

Supplementary Materials

Exploring New Structural Features of The 18 β -Glycyrrhetic Acid Scaffold for The Inhibition of Anaplastic Lymphoma Kinase

Dong Cai ¹, ZhiHua Zhang ², Yu Chen ³, YanYan Zhang ⁴, YuQi Sun ^{4*} and YiXia Gong ^{1,*}

¹ College of Public Basic Sciences, Jinzhou Medical University, Jinzhou 121001, China

² School of Chemical and Environmental Engineering, Liaoning University of Technology, Jinzhou 121001, China

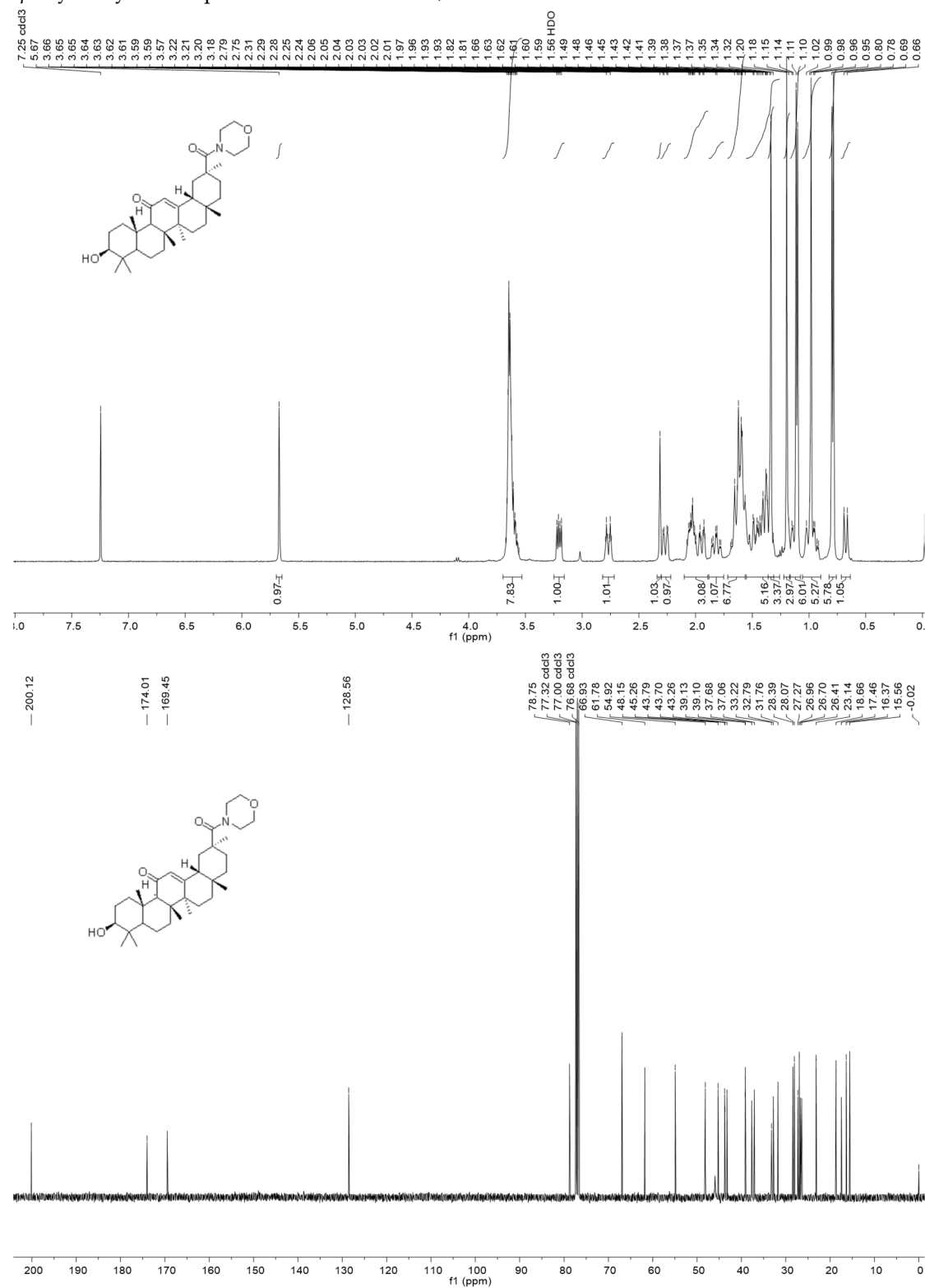
³ School of Life Science and Biopharmaceutics, Shenyang Pharmaceutical University, Shenyang 110016, China

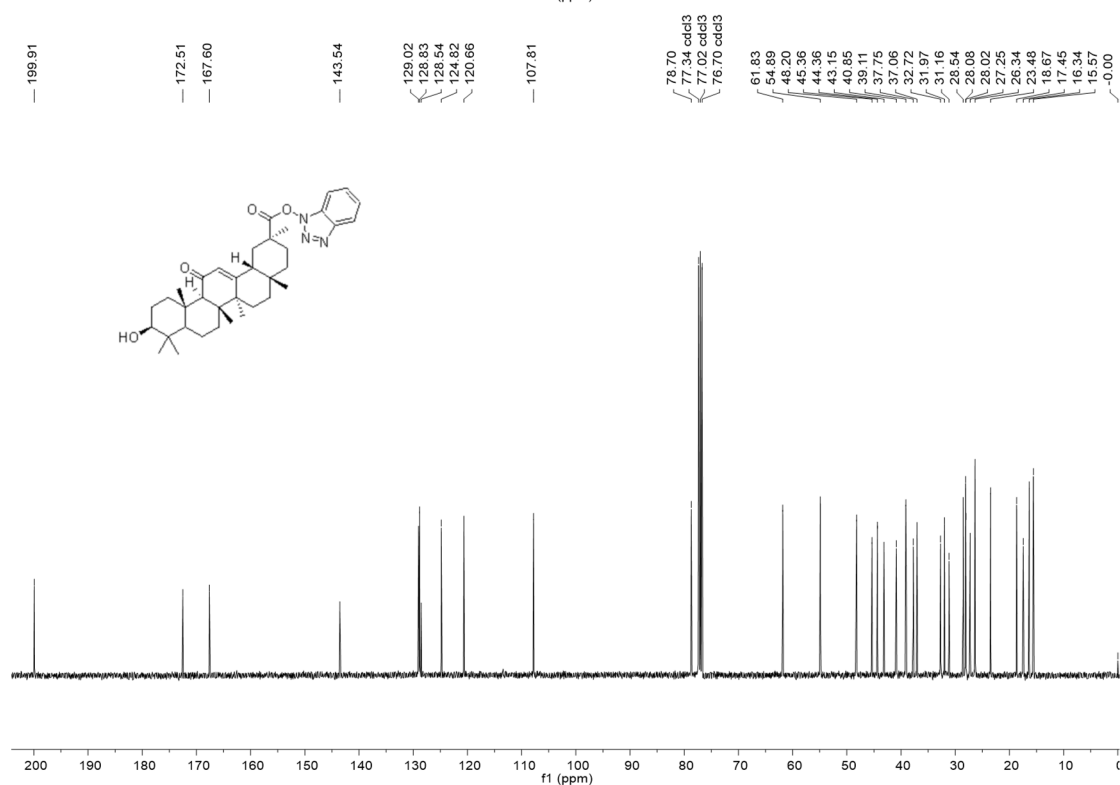
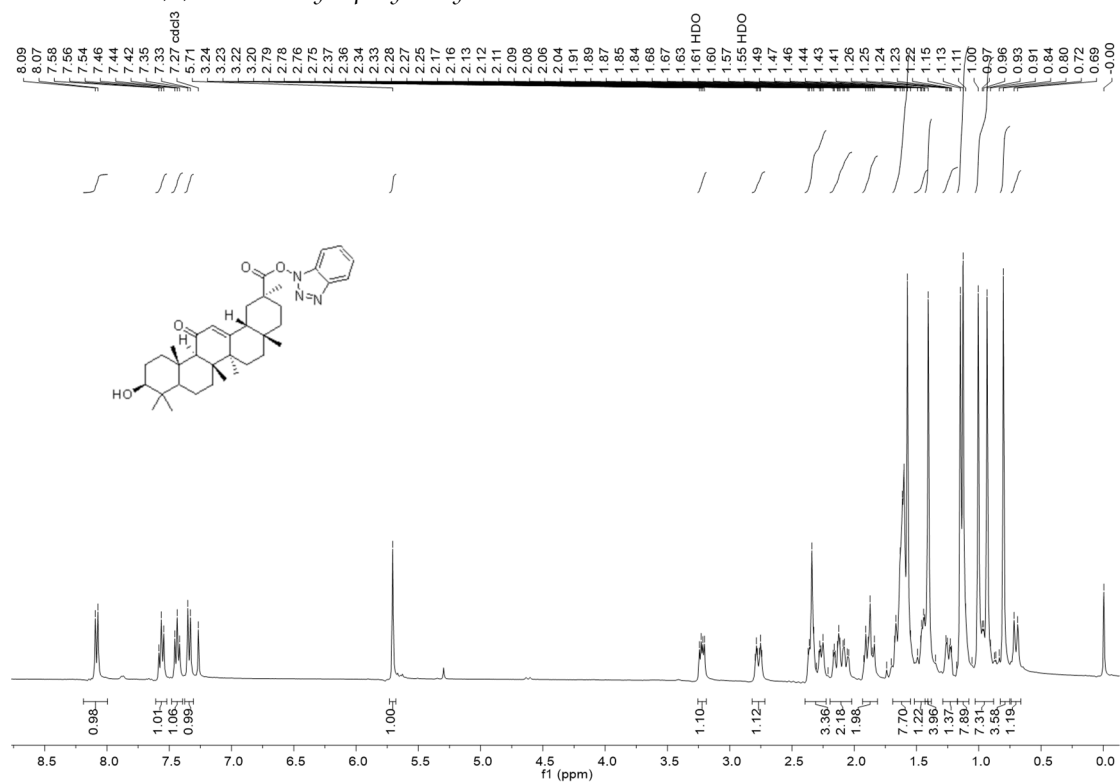
⁴ School of Chemical and Environmental Engineering, Liaoning University of Technology, Jinzhou, 121001, China

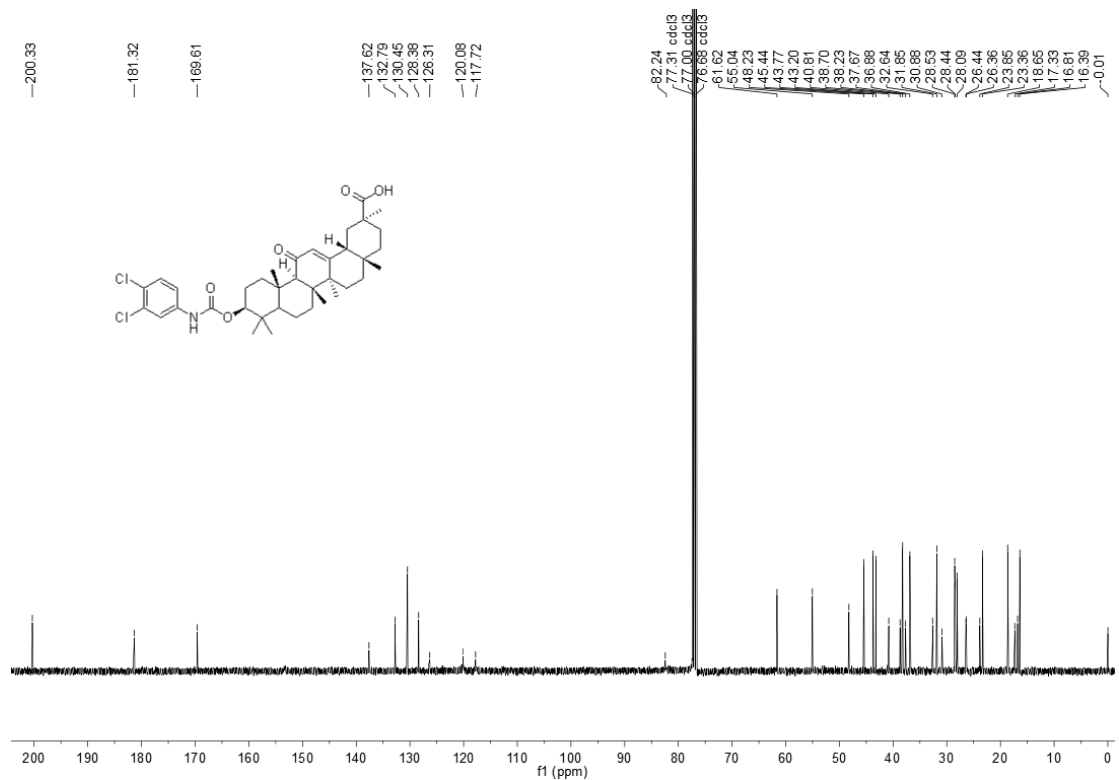
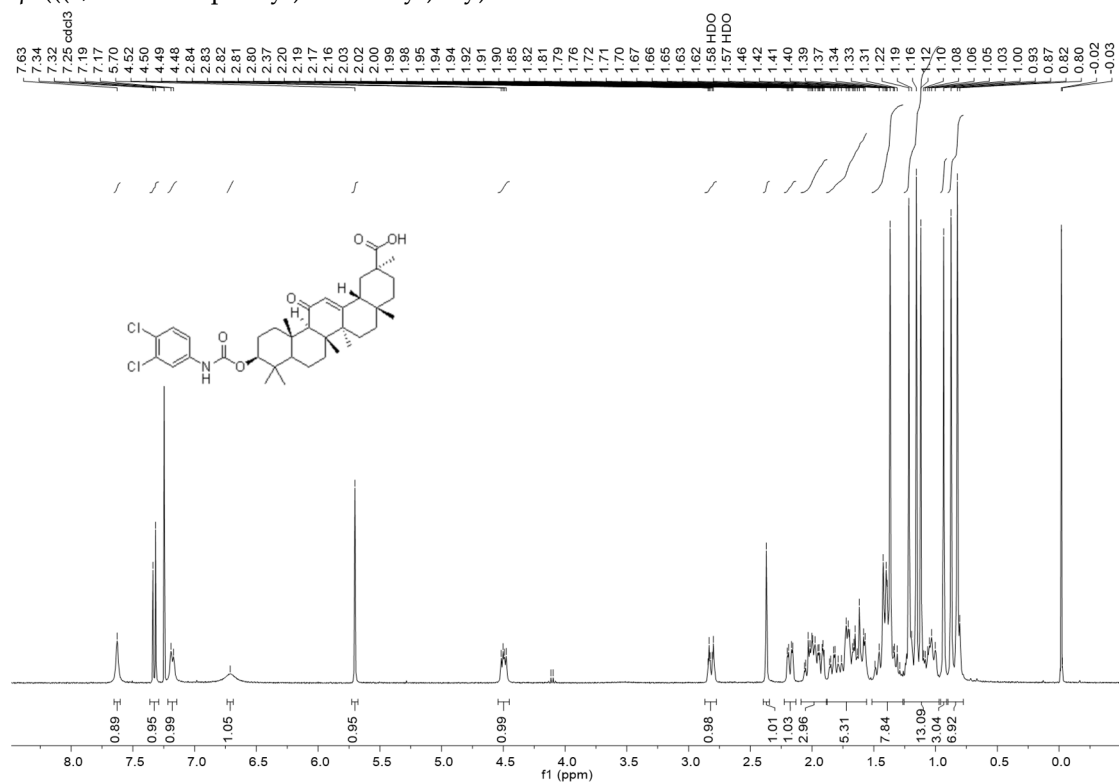
* Correspondence: cpusyq@jzmu.edu.cn (Y.S.); gongyixia_2006@163.com (Y.G.); Tel.: +86-0461-467-3404 (Y.S.)

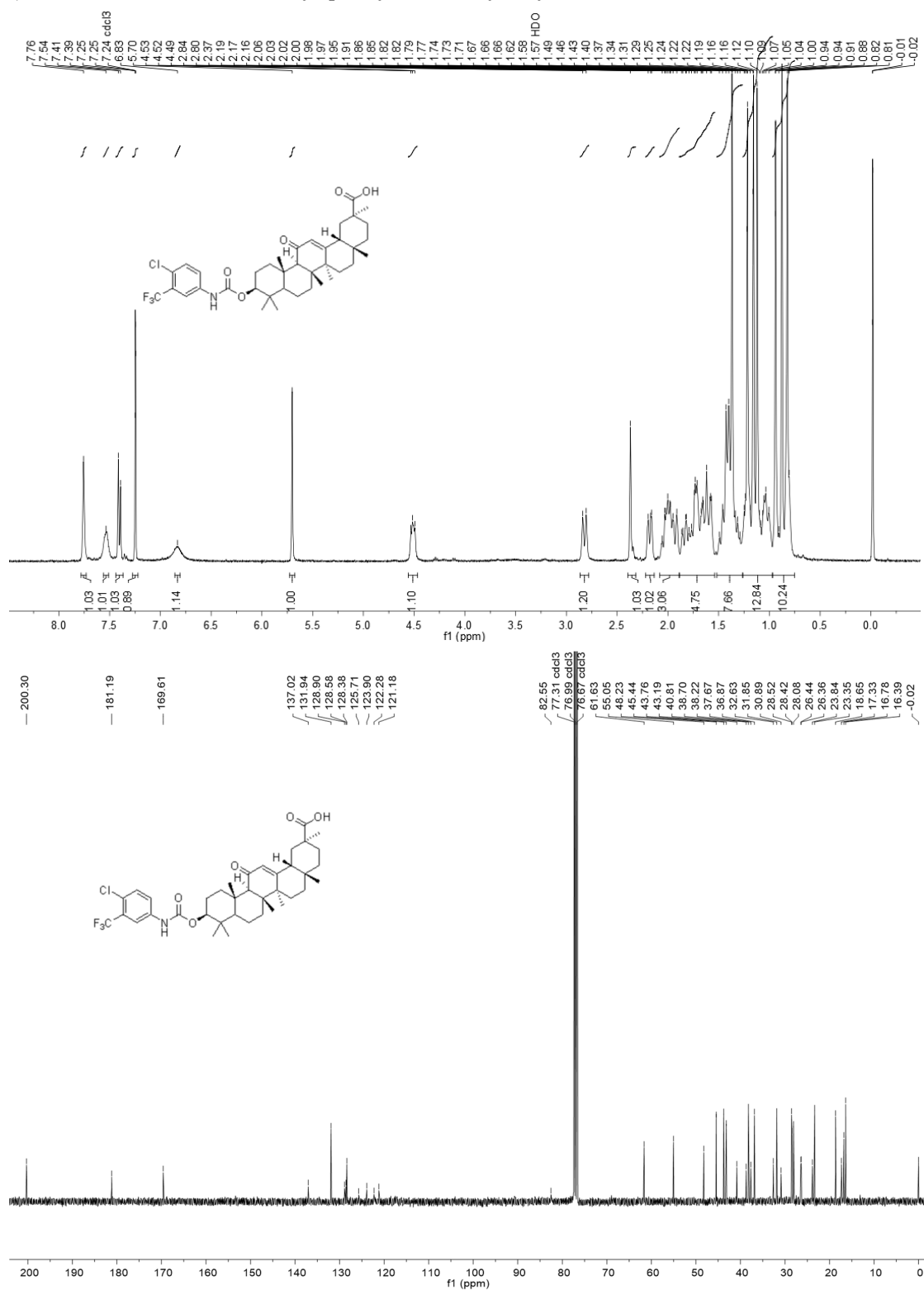
Table of Contents.

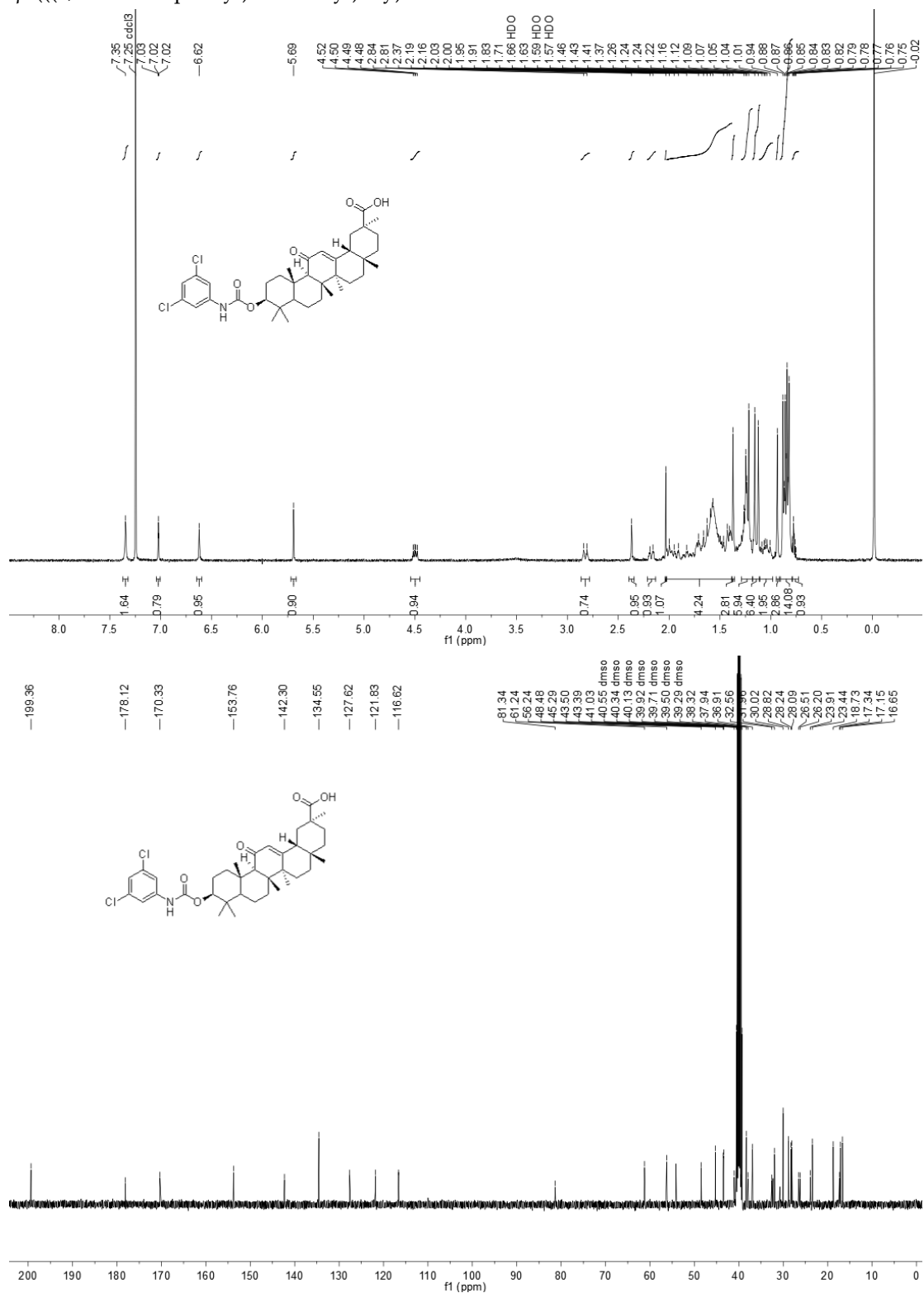
¹ H- and ¹³ C-NMR and HRMS of compound (2).....	S2
¹ H- and ¹³ C-NMR and HRMS of compound (2a)	S3
¹ H- and ¹³ C-NMR and HRMS of compound (3a–3o)	S4-18
¹ H- and ¹³ C-NMR and HRMS of compound (4a–4p)	S19-32
¹ H- and ¹³ C-NMR and HRMS of compound (5)	S33
¹ H- and ¹³ C-NMR and HRMS of compound (6a–6d)	S34-37
¹ H- and ¹³ C-NMR and HRMS of compound (7a–7b)	S38-39

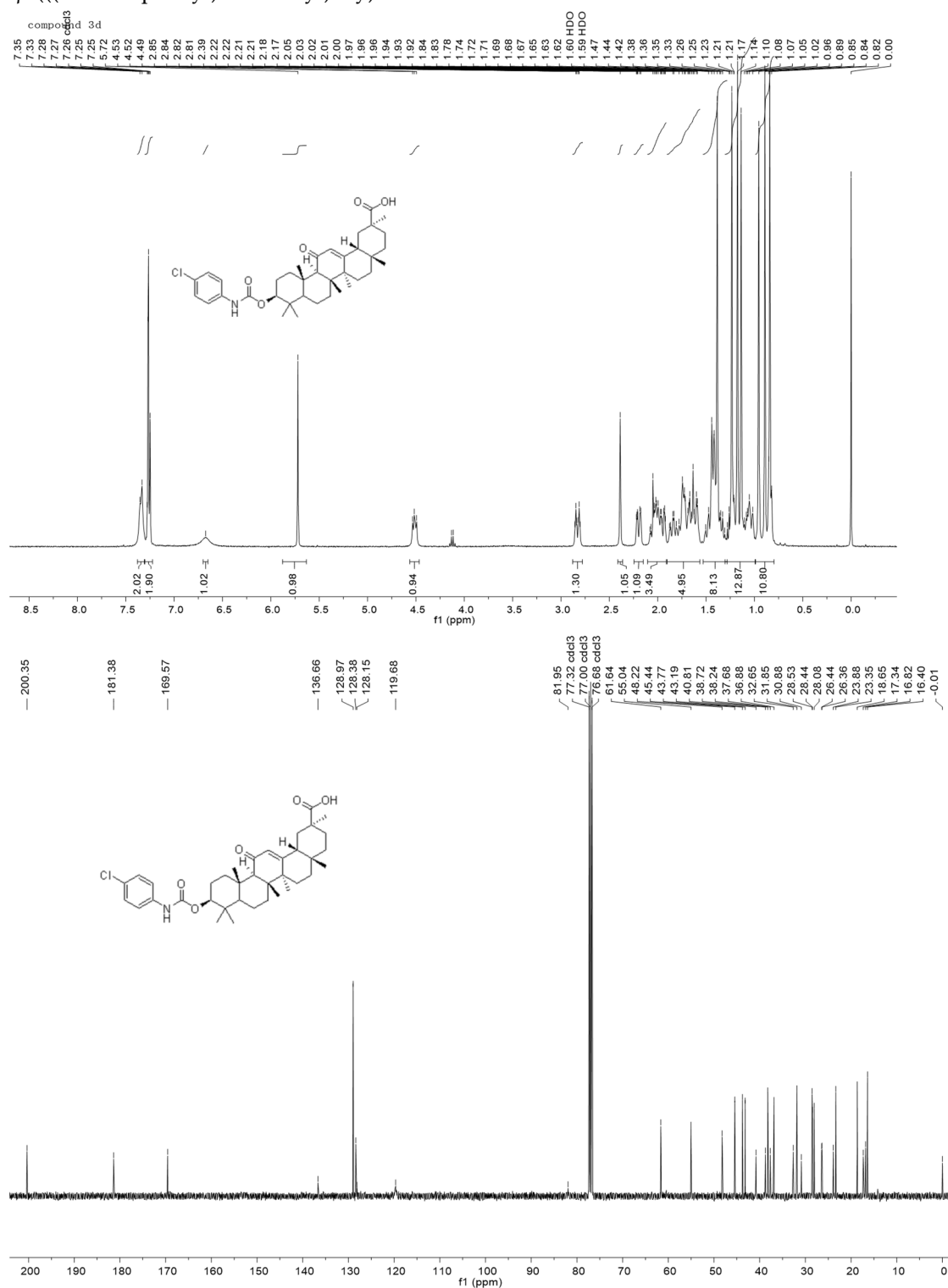
3 β -Hydroxy-30-morpholino-olean-12-ene-11,30-dione 2

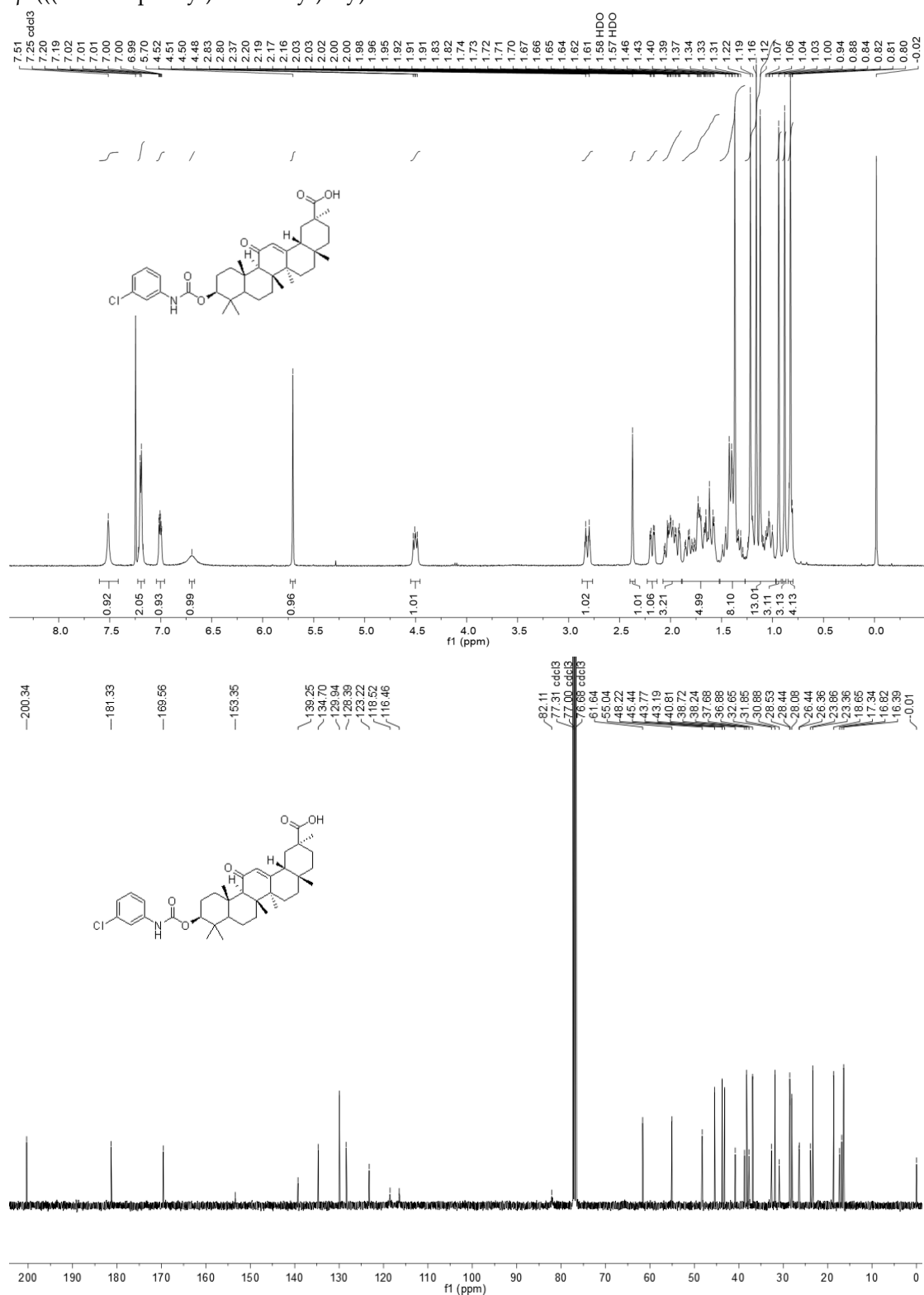
1H-benzo[d][1,2,3]triazol-1-yl 3 β -hydroxy -11-oxo-olean-12-en-30-oate **2a**

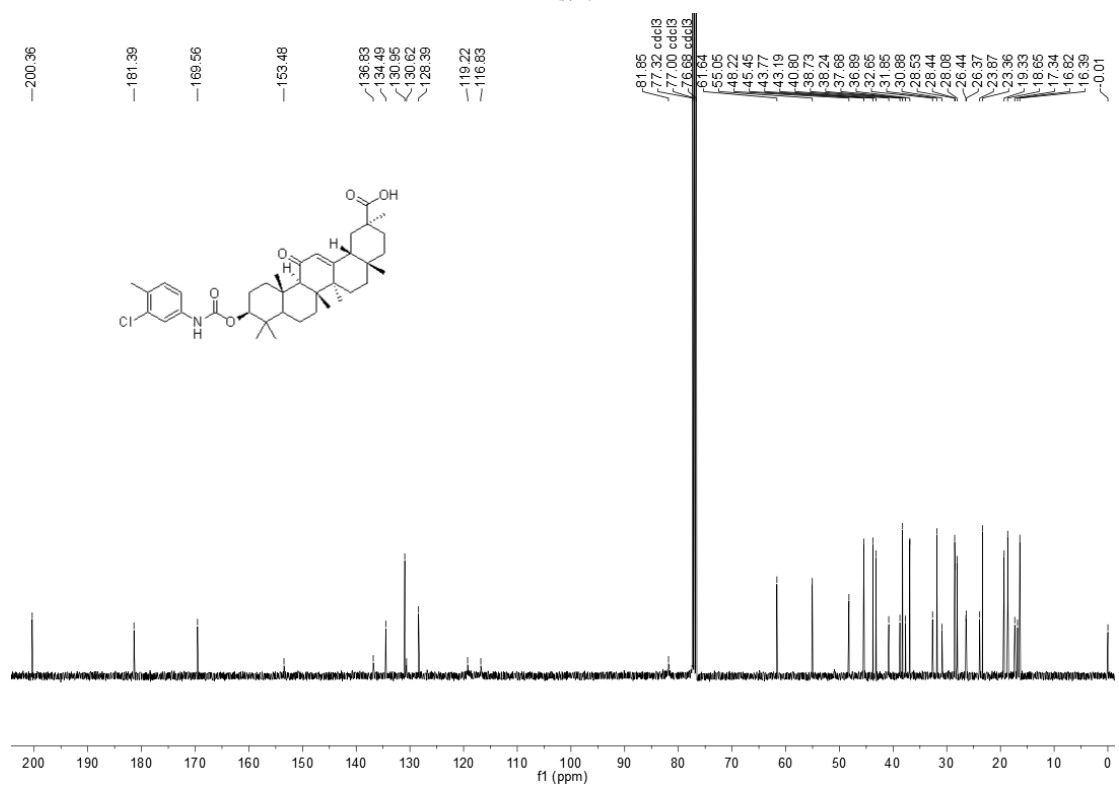
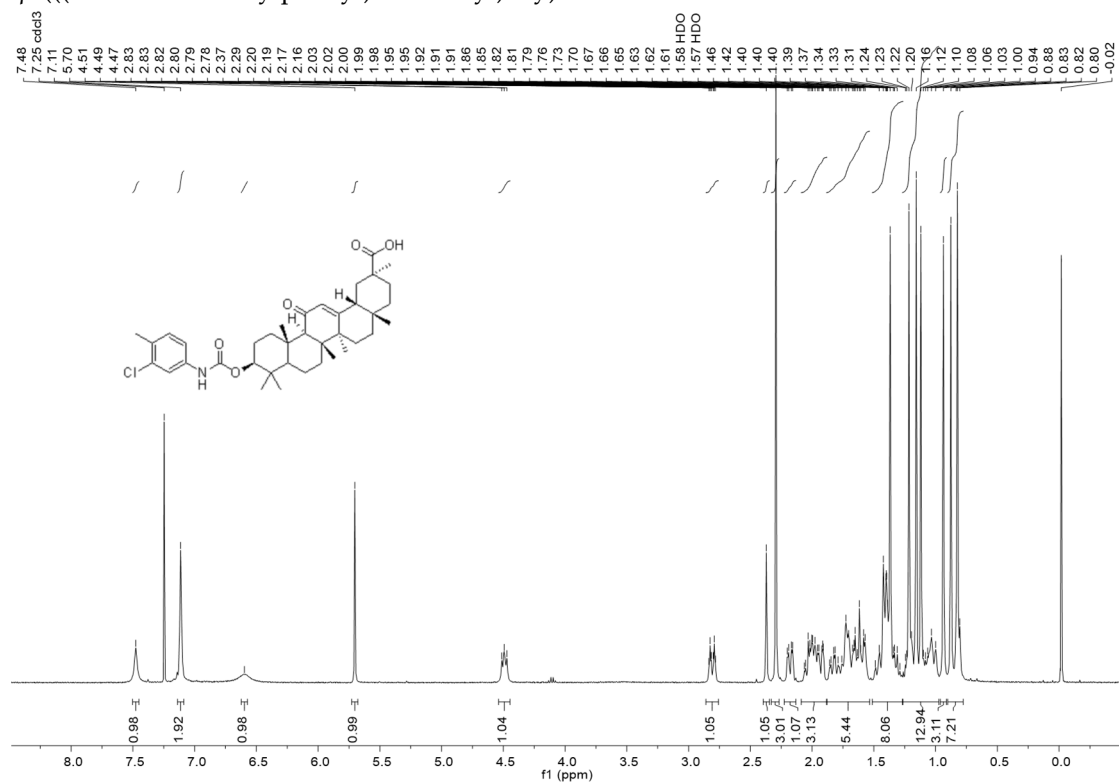
3 β -(((3,4-dichlorophenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oic acid **3a**

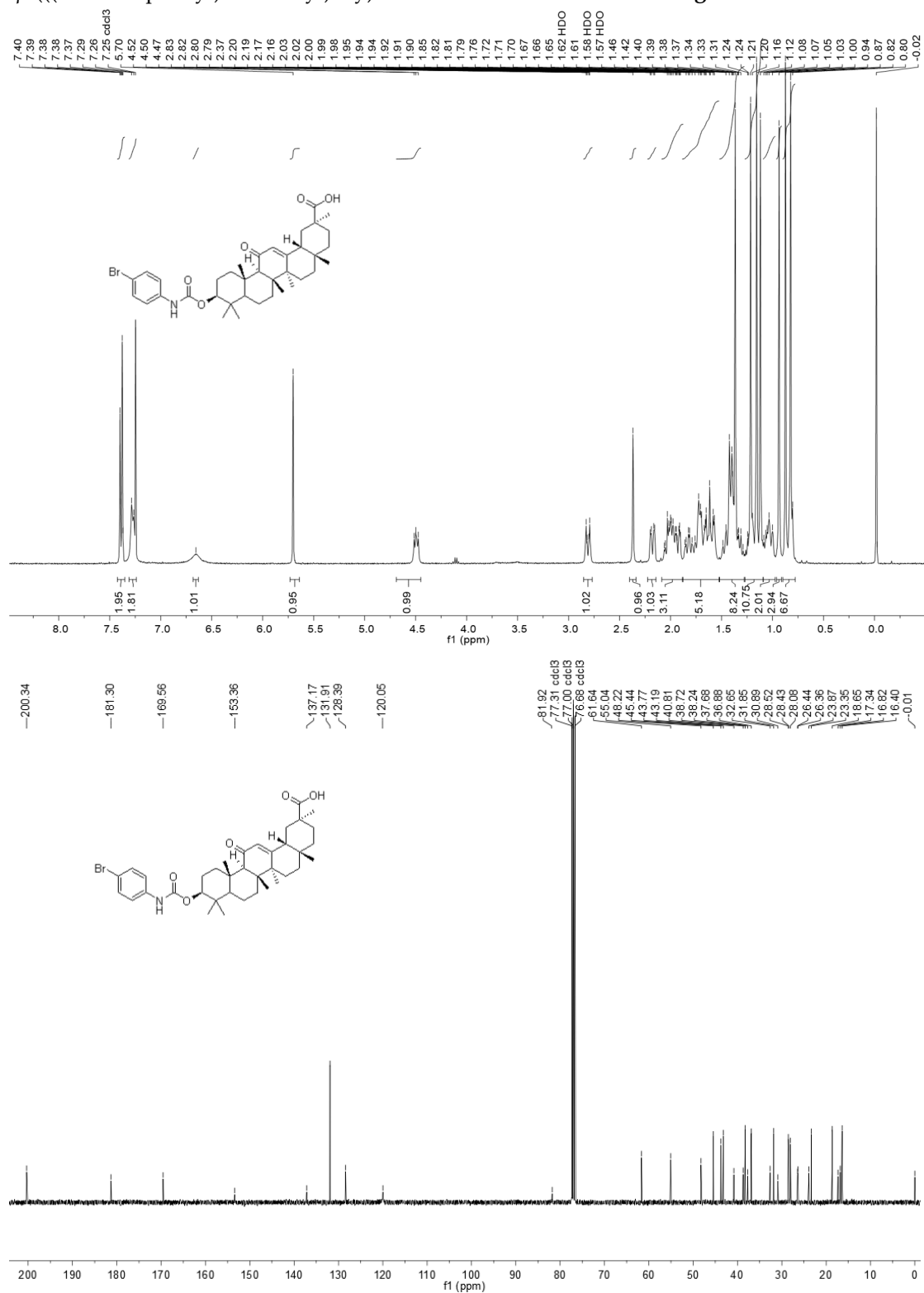
3 β -(((4-chloro-3-(trifluoromethyl)phenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oic acid **3b**

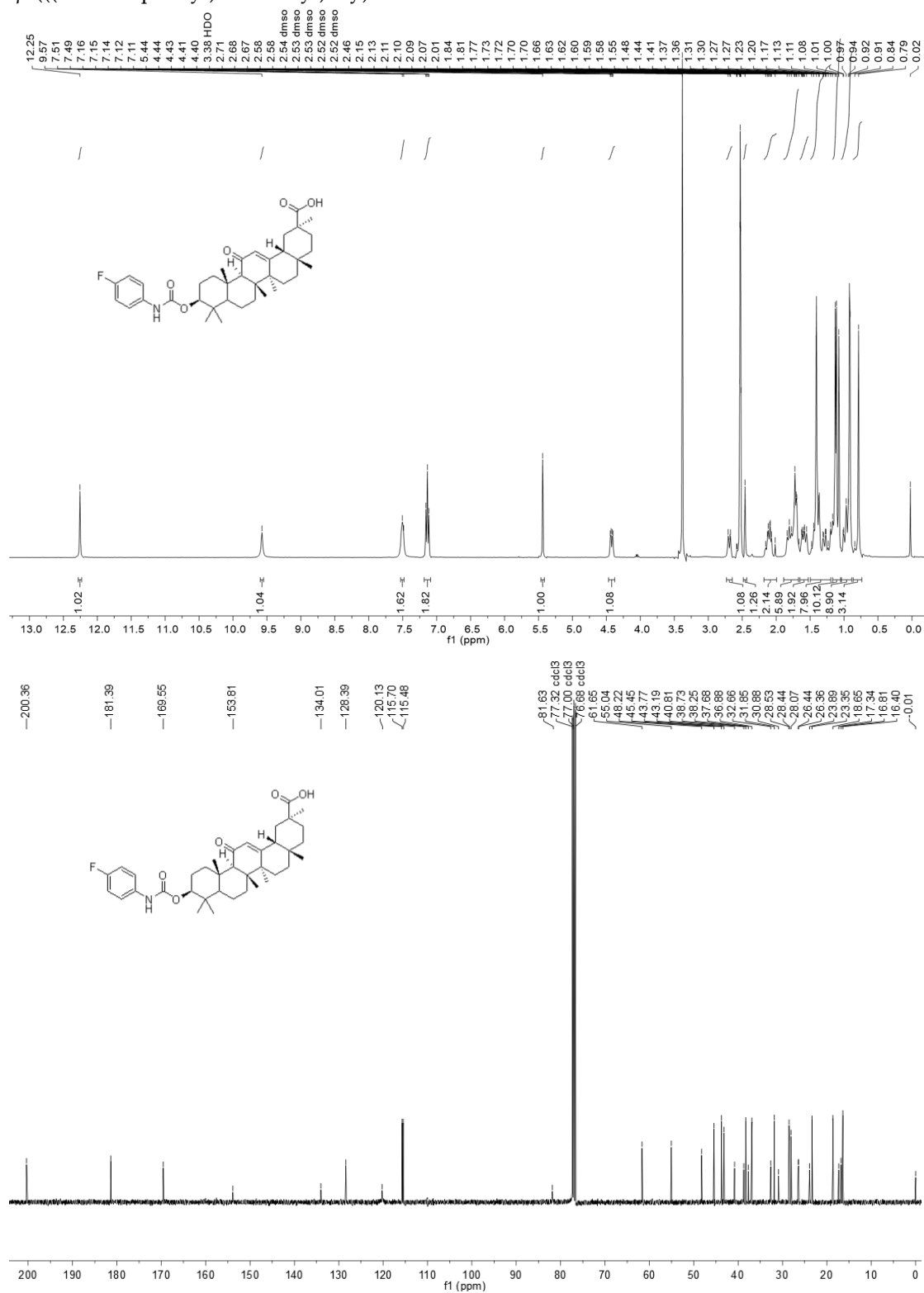
3β -(((3,5-dichlorophenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oic acid **3c**

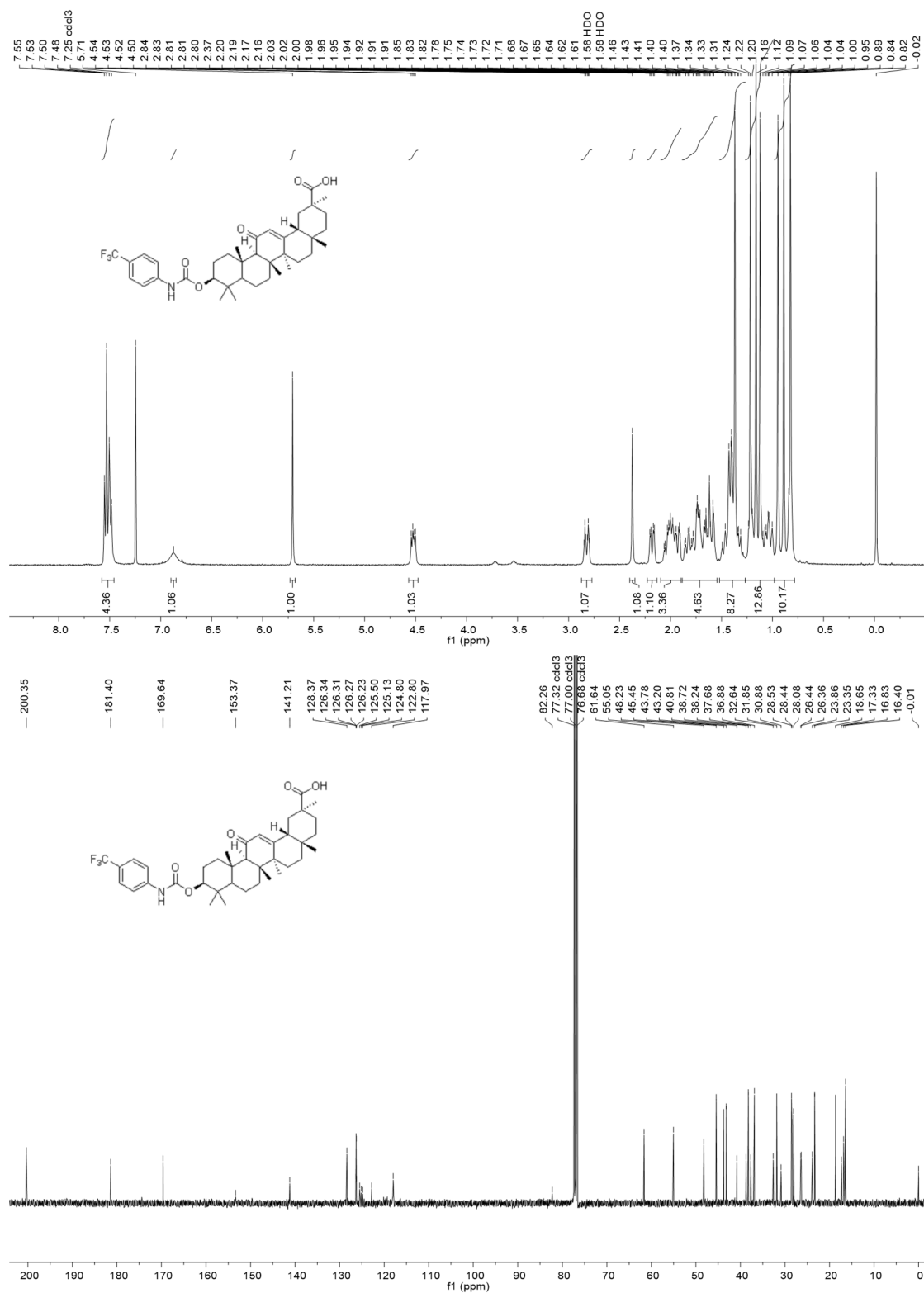
3-(((4-chlorophenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oic acid **3d**

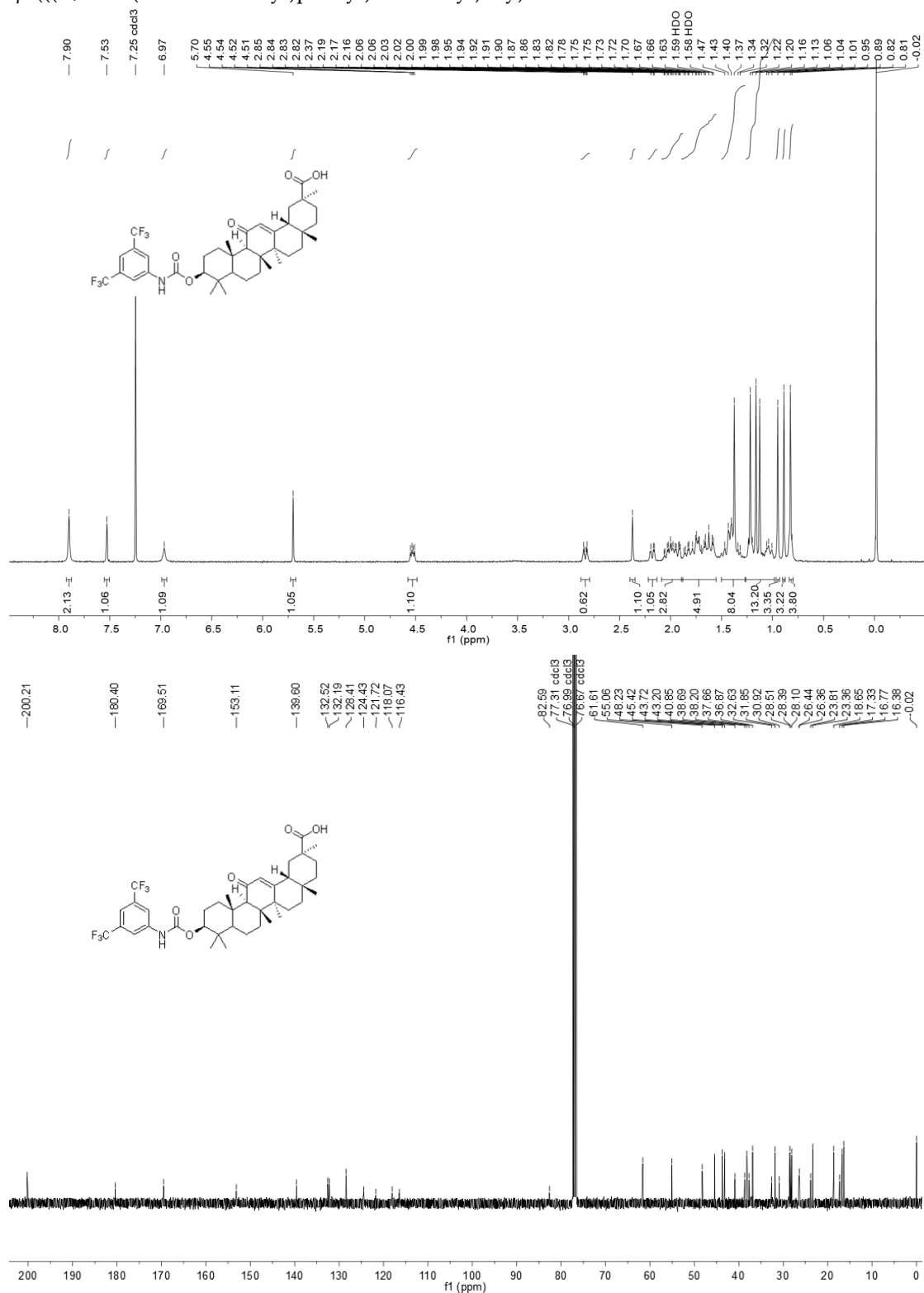
3 β -(((3-chlorophenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oic acid **3e**

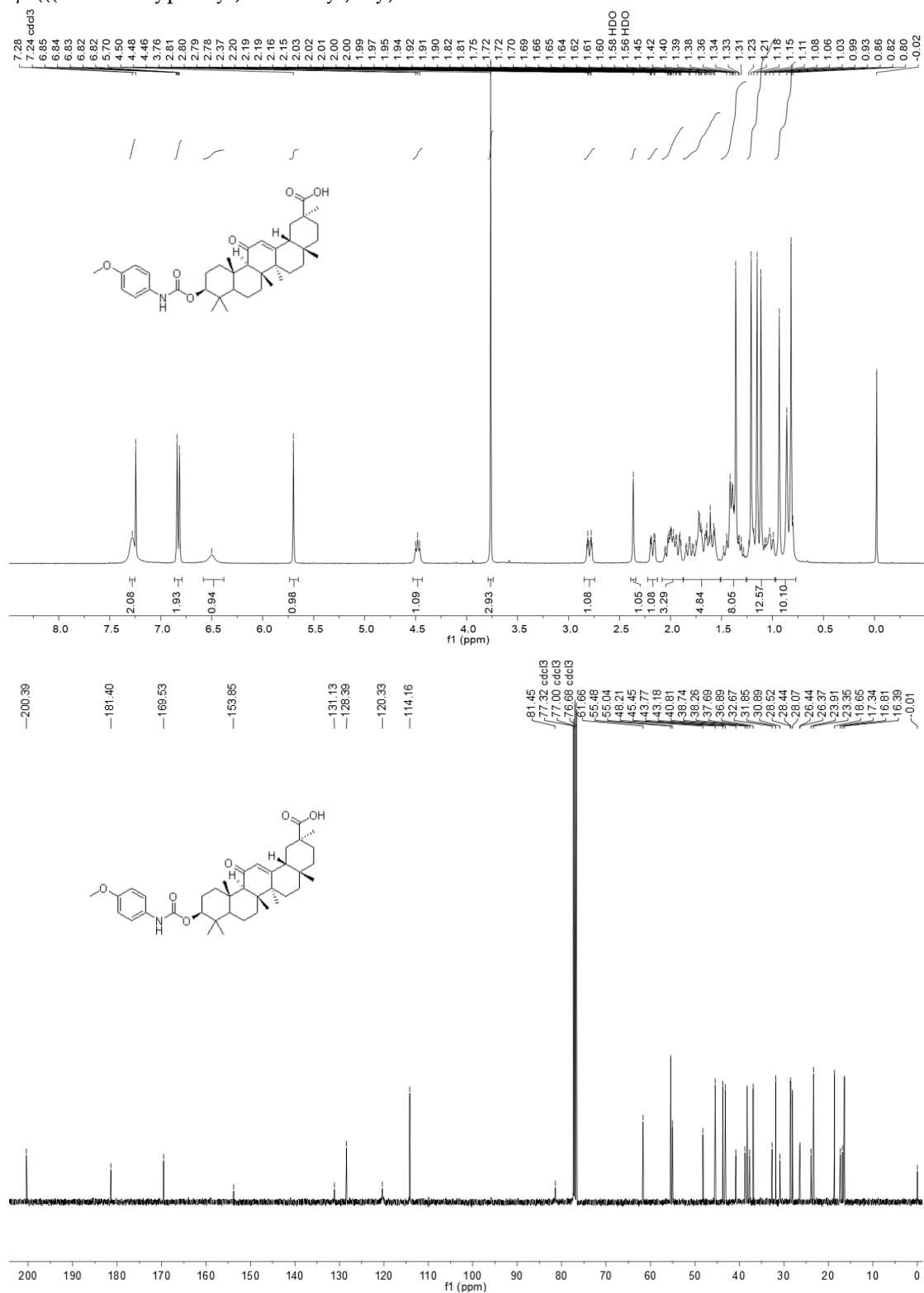
3 β -(((3-chloro-4-methylphenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oic acid 3f

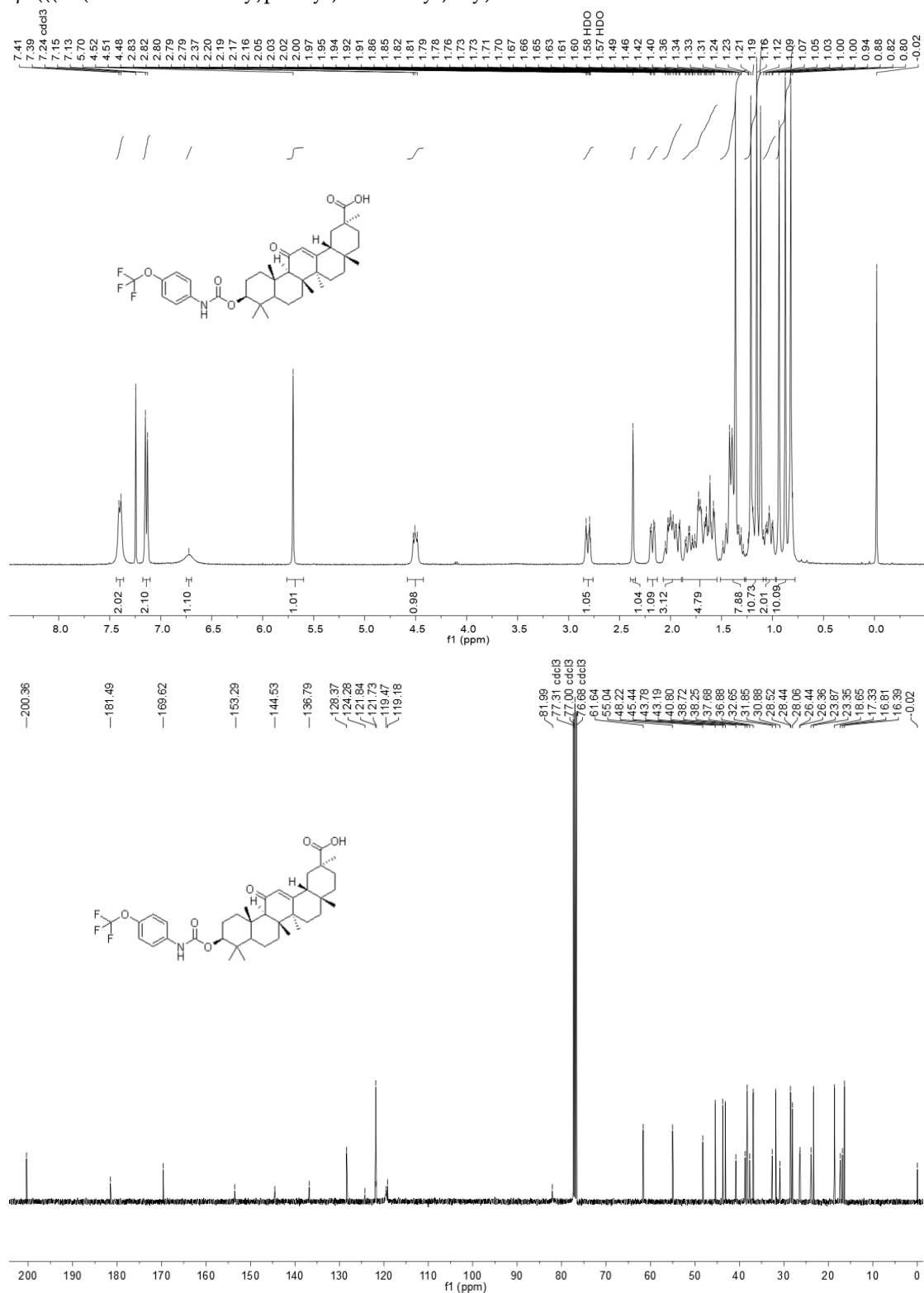
3 β -(((4-bromophenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oic acid **3g**

3 β -(((4-fluorophenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oic acid 3h

3 β -(((4-(trifluoromethyl)phenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oic acid 3i

3 β -(((3,5-bis(trifluoromethyl)phenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oic acid **3k**

3 β -(((4-methoxyphenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oic acid **3m**

3 β -(((4-(trifluoromethoxy)phenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oic acid 3n

¹H NMR (400 MHz, CDCl₃)

Chemical structure of compound 10 is shown above the spectrum.

Peak list (ppm): 7.25, 7.01, 6.68, 6.55, 6.71, 4.51, 4.49, 4.46, 2.82, 2.80, 2.79, 2.37, 2.27, 2.20, 2.19, 2.17, 2.05, 2.03, 2.02, 2.00, 1.98, 1.96, 1.95, 1.92, 1.91, 1.85, 1.83, 1.82, 1.81, 1.79, 1.73, 1.71, 1.70 (H₂O), 1.66 (H₂O), 1.65, 1.62, 1.61, 1.56, 1.57, 1.57, 1.49, 1.46, 1.42, 1.40, 1.40, 1.39, 1.37, 1.34, 1.33, 1.31, 1.22, 1.19, 1.16, 1.12, 1.10, 1.08, 1.04, 1.00, 0.94, 0.88, 0.82, 0.80, 0.02, 0.02.

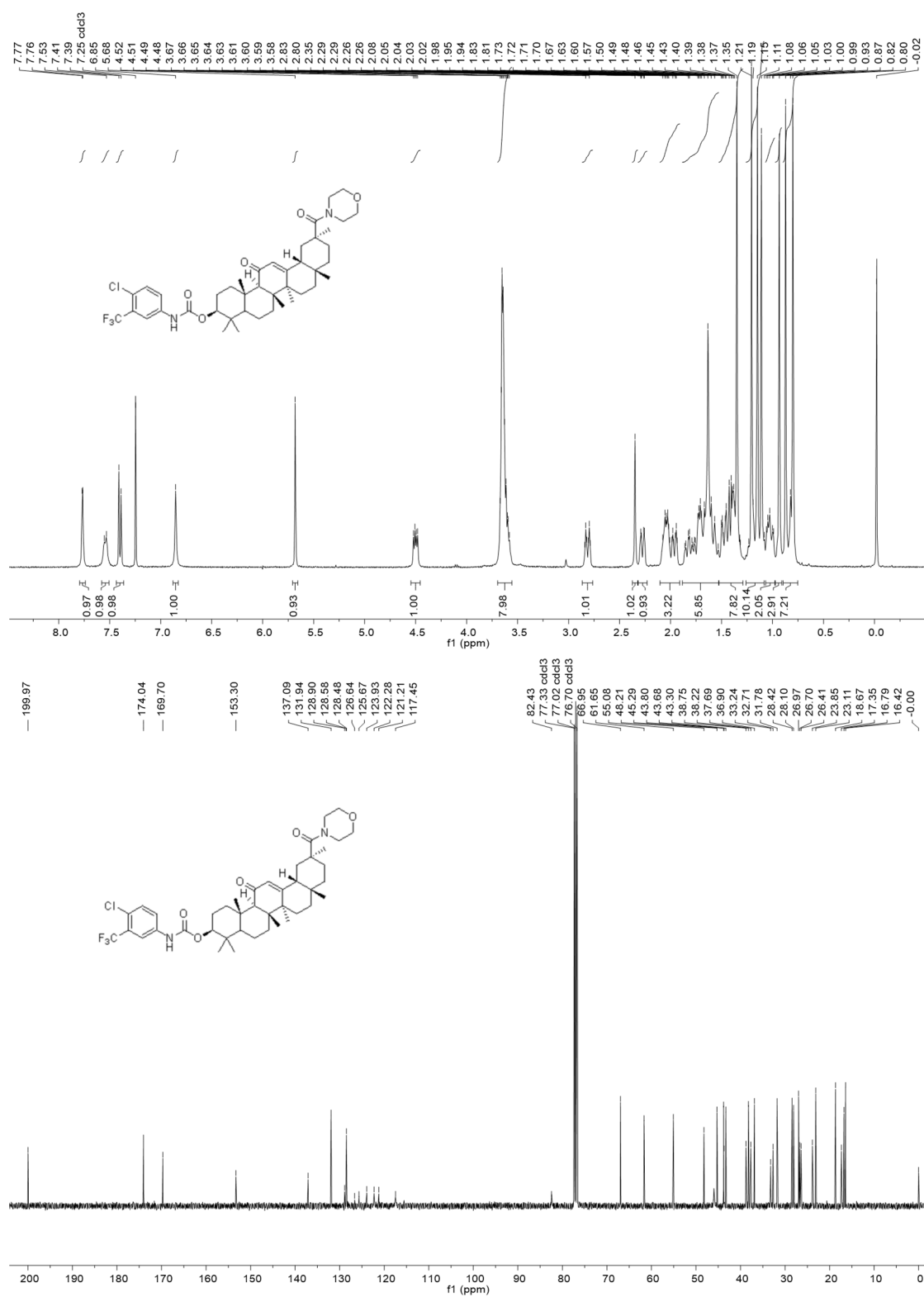
Integration values: 1.98, 0.94, 1.06, 1.02, 1.03, 1.08, 6.05, 1.28, 6.44, 8.40, 3.75, 9.95, 3.23, 3.12, 3.65.

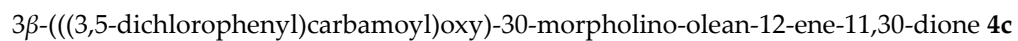
¹³C NMR (100 MHz, CDCl₃)

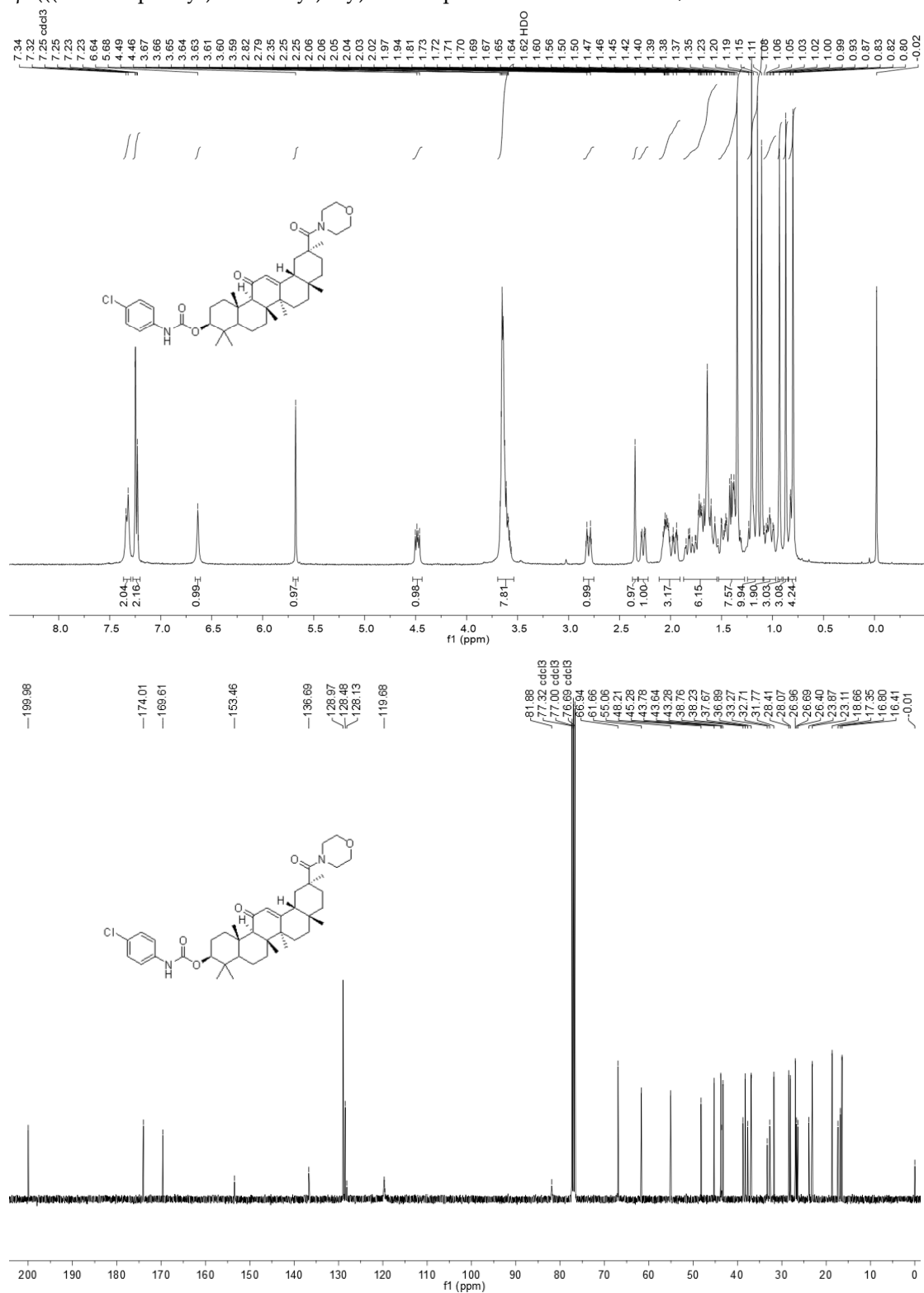
Chemical structure of compound 10 is shown above the spectrum.

Peak list (ppm): 200.38, 181.43, 169.53, 153.61, 138.68, 137.84, 128.40, 124.95, 119.26, 81.69, 77.32 (CDCl₃), 77.00 (CDCl₃), 76.68 (CDCl₃), 61.65, 55.07, 48.22, 45.45, 43.77, 43.19, 40.61, 38.75, 38.44, 37.69, 36.90, 32.67, 31.85, 30.89, 28.53, 28.44, 28.09, 26.44, 26.37, 23.90, 23.37, 21.37, 21.34, 18.66, 17.35, 16.62, 16.39, 0.01.

3 β -(((4-chloro-3-(trifluoromethyl)phenyl)carbamoyl)oxy)-30-morpholino-olean-12-ene-11,30-dione
4b



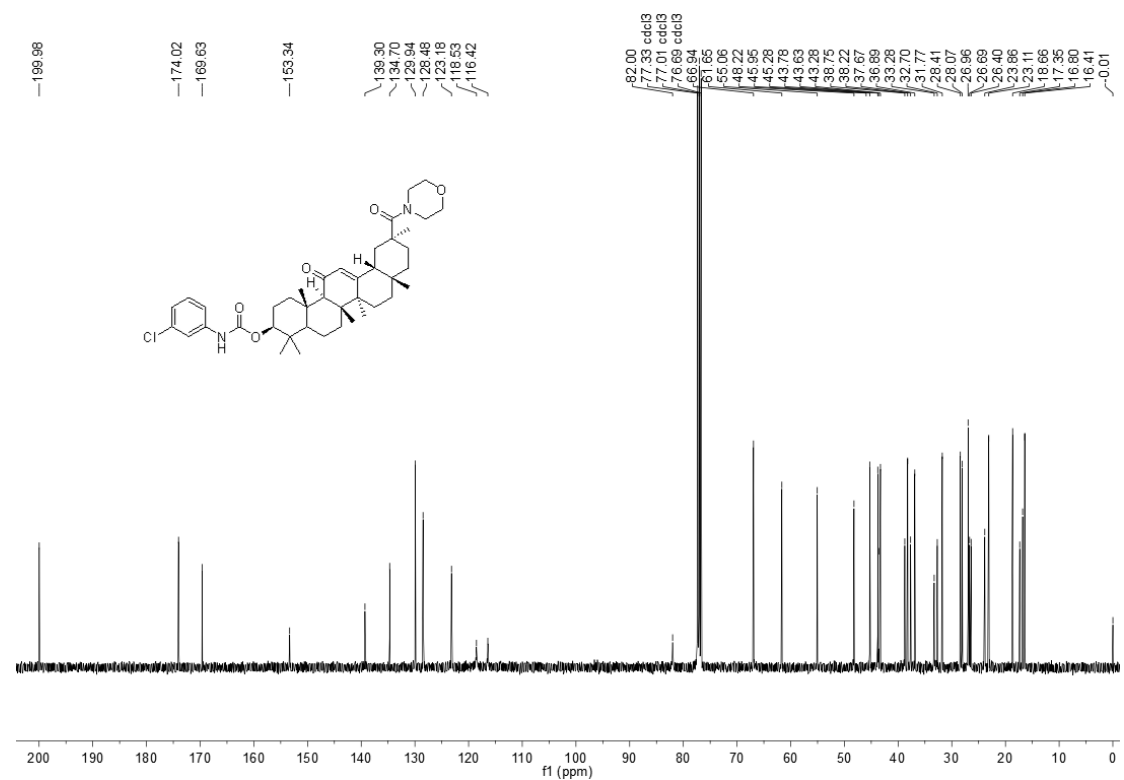


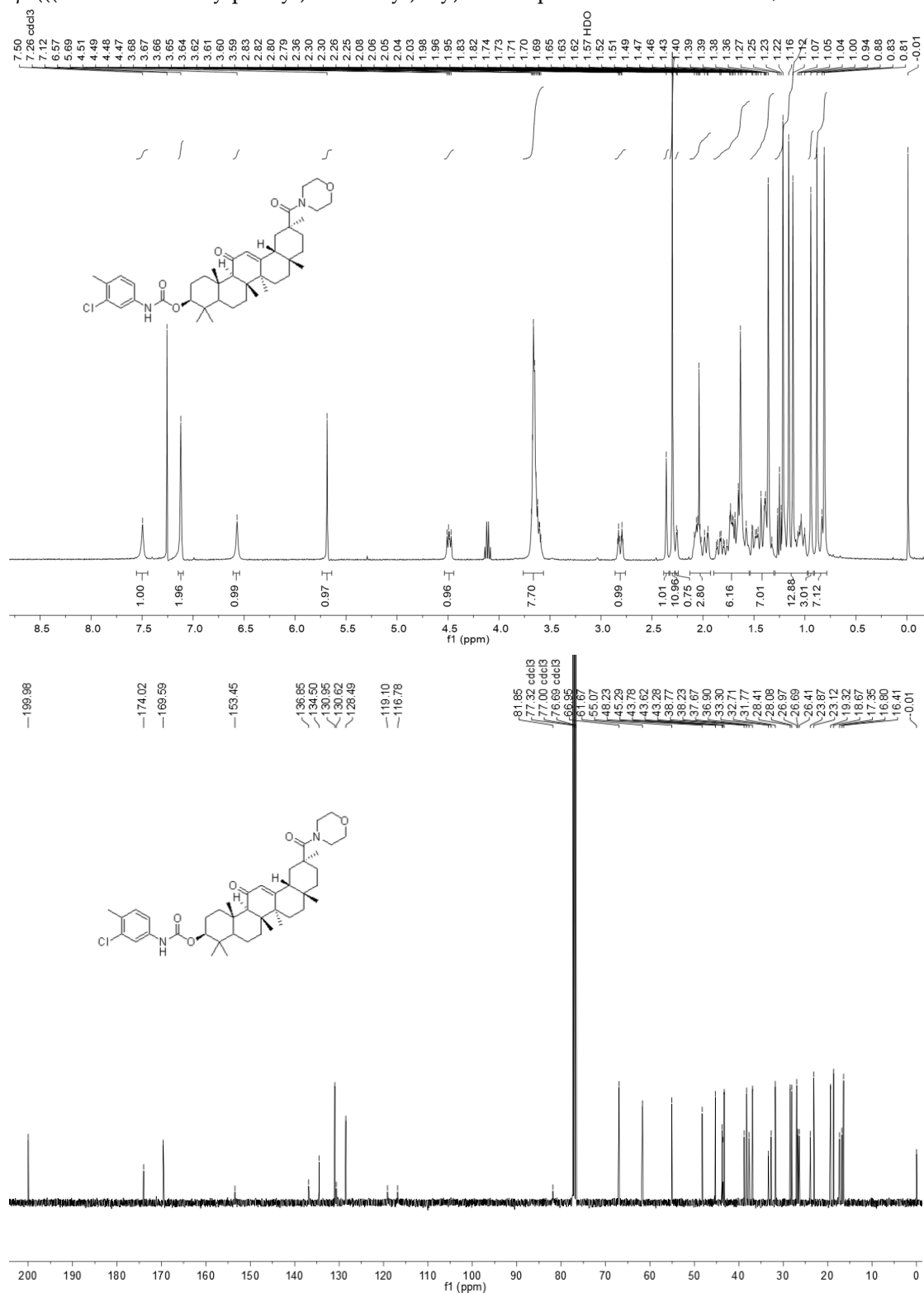
3 β -(((4-chlorophenyl)carbamoyl)oxy)-30-morpholino-olean-12-ene-11,30-dione 4d

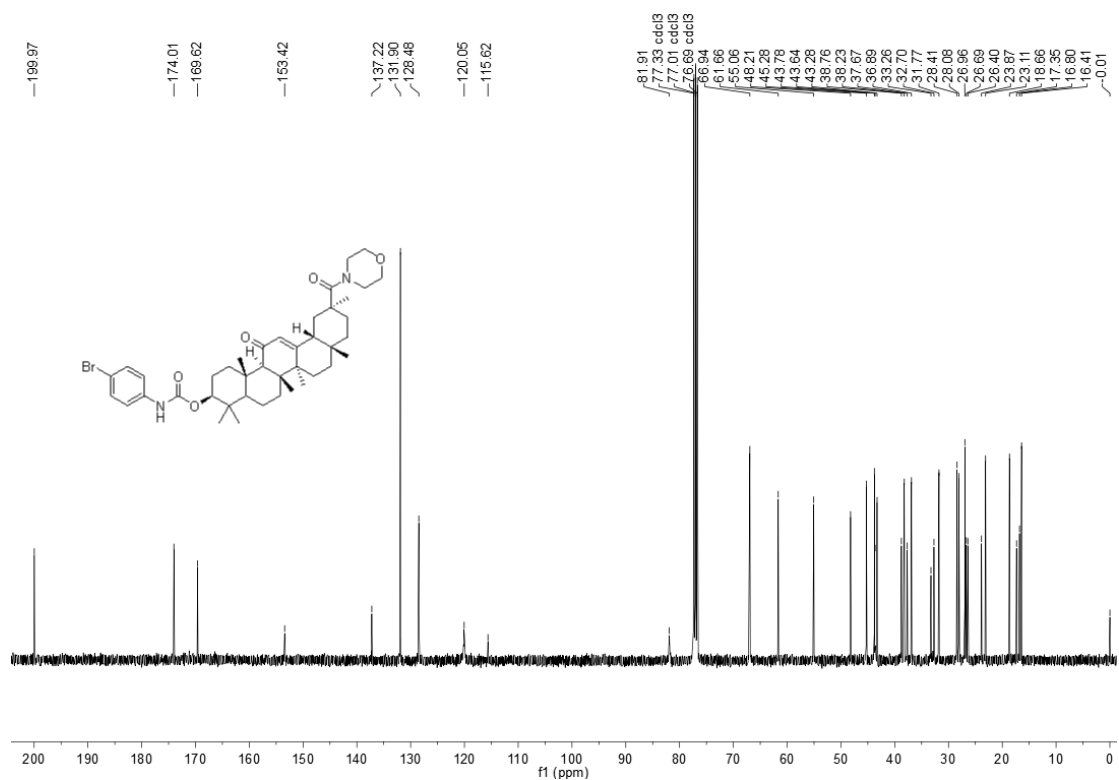
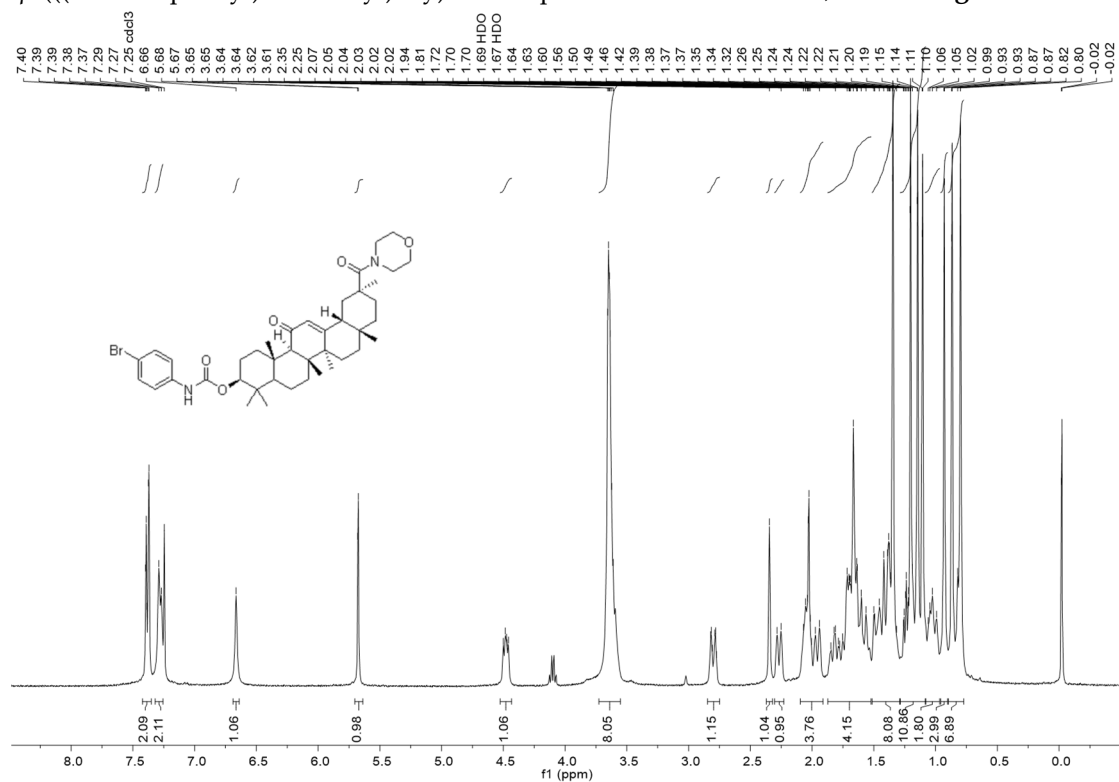
Chemical structure of compound 10 is shown above the spectrum. The structure is a complex steroid derivative with a 4-chlorobenzoyl group at C3, a 4-morpholinyl group at C17, and a 4-methylpent-1-en-1-yl group at C13.

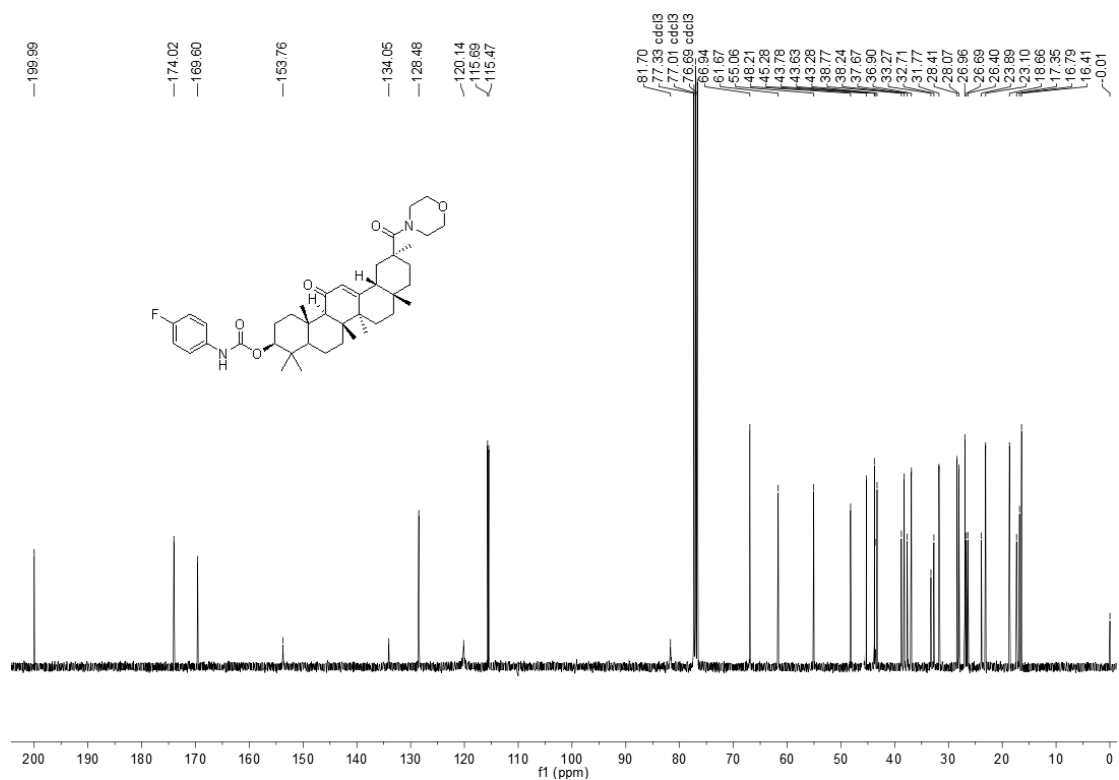
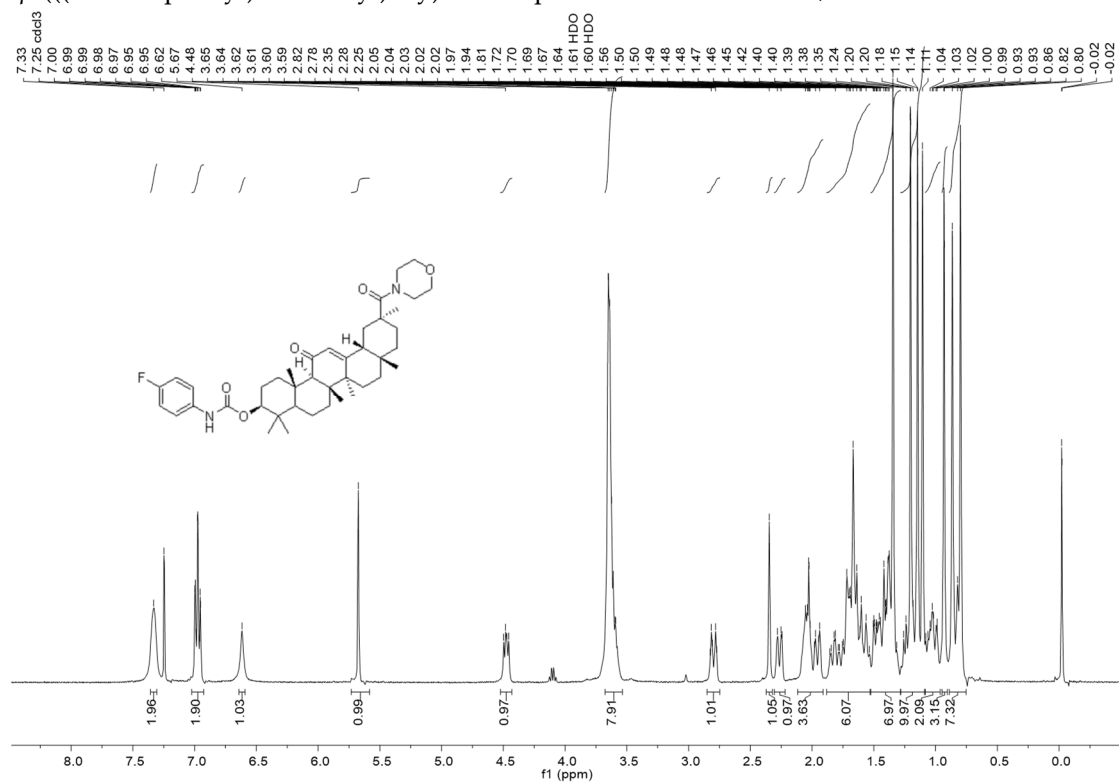
Integration values (from left to right): 1.05, 1.94, 0.99, 1.13, 1.07, 1.13, 7.91, 1.14, 1.13, 1.02, 3.55, 4.06, 8.68, 2.91, 8.07, 3.22, 7.99.

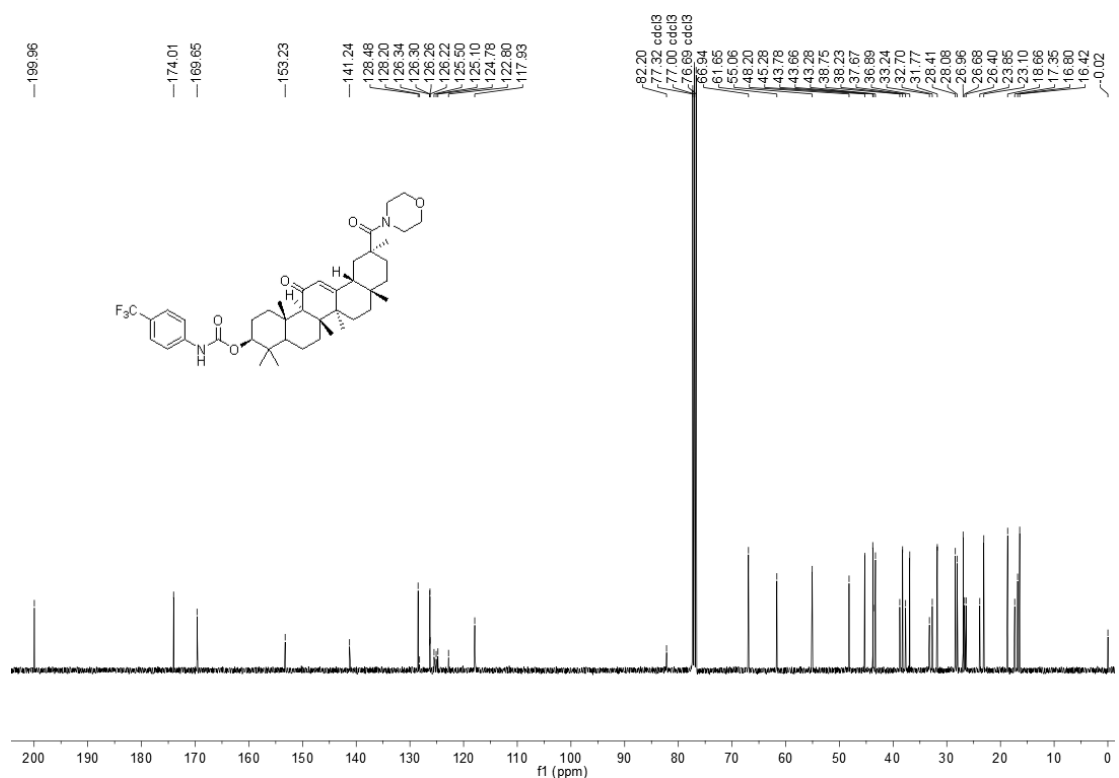
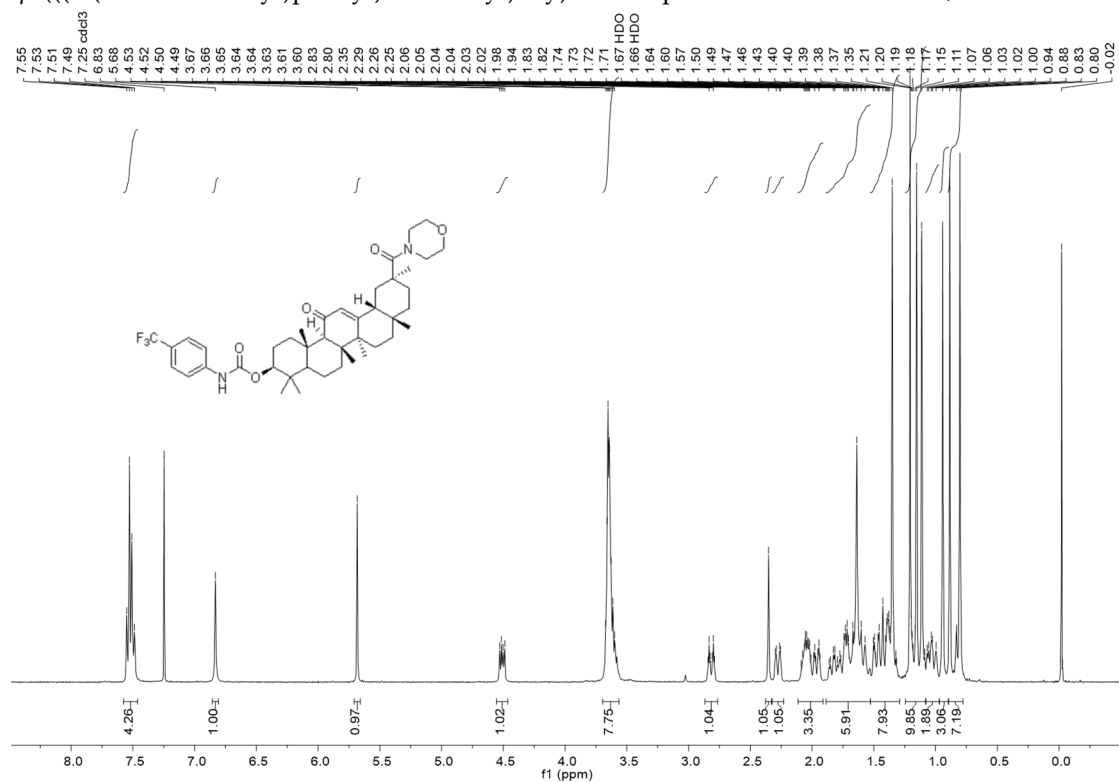
Peak positions (ppm) listed at the top: 7.52, 7.25, 7.20, 7.19, 7.01, 7.00, 6.99, 6.70, 5.68, 4.49, 3.67, 3.66, 3.65, 3.64, 3.62, 3.61, 2.82, 2.79, 2.35, 2.28, 2.25, 2.07, 2.06, 2.04, 2.02, 2.02, 1.97, 1.95, 1.94, 1.82, 1.81, 1.76, 1.75, 1.73, 1.72, 1.70, 1.67, 1.65, 1.64, 1.62, 1.60, 1.57, 1.50, 1.50, 1.46, 1.46, 1.45, 1.42, 1.40, 1.39, 1.38, 1.35, 1.31, 1.31, 1.20, 1.15, 1.11, 1.08, 1.06, 1.05, 1.03, 1.00, 0.99, 0.93, 0.87, 0.83, 0.82, 0.80, -0.02, -0.02.

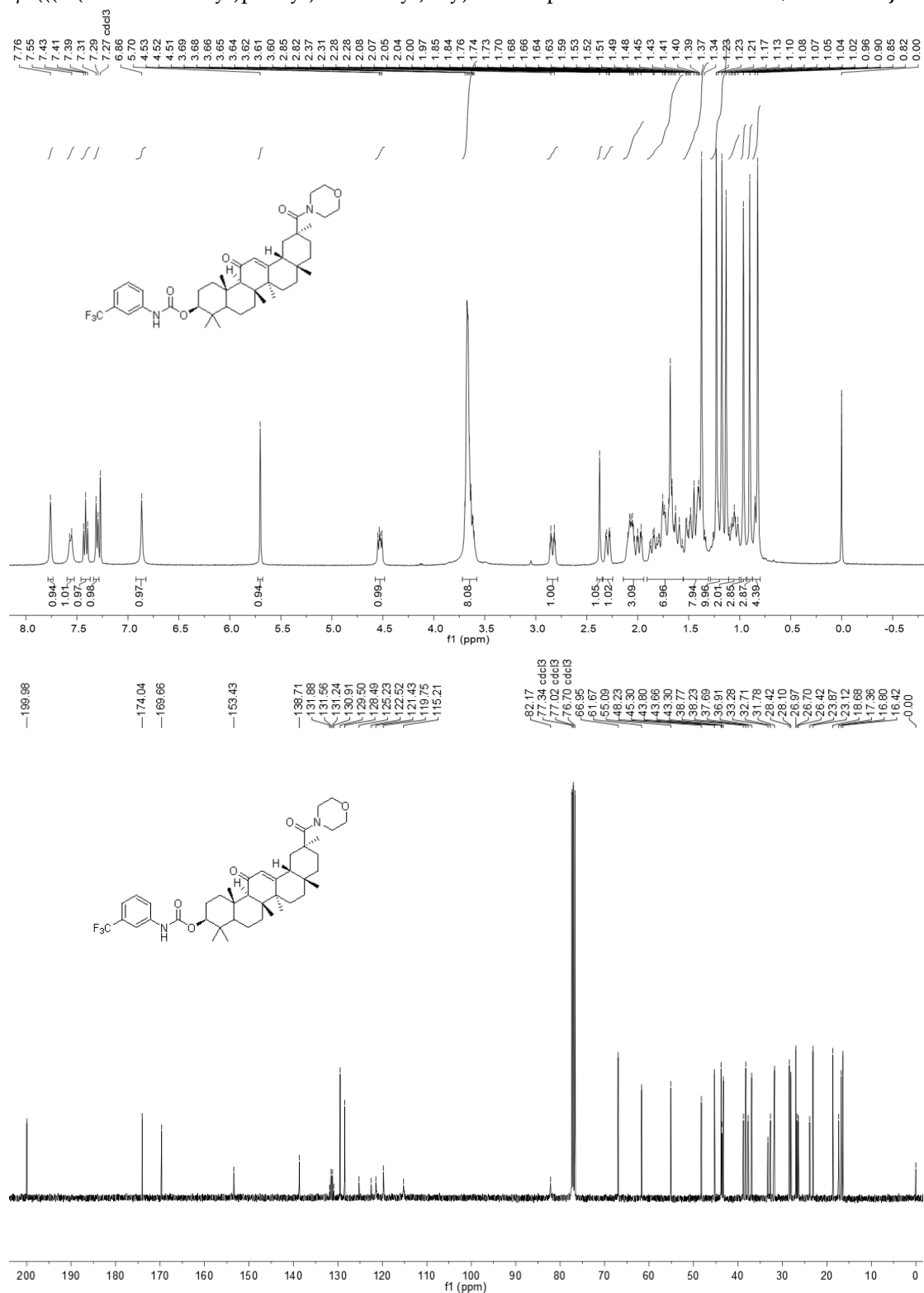


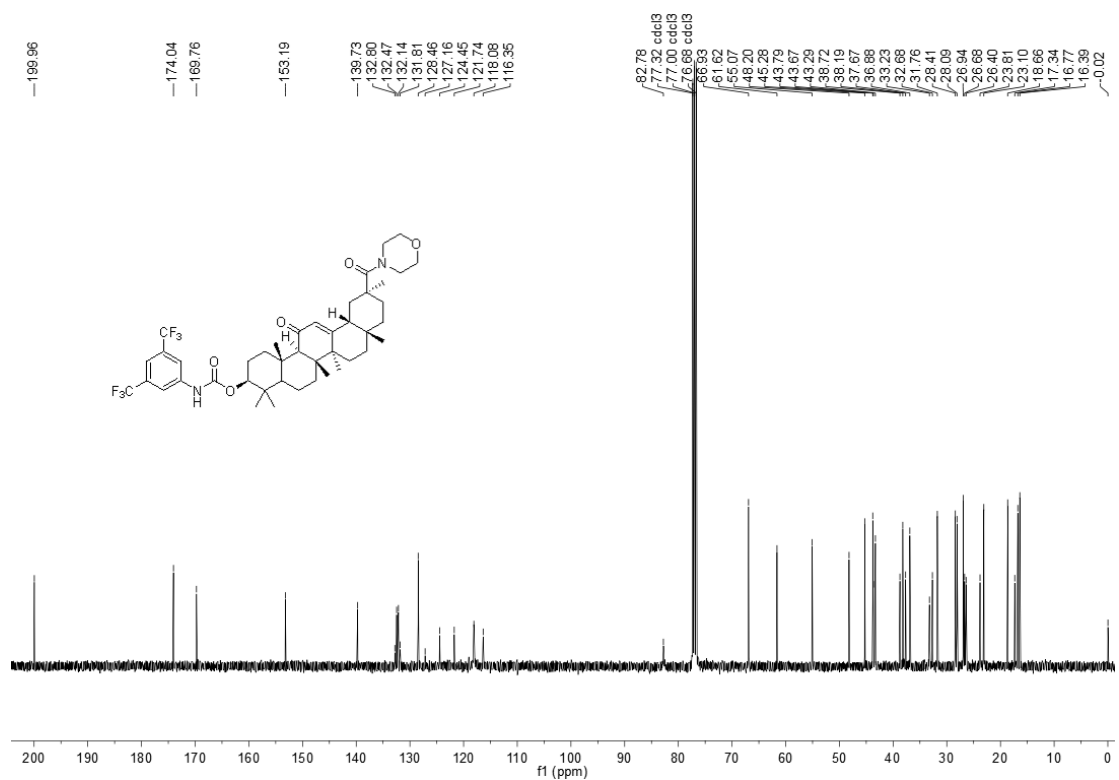
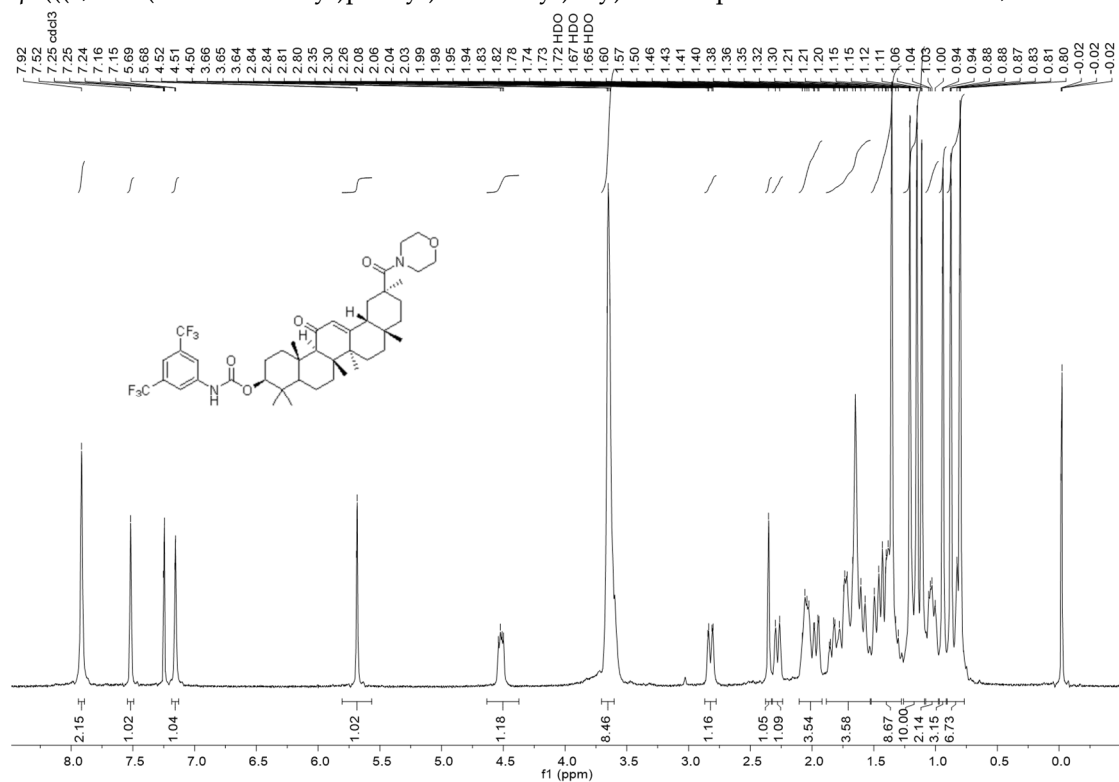
3 β -(((3-chloro-4-methylphenyl)carbamoyl)oxy)-30-morpholino-olean-12-ene-11,30-dione **4f**

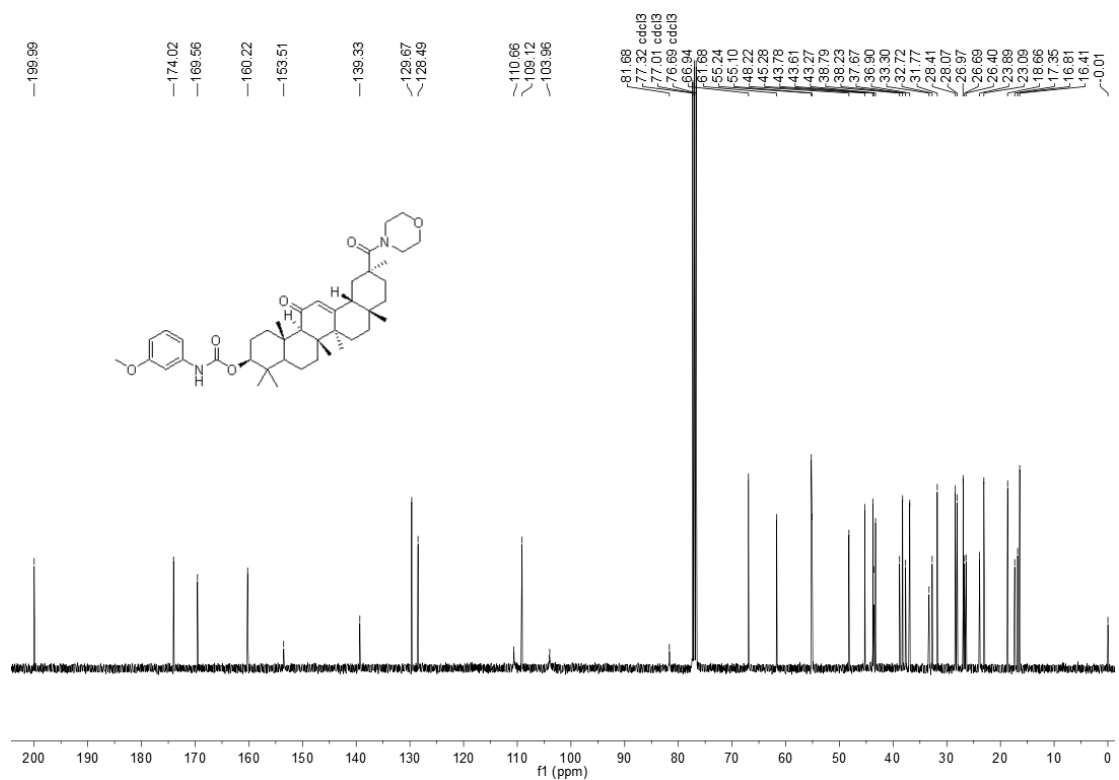
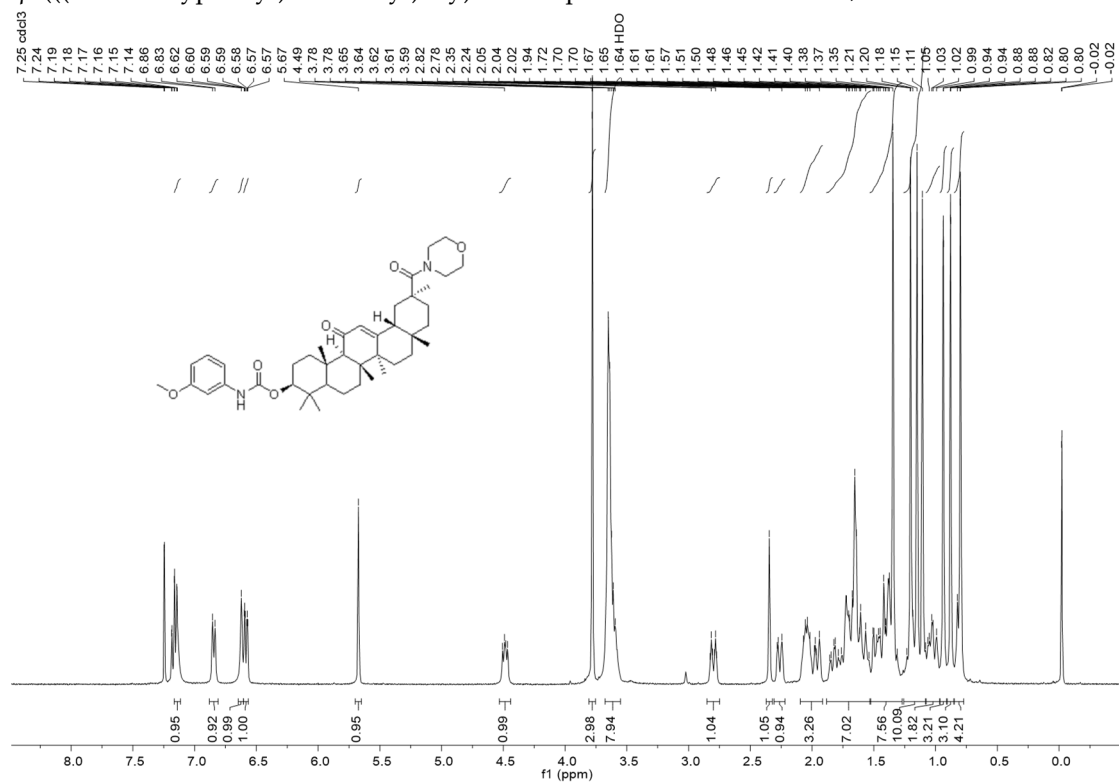
3 β -(((4-bromophenyl)carbamoyl)oxy)-30-morpholino-olean-12-ene-11,30-dione 4g

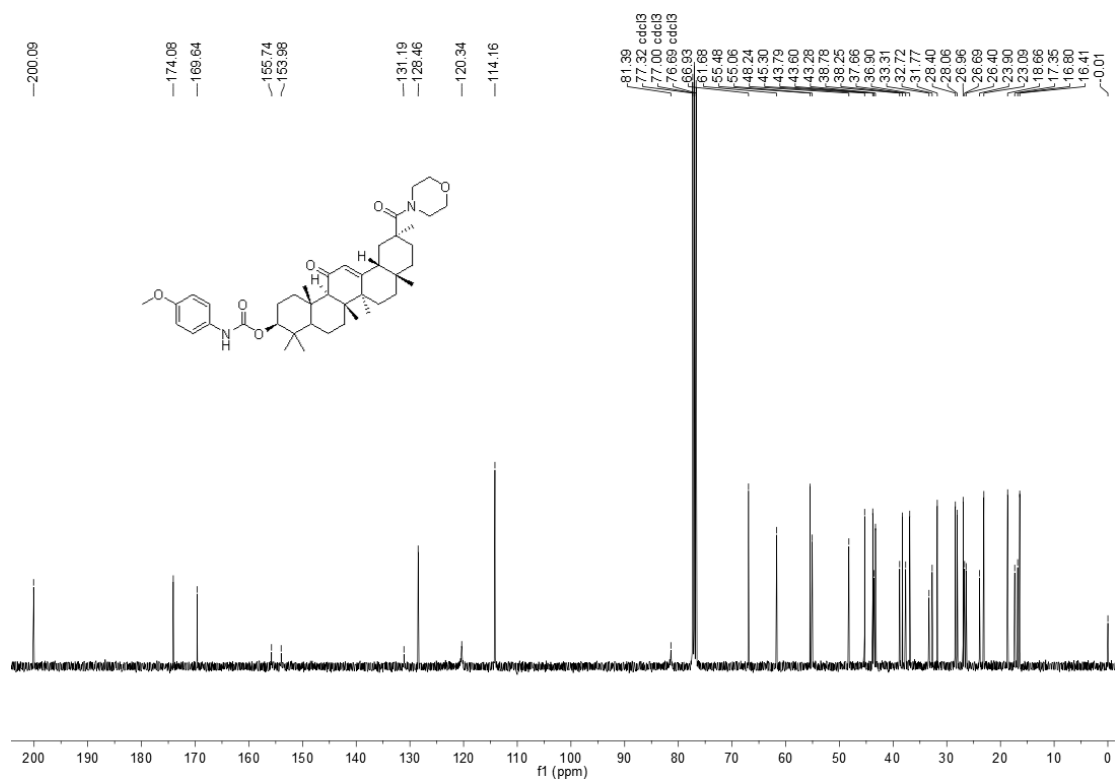
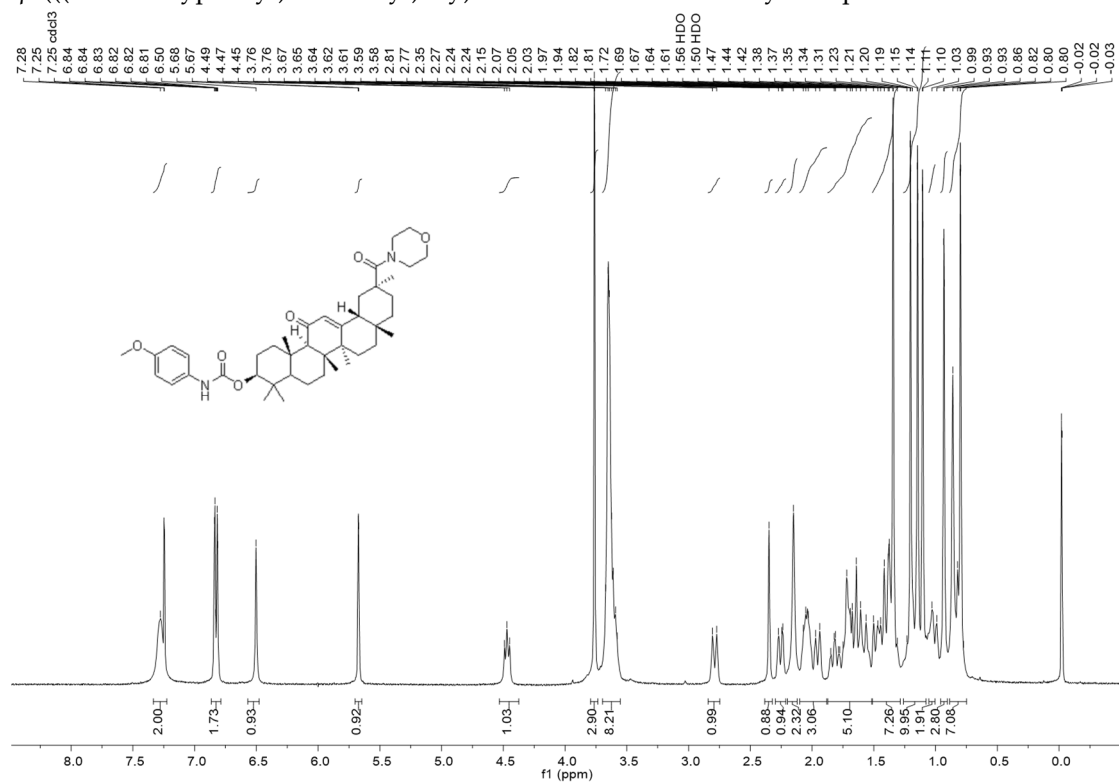
3 β -(((4-fluorophenyl)carbamoyl)oxy)-30-morpholino-olean-12-ene-11,30-dione 4h

3 β -(((4-(trifluoromethyl)phenyl)carbamoyl)oxy)-30-morpholino-olean-12-ene-11,30-dione 4i

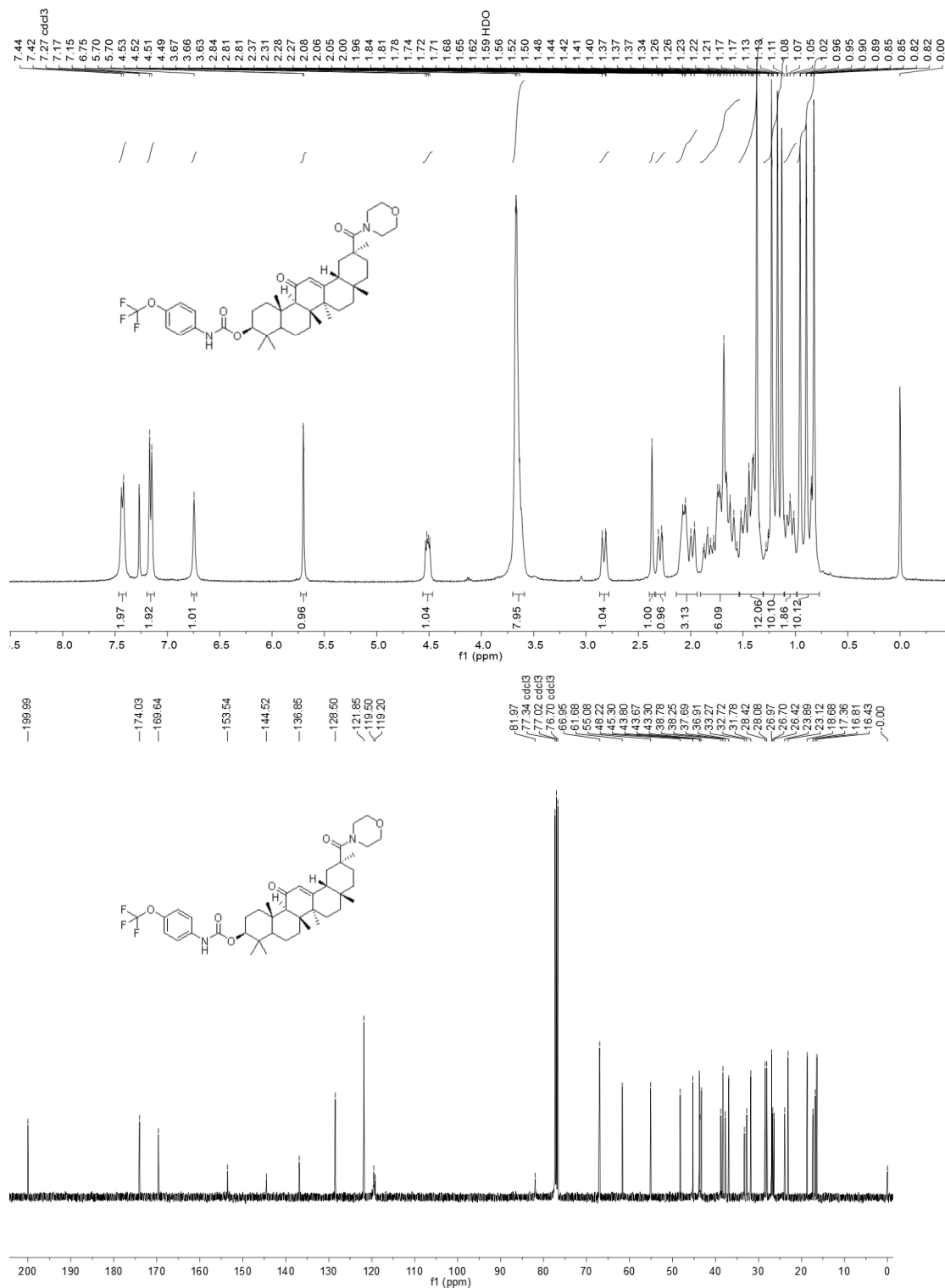
3 β -(((3-(trifluoromethyl)phenyl)carbamoyl)oxy)-30-morpholino-olean-12-ene-11,30-dione 4j

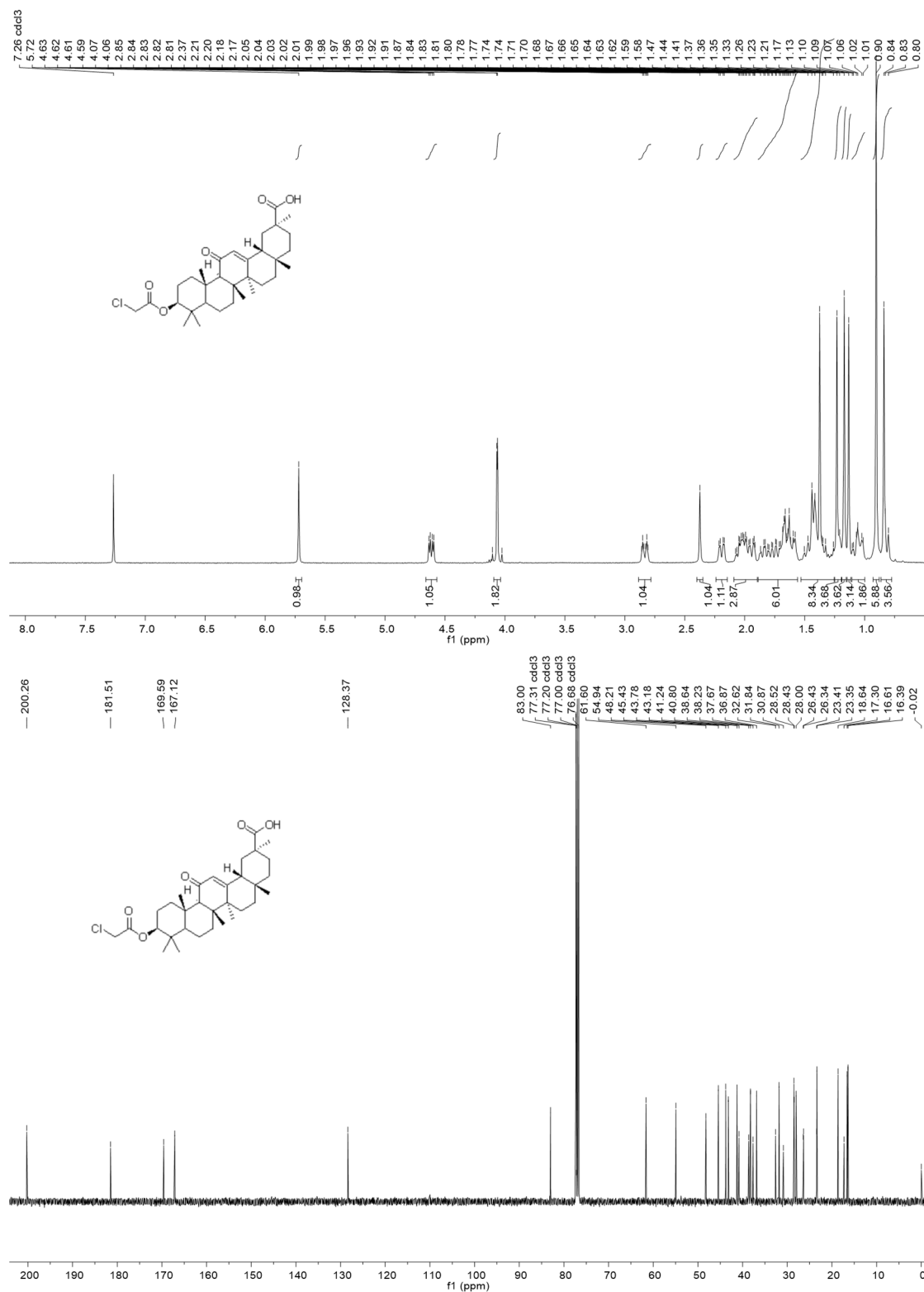
3 β -(((3,5-bis(trifluoromethyl)phenyl)carbamoyl)oxy)-30-morpholino-olean-12-ene-11,30-dione **4k**

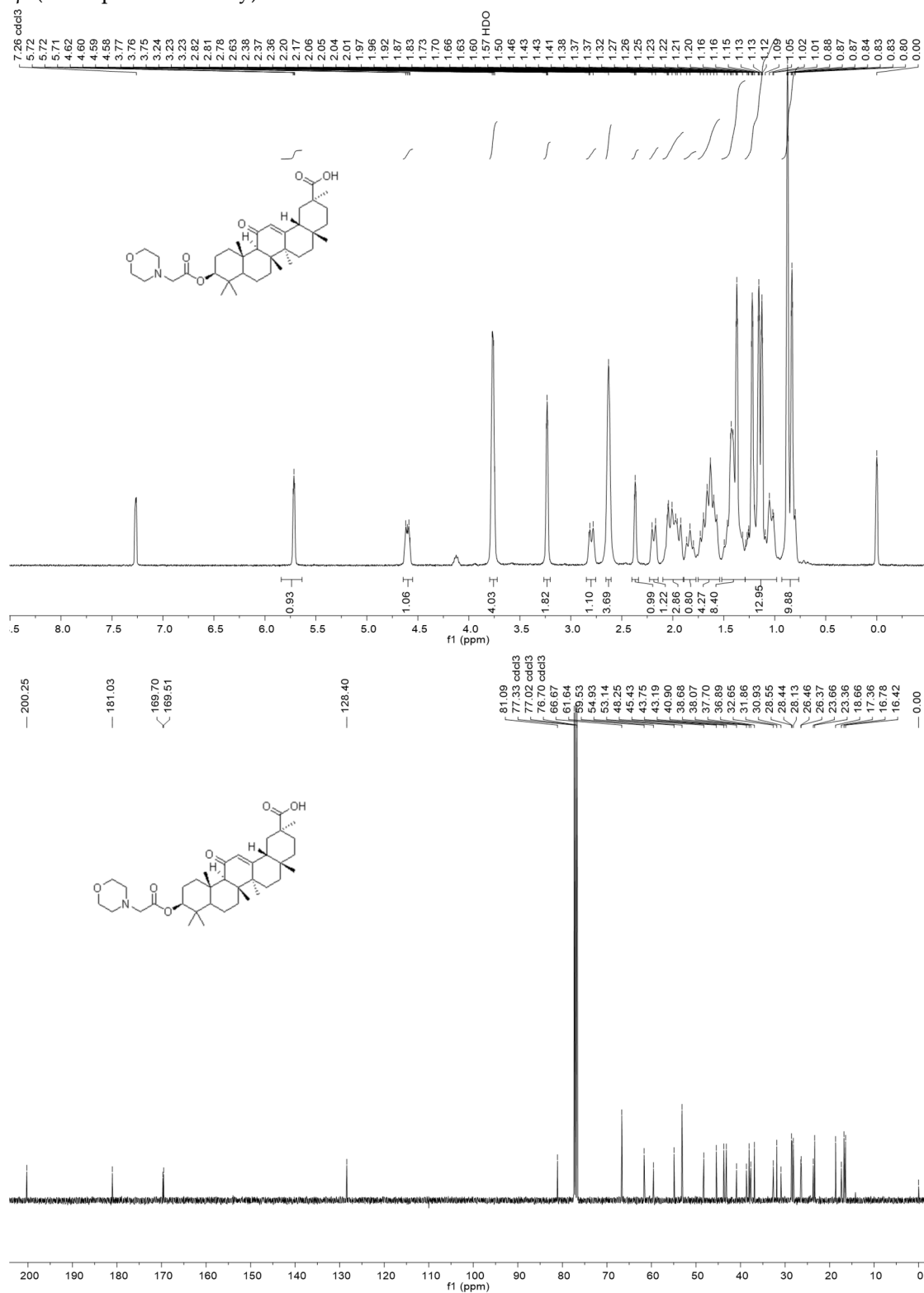
3 β -(((3-methoxyphenyl)carbamoyl)oxy)-30-morpholino-olean-12-ene-11,30-dione 41

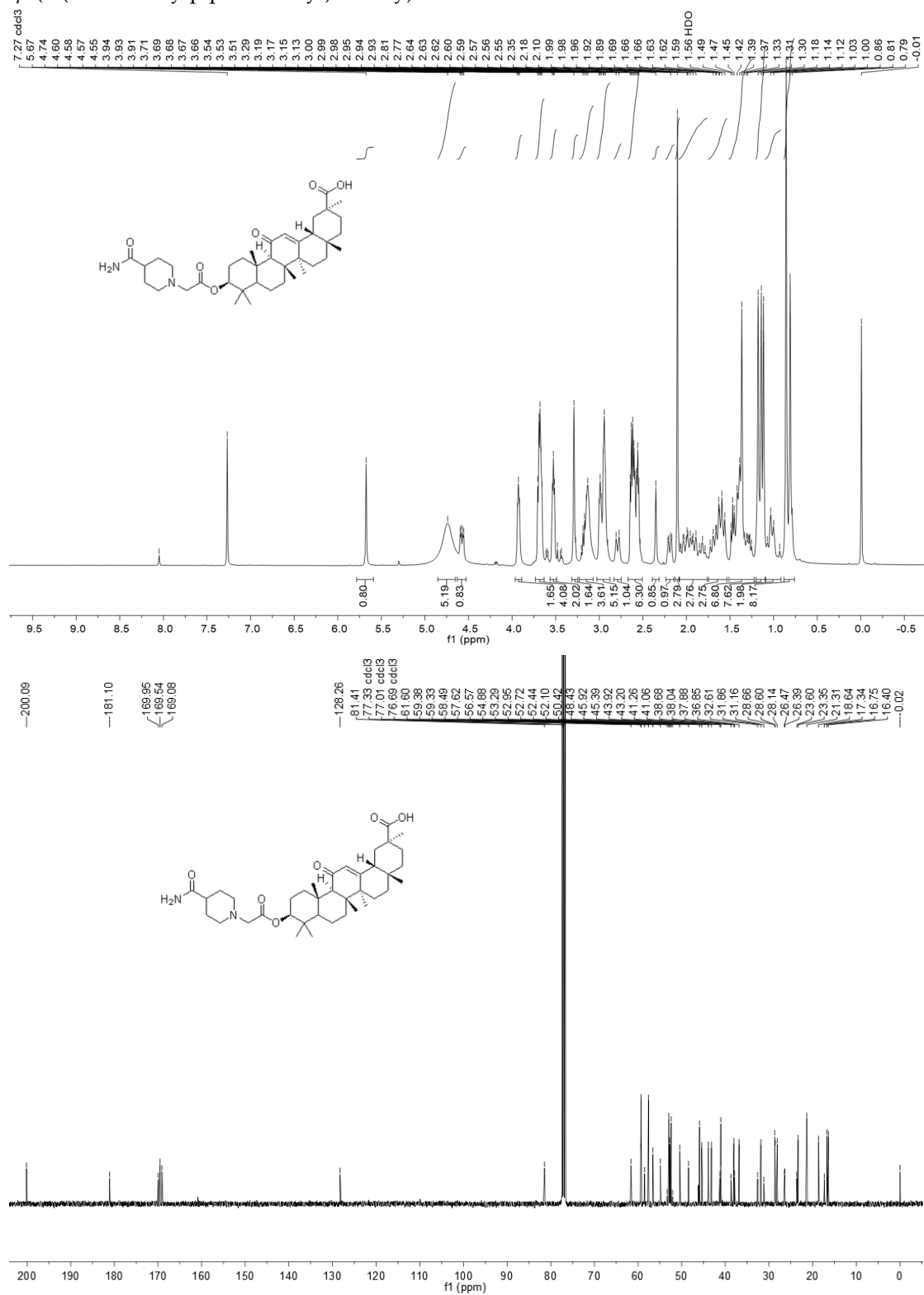
3 β -(((4-methoxyphenyl)carbamoyl)oxy)-11-oxo-olean-12-en-30-oyl morpholine 4m

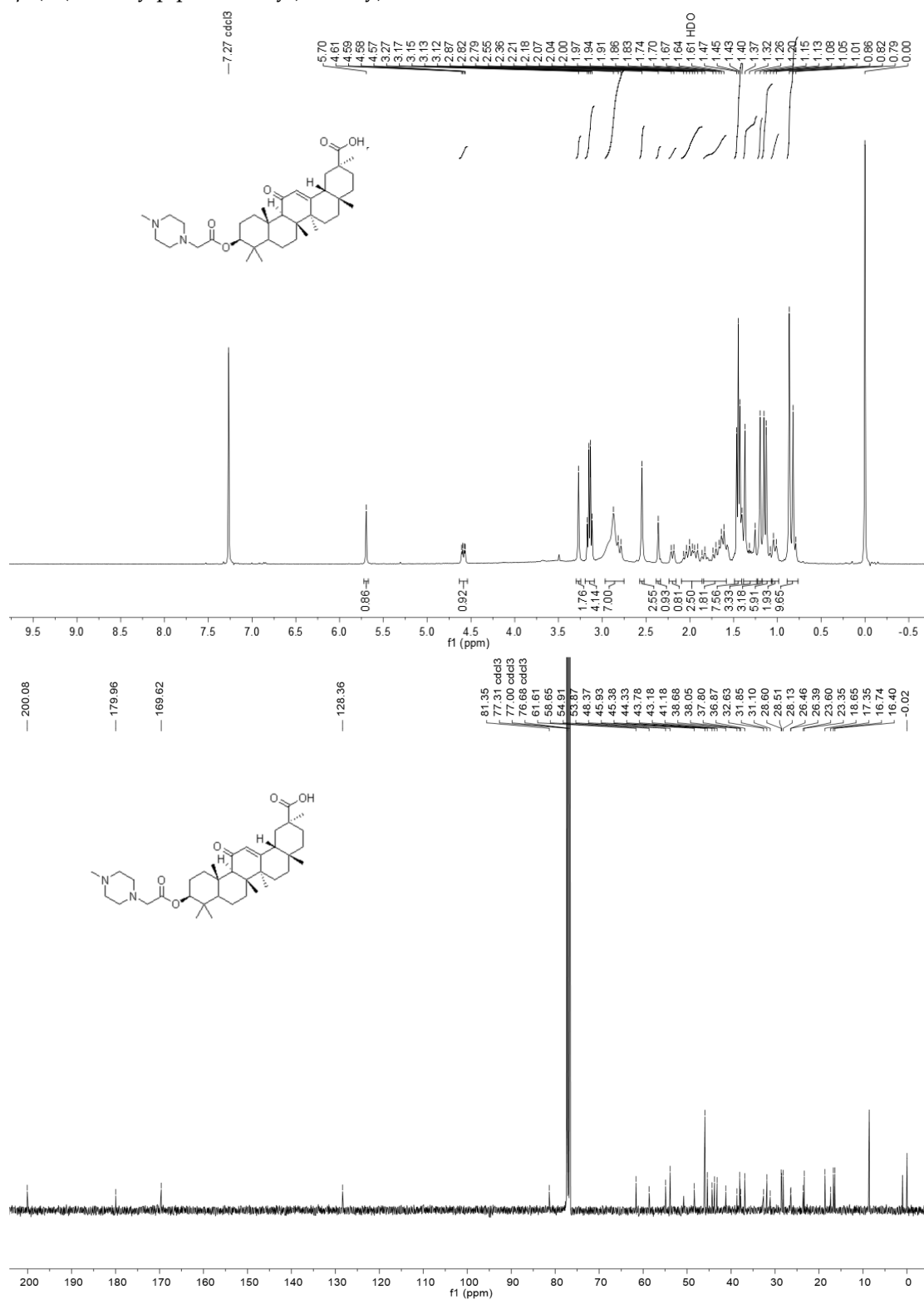
4n

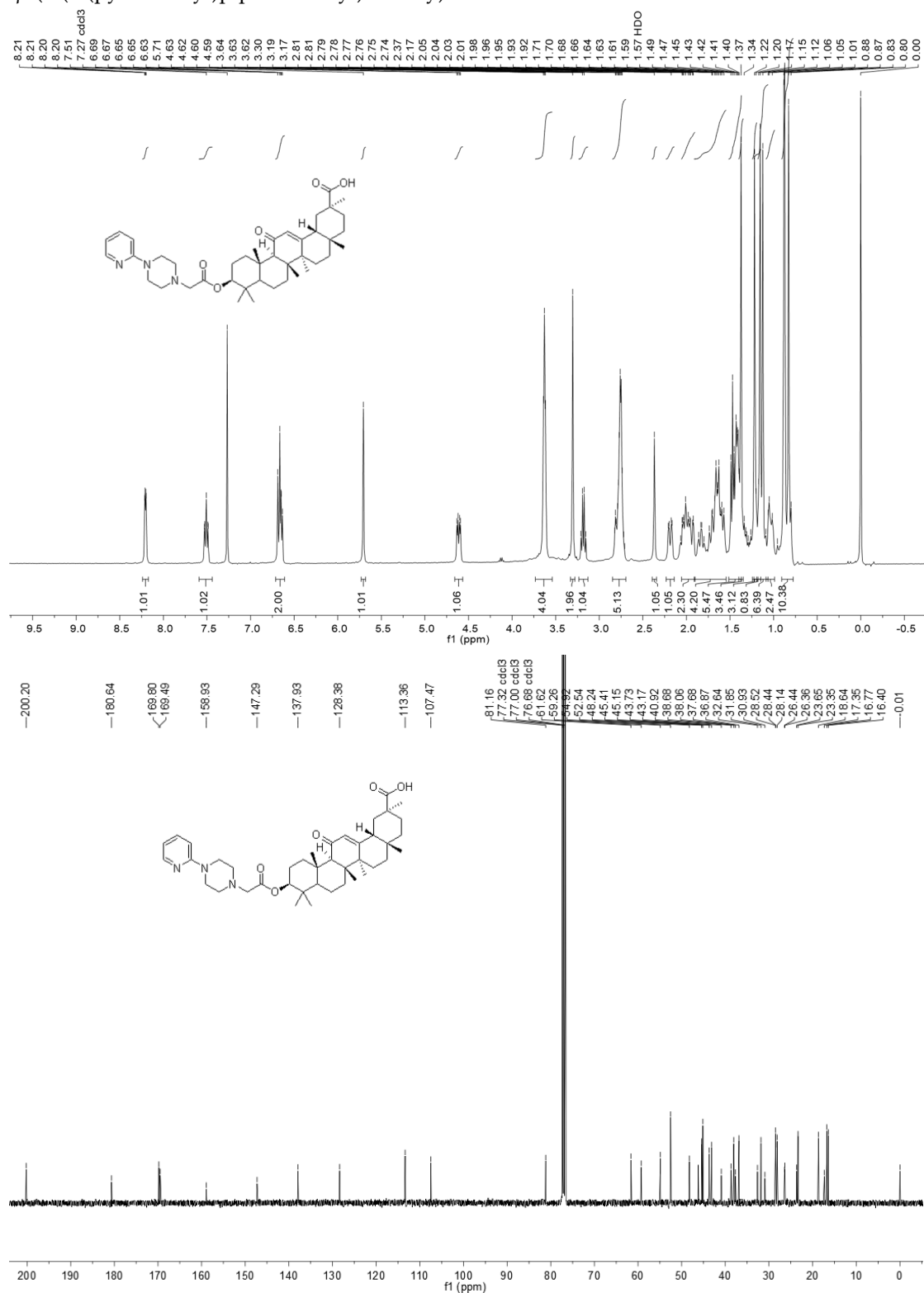


3 β -(2-chloroacetyl)-11-oxo-olean-12-en-30-oic acid 5

3 β -(2-morpholinoacetoxy)-11-oxo-olean-12-en-30-oic acid 6a

3 β -(2-(4-carbamoylpiperidin-1-yl)acetoxy)-11-oxo-olean-12-en-30-oic acid 6b

3 β -(2-(4-methylpiperazin-1-yl)acetoxy)-11-oxo-olean-12-en-30-oic acid 6c

3 β -(2-(4-(pyridin-2-yl)piperazin-1-yl)acetoxy)-11-oxo-olean-12-en-30-oic acid 6d

¹H NMR spectrum (top): The x-axis represents the chemical shift in ppm, ranging from 0.00 to 13.08. The spectrum shows several peaks, with integrations provided below the baseline. The integrations are: 0.31, 2.51, 2.32, 0.90, 1.19, 0.31, 1.13, 0.28, 0.30, 0.03, 0.64, 1.25, 1.23, 1.25, 1.27, 1.10, 0.63, 0.56, 0.66, 0.04, 10.67, and 0.81. The chemical structure of compound 10 is shown above the spectrum.

¹³C NMR spectrum (bottom): The x-axis represents the chemical shift in ppm, ranging from 0 to 200.29. The spectrum shows several peaks, with integrations provided below the baseline. The integrations are: 0.01, 16.13, 16.33, 16.61, 17.27, 18.63, 19.56, 23.47, 26.34, 27.91, 28.01, 28.41, 28.51, 30.87, 31.83, 32.60, 36.80, 36.83, 37.66, 38.04, 38.11, 38.17, 38.23, 40.79, 41.27, 43.16, 43.75, 45.39, 45.41, 47.95, 48.00, 54.84, 54.91, 76.68, 77.00, 77.31, 104.33, 128.38, 128.55, 128.60, 128.87, 128.90, 129.01, 130.53, 130.65, 130.89, 132.65, 132.79, 133.20, 134.70, 169.87, 170.87, 172.11, 173.18, 181.25, 200.23, and 200.29. The chemical structure of compound 10 is shown above the spectrum.

3 β -(2-(4-fluorophenyl)acetoxy)-11-oxo-olean-12-en-30-oic acid 7b