Decision Letter (LSYC-2013-8495.R1)

From: p.page@uea.ac.uk

To: amoglio@ffyb.uba.ar

CC:

Subject: Synthetic Communications - Decision on Manuscript ID LSYC-2013-8495.R1

Body: 10-Dec-2013

Dear Dr. Moglioni:

Ref: An efficient microwave-assisted esterification reaction employing methanesulfonic acid supported on alumina as catalyst.

Our referees have now considered your paper and have recommended publication in Synthetic Communications; their comments, if any, appear below. We are pleased to accept your paper in its current form which will now be forwarded to the publisher for copy editing and typesetting.

You will receive proofs for checking, and instructions for transfer of copyright in due course.

The publisher also requests that proofs are checked and returned within 48 hours of receipt.

Thank you for your contribution to Synthetic Communications and we look forward to receiving further submissions from you.

Yours sincerely

Prof. Philip Page
Editor in Chief, Synthetic Communications
p.page@uea.ac.uk

Date Sent: 10-Dec-2013

An efficient microwave-assisted esterification reaction employing methanesulfonic acid supported on alumina as catalyst.

Lucas Fabian,[a] Matías Gómez,[a] Juan A. Caturelli Kuran,[a]

Graciela Moltrasio[b] and Albertina Moglioni.[a]*

[a]Departamento de Farmacología. [b]Departamento de Química Orgánica. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires. Junín 956, Buenos Aires, C1113AAD, Argentina.

Email: amoglio@ffyb.uba.ar

Abstract

A rapid and efficient protocol assisted by microwave for the synthesis of esters using methanesulfonic acid(CH_3SO_3H) supported on Al_2O_3 (AMA) as catalyst and free of solvent is described. The products were obtained in high yields and purity, with reduced reaction time and the process is simple and environmentally benign.

Keywords: Synthesis of esters,microwave irradiation, AMA catalyst, solvent-free

INTRODUCTION

In the past few years, chemistry using microwave-assisted protocols has been under intense study with significant benefits in the area of organic synthesis.[1]

]Esterification between an alcohol and an acid, catalyzed by mineral acids, is a very important reaction in the organic synthesis and a large number of experimental conditions have been developed for this reaction. Nowadays, catalyzed esterifications area currently active area of research. Stoichiometric reactions between an alcohol and an acid reported by Yamamoto[2] and Tanabe[3] are among the best, especially from the atom economy viewpoint.

There has been growing interest in microwave-assisted reactions since 1986, when pioneering investigations were performed.[4]Microwave activation of a large number of organic synthetic and metal catalyzed reactions[5] have appeared in the last decade, attracting attention due to time economy. Lidstrom[6] andBodgal[7] reviewed microwave assisted experiments reported between 1994 and 2007.Although these reports include a number of esterification reactions, the scope of the individual reactions is rather narrow. Simple and efficient esterification methods are needed in pharmaceutical chemistry and organic synthesis. Recently several authors described examples of microwave-assisted syntheses employing supported reagents with excellent results.[8]

The synthesis of esters from carboxylic acids and alcohols using CH_3SO_3H supported Al_2O_3 (AMA) as catalyst under classical reaction conditions is well documented, especially for the selective synthesis of monoesters obtained from diols.[9]This synthesis involves very large quantities of AMA (15 mmol de CH_3SO_3H /3 mmol de Al_2O_3 /1 mmol de carboxylic acid) making it difficult to separate the catalyst from the reaction product.

Herein we report our results on the use of AMA as and inorganic acid catalyst in microwave induced esterification reactions. With these conditions we were able to reduce the proportion of AMA / carboxylic acid (1 mol / 1.6 mol), get cleaner reactions, with high yields and reduced reaction times.

RESULTSAND DISCUSSION

Using a ternary mixture of alcohol (methanol, ethanol, *n*- and isopropanol), aromatic and aliphatic carboxylic acid and AMA, previously prepared from CH_3SO_3H (2 mol) and Al_2O_3 (3 mol) (called by us AMA 2:3), a wide range of acids were conveniently and efficiently converted into esters (Table 1). The ternary mixture was simply loaded into asealed reaction vessel equipped with a magnetic stirring and irradiated in an Anton Paar MW 300 microwave oven at 80 ºC during 8 min or 120 ºC during 20 min.The compounds chosen for these experiments (see Table I) are important in a wide range of applications.

Given the good results obtained in the preparation of these derivatives from several carboxylic acids with very different reactivity, extension of the developed methodology to the synthesis of some α-amino acid esters was assayed.

Amino acid esters are important intermediates in organic synthesis because they have been used in various areas such as peptide synthesis,[17] medicinal chemistry,[18,19]as chiral sources[20-23] and polymer materials.[24,25] A variety of reagents have been reported for the transformation of amino acids into amino acid esters, which include protic acids[26,27] (gaseous hydrochloric acid, sulphuric acid and *p*-toluenesulfonic acid), thionyl chloride,[28] and ion-exchange resins.[29] There are other methods which require multistep reactions to obtain the products, such as the sequence of *N*-protection, esterification and deprotection. Although some of them

are widely used, they still have several disadvantages, including tedious workup procedures, safety and waste disposal problems and harsh reaction conditions.

The use of AMA 2:3 employing microwave irradiation as an energy source showed the applicability of this methodology for the preparation of methyl, ethyl, *n*- and isopropyl esters of some α-amino acids with excellent yields (69-95%) at 120 ºC and short reaction times (20 min) (Table II). Some of these compounds were isolated as base and others as the ammonium cations.

This methodology also was assayed in the ester synthesis of homochiral ketoacids. In this case, the traditional esterification methods, using protic acids, favour the isomerisation of the chiral centre bearing the keto group. Therefore, the use of diazomethane is almost the only suitable method. In this context and pinononic and pinonic acid methyl esters, obtained from (-)-verbenone and (-)-α−pinene, were synthesized by this new methodology (Scheme 1).[33] These esters were obtained in good yields after irradiation at 70 °C for 20 min, but this could not prevent a certain percentage of isomerisation in both cases (29% for the pinononic acid and 25% for the pinonic acid).

CONCLUSION

In conclusion, a simple and quick method was described for the esterification of a wide range of carboxylic acids and amino acids with several primary and secondary alcohols, using AMA 2:3 as heterogeneous catalyst and microwave irradiation. In using this methodology, further purification is overcome because the products are obtained with high purity. This method should be of use in research, education and industry.

EXPERIMENTAL

Commercially available reagents were used as supplied (analytical or HPLC grade) without prior purification.Reactions were performed on an Anton Parr Monowave 300 reactor and the reaction mixture temperature was monitored by an IR sensor. All the isolated compounds were characterized by ^{1}H-NMR and ^{13}C-NMR. Elemental analysis was done for all the new compounds. Thin layer chromatography was performed on aluminum plates coated with 60 F_{254} silica. Plates were visualized using UV light (254 nm), iodine, or a solution of *p*-anisaldehyde 2.2% in ethanol. NMR spectra were recorded on a Bruker Avance 500 or a Bruker AC 300 spectrometer in deuterated solvents. Chemical shifts (δ) are reported in ppm. Proton-proton coupling constants (*J*) are given in Hertz and spectral splitting patterns are designated as singlet (s), doublet (d), double doublet (dd), triplet (t), quartet (q), multiplet (m), complex absorption (ca) and broad singlet (brs). Elemental analyses were performed on a Perkin–Elmer C, H, N, S-Analyzer 2400.

Prepartion of methanesulfonic acid supported on Al_2O_3 (AMA)

AMA 2:3 was prepared mixing Al_2O_3 (3 mol), previously activated in an over at 150 ºC during 72 h, with CH_3SO_3H (2 mol) in a mortar until homogeneity.

General procedure for the preparation of aromatic and aliphatic esters (Table 1)

In a typical reaction, AMA 2:3 (332g, 0.6 mol), the corresponding carboxylic acid (1 mol) and alcohol (1.5-2 mol)were mixed in the provided reaction glass tube equipped with a screw cap and magnetic agitation until a wet mixture was achieved. The reaction mixture was irradiated with microwaves (Anton Parr Monowave 300 reactor) at 80 ºC for 8 min or 120 ºC for 20 min. On cooling, the mixture was diluted with dichloromethane (41 mL), filtered under gravity and washed with dichloromethane, then the filtrate was washed with Na_2CO_3 (ss) and with water. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the ester.

General procedure for the preparation of α-amino acids esters(Table 2)

In a typical reaction, AMA 2:3 (498g, 1 mol), the corresponding aminoacid (1 mol) and alcohol (1.5-2 mol), were mixed in the provided reaction glass tube equipped with a screw cap and magnetic agitation until a wet mixture was achieved. The reaction mixture was irradiated with microwaves (Anton Parr Monowave 300 reactor) at 120 ºC for 20 min. On cooling, the mixture was diluted with chloroform (41 mL), filtered with glass frit over Celite under vacuum and washed with chloroform, then the filtrate was washed with Na_2CO_3 (ss) and with water. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the ester.

Propyl octadecanoate (3c)[11]: yellow oil; ^{13}C NMR (125 MHz, $CDCl_3$): δ 10.3, 14.1, 22.0, 22.7, 25.0, 29.1, 29.2, 29.4, 29.6, 31.9, 34.3, 65.8, 173.9.

Propyl cyclohexylacetate (5c): yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.94 (m, 5H), 1.15 (m, 1H), 1.28 (m, 2H), 1.64 (m, 3H), 1.71 (m, 4H), 1.78 (m, 1H), 2.18 (d, *J*=7.1 Hz, 2 H), 4.02 (t, *J*=6.8 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 10.4, 22.0, 26.0, 26.1, 33.0, 34.9, 42.2, 65.7, 173.2; Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.69; H, 10.99.

Isopropyl cyclohexylacetate (5d)[13]: yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93 (m, 2H), 1.18 (d, *J*=6.4 Hz, 6H), 1.2 (m, 1H), 1.66 (m, 8H), 2.19 (d, *J*=6.9 Hz, 2H), 4.95 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.8, 25.9, 26.1, 32.9, 34.9, 42.4, 67.1, 172.6.

Propyl 3,5-dinitrobenzoate (6c)[14]: yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ1.01 (t, *J*=7.4 Hz, 3 H), 1.82 (m, 2 H), 4.38 (t, *J*=6.8 Hz, 2 H), 9.08 (d, *J*=2.3 Hz, 2 H), 9.15 (t, *J*=2.2 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 10.3, 25.8, 68.5, 122.3, 129.4, 134.1, 148.7, 162.6.

Isopropyl 3,5-dinitrobenzoate (6d)[14]: yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ1.44 (d, *J*=6.4 Hz, 6 H), 5.35 (m, 1 H), 9.13 (d, *J*=2.3 Hz, 2 H), 9.20 (t, *J*=2.2 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.9, 71.2, 122.2, 129.4, 134.6, 148.7, 162.0.

Methyl 3,4-dimethoxyphenylacetate (7a)[34]: yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.51 (s, 2 H), 3.63 (s, 3 H), 3.79 (s, 3 H), 3,81 (s, 3H), 6.76 (m, 3H).

Propyl 3,4-dimethoxyphenylacetate (7c): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.75 (t, *J*=7.4 Hz, 3 H), 1.46 (m, 2 H), 3.39 (s, 2 H), 3,66 (s, 3H), 3,69 (s, 3H), 3,88 (t, *J*=7.0 Hz, 2 H), 6.66 (d, *J*=10.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ10.4, 22.0, 40.9, 55.7, 55.8, 66.3,

111.3, 112.5, 121.4, 126.8, 148.2, 149.0, 171.8; Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.40; H, 7.80.

Isopropyl 3,4-dimethoxyphenylacetate (7d)[16]: yellowoil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.19 (d, *J*=6.2 Hz, 6 H), 3.49 (s, 2 H), 3.82 (s, 3 H), 3,84 (s, 3H), 4,98 (m, 1 H), 6.78 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ10.4, 22.0, 40.9, 55.7, 55.8, 66.3, 111.3, 112.5, 121.4, 126.8, 148.2, 149.0, 171.8.

Dipropylsuccinate (10c)[34]: yellowoil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.87 (t, *J*=7.4 Hz, 6 H), 1.59 (m, 4 H), 2.56 (s, 4 H), 3.99 (t, *J*=6.8 Hz, 4 H).

***rac*-Phenylalaninemethylestermethanesulfonate (11a)**[35]: whitesolid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.65 (s, 3H, $CH_3SO_3^-$), 3.18 (m, 1H), 3.30 (m, 1H), 3.62 (s, 3H), 4.30 (m, 1H), 7.25 (brs, 5H); 8,03 (brs, 3H, NH_3^+); ^{13}C NMR (125 MHz, $CDCl_3$):δ 36.5, 39.3, 53.0, 54.6, 127.7, 129.0, 129.6, 134.4, 169.6.

***rac*-Phenylalanineethylestermethanesulfonate (11b)**[36]: whitesolid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.08 (t, *J*=6.8 Hz, 3H), 2.66 (s, 3H, $CH_3SO_3^-$), 3.17 (dd, *J*=8.0 Hz, *J'*=13.2 Hz, 1H), 3.32 (m, 1H), 4.07 (d, *J*=6.4 Hz, 2H), 4.30 (m, 1H), 7.25 (brs, 5H); 8,03 (brs, 3H, NH_3^+); ^{13}C NMR (125 MHz, $CDCl_3$):δ 13.7, 36.4, 39.1, 54.2, 62.1, 127.4, 128.7, 129.5, 134.3, 169.1.

***rac*-Phenylalaninepropylestermethanesulfonate (11c)**[30]: whitesolid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.78 (t, *J*=7.4 Hz, 3H), 1.49 (m, 2H), 2.70 (s, 3H, $CH_3SO_3^-$), 3.26 (dd, *J*=8.0 Hz,

J'=14.0 Hz, 1H), 3.43 (dd, *J*=5.5 Hz, *J'*=14.0 Hz, 1H), 3.99 (t, *J*=6.6 Hz, 2H), 4.38 (m, 1H), 7.28 (m, 5H), 8.29 (brs, 3H, NH_3^+); ^{13}C NMR (125 MHz, $CDCl_3$): δ10.0, 21.4, 36.3, 39.0, 54.2, 67.7, 127.3, 128.6, 129.4, 134.2, 169.0.

***rac*-Phenylalanineisopropylester (11d)**[31]: whitesolid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.15 (d, *J*=6.4 Hz, 3H), 1.20 (d, *J*=6.2 Hz, 3H), 2.15 (brs, 2H, NH_2), 2.86 (dd, *J*=7.7 Hz, *J'*=13.6 Hz, 1H), 3.03 (dd, *J*=5.7 Hz,*J'*=13.5 Hz, 1H), 3.68 (t, *J*=6.6 Hz, 1H), 4.98 (m, 1H), 7.19 (m, 3H), 7.27 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.7, 40.7, 55.7, 68.4, 126.7, 128.4, 129.3, 137.0, 174.0.

L-Valinemethylestermethanesulfonate (12a)[35]: yellowoil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.07 (d, *J*=7.1 Hz, 6H), 2.34 (m, 1H), 2.75 (s, 3H, $CH_3SO_3^-$), 3.80 (s, 3H), 7.75-7.93 (ca, 3H).

L-Valineethylestermethanesulfonate (12b)[36]: yellowoil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.06 (d, *J*=7.1 Hz, 3H), 1.08 (d, *J*=6.9 Hz, 3H), 1.29 (t, *J*=7.1 Hz, 3H), 2.35 (m, 1H), 2.75 (s, 3H, $CH_3SO_3^-$), 3.97 (m, 1H), 4.26 (ca, 2H), 7.75-7.91 (ca, 3H).

L-Valinepropylestermethanesulfonate (12c): yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.97 (t, 3H), 1.08 (d, 3H), 1.11 (d, 3H), 1.71 (m, 2H), 2.37 (m, 1H), 2.77 (s, 3H, $CH_3SO_3^-$), 4.01 (ca, 1H), 4.16 (m, 2H), 7.75-7.91 (brs, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 10.3, 17.5, 18.3, 21.7, 29.3, 58.4, 67.7, 169.0; Anal. Calcd for $C_9H_{21}NO_5S$: C, 42.34; H, 8.29; N, 5.49. Found: C, 42.10; H, 8.40; N, 5.30.

L-Valineisopropylester (12d): yellow oil;^{1}H NMR (500 MHz, $CDCl_3$): δ0.88 (d, *J*=6.9 Hz, 3H), 0.96 (d, *J*=6.9 Hz, 3H), 1.24 (dd, *J*=6.4 Hz, *J'*=6.2 Hz, 6H), 2.00 (dd, *J*=6.9 Hz, *J'*=5.0 Hz, 1H), 3.22 (d, *J*=5.0 Hz, 1H), 5.00 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ17.3, 22.1, 32.4, 60.2, 68.3, 175.3; Anal. Calcd for $C_8H_{17}NO_2$: C, 60.35; H, 10.76; N, 8.80. Found: C, 60.20; H, 10.90.; N, 8.71.

L-Glutamic acid methyl ester methanesulfonate (13a)[35]: yellow oil; ^{13}C NMR (125 MHz, $CDCl_3$): δ25.2, 29.4, 39.2, 52.0, 53.3, 169.6, 172.9.

L-Glutamic acid ethyl ester methanesulfonate (13b)[37]: yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$):δ1.23 (t, *J*=7.1 Hz, 3H), 1.29 (t, *J*=7.1 Hz, 3H), 2.28 (m, 2H), 2.61 (dd, *J*=8.7 Hz, *J*=14.4 Hz, 2H), 2.76 (s, 3H, $CH_3SO_3^-$), 3.71 (dd, *J*=7.1 Hz, *J*=14.2 Hz, 2H), 4.12 (m, *J*=5.1 Hz, *J*=14.2 Hz, 2H), 4.26 (dd, *J*=7.1 Hz, *J*=14.2 Hz, 2H), 8.05 (brs, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ14.0, 25.2, 29.5, 39.1, 53.4, 60.8, 62.6, 169.0, 172.3.

L-Glutamic acid dipropyl ester (13c): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$):δ0.82 (m, 6H), 1.54 (m, 4H), 1.72 (m, 1H), 1.96 (m, 1H), 2.34 (t, *J*=7.7 Hz, 2H), 3.33 (dd, *J*=5.1 Hz, *J'*=8.2 Hz, 1H), 3.94 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$):δ10.1, 21.7, 29.6, 30.3, 53.5, 65.8, 66.3, 172.9, 175.4; Anal. Calcd for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06. Found: C, 56.96; H, 9.20; N, 6.03.

L-Glutamic acid diisopropyl ester methanesulfonate (13d)[32]: yellow oil; ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.7, 25.3, 29.7, 39.2, 64.4, 68.5, 168.6, 174.8.

L-Alanine methyl ester methanesulfonate (14a)[35]: yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$):δ1.61 (d, *J*=7.3 Hz, 3H), 2.75 (s, 3H, $CH_3SO_3^-$), 3.80 (s, 3H), 4.17 (m, 1H), 8.09 (brs, 3H, NH_3^+); ^{13}C NMR (125 MHz, $CDCl_3$): δ15.9, 39.2, 49.0, 53.1, 170.7.

L-Alanine ethyl ester methanesulfonate (14b)[38]: yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$):δ1.29 (t, *J*=7.1 Hz, 3H), 1.61 (d, *J*=7.3 Hz, 3H), 2.75 (s, 3H, $CH_3SO_3^-$), 4.14 (m, 1H), 4.24 (m, 2H);^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 15.9, 39.2, 49.1, 62.4, 170.3.

L-Alanine propyl ester methanesulfonate (14c)[39]: yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$):δ 0.91 (m, 3H), 1.61 (m, 5H), 2.74 (s, 3H, $CH_3SO_3^-$), 3.55 (t, *J*=6.7 Hz, 1H), 4.12 (m, 2H), 7.86 (brs, 3H, NH_3^+). ^{13}C NMR (75 MHz, $CDCl_3$):δ 10.1, 15.7, 21.7, 39.2, 49.1, 67.8, 170.3.

L-Alanine isopropyl ester (14d)[39]: yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$):δ 1.24 (d, *J*=6.2 Hz, 6H), 1.31 (d, *J*=7.0 Hz, 3H), 2.05 (brs, 2H, NH_2), 3.50 (q, *J*=7.0 Hz, 1H), 5.01 (q, *J*=6.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.5, 21.7, 50.1, 68.3, 175.9.

Acknowledgments

This work was supported by SECYT/University of Buenos Aires and CONICET (Argentina). We thank SANICO S.A.I.&C. (Argentina) because it allocated the Anton Parr Monowave 300

reactor to check the first reactions developed in this paper. J.A.C.K. is grateful to CONICET for a research fellowship.

References

1. Kappe, C. O. Controlled microwave heating in modern organic synthesis. *Angew. Chem. Int. Ed*. **2004**, *43*, 6250-6284.
2. Ishihara, K.; Ohara, S.; Yamamoto, H. Direct condensation of carboxylic acids with alcohols catalyzed by hafnium(IV) Salts. *Science* **2000**, *290*, 1140-1142.
3. Wakasugi, K.; Misaki, T.; Yamada, K.; Tanabe, Y. Diphenylammonium triflate (DPAT): Efficient catalyst for esterification of carboxylic acids and for transesterification of carboxylic esters with nearly equimolar amounts of alcohols. *Tetrahedron Lett*. **2000**, *41*, 5249-5252.
4. Gedye, R.; Smith, F.; Westaway, K.; Ali, H.; Baldisera, L.; Laberge, L.; Rousell, J. The use of microwave ovens for rapid organic synthesis. *Tetrahedron Lett.* **1986**, 27, 279-283.
5. Larhed, M.; Moberg, C.; Hallberg, A. Microwave-accelerated homogeneous catalysis in organic chemistry. *Acc. Chem. Res*. **2002**, *35*, 717-727.
6. Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. Microwave assisted organic synthesis-a review. *Tetrahedron* **2001**, 57, 9225-9283.
7. Bogdal, D.; Loupy, A. Application of microwave irradiation to phase-transfer catalyzed reactions. *Org. Process Res. Dev.* **2008**, 12, 710-722.

8. Radi, M.; Saletti, S.; Botta, M. A one-pot, two-step microwave-assisted synthesis of highly functionalized benzoxazoles using solid-supported reagents (SSRs). *Tetrahedron Lett.* **2008**, 49, 4464-4466.

9. Sharghi, H; Sarvari, M. H. Al_2O_3/$MeSO_3H$ (AMA) as a new reagent with high selective ability for monoesterification of diols. *Tetrahedron* **2003**, 59, 3627-3633.

10. Cepanec, I.; Živković, A.; Bartolinčić, A.; Mikuldaš, H.; Litvić, M.; Merkaš, S. Photassium phosphate / benzyltriethylammonium chloride as efficient catalytic system for transesterification. *Croat. Chem. Acta* **2008**, *81*, 519-523.

11. Urioste, D.; Castro, M. B. A.; Biaggio, F. C.; de Castro, H. F. Synthesis of chromatographic standards and establishment of a method for the quantification of the fatty ester composition of biodiesel from babassu oil. *Quim. Nova* **2008**, *31*, 407-412.

12. Sanna,V.; Mariani, A.; Caria, G.; Sechi, M. Synthesis and evaluation of different fatty acid esters formulated into Precirol® ATO-based lipid nanoparticles as vehicles for topical delivery. *Chem. Pharm. Bull*. **2009**, *57*, 680-684.

13. Parrish, J. P.; Dueno, E. E.; Kim, S. I.; Jung, K. W. Improved Cs_2CO_3 Promoted O-Alkylation of Acids. *Synth. Commun*. **2000**, *30*, 2687-2700.

14. Malone, G. B.; Reid, E. E. The regularities in the melting points of some crystalline derivatives of various aliphatic alcohols. *J. Am. Chem. Soc.* **1929**, 51, 3424-3427.

15. Ríos-Lombardía, N.; Busto, E.; García-Urdiales, E.; Gotor-Fernández, V.; Gotor, V. Enzymatic desymmetrization of prochiral 2-substituted-1,3-diamines: Preparation of valuable nitrogenated compounds. *J. Org. Chem.* **2009**, 74, 2571-2574.

16. Leighton, H. J.; Maguire, M. P.; Rioux, E. WO Patent 2008156820 A1, 2008.

17. Barrett, G. C. 'Amino Acids, Peptides and Proteins' R.S.C. Publications: London, 1996**.**

18. Lall, M. S.; Ramtohul, Y. K.; James, M. N. G.; Vederas, J. C. Serine and threonine β-lactones: A new class of hepatitis A virus 3C cysteine proteinase inhibitors. *J. Org. Chem.* **2002**, 67, 1536-1547.

19. Jiabo, L.; Yaowu, S. A Convenient synthesis of amino acid methyl esters. *Molecules* **2008**, *13*, 1111-1119.

20. Tomasz, Z.; Michał, A.; Janusz, J. A simple synthesis of chiral macrocyclic tetraamides derived from α-amino acids. *Tetrahedron: Asymmetry* **2002**, *13*, 2053-2059.

21. Kim, J.; Kim, J.; Song, S.; Jung, O.; Suh, H. Enantiomeric recognition of d- and l-amino acid methyl ester hydrochlorides by new chiral *Bis*-pyridino-18-crown-6 substituted with urea, and diphenyl groups. *J. Incl. Phenom. Macrocycl. Chem.* **2007**, *58*, 187-192.

22. Somlai, C.; Peter, A.; Forgo, P.; Penke, B. One-pot synthesis of N-protected β-chiral amino alcohols. *Synth. Commun.* **2003**, *33*, 1815-1820.

23. Pollini, G.; Baricordi, N.; Benetti, S.; De Risi, C.; Zanirato, V. A simple entry to chiral non-racemic 2-piperazinone derivatives. *Tetrahedron Lett*. **2005**, *46*, 3699-3701.

24. Atsushi, N.; Toyoharu, M.; Hiroto, K.; Takeshi, E. Controlled cationic ring-opening polymerization of 1,3-oxazolidine-2-thione derived from l-serine. *Macromolecules* **2003**, *36*, 9335-9339.

25. Fumio, S.; Takeshi, E. Syntheses and functions of polymers based on amino acids. *Macromol. Chem. Phys*. **1999**, *200***,** 2651-2661.

26. Andersson, P. G.; Guijarro, D.; Tanner, D. Preparation and use of aziridino alcohols as promoters for the enantioselective addition of dialkylzinc reagents to N-(diphenylphosphinoyl) imines. *J. Org.Chem.* **1997**, *62*, 7364-7375.

27. Rachele, J. R. The methyl esterification of amino acids with 2,2-dimethoxypropane and aqueous hydrogen chloride. *J. Org. Chem.* **1963**, *28*, 2898-2898.

28. Jones, S. M.; Urch, J. E.; Kaiser, M.; Brun, R.; Harwood, J. L.; Berry, C.; Gilbert, I. H. Analogues of thiolactomycin as potential antimalarial agents. *J. Med. Chem.* **2005**, *48*, 5932-5941.

29. Ramesh, C. A.; Vimal. A mild and convenient procedure for the esterification of amino acids. *Synth. Commun.* **1998**, *28*, 1963-1965.

30. Allen, G. R.; Baker, B. R.; Dornbush, A. C.; Joseph, J. P.; Kissman, H. M.; Weiss, M. J. The preparation of various esters of certain L-phenylalanine derivatives and their antifungal and antibacterial activity. *J. Med. Chem.* **1960**, 2, 391-413.

31. Arvid, K.; Wretlind, J. The availability of the isopropyl ester of L- and D-phenylalanine and 3,6-dibenzyl-2,5-diketopiperazine for growth in rats. *Acta Physiol. Scand*. **1954**, *30*, 97-104.

32. Buckley, T. F.; Rapoport, H. Amino acids as chiral aducts for asymmetric products. Chirally specific syntheses of tylophorine and cryptopleurine. *J. Org. Chem.* **1983**, *48*, 4222-4232.

33. Moglioni, A. G.; García-Expósito, E; Aguado, G. P.; Parella, T.; Branchadell, V.; Moltrasio, G. Y.; Ortuño, R. M. Divergent routes to chiral cyclobutane synthons from (−)-α-pinene and their use in the stereoselective synthesis of dehydro amino acids. *J. Org. Chem.* **2000**, *65*, 3934-3940.

34. ^{13}C-NMR spectra are in WSS: Wiley Subscription Services, Inc. (US).

35. The corresponding hydrochloride has been described previously in: Omata, K.; Aoyagi, S.; Kabuto, K. Observing the enantiomeric ^{1}H chemical shift non-equivalence of several

α-amino ester signals using tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorato]samarium(III): a chiral lanthanide shift reagent that causes minimal line broadening. *Tetrahedron: Asymmetry* **2004**, *15*, 2351-2356.

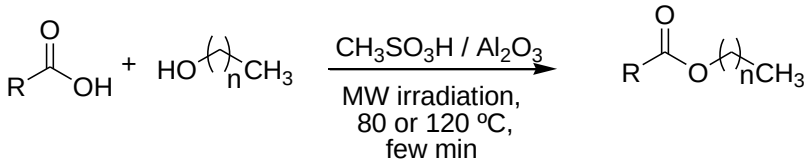
36. The corresponding hydrochloride has been described previously in: Spectral database for organic compounds, SDBS, by National Institute of Advanced Industrial Science and Technology (AIST), Japan.

37. The corresponding hydrochloride has been described previously in: Chiles, H. M.; Noyes, W. A. Optically active diazo compounds. II. *J. Am. Chem. Soc.* **1922**, *44*, 1798-1810.

38. The free base has been described previously in: Li, G.; Liang, Y.; Antilla, J. C. A vaulted biaryl phosphoric acid-catalyzed reduction of α-imino esters: the highly enantioselective preparation of α-amino esters. *J. Am. Chem. Soc.* **2007**, *129*, 5830-5831.

39. The corresponding hydrochloride has been described previously in: Mazur, R. H.; Reuter, J. A.; Swiatek, K. A.; Schlatter, J. M. Synthetic sweeteners. 3. Aspartyl dipeptide esters from L- and D-alkylglycines. *J. Med. Chem.* **1973**, *16*, 1284-1287.

Table I. Esters prepared from aromatic and aliphatic carboxylic acids

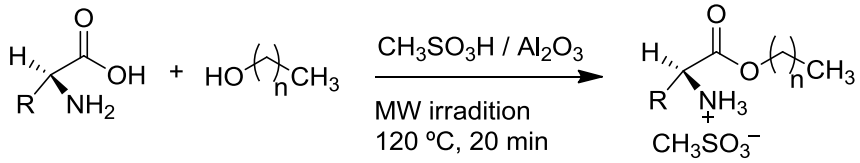


R = alkyl, arylalkyl, aryl; n = 1, 2 or 3

		Methanol		*Ethanol*		*n-Propanol*		*Isopropanol*	
Entry	*Acid*	Time (min)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield(%)
1	Salicylic	20	96[a]	20	96[a]	20	96[b]	20	90[10]
2	Palmitic	20	97[b]	20	97[b]	20	97[11],c	20	97[a]
3	Stearic	20	97[b]	20	97[b]	20	97[11]	20	97[12],c
4	Decanoic	20	97[b]	20	97[b]	20	97[b]	20	97[b]
5	Cyclohexylacetic	8	98[a]	8	98[a]	8	98	8	98[13]
6	3,5-Dinitrobenzoic	8	89[a]	8	88[14]	8	88[14]	8	88[14]
7	3,4-Dimethoxyphenylacetic	20	88[c]	20	90[15]	20	90	20	90[16]
8	Benzoic	8	98[a]	8	98[a]	8	98[a]	8	98[10]
9	Phenylacetic	8	97[a]	8	97[a]	8	97[a]	8	97[13]
10	Succinic[d]	8	97[b]	8	97[a]	8	97[c]	8	97[b]

All compounds were fully characterized by ^{1}H and ^{13}C-NMR spectra.[a] NMR spectra are in accordance with those reported in NMR Catalogues: Poucher et Campbell -AldrichLibrary ofNMR Spectra Aldrich NMR Library and Aldrich Spectral Viewer v 1.1.10.[b]NMR spectra are in accordance with those reported in theSpectral Database for Organic Compounds, SDBS, by National Institute of Advanced Industrial Science and Technology (AIST), Japan. [c]WSS: Spectral data were obtained from Wiley Subscription Services, Inc. (US). [d]Diester derivatives.

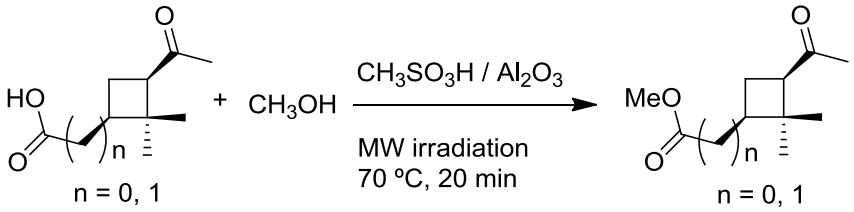
Table II. Esters prepared from α-amino acids.



R = alkyl, aryl; n = 1, 2 or 3

Entry	*Amino acid*	*Methanol* (%)	*Ethanol* (%)	*n-Propanol* (%)	*Isopropanol* (%)
11	Phenylalanine	90	88	92[30]	72[31]
12	Valine	93	92	88	69
13	Glutamic acid[a]	88	86	70	90[32]
14	Alanine	93	95	88	74

All compounds were fully characterized by ^{1}H and ^{13}C-NMR spectra.[a]Diester derivatives.



Scheme 1. Esters prepared from homochiral ketoacids.

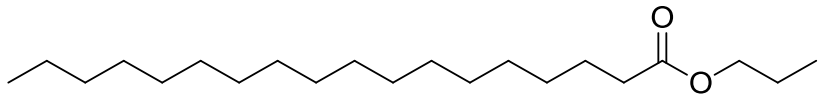
Supplementary Material

An efficient microwave-assisted esterification reaction employing methanesulfonic acid supported on alumina as catalyst.

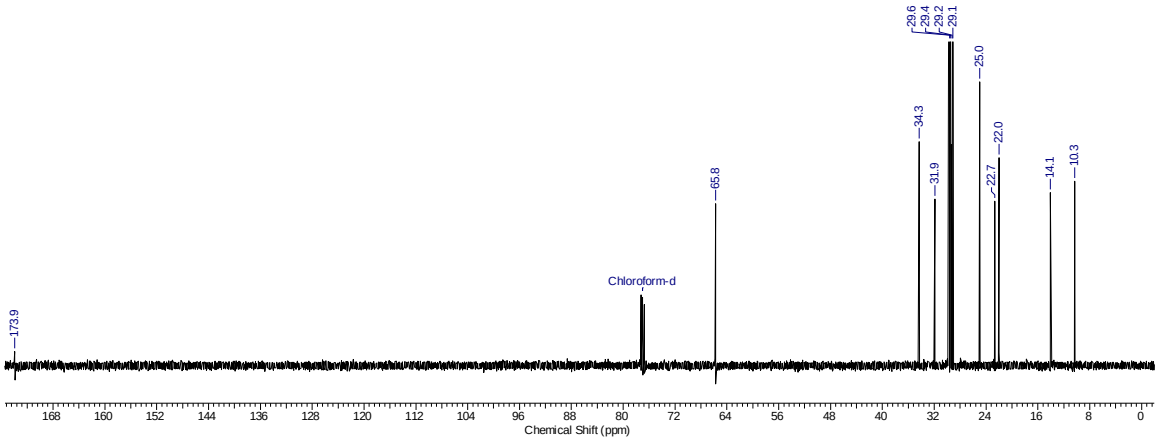
Lucas Fabian,[a] Matías Gómez,[a] Juan A. Caturelli Kuran,[a] Graciela Moltrasio[b] and Albertina Moglioni.[a]*

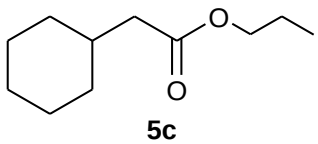
[a]Departamento de Farmacología. [b]Departamento de Química Orgánica. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires. Junín 956, Buenos Aires, C1113AAD, Argentina. Email: amoglio@ffyb.uba.ar

Table of Contents

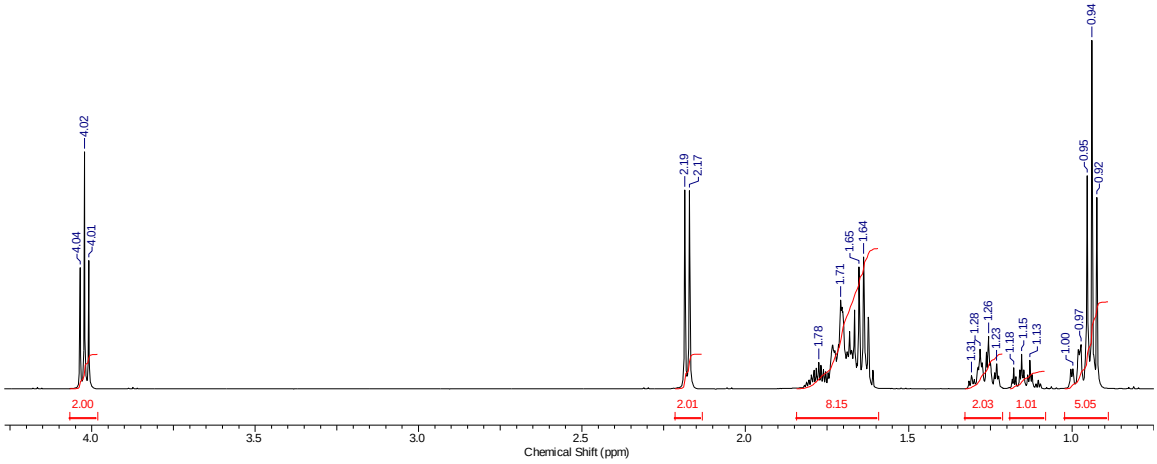


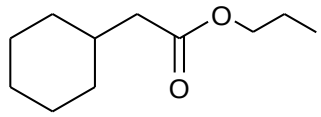
3c


29.6
29.4
29.2
29.1
25.0
34.3
22.0
31.9
22.7
14.1
10.3
65.8
Chloroform-d
173.9
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

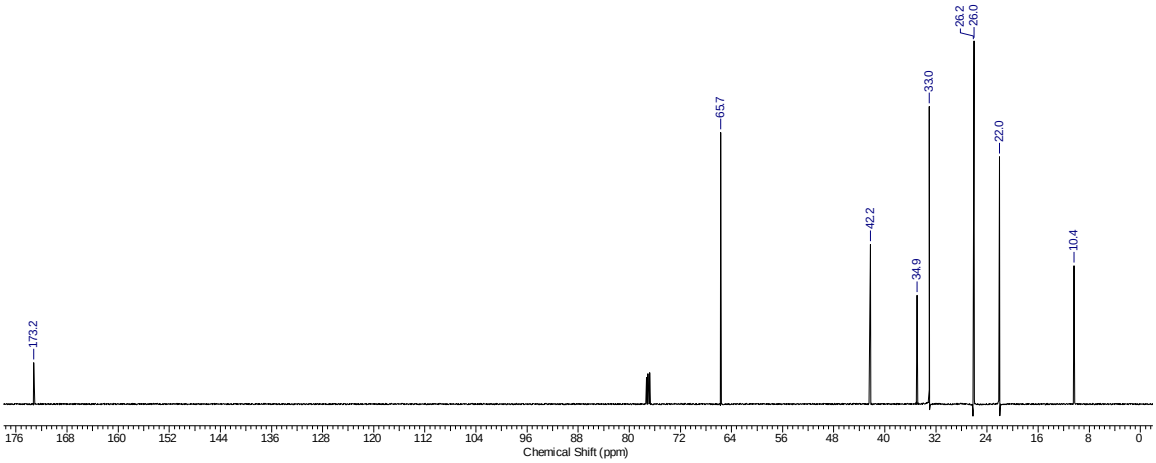


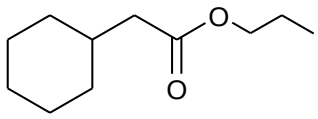
5c


0.94
4.02
2.19
2.17
0.95
0.92
4.04
4.01
1.65
1.64
1.71
1.78
1.31
1.28
1.26
1.23
1.18
1.15
1.13
1.00
0.97
2.00
2.01
8.15
2.03
1.01
5.05
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

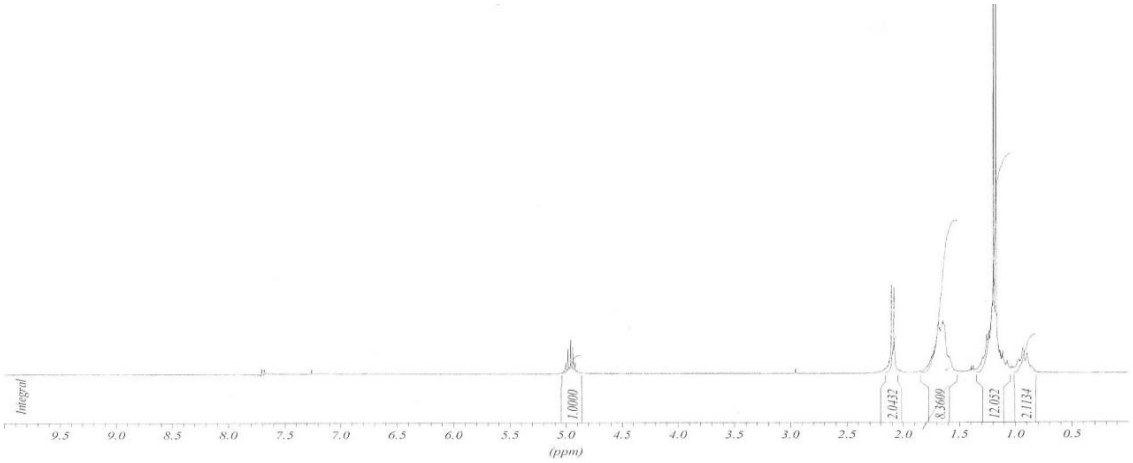


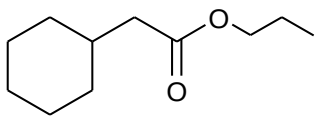
5c


173.2
65.7
42.2
34.9
33.0
26.2
26.0
22.0
10.4
176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

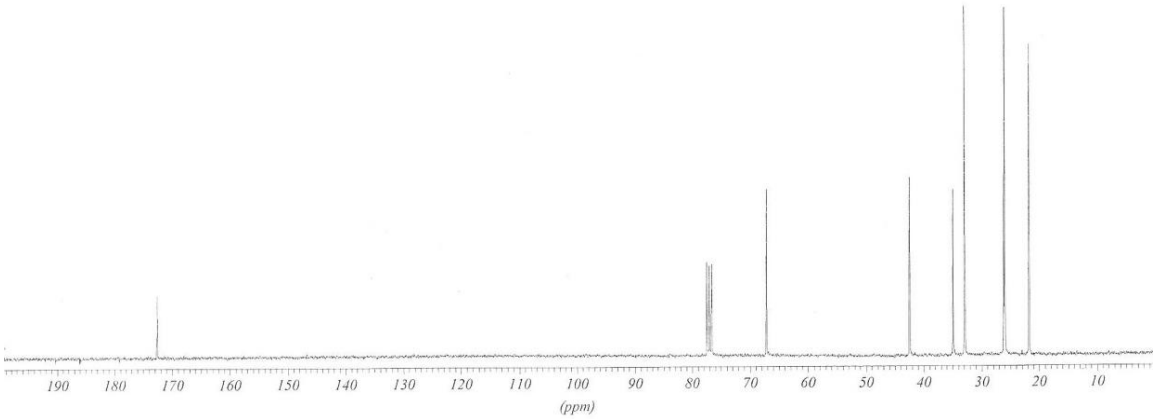


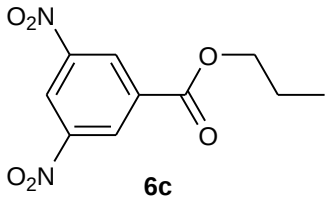
5c


Integral
1.0000
2.0432
8.3600
12.052
2.1134
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
(ppm)

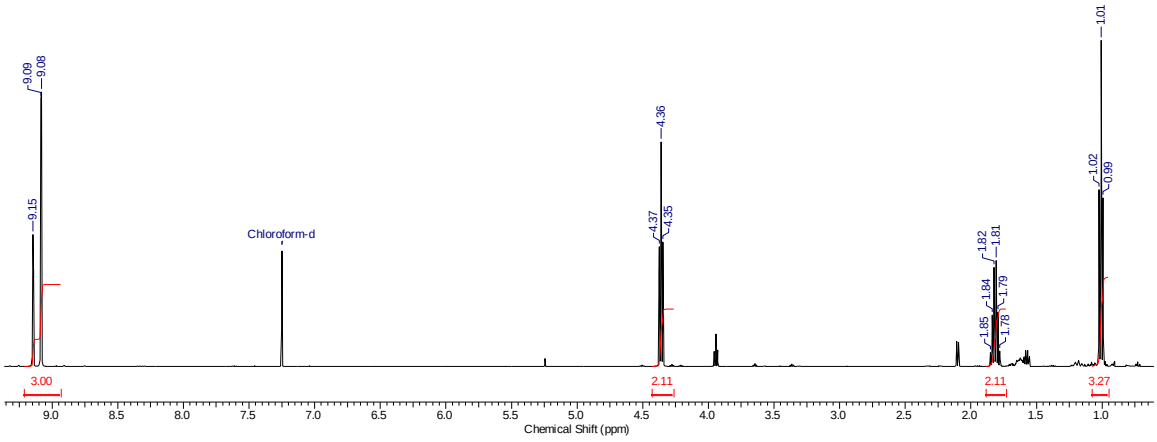

O
O

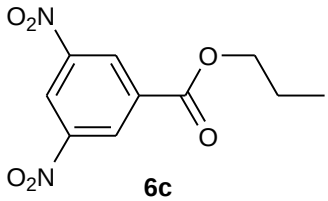
5c


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

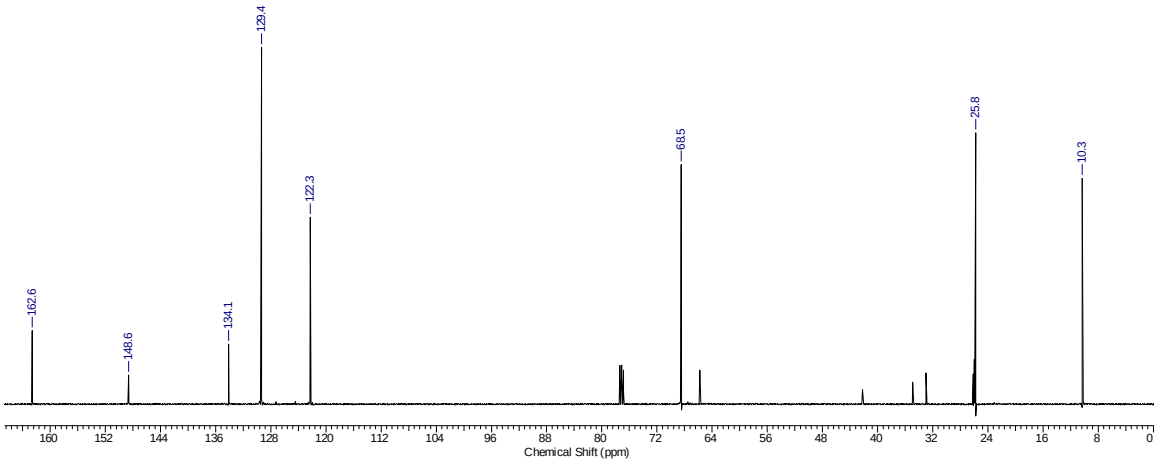

O2N
O
O
O2N

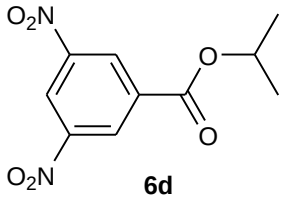
6c


9.09
9.08
9.15
Chloroform-d
4.36
4.37
4.35
1.82
1.81
1.84
1.79
1.85
1.78
1.01
1.02
0.99
3.00
2.11
2.11
3.27
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
Chemical Shift (ppm)

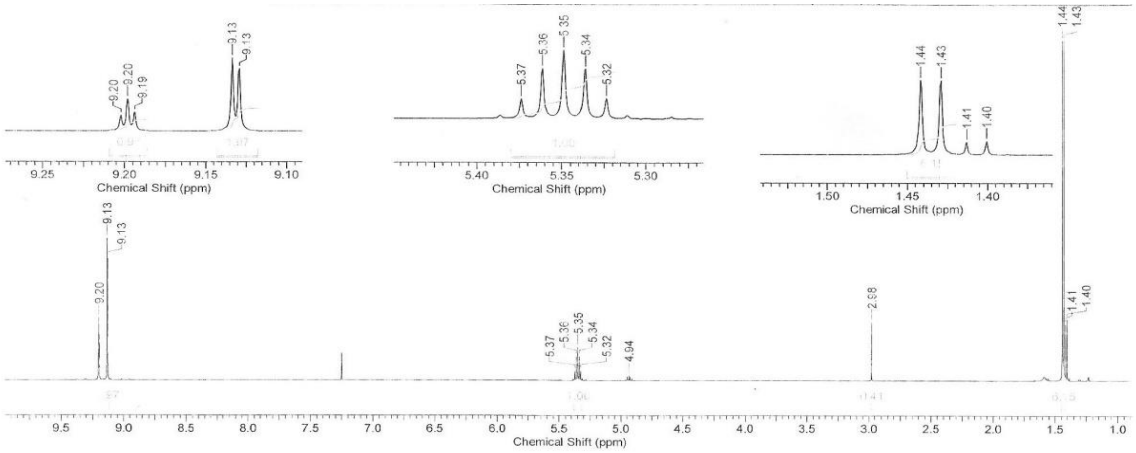


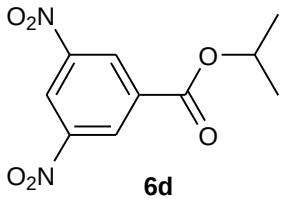
6c


162.6
148.6
134.1
129.4
122.3
68.5
25.8
10.3
Chemical Shift (ppm)

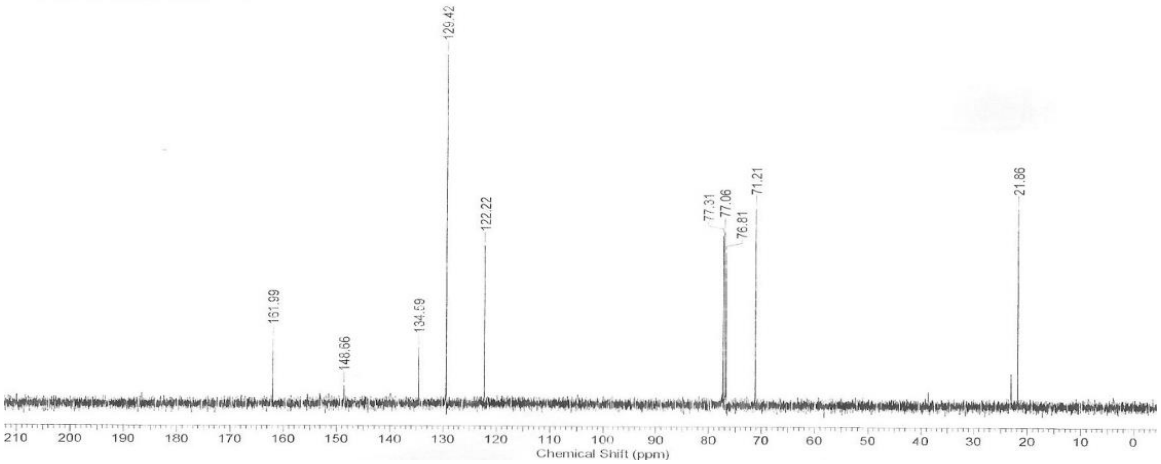


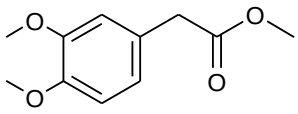
6d


9.20
9.19
9.13
9.13
5.37
5.36
5.35
5.34
5.32
1.44
1.43
1.41
1.40
4.04
2.68
Chemical Shift (ppm)

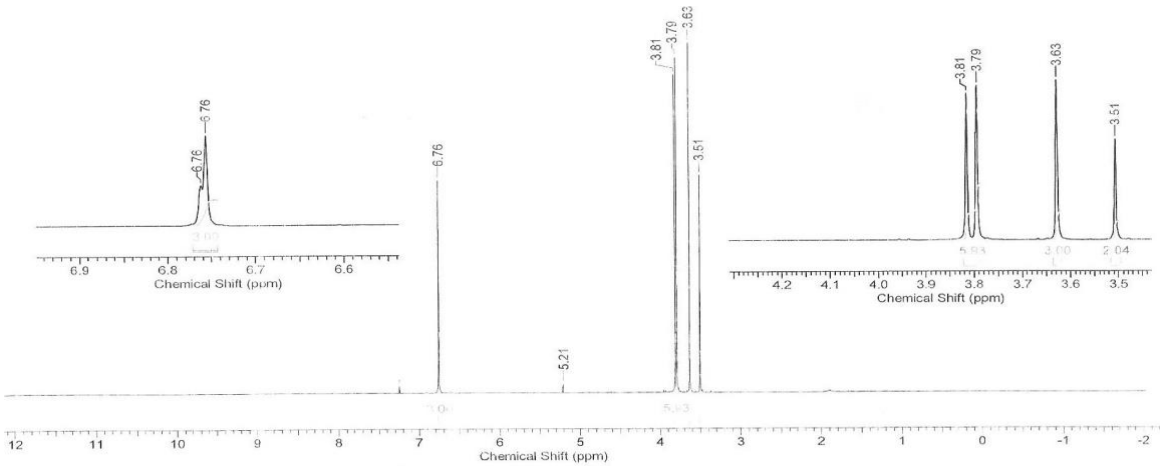


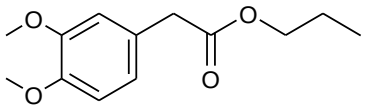
6d


129.42
161.99
146.66
134.69
122.22
77.31
77.06
76.81
71.21
21.86
Chemical Shift (ppm)

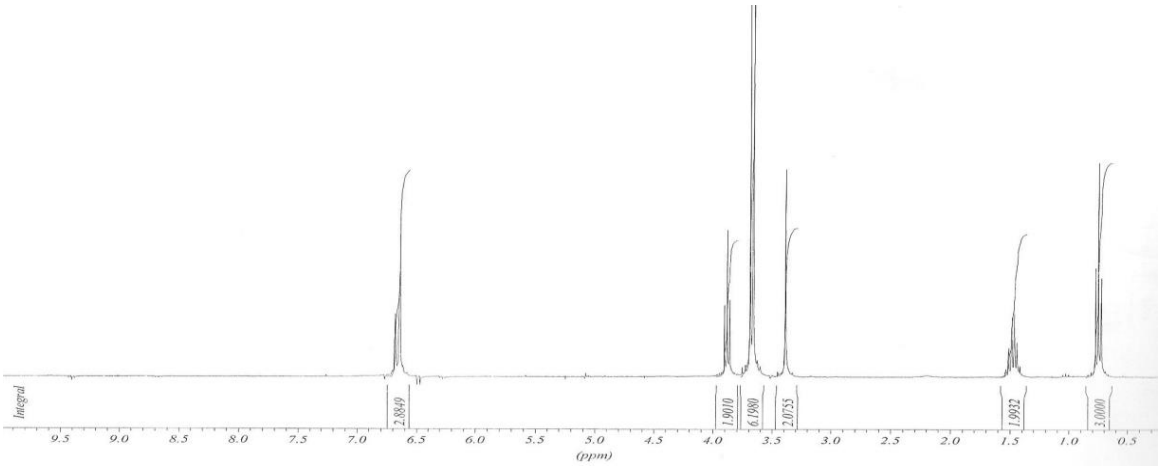


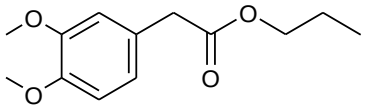
7a


6.76
6.76
3.81
3.79
3.63
3.51
5.21
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)

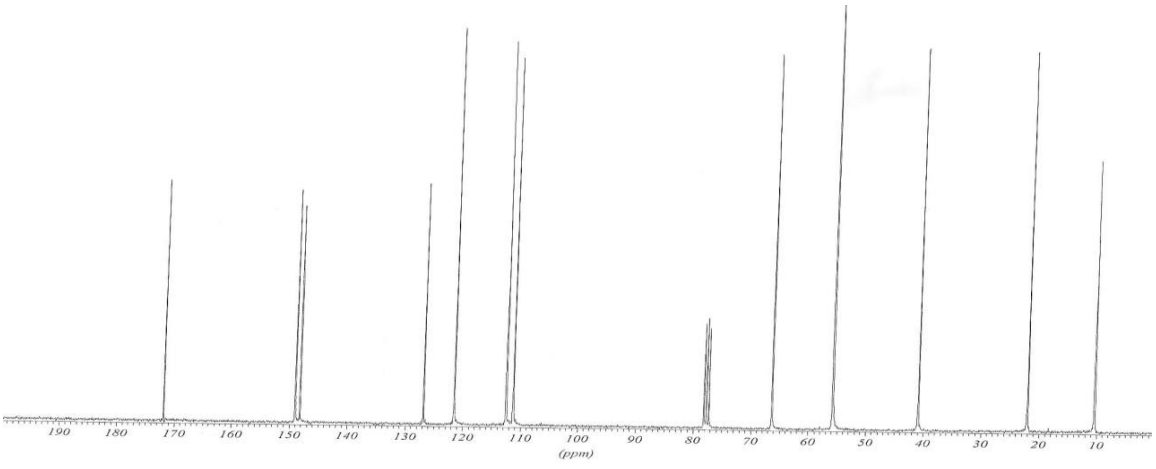


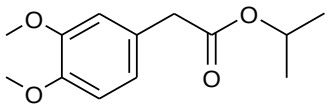
7c


Integral
2.0849
1.9010
6.1980
2.0755
1.9932
3.0000
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
(ppm)

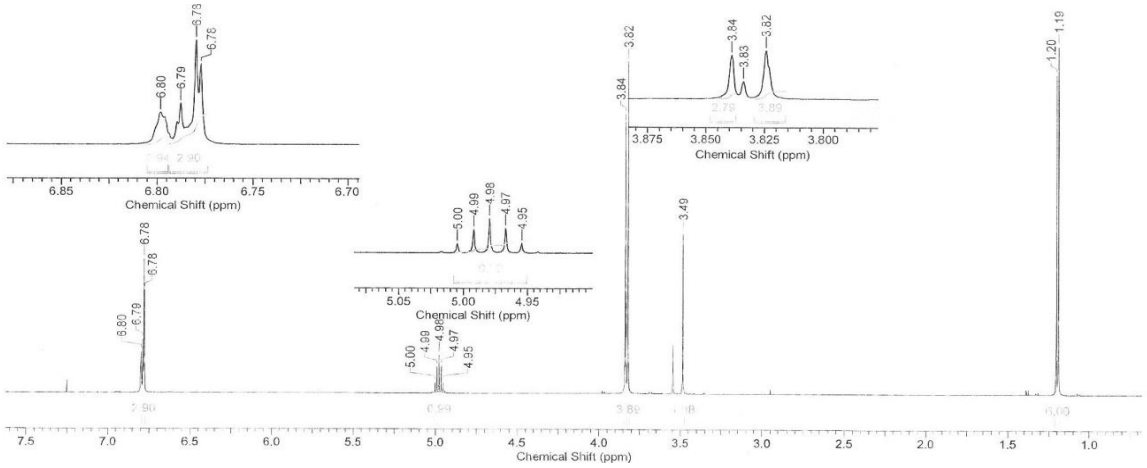


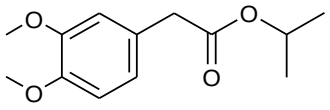
7c


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

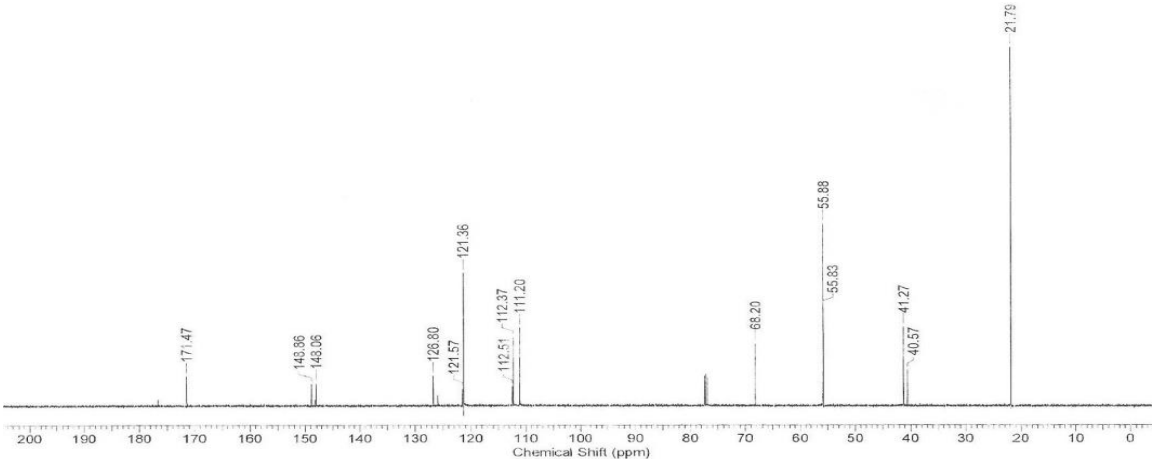


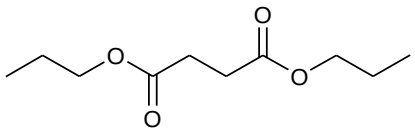
7d


6.80
6.79
6.78
6.76
6.73
6.85
6.80
6.75
6.70
Chemical Shift (ppm)
5.00
4.99
4.98
4.97
4.95
5.05
5.00
4.95
Chemical Shift (ppm)
3.84
3.83
3.82
3.875
3.850
3.825
3.800
Chemical Shift (ppm)
3.49
1.20
1.19
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

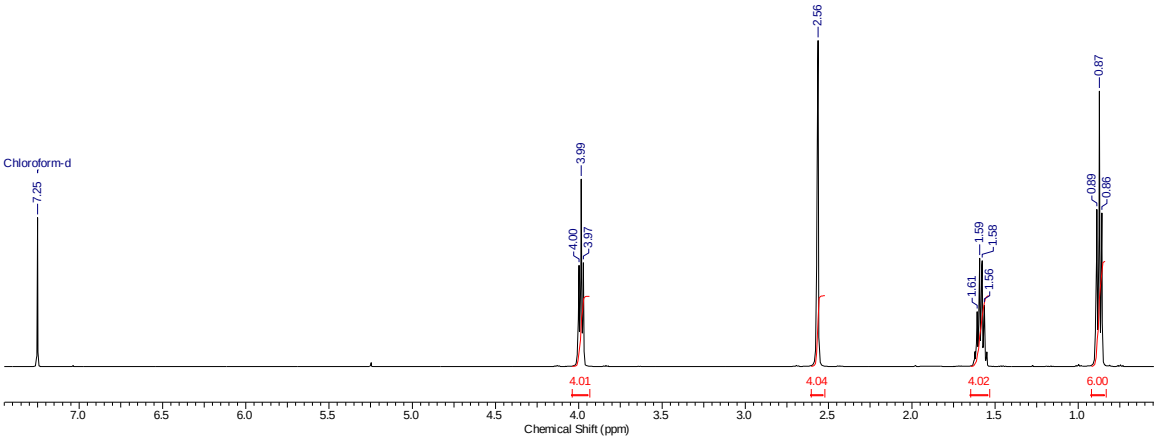


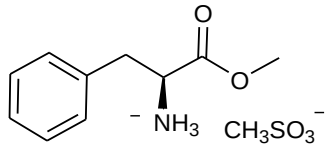
7d


171.47
143.86
143.06
126.80
121.57
121.36
112.51
112.37
111.20
68.20
55.88
55.83
41.27
40.57
21.79
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

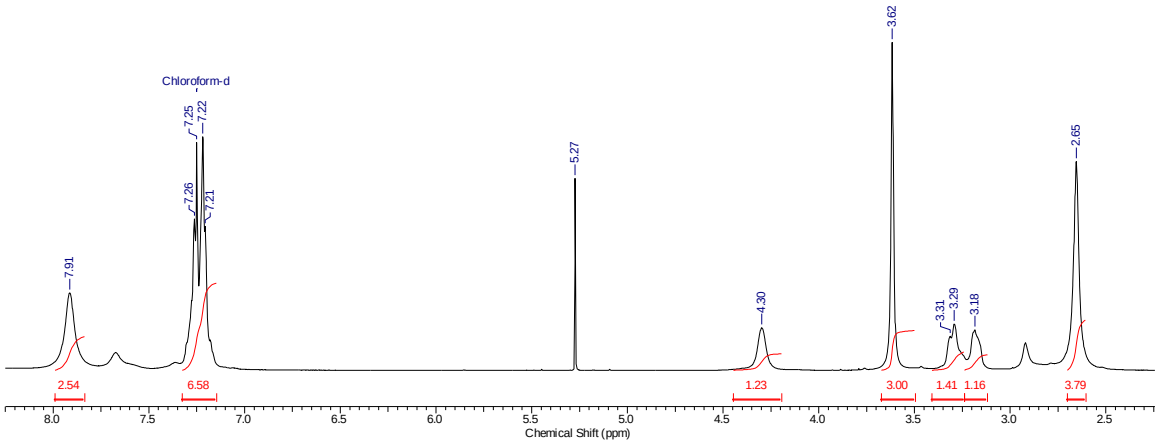


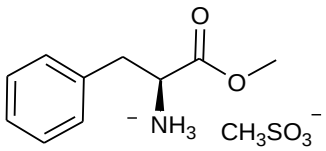
10c


Chloroform-d
7.25
3.99
4.00
3.97
2.56
1.61
1.59
1.58
1.56
0.89
0.87
0.86
4.01
4.04
4.02
6.00
Chemical Shift (ppm)

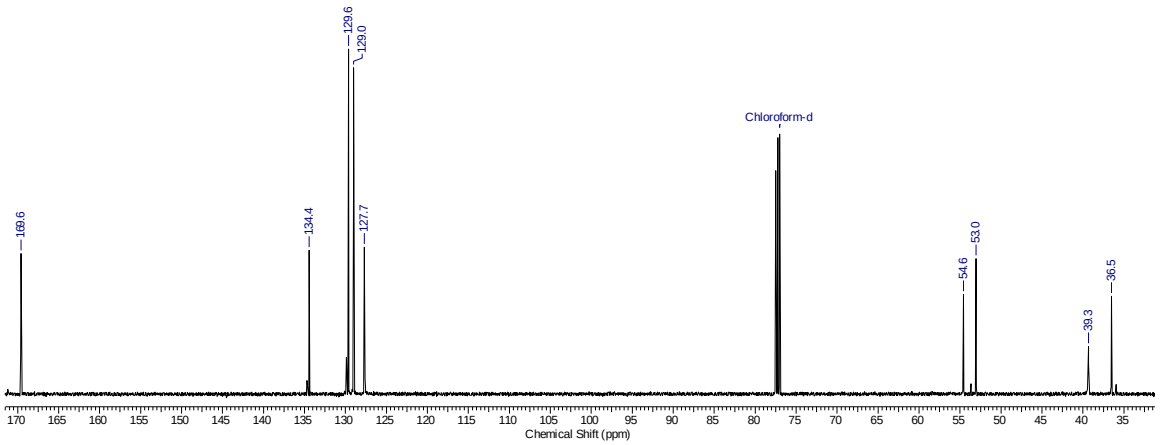


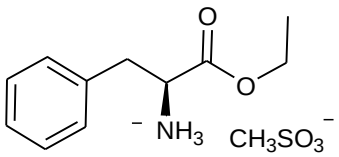
11a


Chloroform-d
7.91
7.25
7.22
7.26
7.21
5.27
4.30
3.62
3.31
3.29
3.18
2.65
2.54
6.58
1.23
3.00
1.41
1.16
3.79
Chemical Shift (ppm)

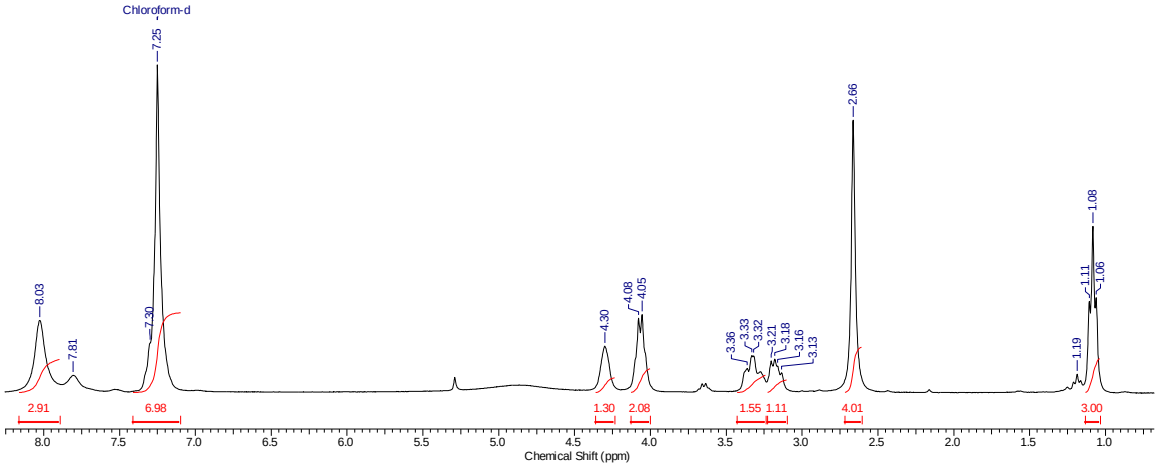


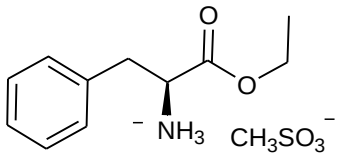
11a


169.6
134.4
129.6
129.0
127.7
Chloroform-d
54.6
53.0
39.3
36.5
Chemical Shift (ppm)

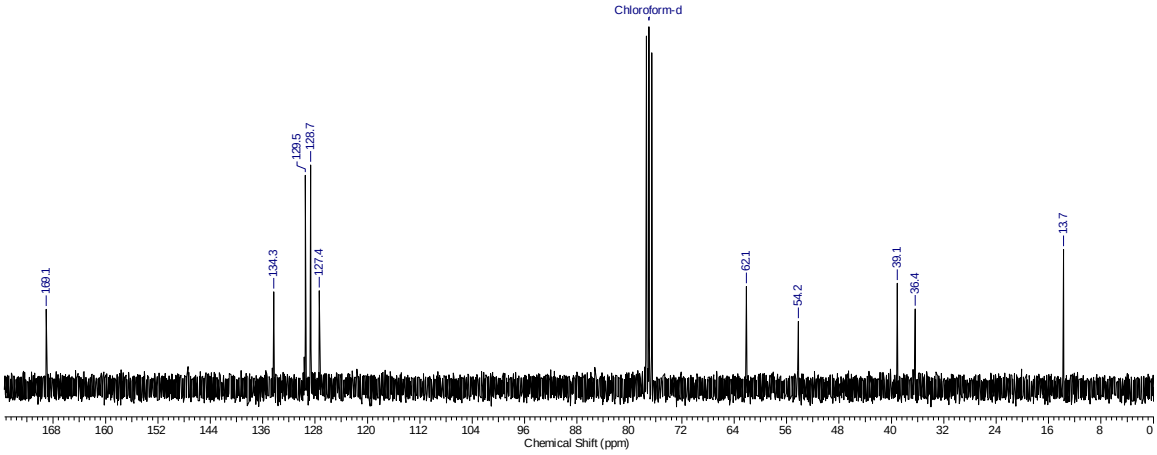


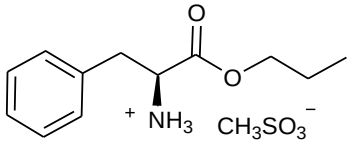
11b


Chloroform-d
8.03
7.81
7.30
7.25
4.30
4.08
4.05
3.36
3.33
3.32
3.21
3.18
3.16
3.13
2.66
1.19
1.11
1.06
1.08
2.91
6.98
1.30
2.08
1.55
1.11
4.01
3.00
Chemical Shift (ppm)

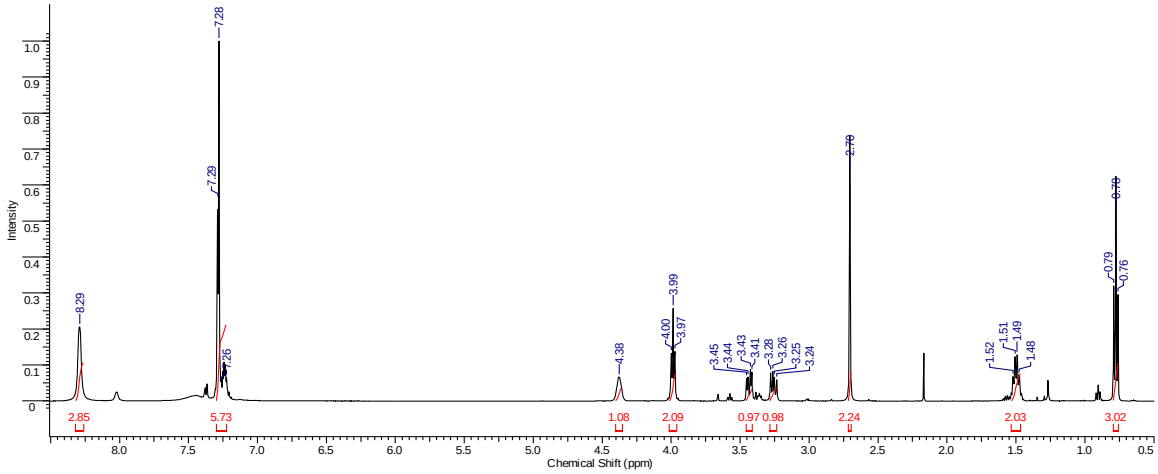

O
O
NH3
CH3SO3

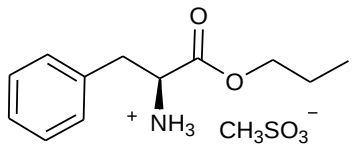
11b


Chloroform-d
169.1
134.3
129.5
128.7
127.4
62.1
54.2
39.1
36.4
13.7
Chemical Shift (ppm)

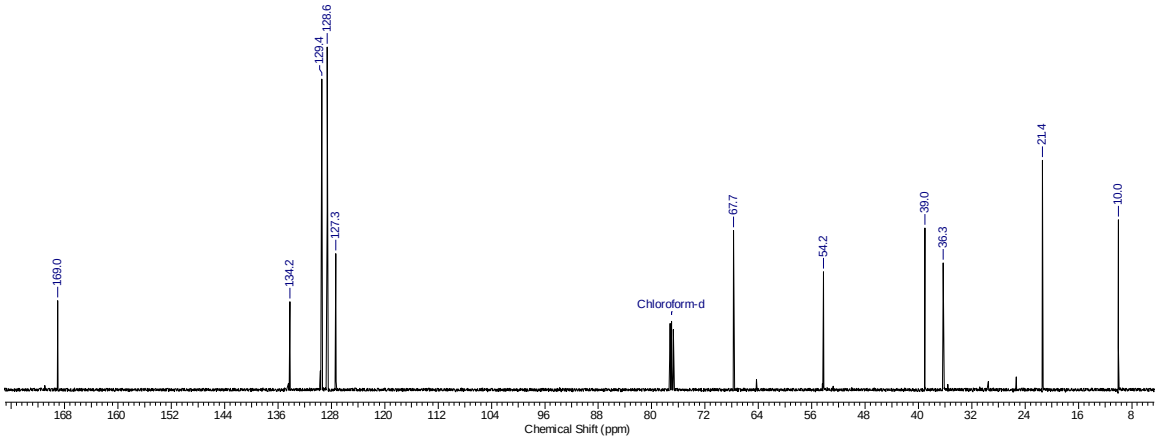

O
O
NH3
CH3SO3

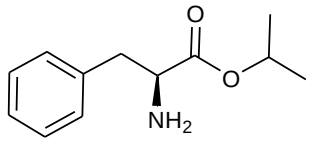
11c


Intensity
8.29
7.29
7.28
7.26
4.38
4.00
3.99
3.97
3.45
3.44
3.43
3.41
3.28
3.26
3.25
3.24
2.70
1.52
1.51
1.49
1.48
0.79
0.76
2.85
5.73
1.08
2.09
0.97
0.98
2.24
2.03
3.02
Chemical Shift (ppm)

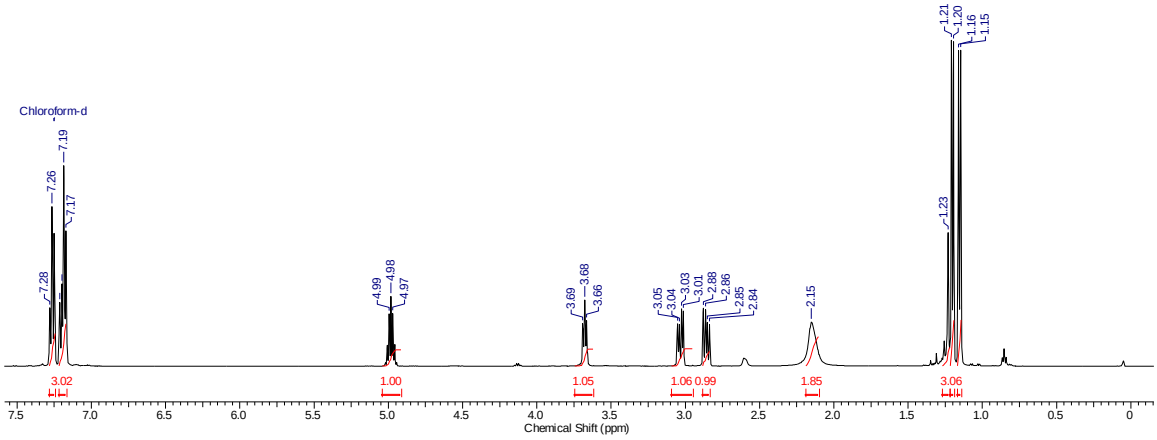

O
O
+ NH3
CH3SO3 −

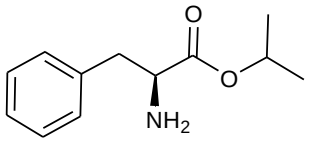
11c


169.0
134.2
129.4
128.6
127.3
Chloroform-d
67.7
54.2
39.0
36.3
21.4
10.0
Chemical Shift (ppm)

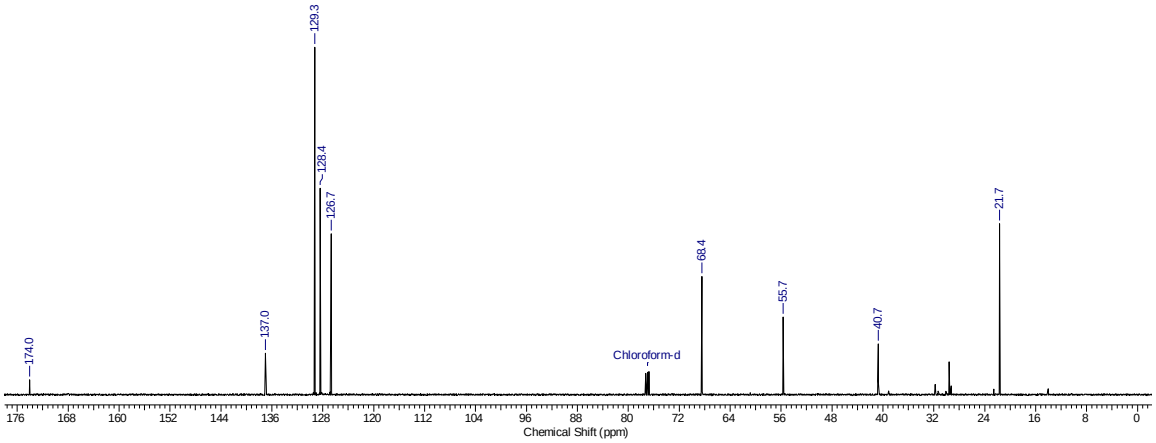

O
O
NH2

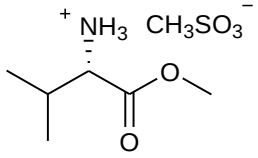
11d


Chloroform-d
7.28
7.26
7.19
7.17
4.99
4.98
4.97
3.69
3.68
3.66
3.05
3.04
3.03
3.01
2.88
2.86
2.85
2.84
2.15
1.23
1.21
1.20
1.16
1.15
3.02
1.00
1.05
1.06
0.99
1.85
3.06
Chemical Shift (ppm)

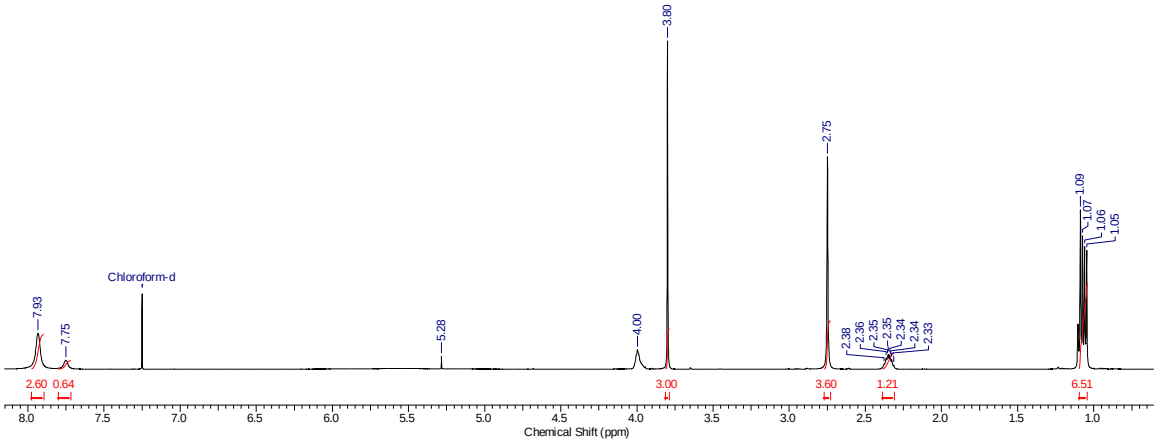

O
O
NH2

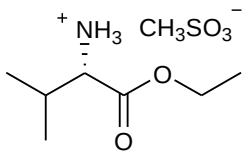
11d


129.3
128.4
126.7
137.0
174.0
Chloroform-d
68.4
55.7
40.7
21.7
Chemical Shift (ppm)

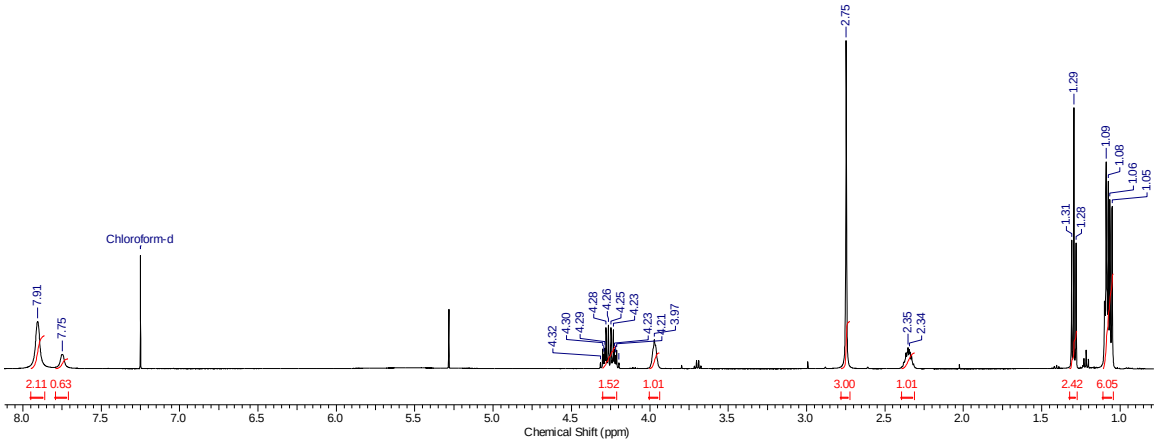

+
NH3
CH3SO3
−
O
O

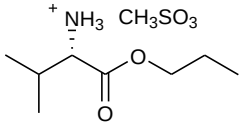
12a


3.80
2.75
1.09
1.07
1.06
1.05
Chloroform-d
7.93
7.75
5.28
4.00
2.38
2.36
2.35
2.34
2.34
2.33
2.60
0.64
3.00
3.60
1.21
6.51
Chemical Shift (ppm)

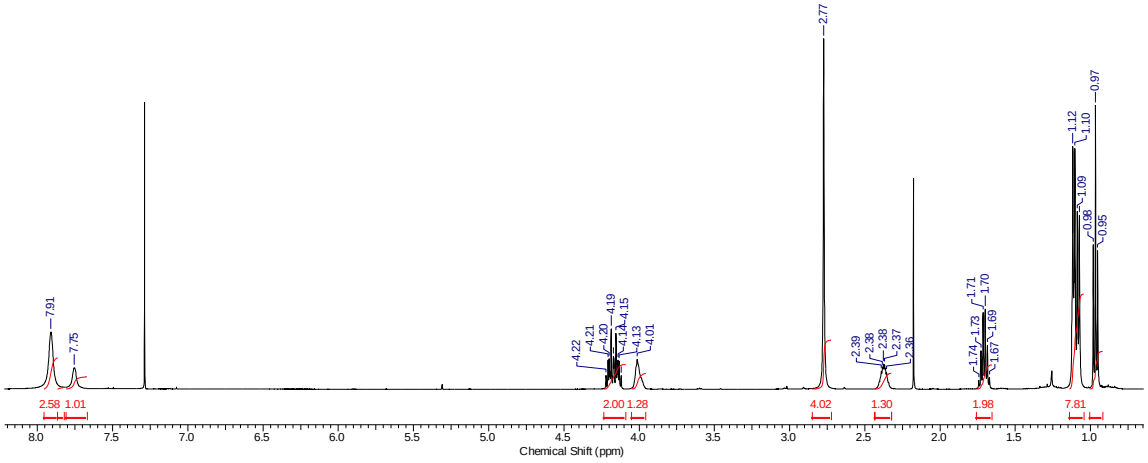


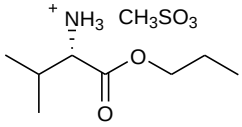
12b



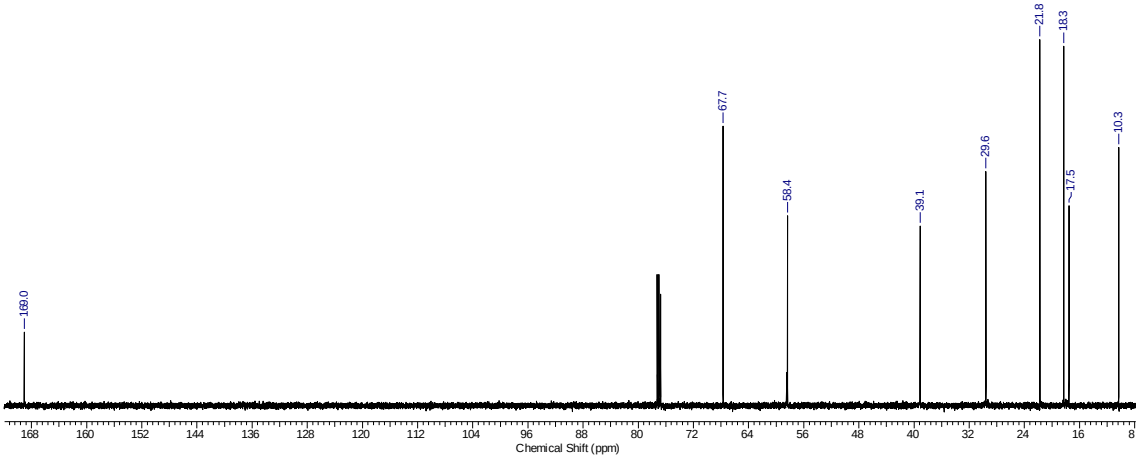


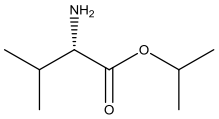
12c



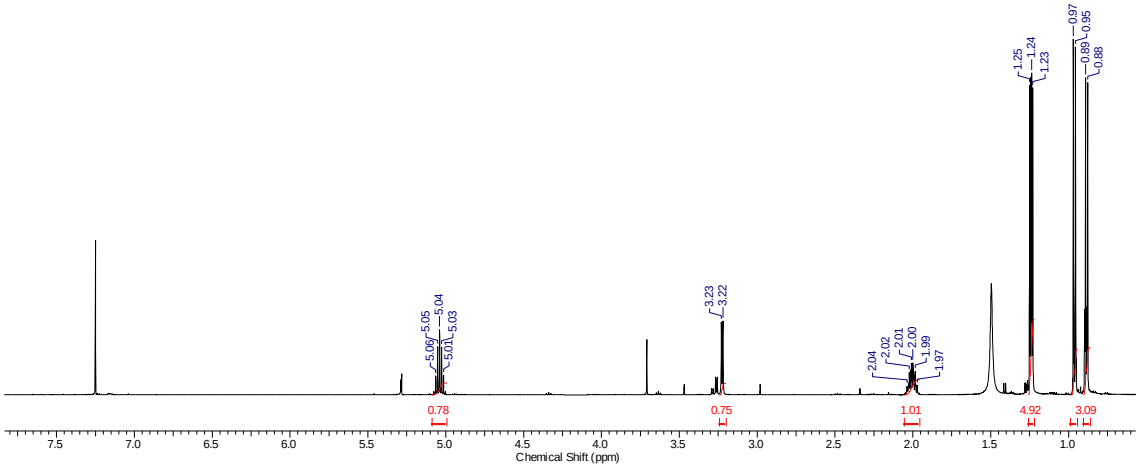

+
NH3
CH3SO3
O
O

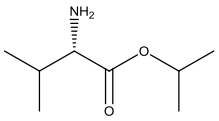
12c


169.0
67.7
58.4
39.1
29.6
21.8
18.3
17.5
10.3
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

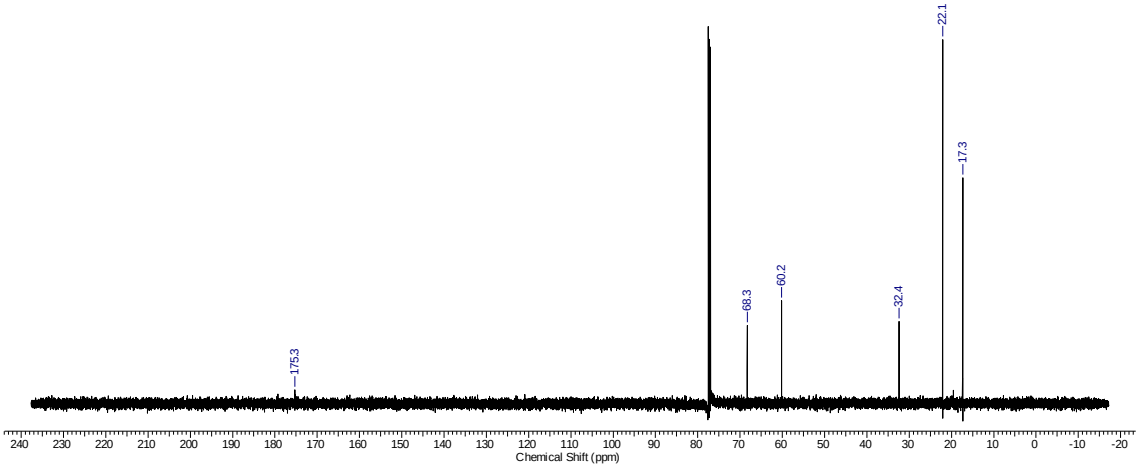

NH2
O
O

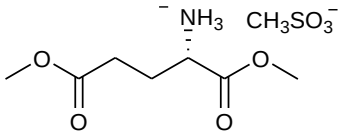
12d


5.05
5.04
5.03
5.01
5.00
3.23
3.22
2.04
2.02
2.01
2.00
1.99
1.97
1.25
1.24
1.23
0.97
0.95
0.89
0.88
0.78
0.75
1.01
4.92
3.09
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

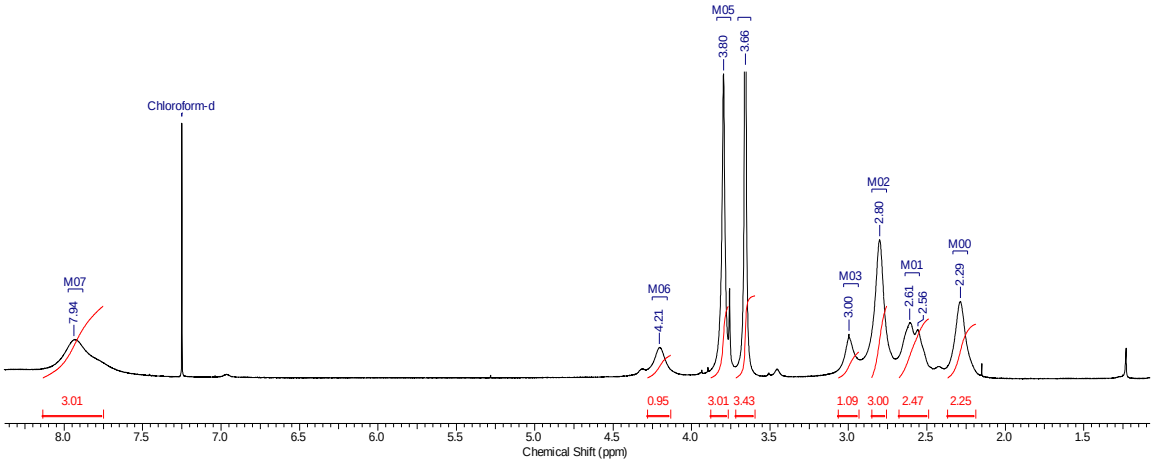

NH2
O
O

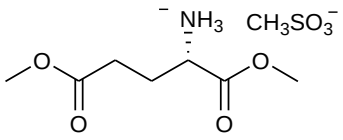
12d


175.3
68.3
60.2
32.4
22.1
17.3
Chemical Shift (ppm)

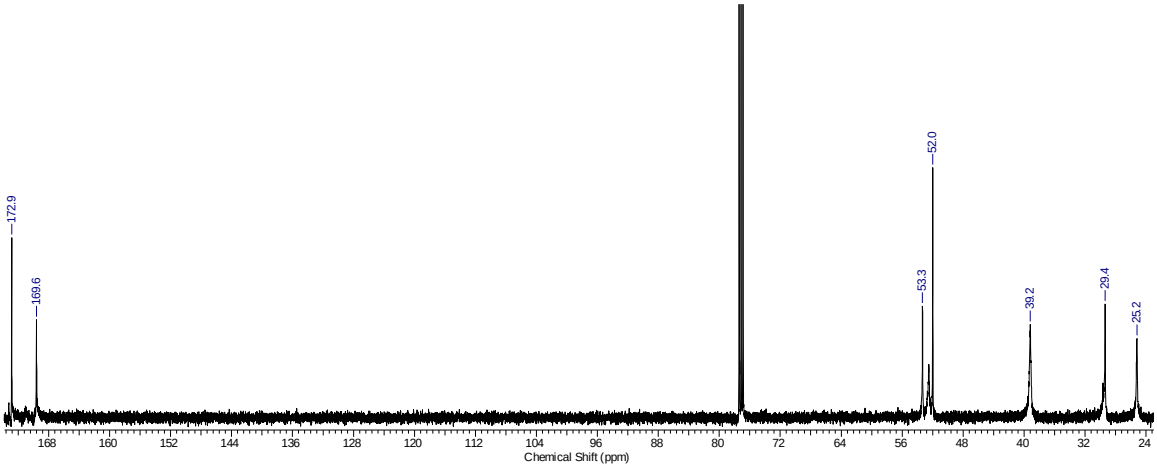

NH3
CH3SO3
O
O
O
O

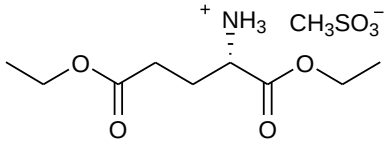
13a


Chloroform-d
M07
7.94
M06
4.21
M05
3.80
3.66
M03
3.00
M02
2.80
M01
2.61
2.56
M00
2.29
3.01
0.95
3.01
3.43
1.09
3.00
2.47
2.25
Chemical Shift (ppm)

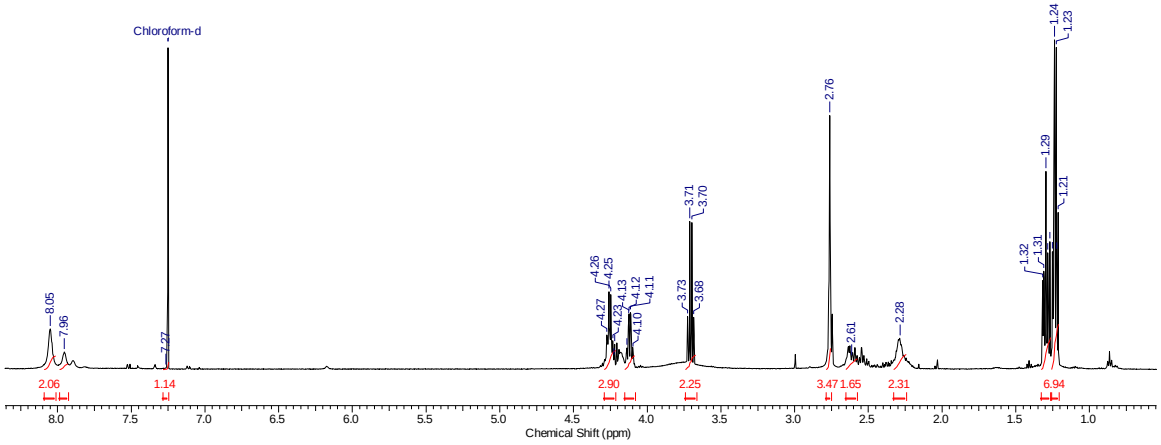

NH3
CH3SO3
O
O
O
O

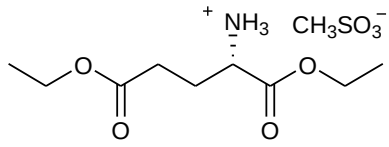
13a


172.9
169.6
53.3
52.0
39.2
29.4
25.2
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)

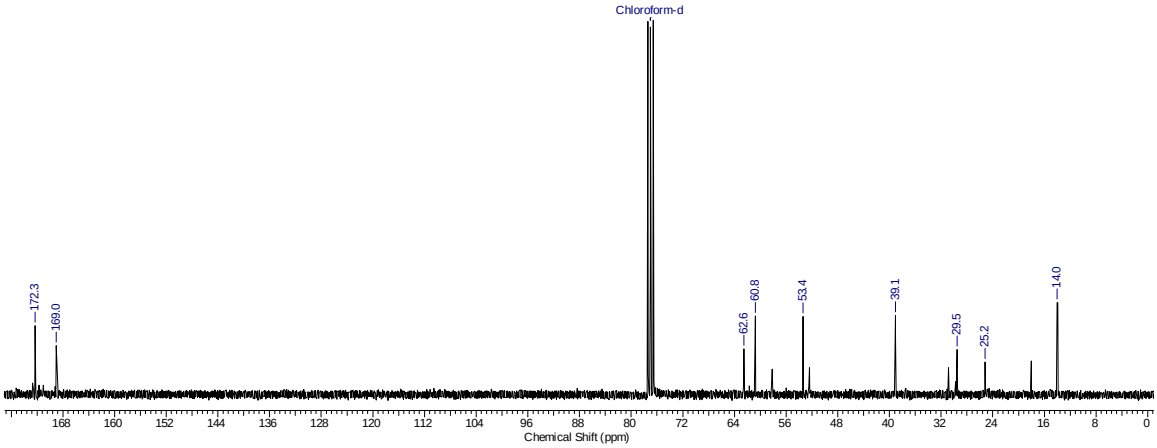

NH3
CH3SO3
O
O
O
O

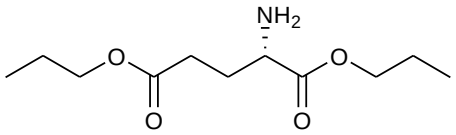
13b


Chloroform-d
8.05
7.96
7.27
4.26
4.25
4.27
4.23
4.13
4.12
4.11
4.10
3.71
3.70
3.73
3.68
2.76
2.61
2.28
1.32
1.31
1.29
1.24
1.23
1.21
2.06
1.14
2.90
2.25
3.47
1.65
2.31
6.94
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

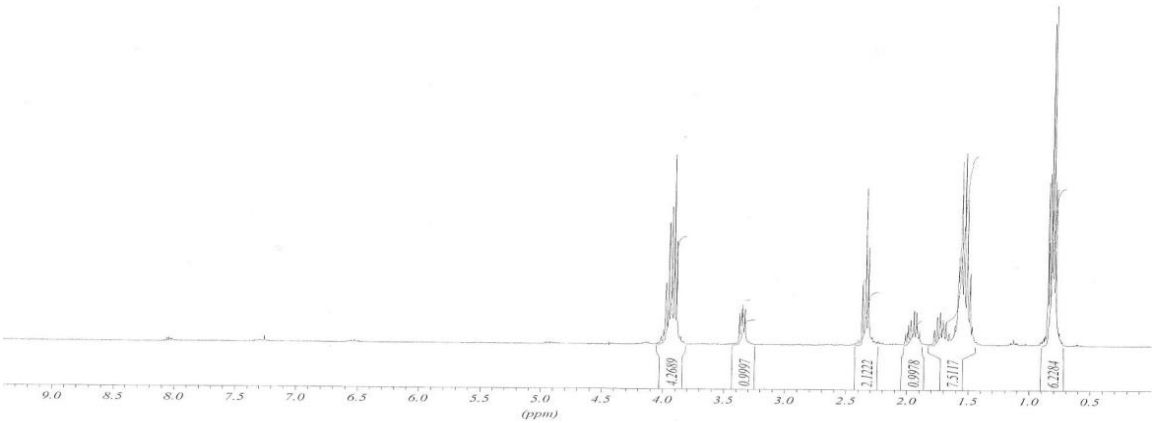

+ NH3 CH3SO3−
O
O
O
O

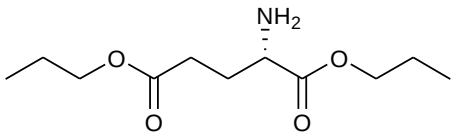
13b


Chloroform-d
172.3
169.0
62.6
60.8
53.4
39.1
29.5
25.2
14.0
168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

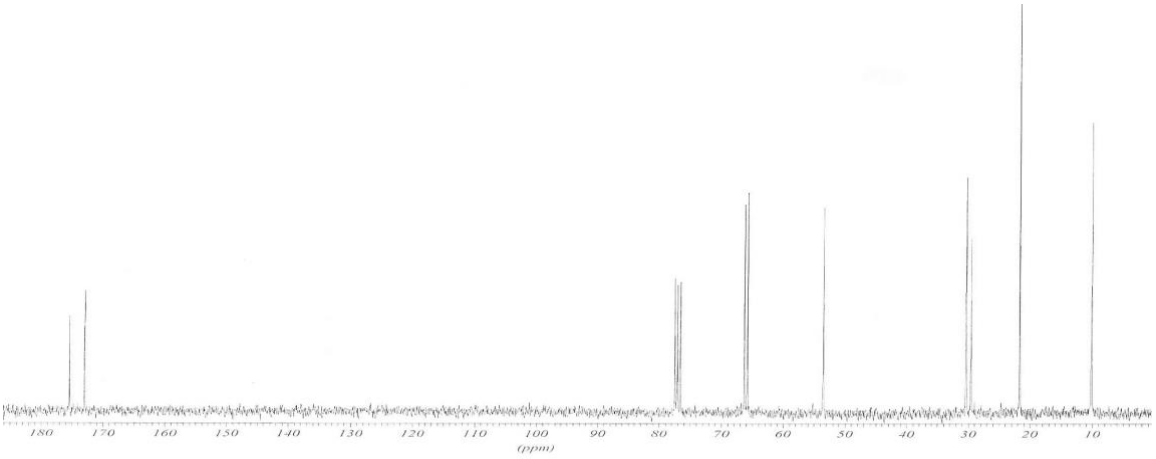

NH2
O
O
O
O

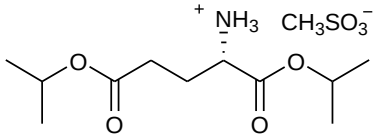
13c


4.2689
0.9997
2.1222
0.9978
2.5117
6.2284
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
(ppm)

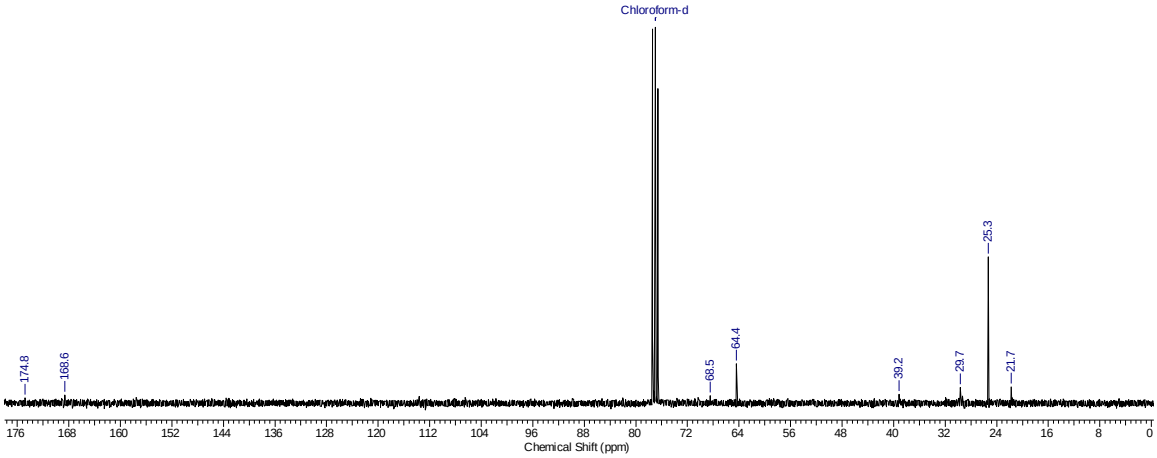

NH2
O
O
O
O

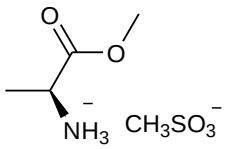
13c


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

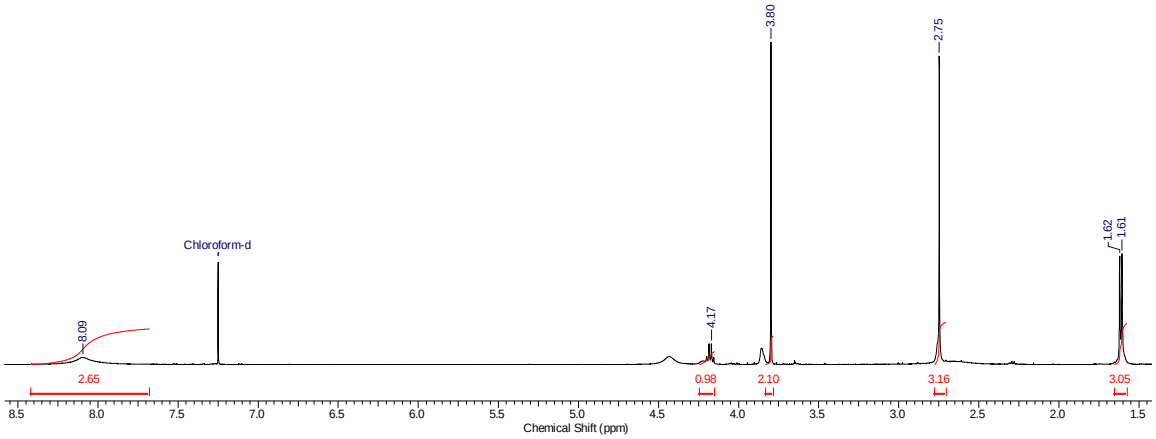

+
NH3
CH3SO3−
O
O
O
O

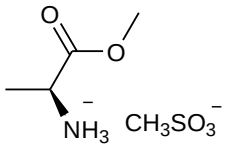
13d


Chloroform-d
174.8
168.6
68.5
64.4
39.2
29.7
25.3
21.7
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

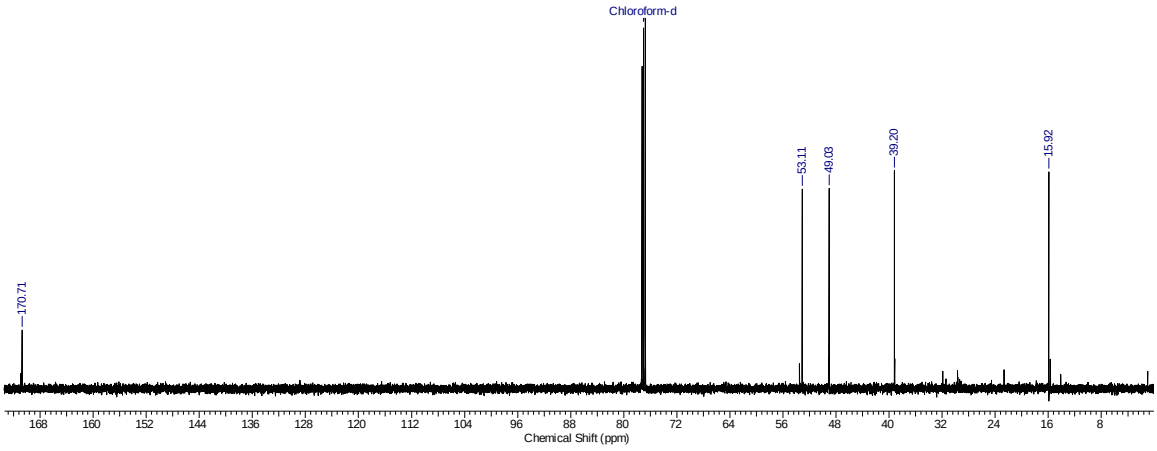


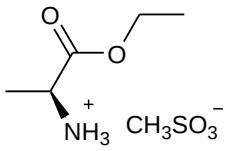
14a


3.80
2.75
1.62
1.61
Chloroform-d
8.09
4.17
2.65
0.98
2.10
3.16
3.05
Chemical Shift (ppm)

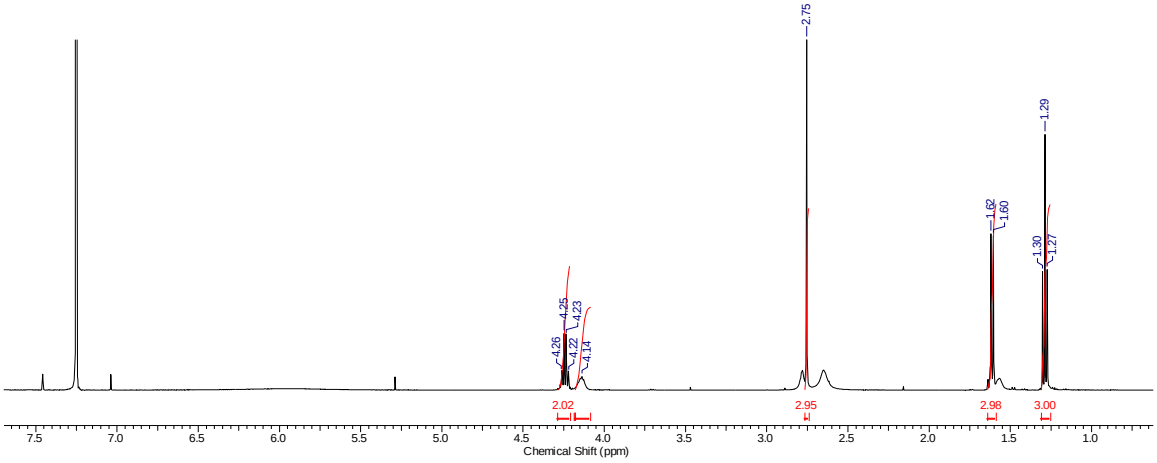


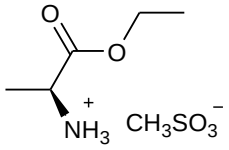
14a


Chloroform-d
53.11
49.03
39.20
15.92
170.71
Chemical Shift (ppm)

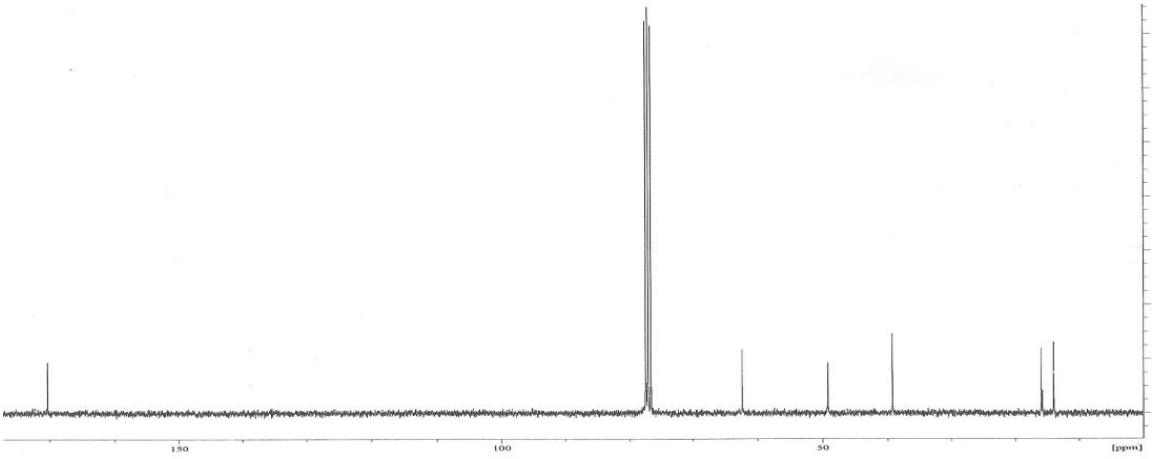

O
O
+
NH3
CH3SO3−

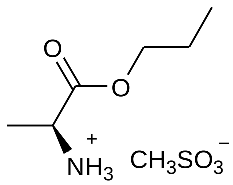
14b


2.75
1.29
1.62
1.60
1.30
1.27
4.25
4.23
4.26
4.22
4.14
2.02
2.95
2.98
3.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

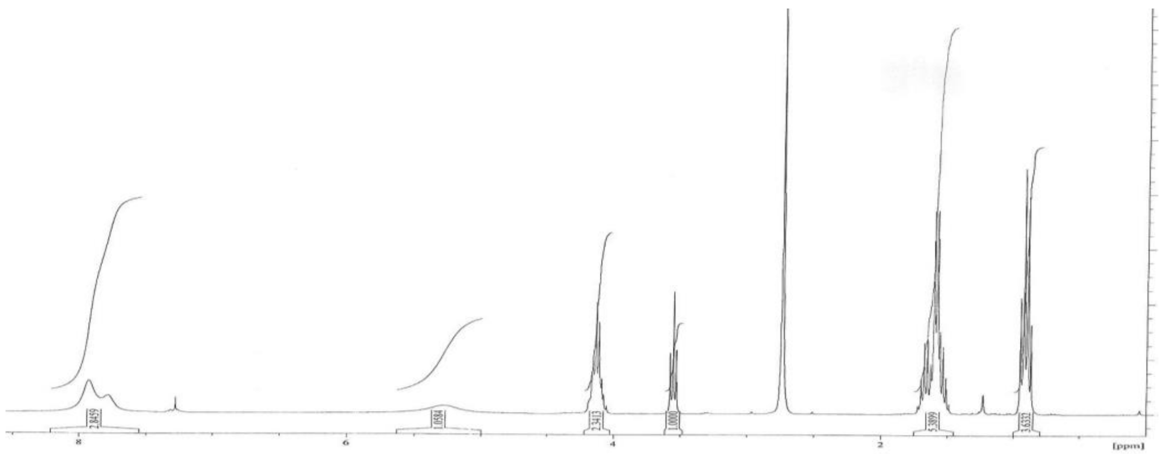

O
O
+
NH3
CH3SO3−

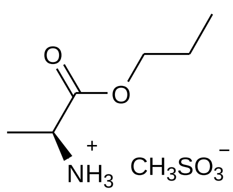
14b


150
100
50
[ppm]

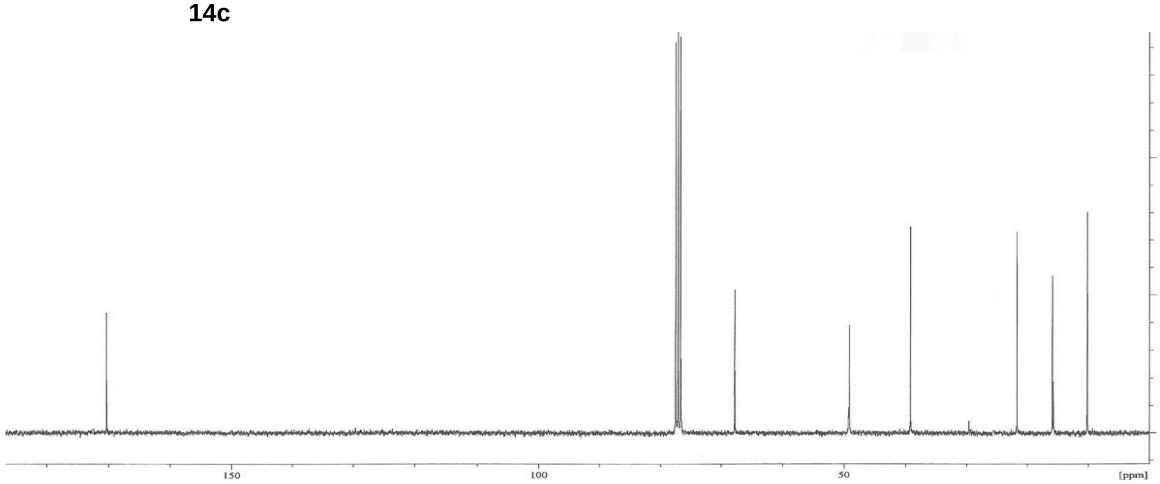


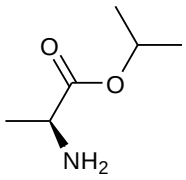
14c



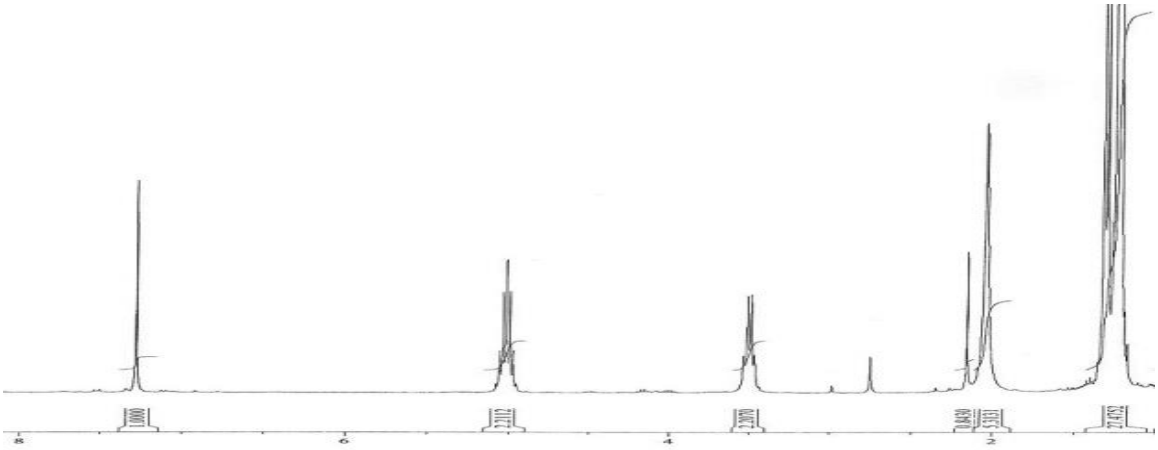


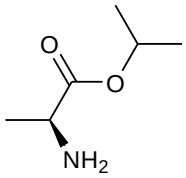
14c



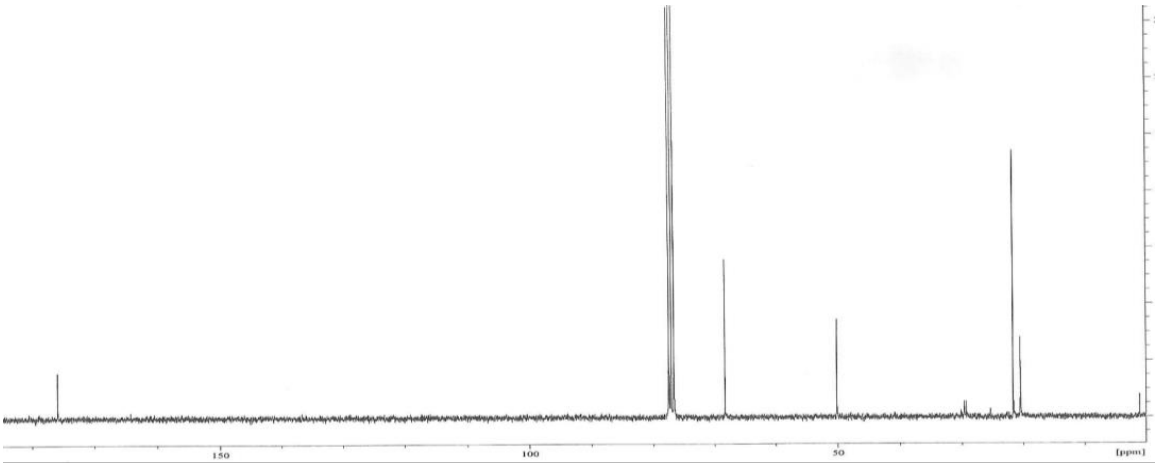


14d





14d



Elemental analysis results

Propyl cyclohexylacetate (**5c**): Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.69; H, 10.99.

Propyl 3,4-dimethoxyphenylacetate (**7c**): Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.40; H, 7.80.

L-Valine propyl ester methanesulfonate (**12c**): Anal. Calcd for $C_9H_{21}NO_5S$: C, 42.34; H, 8.29; N, 5.49. Found: C, 42.10; H, 8.40; N, 5.30.

L-Valine isopropyl ester (**12d**): Anal. Calcd for $C_8H_{17}NO_2$: C, 60.35; H, 10.76; N, 8.80. Found: C, 60.20; H, 10.90.; N, 8.71.

L-Glutamic acid dipropyl ester (**13c**): Anal. Calcd for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06. Found: C, 56.96; H, 9.20; N, 6.03.