

Supplementary Information

A molecular hybridization approach to design and study the *in vitro* and
in silico properties of N-phenyl-4-oxo-butanamide derivatives

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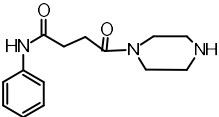
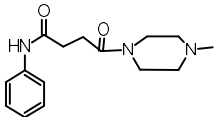
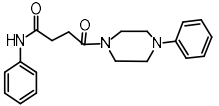
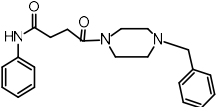
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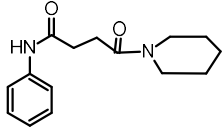
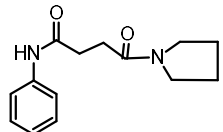
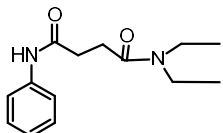
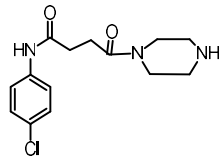
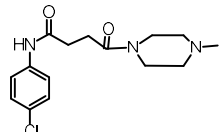
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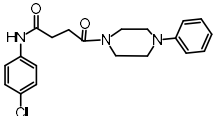
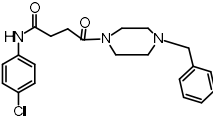
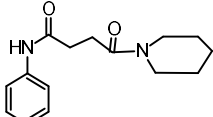
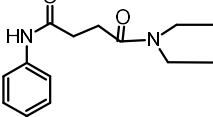
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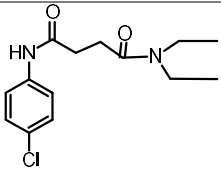
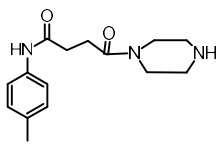
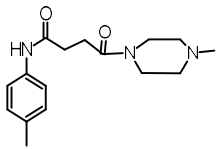
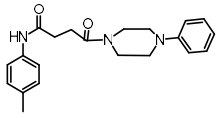
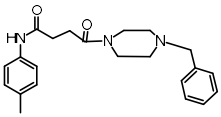
1) Table 1: Physico-Chemical Characteristics of Synthesized compounds

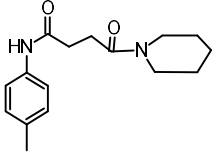
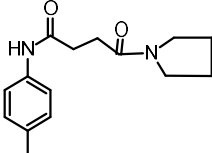
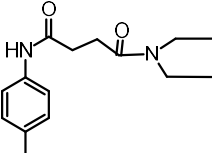
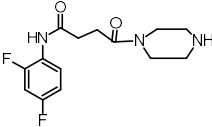
Compound codes	Structure& IUPAC Name	Yield %	M.P ⁰ C	Molecular mass	Empirical formula
1a	 4-oxo- <i>N</i> -phenyl-4-(piperazin-1-yl)butanamide	67.33%	128-131	261.319	C ₁₄ H ₁₉ N ₃ O ₂
1b	 4-(4-methylpiperazin-1-yl)-4-oxo- <i>N</i> -phenylbutanamide	63.66%	129-132	275.346	C ₁₅ H ₂₁ N ₃ O ₂
1c	 4-oxo- <i>N</i> -phenyl-4-(4-phenylpiperazin-1-yl)butanamide	73%	156-158	337.415	C ₂₀ H ₂₃ N ₃ O ₂
1d	 4-oxo- <i>N</i> -phenyl-4-(4-benzylpiperazin-1-yl)butanamide	74.33%	124-129	351.442	C ₂₁ H ₂₅ N ₃ O ₂

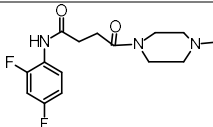
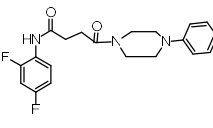
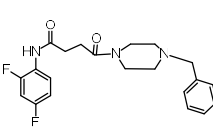
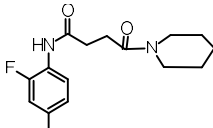
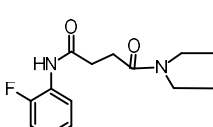
1e		71.73%	127-129	260.331	C ₁₅ H ₂₀ N ₂ O ₂
	4-oxo- <i>N</i> -phenyl-4-(piperidin-1-yl)butanamide				
1f		73.20%	125-127	246.304	C ₁₄ H ₁₈ N ₂ O ₂
	4-oxo- <i>N</i> -phenyl-4-(pyrrolidin-1-yl)butanamide				
1g		70.75%	89-91	248.320	C ₁₄ H ₂₀ N ₂ O ₂
	<i>N</i> ¹ , <i>N</i> ¹ -diethyl- <i>N</i> ⁴ -phenylbutanediamide				
2a		60.93%	133-135	295.764	C ₁₄ H ₁₈ ClN ₃ O ₂
	<i>N</i> -(4-chlorophenyl)-4-oxo-4-(piperazin-1-yl)butanamide				
2b		52.64%	139-141	309.791	C ₁₅ H ₂₀ ClN ₃ O ₂
	<i>N</i> -(4-chlorophenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide				

oxobutanamide

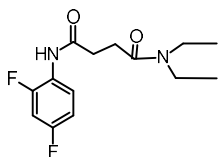
2c		74.14%	156-158	371.86	C ₂₀ H ₂₂ ClN ₃ O ₂
	<i>N</i> -(4-chlorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide				
2d		72.61%	137-139	385.88	C ₂₁ H ₂₄ ClN ₃ O ₂
	<i>N</i> -(4-chlorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide				
2e		70%	134-136	294.776	C ₁₅ H ₁₉ ClN ₂ O ₂
	<i>N</i> -(4-chlorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide				
2f		71.09%	136-141	280.749	C ₁₄ H ₁₇ ClN ₂ O ₂
	<i>N</i> -(4-chlorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide				

2g		70.73%	106-108	282.765	C ₁₄ H ₁₉ ClN ₂ O ₂
	<i>N</i> ⁴ -(4-chlorophenyl)- <i>N</i> ¹ , <i>N</i> ¹ -diethylbutanediamide				
3a		61.51%	134-137	275.346	C ₁₅ H ₂₁ N ₃ O ₂
	<i>N</i> -(4-methylphenyl)-4-oxo-4-(piperazin-1-yl)butanamide				
3b		56.37%	136-139	289.372	C ₁₆ H ₂₃ N ₃ O ₂
	<i>N</i> -(4-methylphenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide				
3c		74.80%	159-161	351.442	C ₂₁ H ₂₅ N ₃ O ₂
	<i>N</i> -(4-methylphenyl)-4-(4-phenylpiperazin-1-yl)-4-oxobutanamide				
3d		75.27%	133-135	365.468	C ₂₂ H ₂₇ N ₃ O ₂
	<i>N</i> -(4-methylphenyl)-4-(4-				

	benzylpiperazin-1-yl)-4-oxobutanamide				
3e	 <i>N</i> -(4-methylphenyl)-4-oxo-4-(piperidin-1-yl)butanamide	75.38%	124-127	274..358	C ₁₆ H ₂₂ N ₂ O ₂
3f	 <i>N</i> -(4-methylphenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide	73.22%	135-138	260.331	C ₁₅ H ₂₀ N ₂ O ₂
3g	 <i>N</i> ¹ , <i>N</i> ¹ -diethyl- <i>N</i> ⁴ -(4-methylphenyl)butanediamide	70.14%	94-97	262.347	C ₁₅ H ₂₂ N ₂ O ₂
4a	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(piperazin-1-yl)butanamide	63.12%	136-141	297.300	C ₁₄ H ₁₇ F ₂ N ₃ O ₂

4b	 <p><i>N</i>-(2,4-difluorophenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide</p>	57.76%	134-138	311.327	C ₁₅ H ₁₉ F ₂ N ₃ O ₂
4c	 <p><i>N</i>-(2,4-difluorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide</p>	75.49%	125-128	373.396	C ₂₀ H ₂₁ F ₂ N ₃ O ₂
4d	 <p><i>N</i>-(2,4-difluorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide</p>	71.80%	149-151	387.423	C ₂₁ H ₂₃ F ₂ N ₃ O ₂
4e	 <p><i>N</i>-(2,4-difluorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide</p>	73.53%	129-131	296.312	C ₁₅ H ₁₈ F ₂ N ₂ O ₂
4f	 <p><i>N</i>-(2,4-difluorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide</p>	70.53%	128-130	282.285	C ₁₄ H ₁₆ F ₂ N ₂ O ₂

4g



71.12%

97-101

284.30

C₁₄H₁₈F₂N₂O₂

*N*⁴-(2,4-difluorophenyl)-
*N*¹,*N*¹-diethylbutanediamide

2) Structural Elucidation of a Synthesized Compounds by Spectroscopic Techniques

Compound (1a): 4-oxo-*N*-phenyl-4-(piperazin-1-yl)butanamide

Yield: 67%; mp: 128-131⁰C; IR (KBr): 1634, 1679, 3297, 3418 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.34 (1H, s, Aryl NHCO), 7.53 (2H,m, Ar-H), 7.30 (2H, m, Ar-H),7.07 (2H, m, Ar-H), 3.51 (4H, m,CH₂), 2.76 (2H, t,CH₂), 2.63 (2H, t,CH₂), 2.07 (4H, m, CH₂); ¹³CNMR (100 MHz, CDCl₃): δ 170.90 (Aryl C(=O)NH), 170.58 (Aryl C(=O)NH), 138.14 (CH), 128.92 (CH),124.05 (CH), 119.69 (CH), 45.14 (CH₂),41.57 (CH₃), 32.44 (CH₂), 28.72 (CH₂); HRMS (ESI): m/z calcd. for C₁₄H₁₉N₃O₂: [M+H]⁺: 262.15, found 262.15; Anal calcd. for C₁₄H₁₉N₃O₂: C: 64.35; H: 7.33; N: 16.08; O: 12.25%; found C: 64.33; H: 7.31; N: 16.04; O: 12.24%.

Compound (1b): 4-(4-methylpiperazin-1-yl)-4-oxo-*N*-phenylbutanamide

Yield: 63.6%; mp: 129-132 ⁰C; IR (KBr): 1639, 1697, 3294, 3636 cm⁻¹; ¹HNMR (400 MHz, DMSO-D₆): δ 9.92 (1H, s, Aryl NHCO), 7.59 (1H, m, Ar-H), 7.25 (2H, m, Ar-H),7.01 (2H, m, Ar-H), 2.60 (2H, t,CH₂), 2.51 (2H, t,CH₂), 2.32 (4H, m, CH₂), 2.20 (4H, m, CH₂), 2.17 (3H, s, CH₃); ¹³CNMR (100 MHz, DMSO-D₆): δ 171.04 (Aryl C(=O)NH), 170.19 (Aryl C(=O)NH), 139.89 (CH), 129.09 (CH),123.26 (CH), 119.30 (CH), 54.79 (CH₂), 46.13 (CH₂),45.04 (CH₃), 31.84 (CH₂), 27.96 (CH₂); HRMS (ESI): m/z calcd. for C₁₅H₂₁N₃O₂: [M+H]⁺: 276.17, found 276.17; Anal calcd. for C₁₅H₂₁N₃O₂ : C: 65.43; H: 7.69; N: 15.26; O: 11.62%; found C: 65.42; H: 7.68; N: 15.27; O: 11.61%.

Compound (1c): 4-oxo-*N*-phenyl-4-(4-phenylpiperazin-1-yl)butanamide

Yield: 73%; mp: 156-158 ⁰C; IR (KBr): 1633, 1652, 3296, 3318 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.45 (1H, s, Aryl NHCO), 7.54 (2H,d, Ar-H), 7.32 (2H, m, Ar-H), 7.12 (2H, m, Ar-H), 7.07 (1H, m, Ar-H), 6.95 (1H, m, Ar-H), 6.91 (2H, m, Ar-H), 3.83-3.67 (4H, m,CH₂), 3.23-3.16 (4H, m,CH₂), 2.81 (2H, t,CH₂), 2.78 (2H, t,CH₂); ¹³CNMR (100 MHz, CDCl₃): δ 170.78 (Aryl C(=O)NH), 170.59 (Aryl C(=O)NH), 150.85 (CH), 138.25(CH),129.28 (CH), 128.90 (CH), 123.95 (CH),120.67 (CH), 119.68(CH),116.72(CH),49.60 (CH₂), 45.34 (CH₂), 32.74 (CH₂), 28.97 (CH₂); HRMS (ESI): m/z calcd. for C₂₀H₂₃N₃O₂ : [M+H]⁺: 338.18, found 338.18; Anal

calcd. for $C_{20}H_{23}N_3O_2$: C: 71.19; H: 6.87; N: 12.45; O: 9.48%; found C: 71.18; H: 6.86; N: 12.44; O: 9.47%.

Compound (1d): 4-oxo-*N*-phenyl-4-(4-benzylpiperazin-1-yl)butanamide

Yield: 72.3%; mp: 124-129 °C; IR (KBr): 1641, 1684, 3273, 3317 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 8.63 (1H, s, Aryl NHCO), 7.54 (2H,d, Ar-H), 7.36-7.28 (7H, m, Ar-H), 7.08 (1H, m, Ar-H), 3.66 (2H, m, CH_2), 3.50 (4H, m, CH_2), 2.75 (2H, t, CH_2), 2.76 (2H, t, CH_2), 2.47-2.42 (4H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.92 (Aryl C(=O)NH), 170.47 (Aryl C(=O)NH), 138.34 (CH), 137.52 (CH), 129.12 (CH), 127.33 (CH), 123.86 (CH), 119.67 (CH), 62.83 (CH_2), 52.64 (CH_2), 45.40 (CH_2), 32.80 (CH_2), 29.00 (CH_2); HRMS (ESI): m/z calcd. For $C_{21}H_{25}N_3O_2$: $[M+H]^+$: 352.20, found 352.20; Anal calcd. for $C_{21}H_{25}N_3O_2$: C: 71.77; H: 7.17; N: 11.96; O: 9.10%; found C: 71.76; H: 7.16; N: 11.94; O: 9.09%.

Compound (1e): 4-oxo-*N*-phenyl-4-(piperidin-1-yl)butanamide

Yield: 71.73%; mp: 127-129 °C; IR (KBr): 1625, 1694, 3273, 3304 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 9.93 (1H, s, Aryl NHCO), 7.59 (2H, m, Ar-H), 7.27 (2H, m, Ar-H), 7.02 (1H, m, Ar-H), 2.89 (4H, m, CH_2), 2.73 (2H, t, CH_2), 2.60 (2H, t, CH_2), 1.51 (4H, m, CH_2), 1.50 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.12 (Aryl C(=O)NH), 170.27 (Aryl C(=O)NH), 138.43 (CH), 128.83 (CH), 123.76 (CH), 119.63 (CH), 43.09 (CH_2), 33.03 (CH_2), 29.19 (CH_2), 25.53 (CH_2), 24.42 (CH_2); HRMS (ESI): m/z calcd. for $C_{15}H_{20}N_2O_2$: $[M+H]^+$: 261.16, found 261.16; Anal calcd. for $C_{15}H_{20}N_2O_2$: C: 69.20; H: 7.74; N: 10.76; O: 12.29%; found C: 69.19; H: 7.72; N: 10.75; O: 12.28%.

Compound (1f): 4-oxo-*N*-phenyl-4-(pyrrolidin-1-yl)butanamide

Yield: 69.2%; mp: 125-127 °C; IR (KBr): 1623, 1692, 3276, 3302 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 9.11 (1H, s, Aryl NHCO), 7.55 (2H, m, Ar-H), 7.26 (2H, m, Ar-H), 7.04 (1H, m, Ar-H), 3.48 (4H, m, CH_2), 2.71 (2H, t, CH_2), 2.70 (2H, t, CH_2), 1.96 (4H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.15 (Aryl C(=O)NH), 170.76 (Aryl C(=O)NH), 138.53 (CH), 128.92 (CH), 124.05 (CH), 122.66 (CH), 46.65 (CH_2), 32.60 (CH_2), 30.47 (CH_2), 25.35 (CH_2); HRMS (ESI): m/z calcd. for $C_{14}H_{18}N_2O_2$: $[M+H]^+$: 247.14, found 247.14; Anal calcd. for

C₁₄H₁₈N₂O₂ : C: 68.27; H: 7.37; N: 11.37; O: 12.99%; found C: 68.26; H: 7.36; N: 11.35; O: 12.98%.

Compound (1g): *N*¹,*N*¹-diethyl-*N*⁴-phenylbutanediamide

Yield: 65.7%; mp: 89-91 °C; IR (KBr): 1617, 1688, 3375, 3492 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 9.15 (1H, s, Aryl NHCO), 7.55 (2H,m, Ar-H), 7.26 (2H, m, Ar-H),7.04 (1H, m, Ar-H), 3.31 (4H, m,CH₂), 2.75 (2H, t,CH₂), 2. 70 (2H, t,CH₂), 1.21-1.10 (6H, m, CH₂); ¹³CNMR (100 MHz, CDCl₃): δ 176.29 (Aryl C(=O)NH), 171.20 (Aryl C(=O)NH), 138.59 (CH), 128.66(CH),126.50 (CH), 123.67 (CH), 41.93 (CH₂), 32.76 (CH₂), 28.83 (CH₂), 14.20 (CH₂); HRMS (ESI): m/z calcd. for C₁₄H₂₀N₂O₂: [M+H]⁺: 249.16, found 249.15; Anal calcd. for C₁₄H₂₀N₂O₂ : C: 67.71; H: 8.12; N: 11.28; O: 12.89%; found C: 67.70; H: 8.10; N: 11.26; O: 12.88%.

Compound (2a): *N*-(4-chlorophenyl)-4-oxo-4-(piperazin-1-yl)butanamide

Yield: 60.9%; mp: 133-135 °C; IR (KBr): 1622, 1647, 3418, 3448 cm⁻¹; ¹HNMR (400 MHz, DMSO-D₆): δ 10.12 (1H, s, Aryl NHCO), 7.63 (2H,m, Ar-H), 7.32 (3H, m, Ar-H), 3.32 (4H, m,CH₂), 2.86 (4H,m,CH₂), 2.59 (2H, t,CH₂), 2. 50 (2H, t,CH₂); ¹³CNMR (100 MHz, DMSO-D₆): δ 172.61 (Aryl C(=O)NH), 171.24 (Aryl C(=O)NH), 138.73 (CH), 129.01 (CH), 126.96 (CH), 120.96 (CH), 56.37 (CH₂), 45.92 (CH₂),31.78 (CH₂), 28.14 (CH₂); HRMS (ESI): m/z calcd. for C₁₄H₁₈ClN₃O₂ : [M+H]⁺: 296.11, found 296.11; Anal calcd. for C₁₄H₁₈ClN₃O₂ : C: 56.85; H: 6.13; Cl: 11.99; N: 14.21; O: 10.82%; found : C: 56.84; H: 6.11; Cl: 11.98; N: 14.20; O: 10.81%.

Compound (2b): *N*-(4-chlorophenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide

Yield: 52.6%; mp: 139-141 °C; IR (KBr): 1492, 1708, 3100, 3468 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 9.4 (1H, s, Aryl NHCO), 7.62 (2H,m, Ar-H), 7.35 (2H, m, Ar-H), 3.53 (4H, m,CH₂), 3.16 (4H,m,CH₂), 2.77 (2H, t,CH₂), 2. 75 (2H, t,CH₂), 2.31 (3H, s, CH₃); ¹³CNMR (100 MHz, CDCl₃): δ 172.37 (Aryl C(=O)NH), 170.70 (Aryl C(=O)NH), 135.72 (CH), 133.45 (CH),128.89 (CH), 126.29 (CH),120.35 (CH), 54.56 (CH₂), 45.93 (CH₂),43.57 (CH₃), 32.71 (CH₂), 29.70 (CH₂); HRMS (ESI): m/z calcd. for C₁₅H₂₀ClN₃O₂ : [M+H]⁺: 310.13, found 310.18; Anal calcd.

for $C_{15}H_{20}ClN_3O_2$: C: 58.16; H: 6.51; Cl: 11.44; N: 13.56; O: 10.33%; found : C: 58.18; H: 6.50; Cl: 11.43; N: 13.54; O: 10.35%.

Compound (2c): *N*-(4-chlorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide

Yield: 74.1%; mp: 156-158 °C; IR (KBr): 1596, 1648, 3214, 3299 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 8.66 (1H, s, Aryl NHCO), 7.51 (2H,d, Ar-H), 7.33-7.25 (4H, m, Ar-H), 6.93 (3H, m, Ar-H), 3.81-3.67 (4H, m,CH₂), 3.22-3.19 (4H, m,CH₂), 2.81 (2H, t,CH₂), 2.75 (2H, t,CH₂); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.11 (Aryl C(=O)NH), 165.90 (Aryl C(=O)NH), 146.04 (CH), 132.23(CH),124.55 (CH), 124.06 (CH), 123.95 (CH),116.10 (CH), 115.98 (CH),111.89 (CH),44.85 (CH₂), 40.62 (CH₂), 37.15 (CH₂), 27.81 (CH₂); HRMS (ESI): m/z calcd. for $C_{20}H_{22}ClN_3O_2$: $[M+H]^+$: 372.14, found 372.14; Anal calcd. for $C_{20}H_{22}ClN_3O_2$: C: 64.60; H: 5.96; Cl: 9.53; N: 11.30; O: 8.61%; found : C: 64.59; H: 5.95; Cl: 9.52; N: 11.29; O: 8.60%.

Compound (2d): *N*-(4-chlorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide

Yield: 72.6%; mp: 137-139 °C; IR (KBr): 1610, 1672, 3306, 3400 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 8.81 (1H, s, Aryl NHCO), 7.50 (2H,d, Ar-H), 7.34-7.24 (7H, m, Ar-H), 3.65 (2H, m,CH₂), 3.51 (4H, m,CH₂), 2.74 (2H, t,CH₂), 2.68 (2H, t,CH₂),2.46-2.44(4H,m,CH₂); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.23 (Aryl C(=O)NH), 165.74 (Aryl C(=O)NH), 132.70 (CH), 132.22(CH),124.37 (CH), 124.05 (CH), 123.91 (CH),123.63 (CH), 122.61 (CH), 58.07 (CH₂), 48.10 (CH₂), 47.85 (CH₂), 37.25 (CH₂), 27.99 (CH₂); HRMS (ESI): m/z calcd. for $C_{21}H_{24}ClN_3O_2$: $[M+H]^+$: 386.16, found 386.16; Anal calcd. for $C_{21}H_{24}ClN_3O_2$: C: 65.36; H: 6.27; Cl: 9.19; N: 10.89; O: 8.29%; found : C: 65.35; H: 6.26; Cl: 9.18; N: 10.80; O: 8.28%.

Compound (2e): *N*-(4-chlorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide

Yield: 70%; mp: 134-136 °C; IR (KBr): 1621, 1697, 3361, 3680 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 9.06 (1H, s, Aryl NHCO), 7.49 (2H,d, Ar-H), 7.25 (2H, m, Ar-H), 3.44 (4H, m,CH₂), 2.92 (2H, t,CH₂), 2.75 (2H, t,CH₂), 1.66-1.57(6H,m,(CH₂); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.17 (Aryl C(=O)NH), 170.30 (Aryl C(=O)NH), 137.09 (CH), 128.77 (CH), 128.54 (CH), 120.80 (CH), 46.52 (CH₂), 32.95 (CH₂),29.10 (CH₂), 25.53 (CH₂), 24.39 (CH₂); HRMS (ESI): m/z calcd. for $C_{15}H_{19}ClN_2O_2$: $[M+H]^+$: 295.11, found 295.11; Anal calcd. for

C₁₅H₁₉ClN₂O₂ : C: 61.12; H: 6.50; Cl: 12.03; N: 9.50; O: 10.86%; found : C: 61.11; H: 6.49; Cl: 12.02; N: 9.49; O: 10.85%.

Compound (2f): *N*-(4-chlorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide

Yield: 71.09%; mp: 136-141 °C; IR (KBr): 1626, 1707, 3279, 3312 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 9.25 (1H, s, Aryl NHCO), 7.52 (2H,m, Ar-H), 7.27 (2H, m, Ar-H), 3.50-3.45 (4H, m,CH₂), 2.92 (2H, t,CH₂), 2.72 (2H, t,CH₂), 1.91 (4H,m,(CH₂); ¹³CNMR (100 MHz, CDCl₃): δ 175.85 (Aryl C(=O)NH), 170.75 (Aryl C(=O)NH), 137.16 (CH), 129.40 (CH), 128.75 (CH), 120.80 (CH), 46.67 (CH₂), 32.70 (CH₂), 30.50 (CH₂), 26.02 (CH₂); HRMS (ESI): m/z calcd. for C₁₄H₁₇ClN₂O₂: [M+H]⁺: 281.10, found 281.10; Anal calcd. for C₁₄H₁₇ClN₂O₂ : C: 59.89; H: 6.10; Cl: 12.63; N: 9.98; O: 11.40%; found : C: 59.88; H: 6.09; Cl: 12.62; N: 9.96; O: 11.39%.

Compound (2g): *N*⁴-(4-chlorophenyl)-*N*¹,*N*¹-diethylbutanediamide

Yield: 70.7%; mp: 106-108 °C; IR (KBr): 1623, 1708, 3249, 3307 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 9.06 (1H, s, Aryl NHCO), 7.46 (2H,d, Ar-H), 7.27 (2H, d, Ar-H), 3.43-3.35 (4H, m,CH₂), 2.75 (2H, t,CH₂), 2.74 (2H, t,CH₂), 1.27-1.14(6H,m,(CH₃); ¹³CNMR (100 MHz, CDCl₃): δ 175.85 (Aryl C(=O)NH), 171.30 (Aryl C(=O)NH), 129.40 (CH), 127.67 (CH), 120.80 (CH), 40.70 (CH₂), 32.95 (CH₂),28.39 (CH₂), 14.06 (CH₃); HRMS (ESI): m/z calcd. for C₁₄H₁₉ClN₂O₂: [M+H]⁺: 283.12, found 283.10; Anal calcd. for C₁₄H₁₉ClN₂O₂: C: 59.47; H: 6.77; Cl: 12.54; N: 9.91; O: 11.32%; found C₁₄H₁₉ClN₂O₂ : C: 59.46; H: 6.76; Cl: 12.53; N: 9.90; O: 11.31%.

Compound (3a): *N*-(4-methylphenyl)-4-oxo-4-(piperazin-1-yl)butanamide

Yield: 61.5%; mp: 134-137 °C; IR (KBr): 1630, 1663, 3462, 3581 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.52 (1H, s, Aryl NHCO), 7.44 (2H,m, Ar-H), 7.09 (3H, m, Ar-H), 3.69 (4H, m,CH₂), 3.10 (4H,m,CH₂), 2.77 (2H, t,CH₂), 2.76 (2H, t,CH₂), 2.31 (3H, s, CH₃); ¹³CNMR (100 MHz, CDCl₃): δ 170.67 (Aryl C(=O)NH), 170.70 (Aryl C(=O)NH), 135.73 (CH), 133.51 (CH),129.36 (CH), 120.29 (CH), 49.35 (CH₂),45.35 (CH₃), 32.57 (CH₂), 28.08 (CH₂), 20.86 (CH₃); HRMS (ESI): m/z calcd. for C₁₅H₂₁N₃O₂ : [M+H]⁺: 276.17, found 276.17; Anal calcd. for C₁₅H₂₁N₃O₂ : C: 65.43; H: 7.69; N: 15.26; O: 11.62%; found : C: 65.42; H: 7.68; N: 15.25; O: 11.61%.

Compound (3b): *N*-(4-methylphenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide

Yield: 56.3%; mp: 136-139 °C; IR (KBr): 1625, 1694, 3274, 3302 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.4 (1H, s, Aryl NHCO), 7.42 (2H, m, Ar-H), 7.15 (2H, m, Ar-H), 3.73 (4H, m, CH₂), 3.16 (4H, m, CH₂), 2.77 (2H, t, CH₂), 2.75 (2H, t, CH₂), 2.31 (3H, s, CH₃), 2.16 (3H, s, CH₃); ¹³CNMR (100 MHz, CDCl₃): δ 176.37 (Aryl C(=O)NH), 170.70 (Aryl C(=O)NH), 135.72 (CH), 133.45 (CH), 129.89 (CH), 126.29 (CH), 129.35 (CH), 54.56 (CH₂), 45.93 (CH₂), 43.57 (CH₃), 32.71 (CH₂), 29.70 (CH₂), 23.42 (CH₃); HRMS (ESI): m/z calcd. for C₁₆H₂₃N₃O₂ : [M+H]⁺: 290.18, found 290.18; Anal calcd. for C₁₆H₂₃N₃O₂ : C: 66.41; H: 8.01; N: 14.52; O: 11.06%; found : C: 66.40; H: 8.00; N: 14.51; O: 11.05%.

Compound (3c): *N*-(4-methylphenyl)-4-(4-phenylpiperazin-1-yl)-4-oxobutanamide

Yield: 74.8%; mp: 159-161 °C; IR (KBr): 1635, 1679, 3262, 3292 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.36 (1H, s, Aryl NHCO), 7.43 (2H, d, Ar-H), 7.30 (2H, m, Ar-H), 7.12 (2H, m, Ar-H), 6.93 (3H, m, Ar-H), 3.82-3.67 (4H, m, CH₂), 3.22-3.15 (4H, m, CH₂), 2.78 (2H, t, CH₂), 2.66 (2H, t, CH₂), 2.31 (3H, s, CH₃); ¹³CNMR (100 MHz, CDCl₃): δ 170.64 (Aryl C(=O)NH), 170.52 (Aryl C(=O)NH), 150.85 (CH), 135.70 (CH), 133.53 (CH), 129.37 (CH), 129.27 (CH), 120.65 (CH), 119.79 (CH), 116.71 (CH), 49.60 (CH₂), 45.35 (CH₂), 32.62 (CH₂), 28.92 (CH₂), 20.85 (CH₃); HRMS (ESI): m/z calcd. for C₂₁H₂₅N₃O₂ : [M+H]⁺: 352.20, found 352.20; Anal calcd. for C₂₁H₂₅N₃O₂ : C: 71.77; H: 7.17; N: 11.96; O: 9.10%; found : C: 71.76; H: 7.16; N: 11.95; O: 9.09%.

Compound (3d): *N*-(4-methylphenyl)-4-(4-benzylpiperazin-1-yl)-4-oxobutanamide

Yield: 75.2%; mp: 133-135 °C; IR (KBr): 1631, 1693, 3274, 3299 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.38 (1H, s, Aryl NHCO), 7.42 (2H, m, Ar-H), 7.35 (2H, m, Ar-H), 7.28 (2H, m, Ar-H), 7.10 (3H, m, Ar-H), 3.64 (2H, m, CH₂), 3.51 (4H, m, CH₂), 2.77 (2H, t, CH₂), 2.64 (2H, t, CH₂), 2.47-2.42 (4H, m, CH₂), 2.31 (3H, s, CH₃); ¹³CNMR (100 MHz, CDCl₃): δ 170.75 (Aryl C(=O)NH), 170.42 (Aryl C(=O)NH), 137.88 (CH), 135.45 (CH), 133.65 (CH), 129.35 (CH), 129.12 (CH), 128.36 (CH), 127.32 (CH), 119.73 (CH), 62.83 (CH₂), 52.91 (CH₂), 45.39 (CH₂), 32.78 (CH₂), 29.04 (CH₂), 20.85 (CH₃); HRMS (ESI): m/z calcd. for C₂₂H₂₇N₃O₂ : [M+H]⁺: 366.21, found 366.21; Anal calcd. for C₂₂H₂₇N₃O₂ : C: 72.30; H: 7.45; N: 11.50; O: 8.76%; found : C: 72.29; H: 7.44; N: 11.49; O: 8.75%.

Compound (3e): *N*-(4-methylphenyl)-4-oxo-4-(piperidin-1-yl)butanamide

Yield: 75.3%; mp: 124-127 °C; IR (KBr): 1625, 1729, 3269, 3303 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.69 (1H, s, Aryl NHCO), 7.43 (2H,m, Ar-H), 7.09 (2H, m, Ar-H), 3.59-3.42 (4H, m,CH₂), 2.77 (2H, t,CH₂), 2.70 (2H, t,CH₂), 2.31 (3H, s, CH₃), 1.67-1.58 (6H, m, CH₂); ¹³CNMR (100 MHz, CDCl₃): δ 170.97 (Aryl C(=O)NH), 170.28 (Aryl C(=O)NH), 135.88 (CH), 133.28 (CH),129.29 (CH), 119.71(CH), 46.48 (CH₂), 32.87 (CH₂), 29.12 (CH₂), 26.29 (CH₂), 25.52 (CH₂), 20.83(CH₃); HRMS (ESI): m/z calcd. for C₁₆H₂₂N₂O₂ : [M+H]⁺: 275.17, found 275.17; Anal calcd. for C₁₆H₂₂N₂O₂ : C: 70.04; H: 8.08; N: 10.21; O: 11.66%; found : C: 70.03; H: 8.07; N: 10.20; O: 11.65%.

Compound (3f): *N*-(4-methylphenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide

Yield: 73.2%; mp: 135-138 °C; IR (KBr): 1625, 1693, 3269, 3304 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.81 (1H, s, Aryl NHCO), 7.42 (2H,m, Ar-H), 7.11 (2H, m, Ar-H), 3.43-3.32 (4H, m,CH₂), 2.77 (2H, t,CH₂), 2.72 (2H, t,CH₂), 2.30 (3H, s, CH₃),2.00-1.87 (4H, m, CH₂);¹³CNMR (100 MHz, CDCl₃): δ 170.93 (Aryl C(=O)NH), 170.71 (Aryl C(=O)NH), 135.88 (CH), 133.28 (CH),129.79 (CH), 124.23 (CH), 119.68(CH), 45.80 (CH₂), 43.57 (CH₂), 34.00 (CH₂), 32.71 (CH₂), 26.03 (CH₂), 24.36 (CH₃); HRMS (ESI): m/z calcd. for C₁₅H₂₀N₂O₂: [M+H]⁺: 261.15, found 261.15; Anal calcd. for C₁₅H₂₀N₂O₂: C: 69.20; H: 7.74; N: 10.76; O: 12.29%; found : C: 69.19; H: 7.73; N: 10.75; O: 12.28%.

Compound (3g): *N*¹,*N*¹-diethyl-*N*⁴-(4-methylphenyl)butanediamide

Yield: 70.1%; mp: 94-97 °C; IR (KBr): 1629, 1679, 3272, 3313 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.765 (1H, s, Aryl NHCO), 7.43 (2H,m, Ar-H), 7.16 (2H, m, Ar-H), 3.51-3.43 (4H, m,CH₂), 2.74 (2H, t,CH₂), 2.69 (2H, t,CH₂), 2.31 (3H, s, CH₃),1.22-1.11 (6H, m, CH₃); ¹³CNMR (100 MHz, CDCl₃): δ 176.38 (Aryl C(=O)NH), 171.30 (Aryl C(=O)NH), 135.91 (CH), 133.26 (CH),129.89 (CH), 119.73 (CH), 42.09 (CH₂), 32.92 (CH₂), 29.05 (CH₂), 14.09 (CH₃); HRMS (ESI): m/z calcd. for C₁₅H₂₂N₂O₂ : [M+H]⁺: 263.17, found 263.17; Anal calcd. for C₁₅H₂₂N₂O₂ : C: 66.41; H: 8.01; N: 14.52; O: 11.06%; found : C: 66.40; H: 8.00; N: 14.51; O: 11.05%.

Compound (4a): *N*-(2,4-difluorophenyl)-4-oxo-4-(piperazin-1-yl)butanamide

Yield: 63.1%; mp: 136-141 °C; IR (KBr): 1623, 1687, 3220, 3436 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 9.74 (1H, s, Aryl NHCO), 7.83 (1H,m, Ar-H), 7.29 (2H, m, Ar-H), 7.26 (1H, m, Ar-H), 3.53 (4H, m,CH₂), 2.73 (4H, m,CH₂), 2.69 (2H, t,CH₂), 2.64 (2H, t, CH₂); ¹³CNMR (100 MHz, CDCl₃): δ 171.47 (Aryl C(=O)NH), 170.49 (Aryl C(=O)NH), 160.51 (Ar-C), 159.26 (Ar-C),125.78 (CH), 123.32 (Ar-C), 111.33(CH), 104.73(CH), 49.64 (CH₂), 45.19 (CH₂), 31.22 (CH₂), 28.01 (CH₂); HRMS (ESI): m/z calcd. for C₁₄H₁₇F₂N₃O₂ : [M+H]⁺: 298.13, found 298.13; Anal calcd. for C₁₄H₁₇F₂N₃O₂: C: 56.56; H: 5.76; F: 12.78; N: 14.13; O: 10.76%; found : C: 56.55; H: 5.75; F: 12.77; N: 14.12; O: 10.75%.

Compound (4b): *N*-(2,4-difluorophenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide

Yield: 57.7%; mp: 134-138 °C; IR (KBr): 1551, 1628, 3372, 3581 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.37 (1H, s, Aryl NHCO), 8.16 (1H,m, Ar-H), 6.97 (1H, m, Ar-H), 6.81 (1H, m, Ar-H), 3.64 (4H, m,CH₂), 2.66 (4H, m,CH₂), 2.93 (2H, t,CH₂), 2.41 (2H, t, CH₂),2.37(3H,s,CH₃); ¹³CNMR (100 MHz, CDCl₃): δ 175.21 (Aryl C(=O)NH), 170.17 (Aryl C(=O)NH), 166.96 (Ar-C), 161.78 (Ar-C),125.03 (CH), 112.22 (Ar-C), 111.09(CH), 103.75(CH), 54.44 (CH₂), 45.92 (CH₂), 41.76 (CH₃), 32.21 (CH₂),29.70 (CH₂); HRMS (ESI): m/z calcd. for C₁₅H₁₉F₂N₃O₂: [M+H]⁺: 312.15, found 312.15; Anal calcd. for C₁₅H₁₉F₂N₃O₂ : C: 57.87; H: 6.15; F: 12.20; N: 13.50; O: 10.28%; found : C: 57.86; H: 6.14; F: 12.19; N: 13.49; O: 10.27%.

Compound (4c): *N*-(2,4-difluorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide

Yield: 75.4%; mp: 125-128 °C; IR (KBr): 1625, 1729, 3260, 3272 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.42 (1H,m, Ar-H), 8.21 (1H, m, Ar-H), 7.29 (1H, m, Ar-H), 6.94 (3H, m, Ar-H), 6.84 (2H, m, Ar-H), 3.69 (4H, m,CH₂), 3.18 (4H, m,CH₂), 2.82 (2H, t,CH₂), 2.81 (2H, t, CH₂); ¹³CNMR (100 MHz, CDCl₃): δ 170.99 (Aryl C(=O)NH), 170.33 (Aryl C(=O)NH), 164.96 (Ar-C), 161.08 (Ar-C), 150.85 (Ar-C), 129.28 (CH), 123.07 (CH), 120.64 (CH), 116.69 (Ar-C), 111.10 (CH), 110.85 (CH), 103.78 (CH), 49.59 (CH₂), 45.32 (CH₂), 30.93 (CH₂), 28.74 (CH₂); HRMS (ESI): m/z calcd. for C₂₀H₂₁F₂N₃O₂: [M+H]⁺: 374.16, found 374.16; Anal calcd. for C₂₀H₂₁F₂N₃O₂ : C: 64.33; H: 5.67; F: 10.18; N: 11.25; O: 8.57%; found : 64.32; H: 5.66; F: 10.17; N: 11.24; O: 8.56%.

Compound (4d): *N*-(2,4-difluorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide

Yield: 71.8%; mp: 149-151 °C; IR (KBr): 1642, 1683, 3215, 3274 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.48 (1H,m, Ar-H), 8.20 (1H, m, Ar-H), 7.79 (1H, m, Ar-H), 7.62 (1H, m, Ar-H), 7.28 (2H, m, Ar-H), 6.83 (2H, m, Ar-H), 3.66 (2H, m,CH₂), 3.54 (4H, m,CH₂), 2.75 (2H, t, CH₂), 2.74(2H,t,CH₂) 2.45 (4H, m,CH₂); ¹³CNMR (100 MHz, CDCl₃): δ 173.11 (Aryl C(=O)NH), 170.17 (Aryl C(=O)NH), 168.8 (Ar-C), 159.73 (Ar-C), 136.10 (Ar-C), 128.37 (CH), 127.36 (CH), 125.05 (CH), 124.14 (Ar-C), 118.53 (CH), 110.11(CH), 104.61 (CH), 62.82 (CH₂), 52.63 (CH₂), 45.34 (CH₂), 32.58 (CH₂), 28.86 (CH₂); HRMS (ESI): m/z calcd. for C₂₁H₂₃F₂N₃O₂: [M+H]⁺: 388.18, found 388.18; Anal calcd. for C₂₁H₂₃F₂N₃O₂: C: 65.10; H: 5.98; F: 9.81; N: 10.85; O: 8.26%; found: C: 65.09; H: 5.97; F: 9.80; N: 10.84; O: 8.25%.

Compound (4e): *N*-(2,4-difluorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide

Yield: 73.5%; mp: 129-131 °C; IR (KBr): 1639, 1720, 3222, 3281 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.59 (1H, s, Aryl NHCO), 8.23 (1H,m, Ar-H), 7.01 (1H, m, Ar-H), 6.83 (1H, m, Ar-H), 3.44 (4H, m,CH₂), 2.76 (2H, t,CH₂), 2.72 (2H, t, CH₂), 1.30 (6H, m,CH₂); ¹³CNMR (100 MHz, CDCl₃): δ 175.22 (Aryl C(=O)NH), 171.30 (Aryl C(=O)NH), 161.61 (Ar-C), 159.56 (Ar-C),122.98 (CH), 114.13 (Ar-C), 111.02(CH), 103.72(CH), 45.54 (CH₂), 30.92 (CH₂), 29.02 (CH₂), 26.29 (CH),25.50(CH₂); HRMS (ESI): m/z calcd. for C₁₅H₁₈F₂N₂O₂: [M+H]⁺: 297.14, found 297.14; Anal calcd. for C₁₅H₁₈F₂N₂O₂: C: 60.80; H: 6.12; F: 12.82; N: 9.45; O: 10.80%; found : C: 60.79; H: 6.11; F: 12.81; N: 9.44; O: 10.79%.

Compound (4f): *N*-(2,4-difluorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide

Yield: 70.5%; mp: 128-130 °C; IR (KBr): 1620, 1694, 3271, 3559 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.82 (1H, s, Aryl NHCO), 8.14 (1H,m, Ar-H), 6.84 (2H, m, Ar-H), 6.78 (2H, m, Ar-H), 3.46 (4H, m,CH₂), 2.66 (2H, t,CH₂), 2.60 (2H, t, CH₂), 1.96 (4H, m,CH₂); ¹³CNMR (100 MHz, CDCl₃): δ 171.28 (Aryl C(=O)NH), 170.40 (Aryl C(=O)NH), 159.69 (Ar-C), 157.25 (Ar-C),123.06 (CH), 111.06 (Ar-C), 110.74(CH), 103.74(CH), 46.58 (CH₂), 32.49 (CH₂), 30.38 (CH₂), 26.03 (CH); HRMS (ESI): m/z calcd. for C₁₄H₁₆F₂N₂O₂: [M+H]⁺: 283.12, found 283.12; Anal calcd. for C₁₅H₁₈F₂N₂O₂: C: 59.57; H: 5.71; F: 13.46; N: 9.92; O: 11.34%; found : C: 59.56; H: 5.70; F: 13.45; N: 9.91; O: 11.33%.

Compound (4g): *N*⁴-(2,4-difluorophenyl)-*N*¹,*N*¹-diethylbutanediamide

Yield: 71.1%; mp: 97-101 °C; IR (KBr): 1679, 1693, 3302, 3361 cm⁻¹; ¹HNMR (400 MHz, CDCl₃): δ 8.70 (1H, s, Aryl NHCO), 8.17 (1H, m, Ar-H), 7.21 (1H, m, Ar-H), 6.94 (1H, m, Ar-H), 3.37 (4H, m, CH₂), 2.96 (2H, t, CH₂), 2.76 (2H, t, CH₂), 1.21 (6H, m, CH₃); ¹³CNMR (100 MHz, CDCl₃): δ 175.22 (Aryl C(=O) NH), 171.35 (Aryl C(=O) NH), 164.40 (Ar-C), 161.78 (Ar-C), 130.18 (CH), 116.02 (Ar-C), 111.95 (CH), 105.30 (CH), 41.95 (CH₂), 29.00 (CH₂), 28.54 (CH₂), 14.05 (CH₃); HRMS (ESI): m/z calcd. for C₁₄H₁₈F₂N₂O₂: [M+H]⁺: 285.14, found 285.14; Anal calcd. for C₁₄H₁₈F₂N₂O₂: C: 59.14; H: 6.38; F: 13.36; N: 9.85; O: 11.26%; found: C: 59.13; H: 6.37; F: 13.35; N: 9.84; O: 11.25%.

Fig. 1: IR Spectrum of 4-oxo-N-phenyl-4-(4-phenylpiperazin-1-yl)butanamide(1c)

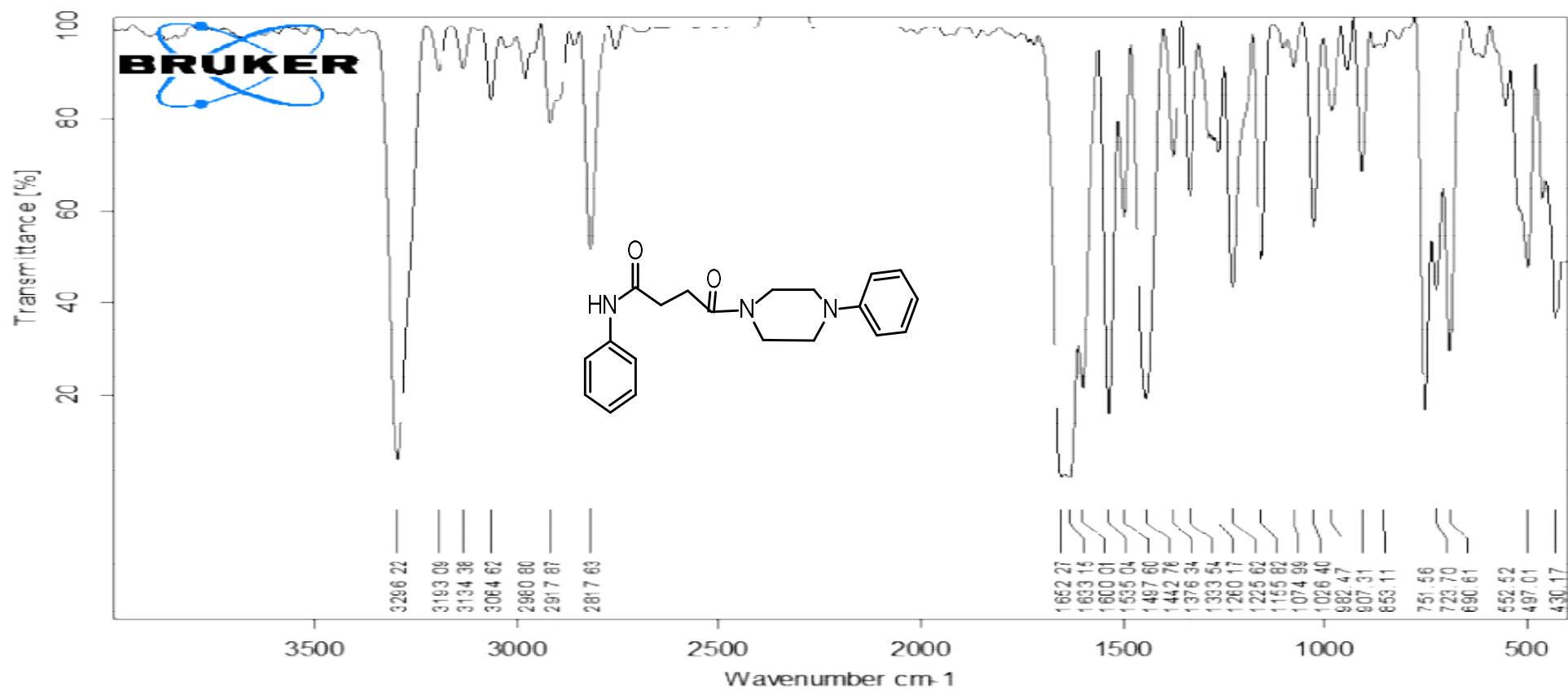


Fig. 2: ¹H NMR Spectrum of 4-oxo-*N*-phenyl-4-(4-phenylpiperazin-1-yl)butanamide(1c)

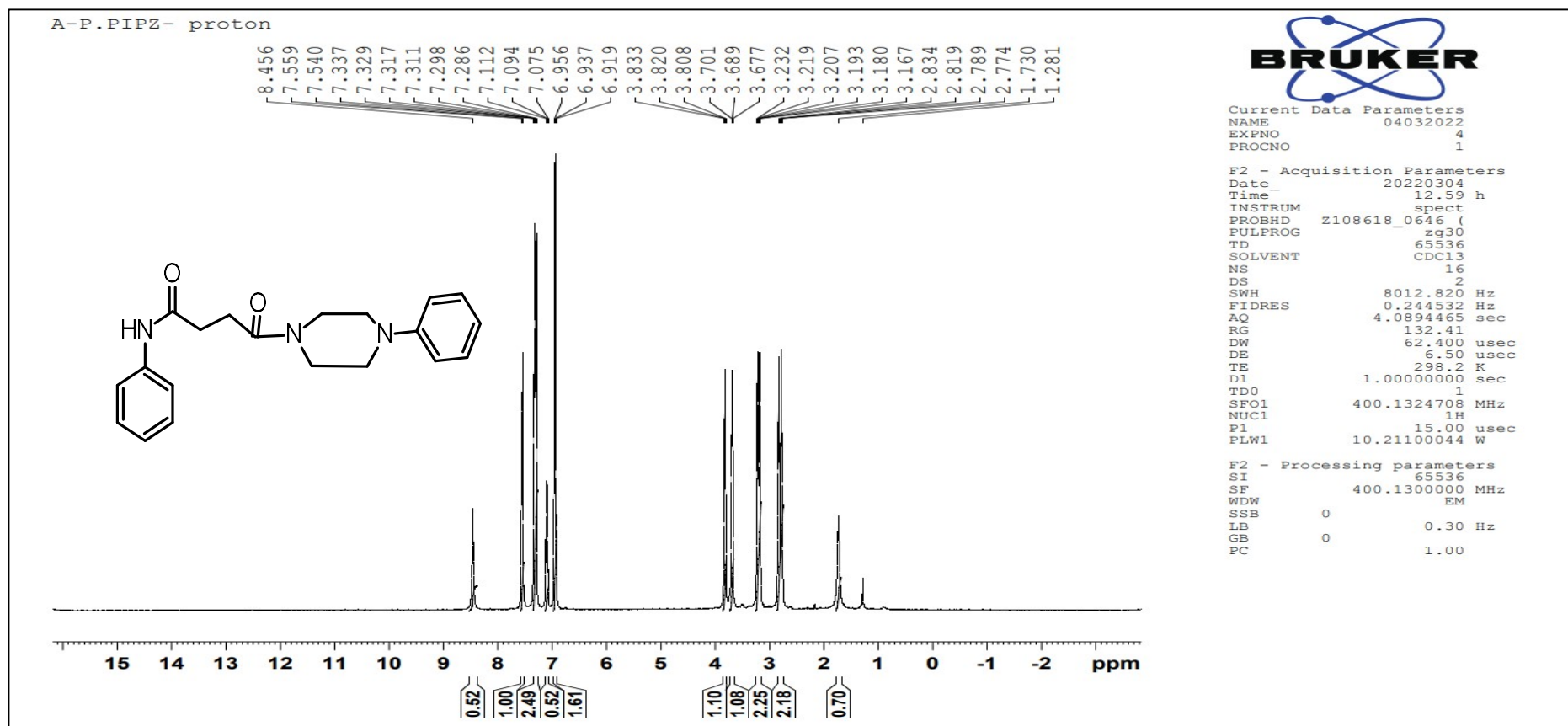


Fig. 3: ^{13}C NMR Spectrum of 4-oxo-*N*-phenyl-4-(4-phenylpiperazin-1-yl)butanamide(1c)

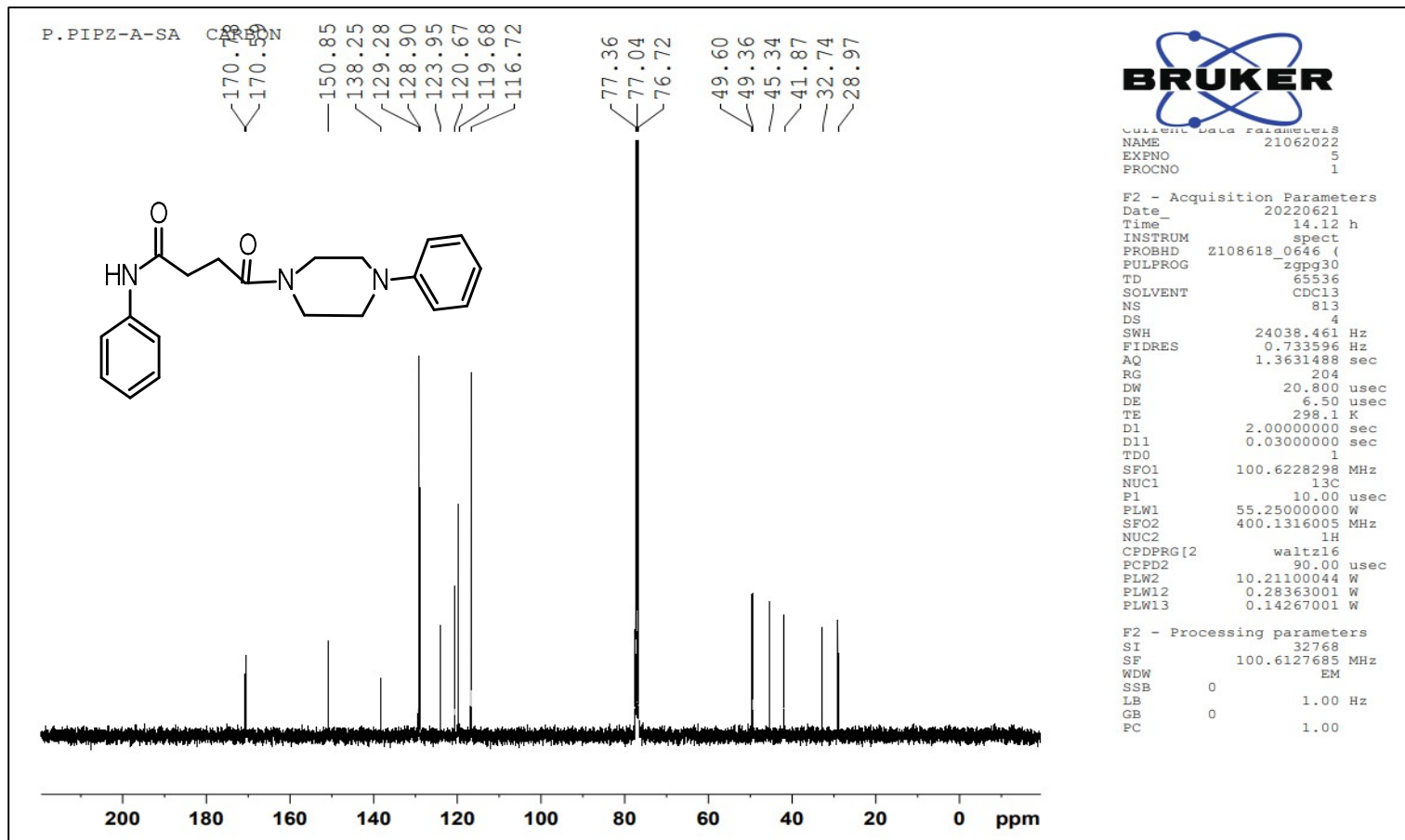


Fig. 4: Mass Spectrum of 4-oxo-N-phenyl-4-(4-phenylpiperazin-1-yl)butanamide(1c)

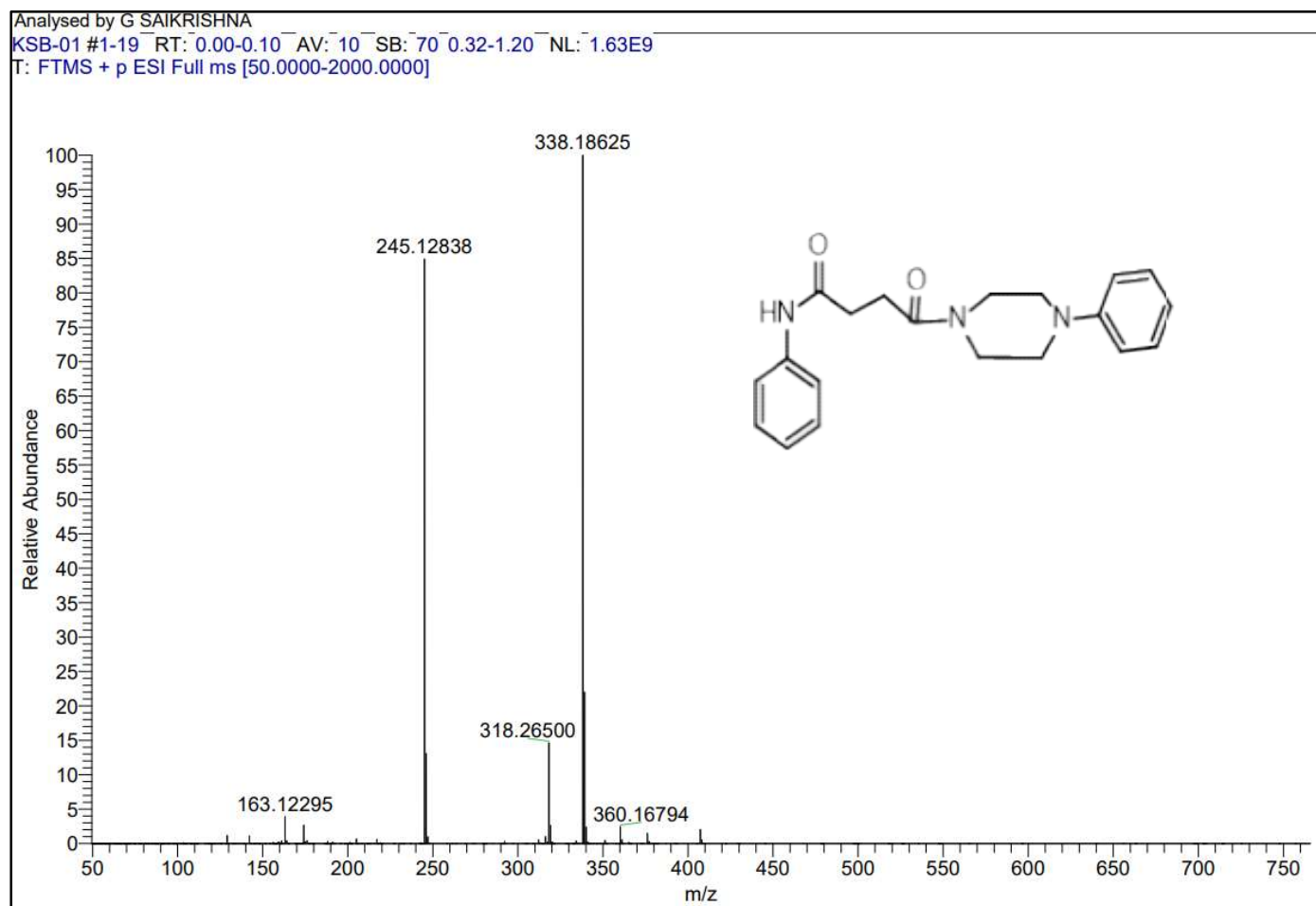


Fig. 5: IR Spectrum of 4-oxo-N-phenyl-4-(4-benzylpiperazin-1-yl)butanamide (1d)

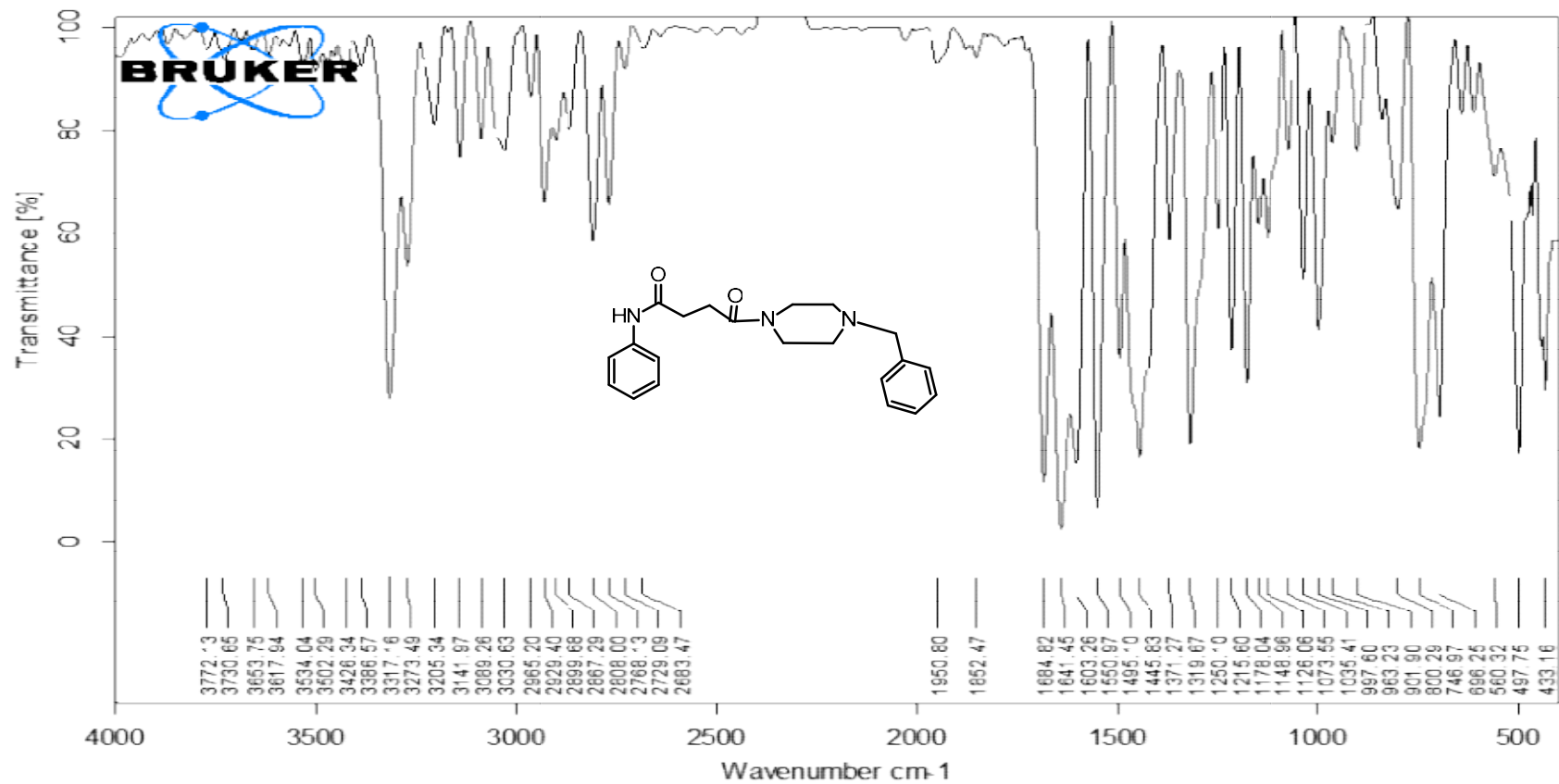


Fig. 6: ^1H NMR Spectrum of 4-oxo-*N*-phenyl-4-(4-benzylpiperazin-1-yl)butanamide (1d)

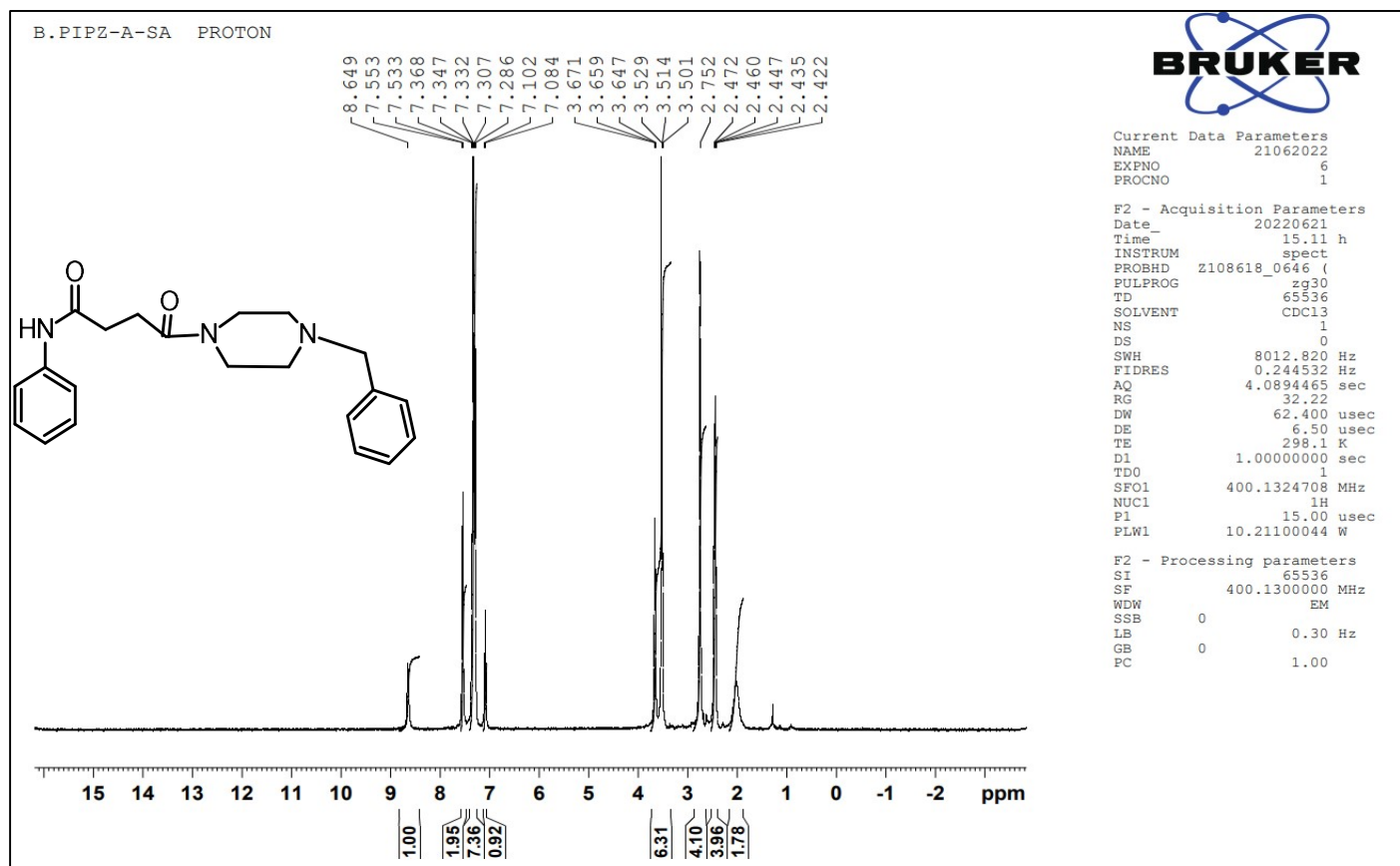


Fig. 7: ^{13}C NMR Spectrum of 4-oxo-*N*-phenyl-4-(4-benzylpiperazin-1-yl)butanamide (1d)

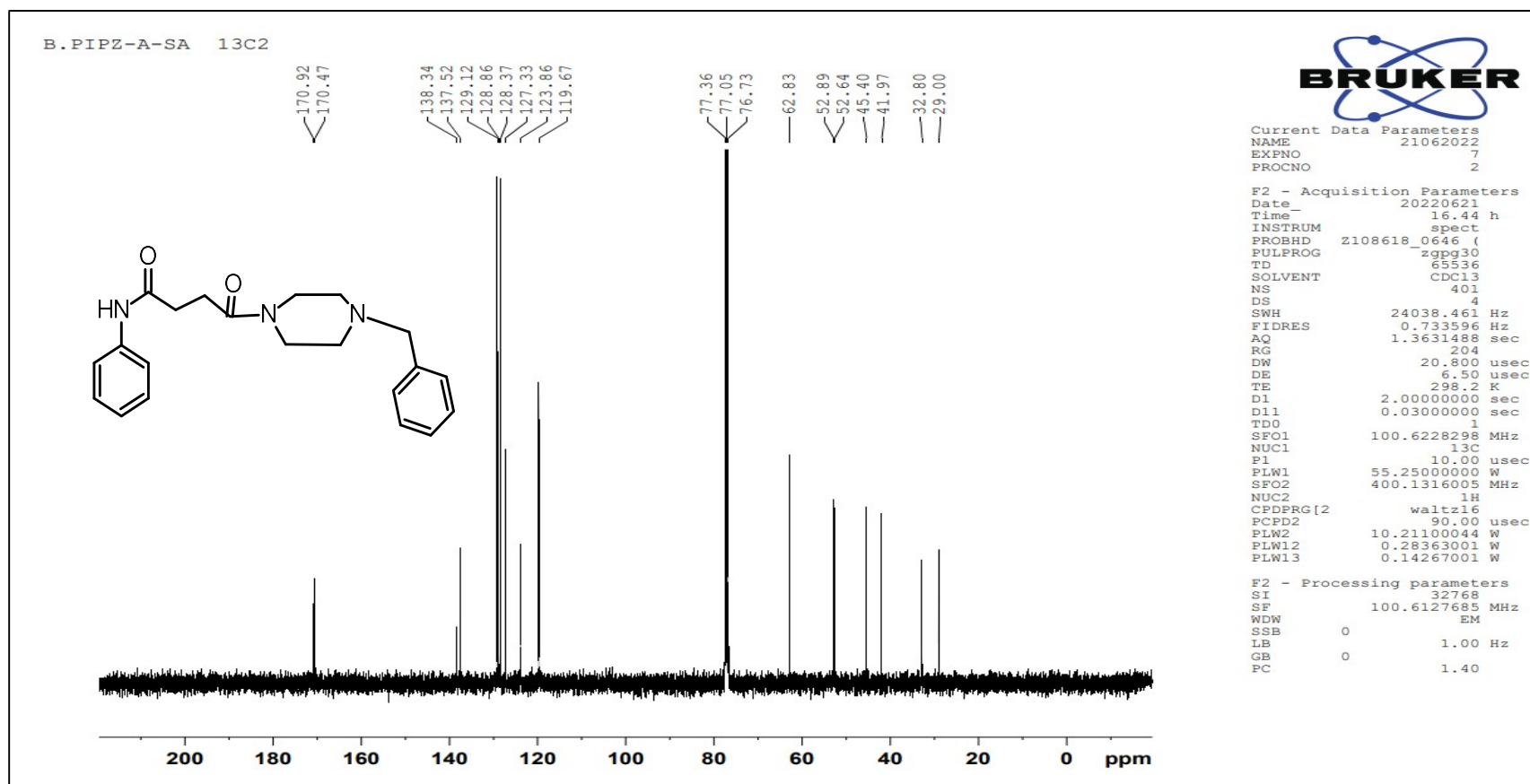


Fig. 8: IR Spectrum of 4-oxo-N-phenyl-4-(piperidin-1-yl)butanamide(1e)

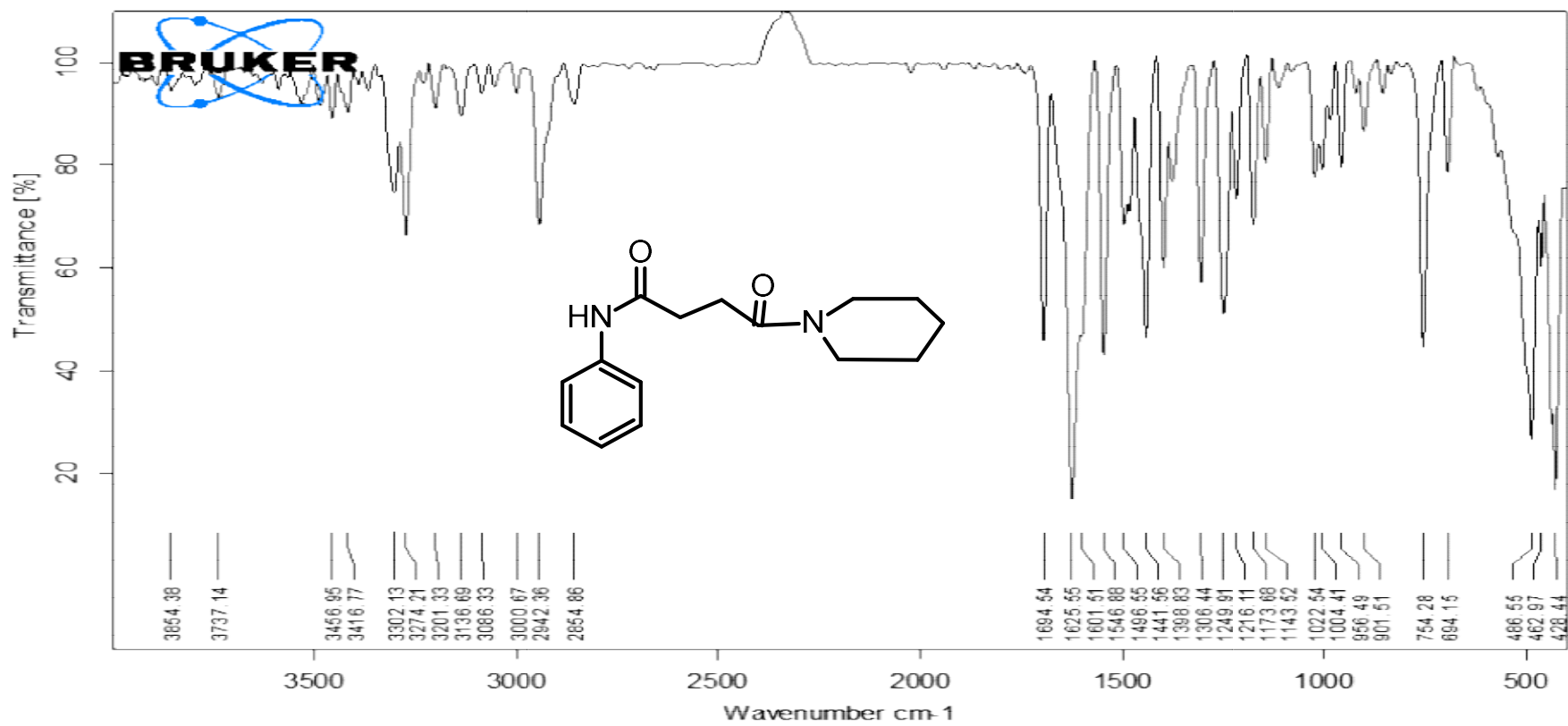


Fig. 9: ^1H NMR Spectrum of 4-oxo-*N*-phenyl-4-(piperidin-1-yl)butanamide(1e)

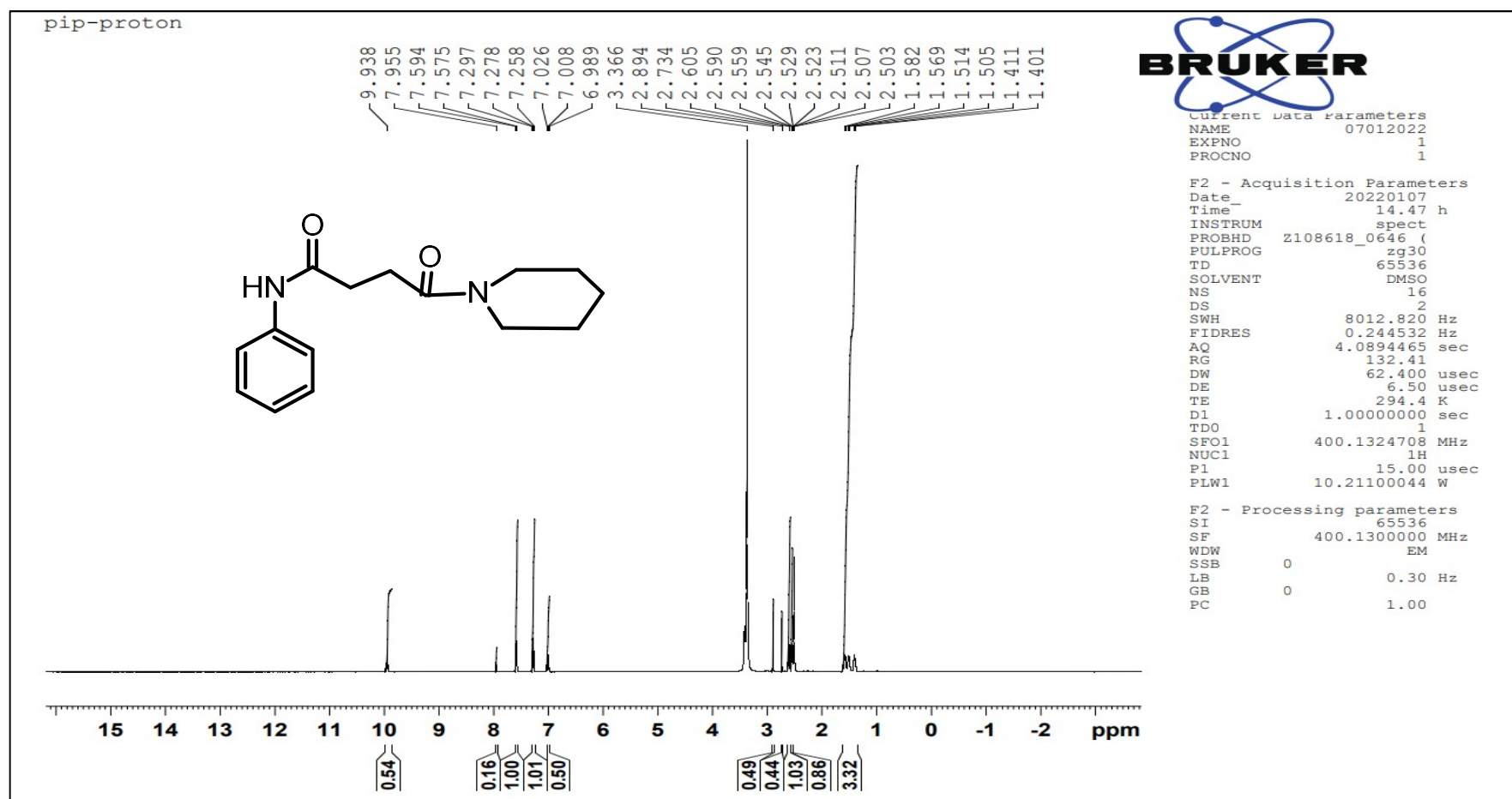


Fig. 10: ^{13}C NMR Spectrum of 4-oxo-*N*-phenyl-4-(piperidin-1-yl)butanamide(1e)

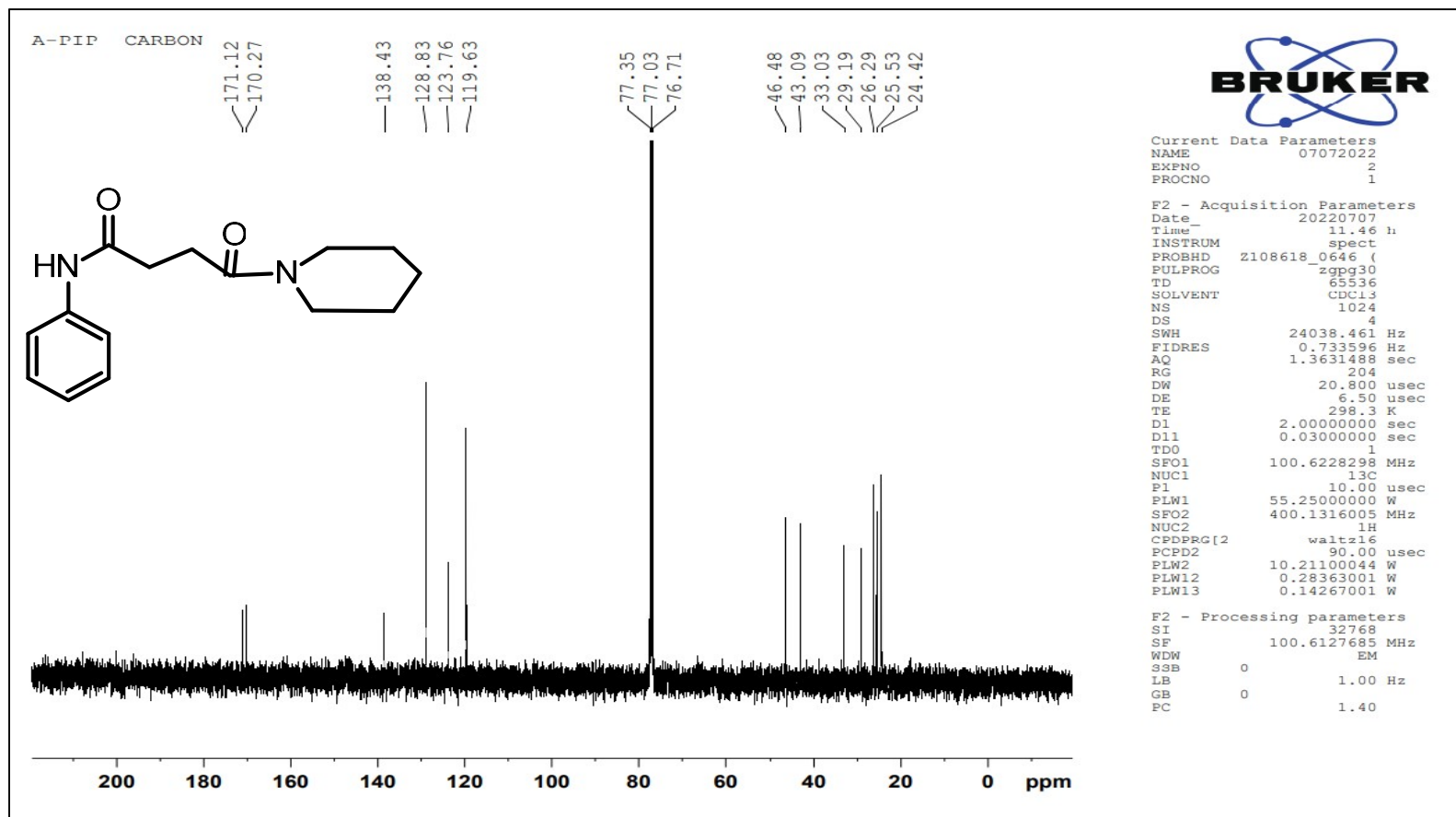


Fig. 11: IR Spectrum of 4-oxo-N-phenyl-4-(pyrrolidin-1-yl)butanamide (1f)

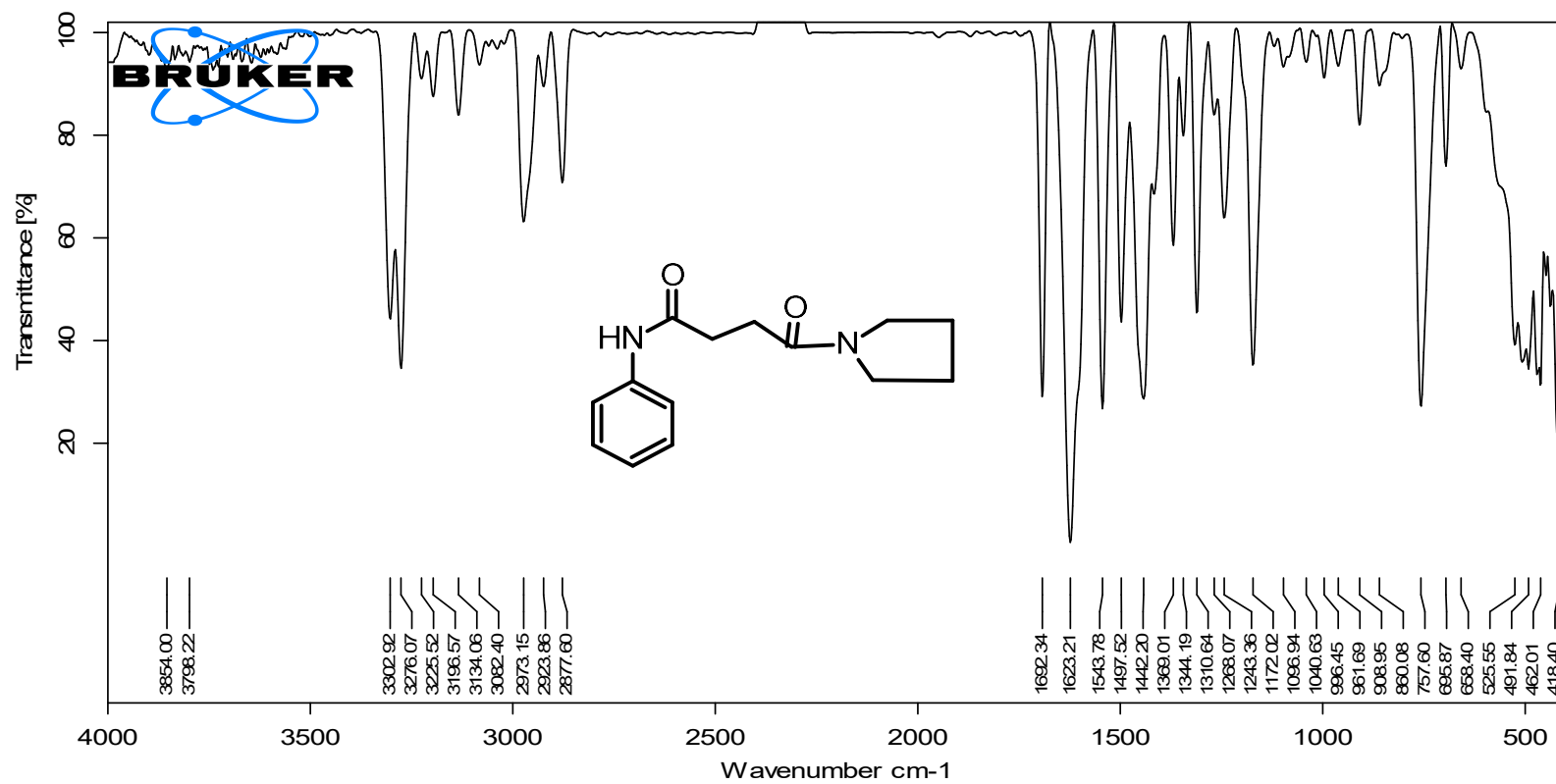


Fig. 12: ^1H NMR Spectrum of 4-oxo-*N*-phenyl-4-(pyrrolidin-1-yl)butanamide (1f)

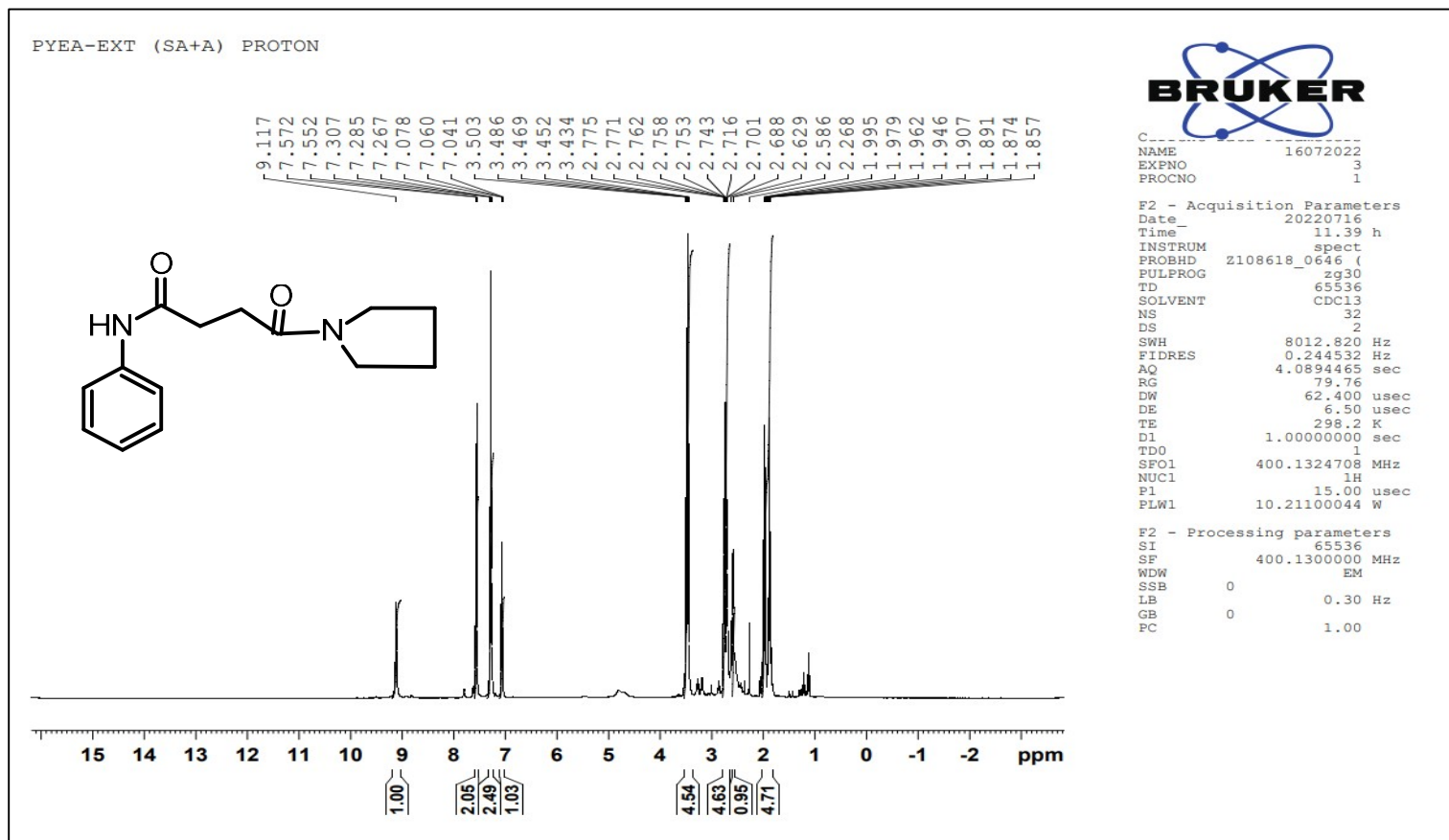


Fig. 13: ^{13}C NMR Spectrum of 4-oxo-*N*-phenyl-4-(pyrrolidin-1-yl)butanamide (1f)

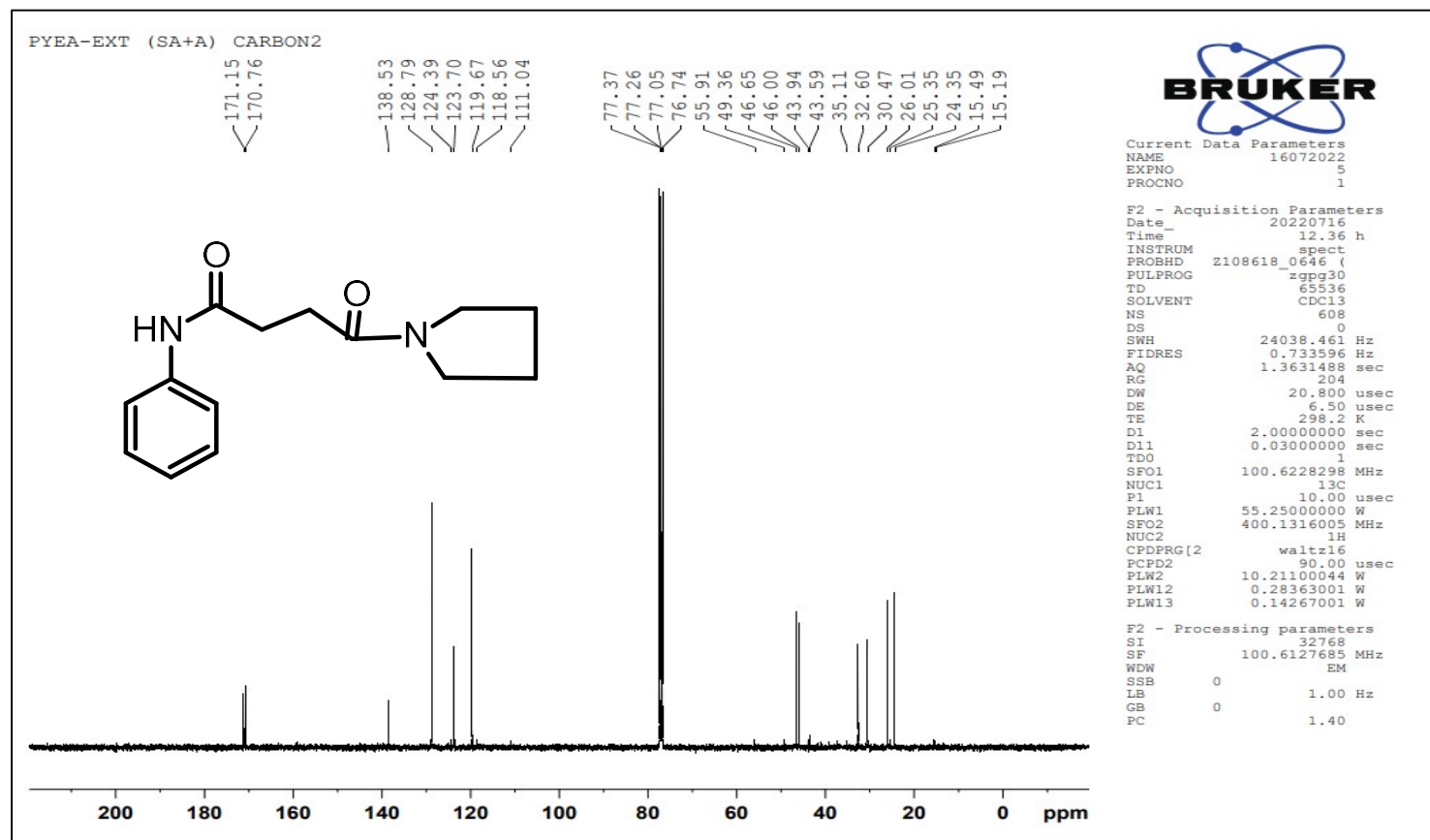


Fig. 14: IR Spectrum of N^1,N^1 -diethyl- N^4 -phenylbutanediamide (1g)

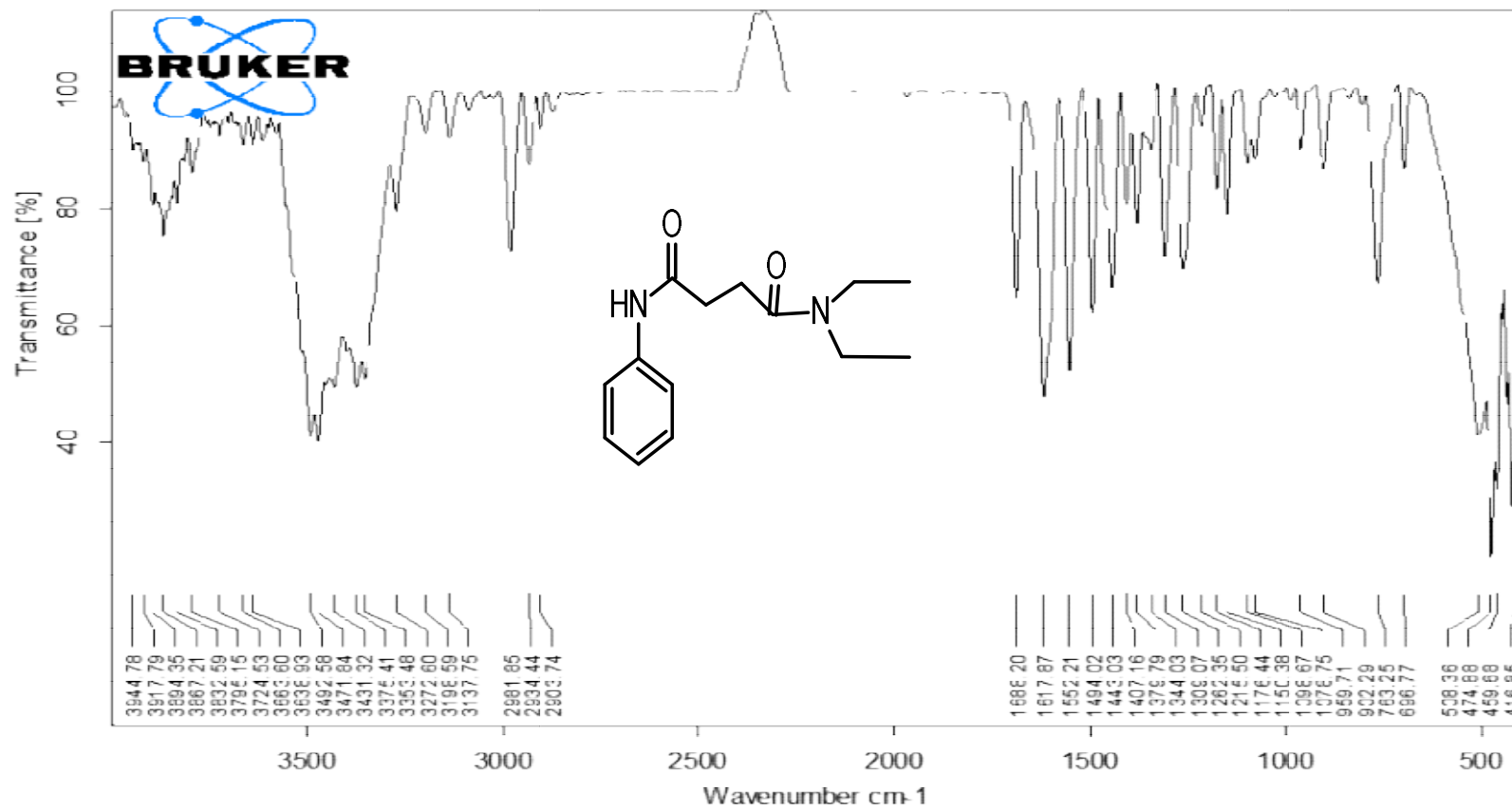


Fig. 15: ^1H NMR Spectrum of N^1, N^1 -diethyl- N^4 -phenylbutanediamide (1g)

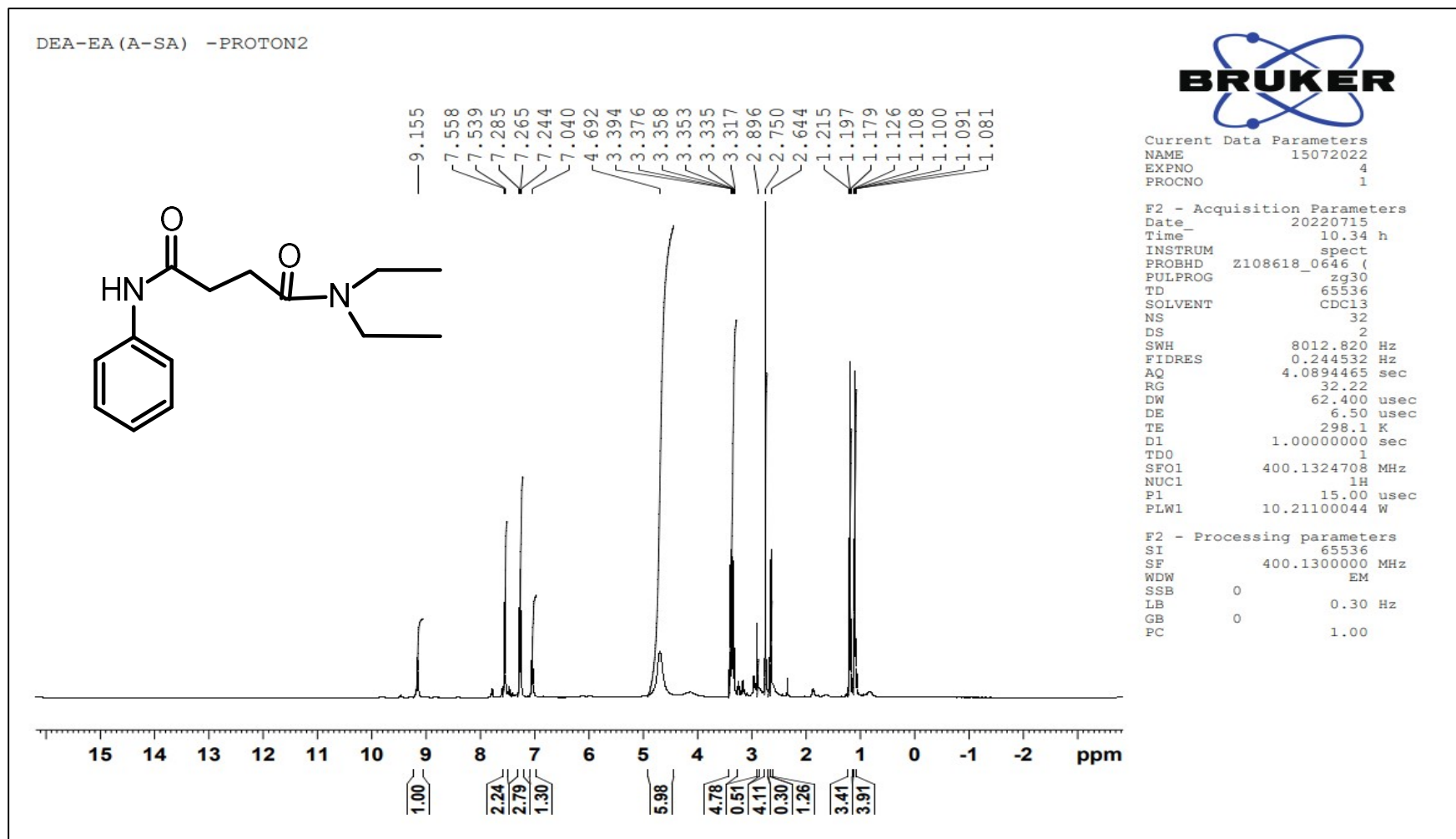


Fig. 16: ^{13}C NMR Spectrum of N^1,N^1 -diethyl- N^4 -phenylbutanediamide (1g)

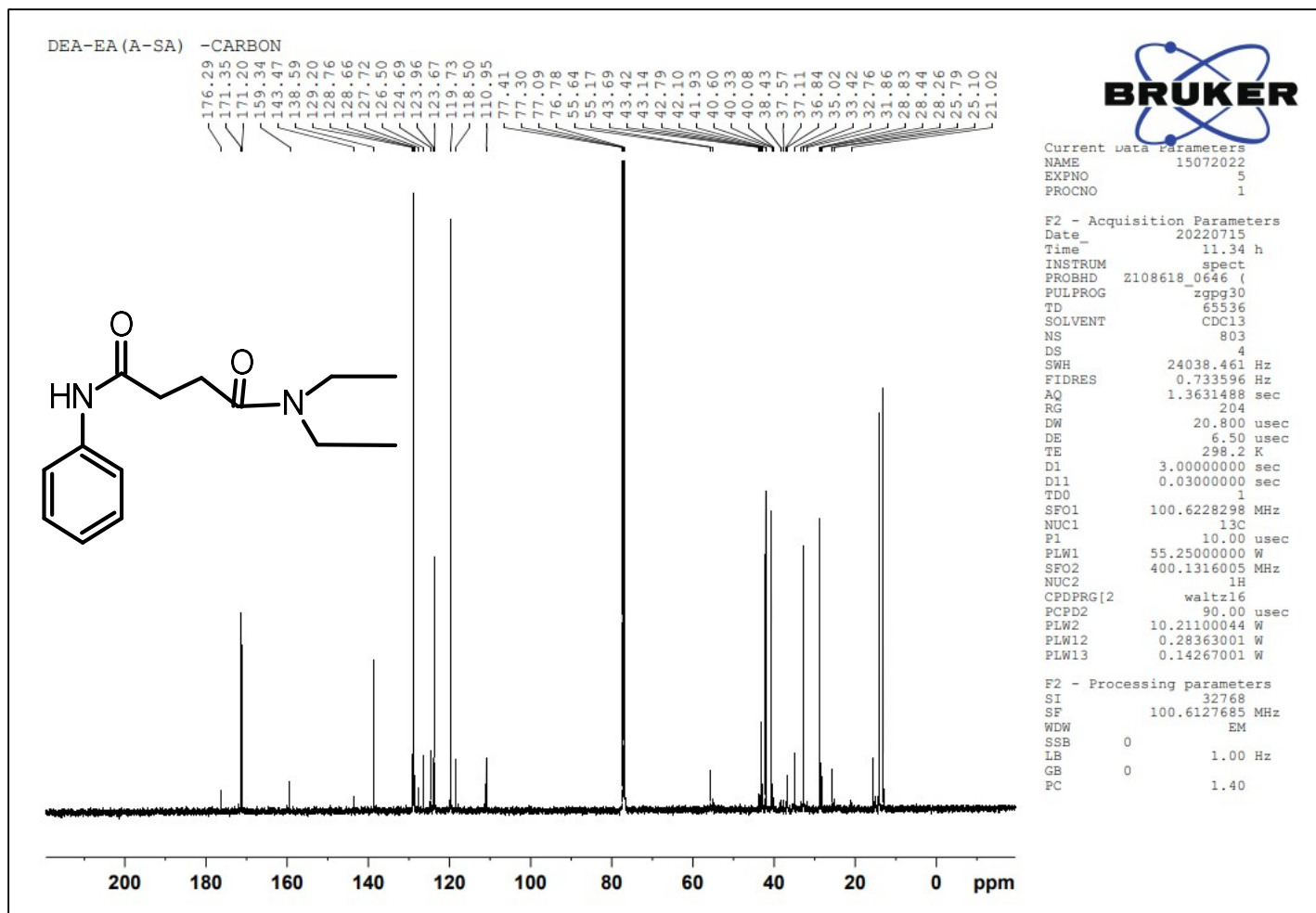


Fig. 17: IR Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide(2c)

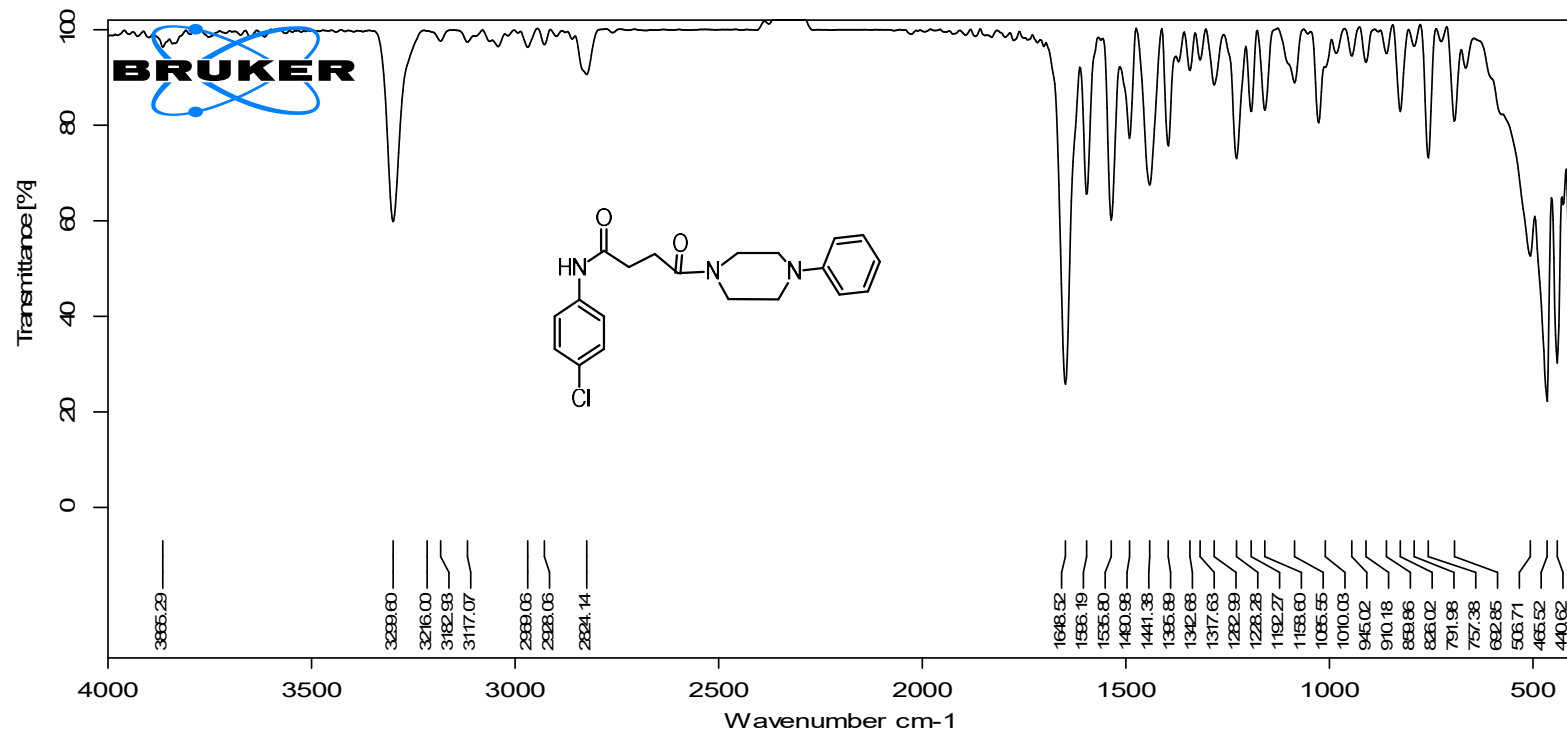


Fig. 18: ^1H NMR Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide(2c)

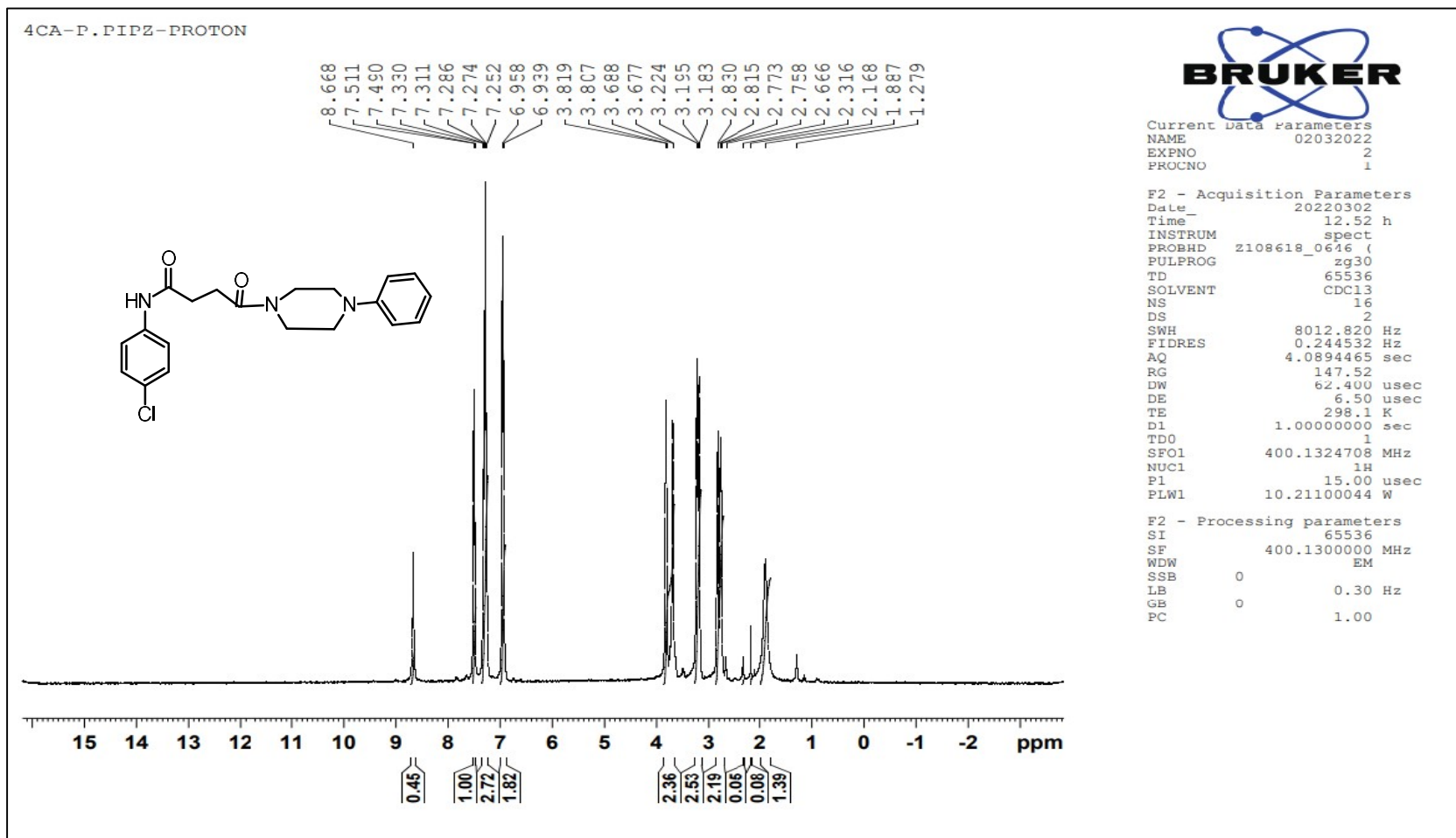


Fig. 19: ^{13}C NMR Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide(2c)

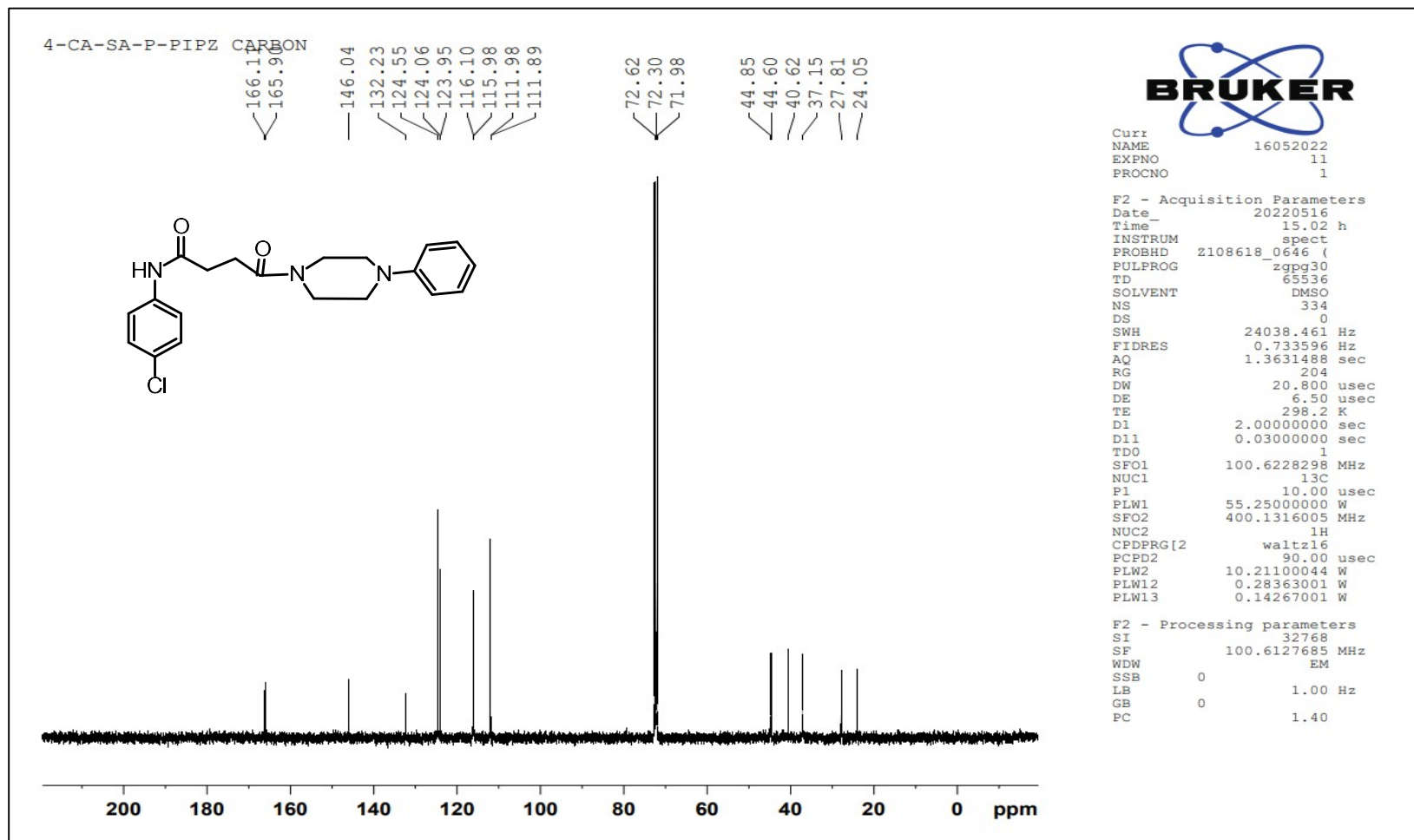


Fig. 20: IR Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide(2d)

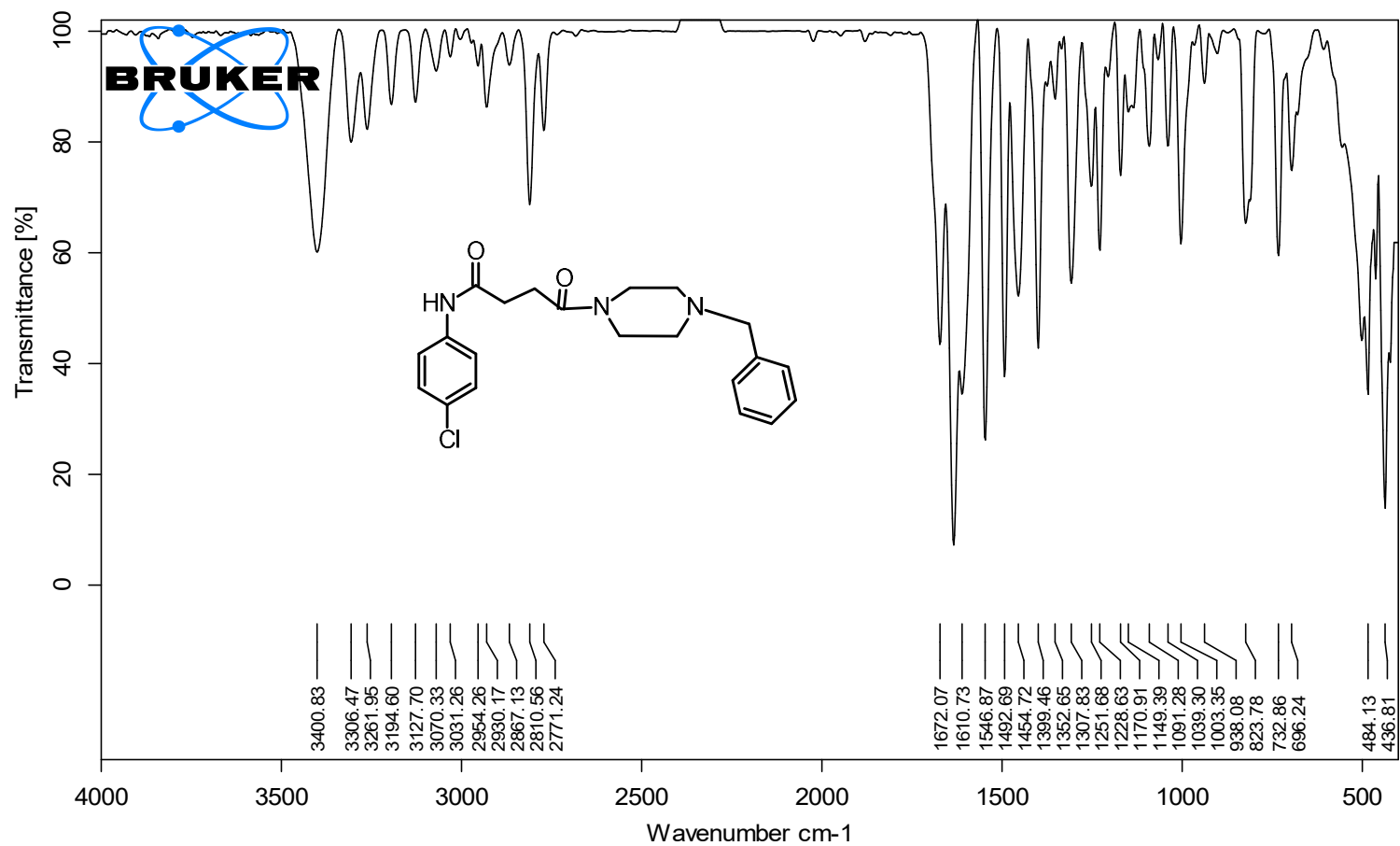


Fig. 21: ^1H NMR Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide(2d)

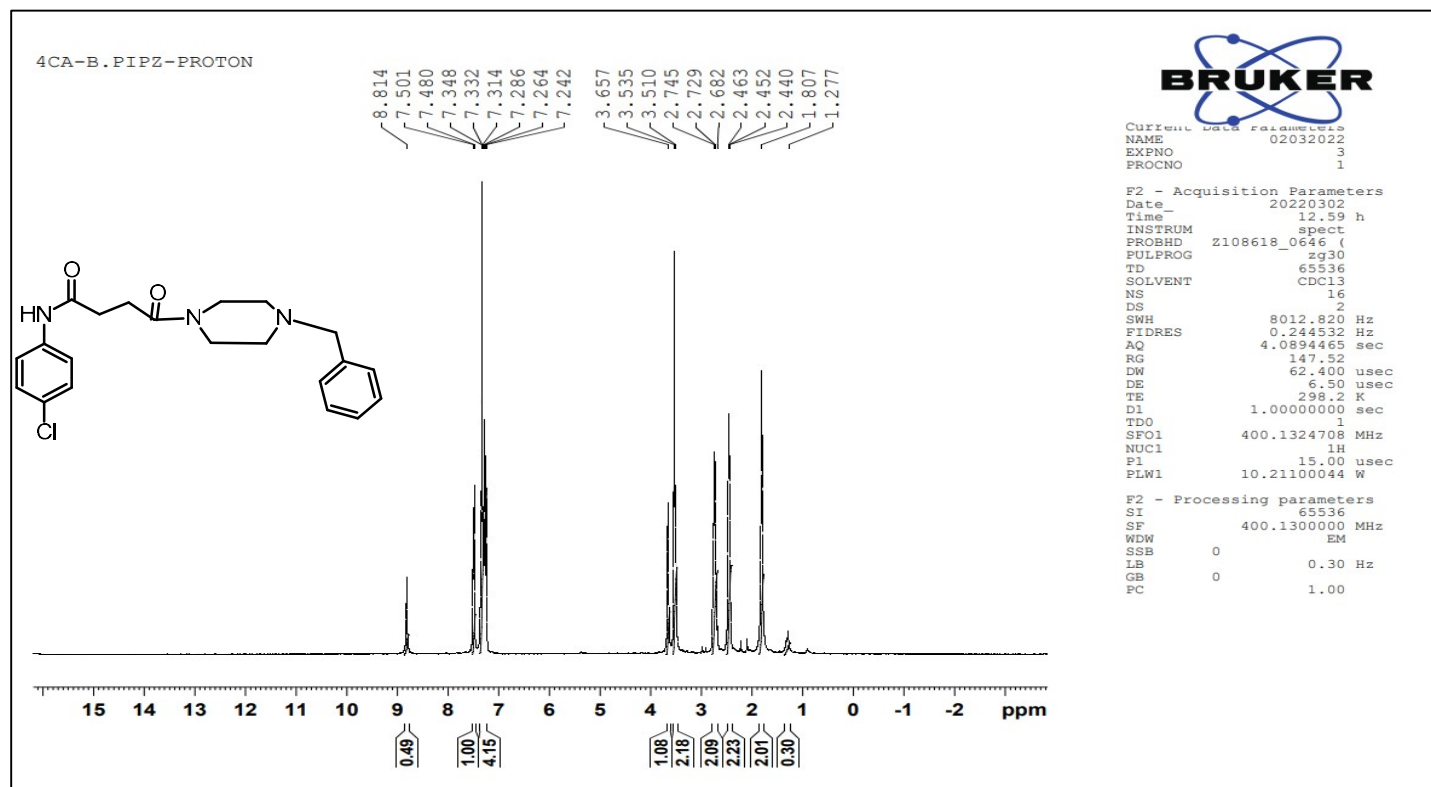


Fig. 22: ^{13}C NMR Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide(2d)

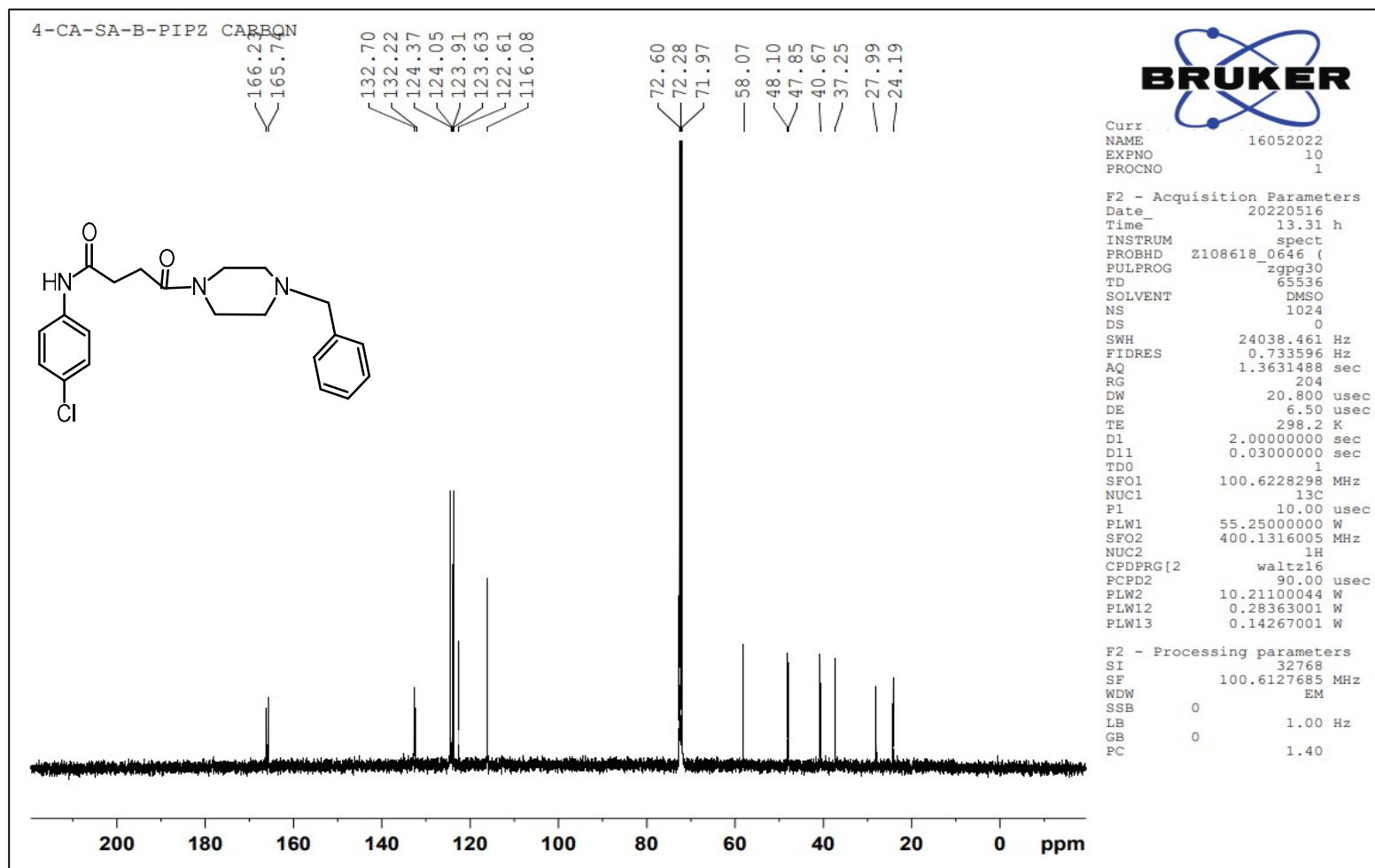


Fig. 23: Mass Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide(2d)

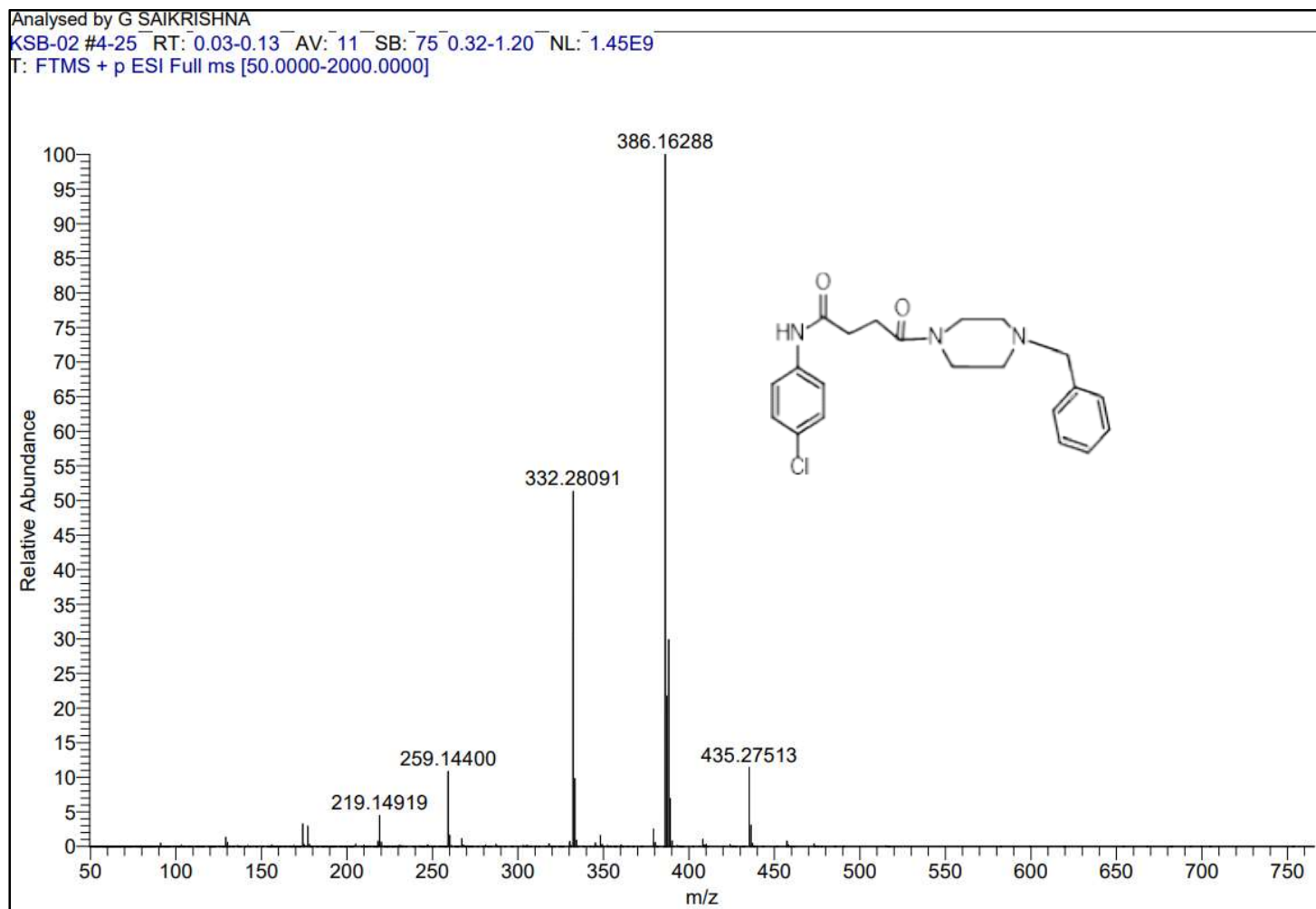


Fig. 24: IR Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide (2e)

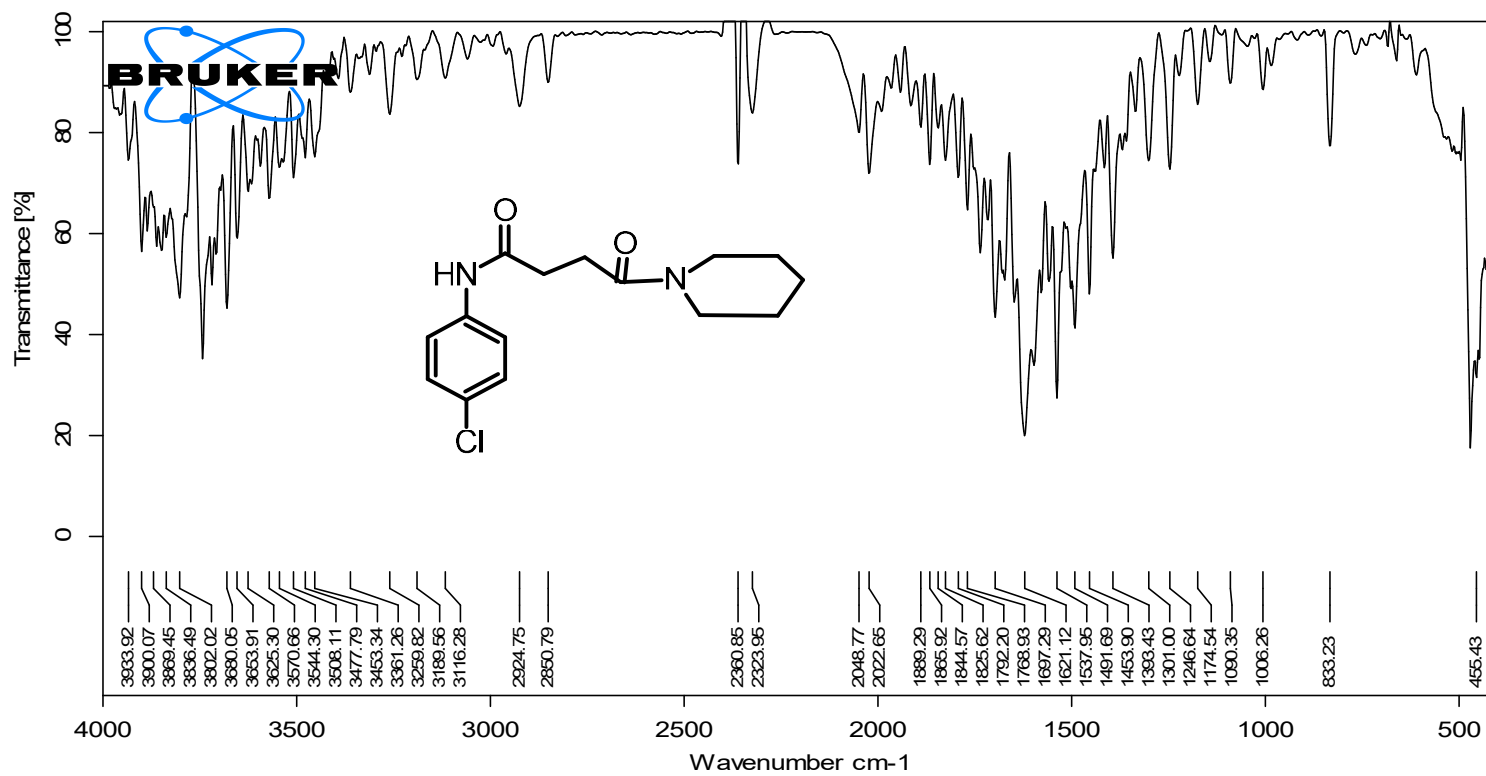


Fig. 25: ^1H NMR Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide (2e)

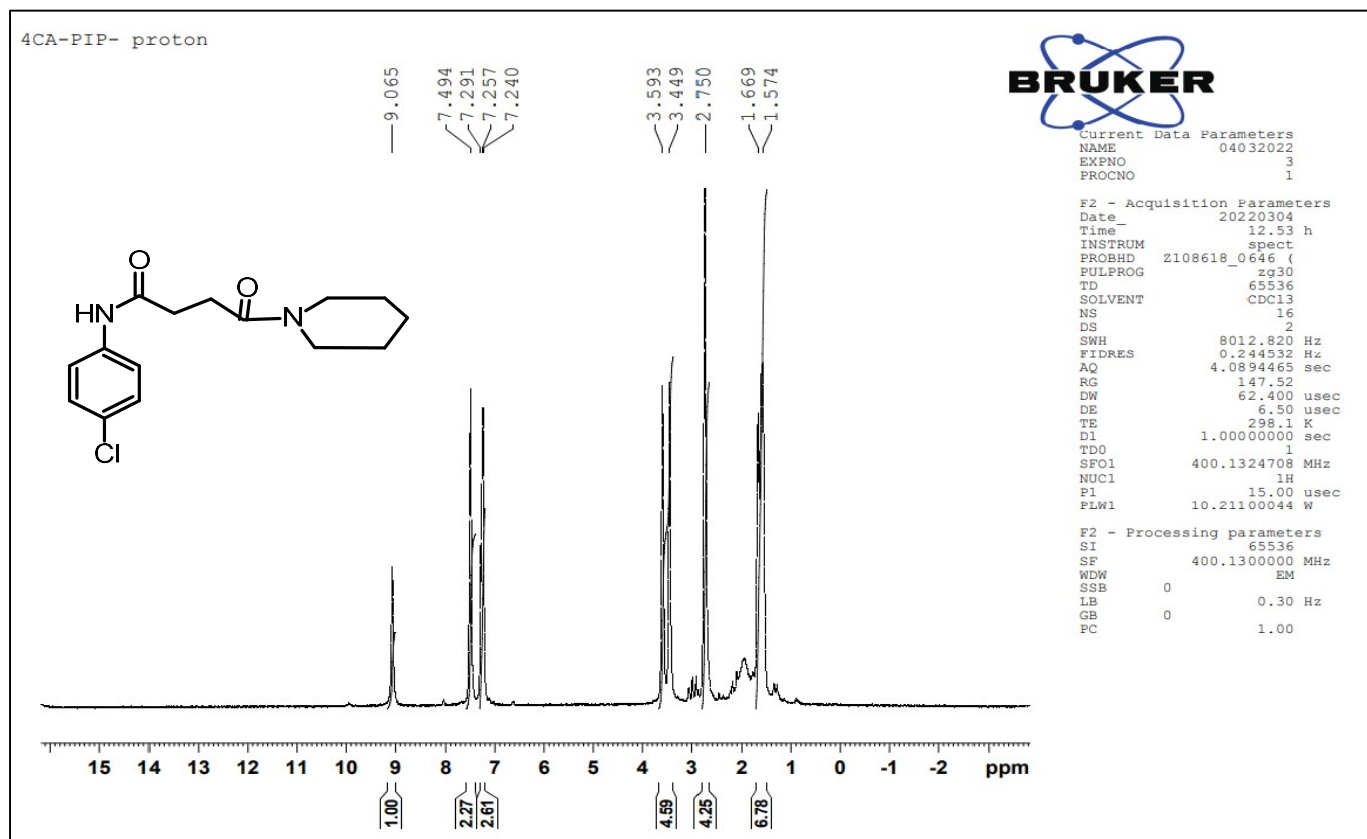


Fig. 26: ^{13}C NMR Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide (2e)

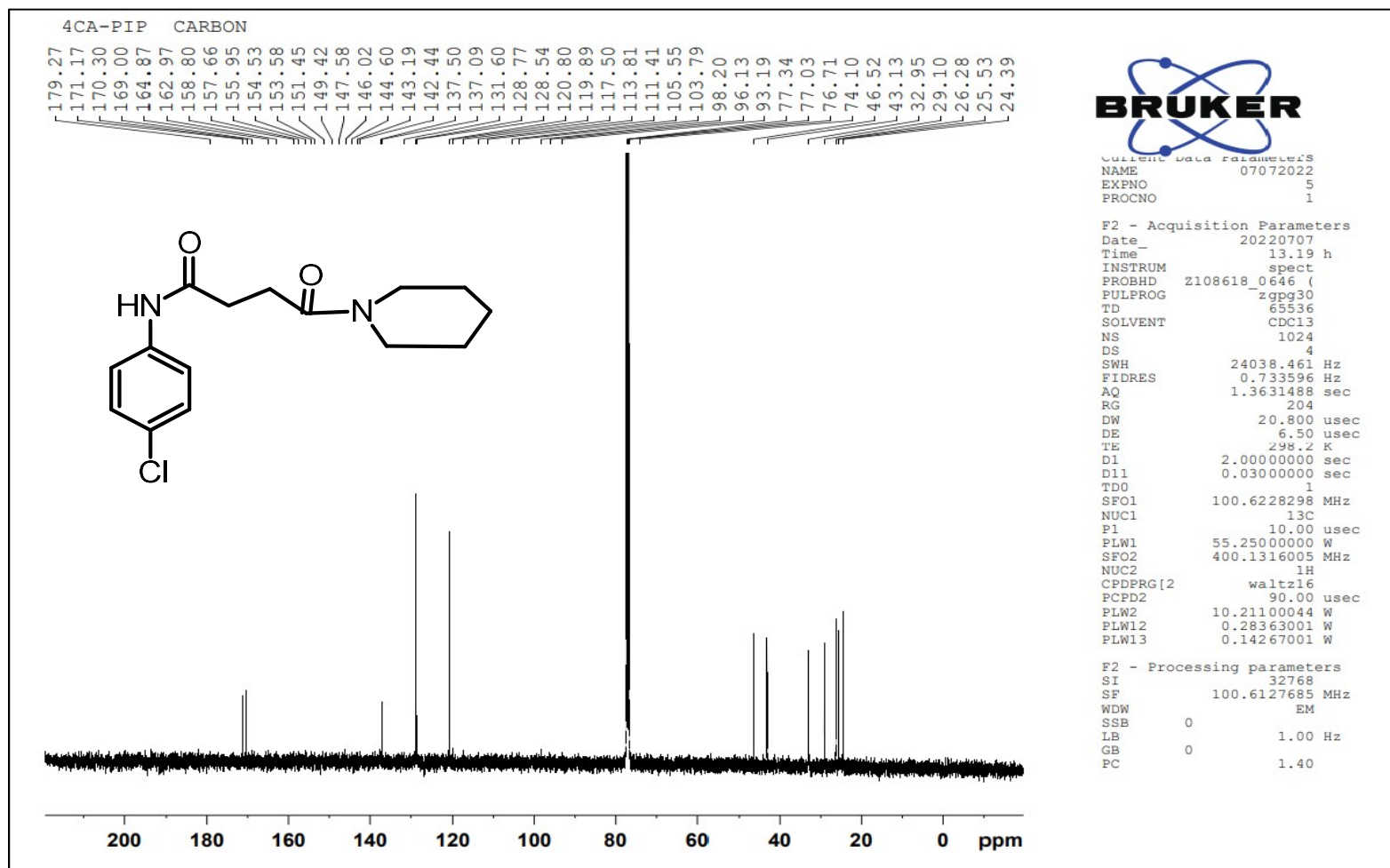


Fig. 27: IR Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide (2f)

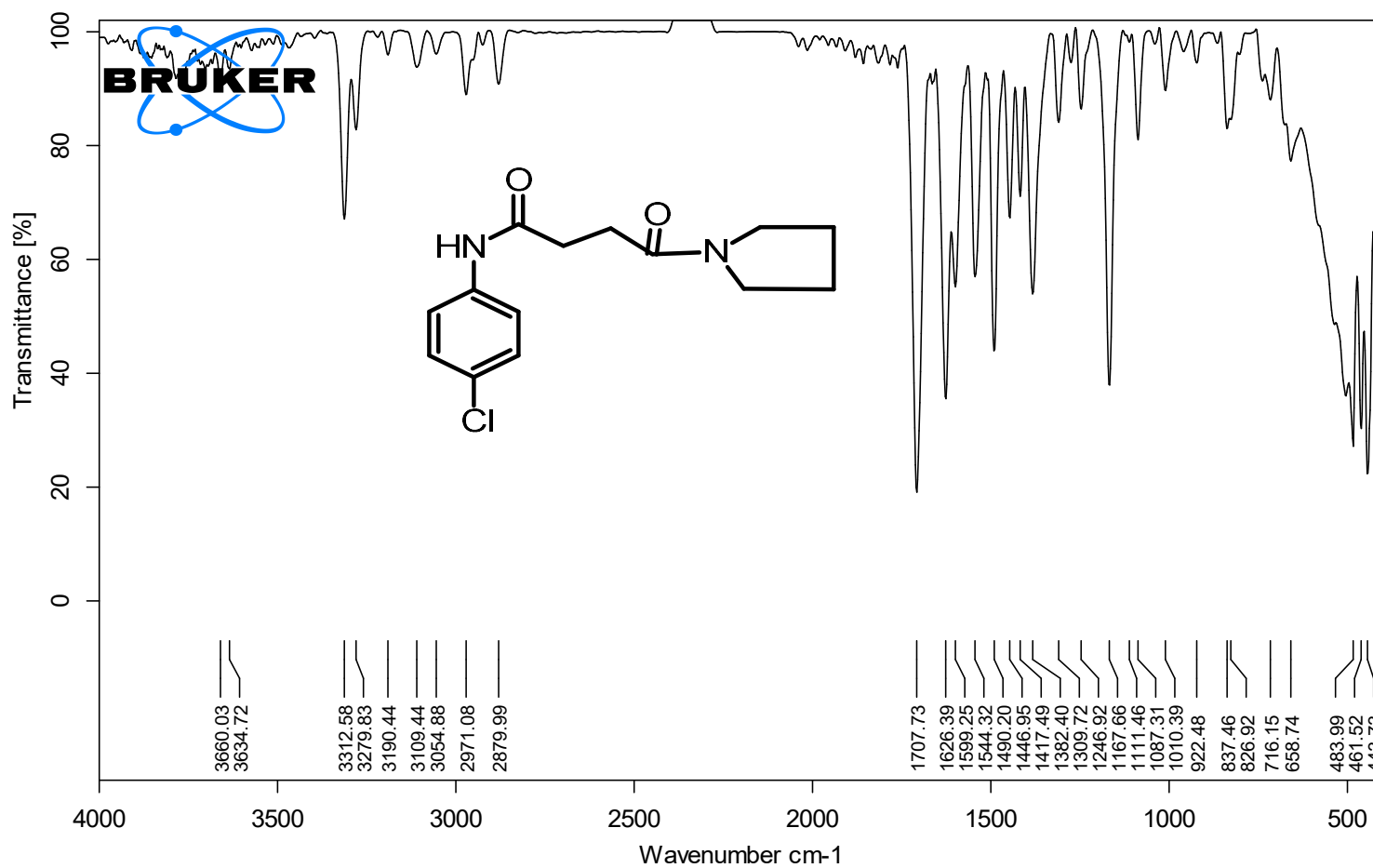


Fig. 28: ^1H NMR Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide (2f)

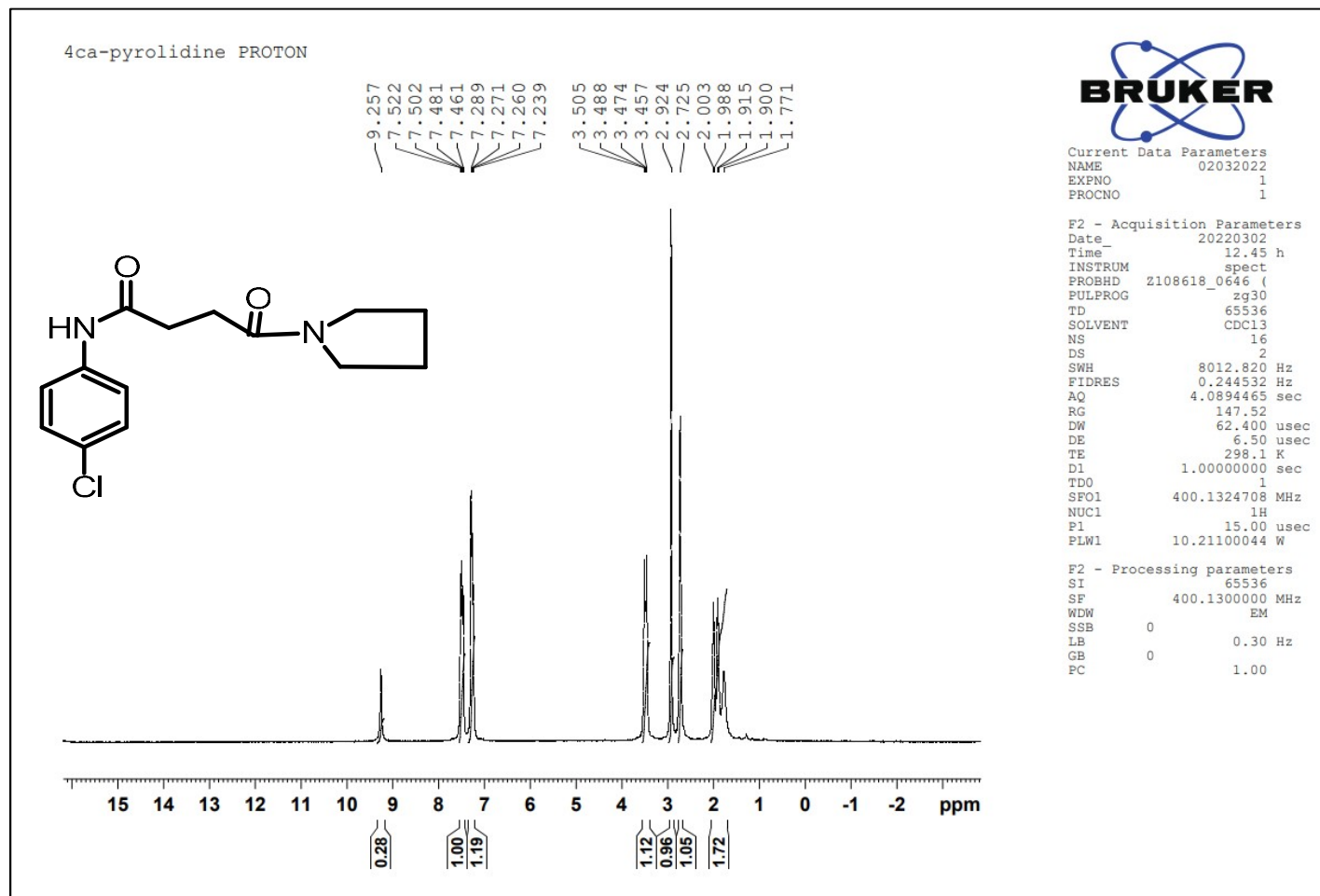


Fig. 29: ^{13}C NMR Spectrum of *N*-(4-chlorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide (2f)

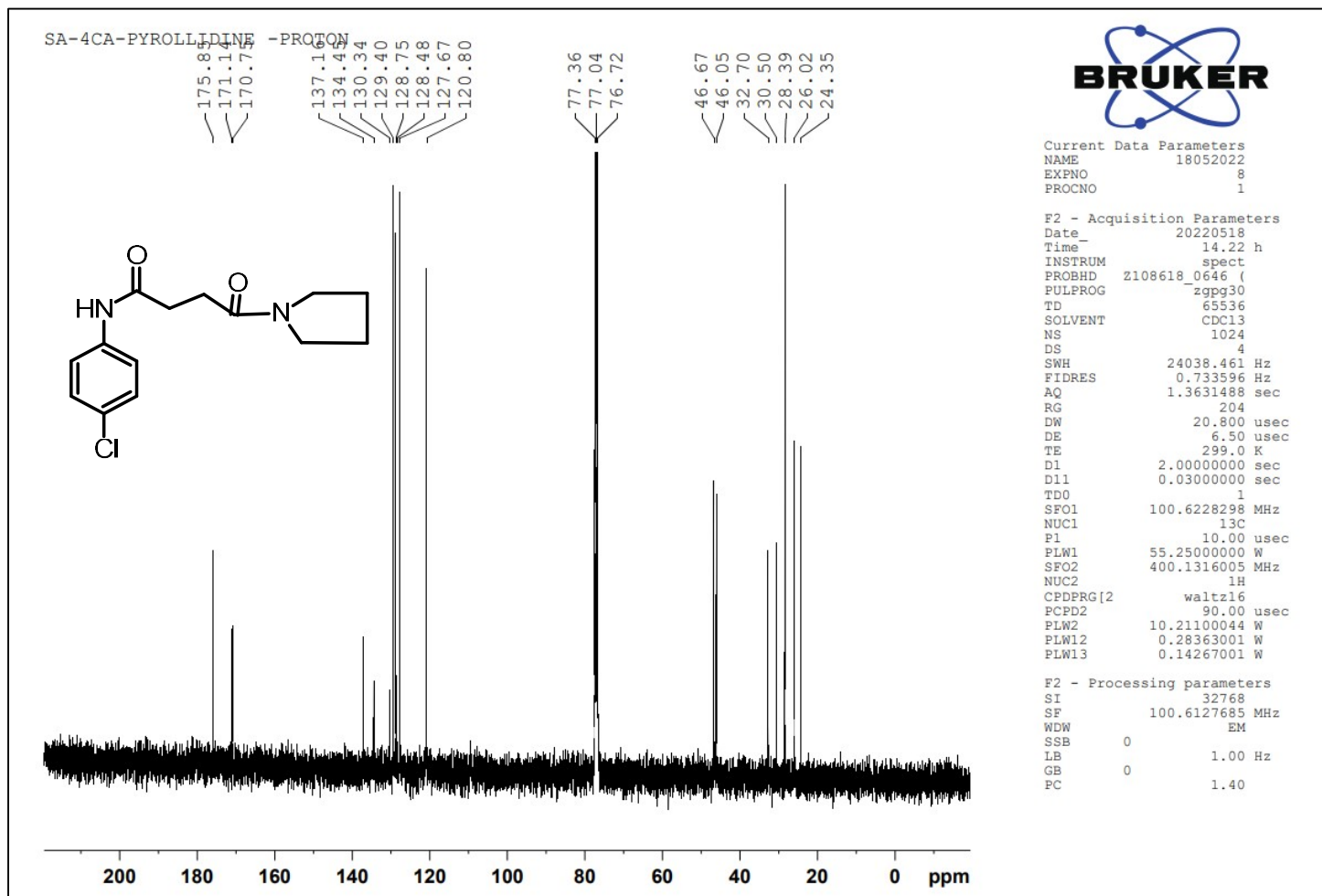


Fig. 30: IR Spectrum of N^4 -(4-chlorophenyl)- N^1,N^1 -diethylbutanediamide(2g)

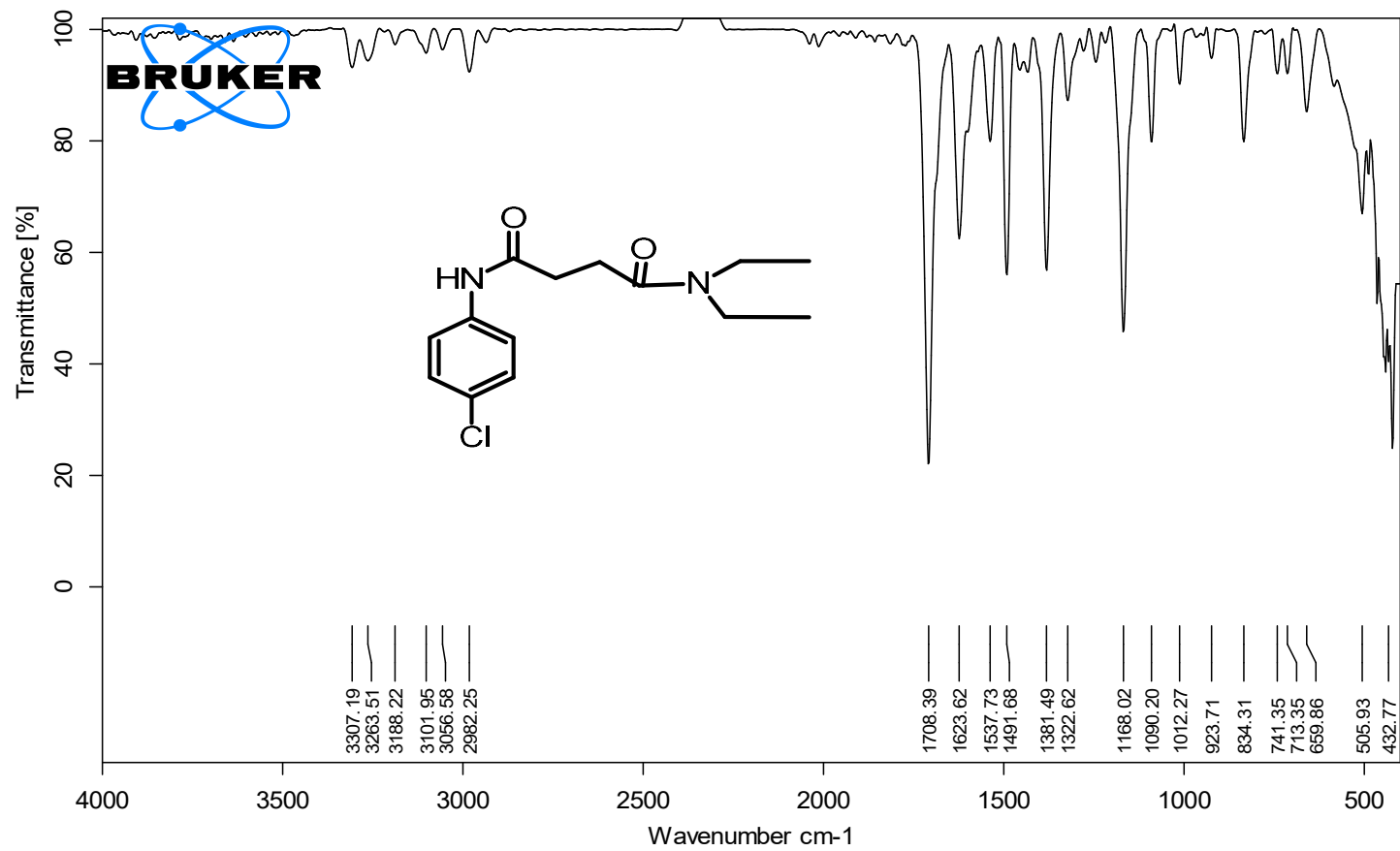


Fig. 31: ^1H NMR Spectrum of N^4 -(4-chlorophenyl)- N^1,N^1 -diethylbutanediamide(2g)

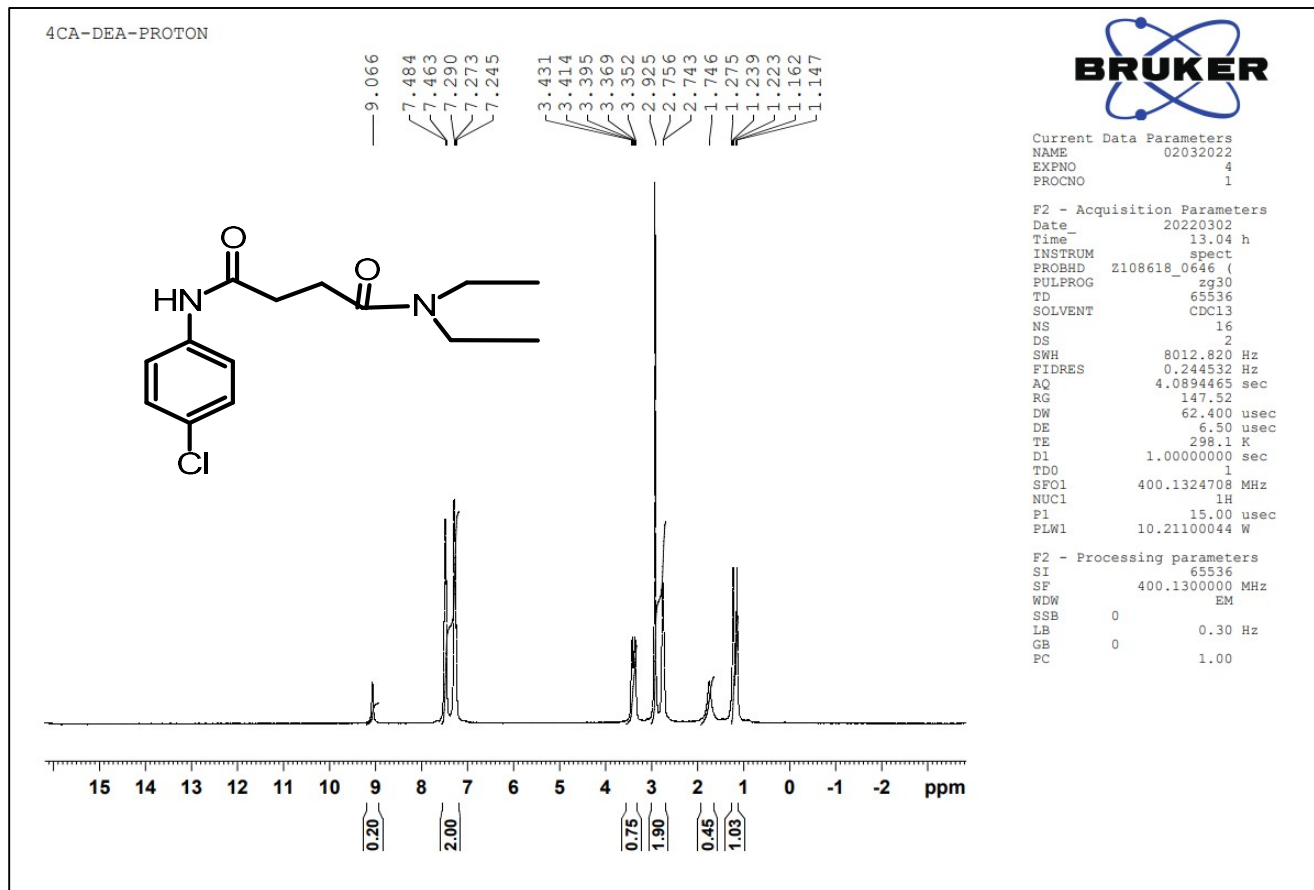


Fig. 32: ^{13}C NMR Spectrum of N^4 -(4-chlorophenyl)- N^1,N^1 -diethylbutanediamide(2g)

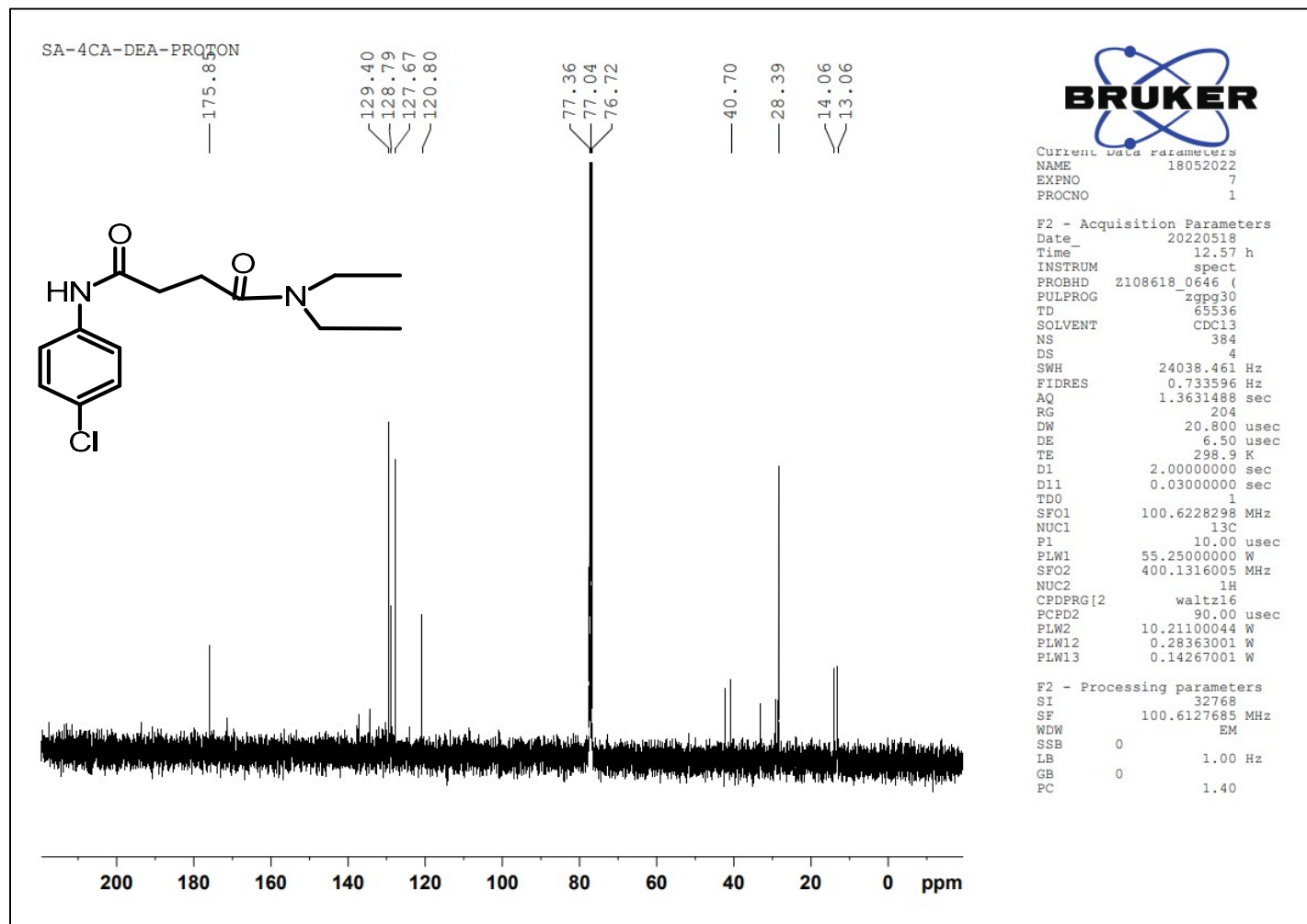


Fig. 33: IR Spectrum of *N*-(4-methylphenyl)-4-(4-phenylpiperazin-1-yl)-4-oxobutanamide(3c)

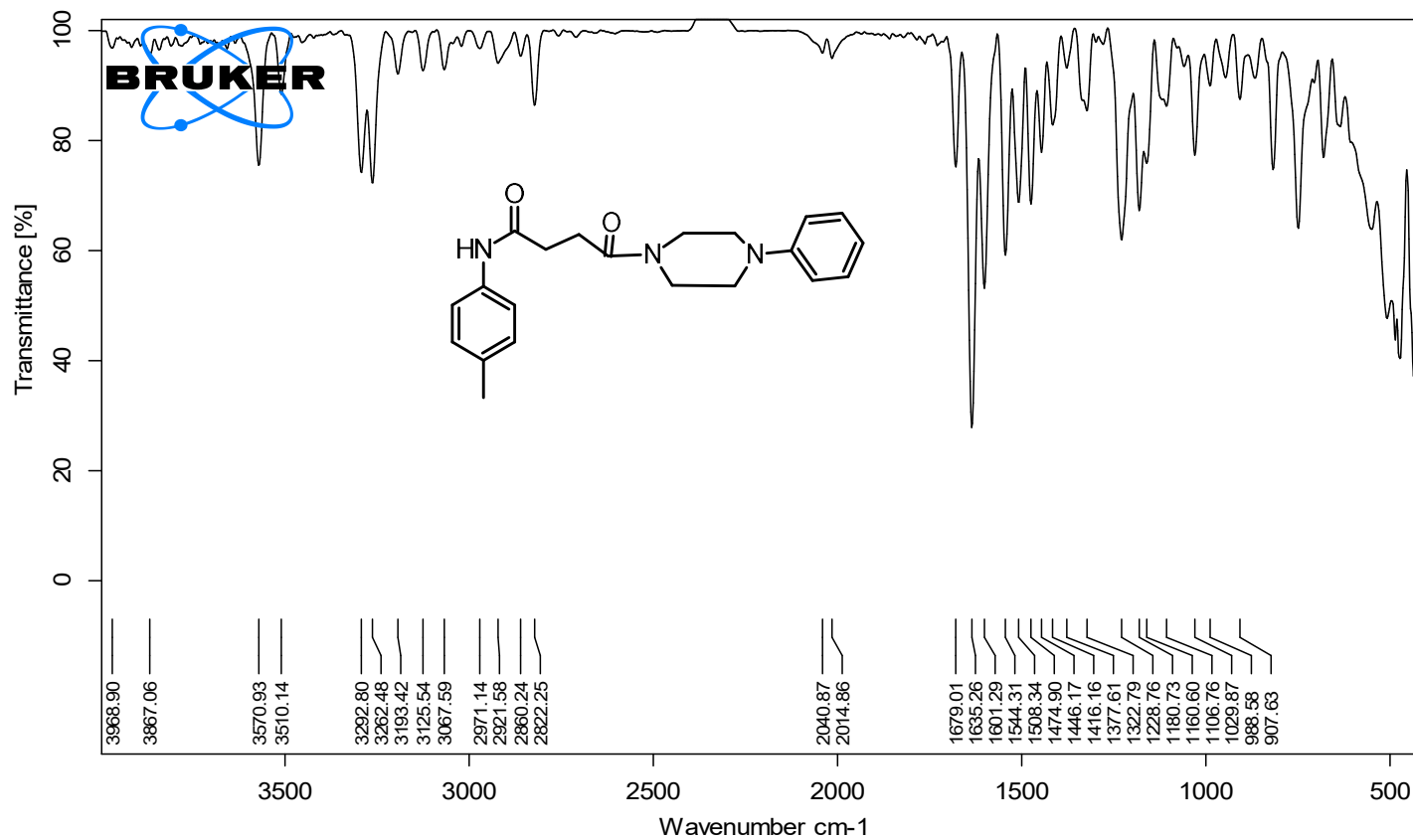


Fig. 34: ¹H NMR Spectrum of *N*-(4-methylphenyl)-4-(4-phenylpiperazin-1-yl)-4-oxobutanamide(3c)

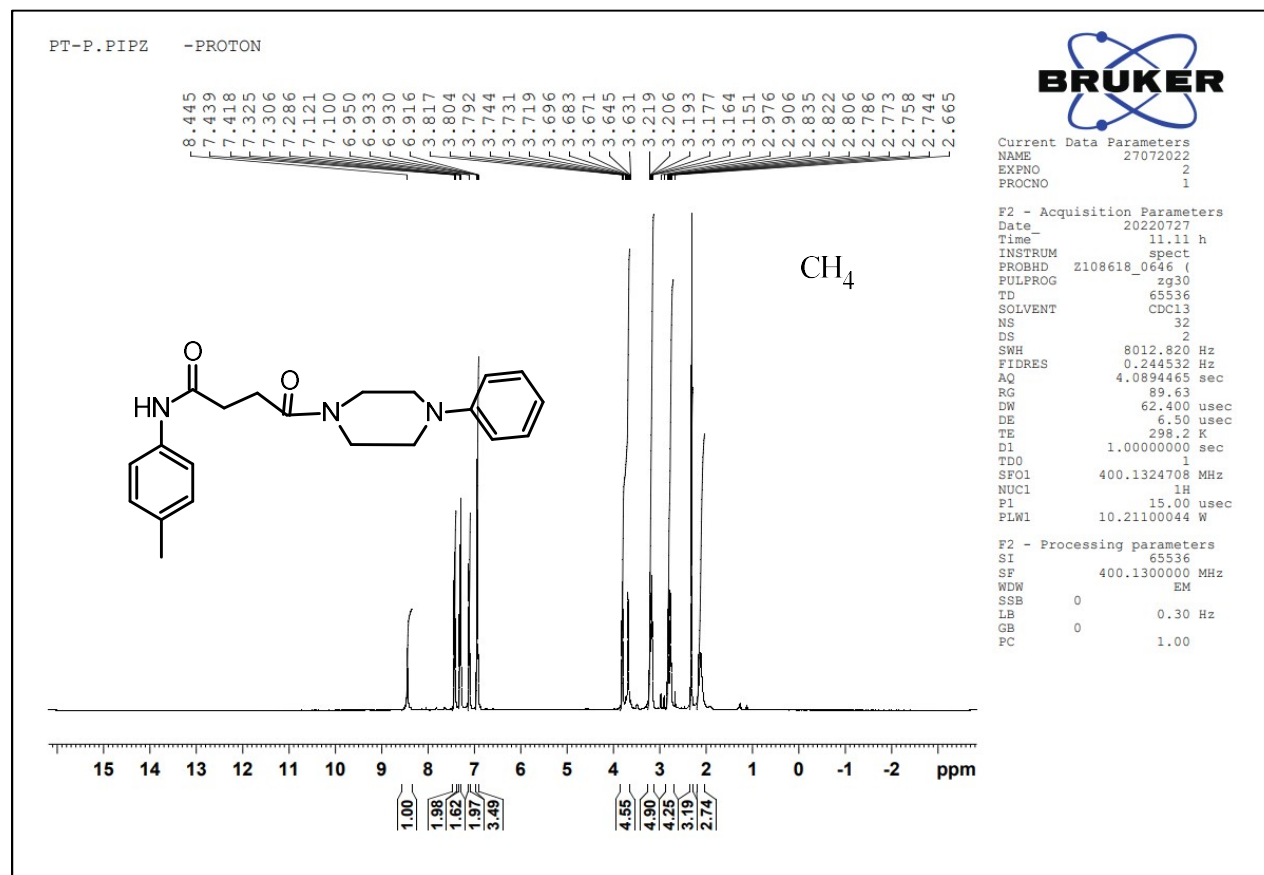


Fig. 35: ^{13}C NMR Spectrum of *N*-(4-methylphenyl)-4-(4-phenylpiperazin-1-yl)-4-oxobutanamide(3c)

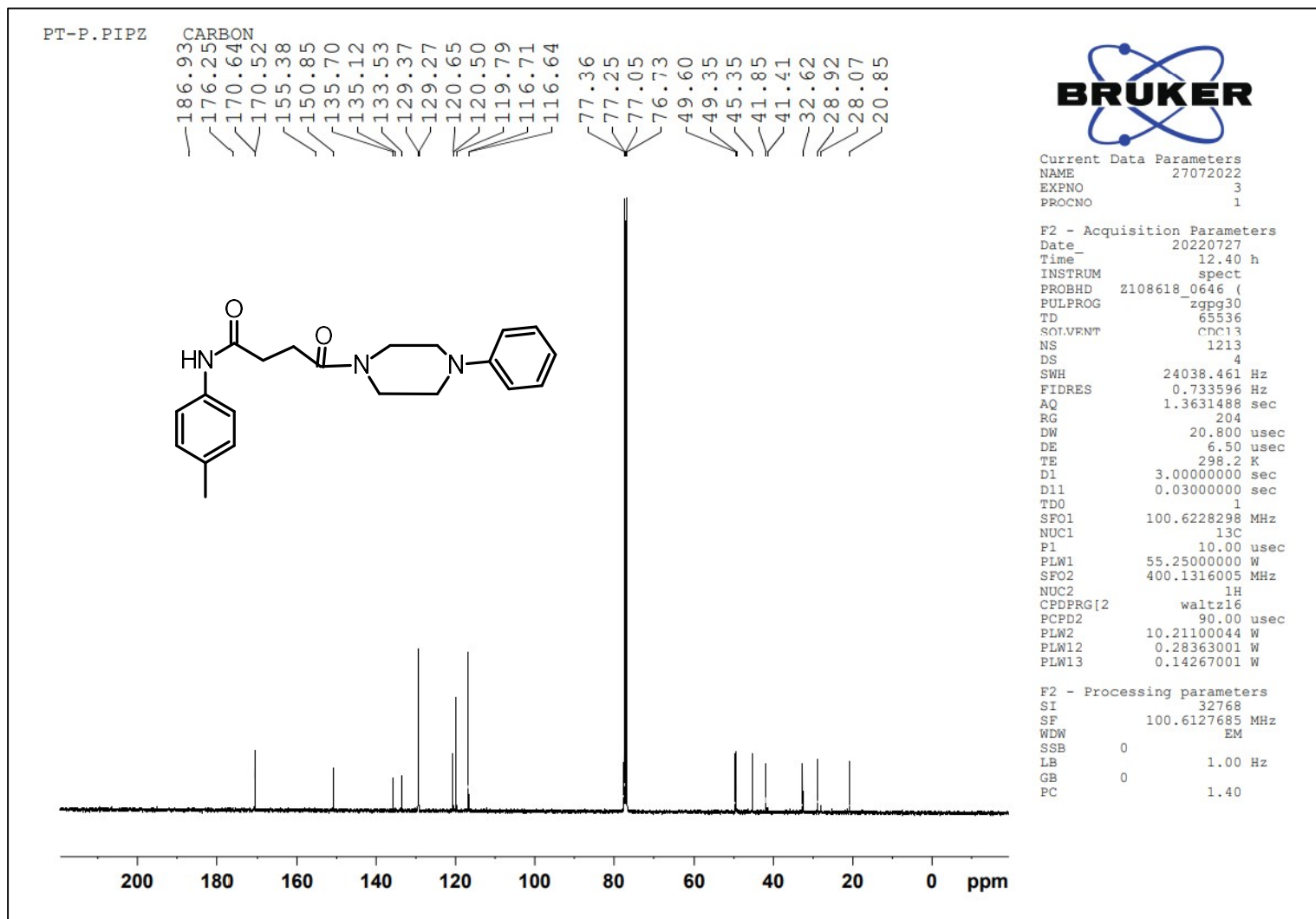


Fig. 36: IR Spectrum of *N*-(4-methylphenyl)-4-(4-benzylpiperazin-1-yl)-4-oxobutanamide(3d)

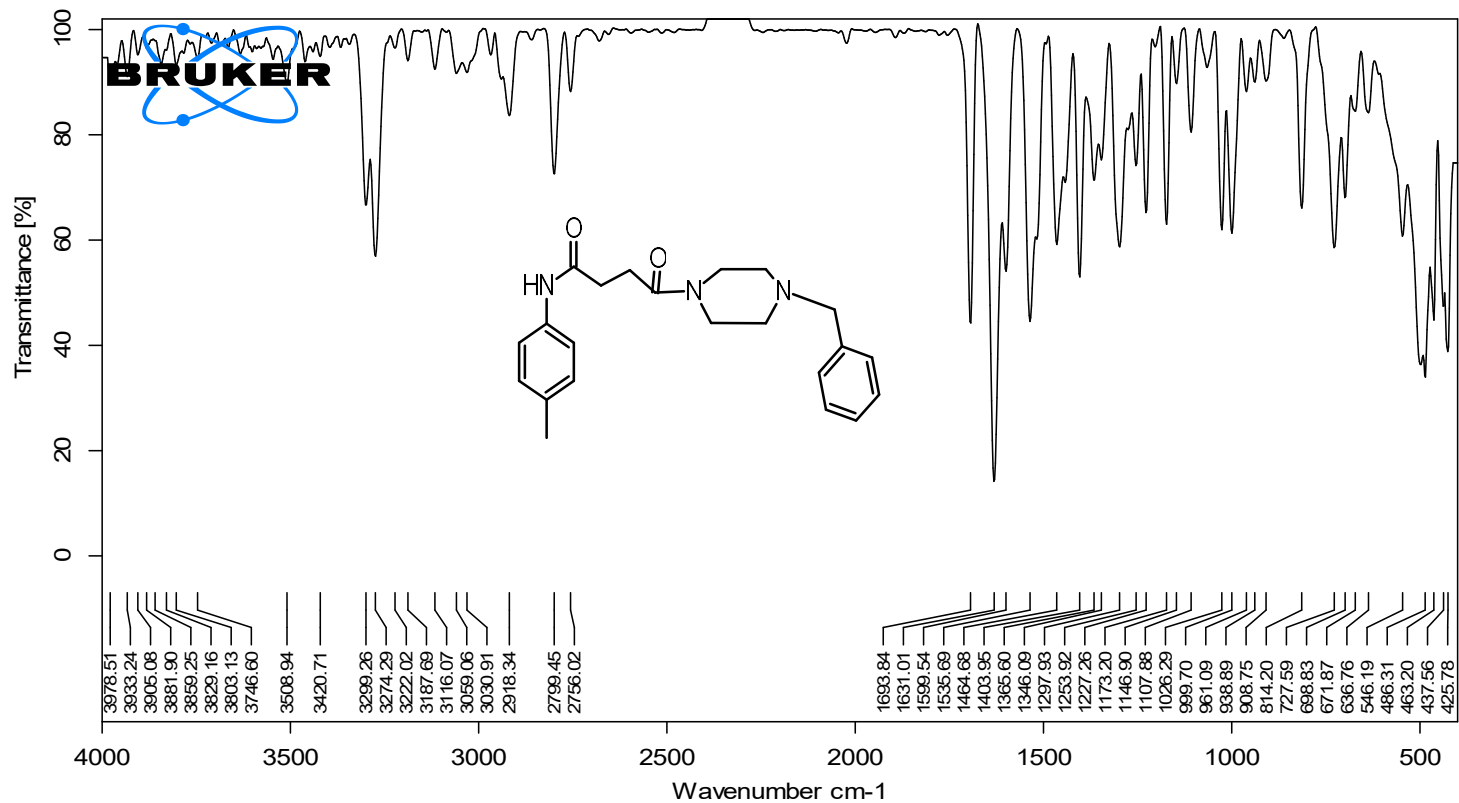


Fig. 37: ^1H NMR Spectrum of *N*-(4-methylphenyl)-4-(4-benzylpiperazin-1-yl)-4-oxobutanamide(3d)

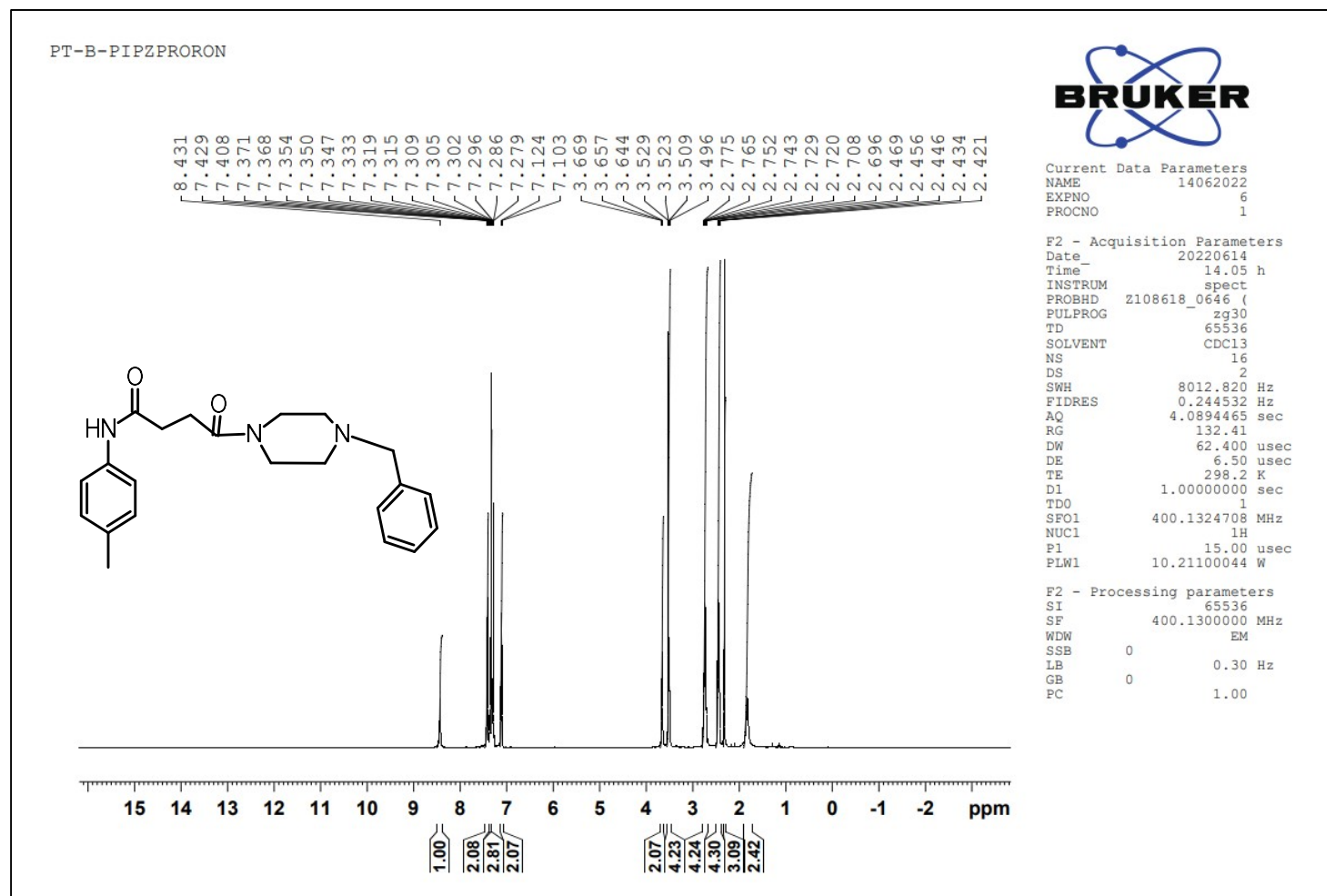


Fig. 38: ^{13}C NMR Spectrum of *N*-(4-methylphenyl)-4-(4-benzylpiperazin-1-yl)-4-oxobutanamide(3d)

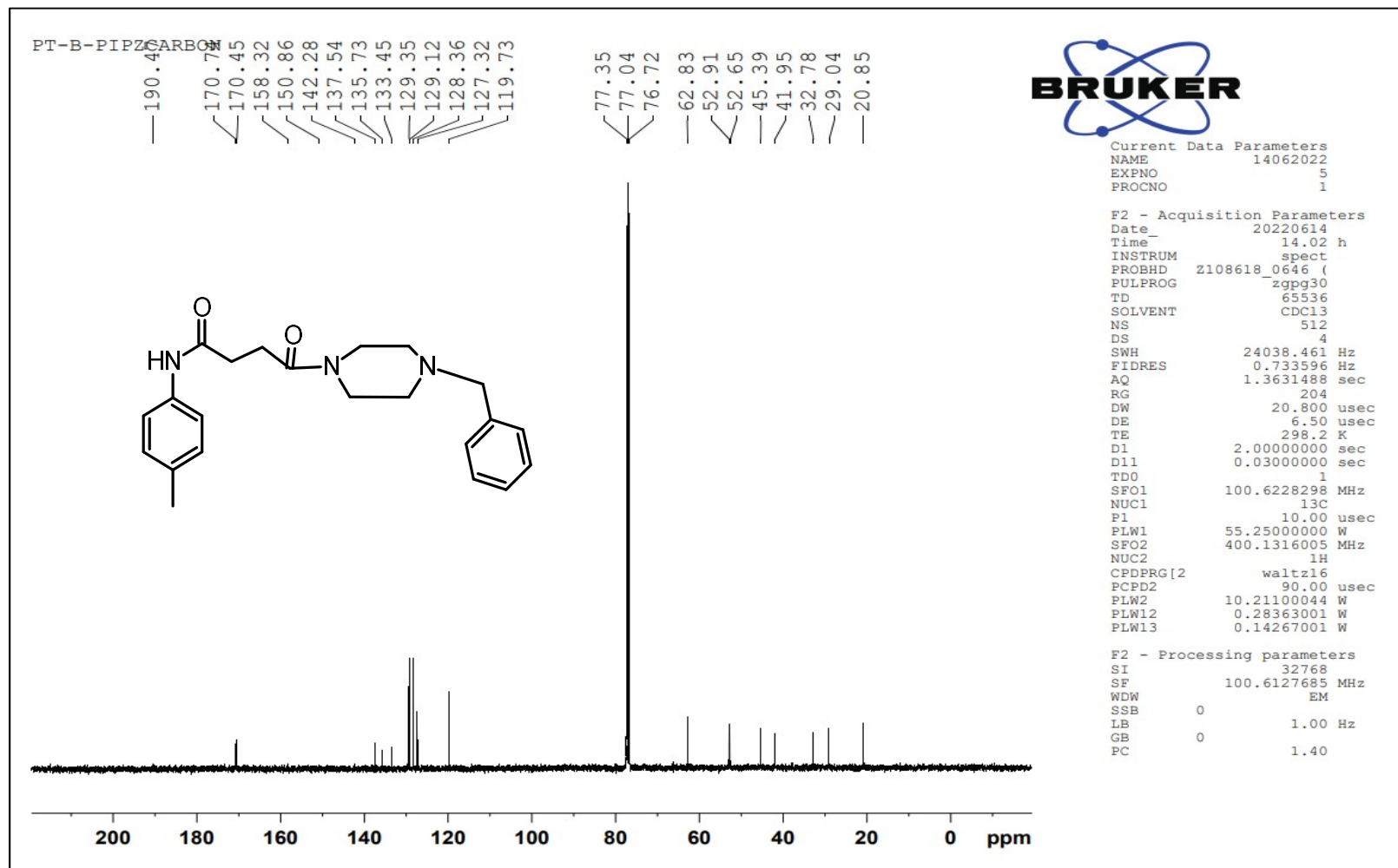


Fig. 39: IR Spectrum of *N*-(4-methylphenyl)-4-oxo-4-(piperidin-1-yl)butanamide(3e)

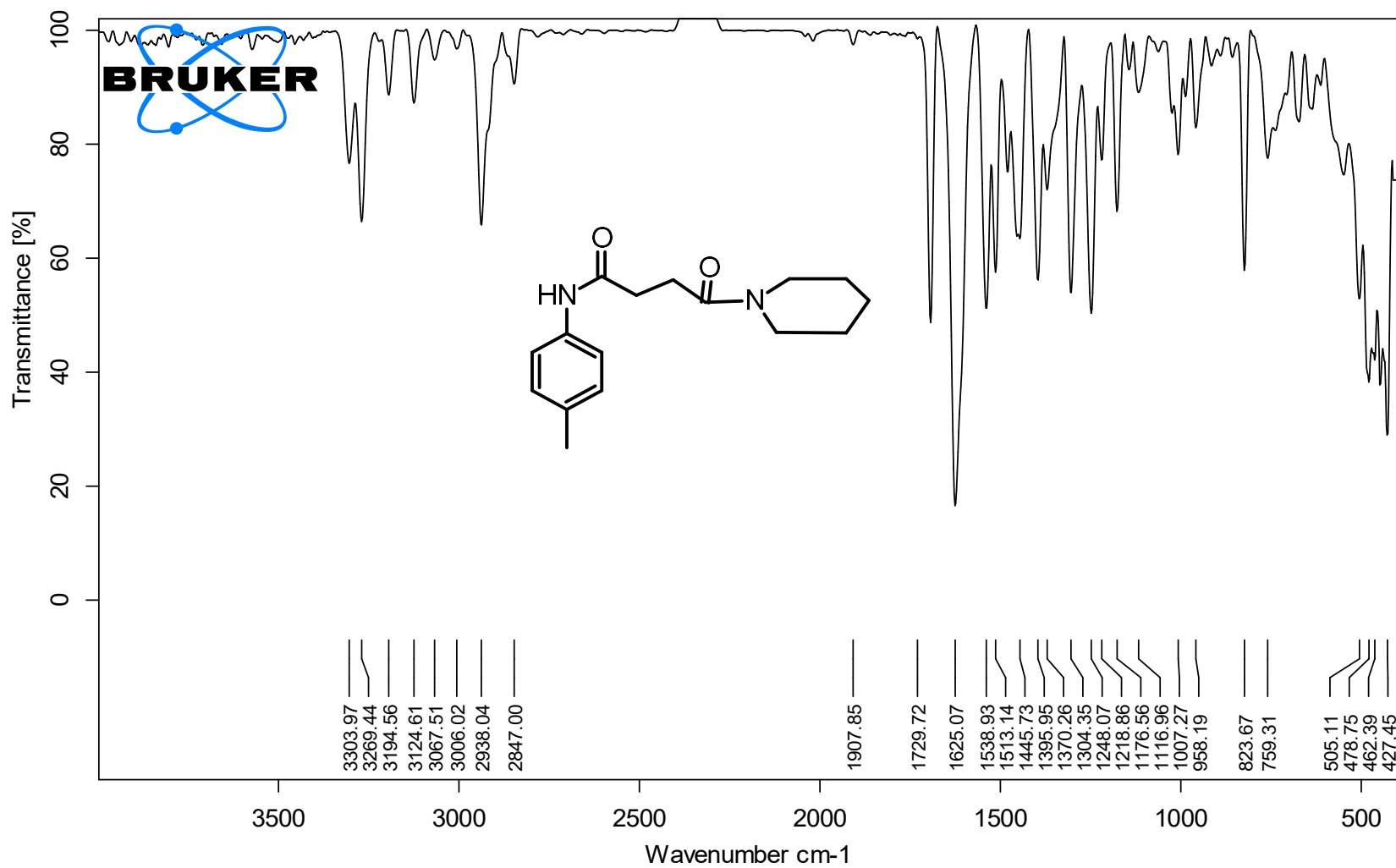


Fig. 40: ^1H NMR Spectrum of *N*-(4-methylphenyl)-4-oxo-4-(piperidin-1-yl)butanamide(3e)

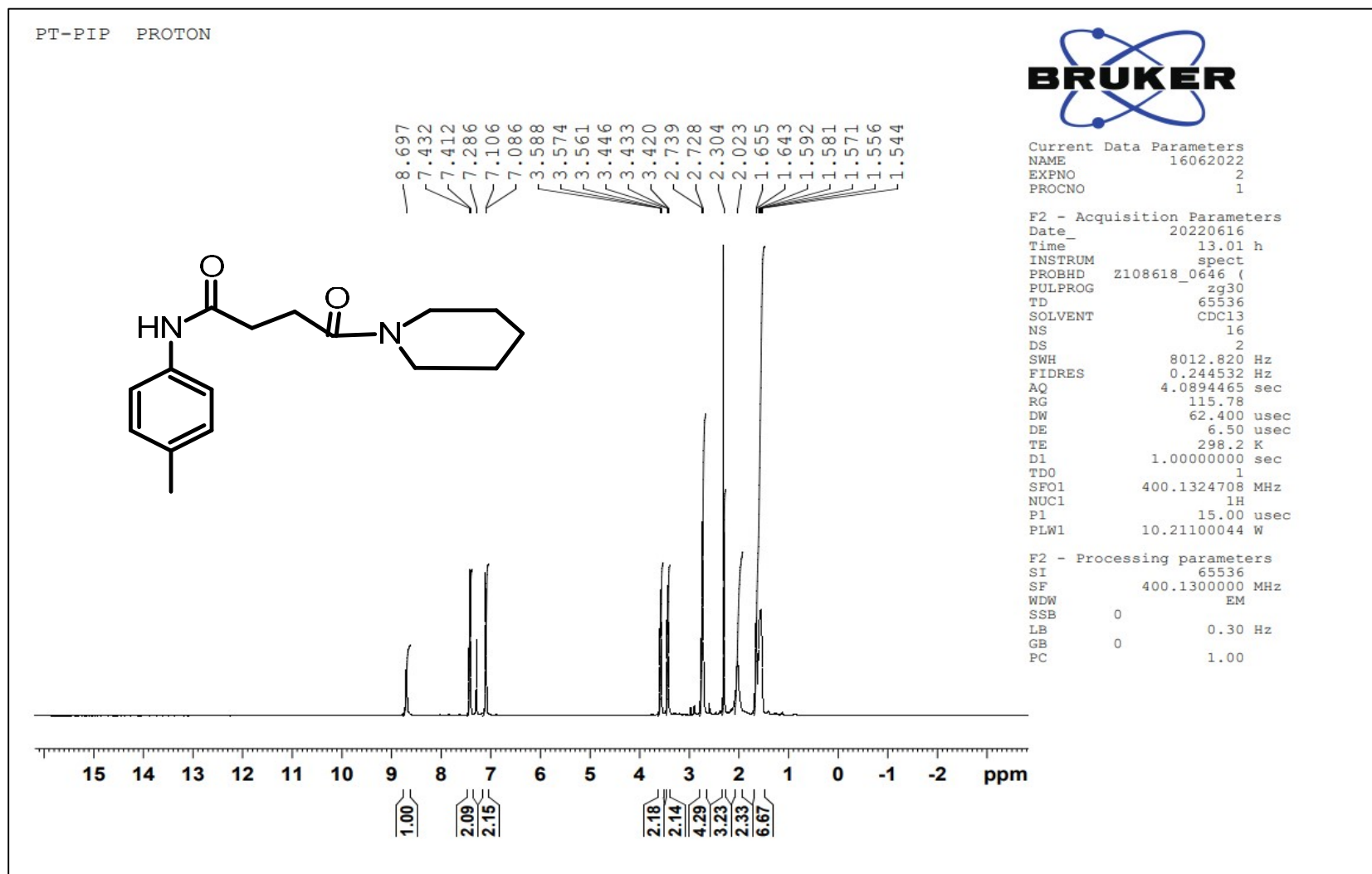


Fig. 41: ^{13}C NMR Spectrum of *N*-(4-methylphenyl)-4-oxo-4-(piperidin-1-yl)butanamide(3e)

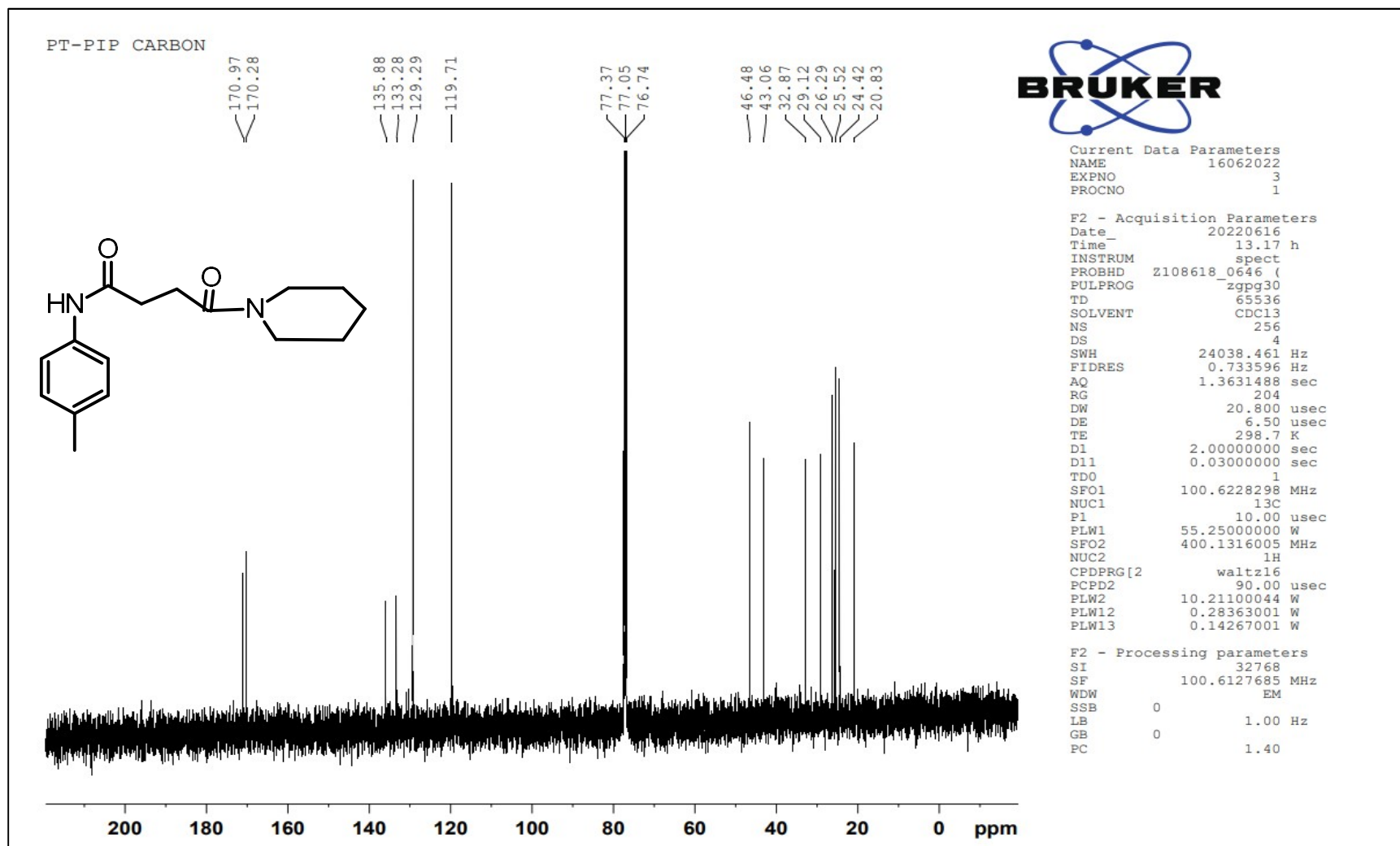


Fig. 42: IR Spectrum of *N*-(4-methylphenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide(3f)

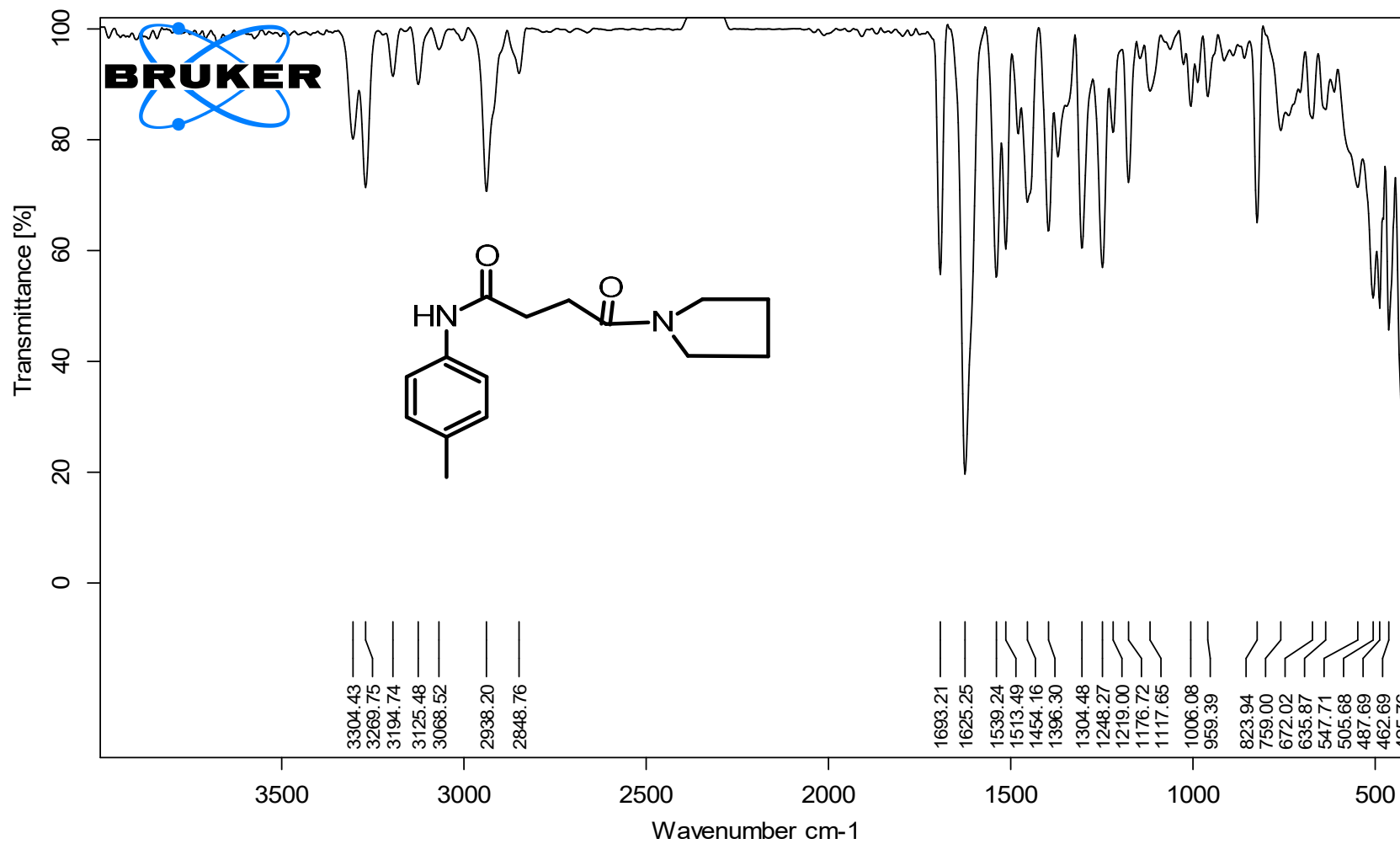


Fig. 43: ^1H NMR Spectrum of *N*-(4-methylphenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide(3f)

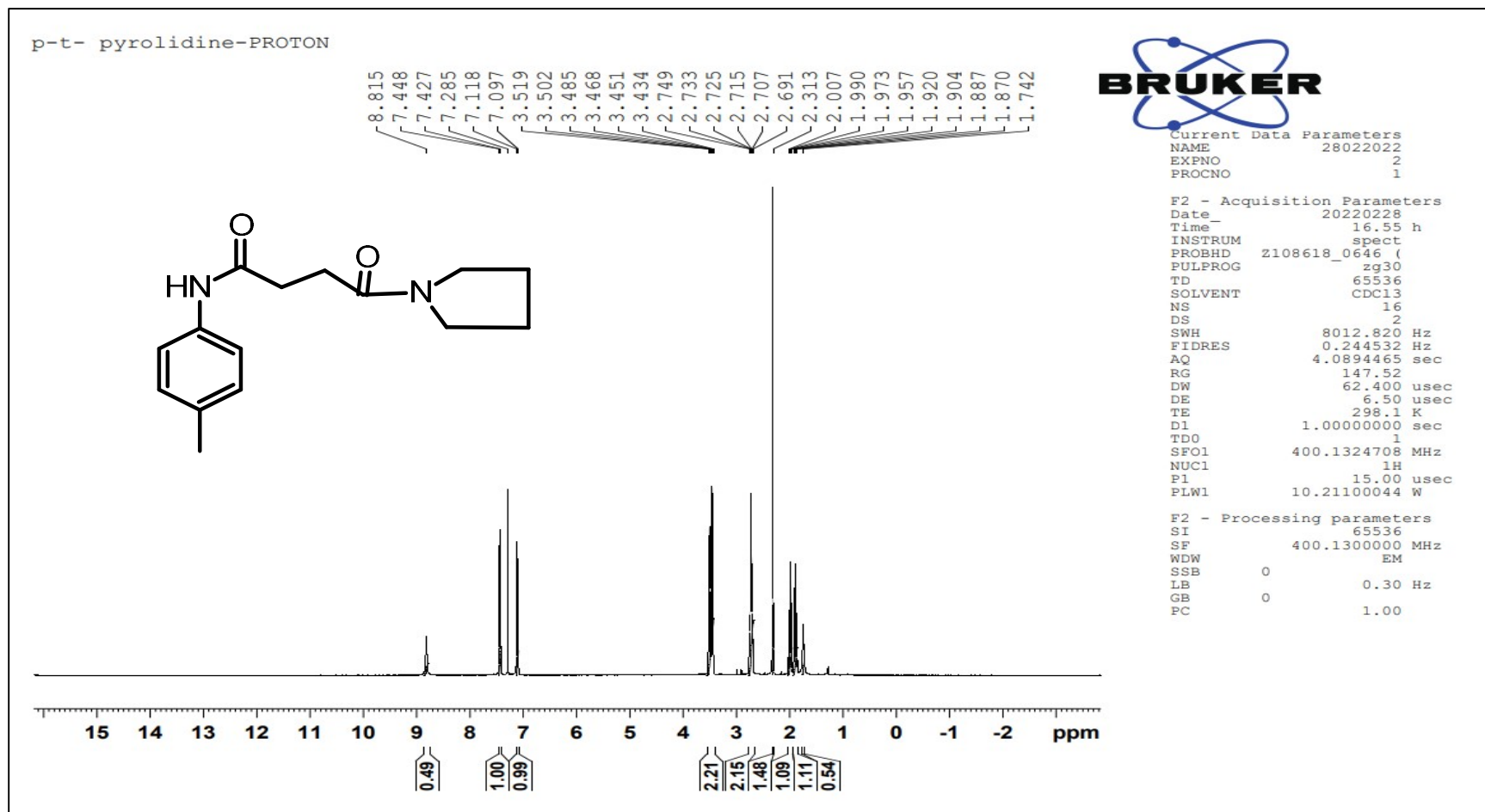


Fig. 44: ^{13}C NMR Spectrum of *N*-(4-methylphenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide(3f)

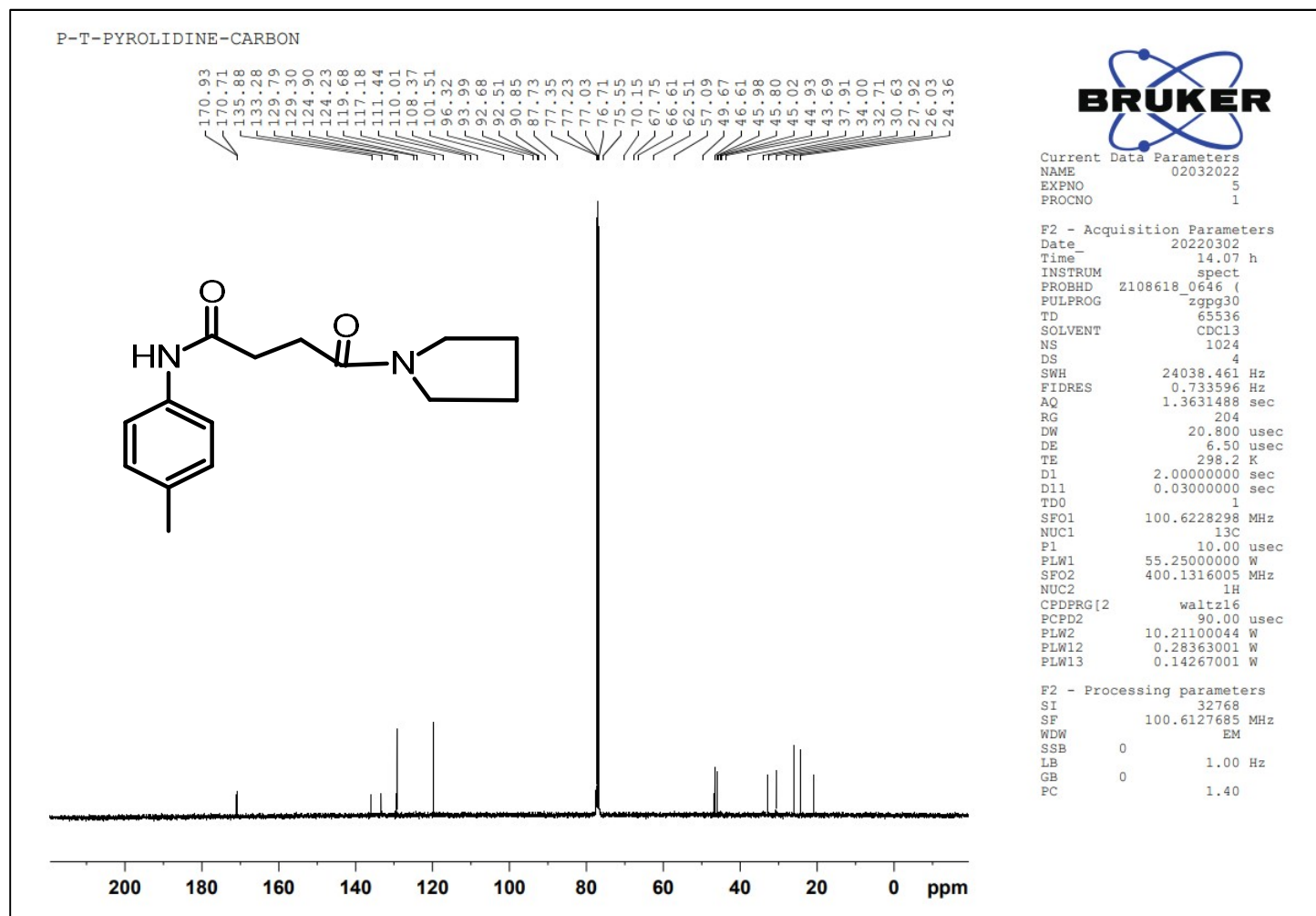


Fig. 45: Mass Spectrum of *N*-(4-methylphenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide(3f)

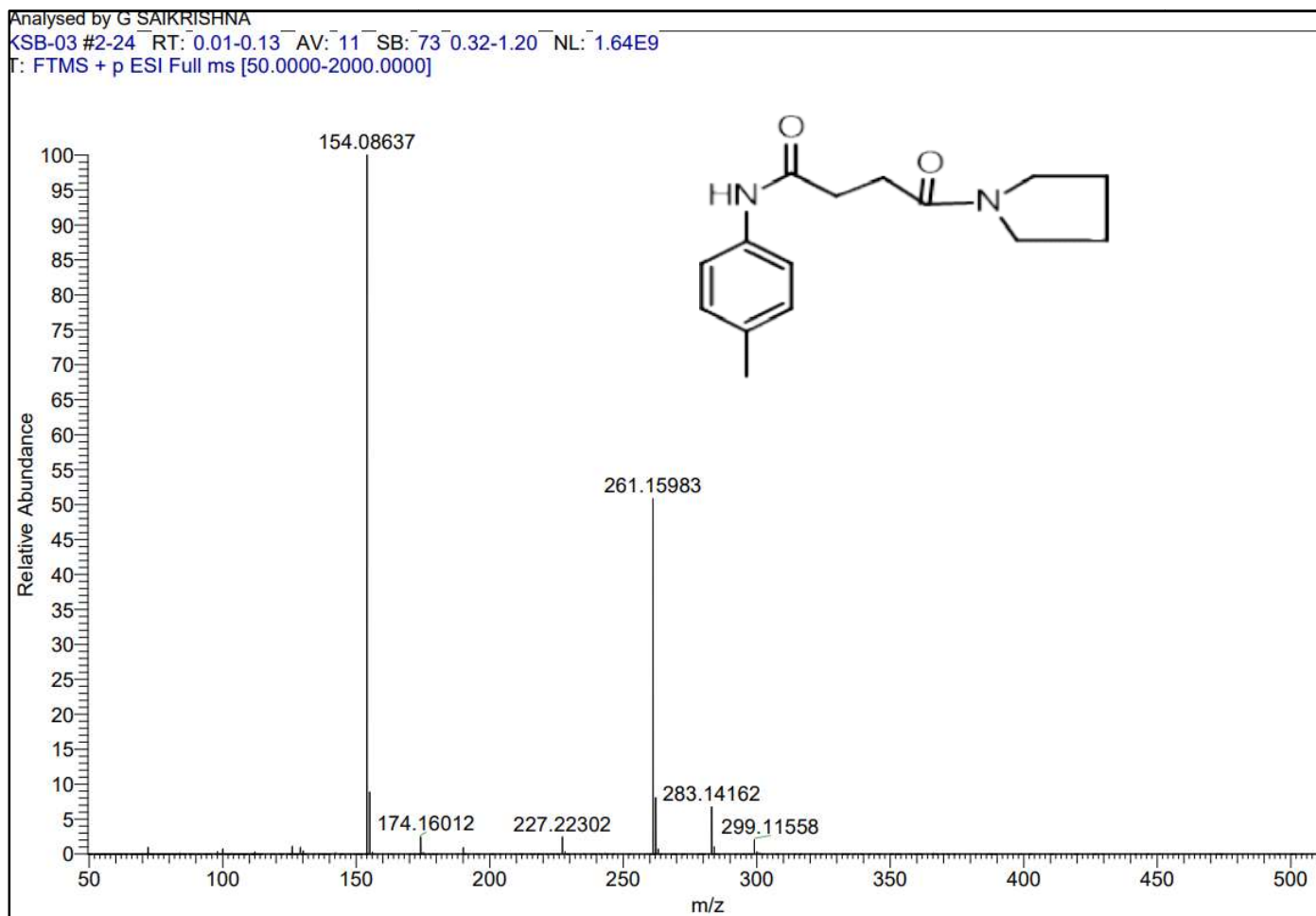


Fig. 46: IR Spectrum of N^1,N^1 -diethyl- N^4 -(4-methylphenyl)butanediamide(3g)

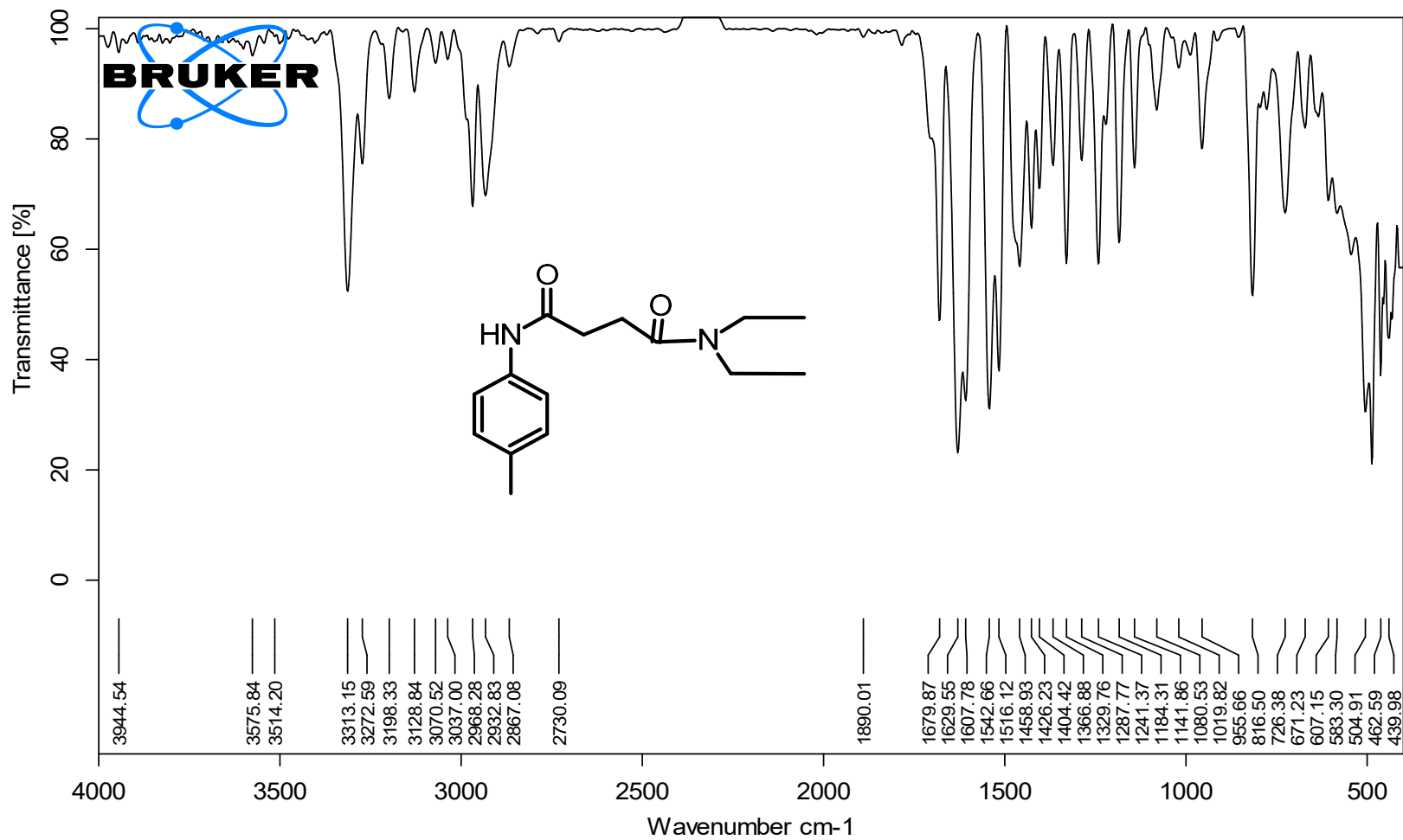


Fig. 47: ^1H NMR Spectrum of N^1, N^1 -diethyl- N^4 -(4-methylphenyl)butanediamide(3g)

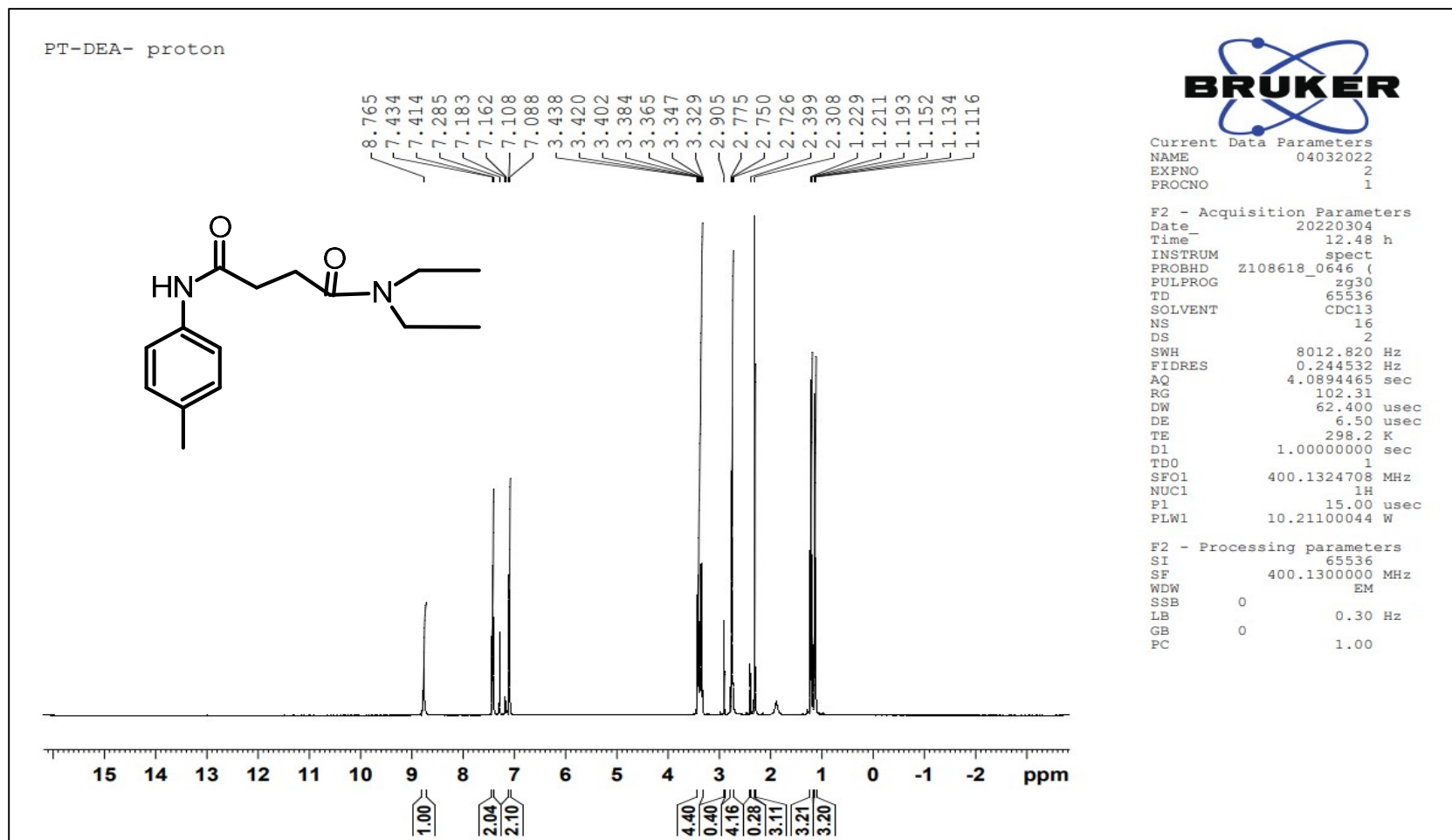


Fig. 48: ^{13}C NMR Spectrum of N^1,N^1 -diethyl- N^4 -(4-methylphenyl)butanediamide(3g)

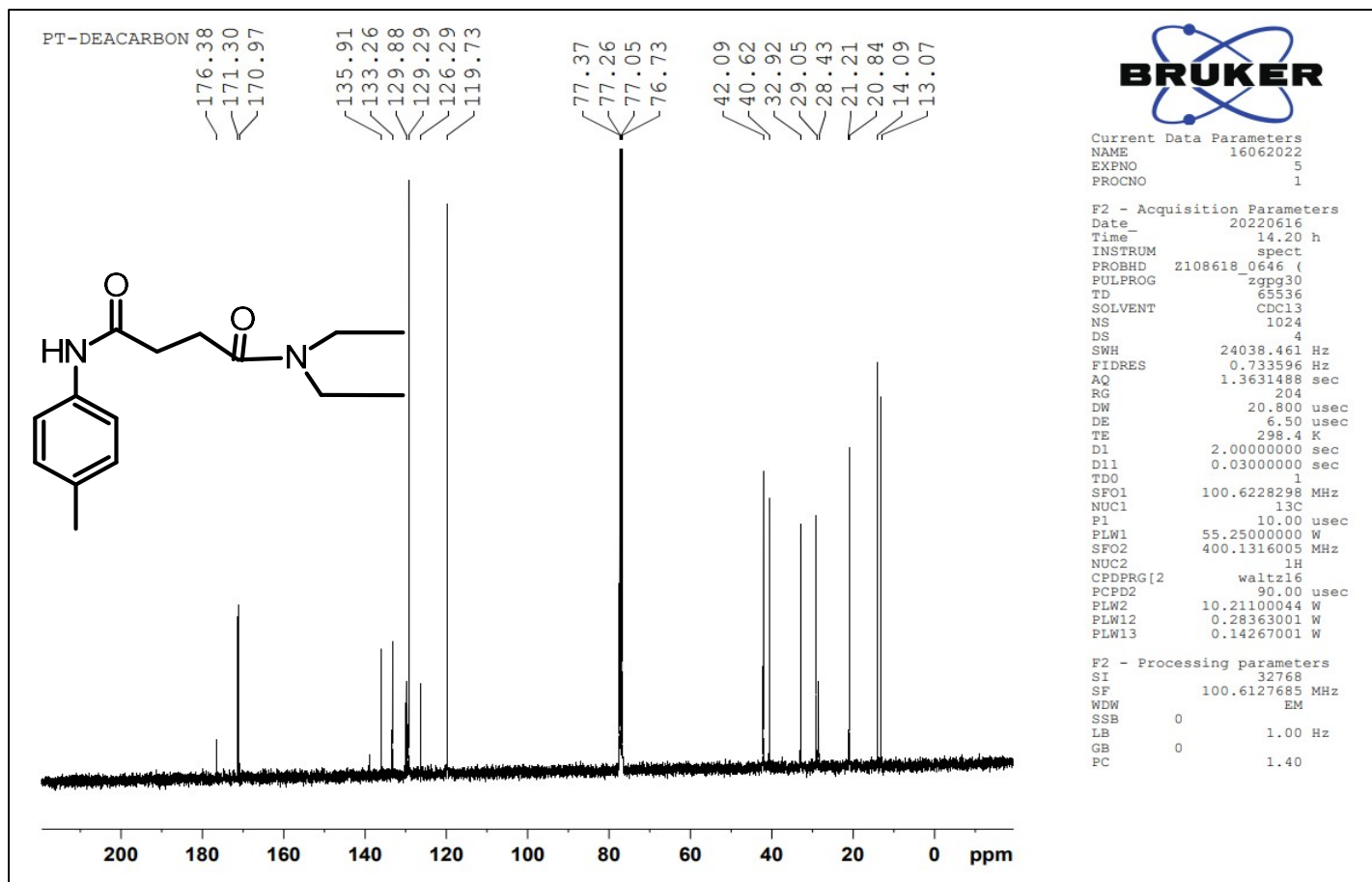


Fig. 49: IR Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide(4c)

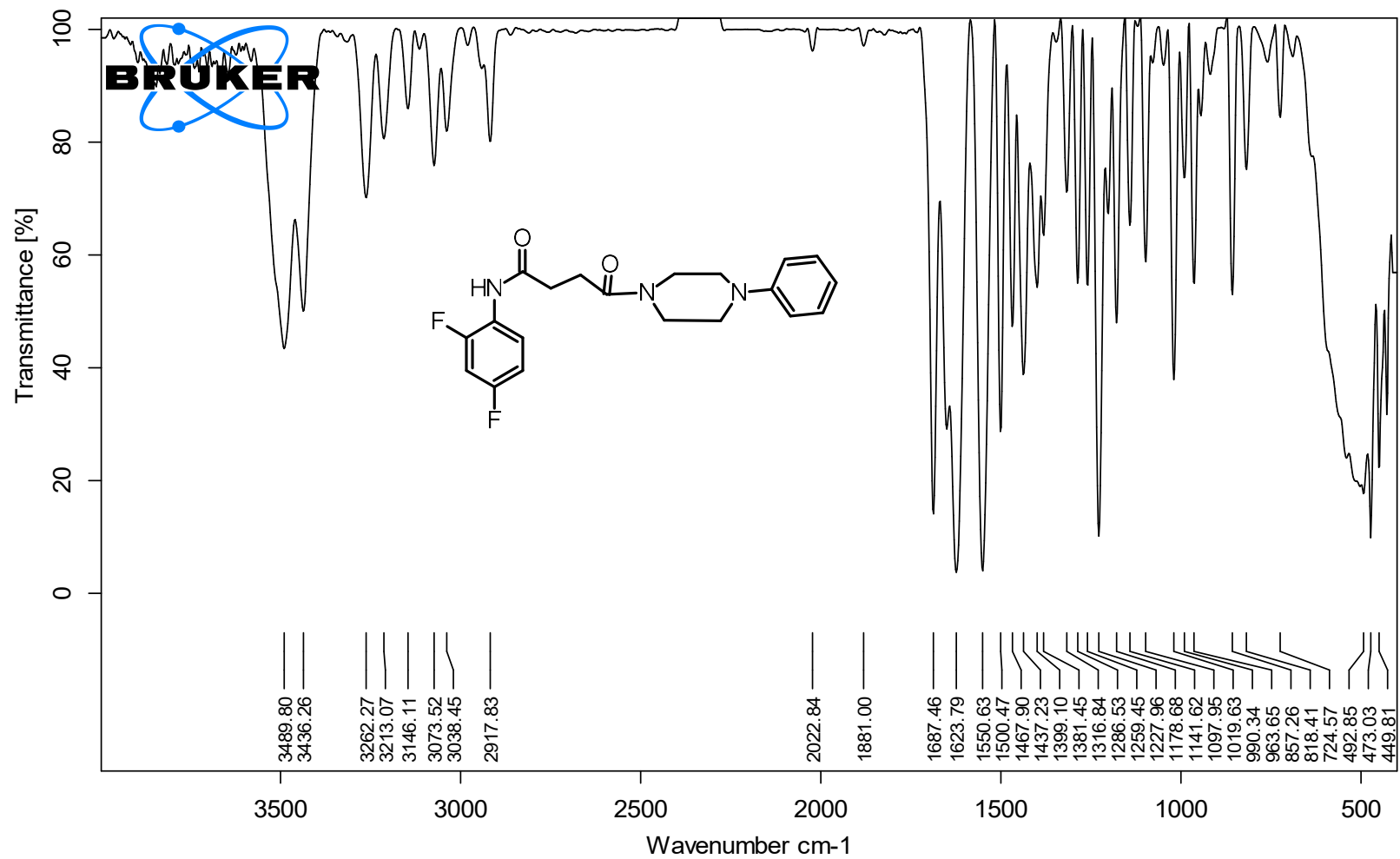


Fig. 50: ¹H NMR Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide(4c)

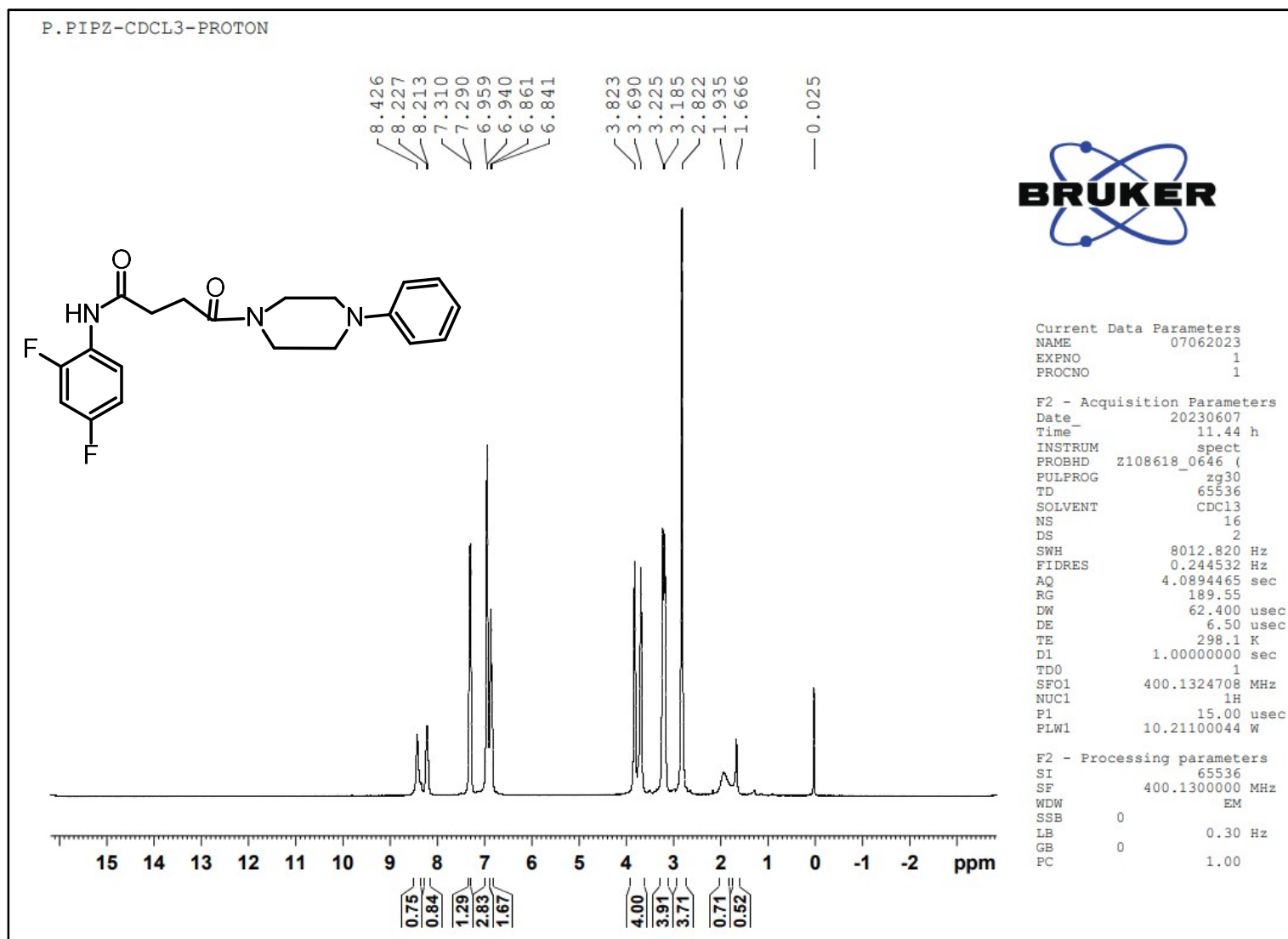


Fig. 51: ^{13}C NMR Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide(4c)

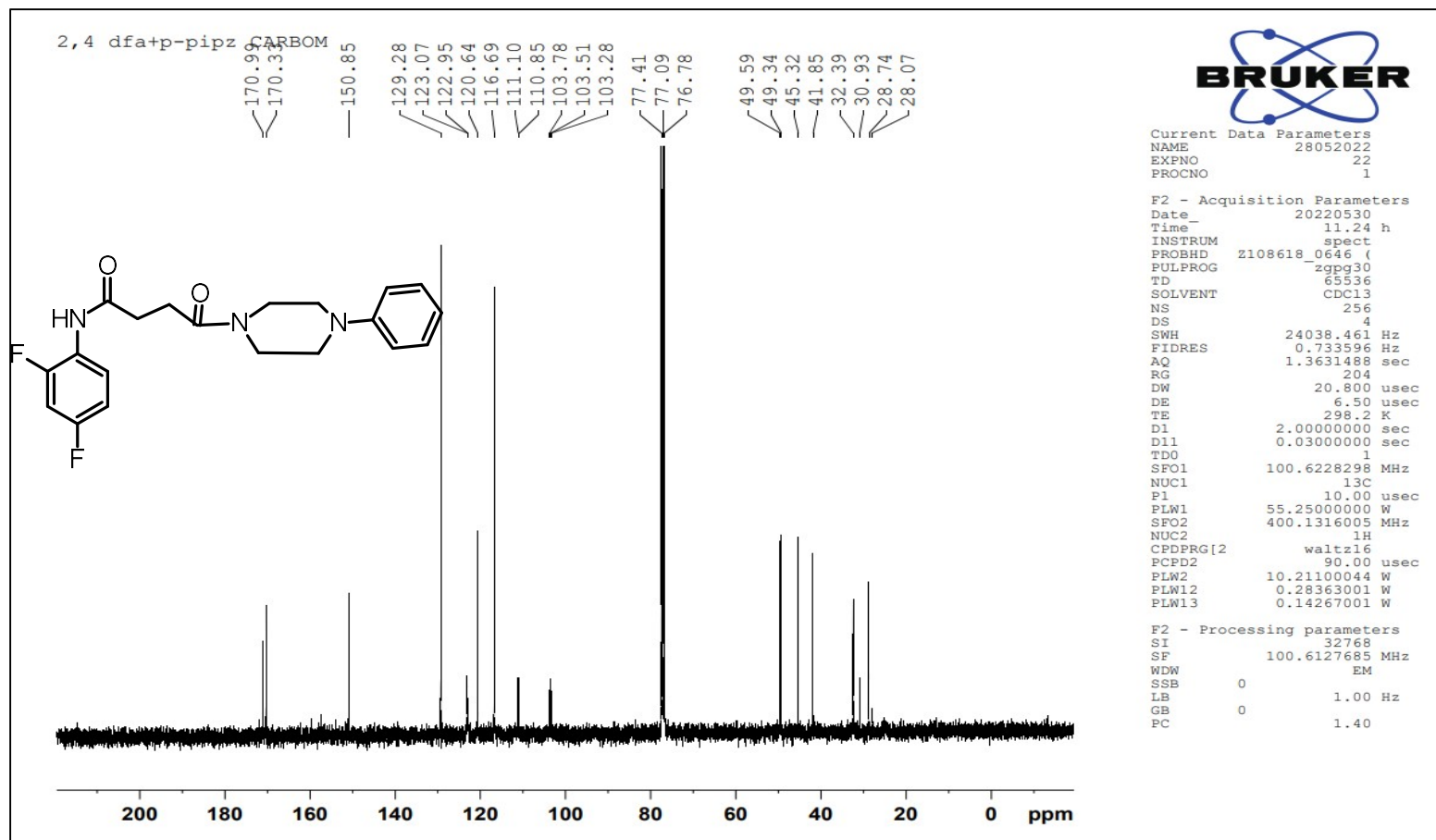


Fig. 52: Mass Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide(4c)

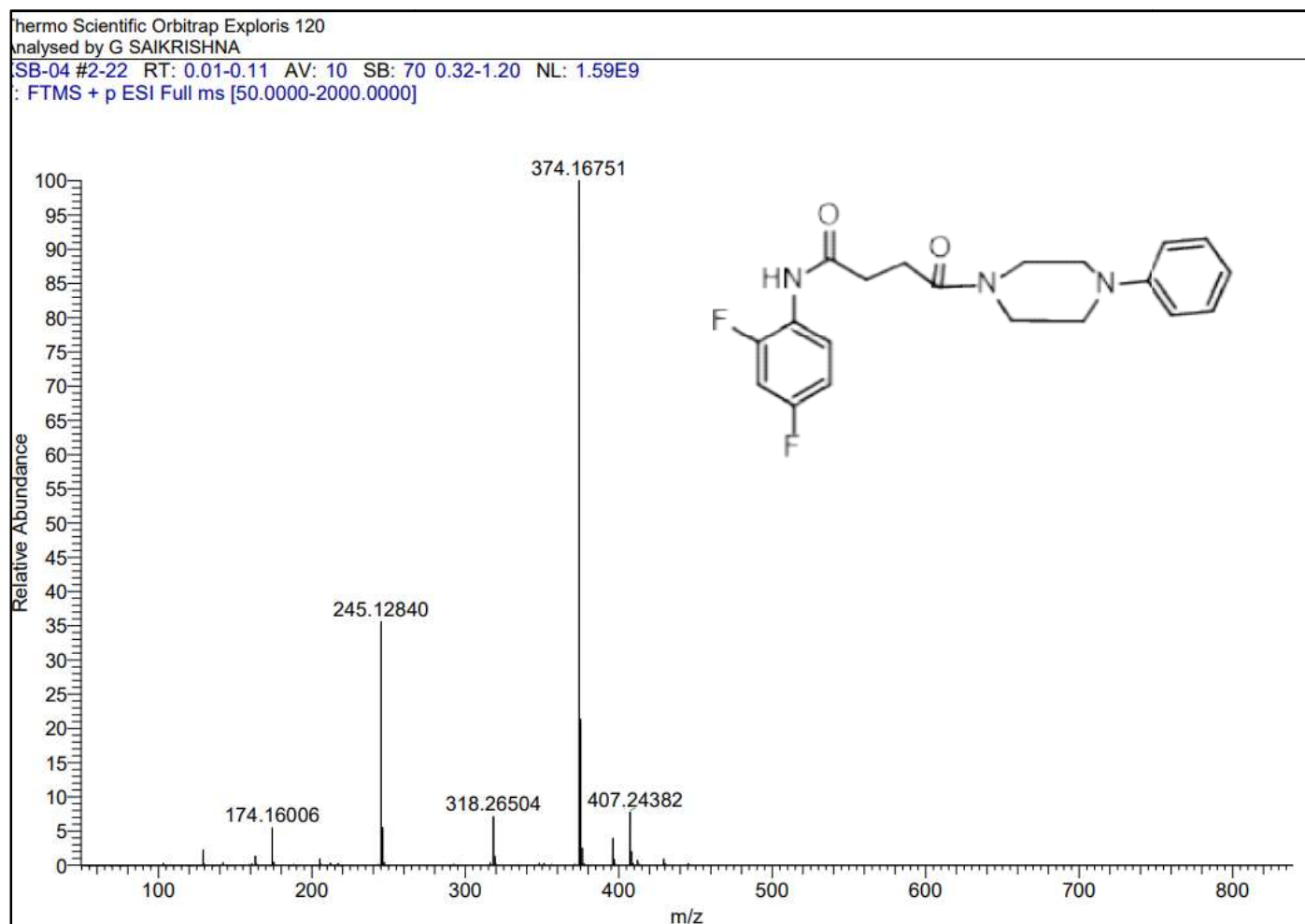


Fig. 53: IR Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide(4d)

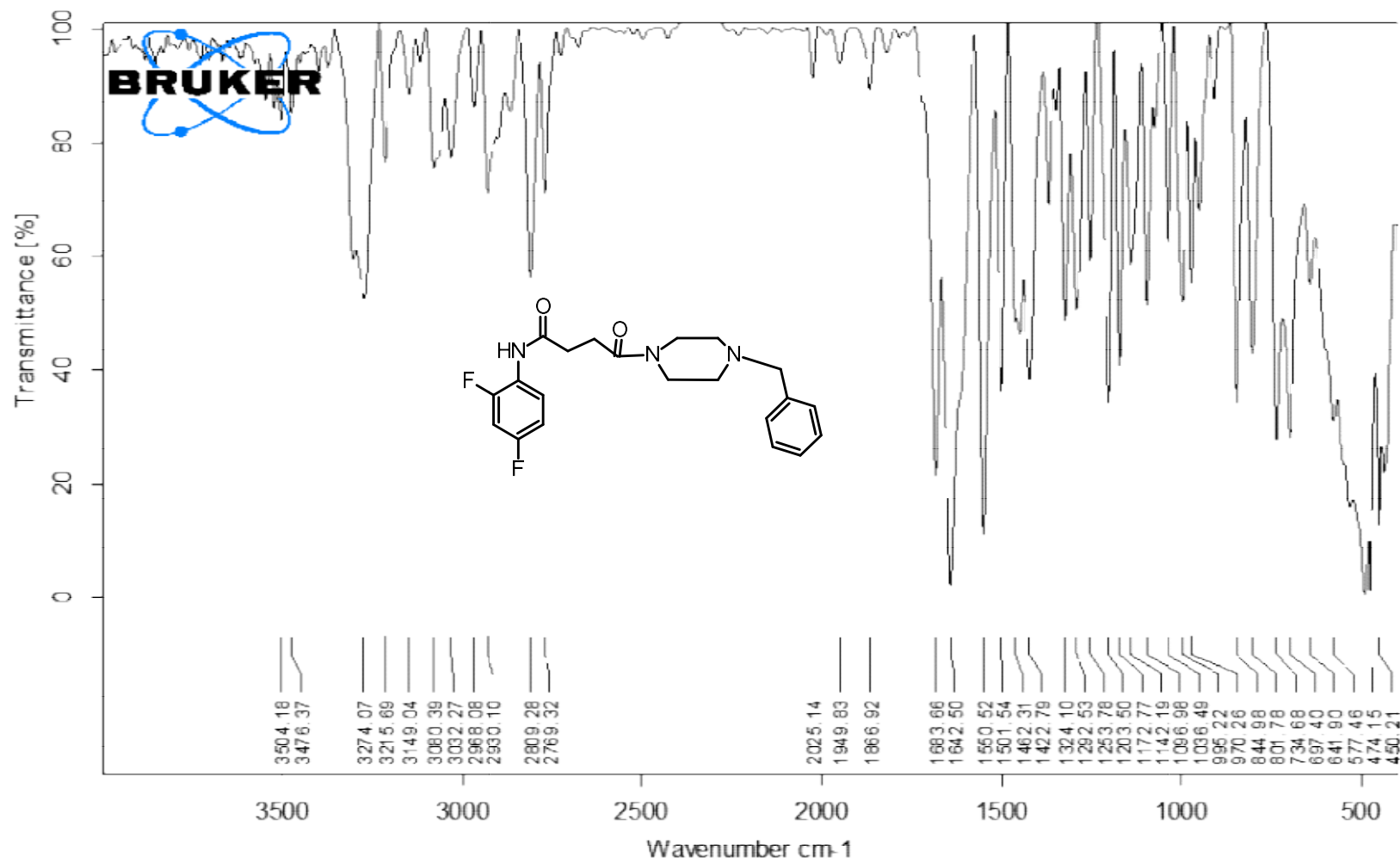


Fig. 54: ¹H NMR Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide(4d)

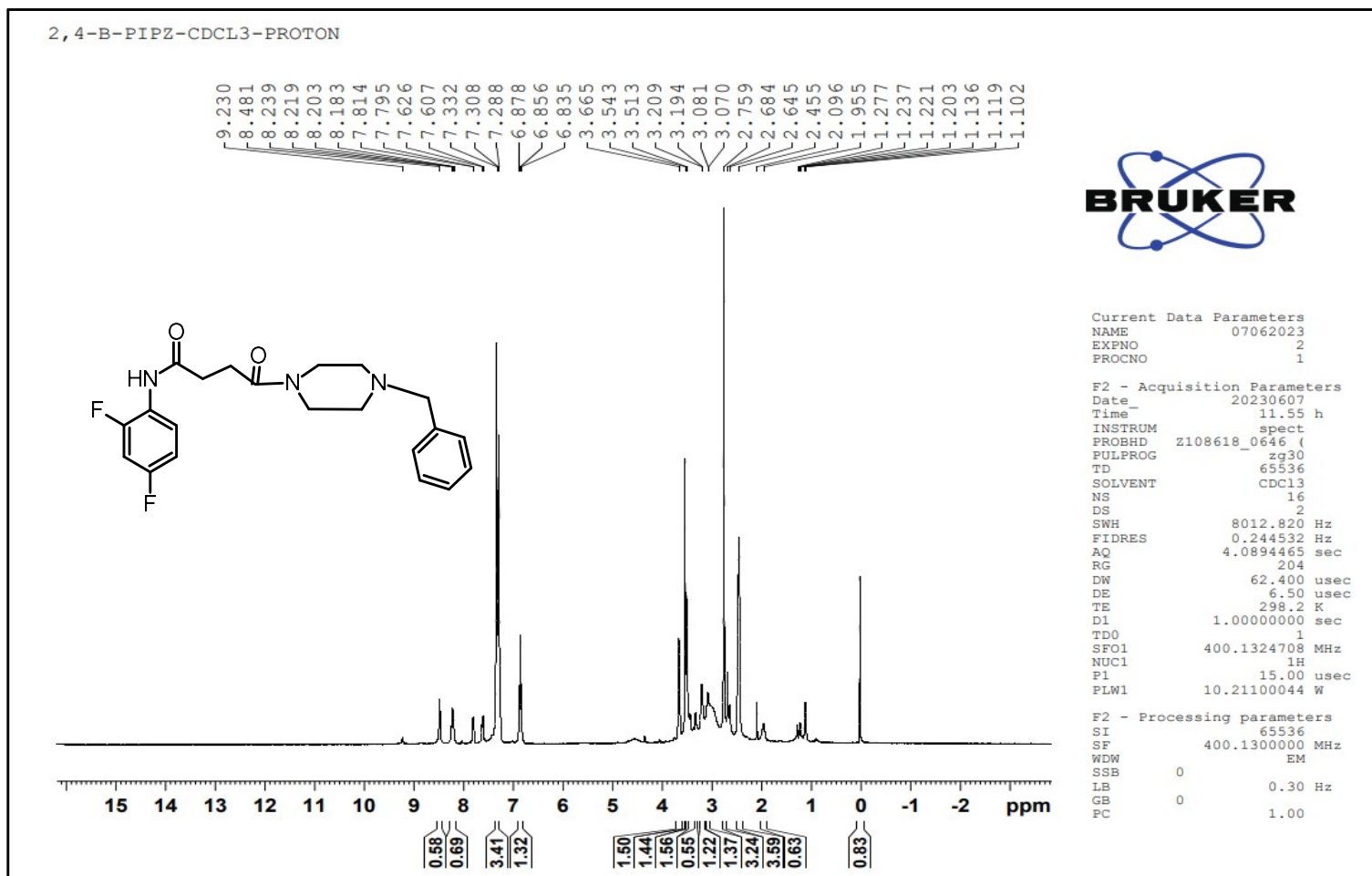


Fig. 55: ^{13}C NMR Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide(4d)

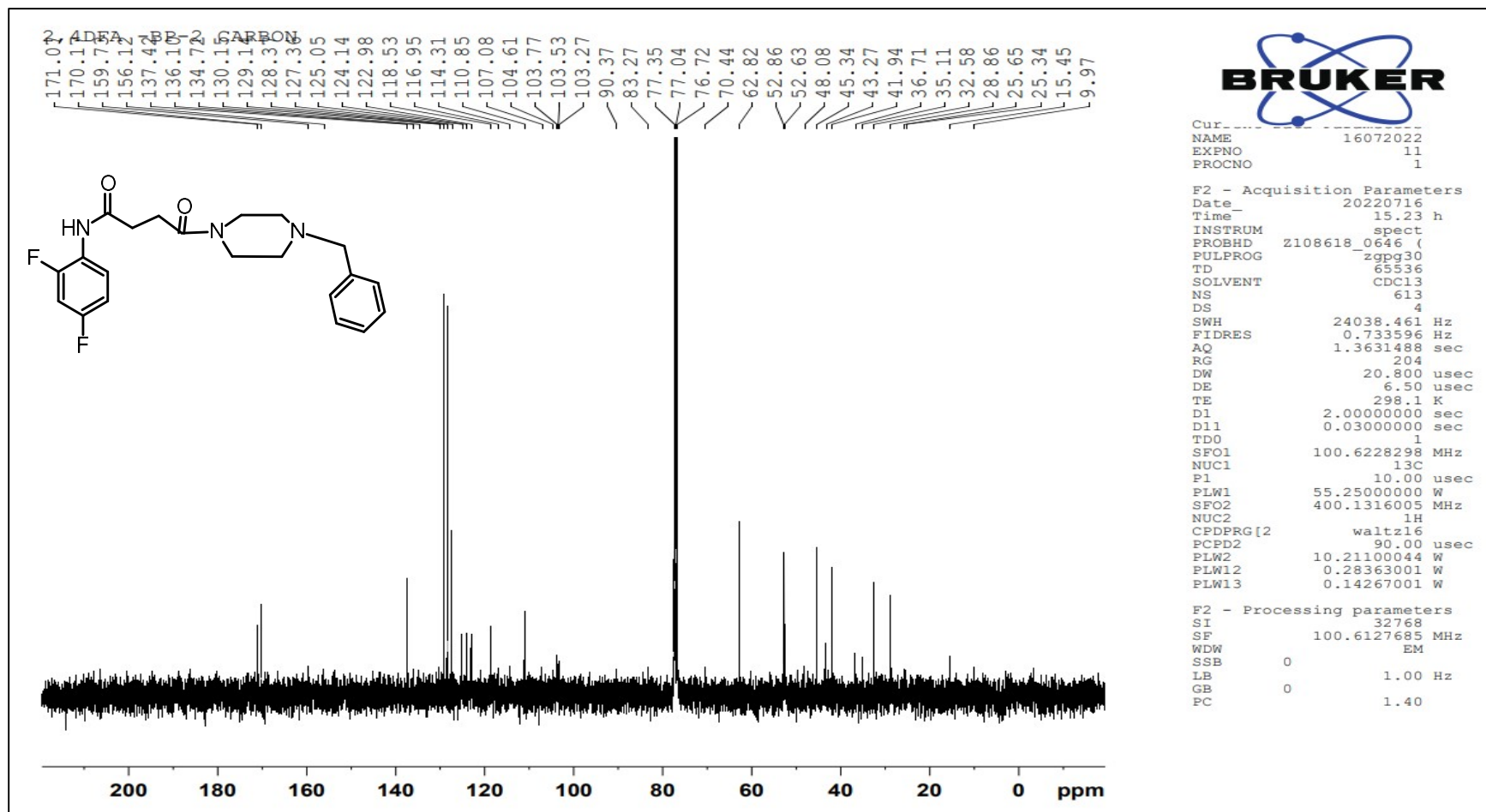


Fig. 56: Mass Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide(4d)

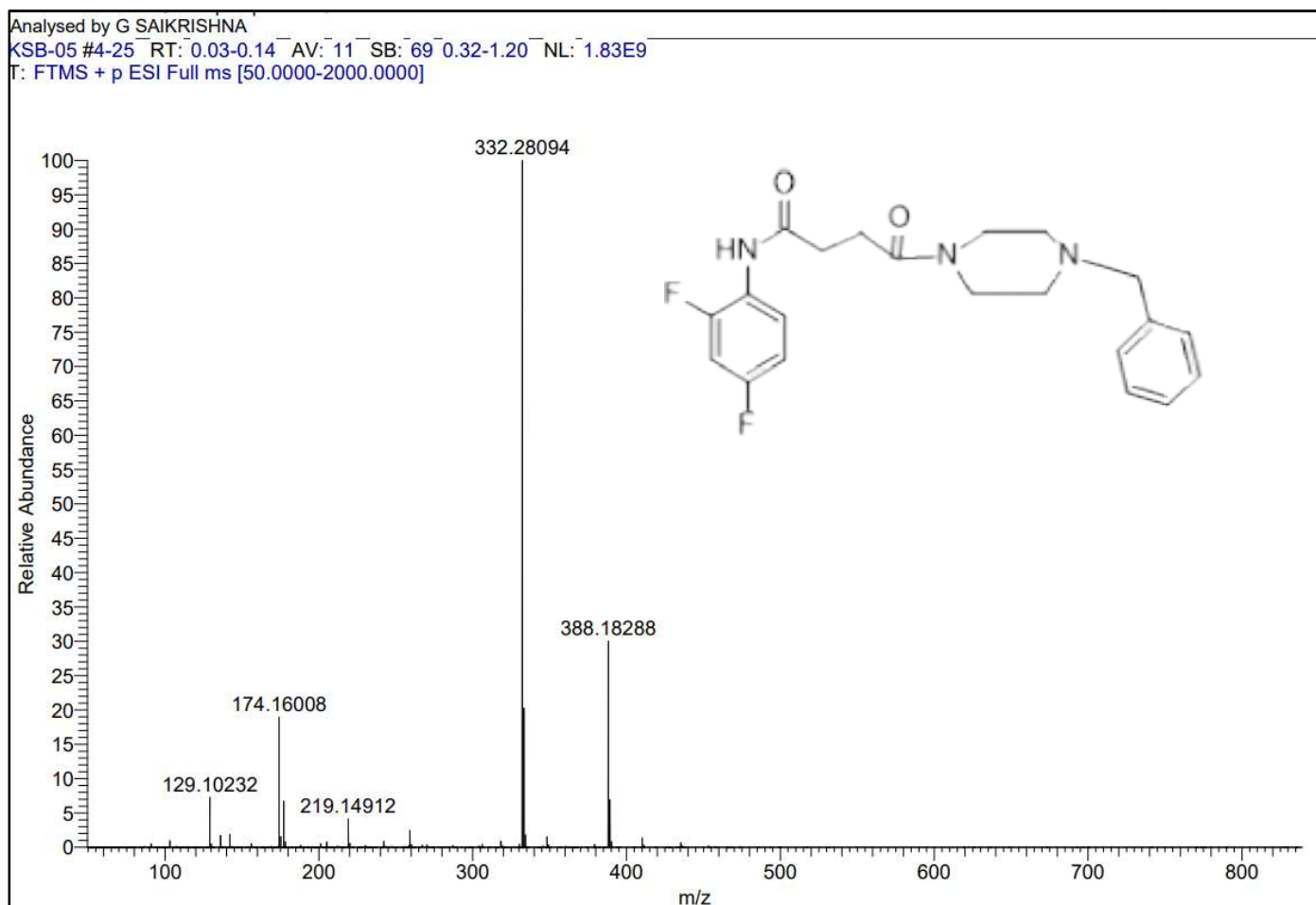


Fig. 57: IR Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide(4e)

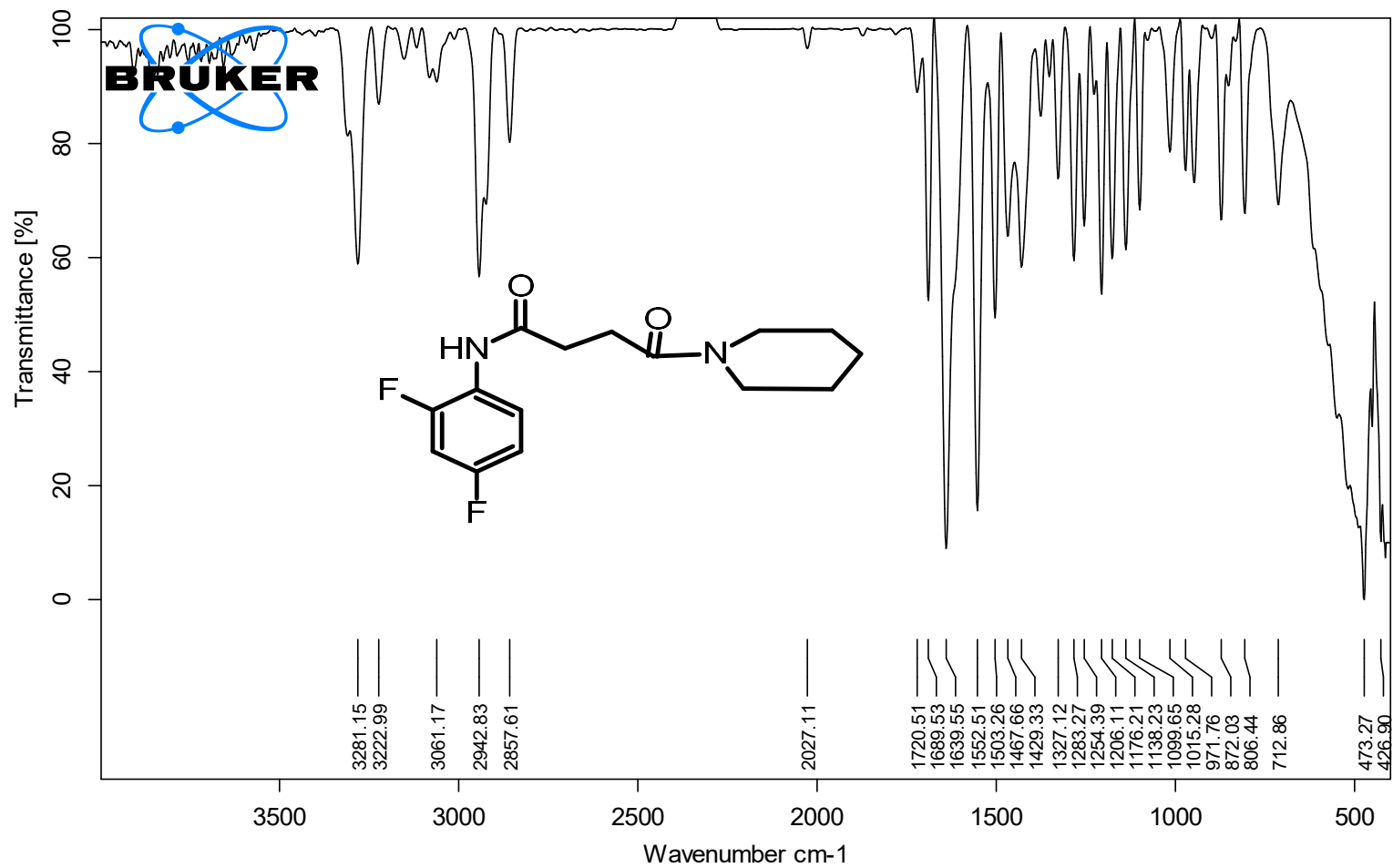


Fig. 58: ¹H NMR Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide(4e)

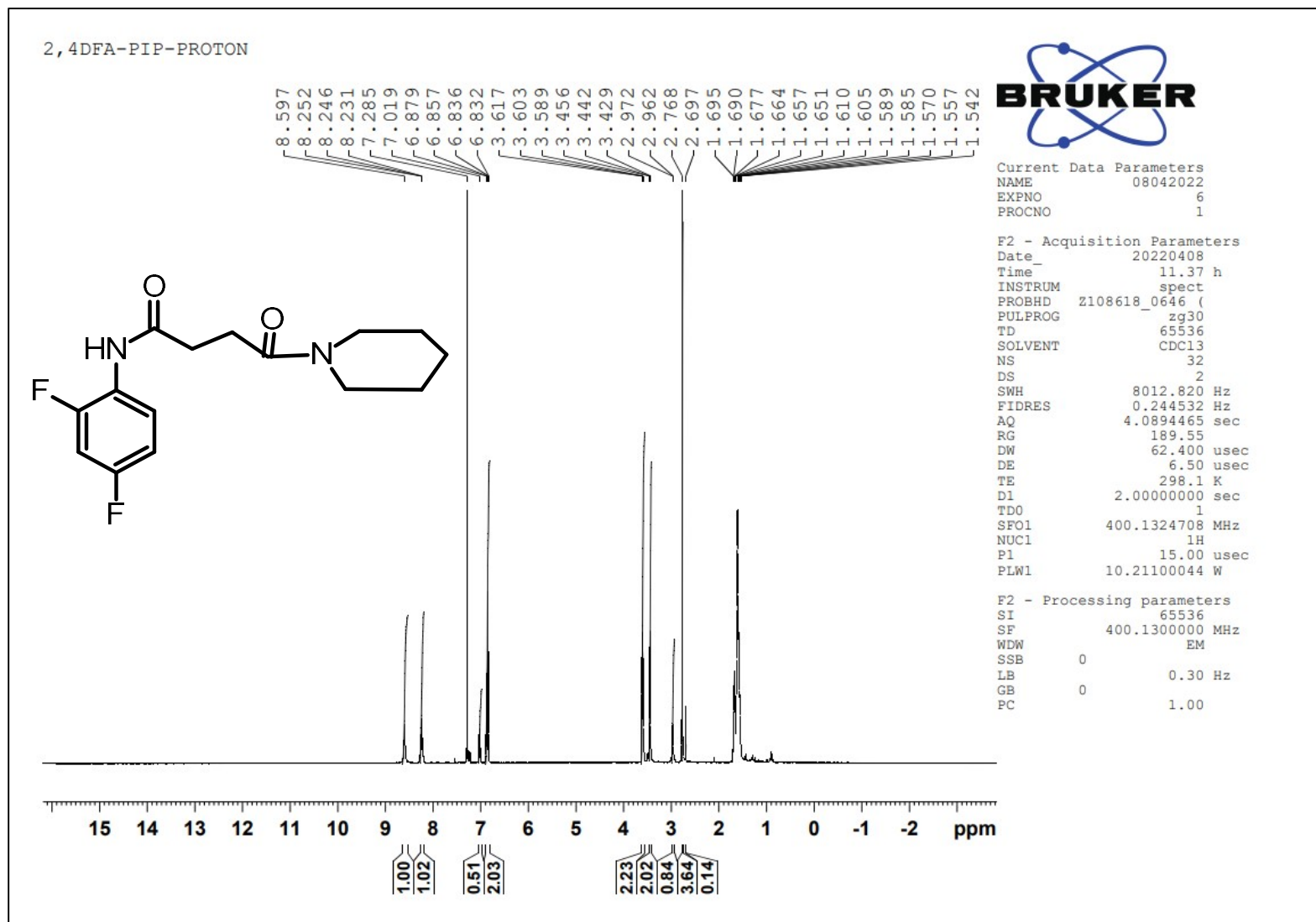


Fig. 59: ^{13}C NMR Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide(4e)

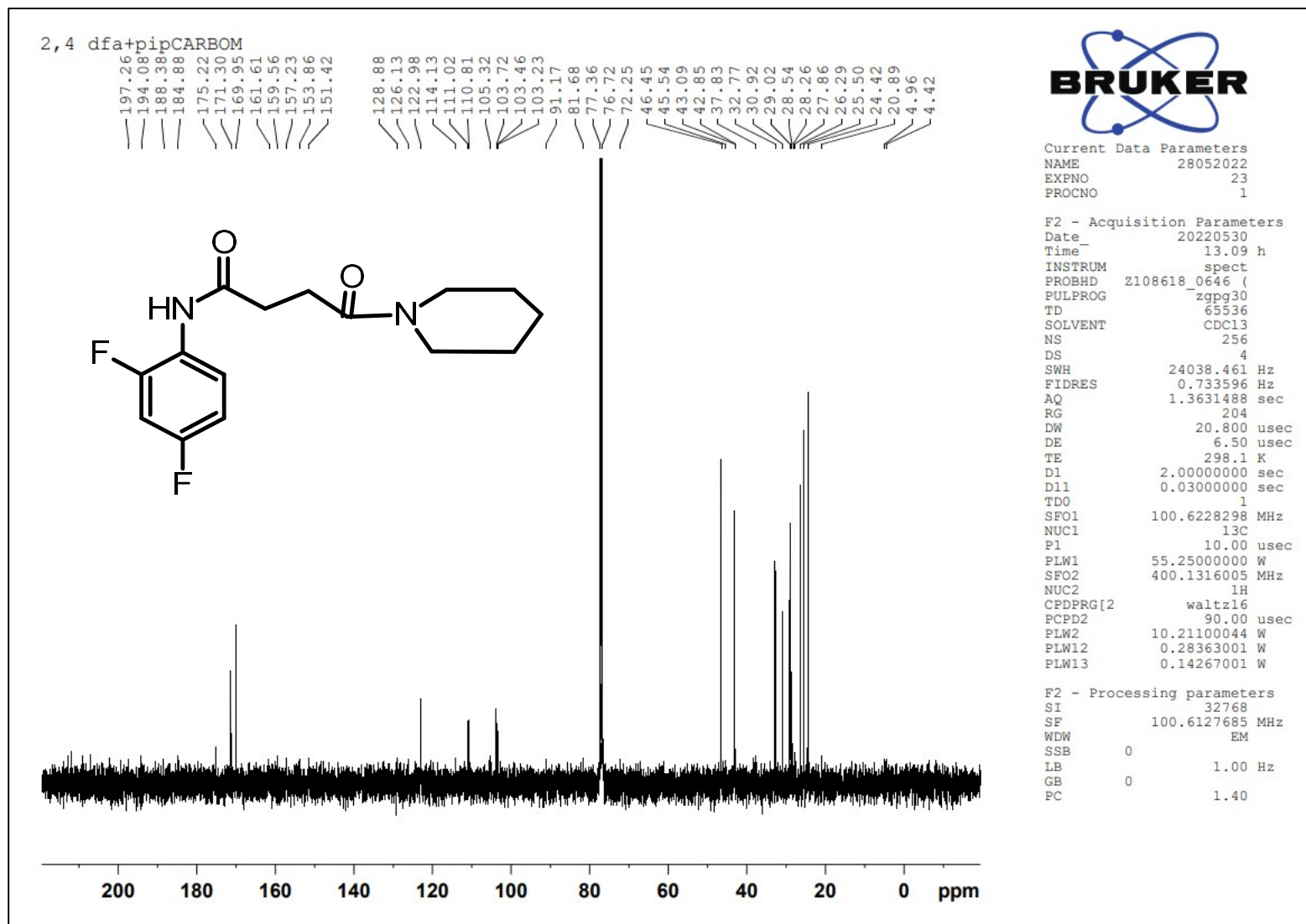


Fig. 60: IR Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide(4f)

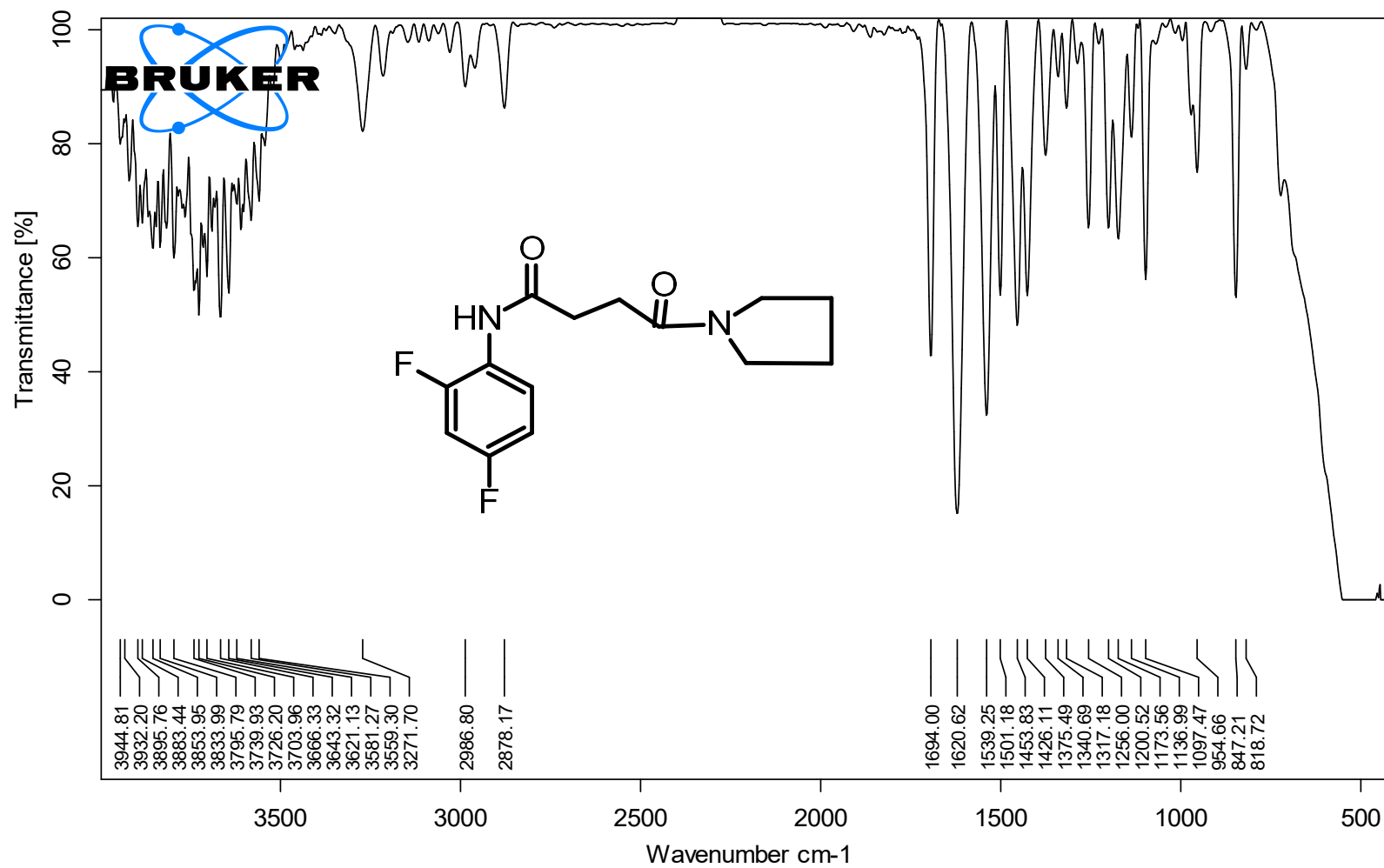


Fig. 61: ¹H NMR Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide(4f)

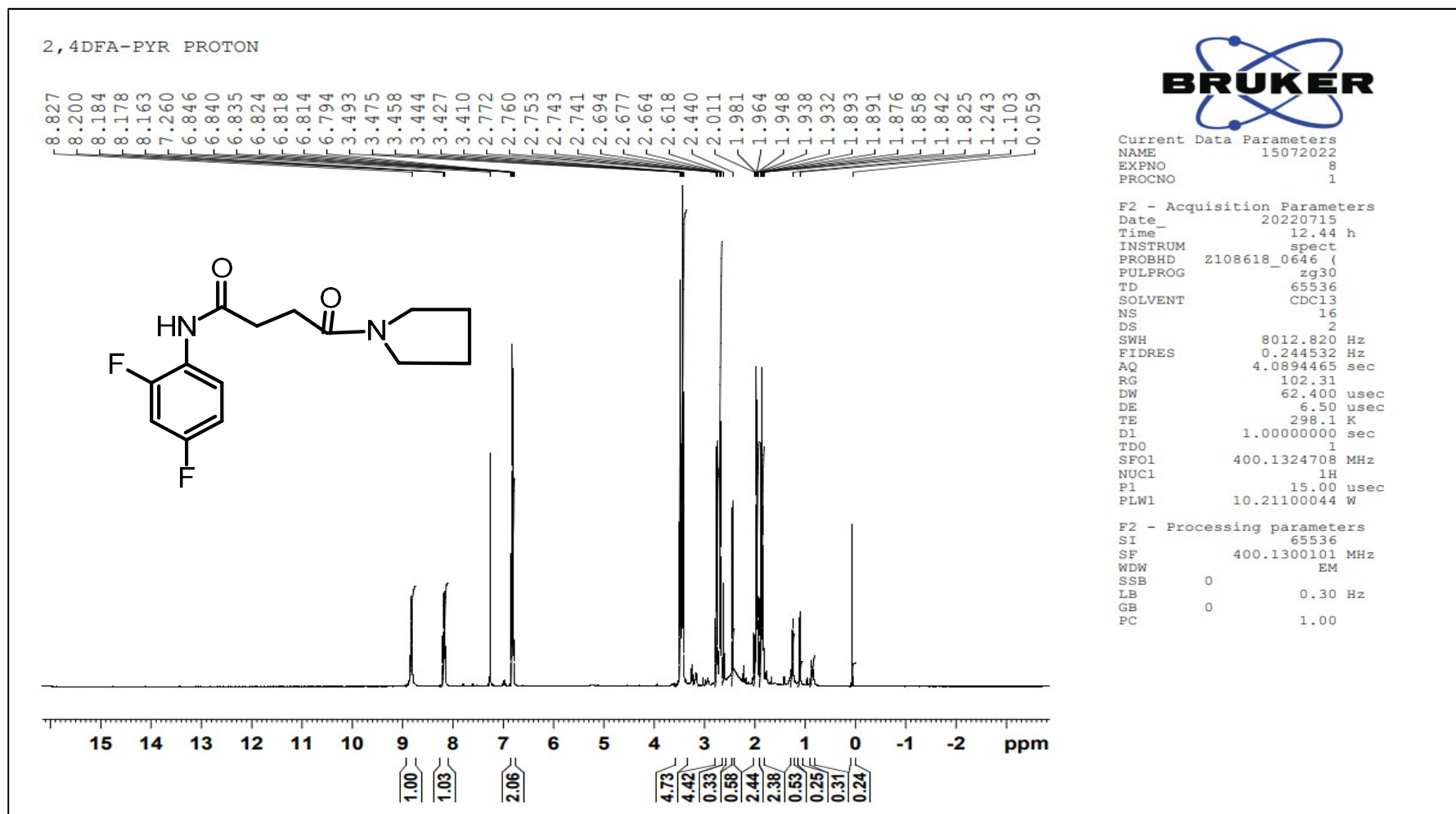


Fig. 62: ^{13}C NMR Spectrum of *N*-(2,4-difluorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide(4f)

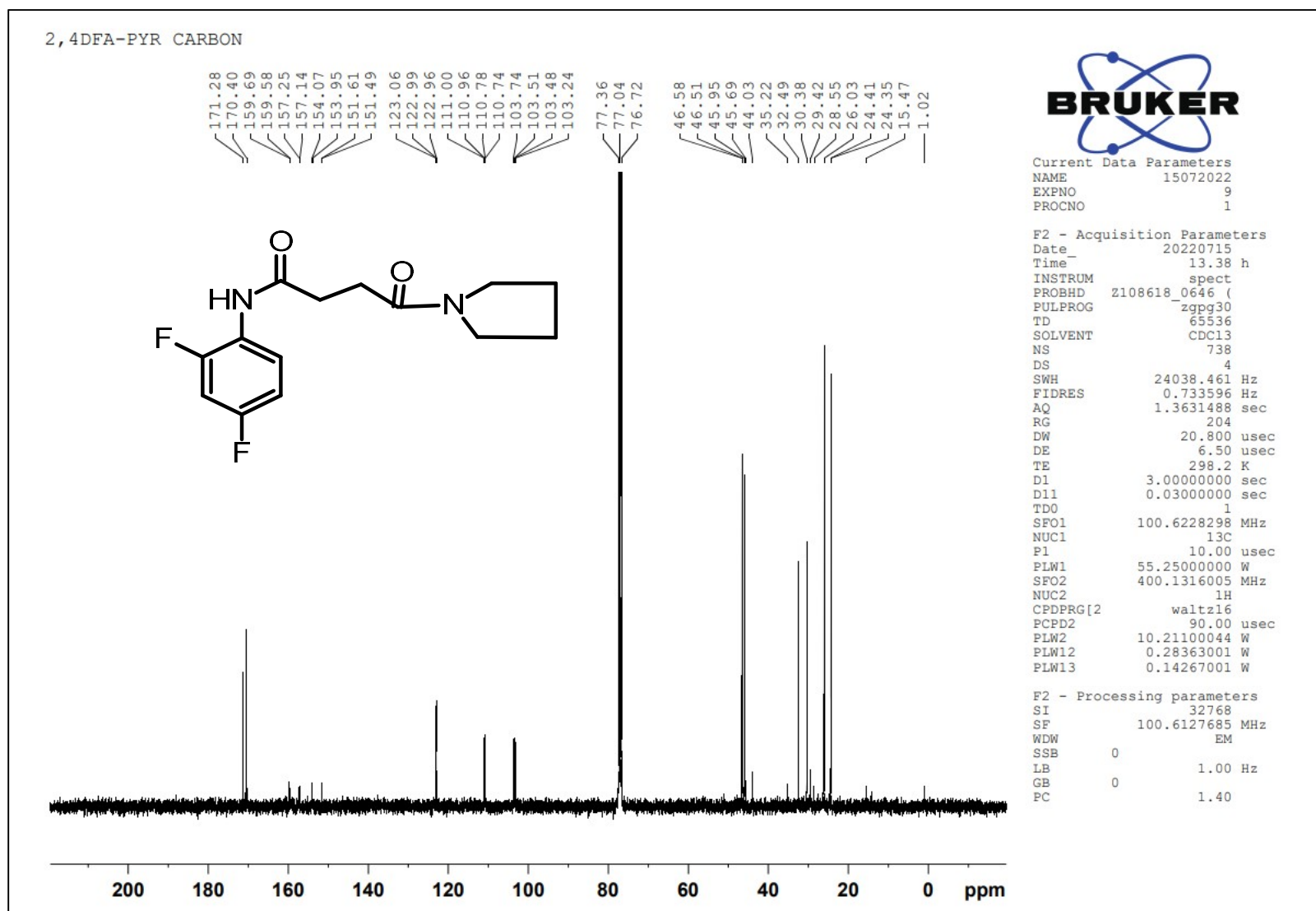


Fig. 63: IR Spectrum of N^4 -(2,4-difluorophenyl)- N^1,N^1 -diethylbutanediamide(4g)

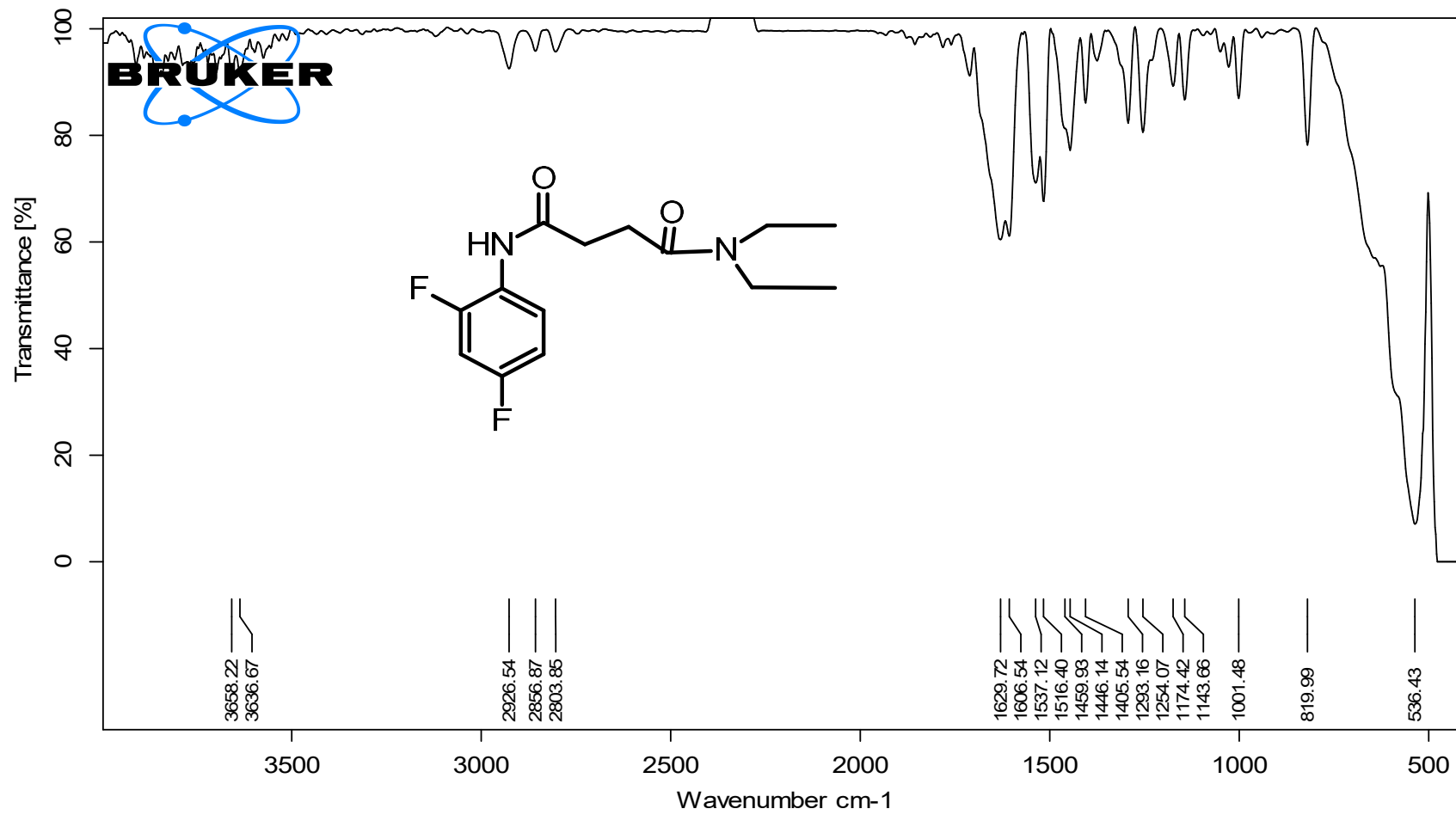


Fig. 64. ^1H NMR Spectrum of N^4 -(2,4-difluorophenyl)- N^1,N^1 -diethylbutanediamide(4g)

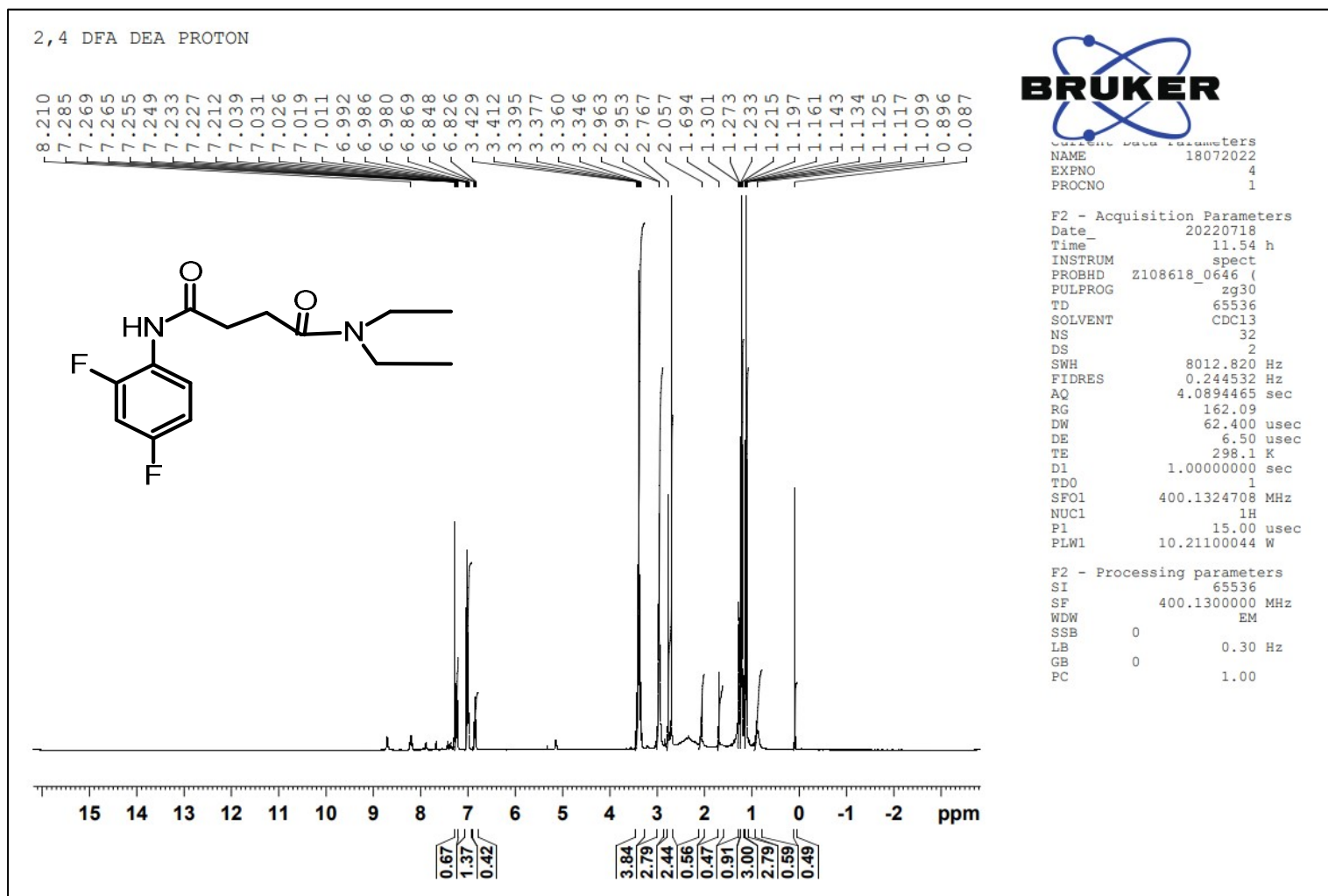
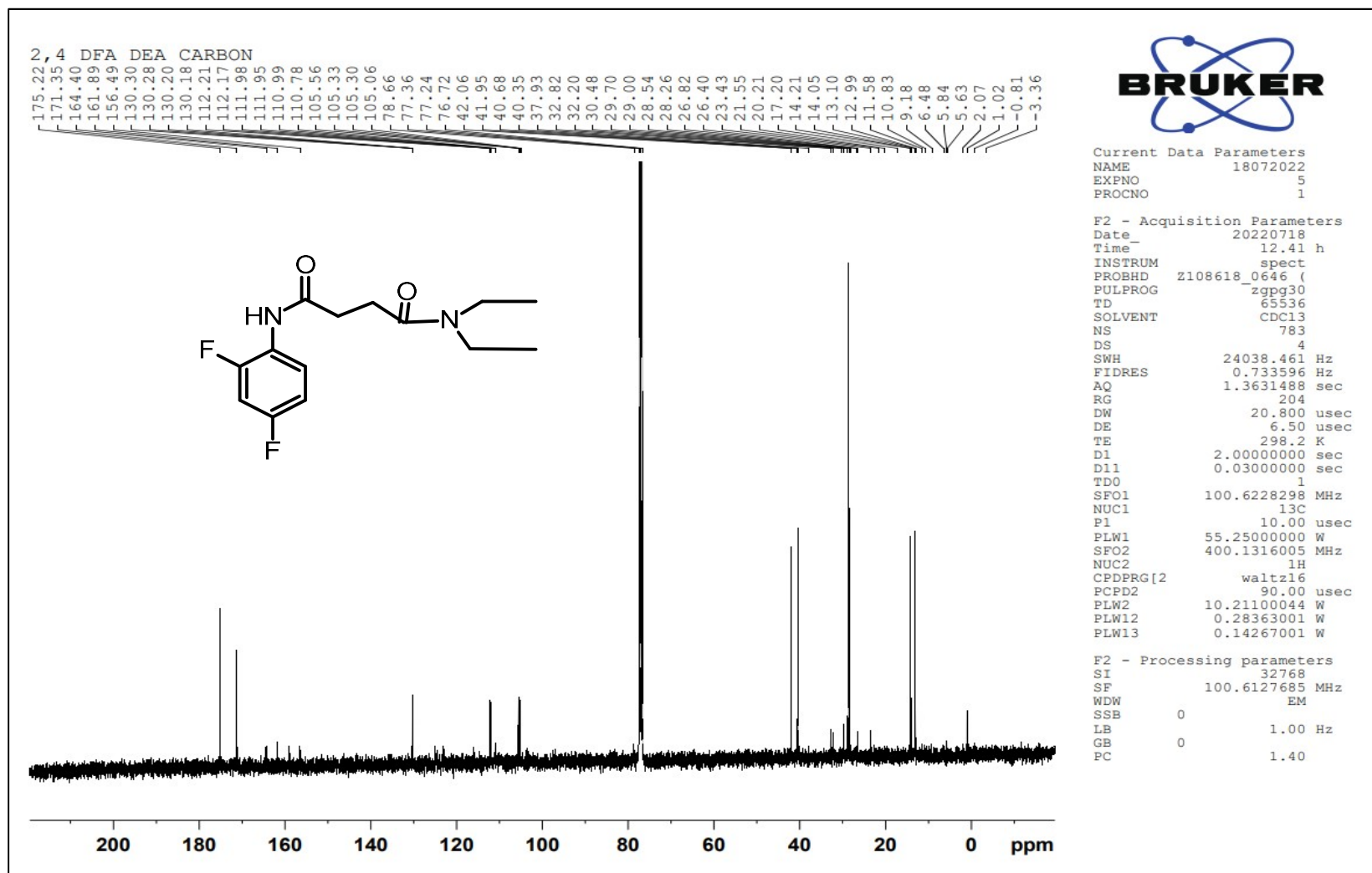


Fig. 65: ^{13}C NMR Spectrum of N^4 -(2,4-difluorophenyl)- N^1,N^1 -diethylbutanediamide(4g)



3) **Antibacterial activity:**

4) Table 2: Zone of inhibition for anti-bacterial activity of N-phenyl-4-oxo-butanamide derivatives (cup plate method)

Sample codes	Gram+Ve (<i>Staphylococcus aureus</i>)		Gram -Ve (<i>Escherichia coli</i>)	
	Zone of Inhibition (mm)		Zone of Inhibition (mm)	
	100µg/ml	50µg/ml	100µg/ml	50µg/ml
Rifampicin	20	19	19	18
1a	4	4	5	4
1b	4	5	5	4
1c	6	4	5	5
1d	5	6	6	5
1e	5	5	5	5
1f	5	5	5	5
1g	5	5	3	3
2a	5	4	5	5
2b	4	3	4	3
2c	4	4	3	5
2d	6	2	4	6
2e	6	5	5	6
2f	5	4	4	5
2g	5	4	4	4
3a	6	5	5	4
3b	5	4	4	5
3c	6	5	5	6
3d	5	5	4	5
3e	5	5	5	5
3f	5	5	5	5
3g	6	5	4	4
4a	6	5	5	5
4b	5	5	5	5
4c	4	5	5	5
4d	5	5	5	5
4e	5	4	5	6
4f	5	4	6	5
4g	5	4	5	5

Fig. 66. Anti-bacterial activity of N-phenyl-4-oxo-butanamide derivatives against gram positive bacteria (*Staphylococcus aureus*) at 50 μ g and 100 μ g concentrations

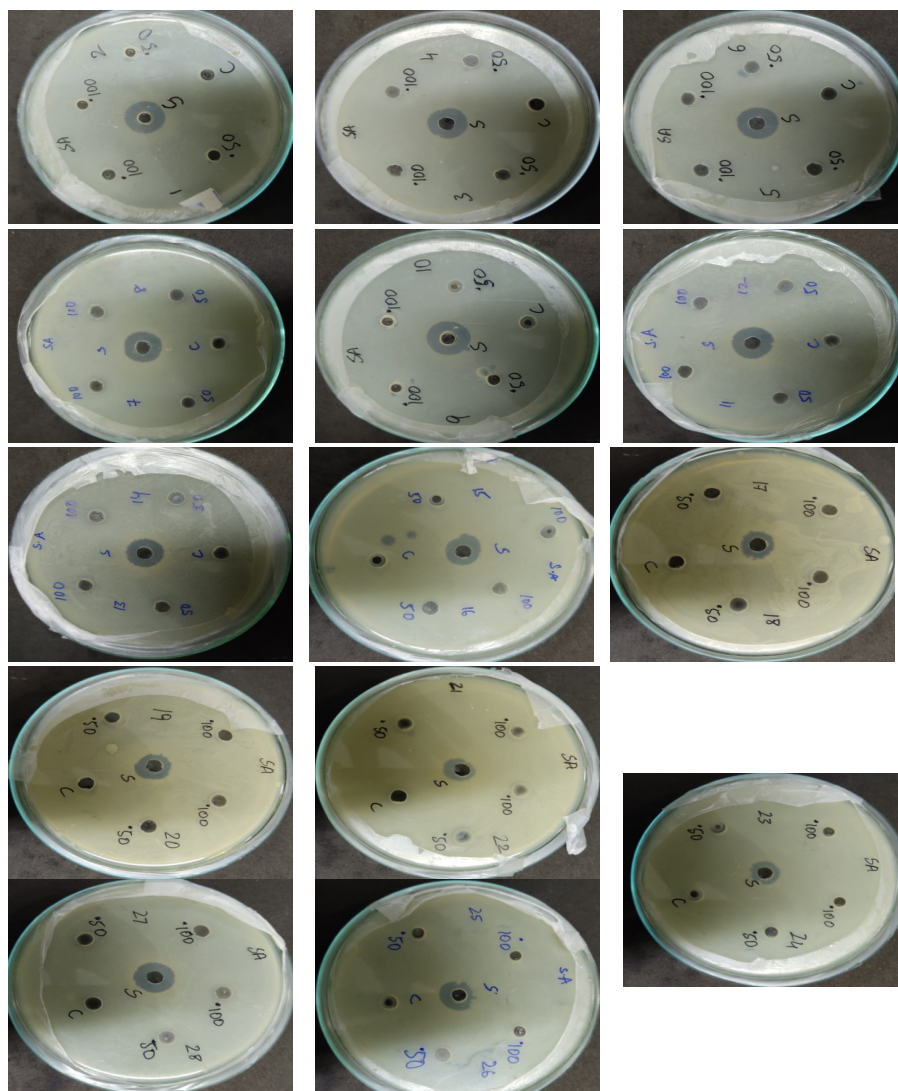
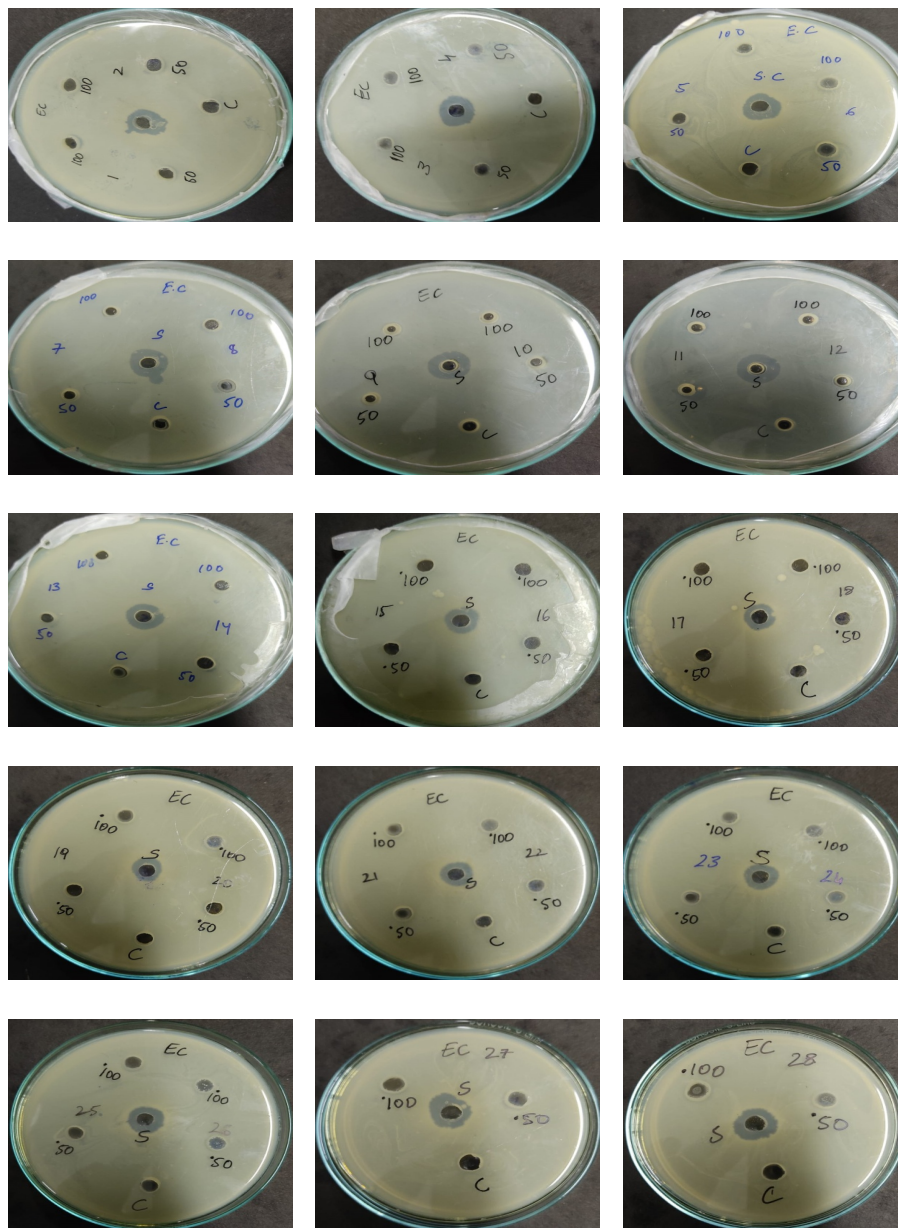


Fig. 67. Anti-bacterial activity of N-phenyl-4-oxo-butanamide derivatives against gram negative bacteria (*Escherichia coli*) at 50 μ g and 100 μ g concentrations

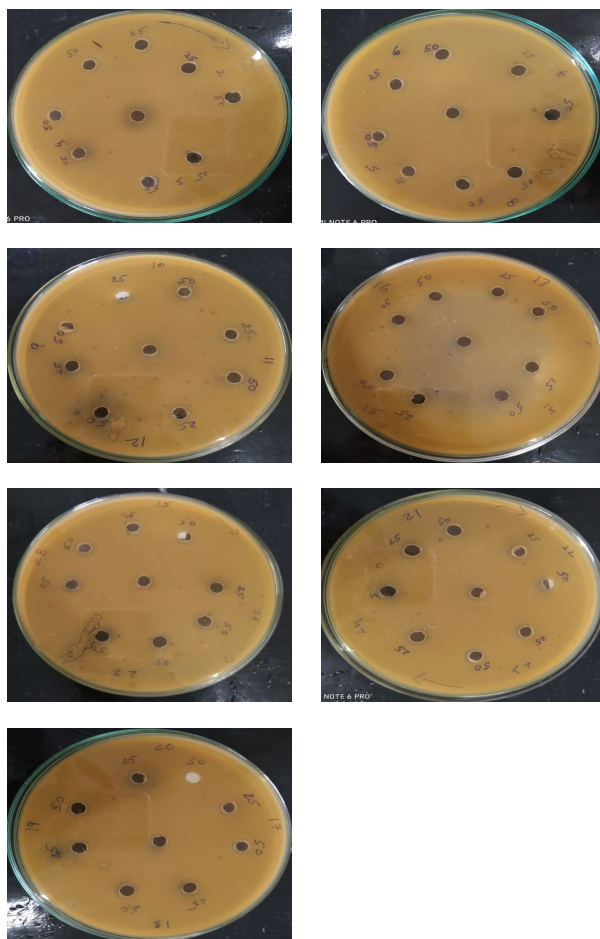


5) Antifungal activity:

6) Table 3: Zone of inhibition for Anti-fungal activity of N-phenyl-4-oxo-butanamide derivatives (Agar well diffusion method)

Sample codes	<i>Candida albicans</i>	
	Zone of Inhibition (mm)	
	100µg/ml	50µg/ml
Rifampicin	13	12
1a	NA	NA
1b	NA	NA
1c	NA	NA
1d	NA	NA
1e	NA	NA
1f	NA	NA
1g	NA	NA
2a	NA	NA
2b	NA	NA
2c	NA	NA
2d	NA	NA
2e	NA	NA
2f	NA	NA
2g	NA	NA
3a	NA	NA
3b	NA	NA
3c	NA	NA
3d	NA	NA
3e	NA	NA
3f	NA	NA
3g	NA	NA
4a	NA	NA
4b	NA	NA
4c	NA	NA
4d	NA	NA
4e	NA	NA
4f	NA	NA
4g	NA	NA

Fig. 68. Anti-fungal activity of N-phenyl-4-oxo-butanamide derivatives against *Candida albicans* at 50 μ g and 100 μ g concentrations



7) *In vitro* anti-TB activity:

8) Table 4: Results of Antitubercular activity of N-phenyl-4-oxo-butanamide derivatives (MABA Assay)

S. No	Sample code	MIC (µg/ml)	S. No	Sample Code	MIC (µg/ml)
1	1a	25	16	3b	25
2	1b	25	17	3c	6.25
3	1c	25	18	3d	12.5
4	1d	25	19	3e	25
5	1e	25	20	3f	25
6	1f	25	21	3g	12.5
7	1g	25	22	4a	25
8	2a	25	23	4b	25
9	2b	12.5	24	4c	1.56
10	2c	25	25	4d	1.56
11	2d	25	26	4e	25
12	2e	12.5	27	4f	12.5
13	2f	25	28	4g	25
14	2g	25	29	Streptomycin	6.25
15	3a	12.5	30	Rifampicin	3.125

Fig. 69: Anti-Tubercular Activity of N-phenyl-4-oxo-butanamide derivatives (MABA)

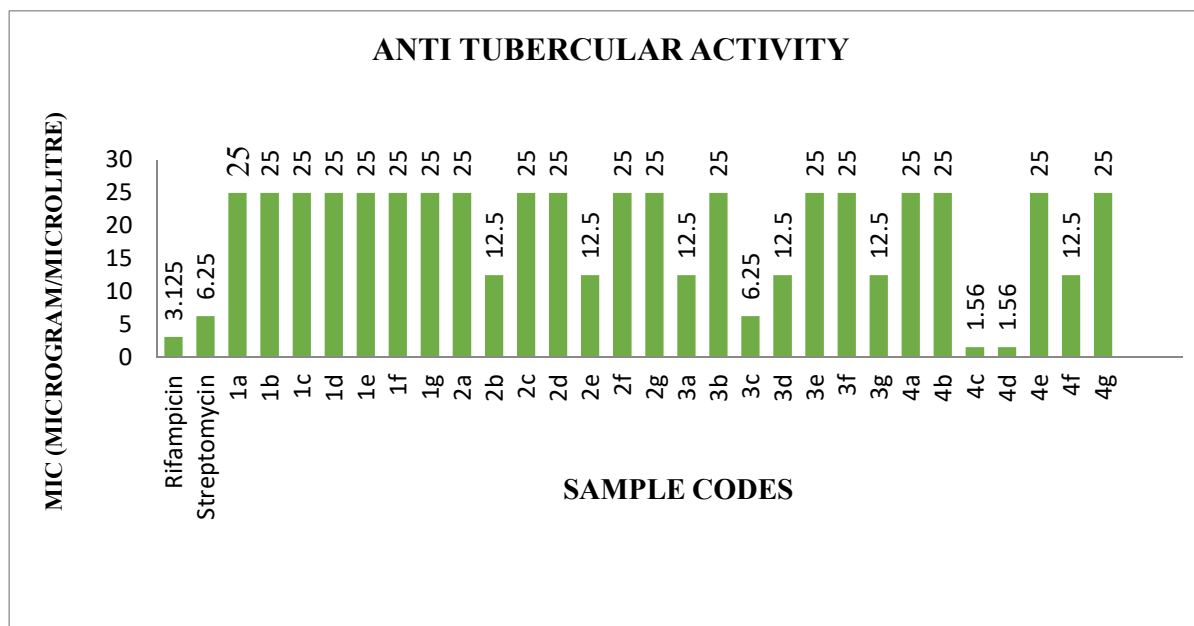
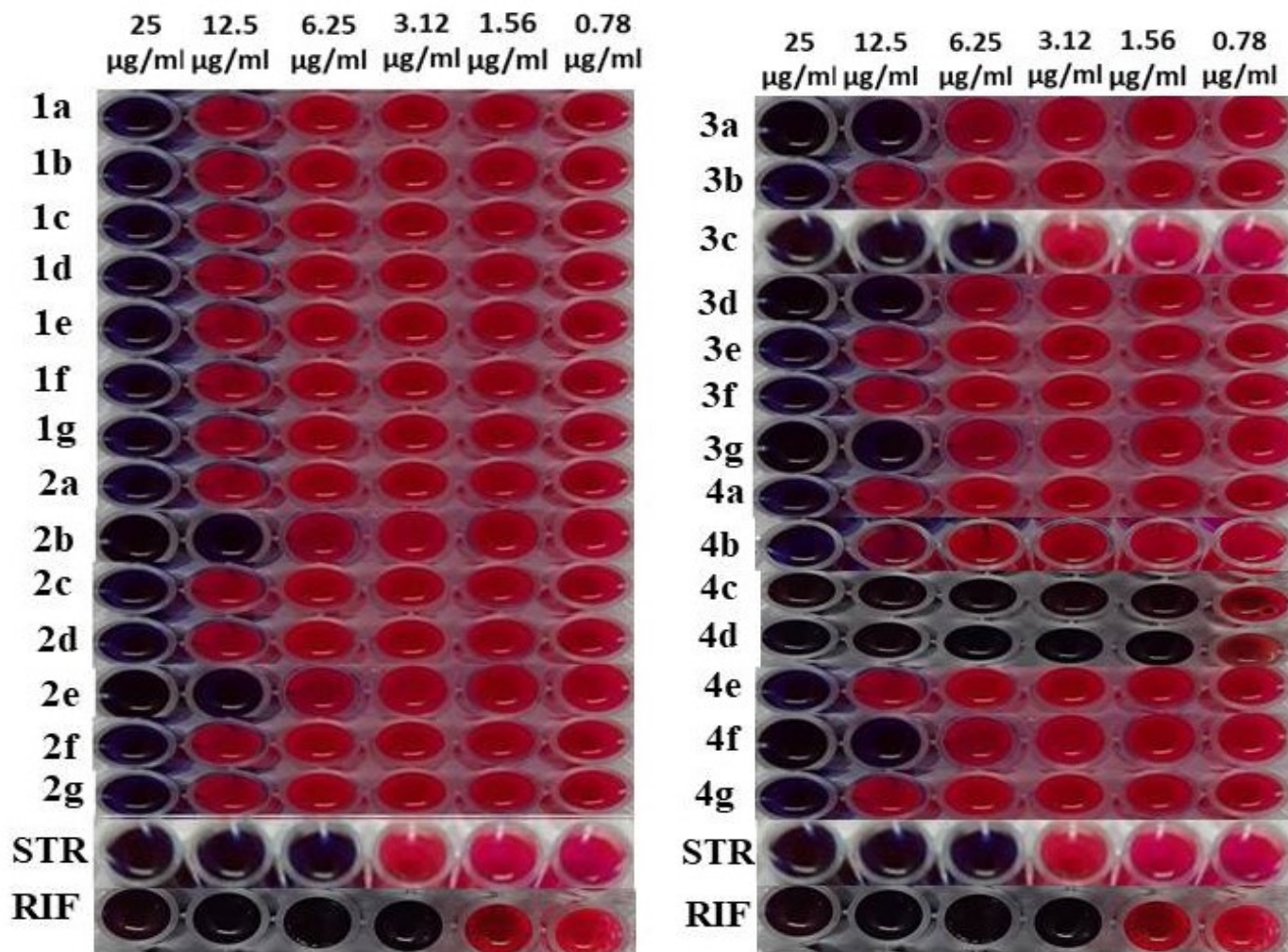


Fig. 70: MABA assay for the synthesized compounds [1(a-g);2(a-g);3(a-g);4(a-g)]
Against *Mtb* H37Rv



9) *In silico* studies:

10) Table 5: Drug likeness score for the synthesized N-phenyl-4-oxo-butanamide derivatives predicted using molinspiration

Compound	miLog P ^a	TPSA ^b	nAtoms	nON ^c	nOHNH ^d	nviolations	nrotb ^e	%ABS ^f	MW
1a	0.30	61.43	19	5	2	0	4	87.806	261.32
1b	0.90	52.65	20	5	1	0	4	90.846	275.35
1c	2.60	52.65	25	5	1	0	5	90.846	337.42
1d	2.30	52.65	26	5	1	0	6	90.846	351.45
1e	1.92	49.41	19	4	1	0	4	91.953	260.34
1f	1.41	49.41	18	4	1	0	4	91.953	246.31
1g	1.76	49.41	18	4	1	0	6	91.953	248.33
2a	0.98	61.43	20	5	2	0	4	87.806	295.77
2b	1.58	52.65	21	5	1	0	4	90.846	309.80
2c	3.27	52.65	26	5	1	0	5	90.846	371.87
2d	2.98	52.65	27	5	1	0	6	90.846	385.89
2e	2.59	49.41	20	4	1	0	4	91.953	294.78
2f	2.09	49.41	19	4	1	0	4	91.953	280.75
2g	2.44	49.41	19	4	1	0	6	91.953	282.77
3a	0.75	61.43	20	5	2	0	4	87.806	275.35
3b	1.35	52.65	21	5	1	0	4	90.846	289.38
3c	3.05	52.65	26	5	1	0	5	90.846	351.45
3d	2.75	52.65	27	5	1	0	6	90.846	365.48
3e	2.37	49.41	20	4	1	0	4	91.953	274.36
3f	1.86	49.41	19	4	1	0	4	91.953	260.34
3g	2.21	49.41	19	4	1	0	6	91.953	262.35
4a	0.56	61.43	21	5	2	0	4	87.806	297.31
4b	1.16	52.65	22	5	1	0	4	90.846	311.33
4c	2.85	52.65	27	5	1	0	5	90.846	373.40
4d	2.55	52.65	28	5	1	0	6	90.846	387.43
4e	2.17	49.41	21	4	1	0	4	91.953	296.32
4f	1.67	49.41	20	4	1	0	4	91.953	282.29
4g	2.02	49.41	20	4	1	0	6	91.953	284.31

^aLogarithm of partition coefficient between n-octanol and water (miLogP); ^btopological polar surface area (TPSA); ^cnumber of hydrogen bond acceptors (n-ON); ^dnumber of hydrogen bond donors (n-OHNH); ^enumber of rotatable bonds (n-rotb); ^fpercentage absorption (%ABS); gmolecular weight (MW).


11) Table 6: Predicted Bioactivity score of N-phenyl-4-oxo-butanamide derivatives according to molinspiration


Compound	GPCR	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1a	-0.06	-0.10	-0.19	-0.53	-0.10	-0.12
1b	-0.04	-0.12	-0.12	-0.46	-0.11	-0.12
1c	0.03	-0.14	-0.08	-0.29	-0.02	-0.14
1d	0.03	-0.14	-0.08	-0.29	0.03	-0.10
1e	-0.10	-0.15	-0.27	-0.46	-0.14	-0.12
1f	-0.19	-0.18	-0.32	-0.52	-0.13	-0.18
1g	-0.23	-0.24	-0.38	-0.58	-0.29	-0.21
2a	-0.07	-0.19	-0.20	-0.49	-0.12	-0.17
2b	-0.06	-0.20	-0.14	-0.42	-0.14	-0.18
2c	-0.01	-0.21	-0.13	-0.30	-0.07	-0.20
2d	-0.01	-0.21	-0.12	-0.31	-0.03	-0.15
2e	-0.11	-0.24	-0.28	-0.42	-0.15	-0.18
2f	-0.19	-0.28	-0.32	-0.47	-0.15	-0.23
2g	-0.22	-0.32	-0.37	-0.53	-0.30	-0.26
3a	-0.02	-0.10	-0.16	-0.48	-0.10	-0.14
3b	-0.01	-0.12	-0.11	-0.42	-0.12	-0.15
3c	0.02	-0.14	-0.10	-0.30	-0.06	-0.17
3d	0.02	-0.14	-0.10	-0.30	-0.01	-0.13
3e	-0.06	-0.15	-0.24	-0.41	-0.14	-0.14
3f	-0.13	-0.18	-0.28	-0.46	-0.13	-0.19
3g	-0.17	-0.23	-0.34	-0.52	-0.28	-0.23
4a	-0.03	-0.09	-0.02	-0.40	0.03	-0.10
4b	-0.03	-0.11	0.01	-0.35	-0.00	-0.11
4c	-0.01	-0.13	-0.02	-0.28	0.01	-0.14
4d	-0.01	-0.13	-0.02	-0.28	0.05	-0.10
4e	-0.07	-0.14	-0.09	-0.34	-0.01	-0.10
4f	-0.13	-0.17	-0.12	-0.37	0.01	-0.13
4g	-0.17	-0.21	-0.17	-0.42	-0.14	-0.17

12) Table 7: Toxicity predictions of N-phenyl-4-oxo-butanamide derivatives based on Osiris Property Explorer

Compound	Mutagenic	Tumorigenic	Reproductive effect	Irritant effect
1a	Yellow	Yellow	Yellow	Green
1b	Yellow	Yellow	Yellow	Yellow
1c	Yellow	Yellow	Yellow	Green
1d	Yellow	Yellow	Yellow	Green
1e	Yellow	Yellow	Yellow	Green
1f	Yellow	Yellow	Yellow	Green
1g	Yellow	Yellow	Yellow	Green
2a	Yellow	Yellow	Yellow	Green
2b	Yellow	Yellow	Yellow	Yellow
2c	Yellow	Yellow	Yellow	Green
2d	Yellow	Yellow	Yellow	Green
2e	Yellow	Yellow	Yellow	Green
2f	Yellow	Yellow	Yellow	Green
2g	Yellow	Yellow	Yellow	Green
3a	Yellow	Yellow	Yellow	Green
3b	Yellow	Yellow	Yellow	Yellow
3c	Yellow	Yellow	Yellow	Green
3d	Yellow	Yellow	Yellow	Green
3e	Yellow	Yellow	Yellow	Green
3f	Yellow	Yellow	Yellow	Green
3g	Yellow	Yellow	Yellow	Green
4a	Yellow	Yellow	Yellow	Green
4b	Yellow	Yellow	Yellow	Yellow
4c	Yellow	Yellow	Yellow	Green
4d	Yellow	Yellow	Yellow	Green
4e	Yellow	Yellow	Yellow	Green
4f	Yellow	Yellow	Yellow	Green
4g	Yellow	Yellow	Yellow	Green

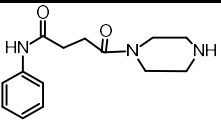
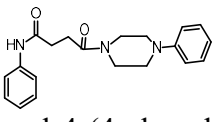
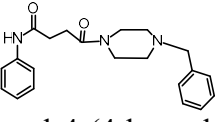
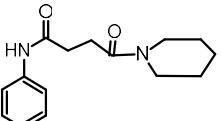
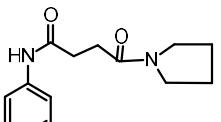
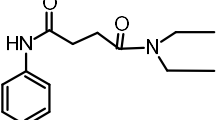
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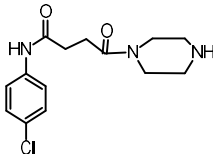
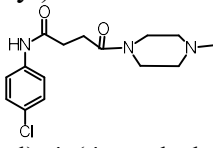
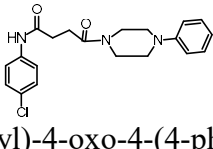
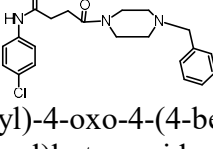
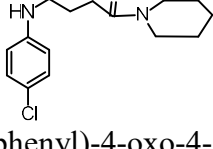
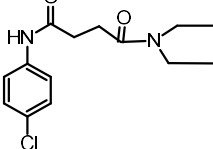
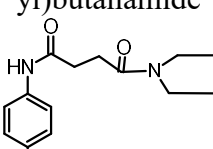
 = low toxicity

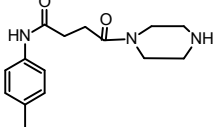
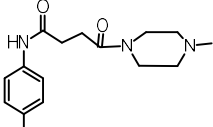
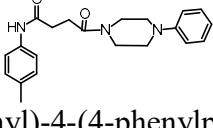
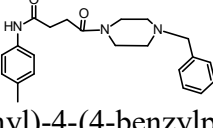
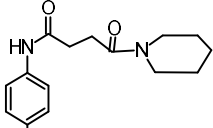
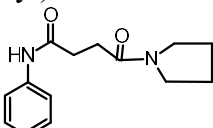
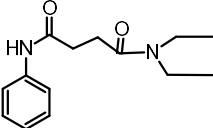
 = moderate toxicity

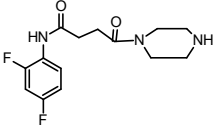
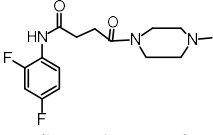
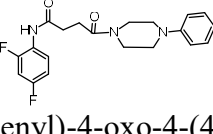
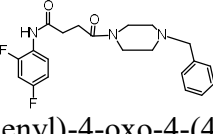
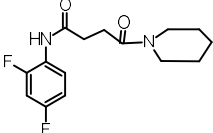
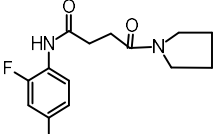
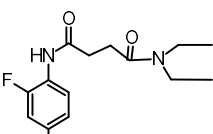
13) Molecular Docking Studies:

14) Table 8: Binding energies of N-phenyl-4-oxo-butanamide derivatives against receptor 2-transenoyl-acyl carrier protein (ACP) reductase (5MTP)

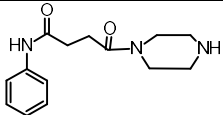
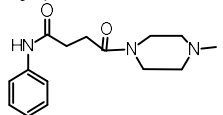
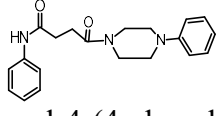
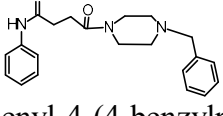
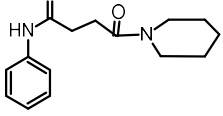
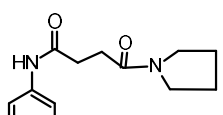
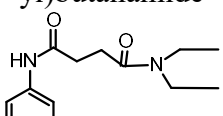
Compound codes	Structure & IUPAC Name	Docking Score	Interaction residues
1a	 4-oxo- <i>N</i> -phenyl-4-(piperazin-1-yl)butanamide	-7.7	Tyr-158
1b	 4-(4-methylpiperazin-1-yl)-4-oxo- <i>N</i> -phenylbutanamide	-8.1	Tyr-158 Lys-165
1c	 4-oxo- <i>N</i> -phenyl-4-(4-phenylpiperazin-1-yl)butanamide	-10.0	Gly-14 Ala-22 Ser-20
1d	 4-oxo- <i>N</i> -phenyl-4-(4-benzylpiperazin-1-yl)butanamide	-9.9	Gly-14 Ala-22 Ser-20
1e	 4-oxo- <i>N</i> -phenyl-4-(piperidin-1-yl)butanamide	-8.5	Gln-214
1f	 4-oxo- <i>N</i> -phenyl-4-(pyrrolidin-1-yl)butanamide	-8.1	Gly-96
1g	 <i>N</i> ¹ , <i>N</i> ¹ -diethyl- <i>N</i> ⁴ -phenylbutanediamide	-7.4	Gln-214

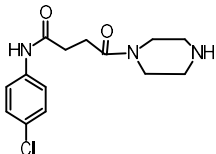
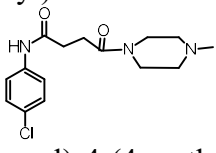
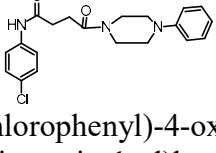
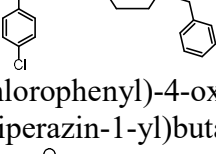
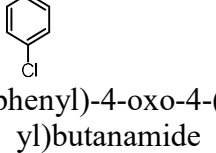
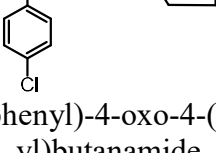
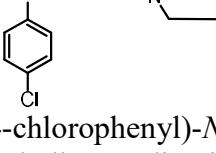
2a	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(piperazin-1-yl)butanamide</p>	-8.3	Tyr- 158
2b	 <p><i>N</i>-(4-chlorophenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide</p>	-8.6	Gln-214
2c	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide</p>	-10.0	Gln-214 Ala-22
2d	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide</p>	-10.0	Gly-14 Ser-20
2e	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide</p>	-8.8	Gln-214
2f	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide</p>	-8.3	Gly-96
2g	 <p><i>N</i>⁴-(4-chlorophenyl)-<i>N</i>¹,<i>N</i>¹-diethylbutanediamide</p>	-7.8	Gln-214

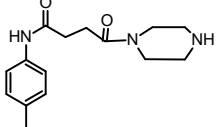
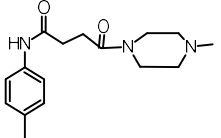
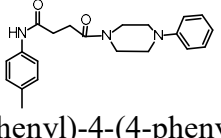
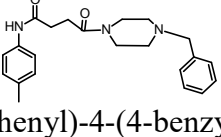
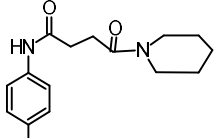
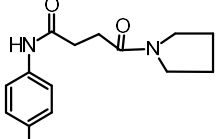
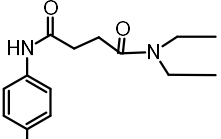
3a	 <i>N</i> -(4-methylphenyl)-4-oxo-4-(piperazin-1-yl)butanamide	-8.5	Ile-194 Thr-196
3b	 <i>N</i> -(4-methylphenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide	-8.6	Tyr-158
3c	 <i>N</i> -(4-methylphenyl)-4-(4-phenylpiperazin-1-yl)-4-oxobutanamide	-10.2	Gly-14 Ala-22
3d	 <i>N</i> -(4-methylphenyl)-4-(4-benzylpiperazin-1-yl)-4-oxobutanamide	-10.3	Gly-14 Ser-20 Ala-22
3e	 <i>N</i> -(4-methylphenyl)-4-oxo-4-(piperidin-1-yl)butanamide	-9.1	Gln-214
3f	 <i>N</i> -(4-methylphenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide	-8.5	Gly-96
3g	 <i>N</i> ¹ , <i>N</i> ¹ -diethyl- <i>N</i> ⁴ -(4-methylphenyl)butanediamide	-7.9	Gln-214

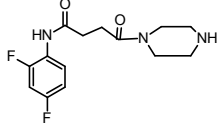
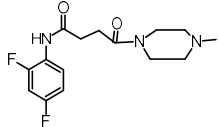
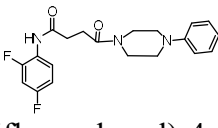
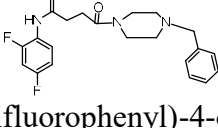
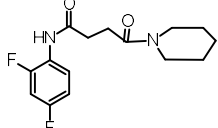
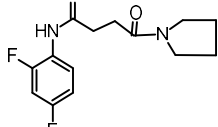
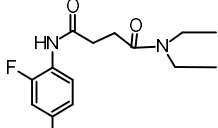
4a	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(piperazin-1-yl)butanamide	-8.6	Thr-196
4b	 <i>N</i> -(2,4-difluorophenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide	-8.5	Gly-14 Ala-22 Ser-94
4c	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide	-10.6	Tyr-158 Ala-22 Met-98
4d	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide	-10.4	Gly-96 Tyr-158 Ala-157
4e	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide	-8.5	Lys-165 Ile-194
4f	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide	-8.5	Gly-96
4g	 <i>N</i> ⁴ -(2,4-difluorophenyl)- <i>N</i> ¹ , <i>N</i> ¹ -diethylbutanediamide	-7.4	Tyr-158

15) Table 9: Binding energies of N-phenyl-4-oxo-butanamide derivatives against receptor β -ketoacyl-ACP reductase (1UZN)

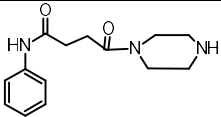
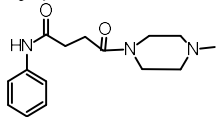
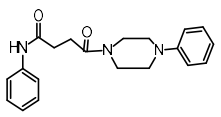
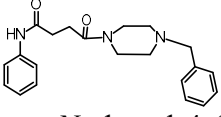
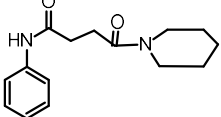
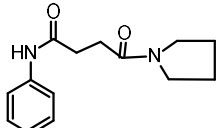
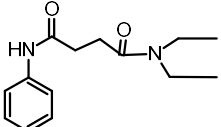
Compound codes	Structure& IUPAC Name	Docking Score	Interaction residues
1a	 4-oxo- <i>N</i> -phenyl-4-(piperazin-1-yl)butanamide	-7.2	Gly-22 Arg-25 Thr-45
1b	 4-(4-methylpiperazin-1-yl)-4-oxo- <i>N</i> -phenylbutanamide	-7.4	Gly-22 Arg -25 Thr-45
1c	 4-oxo- <i>N</i> -phenyl-4-(4-phenylpiperazin-1-yl)butanamide	-8.5	Arg -25
1d	 4-oxo- <i>N</i> -phenyl-4-(4-benzylpiperazin-1-yl)butanamide	-8.3	Gly-22 Arg-25 Thr-45
1e	 4-oxo- <i>N</i> -phenyl-4-(piperidin-1-yl)butanamide	-7.0	Gly-22 Thr-45 Arg-47
1f	 4-oxo- <i>N</i> -phenyl-4-(pyrrolidin-1-yl)butanamide	-7.0	Arg-25 Gly-90
1g	 <i>N</i> ¹ , <i>N</i> ¹ -diethyl- <i>N</i> ⁴ -phenylbutanediamide	-6.4	Gly-22 Thr-45 Arg-47

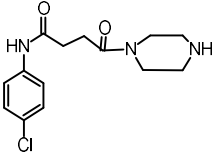
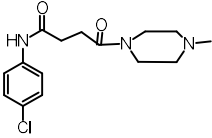
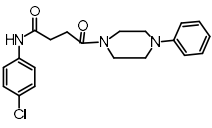
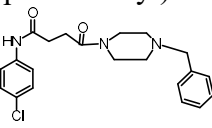
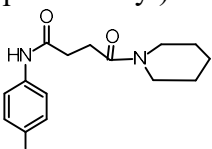
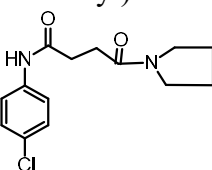
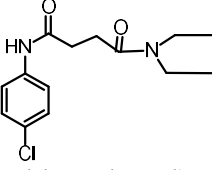
2a	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(piperazin-1-yl)butanamide</p>	-7.5	Asn-88 Ser-40
2b	 <p><i>N</i>-(4-chlorophenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide</p>	-7.3	Tyr-153, Lys-157
2c	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide</p>	-8.5	Tyr-153 Lys-157
2d	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide</p>	-8.4	Tyr-153, Lys-157
2e	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide</p>	-7.1	Gly-90 Tyr-153 Lys-157
2f	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide</p>	-7.0	Arg-25 Asn-88 Gly-90
2g	 <p><i>N</i>⁴-(4-chlorophenyl)-<i>N</i>¹,<i>N</i>¹-diethylbutanediamide</p>	-6.4	Trp-153 Lys-157

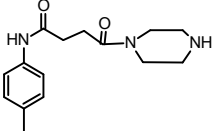
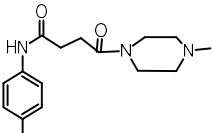
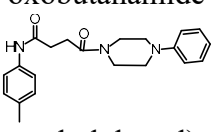
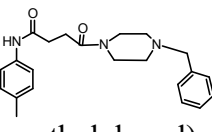
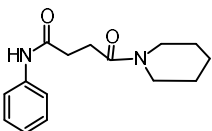
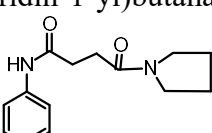
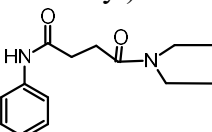
3a	 <p><i>N</i>-(4-methylphenyl)-4-oxo-4-(piperazin-1-yl)butanamide</p>	-7.4	Ser-140
3b	 <p><i>N</i>-(4-methylphenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide</p>	-7.4	Tyr-153 Lys-157
3c	 <p><i>N</i>-(4-methylphenyl)-4-(4-phenylpiperazin-1-yl)-4-oxobutanamide</p>	-8.5	Tyr-153 Lys-157
3d	 <p><i>N</i>-(4-methylphenyl)-4-(4-benzylpiperazin-1-yl)-4-oxobutanamide</p>	-8.3	Tyr-153 Lys-157
3e	 <p><i>N</i>-(4-methylphenyl)-4-oxo-4-(piperidin-1-yl)butanamide</p>	-7.4	Tyr-153 Lys-157
3f	 <p><i>N</i>-(4-methylphenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide</p>	-7.2	Arg-25 Gly-90
3g	 <p><i>N</i>¹,<i>N</i>¹-diethyl-<i>N</i>⁴-(4-methylphenyl)butanediamide</p>	-6.4	Trp-153 Lys-157

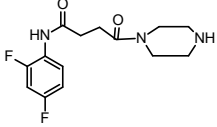
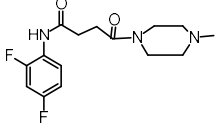
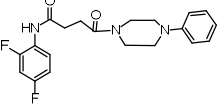
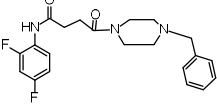
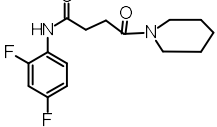
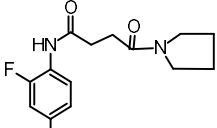
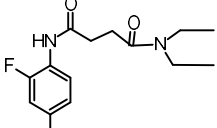
4a	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(piperazin-1-yl)butanamide	-7.5	Thr-45 Val-60 Gly-90
4b	 <i>N</i> -(2,4-difluorophenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide	-7.6	Arg-25 Gly-90
4c	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide	-9.1	Arg-25
4d	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide	-8.8	Arg-25 Gly-90
4e	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide	-7.8	Arg-25 Gly-90
4f	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide	-7.4	Arg-25 Gly-90
4g	 <i>N</i> ⁴ -(2,4-difluorophenyl)- <i>N</i> ¹ , <i>N</i> ¹ -diethylbutanediamide	-6.4	Trp-153 Lys-157

16) Table 10: Binding energies of N-phenyl-4-oxo-butanamide derivatives against receptor mycolic acid methyl transferase (MmaA1)

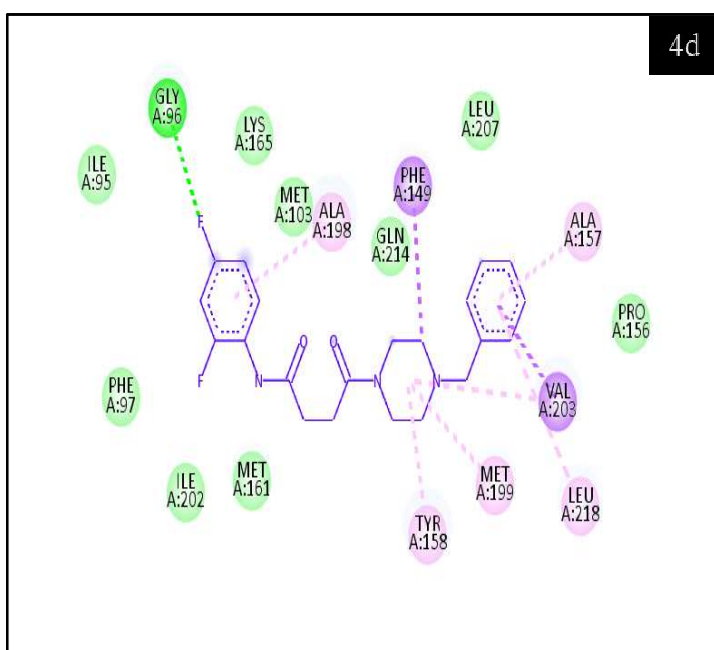
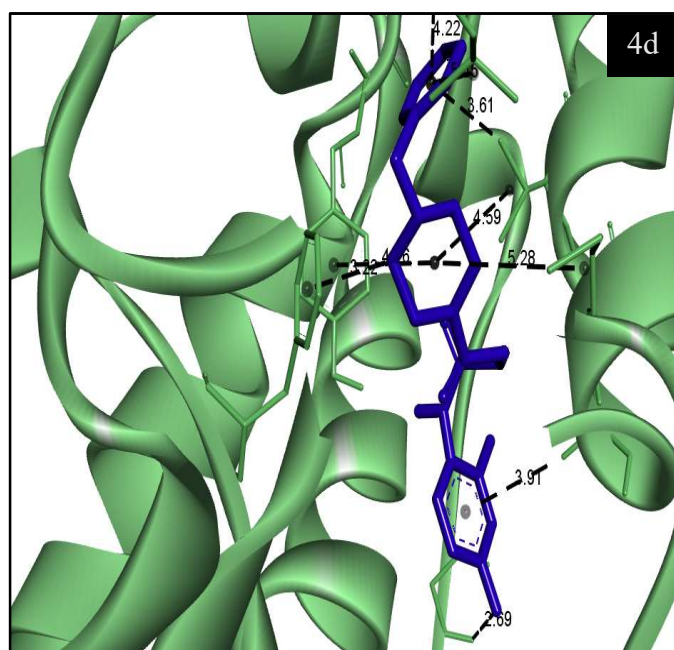
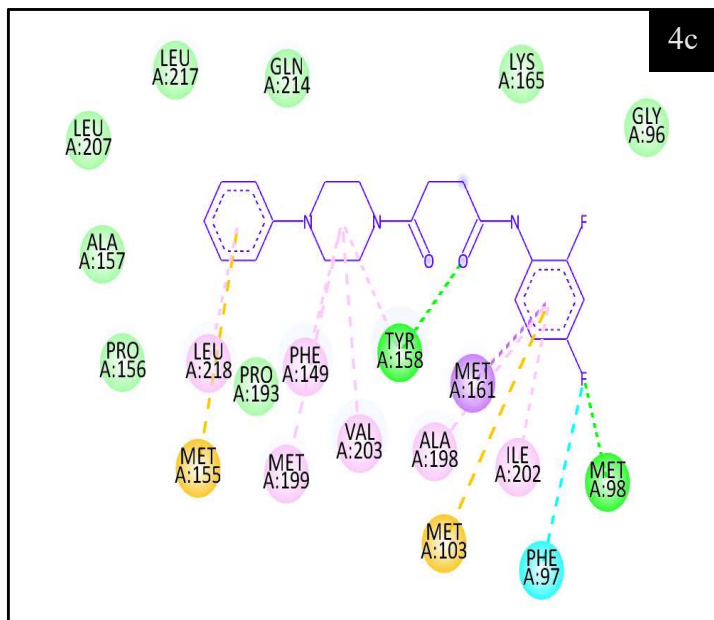
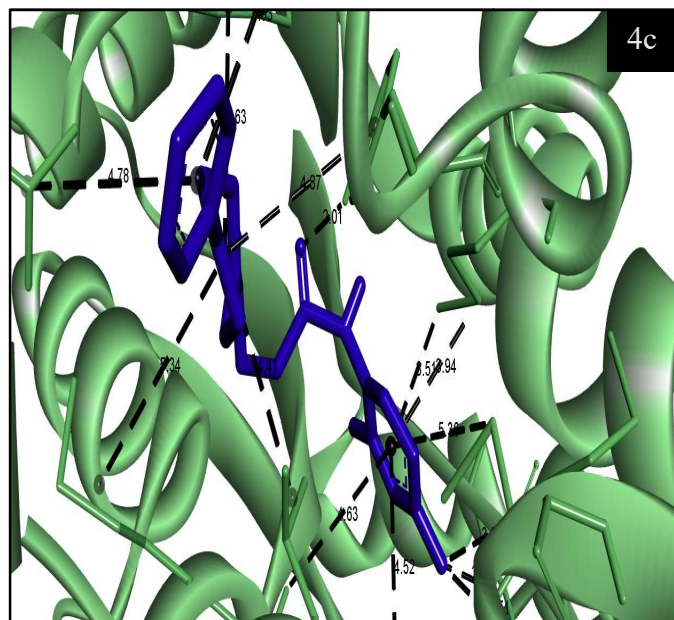
Compound codes	Structure& IUPAC Name	Docking Score	Interaction residues
1a	 4-oxo- <i>N</i> -phenyl-4-(piperazin-1-yl)butanamide	-7.2	His-98
1b	 4-(4-methylpiperazin-1-yl)-4-oxo- <i>N</i> -phenylbutanamide	-7.2	Ser-95
1c	 4-oxo- <i>N</i> -phenyl-4-(4-phenylpiperazin-1-yl)butanamide	-8.2	Lys-143
1d	 4-oxo- <i>N</i> -phenyl-4-(4-benzylpiperazin-1-yl)butanamide	-9.9	His-98
1e	 4-oxo- <i>N</i> -phenyl-4-(piperidin-1-yl)butanamide	-7.9	Lys-143
1f	 4-oxo- <i>N</i> -phenyl-4-(pyrrolidin-1-yl)butanamide	-8.2	Trp-30 Trp 74
1g	 <i>N</i> ¹ , <i>N</i> ¹ -diethyl- <i>N</i> ⁴ -phenylbutanediamide	-6.5	Ala-137

2a	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(piperazin-1-yl)butanamide</p>	-7.7	Ala-140
2b	 <p><i>N</i>-(4-chlorophenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide</p>	-8.1	Phe-135
2c	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide</p>	-10.3	His-98
2d	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide</p>	-10.5	His-98
2e	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide</p>	-8.6	Gly-71 Phe-135
2f	 <p><i>N</i>-(4-chlorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide</p>	-7.9	Trp-30 Trp-74
2g	 <p><i>N</i>⁴-(4-chlorophenyl)-<i>N</i>¹,<i>N</i>¹-diethylbutanediamide</p>	-7.0	His-98 Gly-71

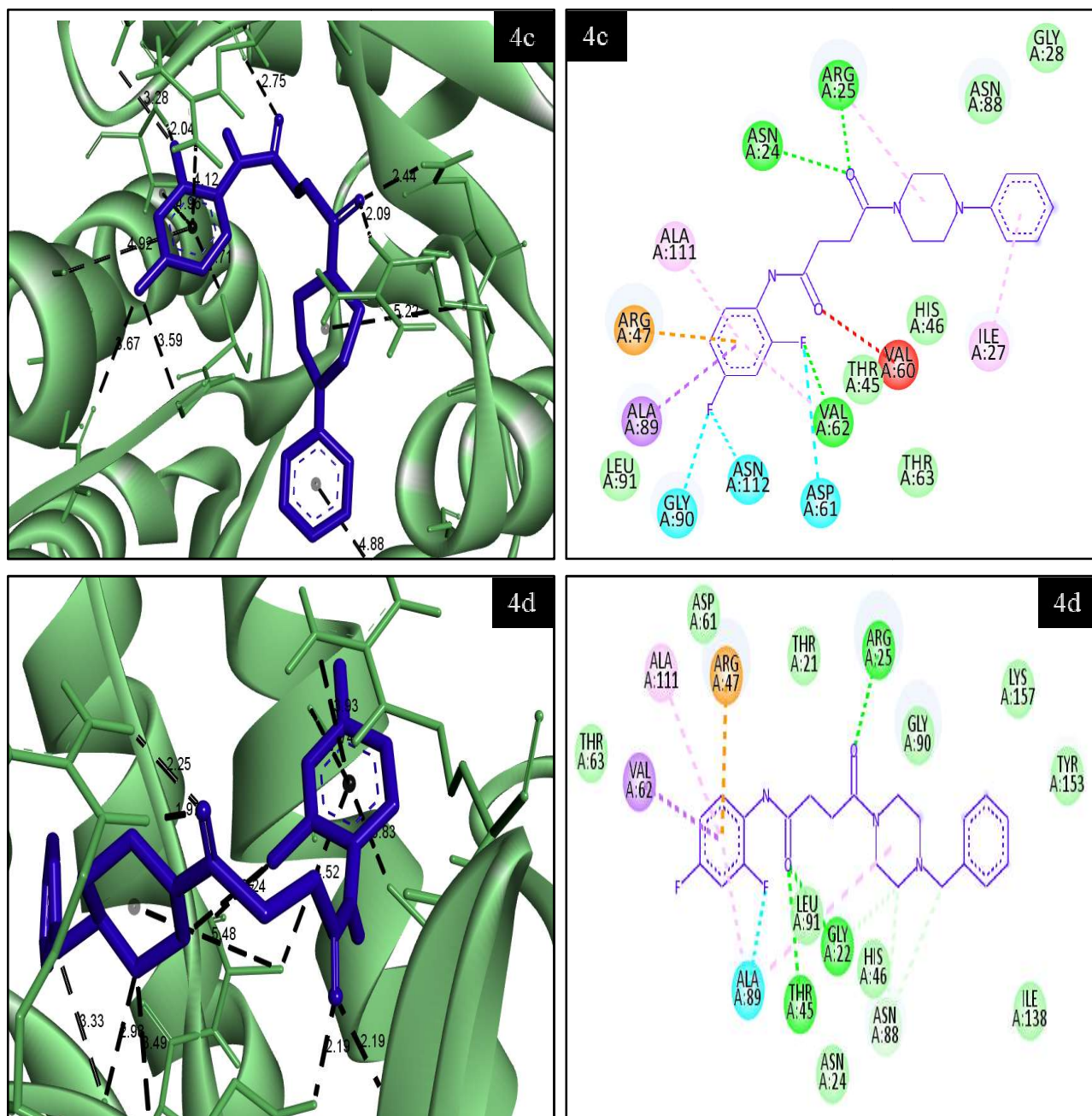
3a	 <p><i>N</i>-(4-methylphenyl)-4-oxo-4-(piperazin-1-yl)butanamide</p>	-7.9	Phe-135
3b	 <p><i>N</i>-(4-methylphenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide</p>	-8.0	Trp-30 Trp-74
3c	 <p><i>N</i>-(4-methylphenyl)-4-(4-phenylpiperazin-1-yl)-4-oxobutanamide</p>	-10.3	Gly-73 Trp-30
3d	 <p><i>N</i>-(4-methylphenyl)-4-(4-benzylpiperazin-1-yl)-4-oxobutanamide</p>	-8.6	His-98 Phe-22
3e	 <p><i>N</i>-(4-methylphenyl)-4-oxo-4-(piperidin-1-yl)butanamide</p>	-8.7	Gly-71 Phe-135
3f	 <p><i>N</i>-(4-methylphenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide</p>	-8.3	Trp-30 Trp-74
3g	 <p><i>N</i>¹,<i>N</i>¹-diethyl-<i>N</i>⁴-(4-methylphenyl)butanediamide</p>	-7.0	Ala -140

4a	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(piperazin-1-yl)butanamide	-8.0	Ser -134 Lys 143
4b	 <i>N</i> -(2,4-difluorophenyl)-4-(4-methylpiperazin-1-yl)-4-oxobutanamide	-8.0	Tyr-32
4c	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(4-phenylpiperazin-1-yl)butanamide	-9.5	Ala-137 Gly-75 Gly-76 Ala-77
4d	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(4-benzylpiperazin-1-yl)butanamide	-10.2	Ala-137 His-98 Trp-74 Glu-136 Phe-135
4e	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(piperidin-1-yl)butanamide	-9.2	Gly-71 Phe-135
4f	 <i>N</i> -(2,4-difluorophenyl)-4-oxo-4-(pyrrolidin-1-yl)butanamide	-8.8	His-98
4g	 <i>N</i> ⁴ -(2,4-difluorophenyl)- <i>N</i> ¹ , <i>N</i> ¹ -diethylbutanediamide	-7.7	Trp-122

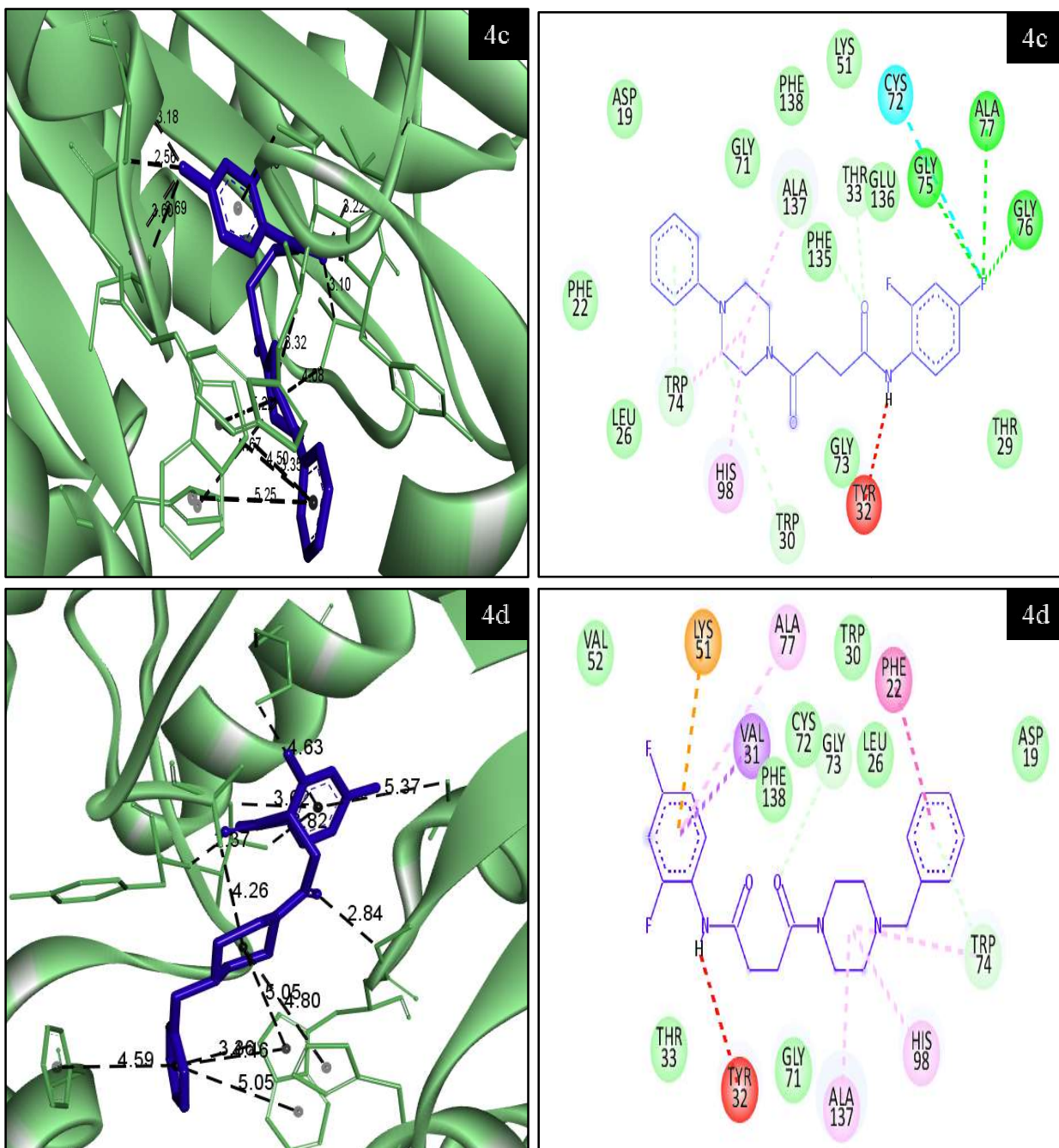
17) Fig. 71: Docking poses of the potent molecules (4c, 4d) with InhA enzyme. The protein is shown as green color solid ribbon model and the ligand is shown as dark blue stick model. The 2D interaction diagram of the protein-ligand interaction is shown on the right side.



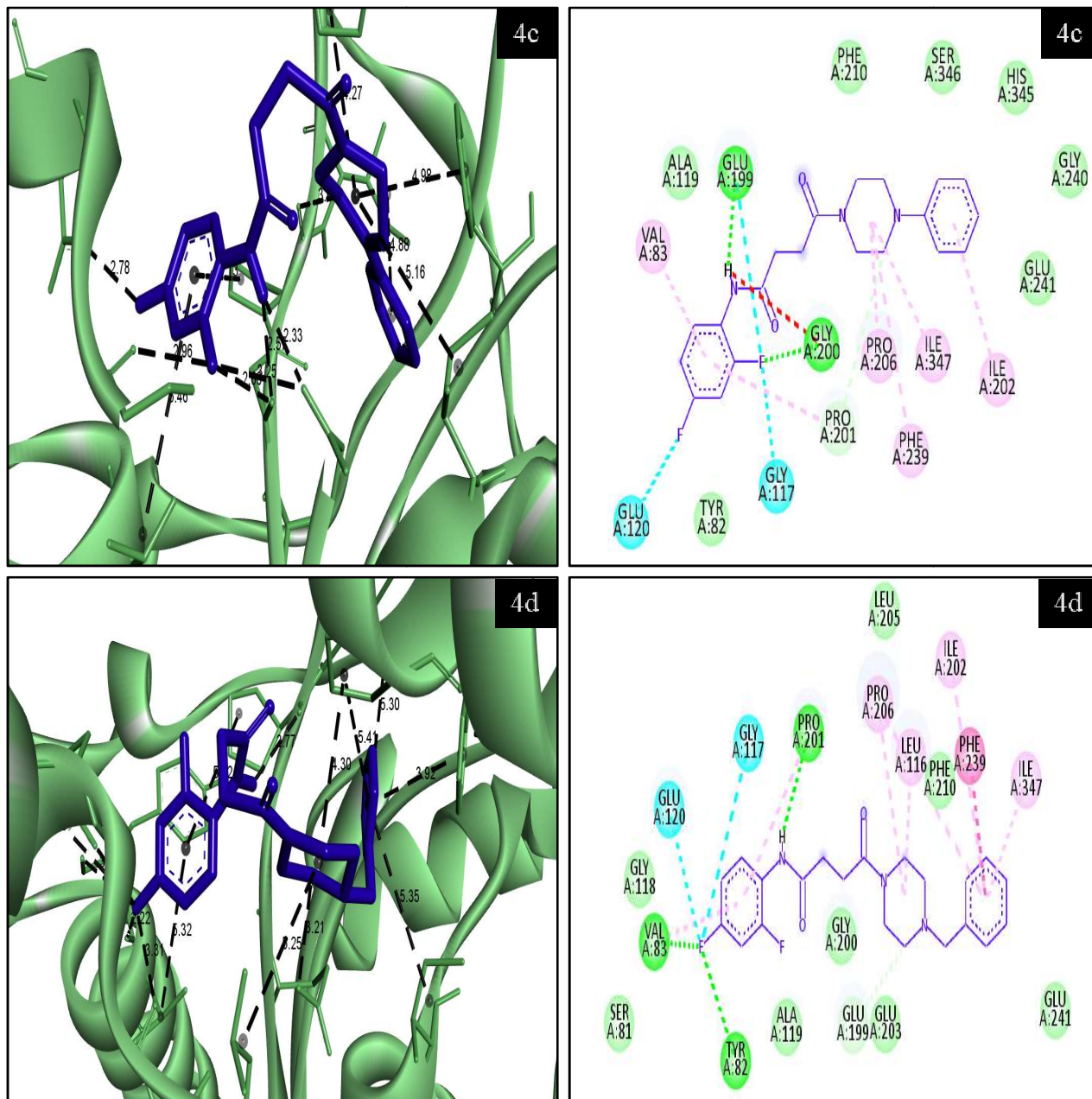
18) Fig. 72: Docking poses of the potent molecules (4c, 4d) with MabA enzyme. The protein is shown as green color solid ribbon model and the ligand is shown as dark blue stick model. The 2D interaction diagram of the protein-ligand interaction is shown on the right side.



19) Fig. 73: Docking poses of the potent molecules (4c, 4d) with MmaA1 enzyme. The protein is shown as green color solid ribbon model and the ligand is shown as dark blue stick model. The 2D interaction diagram of the protein-ligand interaction is shown on the right side.



20) Fig. 74: Docking poses of the potent molecules (4c, 4d) with KasA enzyme. The protein is shown as green color solid ribbon model and the ligand is shown as dark blue stick model. The 2D interaction diagram of the protein-ligand interaction is shown on the right side.



21) Fig. 75: Docking poses of the potent molecules (4c, 4d) with FabH enzyme. The protein is shown as ribbon model and the ligand is shown as green color stick model. The 2D interaction diagram of the protein-ligand interaction is shown on the right side.

