

Supplementary Material

TRYPANOCIDAL POTENTIAL OF SEMI-SYNTHETIC DERIVATIVES OBTAINED FROM NATURAL LABDANE DITERPENES

Aline N. S. Parra, Ana Carolina F. S. Rocha, Julian C. S. Pavan, Analuz da Silva Machado, Vinícius J. Miranda Rodrigues, Daiane Albino dos Santos, Lizandra G. Magalhães, Sérgio de Albuquerque and Vladimir C. G. Heleno*

In this paper is described the obtention of fourteen derivatives from four natural labdane diterpenes isolated from *Copaifera* oleoresin, named *ent*-copalic acid (**1**), *ent*-3b-acetoxy copalic acid (**2**), *ent*-3b-hydroxy copalic acid (**3**) and *ent*-agathic acid (**4**). All eighteen compounds were assayed against *Trypanosoma cruzi*, revealing three promising compounds with trypanocidal activity, two of them ($IC_{50} = 13.31mM$ and $IC_{50} = 15.05mM$) displaying similar activity as the reference drug ($IC_{50} = 13.12mM$) and one of them even more potent with $IC_{50} = 0.425mM$.

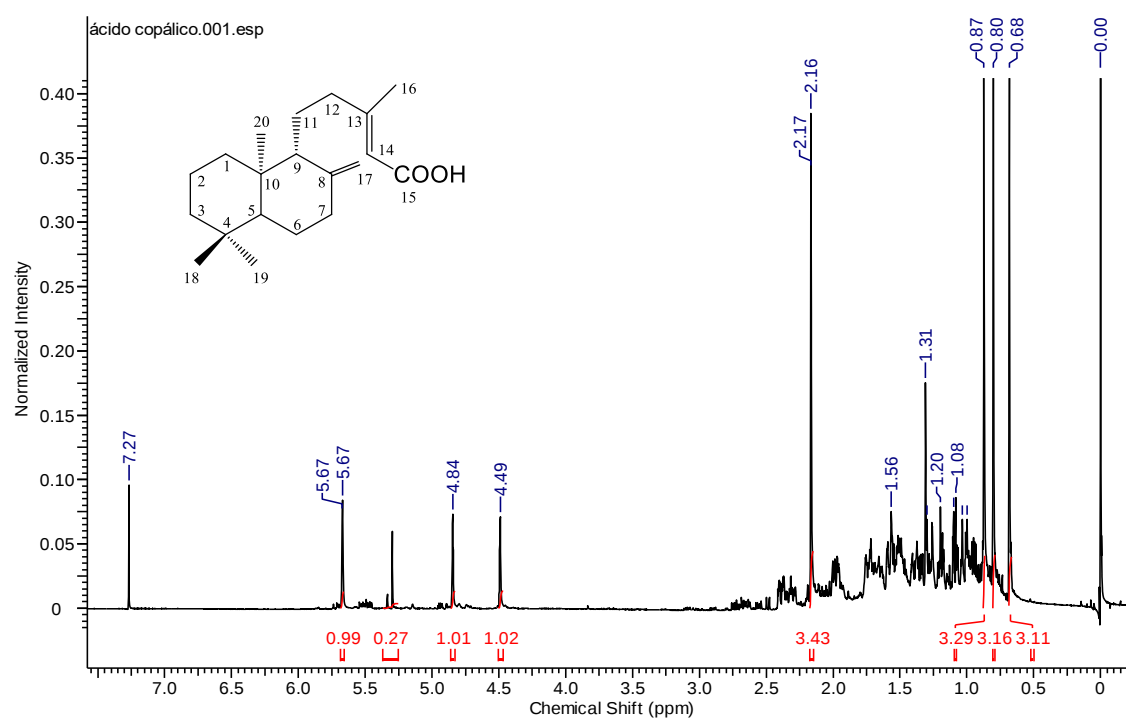


Figure 1S: ¹H NMR spectrum for ent-copalic acid (1) (400 MHz, CDCl₃).

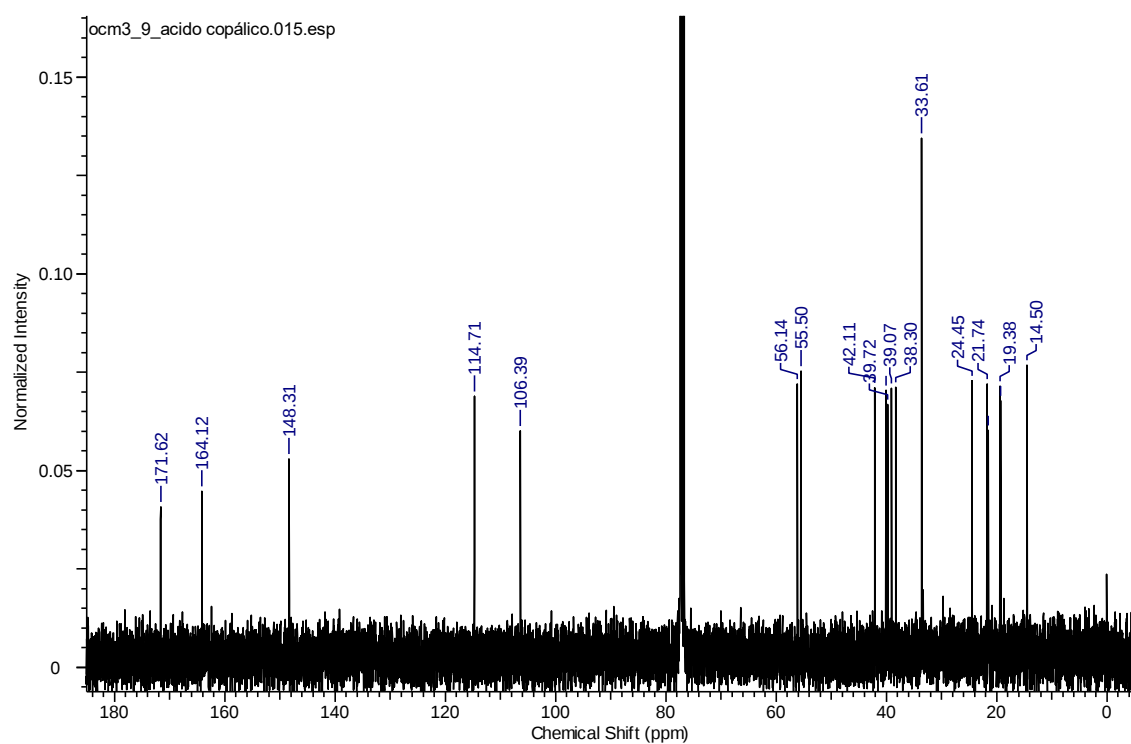


Figure 2S: ¹³C NMR spectrum for ent-copalic acid (1) (100 MHz, CDCl₃).

Table 1S. ^1H NMR data for *ent*-copalic acid (**1**). (400 MHz, CDCl_3)

^1H	Ohsaki <i>et al.</i> , 1994	9
H-14	5.67 s	5.66 s(<i>l</i>)
H-15	2.17 s	2.16 s
H-17a	4.49 s(<i>l</i>)	4.48 s(<i>l</i>)
H-17b	4.85 s(<i>l</i>)	4.84 s(<i>l</i>)
H-18	0.87 s	0.86 s
H-19	0.80 s	0.79 s
H-20	0.68 s	0.68 s

Table 2S. ^{13}C NMR data for *ent*-copalic acid (**1**). (100 MHz, CDCl_3)

^{13}C	Ohsaki <i>et al.</i> , 1994	9
C-1	42.1	42.2
C-2	19.3	19.4
C-3	39.0	39.1
C-4	33.5	33.6
C-5	55.5	55.5
C-6	24.4	24.4
C-7	38.3	38.3
C-8	148.2	148.3
C-9	56.1	56.1
C-10	39.7	39.7
C-11	21.5	21.5
C-12	40.1	40.1
C-13	164.0	164.1
C-14	114.9	114.7
C-15	19.2	19.3
C-16	172.4	171.6
C-17	106.3	106.3
C-18	33.5	33.6
C-19	21.7	21.7
C-20	14.4	14.5

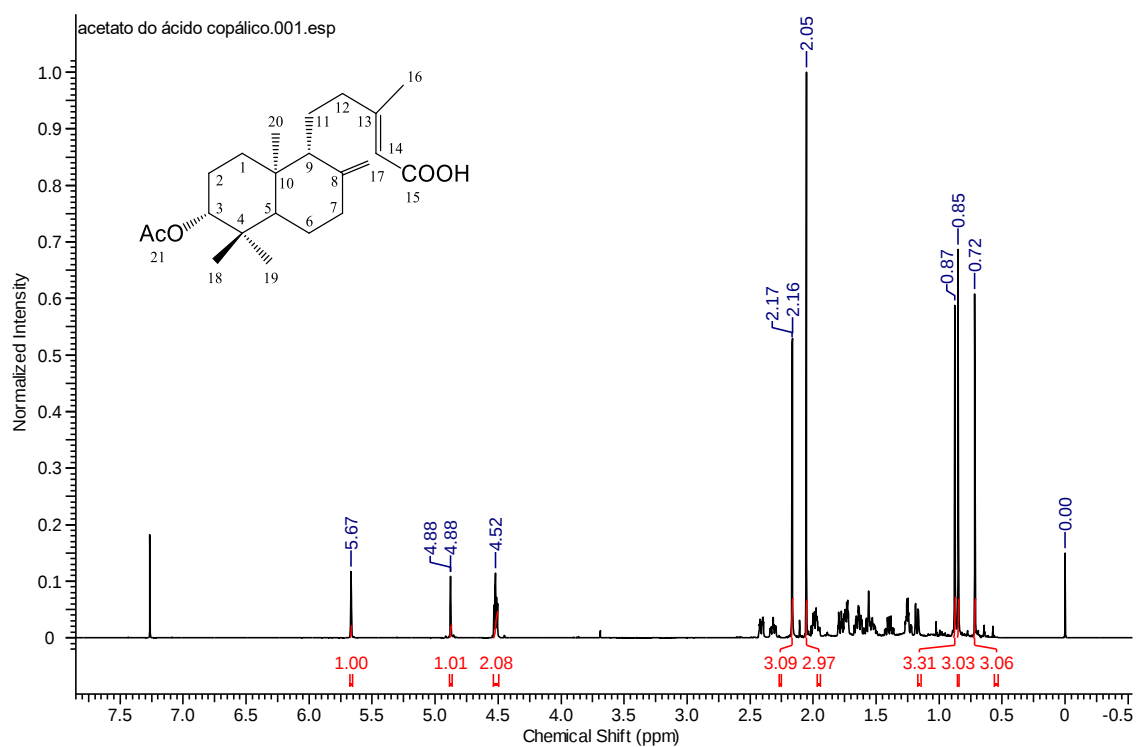


Figure 3S: ^1H NMR spectrum for ent-3b-acetoxycopallic acid (**2**) (400 MHz, CDCl_3).

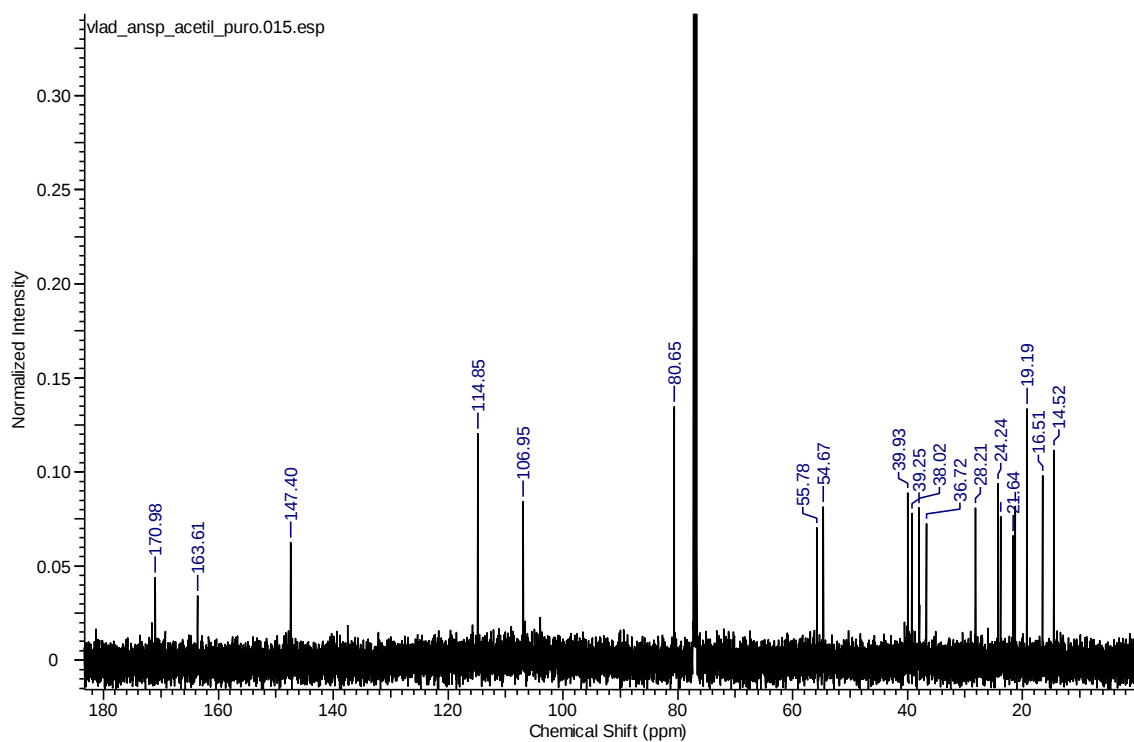


Figure 4S: ^{13}C NMR spectrum for ent-3b-acetoxycopallic acid (**2**) (100 MHz, CDCl_3).

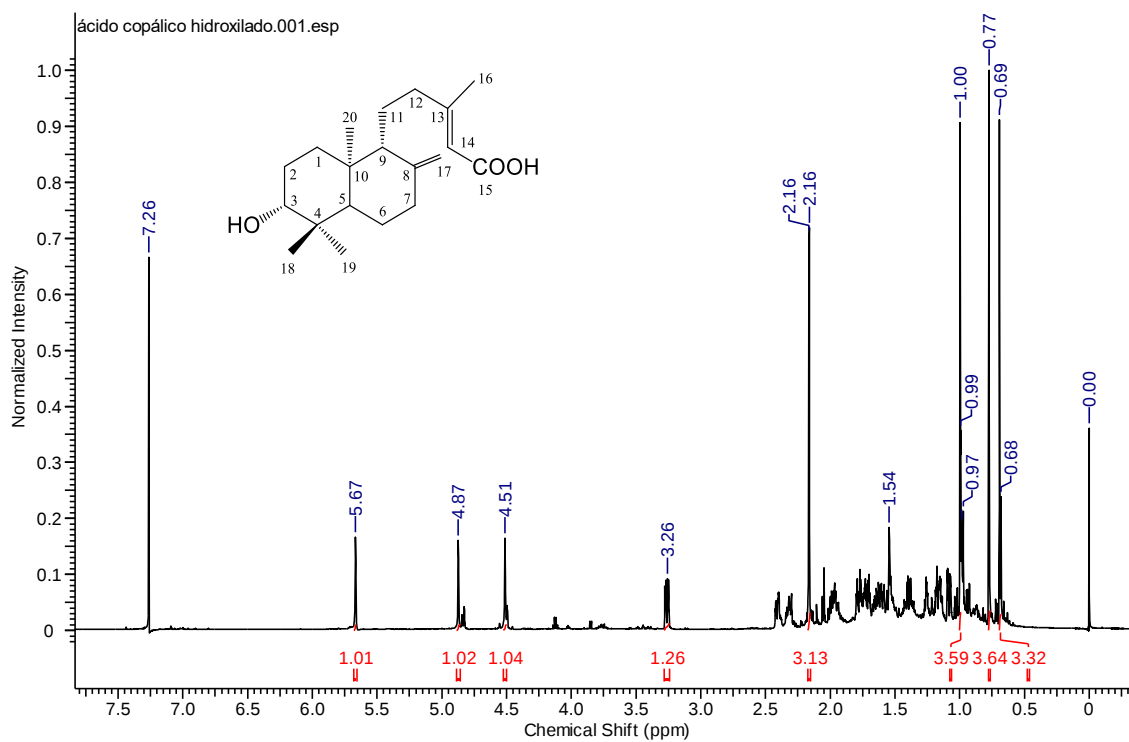


Figure 5S: ¹H NMR spectrum for *ent*-3*b*-hydroxy copalic acid (3) (400 MHz, CDCl₃).

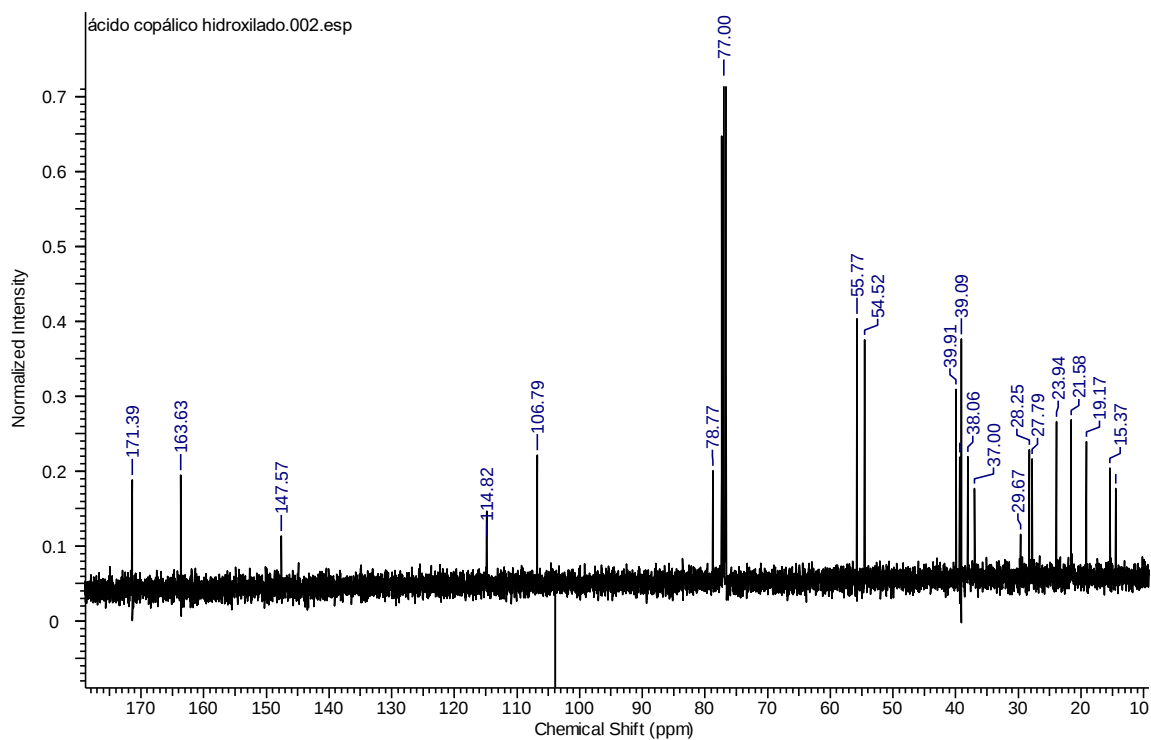


Figure 6S: ¹³C NMR spectrum for *ent*-3*b*-hydroxy copalic acid (3) (100 MHz, CDCl₃).

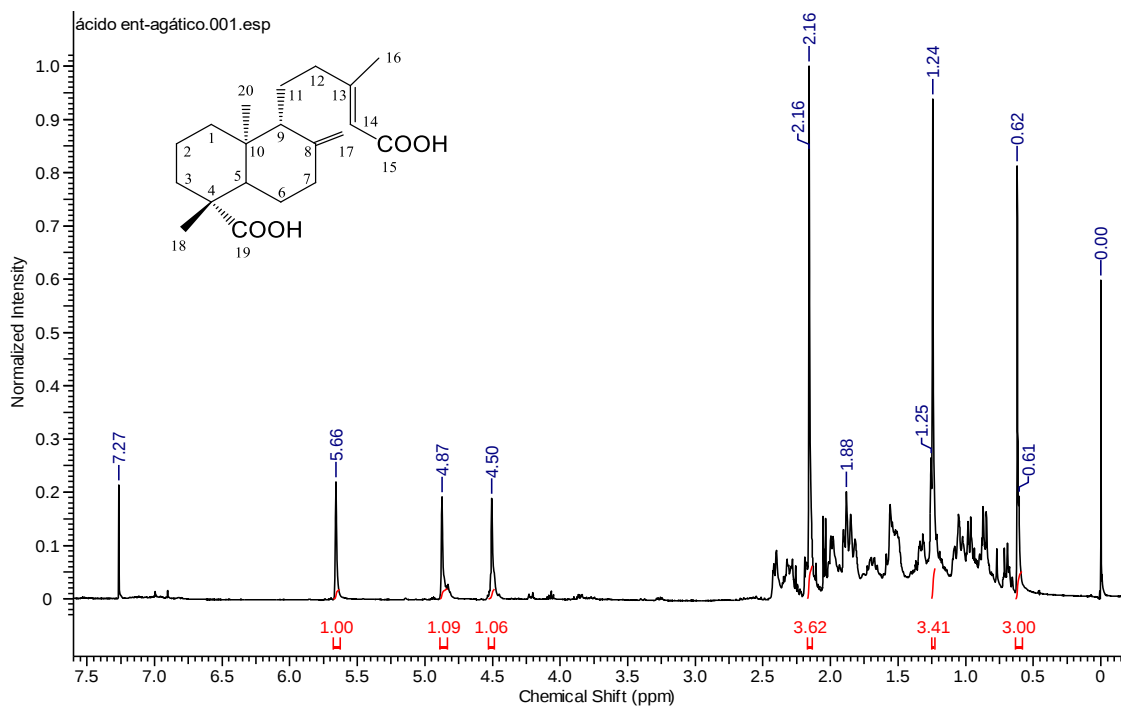


Figure 7S: ^1H NMR spectrum for ent-agatic acid (3) (400 MHz, CDCl_3).

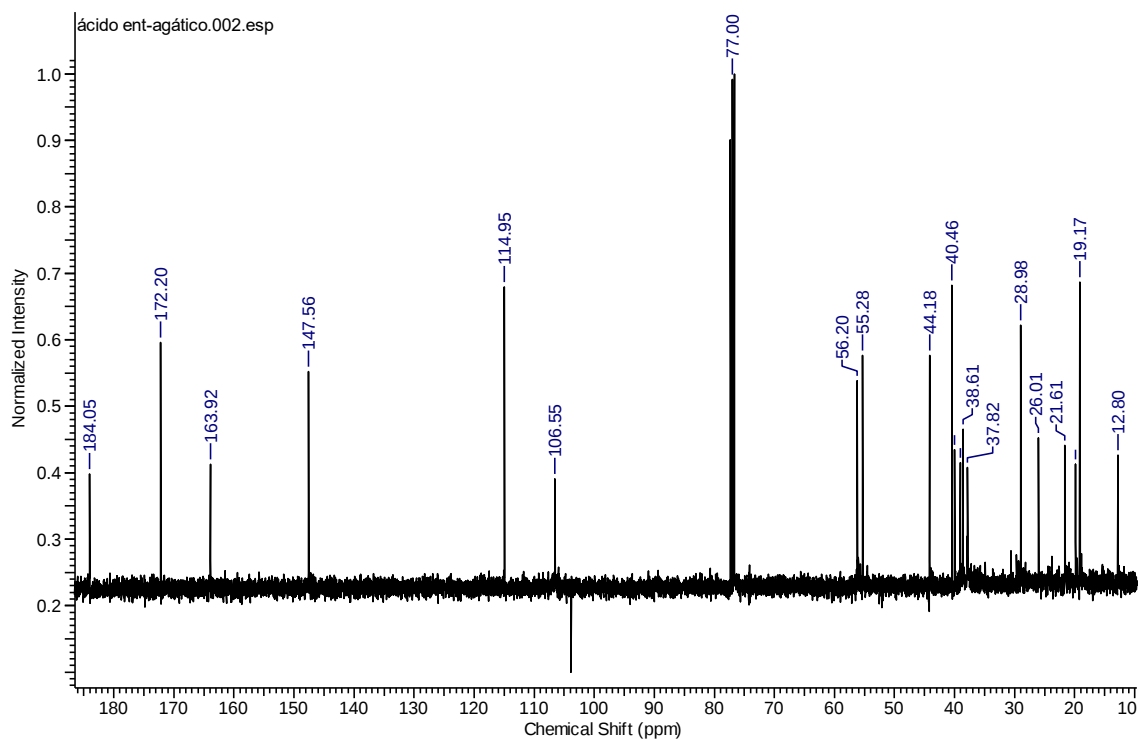


Figure 8S: ^{13}C NMR spectrum for ent-agatic acid (4) (100 MHz, CDCl_3).

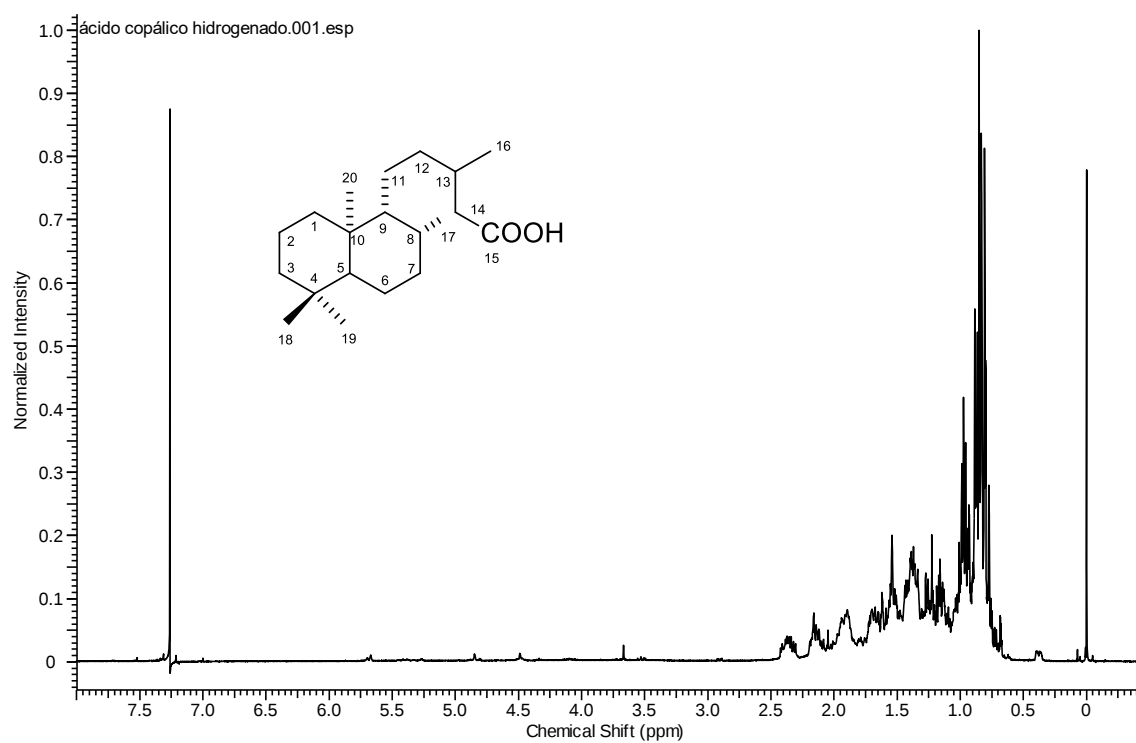


Figure 9S: ^1H NMR spectrum for compound 5 (400 MHz, CDCl_3).

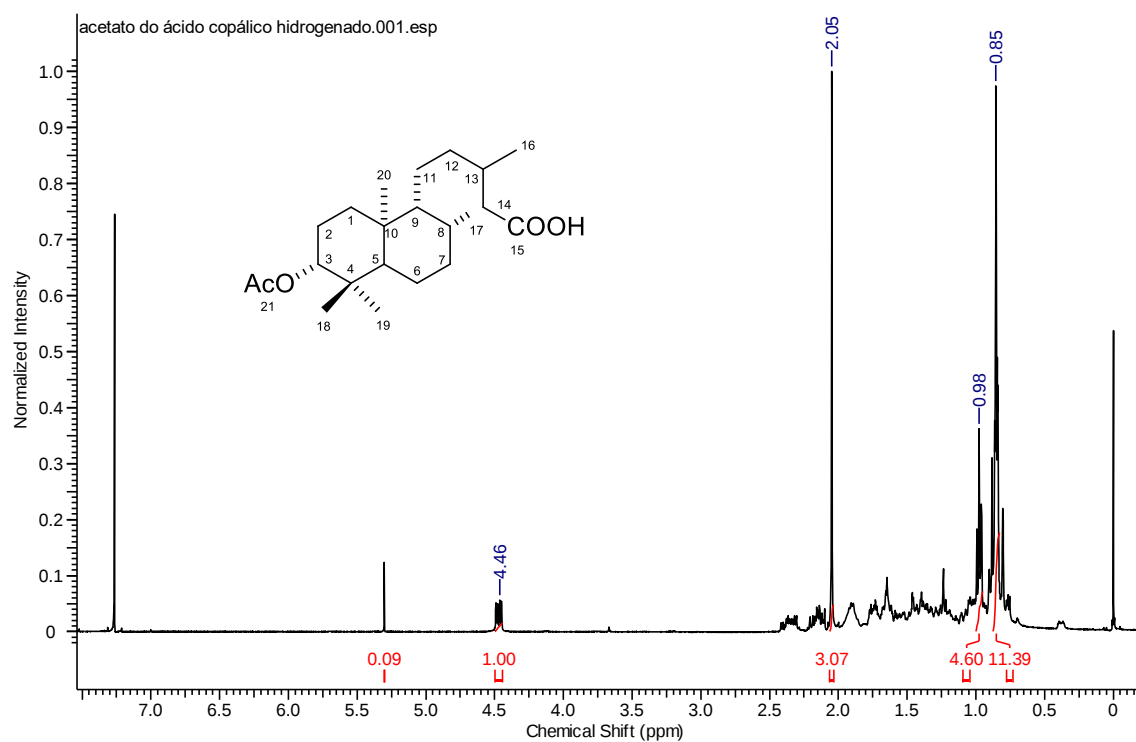


Figure 10S: ^1H NMR spectrum for compound 6 (400 MHz, CDCl_3).

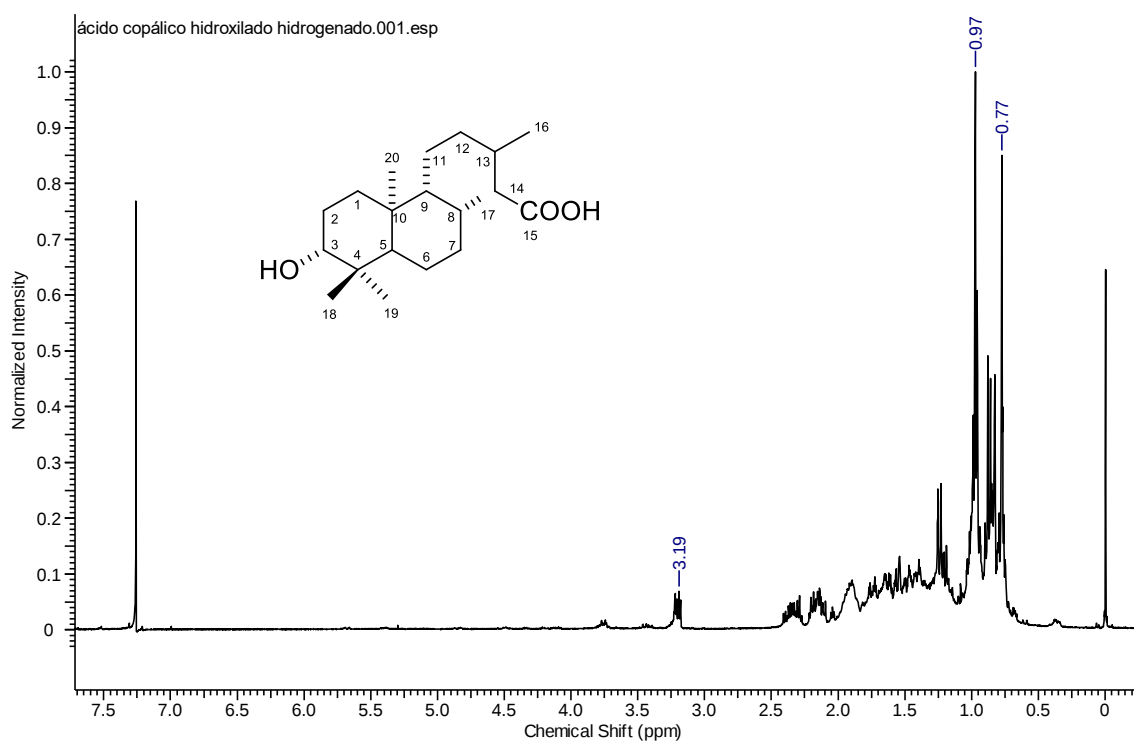


Figure 11S: ^1H NMR spectrum for compound **7** (400 MHz, CDCl₃).

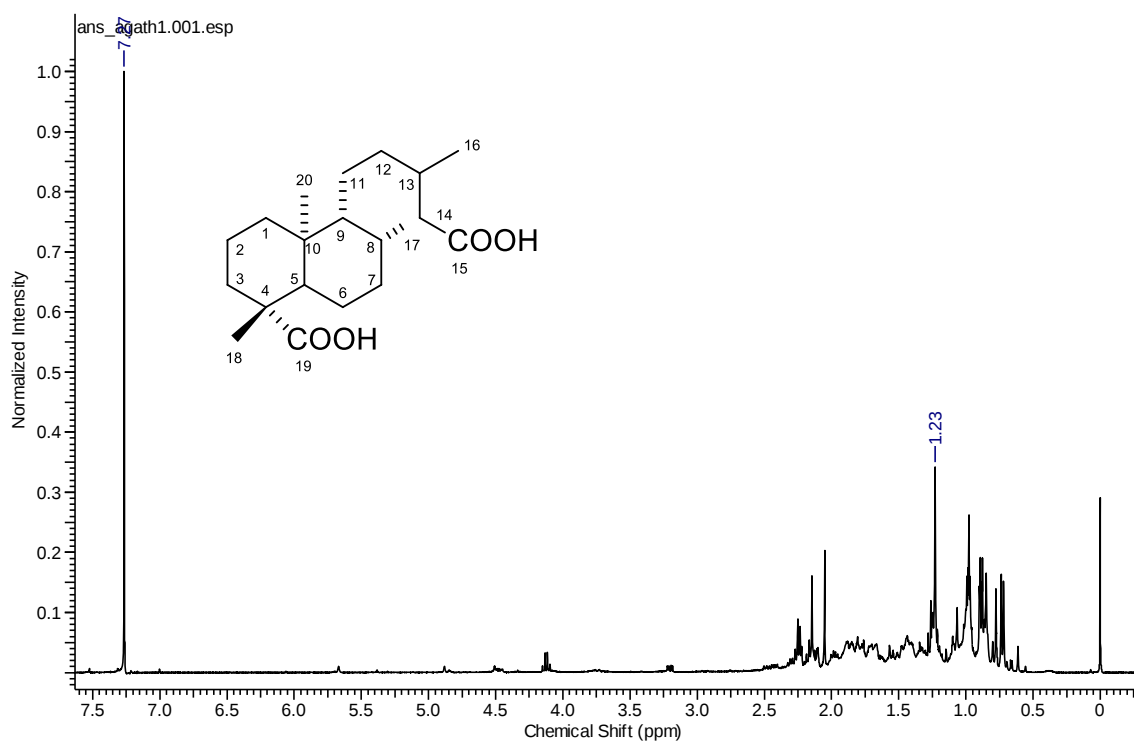


Figure 12S: ^1H NMR spectrum for compound **8** (400 MHz, CDCl₃).

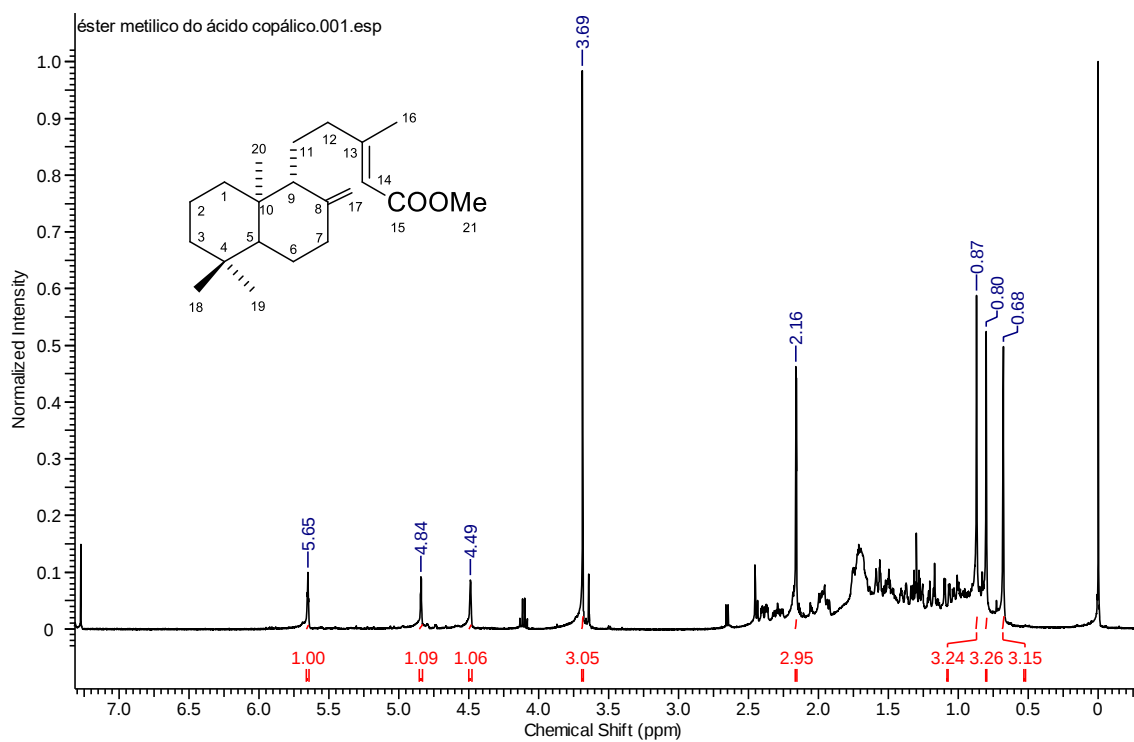


Figure 13S: ¹H NMR spectrum for compound **9** (400 MHz, CDCl₃).

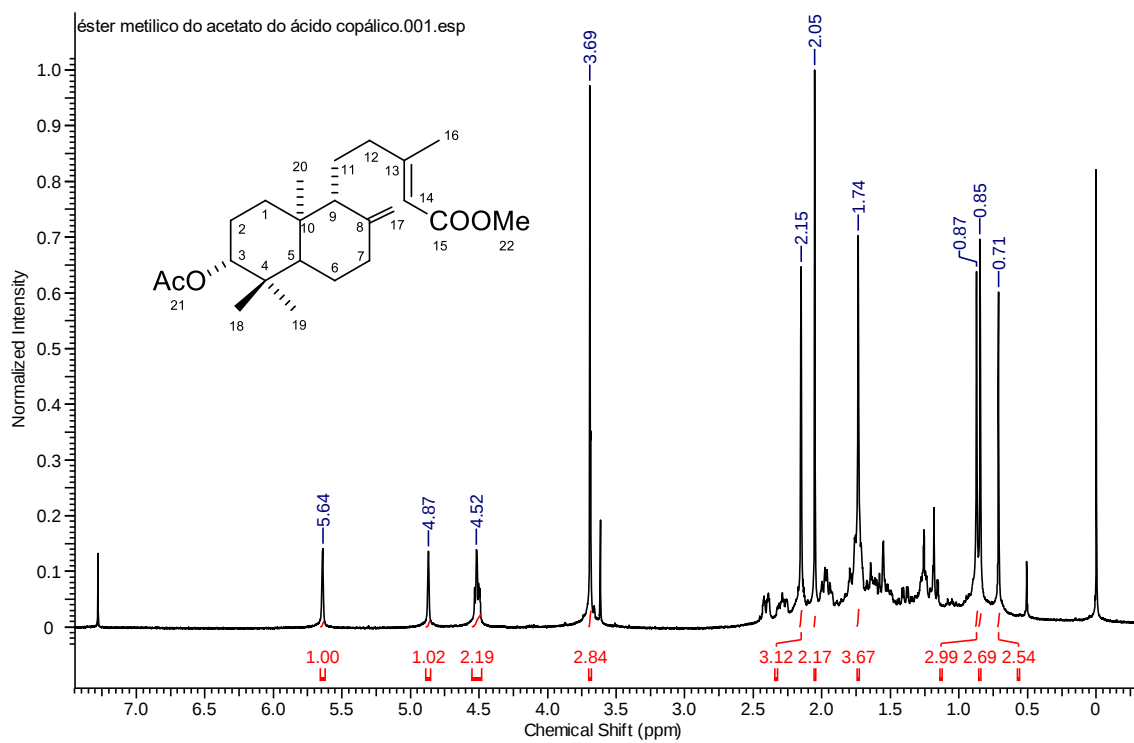


Figure 14S: ¹H NMR spectrum for compound **10** (400 MHz, CDCl₃).

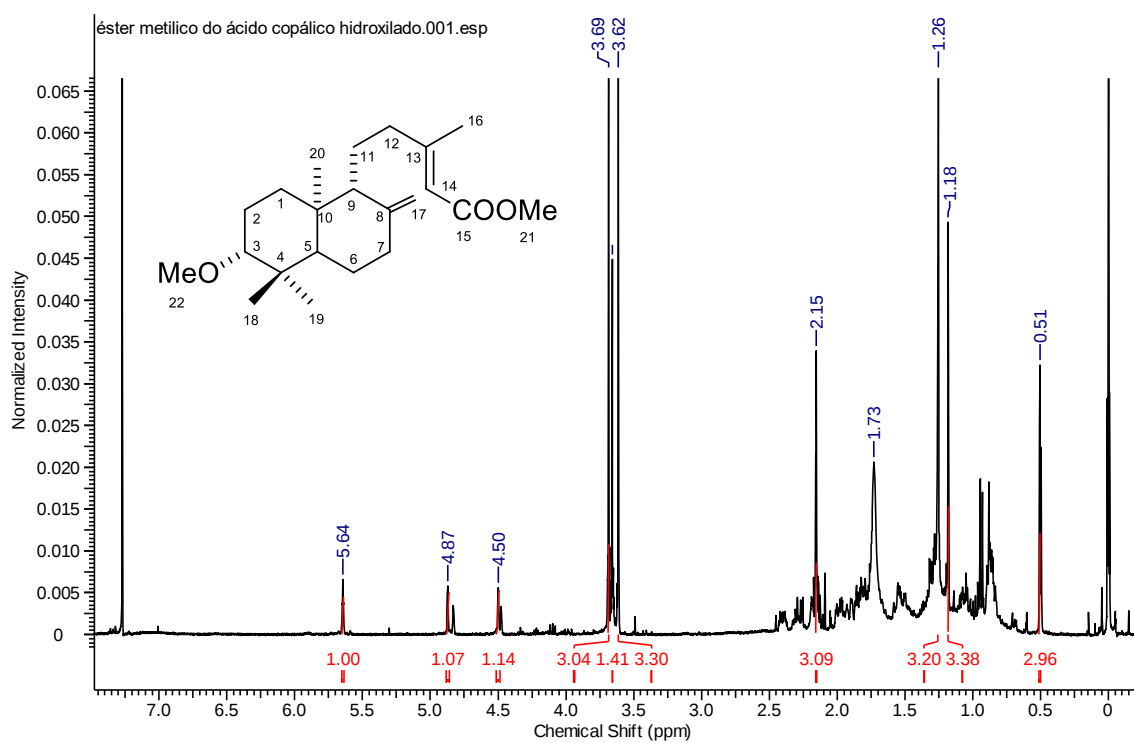


Figure 15S: ^1H NMR spectrum for compound **11** (400 MHz, CDCl_3).

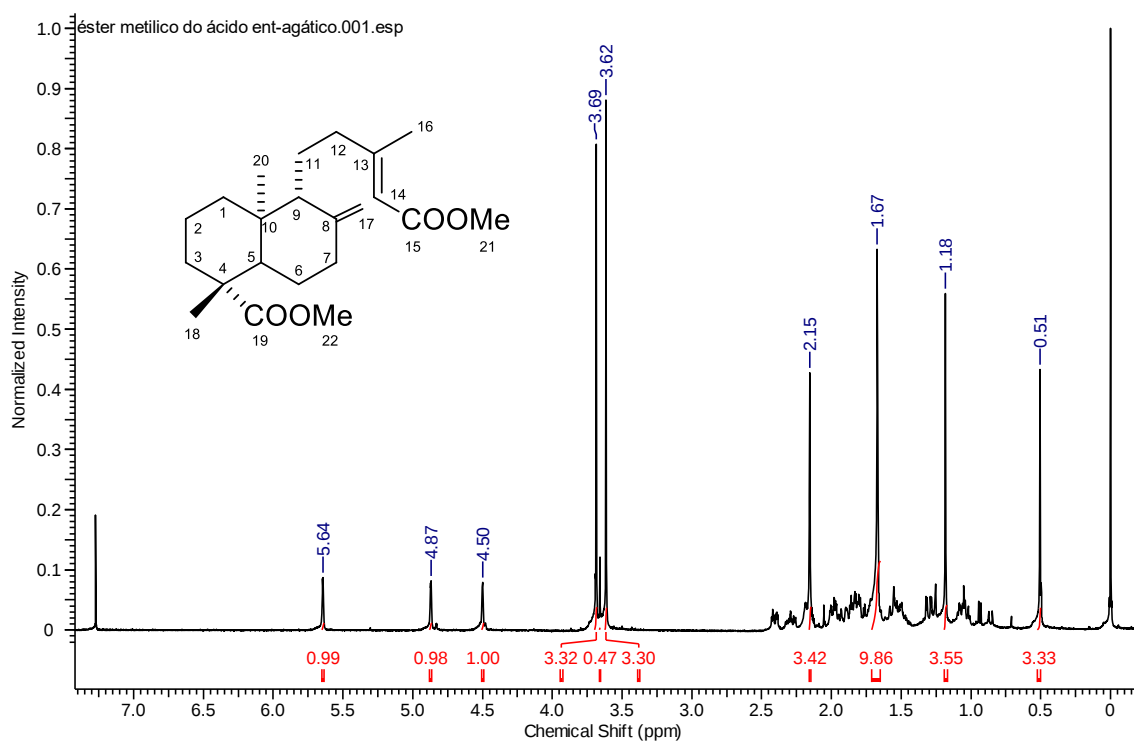


Figure 16S: ^1H NMR spectrum for compound **12** (400 MHz, CDCl_3).

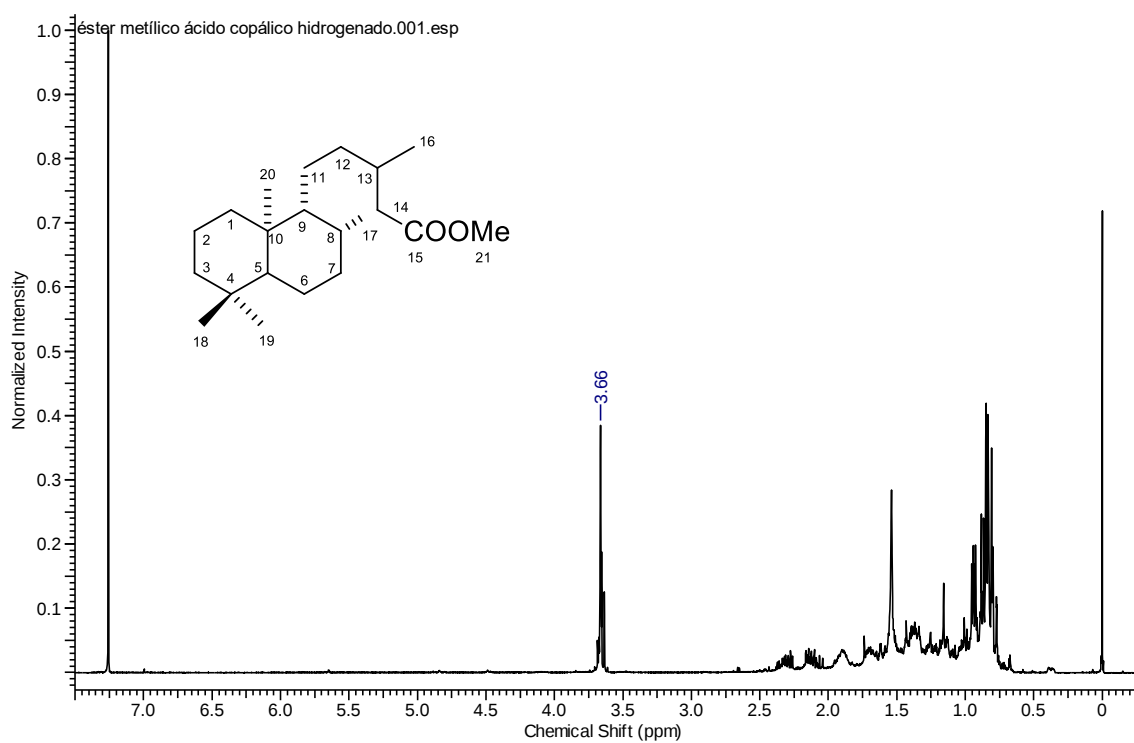


Figure 17S: ^1H NMR spectrum for compound **13** (400 MHz, CDCl_3).

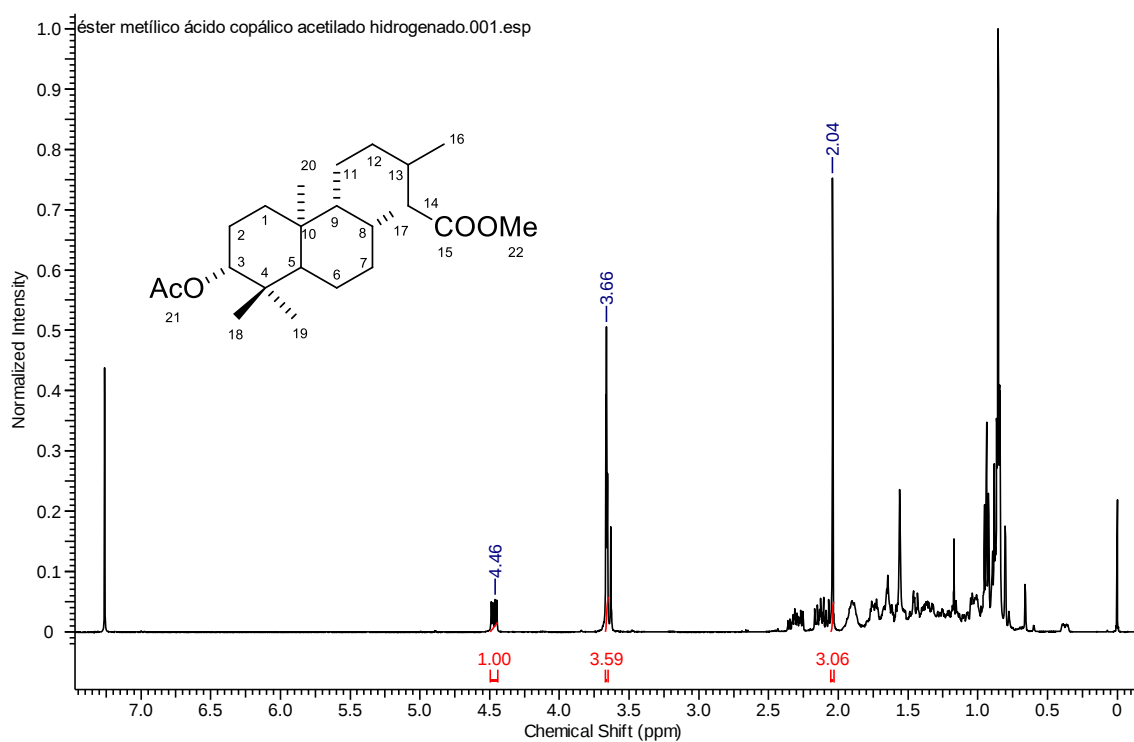


Figure 18S: ^1H NMR spectrum for compound **14** (400 MHz, CDCl_3).

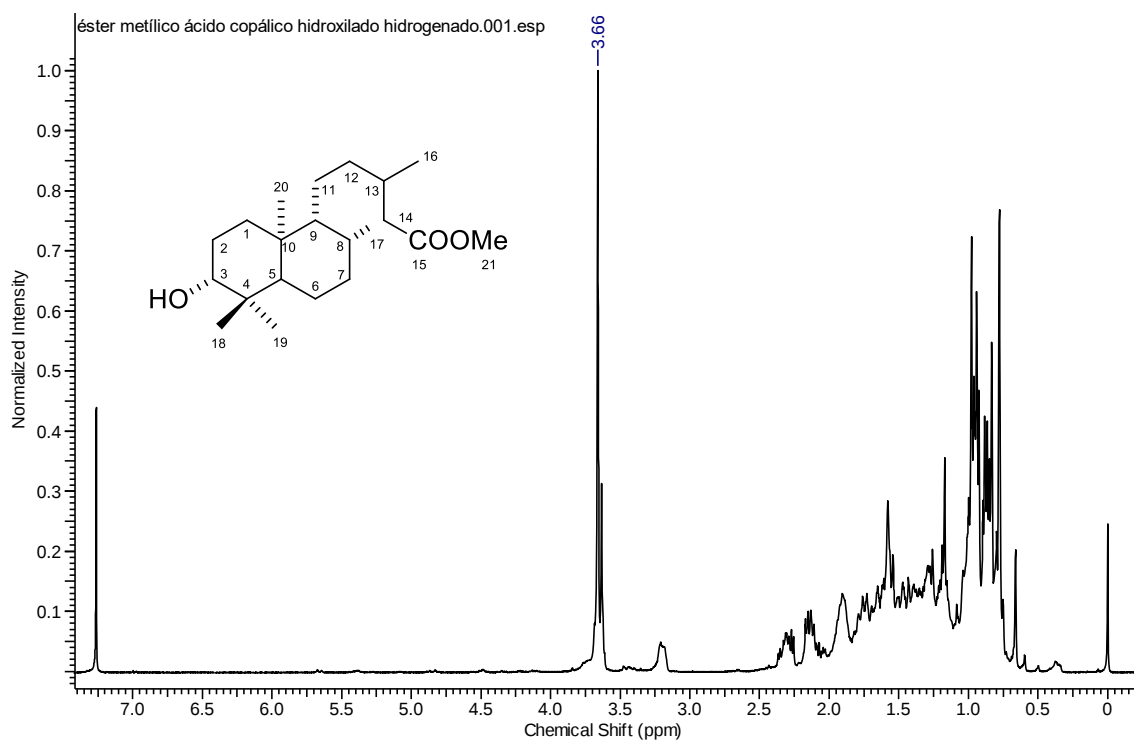


Figure 19S: ^1H NMR spectrum for compound **15** (400 MHz, CDCl_3).

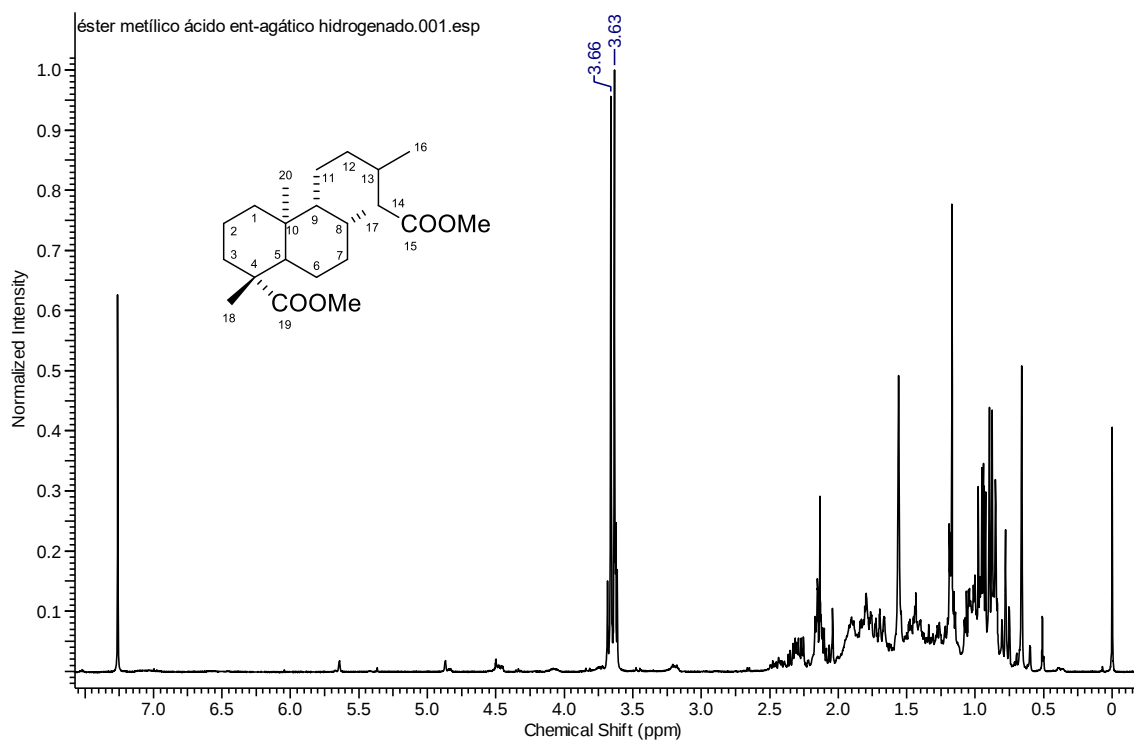


Figure 20S: ^1H NMR spectrum for compound **16** (400 MHz, CDCl_3).

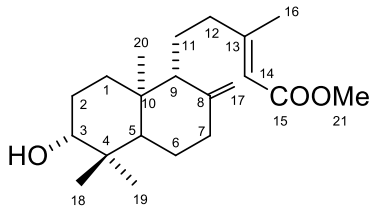


Figure 21S: ^1H NMR spectrum for compound **17** (400 MHz, CDCl_3).

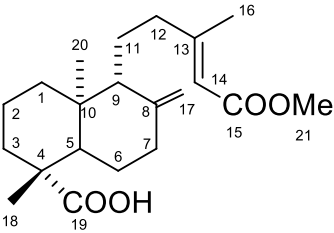


Figure 22S: ^1H NMR spectrum for compound **18** (400 MHz, CDCl_3).

Reference

Ohsaki A, Yan LT, Ito S, Edatsugi H, Iwata D, Komoda Y. 1994. The isolation and in vivo Potent Antitumor activity of clerodane diterpenoid from the oleoresin of the brazilian medicinal plant, *copaifera langsdorfi* desfon. *Bioorganic Med Chem Lett.* 4(24):2889–2892