

Chemoreversal agents from Taiwanofungus genus and their more potent methyl derivatives targeting STAT3 phosphorylation

Ko-Hua Yu ¹ Chin-Chuan Hung ^{2,3,4}, Tian-Shung Wu ^{1,5}, Chin-Fu Chen ⁶, I-Ting Wu ²,
Ping-Chung Kuo ¹, Sio-Hong Lam ¹ and Hsin-Yi Hung ^{1,*}

¹ School of Pharmacy, College of Medicine, National Cheng Kung University,
Tainan 701, Taiwan; s68071061@gs.ncku.edu.tw (K.-H.Y.); tswu@mail.ncku.edu.tw
(T.-S.W.); z10502016@email.ncku.edu.tw (P.-C.K.); shlam@mail.ncku.edu.tw (S.-
H.L.)

² Department of Pharmacy, College of Pharmacy, China Medical University,
Taichung 406, Taiwan; cchung@mail.cmu.edu.tw (C.-C.H.); 105015202@cmu.edu.tw
(I.-T.W.)

³ Department of Pharmacy, China Medical University Hospital, Taichung 404,
Taiwan

⁴ Department of Healthcare Administration, Asia University, Taichung 500,
Taiwan

⁵ Department of Pharmacy, College of Pharmacy and Health Care, Tajen
University, Pingtung, 907, Taiwan

6 Department of Life Sciences, National Cheng Kung University, Tainan 701,
Taiwan; chin-fu9999@gmail.com

* Correspondence: z10308005@email.ncku.edu.tw

Table of Content

Figure S1 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl $3\alpha,7\alpha,12\alpha$ -trihydroxy- 4α -methylergosta-8,24(28)-dien-11-on-26-oate. (6).....	5
Figure S2 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl $3\alpha,7\alpha,12\alpha$ -trihydroxy- 4α -methylergosta-8,24(28)-dien-11-on-26-oate. (6).....	6
Figure S3 ^1H NMR (500 MHz, CDCl_3) spectrum of zhankuic acid A methyl ester. (8).....	7
Figure S4 ^{13}C NMR (125 MHz, CDCl_3) spectrum of zhankuic acid A methyl ester. (8).....	8
Figure S5 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl $7\alpha,12\alpha$ -dihydroxy-3,11-dioxo- 4α -methylergosta-8,24(28)-dien-26-oate. (10).....	9
Figure S6 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl $7\alpha,12\alpha$ -dihydroxy-3,11-dioxo- 4α -methylergosta-8,24(28)-dien-26-oate. (10).....	10
Figure S7 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl- 7β -hydroxy-3,11-dioxo- 4α -methylergosta-8,24(28)-dien-26-oate. (12)	11
Figure S8 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl- 7β -hydroxy-3,11-dioxo- 4α -methylergosta-8,24(28)-dien-26-oate. (12)	12
Figure S9 ^1H NMR (500 MHz, acetone- d_6) spectrum of methyl $3\alpha,4\beta,7\beta$ -trihydroxyergosta-8,24(28)-dien-11-on-26-oate (methyl antcamphorol D, 14).....	13
Figure S10 ^{13}C NMR (125 MHz, acetone- d_6) spectrum of methyl $3\alpha,4\beta,7\beta$ -trihydroxyergosta-8,24(28)-dien-11-on-26-oate (methyl antcamphorol D, 14).....	14
Figure S11 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl $3\alpha,12\alpha$ -dihydroxy 4α -methylergosta-8,24(28)-diene-7,11-dion-26-oate (methyl antcinate H, 16).	15
Figure S12 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl $3\alpha,12\alpha$ -dihydroxy 4α -methylergosta-8,24(28)-diene-7,11-dion-26-oate (methyl antcinate H, 16)	16
Figure S13 ^1H NMR (500 MHz, CDCl_3) spectrum of zhankuic acid methyl ester C 3-O-formate. (18).....	17
Figure S14 ^{13}C NMR (125 MHz, CDCl_3) spectrum of zhankuic acid methyl ester C 3-O-formate. (18).....	18

Figure S15 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 3 α -hydroxy-7,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate. (20)	19
Figure S16 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 3 α -hydroxy-7,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate. (20)	20
Figure S17 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 7 β -hydroxy-3,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate. (22)	21
Figure S18 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 7 β -hydroxy-3,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate. (22)	22
Figure S19 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 4 α -methylergosta-8,24(28)-diene-3,11-dien-26-oate. (24).....	23
Figure S20 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 4 α -methylergosta-8,24(28)-diene-3,11-dien-26-oate. (24).....	24
Figure S21 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 3 α ,7 β -dihydroxy-4 α -methylergosta-8,24(28)-dien-11-on-26-oate. (26).....	25
Figure S22 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 3 α ,7 β -dihydroxy-4 α -methylergosta-8,24(28)-dien-11-on-26-oate. (26).....	26
Figure S23 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 3 β ,12 β -dihydroxy-11-oxo-4 β -methylergosta-8,24(28)-dien-26-oate (methyl antcin M). (28)	27
Figure S24 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 3 β ,12 β -dihydroxy-11-oxo-4 β -methylergosta-8,24(28)-dien-26-oate (methyl antcin M). (28)	28
Figure S25 References for known compounds.....	29

Figure S1 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 3 α ,7 α ,12 α -trihydroxy-4 α -methylergosta-8,24(28)-dien-11-on-26-oate. (6)

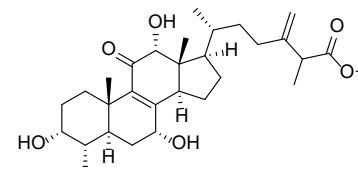
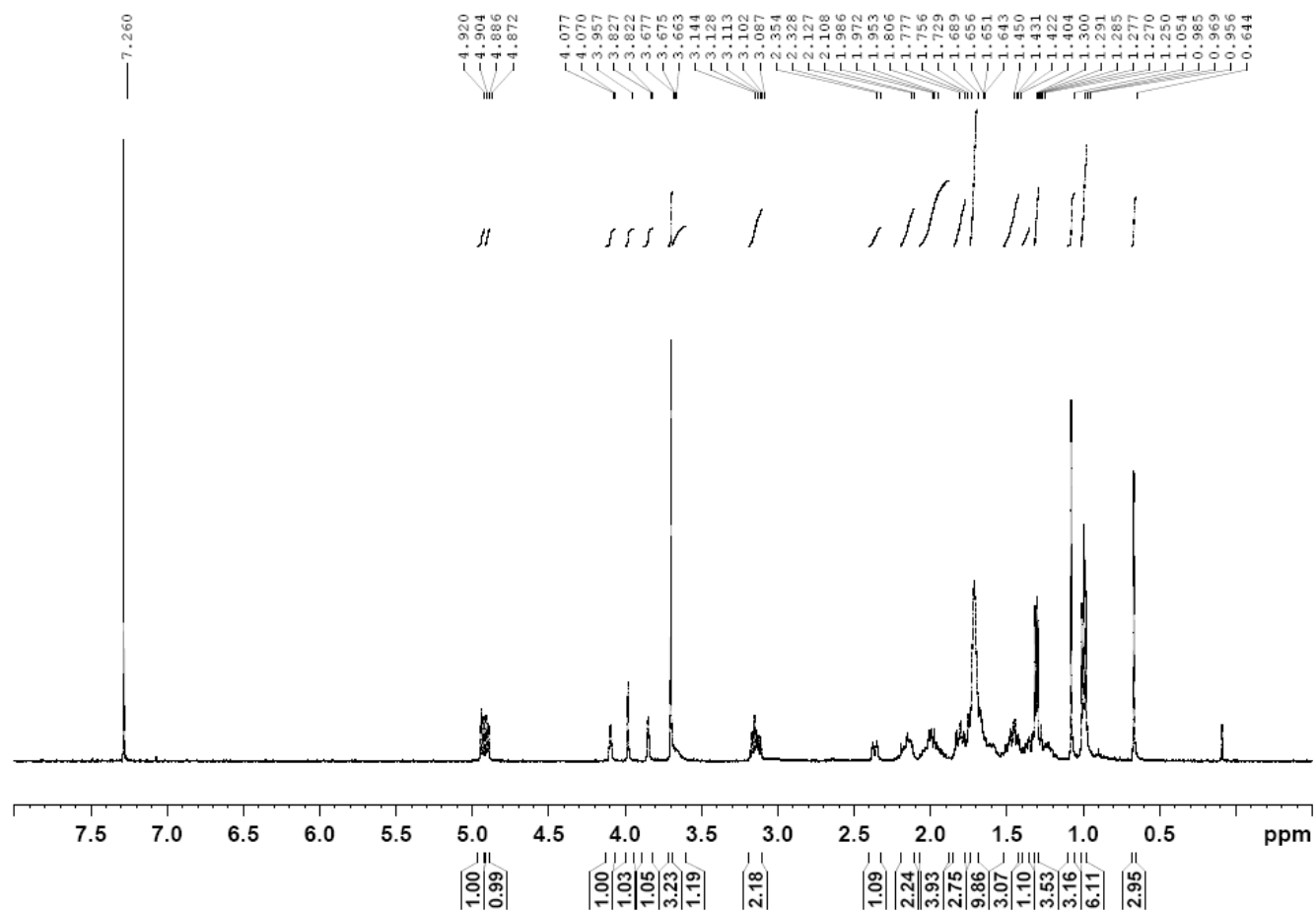


Figure S2 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 3 α ,7 α ,12 α -trihydroxy-4 α -methylergosta-8,24(28)-dien-11-on-26-oate.
(6)

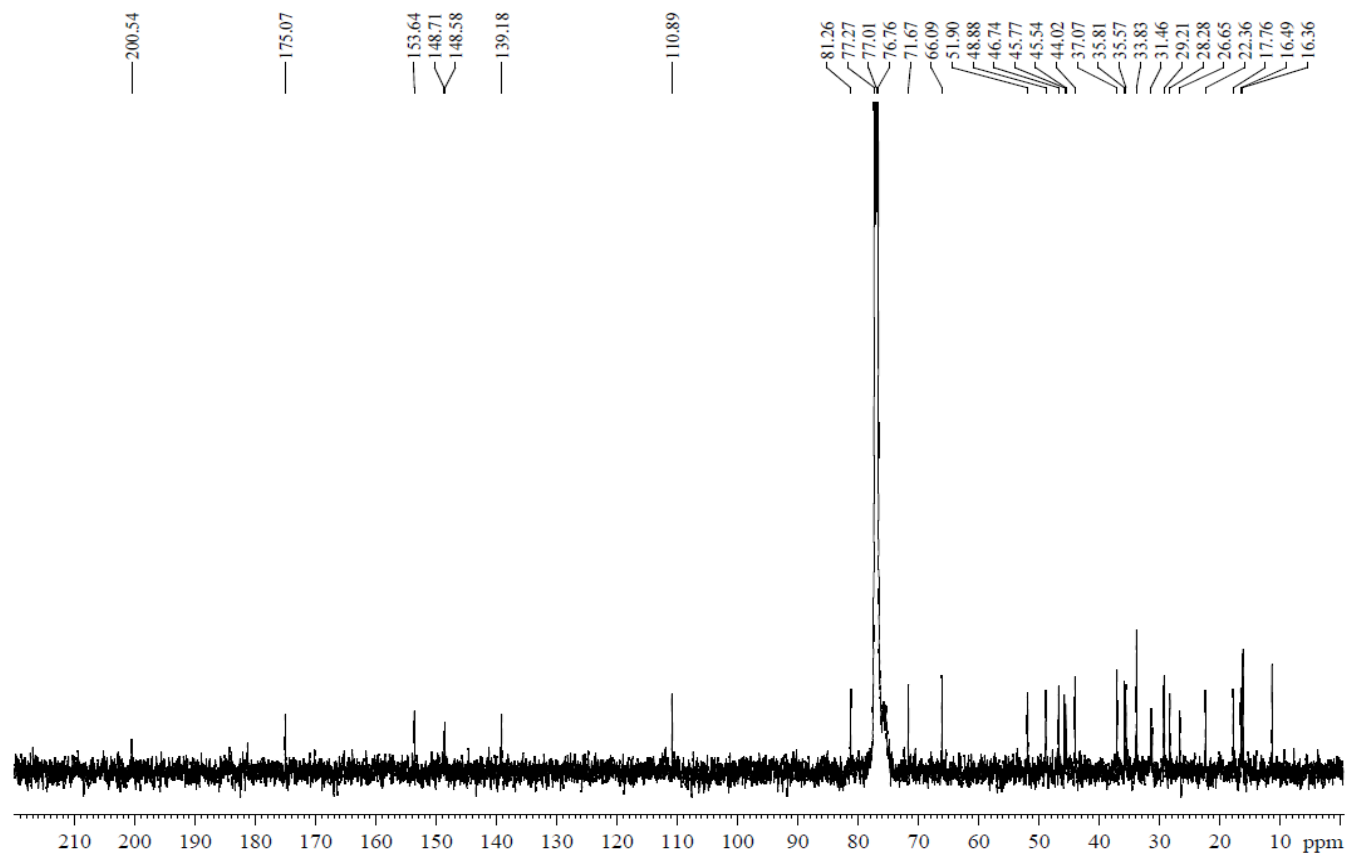


Figure S3 ^1H NMR (500 MHz, CDCl_3) spectrum of zhankuic acid A methyl ester. (8)

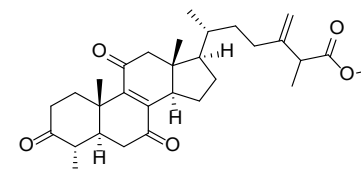
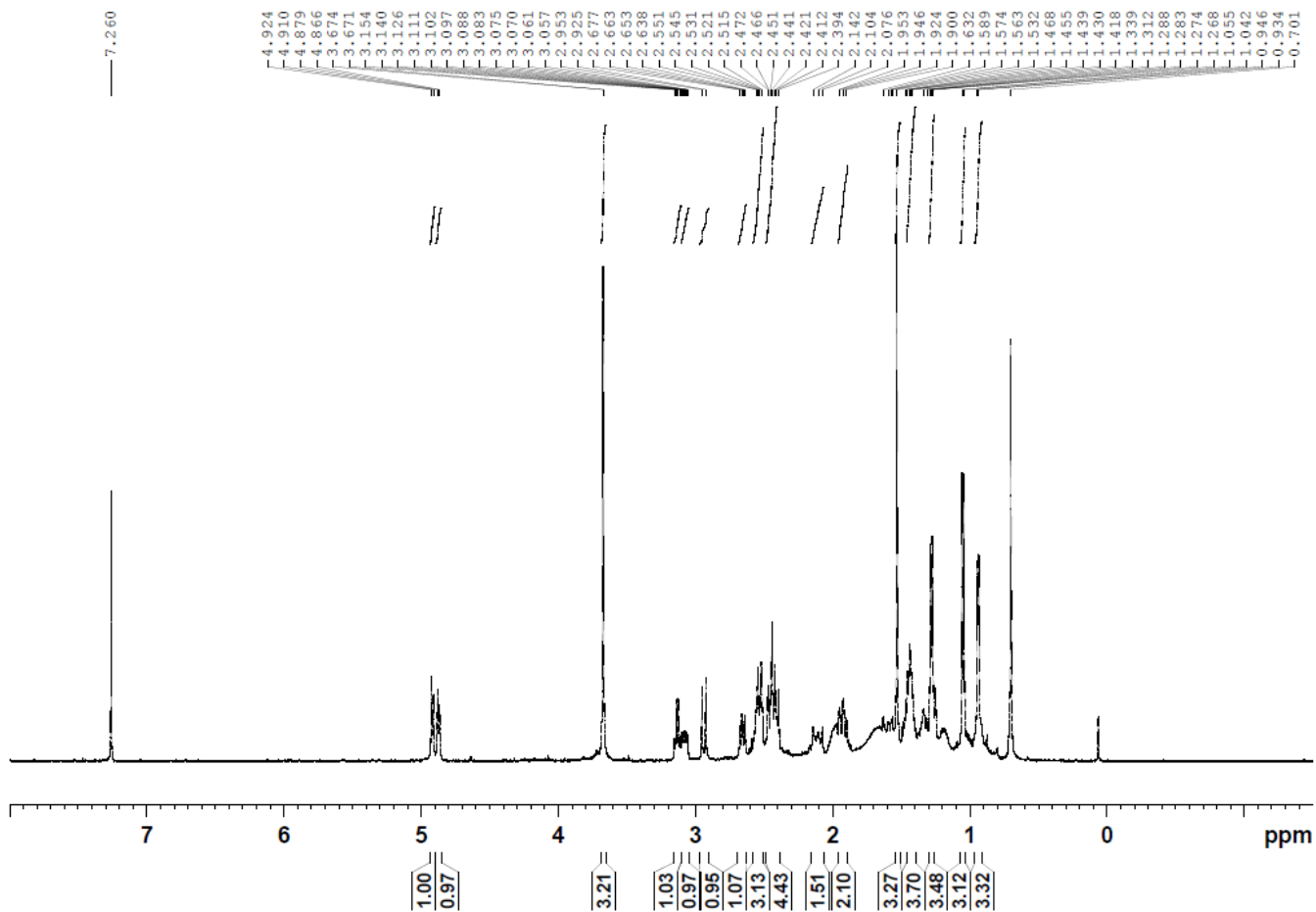


Figure S4 ^{13}C NMR (125 MHz, CDCl_3) spectrum of zhankuic acid A methyl ester. (8)

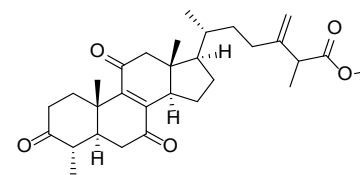
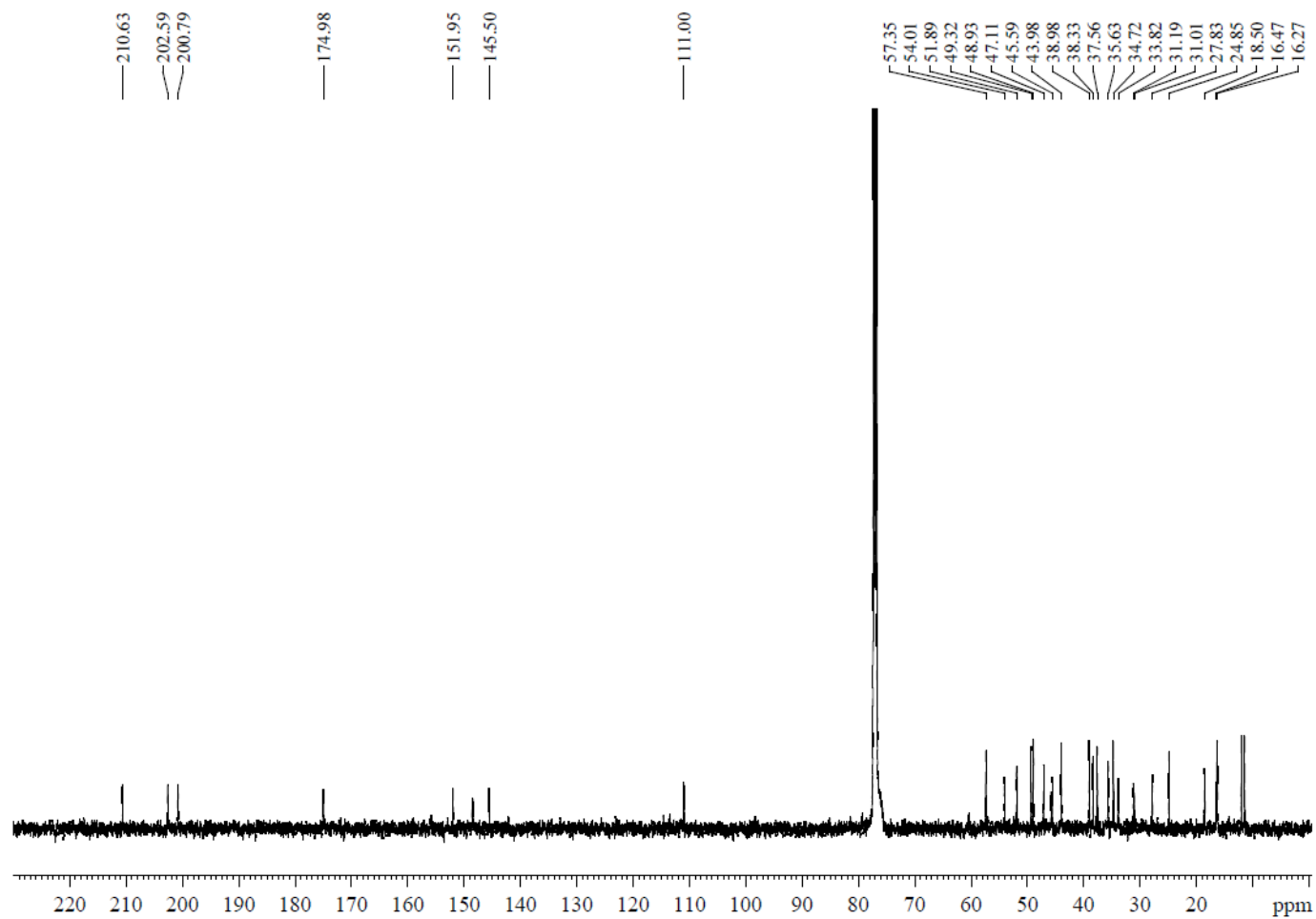


Figure S5 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 7 α , 12 α -dihydroxy-3,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate. (10)

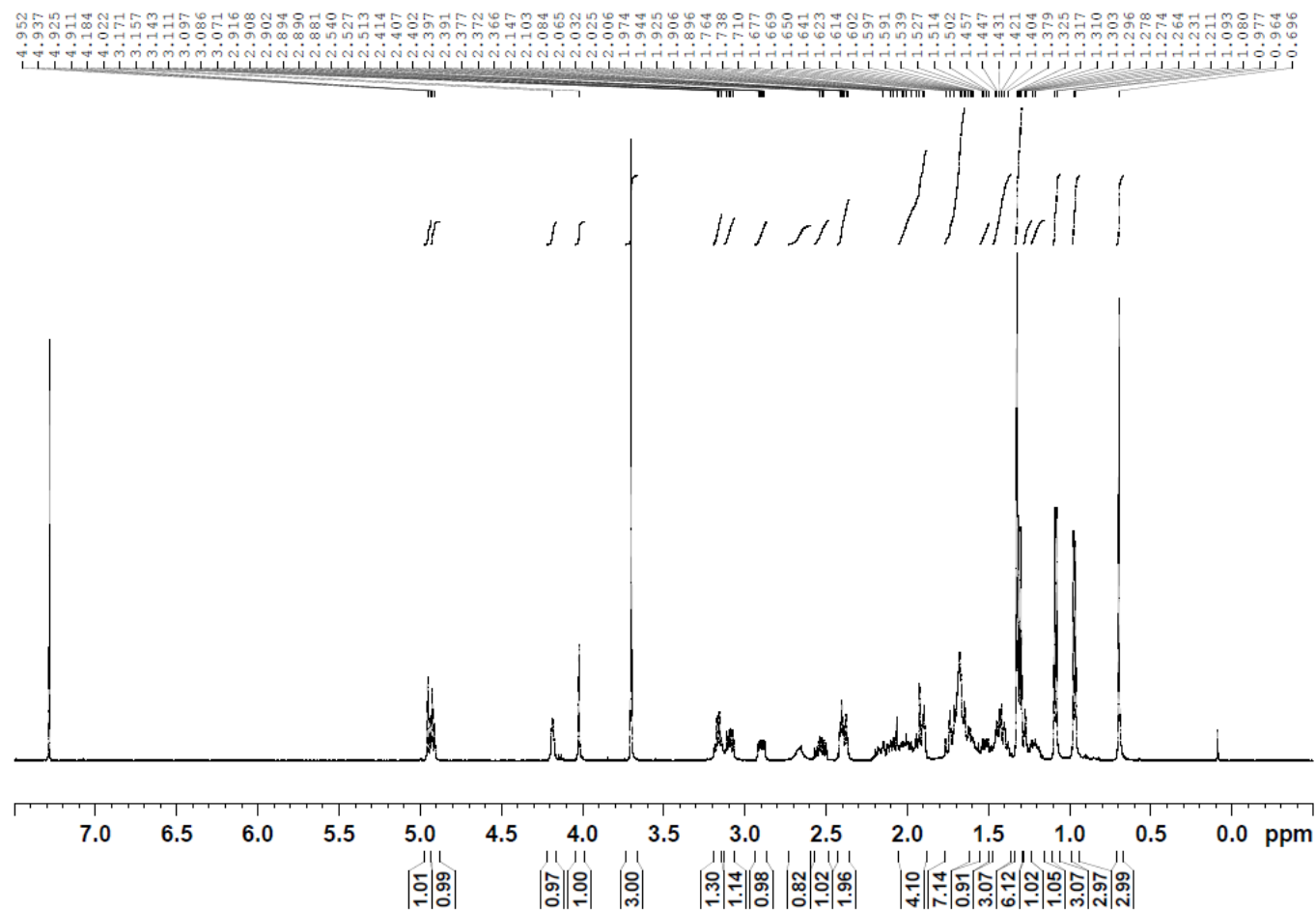


Figure S6 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 7 α , 12 α -dihydroxy-3,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate. (10)

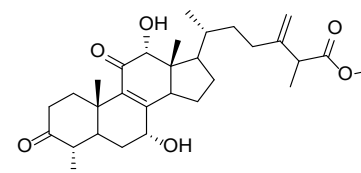
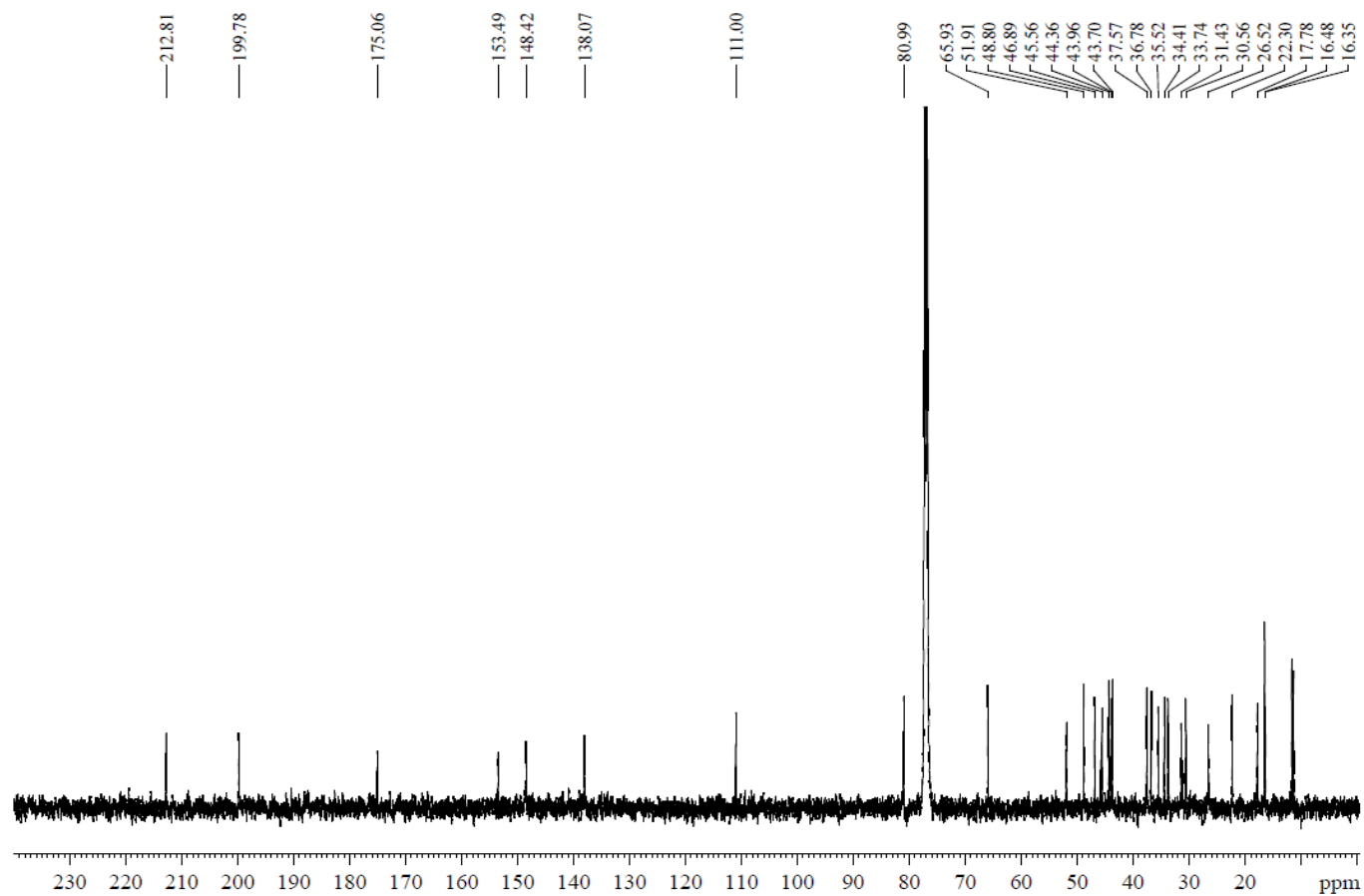


Figure S7 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl-7 β -hydroxy-3,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate. (12)

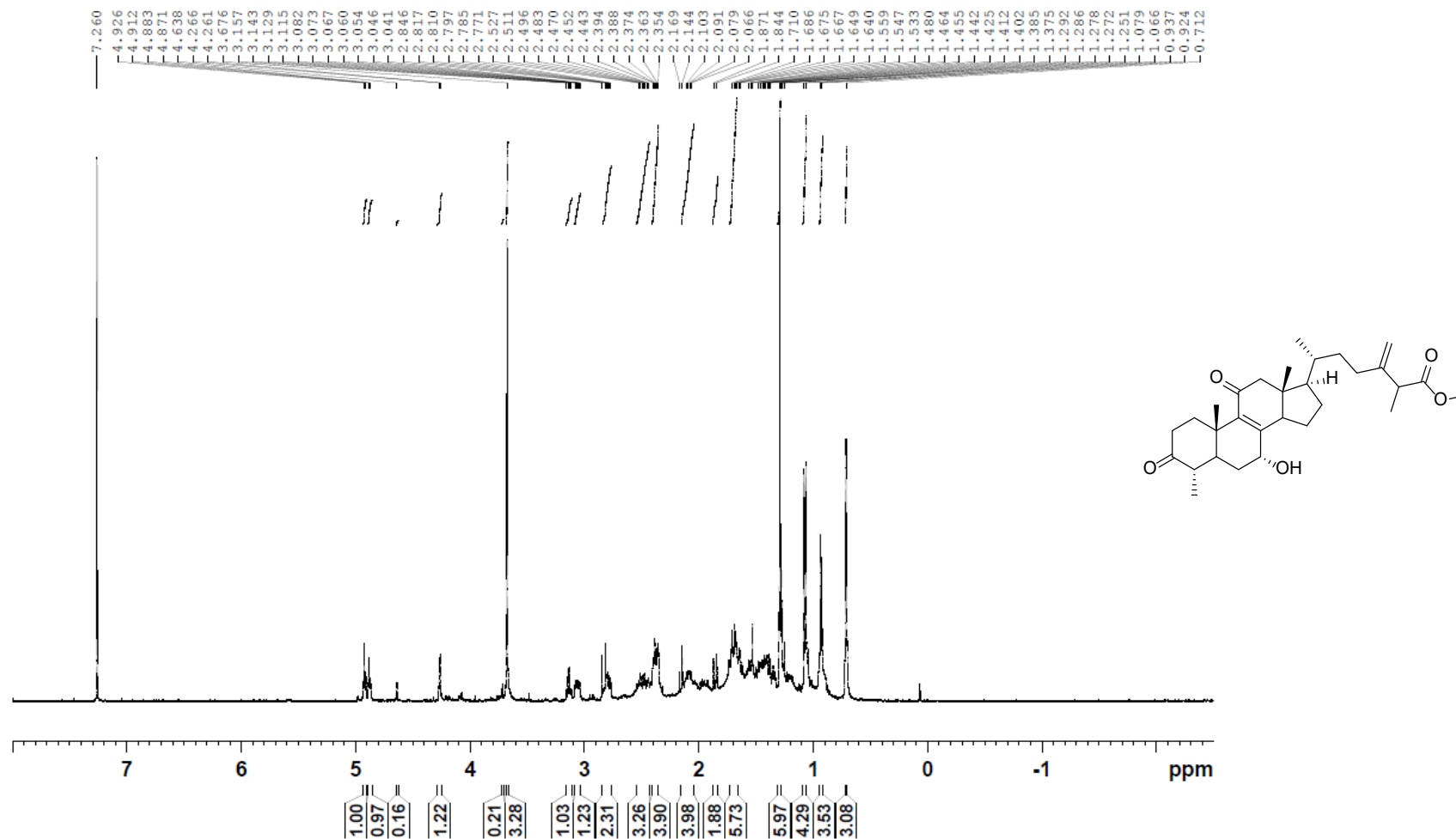


Figure S8 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl-7 β -hydroxy-3,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate. (12)

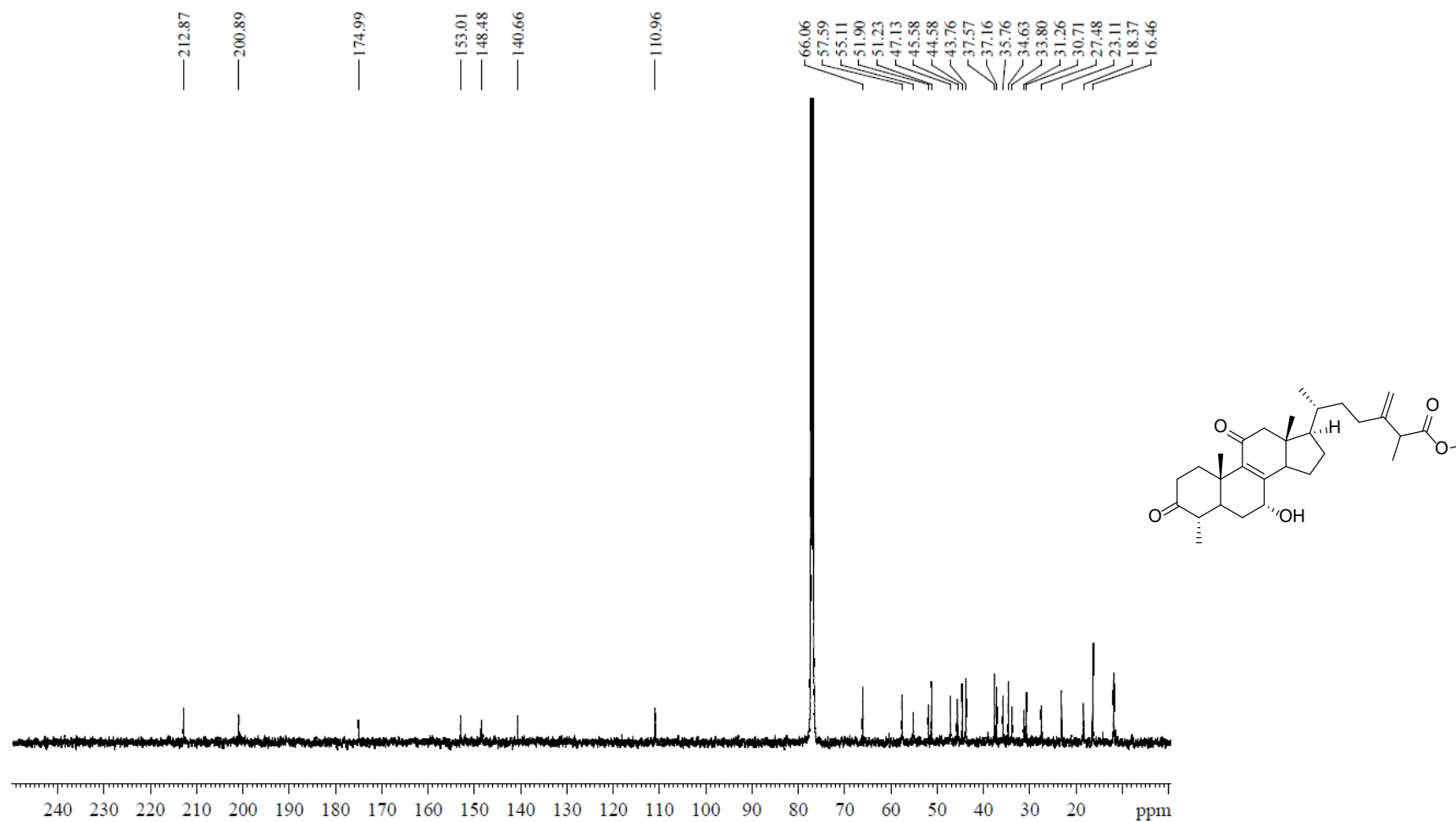


Figure S9 ^1H NMR (500 MHz, acetone- d_6) spectrum of methyl 3 α ,4 β ,7 β -trihydroxyergosta-8,24(28)-dien-11-on-26-oate (methyl antcamphorol D, 14).

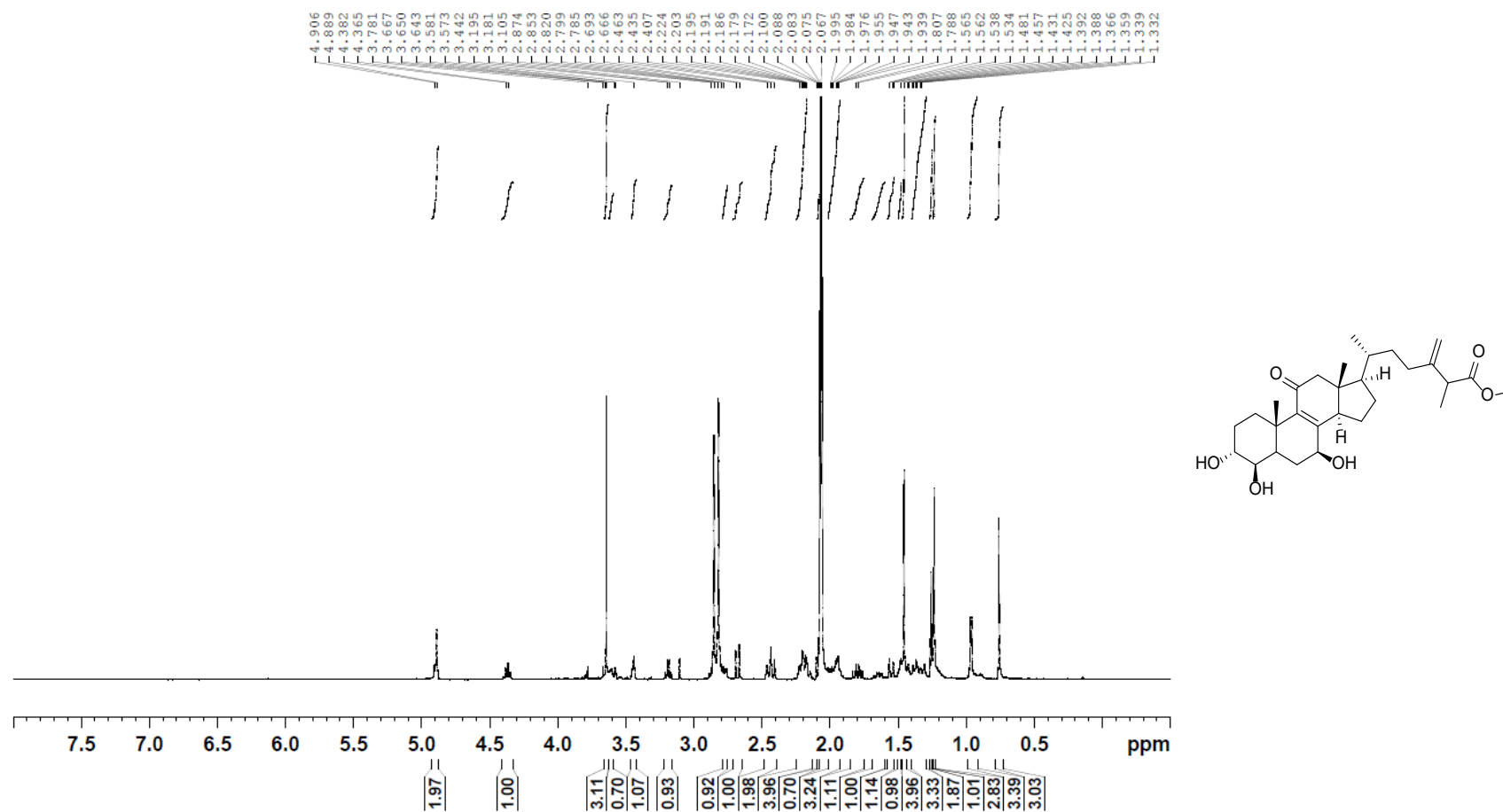


Figure S10 ^{13}C NMR (125 MHz, acetone- d_6) spectrum of methyl 3 α ,4 β ,7 β -trihydroxyergosta-8,24(28)-dien-11-on-26-oate (methyl antcamphorol D, 14).

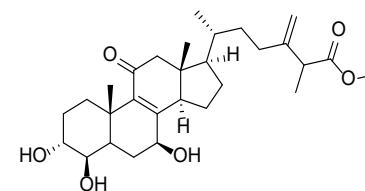
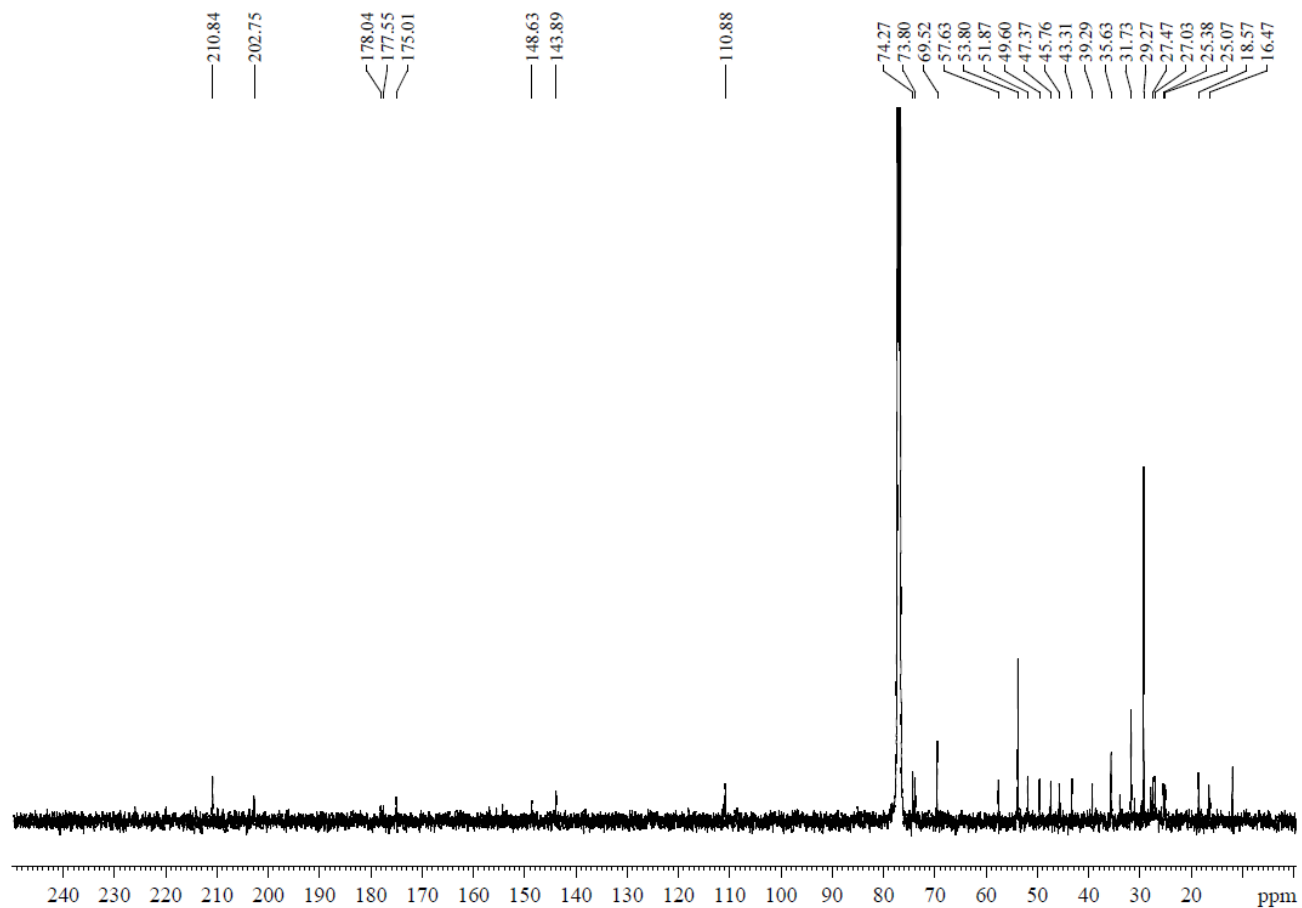


Figure S11 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 3 α ,12 α -dihydroxy 4 α -methylergosta-8,24(28)-diene-7,11-dione-26-oate (methyl antcinate H, 16).

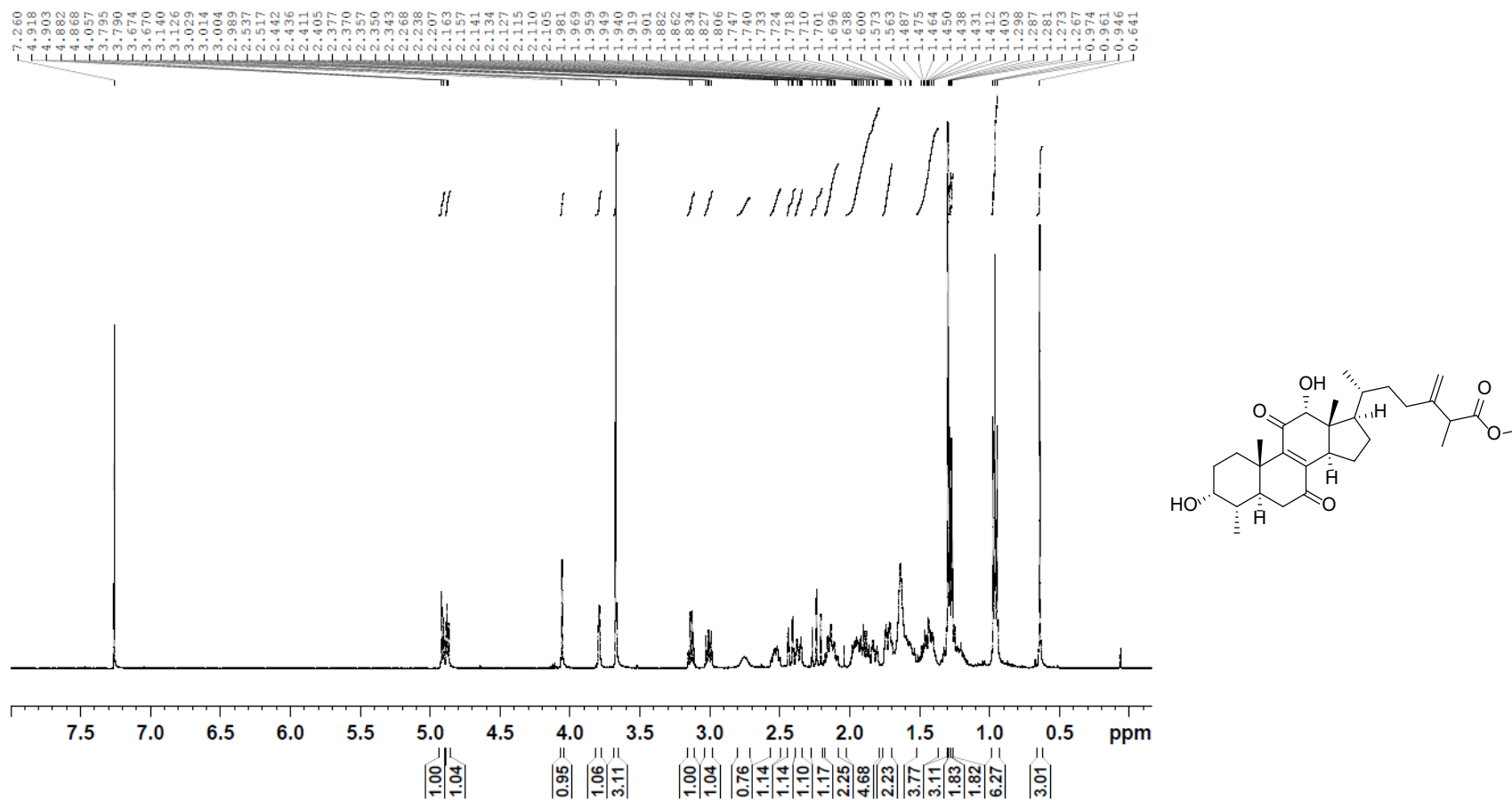


Figure S12 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 3 α ,12 α -dihydroxy 4 α -methylergosta-8,24(28)-diene-7,11-dione-26-oate (methyl antcinate H, 16)

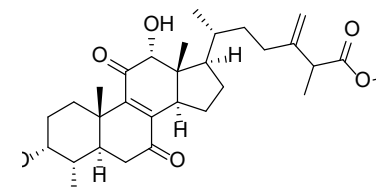
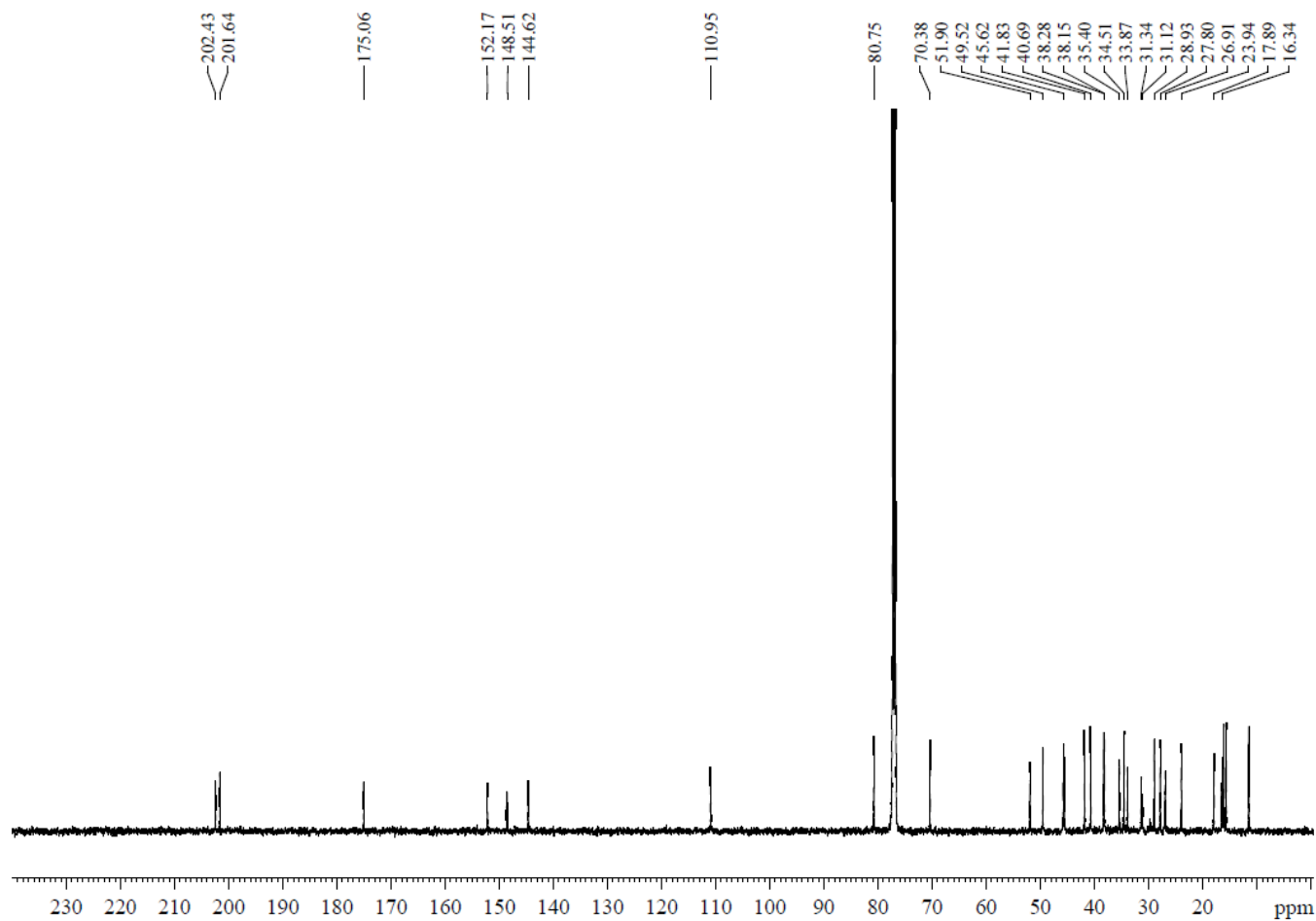


Figure S13 ^1H NMR (500 MHz, CDCl_3) spectrum of zhankuic acid methyl ester C 3-O-formate. (18)

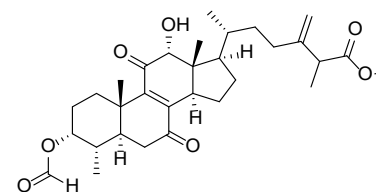
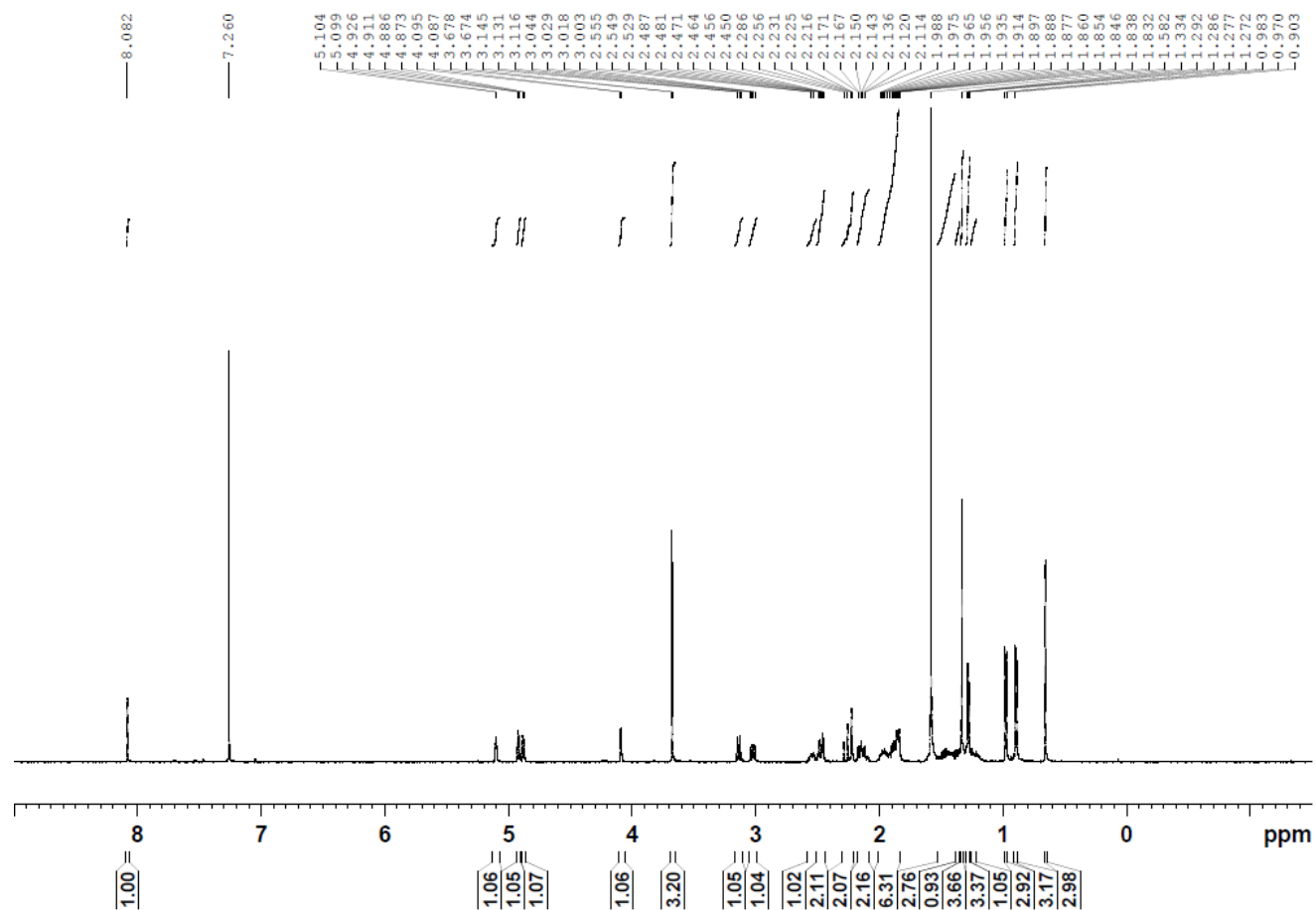


Figure S14 ^{13}C NMR (125 MHz, CDCl_3) spectrum of zhankuic acid methyl ester C 3-O-formate. (18)

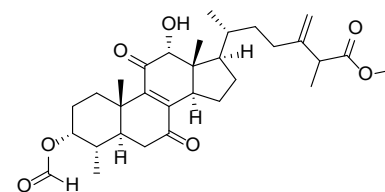
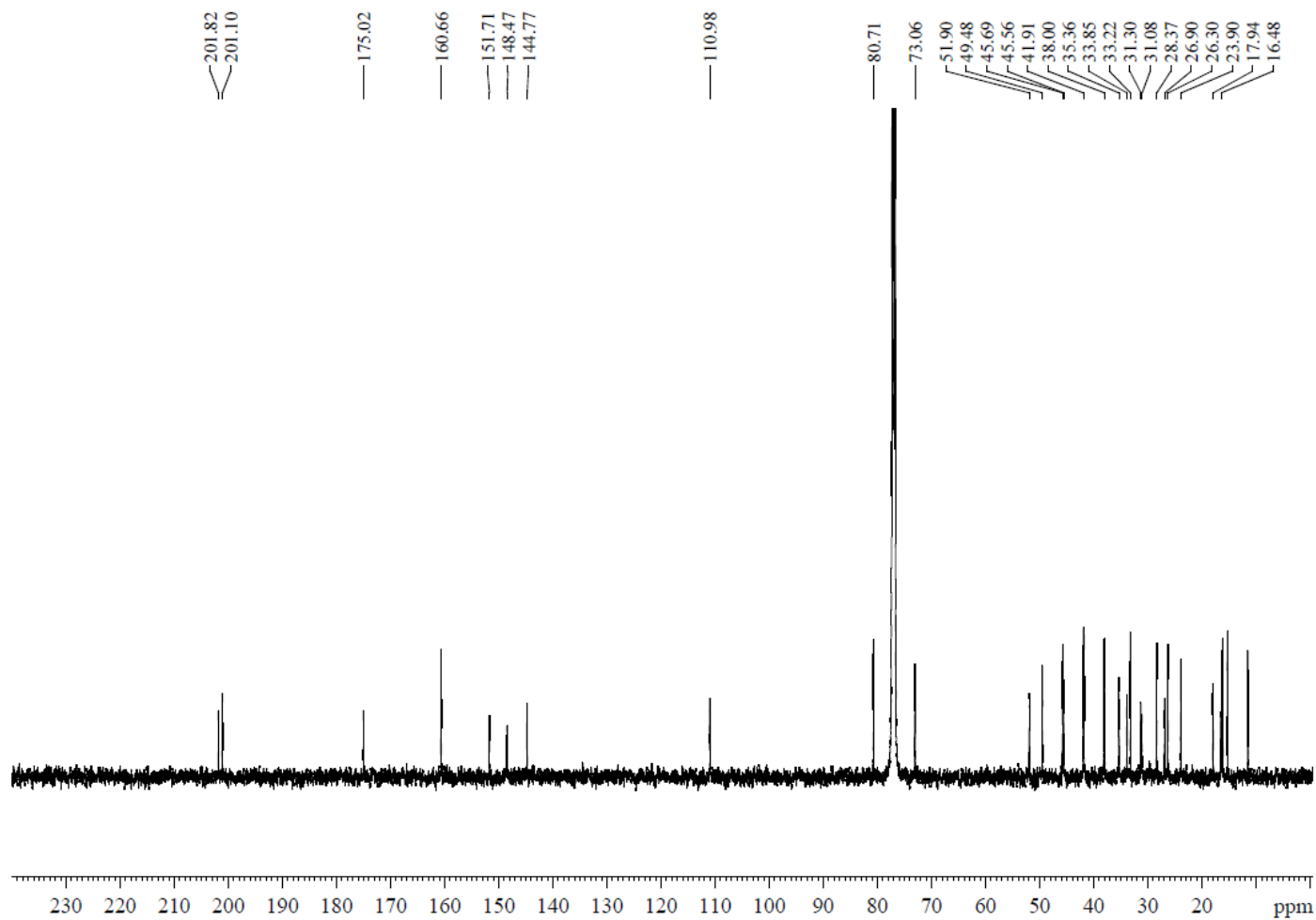


Figure S15 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 3 α -hydroxy-7,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate. (20)

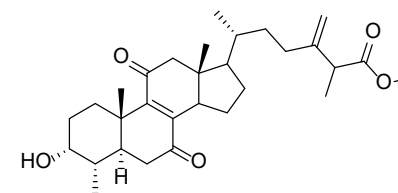
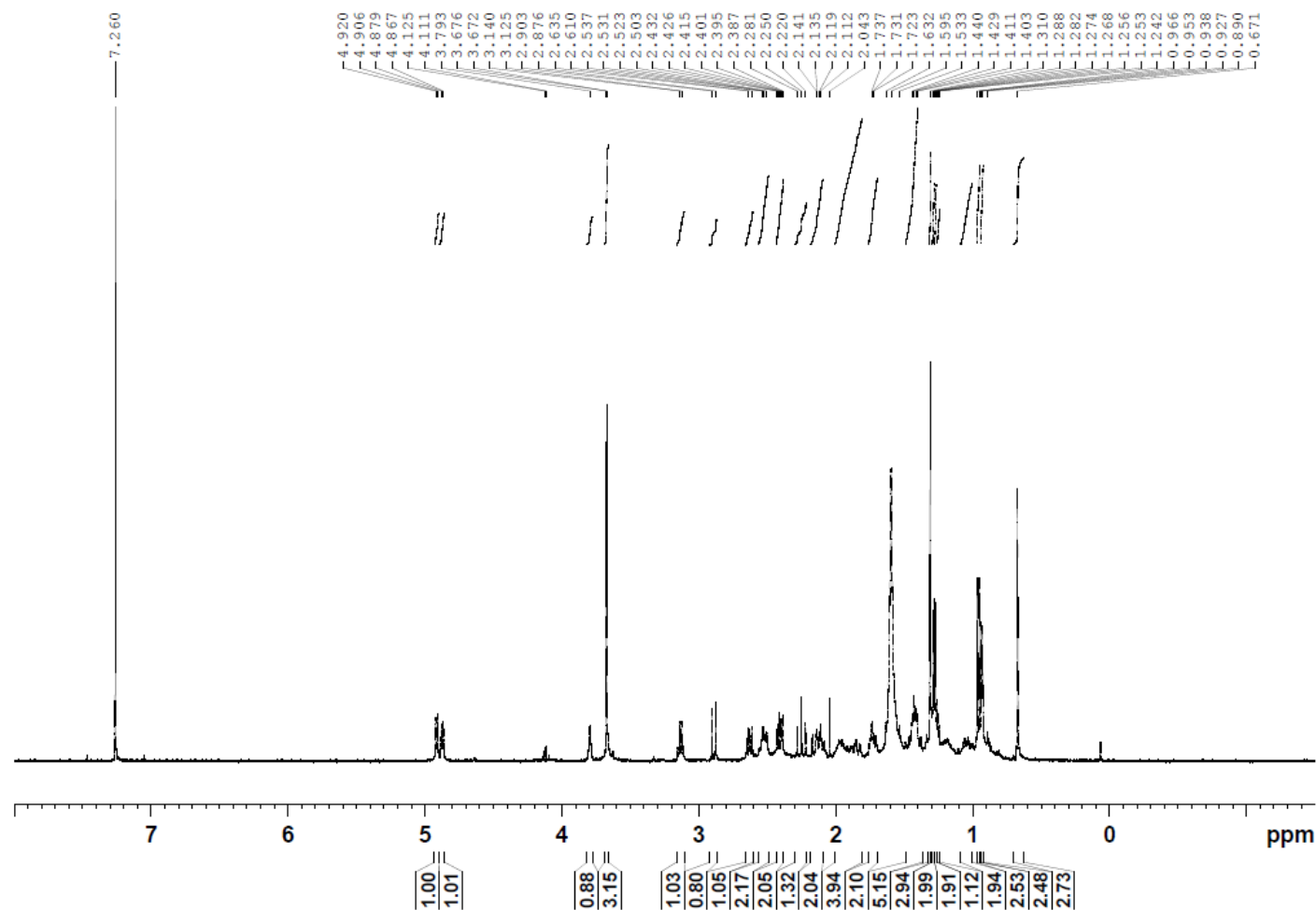


Figure S16 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 3 α -hydroxy-7,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate. (20)

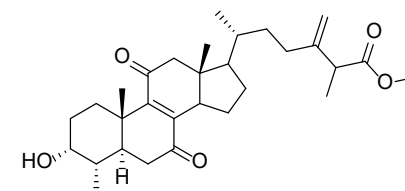
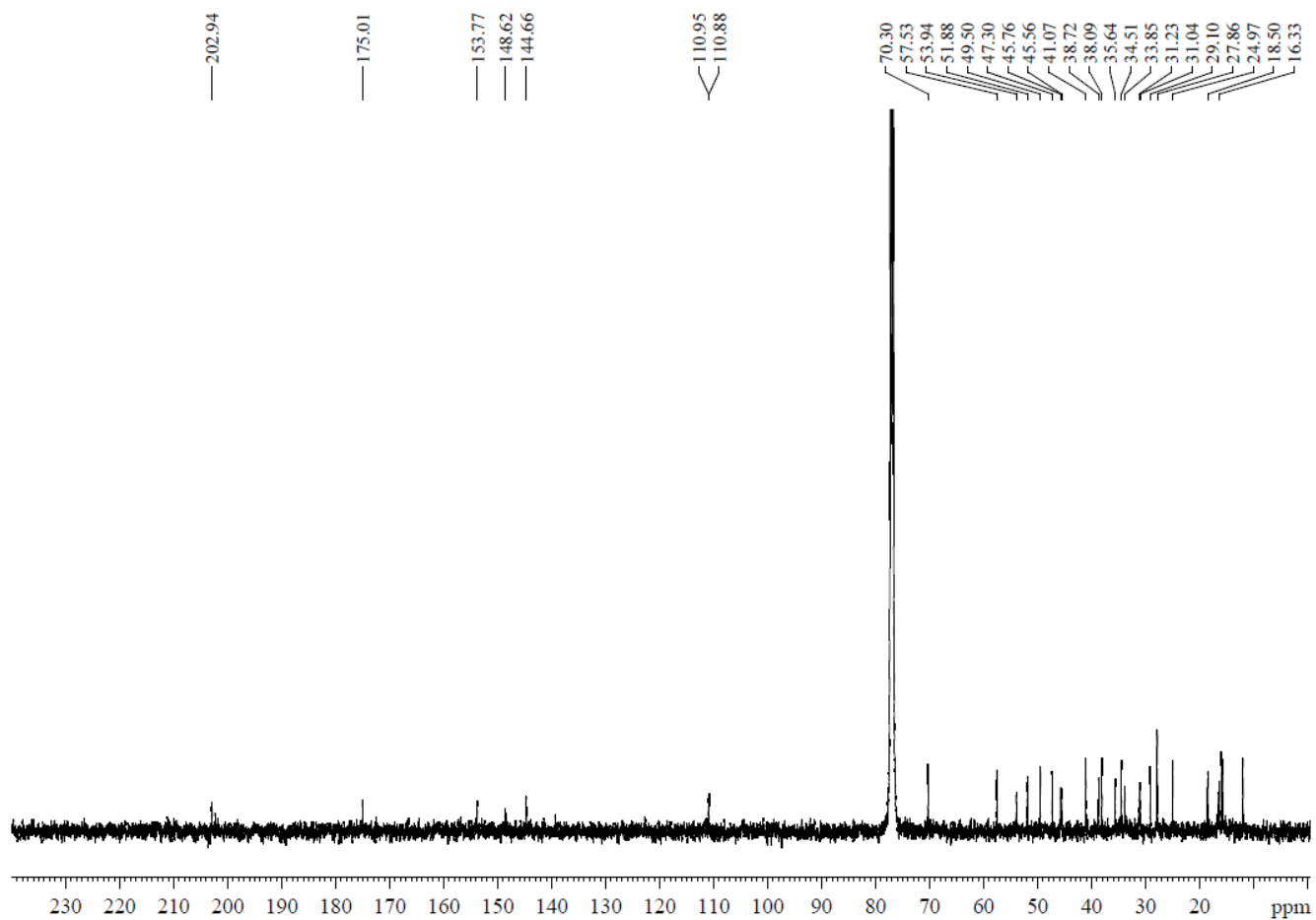


Figure S17 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 7 β -hydroxy-3,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate. (22)

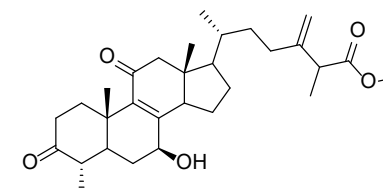
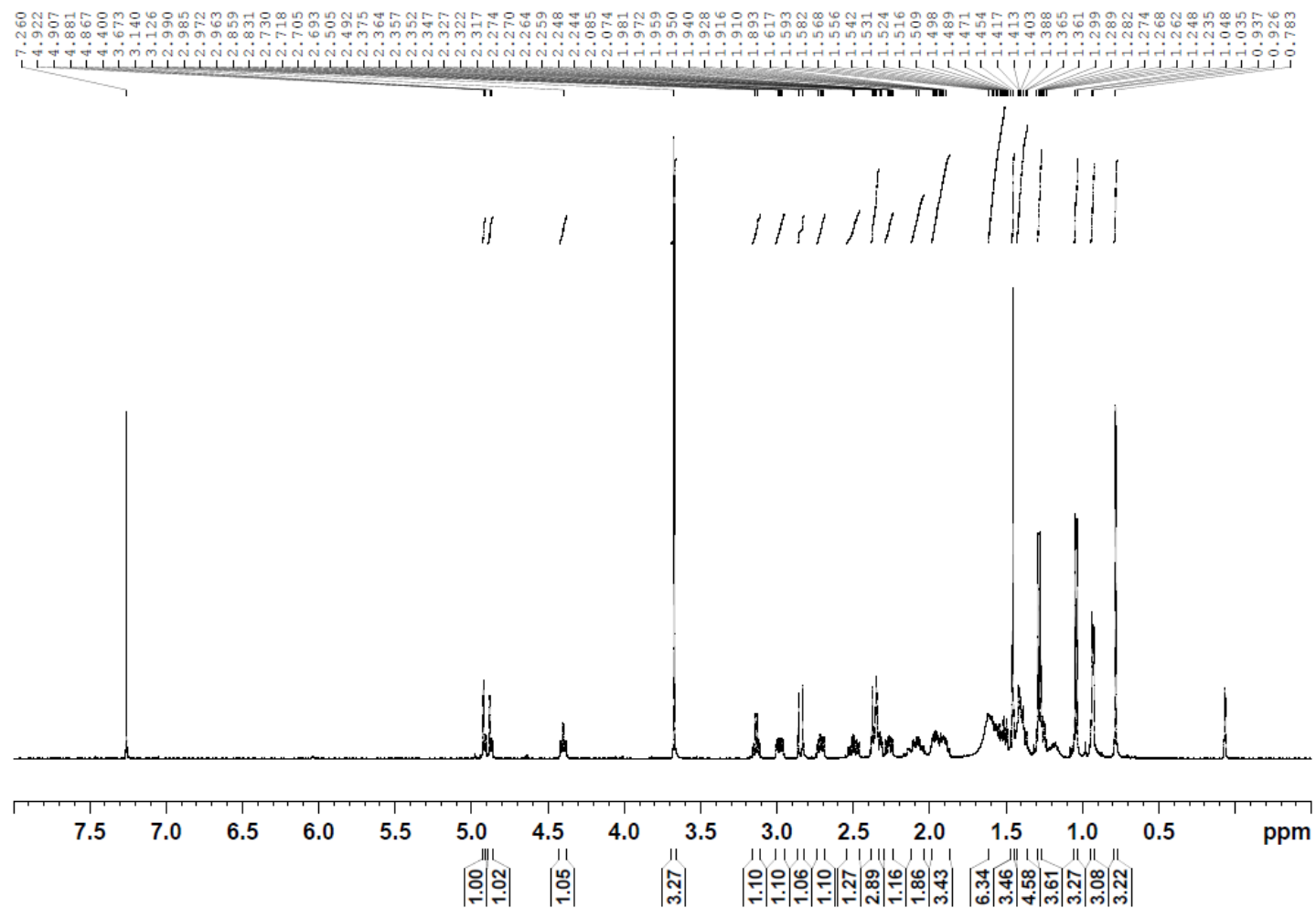


Figure S18 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 7 β -hydroxy-3,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate. (22)

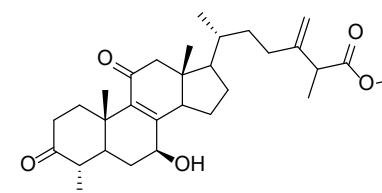
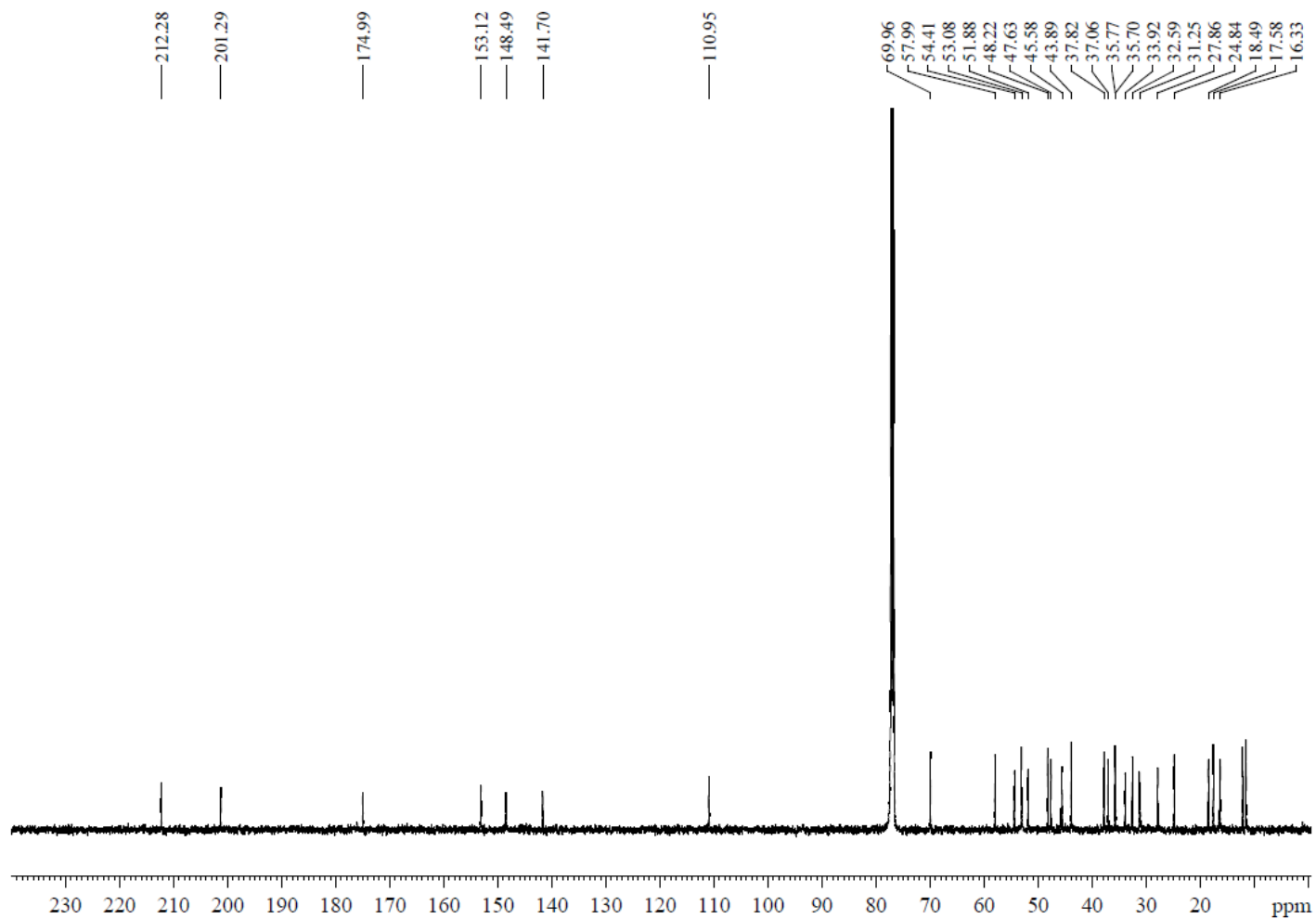


Figure S19 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 4 α -methylergosta-8,24(28)-diene-3,11-dione-26-oate. (24)

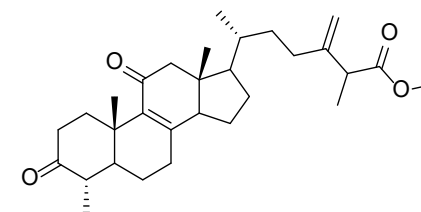
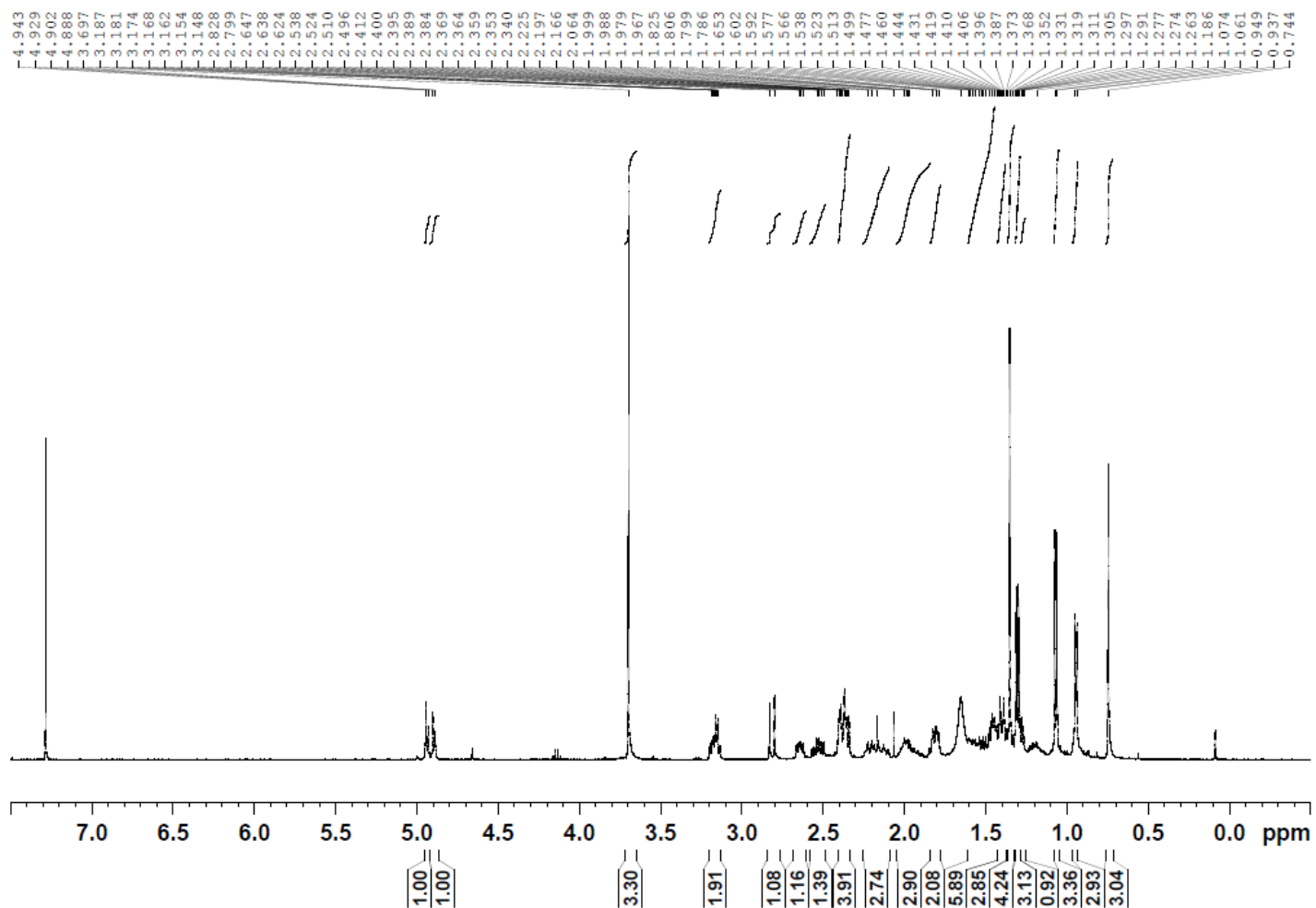


Figure S20 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 4 α -methylergosta-8,24(28)-diene-3,11-dione-26-oate. (24)

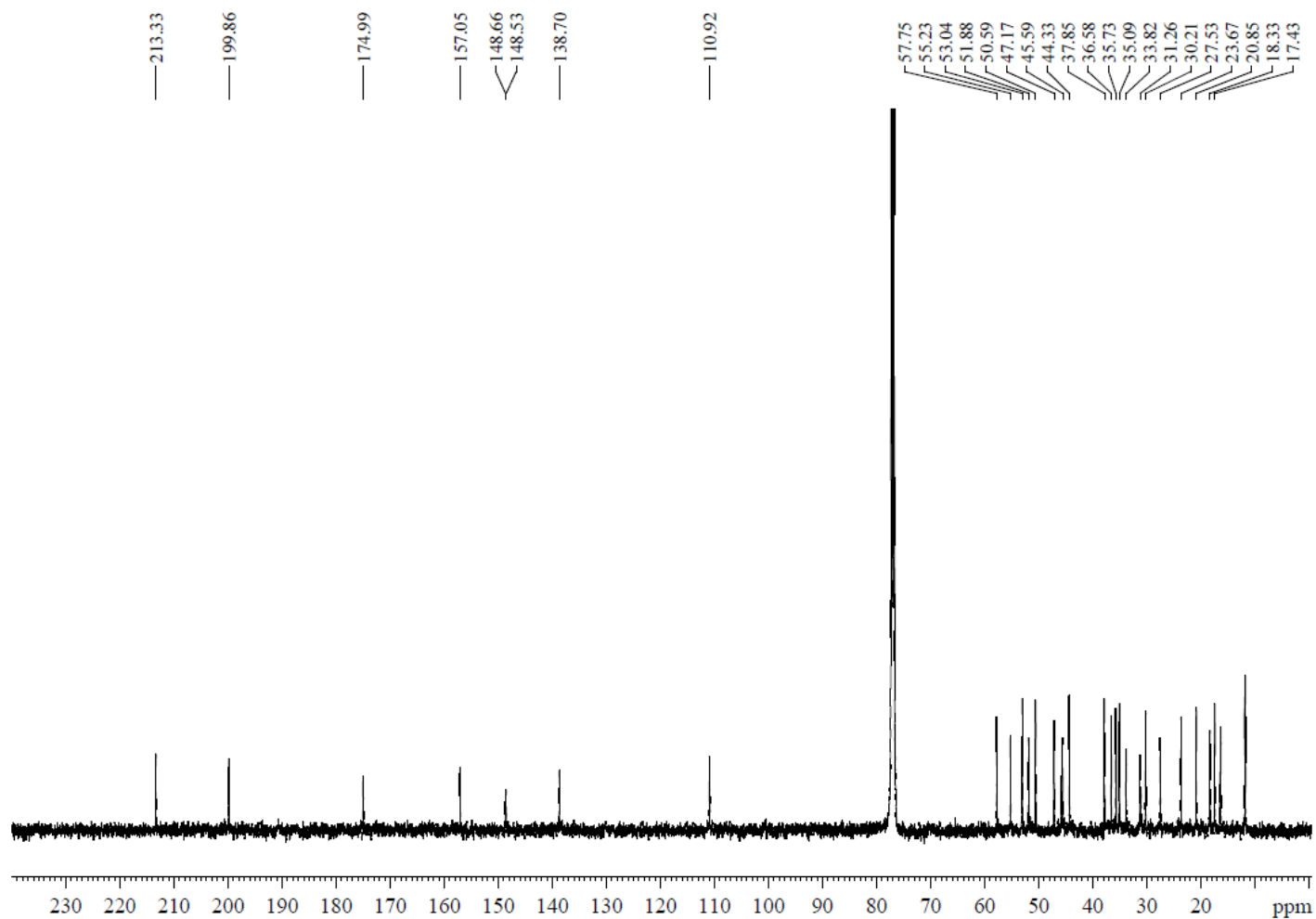


Figure S21 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 3 α ,7 β -dihydroxy-4 α -methylergosta-8,24(28)-dien-11-on-26-oate. (26)

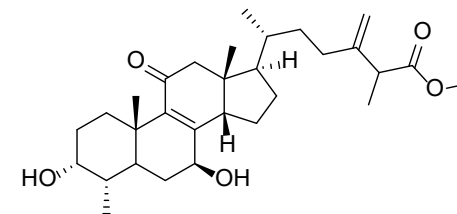
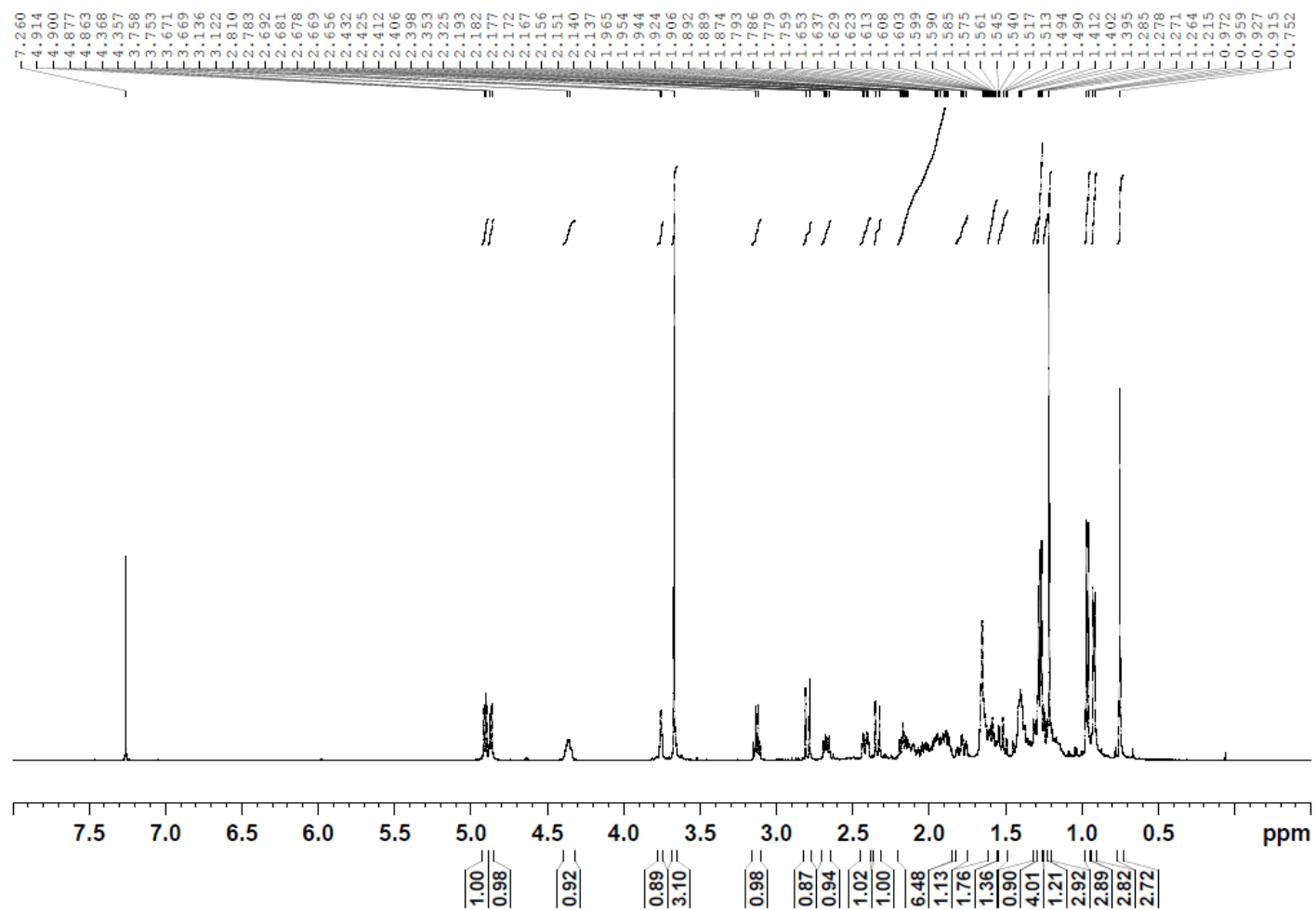


Figure S22 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 3 α ,7 β -dihydroxy-4 α -methylergosta-8,24(28)-dien-11-on-26-oate. (26)

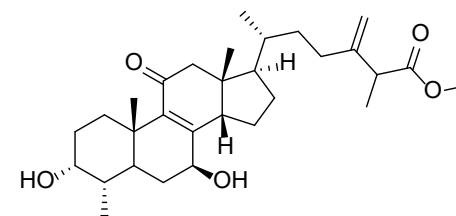
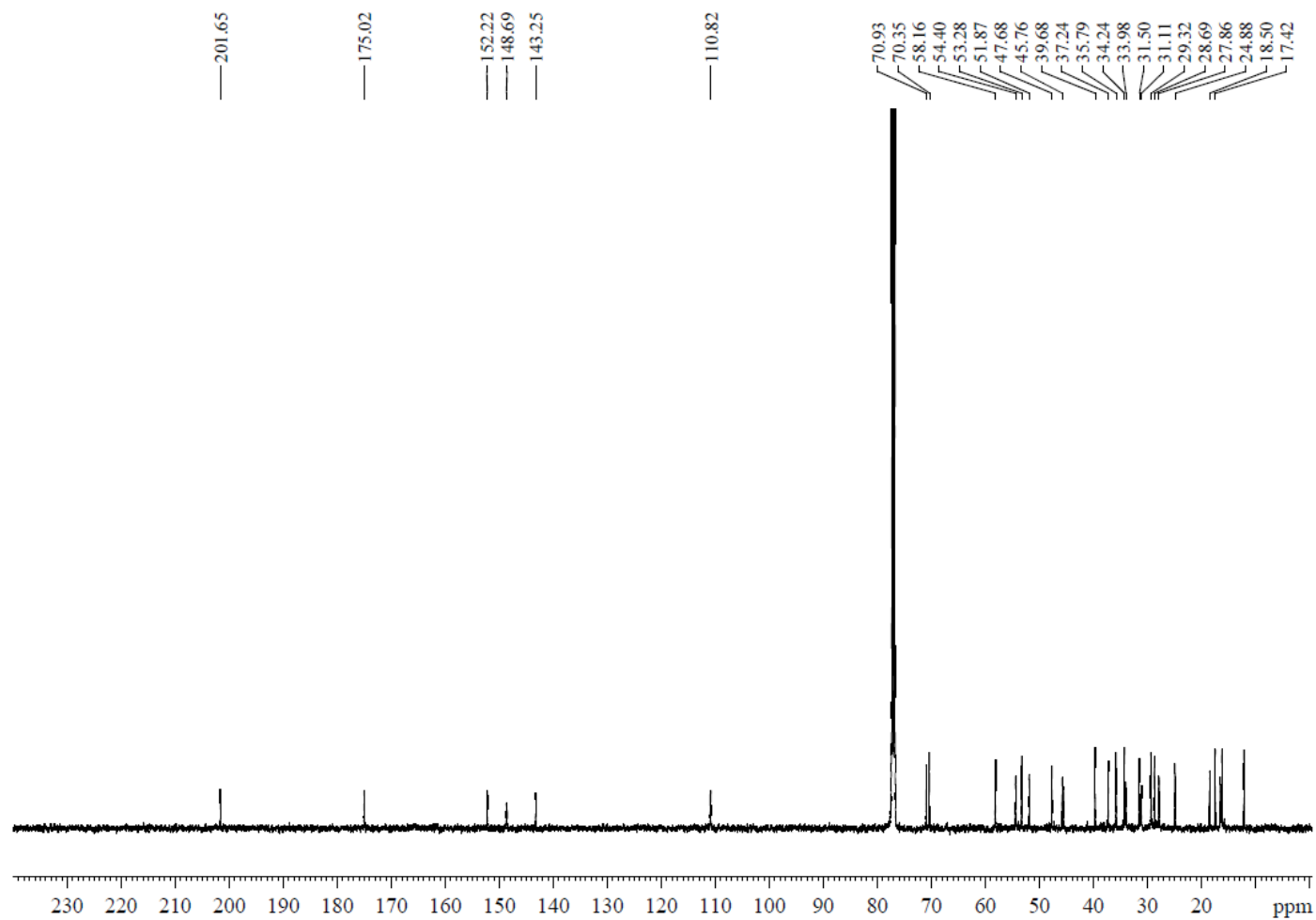


Figure S23 ^1H NMR (500 MHz, CDCl_3) spectrum of methyl 3 β ,12 β -dihydroxy-11-oxo-4 β -methylergosta-8,24(28)-dien-26-oate (methyl antcin M). (28)

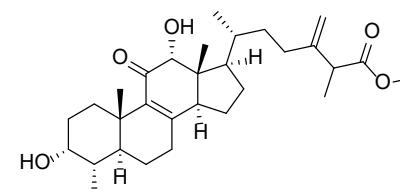
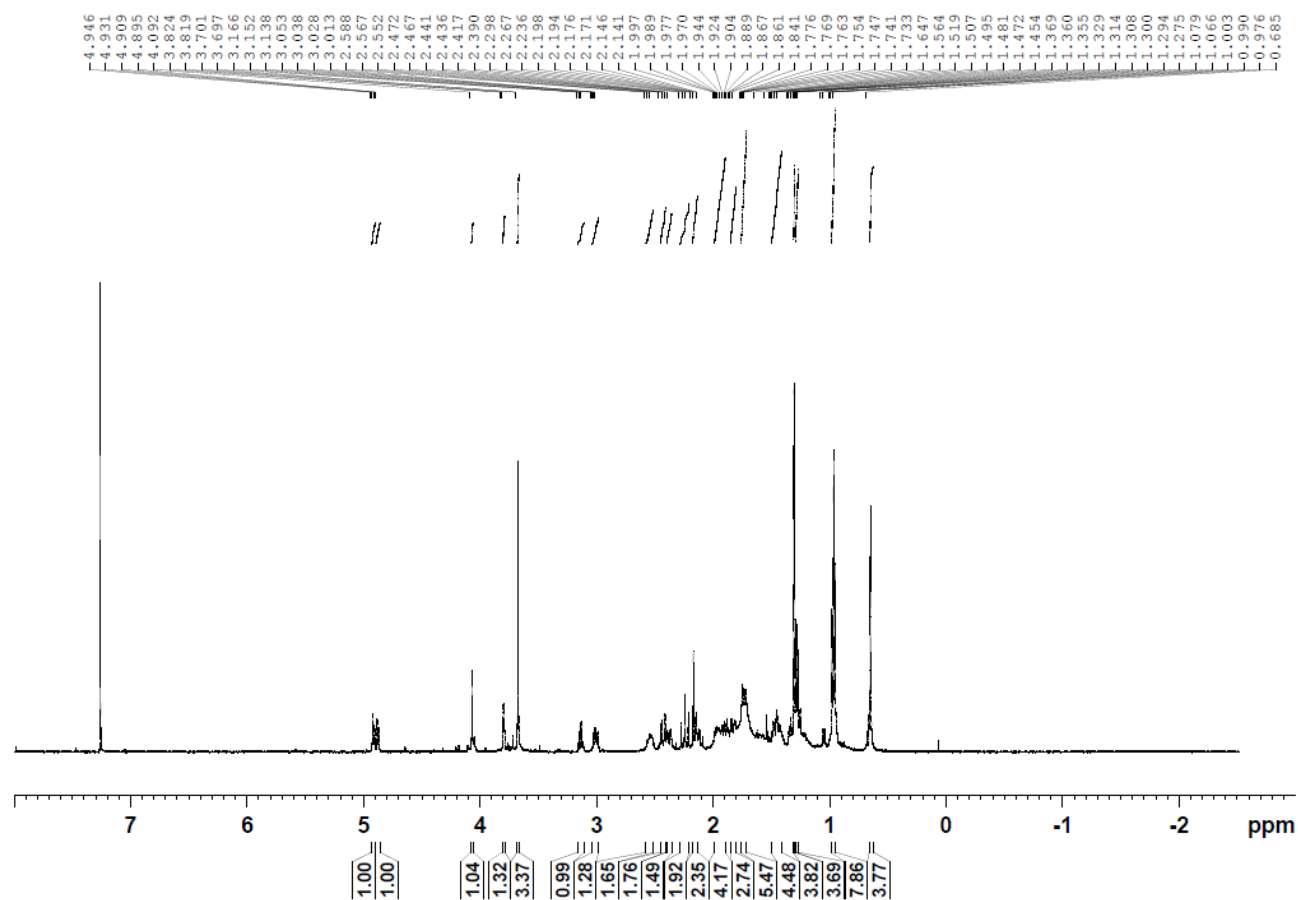


Figure S24 ^{13}C NMR (125 MHz, CDCl_3) spectrum of methyl 3 β ,12 β -dihydroxy-11-oxo-4 β -methylergosta-8,24(28)-dien-26-oate (methyl antcin M). (28)

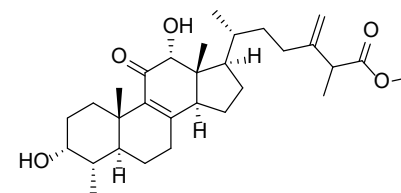
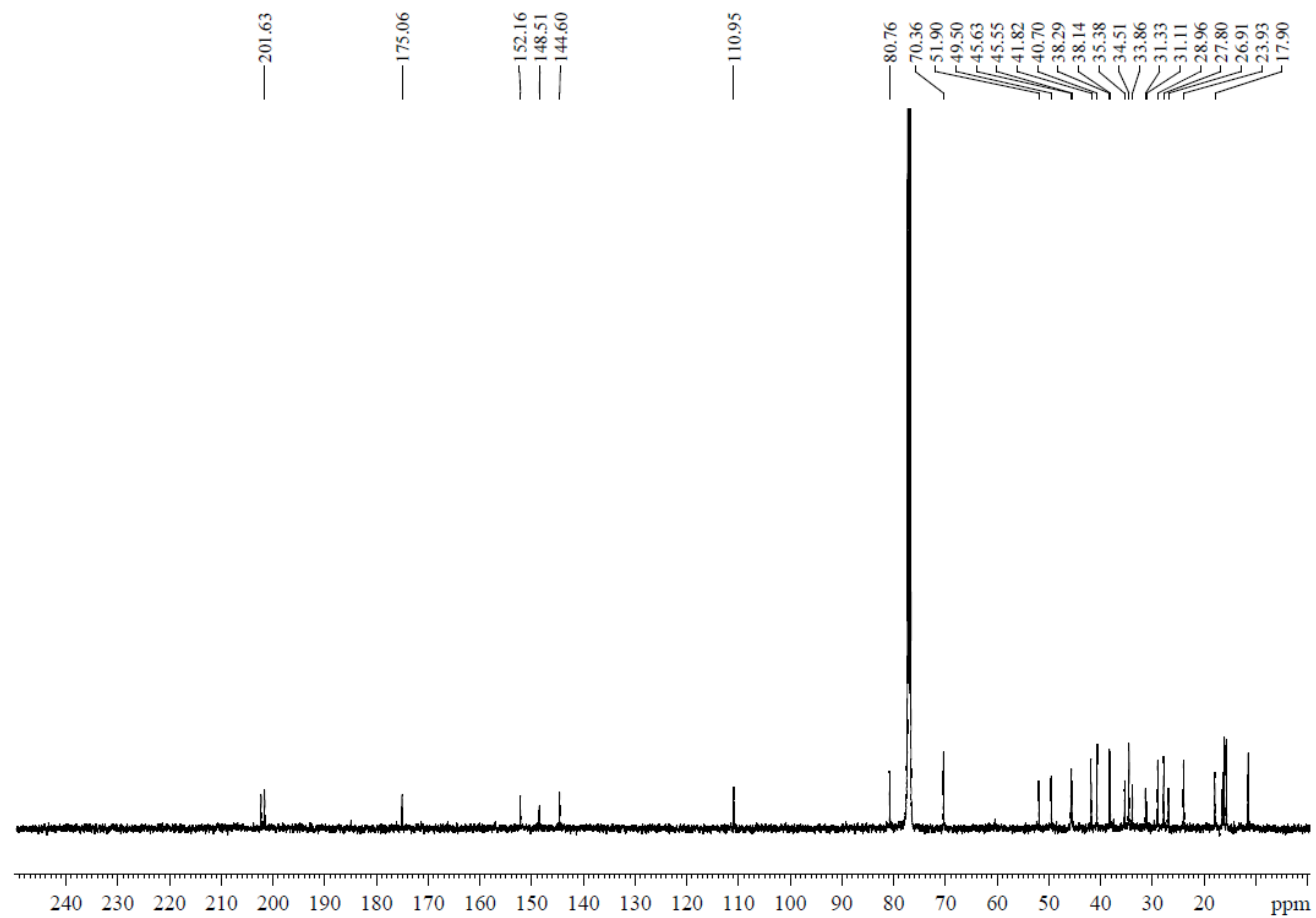


Figure S25 References for known compounds

- methyl 3 α ,7 α ,12 α -trihydroxy-4 α -methylergosta-8,24(28)-dien-11-on-26-oate (**6**), [1]
- zhankuic acid A methyl ester (**8**), [2]
- methyl-7 β -hydroxy-3,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate (**12**), [2]
- methyl 3 α ,12 α -dihydroxy 4 α -methylergosta-8,24(28)-diene-7,11-dion-26-oate (methyl antcinatate H, **16**), [3]
- methyl 3 α -hydroxy-7,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate (**20**), [2]
- methyl 7 β -hydroxy-3,11-dioxo-4 α -methylergosta-8,24(28)-dien-26-oate (**22**), [2]
- methyl 4 α -methylergosta-8,24(28)-diene-3,11-dion-26-oate (**24**), [2]
- methyl 3 β ,12 β -dihydroxy-11-oxo-4 β -methylergosta-8,24(28)-dien-26-oate (methyl antcin M, **26**) [4]

Reference

- [1] C.C. Shen, Y.H. Wang, T.T. Chang, L.C. Lin, M.J. Don, Y.C. Hou, K.T. Liou, S. Chang, W.Y. Wang, H.C. Ko, Y.C. Shen, Anti-inflammatory ergostanes from the basidiomata of *Antrodia salmonea*, *Planta Med.* 73 (2007) 1208-1213. <http://doi.org/10.1055/s-2007-981591>
- [2] S.J. Wu, W.L. Leu, C.H. Chen, C.H. Chao, D.Y. Shen, H.H. Chan, E.J. Lee, T.S. Wu, Y.H. Wang, Y.C. Shen, K. Qian, K.F. Bastow, K.H. Lee, Camphorastins A–J, Potent Cytotoxic and Anti-inflammatory Triterpenoids from the Fruiting Body of *Taiwanofungus camphoratus*, *J. Nat. Prod.* 73 (2010) 1756-1762. <http://doi.org/10.1021/np1002143>
- [3] S.W. Yang, Y.C. Shen, C.H. Chen, Steroids and triterpenoids of *Antrodia cinnamomea*—A fungus parasitic on *Cinnamomum micranthum*, *Phytochemistry* 41 (1996) 1389-1392. [http://doi.org/https://doi.org/10.1016/0031-9422\(95\)00767-9](http://doi.org/https://doi.org/10.1016/0031-9422(95)00767-9)
- [4] R. Gautam, S.M. Jachak, Recent developments in anti-inflammatory natural products, *Med. Res. Rev.* 29 (2009) 767-820. <http://doi.org/https://doi.org/10.1002/med.20156>