Supplementary Information

Design, synthesis and evaluation of antitubercular activity of 4-oxo-butanamido benzoate derivatives

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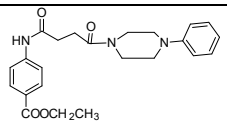
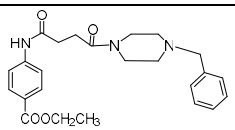
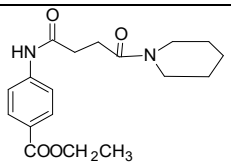
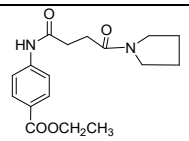
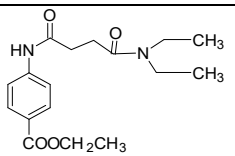
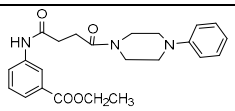
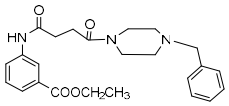
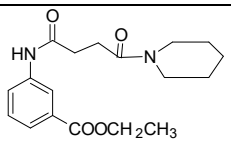
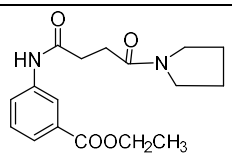
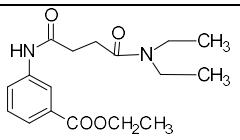
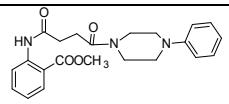
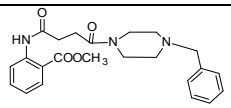
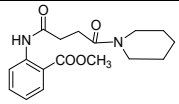
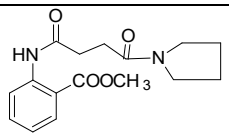
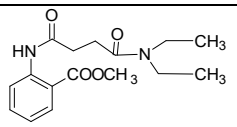
1) Table 1: Physico-Chemical Characteristics of Synthesized compounds

Compound codes	Structure& IUPAC Name	Yield (%)	M.P^{0}C	Molecular mass	Empirical formula
SA1a	 ethyl 4-[4-(4-Phenylpiperazin-1-yl)-4-oxobutanamido]benzoate	73.69	162	409.49	$C_{23}H_{27}N_3O_4$
SA1b	 ethyl 4-[4-(4-Benzylpiperazin-1-yl)-4-oxobutanamido]benzoate	74.33	186	423.51	$C_{24}H_{29}N_3O_4$
SA1c	 ethyl 4-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate	71.73	143	332.40	$C_{18}H_{24}N_2O_4$

SA1d	 ethyl 4-[4-oxo-4-(pyrrolidin-1-yl)butanamido]benzoate	73.20	123	318.37	$C_{17}H_{22}N_2O_4$
SA1e	 ethyl 4-[4-(diethylamino)-4-oxobutanamido]benzoate	68.75	101	320.39	$C_{17}H_{24}N_2O_4$
SA2a	 ethyl 3-(4-oxo-4-(4-phenylpiperazin-1-yl)butanamido)benzoate	72.14	158	409.49	$C_{23}H_{27}N_3O_4$
SA2b	 ethyl 3-(4-(4-benzylpiperazin-1-yl)-4-oxobutanamido)benzoate	76.61	161	423.51	$C_{24}H_{29}N_3O_4$
SA2c	 ethyl 3-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate	70.11	136	332.40	$C_{18}H_{24}N_2O_4$

SA2d	 ethyl 3-[4-oxo-4-(pyrrolidin-1-yl)butanamido]benzoate	71.09	133	318.37	$C_{17}H_{22}N_2O_4$
SA2e	 ethyl 3-[4-(diethylamino)-4-oxobutanamido]benzoate	67.73	104	320.39	$C_{17}H_{24}N_2O_4$
SA3a	 methyl 2-[4-(4-phenylpiperazin-1-yl)-4-oxobutanamido]benzoate	74.80	148	395.46	$C_{22}H_{25}N_3O_4$
SA3b	 methyl 2-[4-(4-benzylpiperazin-1-yl)-4-oxobutanamido]benzoate	75.27	162	409.49	$C_{23}H_{27}N_3O_4$
SA3c		74.38	111	318.37	$C_{17}H_{22}N_2O_4$

	methyl 2-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate				
SA3d	 methyl 2-[4-oxo-4-(pyrrolidin-1-yl)butanamido]benzoate	73.22	130	304.35	$C_{16}H_{20}N_2O_4$
SA3e	 methyl 2-[4-(diethylamino)-4-oxobutanamido]benzoate	67.14	92	306.36	$C_{16}H_{22}N_2O_4$

2) Structural Elucidation of a Synthesized Compounds by Spectroscopic Techniques

Compound (SA1a): ethyl 4-[4-(4-Phenylpiperazin-1-yl)-4-oxobutanamido]benzoate

Yield: 73.6%; mp: 162 ^{0}C; IR (KBr): 1233 (C-O), 1589 (C=O), 1736 (C=O), 3146 (Ar C-H), 3368 (NH) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 9.01 (1H, s), 7.99 (2H, m, J = 8.3 Hz), 7.63 (2H, m, J = 8.4 Hz), 7.28 (2H, m, J = 7.74 Hz), 6.95 (3H, m, J = 7.71 Hz), 4.37 (2H, q, J = 7.1 Hz), 3.81 (4H, m), 3.21 (4H, m), 2.94 (4H, t, J = 7.3 Hz), 1.39 (3H, t, J = 7.1 Hz); ^{13}CNMR (100 MHz, $CDCl_3$): δ 171.12, 166.23,150.78, 142.43, 130.67, 129.30, 125.53, 120.74, 118.67, 116.74, 60.78, 49.36, 45.38, 41.94, 32.83, 28.88, 14.36; HRMS (ESI): m/z calcd. for $C_{23}H_{27}N_3O_4$: $[M+H]^+$: 410.20, found 410.20; Anal calcd. for $C_{23}H_{27}N_3O_4$: C: 67.46; H: 6.65; N:10.26;O:15.63%; found C: 67.46; H: 6.65; N:10.26;O:15.63%

Compound (SA1b): ethyl 4-[4-(4-benzylpiperazin-1-yl)-4-oxobutanamido]benzoate

Yield: 74.3%; mp: 186 ^{0}C; IR (KBr): 1293 (C-O), 1644 (C=O), 1732 (C=O), 2875, 3102 (Ar C-H), 3377 (NH) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 9.15 (1H, s), 7.95 (2H, m, J = 8.5 Hz), 7.61 (2H, m, J = 8.47 Hz), 7.33 (3H, m, J = 7.74 Hz), 7.28 (2H, m, J = 7.71 Hz), 4.37 (2H, q, J = 7.1 Hz), 3.66 (2H, m), 3.53 (4H, m), 2.77 (4H, t, J = 7.3 Hz); 2.45 (4H, m), 1.39 (3H, t, J = 7.1 Hz); ^{13}CNMR (100 MHz, $CDCl_3$): δ 175.72, 171.24, 165.70,142.57, 137.47, 130.43, 127.35, 118.65, 62.81, 60.75, 52.61, 45.46, 42.05, 32.81, 28.80, 14.36; HRMS (ESI): m/z calcd. For $C_{24}H_{29}N_3O_4$: $[M+H]^+$: 424.22, found 424.22; Anal calcd. for $C_{24}H_{29}N_3O_4$: C: 68.06; H: 6.90; N:9.92 ;O:15.11%; found C: 68.06; H: 6.90; N:9.92;O:15.11%

Compound (SA1c): ethyl 4-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

Yield: 71.7%; mp: 143 ^{0}C; IR (KBr): 1199 (C-O), 1619 (C=O), 1716 (C=O), 3230 (Ar C-H), 3405(NH) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 9.321 (1H, s), 7.95 (2H, m, J = 8.3 Hz), 7.60 (2H, m, J = 8.4 Hz), 4.33 (2H, q, J = 7.1 Hz), 3.58 (4H, m), 2.77 (4H, t, J = 7.3 Hz); 1.6 (2H), 1.56 (4H, m), 1.39 (3H, t, J = 7.1 Hz);^{13}CNMR (100 MHz, $CDCl_3$): δ 171.46, 170.28,

166.28,142.63, 130.62, 125.33, 118.64, 60.74, 46.54, 43.17, 33.11, 29.05, 25.53, 24.38, 14.36; HRMS (ESI): m/z calcd. for $C_{18}H_{24}N_2O_4$: $[M+H]^+$: 333.18, found 333.18; Anal calcd. for $C_{18}H_{24}N_2O_4$: C:65.04; H:7.28; N: 8.43; O: 19.25 %; found C:65.04; H:7.28; N: 8.43; O: 19.25%.

Compound (SA1d): ethyl 4-[4-oxo-4-(pyrrolidin-1-yl)butanamido]benzoate

Yield: 73.2%; mp: 123 ^{0}C; IR (KBr): 1208 (C-O), 1539 (C=O), 1747 (C=O), 3024 (Ar C-H), 3495 (NH) cm^{-1}; ^{1}HNMR (400 MHz, DMSO): δ 7.87 (2H, m, J = 8.4 Hz), 7.73 (2H, m, J = 8.4 Hz), 4.28 (2H, q, J = 7.1 Hz), 3.28 (4H, m), 2.63-2.50 (4H, t, J = 7.3 Hz), 1.89 (4H, m), 1.32 (3H, t, J = 7.1 Hz);^{13}CNMR (100 MHz, DMSO): δ 171.86, 169.86, 165.85, 144.27, 130.62, 124.22, 118.67, 60.84, 46.25, 45.76, 31.71, 29.26, 26.05, 24.43, 14.68; HRMS (ESI): m/z calcd. for $C_{17}H_{22}N_2O_4$: $[M+H]^+$: 319.16, found 319.16; Anal calcd. For $C_{17}H_{22}N_2O_4$: C:64.13; H:6.97; N: 8.80; O: 20.10 %; found C:64.13; H:6.97; N: 8.80; O: 20.10%.

Compound (SA1e): ethyl 4-[4-(diethylamino)-4-oxobutanamido]benzoate

Yield: 68.7%; mp: 101 ^{0}C; IR (KBr): 1133 (C-O), 1629 (C=O), 1763 (C=O), 3012 (Ar C-H), 3501 (NH) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 7.93 (2H, m, J = 8.4 Hz), 7.72 (2H, m, J = 8.4 Hz), 4.24 (2H, q, J = 7.1 Hz), 3.36 (4H, m), 2.87 (4H, t, J = 7.3 Hz), 1.32 (3H, t, J = 7.1 Hz), 1.14 (6H, t, J = 7.1 Hz);^{13}CNMR (100 MHz, $CDCl_3$): δ 170.16, 167.86, 165.85, 144.27, 132.62, 124.22, 117.97, 61.24, 46.25, 45.76, 31.71, 27.26, 24.15, 14.68, 12.6; HRMS (ESI): m/z calcd. for $C_{17}H_{24}N_2O_4$: $[M+H]^+$: 321.18, found 321.18; Anal calcd. for $C_{17}H_{24}N_2O_4$: C: 63.73; H: 7.55; N: 8.74; O: 19.97%; found C: 63.73; H: 7.55; N: 8.74; O: 19.97%.

Compound (SA2a): ethyl 3-(4-oxo-4-(4-phenylpiperazin-1-yl)butanamido)benzoate

Yield: 72.1%; mp: 158 ^{0}C; IR (KBr): 1290 (C-O), 1651 (C=O), 1706 (C=O), 3121 (Ar C-H), 3379(NH) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.88 (1H, s), 8.10 (1H, m,), 7.88 (1H, m, J = 7.79 Hz), 7.74 (1H, m, J = 7.82 Hz), 7.50 (1H, m, J = 7.81 Hz), 7.23 (3H, m, J = 7.7 Hz), 6.93 (2H, m, J = 7.74 Hz), 4.37 (2H, q, J = 7.1 Hz), 3.87 (4H, m), 3.18 (4H, m), 2.82 (4H, t, J = 7.3 Hz), , 1.94 (3H, t, J = 7.1 Hz);^{13}CNMR (100 MHz, $CDCl_3$): δ 170.62, 166.85, 150.82, 138.55, 130.75, 129.28, 124.19, 120.69, 116.72, 61.1, 52.19, 49.60, 45.38, 41.93, 32.61, 28.83, 14.3 ; HRMS (ESI): m/z calcd. for $C_{23}H_{27}N_3O_4$: $[M+H]^+$: 410.20; found 410.20; Anal calcd. for $C_{23}H_{27}N_3O_4$: C:67.46; H: 6.65; N: 10.26; O:15.63%; found : C:67.46; H: 6.65; N: 10.26; O:15.63%.

Compound (SA2b): ethyl 3-(4-(4-benzylpiperazin-1-yl)-4-oxobutanamido)benzoate

Yield: 76.6%; mp: 161 ^{0}C; IR (KBr): 1244 (C-O), 1562 (C=O), 1718 (C=O), 3130 (Ar C-H), 3488 (NH)cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.08 (1H, m,), 7.99 (1H, m, J = 7.79 Hz), 7.57 (1H, m, J = 7.82 Hz), 7.50 (1H, m, J = 7.81 Hz), 7.36 (2H, m, J = 7.74 Hz), 7.30 (3H, m, J = 7.7 Hz), 4.37 (2H, q, J = 7.1 Hz), 3.66 (2H, m), 3.51 (4H, m), 2.93 (4H, t, J = 7.3 Hz), 2.43 (4H, m), 1.69 (3H, t, J = 7.1 Hz); ^{13}CNMR (100 MHz, $CDCl_3$): δ 170.49, 165.70, 142.57, 137.47, 130.43, 129.28, 127.35, 125.38, 118.65, 62.81, 60.75, 52.61, 45.46, 42.05, 32.81, 28.45, 14.36; HRMS (ESI): m/z calcd. for $C_{24}H_{29}N_3O_4$: $[M+H]^+$: 424.22, found 424.22; Anal calcd. for $C_{24}H_{29}N_3O_4$: C: 68.06; H: 6.90; N: 9.92; O:15.11%; found : C: 68.06; H: 6.90; N: 9.92; O:15.11%.

Compound (SA2c): ethyl 3-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

Yield: 70.1%; mp: 136 ^{0}C; IR (KBr): 1221 (C-O), 1544 (C=O), 1728 (C=O), 3088 (Ar C-H), 3309 (NH)cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.08 (1H, m, J = 7.79 Hz), 7.88 (1H, m, J = 7.79 Hz), 7.74 (1H, m, J = 7.82 Hz), 7.37 (1H, m, J = 7.8 Hz), 4.37 (2H, q, J = 7.1 Hz), 3.45 (4H, m), 2.77 (4H, t, J = 7.3 Hz), 1.60 (6H, m), 1.56 (3H, t, J = 7.1 Hz); ^{13}CNMR (100 MHz, $CDCl_3$): δ 171.37, 170.24, 166.39, 138.59, 131.11, 128.89, 124.11, 120.52, 61.04, 46.51, 43.13, 32.95, 29.10, 24.40, 14.3; HRMS (ESI): m/z calcd. for $C_{18}H_{24}N_2O_4$: $[M+H]^+$: 333.18, found 333.18; Anal calcd. for $C_{18}H_{24}N_2O_4$: C: 65.04; H: 7.28; N: 8.43; O:19.25%; found : C: 65.04; H: 7.28; N: 8.43; O:19.25%.

Compound (SA2d): ethyl 3-[4-oxo-4-(pyrrolidin-1-yl)butanamido]benzoate

Yield: 71.0%; mp: 133 ^{0}C; IR (KBr): 1266 (C-O), 1509 (C=O), 1722 (C=O), 3125 (Ar C-H), 3489 (NH) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 9.35 (1H, s), 8.11 (1H, m, J = 7.79 Hz), 7.88 (1H, m, J = 7.79 Hz), 7.73 (1H, m, J = 7.82 Hz), 7.34 (1H, m, J = 7.81 Hz), 4.37 (2H, q, J = 7.1 Hz), 3.49 (4H, m), 2.74 (4H, t, J = 7.3 Hz), 2.0 (4H, m), 1.7 (3H, t, J = 7.1 Hz); ^{13}CNMR (100 MHz, $CDCl_3$): δ 171.32, 170.73, 166.89, 138.76, 130.70, 128.90, 124.15, 120.54, 61.02, 52.13, 46.08, 32.63, 30.43, 26.02, 24.37, 14.34 ; HRMS (ESI): m/z calcd. for $C_{17}H_{22}N_2O_4$: $[M+H]^+$: 319.16, found 319.16; Anal calcd. for $C_{17}H_{22}N_2O_4$: C: 64.13; H: 6.97; N: 8.80; O:20.10%; found : C: 64.13; H: 6.97; N: 8.80; O:20.10%.

Compound (SA2e): ethyl 3-[4-(diethylamino)-4-oxobutanamido]benzoate

Yield: 67.7%; mp: 104 ^{0}C; IR (KBr): 1193 (C-O), 1596 (C=O), 1737 (C=O), 3006 (Ar C-H), 3480 (NH) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.10 (1H, m, J = 7.79 Hz), 8.0 (1H, m, J = 7.79 Hz), 7.60 (1H, m, J = 7.82 Hz), 7.50 (1H, m, J = 7.81 Hz), 4.37 (2H, q, J = 7.1 Hz), 3.92 (4H, m), 2.9 (4H, t, J = 7.3 Hz), 1.20 (6H, t, J = 7.1 Hz), 1.39 (3H, t, J = 7.1 Hz); ^{13}CNMR (100 MHz, $CDCl_3$): δ 171.16, 168.86, 166.85, 138.42, 129.62, 127.88, 124.22, 119.71, 117.97, 60.24, 46.2, 43.76, 31.71, 27.26, 14.68, 12.4; HRMS (ESI): m/z calcd. for $C_{17}H_{24}N_2O_4$: $[M+H]^+$: 321.18, found 321.18; Anal calcd. for $C_{17}H_{24}N_2O_4$: C: 63.73; H: 7.55; N: 8.74; O:19.97%; found : C: 63.73; H: 7.55; N: 8.74; O:19.97%.

Compound (SA3a): methyl 2-[4-(4-phenylpiperazin-1-yl)-4-oxobutanamido]benzoate

Yield: 74.8%; mp: 148 ^{0}C; IR (KBr): 1230 (C-O), 1579 (C=O), 1750 (C=O), 3076 (Ar C-H), 3518 (NH) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.69 (1H, m, J = 8.13 Hz), 8.13 (1H, m, J = 7.88 Hz), 8.01 (1H, m, J = 7.81 Hz), 7.50 (1H, m, J = 8.13 Hz), 7.27 (2H, m, J = 8.28 Hz), 7.07 (1H, m, J = 8.10 Hz), 6.89 (2H, m, J = 8.28 Hz), 3.93 (3H), 3.71 (4H, m), 3.68 (4H, m), 2.85-2.75 (4H, t, J = 7.3 Hz); ^{13}CNMR (100 MHz, $CDCl_3$): δ 173.03, 171.17, 168.71, 164.94, 150.98, 141.52, 134.66, 132.67, 130.79, 129.24, 127.12, 122.49, 122.38, 120.39, 115.01, 52.35, 49.36, 45.27, 41.71, 33.06, 28.87; HRMS (ESI): m/z calcd. for $C_{22}H_{25}N_3O_4$: $[M+H]^+$: 396.19, found 396.19; Anal calcd. for $C_{22}H_{25}N_3O_4$: C:66.82; H: 6.37; N:10.63; O:16.18%; found : C:66.82; H: 6.37; N:10.63; O:16.18%.

Compound (SA3b): methyl 2-[4-(4-benzylpiperazin-1-yl)-4-oxobutanamido]benzoate

Yield: 75.2%; mp: 162 ^{0}C; IR (KBr): 1159 (C-O), 1601 (C=O), 1724 (C=O), 3014 (Ar C-H), 3546 (NH)cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.71 (1H, m, J = 8.13 Hz), 8.16 (1H, m, J = 7.88 Hz), 8.03 (1H, m, J = 7.51 Hz), 7.68 (1H, m, J = 8.13 Hz), 7.53 (2H, m, J = 8.28 Hz), 7.32 (1H, m, J = 8.10 Hz), 7.09 (2H, m, J = 8.28 Hz), 3.56 (2H, m), 3.94 (3H), 3.56 (4H, m), 3.37 (4H, m), 2.84-2.73 (4H, t, J = 7.38 Hz); ^{13}CNMR (100 MHz, $CDCl_3$): δ 171.27, 169.79, 168.59, 164.93, 160.75, 141.53, 137.55, 138.55, 131.78, 129.43, 128.37,127.35, 122.33, 120.40, 115.01, 62.89, 53.02, 52.32, 45.68, 41.80, 33.12, 28.87; HRMS (ESI): m/z calcd. for $C_{23}H_{27}N_3O_4$: $[M+H]^+$: 410.20, found 410.20; Anal calcd. for $C_{23}H_{27}N_3O_4$: C: 67.46; H:6.65; N: 10.26; O:15.63%; found : C: 67.46; H:6.65; N: 10.26; O:15.63%.

Compound (SA3c): methyl 2-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

Yield: 74.3%; mp: 111 ^{0}C; IR (KBr): 1190 (C-O), 1559 (C=O), 1746 (C=O), 3069 (Ar C-H), 3365 (NH) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.70 (1H, m, J = 8.13 Hz), 8.01 (1H, m, J = 7.88 Hz), 7.5 (1H, m, J = 7.51 Hz), 7.0 (1H, m, J = 8.13 Hz), 3.93 (3H), 3.55 (4H, m), 2.80 (2H, t, J = 7.3 Hz), 2.76 (2H, t, J = 7.3 Hz), 1.66-1.54 (6H, m); ^{13}CNMR (100 MHz, $CDCl_3$): δ 171.46, 169.55, 168.57, 141.57, 134.49, 130.74, 122.28, 120.42, 115.01, 52.31, 46.39, 42.88, 33.27, 28.21, 23.53, 24.56; HRMS (ESI): m/z calcd. for $C_{17}H_{22}N_2O_{42}$: $[M+H]^+$: 319.16, found 319.16; Anal calcd. for $C_{17}H_{22}N_2O_4$: C:64.13; H: 6.97; N: 8.80; O:20.10%; found : C:64.13; H: 6.97; N: 8.80; O:20.10%.

Compound (SA3d): methyl 2-[4-oxo-4-(pyrrolidin-1-yl)butanamido]benzoate

Yield: 73.2%; mp: 130 ^{0}C; IR (KBr): 1243 (C-O), 1590 (C=O), 1761 (C=O), 3046 (Ar C-H), 3468 (NH) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.21 (1H, m, J = 8.13 Hz), 8.01 (1H, m, J = 7.88 Hz), 7.66 (1H, m, J = 7.51 Hz), 7.1 (1H, m, J = 8.13 Hz), 3.74 (3H), 3.12 (4H, m), 2.97 (4H, t, J = 7.3 Hz), 1.89 (4H, m); ^{13}CNMR (100 MHz, $CDCl_3$): δ 171.4, 169.35, 168.57, 140.57, 131.74, 128.48, 126.46, 119.1, 117.3, 52.31, 45.10, 31.27, 30.71, 23.1; HRMS (ESI): m/z calcd. For $C_{16}H_{20}N_2O_4$ $[M+H]^+$: 305.15, found 305.15; Anal calcd. for $C_{16}H_{20}N_2O_4$: C:63.14; H: 6.62; N: 9.20; O:21.03%; found : C:63.14; H: 6.62; N: 9.20; O:21.03%.

Compound (SA3e): methyl 2-[4-(diethylamino)-4-oxobutanamido]benzoate

Yield: 67.1%; mp: 92 ^{0}C; IR (KBr): 1235 (C-O), 1586 (C=O), 1769 (C=O), 3094 (Ar C-H), 3490 (NH) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ 7.99 (1H, m, J = 8.13 Hz), 7.83 (1H, m, J = 7.88 Hz), 7.4 (1H, m, J = 7.51 Hz), 6.9 (1H, m, J = 8.13 Hz), 3.94 (3H), 3.56 (4H, m), 2.84 (4H, t, J = 7.3 Hz), 1.12 (6H, t, J = 7.1 Hz); ^{13}CNMR (100 MHz, $CDCl_3$): δ 171.59, 168.45, 167.37, 141.57, 132.74, 127.48, 125.46, 119.1, 112.41, 52.22, 42.5, 32.9, 31.71, 12.4; HRMS (ESI): m/z calcd. for $C_{16}H_{22}N_2O_4$: $[M+H]^+$: 307.16, found 307.16; Anal calcd. for $C_{16}H_{22}N_2O_4$: C: 62.73; H: 7.24; N: 9.14; O: 20.89%; found : C: 62.73; H: 7.24; N: 9.14; O: 20.89%.

Figure 1: IR Spectrum of ethyl 4-[4-(4-Phenylpiperazin-1-yl)-4-oxobutanamido]benzoate

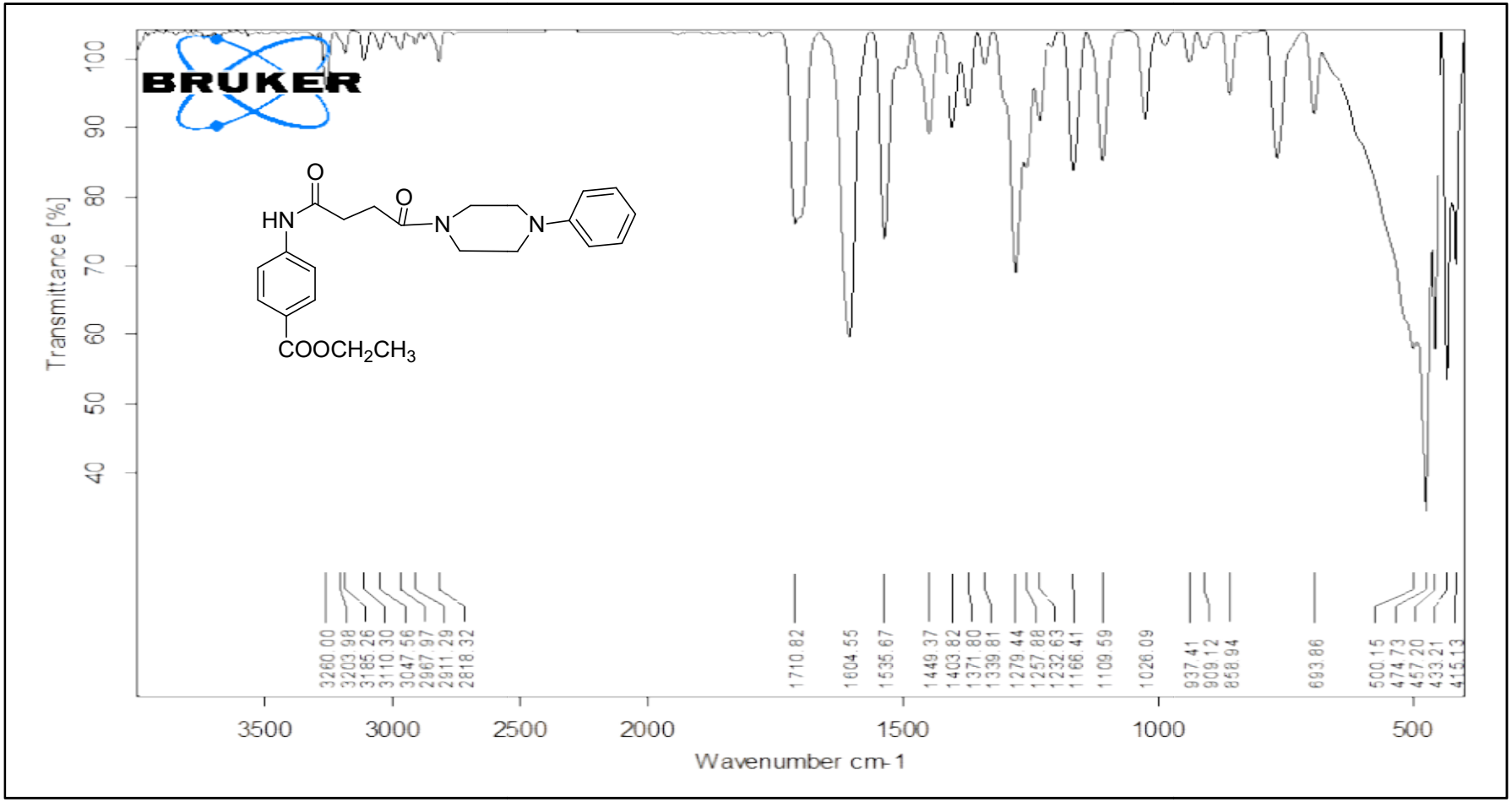


Figure 2: ^{1}H NMR Spectrum of ethyl 4-[4-(4-Phenylpiperazin-1-yl)-4-oxobutanamido]benzoate

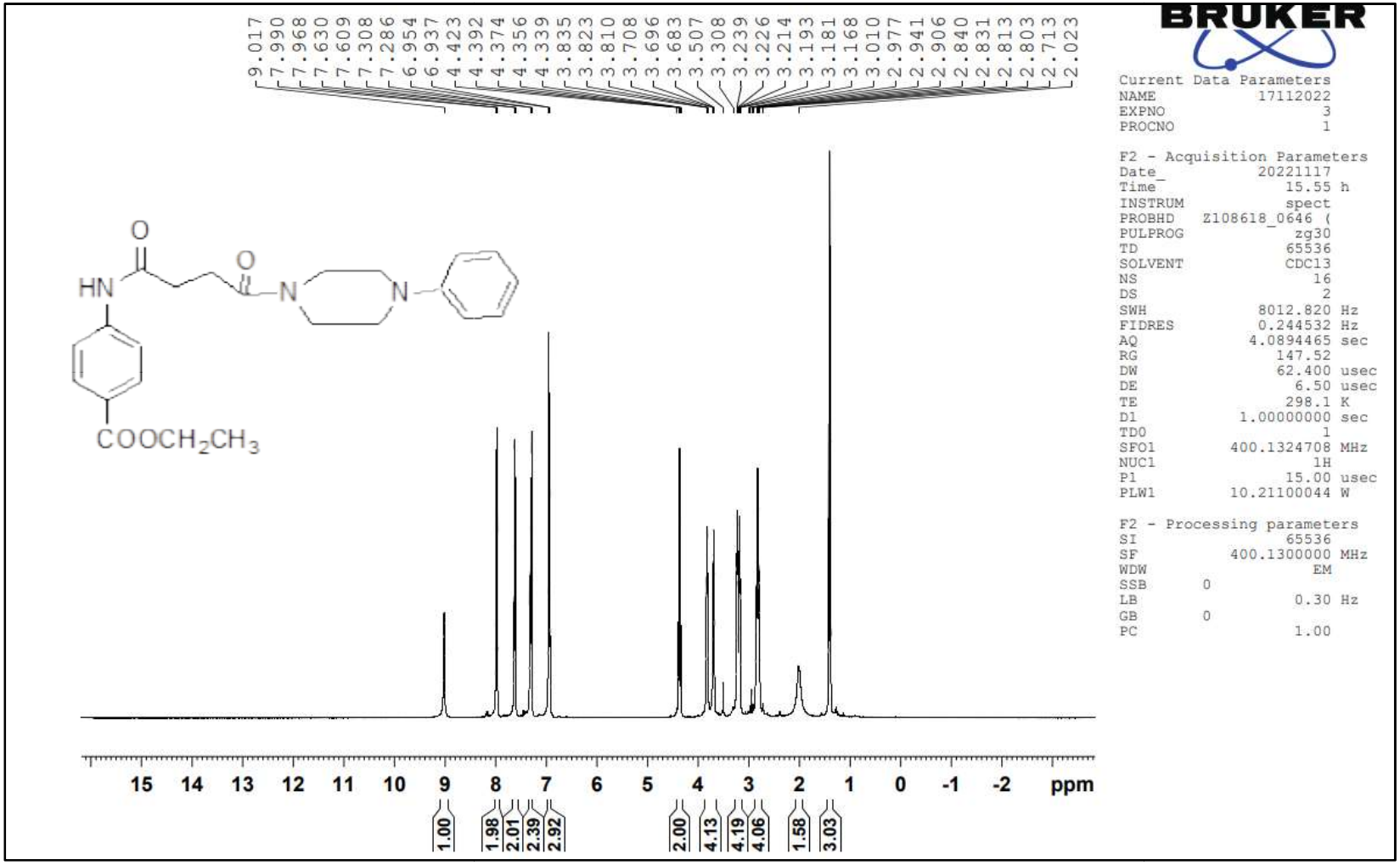


Figure 3: ^{13}C NMR Spectrum of ethyl 4-[4-(4-Phenylpiperazin-1-yl)-4-oxobutanamido]benzoate

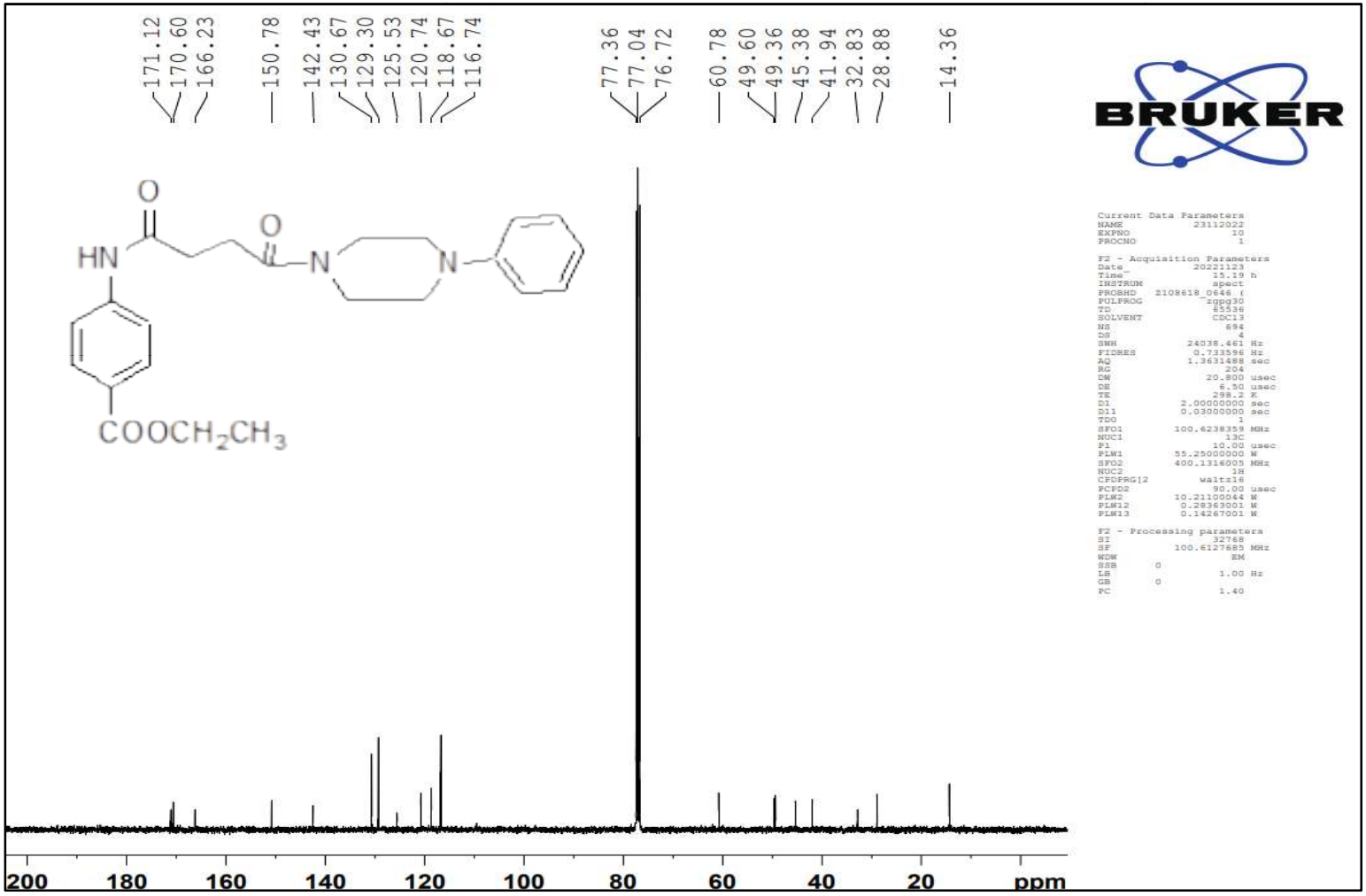


Figure 4: Mass Spectrum of ethyl 4-[4-(4-Phenylpiperazin-1-yl)-4-oxobutanamido]benzoate

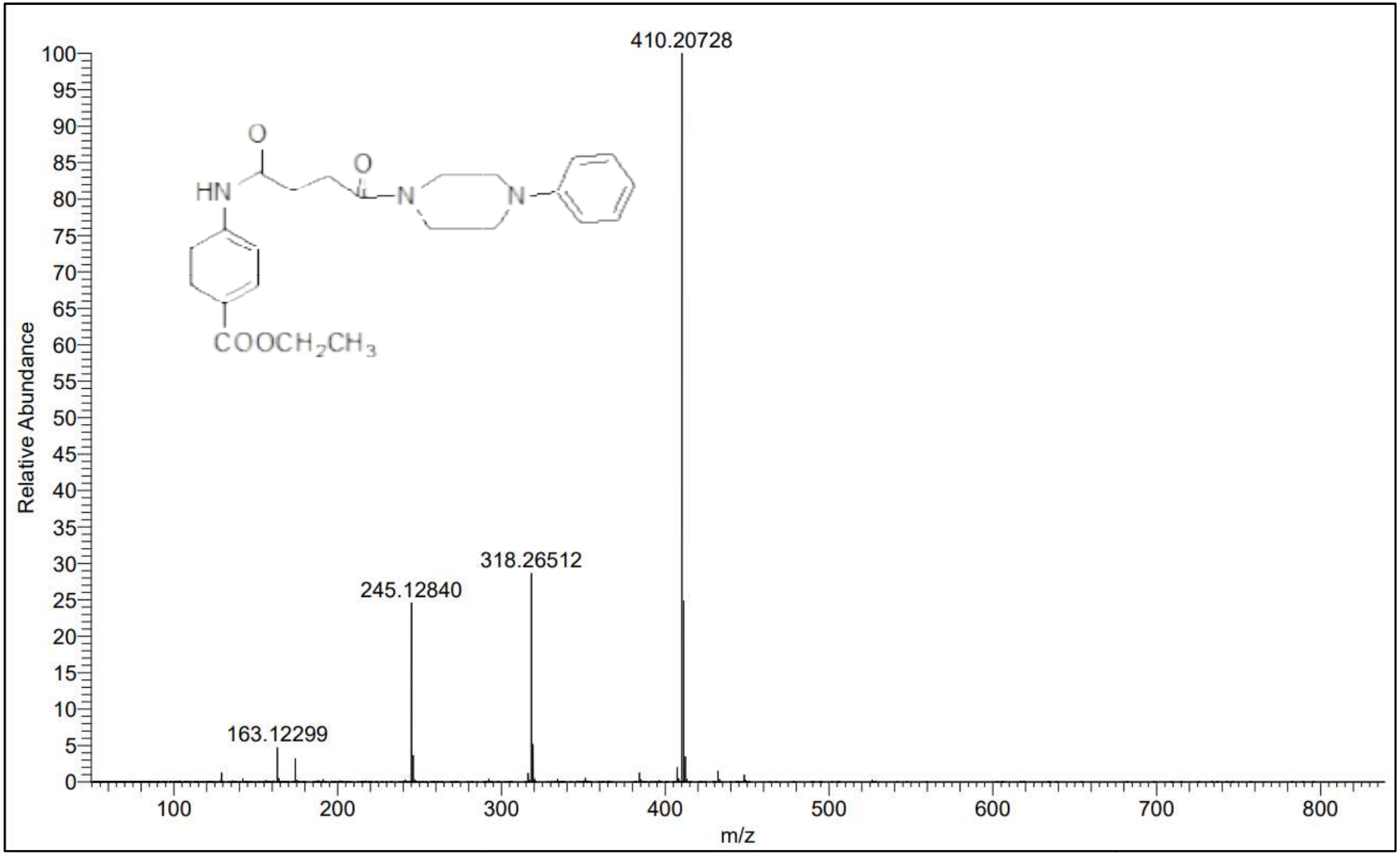


Figure 5: IR Spectrum of ethyl 4-[4-(4-Benzylpiperazin-1-yl)-4-oxobutanamido]benzoate

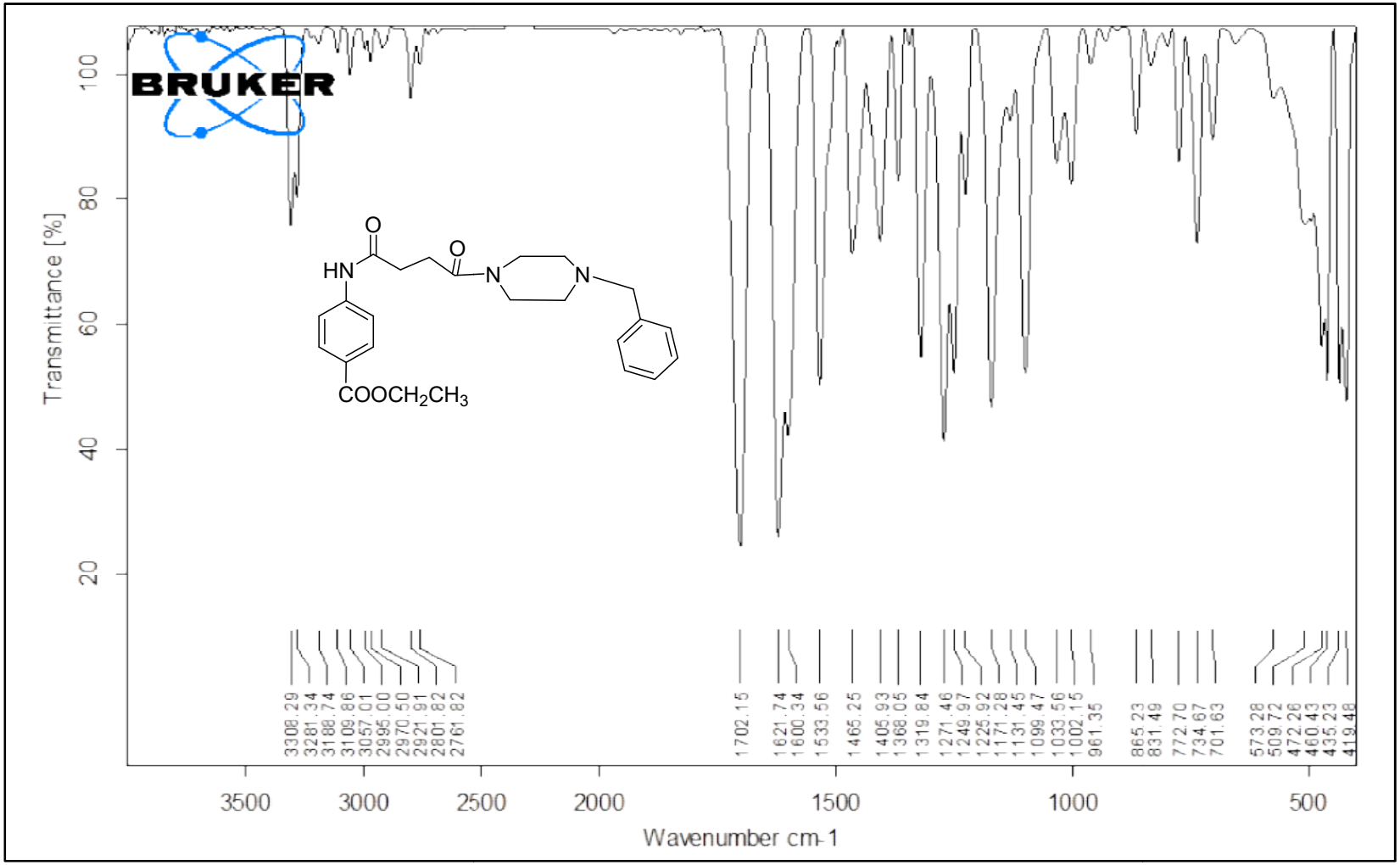


Figure 6: ^{1}H NMR Spectrum of ethyl 4-[4-(4-Benzylpiperazin-1-yl)-4-oxobutanamido]benzoate

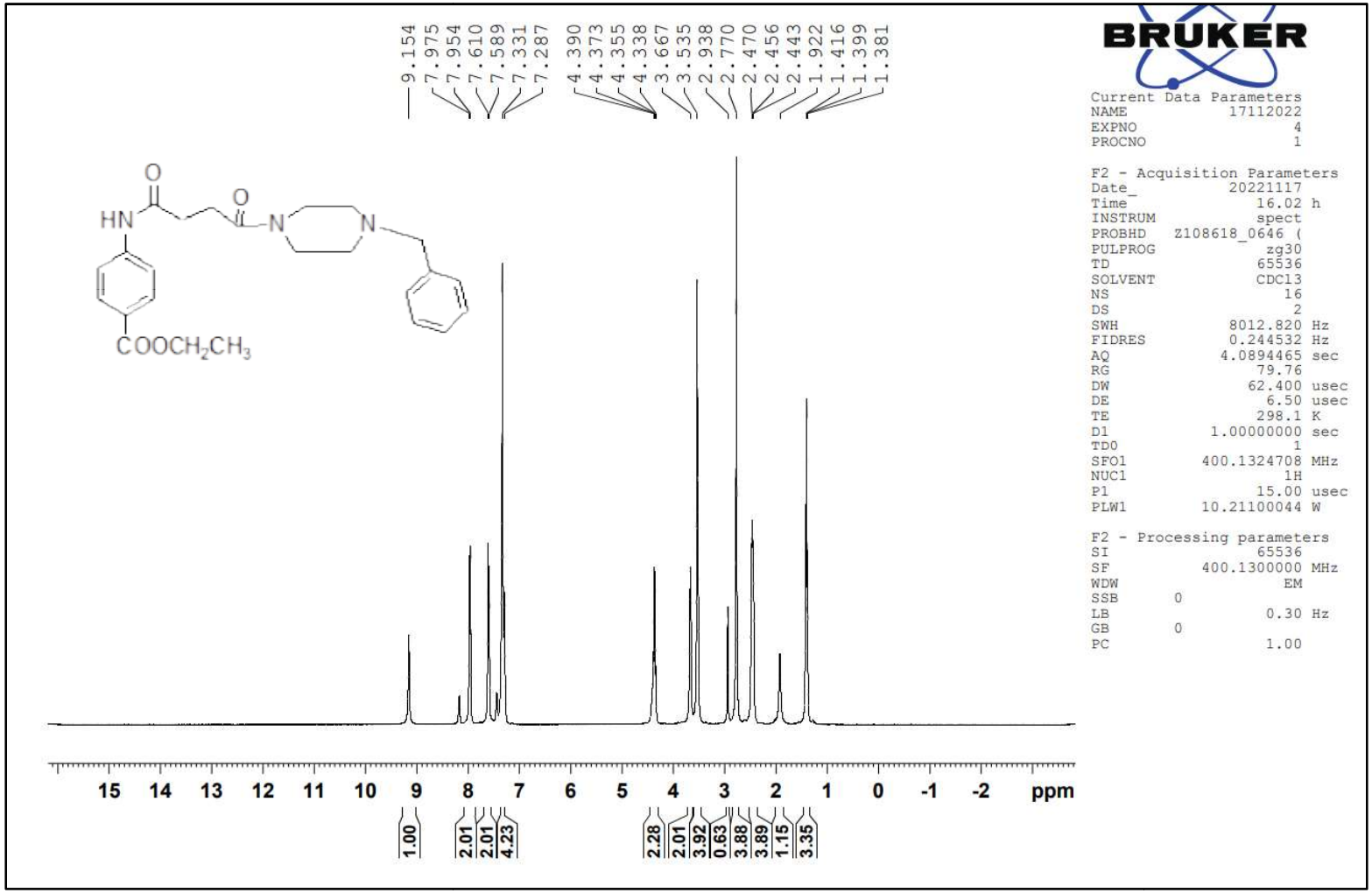


Figure 7: ^{13}C NMR Spectrum of ethyl 4-[4-(4-Benzylpiperazin-1-yl)-4-oxobutanamido]benzoate

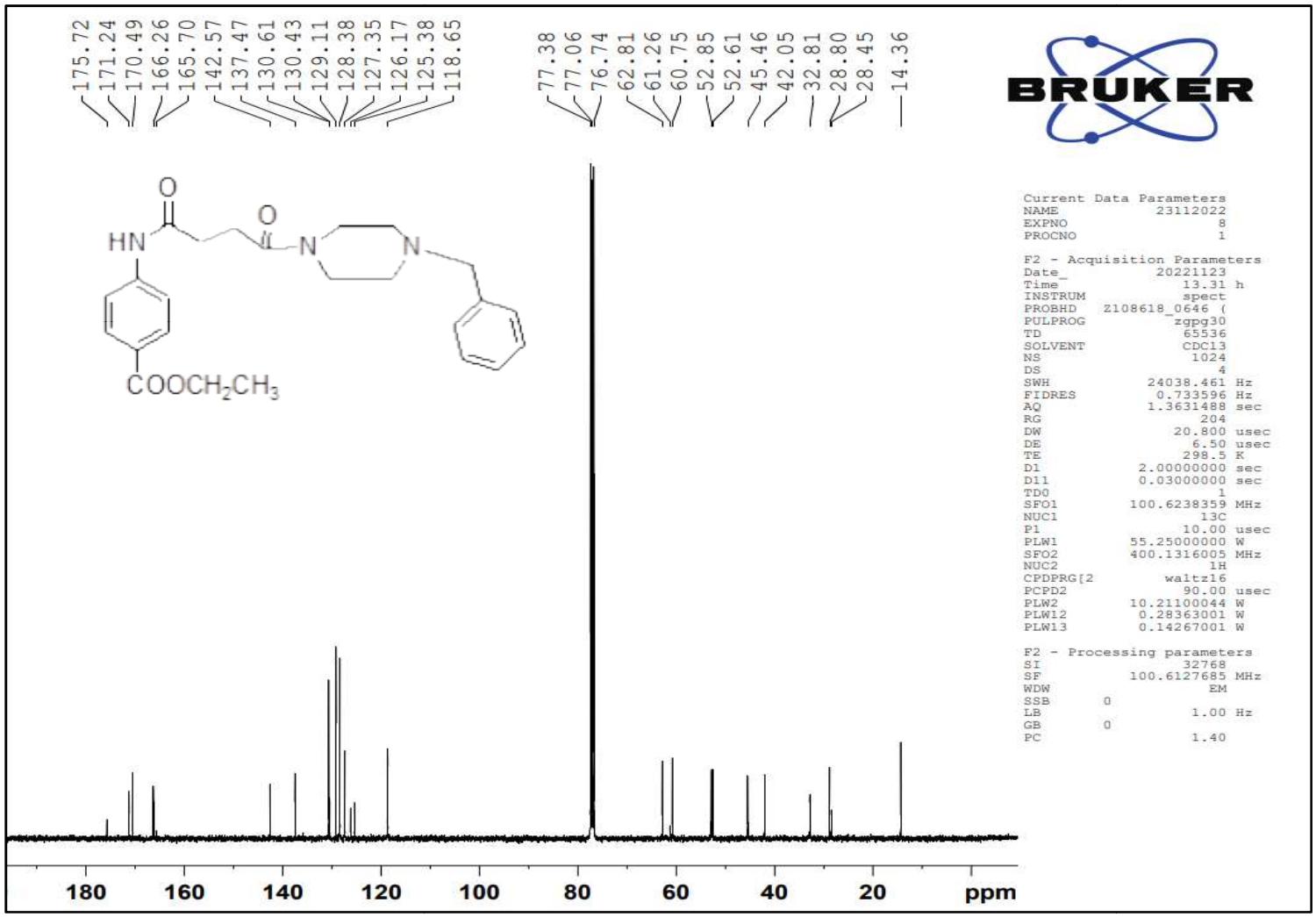


Figure 8: Mass Spectrum of ethyl 4-[4-(4-Benzylpiperazin-1-yl)-4-oxobutanamido]benzoate

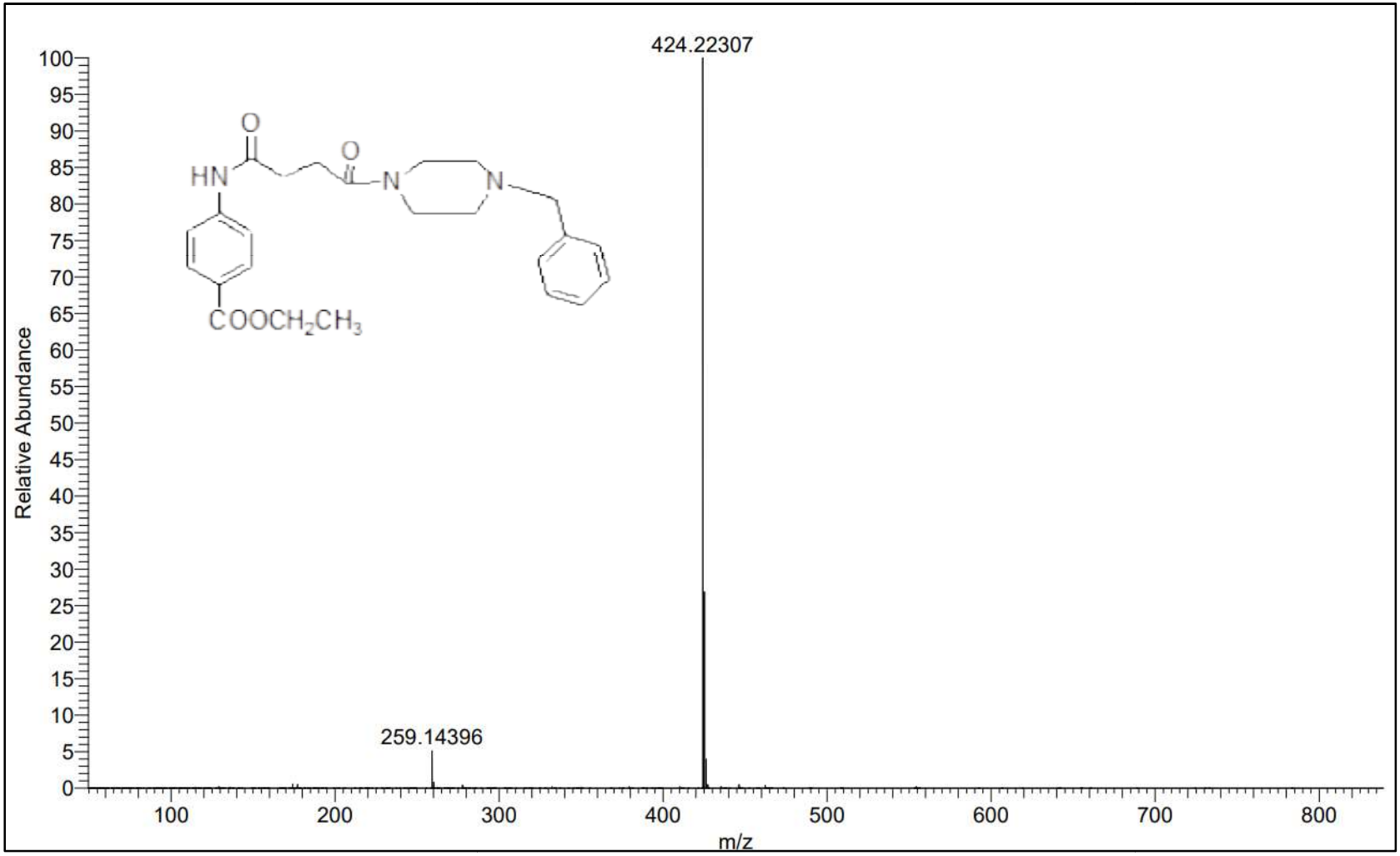


Figure 9: IR Spectrum of ethyl 4-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

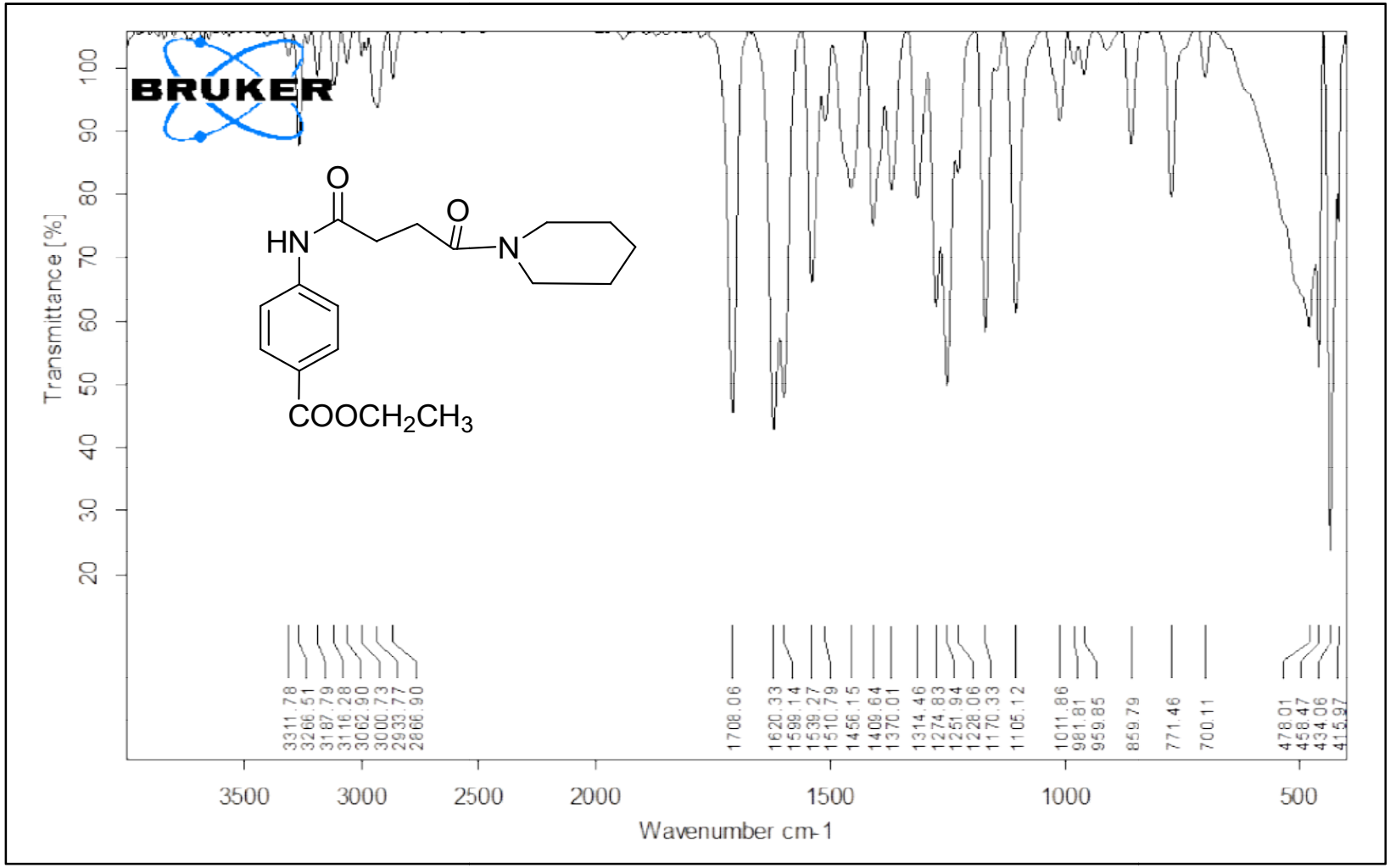


Figure 10: ^{1}H NMR Spectrum of ethyl 4-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

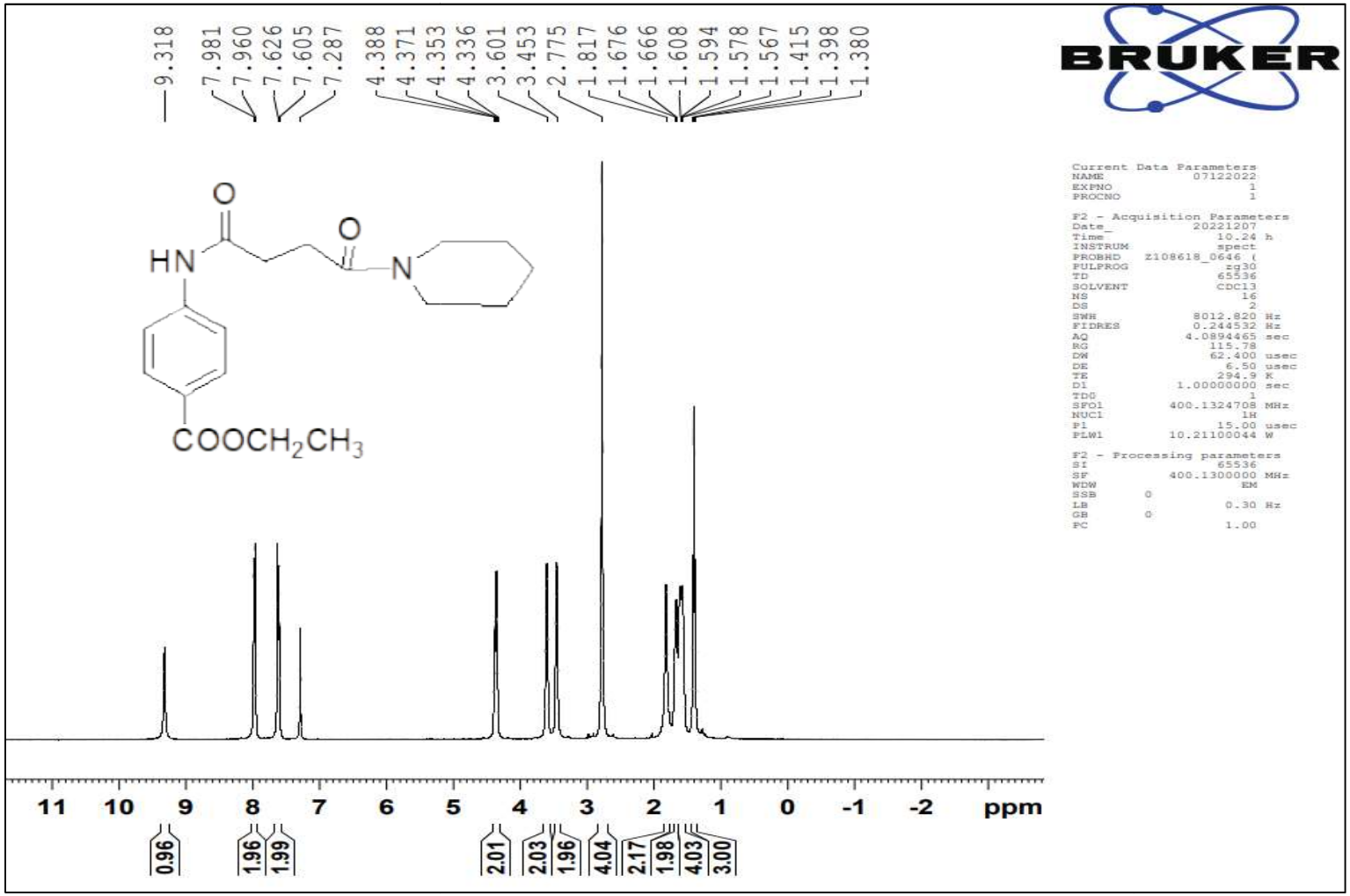


Figure 11: ^{13}C NMR Spectrum of ethyl 4-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

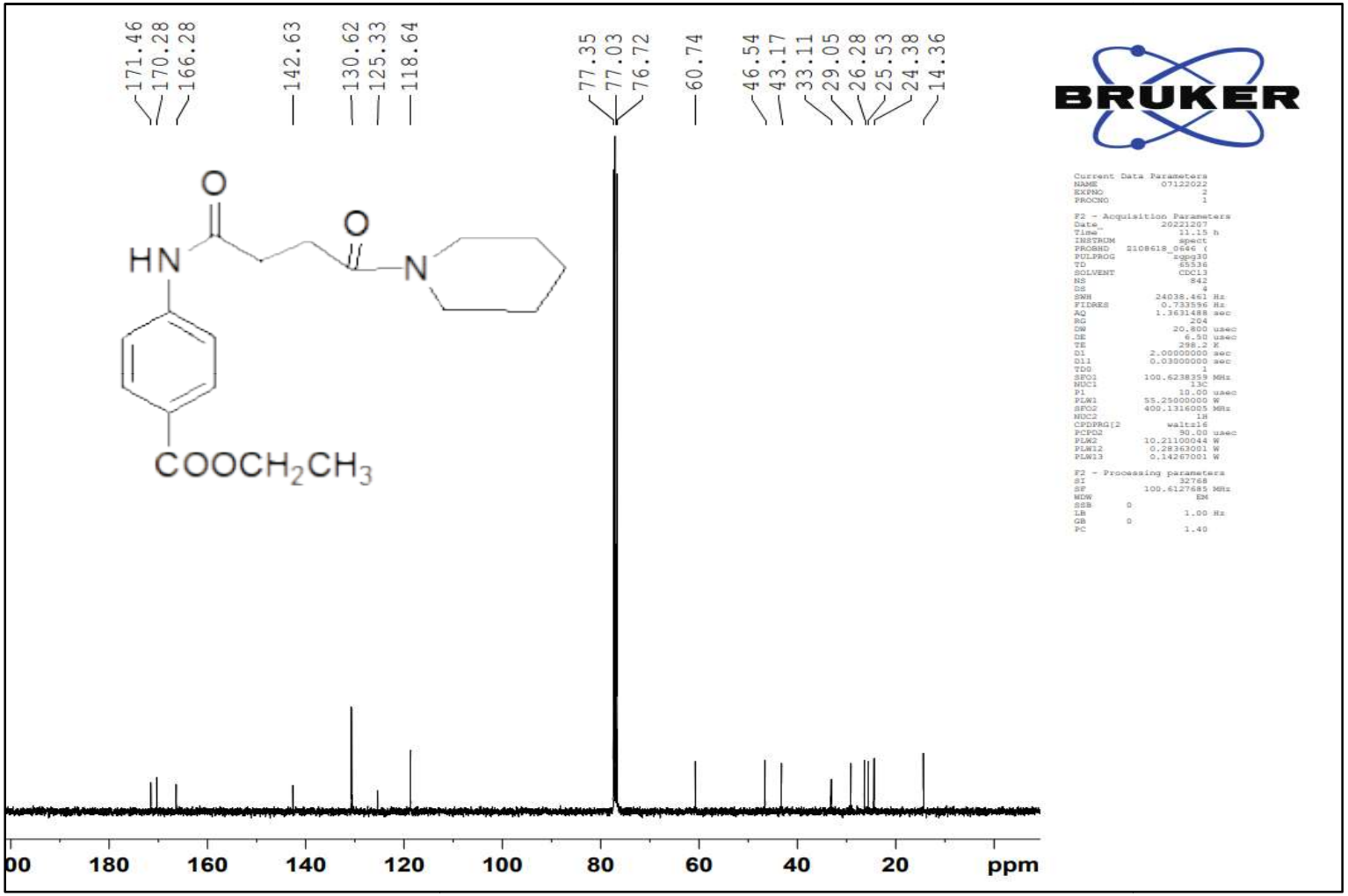


Figure 12: Mass Spectrum of ethyl 4-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

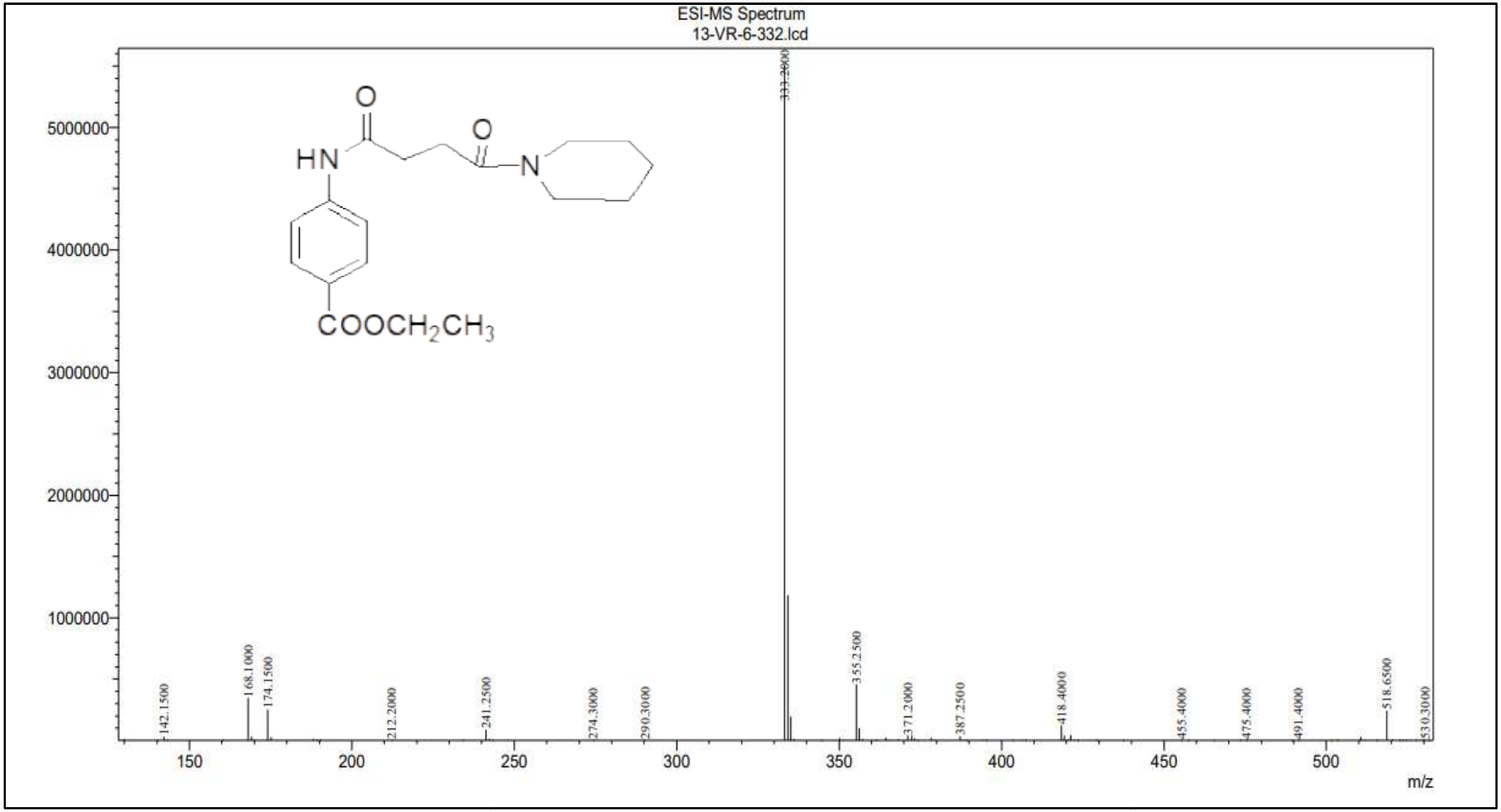


Figure 13: IR Spectrum of ethyl 4-[4-oxo-4-(pyrrolidin-1-yl)butanamido]benzoate

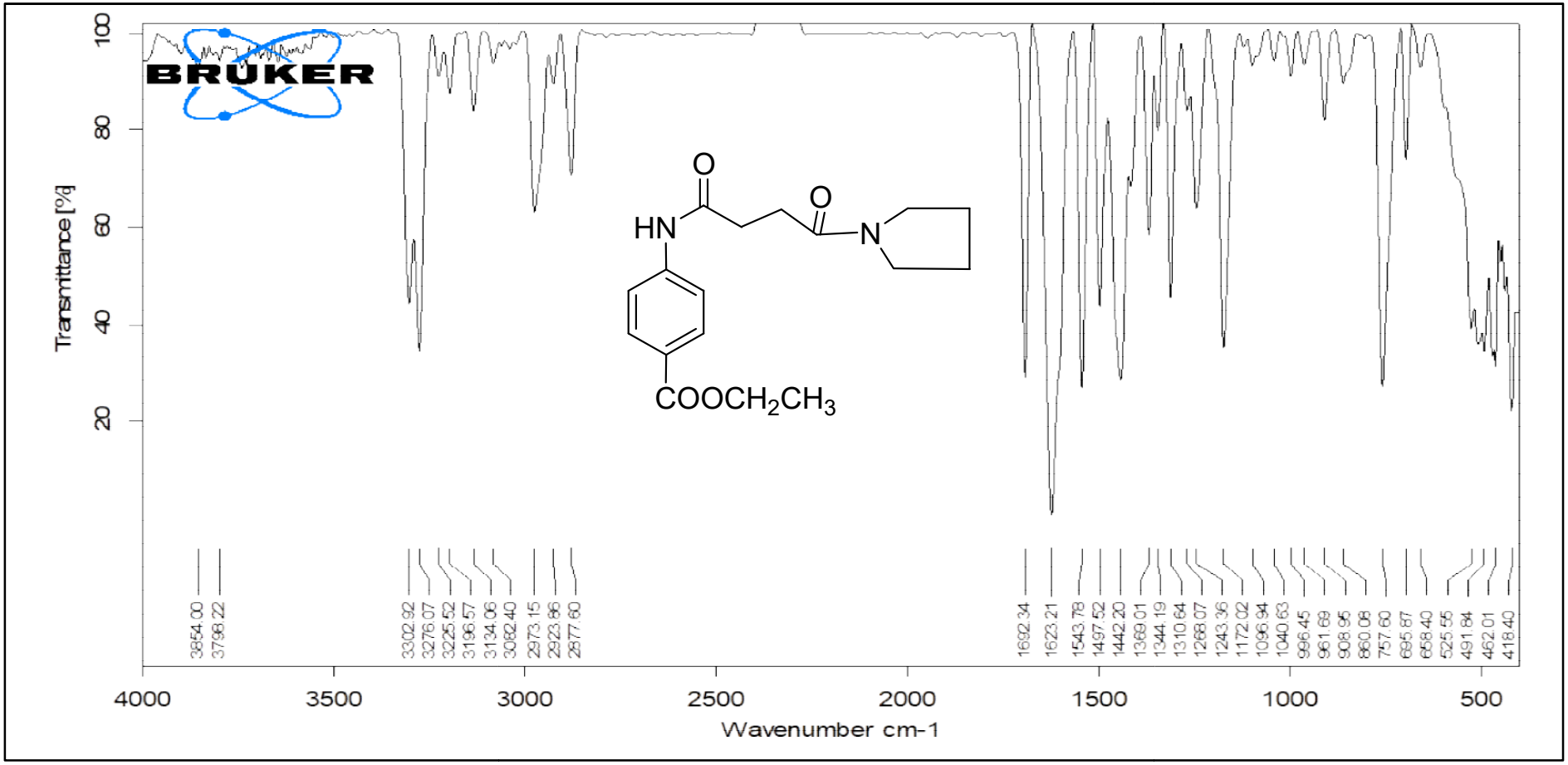


Figure 14: ^{1}H NMR Spectrum of ethyl 4-[4-oxo-4-(pyrrolidin-1-yl)butanamido]benzoate

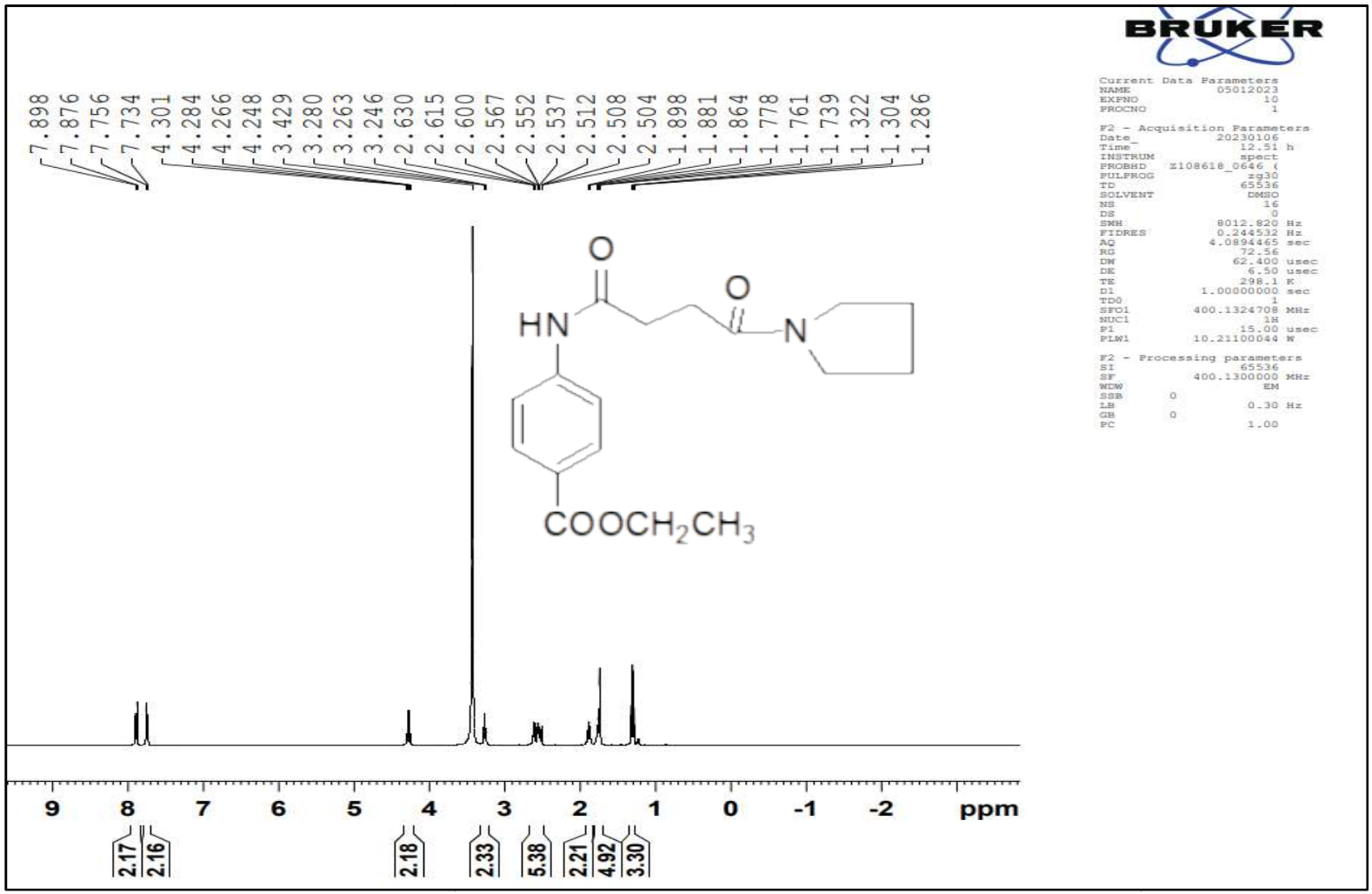


Figure 15: ^{13}C NMR Spectrum of ethyl 4-[4-oxo-4-(pyrrolidin-1-yl)butanamido]benzoate

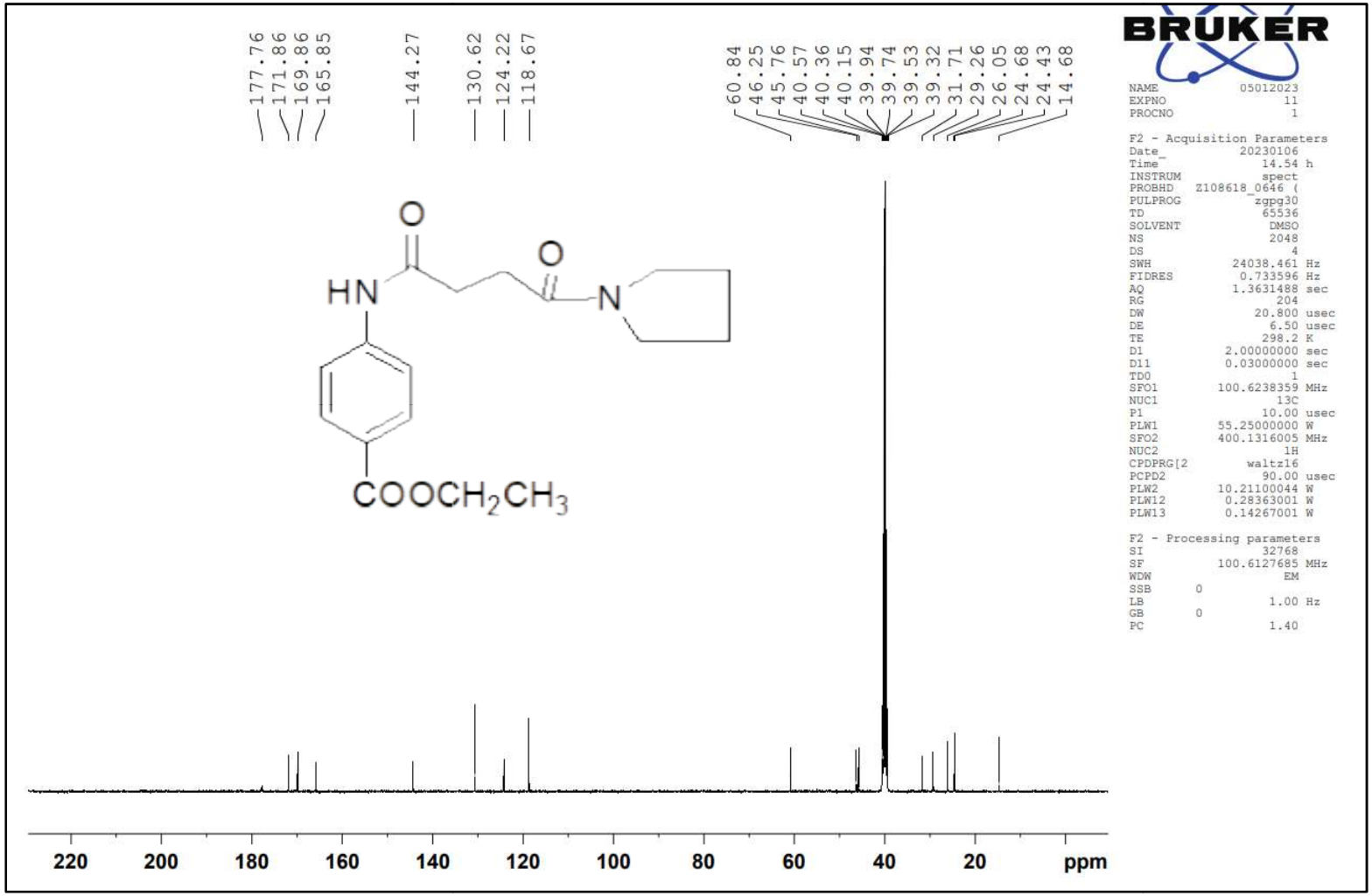


Figure 16: IR Spectrum of ethyl 3-(4-oxo-4-(4-phenylpiperazin-1-yl)butanamido)benzoate

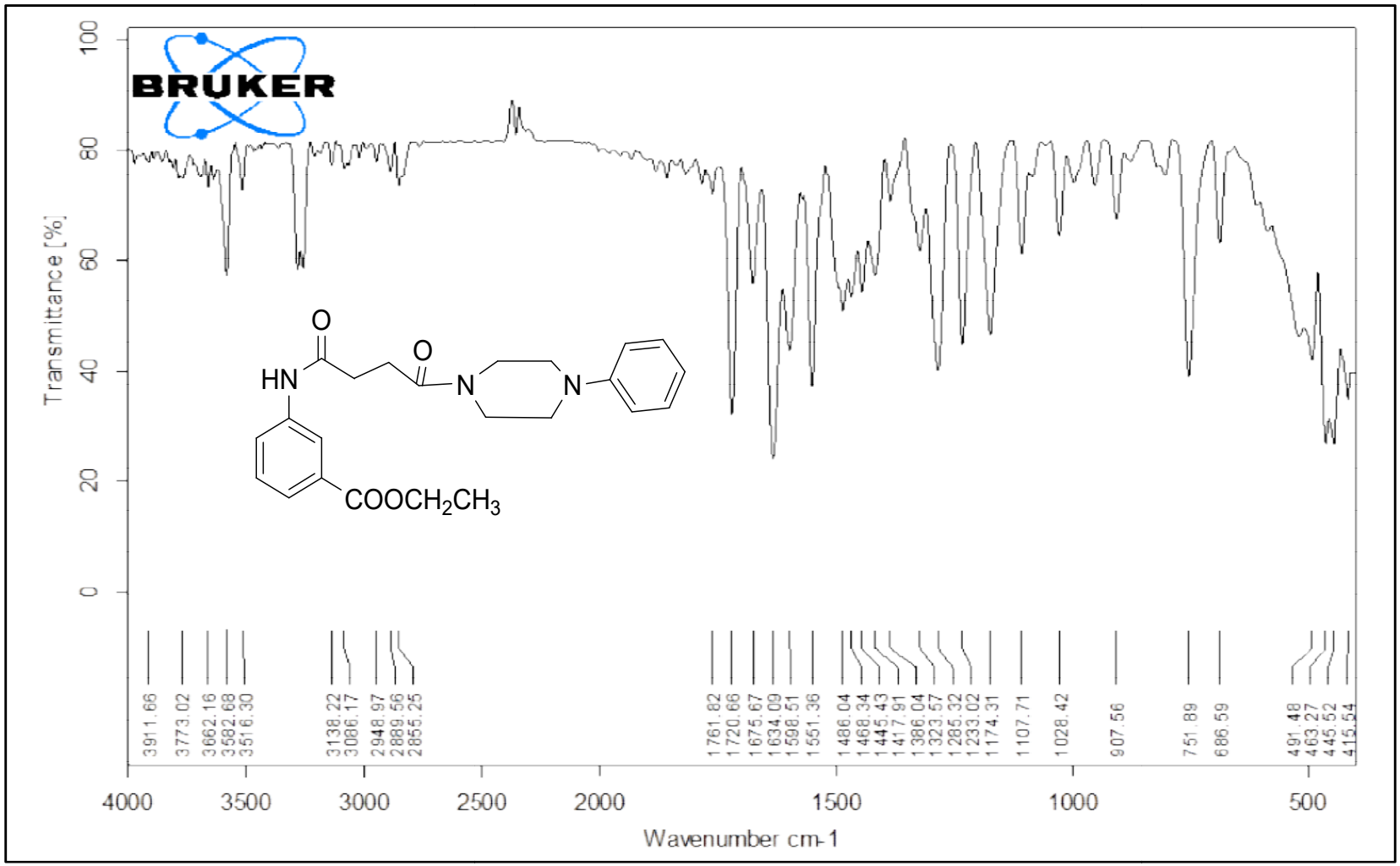


Figure 17: ^{1}H NMR Spectrum of ethyl 3-(4-oxo-4-(4-phenylpiperazin-1-yl)butanamido)benzoate

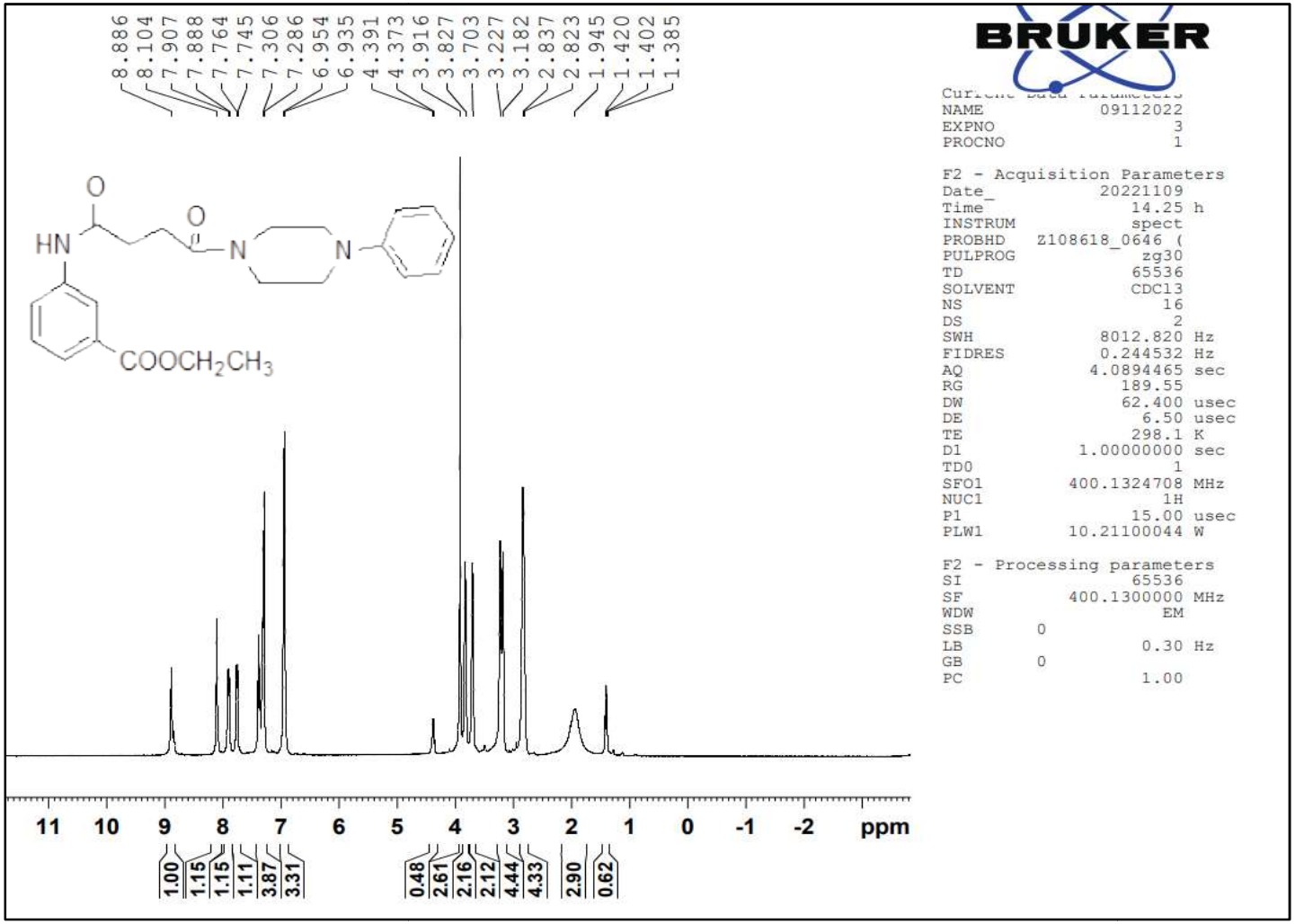


Figure 18: ^{13}C NMR Spectrum of ethyl 3-(4-oxo-4-(4-phenylpiperazin-1-yl)butanamido)benzoate

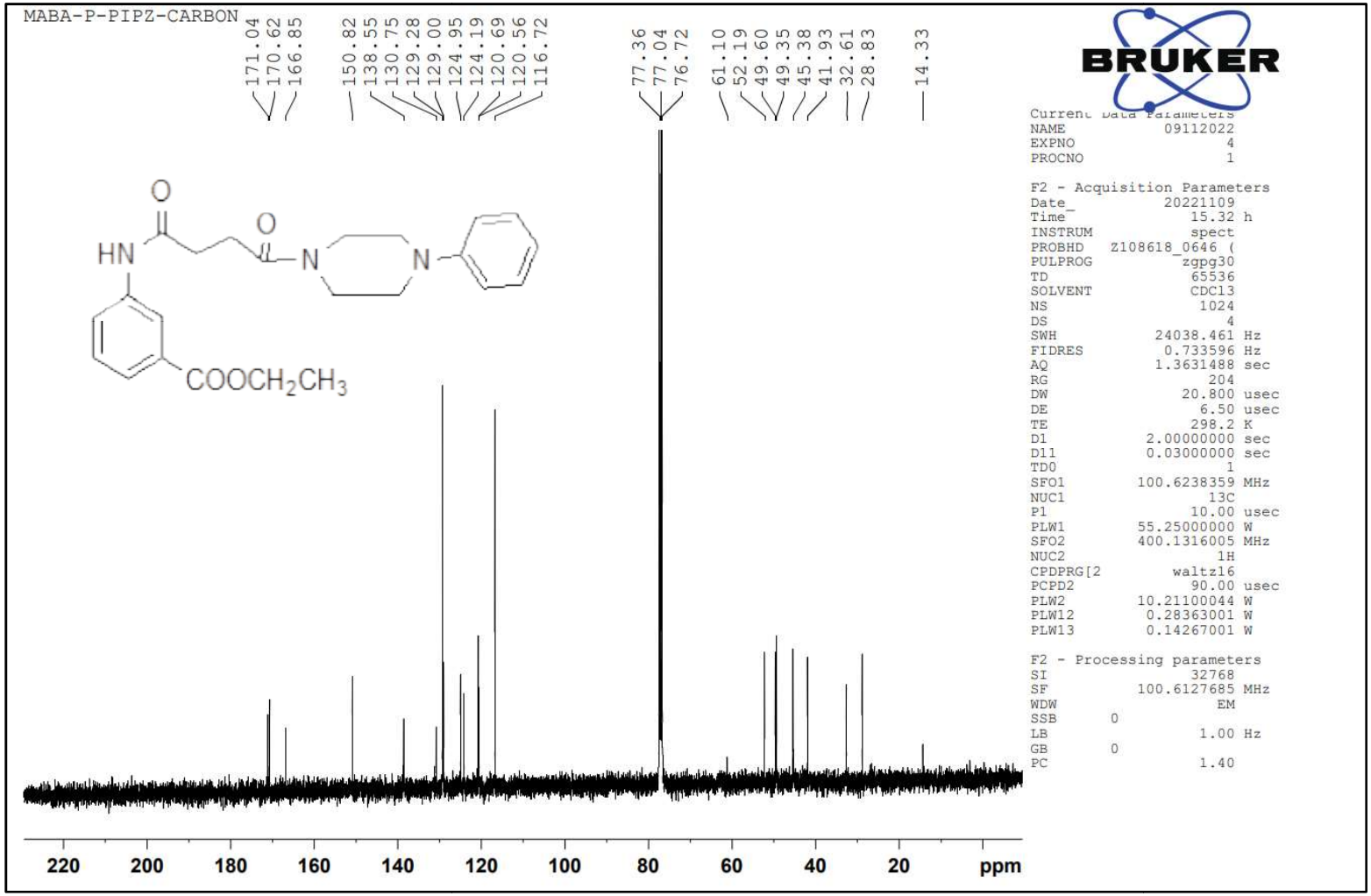


Figure 19: Mass Spectrum of ethyl 3-(4-oxo-4-(4-phenylpiperazin-1-yl)butanamido)benzoate

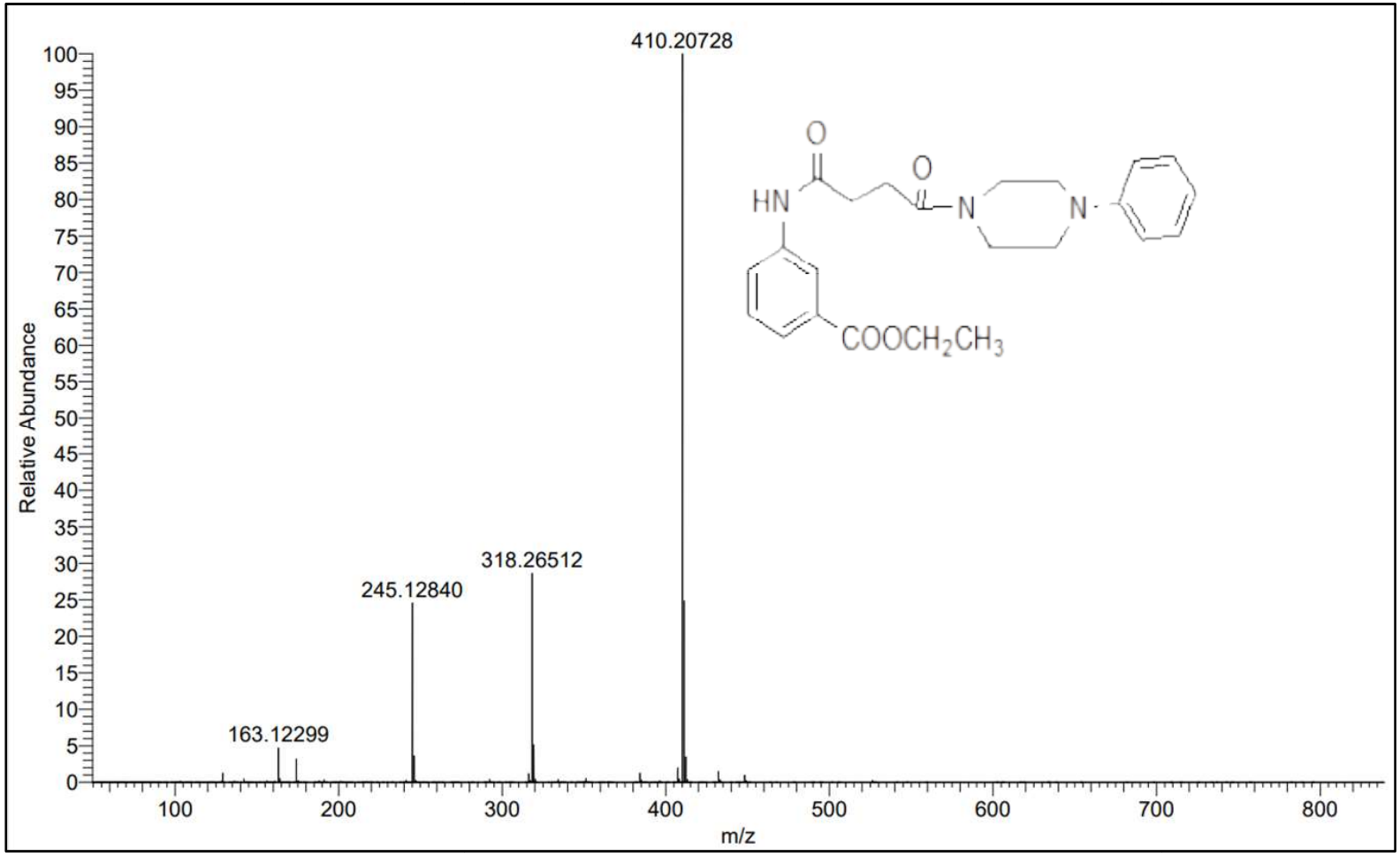


Figure 20: IR Spectrum of ethyl 3-(4-(4-benzylpiperazin-1-yl)-4-oxobutanamido)benzoate

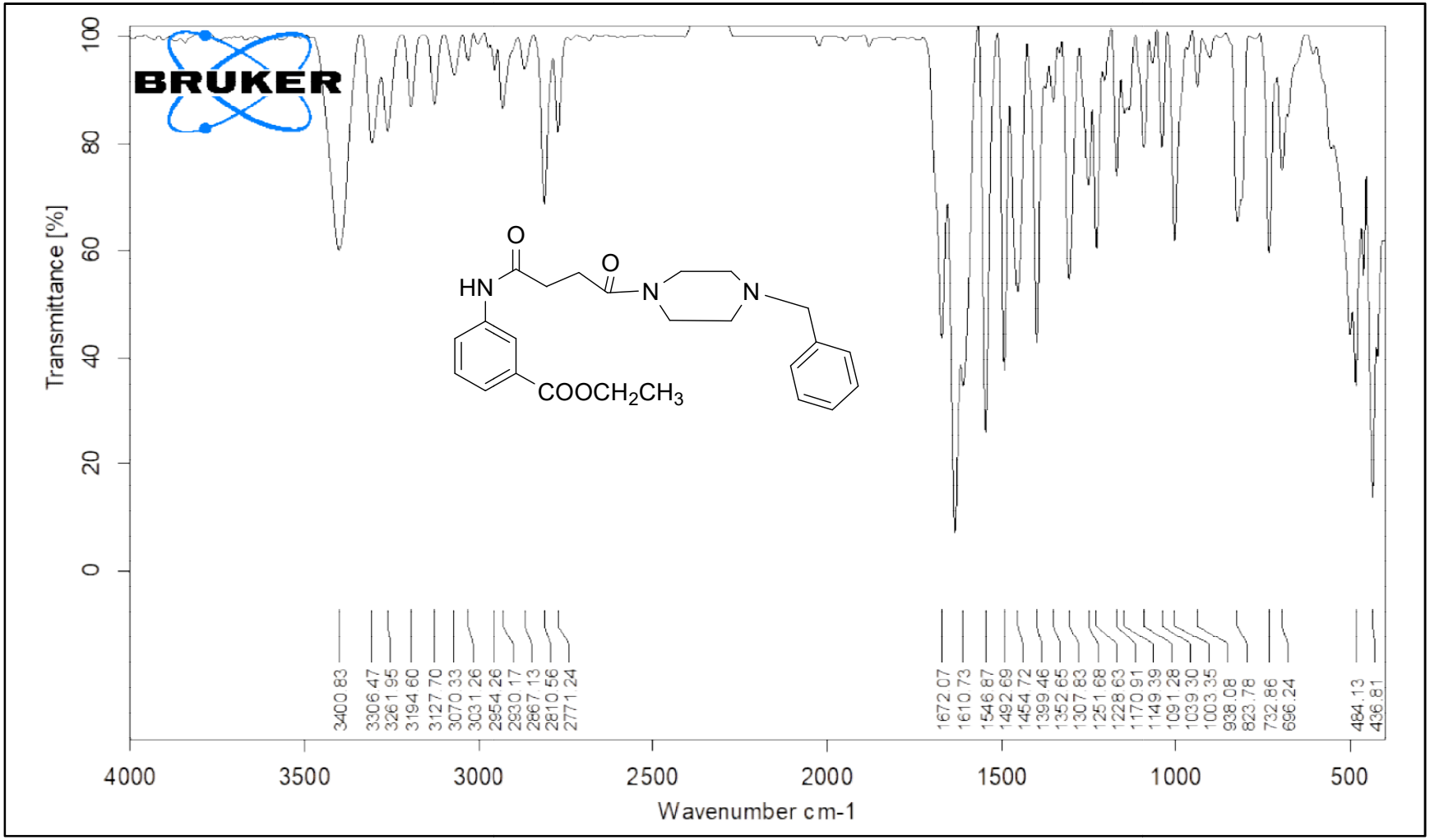


Figure 21: ^{1}H NMR Spectrum of ethyl 3-(4-(4-benzylpiperazin-1-yl)-4-oxobutanamido)benzoate

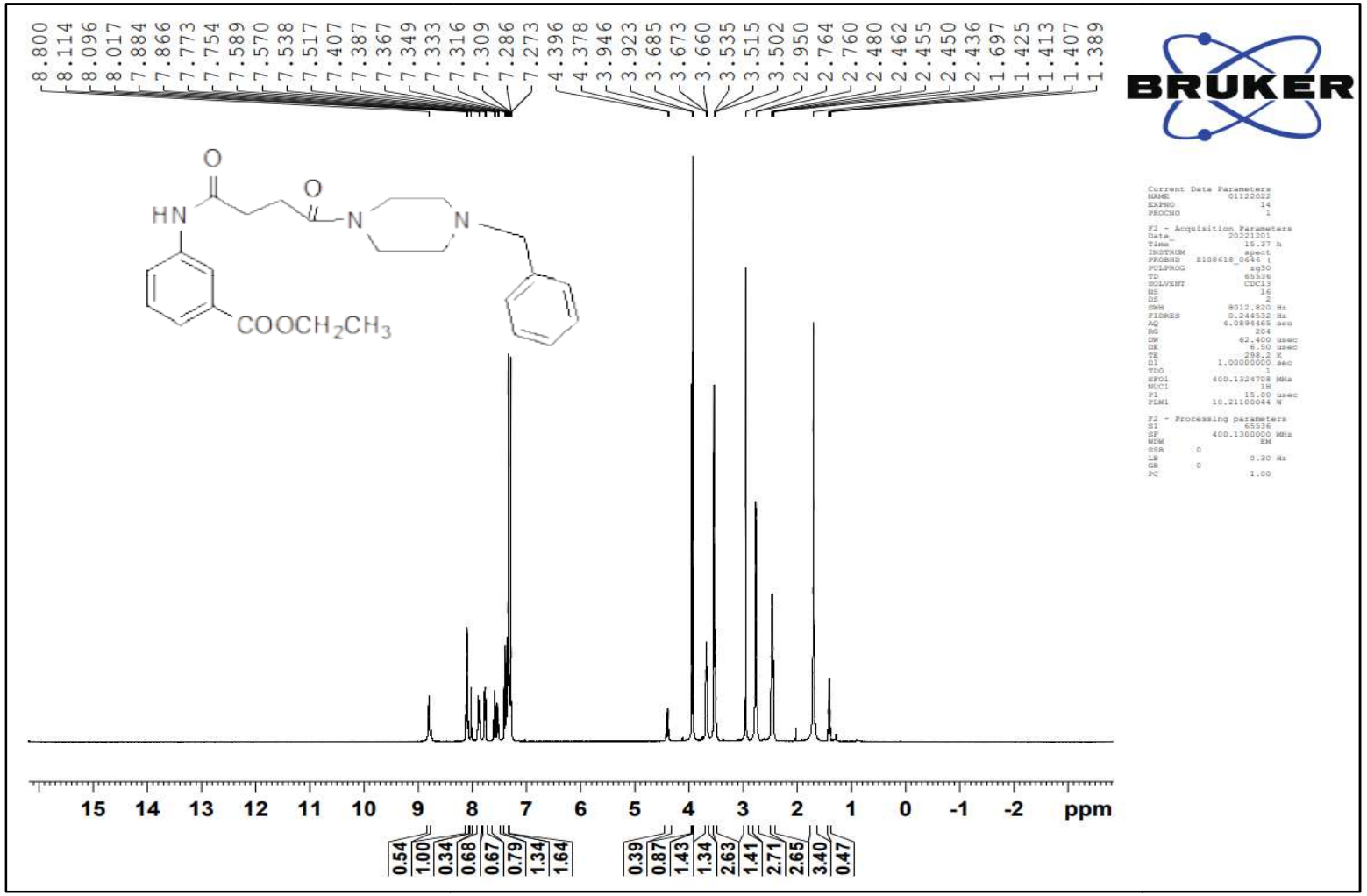


Figure 22: ^{13}C NMR Spectrum of ethyl 3-(4-(4-benzylpiperazin-1-yl)-4-oxobutanamido)benzoate

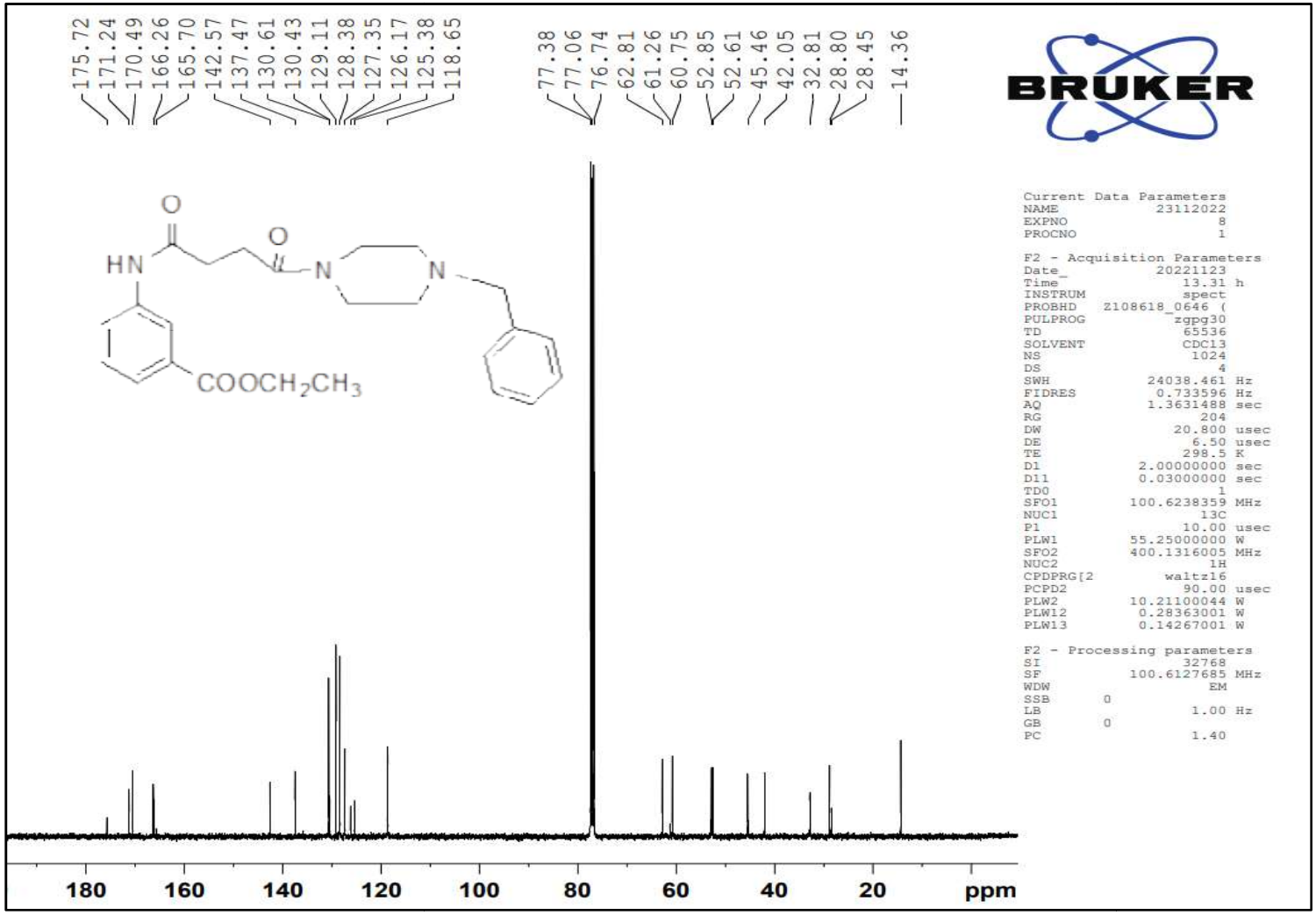


Figure 23: Mass Spectrum of ethyl 3-(4-(4-benzylpiperazin-1-yl)-4-oxobutanamido)benzoate

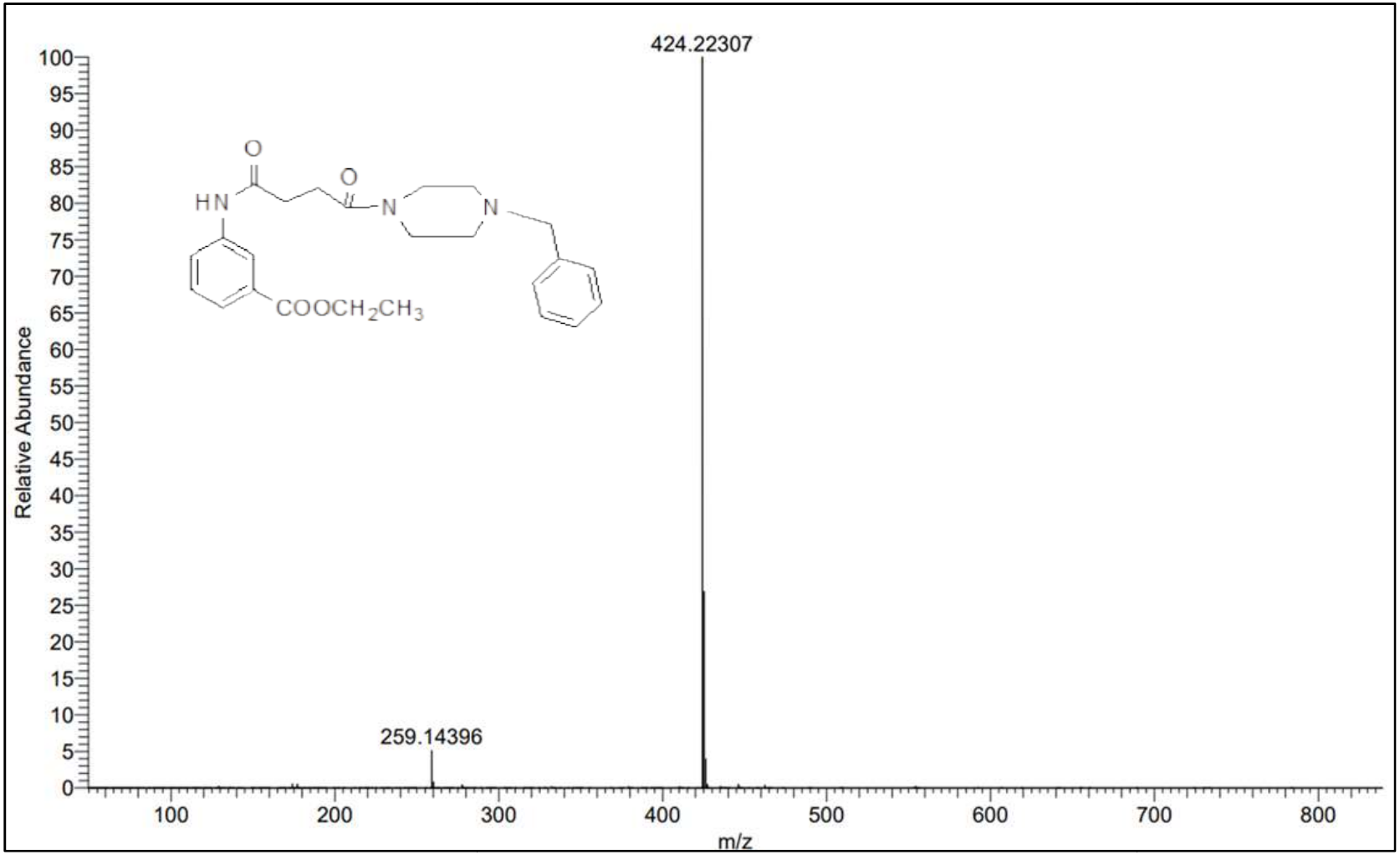


Figure 24: IR Spectrum of ethyl 3-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

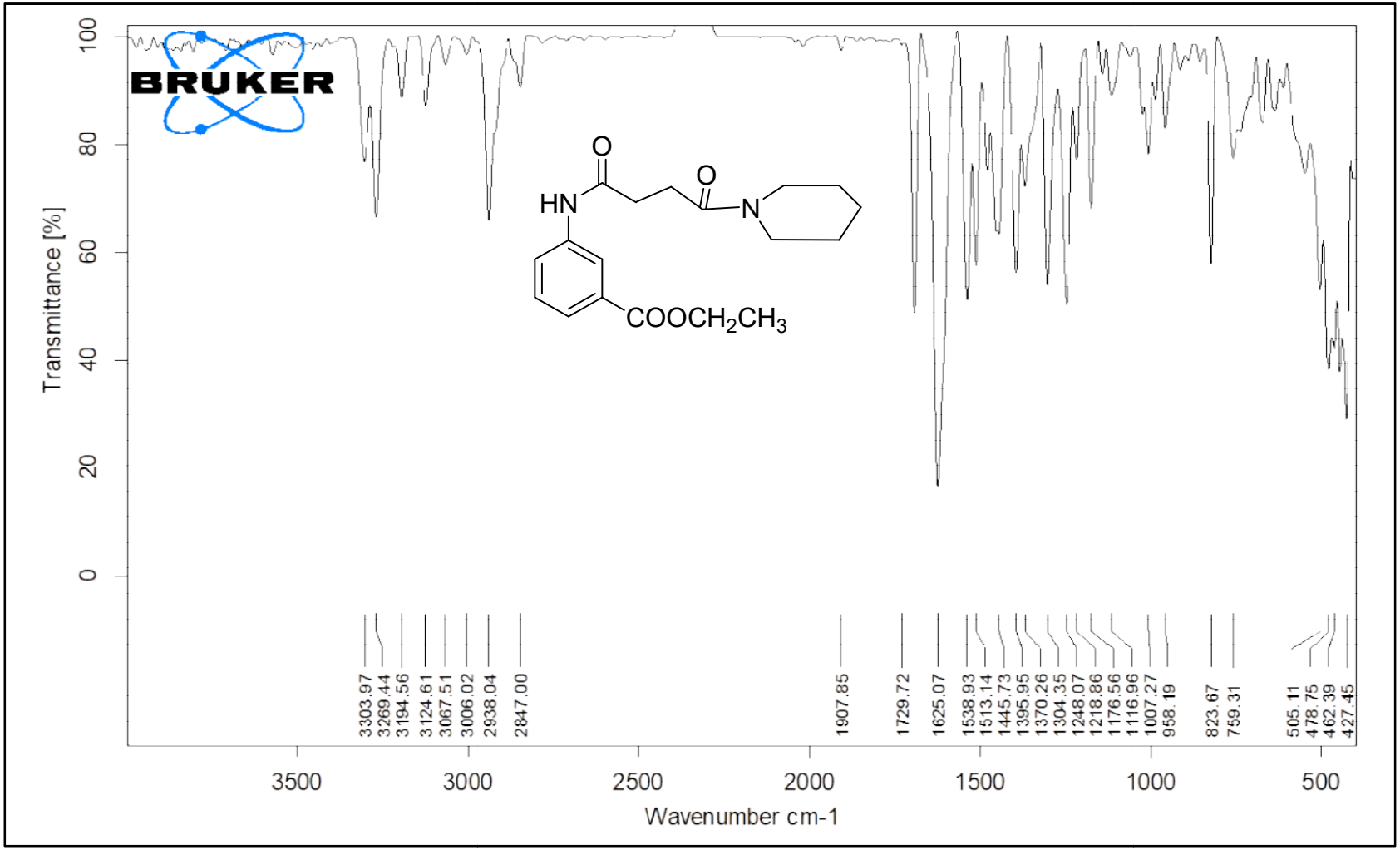


Figure 25: ^{1}H NMR Spectrum of ethyl 3-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

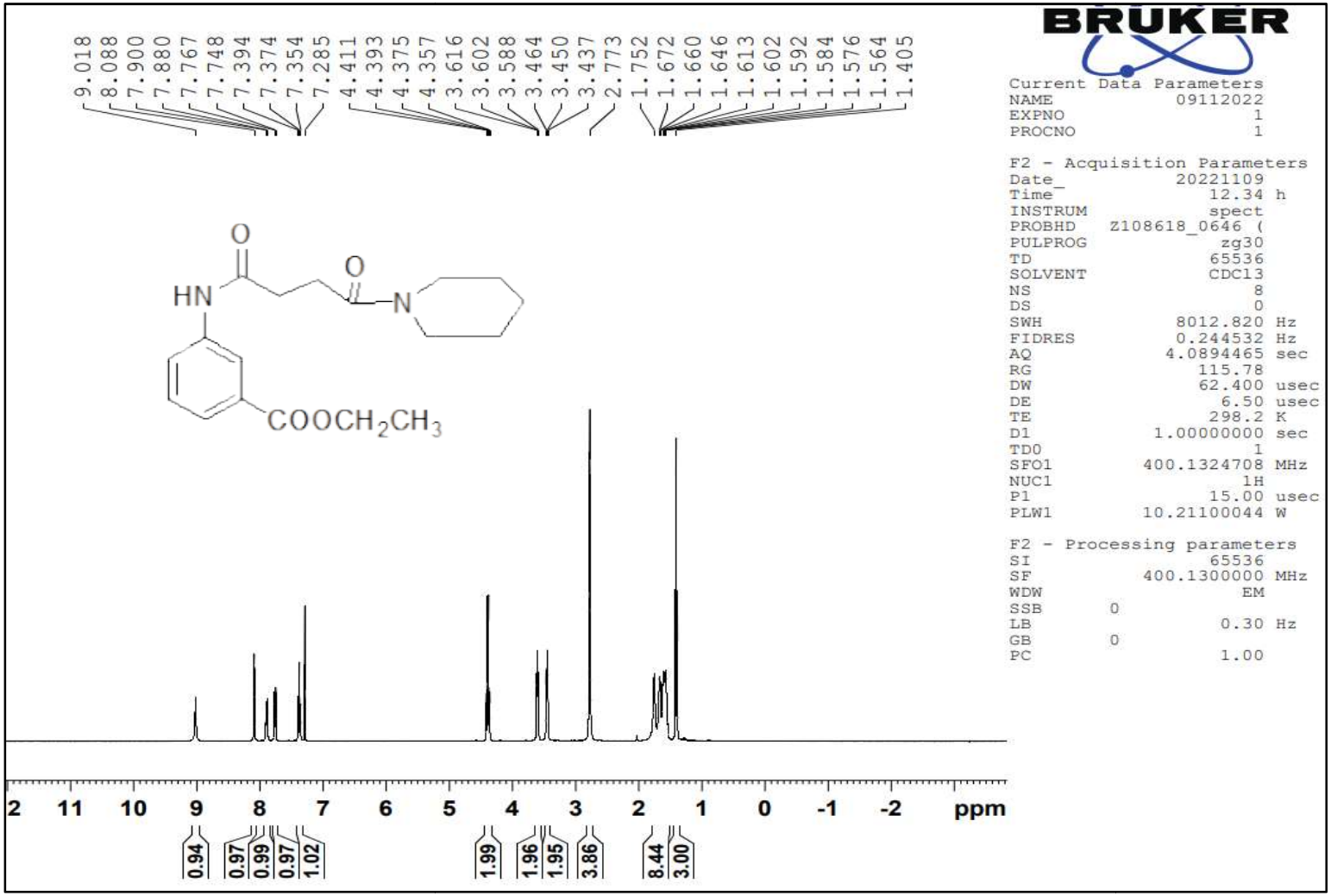


Figure 26: ^{13}C NMR Spectrum of ethyl 3-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

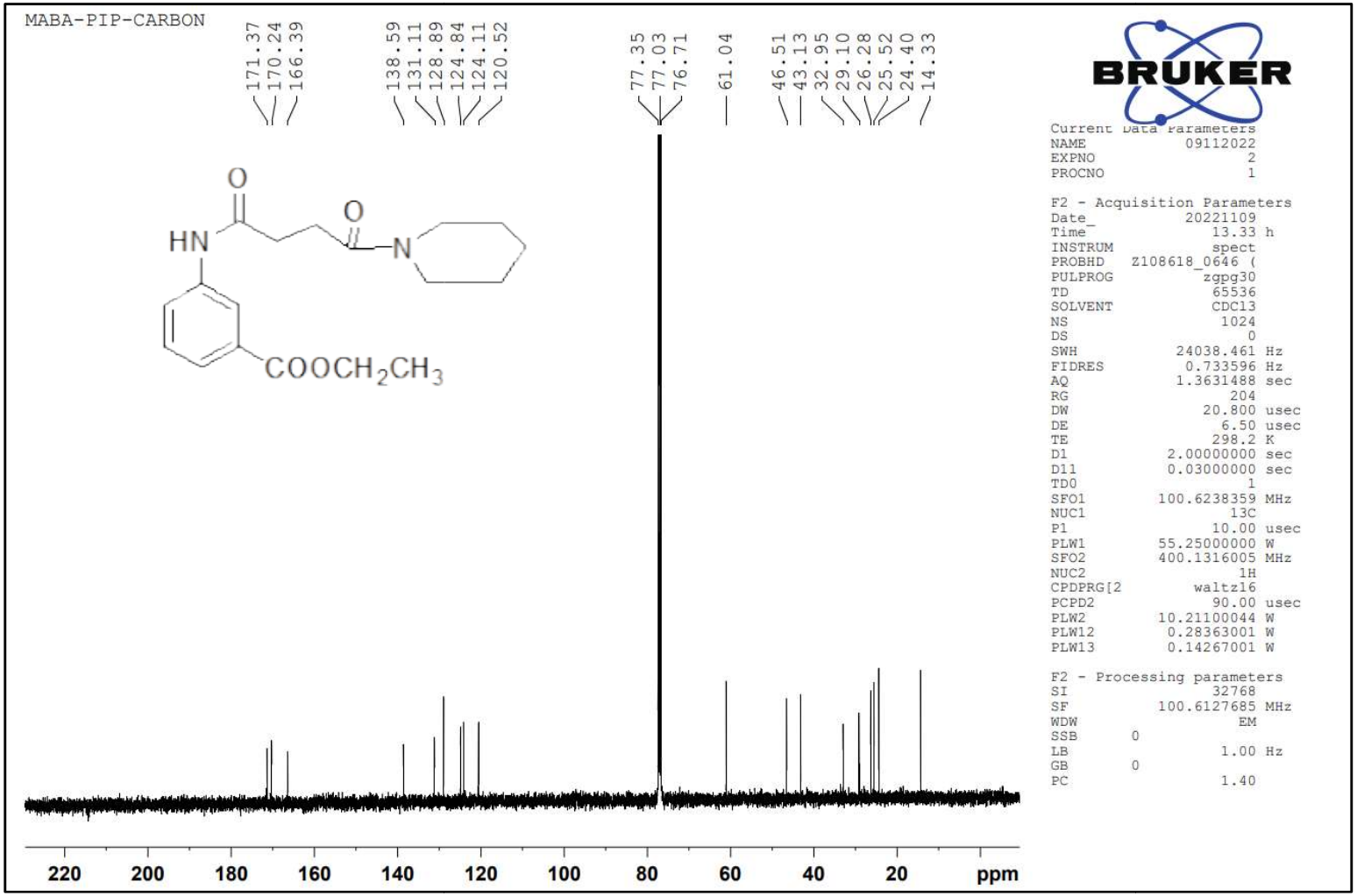


Figure 27: Mass Spectrum of ethyl 3-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

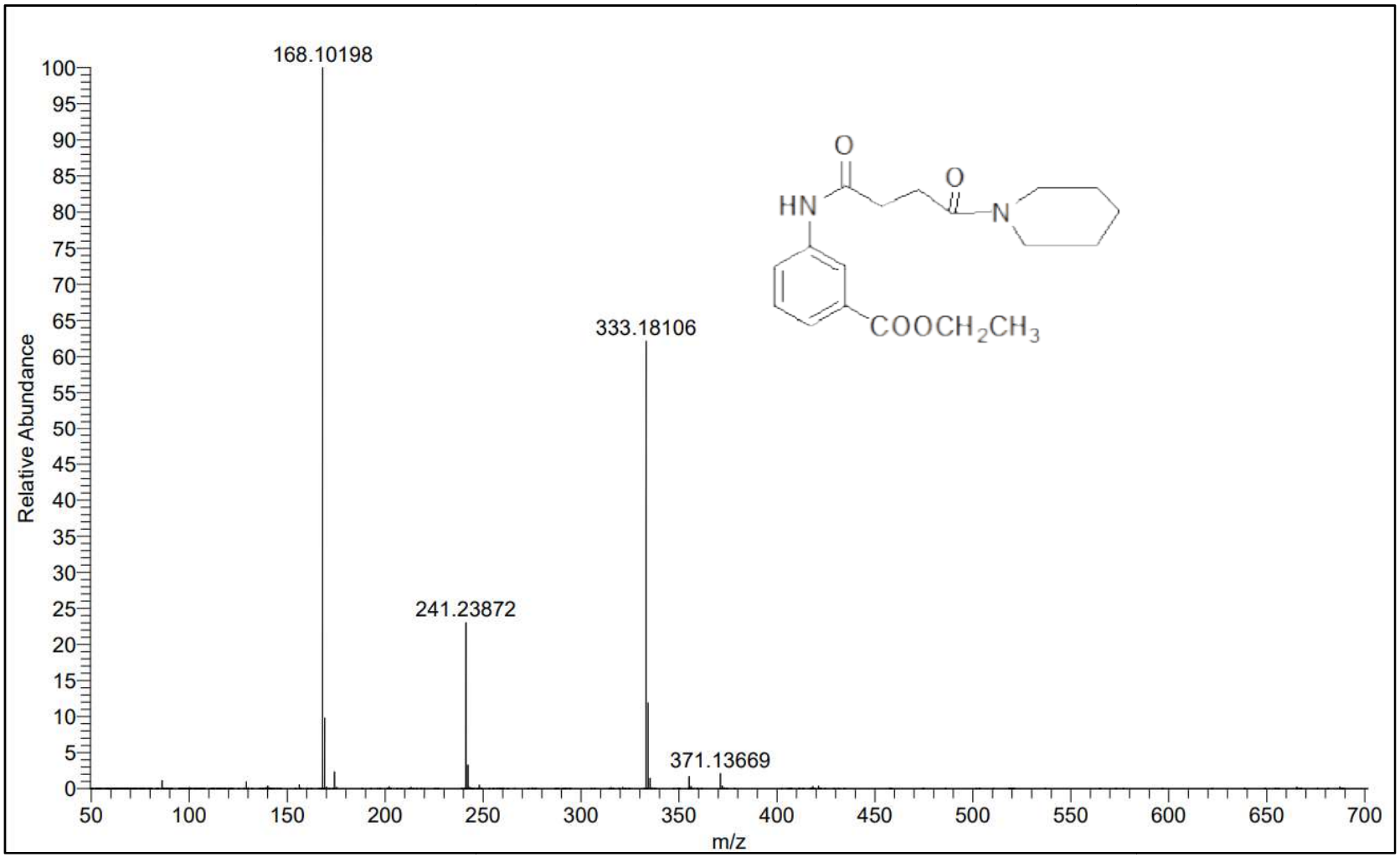


Figure 28: IR Spectrum of ethyl 3-[4-oxo-4-(pyrrolidin-1-yl)butanamido]benzoate

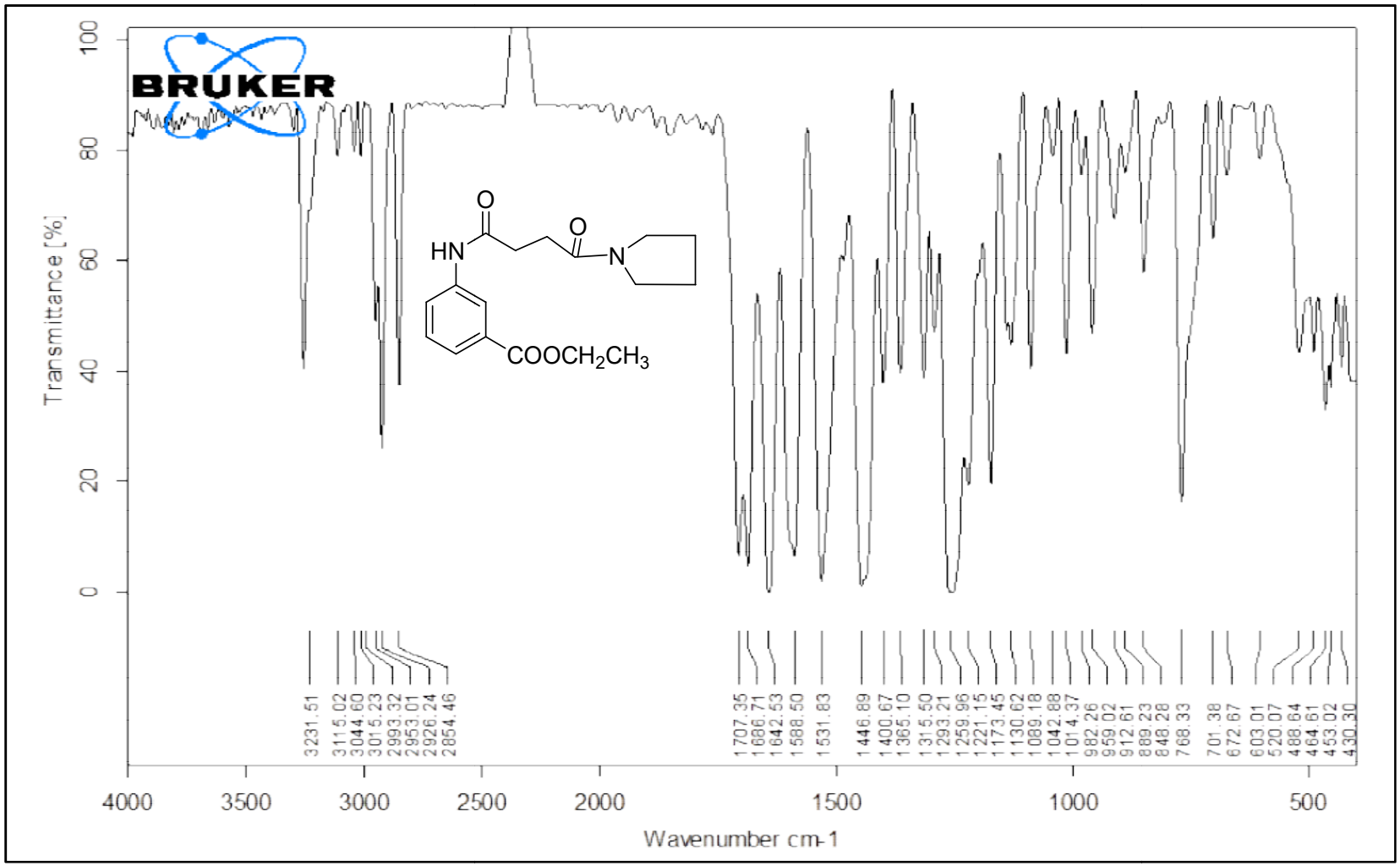


Figure 29: ^{1}H NMR Spectrum of ethyl 3-[4-oxo-4-(pyrrolidin-1-yl)butanamido]benzoate

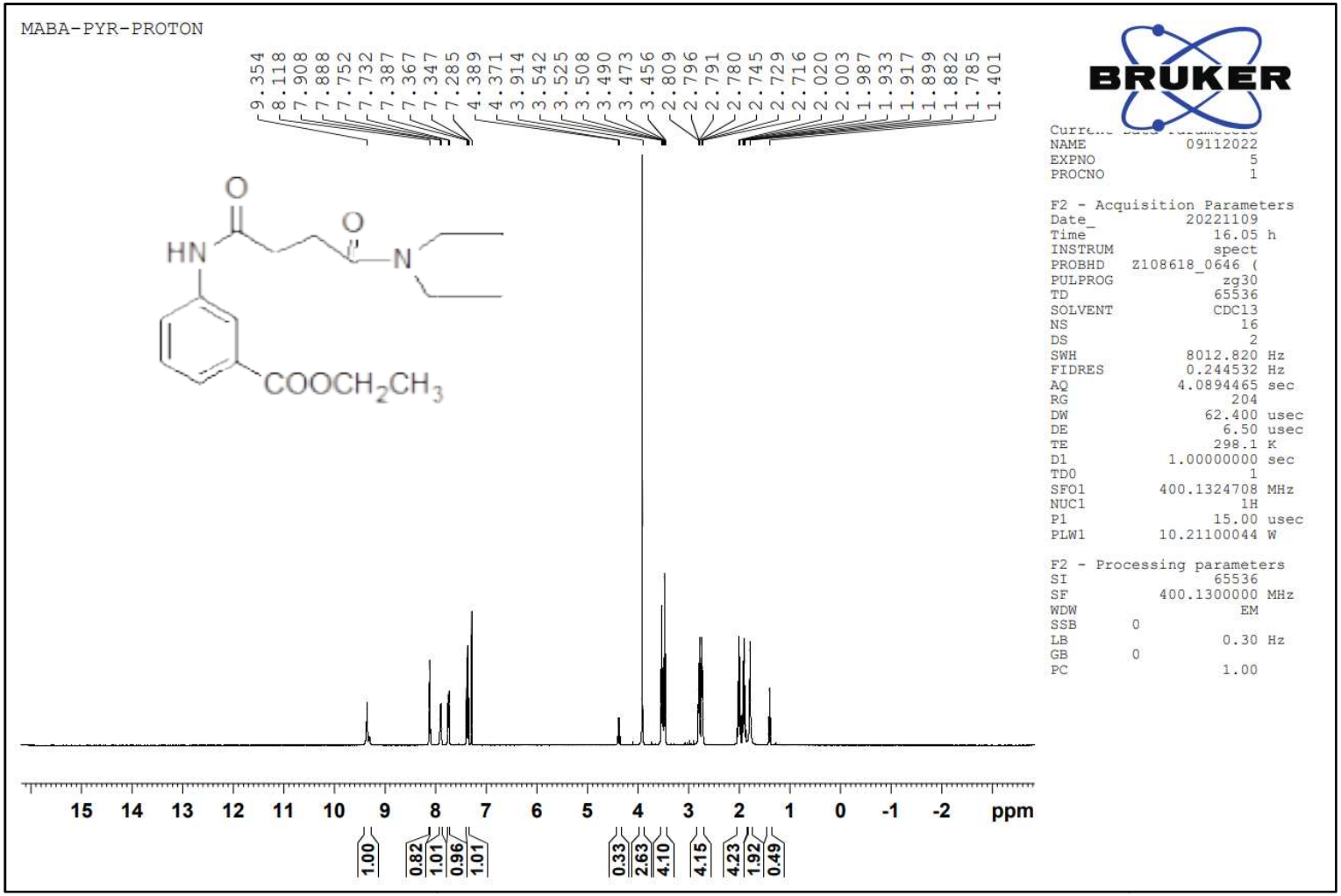


Figure 30: ^{13}C NMR Spectrum of ethyl 3-[4-oxo-4-(pyrrolidin-1-yl)butanamido]benzoate

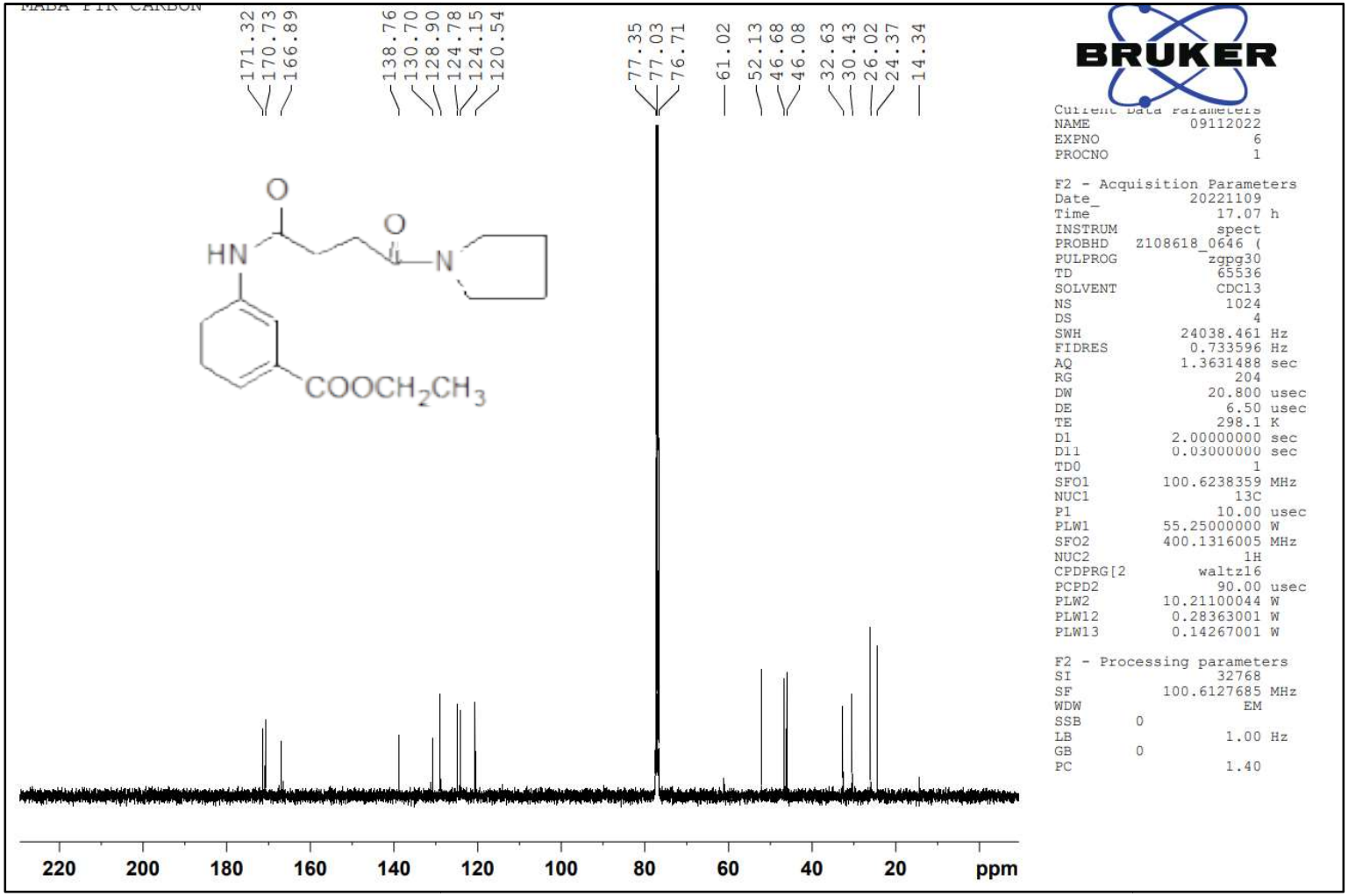


Figure 31: IR Spectrum of methyl 2-[4-(4-phenylpiperazin-1-yl)-4-oxobutanamido]benzoate

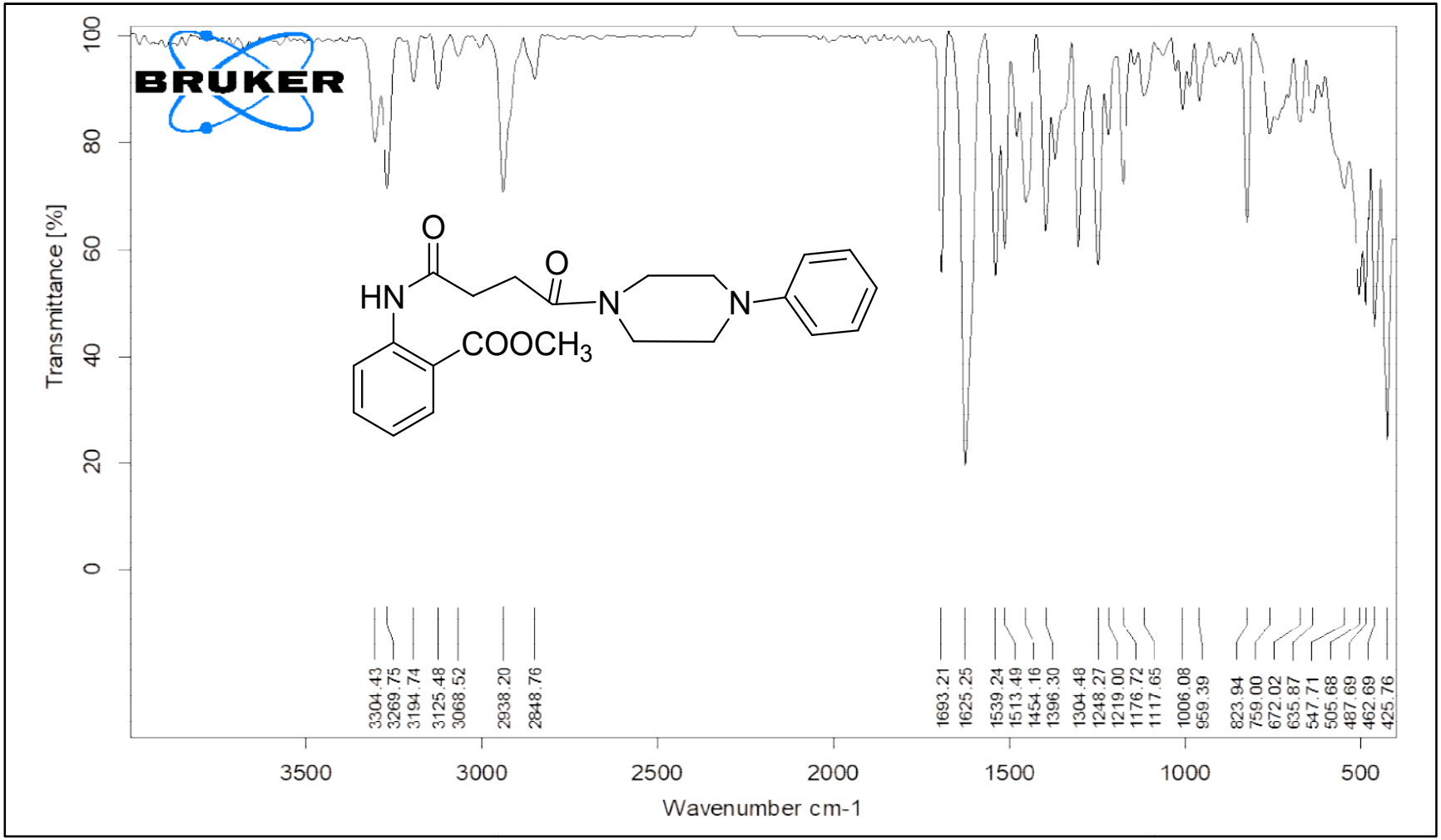


Figure 32: ^{1}H NMR Spectrum of methyl 2-[4-(4-phenylpiperazin-1-yl)-4-oxobutanamido]benzoate

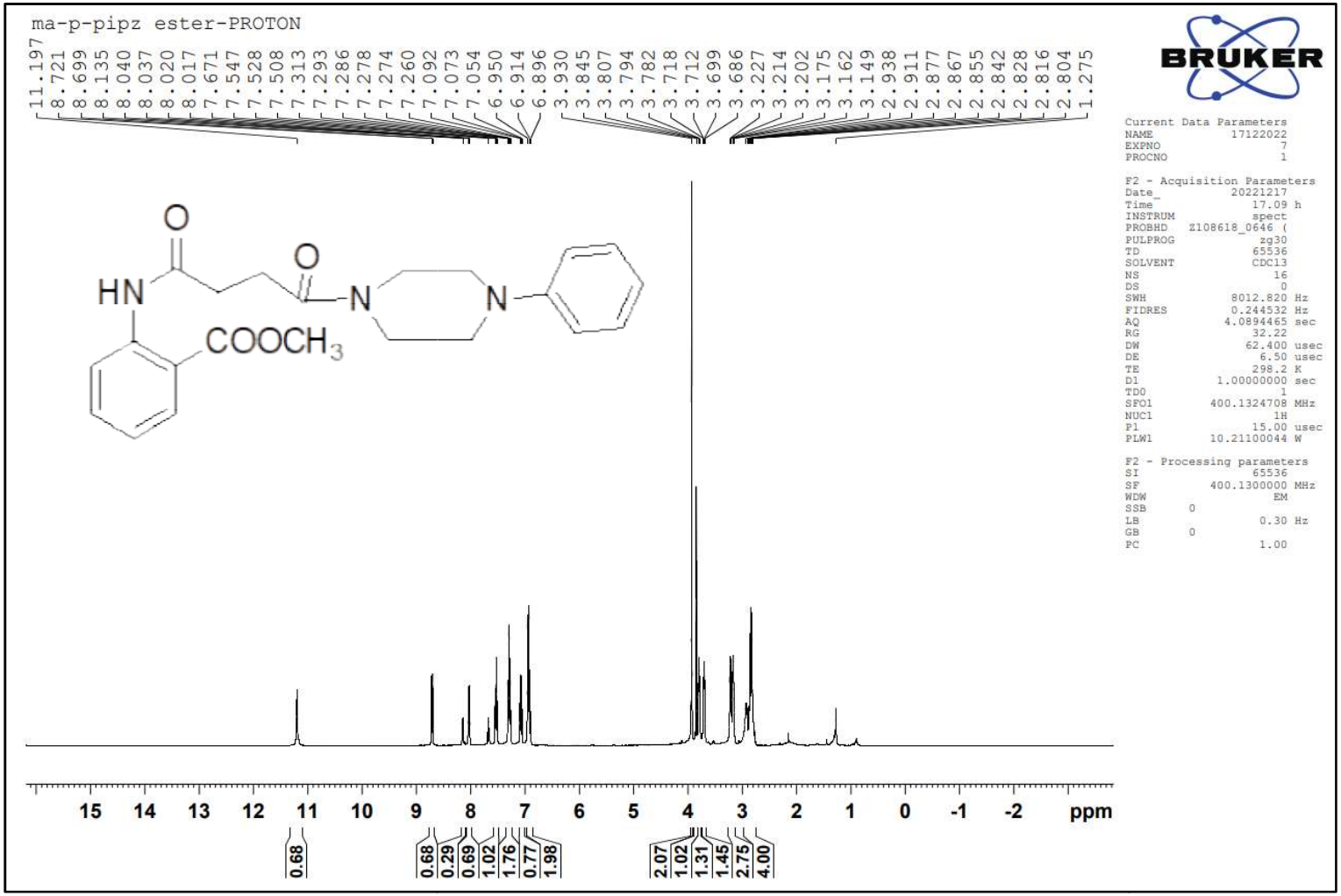


Figure 33: ^{13}C NMR Spectrum of methyl 2-[4-(4-phenylpiperazin-1-yl)-4-oxobutanamido]benzoate

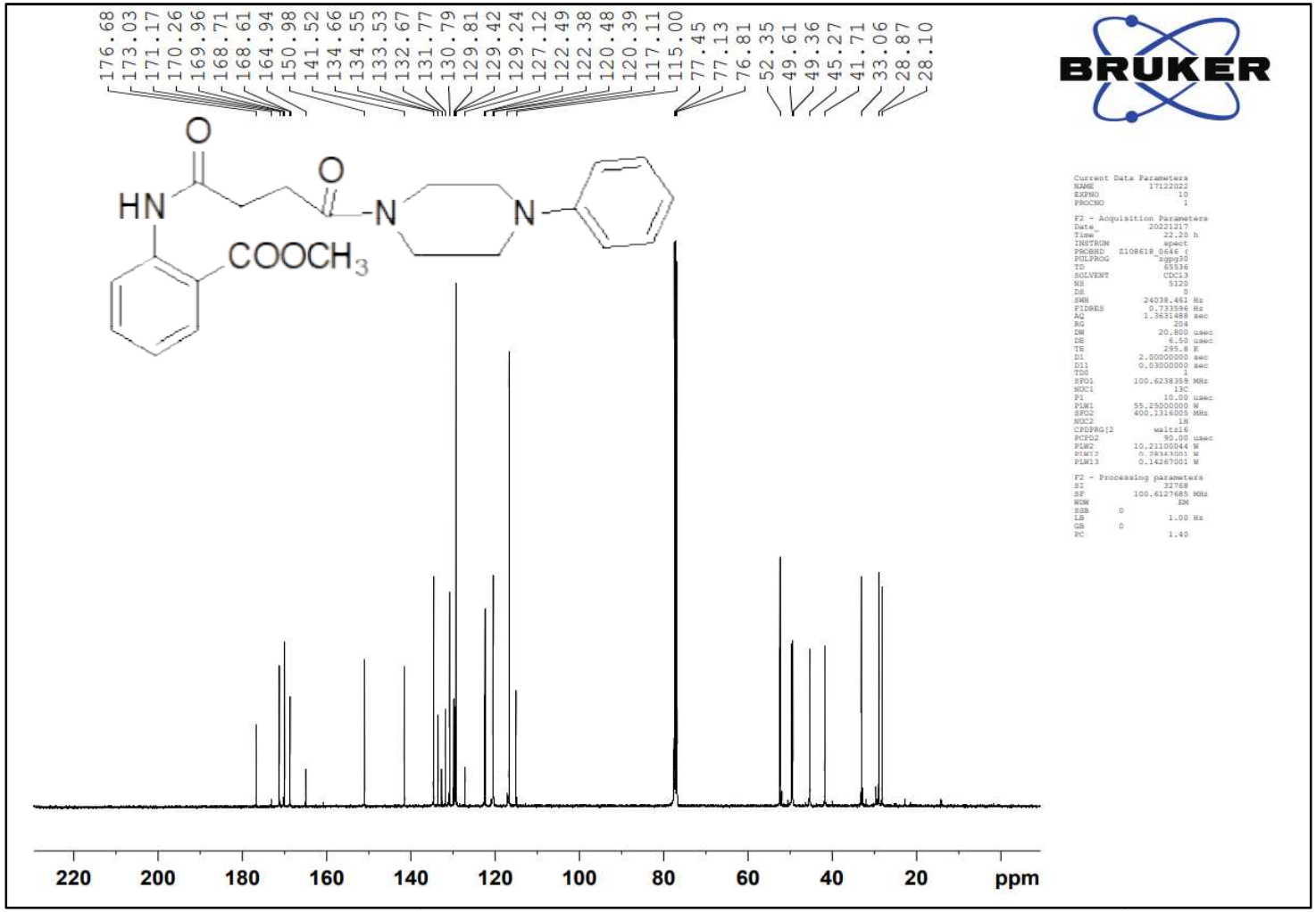


Figure 34: IR Spectrum of methyl 2-[4-(4-benzylpiperazin-1-yl)-4-oxobutanamido]benzoate

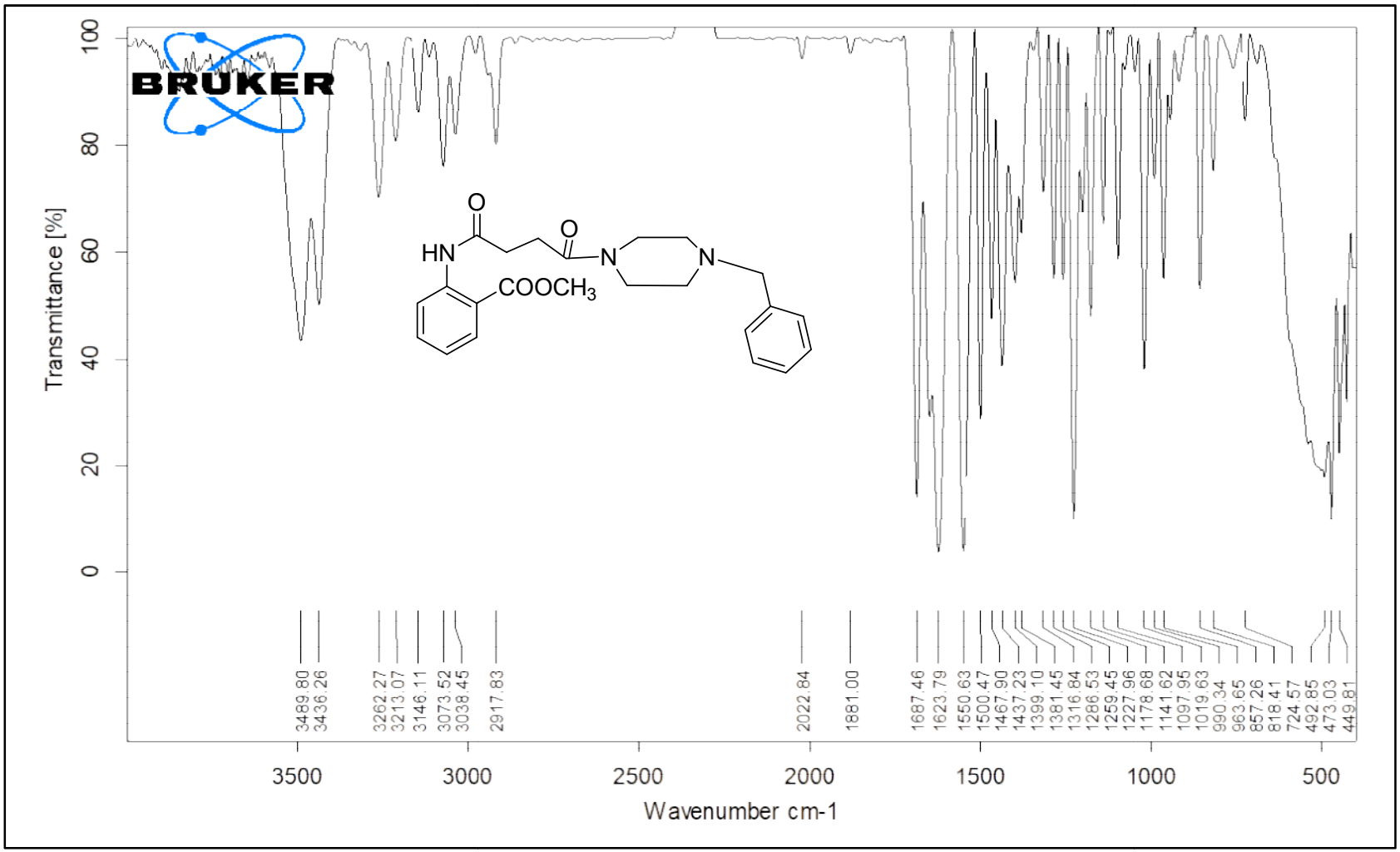


Figure 35: ^{1}H NMR Spectrum of methyl 2-[4-(4-benzylpiperazin-1-yl)-4-oxobutanamido]benzoate

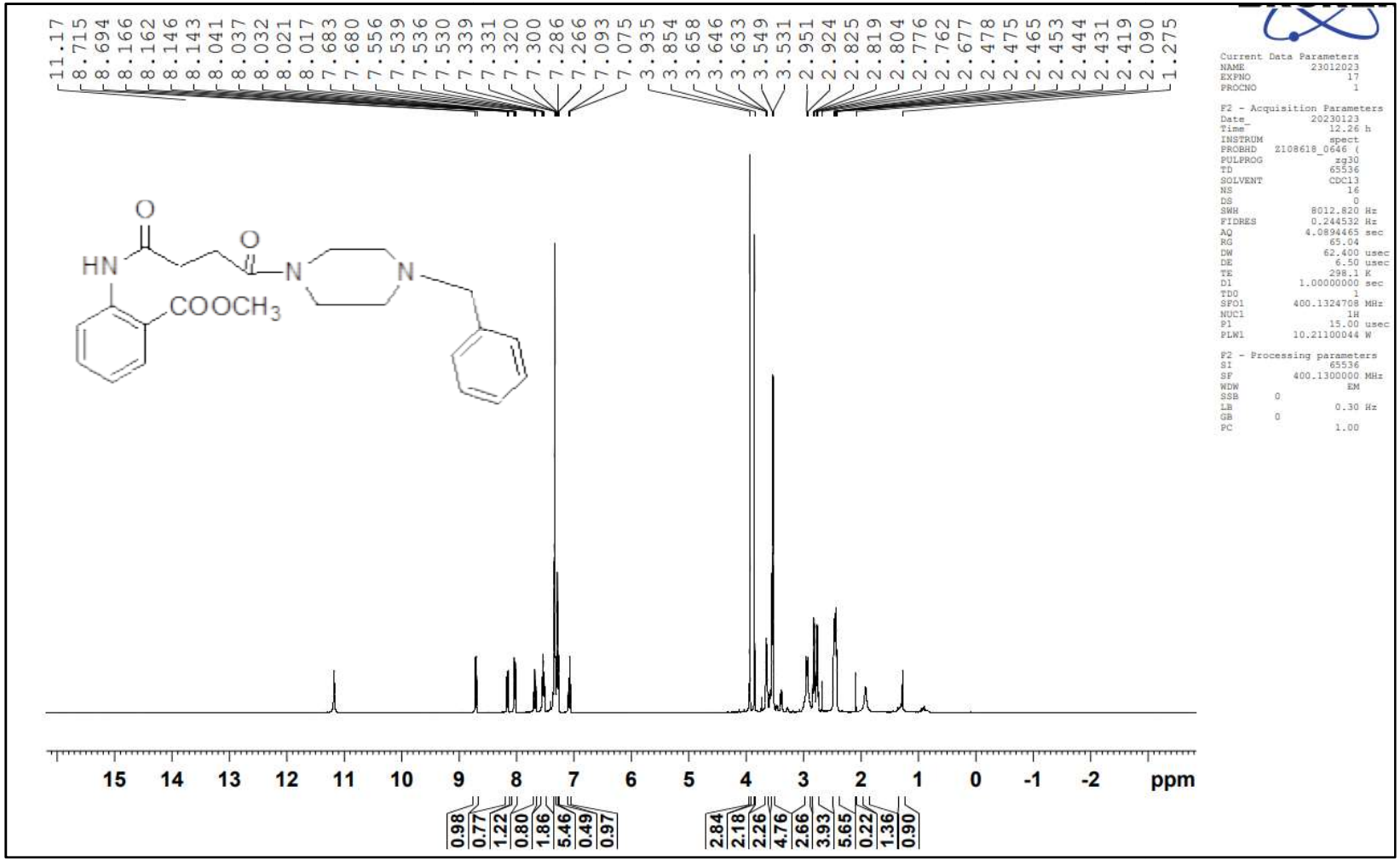


Figure 36: ^{13}C NMR Spectrum of methyl 2-[4-(4-benzylpiperazin-1-yl)-4-oxobutanamido]benzoate

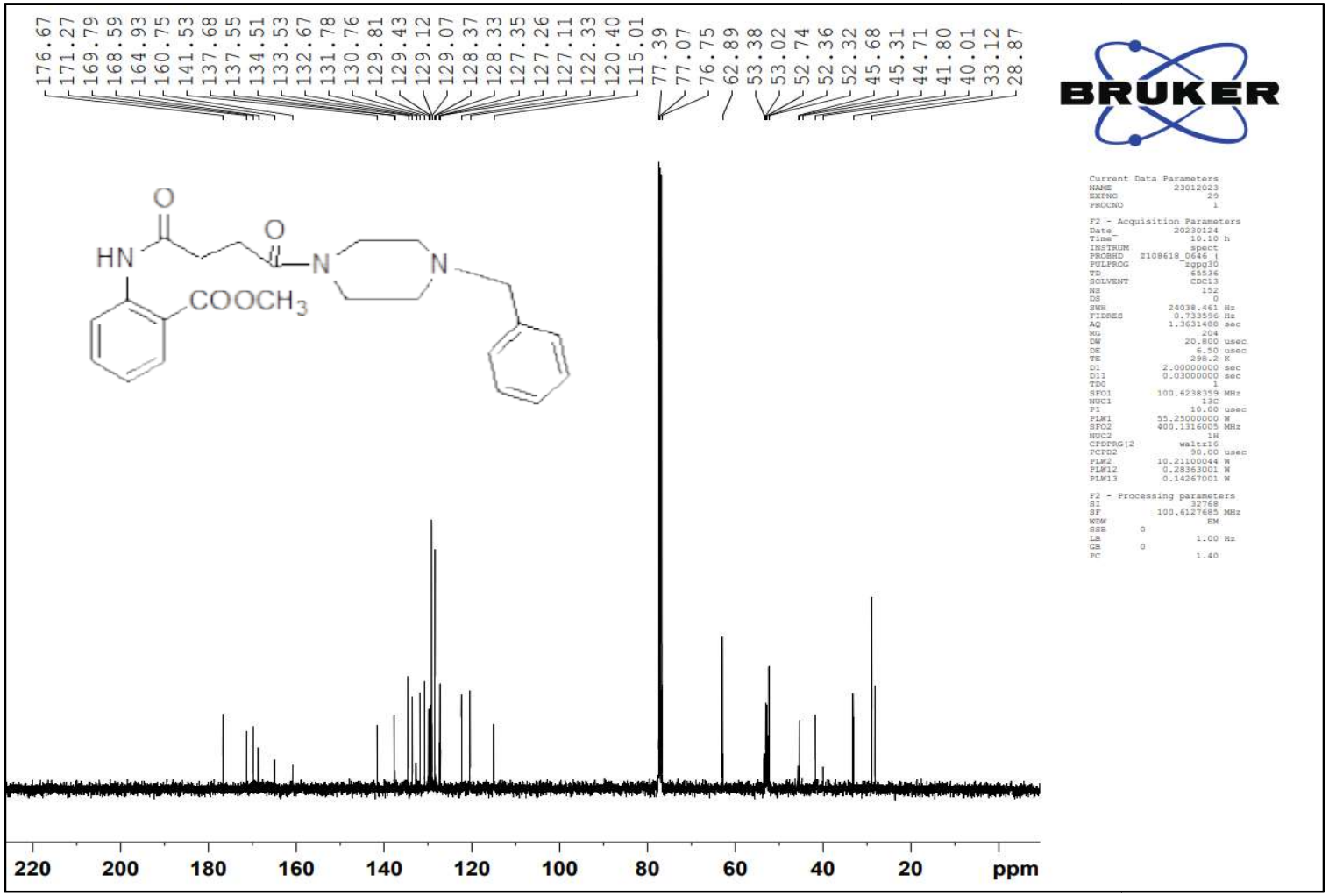


Figure 37: IR Spectrum of methyl 2-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

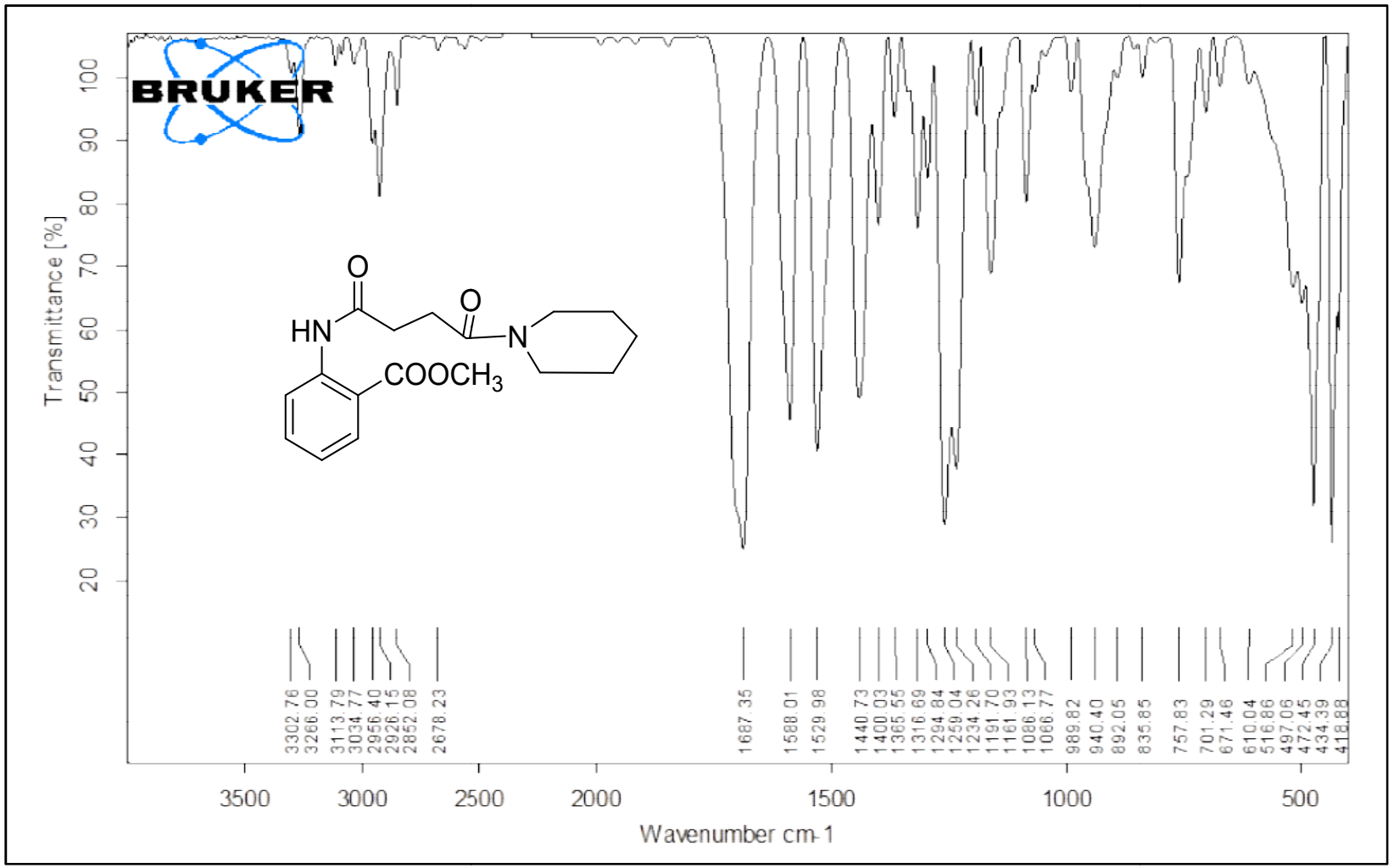


Figure 38: ^{1}H NMR Spectrum of methyl 2-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

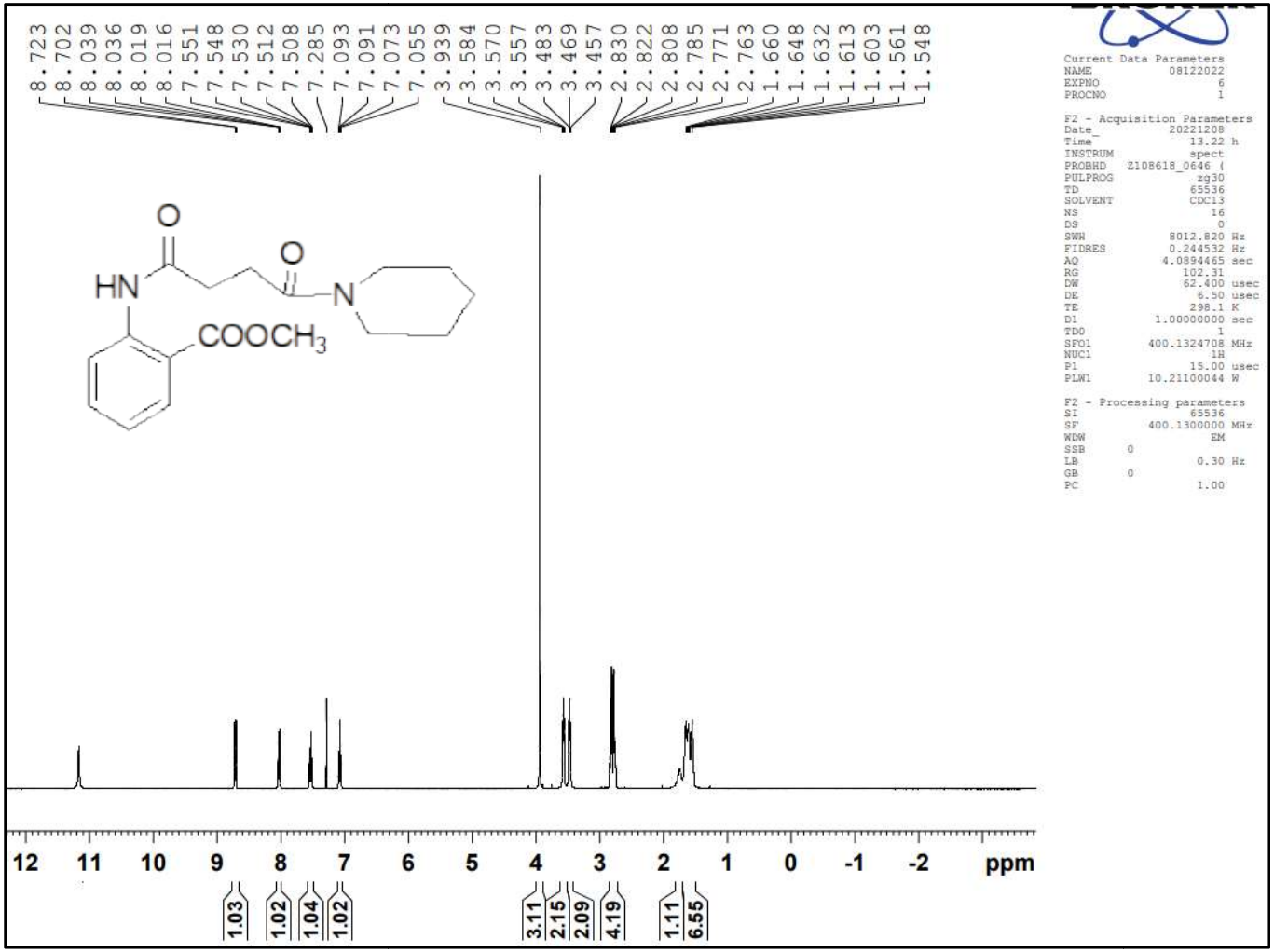


Figure 39: ^{13}C NMR Spectrum of methyl 2-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate

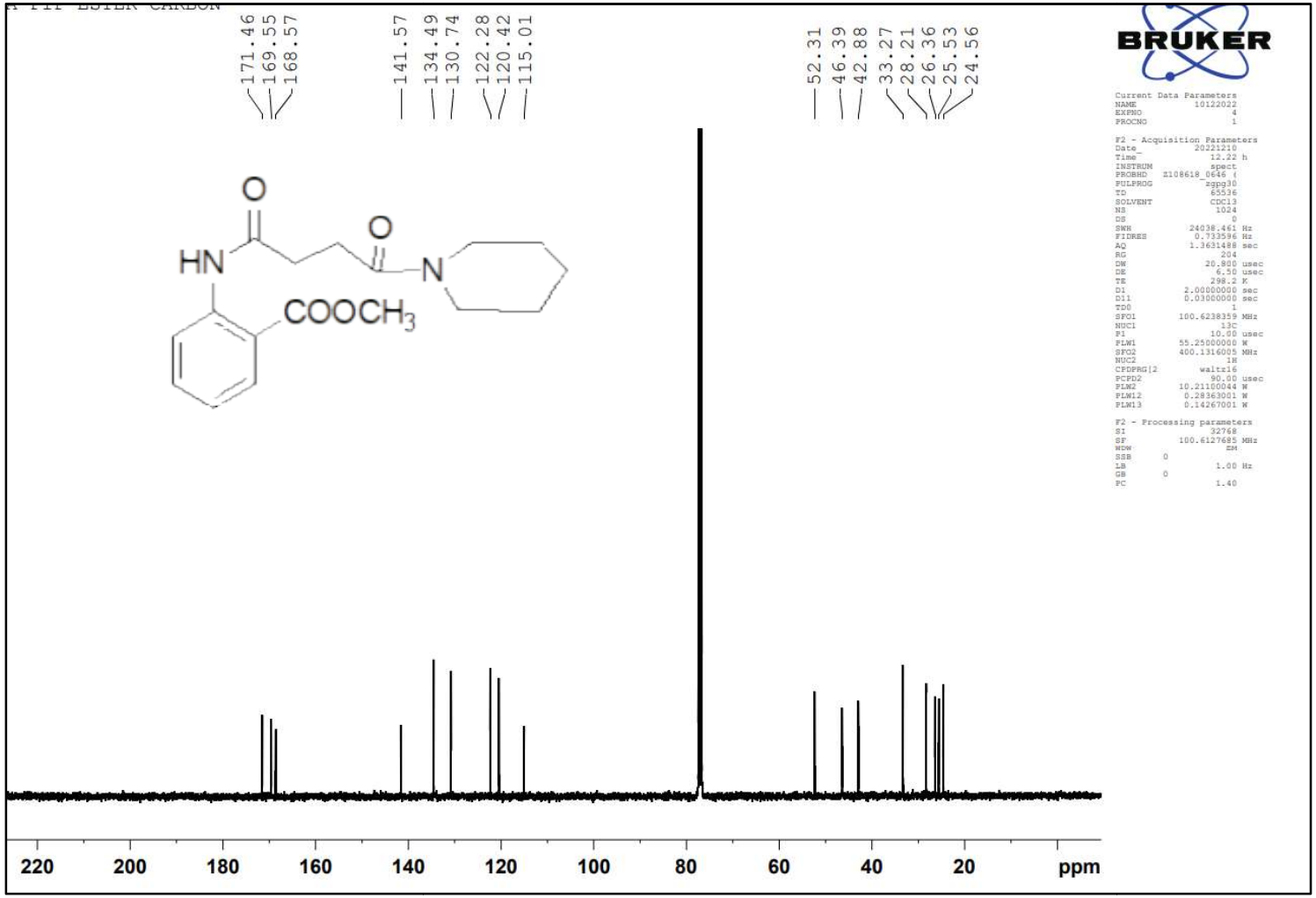
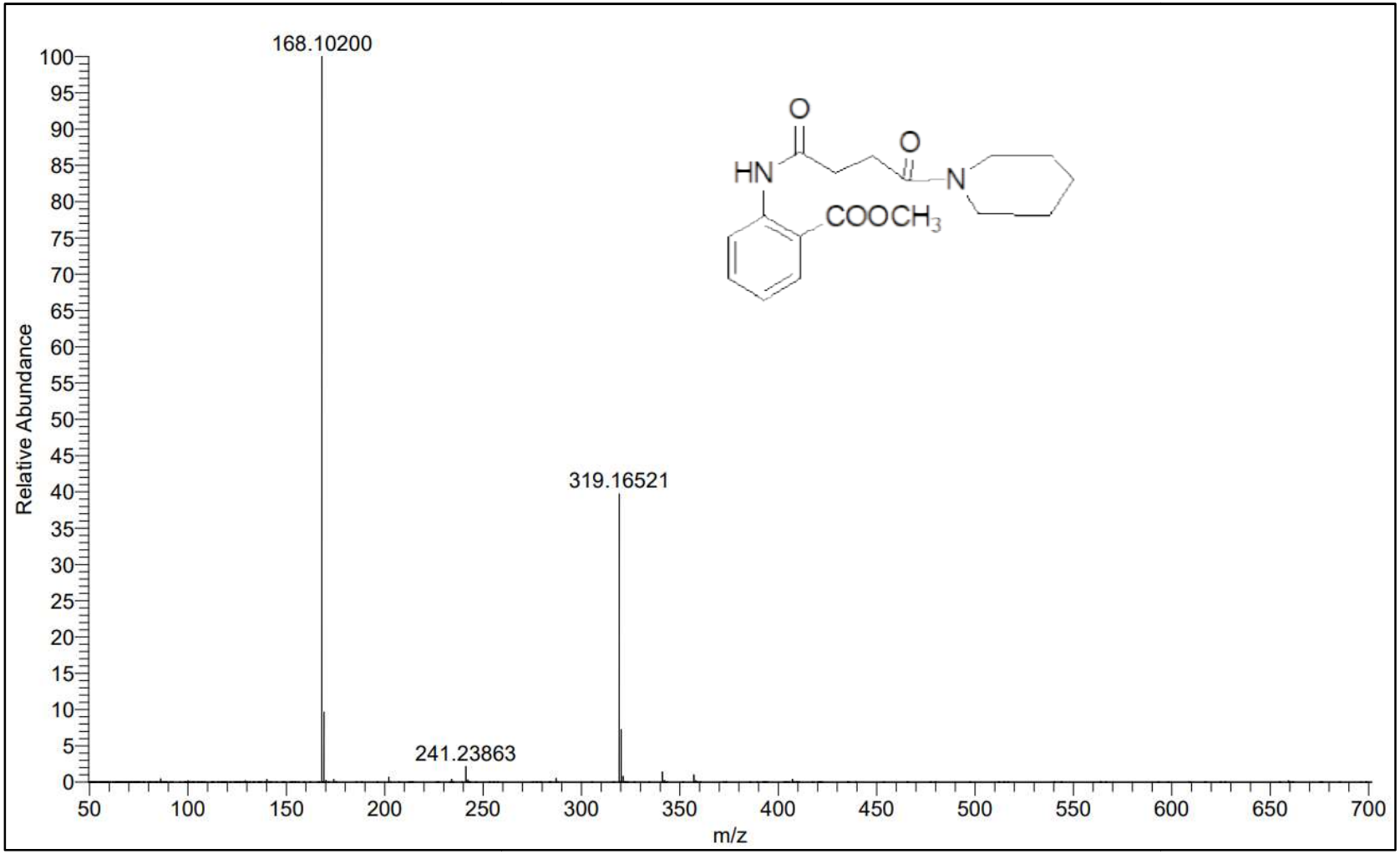


Figure 40: Mass Spectrum of methyl 2-[4-oxo-4-(piperidin-1-yl)butanamido]benzoate



3) Antibacterial activity:

4) Table 2: Zone of inhibition for anti-bacterial activity of 4-oxo-butanamido benzoate derivatives (cup plate method)

Sample codes	Gram +Ve		Gram -Ve	
	Zone of Inhibition (mm)[a]		Zone of Inhibition (mm)[a]	
	100µg/ml	50µg/ml	100µg/ml	50µg/ml
STD	**20**	**19**	**19**	**18**
SA1a	NA	NA	NA	NA
SA1b	NA	NA	NA	NA
SA1c	NA	NA	NA	NA
SA1d	NA	NA	NA	NA
SA1e	NA	NA	NA	NA
SA2a	NA	NA	NA	NA
SA2b	NA	NA	NA	NA
SA2c	NA	NA	NA	NA
SA2d	NA	NA	NA	NA
SA2e	NA	NA	NA	NA
SA3a	NA	NA	NA	NA
SA3b	NA	NA	NA	NA
SA3c	NA	NA	NA	NA
SA3d	NA	NA	NA	NA
SA3e	NA	NA	NA	NA

a- Excluding the diameter of the well/cup (6 mm);
Standard (Rifampicin)-20mm (against SA) and 19mm (against EC); Control (Methanol)-No zone; NA = not active

Figure 41: Anti-bacterial activity of 4-oxo-butanamido benzoate derivatives with concentrations of 50µg and 100µg against gram positive (*Staphylococcus aureus*) bacteria.

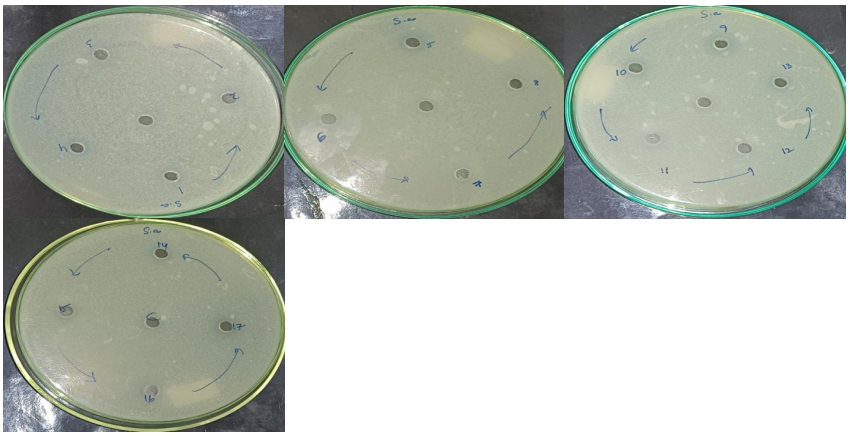
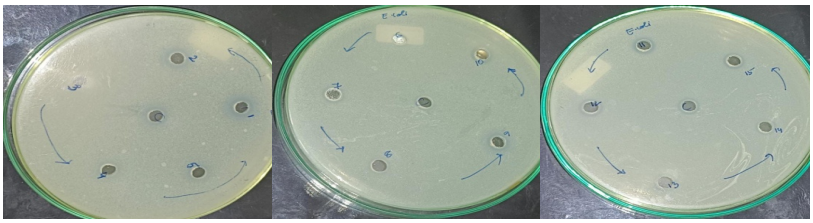


Figure 42: Anti-bacterial activities of 4-oxo-butanamido benzoate derivatives with concentrations of 50µg and 100µg against gram negative (*Escherichia coli*) bacteria.



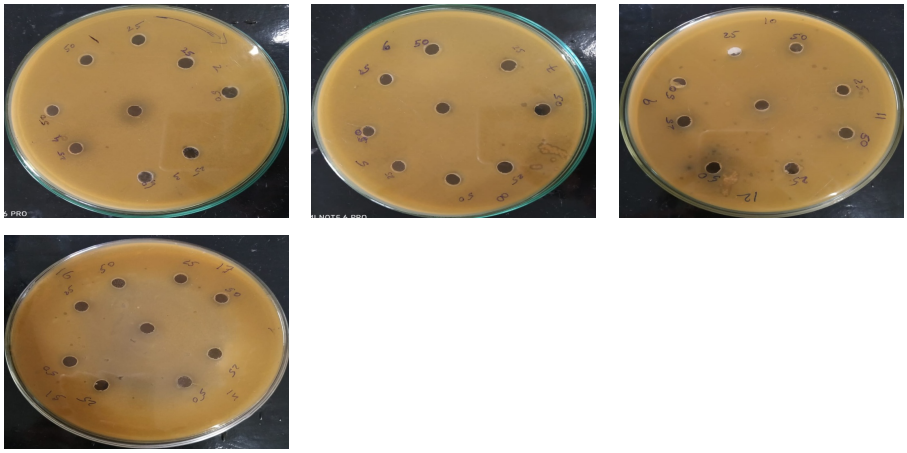
5) Antifungal activity:

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

Sample codes	*A. niger*		*C. albicans*	
	Zone of Inhibition (mm)[a]		Zone of Inhibition (mm)[a]	
	100µg/ml	50µg/ml	100µg/ml	50µg/ml
SA1a	NA	NA	NA	NA
SA1b	NA	NA	NA	NA
SA1c	NA	NA	NA	NA
SA1d	NA	NA	NA	NA
SA1e	NA	NA	NA	NA
SA2a	NA	NA	NA	NA
SA2b	NA	NA	NA	NA
SA2c	NA	NA	NA	NA
SA2d	NA	NA	NA	NA
SA2e	NA	NA	NA	NA
SA3a	NA	NA	NA	NA
SA3b	NA	NA	NA	NA
SA3c	NA	NA	NA	NA
SA3d	NA	NA	NA	NA
SA3e	NA	NA	NA	NA

a- Excluding the diameter of the well/cup (6 mm);
Standard (Ketoconazole)-35mm (against AN) and 38mm (against CA); Control (Methanol)-No zone; NA = not active

Figure 43: Antifungal activity of compounds against *Candida albicans* at 50µg and 100µg concentrations



7) *In vitro* anti-TB activity:

8) Table 4: Results of Antitubercular activity of 4-oxo-butanamido benzoate derivatives (MABA Assay)

S. No	Sample code	MIC(µg/ml)
1	SA1a	**1.56**
2	SA1b	**1.56**
3	SA1c	12.5
4	SA1d	12.5
5	SA1e	25
6	SA2a	**1.56**
7	SA2b	**3.12**
8	SA2c	12.5
9	SA2d	25
10	SA2e	25
11	SA3a	**3.125**
12	SA3b	**6.25**
13	SA3c	12.5
14	SA3d	25
15	SA3e	25
16	Streptomycin	**6.25**
17	Rifampicin	**3.12**

Figure 44: *In vitro* MABA assay results of the 4-oxo-butanamido benzoate derivatives SA1(a-e);SA2(a-e);SA3(a-e)

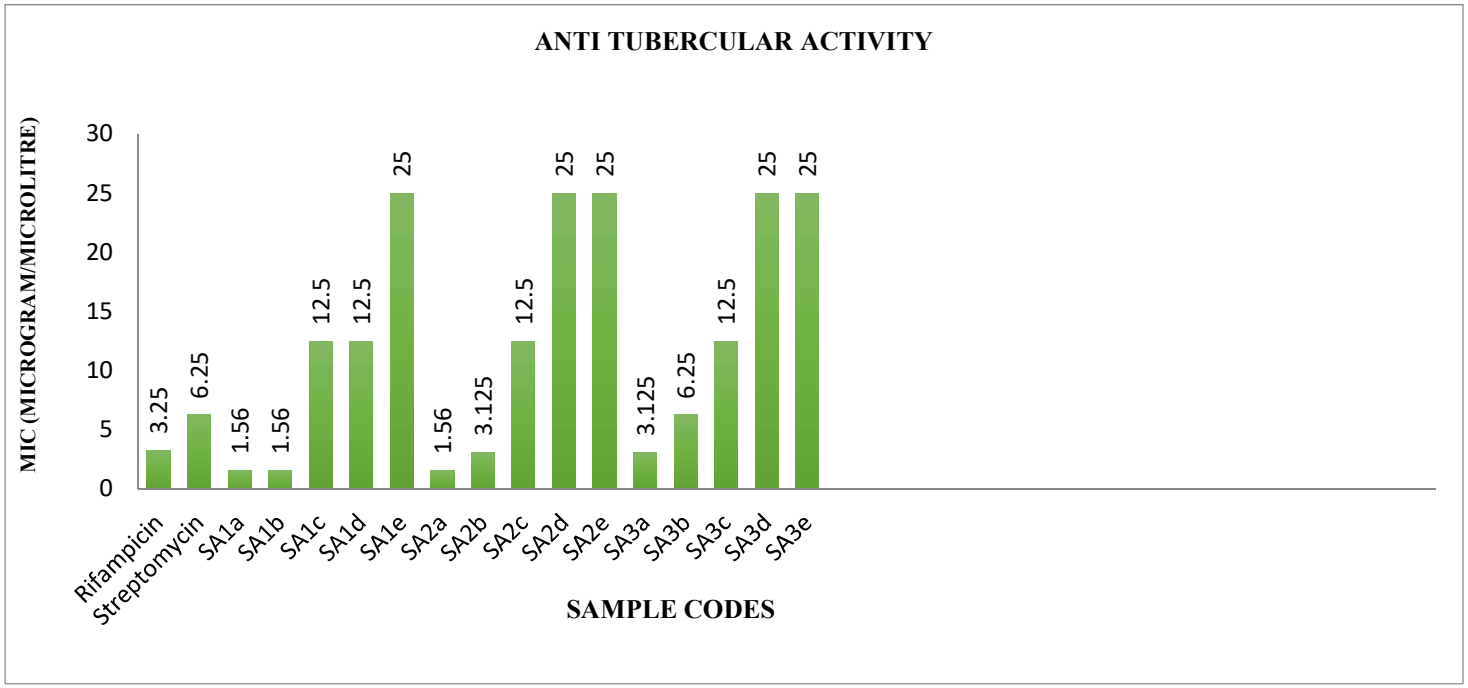
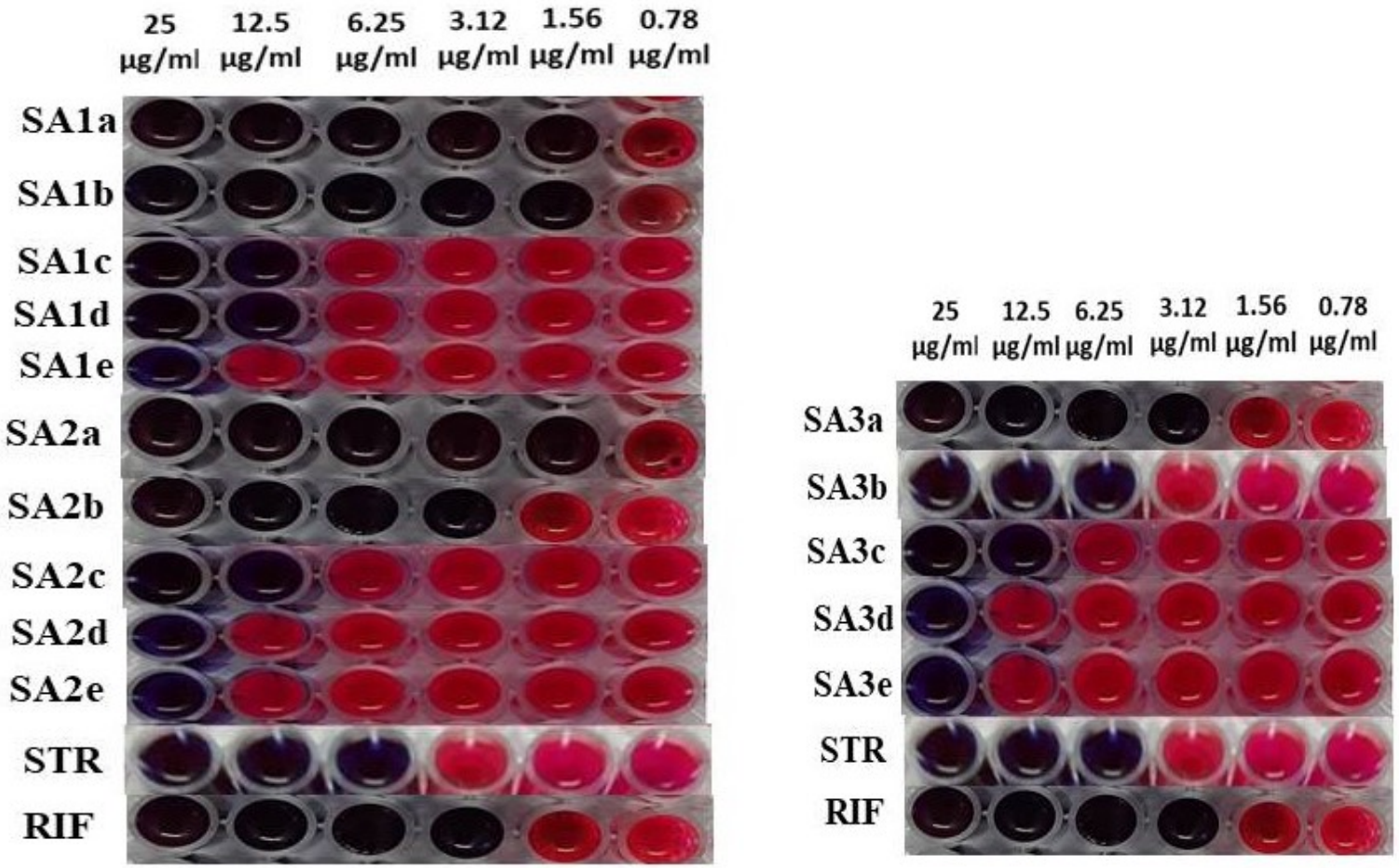


Figure 45: MABA assay of 4-oxo-butanamido benzoate derivatives SA1(a-e); SA2(a-e); SA3(a-e) Against *Mtb* H37Rv



9) *Insilico* studies:

10) Table 5: Drug likeness score for the synthesized 4-oxo-butanamido benzoate derivatives predicted using molinspiration& Osiris Property Explorer

Compound	miLog P[a]	TPSA[b]	nAtoms	nON[c]	nOHNH[d]	nviolations	nrotb[e]	%ABS[f]	MW
SA1a	3.14	78.95	30	7	1	0	8	81.76	409.49
SA1b	2.85	78.95	31	7	1	0	9	81.76	423.51
SA1c	2.46	75.71	24	6	1	0	7	82.88	332.40
SA1d	1.96	75.71	23	6	1	0	7	82.88	318.37
SA1e	2.31	75.71	23	6	1	0	9	82.88	320.39
SA2a	3.12	78.95	30	7	1	0	8	81.76	409.49
SA2b	2.82	78.95	31	7	1	0	9	81.76	423.51
SA2c	2.44	75.71	24	6	1	0	7	82.88	332.40
SA2d	1.93	75.71	23	6	1	0	7	82.88	318.37
SA2e	2.28	75.71	23	6	1	0	9	82.88	320.39
SA3a	2.90	78.95	29	7	1	0	7	81.76	395.46
SA3b	2.60	78.95	30	7	1	0	8	81.76	409.49
SA3c	2.22	75.71	23	6	1	0	6	82.88	318.37
SA3d	1.71	75.71	22	6	1	0	6	82.88	304.35
SA3e	2.06	75.71	22	6	1	0	8	82.88	306.36

[a]Logarithm of partition coefficient between n-octanol and water (miLogP); [b]topological polar surface area (TPSA); [c]number of hydrogen bond acceptors (n-ON); [d]number of hydrogen bond donors (n-OHNH); [e]number of rotatable bonds (n-rotb); [f]percentage absorption (%ABS); gmolecular weight (MW).

11) Table 6: Predicted Bioactivity score of 4-oxo-butanamido benzoate derivatives according to molinspiration

Compound code	GPCR	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
SA1a	-0.11	-0.20	-0.23	-0.26	-0.14	-0.23
SA1b	-0.11	-0.20	-0.21	-0.26	-0.10	-0.19
SA1c	-0.14	-0.23	-0.30	-0.25	-0.11	-0.22
SA1d	-0.17	-0.25	-0.11	-0.25	-0.08	-0.25
SA1e	-0.20	-0.28	-0.33	-0.31	-0.20	-0.27
SA2a	-0.12	-0.21	-0.22	-0.26	-0.15	-0.24
SA2b	-0.12	-0.21	-0.21	-0.26	-0.10	-0.20
SA2c	-0.15	-0.24	-0.30	-0.26	-0.12	-0.23
SA2d	-0.18	-0.27	-0.30	-0.25	-0.09	-0.27
SA2e	-0.21	-0.30	-0.33	-0.31	-0.21	-0.29
SA3a	-0.09	-0.20	-0.21	-0.28	-0.15	-0.21
SA3b	-0.09	-0.20	-0.20	-0.29	-0.`0	-0.17
SA3c	-0.11	-0.23	-0.29	-0.30	-0.14	-0.20
SA3d	-0.16	-0.26	-0.30	-0.30	-0.11	-0.23
SA3e	-0.19	-0.29	-0.34	-0.36	-0.24	-0.25

12) Table 7: Toxicity predictions of 4-oxo-butanamido benzoate derivatives based on Osiris Property Explorer

Compound	Mutagenic	Tumorigenic	Reproductive effect	Irritant effect
SA1a	none	none	none	none
SA1b	none	none	none	none
SA1c	none	none	none	none
SA1d	none	none	none	none
SA1e	none	none	none	none
SA2a	none	none	none	none
SA2b	none	none	none	none
SA2c	none	none	none	none
SA2d	none	none	none	none
SA2e	none	none	none	none
SA3a	none	none	none	none
SA3b	none	none	none	none
SA3c	none	none	none	none
SA3d	none	none	none	none
SA3e	none	none	none	none

13) Molecular DockingStudies:

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

Compound codes	Docking Score	Interaction residues
SA1a	-10.4	ALA-22
SA1b	-10.1	GLY-14, ILE-21, ALA-22
SA1c	-8.5	ALA-22, TYR-158, LYS-165
SA1d	-8.4	ALA-22
SA1e	-7.8	ILE-21, ALA-22, ILE-194
SA2a	-10.3	GLY-14, SER-20, ALA-22, GLY-96
SA2b	-10.3	GLN-14, SER-20, ILE-21, GLY-96
SA2c	-8.9	GLN-214
SA2d	-8.3	LYS-165, GLN-214
SA2e	-8.2	TYR-158
SA3a	-10.2	GLN-214
SA3b	-9.7	SER-94, GLY-96
SA3c	-8.8	ILE-194, GLN-214
SA3d	-8.1	LYS-165, ILE-194
SA3e	-7.4	LYS-165, ILE-194

15) Table 9: Binding energies of 4-oxo-butanamido benzoate derivatives against receptor β-ketoacyl ACP synthase I (5LD8)

Compound codes	Docking Score	Interaction residues
SA1a	-8.0	GLY-117
SA1b	-9.2	ARG-85, GLU-120
SA1c	-7.1	GLU-120
SA1d	-7.4	ARG-85
SA1e	-7.0	GLU-120
SA2a	-8.7	GLU-199, GLU-120, ALA-119
SA2b	-8.8	GLU-199, ALA-119
SA2c	-8.3	GLU-199
SA2d	-8.1	GLU-199
SA2e	-7.4	GLU-199
SA3a	-8.6	GLU-199, PHE-239
SA3b	-8.6	PHE-239
SA3c	-8.6	GLU-199, PHE-239
SA3d	-7.3	ALA-119, GLU-120
SA3e	-6.3	GLY-117, LEU-116

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

Compound codes	Docking Score	Interaction residues
SA1a	-8.0	TRP-74
SA1b	-8.6	ASP-139, HIS-98
SA1c	-8.2	TRP-30, TRP-74
SA1d	-7.9	TRP-74, HIS-98
SA1e	-6.5	GLY-73, THR-93, HIS-98
SA2a	-8.9	THR-93
SA2b	-8.1	HIS-98, TYR-32, PHE-22
SA2c	-8.5	TYR-33, TRP-74, HIS-98
SA2d	-8.4	TYR-32, THR-33
SA2e	-7.1	GLY-71, PHE-135
SA3a	-8.0	HIS-98
SA3b	-8.3	PHE-22
SA3c	-7.0	ASN-260
SA3d	-8.3	TRP-74
SA3e	-6.5	TYR-32, TRP-74, HIS-98

17) Table 11: Binding energies of 4-oxo-butanamido benzoate derivatives against receptor β-ketoacyl-ACP reductase (1UZN)

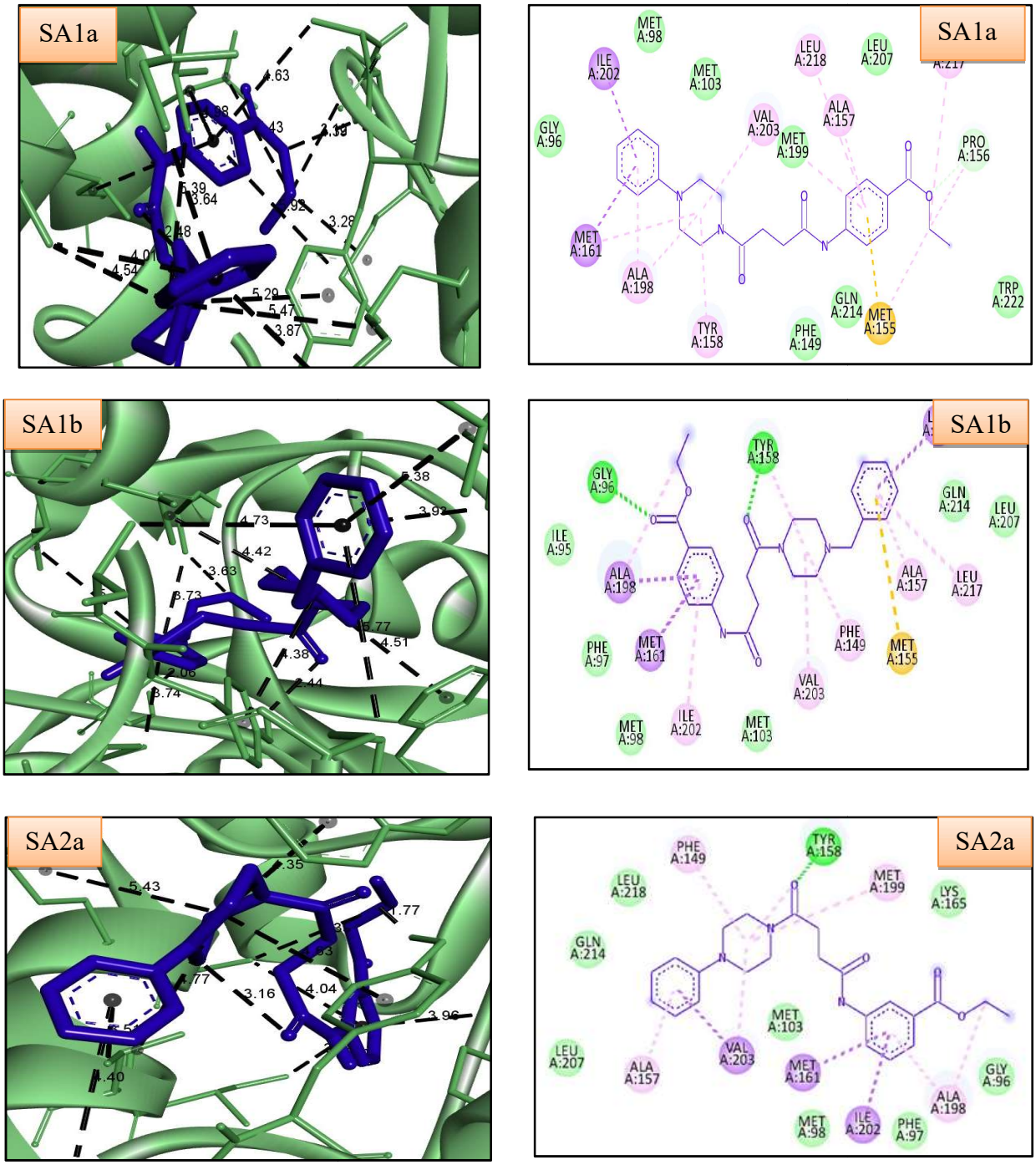
Compound codes	Docking Score	Interaction residues
SA1a	-8.6	ILE-27, ARG-25, ASN-88 GLY-28, GLY-22, ARG-47
SA1b	-8.9	ILE-27, TYR-185
SA1c	-8.0	GLY-22, ARG-25, GLY-28, ILE-27, ARG-47
SA1d	-7.2	GLY-28, ARG-47
SA1e	-6.9	GLY-22, ILE-27, ARG-47, ASN-88
SA2a	-8.8	ILE-27, TYR-153
SA2b	-8.6	ILE-27, GLY-28, TYR-153, LYS-157
SA2c	-7.4	ILE-27, GLY-28, ILE-186
SA2d	-7.4	ILE-27, GLY-28, TYR-153, LYS-157
SA2e	-7.0	ILE-27, GLY-28
SA3a	-7.1	GLY-22, THR-45, ARG-47
SA3b	-7.8	ARG-25
SA3c	-7.0	ARG-25, ARG-47, GLY-90
SA3d	-7.7	GLY-22, ARG-25, THR-45, GLY-90
SA3e	-7.1	ARG-25, THR-45, GLY-90

-

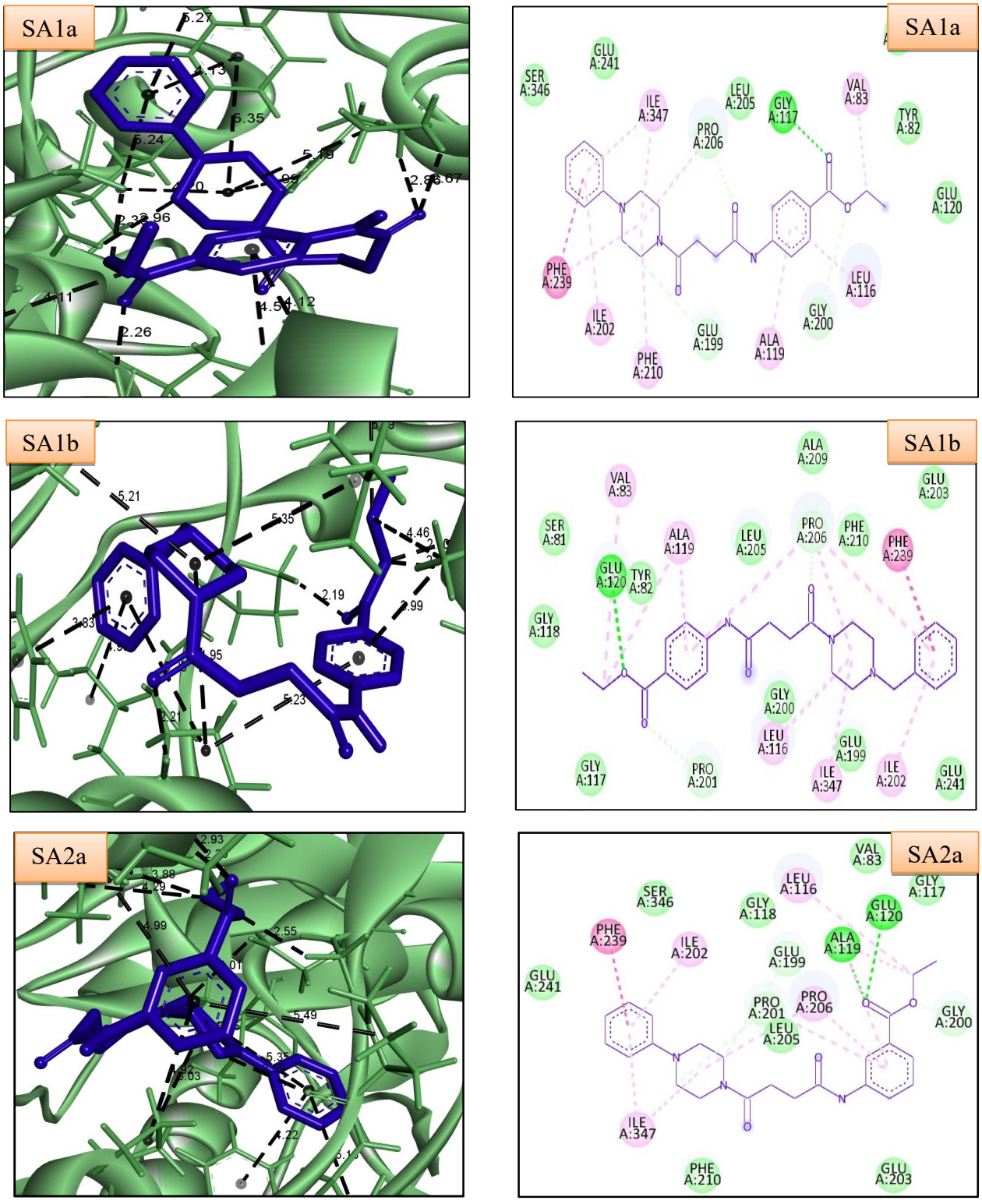
18) Table 12: Binding energies of 4-oxo-butanamido benzoate derivatives against receptor Beta-Ketoacyl-Acyl Carrier Protein Synthase III (1HZP)

Compound codes	Docking Score	Interaction residues
SA1a	-8.6	GLY-209
SA1b	-9.2	ARG-249, ARG-214
SA1c	-7.9	ASN-274, ARG-151
SA1d	-8.4	ARG-249, ASN-274
SA1e	-7.3	ASN-274
SA2a	-8.6	ARG-151, GLY-152
SA2b	-8.9	GLY-209, ASN-274
SA2c	-7.9	ASN-274
SA2d	-8.0	ASN-274
SA2e	-7.4	ASN-247, ASN-274
SA3a	-8.2	ARG-151
SA3b	-7.6	ARG-151
SA3c	-7.8	ASN-247
SA3d	-7.5	ASN-247, ARG-249
SA3e	-6.6	ASN-274

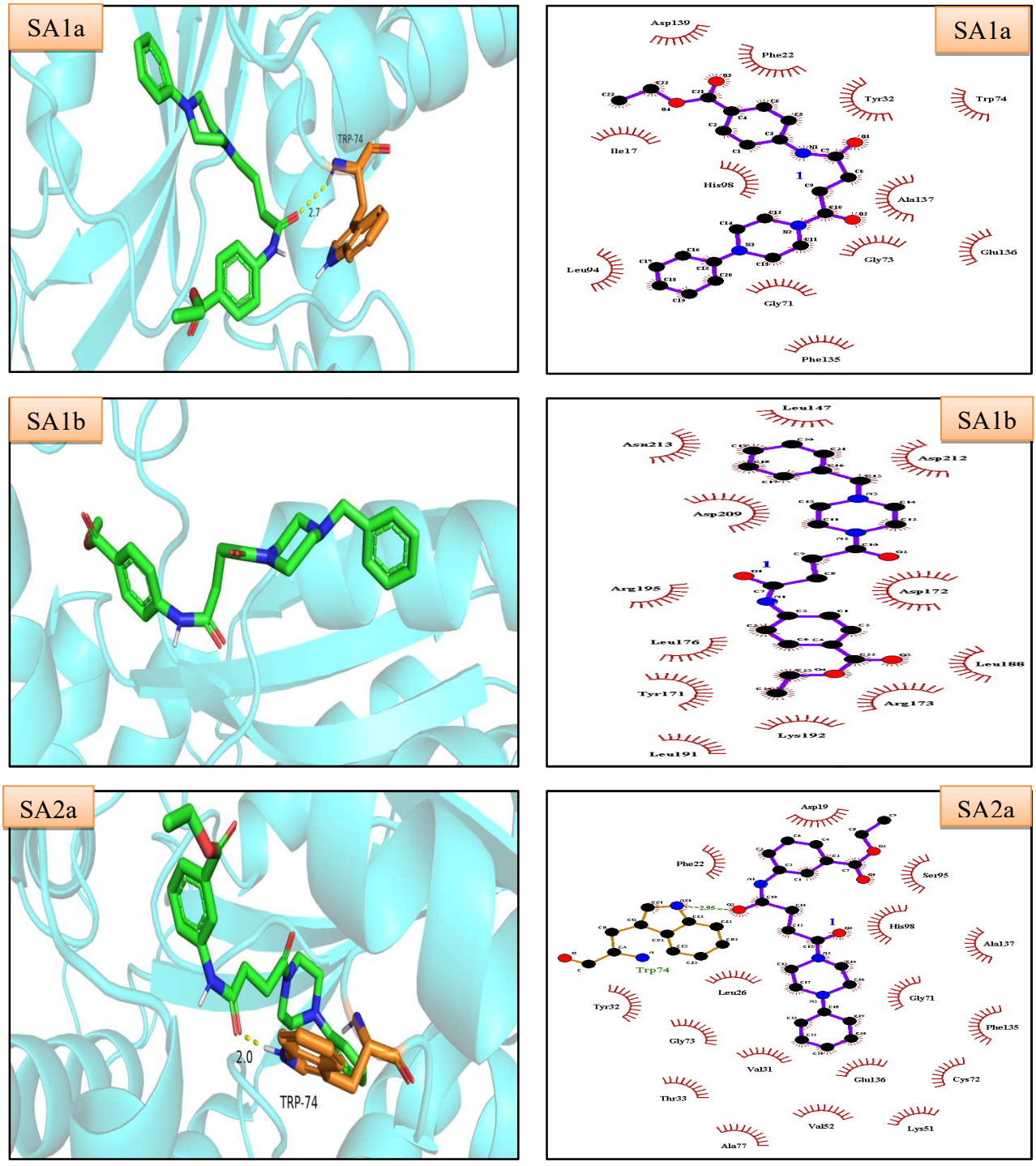
19) **Figure 46: Docking poses of the potent molecules (SA1a, SA1b & SA2a) with InhA enzyme. The protein is shown as green color solid ribbon model and the ligand is shown as dark blue stick model. The 2D interaction diagram of the protein-ligand interaction is shown on the right side.**



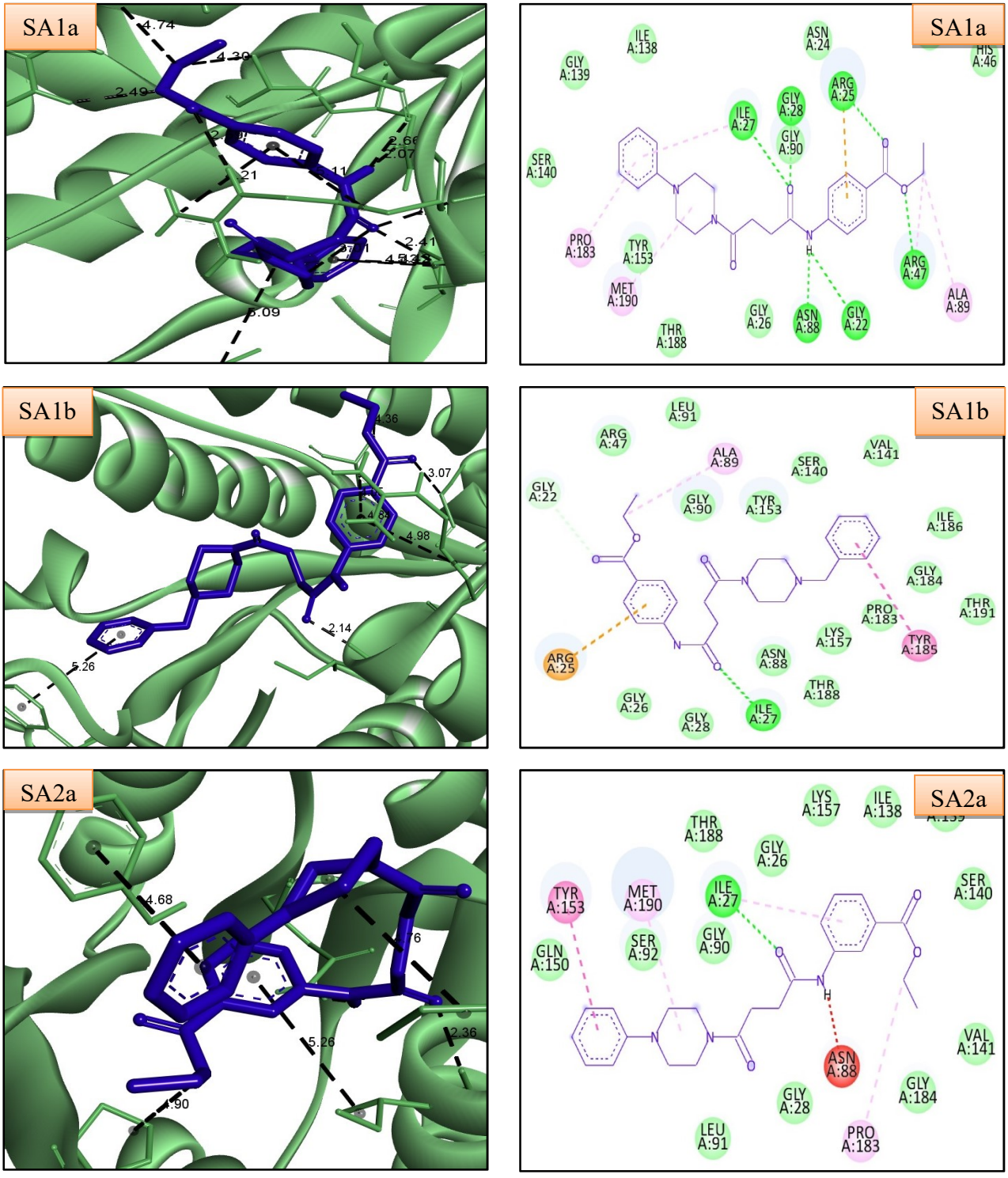
20) **Figure 47: Docking poses of the potent molecules (SA1a, SA1b & SA2a) with KasA enzyme. The protein is shown as green color solid ribbon model and the ligand is shown as dark blue stick model. The 2D interaction diagram of the protein-ligand interaction is shown on the right side.**



21) **Figure 48: Docking poses of the potent molecules (SA1a, SA1b & SA2a) 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.**



22) **Figure 49: Docking poses of the potent molecules (SA1a, SA1b & SA2a) 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.**



23) Figure 50: Docking poses of the potent molecules (SA1a, SA1b & SA2a) 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.