



(43) International Publication Date
19 June 2014 (19.06.2014)

(10) International Publication Number
WO 2014/089680 A1

(51) International Patent Classification:

C07C 311/41 (2006.01) *A01P 1/00* (2006.01)
A01N 35/04 (2006.01) *C07C 303/40* (2006.01)
A01N 41/06 (2006.01) *C09D 5/14* (2006.01)

(21) International Application Number:

PCT/CA2013/001026

(22) International Filing Date:

6 December 2013 (06.12.2013)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/735,890 11 December 2012 (11.12.2012) US

(71) Applicant: **NANO SAFE COATINGS INCORPORATED (A FLORIDA CORPORATION 3 P14000024914)** [US/US]; 1445 Jupiter Park Drive Suite 11, JUPITER, Florida (US).

(72) Inventors: **POROSA, Lukasz**; 108 Bar Harbour Square, Scarborough, Ontario M1C 5E9 (CA). **MOCELLA, Amanda**; 1 Cynthia Crescent, Brampton, Ontario L6P 0S9 (CA). **WOLFAARDT, Gideon**; 1987 Pitagora Court, Mississauga, Ontario L5K 2M4 (CA). **FOUCHER, Daniel**; 768 Shaw Street, Toronto, Ontario M6G 3M1 (CA).

(74) Agent: **SARKIS, Marcelo**; c/o Prima IP, 1948 Heights Road, Dunsford, Ontario K0M 1L0 (CA).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,

BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- of inventorship (Rule 4.17(iv))

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(54) Title: UV CURED BENZOPHENONE TERMINATED QUATERNARY AMMONIUM ANTIMICROBIALS FOR SURFACES

(57) Abstract: The invention relates to benzophenone-terminated quaternary ammonium compounds, processes for preparing benzophenone-terminated quaternary ammonium compounds, environmentally friendly antimicrobial formulations of said quaternary ammonium compounds and their use as durable antimicrobial surface coatings for surfaces.



WO 2014/089680 A1

TITLE OF THE INVENTION

UV CURED BENZOPHENONE TERMINATED QUATERNARY AMMONIUM
ANTIMICROBIALS FOR SURFACES

BACKGROUND OF THE INVENTION

5 One of the main challenges faced by the medical industry is infection control and reducing the spread of microorganisms such as fungi, bacteria and viruses. Several microorganisms have the ability to attach to surfaces, for example porous surfaces and to proliferate forming colonies called biofilms. The use of antibiotics to treat infectious diseases caused by biofilms has become one of the biggest milestones in the history of medicine. However, after widespread use of these
10 antibiotics, and other chemicals used for the purpose of disinfection, several strains of microorganisms (e.g. bacteria), have developed resistance to them. For the growing number of microorganisms with clinical importance (one example is pathogens), there is either no effective therapy or only one or two antibiotics that are hard to administer, expensive and/or have increasingly toxic side effects. Furthermore, when growing on surfaces as biofilms,
15 microorganisms are generally more persistent, and it is now acknowledged that the majority of infections involve biofilms. Biofilms also pose a notable threat of contamination in food processing facilities and spoilage of other products susceptible to microbial attack.

One approach in preventing biofilm formation, and thus the potential to cause spoilage or infection is the use of antimicrobial coatings on surfaces that are not susceptible to the
20 development of resistance by the target microorganisms. These coatings have bacteriostatic (inhibiting) or bactericidal (killing) properties and thus afford a preventative strategy compared to disinfection, which is reactive, often after some damage or infection has occurred. In contrast to conventional antibiotics, bacteria do not readily develop resistance to antimicrobial coatings that inhibit microorganisms in a mechanical, as opposed to a chemical fashion. This important
25 distinction, and the related alarming rate at which the number of effective antibiotics decline, is a primary reason for the rapidly growing interest in these antimicrobial coatings in recent years.

Quaternary ammonium compounds ("QACs") have gained recognition as surfactants with antimicrobial activity. QAC's consist of an irreversibly positively charged quaternary nitrogen atom where often at least one substituent is a long aliphatic chain. The synthesis of these

compounds involves the quaternization of a tertiary amine following the Menshutkin reaction (i.e. a reaction of a tertiary amine with an alkyl halide).

Without being bound by any particular theory, the mode of action of QAC's in killing bacteria is multi-stepped. First, the QAC is adsorbed into the bacterial cell wall. Second, the long hydrophobic alkyl chain of the QAC interacts with the phospholipid bilayer making up the bacteria cell membrane and alters its fluidity and structure which adds stress to the cell wall. Finally, this added stress on the cell wall upsets the bilayer, expelling cytoplasmic material and ultimately caused cell death.

Polymeric antimicrobial coatings have the advantage of being chemically stable, non-toxic and non-volatile making them more efficient, selective and environmentally safe compared to traditional antimicrobial coatings which depend on leaching of the chemical from the substrate. It has become common practice over the past 35 years to incorporate antimicrobial coatings in thermoplastic polymer solutions. Furthermore, solvents commonly used to incorporate the antimicrobials in the thermoplastic polymers include tetrahydrofuran ("THF") and dimethyl formamide ("DMF"). These solvents have the ability of attacking polymeric surfaces including those of polyurethane, polyisoprene, butyl rubber, polycarbonate, etc. This often distorts the surface, altering the integrity of the material at the surface, which in turn may ultimately enhance attachment by microbial cells resistant to the antimicrobial ingredient, and other microbes later when the concentration of the antimicrobial ingredient drops below the threshold required for inhibition. Also, once the prior art coatings are applied to the surfaces, drying times on the order of almost 24 hours are required to completely evaporate the solvent from the surface.

Development of antimicrobial coatings is limited by the availability of suitable antimicrobials that may be incorporated into thermoplastic polymers. Silver is one common agent used both in elemental and salt form. However, the technology to incorporate silver into polymeric materials is tedious, expensive and not environmentally friendly. Moreover, the performance of silver is weak taking up to eight hours to reach efficacious levels against microbes and discolouration is common in silver treated materials. Thus there exists a long-felt need for a composition to eradicate microbes and prevent biofilm formation that is low-cost, durable and efficacious without these deleterious side effects.

In an effort to increase the stability of antimicrobial films on polymer surfaces, irreversible covalent attachment of the antimicrobial is desirable. Methods for grafting antimicrobials to polymer surfaces have been developed usually using functionalized surfaces and/or antimicrobial molecules. However, some of these functionalizing techniques are expensive and require
5 extensive synthetic methodologies. Recently, light-activated systems involving photoreactive groups have been reported. Benzophenone is a popular photoreactive group and is commonly used in fragrances and cosmetics. It now has been found that incorporation of a benzophenone group into a QAC introduces the possibility of permanently binding a QAC to a polymeric surface.

- 10 U.S. Patent No. 3,697,402 teaches photocurable thiol-capped polyalkene polymers which when applied to a surface and exposed to ultra-violet ("UV") light forms a solid product for use, among other things, as a sealant, coating, and adhesive.

U.S. Patent No. 4,948,819 teaches water-soluble, quaternary ammonium methacrylate coatings having a photo-active linking molecule, with uses as an UV-cured lacquer coating.

- 15 U.S. Patent 5,714,360 teaches a chemical cross-linking agent X-Y-X where X is a photoreactive radical and Y is a nitrogen containing group used to attach chemical compounds to other compounds or to substrates.

- J.C. Tiller et al., (Proceedings of the National Academy of Sciences, 2001, 98, 5981) teaches a surface coating composition of polyvinylpyrrolidone ("PVP")-QAC in which the surface is a pre-
20 functionalized glass surface and PVP-QAC is bonded to the functional groups. The surface needs to be pre-functionalized with an acyl-chloride compound in order for the coating to bond to the glass surface.

- U.S. Patent Application Publication No. 2006/0147413 teaches a water-soluble, photo-activatable polymer bonded through a reactive group biomaterial used to deploy molecular
25 therapeutics such as proteins, genes, vectors and cells.

U.S. Patent Application Publication No. 2007/0231291 teaches a polymeric QAC-polyethyleneimine used to protect surfaces against bacteria and fungi attack.

International Patent Application Publication WO2010/065421 teaches UV-curable coatings containing rheology modifiers or antimicrobial agents wherein the antimicrobial agents are not covalently linked to the coating polymer.

International Patent Application Publication WO2010/096444 teaches a UV-curable polyethyleneimine polymer that can be attached to pre-functionalized surfaces giving the surface antimicrobial activity. The surfaces are functionalized by reacting the surfaces with 7-octenyl trichlorosilane.

V.P. Dhende et al (Application of Material Interfaces, 2001, 3, 2830) teaches a UV-curable polyethyleneimine co-polymer that can be attached to pre-functionalized surfaces giving the surface antimicrobial activity. The surfaces are functionalized by reacting the surfaces with octyltrichlorosilane.

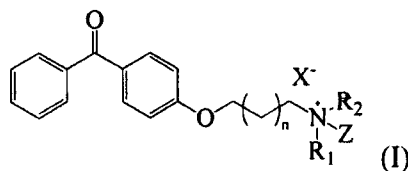
International Patent Application Publication WO2011/139817 teaches a UV-curable vinyl-substituted polyethyleneimine that can be attached to pre-functionalized surfaces and imparting antimicrobial activity to the surfaces. The surfaces are functionalized by reacting the surface with 7-octenyl trichlorosilane.

Mustafa Baris Yagci ("Self-Stratifying Antimicrobial Coatings", Ph.D. dissertation, January 16, 2012) teaches *inter alia* a QAC-bonded polyurethane surface coating.

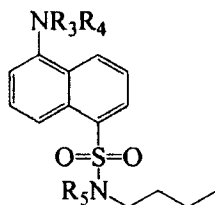
Thus, there has been a long-felt need for a durable and environmentally safe antimicrobial surface coating that minimizes or eliminates bacterial resistance.

SUMMARY OF THE INVENTION

In one aspect of the invention there is provided a novel quaternary ammonium compound of the following formula (I):



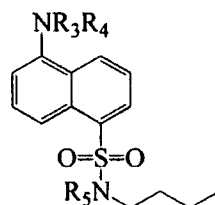
wherein R_1 and R_2 are independently lower alkyl groups defined as saturated hydrocarbon chains being one, two or three carbon atoms in length, Z is $\left(\text{---}\right)_m$ wherein m is at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18; or a group having the formula



5

wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl, preferably R_3 and R_4 are methyl, ethyl, n-propyl or isopropyl and R_5 is hydrogen, X is a halogen atom and n is 1, 2, 3 or 4. R_1 and R_2 are preferably the same, more preferably selected from methyl, ethyl, n-propyl or i-propyl groups, and more preferably methyl groups. Z is preferably

10 $\left(\text{---}\right)_m$ wherein m is at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18 or a group having the formula

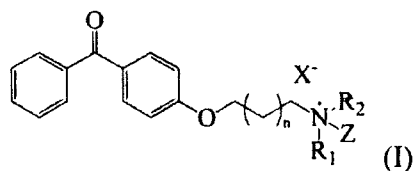


wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl, preferably R_3 and R_4 are methyl, ethyl, n-propyl or isopropyl and R_5 is hydrogen, and more

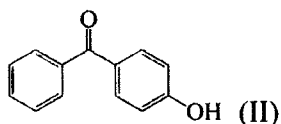
15 preferably $\left(\text{---}\right)_m$ wherein m is at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18. X is preferably selected from the group consisting of chloro, bromo and iodo and more preferably bromo and iodo, with the proviso that when X is bromo, n is 1 and R_1 and R_2 are methyl, m cannot be 17.

In another aspect of the invention there is provided a process for preparing a quaternary ammonium compound of formula (I)

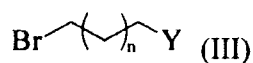
20



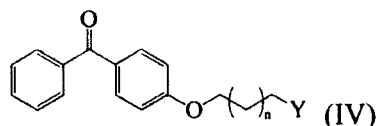
comprising the steps of (a) reacting a compound of formula (II)



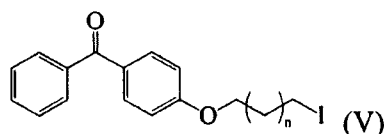
with an alkyl halide of formula (III)



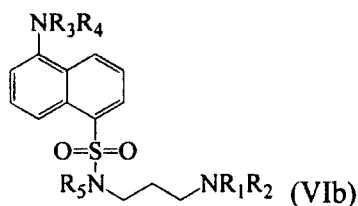
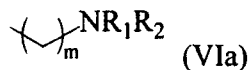
where Y is a halogen selected from chloro or bromo, more preferably bromo, in the presence of an alkali metal carbonate to give a compound of formula (IV)



(b) optionally converting the compound of formula (IV) to a compound of formula (V)

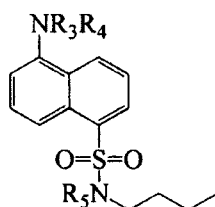


and (c) reacting the compound of formula (IV) or formula (V) with a compound of formula (VIa) or (VIb)



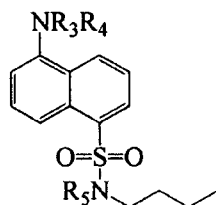
wherein R₁ and R₂ are independently lower alkyl groups defined as saturated hydrocarbon chains being one, two or three carbon atoms in length, R₃, R₄ and R₅ are independently hydrogen, C₁-C₆ linear or branched alkyl or C₆-C₁₀ aryl, preferably R₃ and R₄ are methyl, ethyl, n-propyl or

isopropyl and R_5 is hydrogen, X is a halogen atom, Y is chloro or bromo, Z is $(M)_m$ wherein m is at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18 or a group having the formula



5 wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl, preferably R_3 and R_4 are methyl, ethyl, n-propyl or isopropyl and R_5 is hydrogen, and n is selected from 1, 2, 3 or 4.

R_1 and R_2 are preferably the same, more preferably selected from methyl, ethyl, n-propyl or i-propyl groups, and even more preferably methyl groups. Z is preferably $(M)_m$ wherein m is at
10 least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18 or a group having the formula

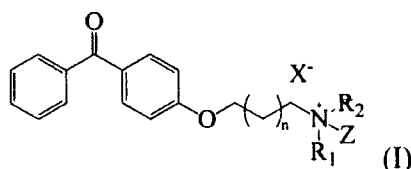


wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl, preferably R_3 and R_4 are methyl, ethyl, n-propyl or isopropyl and R_5 is hydrogen, and more
15 preferably $(M)_m$ wherein m is at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18. X is preferably selected from the group consisting of chloro, bromo and iodo and more preferably bromo or iodo.

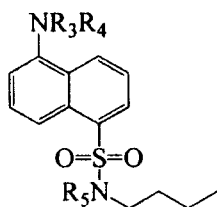
In a preferred embodiment the process may take place in a polar, aprotic reaction solvent, such as DMF, THF or acetonitrile, preferably acetonitrile. The process may be carried out at the
20 refluxing temperature of the reaction solvent. The process duration may be from about 18 to

about 36 hours, preferably 24 hours. The final product optionally may be purified, preferably by chromatography or recrystallization.

In another aspect of the invention there is provided an antimicrobial surface coating composition comprising a compound of formula (I)

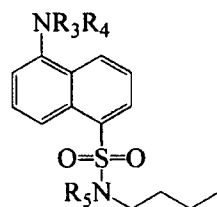


wherein R_1 and R_2 are independently lower alkyl groups defined as saturated hydrocarbon chains being one, two or three carbon atoms in length, Z is $\text{---}(\text{CH}_2)_m\text{---}$ wherein m is at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18 or a group having the formula



wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl, preferably R_3 and R_4 are methyl, ethyl, n-propyl or isopropyl and R_5 is hydrogen, X is a halogen atom and n is 1, 2, 3 or 4, and an environmentally friendly carrier. R_1 and R_2 are preferably the same, more preferably selected from methyl, ethyl, n-propyl or i-propyl groups, and more preferably methyl groups. Z is preferably $\text{---}(\text{CH}_2)_m\text{---}$ wherein m is at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18 or a group having the formula

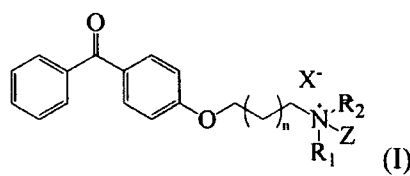
15



wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl, preferably R_3 and R_4 are methyl, ethyl, n-propyl or isopropyl and R_5 is hydrogen, and more

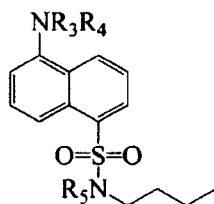
preferably $\text{---}(\text{CH}_2)_m\text{---}$ wherein m is at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18. X is preferably selected from the group consisting of chloro, bromo and iodo and more preferably bromo or iodo. In a preferred embodiment, the environmentally friendly carrier is water, more preferably a mixture of water and an alcohol, said alcohol is selected from a group consisting of methanol, ethanol and isopropanol wherein the alcohol is preferably methanol and said water is preferably distilled water.

- 10 In yet another aspect of the invention there is provided a process for treating a surface with an antimicrobial coating comprising the steps of contacting the surface with a composition comprising a compound of formula (I)



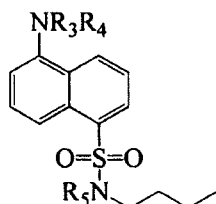
wherein R_1 and R_2 are independently lower alkyl groups defined as saturated hydrocarbon chains

- 15 being one, two or three carbon atoms in length, Z is $\text{---}(\text{CH}_2)_m\text{---}$ wherein m is at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18 or a group having the formula



- 20 wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl, preferably R_3 and R_4 are methyl, ethyl, n-propyl or isopropyl and R_5 is hydrogen, X is a halogen atom and n is 1, 2, 3 or 4, and an environmentally friendly carrier. R_1 and R_2 are preferably the same, more preferably selected from methyl, ethyl, n-propyl or i-propyl groups, and more

preferably methyl groups. Z is preferably $\left(\text{CH}_2\right)_m$ wherein m is at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18 or a group having the formula



- 5 wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl, preferably R_3 and R_4 are methyl, ethyl, n-propyl or isopropyl and R_5 is hydrogen, and more preferably $\left(\text{CH}_2\right)_m$ wherein m is at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18. X is preferably selected from the group consisting of chloro, bromo and iodo and more preferably bromo or iodo, and
- 10 irradiating the coated surface and optionally washing the coated surface. The surface can include, but not be limited to, polymers such as polyethylene, polypropylene, acrylonitrile-butadiene-styrene, polyurethane or nylon articles such as food trays, molded bedding parts, desk chairs and assorted furniture, disposable syringes, plastic handles for appliances, bathroom fixtures, window blinds and the like. Preferably the surface is a polymer or a fibre. Preferably,
- 15 the washing step uses a water and isopropanol mixture. Depending on the article or surface to be coated, the skilled person would take the steps necessary to ensure the composition substantially coats the surface, preferably fully coats the surface. For example, an article may only require one application of the composition, or the article may require multiple applications of the composition to ensure the article is substantially coated. In a preferred embodiment the
- 20 irradiating step comprises irradiating the coated surface, preferably with UV light.

Further and other aspects will be appreciated by the skilled reader.

DETAILED DESCRIPTION OF THE INVENTION

Brief Summary of Figures

- 25 Figure 1 shows a bromophenyl blue stained antimicrobial surface treatment.

Figure 2 shows antimicrobial treatment fluorescing under UV light

Figure 3 shows the ^1H NMR of compound **1a** of Example 1

Figure 4 shows the ^{13}C NMR of compound **1a** of Example 1

Figure 5 shows the ^1H NMR of compound **1b** of Example 2

5 Figure 6 shows the ^{13}C NMR of compound **1b** of Example 2.

Figure 7 shows the ^1H NMR of compound **2a** of Example 3

Figure 8 shows the ^{13}C NMR of compound **2a** of Example 3

Figure 9 shows the ^1H NMR of compound **3a** of Example 4

Figure 10 shows the ^{13}C NMR of compound **3a** of Example 4

10 Figure 11 shows the ^1H NMR of compound **3b** of Example 5

Figure 12 shows the ^{13}C NMR of compound **3b** of Example 5

Figure 13 shows the ^1H NMR of compound **1c** of Example 6

Figure 14 shows the ^{13}C NMR of compound **1c** of Example 6

Figure 15 shows the ^1H NMR of compound **2c** of Example 7.

15 Figure 16 shows the ^{13}C NMR of compound **2c** of Example 7.

Figure 17 shows the ^1H NMR of compound **3c** of Example 8.

Figure 18 shows the ^{13}C NMR of compound **3c** of Example 8.

Figure 19 shows the ^1H NMR of compound **4a** of Example 9.

Figure 20 shows the ^{13}C NMR of compound **4a** of Example 9.

20 Figure 21 shows the ^1H NMR of compound **4b** of Example 10.

Figure 22 shows the ^{13}C NMR of compound **4b** of Example 10.

- Figure 23 shows the ^1H NMR of compound **4c** of Example 11.
- Figure 24 shows the ^{13}C NMR of compound **4c** of Example 11.
- Figure 25 shows the ^1H NMR of compound **5a** of Example 12.
- Figure 26 shows the ^{13}C NMR of compound **5a** of Example 12.
- 5 Figure 27 shows the ^1H NMR of compound **5c** of Example 13.
- Figure 28 shows the ^{13}C NMR of compound **5c** of Example 13.
- Figure 29 shows the ^1H NMR of compound **6a** of Example 14.
- Figure 30 shows the ^{13}C NMR of compound **6a** of Example 14.
- Figure 31 shows the ^1H NMR of compound **6b** of Example 15.
- 10 Figure 32 shows the ^{13}C NMR of compound **6b** of Example 15.
- Figure 33 shows the ^1H NMR of compound **6c** of Example 16.
- Figure 34 shows the ^{13}C NMR of compound **6c** of Example 16.
- Figure 35 shows the ^{13}C NMR of compound **7a** of Example 17.
- Figure 36 shows the ^{13}C NMR of compound **7a** of Example 17.
- 15 Figure 37 shows the ^1H NMR of compound **7b** of Example 18.
- Figure 38 shows the ^{13}C NMR of compound **7b** of Example 18.
- Figure 39 shows the ^1H NMR of compound **7c** of Example 19.
- Figure 40 shows the ^{13}C NMR of compound **7c** of Example 19.
- Figure 41 shows the ^1H NMR of compound **8a** of Example 20.
- 20 Figure 42 shows the ^{13}C NMR of compound **8a** of Example 20.
- Figure 43 shows the ^1H NMR of compound **8c** of Example 21.

Figure 44 shows the ^{13}C NMR of compound **8c** of Example 21.

Figure 45 shows the ^1H NMR of compound **9a** of Example 22.

Figure 46 shows the ^{13}C NMR of compound **9a** of Example 22.

Figure 47 shows the ^1H NMR of compound **9b** of Example 23.

5 Figure 48 shows the ^{13}C NMR of compound **9b** of Example 23.

Figure 49 shows the ^1H NMR of compound **9c** of Example 24.

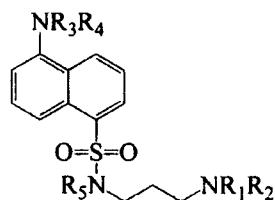
Figure 50 shows the ^{13}C NMR of compound **9c** of Example 24.

10 The present invention is directed to novel quaternary ammonium compounds that are linked to a UV-activatable moiety, methods for manufacturing the compounds and treating surfaces with the compound to provide a durable, antimicrobial-treated article.

15 The quaternary ammonium compound of the present invention comprises a positively charged nitrogen centre linked to two alkyl groups which are independently the same or different, a UV activatable moiety and a long alkyl chain and a halogen counterion. The two alkyl groups are independently methyl, ethyl, n-propyl or i-propyl, most preferably methyl. The alkyl chain is preferably at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18 carbon atoms long. The alkyl chain can be branched or linear and preferably linear. The UV activatable moiety is linked to the positively charged nitrogen centre via an alkyl chain of preferably three to six carbon atoms in length. The alkyl chain is preferably linear. The UV activatable moiety is preferably benzophenone. The halogen counterion is preferably selected from the group consisting of chloro, bromo and iodo, most preferably from chloro or bromo, with the proviso that when the halogen is bromo, the alkyl chain linking the UV activatable moiety to the nitrogen centre is three carbon atoms long and the two alkyl groups are methyl, the long alkyl chain cannot be 18 carbon atoms long.

25 The quaternary ammonium compound of the present invention also comprises a positively charged nitrogen centre linked to two alkyl groups which are independently the same or

different, a UV activatable moiety and a di-N-substituted-dialkylaminopropyl naphthalene-1-sulfonamide group of formula (VIb):



wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl, preferably R_3 and R_4 are methyl, ethyl, n-propyl or isopropyl and R_5 is hydrogen. The two alkyl groups are independently methyl, ethyl, n-propyl or i-propyl, most preferably methyl. The UV activatable moiety is linked to the positively charged nitrogen centre via an alkyl chain of preferably three to six carbon atoms in length. The alkyl chain is preferably linear. The UV activatable moiety is preferably benzophenone. The di-N-substituted-dialkylaminopropyl naphthalene-1-sulfonamide group fluoresces under UV light and acts as an indicator of the presence of the quaternary ammonium compound.

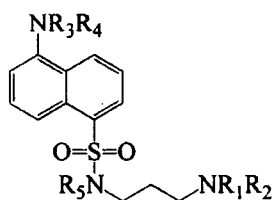
The quaternary ammonium compounds of the present invention can be prepared by modification of known synthetic techniques in the preparation of QACs. Generally, the first step involves reacting benzophenone with a dihaloalkane in the presence of an alkali metal carbonate in a polar, aprotic solvent under refluxing conditions. The dihaloalkane can have the same or different halogen groups, preferably selected from chloro, bromo and iodo. The dihaloalkane is from three to ten carbon atoms long, and is preferably four to nine carbon atoms long, more preferably five to eight carbon atoms long. The alkali metal carbonate is selected from the group consisting of sodium, potassium and cesium carbonate and most preferably potassium carbonate. The polar, aprotic solvent may be any suitable solvent; preferably it is selected from the group consisting of DMF, acetone, THF and acetonitrile. Most preferably the solvent is acetonitrile. The reaction mixture is heated until such time as the reaction mixture becomes substantially clear and a thin-layer chromatography ("TLC") analysis shows the starting material has been consumed. Preferably the reaction mixture is heated to reflux. The final haloalkylbenzophenone product is isolated, preferably by filtration, preferably through CeliteTM to remove the alkali metal halide by-product, which is further washed with a polar, aprotic solvent to extract any final product held in the CeliteTM, evaporating the filtrate to dryness and purifying the final product

preferably using a chromatographic method, most preferably column chromatography. The elution solvent is preferably a solvent mixture comprising ethyl acetate and hexanes. The final haloalkylbenzophenone product optionally can be further purified by recrystallization.

Optionally, the haloalkylbenzophenone product of the previous step can be converted to an iodoalkylbenzophenone by reacting the haloalkylbenzophenone with sodium iodide in a refluxing polar, aprotic solvent, preferably acetone.

The second step in the preparation involves reacting the haloalkylbenzophenone of the previous step where the halo is selected from chloro, bromo or iodo with a trialkylamine in a refluxing polar solvent. One of the alkyl groups of the trialkylamine is preferably at least 12, preferably between 12 and 36 and most preferably selected from the group consisting of 12, 13, 14, 15, 16, 17 and 18 carbon atoms long. The alkyl chain can be branched or linear and preferably linear. The remaining two alkyl groups are independently methyl, ethyl, n-propyl or i-propyl, most preferably methyl. The solvent can be selected from DMF, acetone, THF, ethanol, methanol or acetonitrile. Most preferably the solvent is acetonitrile. The reaction is allowed to go until starting materials are substantially no longer present. One method of monitoring the progress of the reaction is via TLC. Other methods may be applied. The quaternary ammonium product is purified preferably by a chromatographic method, and most preferably by column chromatography. The elution solvent is preferably a solvent mixture comprising 6% sodium bromide in methanol and acetonitrile. The final quaternary ammonium product optionally can be further purified by recrystallization from a mixed solvent, preferably ethanol/acetone.

Synthesis of quaternary ammonium compounds capped with a di-N-substituted-dialkylaminopropyl naphthalene-1-sulfonamide group of formula (VIb):



wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl, preferably R_3 and R_4 are methyl, ethyl, n-propyl or isopropyl and R_5 is hydrogen can be carried out by reacting the haloalkylbenzophenone from the above step with a trialkylamine in which

one of the alkyl groups is 5-dimethylaminonaphthalene-1-sulfonamidopropyl and the other two alkyl groups independently are selected from methyl, ethyl, n-propyl or i-propyl, preferably methyl. The halo group of the haloalkylbenzophenone can be chloro, bromo or iodo. The reaction can be carried out in refluxing polar solvent selected from DMF, acetone, THF, methanol, ethanol or acetonitrile. Most preferably the solvent is acetonitrile. The reaction is allowed to go until starting material are substantially no longer present. One method of monitoring the reaction is via TLC. The quaternary ammonium product is isolated by precipitation from the reaction mixture by addition of cold diethyl ether, more preferably diethyl ether at a temperature of about -10°C to about 10°C and most preferably at a temperature at about 0°C, and evaporation of the reaction solvent.

The quaternary ammonium compounds of the present invention in another embodiment, can be used to antimicrobially treat hard surfaces. Without being bound by any particular theory, the UV activatable moiety of the quaternary ammonium compounds converts to a diradical species in the presence of UV light and reacts with any surface having C-H bonds to form a covalent C-C bond. The result is a fixed, durable antimicrobial coating of quaternary ammonium compounds.

Treatment of articles, including hard surfaces can be done via dipping, painting, spraying or coating the surface with a solution of a quaternary ammonium compound of the present invention. A surface may be an inner and/or outer surface. The solution is environmentally friendly and comprises a water or a water-alcohol solvent mixture carrier, preferably water-methanol, water-ethanol or water-isopropanol, most preferably water or water-isopropanol. The amount of quaternary ammonium compound in the solution ranges from about 0.01% to about 1% and more preferably from about 0.05% to about 0.5% weight by volume. In one embodiment, polyvinylchloride previously washed with isopropanol and dried is treated with a 0.05% or a 0.5% solution of a C18 quaternary ammonium compound in which the UV activatable moiety is linked to the nitrogen centre with a C5 alkyl chain. The carrier is a water-methanol solvent mixture. The previously washed and dried polyvinylchloride ("PVC") substrate is electrosprayed with the above solution followed by UV irradiation until a satisfactory coating is achieved. A typical UV wavelength of between about 200 and 400 nm, preferably

between about 345 to about 365 nm is used. Optionally, the coated PVC substrate is rinsed with a water and isopropanol mixture and dried.

With reference to Figure 1, the PVC substrate treated with C18 quaternary ammonium compound in which the UV activatable moiety is linked to the nitrogen centre with a C5 alkyl chain was washed with water and treated with bromophenyl blue to show the antimicrobial treatment of the present invention. A second PVC substrate sample treated with the same quaternary ammonium compound was washed with ionic detergent, rinsed with water and bromophenyl blue to show the antimicrobial treatment of the present invention.

With reference to Figure 2, the silicone tubing substrate treated with 5-dimethylaminonaphthalene-1-sulfonamidopropyl quaternary ammonium compound fluoresces under UV light showing the presence of the antimicrobial treatment of the present invention.

With reference to Figures 3 to 50, the horizontal axes represent the chemical shift of the NMR peaks in ppm and the vertical axes represent the intensity of the chemical shift peaks.

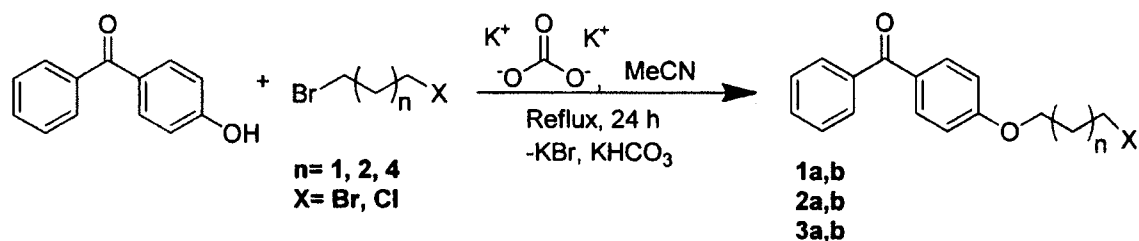
The following non-limiting examples are provided.

Materials. All reagents and solvents, unless otherwise specified were obtained from Sigma-Aldrich and used as received. Potassium carbonate was obtained from Fisher, N,N-dimethyloctadecylamine was retrieved from Acros, and sodium iodide from BDH. 5-(dimethylamino)-N-(3-(dimethylamino)propyl)naphthalene-1-sulfonamide (compound 10) was prepared according to literature procedures: Wang, X. & Schneider, H. Binding of dansylamide derivatives to nucleotides and nucleic acids. *J. Chem. Soc. Perkin Trans. 2*, 1998, 1323-1328; Hillman G.R. et al., Effects of Dansylated Acetylcholine Analogs on *Schistosoma a Mansoni*, *J. Pharm. Sci.*, 1980, 69(5), 516-520. Polyvinylchloride (PVC) was obtained from Oran Industries (Woodbridge ON), while silicone tubing was a VWR brand select silicone (0.062 × 0.125 × 0.032 cm). The UV fumehood used was equipped with a G30T8 30 W germicidal fluorescent bulb whereas the Hanovia utility UV quartz lamp was a 140 W source. Trypticase soy agar used in testing antimicrobial efficiency was provided by Bio Basic Canada Inc. Agar A.

Instrumental Methods. Nuclear magnetic resonance (NMR) experiments were carried out on a 400 MHz Bruker Avance Spectrometer using deuterated chloroform (CDCl₃) as the solvent. ¹H

NMR (400 MHz) spectra were referenced to the residual protonated solvent resonance signal (CHCl_3 : 7.26 ppm) and the ^{13}C (100.6 MHz) to the central carbon resonance signal of the solvent (CDCl_3 : 77.0 ppm). All chemical shifts are given in δ (ppm) relative to the solvent. All thin layer chromatography (TLC) was performed using Silica gel 60 eluting with EtOAc/hexanes (20:80) solution unless otherwise noted. Melting points were measured using a Fischer Scientific melting point apparatus. The UV light source was a quartz mercury lamp with a power of 140 W.

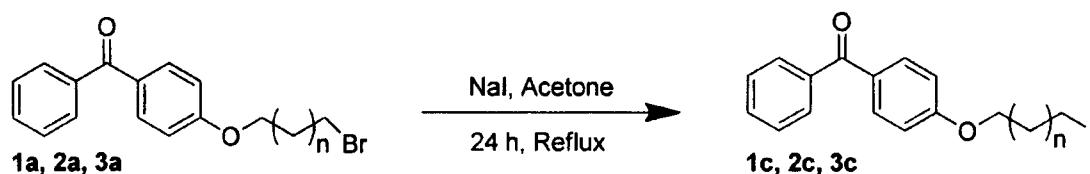
Referential Example 1 - Synthesis of (1a-b; 2a-b; 3a-b)



In a 50 mL round bottom flask dihaloalkane (4 eq.) and potassium carbonate (2 eq.) were dissolved in acetonitrile (10 mL). A solution of 4-hydroxybenzophenone (1 eq.) dissolved in acetonitrile (10 mL) was prepared in a dropping funnel, and then added dropwise under reflux. The resultant yellow mixture was heated at reflux until a clear solution was obtained or until TLC showed the disappearance of starting material 4-hydroxybenzophenone. The excess potassium bromide salt was filtered off through CeliteTM and washed with acetone (10 mL). The mixture was evaporated under reduced pressure to give a crude product.

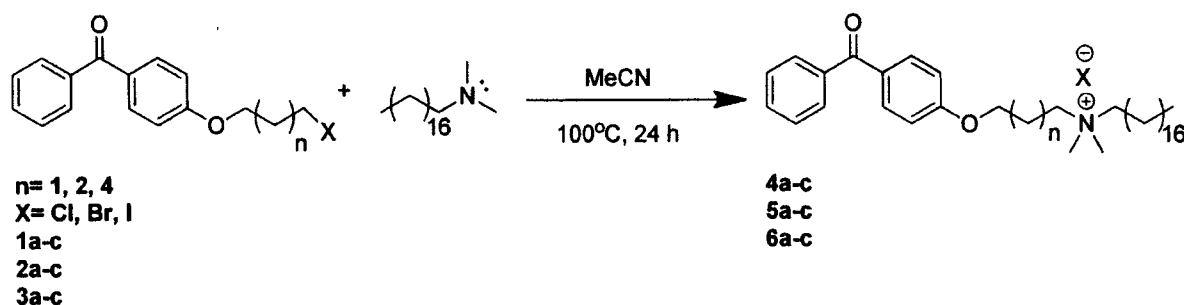
The crude product was packed onto silica and purified by dry column chromatography (4.5 cm x 5.0 cm frit, 40 g silica) eluting with EtOAc/hexanes (20:80) to afford the desired product and further recrystallized in toluene/hexanes (1:3).

Referential Example 2 - Synthesis of 4-O-(n-iodoalkyl)benzophenone precursors (1c, 2c, 3c)



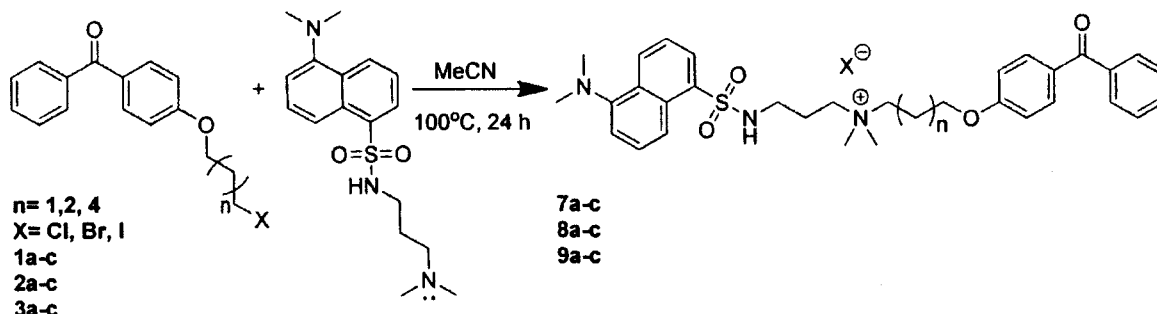
In a 50 mL round bottom flask 4-*O*-(*n*-haloalkyl)benzophenone (1 eq.) and sodium iodide (3 eq.) were mixed in acetone (10 mL) and the resultant mixture was left to reflux for 24 hours or until TLC showed the disappearance of starting material (EtOAc/hexanes 20:80). Excess sodium iodide and sodium bromide salt were filtered through CeliteTM, washing with cold hexanes. The solvent extracts were then evaporated under reduced pressure and the crude residue dry packed onto silica and purified by dry column chromatography (4.5 cm x 5.0 cm frit, 40 g silica), eluting with EtOAc/hexanes (20:80) to yield the desired product. Further recrystallization in toluene/hexanes (1:2) was undertaken.

10 **Referential Example 3 - Synthesis of *N*-(*n*-(4-benzoylphenoxy)alkyl)-*N,N*-dimethyloctadecan-1-ammonium halides**



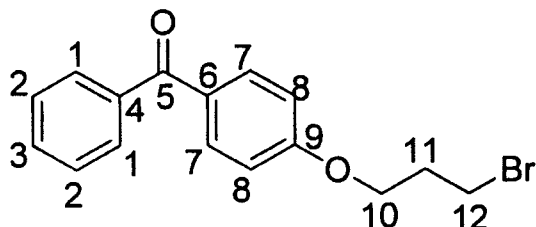
In a 20 mL screw cap vial *N,N*-dimethyloctadecylamine (1.1 eq.) and 4-*O*-(*n*-haloalkyl)benzophenone (1.0 eq.) were mixed in acetonitrile (1 mL). The resultant mixture was left to stir in a 100°C sand bath for 24 hours or until TLC showed the disappearance of starting material (acetone/ammonia 15:1). The vial was then removed from heat and allowed to cool at ambient conditions and a crude product obtained. The crude product was recrystallized using ethanol/acetone (1:3) and evaporated under vacuum to obtain the desired product.

Referential Example 4 - Synthesis of *n*-(4-benzoylphenoxy)-*N*-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-*N,N*-dimethylalkyl-1-ammonium halides



- 5 In a 20 mL screw cap vial 5-(dimethylamino)-*N*-(3-(dimethylamino)propyl)naphthalene-1-sulfonamide **10** (1.0 eq.) and haloalkoxy(phenyl)(phenyl)methanone (1.0 eq.) were dissolved in acetonitrile (2 mL). The resultant solution was left to stir in a 100°C sand bath for 24 hours or until TLC showed the disappearance of starting material (EtOAc/hexanes 20:80). The residue was then precipitated from the resultant solution by the dropwise addition of cold diethyl ether (4
- 10 mL) and evaporated under vacuum to obtain the desired product.

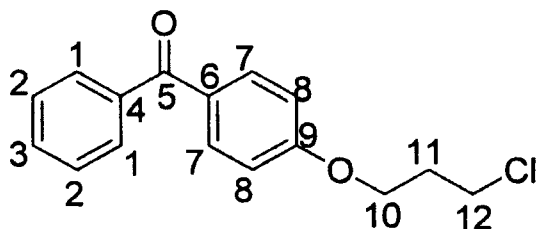
Example 1 - 4-O-(3-bromopropyl)benzophenone **1a**



- 15 According to the general procedure for the halide alkylation of 4-hydroxybenzophenone derived from Saettone *et al.*, *International Journal of Cosmetic Sciences*, **1988**, *10*, 99-109. 1,3-dibromopropane (60.5 mmol, 6.14 mL), potassium carbonate (30.2 mmol, 4.18 g) and 4-hydroxybenzophenone (15.1 mmol, 3.0 g) were stirred in acetonitrile (20 mL) under reflux for 24 hours to give a crude product of 4-O-(3-bromopropyl)benzophenone which was recrystallized in toluene/hexanes to yield compound **1a** (3.22 g, 66.7% yield). $\text{C}_{16}\text{H}_{15}\text{BrO}_2$; off white powder,
- 20 mp 54-66 °C; $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 2.35 (m, $-\text{CH}_2$, 2H), 3.62 (m, $-\text{CH}_2$, 2H), 4.21 (m, $-\text{CH}_2$, 2H), 6.95 (s, Ar, 2H), 7.55 (m, Ar, 2H), 7.60 (m, Ar, 1H), 7.75 (m, Ar, 2H), 7.80 (m, Ar, 2H) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 195.52 (C5), 162.31 (C9), 138.24 (C4), 132.58 (C3),

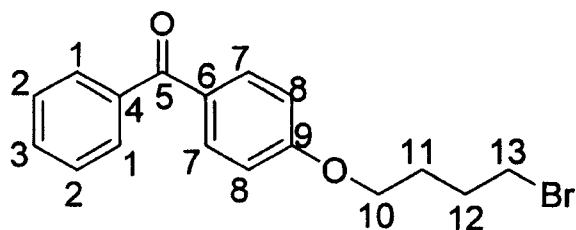
129.74 (C1), 129.73 (C6), 128.21 (C2), 114.04 (C8), 65.53 (C10), 32.14 (C12), 29.74 (C11) ppm. HRMS-DART (m/z): $[M^+]$ calcd. for $C_{16}H_{15}BrO_2$, 319.0334; found, 319.0329.

Example 2 - 4-O-(3-chloropropyl)benzophenone 1b



According to the general method derived from this group, 1-bromo-3-chloropropane (50.4 mmol, 5.00 mL), potassium carbonate (25.3 mmol, 3.49 g) and 4-hydroxybenzophenone (12.6 mmol, 2.50 g) were stirred in acetonitrile (20 mL) under reflux for 24 hours to give a crude product of 4-O-(3-chloropropyl)benzophenone which was recrystallized in toluene/hexanes to yield compound **1b** (1.21 g, 34.9% yield). $C_{16}H_{15}ClO_2$; off white powder; 1H NMR ($CDCl_3$, 400 MHz) δ = 2.29 (m, $-CH_2-$, 2H), 3.79 (m, $Cl-CH_2-$, 2H), 4.23 (m, $-O-CH_2-$, 2H), 6.98 (m, $-Ar$, 2H), 7.45 (m, $-Ar$, 2H), 7.60 (m, $-Ar$, 1H), 7.75 (m, $-Ar$, 2H), 7.82 (m, $-Ar$, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.52 (C5), 162.31 (C9), 138.24 (C4), 132.54 (C3), 130.38 (7), 129.74 (C1), 128.21 (C2), 114.04 (C8), 65.53 (C10), 32.14 (C12), 29.73 (C11) ppm. Note: Chemical properties agree with that of the compounds as prepared previously by Saettone *et al.*, *International Journal of Cosmetic Sciences*, 1988, 10, 99-109.

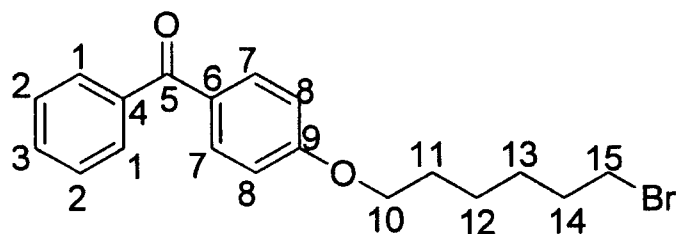
Example 3 - 4-O-(4-bromobutyl)benzophenone 2a



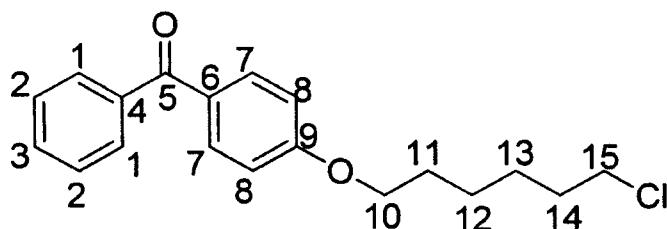
According to the general procedure for the halide alkylation of 4-hydroxybenzophenone derived from Saettone *et al.*, *International Journal of Cosmetic Sciences*, 1988, 10, 99-109, 1,4-dibromobutane (50.4 mmol, 6.02 mL), potassium carbonate (25.3 mmol, 3.49 g) and 4-hydroxybenzophenone (12.6 mmol, 2.50 g) were stirred in acetonitrile (20 mL) under reflux for

24 hours to give a crude product of 4-O-(4-bromobutyl)benzophenone which was recrystallized in toluene/hexanes to yield compound **2a** (3.846 g, 91.6% yield). $C_{17}H_{17}BrO_2$; pale yellow powder; 1H NMR ($CDCl_3$, 400 MHz) δ = 1.99 (m, $-CH_2-$, 2H), 2.09 (m, $-CH_2-$, 2H), 3.51 (m, $-Br-CH_2$, 2H), 4.09 (m, $-O-CH_2$, 2H), 6.95 (m, -Ar, 2H), 7.45 (m, -Ar, 2H), 7.55 (m, -Ar, 1H), 7.75 (m, -Ar, 2H), 7.85 (m, -Ar, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.52 (C5), 162.51 (C9), 138.27 (C4), 132.57 (C3), 131.90 (1), 129.72 (C6), 128.20 (2), 113.99 (8), 67.13 (C10), 33.31 (C13), 29.36 (C11) 27.76 (C12) ppm. **HRMS-DART** (m/z): $[M^+]$ calcd. for $C_{17}H_{17}BrO_2$, 333.0490 found, 333.0486.

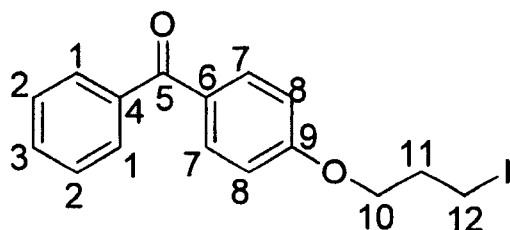
10 Example 4 - 4-O-(6-bromohexyl)benzophenone **3a**



According to the general procedure for the halide alkylation of 4-hydroxybenzophenone derived from Saettone et al., *International Journal of Cosmetic Sciences*, **1988**, 10, 99-109, 1,6-dibromohexane (40.4 mmol, 6.21 mL), potassium carbonate (20.2 mmol, 2.79 g) and 4-hydroxybenzophenone (10.1 mmol, 2.00 g) were stirred in acetonitrile (20 mL) under reflux for 24 hours to give a crude product of 4-O-(6-bromohexyl)benzophenone which was recrystallized in toluene/hexanes to yield compound **3a** (1.495 g, 42.7% yield). $C_{19}H_{21}BrO_2$; white powder; 1H NMR ($CDCl_3$, 400 MHz) δ = 1.55 (m, $-CH_2-$, 4H), 1.88 (m, $-CH_2-$, 4H), 3.45 (m, $-Br-CH_2$, 2H), 4.09 (m, $-O-CH_2$, 2H), 6.95 (m, -Ar, 2H), 7.45 (m, -Ar, 2H), 7.55 (m, -Ar, 1H), 7.79 (m, -Ar, 4H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.52 (C5), 162.75 (C9), 138.22 (C4), 132.57 (C3), 129.98 (C7), 129.72 (C1), 128.18 (C2), 114.00 (C8), 67.99 (C10), 33.78 (C15), 32.63 (C14), 28.94 (C11), 27.88 (C13), 25.25 (C12) ppm. **HRMS-DART** (m/z): $[M^+]$ calcd. for $C_{19}H_{21}BrO_2$, 361.0803; found, 361.0796.

Example 5 - 4-O-(6-chlorohexyl)benzophenone 3b

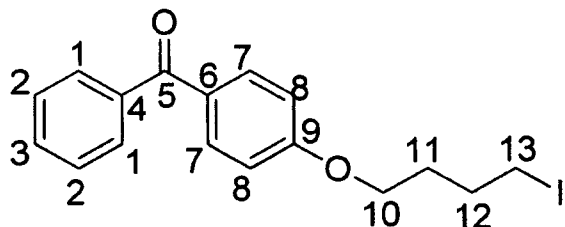
According to the general procedure for the halide alkylation of 4-hydroxybenzophenone, 1-bromo-6-chlorohexane (13.9 mmol, 2.77 mL), potassium carbonate (25.2 mmol, 3.49 g) and 4-hydroxybenzophenone (12.6 mmol, 2.50 g) were stirred in acetonitrile (20.0 mL) under reflux for 24 hours to give a crude product of 4-O-(6-chlorohexyl)benzophenone which was recrystallized in toluene/hexanes to yield compound **3b** (3.07 g, 76.8% yield). $C_{19}H_{21}ClO_2$; off white powder, mp 64-67°C; 1H NMR ($CDCl_3$, 400 MHz) δ = 1.55 (m, $-CH_2-$, 4H), 1.85 (m, $-CH_2-$, 4H), 3.51 (m, $-Cl-CH_2$, 2H), 4.06 (m, $-O-CH_2$, 2H), 6.95 (m, $-Ar$, 2H), 7.49 (m, $-Ar$, 2H), 7.52 (m, $-Ar$, 1H), 7.77 (m, $-Ar$, 4H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.54 (C5), 162.74 (C9), 138.34 (C4), 132.57 (C3), 129.72 (C1), 128.18 (C2), 114.00 (C8), 67.99 (C10), 30.32 (C15), 30.20 (C14), 28.92 (C11), 25.02 (C13) ppm. HRMS-DART (m/z): $[M^+]$ calcd. for $C_{19}H_{21}ClO_2$, 317.1308; found, 317.1311.

Example 6 - 4-O-(3-iodopropyl)benzophenone 1c

According to the general procedure for the halide substitution of bromine for iodine in haloalkoxy(phenyl)(phenyl)methanone compounds, 4-(3-bromopropoxy)(phenyl)(phenyl)methanone (3.13 mmol, 1.00 g) and sodium iodide (9.40 mmol, 1.41 g) were mixed in acetone (10.0 mL) under reflux for 24 hours to give crude product of 4-O-(3-iodopropyl)benzophenone which was recrystallized in toluene/hexanes (1:2) to obtain compound **1c** (0.585 g, 51.0% yield). $C_{15}H_{16}IO_2$; yellow powder; 1H NMR ($CDCl_3$, 400 MHz) δ = 2.31 (m, $-CH_2-$, 2H), 3.39 (m, $-CH_2-$, 2H), 4.15 (m, $-I-CH_2$, 2H), 6.95 (m, $-Ar$, 2H), 7.51 (m, $-Ar$, 3H), 7.70 (m, $-Ar$, 4H) ppm; ^{13}C

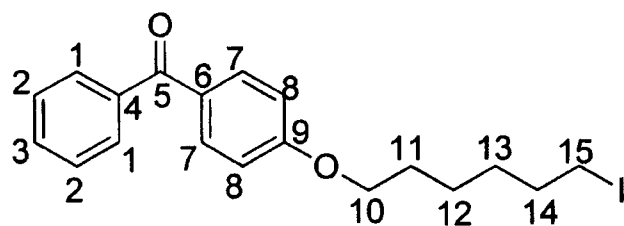
NMR (CDCl₃, 100 MHz) δ 195.47 (C5), 162.32 (C9), 138.27 (C4), 129.75 (C1), 128.28 (C2), 114.09 (C8), 67.54 (C10), 32.74 (C11), 2.19 (C12) ppm. **HRMS-DART** (m/z): [M⁺] calcd. for C₁₆H₁₅IO₂, 367.0195 found, 367.0202.

5 Example 7 - 4-O-(4-iodobutyl)benzophenone 2c



The synthesis of compound **2c** has been previously reported by Acosta *et al.*, *Polymer Degradation and Stability*, **1996**, 52, 11-17. An alternative synthetic approach, following the general procedure for the halide substitution of bromine for iodine in halo-alkoxy(phenyl)(phenyl)methanone compounds, 4-(4-bromobutoxy)(phenyl)(phenyl)methanone (3.00 mmol, 1.00 g) and sodium iodide (6.00 mmol, 0.900 g) were mixed in acetone (10.0 mL) under reflux for 24 hours to give crude product of 4-O-(4-iodobutyl)benzophenone which was recrystallized in toluene/hexanes (1:2) to obtain compound **2c** (1.03 g, 90.2% yield). C₁₅H₁₆IO₂; pale yellow powder; ¹H NMR (CDCl₃, 400 MHz) δ = 2.00 (m, -CH₂-, 4H), 3.39 (m, I-CH₂-, 2H), 4.05 (m, -O-CH₂-, 2H), 6.95 (m, -Ar, 2H), 7.51 (m, -Ar, 3H), 7.79 (m, -Ar, 4H) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ = 195.52 (C5), 162.51 (C9), 138.27 (C4), 132.58 (C3), 131.90 (C7), 129.72 (C1), 128.20 (C2), 113.99 (C8), 66.92 (C10), 30.05 (C11), 30.01 (C12), 6.21 (C13) ppm. ¹H NMR chemical shifts agree with those reported by Acosta *et al.* above.

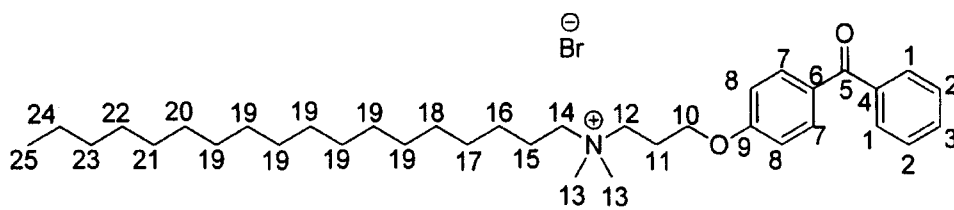
20 Example 8 - 4-O-(6-iodohexyl)benzophenone 3c



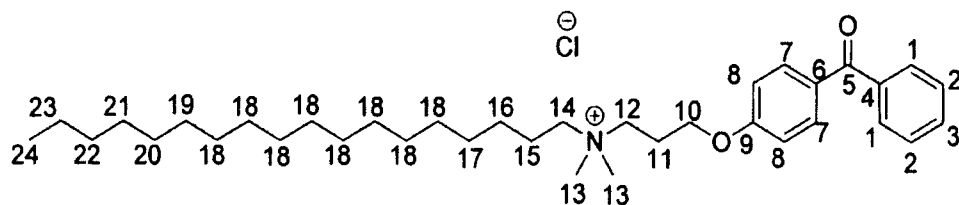
Previous synthesis of this compound has been reported by Acosta *et al.*, *Polymer Degradation and Stability*, **1996**, 52, 11-17. Following an alternative synthetic approach outlined in the

general procedure for the halide substitution of bromine for iodine in haloalkoxy(phenyl)(phenyl)methanone compounds, 4-((3-bromohexyl)oxy)phenyl(phenyl)methanone (1.38 mmol, 0.500 g) and sodium iodide (4.15 mmol, 0.622 g) were mixed in acetone (10.0 mL) under reflux for 24 hours to give crude product of 4-O-(6-iodohexyl)benzophenone which was recrystallized in toluene/hexanes (1:2) to obtain compound **3c** (0.480 g, 85.0% yield). $C_{19}H_{21}IO_2$; off white powder; 1H NMR ($CDCl_3$, 400 MHz) δ = 1.55 (m, $-CH_2-$, 4H), 1.85 (m, $-CH_2-$, 4H), 3.21 (m, $-I-CH_2$, 2H), 4.05 (m, $-O-CH_2$, 2H), 6.95 (m, -Ar, 2H), 7.51 (m, -Ar, 3H), 7.77 (m, -Ar, 4H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.54 (C5), 162.74 (C9), 138.34 (C4), 132.57 (C3), 130.00 (C7), 129.72 (C1), 128.17 (C2), 114.00 (C8), 67.99 (C10), 33.32 (C14), 30.20 (C11), 28.92 (C13), 25.02 (C12), 6.89 (C15) ppm. 1H NMR chemical shifts agree with those reported by Acosta *et al.* above.

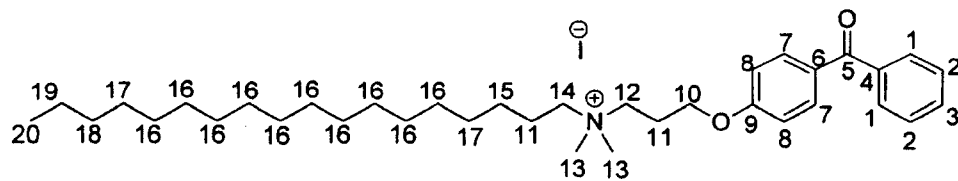
Example 9 - Propyl-dimethyl (benzoylphenoxy)octadecylammonium bromide **4a**



This compound has been previously reported by Saettone *et al.*, *International Journal of Cosmetic Sciences*, **1988**, *10*, 99-109. According to the general procedure for the quaternization of *N*-dimethyloctadecylamine with 4-O-(*n*-haloalkyl)benzophenone, 4-O-(3-bromopropyl)benzophenone (0.313 mmol, 0.100 g) and *N*-dimethyloctadecylamine (0.345 mmol, 0.103 g) and acetonitrile (1 mL) were stirred in an 100°C sand bath for 24 hours to give crude product of propyl-dimethyl (benzoylphenoxy)octadecylammonium bromide **4a** (0.194 g, 101% crude yield). $C_{36}H_{58}BrNO_2$; pale yellow solid; mp 58-68°C (lit. mp 81-83°C); 1H -NMR δ = 0.88 (m, $-CH_3-$, 3H), 1.30 (m, $-CH_2-$, 34H), 3.40 (s, $N-CH_3$, 6H), 3.45 (m, $-CH_2-$, 2H), 3.75 (s, $-CH_2-$, 2H), 4.13 (s, $O-CH_2-$, 2H), 6.95 (m, -Ar, 2H), 7.45 (m, -Ar, 2H), 7.55 (m, -Ar, 1H), 7.75 (m, -Ar, 2H), 7.81 (m, -Ar, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.47 (C5), 161.58 (C9), 137.95 (C4), 132.48 (C3), 131.91 (C7), 130.75 (C1), 129.72 (C6), 128.17 (C2), 114.10 (C8), 68.90 (C10), 64.46 (C14), 61.14 (C12), 51.50 (C13), 31.90 (C23), 29.63 (C19), 29.39 (C17), 29.34 (C22), 27.36 (C16), 26.25 (C15), 23.16 (C11), 22.75 (C24), 14.11 (C25) ppm. HRMS-DART (m/z): [$M^+ - Br$] calcd. for $C_{36}H_{58}BrNO_2$, 536.4478; found, 536.4462.

Example 10 - Propyl-dimethyl (benzoylphenoxy)octadecylammonium chloride 4b

According to the general procedure for the quaternization of *N*-dimethyloctadecylamine with 4-*O*-(*n*-haloalkyl)benzophenone, 4-*O*-(3-chloropropyl)benzophenone (0.910 mmol, 0.250 g) and *N*-dimethyloctadecylamine (1.00 mmol, 0.298 g) and acetonitrile (1 mL) were stirred in an 100°C sand bath for 24 hours to give crude product of propyl-dimethyl (benzoylphenoxy)octadecylammonium chloride **4b** (0.383 g, 77.0% crude yield) C₃₆H₅₈ClNO₂; pale yellow powder; ¹H NMR (CDCl₃, 400 MHz) δ= 0.88 (m, -CH₃-, 3H), 1.30 (m, -CH₂-, 34H), 3.40 (6H, s), 3.45 (m, N-CH₃2H), 3.71 (s, -CH₂-, 2H), 4.06 (s, O-CH₂-, 2H), 6.95 (m, -Ar, 2H), 7.45 (m, -Ar, 2H), 7.55 (m, -Ar, 1H), 7.75 (m, -Ar, 2H), 7.81 (m, -Ar, 2H) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 195.47 (C5), 161.58 (C9), 137.95 (C4), 132.48 (C3), 131.91 (C7), 130.75 (C1), 129.72 (C6), 128.25 (C2), 114.10 (C8), 68.90 (C10), 64.46 (C14), 61.14 (C12), 51.50 (C13), 31.90 (C22), 29.63 (C18), 29.39 (C17), 29.34 (C21), 27.36 (C16), 26.25 (C15), 23.16 (C11), 22.75 (C23), 14.11 (C24) ppm. **HRMS-DART** (m/z): [M⁺ - Cl] calcd. for C₃₆H₅₈ClNO₂, 536.4461; found, 536.4462.

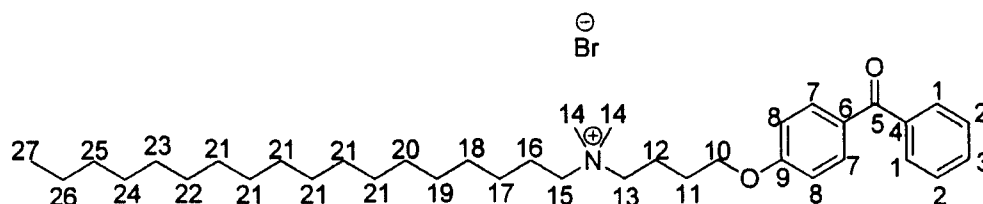
Example 11 - Propyl-dimethyl (benzoylphenoxy)octadecylammonium iodide 4c

According to the general procedure for the quaternization of *N*-dimethyloctadecylamine with 4-*O*-(*n*-haloalkyl)benzophenone, 4-*O*-(3-iodopropyl)benzophenone **1c** (0.575 mmol, 0.211 g) and *N*-dimethyloctadecylamine (0.633 mmol, 0.188 g) were stirred in acetonitrile (1 mL) in an 100°C sand bath for 24 hours to give crude product of propyl-dimethyl (benzoylphenoxy)octadecylammonium iodide to yield the desired product, **4c** (0.363 g, 95.1% yield). C₃₆H₅₈I NO₂; white powder. ¹H NMR (400 MHz, CDCl₃, δ): 0.87 (m, H₂₀, 3H), 1.24 (m,

H18-H16, 26H), 1.84 (m, H11, 2H), 3.37 (s, H13, 6H), 3.48 (m, H14, 2H), 4.05 (m, H 10, 2H), 6.95 (m, -Ar, 2H), 7.45 (m, -Ar, 3H), 7.74 (m, -Ar, 2H), 7.81 (m, -Ar, 2H) ppm; ^{13}C NMR (100 MHz, CDCl_3 , δ): 130.55 (C8), 124.53 (C9), 66.54 (C7), 64.01 (C6), 50.43 (C5), 31.91 (C2), 29.69-26.24 (C2, C14 OVERLAPPING), 26.26 (C3), 22.76 (C4), 14.11 (C1) ppm. **HRMS-**

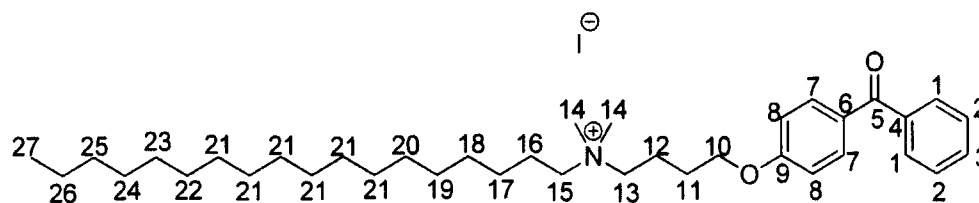
DART (m/z): [$\text{M}^+ - \text{I}$] calcd. for $\text{C}_{36}\text{H}_{58}\text{INO}_2$, 536.4449; found, 536.4462.

Example 12 - Butyl-dimethyl (benzoylphenoxy)octadecylammonium bromide 5a



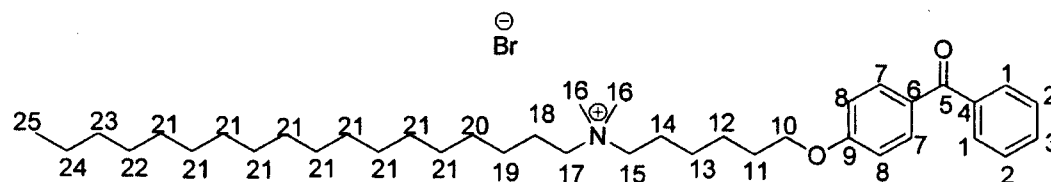
According to the general procedure for the quaternization of *N*-dimethyloctadecylamine with 4-*O*-(*n*-haloalkyl)benzophenone, 4-*O*-(4-bromobutyl)benzophenone (0.752 mmol, 0.251 g) and *N*-dimethyloctadecylamine (0.827 mmol, 0.246 g) and acetonitrile (1 mL) were stirred in an 100°C sand bath for 24 hours to give crude product butyl-dimethyl (benzoylphenoxy)octadecylammonium bromide **5a** (0.551 g, 100% crude yield). $\text{C}_{37}\text{H}_{61}\text{BrNO}_2$; white powder; mp 83-87°C; ^1H NMR (CDCl_3 , 400 MHz) δ = 0.88 (m, $-\text{CH}_3$ -, 3H), 1.30 (m, $-\text{CH}_2$ -, 34H), 3.40 (6H, s), 3.45 (m, $-\text{CH}_2$ -, 2H), 3.71 (s, $-\text{CH}_2$ -, 2H), 4.06 (s, $\text{O}-\text{CH}_2$ -, 2H), 6.95 (m, -Ar, 2H), 7.45 (m, -Ar, 2H), 7.55 (m, -Ar, 1H), 7.75 (m, -Ar, 2H), 7.81 (m, -Ar, 2H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 195.49 (C5), 162.13 (C9), 138.07 (C4), 132.58 (C3), 132.02 (C7), 130.43 (C1), 129.71 (C6), 128.23 (C2), 114.06 (C8), 66.93 (C10), 64.11 (C13), 63.40 (C15), 51.19 (C14), 31.90 (C24), 29.69 (C23), 29.64 (C22), 29.58 (C21), 29.46 (C20), 29.39 (C19), 29.34 (C18), 29.22 (C11), 26.27 (C17), 25.81 (C16), 22.81 (C25), 22.67 (C26), 19.77 (C12), 14.12 (C27) ppm. **HRMS-DART** (m/z): [$\text{M}^+ - \text{Br}$] calcd. for $\text{C}_{37}\text{H}_{60}\text{BrNO}_2$, 550.4632; found, 550.4618.

Example 13 - Butyl-dimethyl (benzoylphenoxy)octadecylammonium iodide 5c



According to the general procedure for the quaternization of *N*-dimethyloctadecylamine with 4-*O*-(*n*-haloalkyl)benzophenone, 4-*O*-(4-iodobutyl)benzophenone **2c** (0.660 mmol, 0.250 g) and *N*-dimethyloctadecylamine (0.720 mmol, 0.215 g) were stirred in acetonitrile (1.00 mL) in an 100°C sand bath for 24 hours to give crude product butyl-dimethyl (benzoylphenoxy)octadecylammonium iodide purified to give compound **5c** (0.207 g, 46.3% yield). C₃₇H₆₀INO₂; white powder. ¹H NMR (400 MHz, CDCl₃, δ): 0.85 (m, H₂₇, 3H), 1.21 (m, H₂₆-H₁₈, 29H), 1.71 (m, H₁₂, 2H), 1.97 (m, H₁₁, 3H), 3.36 (m, H₁₄, 6H), 3.51 (m, H₁₃, 2H), 3.74 (m, H₁₅, 2H), 4.13 (m, H₁₀, 2H), 6.96 (m, -Ar, 2H), 7.42 (m, -Ar, 2H), 7.52 (m, -Ar, 1H), 7.70 (m, -Ar, 2H), 7.77 (m, -Ar, 2H) ppm; ¹³C NMR (100 MHz, CDCl₃, δ): 195.51 (C₅), 162.15 (C₉), 138.06 (C₄), 132.55 (C₃), 132.03 (C₇), 130.36 (C₁), 129.70 (C₆), 128.24 (C₂), 114.16 (C₈), 67.02 (C₁₀), 64.51 (C₁₃), 63.77 (C₁₅), 51.48 (C₁₄), 31.90 (C₂₄), 29.69 (C₂₃), 29.64 (C₂₂), 29.61 (C₂₁), 29.48 (C₂₀), 29.40 (C₁₉), 29.34 (C₁₈), 29.21 (C₁₁), 26.21 (C₁₇), 25.70 (C₁₆), 22.86 (C₂₅), 22.67 (C₂₆), 19.81 (C₁₂), 14.11 (C₂₇) ppm. HRMS-DART (m/z): [M⁺ - Cl] calcd. for C₃₇H₆₀INO₂, 550.4635; found, 550.4618.

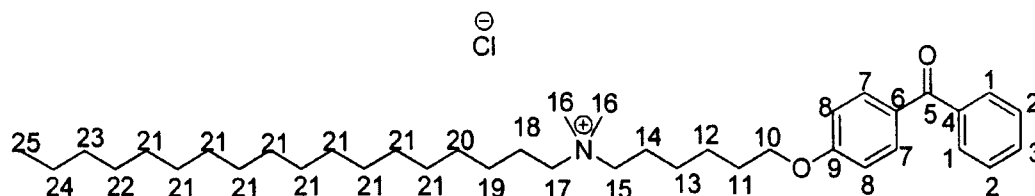
Example 14 - Hexyl-dimethyl (benzoylphenoxy)octadecylammonium bromide **6a**



According to the general procedure for the quaternization of *N*-dimethyloctadecylamine with 4-*O*-(*n*-haloalkyl)benzophenone, 4-*O*-(6-bromohexyl)benzophenone **3a** (0.692 mmol, 0.250 g) and *N*-dimethyloctadecylamine (0.761 mmol, 0.227 g) were stirred in acetonitrile (1 mL) in an 100°C sand bath for 24 hours to give crude product of hexyl-dimethyl (benzoylphenoxy)octadecylammonium bromide to yield the desired product, **6a** (0.429 g, 94.1% yield). C₃₉H₆₄BrNO₂; off white powder. ¹H NMR (400 MHz, CDCl₃, δ): 0.89 (m, H₂₅, 3H), 1.26 (m, H₂₃-H₁₉, H₁₃, 32H), 1.58 (s, H₂₄, H₁₂, H₁₈, H₁₄, H₁₁, 10H), 3.39 (s, H₁₆, 6H), 3.50 (m, H₁₅, 2H), 3.54 (m, H₁₇, 2H), 4.07 (m, H₁₀, 2H), 6.95 (m, -Ar, 2H), 7.42 (m, -Ar, 2H), 7.55 (m, -Ar, 1H), 7.75 (m, -Ar, 2H), 7.80 (m, -Ar, 2H) ppm; ¹³C NMR (100 MHz, CDCl₃, δ): 195.54 (C₅), 162.63 (C₉), 138.22 (C₄), 132.53 (C₃), 131.90 (C₁, C₇ OVERLAPPING), 129.68 (C₆), 128.19 (C₂), 114.03 (C₈), 67.75 (C₁₀, C₁₅ C₁₇ OVERLAPPING), 51.18 (C₁₆), 31.90 (C₂₃),

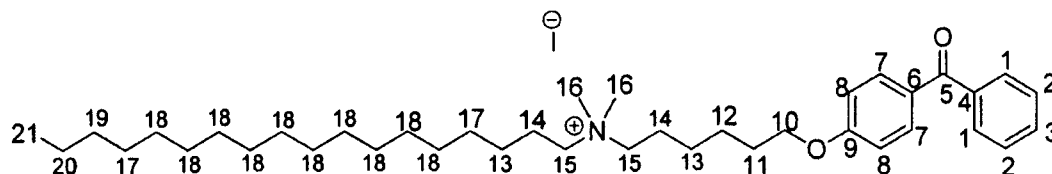
29.68 (C21), 29.63 (C20), 29.58 (C19), 29.38 (C11), 29.34 (C22), 26.27 (C13, C15 OVERLAPPING), 25.68 (C12), 25.36 (C18), 22.81 (C23), 22.68 (C24), 18.46 (C14), 14.12 (C25) ppm. **HRMS-DART** (m/z): [$M^+ - Br$] calcd. for $C_{39}H_{64}BrNO_2$, 578.4958; found, 578.4931.

5 Example 15 - Hexyl-dimethyl (benzoylphenoxy)octadecylammonium chloride 6b



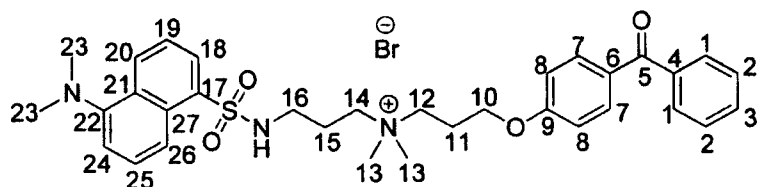
According to the general procedure for the quaternization of *N*-dimethyloctadecylamine with 4-O-(n-haloalkyl)benzophenone, 4-O-(6-chlorohexyl)benzophenone **3b** (0.789 mmol, 0.250 g) and *N*-dimethyloctadecylamine (0.868 mmol, 0.258 g) were stirred in acetonitrile (1 mL) in an 100°C sand bath for 24 hours to give crude product of hexyl-dimethyl (benzoylphenoxy)octadecylammonium chloride purified to yield the desired product, **6b** (0.311 g, 64.1 % yield). $C_{39}H_{64}ClNO_2$; pale yellow powder. 1H NMR (400 MHz, $CDCl_3$, δ): 0.86 (m, H25, 3H), 1.24 (m, H24-H18, 29H), 1.52 (m, H12, H13, 4H), 1.80 (m, H17, 2H), 2.29 (m, H14, 2H), 3.39 (m, H15, H17, 4H), 3.55 (m, H11, 2H), 4.03 (s, H10, 2H), 6.93 (m, -Ar, 2H), 7.44 (m, -Ar, 2H), 7.54 (m, -Ar, 1H), 7.75 (m, -Ar, 2H) 7.81 (m, -Ar, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ): 195.56 (C5), 162.75 (C9), 138.23 (C4), 132.56 (C3), 131.92 (C7), 131.86 (C1), 129.96 (C6), 128.19 (C2), 128.17 (C2), 114.00 (C8), 113.98 (C8), 67.99 (C10), 67.70 (C15), 59.90 (C16), 31.90 (C25), 29.69 (C23), 29.64 (C22), 29.58 (C21), 29.46 (C20), 29.39 (C19), 29.34 (C18), 29.22 (C11), 26.27 (C17), 25.36 (C16), 22.81 (C25), 22.68 (C20), 18.46 (C14), 14.12 (C27) ppm. **HRMS-DART** (m/z): [$M^+ - Cl$] calcd. for $C_{39}H_{64}ClNO_2$, 578.4948; found, 578.4931.

Example 16 - Hexyl-dimethyl (benzoylphenoxy)octadecylammonium iodide 6c.



According to the general procedure for the quaternization of N-dimethyloctadecylamine with 4-O-(n-haloalkyl)benzophenone, 4-O-(6-iodohexyl)benzophenone **3c** (0.612 mmol, 0.250 g) and N-dimethyloctadecylamine (0.674 mmol, 0.200 g) were stirred in acetonitrile (1 mL) in an 100°C sand bath for 24 hours to give crude product of hexyl-dimethyl (benzoylphenoxy)octadecylammonium iodide purified to yield the desired product **6c** (0.373 g, 86.3% yield). $C_{39}H_{64}INO_2$; white powder. 1H NMR (400 MHz, $CDCl_3$, δ): 0.86 (m, H21, 3H), 1.23 (m, H20-H18, H13-H11, 36H), 1.77 (m, H14, 2H), 2.36 (m, H17, 2H), 3.51 (s, H16, 6H), 3.84 (s, H15, 2H), 4.24 (s, H10, 2H), 6.95 (m, -Ar, 2H), 7.45 (m, -Ar, 2H), 7.55 (m, -Ar, 1H), 7.78 (m, -Ar, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ): 195.56 (C5), 162.75 (C9), 138.23 (C4), 132.56 (C3), 131.92 (C7), 131.86 (C1), 129.96 (C6), 128.19 (C2), 128.17 (C2), 114.00 (C8), 113.98 (C8), 67.99 (C10), 67.70 (C15), 59.90 (C16), 31.90 (C25), 29.69 (C23), 29.64 (C22), 29.58 (C21), 29.46 (C20), 29.39 (C19), 29.34 (C18), 29.22 (C11), 26.27 (C17), 25.36 (C16), 22.81 (C25), 22.68 (C20), 18.46 (C14), 14.12 (C27) ppm. HRMS-DART (m/z): $[M^+ - I]$ calcd. for $C_{39}H_{64}INO_2$, 578.4938; found, 578.4931.

Example 17 - 3-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylpropan-1-ammonium bromide **7a**

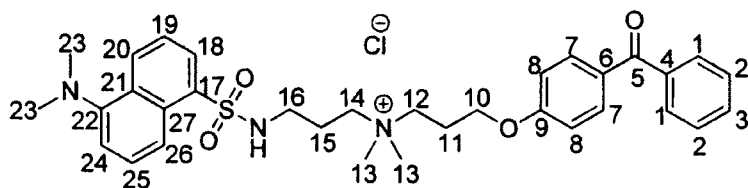


According to the general procedure of quaternization of compound **10** with 4-O-(n-haloalkyl)benzophenone, compound **10** (0.712 mmol, 0.239 g) and 4-O-(3-bromopropyl)benzophenone **1a** (0.783 mmol, 0.250 g) were dissolved in acetonitrile (2 mL) and left to stir in a 100°C sand bath for 24 hours. The resultant residue was precipitated using cold diethyl ether (4 mL) to obtain the desired product 3-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylpropan-1-ammonium

bromide, **7a** (0.345 g, 74.0 % yield). $C_{33}H_{40}BrN_3O_4S$; puffy yellow powder. 1H NMR (400 MHz, $CDCl_3$, δ): 1.78 (m, H15, H16, 4H), 2.22 (m, H11, 2H), 2.82 (s, H23, 6H), 3.10 (m, H17, 2H), 3.22 (m, H13, 6H), 3.62 (m, H14, 2H), 3.72 (m, H12, 2H), 4.07 (m, H10, 2H), 6.85 (m, Ar, 2H), 6.99 (m, Ar, 1H), 7.12 (m, Ar, 1H), 7.55 (m, Ar, 2H), 7.75 (m, Ar, 6H), 7.85 (m, Ar, 1H);

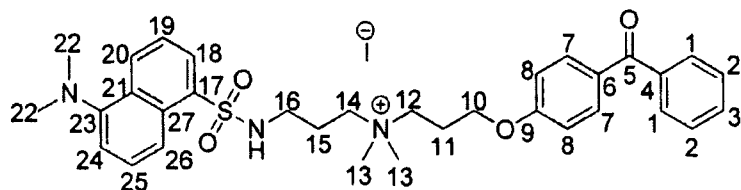
¹³C NMR (100 MHz, CDCl₃, δ): 195.48 (C5), 161.65 (C9), 137.98 (C4), 132.57 (C27), 132.44 (C3), 130.54 (C7), 130.39 (C1), 129.72 (C6), 128.71 (C2), 128.25 (C20), 128.20 (C25), 128.18 (C19), 123.35 (C26), 118.21 (C21), 115.32 (C24), 114.13 (C8), 68.92 (C10), 64.46 (C14), 62.09 (C12), 51.37 (C13), 45.36 (C23), 22.91 (C11) ppm. HRMS-DART (m/z): [M⁺ - Br] calcd. for C₃₃H₄₀BrN₃O₄S, 574.2749; found, 574.2734.

Example 18 - 3-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylpropan-1-ammonium chloride 7b



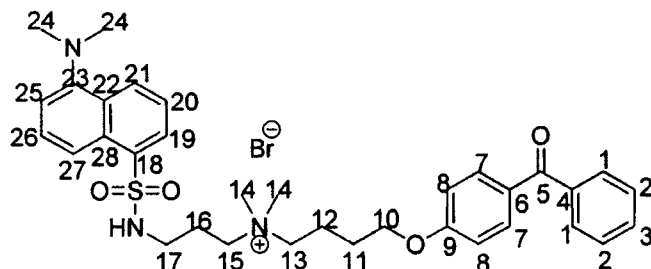
According to the general procedure of quaternization of compound **10** with haloalkoxy(phenyl)(phenyl)methanone, compound **10** (0.870 mmol, 0.291 g) and (4-(3-chloropropoxy)phenyl)(phenyl)methanone **1b** (0.790 mmol, 0.250 g) were dissolved in acetonitrile (2 mL) and left to stir in a 100°C sand bath for 24 hours. The resultant residue was precipitated using cold diethyl ether (4 mL) to obtain the desired product 3-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylpropan-1-ammonium chloride, **7b** (0.250 g, 51.9 % yield). C₃₃H₄₀ClN₃O₄S; puffy yellow powder. ¹H NMR (400 MHz, CDCl₃, δ): 1.55 (m, H16, H15, 4H), 1.99 (m, H11, 2H), 2.82 (m, H12, 2H), 2.85 (s, H23, 6H), 3.15 (m, H13, 6H), 4.21 (m, H10, 2H), 6.81 (m, Ar, 1H), 6.95 (m, Ar, 1H), 7.18 (m, Ar, 3H), 7.51 (m, Ar, 2H), 7.75 (m, Ar, 4H), 7.81 (m, Ar, 2H), 8.21 (m, Ar, 3H), 8.29 (m, Ar, 1H), 8.45 (m, Ar, 1H) ppm; ¹³C NMR (100 MHz, CDCl₃, δ): 195.53 (C5), 162.33 (C9), 138.22 (C4), 132.57 (C27), 132.46 (C3), 130.32 (C7), 130.01 (C1), 129.88 (C6), 128.24 (C2), 128.20 (C20), 128.10 (C25), 123.17 (C26), 118.99 (C21), 115.01 (C24), 114.06 (C8), 64.49 (C14), 59.94 (C12), 59.49 (C13), 45.42 (C23), 32.05 (C16), 24.64 (C11), 24.61 (C15) ppm. HRMS-DART (m/z): [M⁺ - Cl] calcd. for C₃₃H₄₀ClN₃O₄S, 574.2751; found, 574.2734.

Example 19 - 3-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylpropan-1-ammonium iodide 7c



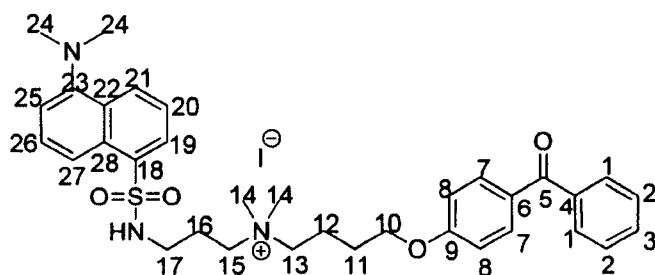
According to the general procedure of quaternization of compound **10** with halo-alkoxy(phenyl)(phenyl)methanone, compound **10** (0.750 mmol, 0.252 g) and (4-(3-iodopropoxy)phenyl)(phenyl)methanone **1c** (0.680 mmol, 0.250 g) were dissolved in acetonitrile (2 mL) and left to stir in a 100°C sand bath for 24 hours. The resultant residue was precipitated using cold di-ethyl ether (4 mL) to obtain the desired product 3-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylpropan-1-ammonium iodide, **7c** (0.267 g, 55.9 % yield) C₃₃H₄₀IN₃O₄S; puffy yellow powder. ¹H NMR (400 MHz, CDCl₃, δ): 1.99 (m, H15, 2H), 2.20 (m, H11, 2H), 2.80 (s, H22, 6H), 3.08 (m, H14, 2H), 3.15 (m, H13, 6H), 3.69 (m, H12, 2H), 3.71 (m, H16, 2H), 4.09 (m, H10, 2H), 6.95 (m, Ar, 2H), 7.18 (m, Ar, 3H), 7.45 (m, Ar, 2H), 7.55 (m, Ar, 1H), 7.75 (m, Ar, 2H), 7.85 (m, Ar, 2H), 8.21 (m, Ar, 3H), 8.29 (m, Ar, 1H) ppm; ¹³C NMR (100 MHz, CDCl₃, δ): 195.48 (C5), 161.65 (C9), 137.98 (C4), 134.79 (C27), 132.57 (C3), 130.54 (C7), 130.39 (C1), 129.72 (C6), 128.71 (C2), 128.25 (C21), 128.20 (C26), 123.35 (C27), 118.21 (C22), 115.32 (C25), 114.13 (C8), 68.92 (C10), 64.46 (C14), 62.09 (C12), 51.37 (C13), 45.36 (C22), 22.91 (C15) ppm. HRMS-DART (m/z): [M⁺ - I] calcd. for C₃₃H₄₀IN₃O₄S, 574.2753; found, 574.2734.

Example 20 - 4-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylbutan-1-ammonium bromide 8a



According to the general procedure of quaternization of compound **10** with haloalkoxy(phenyl)(phenyl)methanone, compound **10** (0.717 mol, 0.240 g) and (4-(4-bromobutoxy)phenyl)(phenyl)methanone **2a** (0.721 mmol, 0.240 g) were dissolved in acetonitrile (2 mL) and left to stir in a 100°C sand bath for 24 hours. The resultant residue was precipitated using cold di-ethyl ether (4 mL) to obtain the desired product 4-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylbutan-1-ammonium bromide, **8a** (0.168 g, 35.0 % yield). C₃₄H₄₂BrN₃O₄S; puffy yellow powder. mp 96-104 °C. ¹H NMR (400 MHz, CDCl₃, δ): 1.84 (m, H17, H16, H12, H11, 8H), 2.84 (s, H24, 6H), 3.14 (m, H15, H14, H13, 10H), 4.03 (m, H10, 2H), 6.90 (m, Ar, 2H), 7.12 (m, Ar, 1H), 7.45 (m, Ar, 3H), 7.56 (m, Ar, 2H), 7.75 (m, Ar, 4H), 8.20 (m, Ar, 1H), 8.47 (m, Ar, 2H) ppm; ¹³C NMR (100 MHz, CDCl₃, δ): 195.56 (C5), 162.22 (C9), 151.83 (C24), 138.09 (C4), 132.51 (C28), 132.00 (C3), 130.38 (C7), 130.20 (C1), 129.74 (C6), 129.45 (C2), 129.27 (C21), 128.23 (C26), 123.33 (C19), 115.34 (C25), 114.11 (C8) 67.00 (C10), 51.11 (C14), 45.39 (C23), 39.81 (C17), 22.86 (C12) ppm. HRMS-DART (m/z): [M⁺ - Br] calcd. for C₃₄H₄₂BrN₃O₄S, 588.2908; found, 588.2890.

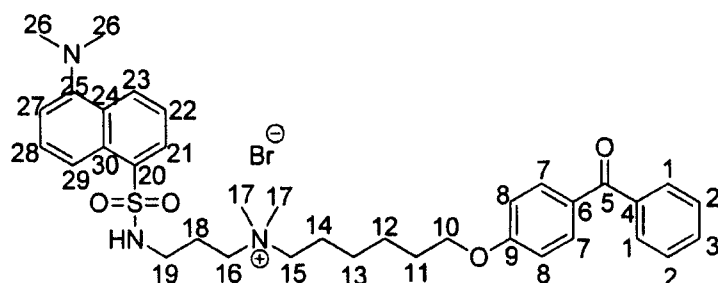
Example 21 - 4-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylbutan-1-ammonium iodide **8c.**



According to the general procedure of quaternization of compound **10** with haloalkoxy(phenyl)(phenyl)methanone, compound **10** (0.598 mmol, 0.201 g) and (4-(4-iodobutoxy)phenyl)(phenyl)methanone **2c** (0.658 mmol, 0.250 g) were dissolved in acetonitrile (2 mL) and left to stir in a 100°C sand bath for 24 hours. The resultant residue was precipitated using cold diethyl ether (4 mL) to obtain the desired product 4-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylbutan-1-ammonium iodide, **8c** (0.244 g, 56.9 % yield). C₃₄H₄₂IN₃O₄S; puffy yellow powder. ¹H NMR (400 MHz, CDCl₃, δ):

1.62 (m, H11, 2H), 1.97 (m, H16, H12, 4H), 2.84 (s, H24, 6H), 3.15 (m, H12, H14, 8H), 3.48 (m, H13, H15, 4H), 3.60 (m, H17, 2H), 4.07 (m, H10, 2H), 6.91 (m, Ar, 3H), 7.15 (m, Ar, 1H), 7.45 (m, Ar, 3H), 7.57 (m, Ar, 2H), 7.75 (m, Ar, 4H), 8.19 (m, Ar, 1H), 8.42 (m, Ar, 1H), 8.50 (m, Ar, 1H); ^{13}C NMR (100 MHz, CDCl_3 , δ): 195.61 (C5), 162.22 (C9), 151.92 (C23), 138.06 (C4), 134.37 (C28), 132.52 (C3), 130.58 (C7), 130.19 (C1), 129.71 (C6), 129.32 (C2), 128.91 (C21), 128.26 (C26), 123.40 (C19), 114.20 (C8), 67.03 (C10), 51.39 (C14), 45.40 (C24), 30.04 (C11), 25.65 (C12), 19.65 (C15) ppm. HRMS-DART (m/z): $[\text{M}^+ - \text{I}]$ calcd. for $\text{C}_{34}\text{H}_{42}\text{IN}_3\text{O}_4\text{S}$, 588.2904; found, 588.2890.

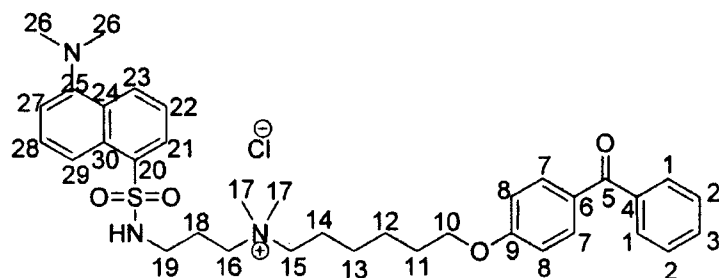
Example 22 - 6-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylhexan-1-ammonium bromide 9a



According to the general procedure of quaternization of compound **10** with haloalkoxy(phenyl)(phenyl)methanone, compound **10** (0.629 mmol, 0.211 g) and 4-((6-bromohexyl)oxy)phenyl)(phenyl)methanone **3a** (0.692 mmol, 0.250 g) were dissolved in acetonitrile (2 mL) and left to stir in a 100°C sand bath for 24 hours. The resultant residue was precipitated using cold diethyl ether (4 mL) to obtain the desired product 6-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylhexan-1-ammonium bromide, **9a** (0.385 g, 87.8 % yield). $\text{C}_{34}\text{H}_{42}\text{BrN}_3\text{O}_4\text{S}$; puffy yellow powder. ^1H NMR (400 MHz, CDCl_3 , δ): 1.36 (m, H13, 2H), 1.48 (m, H12, 2H), 1.76 (m, H18, H14, H11, 6H), 2.84 (s, H26, 6H), 3.12 (s, H17, 6H), 3.33 (m, H19, 2H), 3.63 (m, H16, 2H), 4.06 (m, H10, 2H), 6.95 (m, Ar, 1H), 7.10 (m, Ar, 2H), 7.40 (m, Ar, 1H), 7.60 (m, Ar, 4H), 7.80 (m, Ar, 3H), 8.20 (m, Ar, 1H), 8.45 (m, Ar, 2H) ppm; ^{13}C NMR (100 MHz, CDCl_3 , δ): 195.58 (C5), 162.69 (C9), 151.79 (C26), 138.20 (C4), 134.94 (C30), 132.51 (C3), 131.92 (C7), 131.86 (C1), 129.87 (C6), 128.69 (C2), 128.21 (C22), 128.18 (C27), 123.33 (C21), 115.31 (C25), 114.00 (C8), 67.81 (C10), 51.04 (C17), 45.39 (C26), 33.77 (C19), 32.61 (C11), 28.92 (C11), 28.71 (C18), 27.86 (C13), 25.79

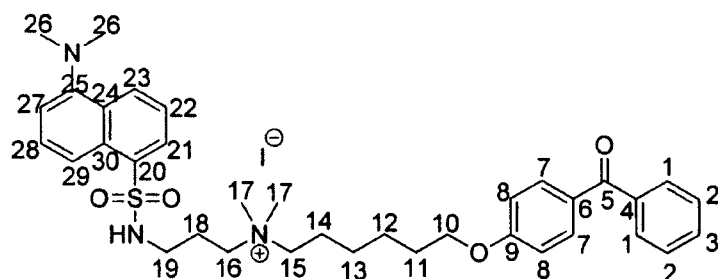
(C12), 25.43 (C14) ppm. **HRMS-DART** (m/z): $[M^+ - Br]$ calcd. for $C_{34}H_{42}BrN_3O_4S$, 616.3224; found, 616.3203.

Example 23 - 6-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylhexan-1-ammonium chloride 9b



According to the general procedure of quaternization of compound **10** with haloalkoxy(phenyl)(phenyl)methanone, compound **10** (0.870 mmol, 0.291 g) and (4-(6-chlorohexyl(oxy)))phenyl(phenyl)methanone **3b** (0.790 mmol, 0.250 g) were dissolved in acetonitrile (2 mL) and left to stir in a 100°C sand bath for 24 hours. The resultant residue was precipitated using cold di-ethyl ether (4 mL) to obtain the desired product 6-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylhexan-1-ammonium chloride, **9b** (0.435 g, 84.5 % yield). $C_{36}H_{46}ClN_3O_4S$; puffy yellow powder. **1H NMR** (400 MHz, $CDCl_3$, δ): 1.18 (m, H13, 2H), 1.51 (m, H12, H19, 4H), 1.83 (m, H14, H18, 4H), 2.20 (m, H11, 2H), 2.81 (m, H15, H16, 4H), 2.87 (s, H26, 6H), 3.03 (s, H17, 6H), 4.03 (m, H10, 2H), 6.95 (m, Ar, 1H), 7.10 (m, Ar, 2H), 7.40 (m, Ar, 1H) 7.60 (m, Ar, 4H), 7.80 (m, Ar, 3H), 8.20 (m, Ar, 1H), 8.45 (m, Ar, 2H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, δ): 195.58 (C5), 162.76 (C9), 151.89 (C25), 138.31 (C4), 134.74 (C29), 132.57 (C3), 131.91 (C7), 131.87 (C1), 129.96 (C6), 129.62 (C2), 128.60 (C24), 128.20 (C28), 128.18 (C23), 115.29 (C27), 114.03 (C8), 68.00 (C10), 50.93 (C16), 45.42 (C26), 44.42 (C19), 32.46 (C11), 28.96 (C18), 28.72 (C13), 26.59 (C12), 25.82 (C14), 25.46 (C17) ppm. **HRMS-DART** (m/z): $[M^+ - Cl]$ calcd. for $C_{36}H_{46}ClN_3O_4S$, 616.3221; found, 616.3203.

Example 24 - 6-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-N,N-dimethylhexan-1-ammonium iodide 9c



According to the general procedure of quaternization of compound **10** with halo-alkoxy(phenyl)(phenyl)methanone, compound **10** (0.366 mmol, 0.272 g) and 4-((6-iodohexyl)oxy)phenyl)(phenyl)methanone **3c** (0.333 mmol, 0.136 g) were dissolved in acetonitrile (2 mL) and left to stir in a 100°C sand bath for 24 hours. The resultant residue was precipitated using cold diethyl ether (4 mL) to obtain the desired product 6-(4-benzoylphenoxy)-N-(3-(5-(dimethylamino) naphthalene-1-sulfonamido)propyl)-N,N-dimethylhexan-1-ammonium iodide, **9c** (0.232 g, 93.5% yield). $C_{36}H_{46}IN_3O_4S$; puffy yellow powder. 1H NMR (400 MHz, $CDCl_3$, δ): 1.34 (m, H13, 2H), 1.46 (m, H18, 2H), 1.73 (m, H12, 2H), 2.00 (m, H11, 2H), 2.83 (s, H26, 6H), 3.10 (m, H16, 17, 8H), 3.29 (m, H15, 2H), 3.54 (m, H19, 2H), 3.95 (m, H10, 2H), 6.90 (m, Ar, 2H), 7.10 (m, Ar, 1H), 7.50 (m, Ar, 6H), 7.75 (m, Ar, 4H), 8.20 (m, Ar, 1H), 8.40 (m, Ar, 1H), 8.49 (m, Ar, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ): 195.63 (C5), 162.69 (C9), 138.21 (C4), 134.45 (C30), 132.54 (C3), 131.95 (C7), 129.92 (C6), 129.74 (C2), 129.72 (C24), 128.22 (C27), 115.29 (C26), 114.11 (C8), 67.83 (C10), 51.35 (C17), 45.42 (C24), 28.96 (C11), 28.71 (C13), 25.47 (C14) ppm. HRMS-DART (m/z): $[M^+ - I]$ calcd. for $C_{36}H_{46}IN_3O_4S$, 616.3217; found, 616.3203.

Table 1: Physio-chemical data of 4-O-(n-haloalkyl)benzophenone derivatives

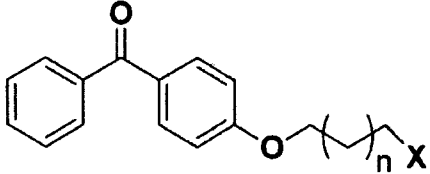
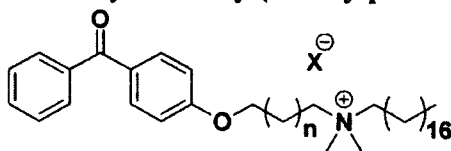
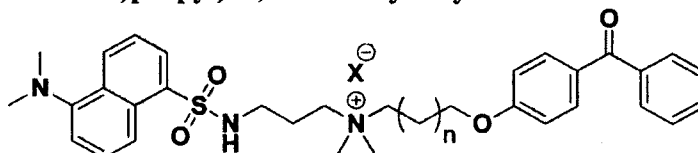
 Compound	n	X	Molecular Formula	MW (g/mol)	m.p. (°C) (Literature)
1a	1	Br	C ₁₆ H ₁₅ BrO ₂	319.19	54-66
1b	1	Cl	C ₁₆ H ₁₅ ClO ₂	274.74	58-63 (53-55)
2a	2	Br	C ₁₇ H ₁₇ BrO ₂	333.22	—
3a	4	Br	C ₁₉ H ₂₁ BrO ₂	361.27	47-55
3b	4	Cl	C ₁₉ H ₂₁ ClO ₂	316.82	—

Table 2: Physio-chemical data of alkyl-dimethyl(benzoylphenoxy)alkylammonium salts

Compound	n	X	Molecular Formula	MW (g/mol)	m.p. (°C)	Percent Yield
4a	1	Br	C ₃₆ H ₅₈ BrNO ₂	616.75	58-68	79.2
4b	1	Cl	C ₃₆ H ₅₈ ClNO ₂	572.30	—	77.0
4c	1	I	C ₃₆ H ₅₈ INO ₂	663.75	—	95.1
5a	2	Br	C ₃₇ H ₆₁ BrNO ₂	630.78	83-87	67.9
5c	2	I	C ₃₇ H ₆₁ INO ₂	677.78	—	46.3
6a	4	Br	C ₃₈ H ₆₁ BrNO ₂	658.83	91-96	94.1
6b	4	Cl	C ₃₈ H ₆₁ ClNO ₂	614.38	58-64	64.1
6c	4	I	C ₃₈ H ₆₁ INO ₂	705.83	—	86.3

Table 3: Physio-chemical data of *n*-(4-benzoylphenoxy)-*N*-(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)-*N,N*-dimethylalkyl-1-ammonium halide derivatives



Compound	n	X	Molecular Formula	Molecular Weight (g/mol)	m.p. (°C)	Percent Yield (%)
7a	1	Br	C₃₃H₄₀BrN₃O₄S	654.65	82-87	74.0
7b	1	Cl	C ₃₃ H ₄₀ ClN ₃ O ₄ S	610.20	--	51.9
7c	1	I	C₃₃H₄₀IN₃O₄S	701.65	--	55.9
8a	2	Br	C₃₄H₄₂BrN₃O₄S	668.68	96-104	35.0
8c	2	I	C₃₄H₄₂BrN₃O₄S	715.68	--	56.9
9a	4	Br	C₃₆H₄₆BrN₃O₄S	696.73	77	87.8
9b	4	Cl	C₃₆H₄₆BrN₃O₄S	652.28	--	84.5
9c	4	I	C₃₆H₄₆BrN₃O₄S	743.73	--	93.5

5

Preparation of Self Assembled Monolayers on Polyvinylchloride (PVC)

PVC was cut into rectangles and substrates were rinsed in isopropyl alcohol (IPA) and water then dried in an oven for 30 minutes. A 0.05% and 0.5% (w/v) solution of **6a** was made in H₂O/MeOH and electrospayed on the clean substrates three consecutive times with 5 minutes of irradiation time with UV in a fumehood in-between each spray. After the last spray substrates were irradiated once more for an additional 25 minutes. Unbound material was later rinsed from the substrates using H₂O.

Preparation of Self Assembled Monolayers on Silicone Tubing**Using peristaltic pump**

Silicone tubing was rinsed with IPA and H₂O using a peristaltic pump then dried by running air through the tubes. A 0.05% (w/v) solution of **8a** in H₂O and a 0.5% (w/v) solution of **4c** in H₂O/IPA were prepared. Tubes were coated using the peristaltic pump and filled tubes were irradiated using a UV fumehood for 25 minutes. Coated tubes were then rinsed with H₂O to remove any unbound materials.

Using a syringe

1.5% (w/v) solutions of **8a** and **4c** in dichloromethane (DCM) were prepared. These solutions were pumped through clean silicone tubing using a syringe and irradiated using a UV quartz lamp for 30 minutes.

Antimicrobial Test Method

The antimicrobial efficacy was determined using a flow-cell method as described in Markison C and Swan J, "The Effect of Humidity on the Survival of MRSA on Hard Surfaces", Indoor and Built Environment, 2006, 15(1), 85-91. A 1% tryptic soy broth and an inoculum of 10×10^4 cfu/mL of *Pseudomonas spp.* CTO7 were pumped through silicone tubing coated with **8a**, **4c** and a control tube for 30 hours. The tubes were then left stagnant for a period of 2 hours after which only the 1% TSB was allowed to flow through the tubes for 48 hours. During these 48 hours effluent samples of 100 μ L were collected periodically and plated on 10% trypticase soy agar (TSA) in a dilution series up to 10×10^4 . Sampling periods were time zero, 3 hours, 6 hours, 24 hours, 27 hours, 30 hours, and 48 hours. The number of colonies grown on each plate was counted in order to determine antimicrobial activity.

Table 4: *Pseudomonas* bacterial cell count on silicone tubing coated with 8a

Time (hr)	Concentration of samples (cfu/mL)				
	10^0	10^{-1}	10^{-2}	10^{-3}	10^{-4}
0	0	0	0	0	0
3	15	0	0	0	0
6	6	0	0	0	0
24	0	0	0	0	0
27	30	0	0	0	0
30	18	4	0	0	0
48	27	1	0	0	0

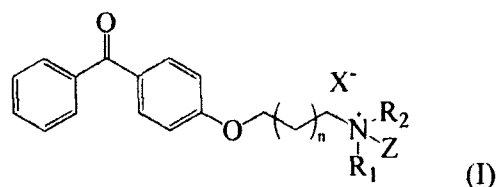
Table 5: *Pseudomonas* spp. CT07 bacterial cell count on silicone tubing coated with 4c

Time (hr)	Concentration of samples (cfu/mL)				
	10^0	10^{-1}	10^{-2}	10^{-3}	10^{-4}
0	300	300	48	8	0
3	20	0	0	0	0
6	160	15	0	0	0
24	300	200	21	4	0
27	300	110	11	0	0
30	300	70	5	0	0
48	289	31	0	0	0

- 5 The scope of the claims should not be limited by the preferred embodiments set forth in the examples, but should be given the broadest interpretation consistent with the description as a whole.

We claim:

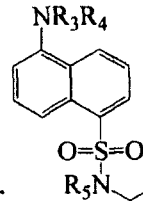
1. A quaternary ammonium compound of formula (I):



wherein n is 1, 2, 3 or 4;

R_1 and R_2 are independently methyl, ethyl, n-propyl or i-propyl;

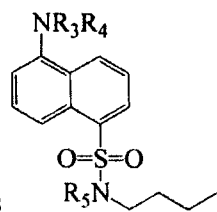
Z is  wherein m is selected from the group consisting of 12, 13, 14, 15, 16, 17 and

18, or  wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl; and

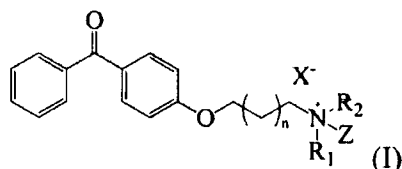
X is a halogen selected from the group consisting of chloro, bromo and iodo, with the proviso that when X is bromo, n is 1 and R_1 and R_2 are methyl, m cannot be 17.

2. The compound of claim 1 wherein R_1 and R_2 are methyl.
3. The compound of claims 1 or 2 wherein X is bromo or iodo.
4. The compound of any one of claims 1 to 3 wherein R_3 and R_4 are independently methyl, ethyl, n-propyl or isopropyl and R_5 is hydrogen.
5. The compound of any one of claims 1 to 3 wherein Z is .
6. The compound of claim 5 wherein m is 17 except when n is 1, X is bromo and R_1 and R_2 are methyl.

7. The compound of any one of claims 1 to 4 wherein Z is



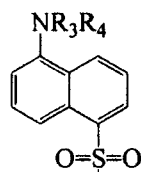
8. A process for preparing a quaternary ammonium compound of formula (I)



wherein n is 1, 2, 3 or 4;

R_1 and R_2 are independently methyl, ethyl, n-propyl or i-propyl;

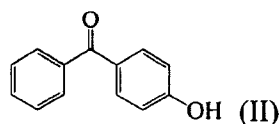
Z is $\text{---}(\text{---})_m\text{---}$ wherein m is selected from the group consisting of 12, 13, 14, 15, 16, 17 and



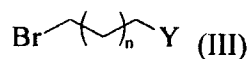
18, or $\text{---}(\text{---})_m\text{---}$, wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl; and

X is a halogen selected from the group consisting of chloro, bromo and iodo,

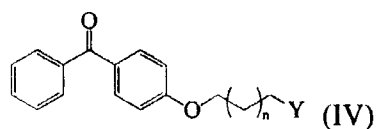
comprising the steps of (a) reacting a compound of formula (II):



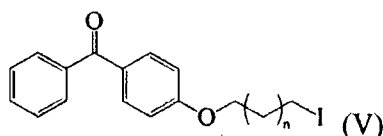
with an alkyl halide of formula (III):



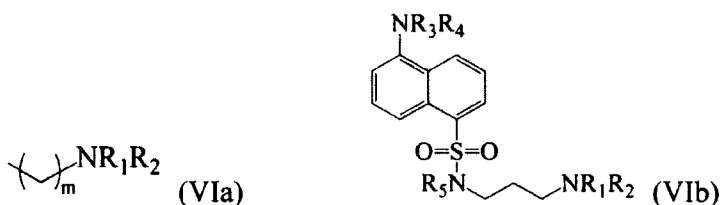
wherein n is as defined above and Y is bromo or chloro, in the presence of an alkali metal carbonate, to give a compound of formula (IV):



wherein n and Y are as defined above; (b) optionally converting a compound of formula (IV) to a compound of formula (V):



and (c) reacting a compound of formula (IV) or formula (V) with a compound of formula (VIa) or (VIb):



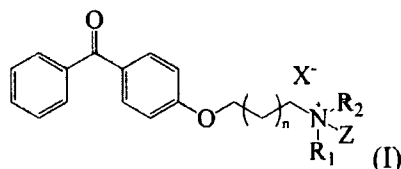
wherein m, R₁, R₂, R₃, R₄ and R₅ are as defined above to give a compound of formula (I).

9. The process of claim 8 wherein R₁ and R₂ are methyl.
10. The process of claims 8 or 9 wherein X is bromo and iodo.
11. The process of any one of claims 8 to 10 wherein R₃ and R₄ are independently methyl, ethyl, n-propyl or isopropyl and R₅ is hydrogen.
12. The process of any one of claims 8 to 10 wherein Z is .
13. The process of claim 12 wherein m is 17.

14. The process of any one of claims 8 to 11 wherein Z is .

15. The process of any one of claims 8 to 14 wherein the alkali metal carbonate is potassium carbonate.

16. An antimicrobial surface coating composition comprising a compound of formula (I)



wherein n is 1, 2, 3 or 4;

R_1 and R_2 are independently methyl, ethyl, n-propyl or i-propyl;

Z is $(\text{CH}_2)_m$ wherein m is selected from the group consisting of 12, 13, 14, 15, 16, 17 and



18, or $\text{R}_5\text{NCH}_2\text{CH}_2\text{CH}_2\text{NR}_1\text{R}_2$, wherein R_3 , R_4 and R_5 are independently hydrogen, C_1 - C_6 linear or branched alkyl or C_6 - C_{10} aryl; and

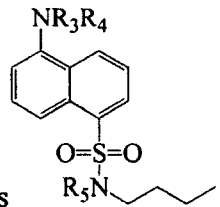
X is a halogen selected from the group consisting of chloro, bromo and iodo;

and an environmentally friendly carrier.

17. The composition of claim 16 wherein R_1 and R_2 are methyl.
18. The composition of claims 16 or 17 wherein X is bromo or iodo.
19. The composition of any one of claims 16 to 18 wherein R_3 and R_4 are independently methyl, ethyl, n-propyl or isopropyl and R_5 is hydrogen.

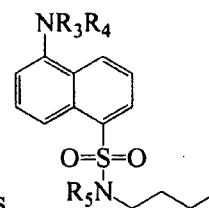
20. The composition of any one of claims 16 to 18 wherein Z is $(\text{CH}_2)_m$.

21. The composition of claim 20 wherein m is 17.



22. The composition of any one of claims 16 to 19 wherein Z is
23. The composition of any one of claims 16 to 22 wherein the carrier is a mixture of water and an alcohol.

24. The composition of claim 23 wherein the alcohol is methanol.
25. A process for coating a surface with an antimicrobial coating, said process comprising the steps of:
- i) contacting the surface with a composition of any one of claims 16 to 24; and
 - ii) irradiating the coated surface.
26. The process of claim 25 wherein the surface comprises a polymer or a fibre.
27. The process of claim 25 or 26 further comprising a washing step wherein the washing step comprises the use of a water and isopropanol mixture.
28. The process of claims 25 or 26 wherein the irradiating step comprises irradiating the coated surface with UV light.
29. A process for assessing antimicrobial treatment of an antimicrobially treated surface by a



quaternary ammonium compound of any one of claims 1 to 4 wherein Z is comprising irradiating the antimicrobially treated surface with a UV light.

Figure 1

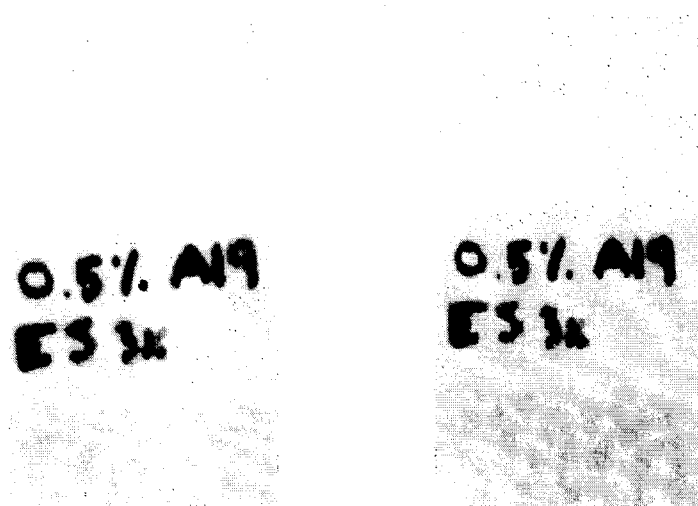


Figure 2

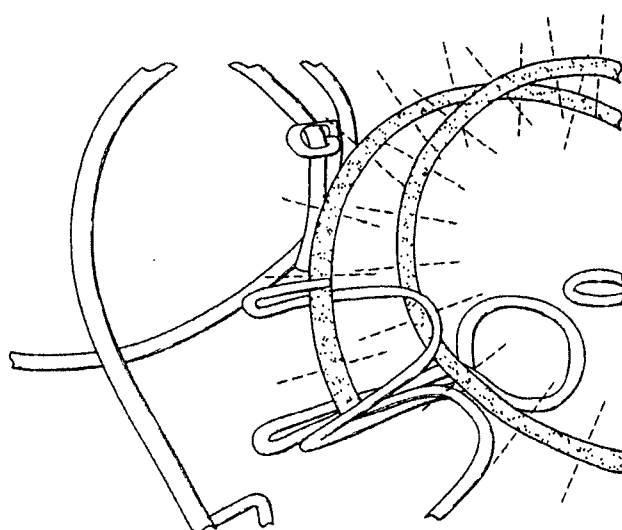


Figure 3

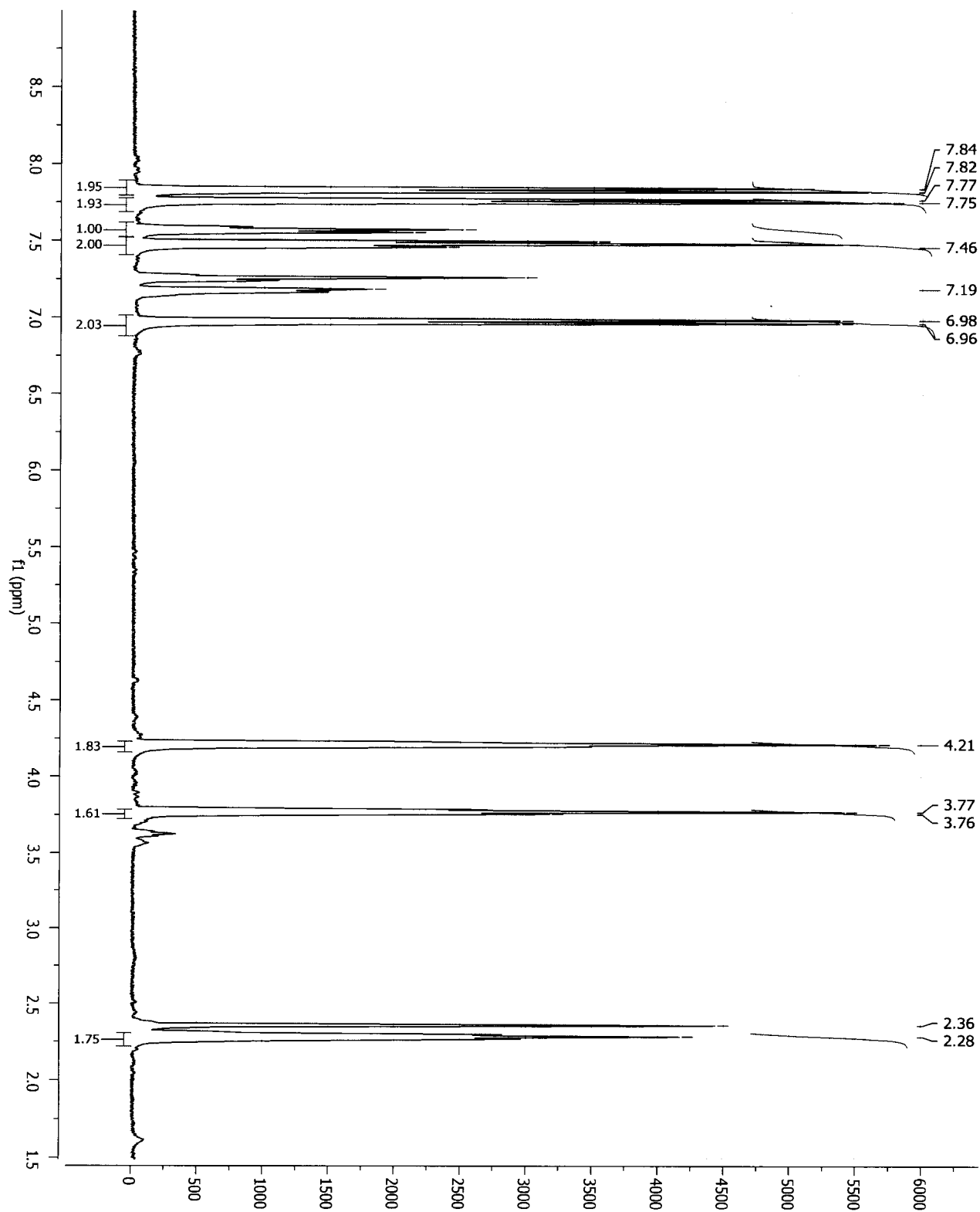


Figure 4

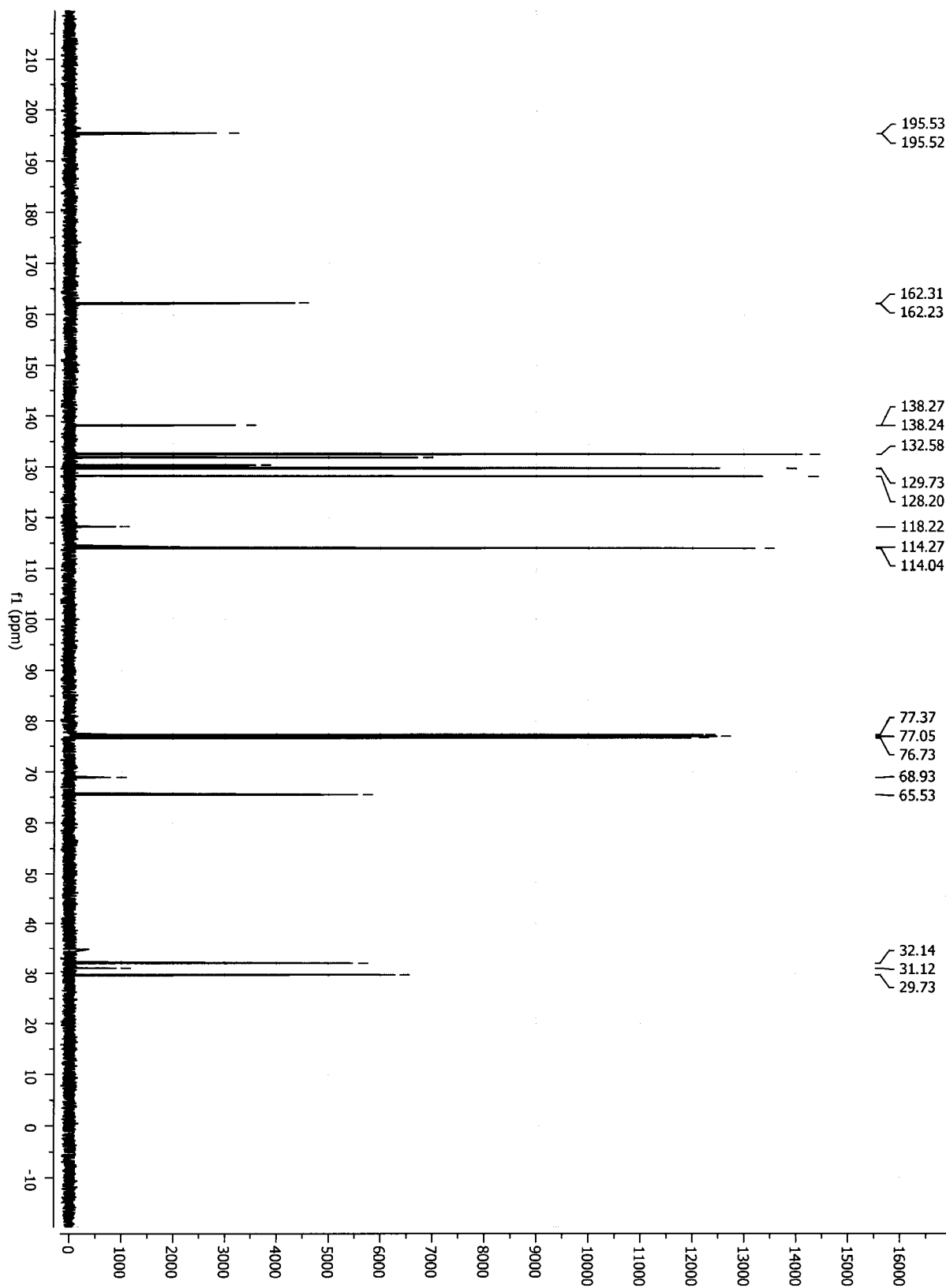


Figure 5

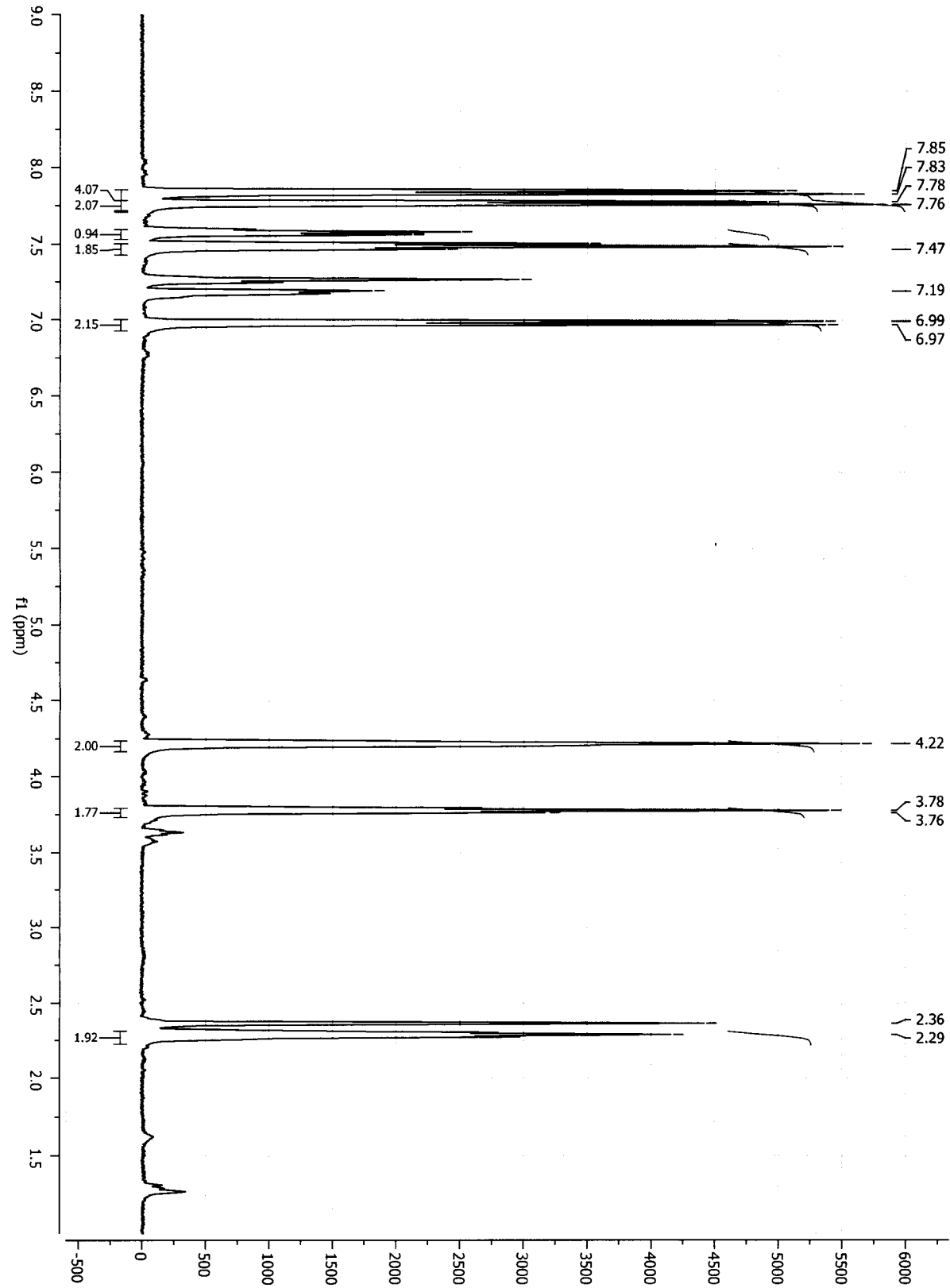


Figure 6

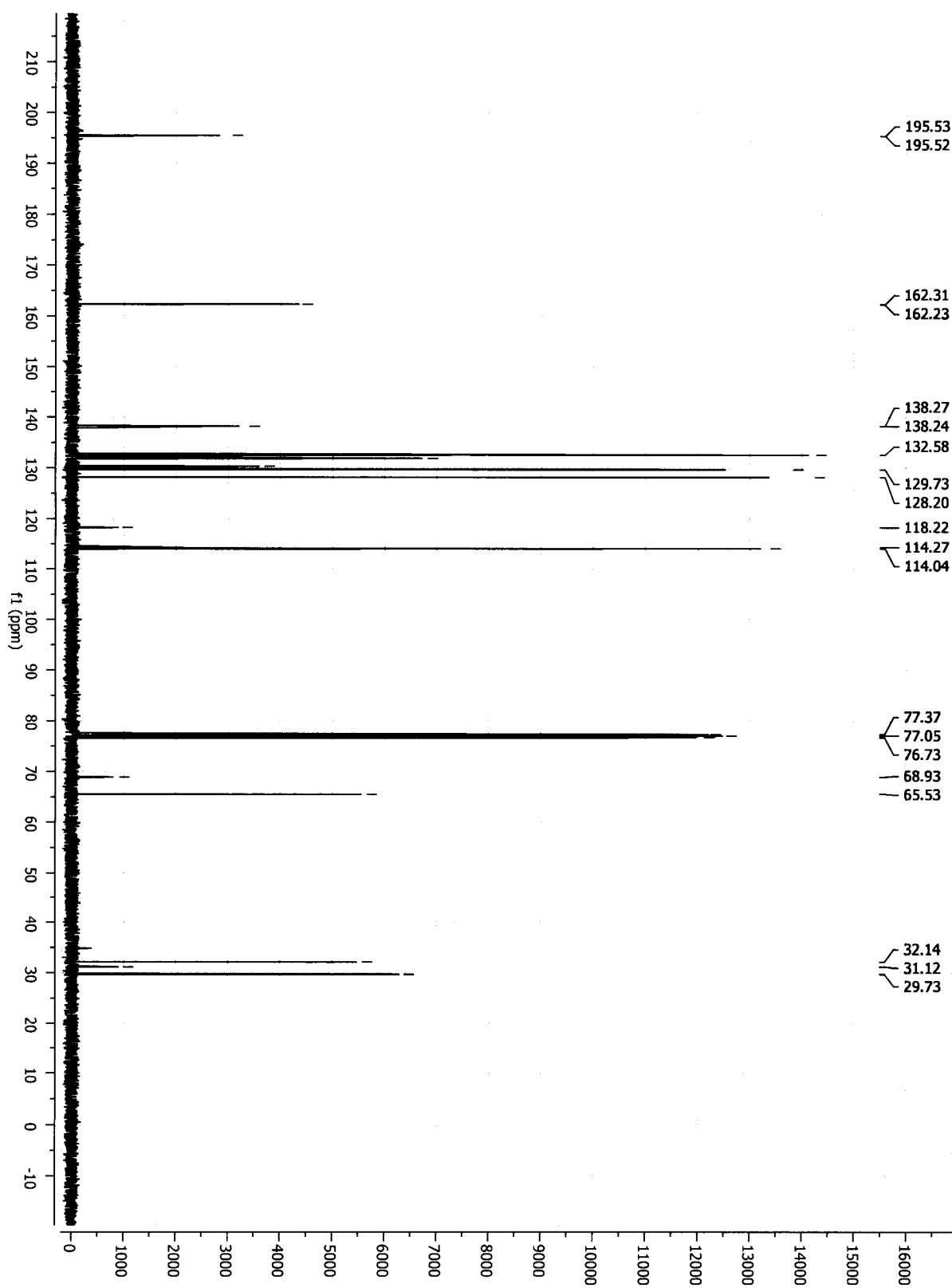


Figure 7

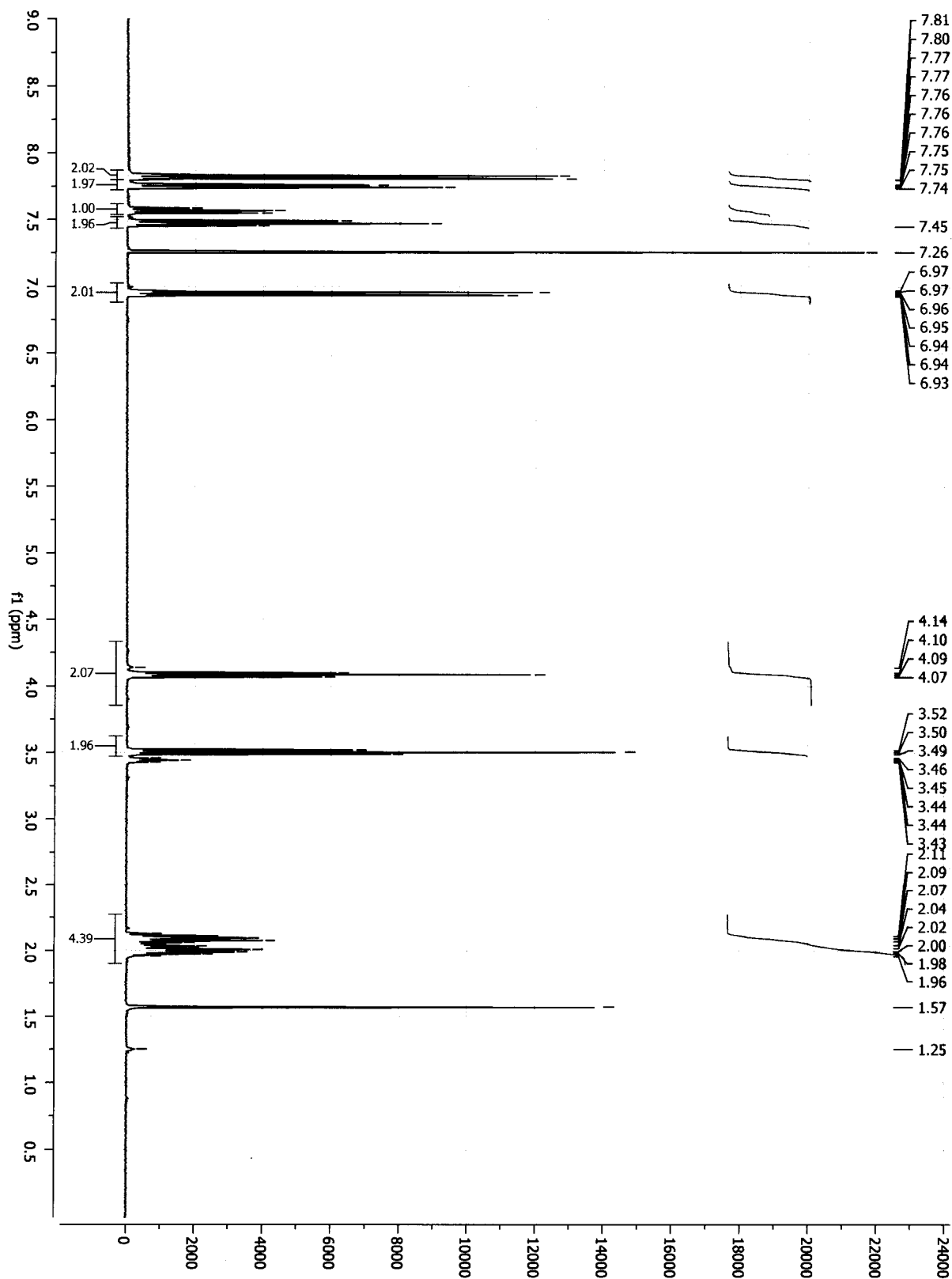


Figure 8

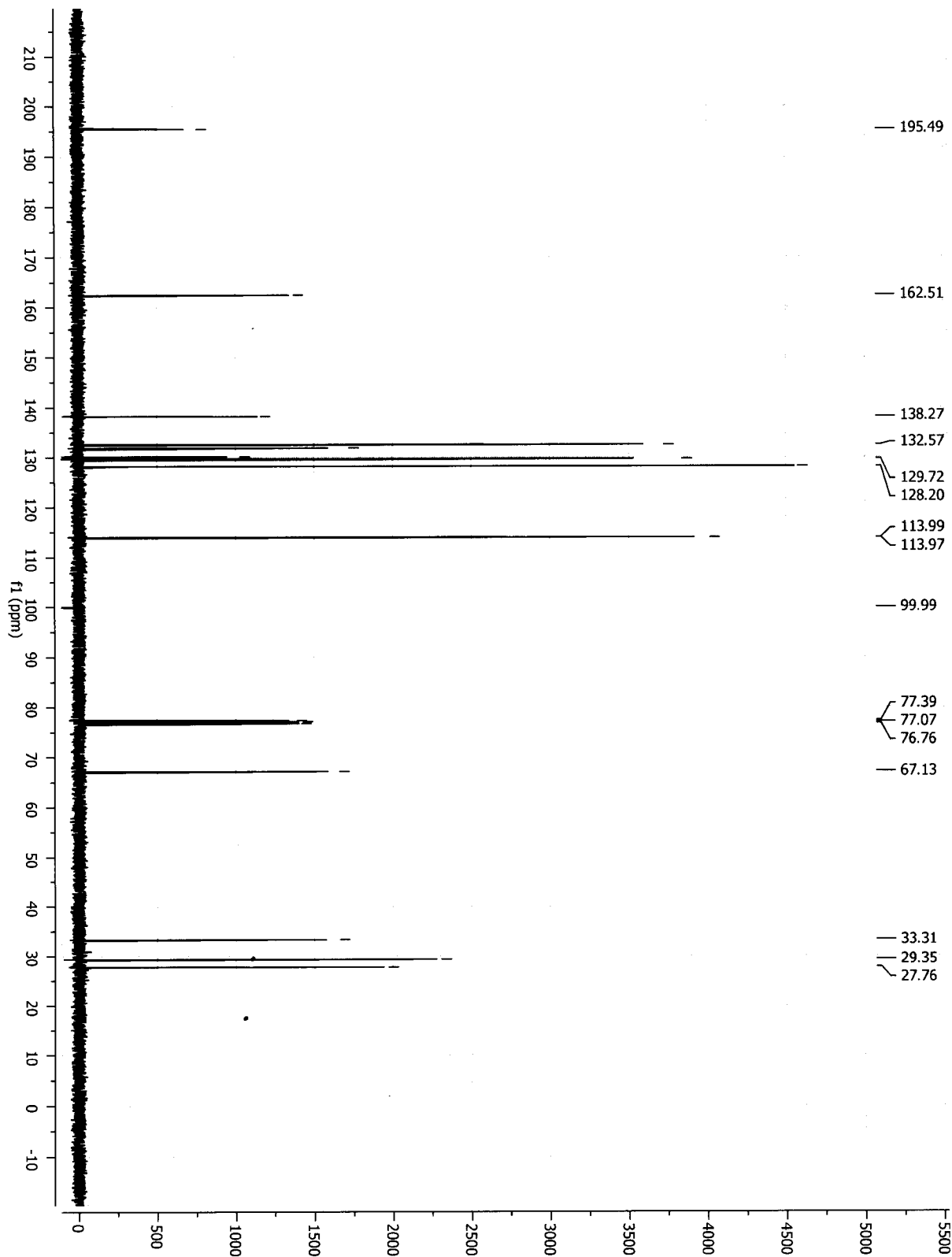


Figure 9

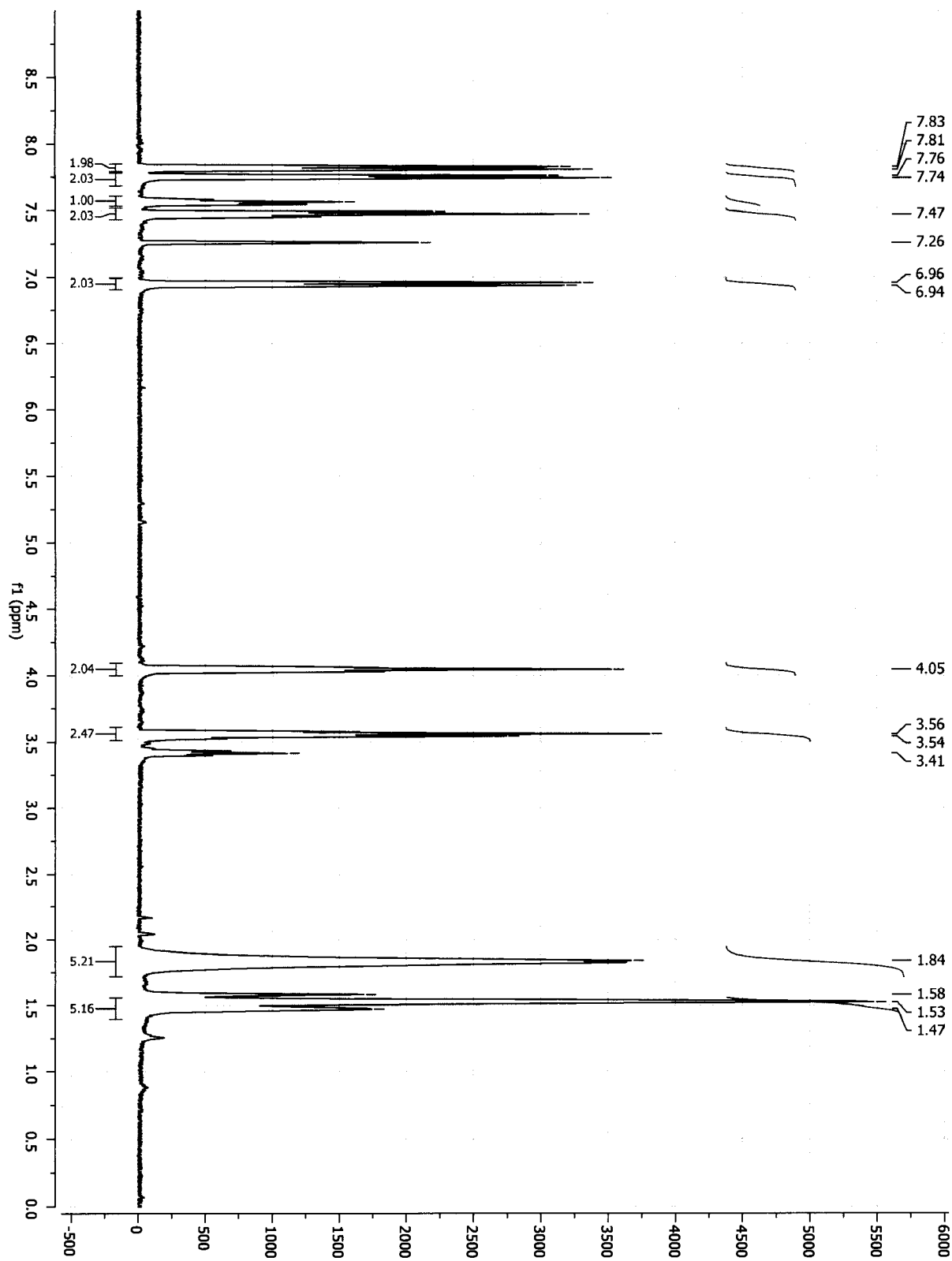


Figure 10

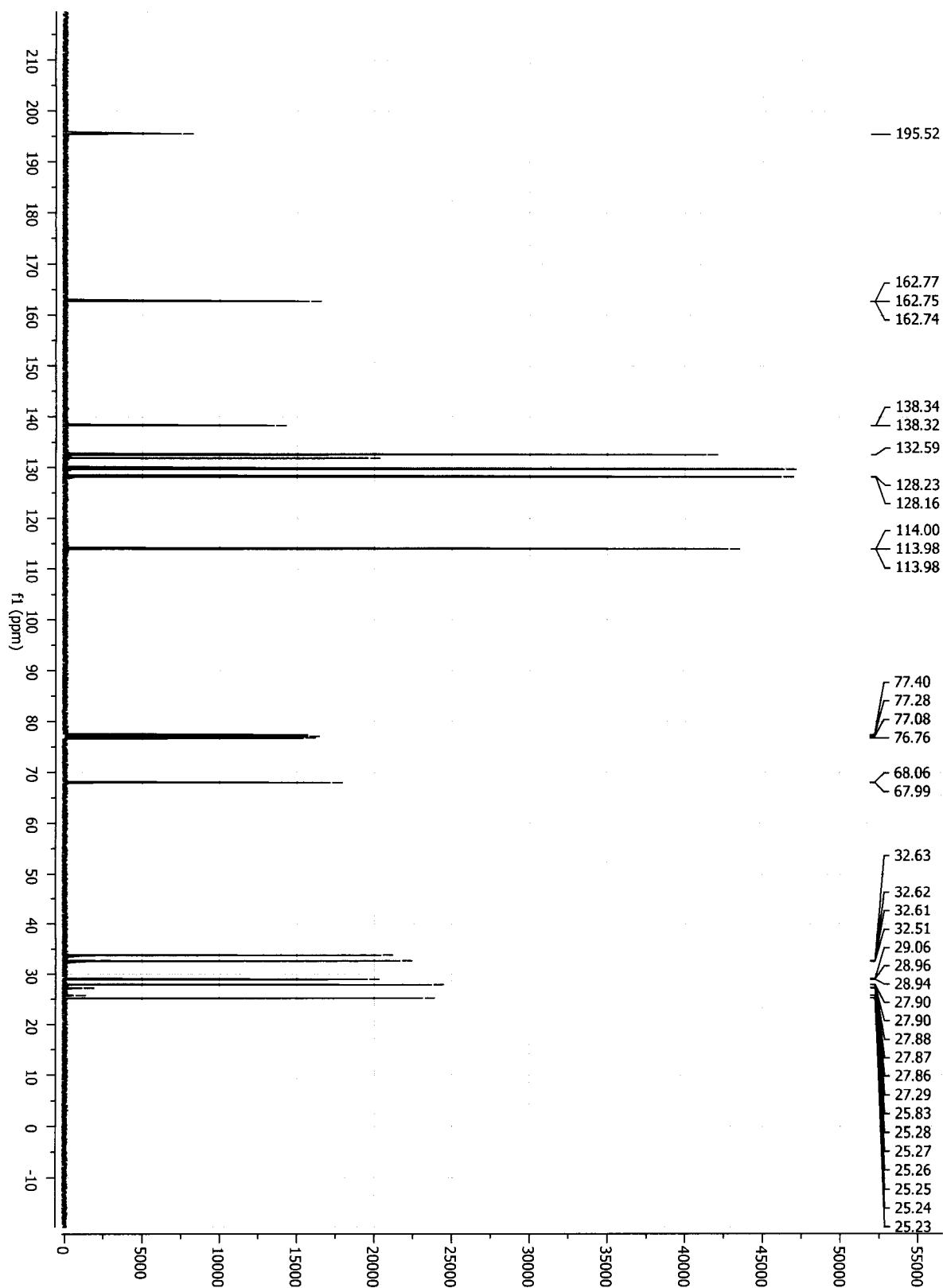


Figure 11

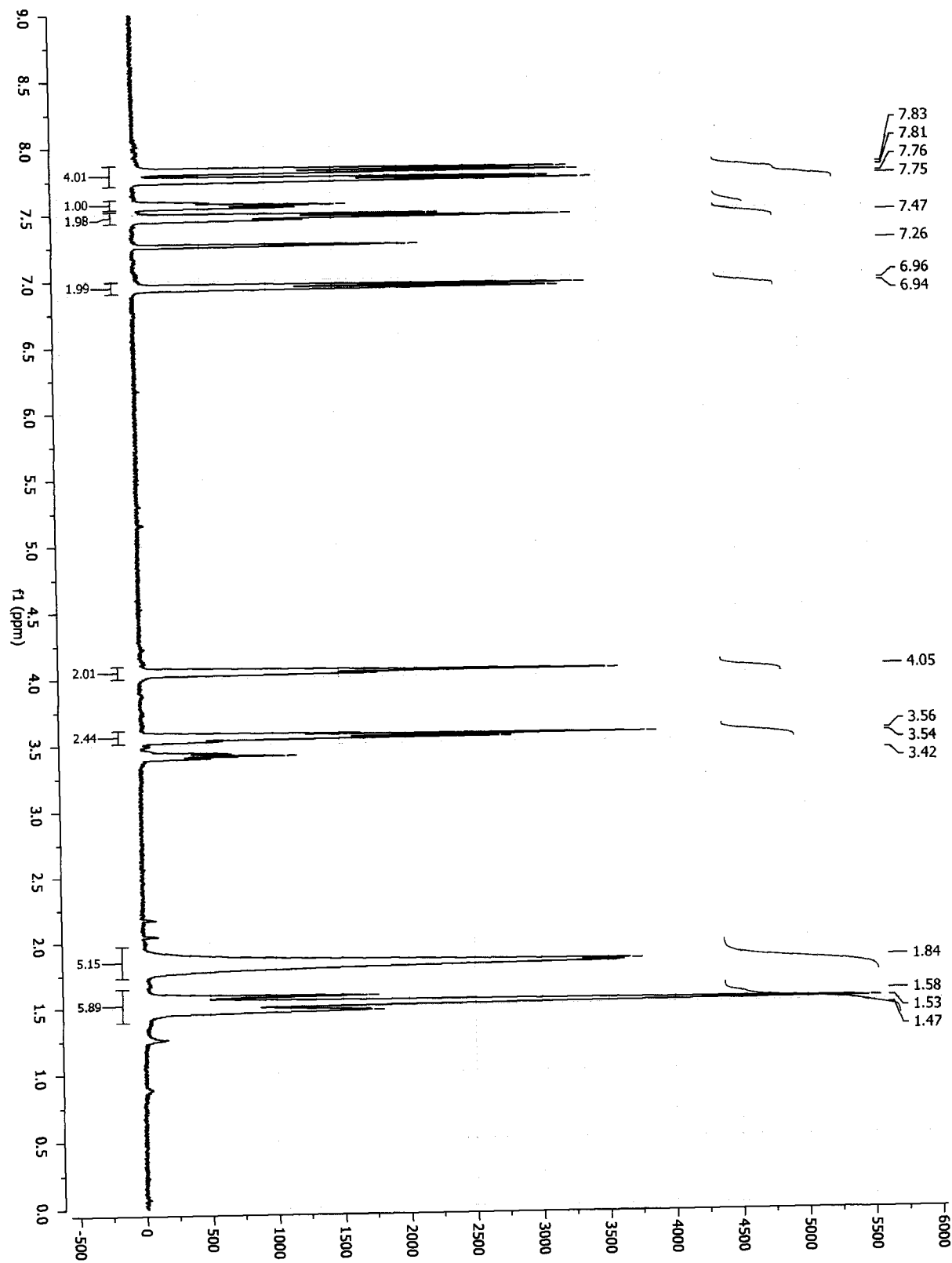


Figure 12

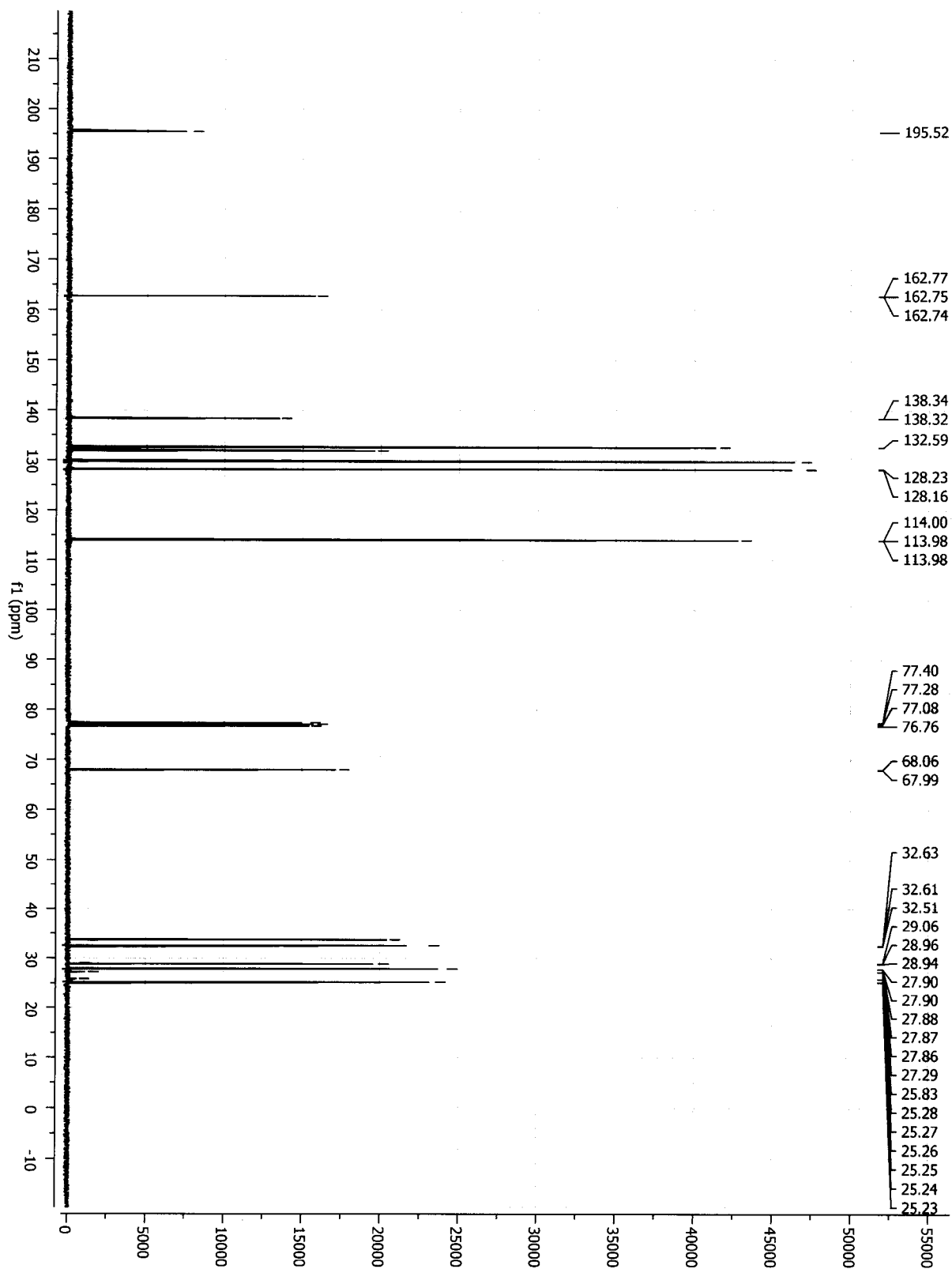


Figure 13

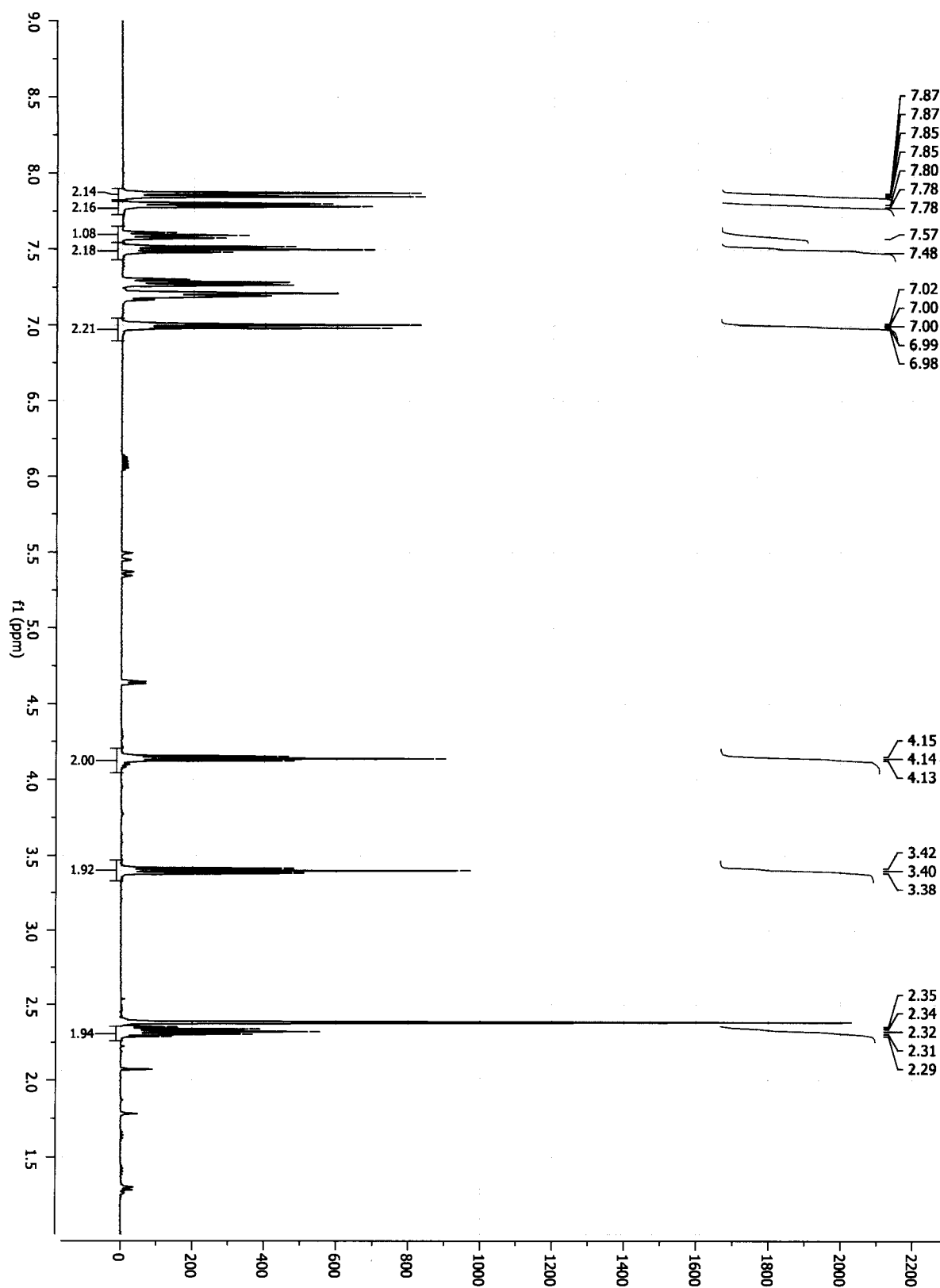


Figure 14

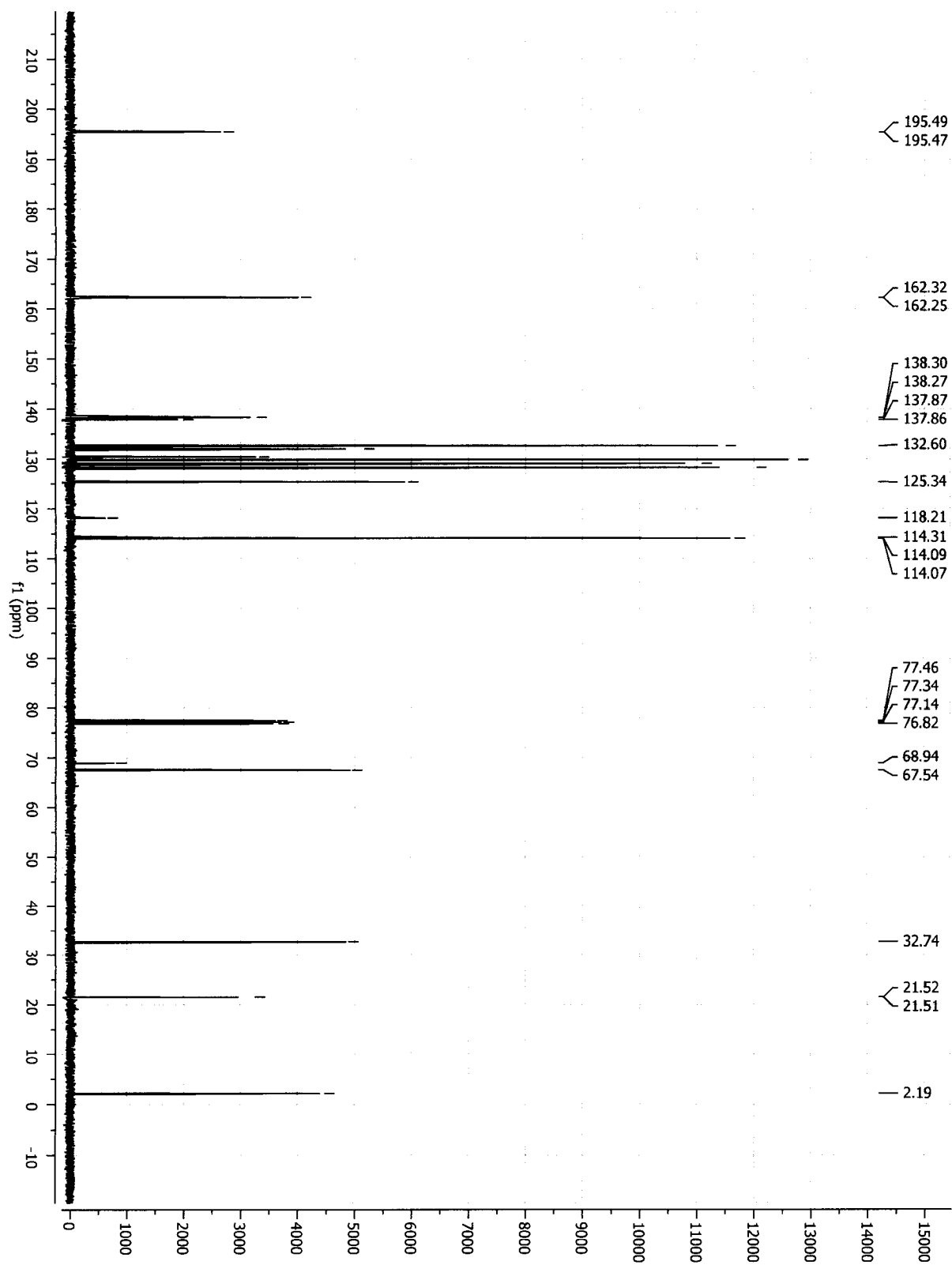


Figure 15

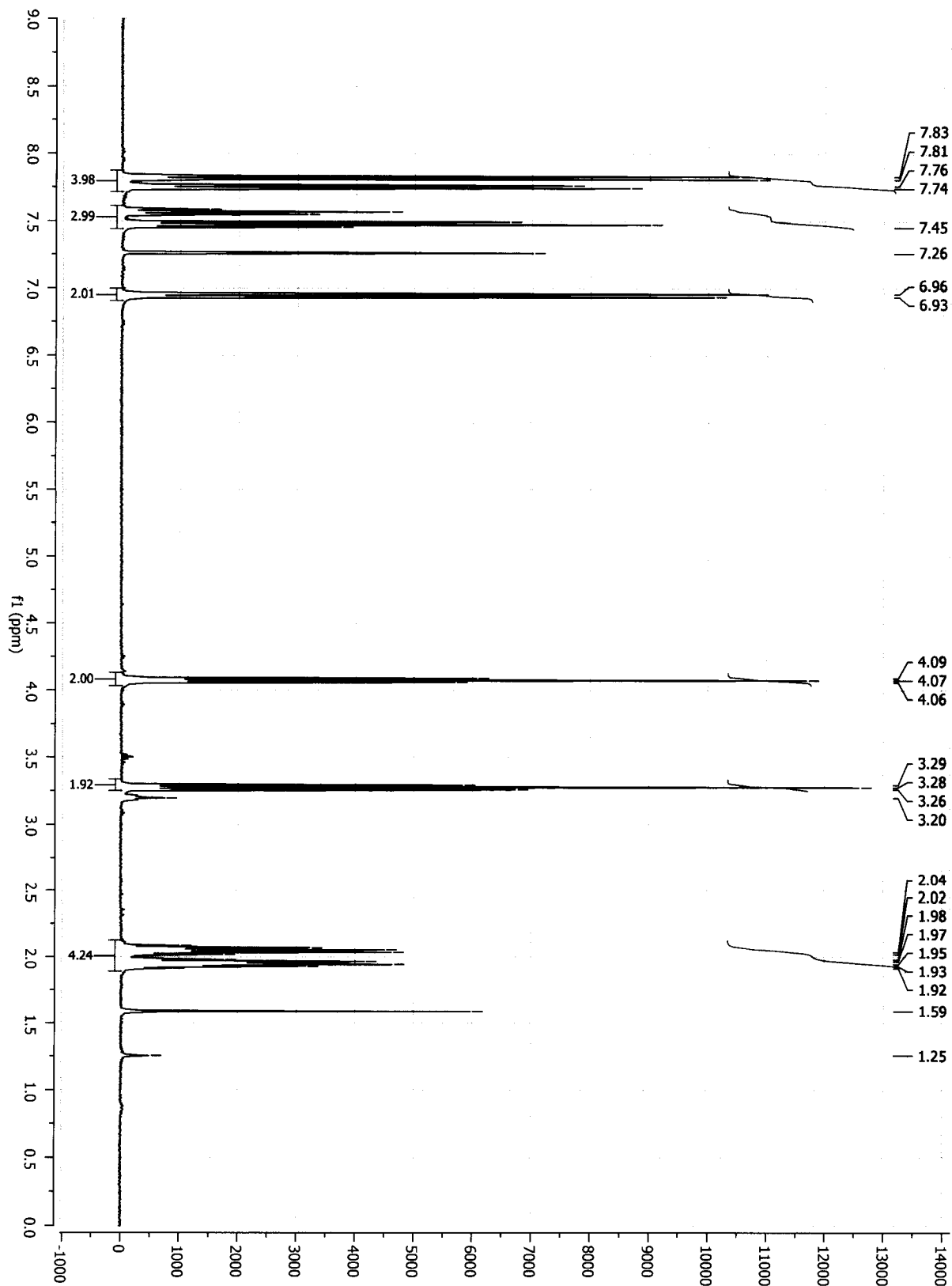


Figure 16

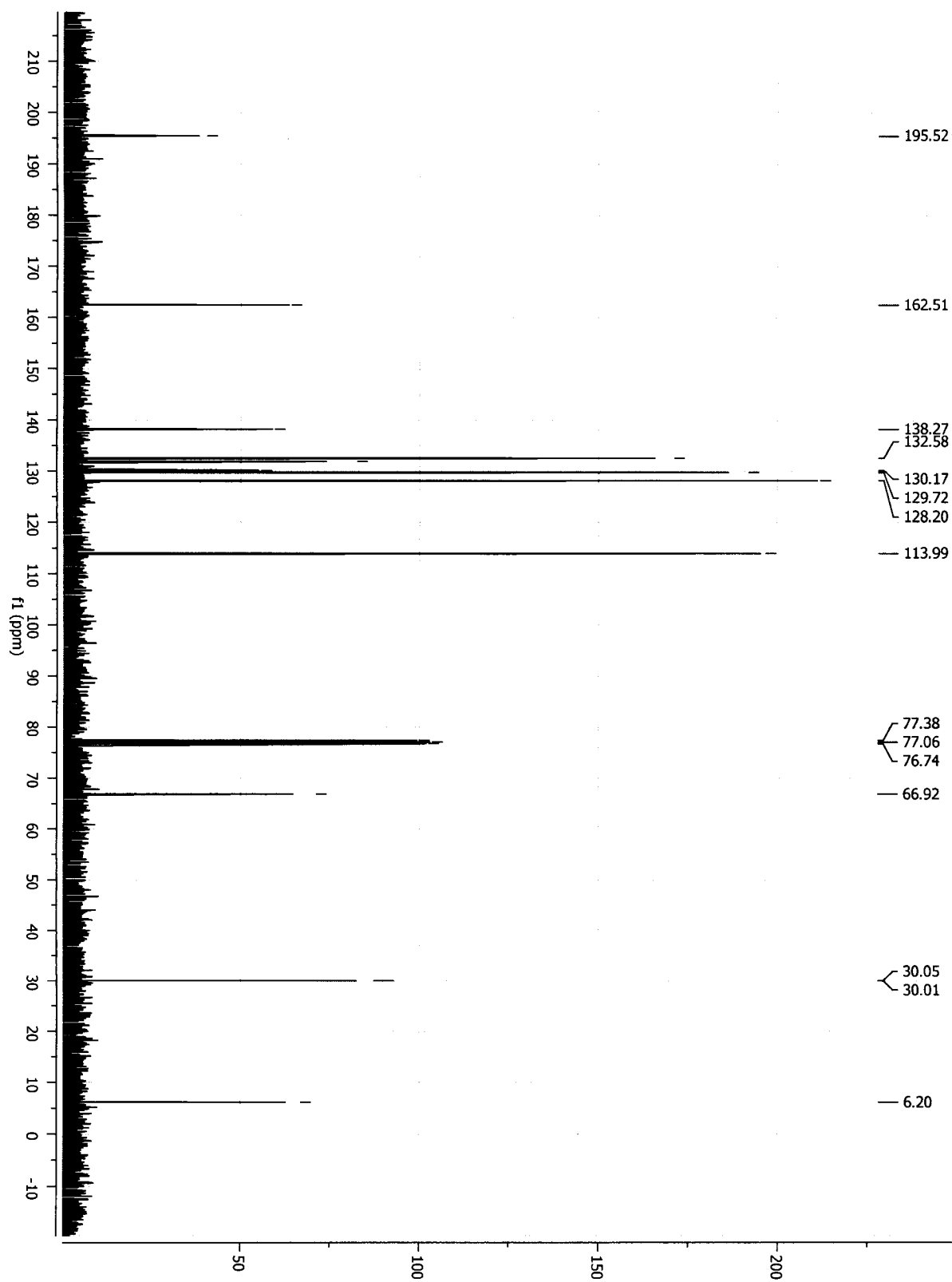


Figure 17

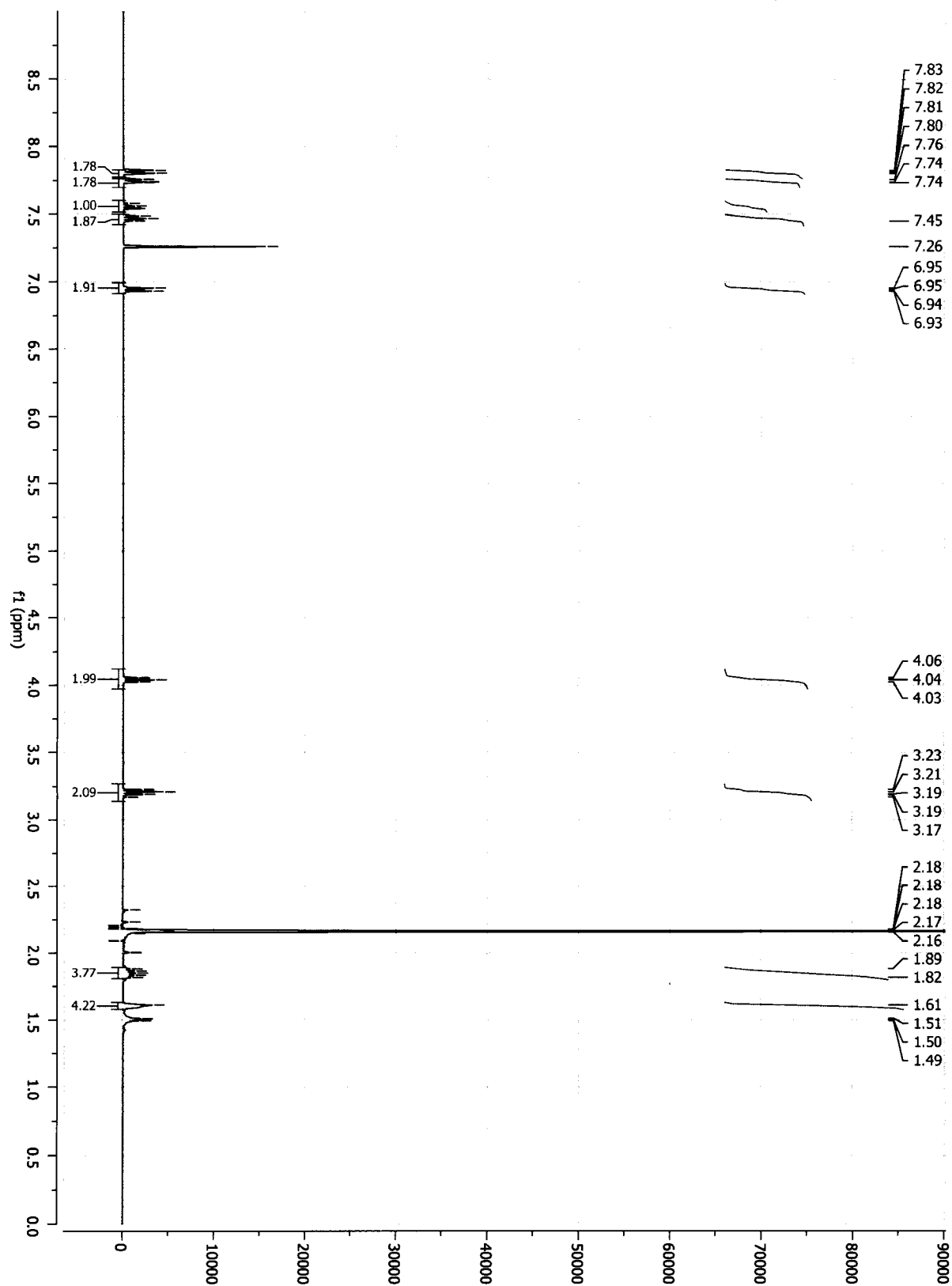


Figure 18

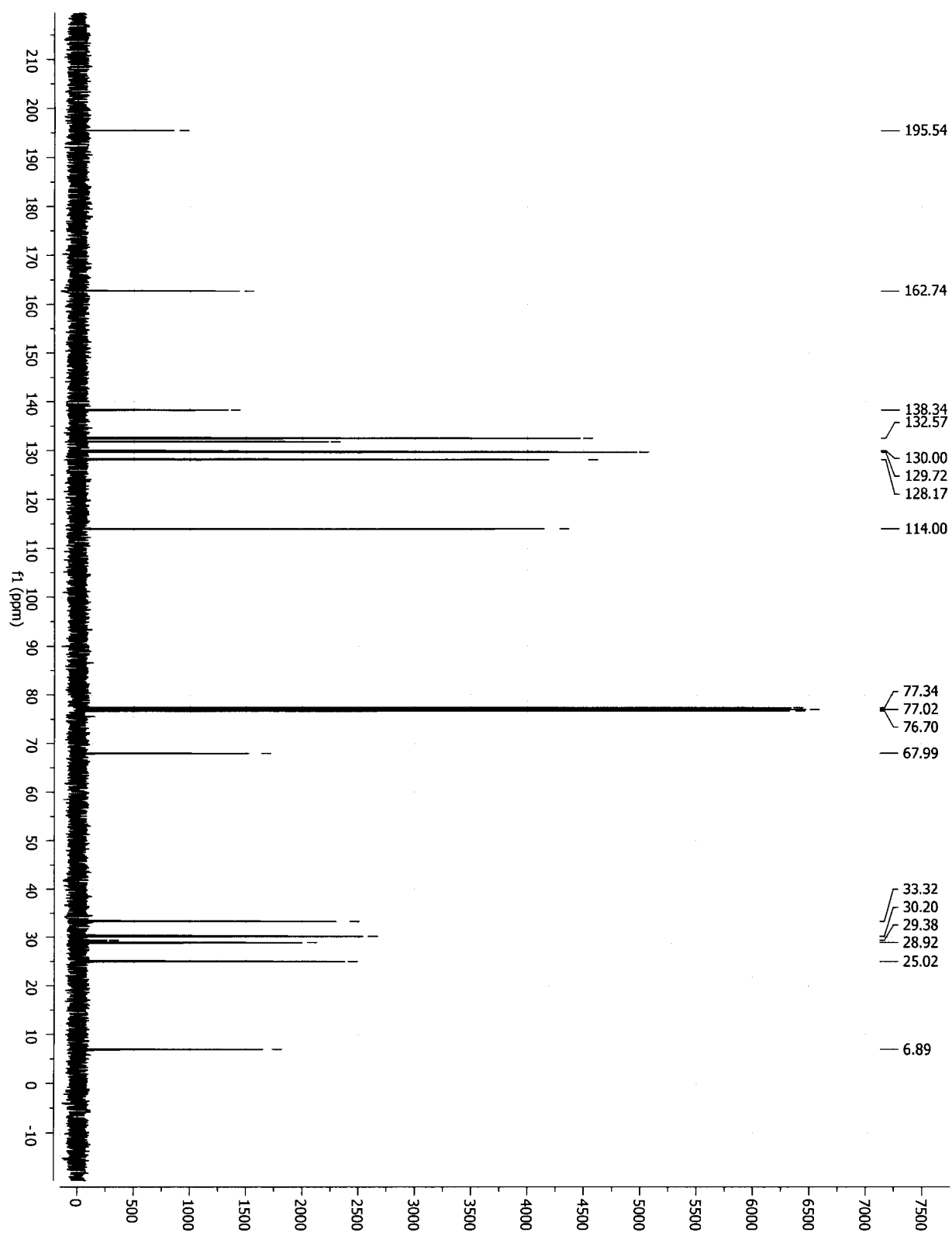


Figure 19

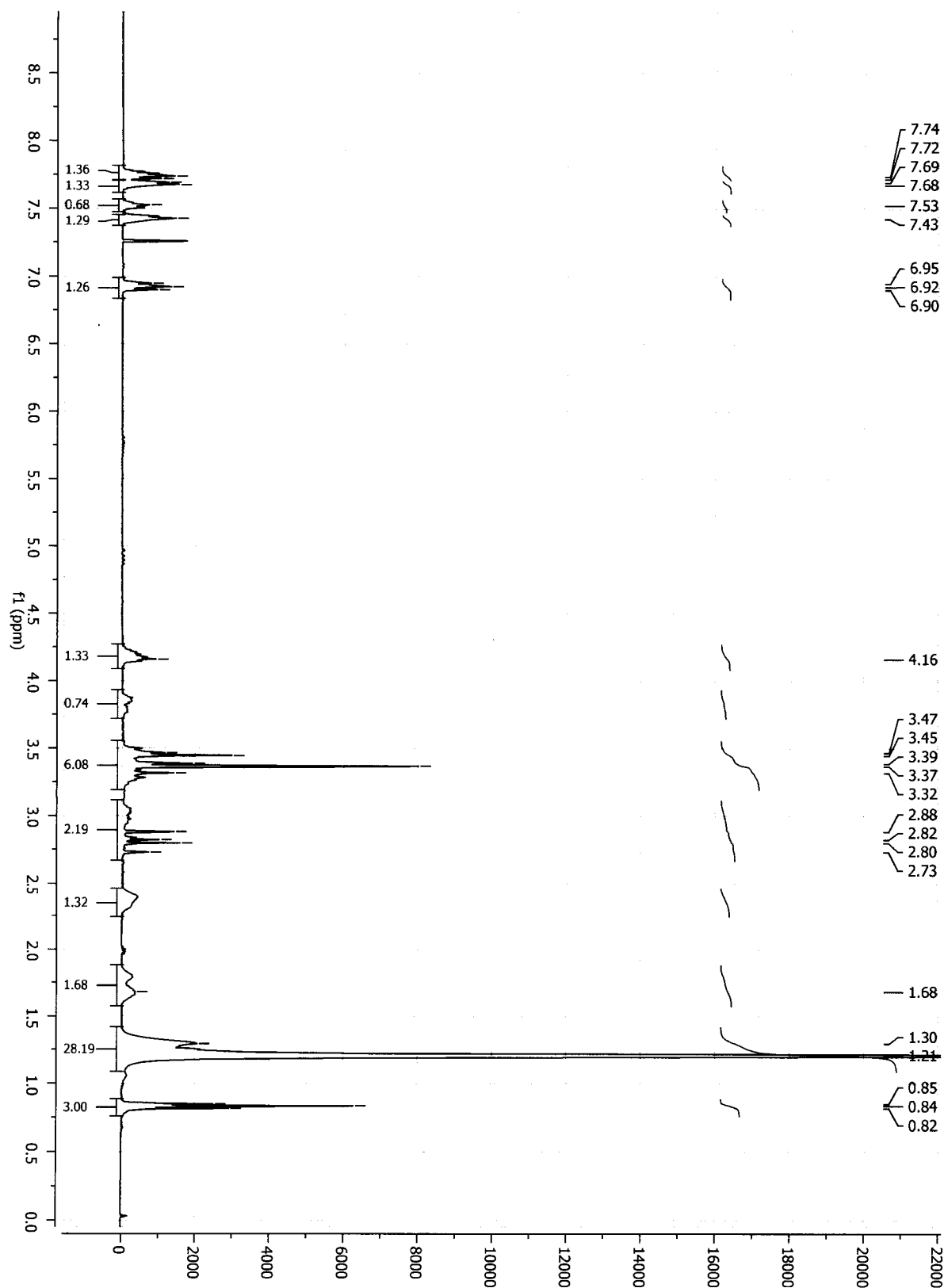


Figure 20

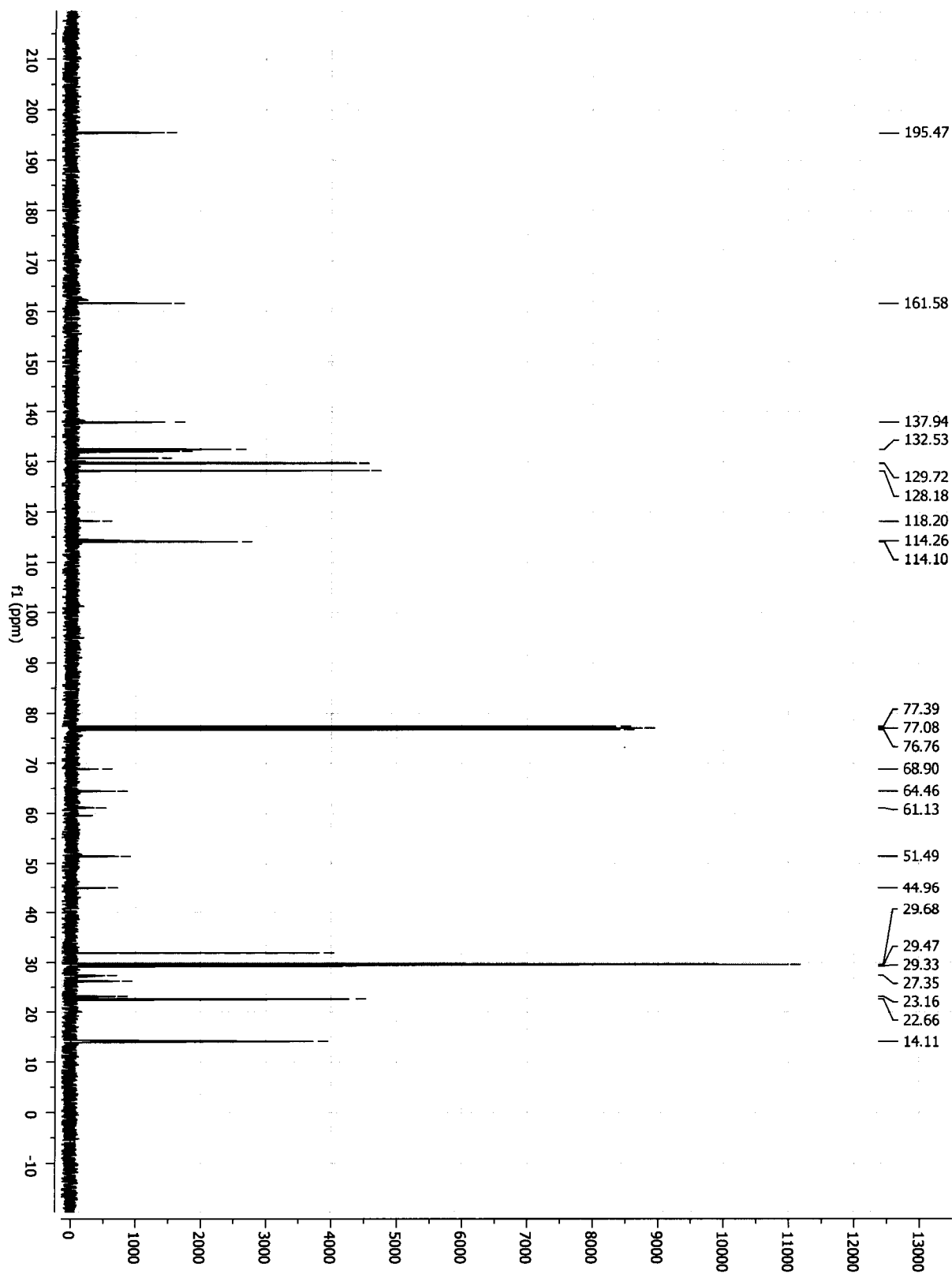


Figure 21

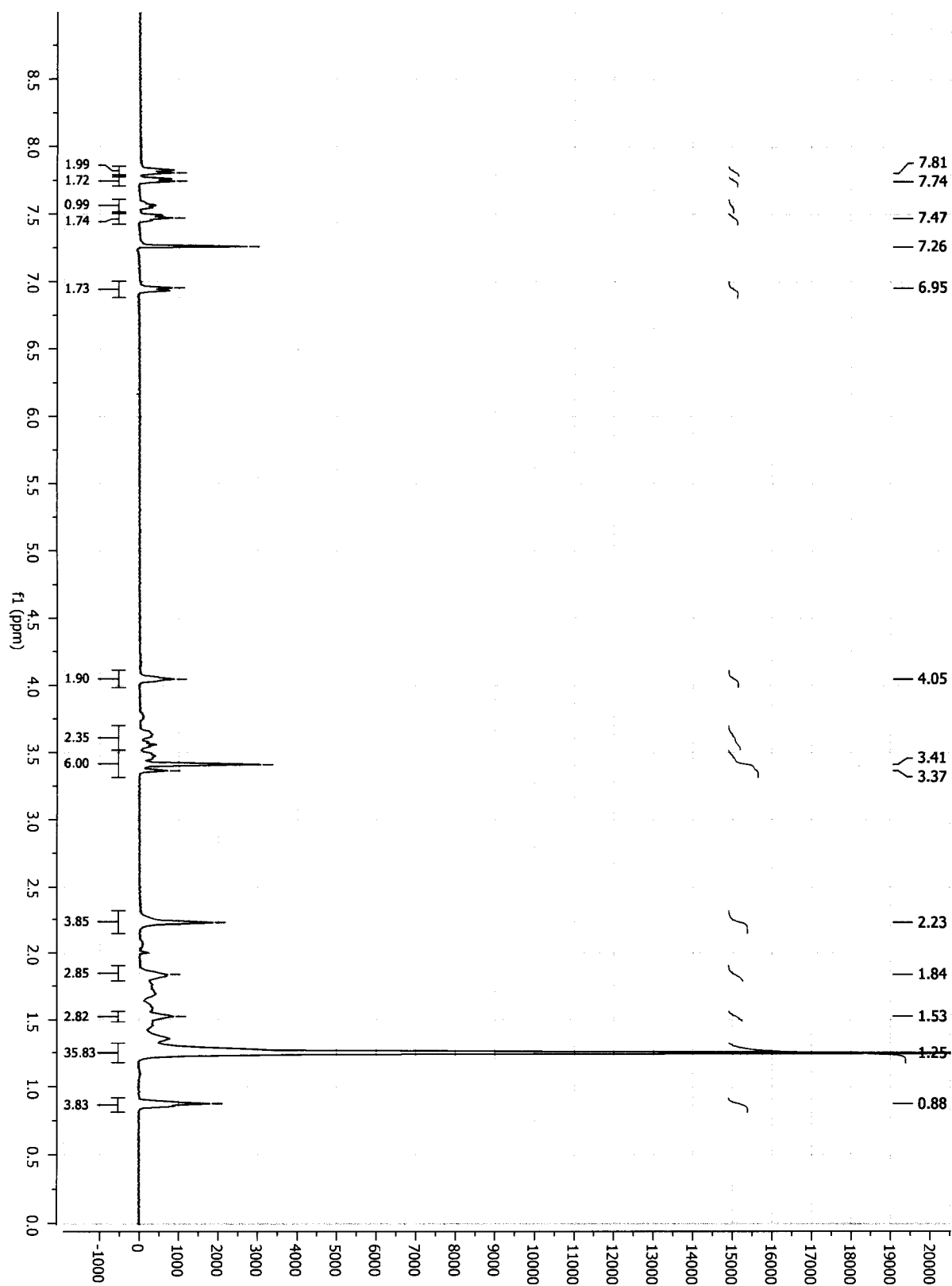


Figure 22

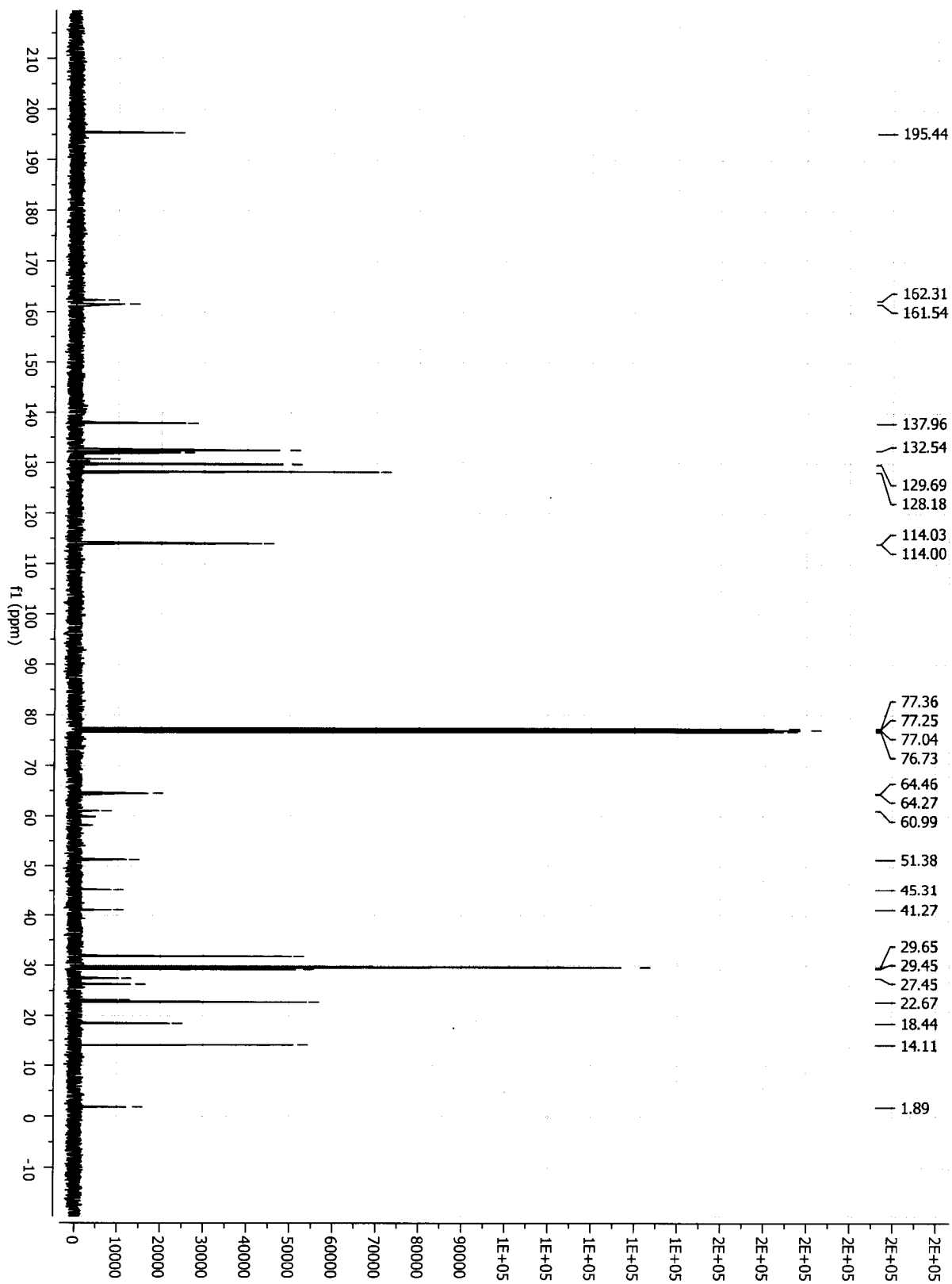


Figure 23

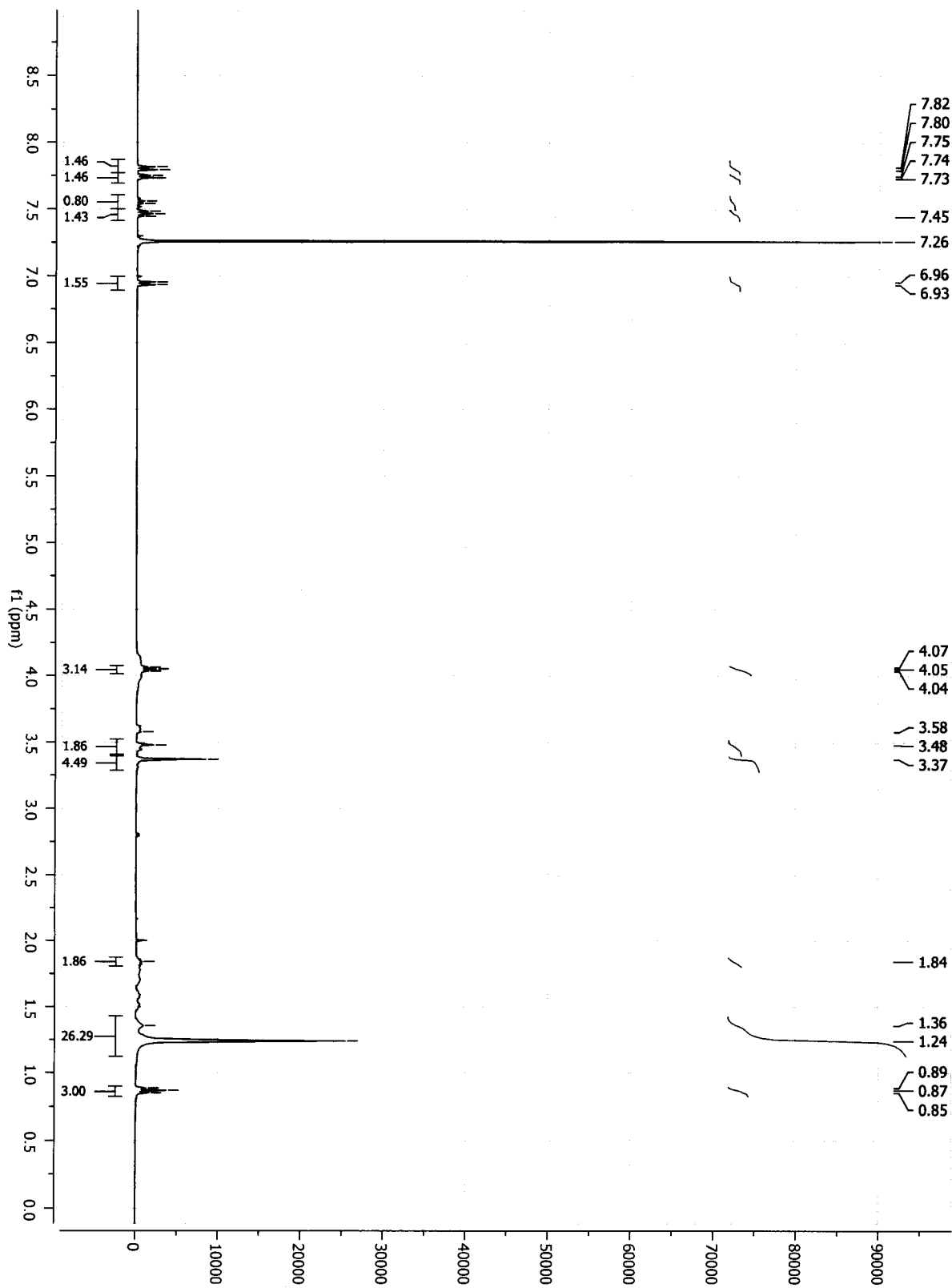


Figure 24

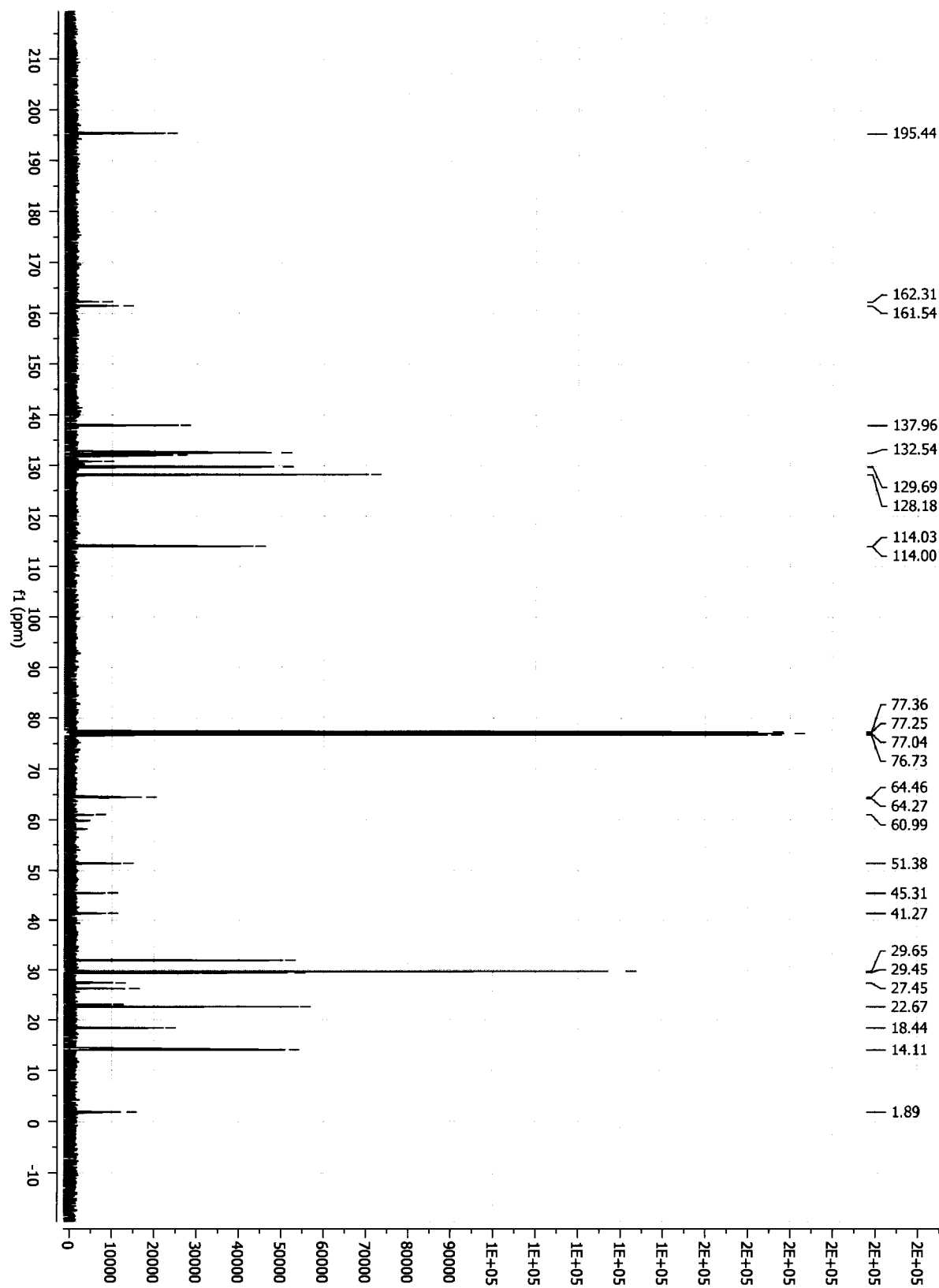


Figure 25

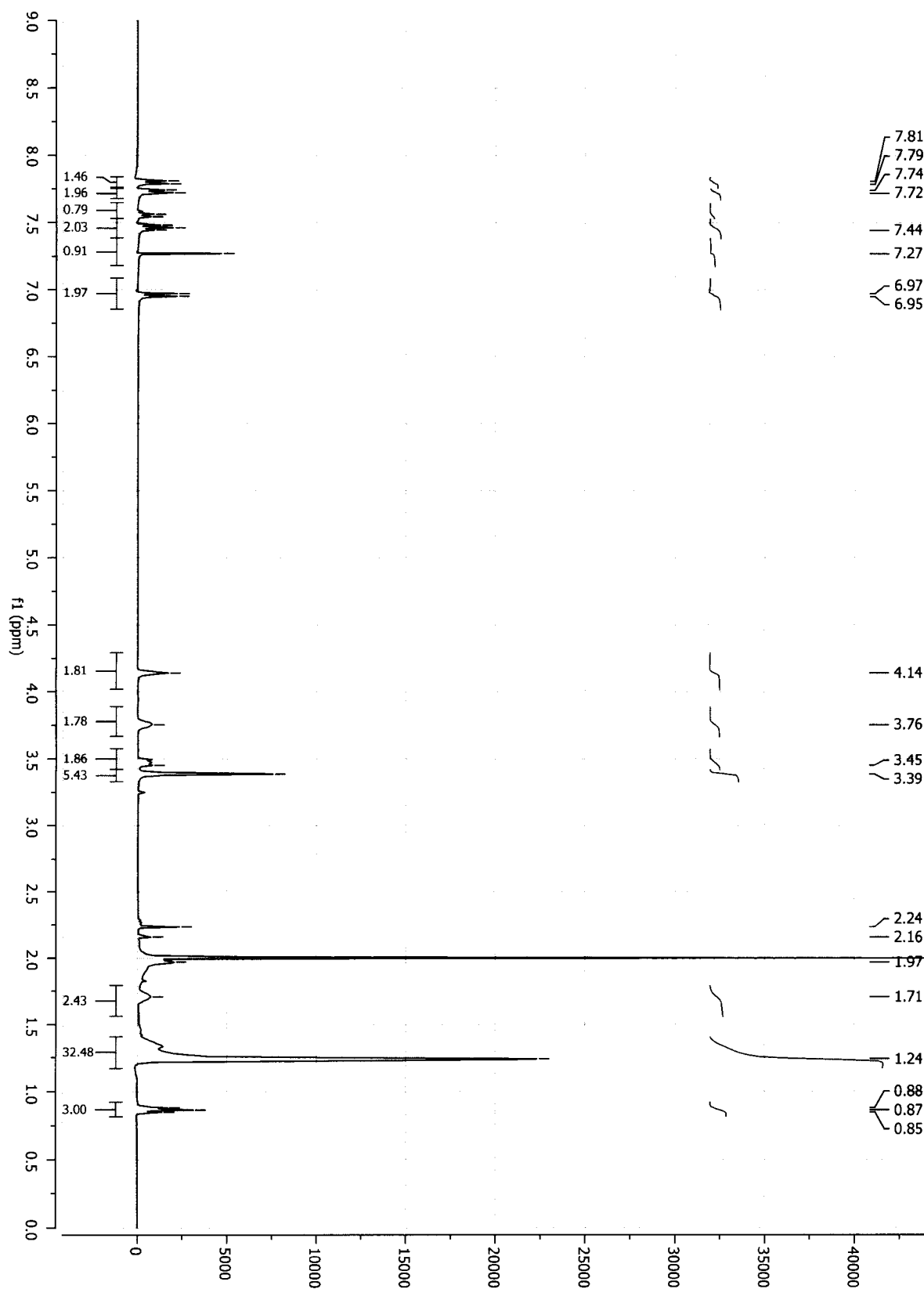


Figure 26

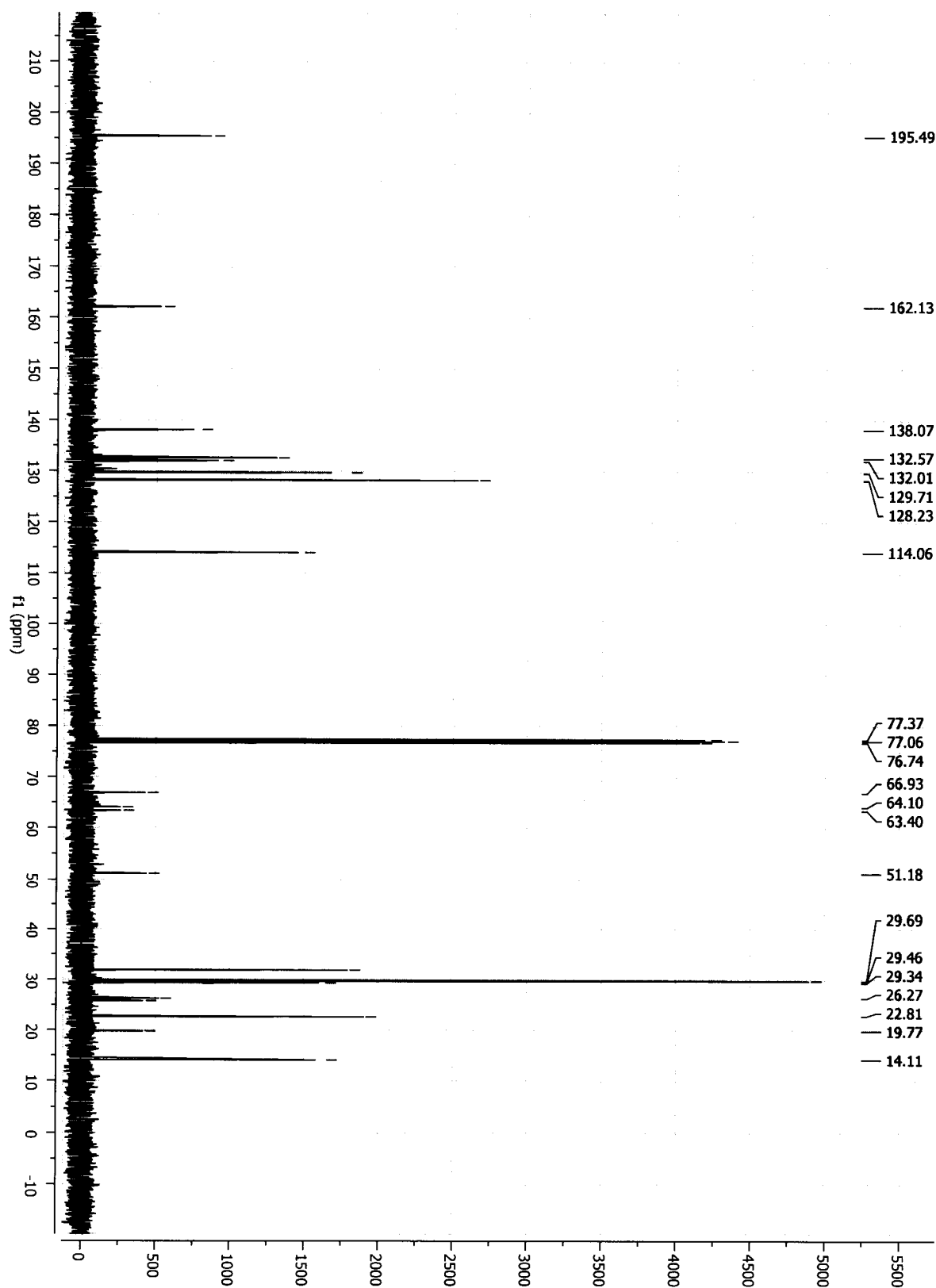


Figure 27

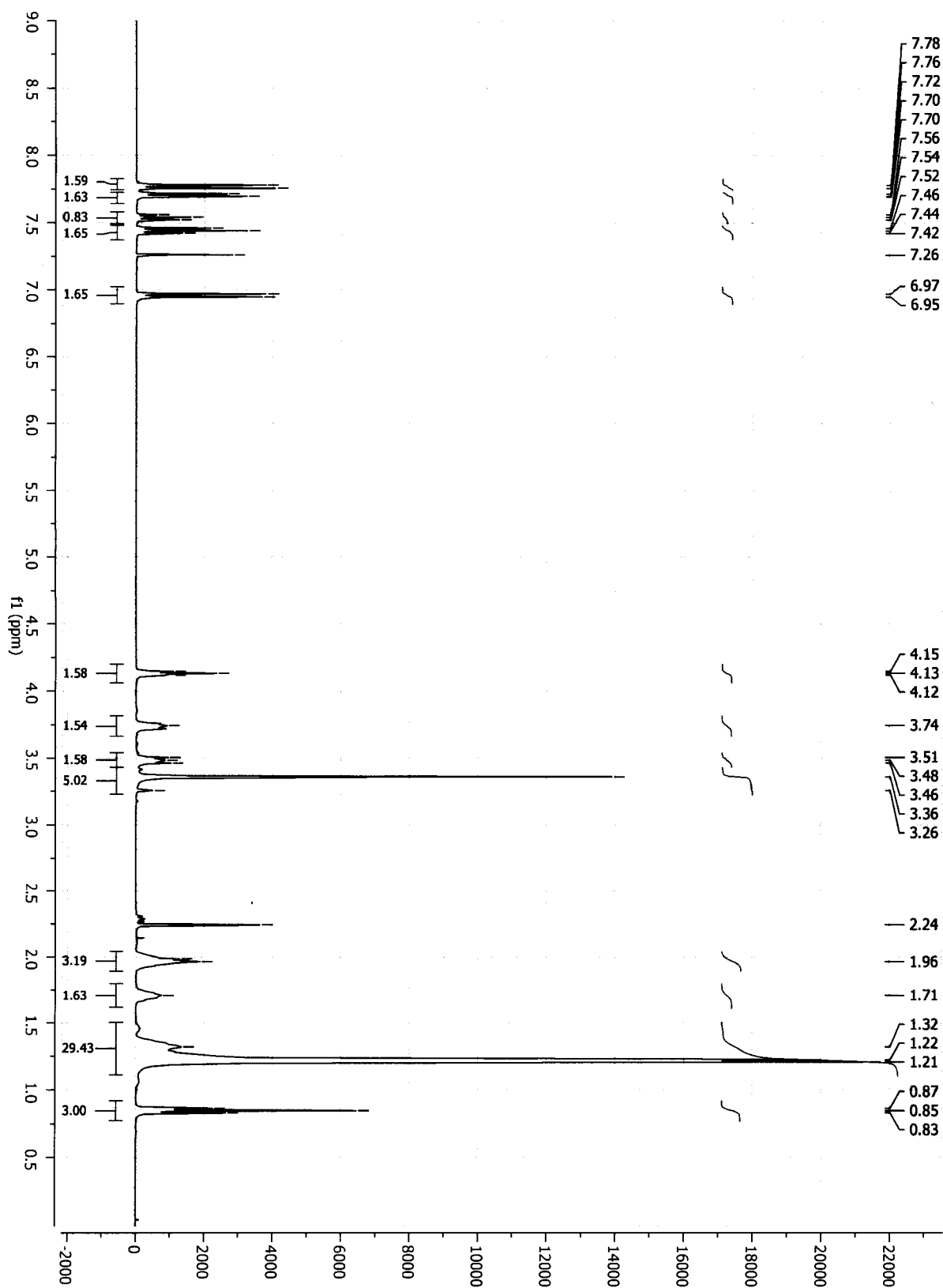


Figure 28

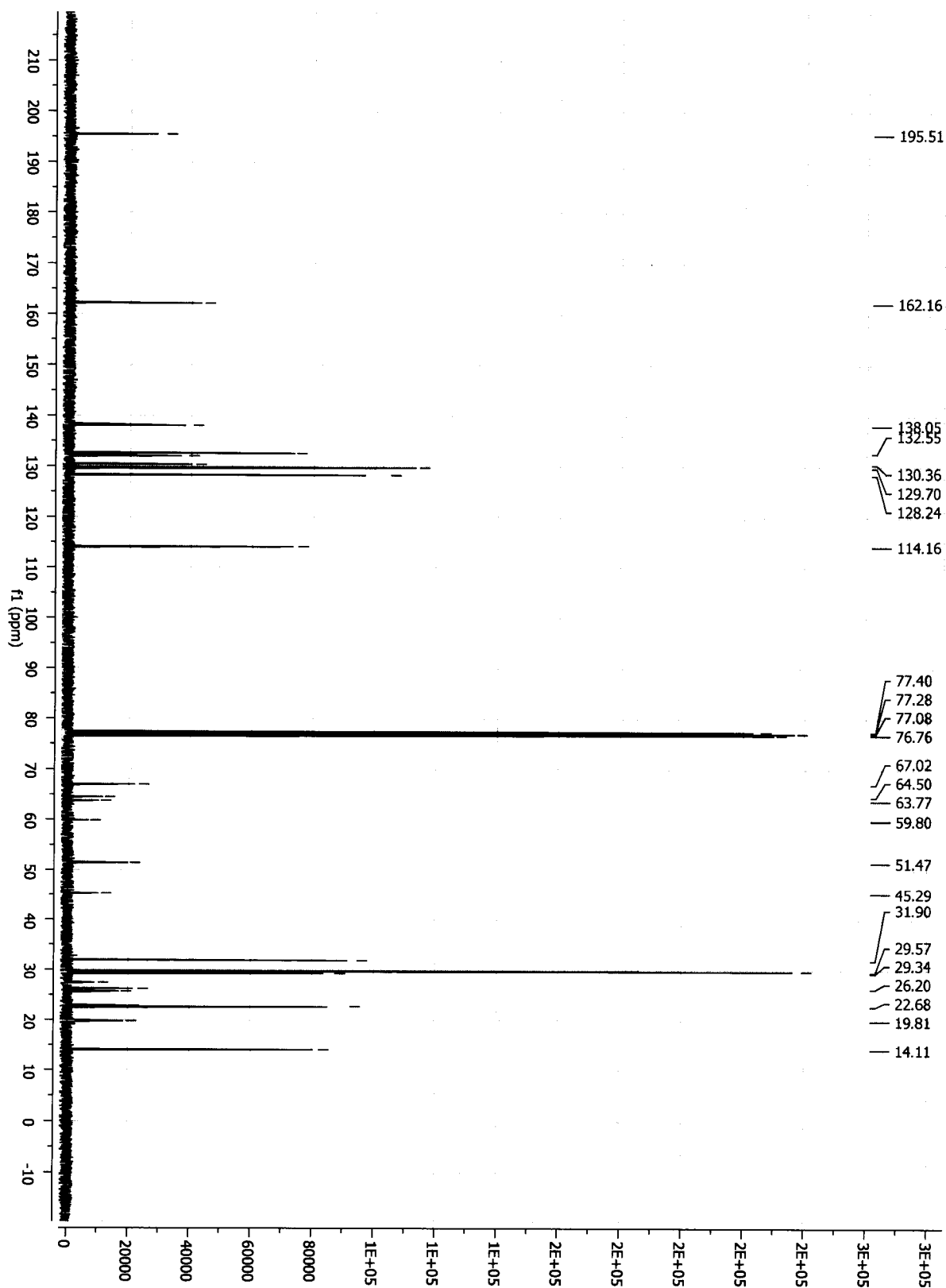


Figure 29

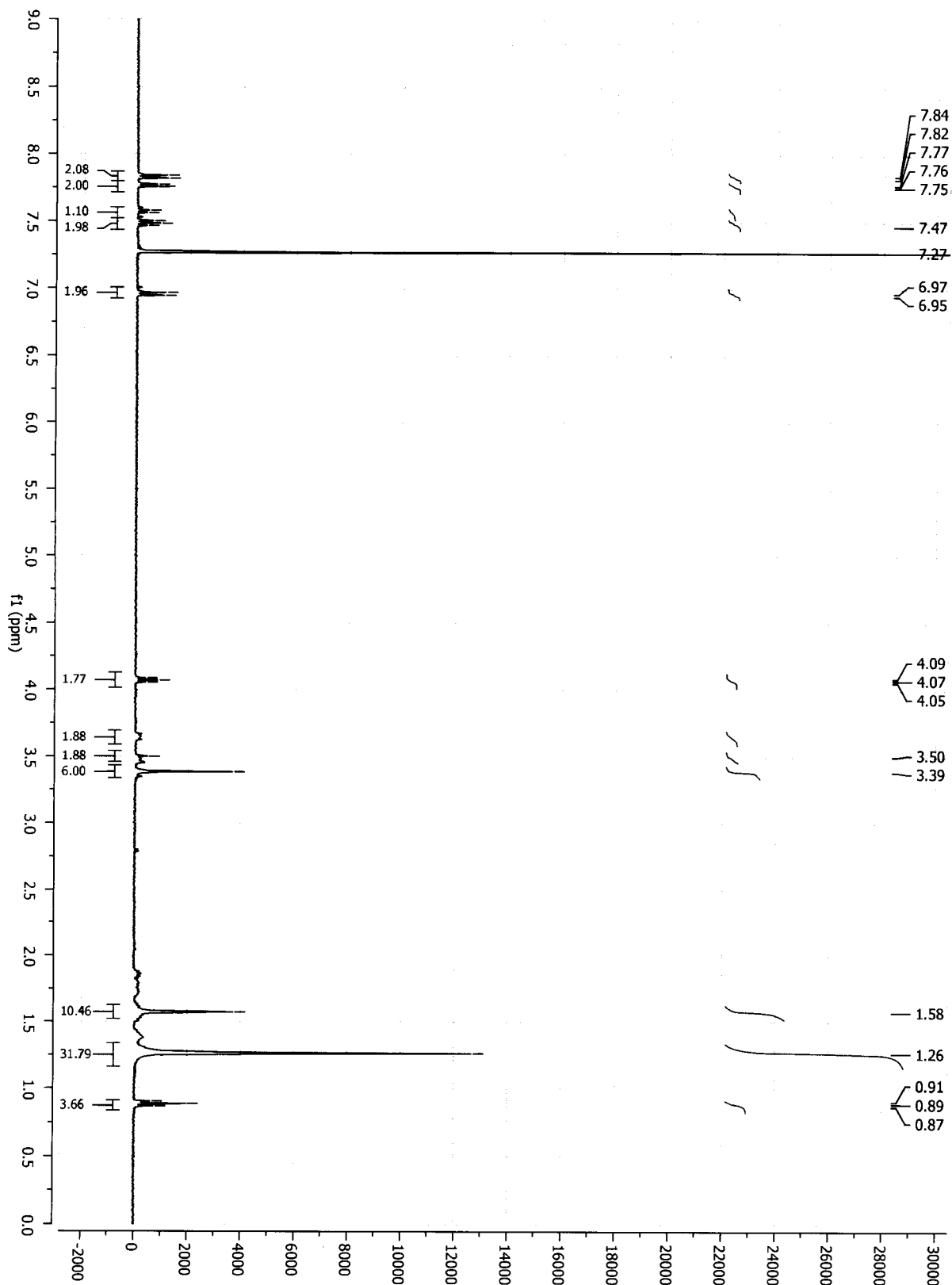


Figure 30

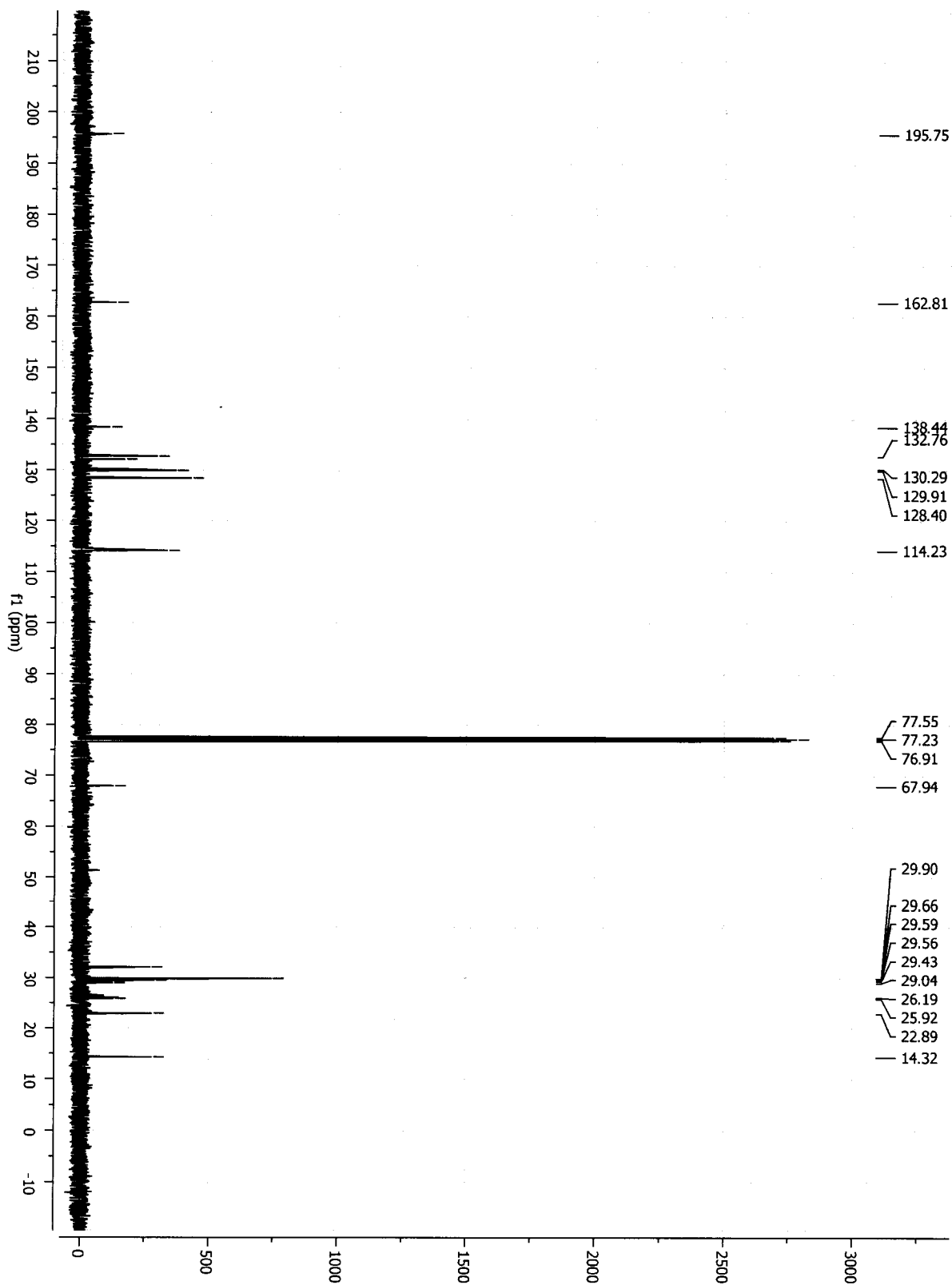


Figure 31

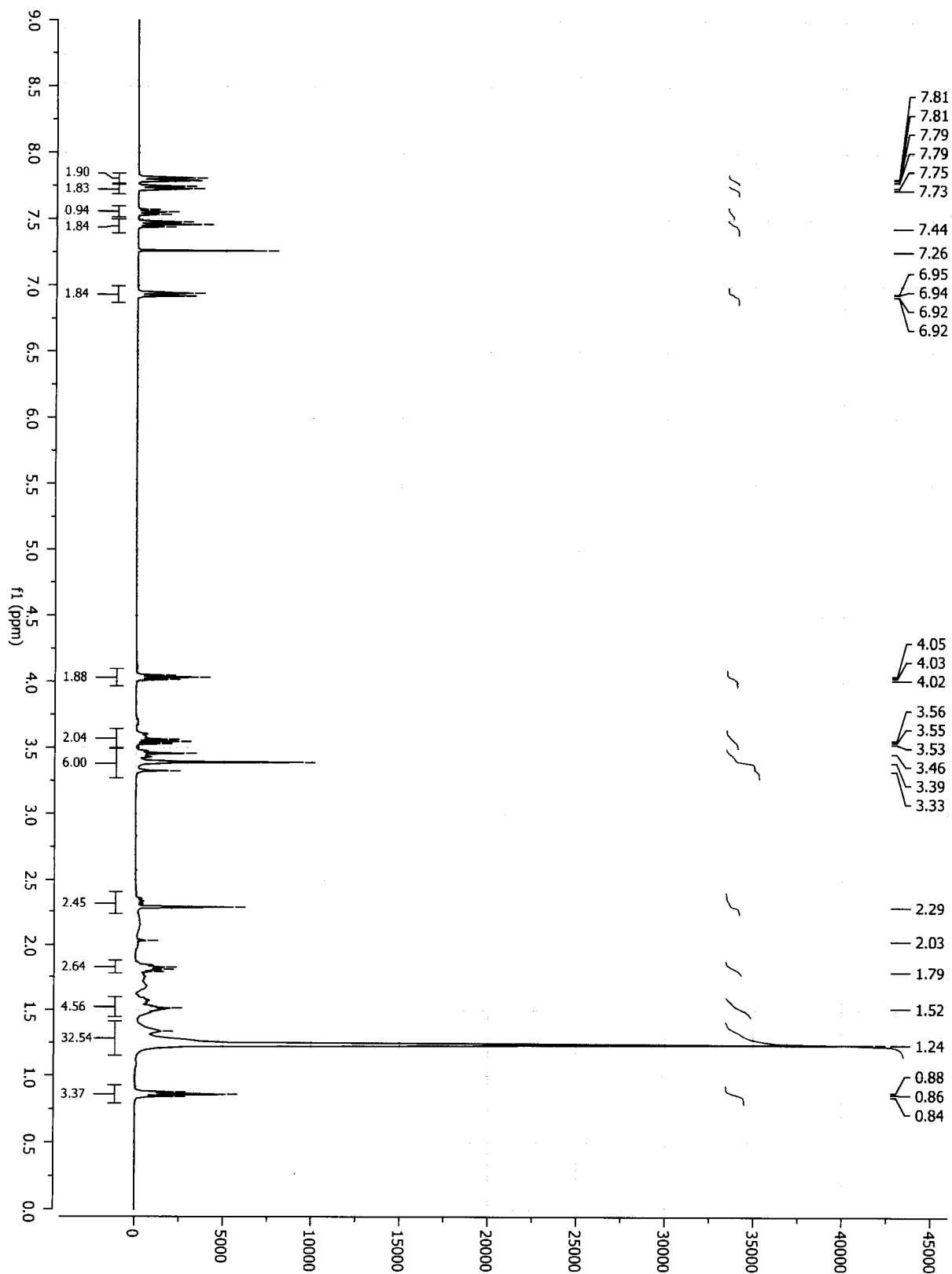


Figure 32

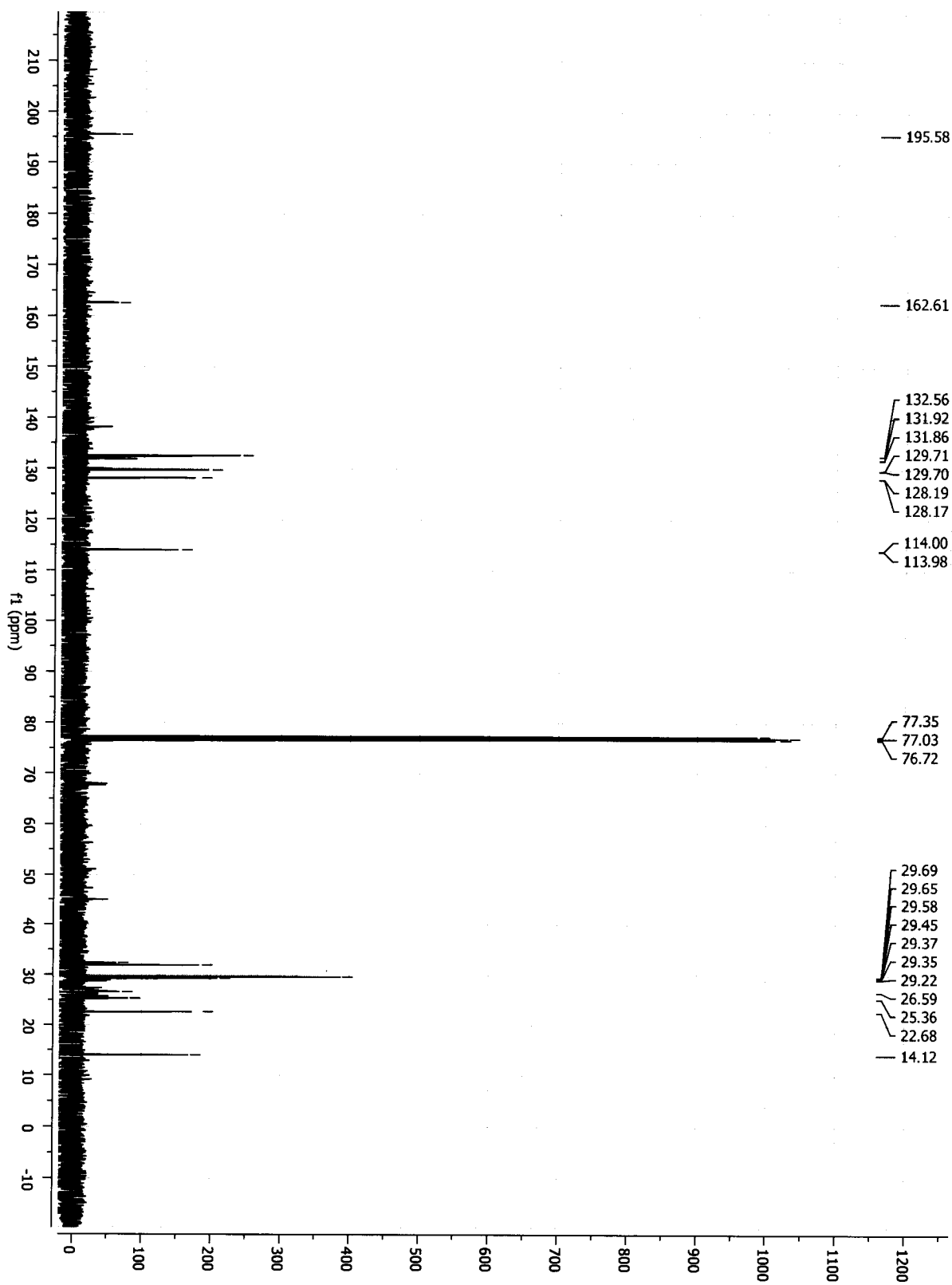


Figure 33

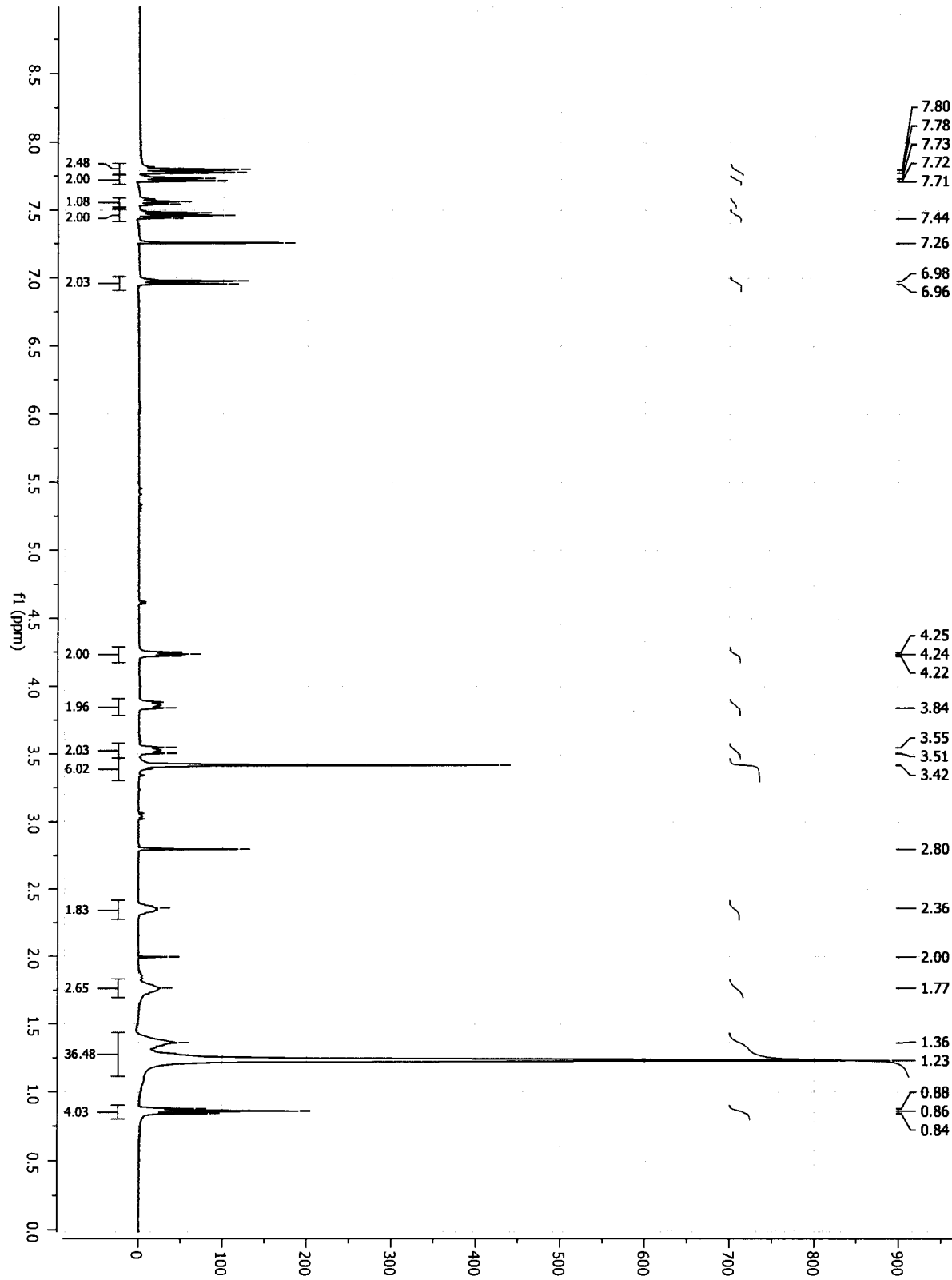


Figure 34

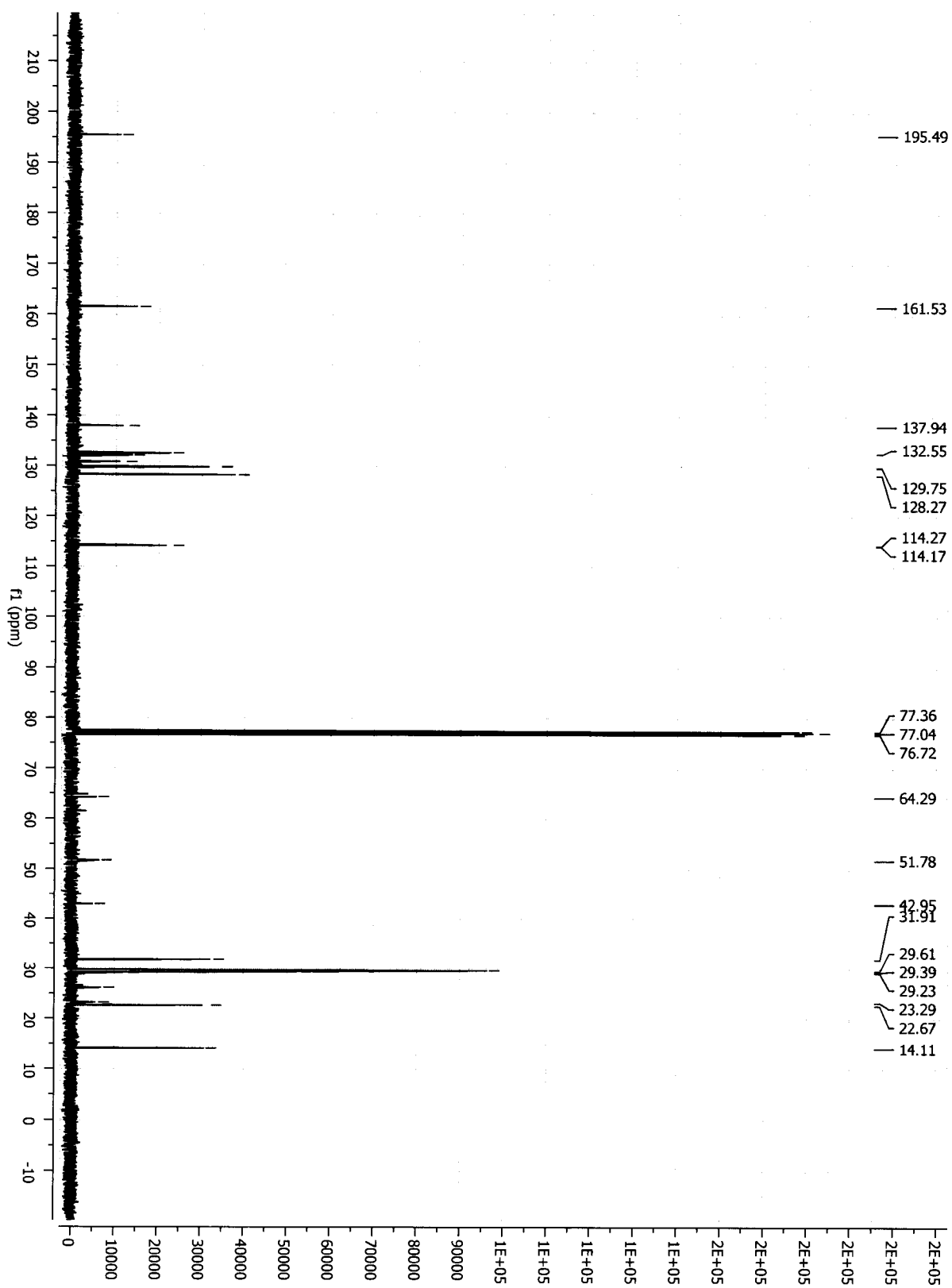


Figure 35

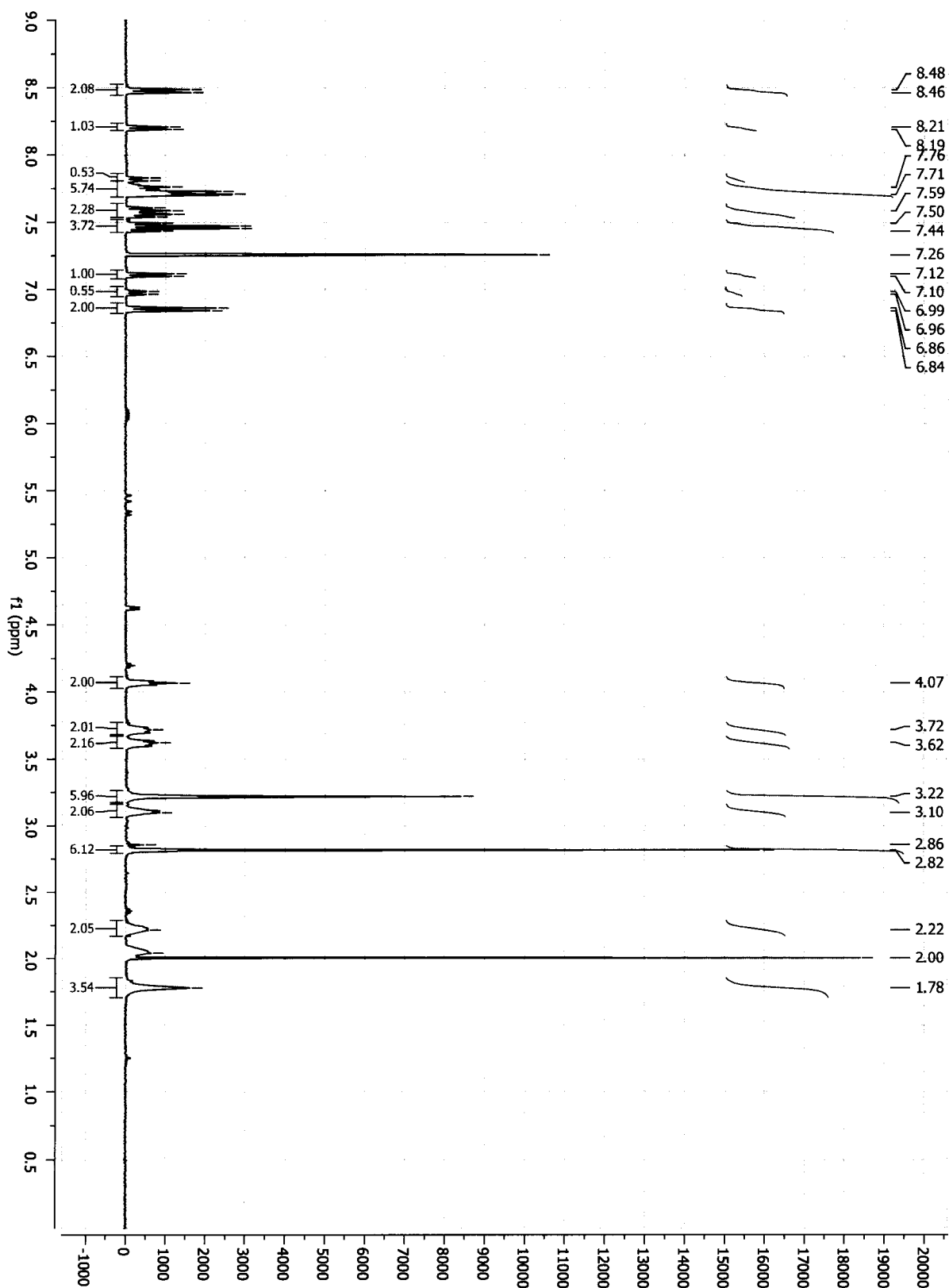


Figure 36

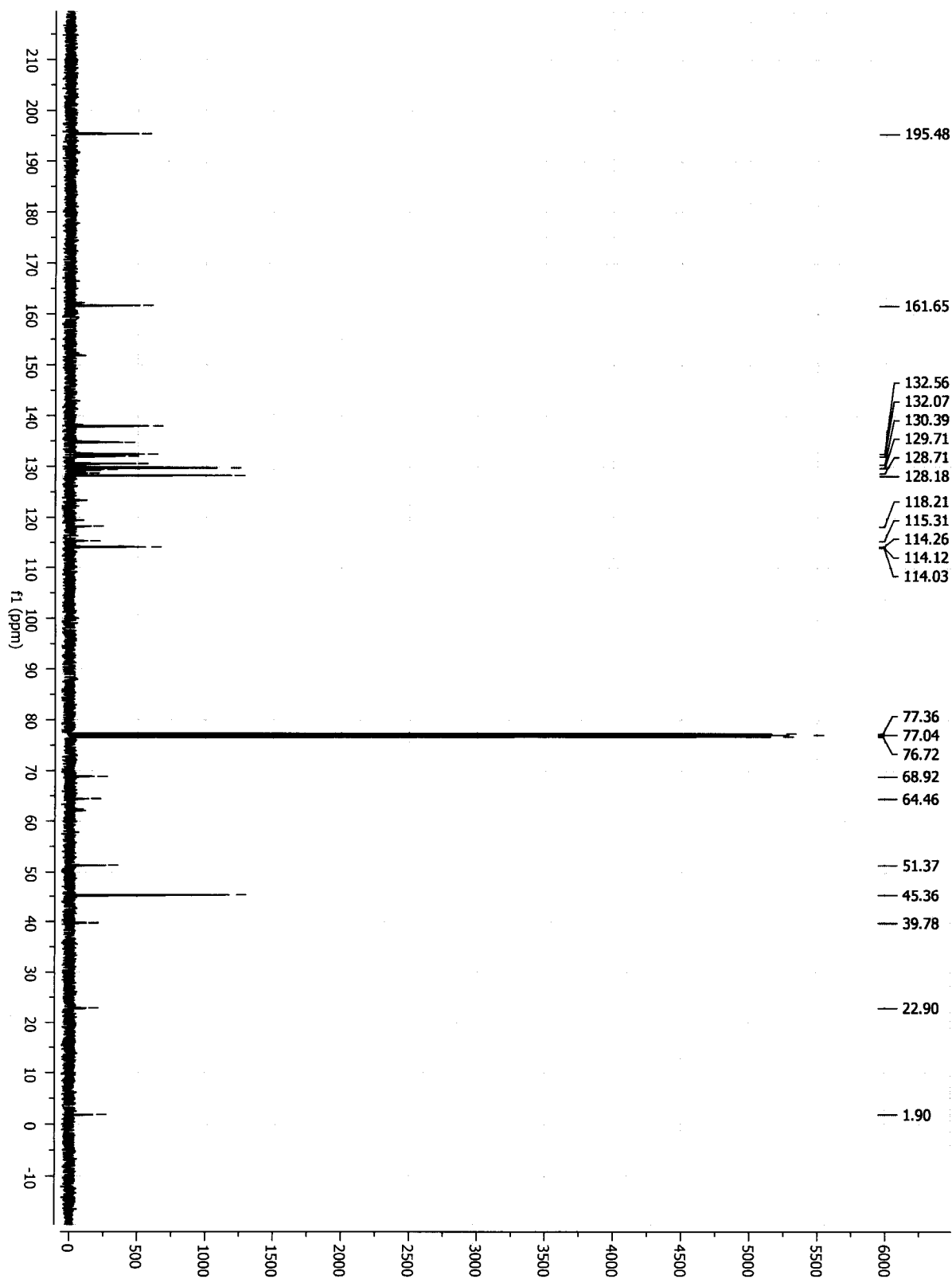


Figure 37

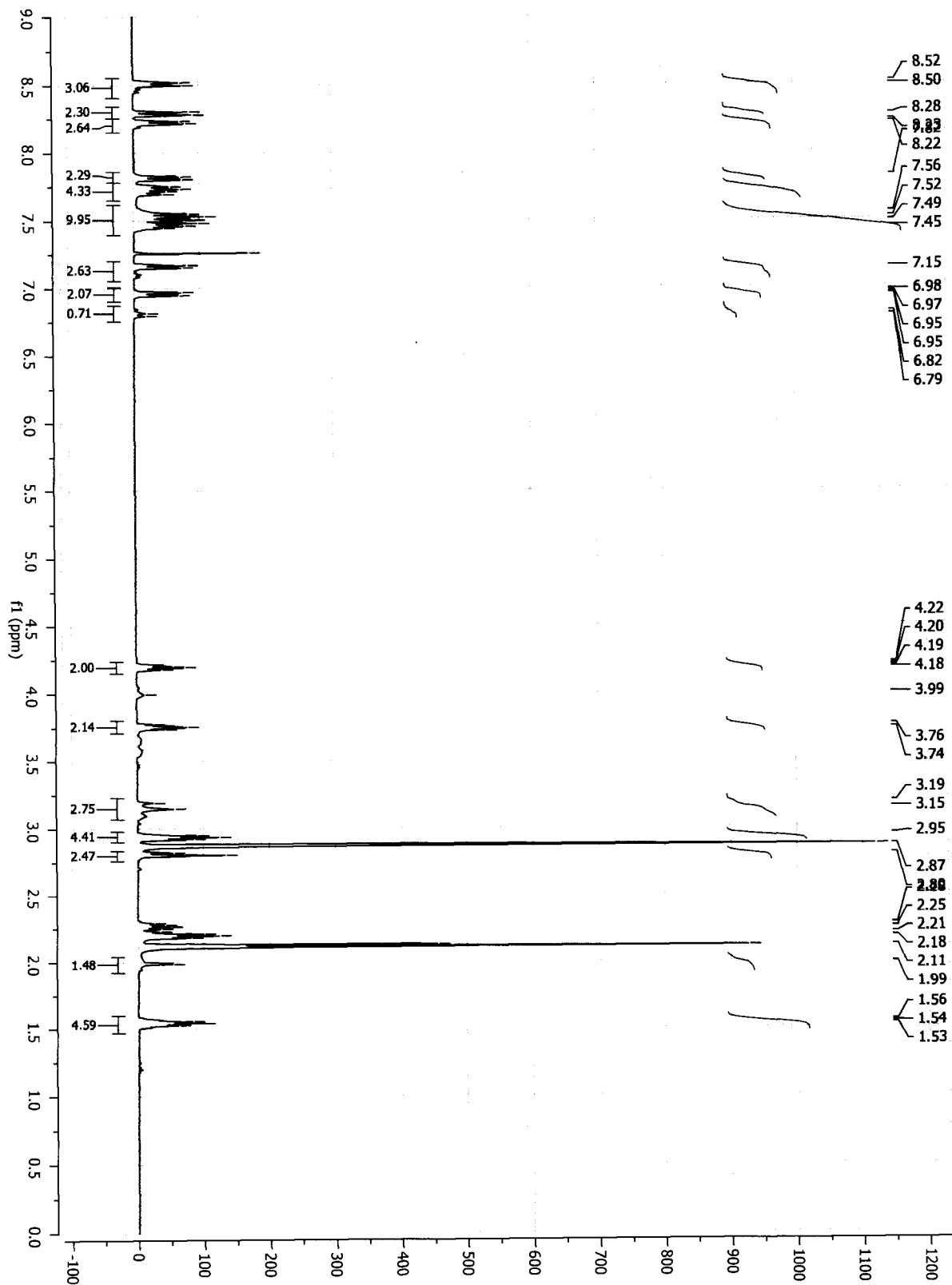


Figure 38

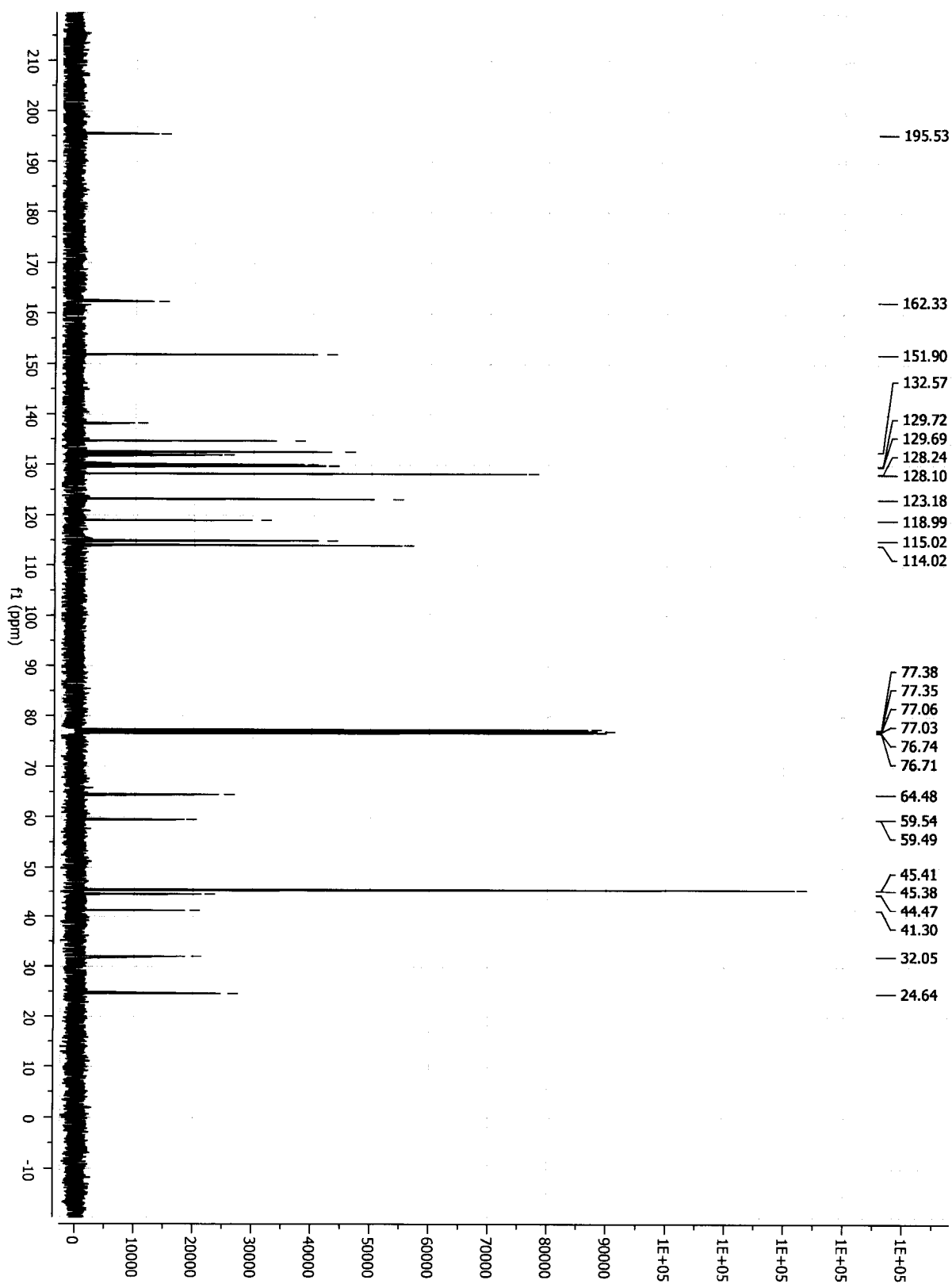


Figure 39

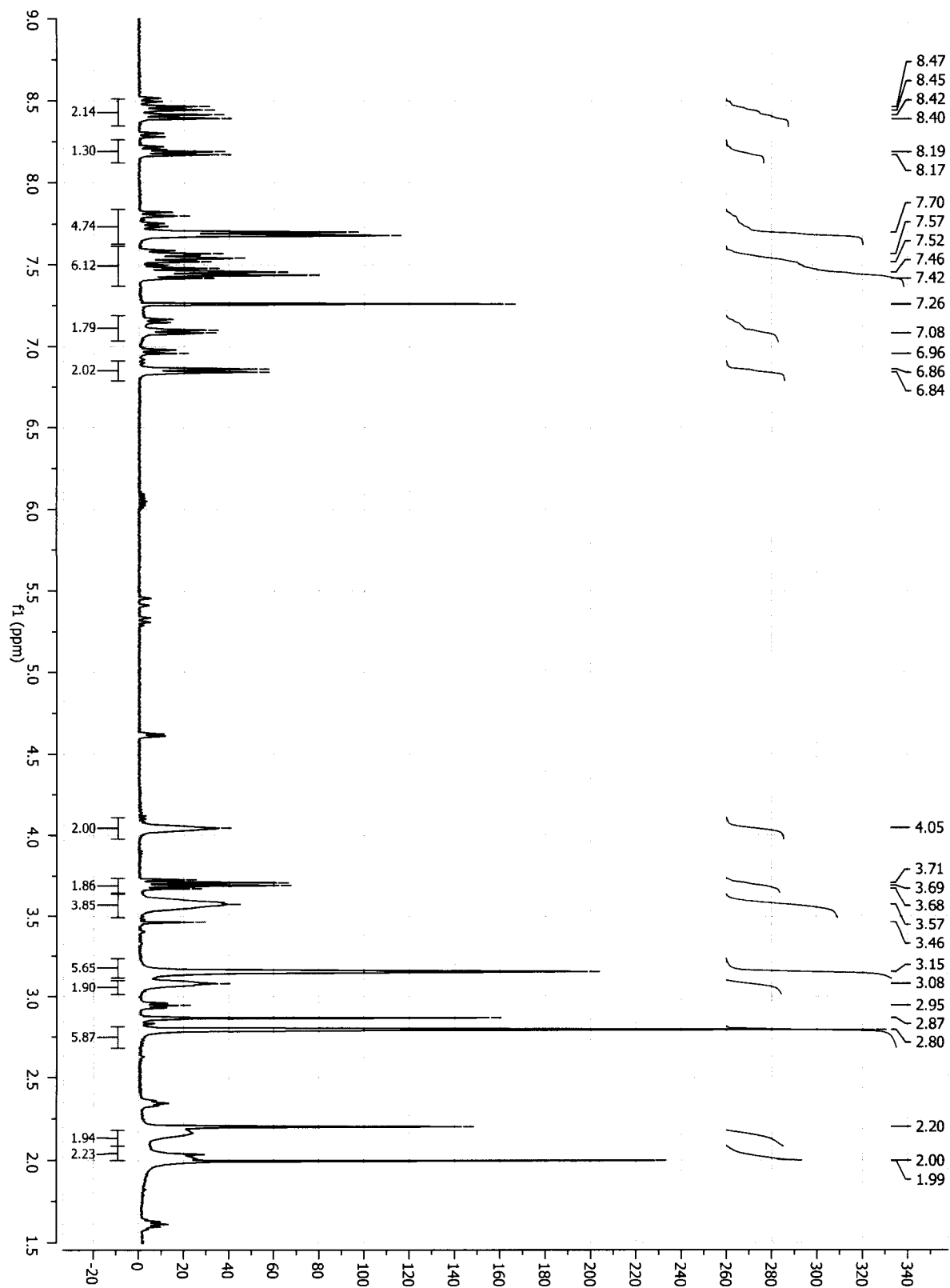


Figure 40

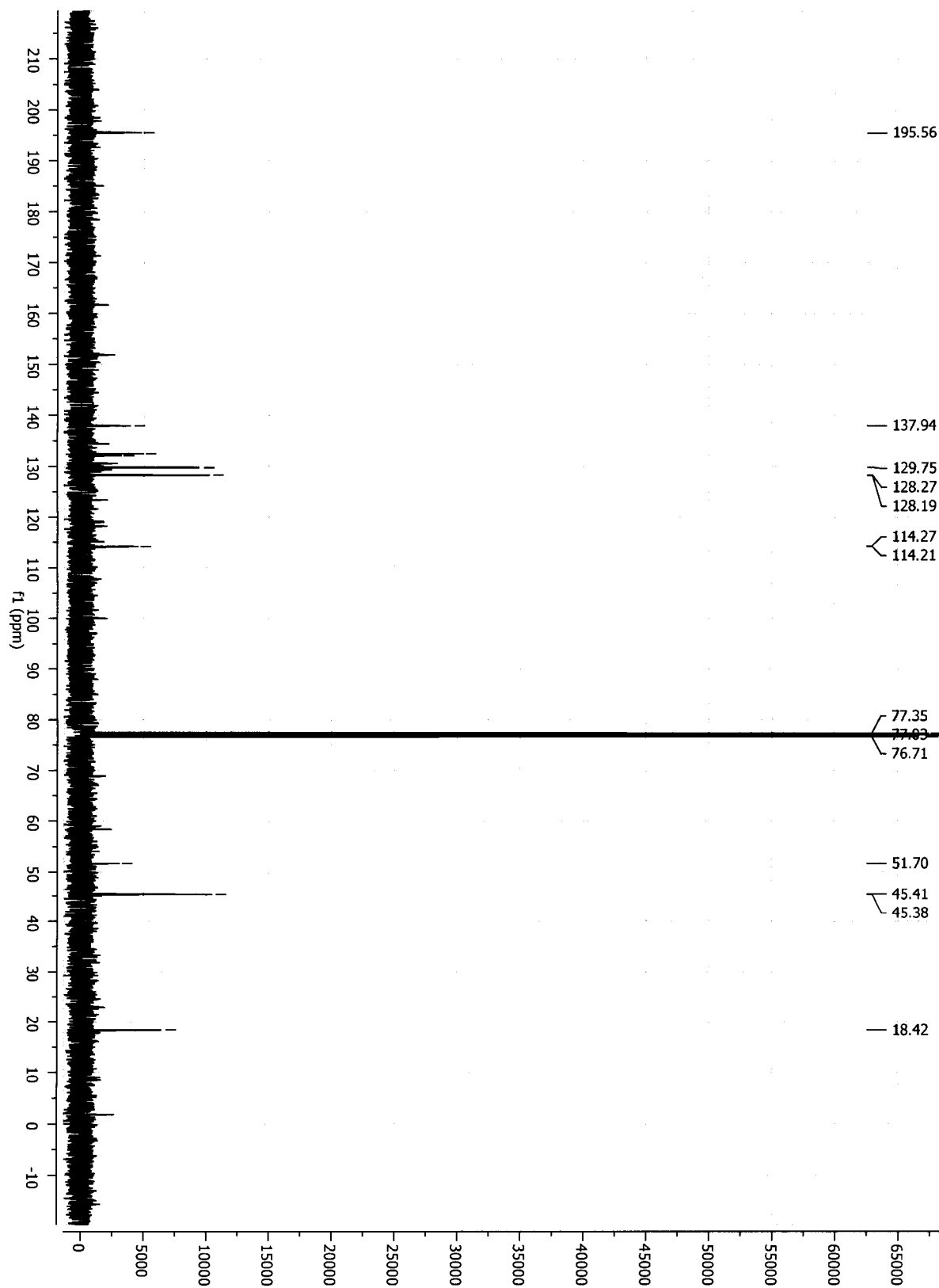


Figure 41

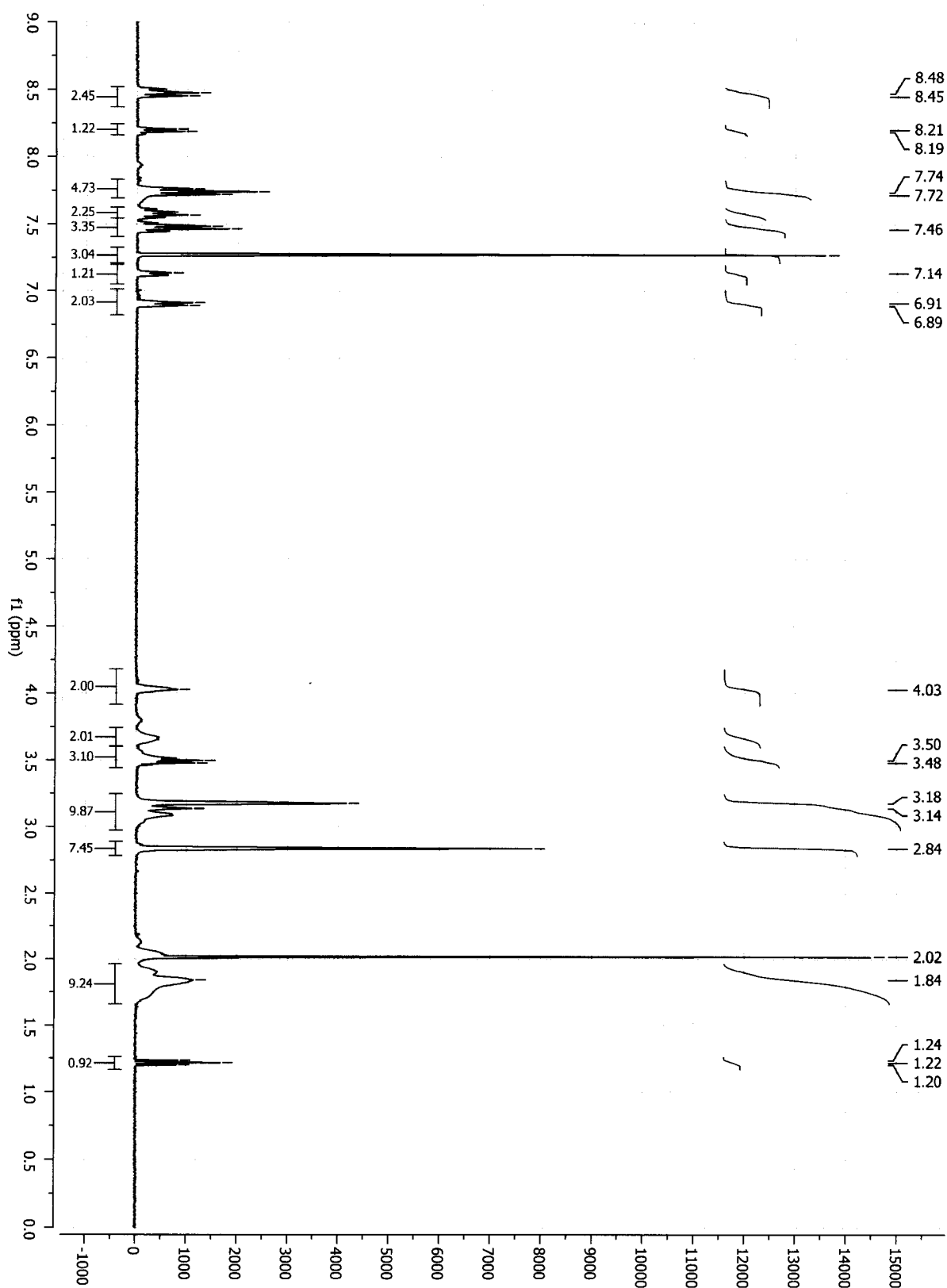


Figure 42

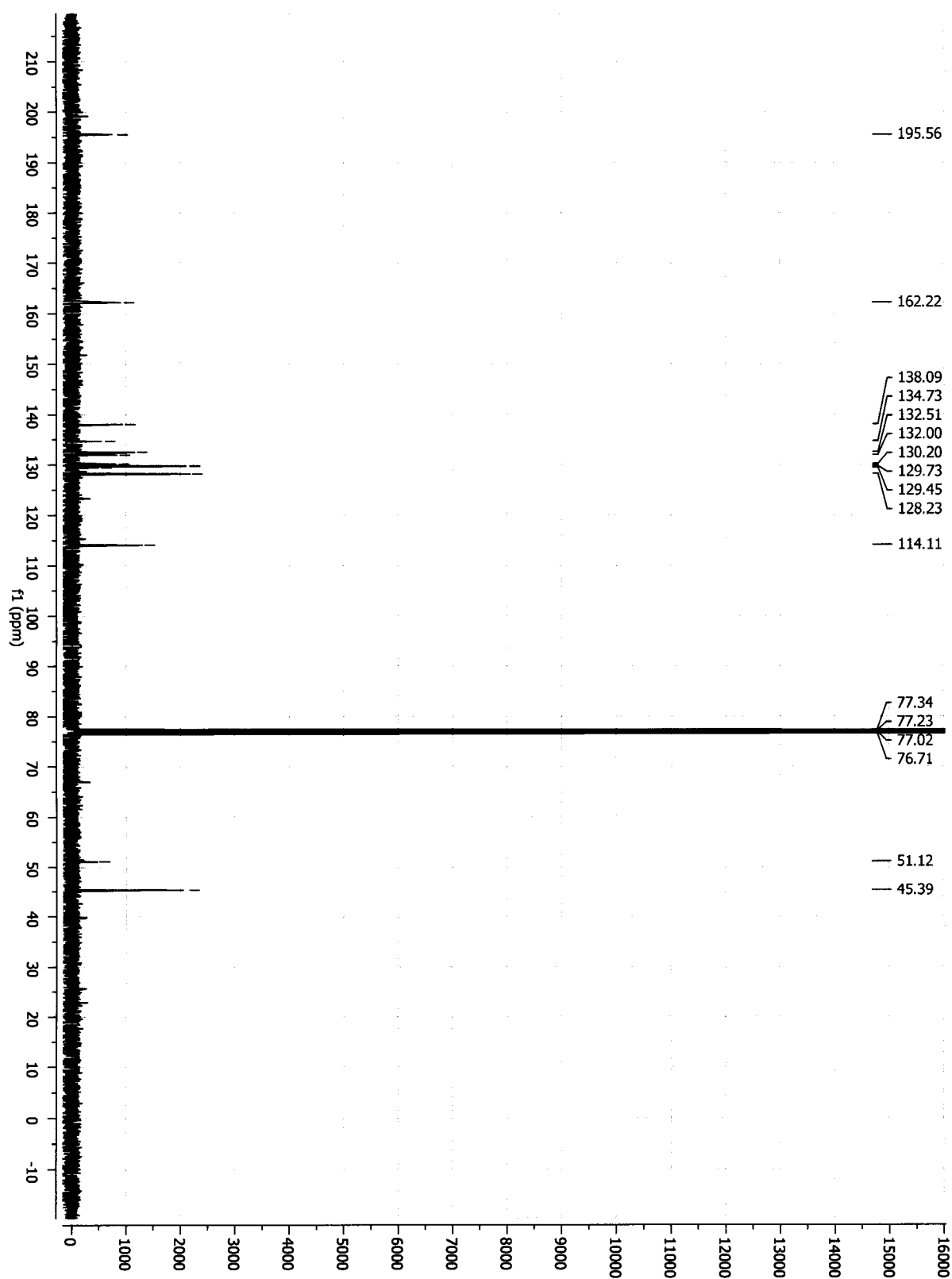


Figure 43

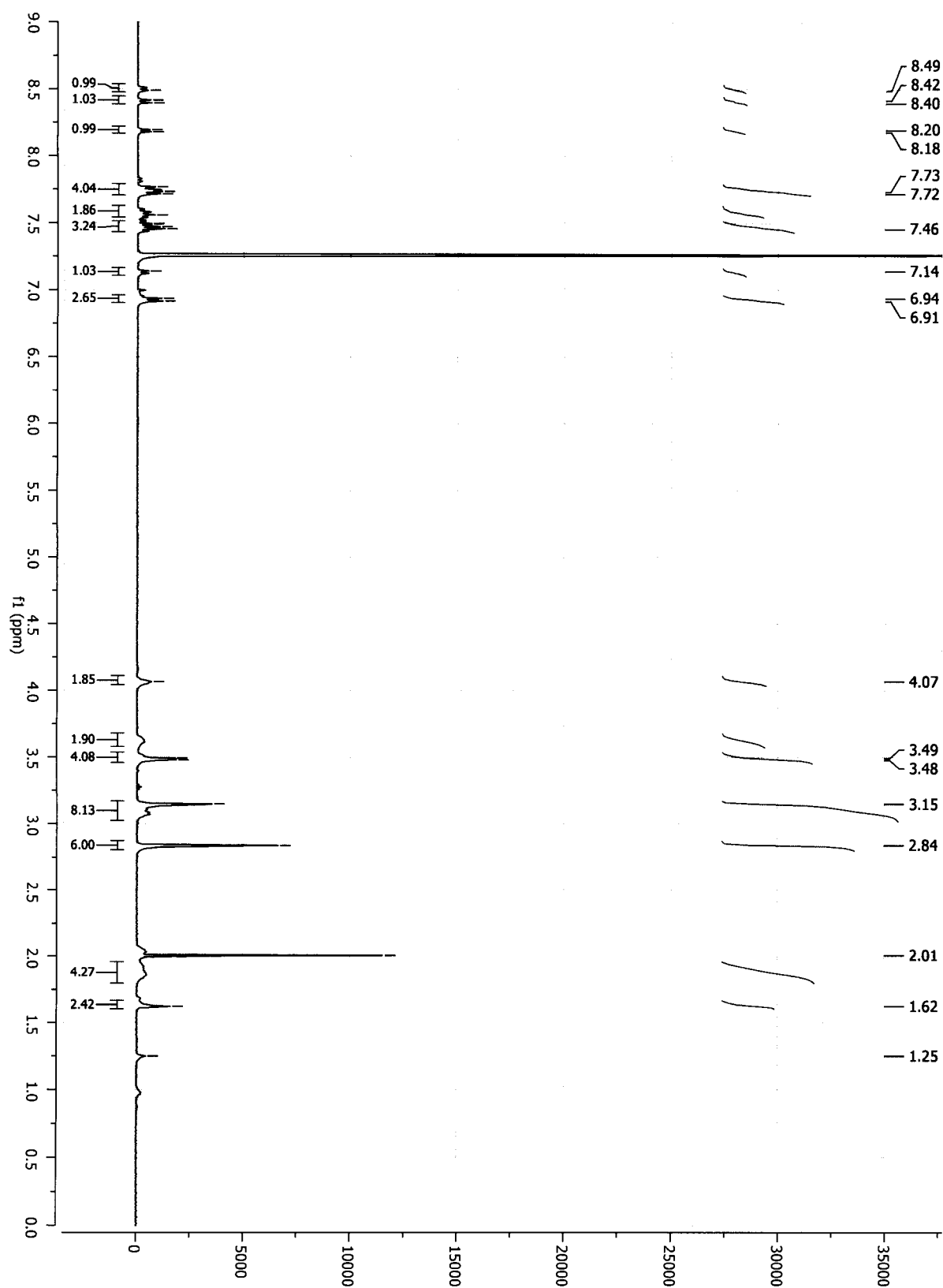


Figure 44

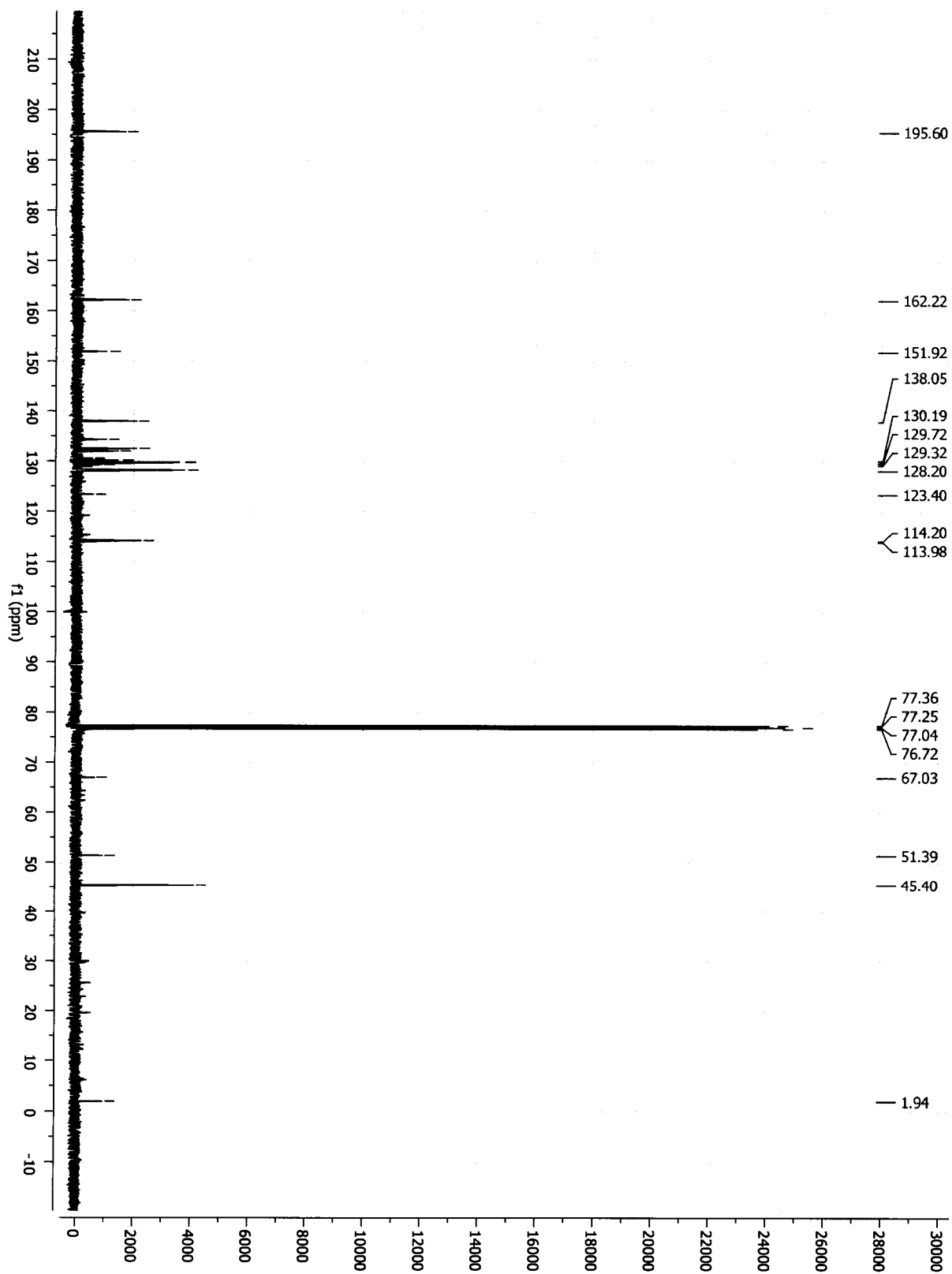


Figure 45

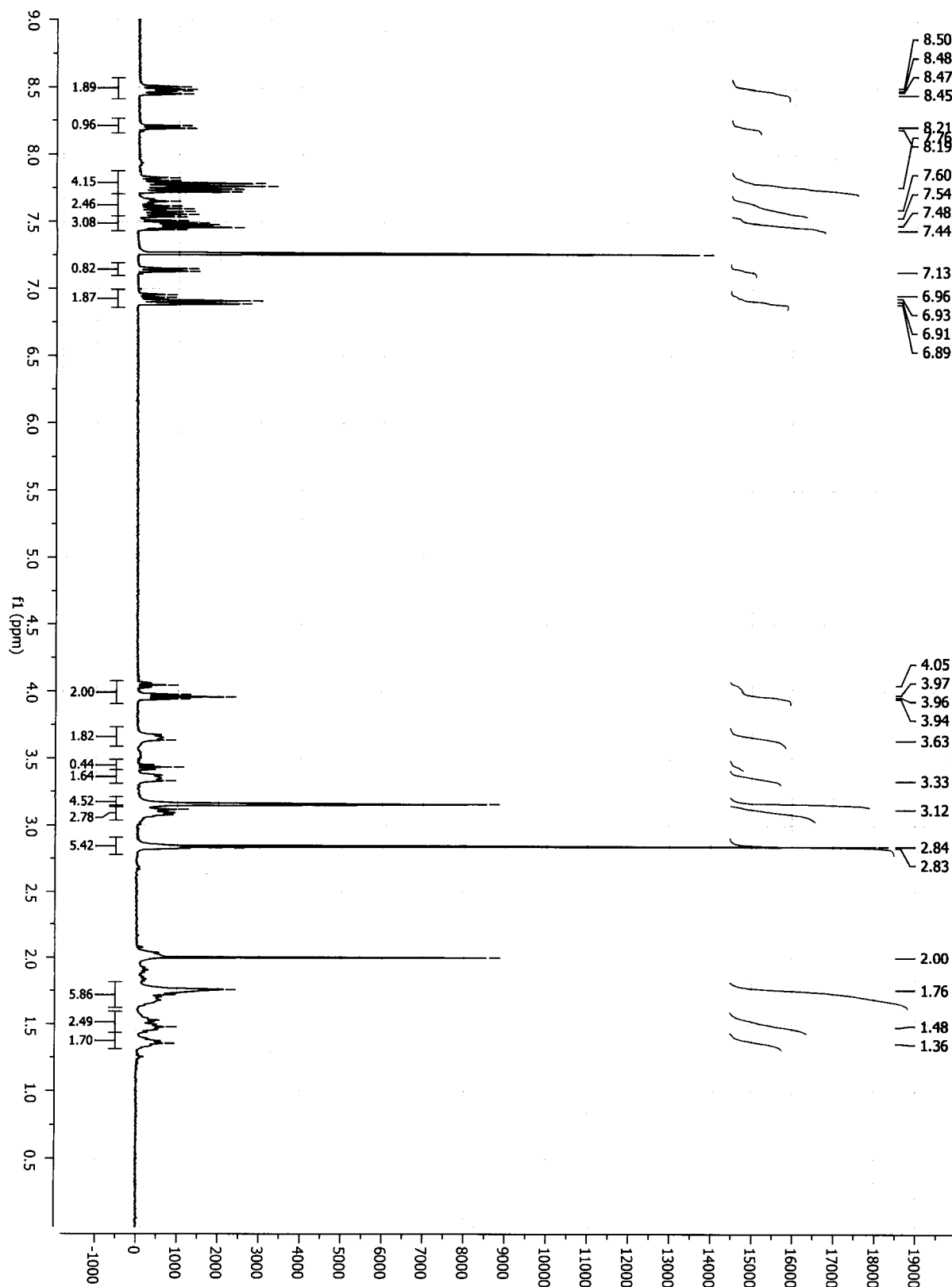


Figure 46

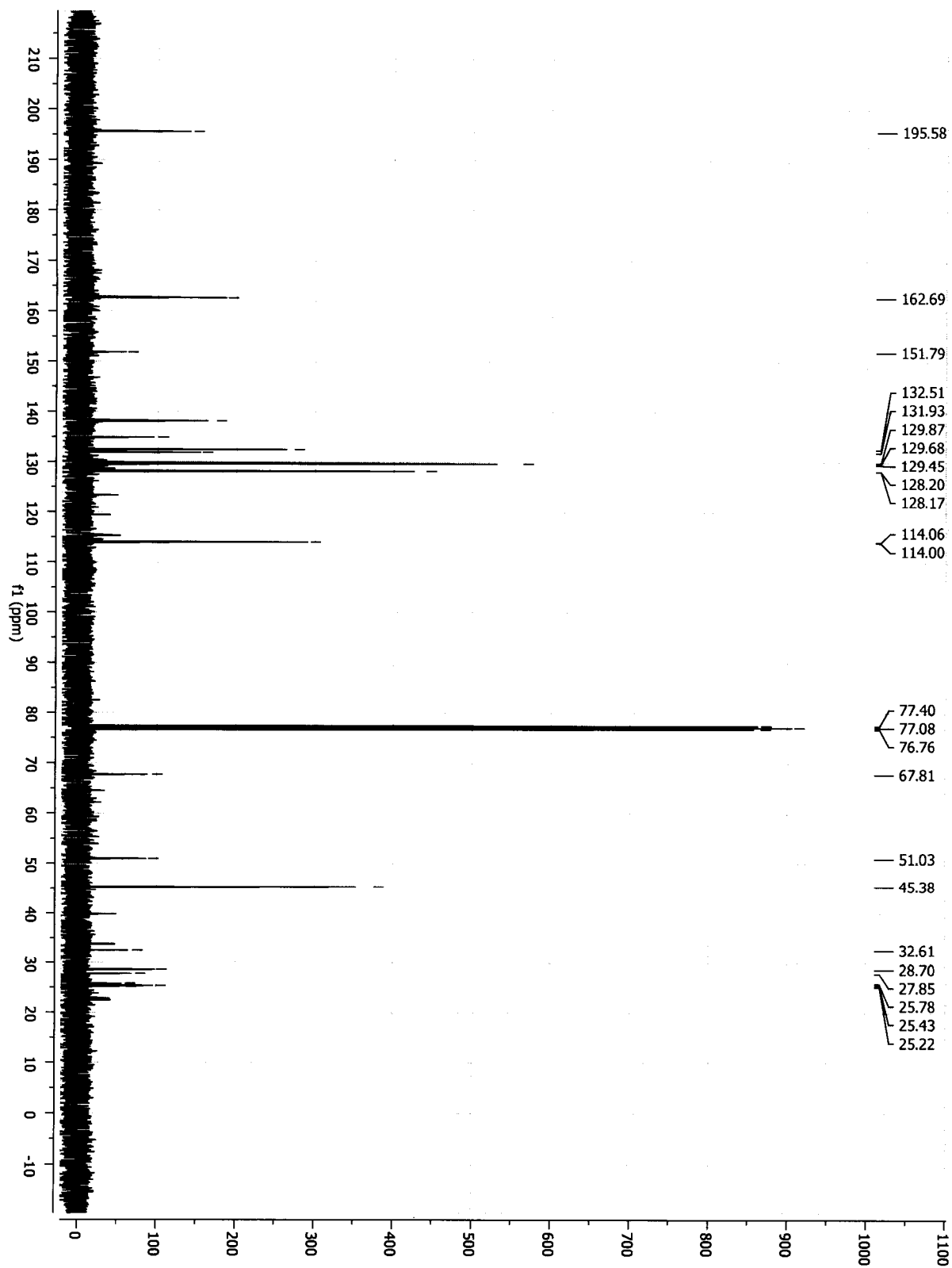


Figure 47

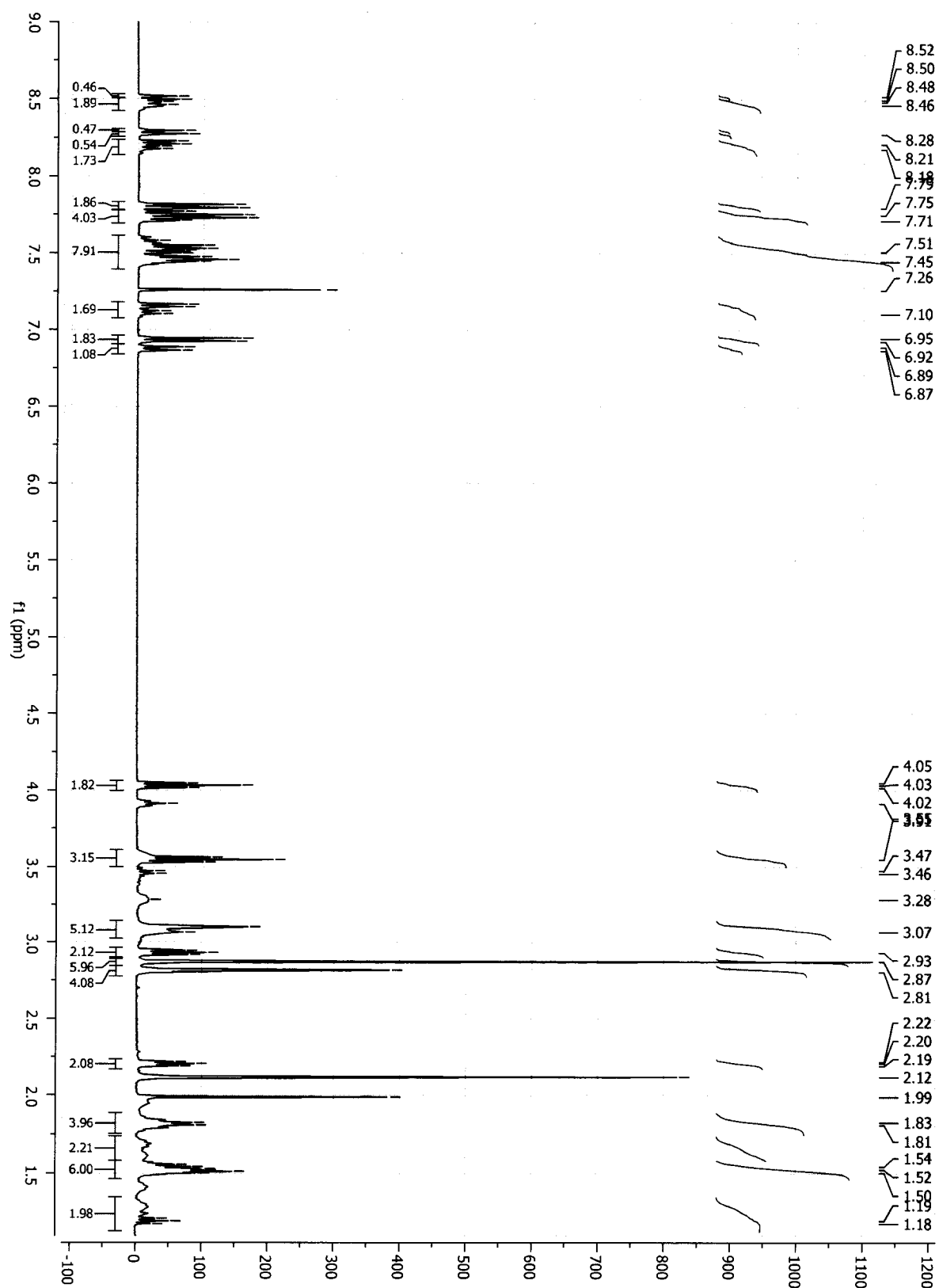


Figure 48

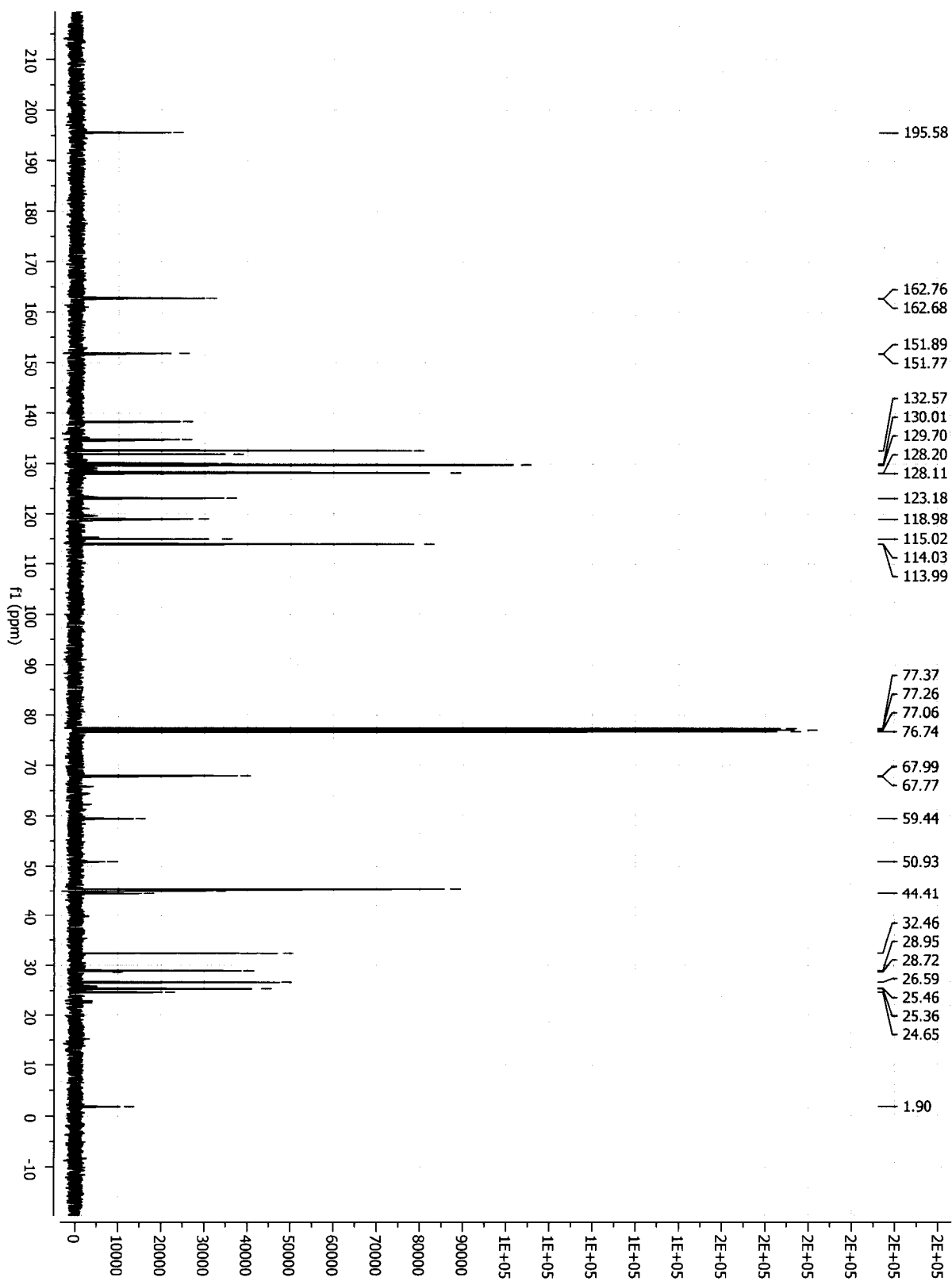


Figure 49

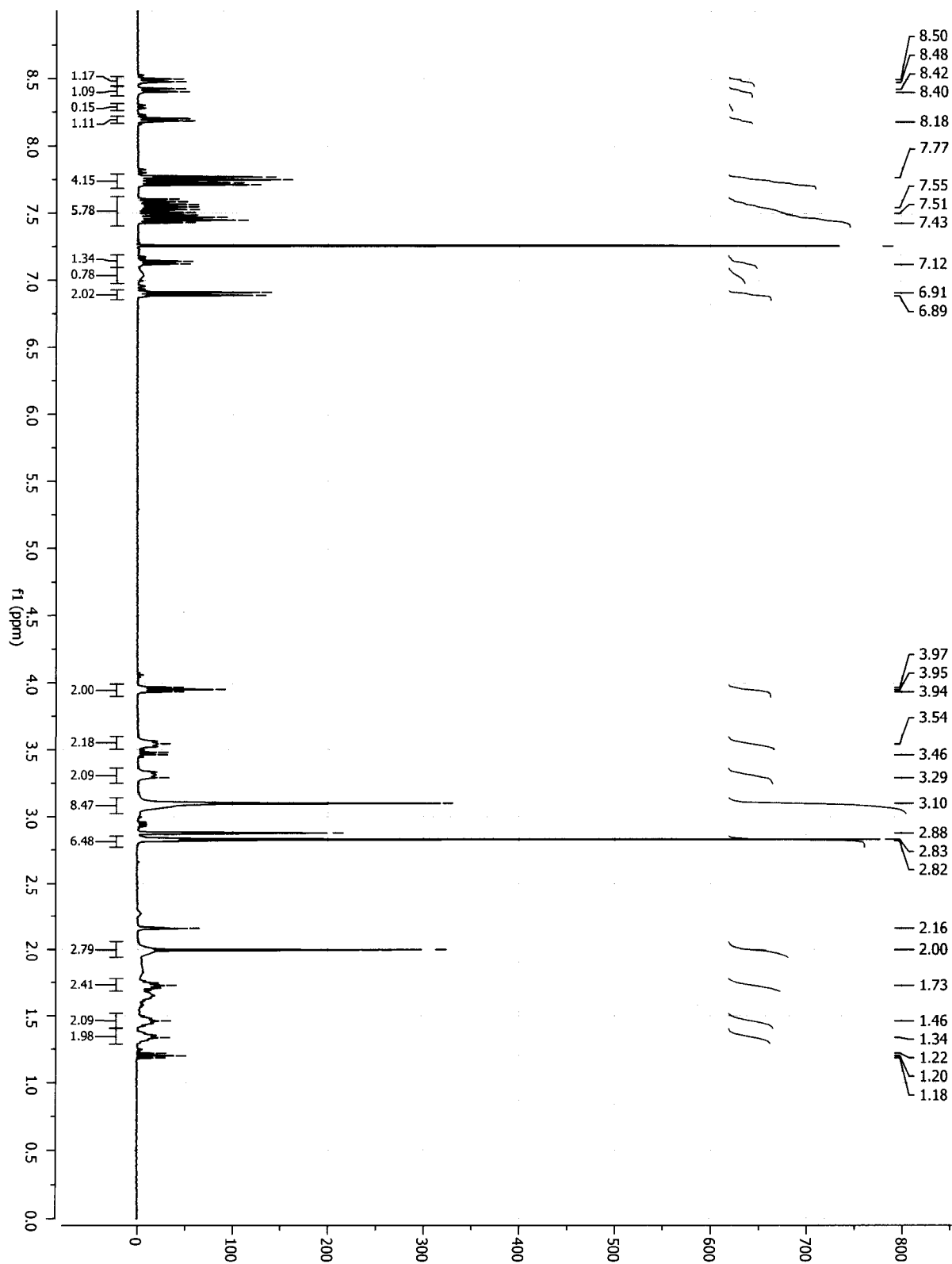
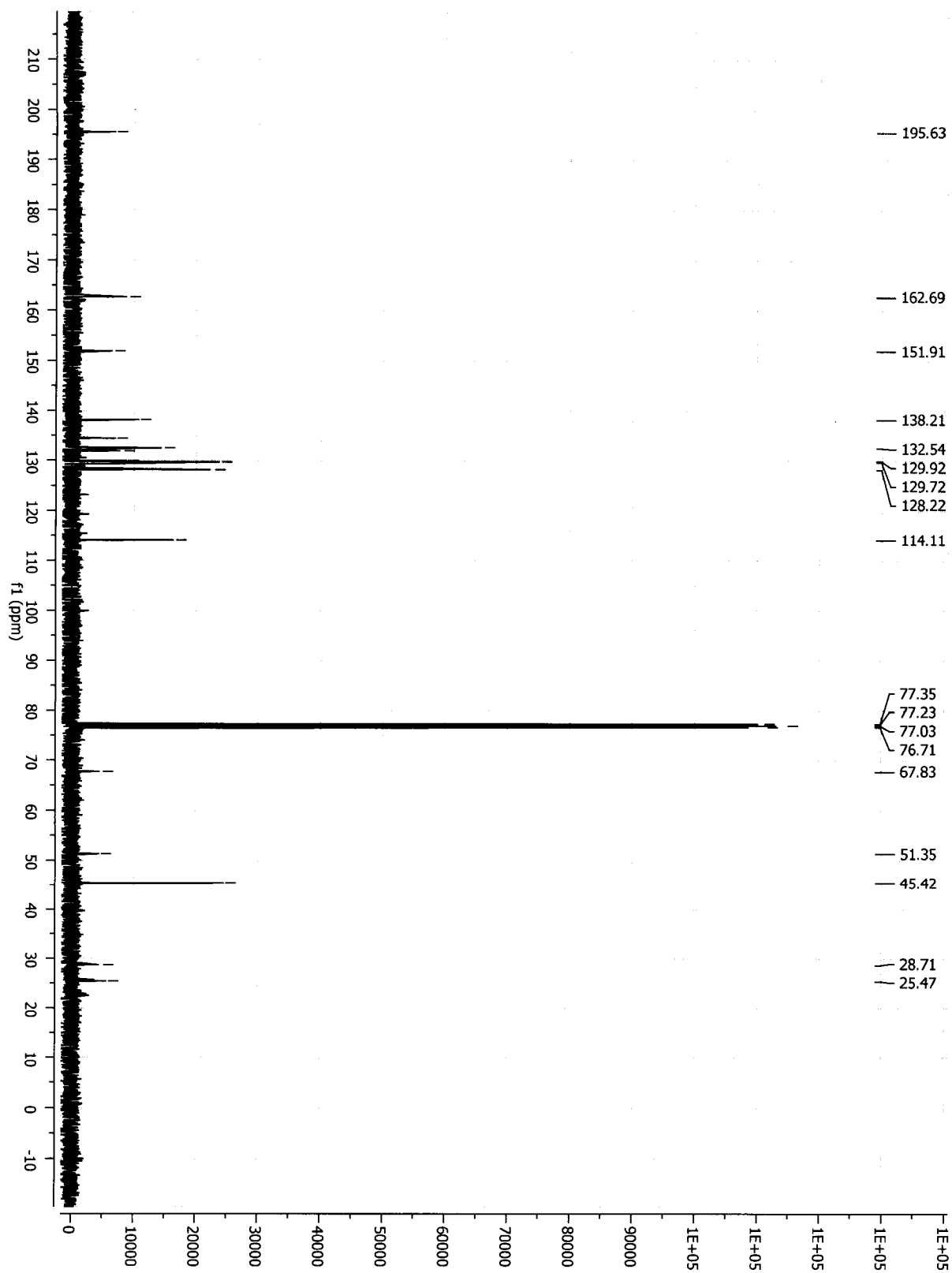


Figure 50



INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA2013/001026

A. CLASSIFICATION OF SUBJECT MATTER IPC: <i>C07C 311/41</i> (2006.01), <i>A01N 35/04</i> (2006.01), <i>A01N 41/06</i> (2006.01), <i>A01P 1/00</i> (2006.01), <i>C07C 213/02</i> (2006.01), <i>C07C 217/18</i> (2006.01) (more IPCs on the last page)		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC: <i>C07C 311/41</i> (2006.01), <i>A01N 35/04</i> (2006.01), <i>A01N 41/06</i> (2006.01), <i>A01P 1/00</i> (2006.01), <i>C07C 213/02</i> (2006.01), <i>C07C 217/18</i> (2006.01), <i>C07C 303/40</i> (2006.01), <i>C09D 5/14</i> (2006.01) Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used) Canadian Patent Database, STN (structure, CAS Registry, MARPAT, CAPlus), TotalPatent, s. terms: benzophenone, quaternary ammonium		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SAETSTONE, M. F. <i>et al.</i> , « Substantivity of sunscreens-preparation and evaluation of some quaternary ammonium benzophenone derivatives », International Journal of Cosmetic Science, 10, pages 99-109, 1988 See compound VI on page 101, compounds 6 to 8 in Table I and page 105, line 7	1 to 5 and 16 to 21
A	CA 1 231 970 (TOTH, E. <i>et al.</i>) 26 January 1988 (26-01-1988) See compound (VI)	1 to 29
A	US 5,824,716 (COQUERET, X. <i>et al.</i>) 20 October 1998 (20-10-1998) See the compound of Figure 3	1 to 29
☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* "A" "E" "L" "O" "P"	Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family
Date of the actual completion of the international search 5 March 2014 (05-03-2014)		Date of mailing of the international search report 14 April 2014 (14-04-2014)
Name and mailing address of the ISA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476		Authorized officer Alain Paquin (819) 997-2068

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/CA2013/001026

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
CA1231970A1	26 January 1988 (26-01-1988)	AT19772T	15 May 1986 (15-05-1986)
		AU558261B2	22 January 1987 (22-01-1987)
		AU2291583A	05 July 1984 (05-07-1984)
		DE3363553D1	19 June 1986 (19-06-1986)
		DK601683D0	27 December 1983 (27-12-1983)
		DK601683A	29 June 1984 (29-06-1984)
		DK163182B	03 February 1992 (03-02-1992)
		DK163182C	22 June 1992 (22-06-1992)
		EP0114410A1	01 August 1984 (01-08-1984)
		EP0114410B1	14 May 1986 (14-05-1986)
		ES528462D0	01 October 1985 (01-10-1985)
		ES8600205A1	01 January 1986 (01-01-1986)
		ES543803D0	16 January 1986 (16-01-1986)
		ES8604102A1	01 June 1986 (01-06-1986)
		ES543804D0	16 July 1986 (16-07-1986)
		ES8608476A1	01 December 1986 (01-12-1986)
		ES543805D0	16 January 1986 (16-01-1986)
		ES8604103A1	01 June 1986 (01-06-1986)
		FI834800A	29 June 1984 (29-06-1984)
		FI78459B	28 April 1989 (28-04-1989)
		FI78459C	10 August 1989 (10-08-1989)
		GR78771A1	02 October 1984 (02-10-1984)
		HU187208B	28 November 1985 (28-11-1985)
		IL70560D0	30 March 1984 (30-03-1984)
		IL70560A	31 December 1986 (31-12-1986)
		JPS59134756A	02 August 1984 (02-08-1984)
		JPS6340780B2	12 August 1988 (12-08-1988)
		US4645779A	24 February 1987 (24-02-1987)
		ZA8309615A	29 August 1984 (29-08-1984)
US5824716A	20 October 1998 (20-10-1998)	AT168404T	15 August 1998 (15-08-1998)
		AU1420295A	08 August 1995 (08-08-1995)
		CA2181701A1	27 July 1995 (27-07-1995)
		CN1142242A	05 February 1997 (05-02-1997)
		DE69411759D1	20 August 1998 (20-08-1998)
		DE69411759T2	01 April 1999 (01-04-1999)
		EP0740691A1	06 November 1996 (06-11-1996)
		EP0740691B1	15 July 1998 (15-07-1998)
		FR2715157A1	21 July 1995 (21-07-1995)
		FR2715157B1	01 March 1996 (01-03-1996)
		JPH09508158A	19 August 1997 (19-08-1997)
		WO9520016A1	27 July 1995 (27-07-1995)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA2013/001026

C07C303/40(2006.01) , *C09D 5/14* (2006.01)