Supporting Information for:

Preparation of (D)-Cycloserine and ^{13}C-labeled (D)-Cycloserine

Nathan C. Thacker,[a] Judit Toth,[a] Judy L. Miska,[a] Raul Barletta,[b] and James M. Takacs[*,a]

[a]Department of Chemistry, University of Nebraska-Lincoln, NE 68588-0304

[b]Department of Veterinary and Biomedical Sciences, University of Nebraska-Lincoln, NE 68583

Contents

Synthesis and Characterization of ^{13}C-labelled D-Cycloserine

DL-Methyl-3-hydroxy-2-(tritylamino)propanoate-1-^{13}C (**11**). Commercially available DL-Serine-1-^{13}C (250 mg, 2.36 mmol) was converted to DL-Serine-1-^{13}C methyl ester hydrochloride using the procedure for unlabeled material (**1**). This material was used immediately without subsequent purification. DL-Serine-1-^{13}C methyl ester hydrochloride was converted to DL-Methyl-3-hydroxy-2-(tritylamino)propanoate-1-^{13}C (**11**) using the procedure for unlabeled material (**2**) affording **11** (738 mg, 86% over 2 steps) as a white powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53–7.51 (6H, m), 7.32–7.28 (5H, m), 7.24–7.21 (3H, m), 3.78–3.72 (1H, m), 3.64–3.55 (2H, m), 3.32 (3H, d, J = 3.8 Hz), 3.05-2.96 (1H, m), 2.37 (1H, t, J = 12.56 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0; HRMS (ESI) cald. For $^{13}CC_{22}H_{23}NO_3$ (M+Na): 385.1609, found 385.1612 m/z.

DL-*O*-(1,3-Dihydro-2,5-dioxy-1-pyrolidinyl)-*N*-(triphenylmethyl)-1-^{13}C methyl ester (**12**). **11** (733 mg, 2.02 mmol) was converted to DL-*O*-(1,3-Dihydro-2,5-dioxy-1-pyrolidinyl)-*N*-(triphenylmethyl)-1-^{13}C methyl ester (**12**) using the procedure for unlabeled material (**3**) affording **12** (660 mg, 71%) as a white powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.53 (6H, m), 7.31–7.26 (6H, m), 7.23–7.18 (3H, m), 4.44–4.40 (1H, m), 4.03–3.98 (1H, m), 3.70–3.63 (1H, m), 3.35 (3H, d, J = 3.8 Hz), 3.10 (1H, dd, J_1 = 10.0 Hz, J_2 = 3.8 Hz), 2.69 (4H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6; HRMS (ESI) cald. For $^{13}CC_{26}H_{26}N_2O_5$ (M+Na): 482.1773, found 482.1781 m/z.

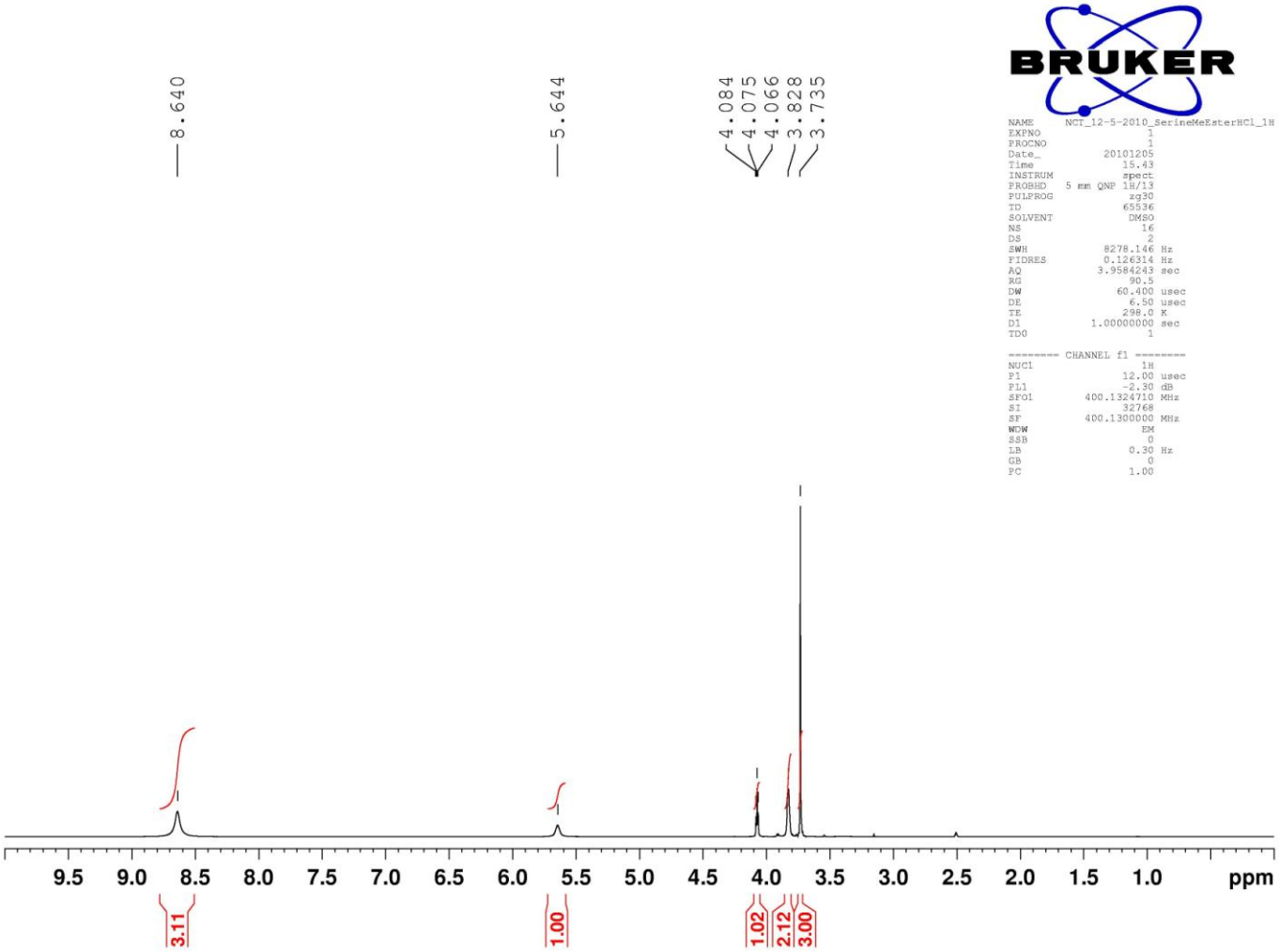
DL-Methyl-γ-Aminooxy-α-amino(triphenylmethyl)butyrate-1-^{13}C (**13**). **12** (653 mg, 1.42 mmol) was converted to DL-Methyl-γ-Aminooxy-α-amino(triphenylmethyl)butyrate-1-^{13}C (**13**) using the procedure for unlabeled material (**4**) affording **13** (526 mg, 98%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.52 (6H, m), 7.31–7.26 (6H, m), 7.23–7.18 (3H, m), 5.47 (2H, bs), 4.06–4.01 (1H, m), 3.77–3.68 (2H, m), 3.24 (3H, d, J = 3.8 Hz), 3.78 (1H, bs); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3; HRMS (ESI) cald. For $^{13}CC_{22}H_{24}N_2O_3$ (M+Na): 400.1718, found 400.1727 m/z.

DL-Cycloserine-1-^{13}C (**14**). **13** (520 mg, 1.38 mmol) was converted to the DiHCl salt using the procedure for unlabeled material (**5**) and used without further purification. DiHCl salt of **13** was then converted to DL-Cycloserine-1-^{13}C (**14**) using the procedure for unlabeled material (**6**) affording **14** (87.2 mg, 61% over 2 steps) as a white powder. ^{1}H NMR (400 MHz, d_6-DMSO) δ 4.44–4.36 (1H, m), 3.76–3.69 (2H, m); ^{13}C NMR (100 MHz, d_6-DMSO) δ 175.0; HRMS (ESI) cald. For $^{13}CC_2H_6N_2O_2$ (M+H): 104.0541, found 104.0542 m/z.

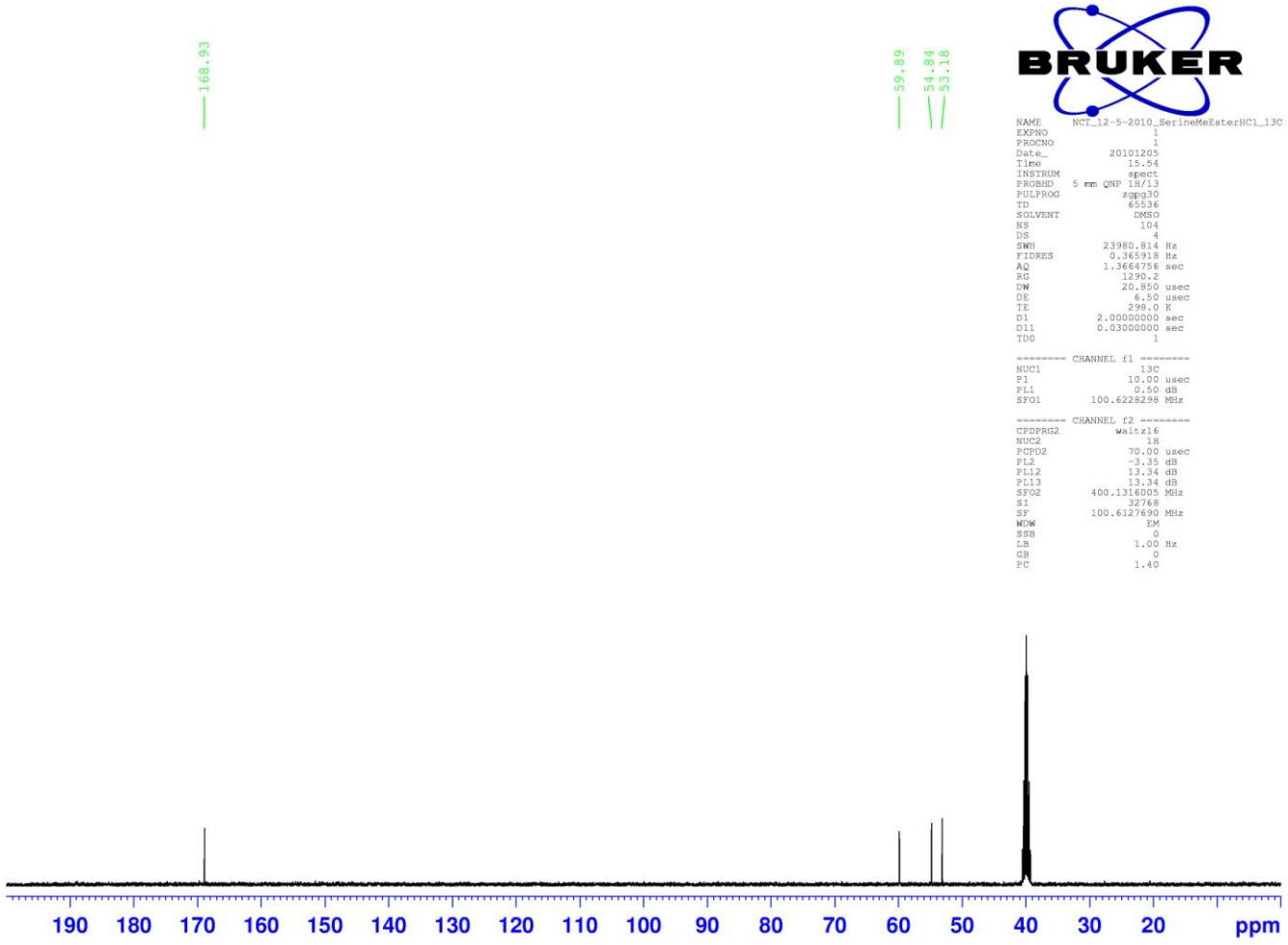
D-Cycloserine-1-^{13}C-L-Tartrate (**15**). **14** (80.3 mg, 0.787 mmol) was converted to D-Cycloserine-1-^{13}C-L-Tartrate (**15**) using the procedure for unlabelled material (**8**) affording **15** (76.7 mg, 77%) as a white crystalline powder. ^{1}H NMR (400 MHz, d_6-DMSO) δ 4.46 (1H, s), 4.05 (2H, s), 3.80 (2H, s); ^{13}C NMR (100 MHz, d_6-DMSO) δ 174.2; HRMS (ESI) cald. For $^{13}CC_6H_{12}N_2O_8$ (M+H): 254.0705, found 254.0700 m/z.

D-Cycloserine-1-^{13}C (**16**). **15** (73 mg, 0.288 mmol) was converted to D-Cycloserine-1-^{13}C (**16**) using the procedure for unlabelled material (**9**) affording **16** (16.9 mg, 57%) as a white powder. ^{1}H NMR (400 MHz, d_6-DMSO) δ 4.43–4.40 (1H, m), 3.76–3.71 (2H, m), 3.60–3.10 (3H, bs); ^{13}C NMR (100 MHz, d_6-DMSO) δ 175.0; HRMS (ESI) cald. For $^{13}CC_2H_6N_2O_2$ (M+H): 104.0541, found 104.0543 m/z.

^{1}H of DL-Serine methyl ester hydrochloride (1)



^{13}C of DL-Serine methyl ester hydrochloride (1)



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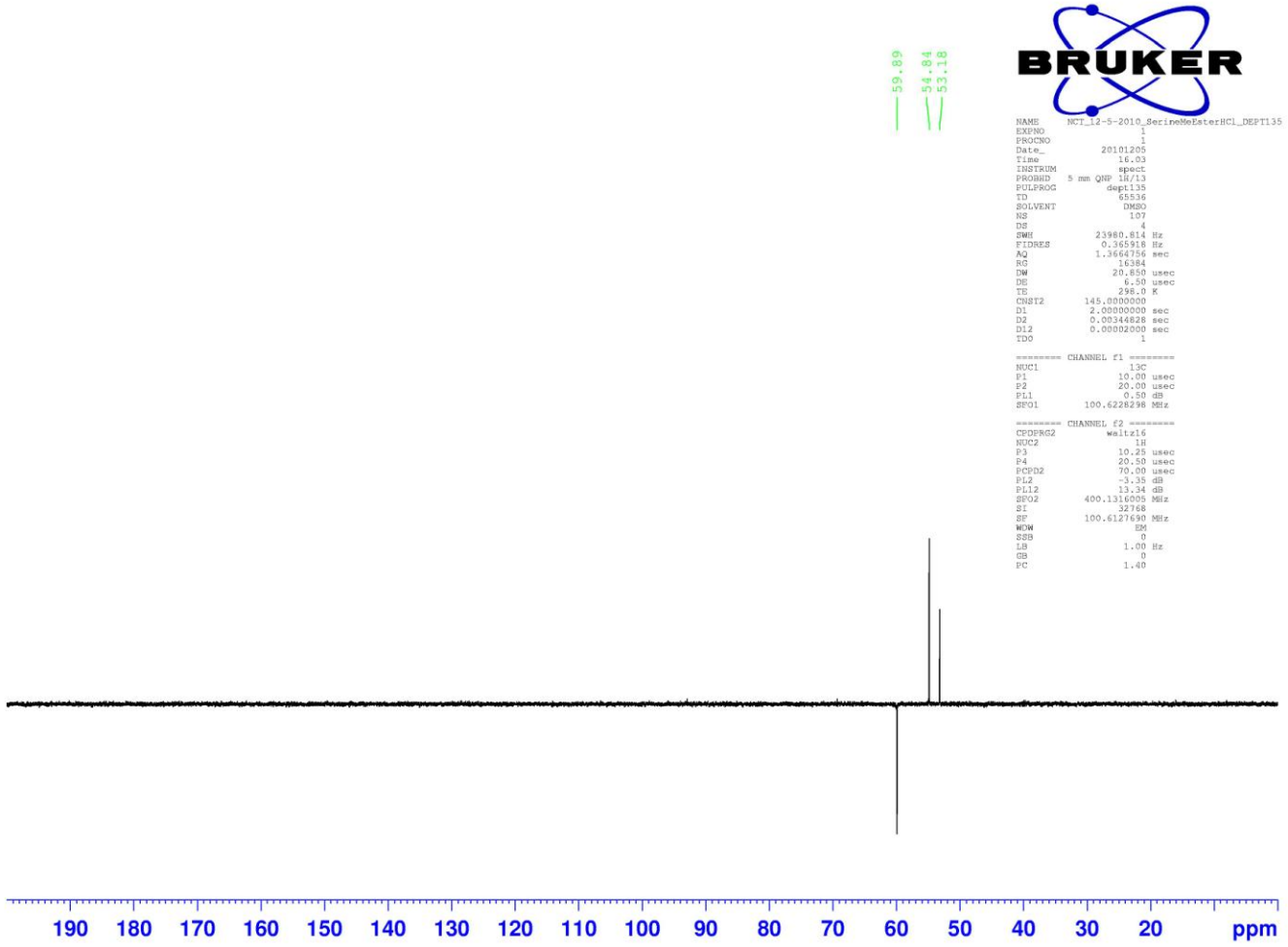

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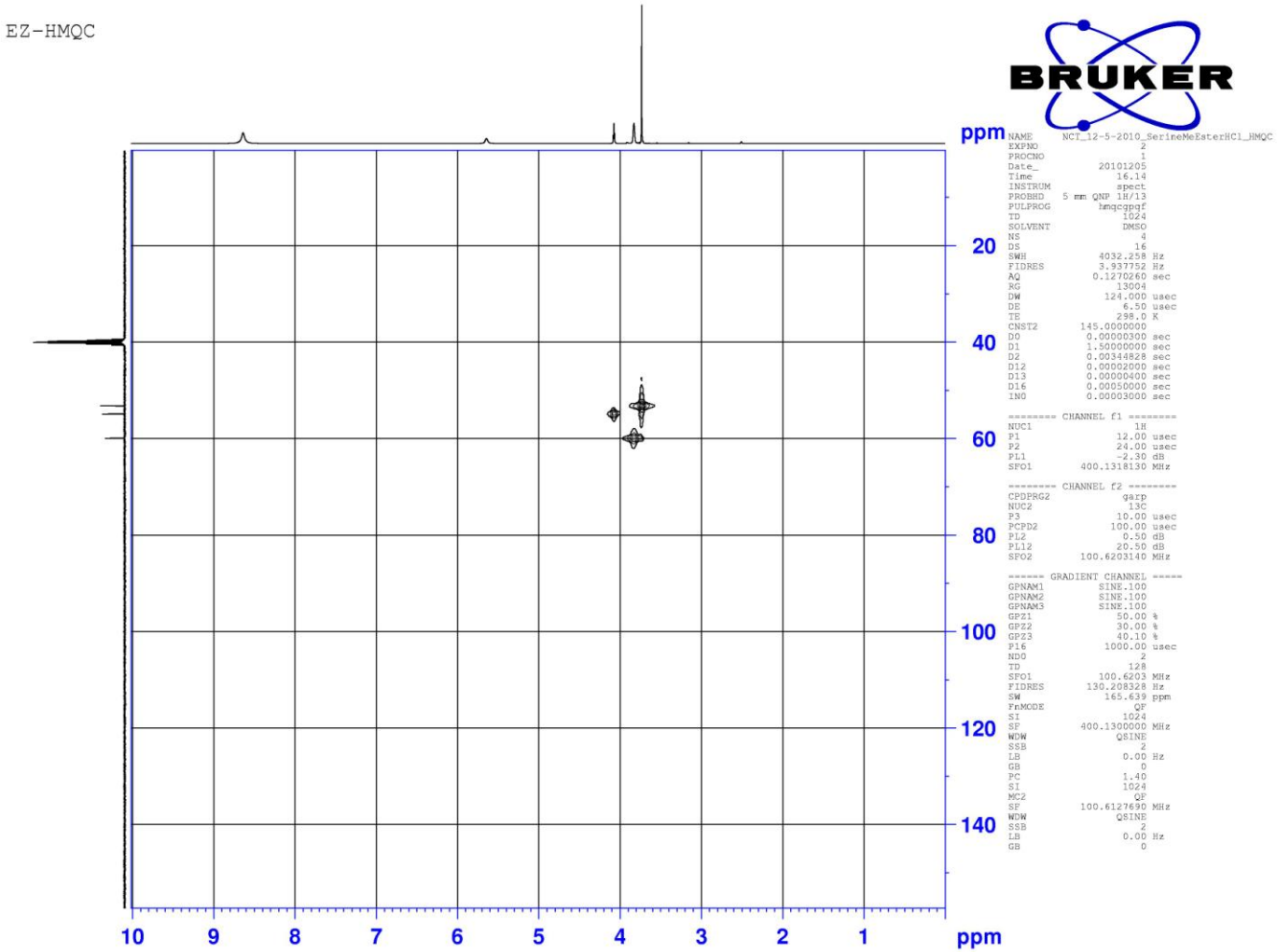

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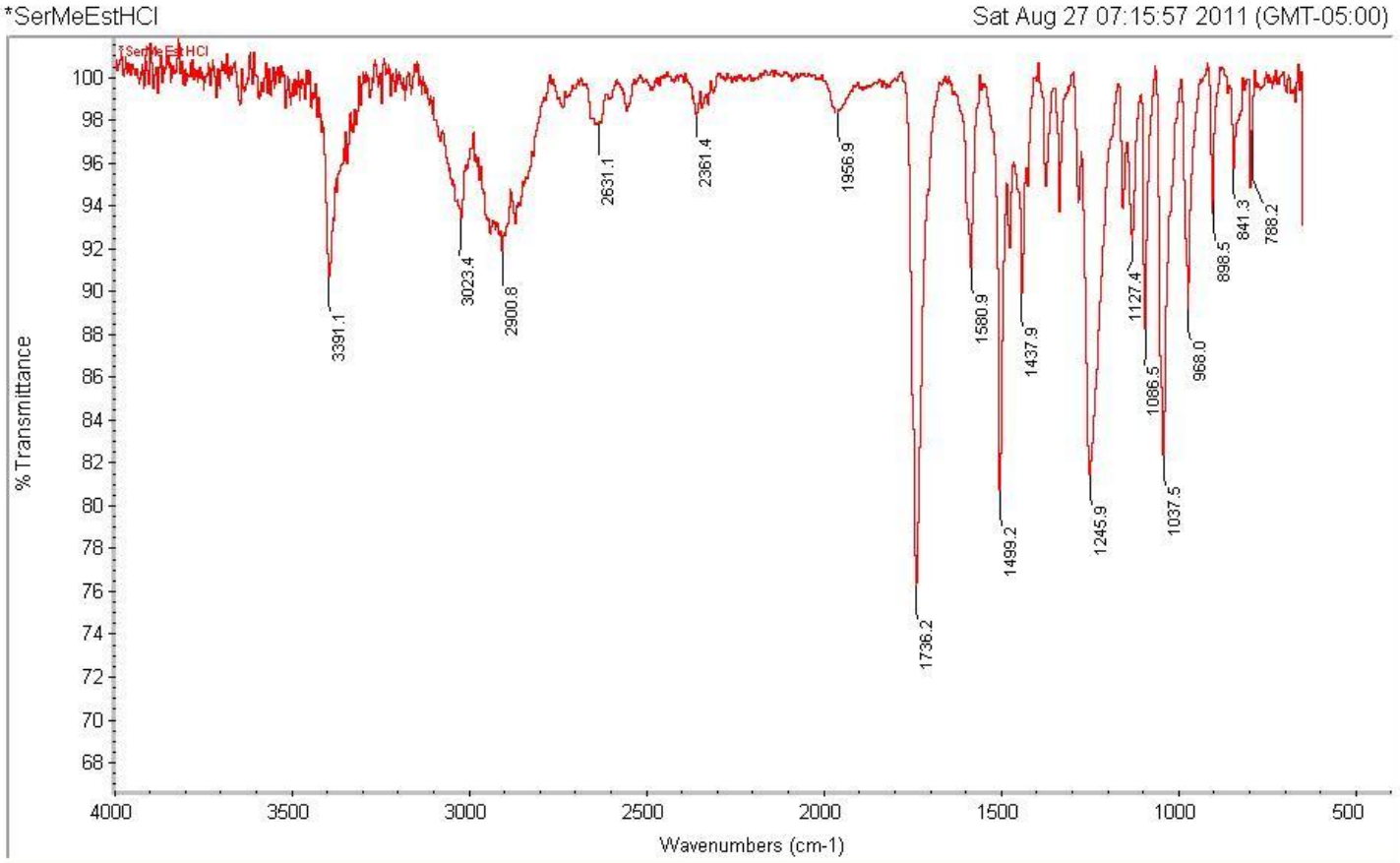

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Resolution: 4.000
Sample gain: 8.0
Optical velocity: 0.6329
Aperture: 100.00

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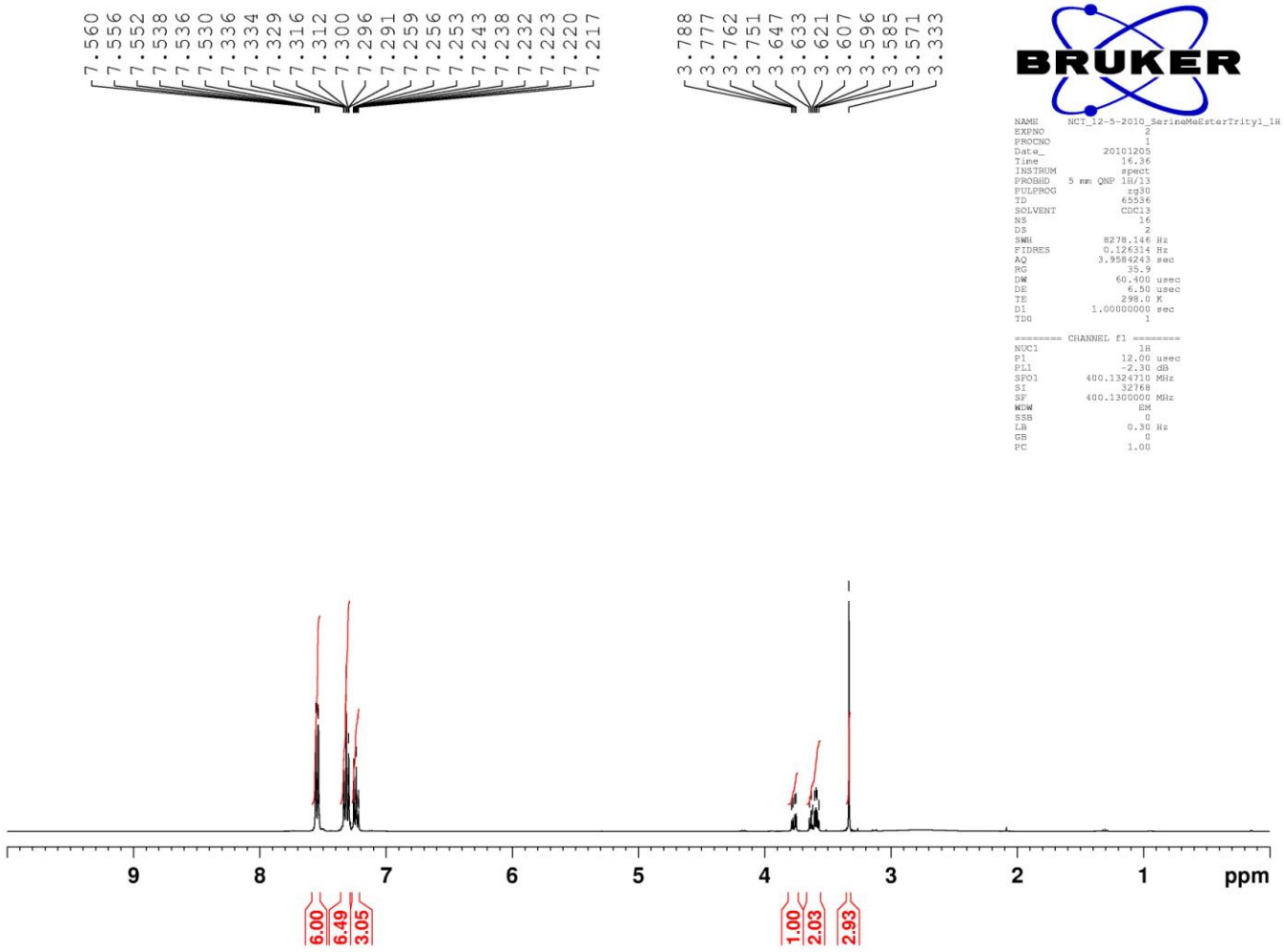

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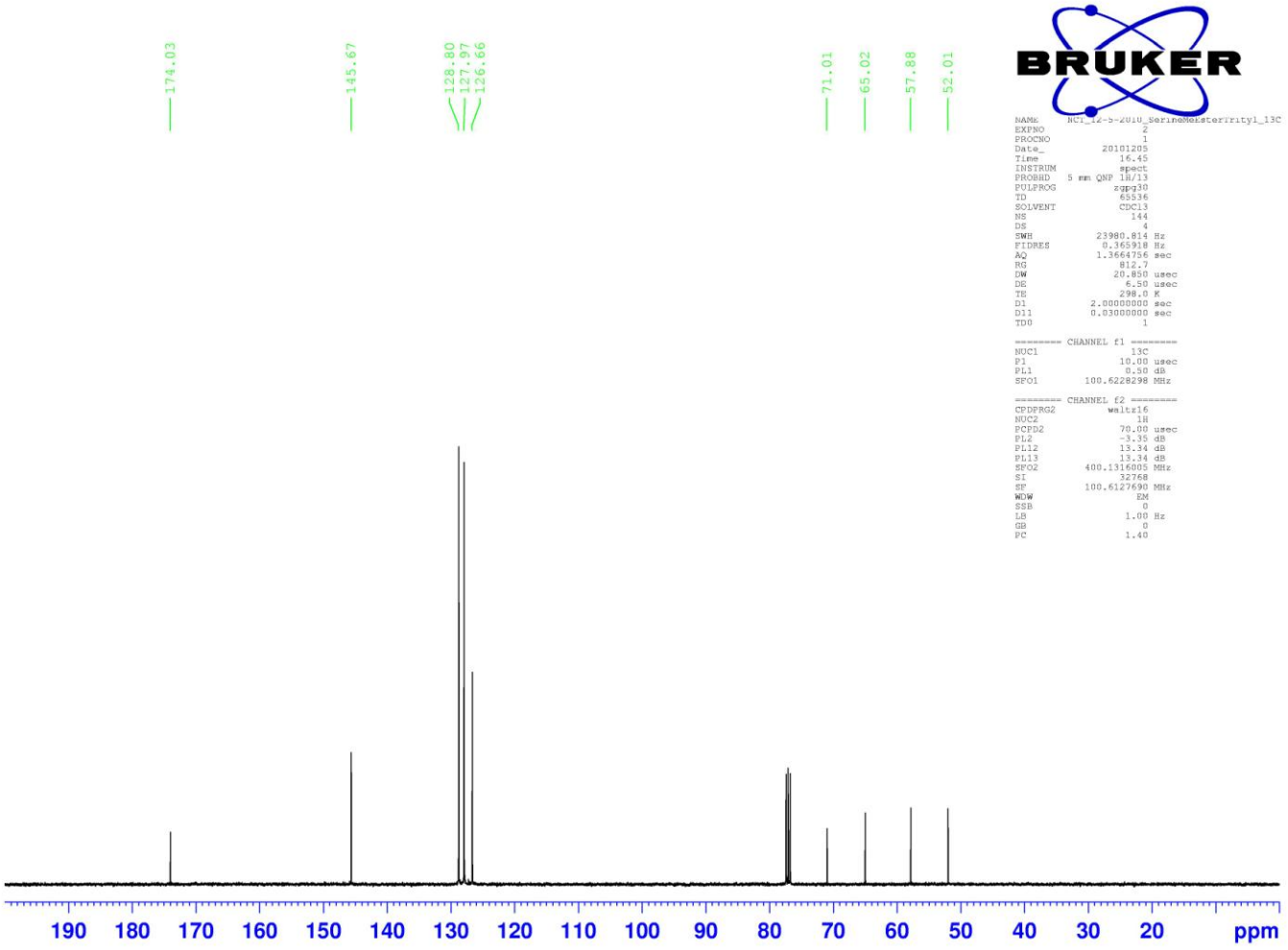

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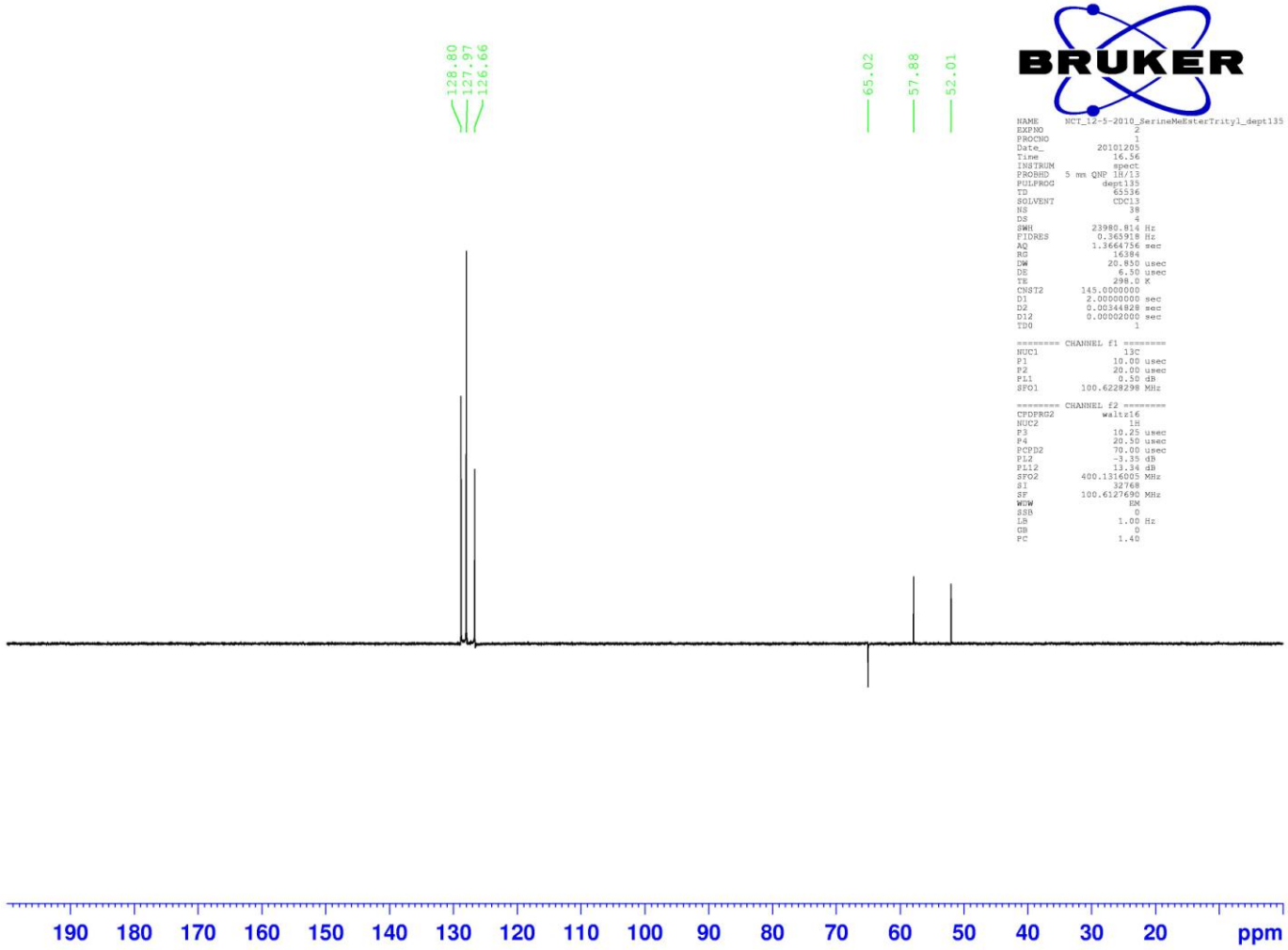

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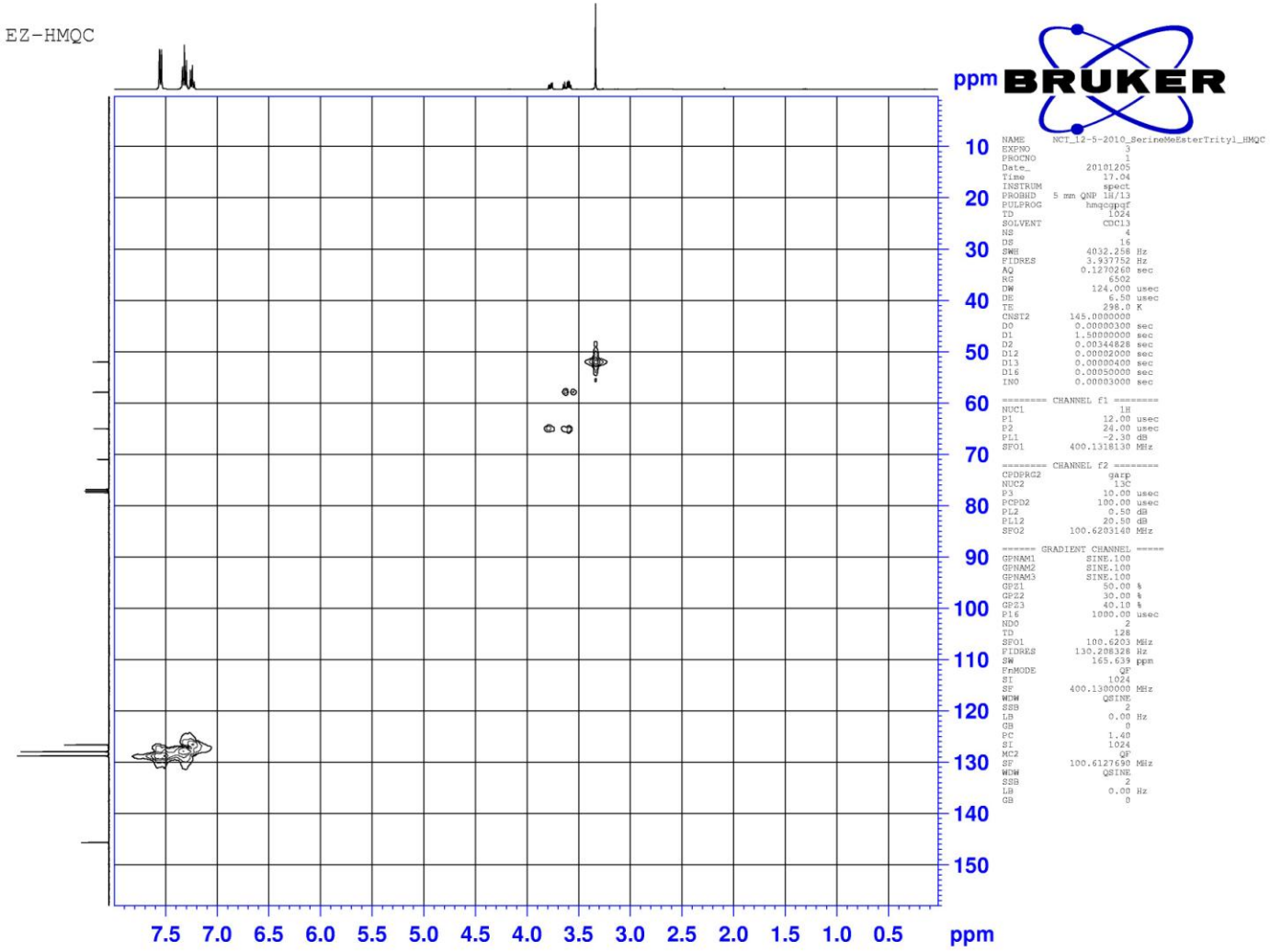

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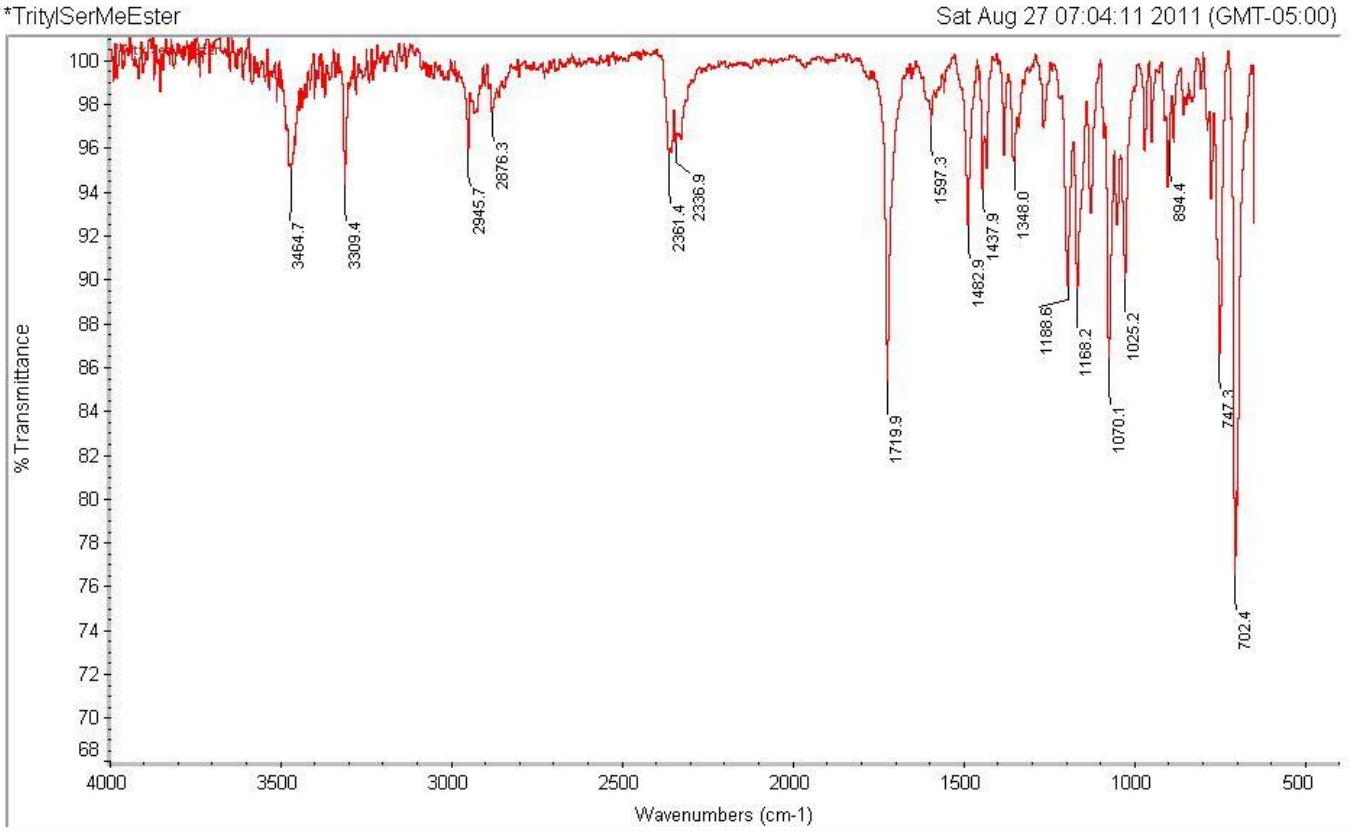

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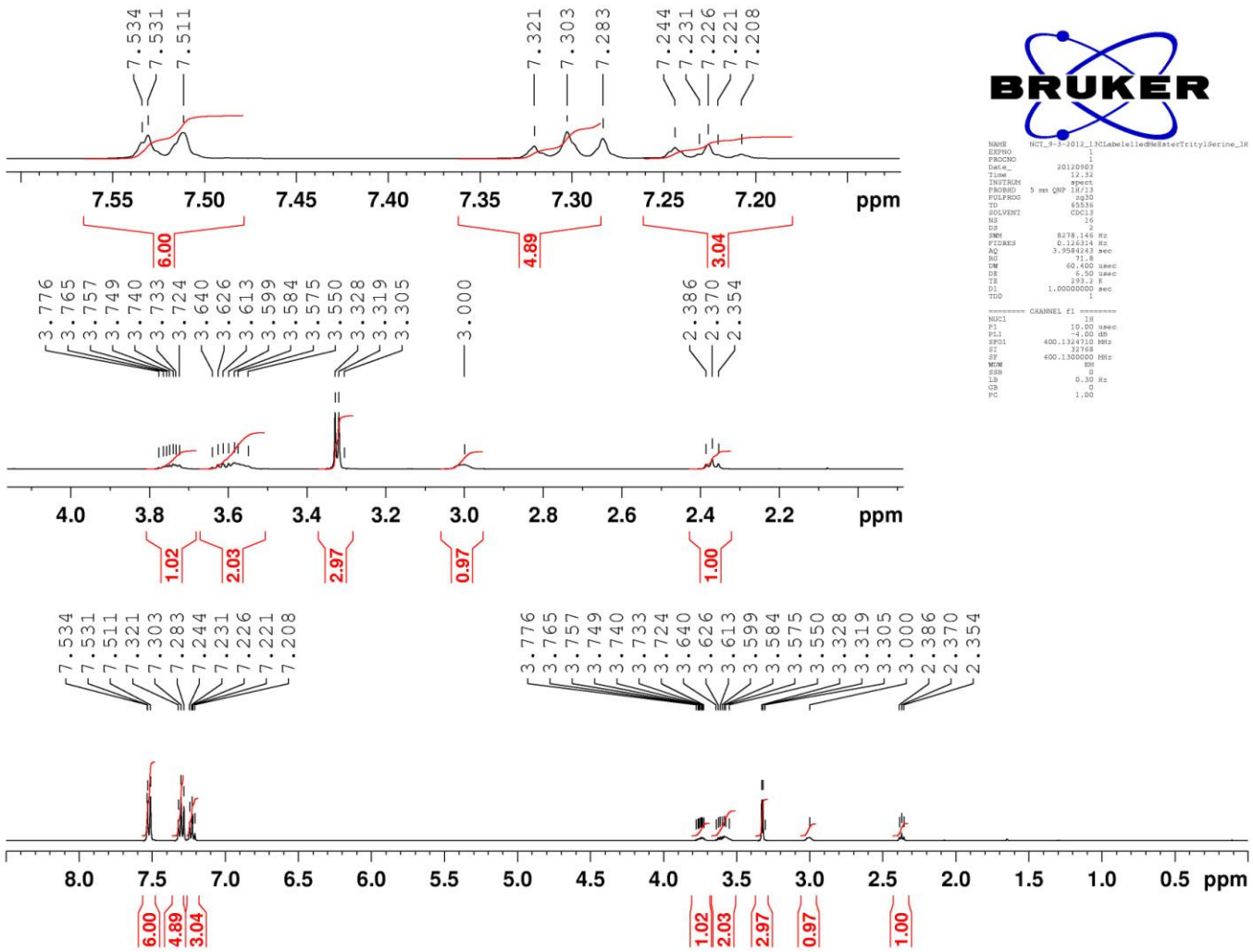
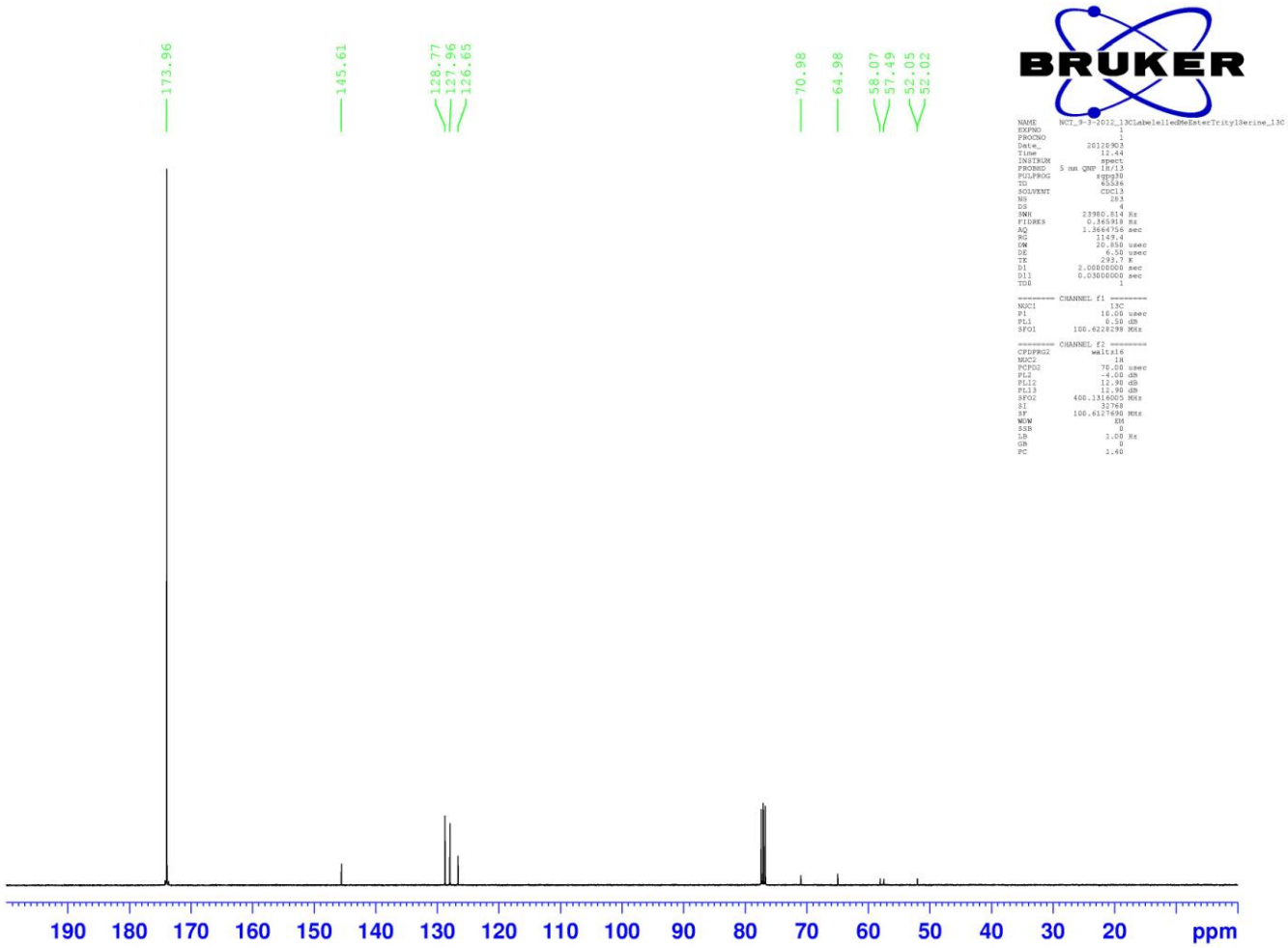
Aperture: 100.00

1H NMR of DL-Methyl-3-hydroxy-2-(tritylamino)propanoate-1-^{13}C (11)



^{13}C NMR of DL-Methyl-3-hydroxy-2-(tritylamino)propanoate-1-^{13}C (11)



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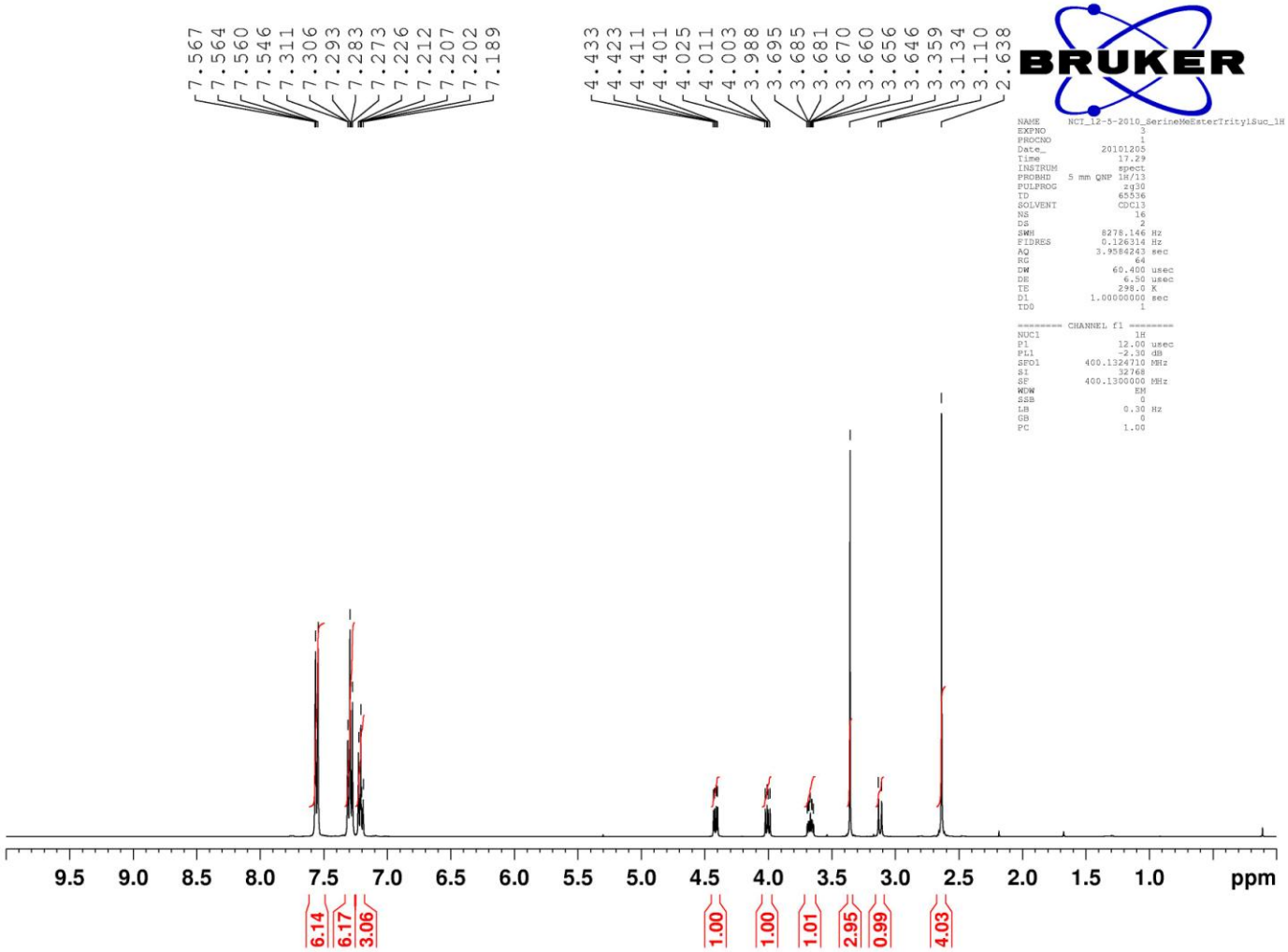

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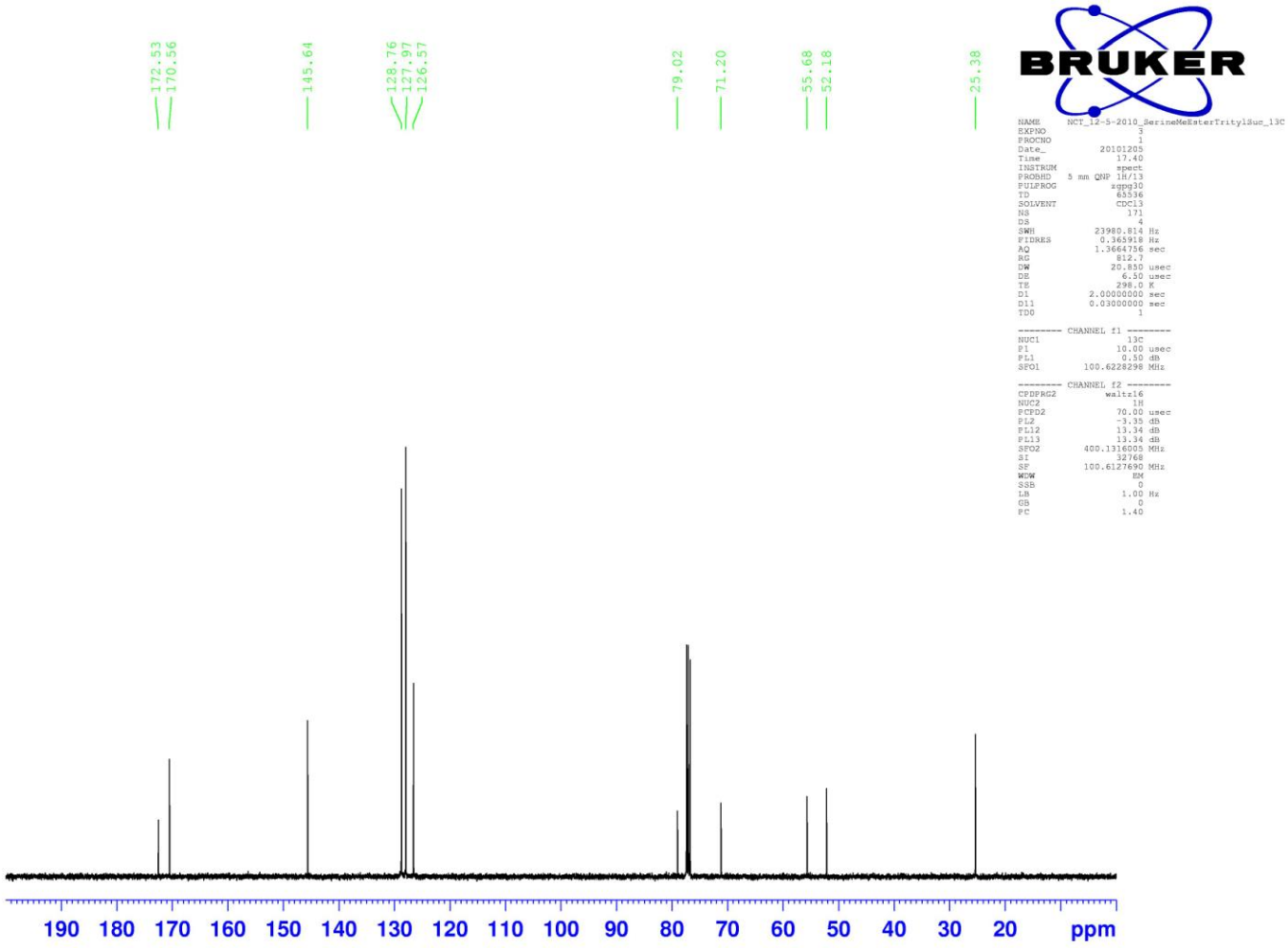

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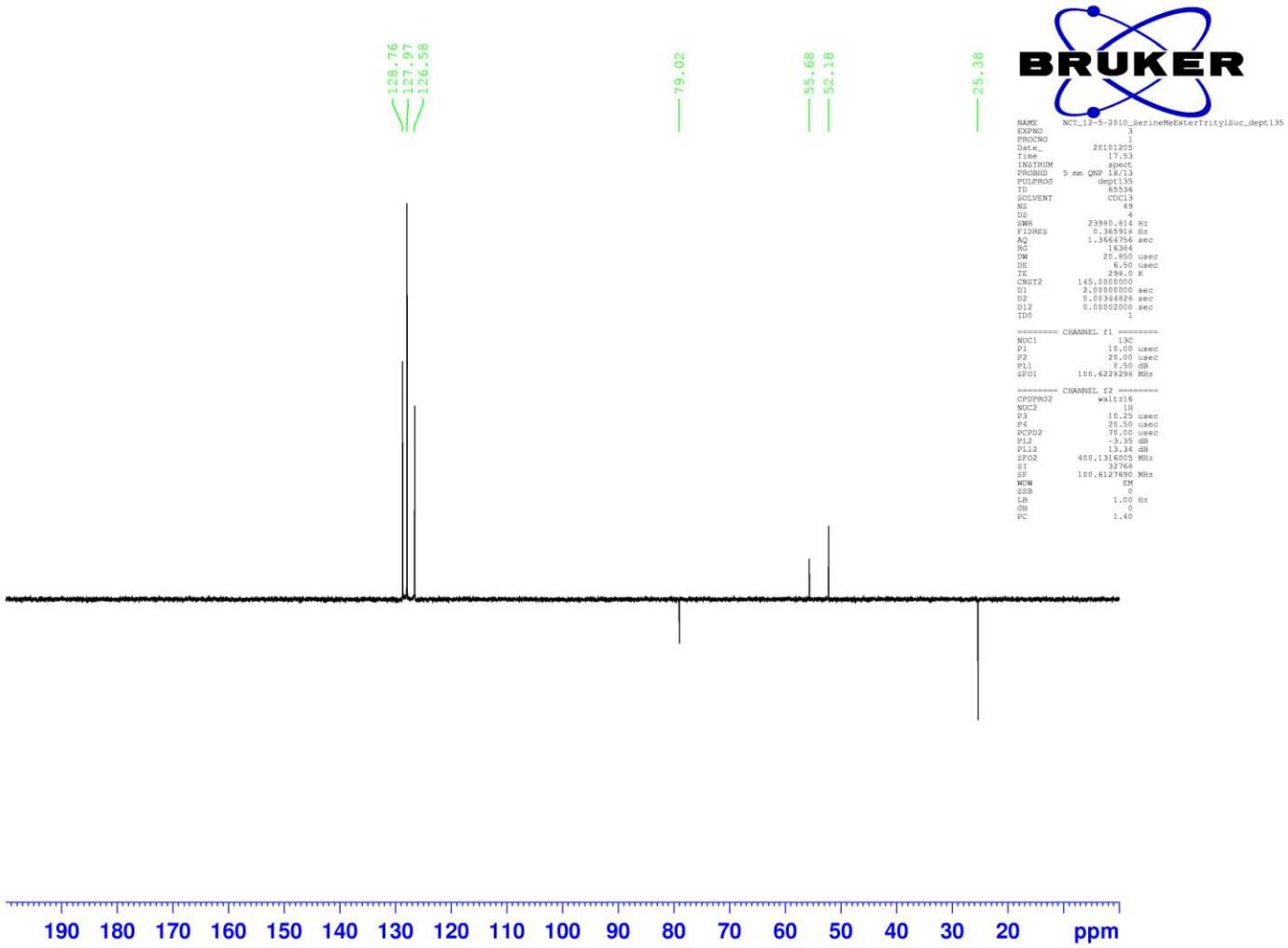
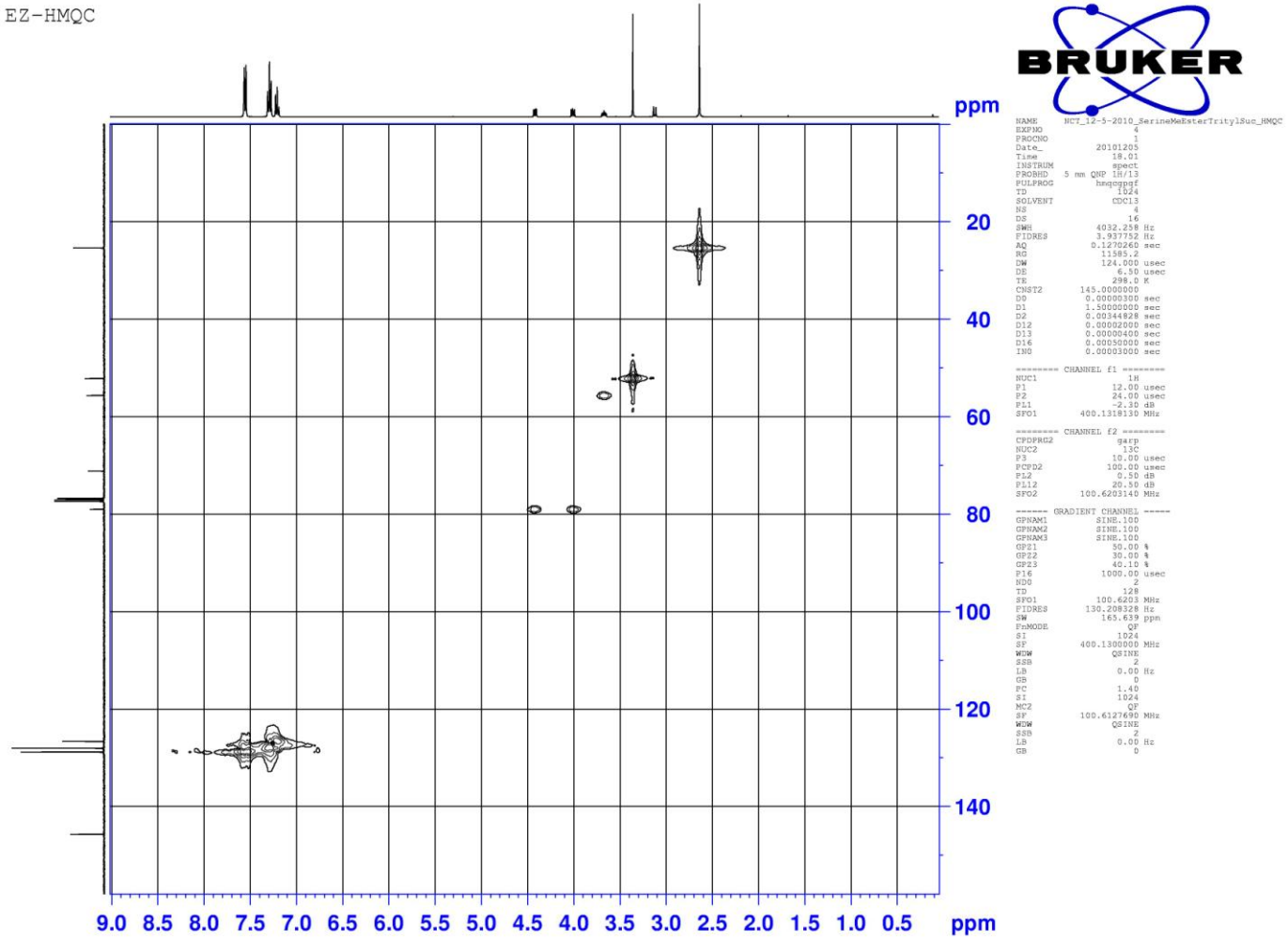
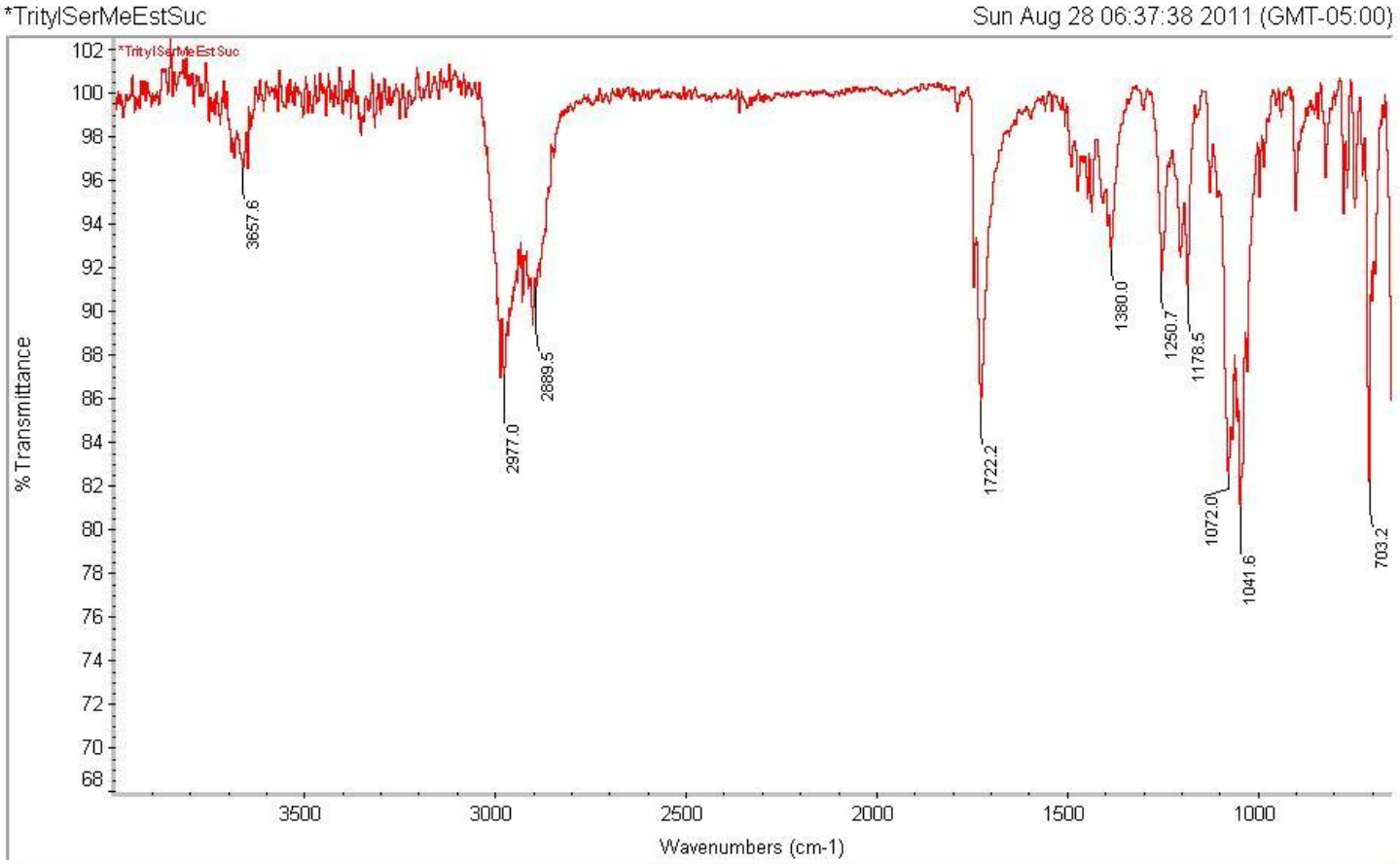


HMQC of DL-O-(1,3-dihydro-2,5-dioxo-1-pyrolidinyl)-N-(triphenylmethyl)-methyl ester (3)



IR of DL-O-(1,3-dihydro-2,5-dioxo-1-pyrolidinyl)-N-(triphenylmethyl)-methyl ester (3)



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Number of background scans: 16
Resolution: 4.000
Sample gain: 8.0
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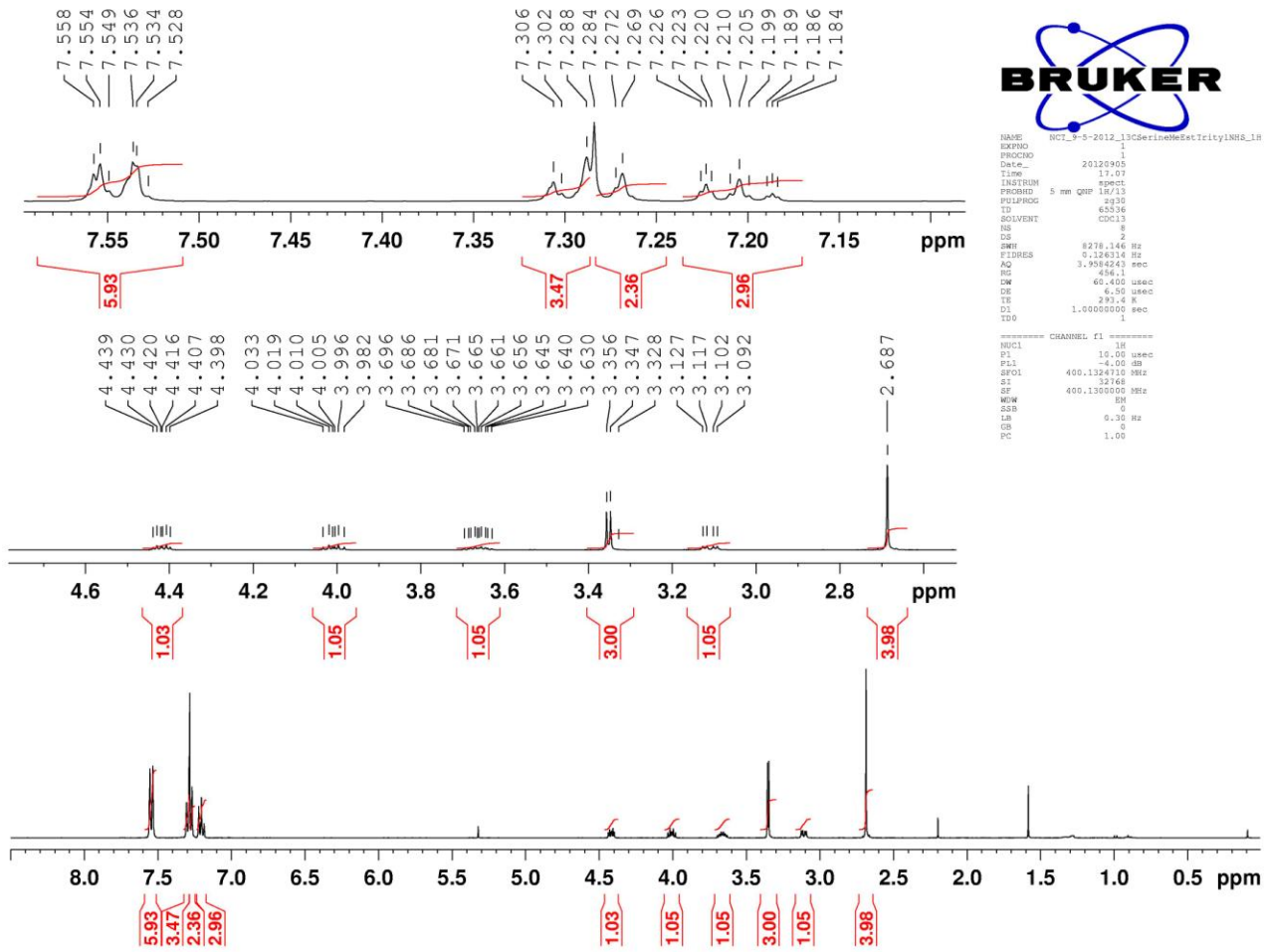
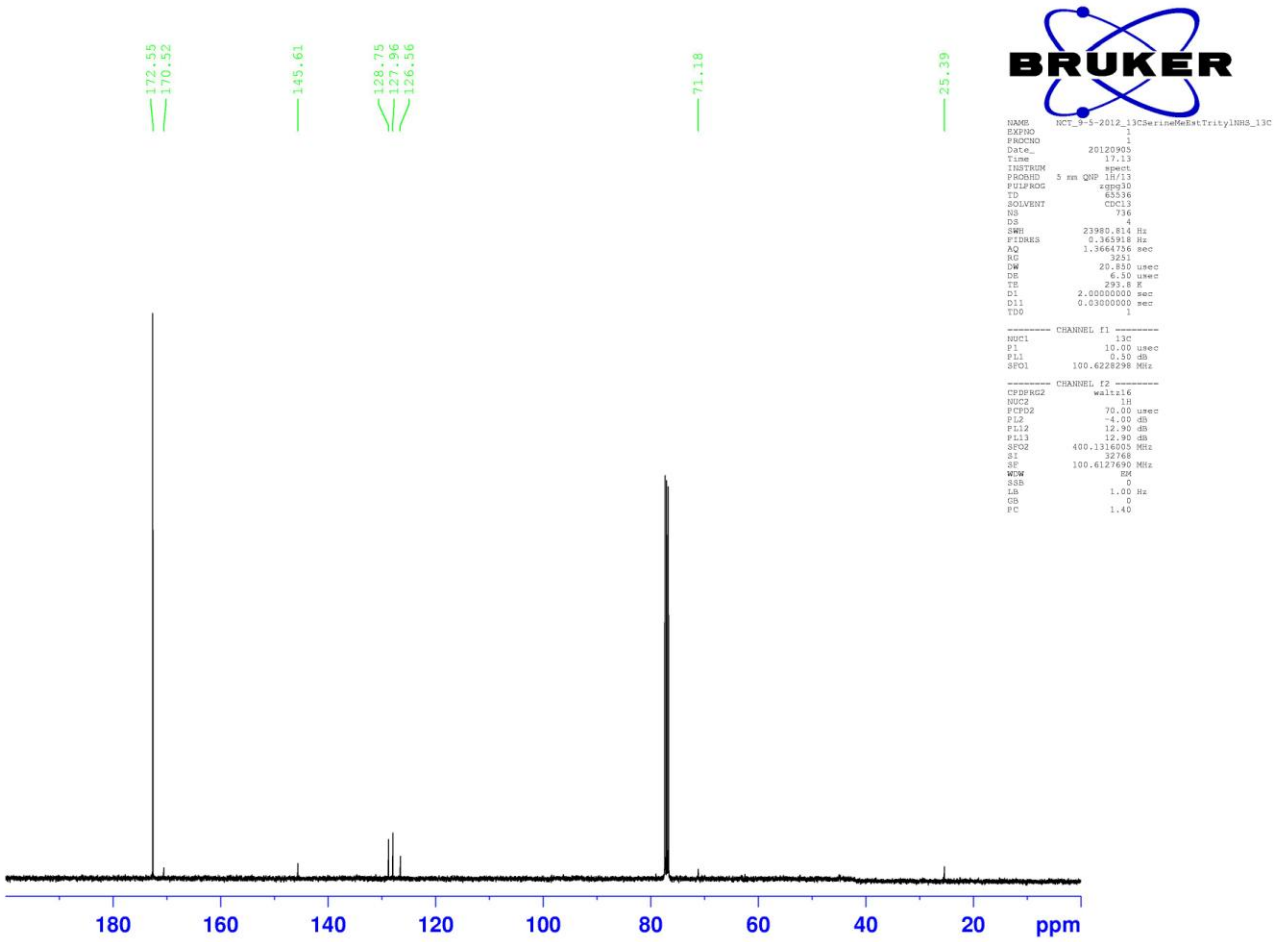
Aperture: 100.00

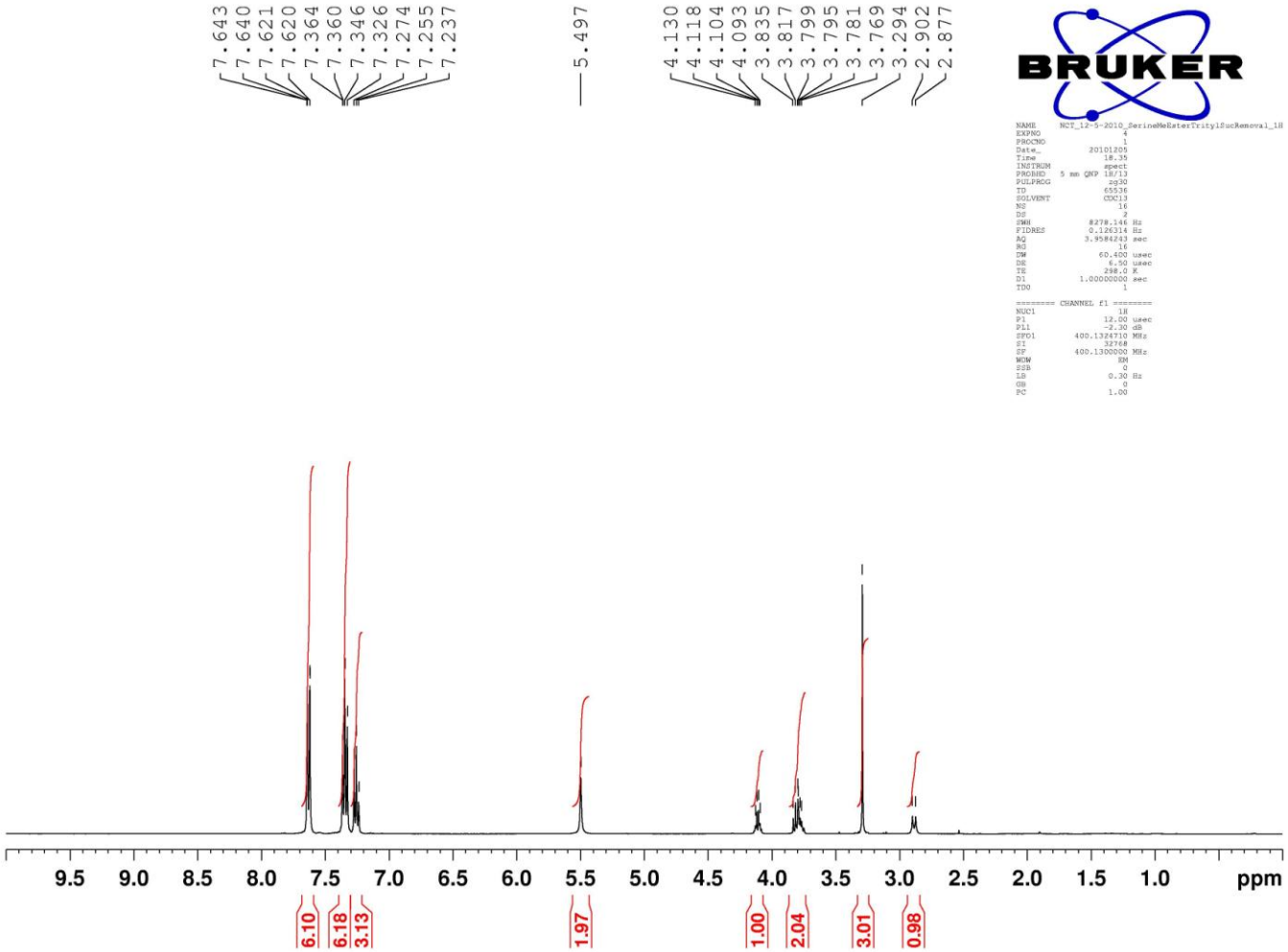
^{1}H NMR of DL-O-(1,3-dihydro-2,5-dioxo-1-pyrolidinyl)-N-(triphenylmethyl)-1-^{13}C methyl ester (12)



^{13}C NMR of DL-O-(1,3-dihydro-2,5-dioxo-1-pyrolidinyl)-N-(triphenylmethyl)-1-^{13}C methyl ester (12)



^{1}H of DL-Methyl-γ-aminooxy-α-amino(triphenylmethyl)butyrate (4)



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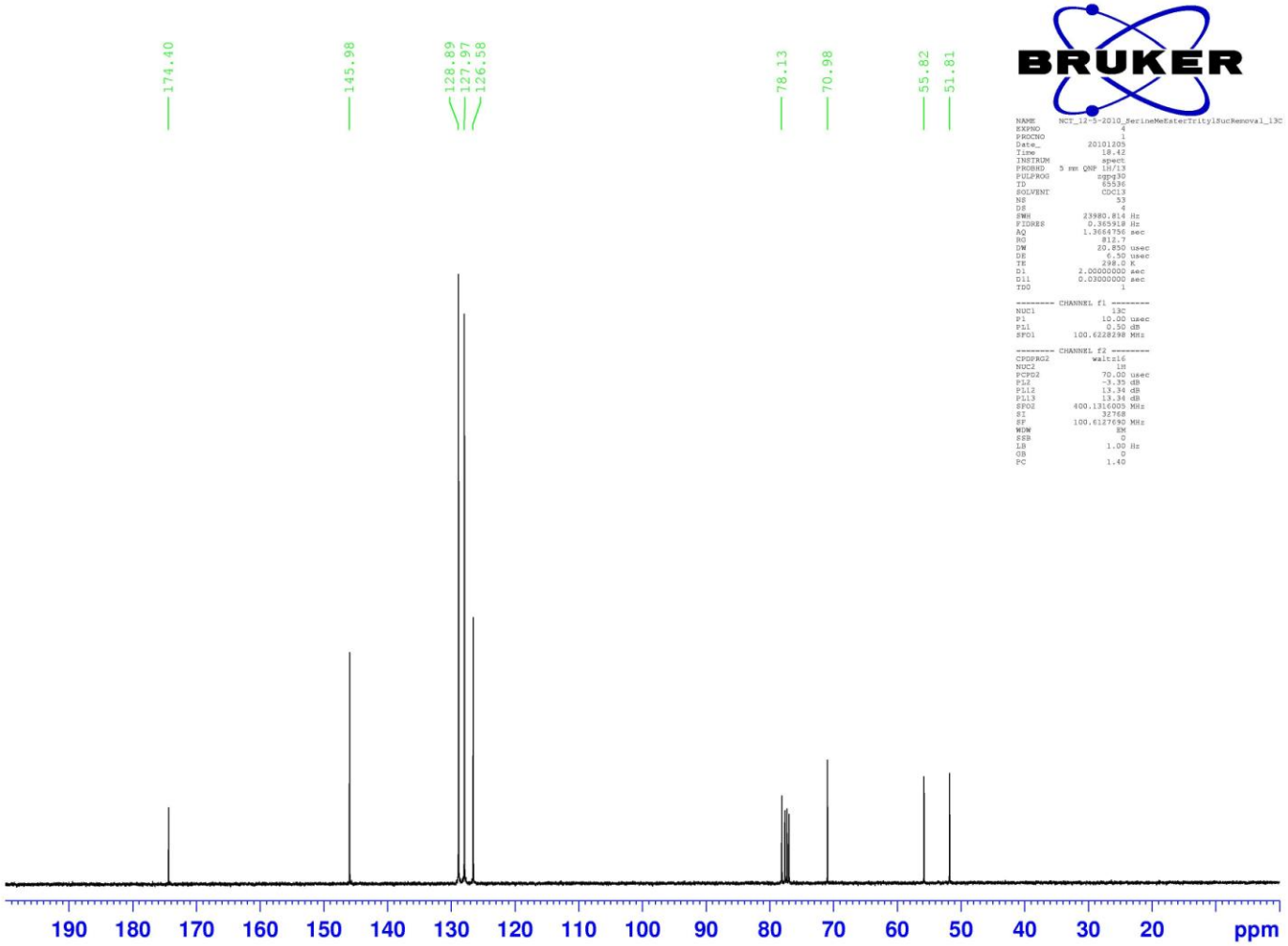
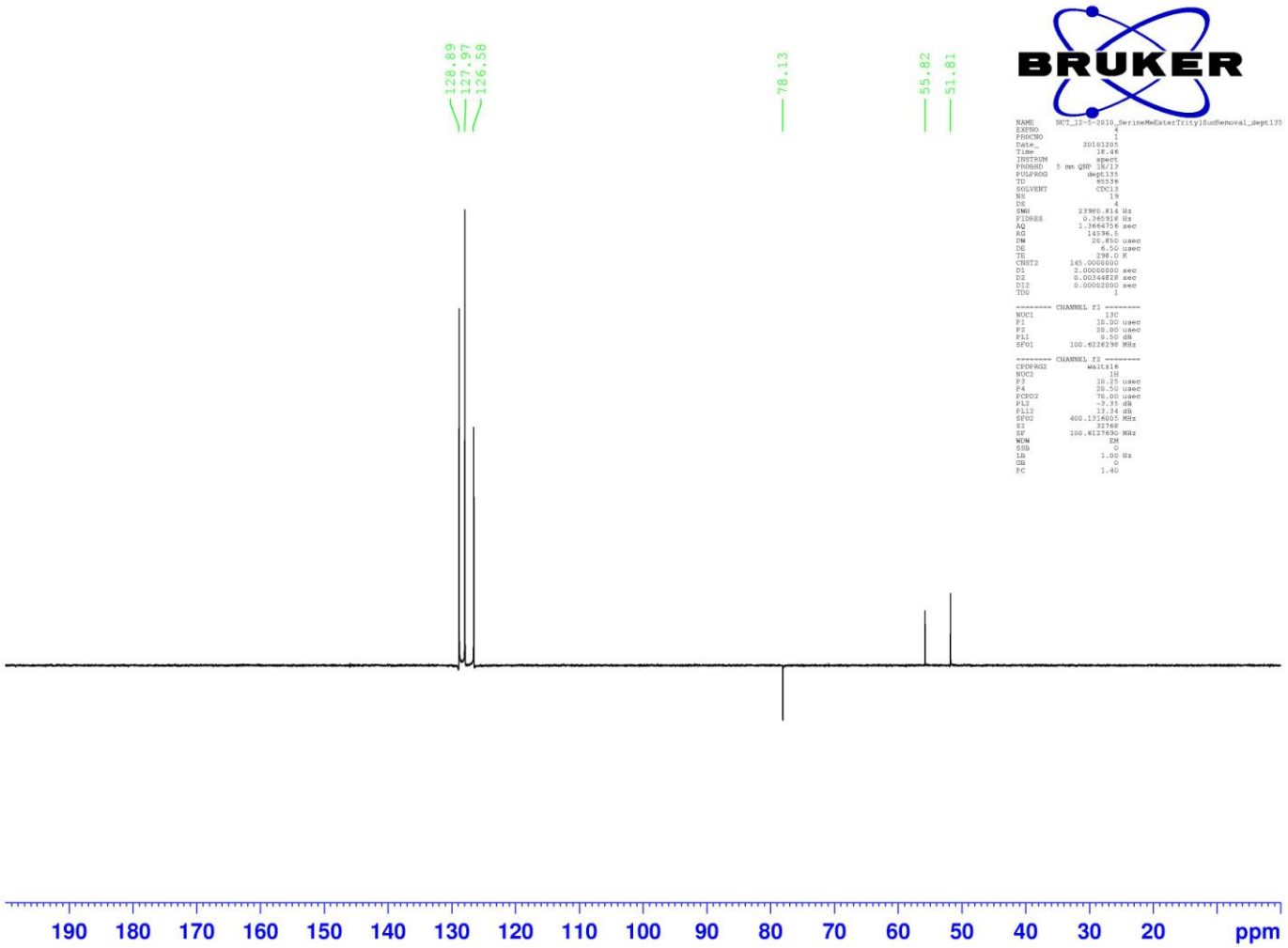
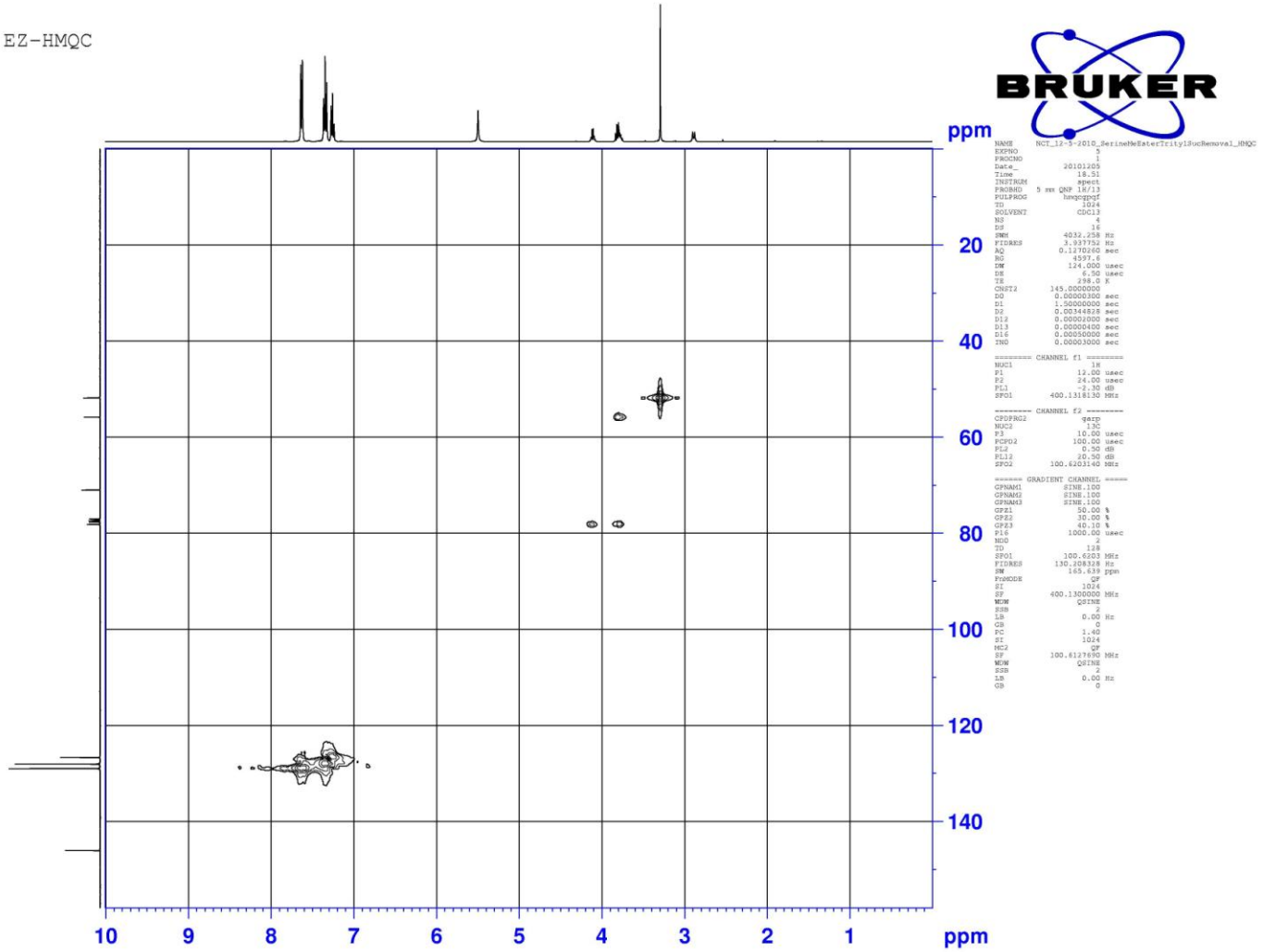


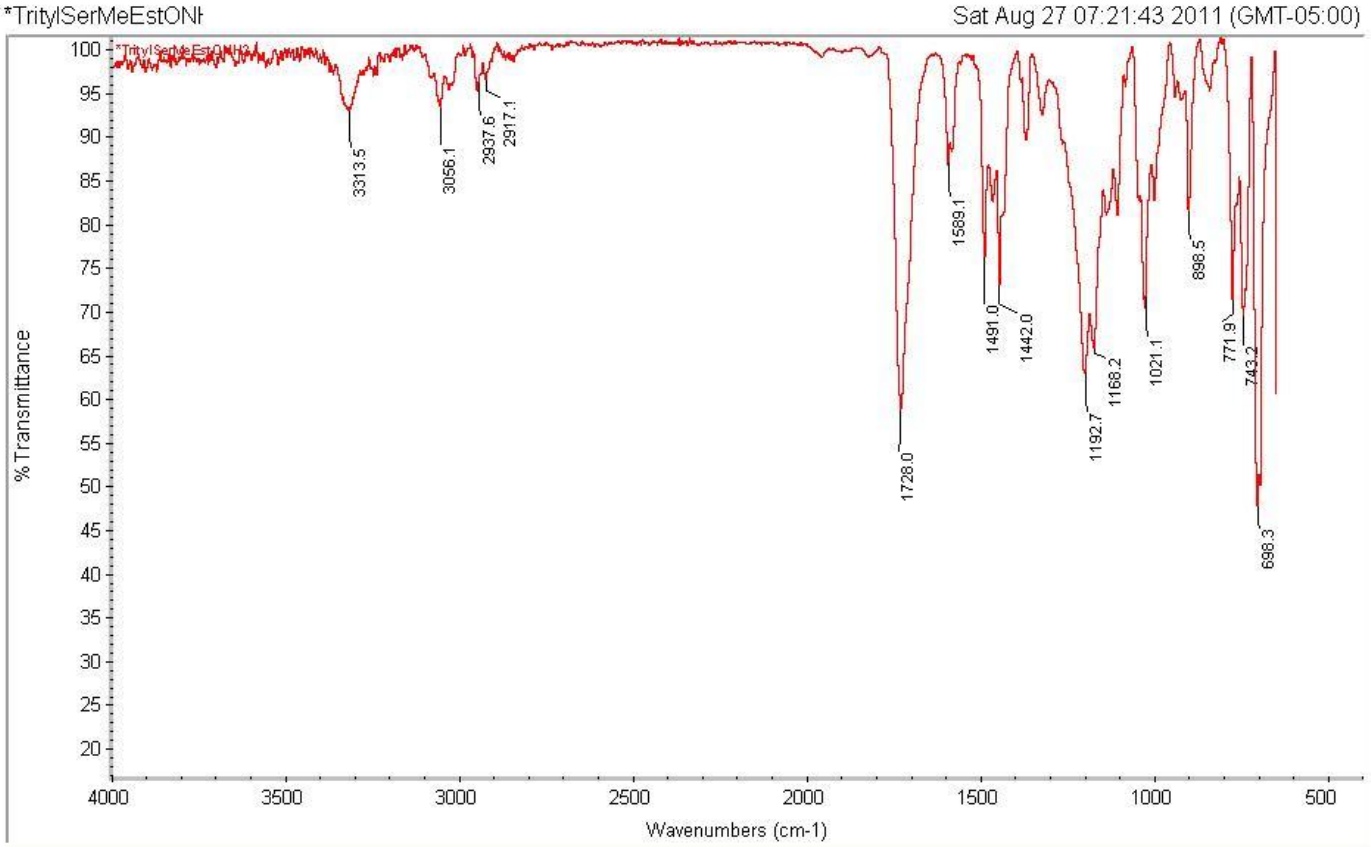
DEPT of DL-Methyl-γ-aminooxy-α-amino(triphenylmethyl)butyrate (4)



HMQC of DL-Methyl-γ-aminooxy-α-amino(triphenylmethyl)butyrate (4)



IR of DL-Methyl-γ-aminooxy-α-amino(triphenylmethyl)butyrate (4)



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Sample gain: 8.0
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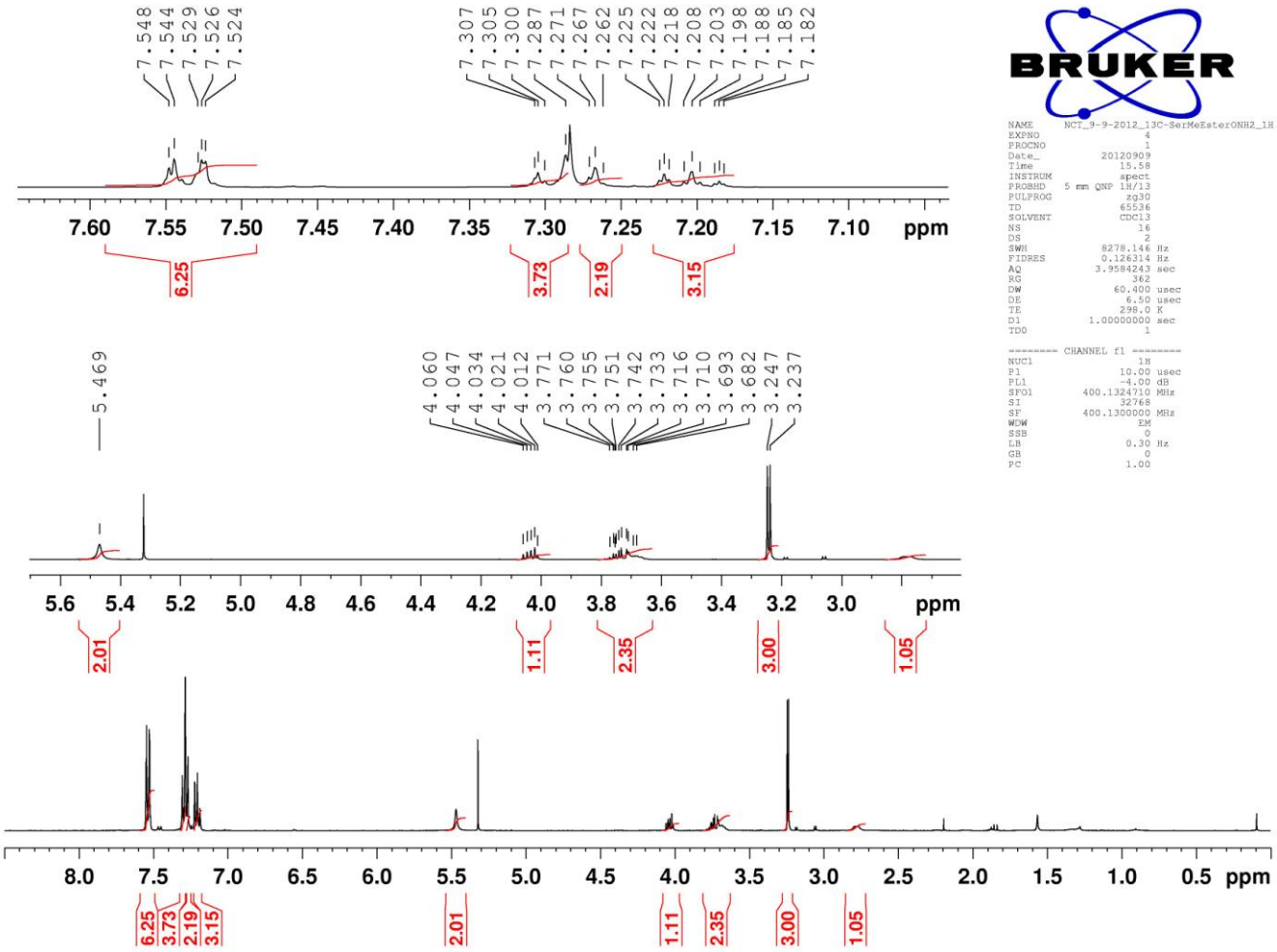
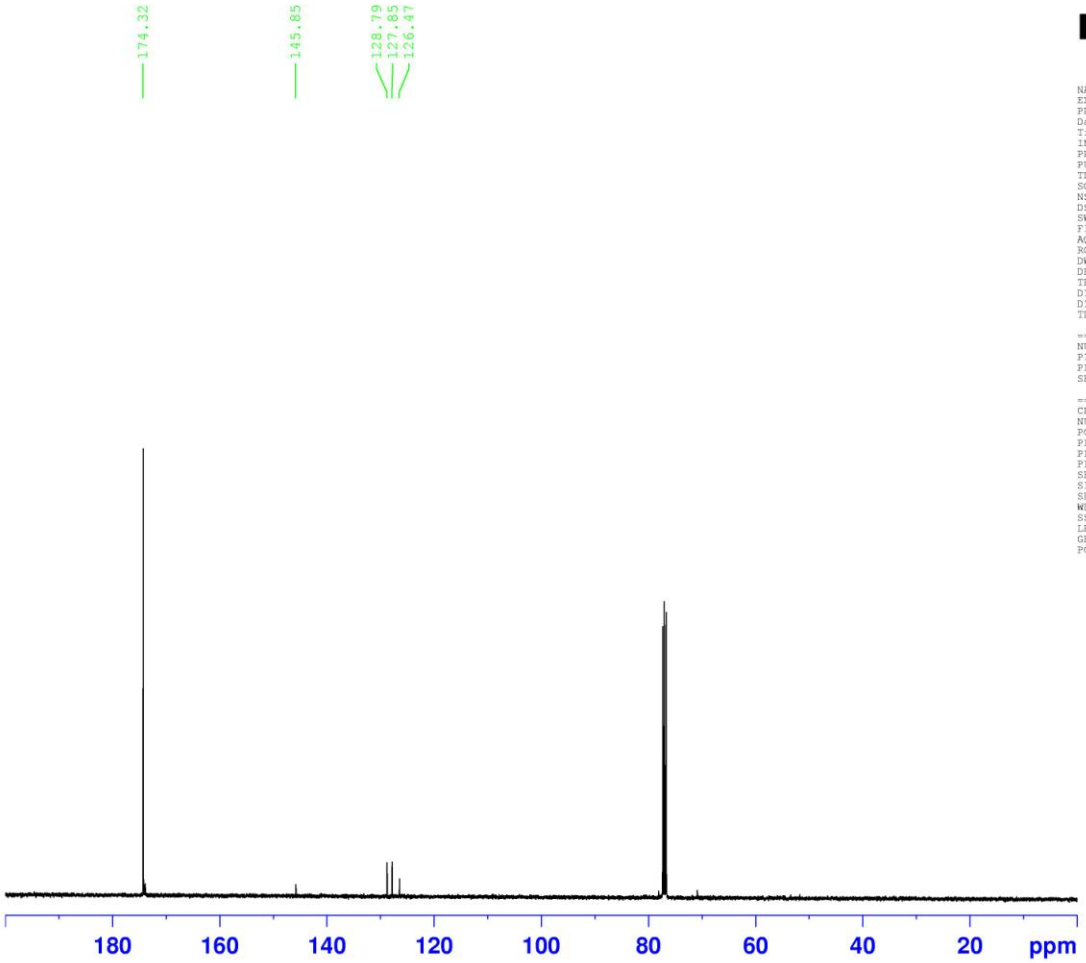
Aperture: 100.00

^{1}H NMR of DL-Methyl-γ-aminooxy-α-amino(triphenylmethyl)butyrate-1-^{13}C (13)



^{13}C NMR of DL-Methyl-γ-aminooxy-α-amino(triphenylmethyl)butyrate-1-^{13}C (13)

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PL1                 0.50 dB
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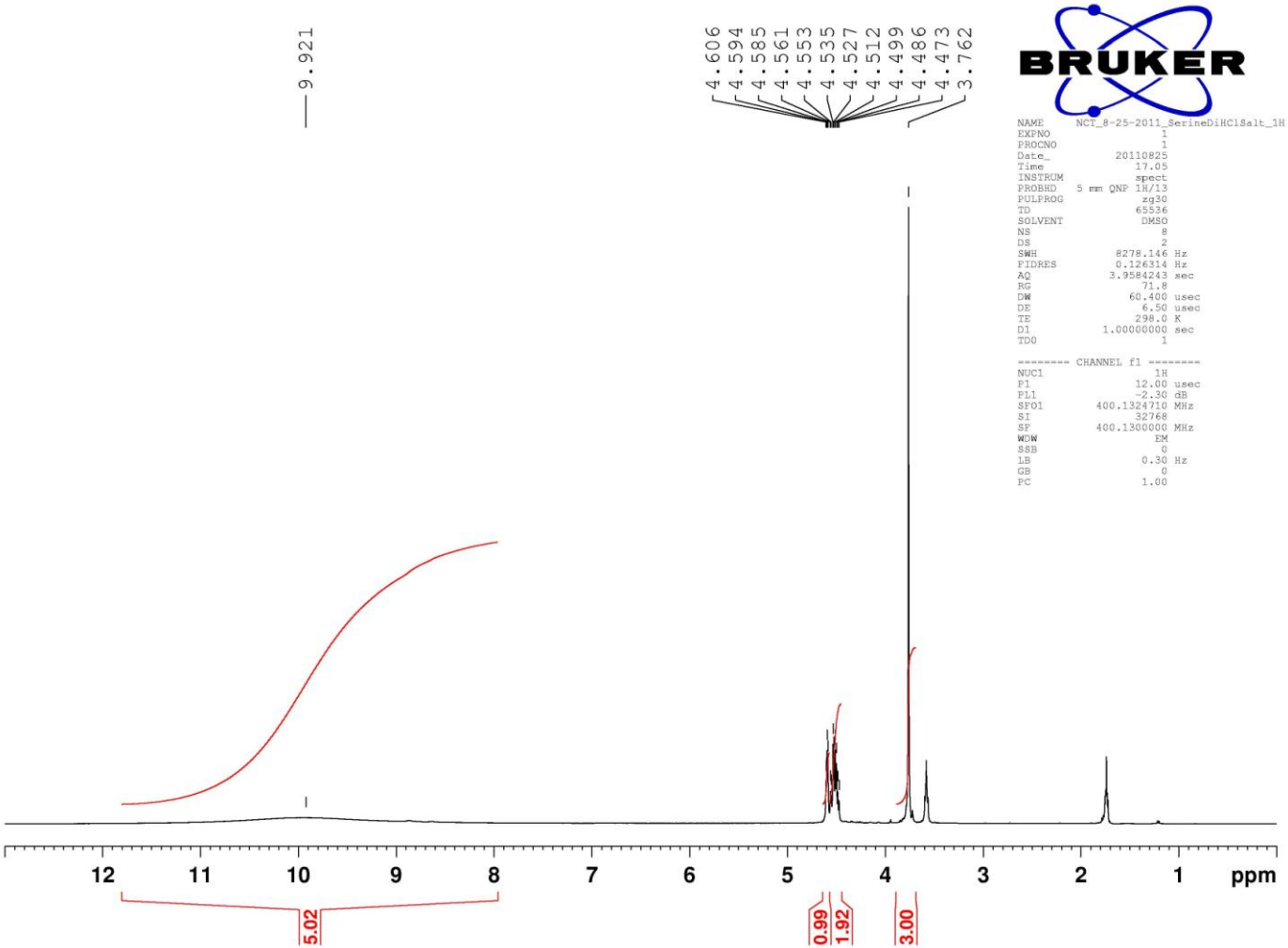
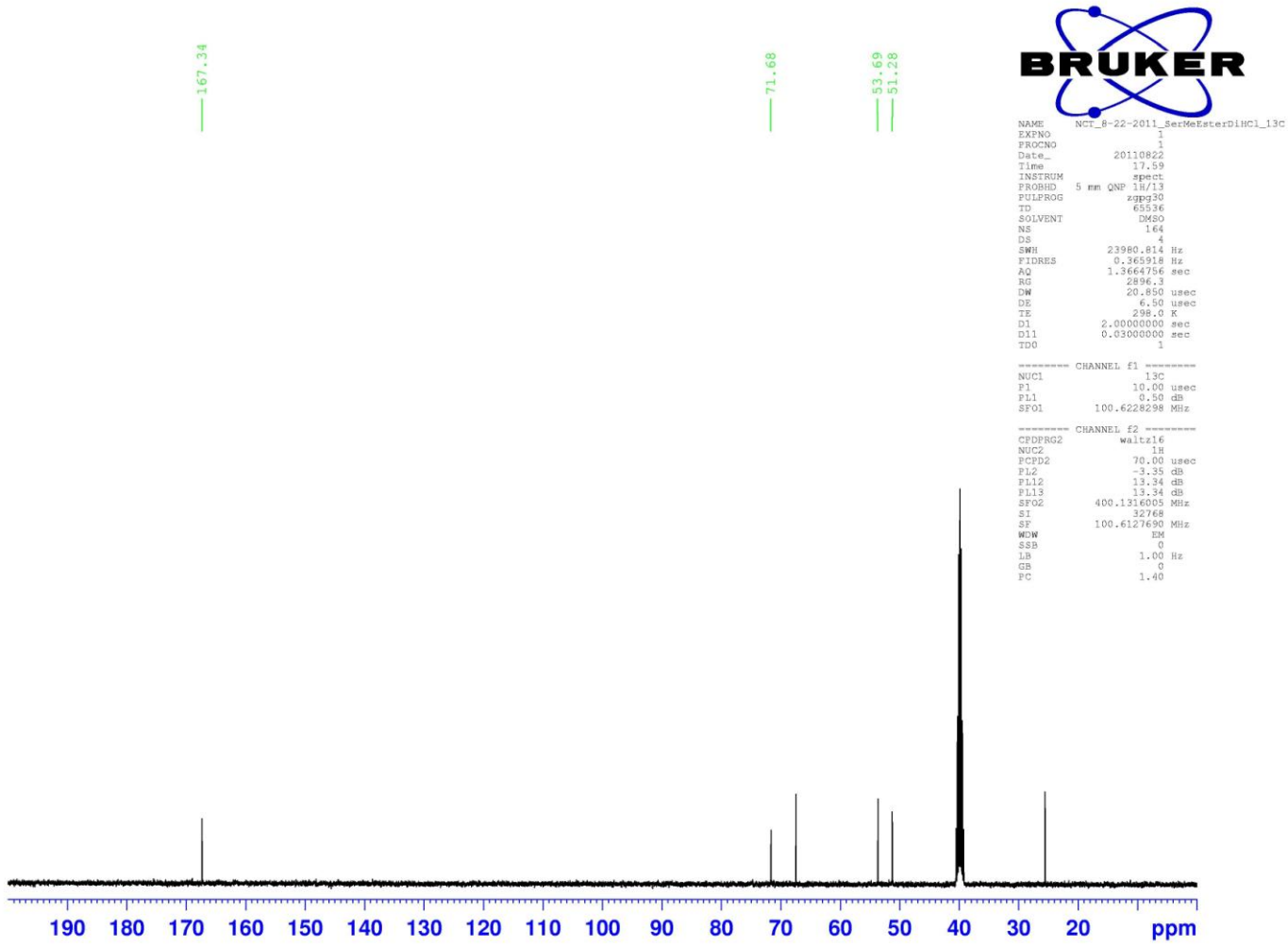
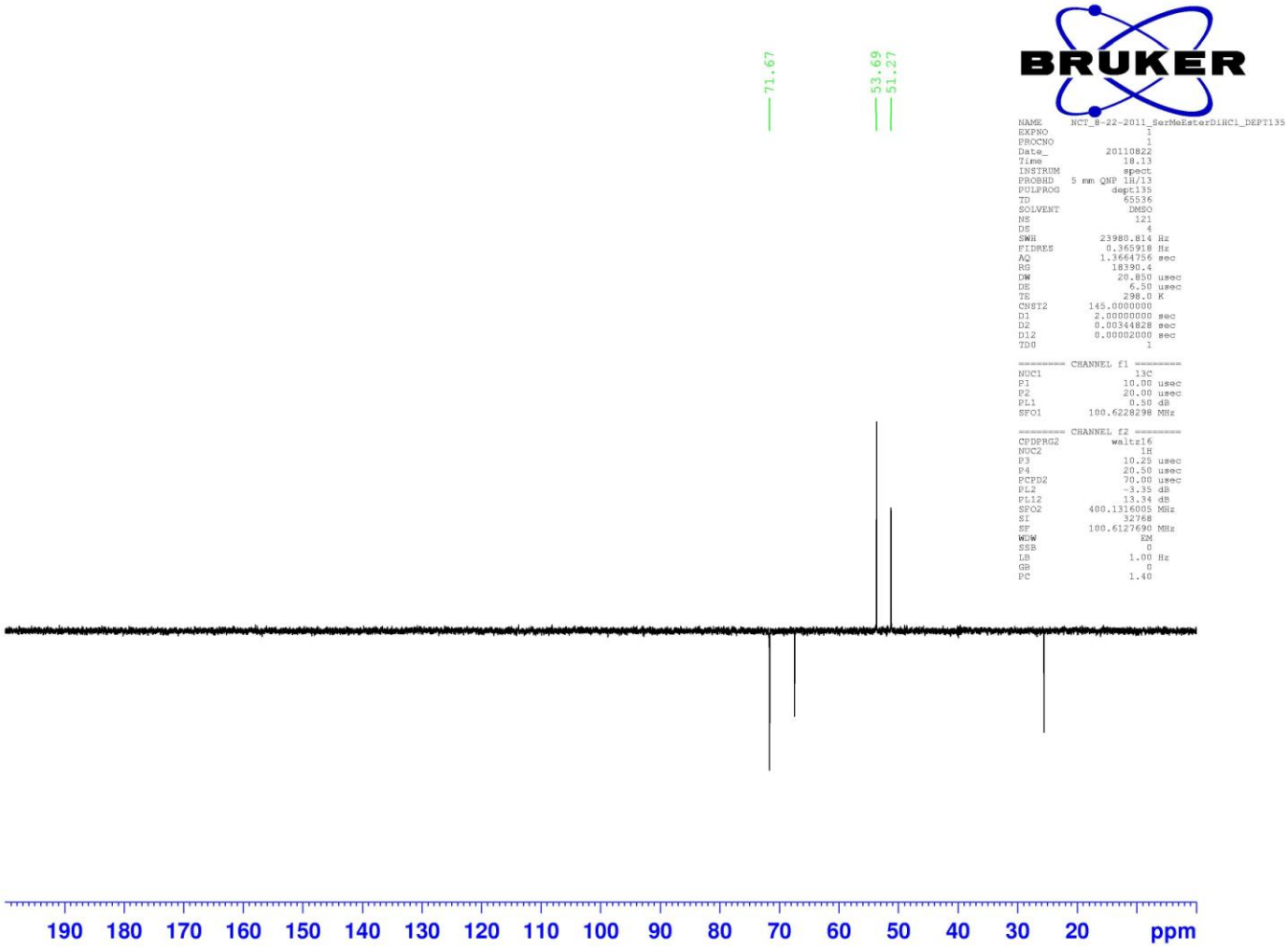
^{1}H of DL-β-aminoxyalanine methyl ester dihydrochloride (5)



^{13}C of DL-β-aminoxyalanine methyl ester dihydrochloride (5)



DEPT of DL-β-aminoxyalanine methyl ester dihydrochloride (5)



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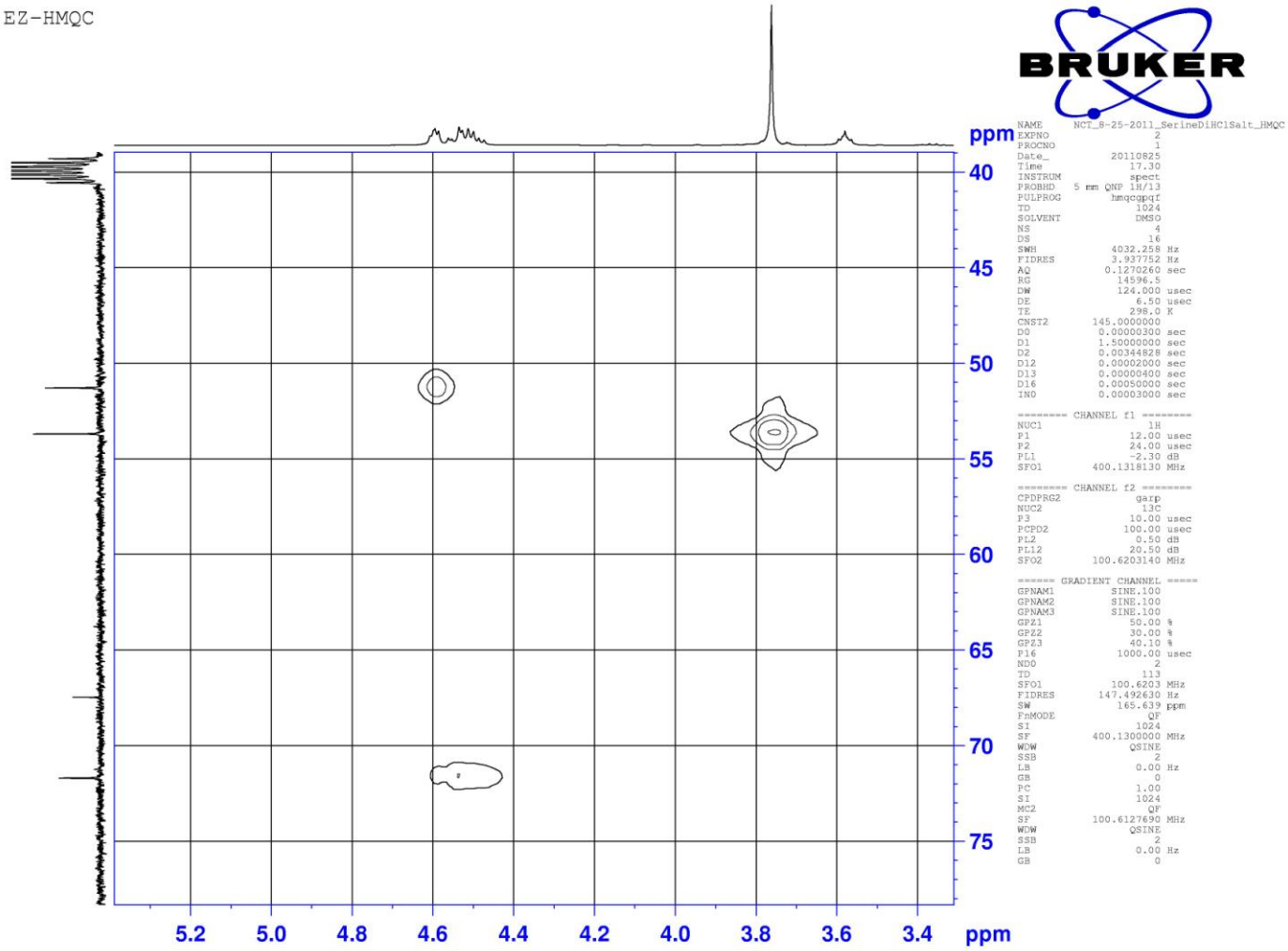
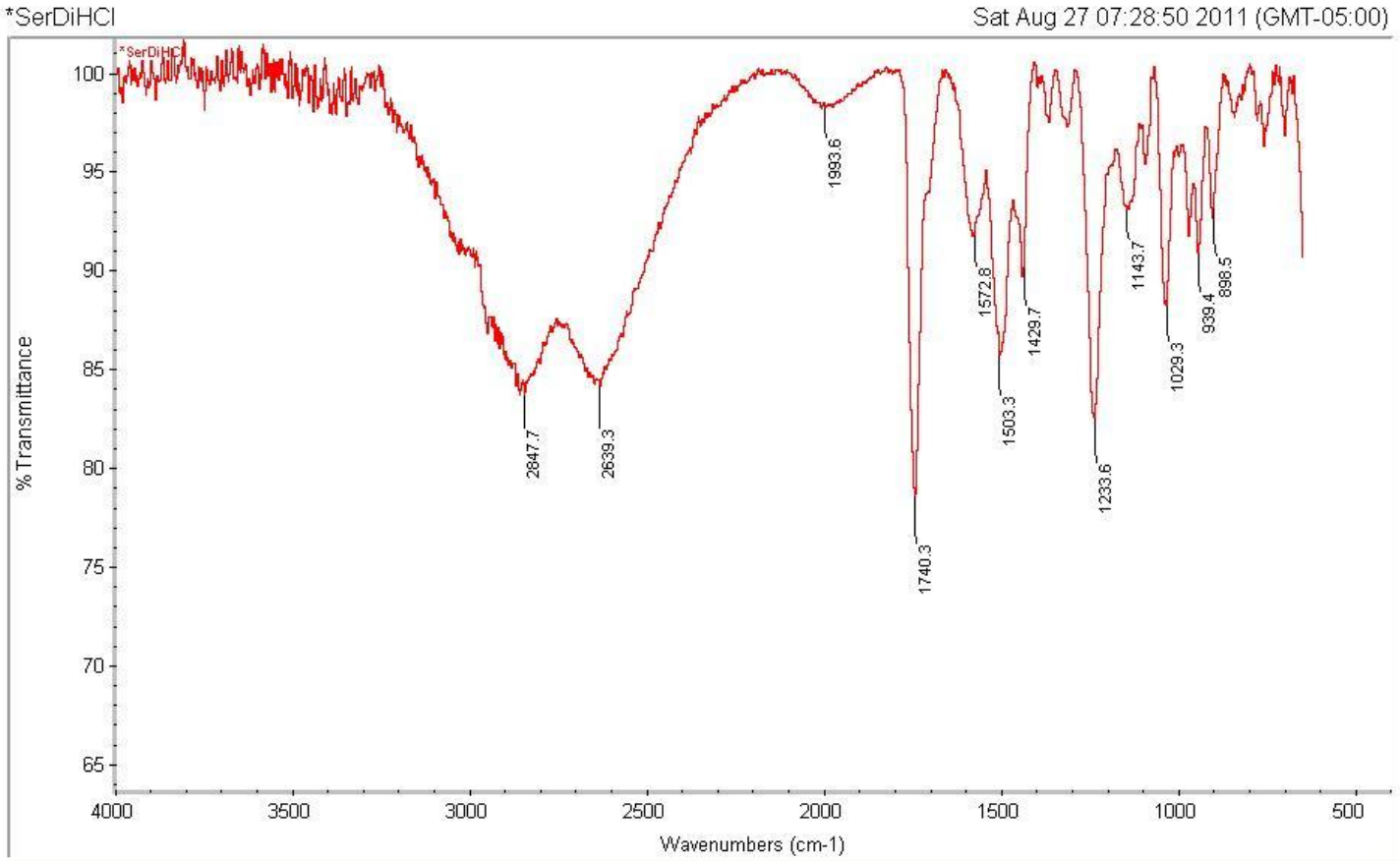
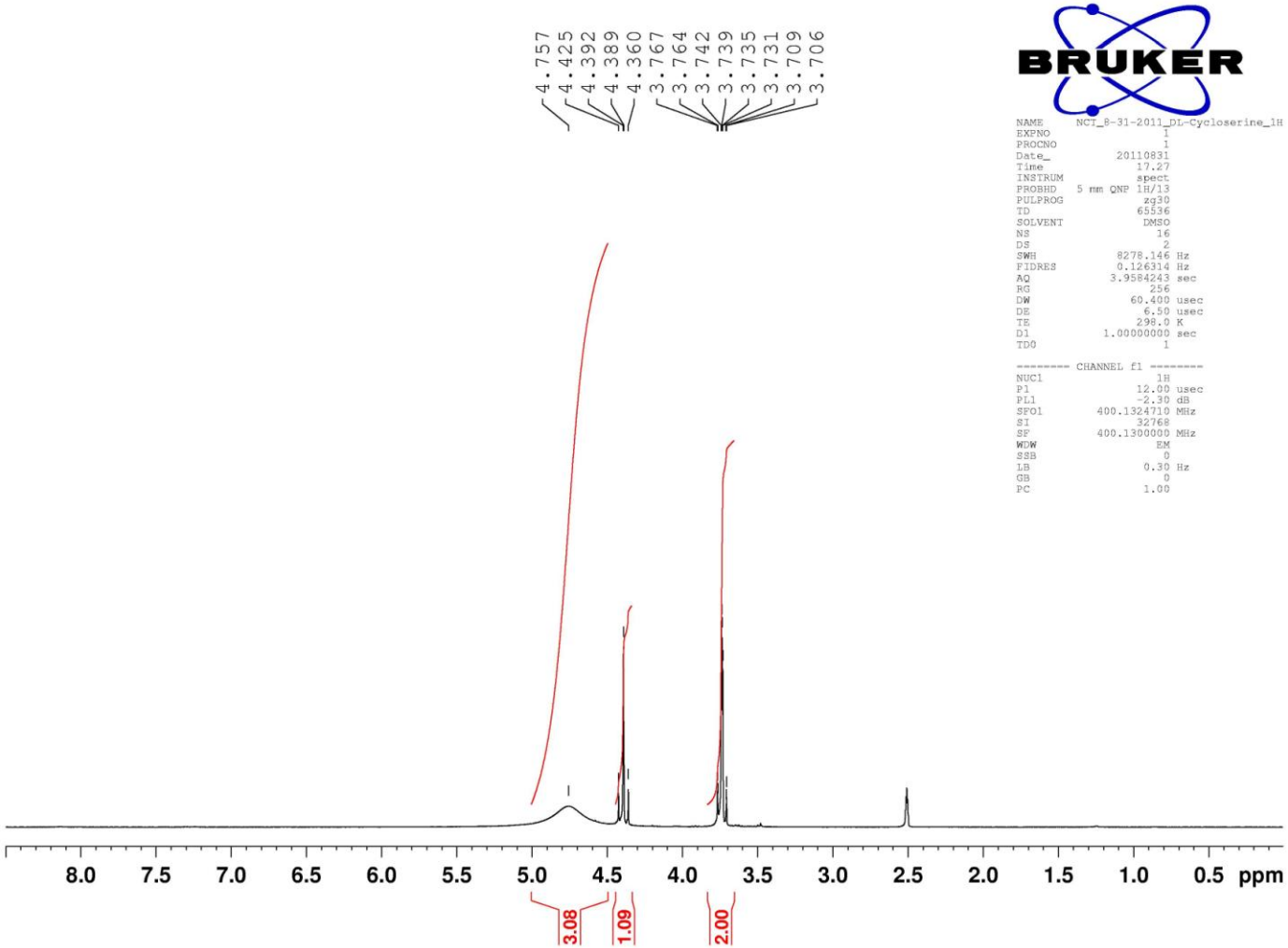


IR of DL-β-aminoxyalanine methyl ester dihydrochloride (5)

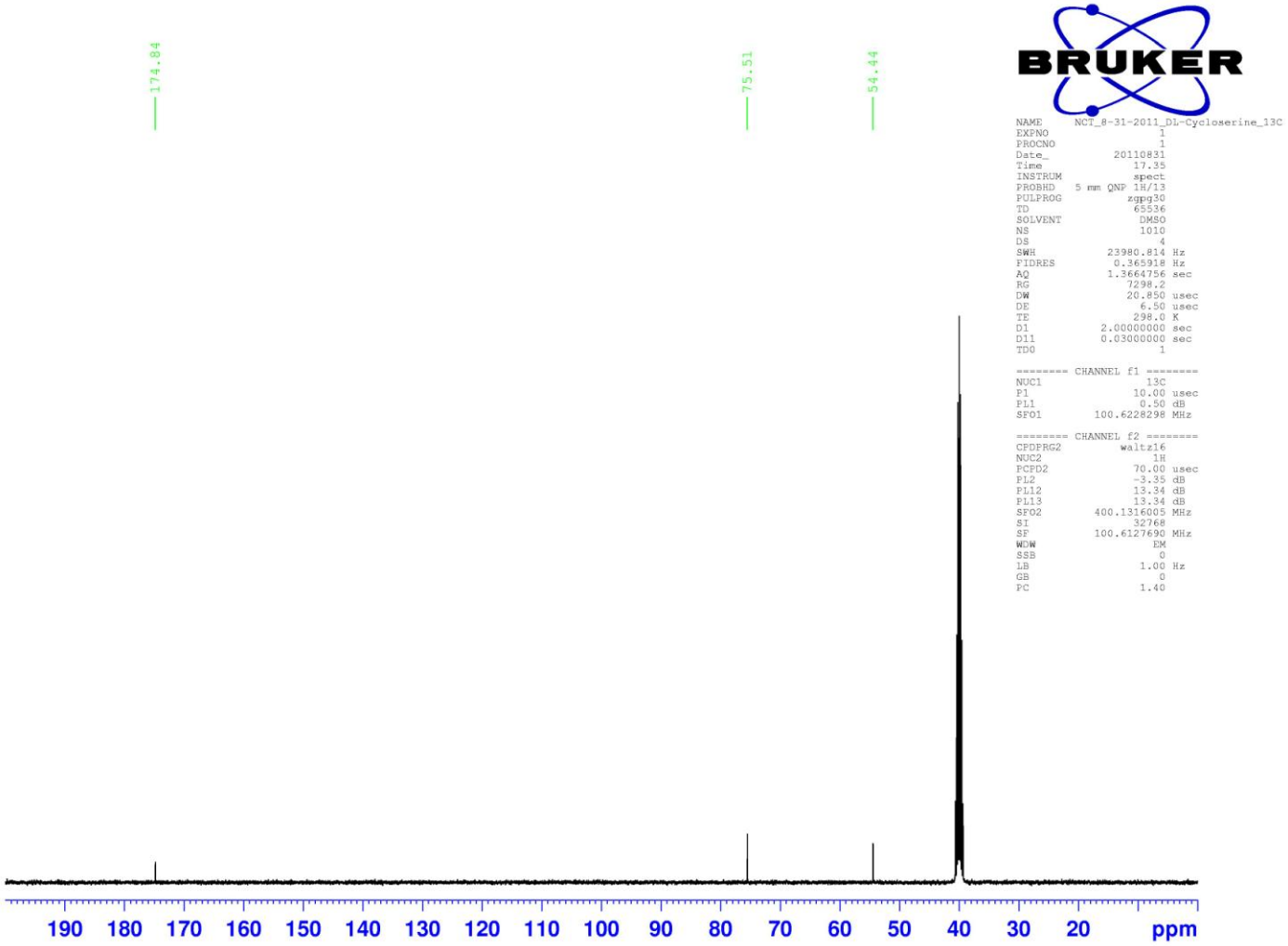


Number of sample scans: 16
Number of background scans: 16
Resolution: 4.000
Sample gain: 8.0
Optical velocity: 0.6329
Aperture: 100.00

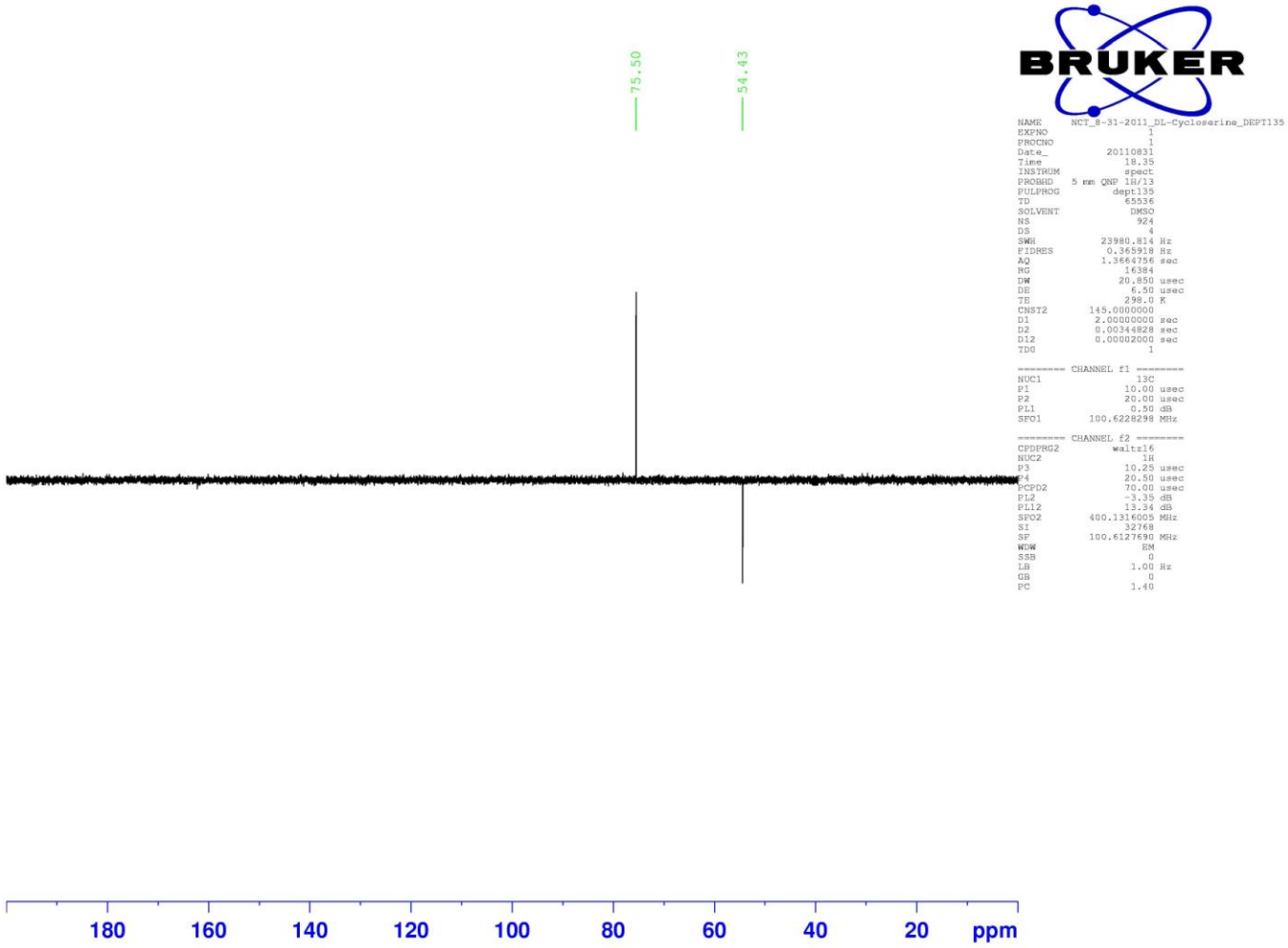
^{1}H of DL-Cycloserine (6)



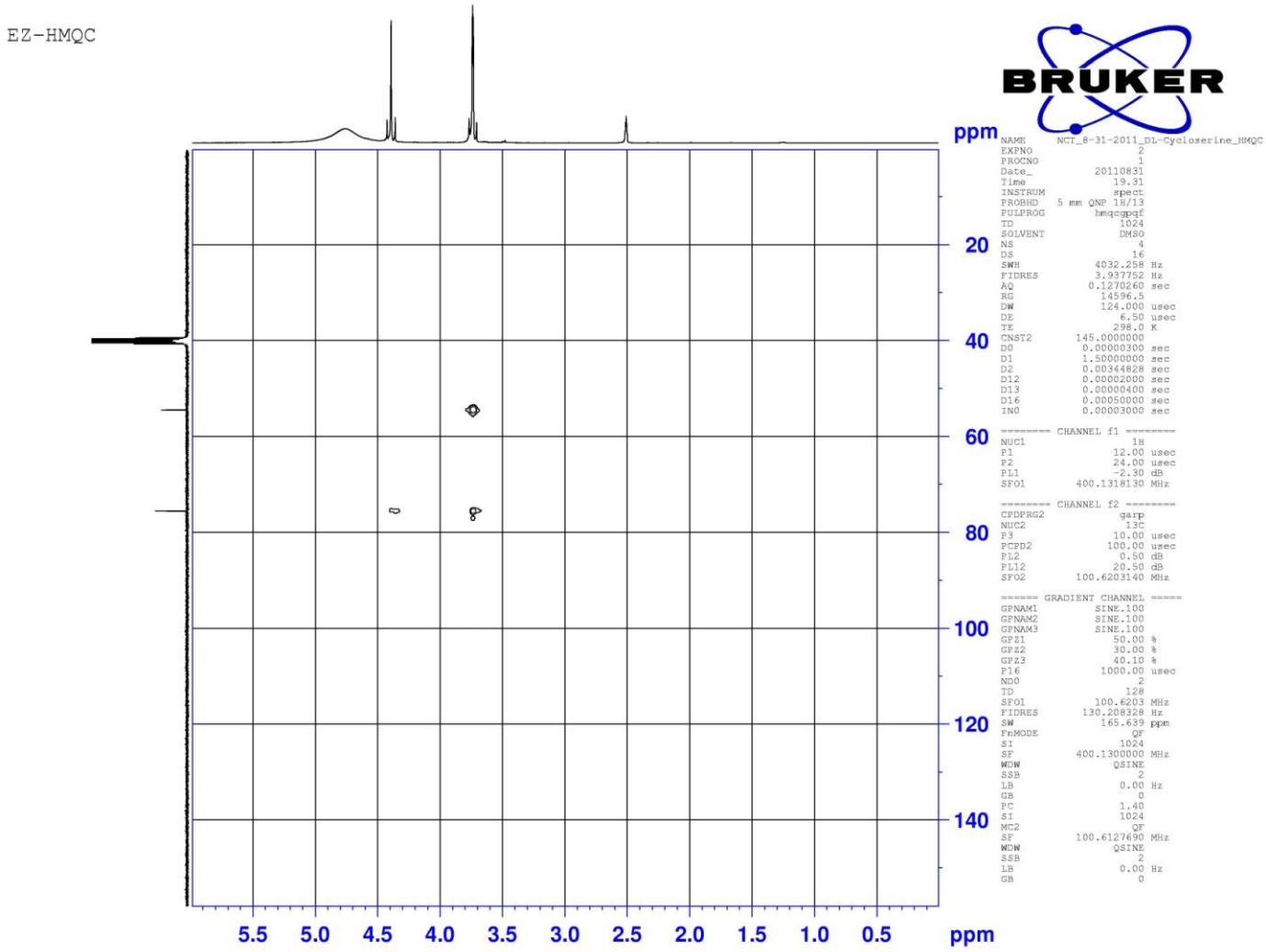
^{13}C of DL-Cycloserine (6)



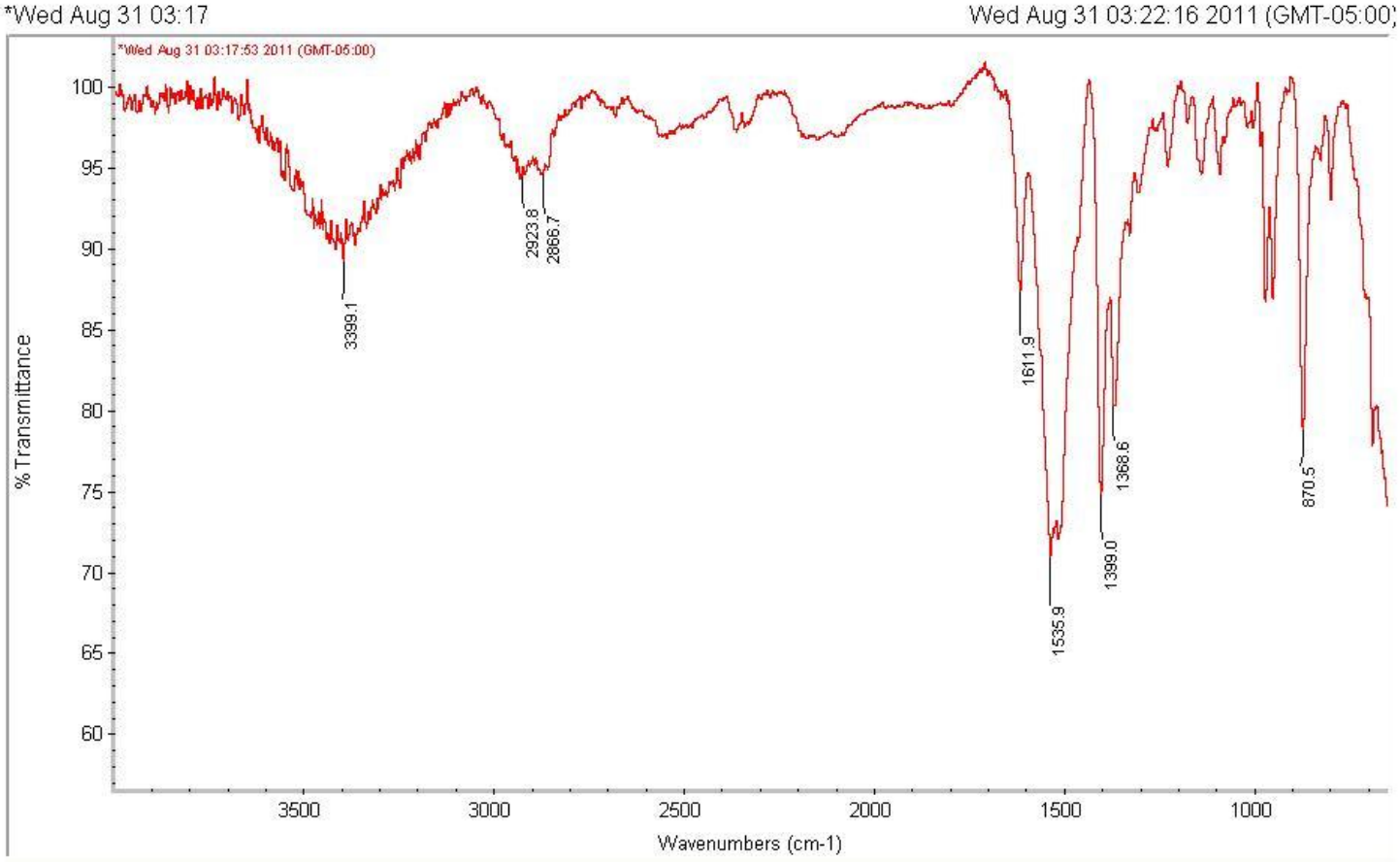
DEPT of DL-Cycloserine (6)



HMQC of DL-Cycloserine (6)

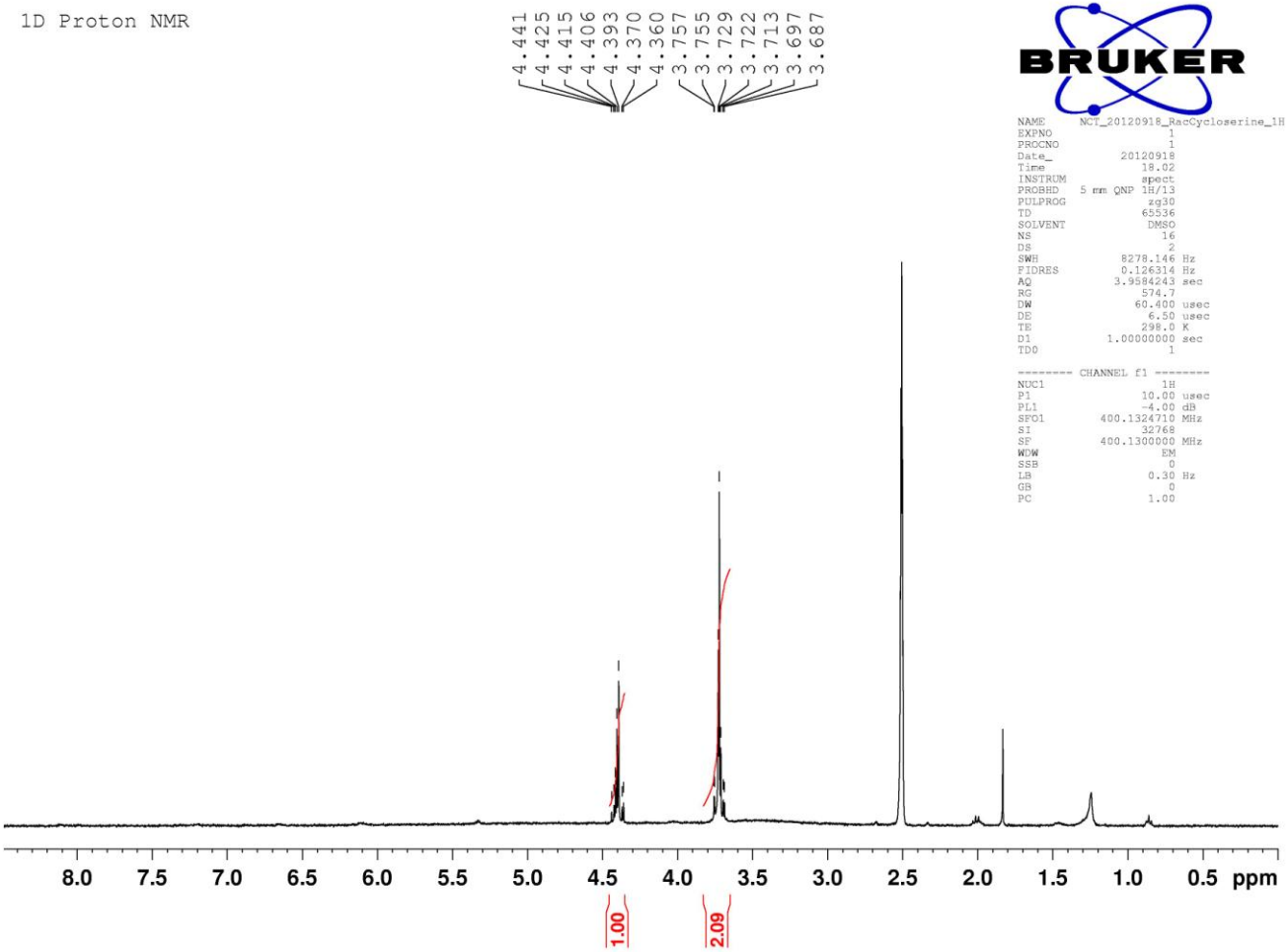


IR of DL-Cycloserine (6)

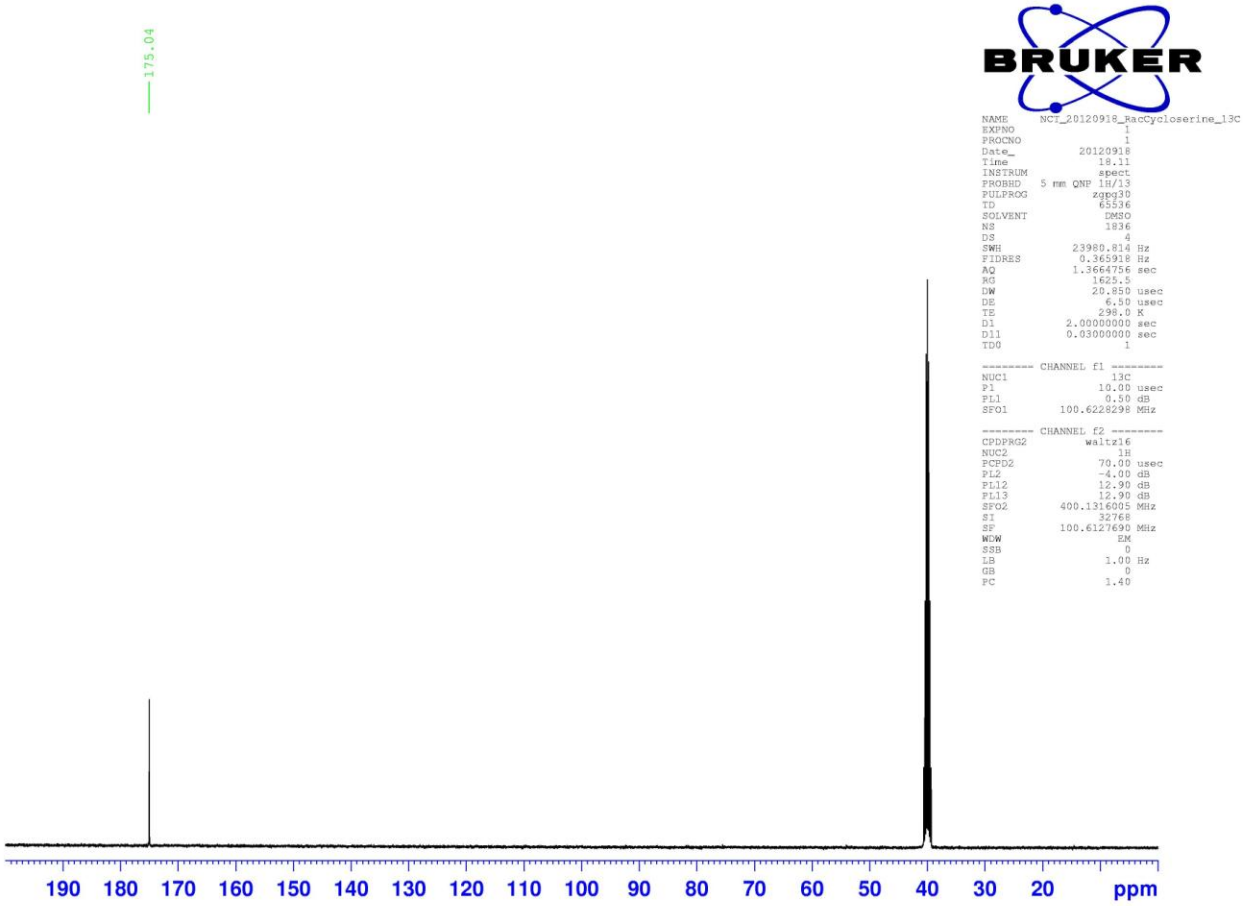


Number of sample scans: 16
Number of background scans: 16
Resolution: 4.000
Sample gain: 8.0
Optical velocity: 0.6329
Aperture: 100.00

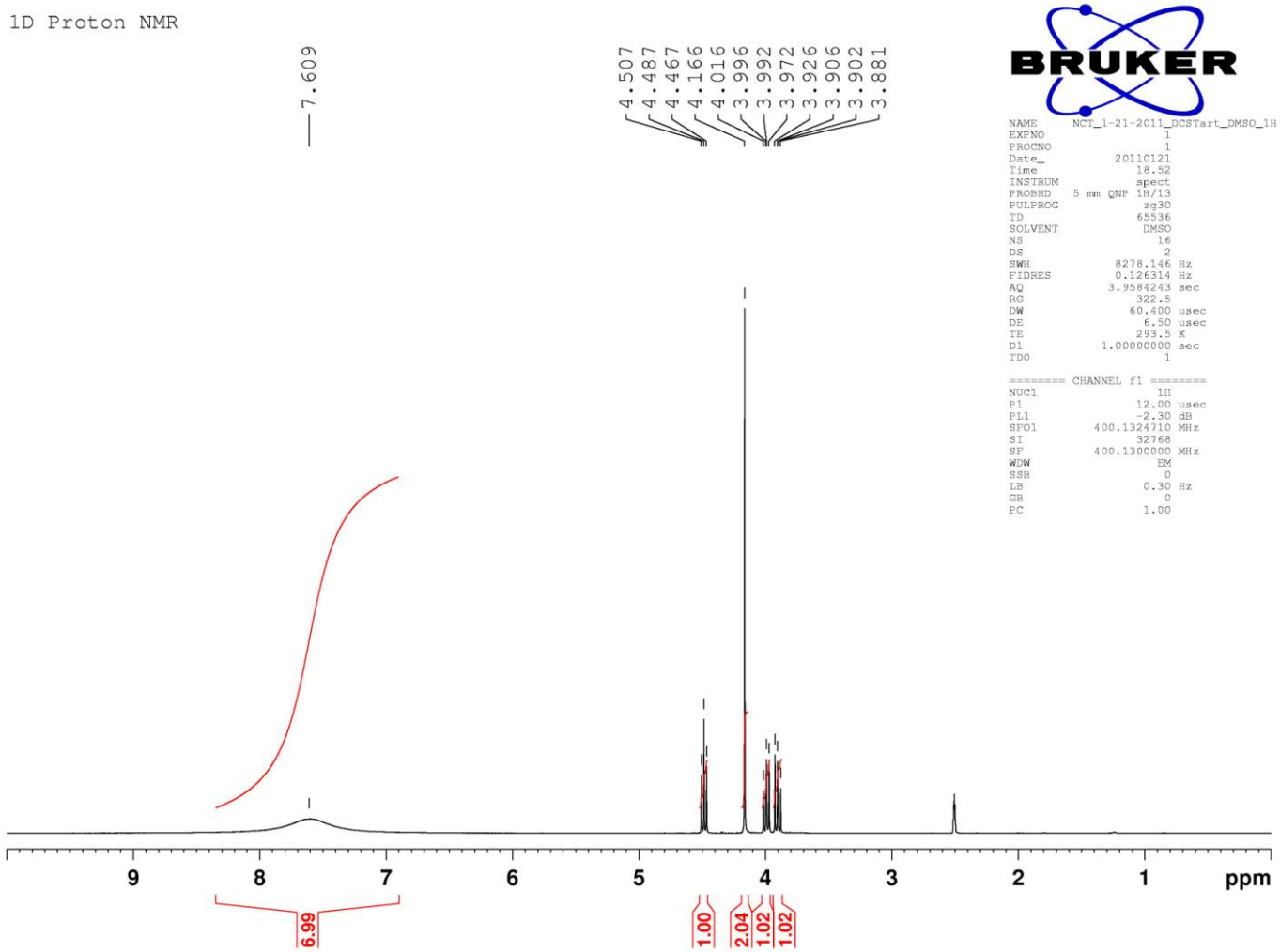
^{1}H NMR of DL-Cycloserine-1-^{13}C (14)



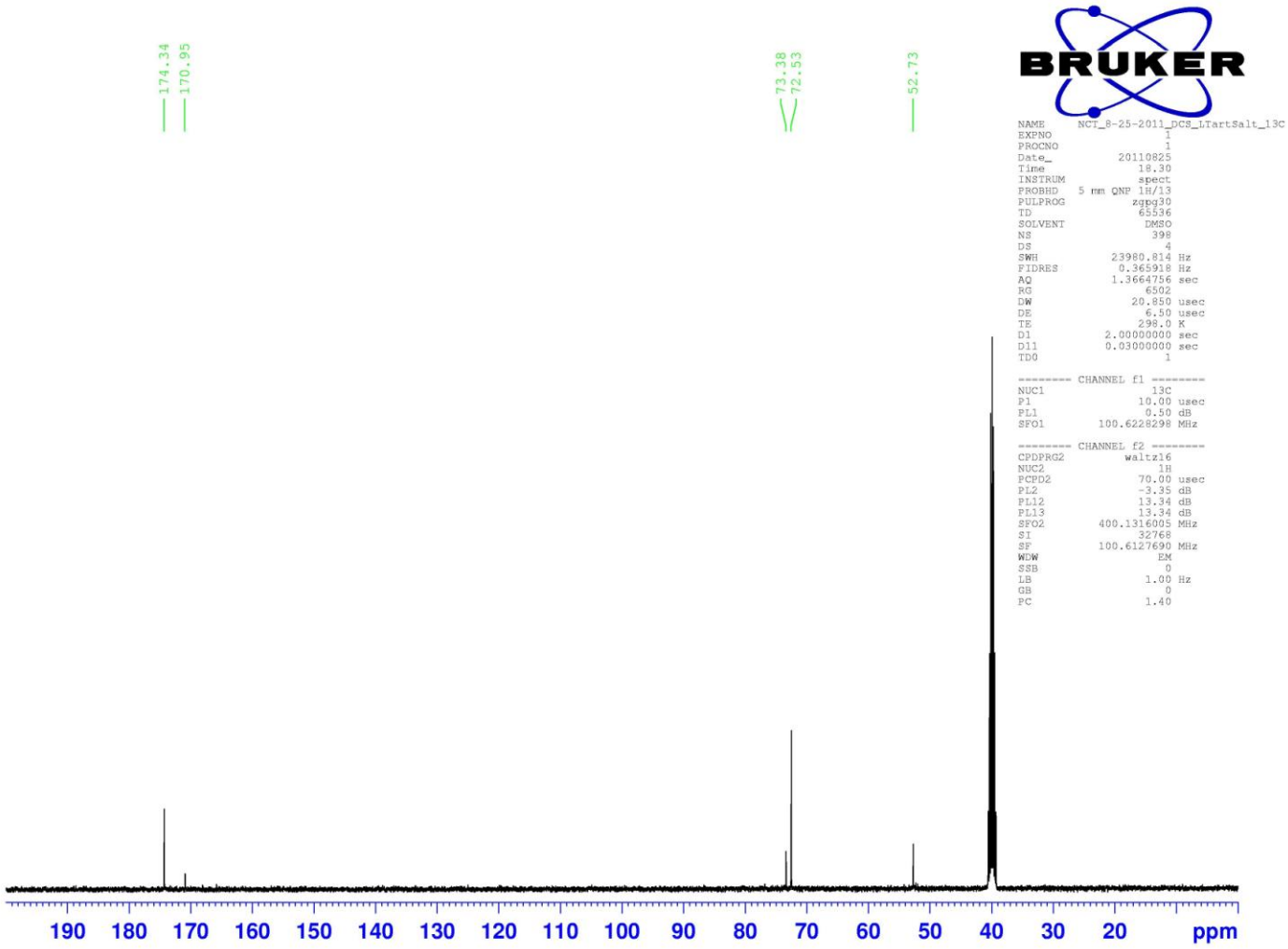
^{13}C NMR of DL-Cycloserine-1-^{13}C (14)



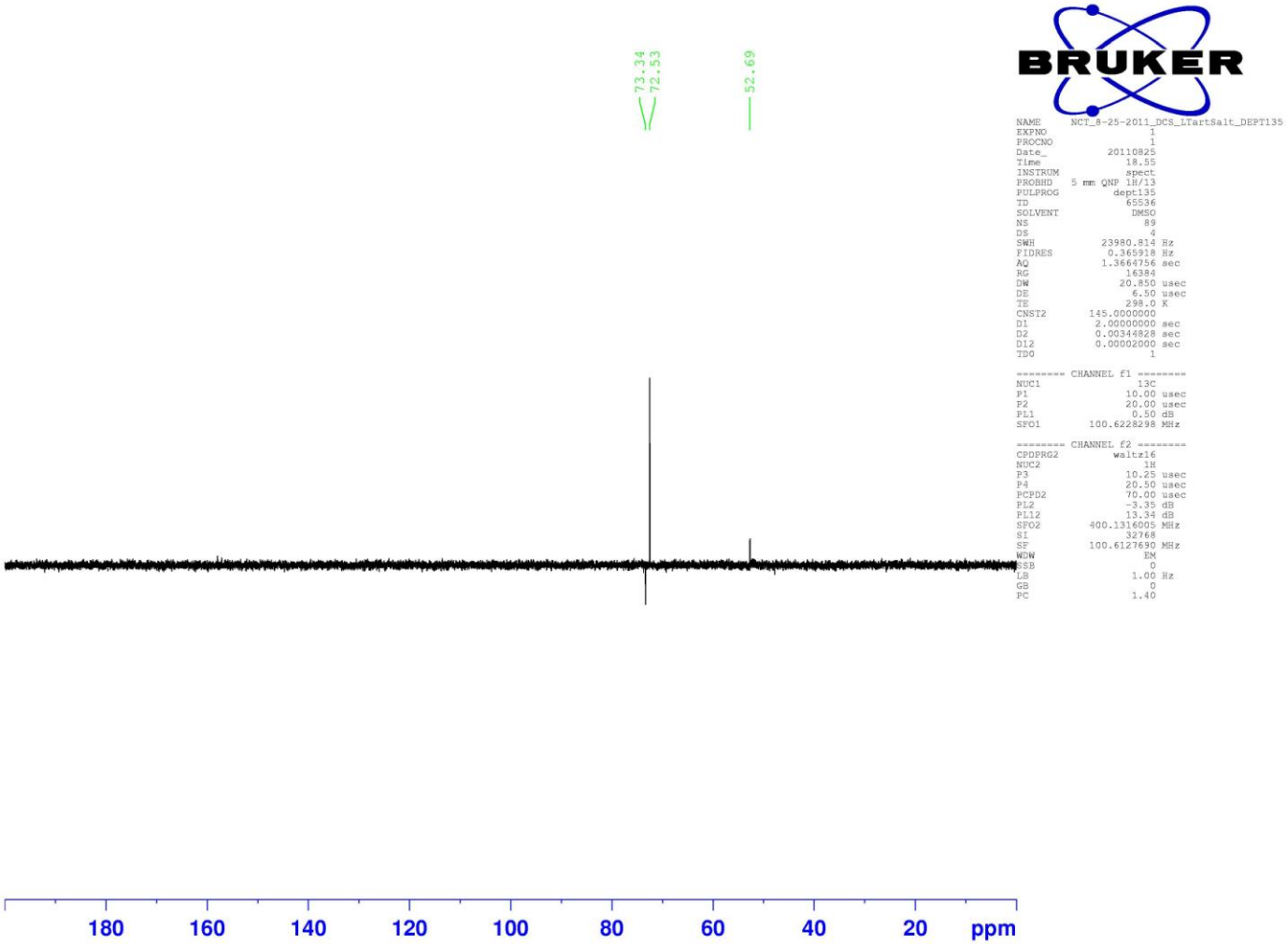
^{1}H of D-Cycloserine – (L)-Tartaric acid (7)



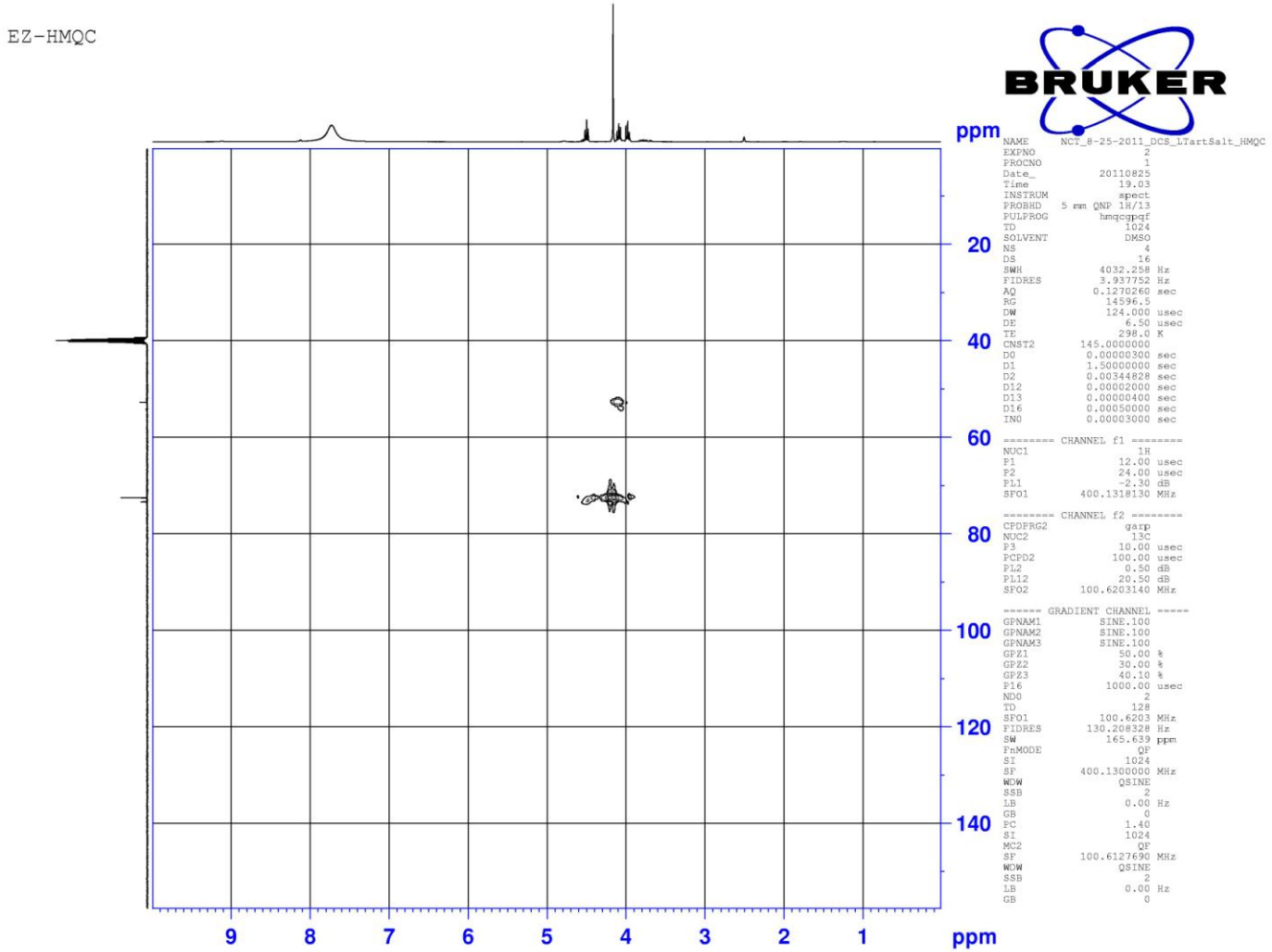
^{13}C of D-Cycloserine – (L)-Tartaric acid (7)



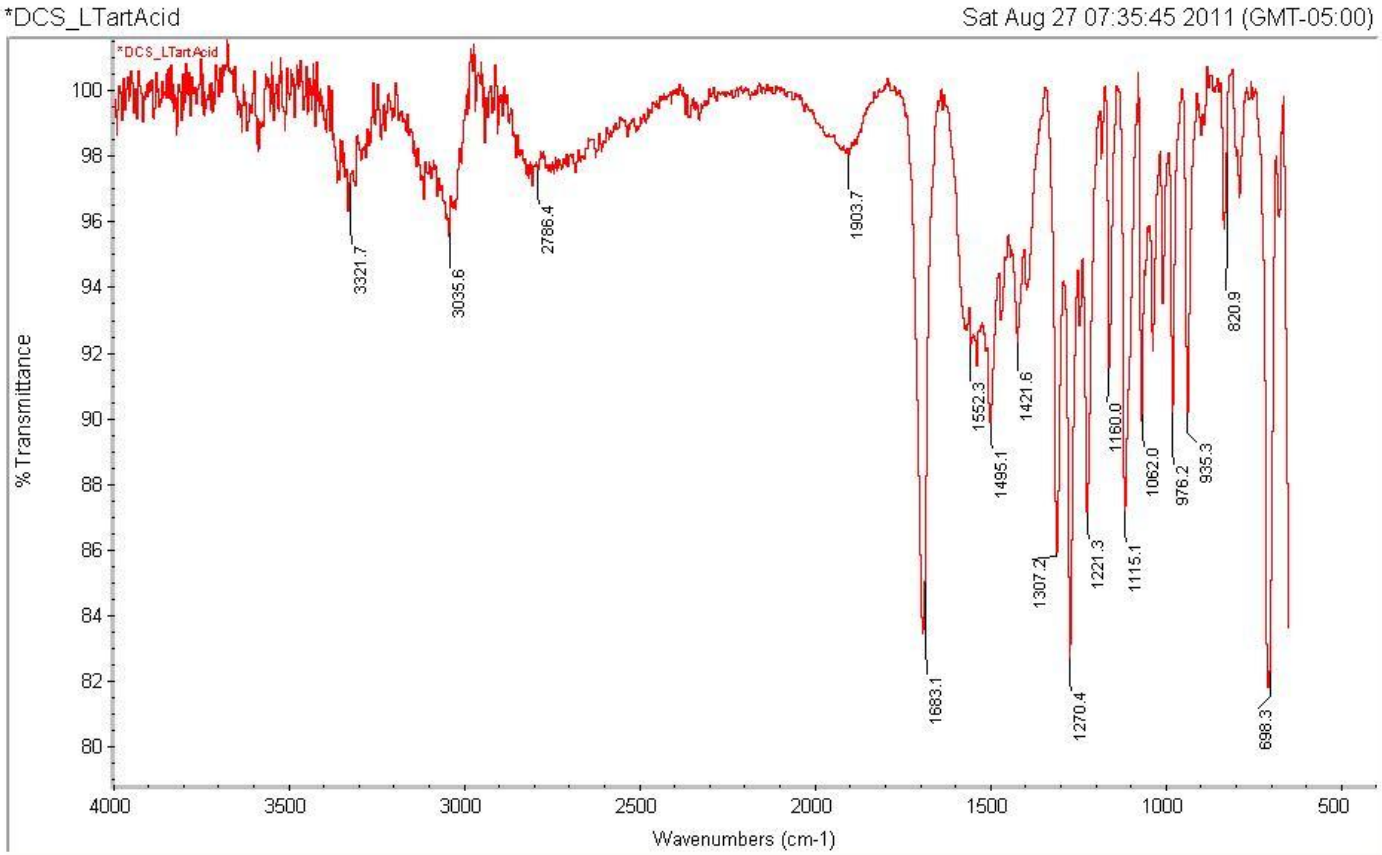
DEPT of D-Cycloserine – (L)-Tartaric acid (7)



HMQC of D-Cycloserine – (L)-Tartaric acid (7)

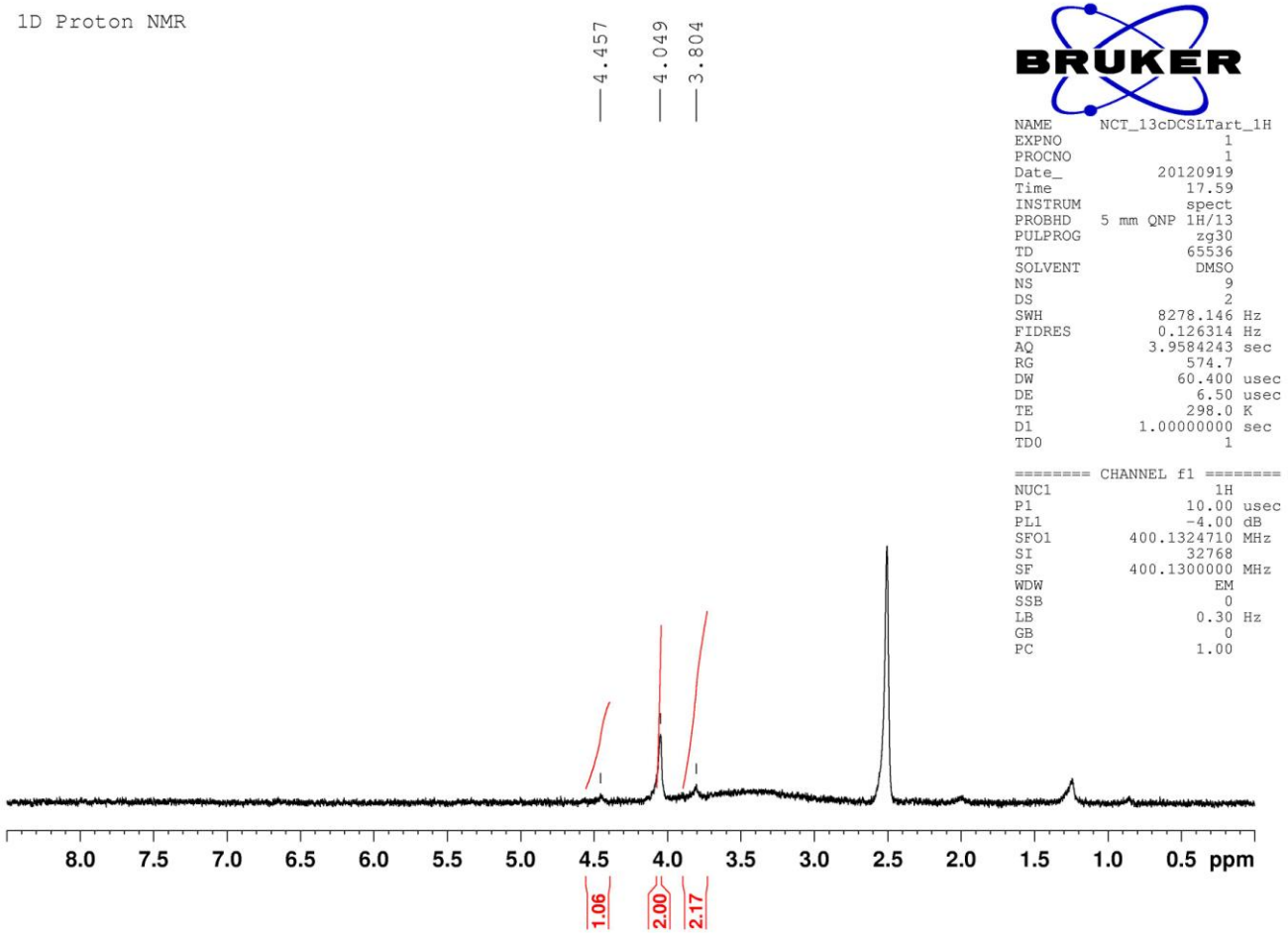


IR of D-Cycloserine – (L)-Tartaric acid (7)

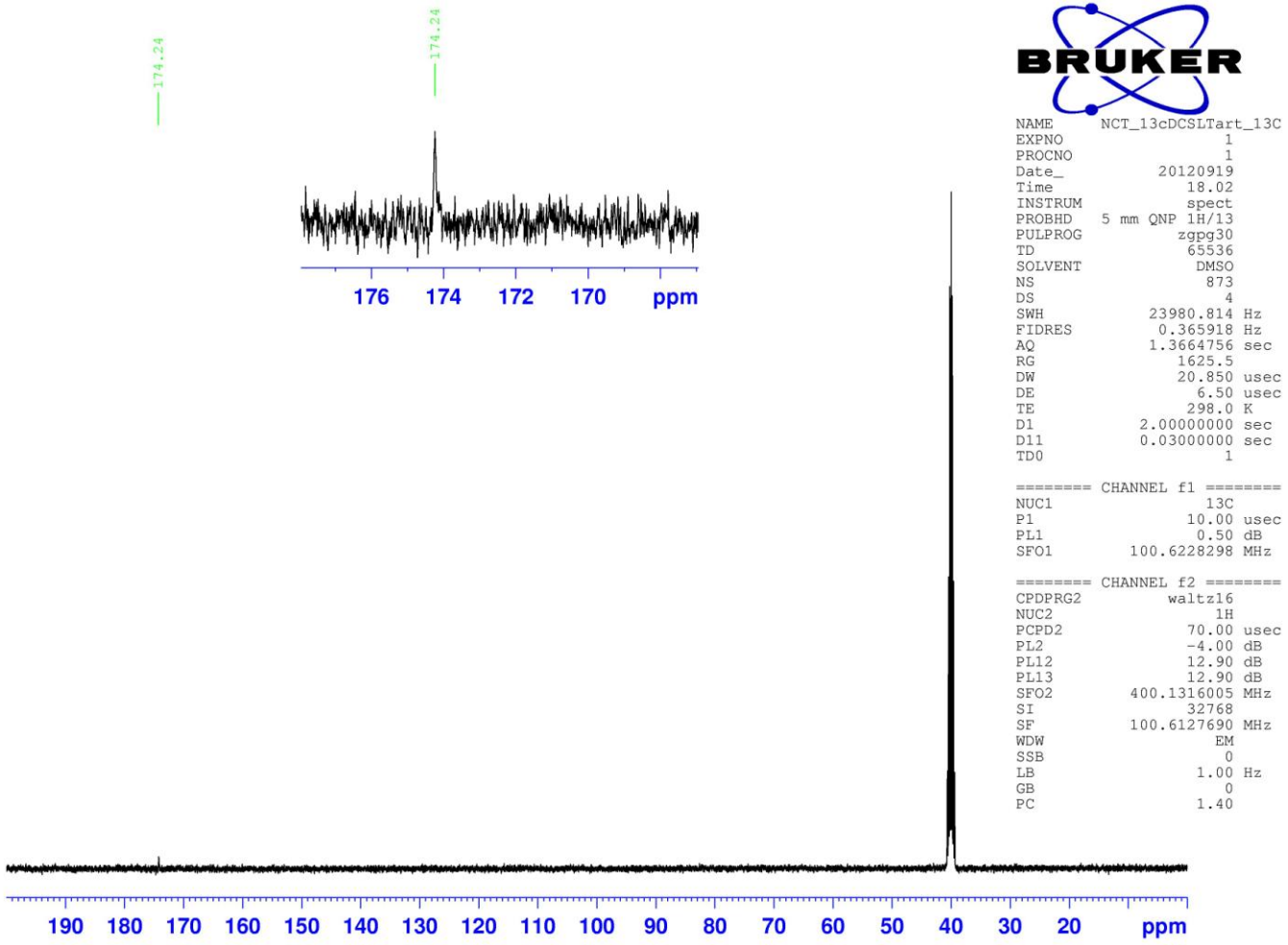


Number of sample scans: 16
Number of background scans: 16
Resolution: 4.000
Sample gain: 8.0
Optical velocity: 0.6329
Aperture: 100.00

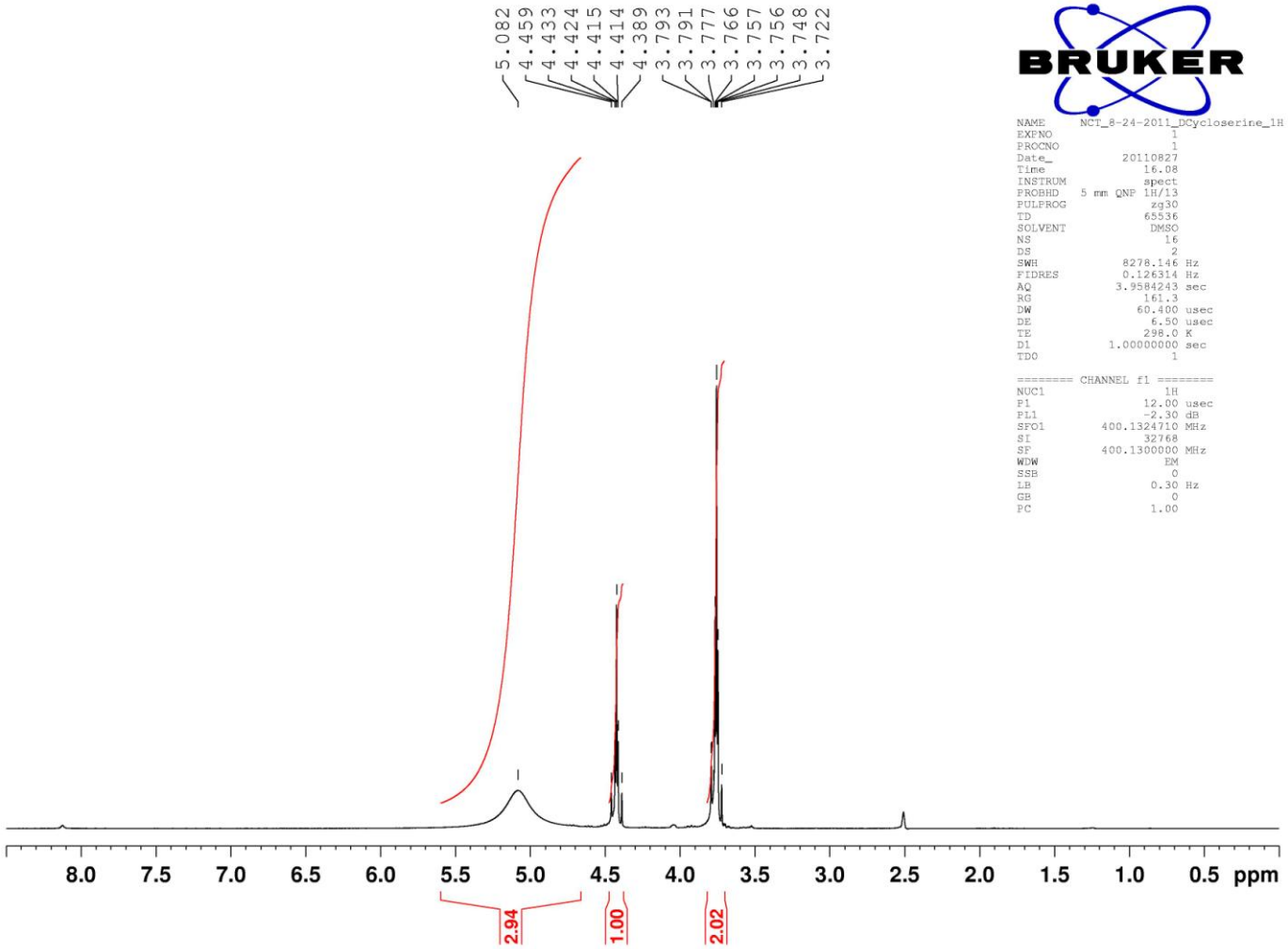
^{1}H of D-Cycloserine-1-^{13}C – (L)-Tartaric acid (15)



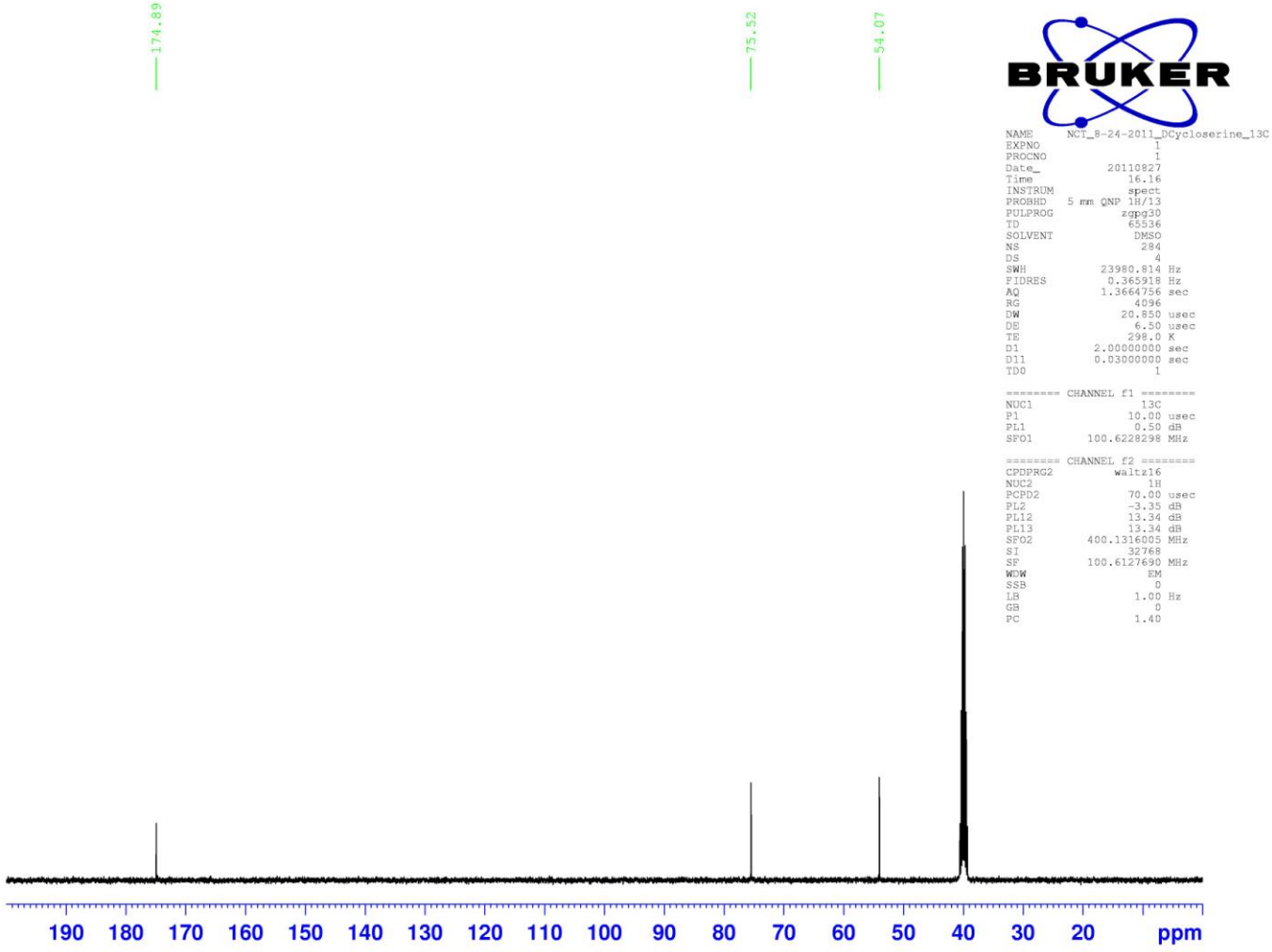
^{13}C of D-Cycloserine-1-^{13}C – (L)-Tartaric acid (15)



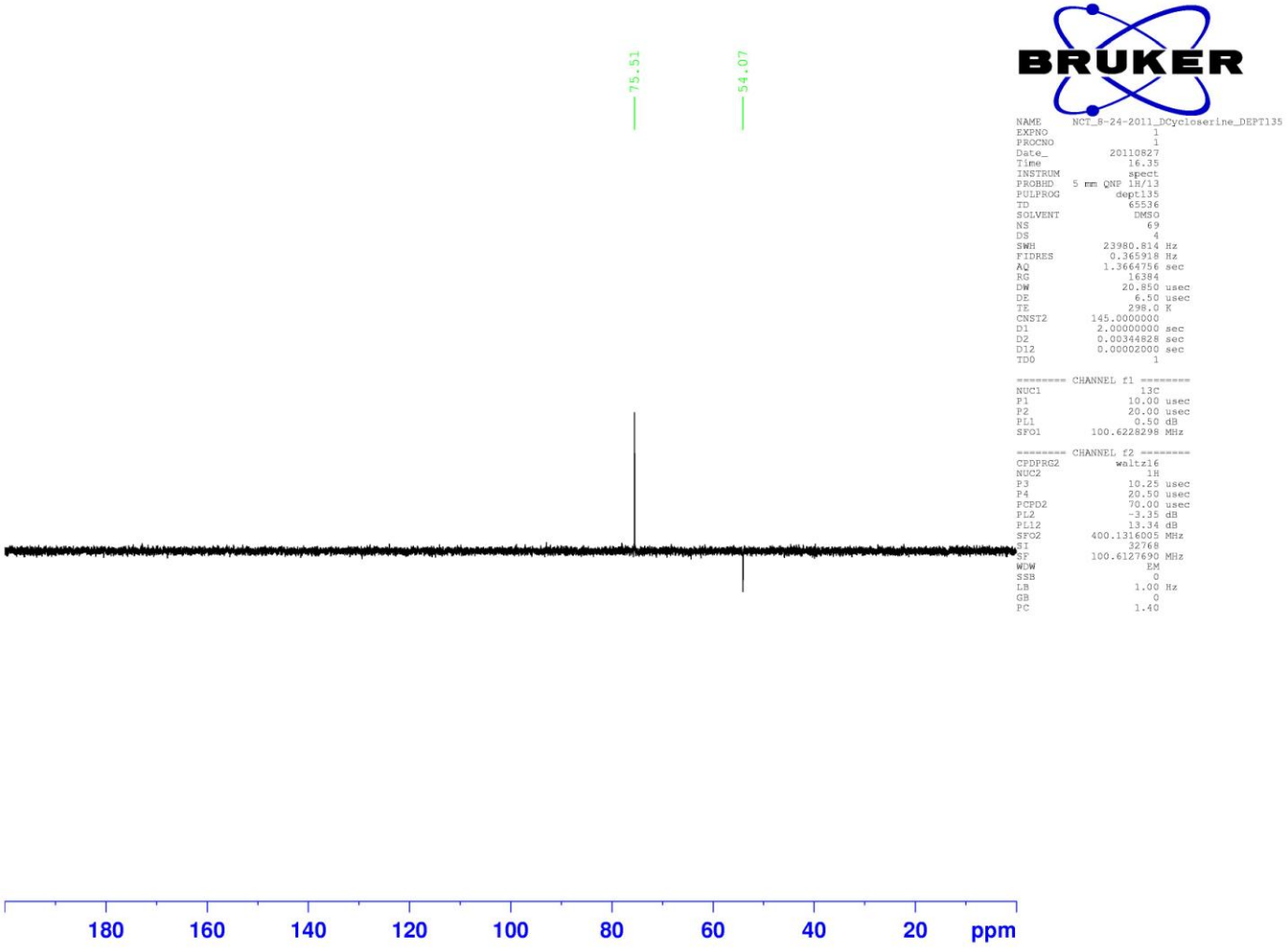
^{1}H of D-Cycloserine (9)



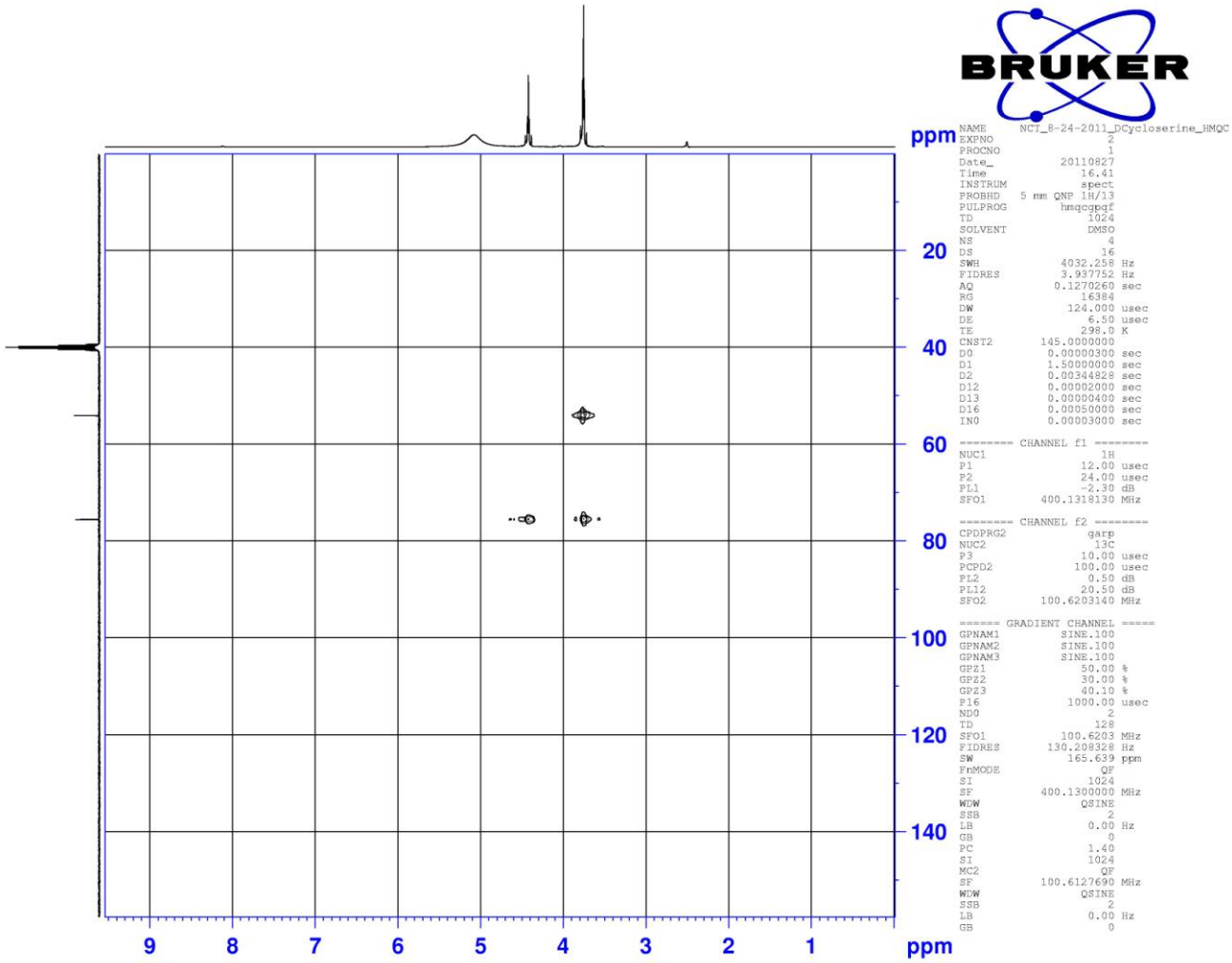
^{13}C of D-Cycloserine (9)



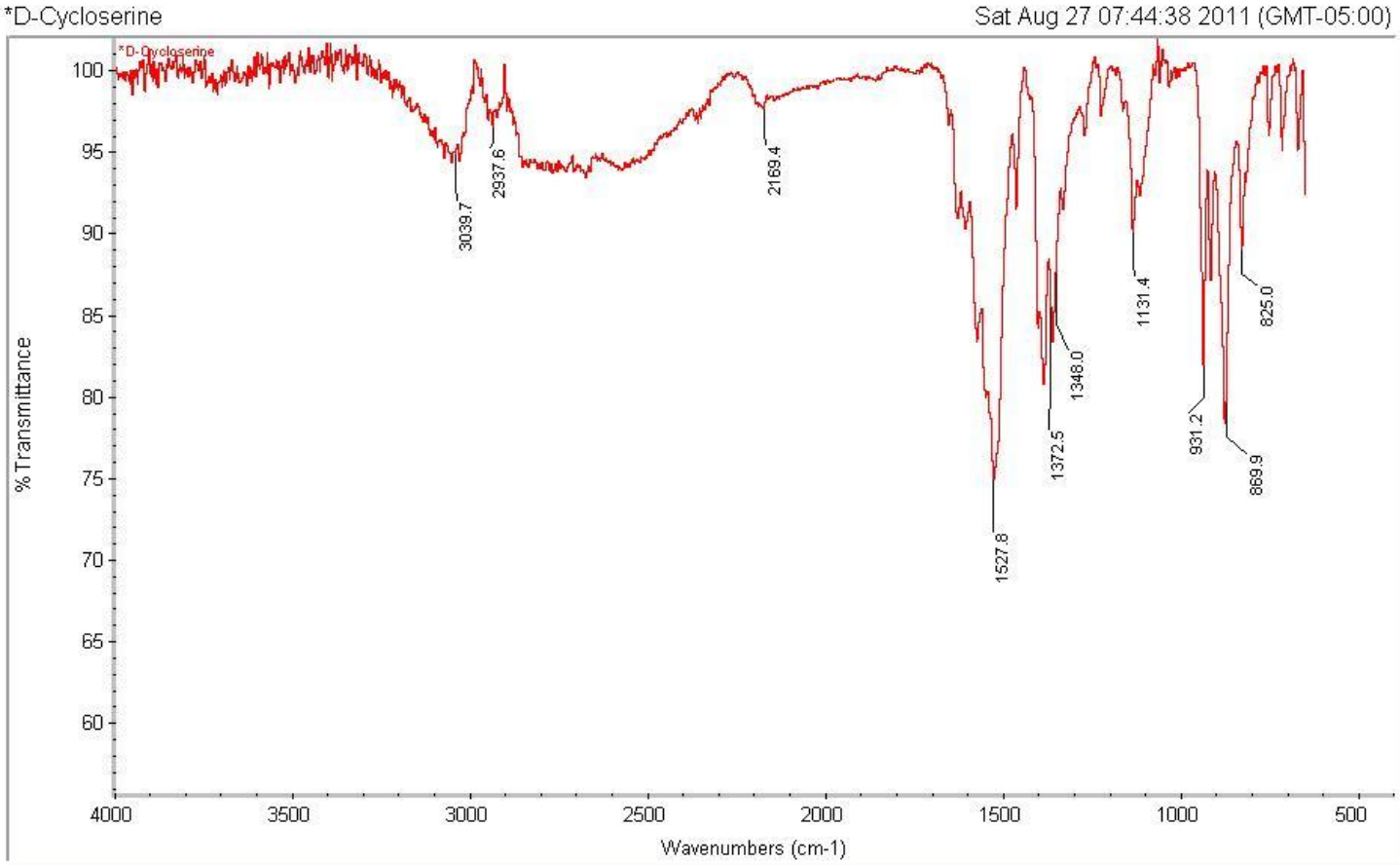
DEPT of D-Cycloserine (9)



HMQC of D-Cycloserine (9)

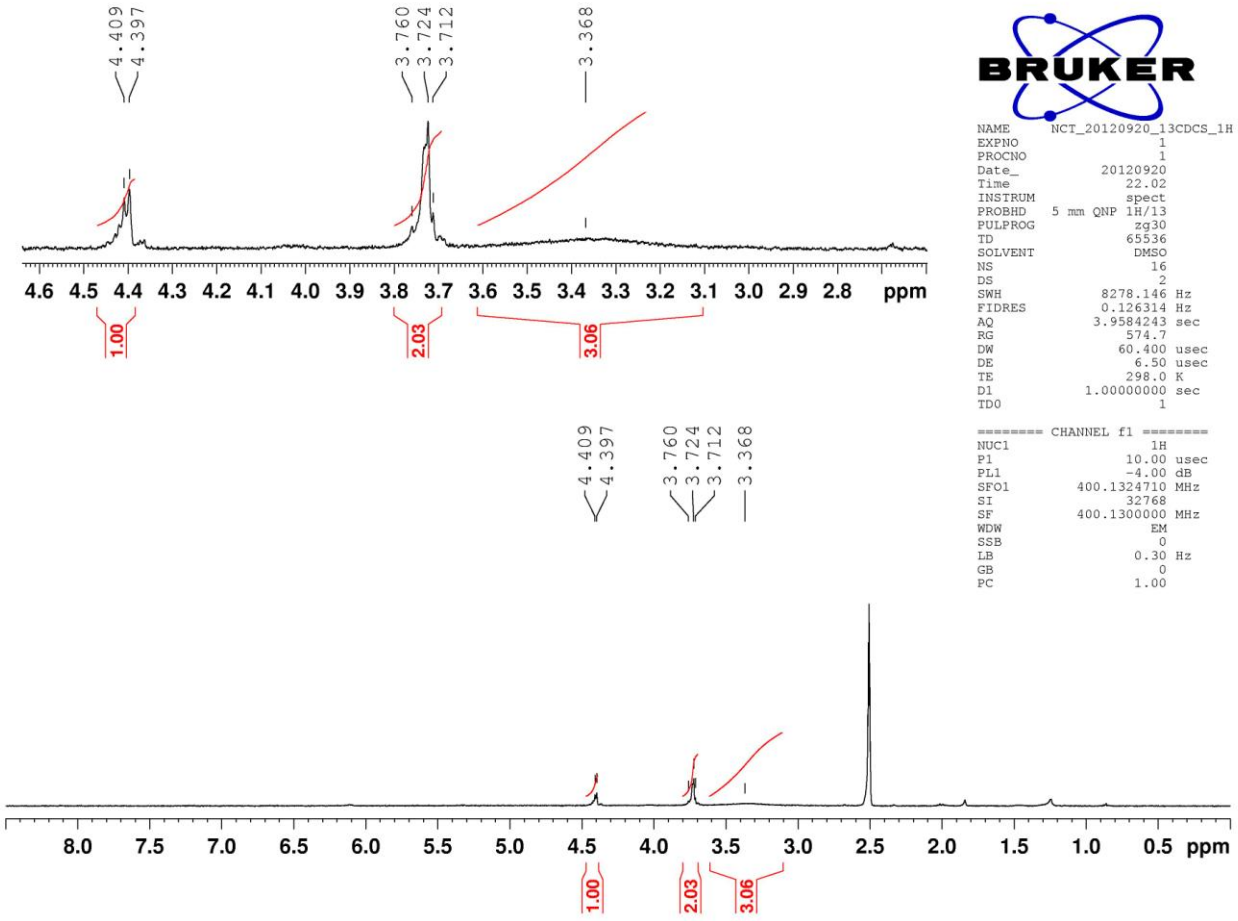


IR of D-Cycloserine (9)

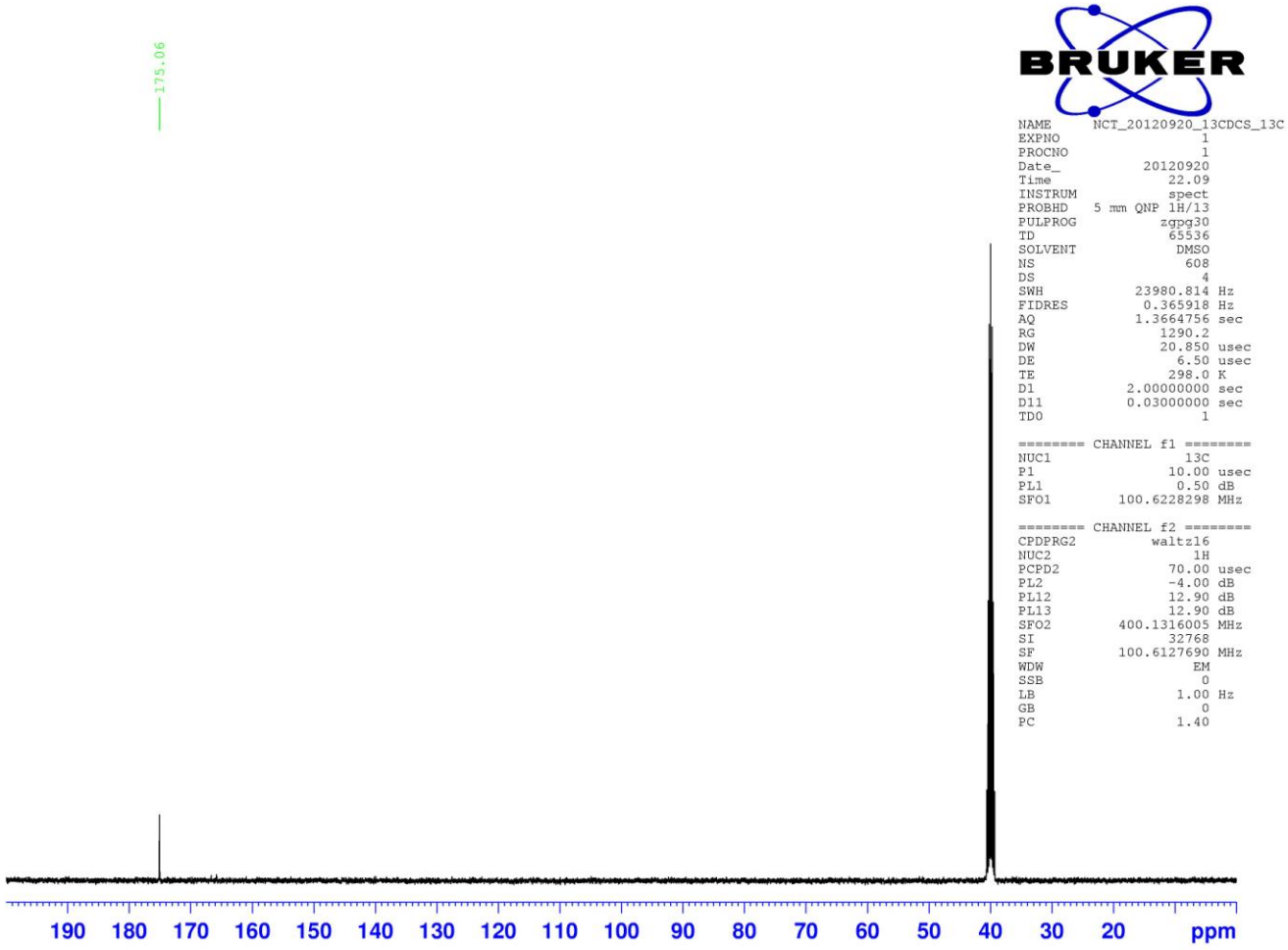


Number of sample scans: 16
Number of background scans: 16
Resolution: 4.000
Sample gain: 8.0
Optical velocity: 0.6329
Aperture: 100.00

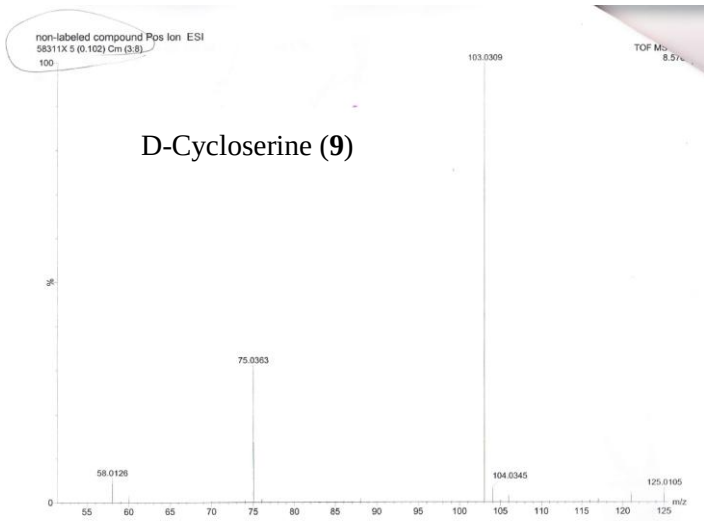
^{1}H of D-Cycloserine-1-^{13}C (16)



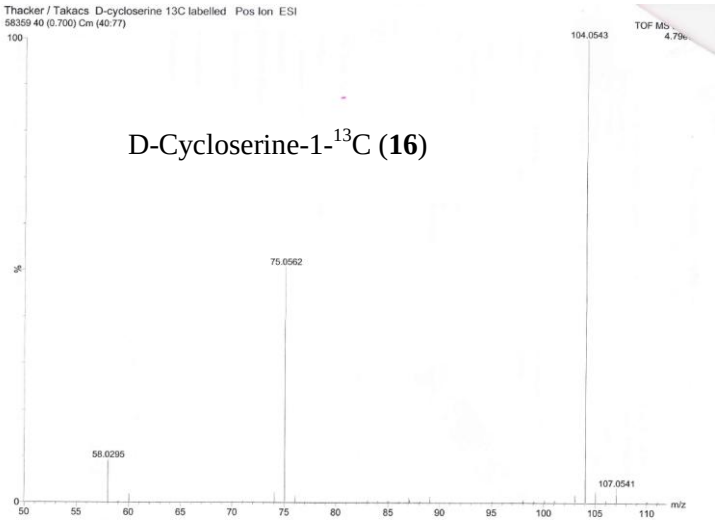
^{13}C NMR of D-Cycloserine-1-^{13}C (16)



HRMS of D-Cycloserine (9) vs D-Cycloserine-1-^{13}C (16)



D-Cycloserine (**9**)



D-Cycloserine-1-^{13}C (**16**)