R* stereoisomer of euphoscopin M (**1**). The relation between H-7/H-8 dihedral angle value and the relative orientation of C-7 C-3 substituents is evidenced . Atoms are coloured by atom type; hydrogens atoms, with the exceptions of those discussed *in NMR data* are omitted for clarity of presentation.