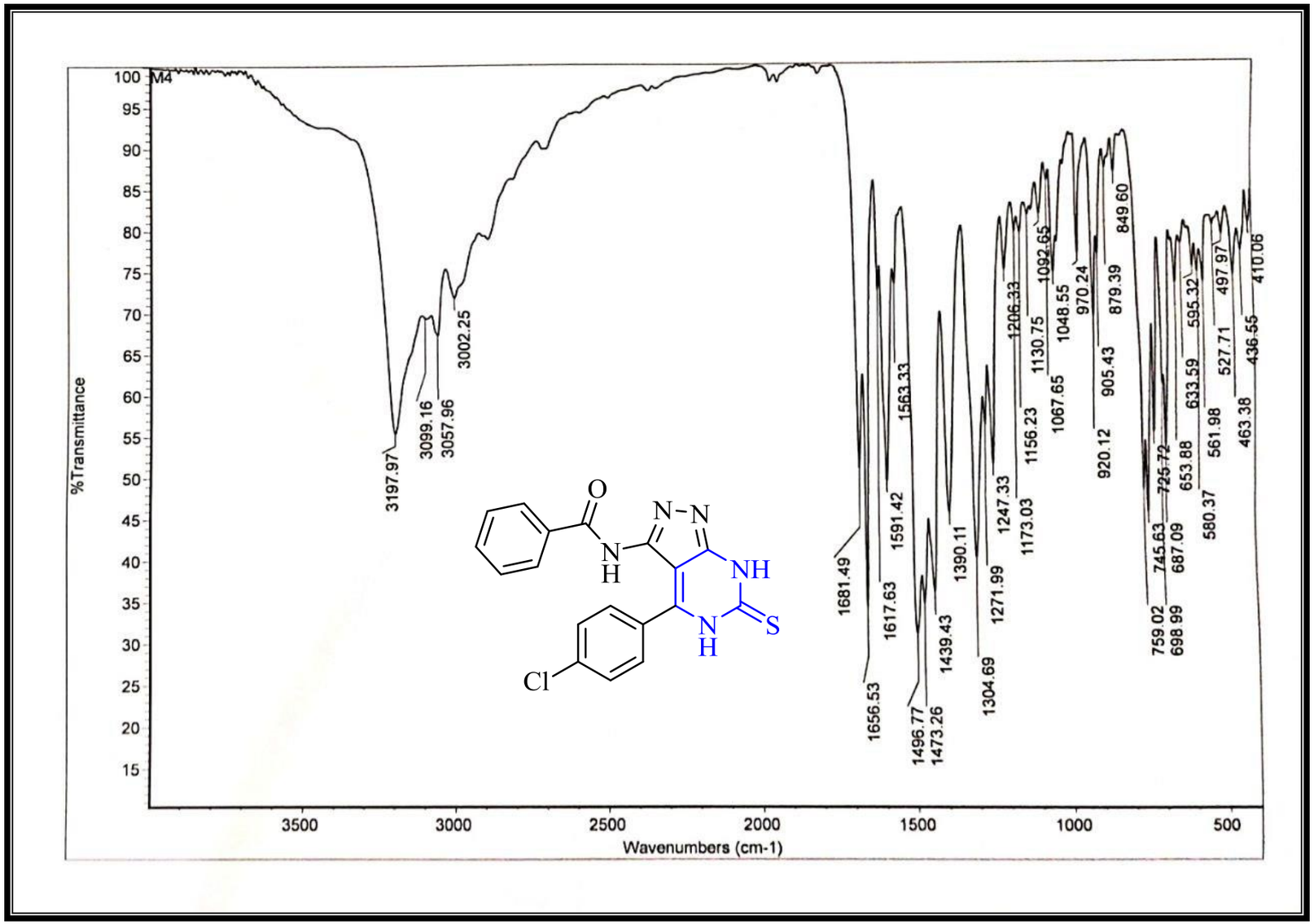
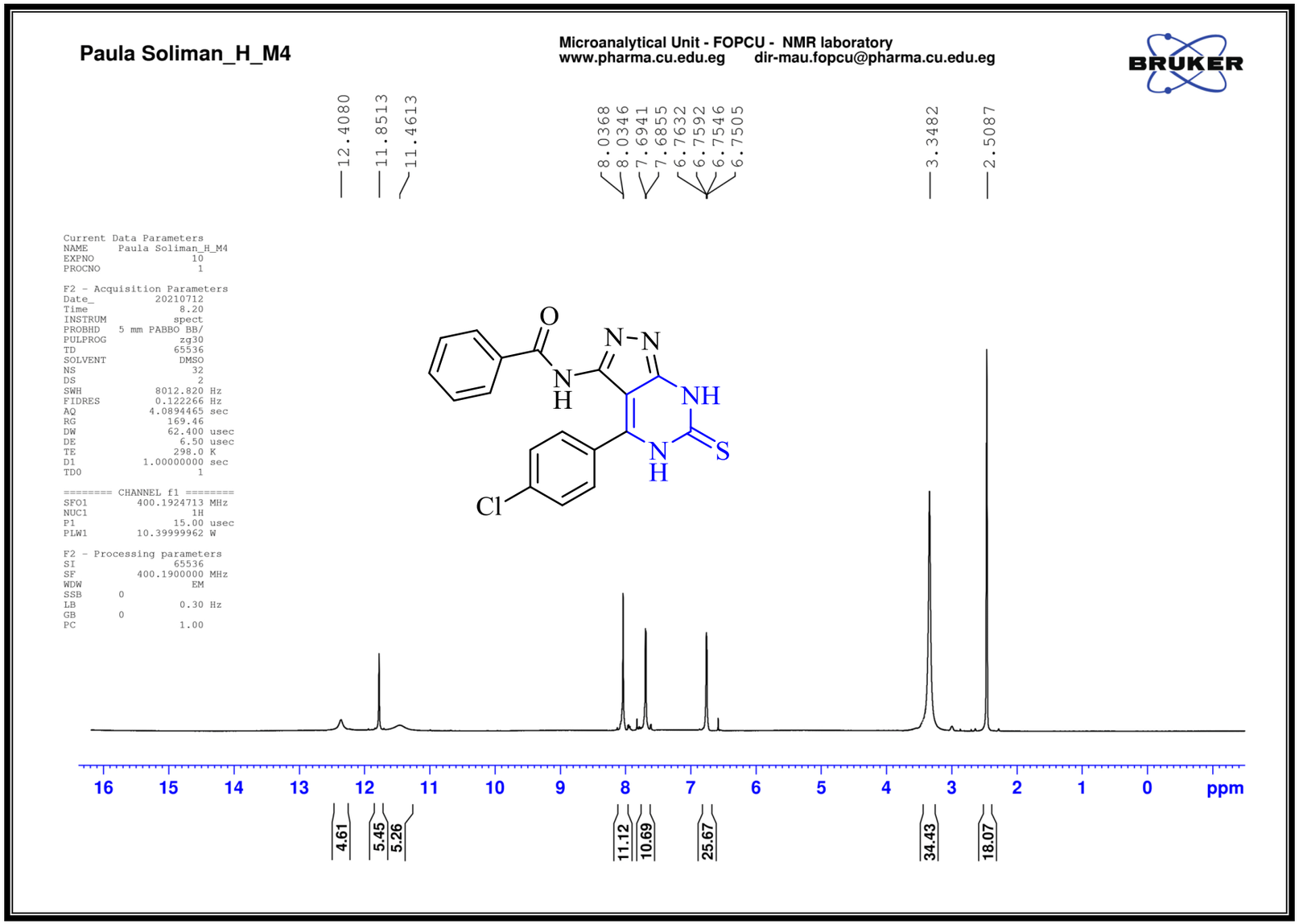
Electronic Supplementary Material (ESI) for RSC Advances.

1. Chemistry

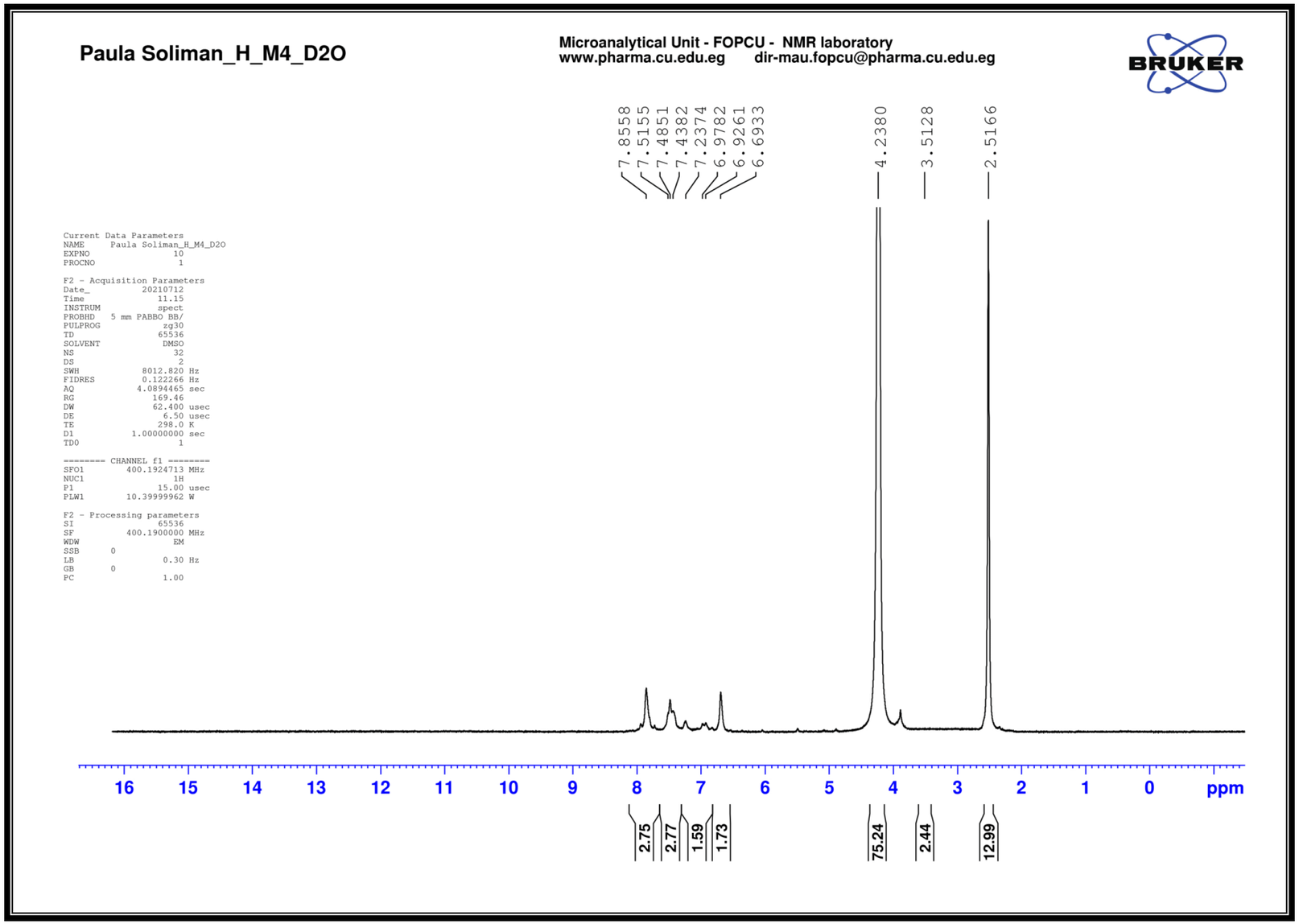
Using a Pye Unicam SP1200 spectrophotometer, IR-spectra were recorded using the KBr wafer method (Pye Unicam Ltd., Cambridge, UK). The 1H-NMR spectra were obtained on a Bruker Avance (III) with a Varian-Gemini 400 MHz and an internal standard of Tetramethyl silane (chemical shifts in scale ppm), while the ^{13}C-NMR spectra were obtained at 100 MHz. TMS was used as an internal standard in deuterated Dimethyl sulfoxide (DMSO-d_6).



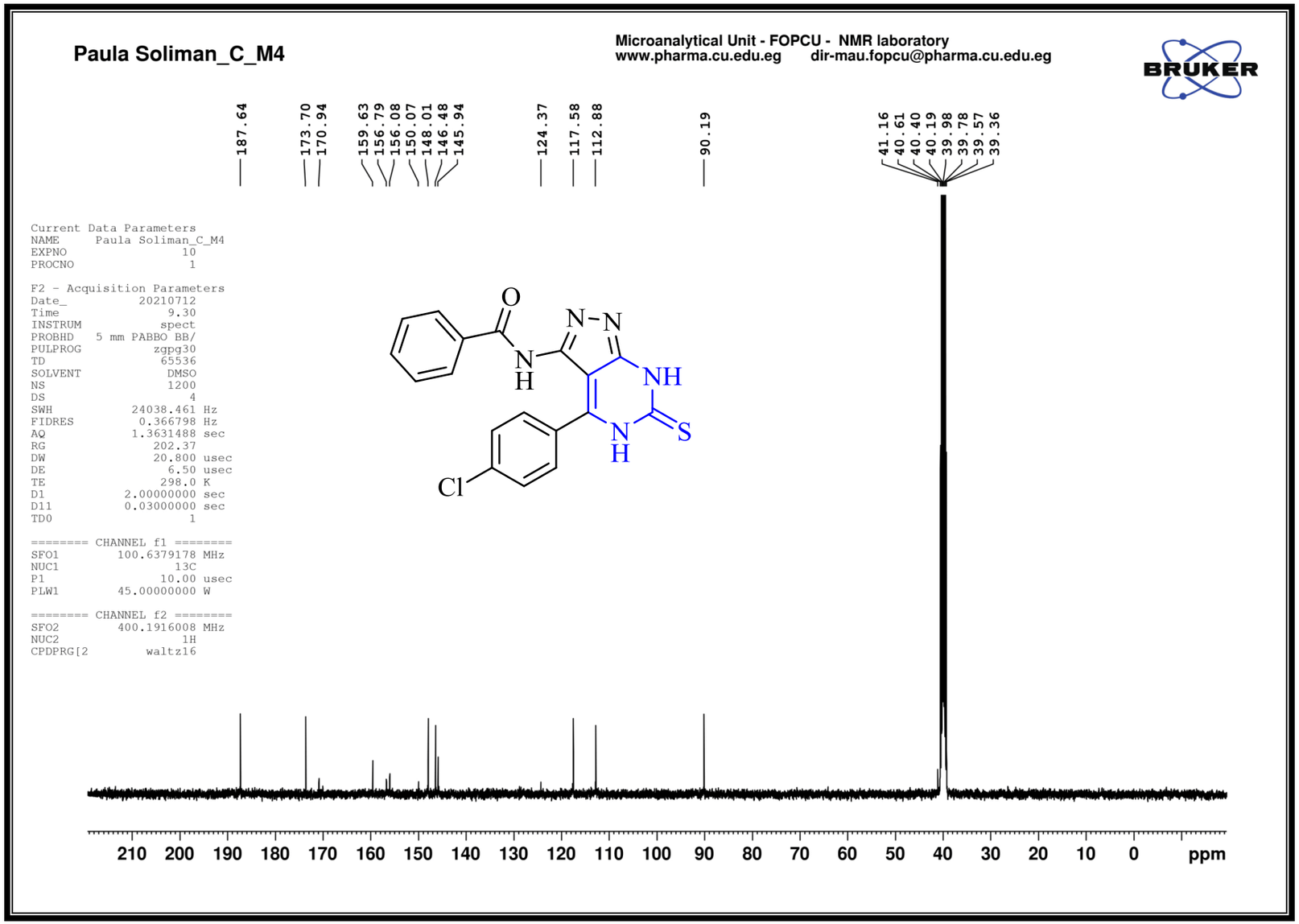
IR of *N*-(4-(4-chlorophenyl)-6-thioxo-6,7-dihydro-5H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (2).



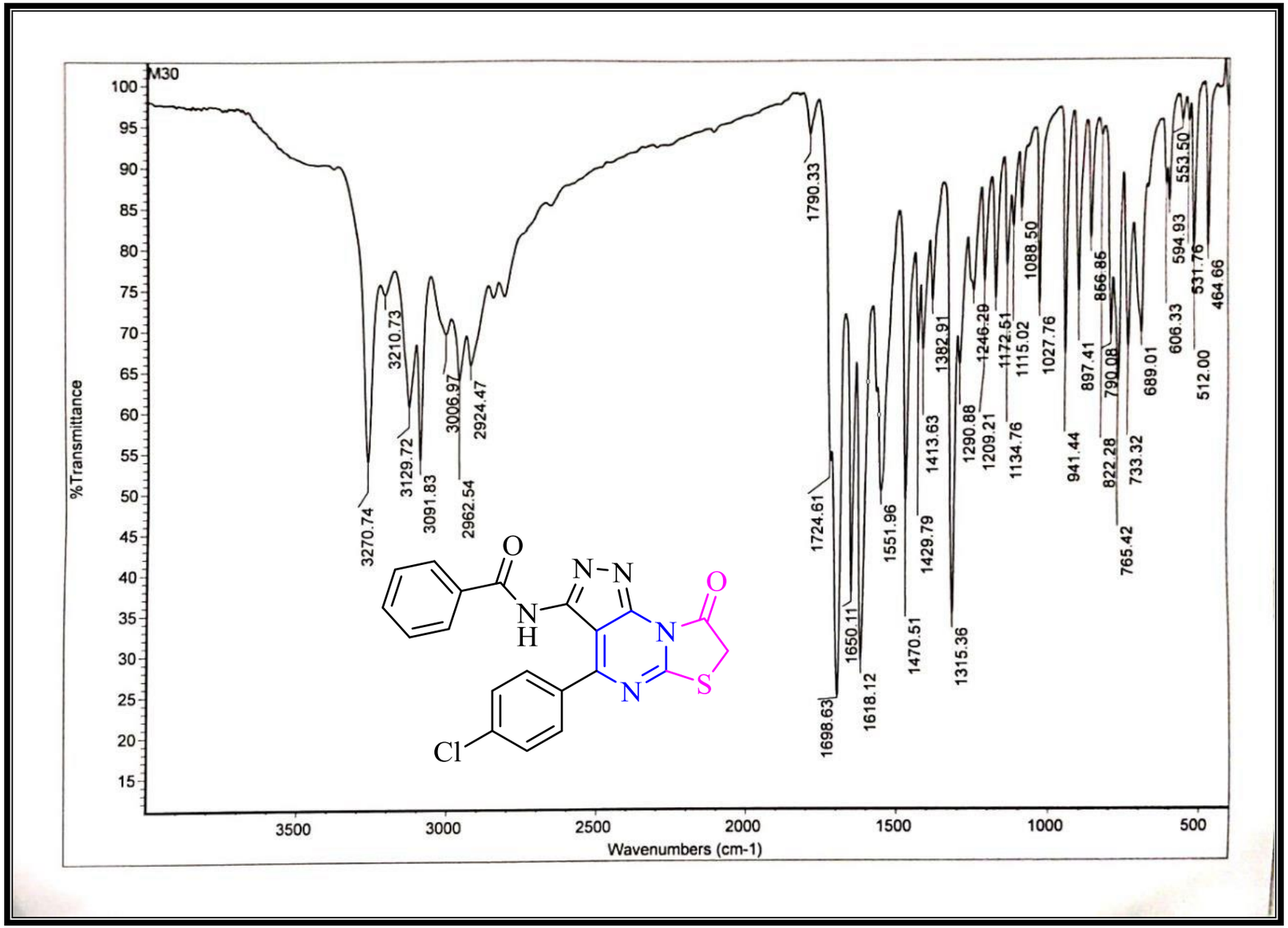
^{1}H-NMR of *N*-(4-(4-chlorophenyl)-6-thioxo-6,7-dihydro-5H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (2).



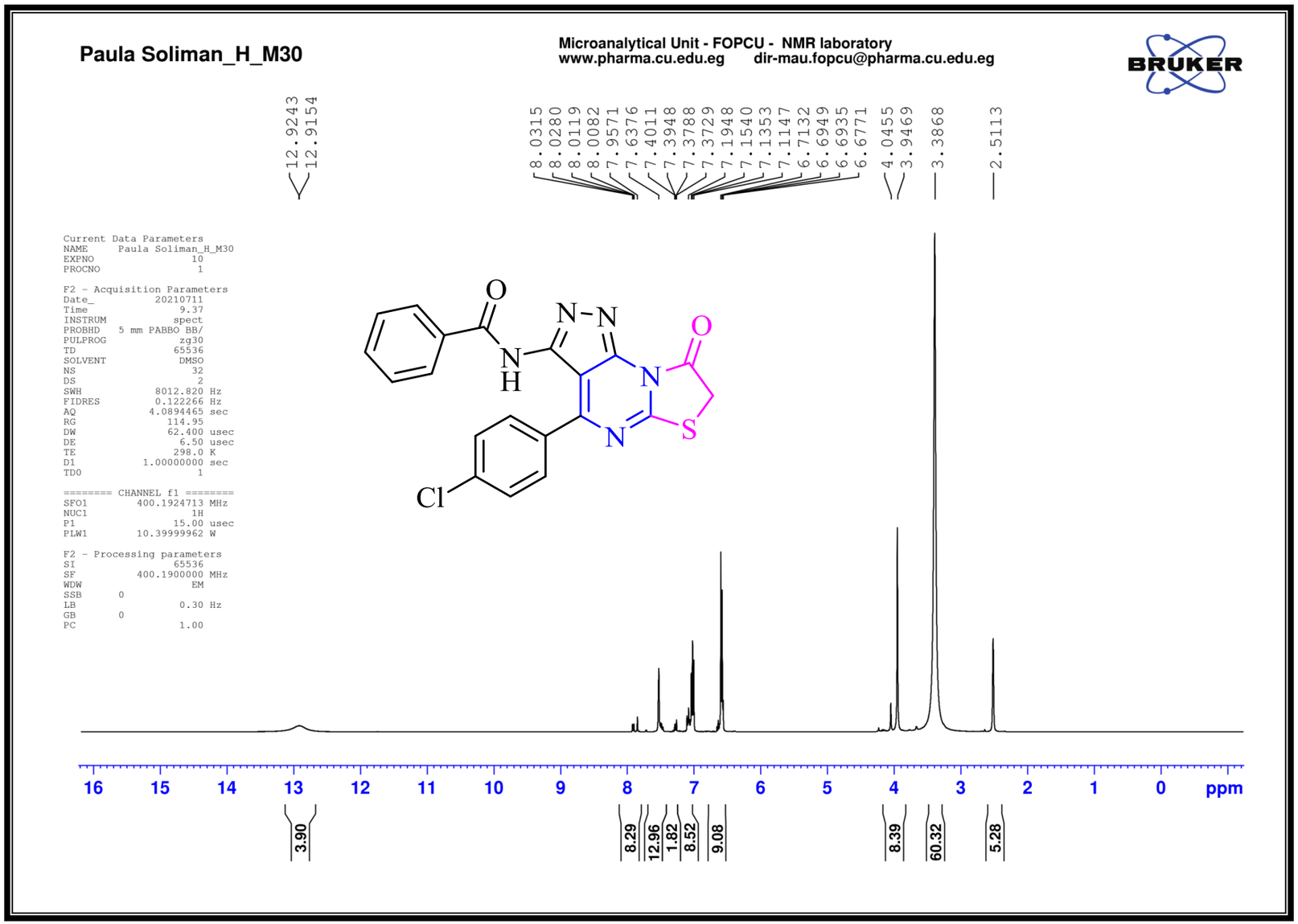
D_2O of *N*-(4-(4-chlorophenyl)-6-thioxo-6,7-dihydro-5H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (2).



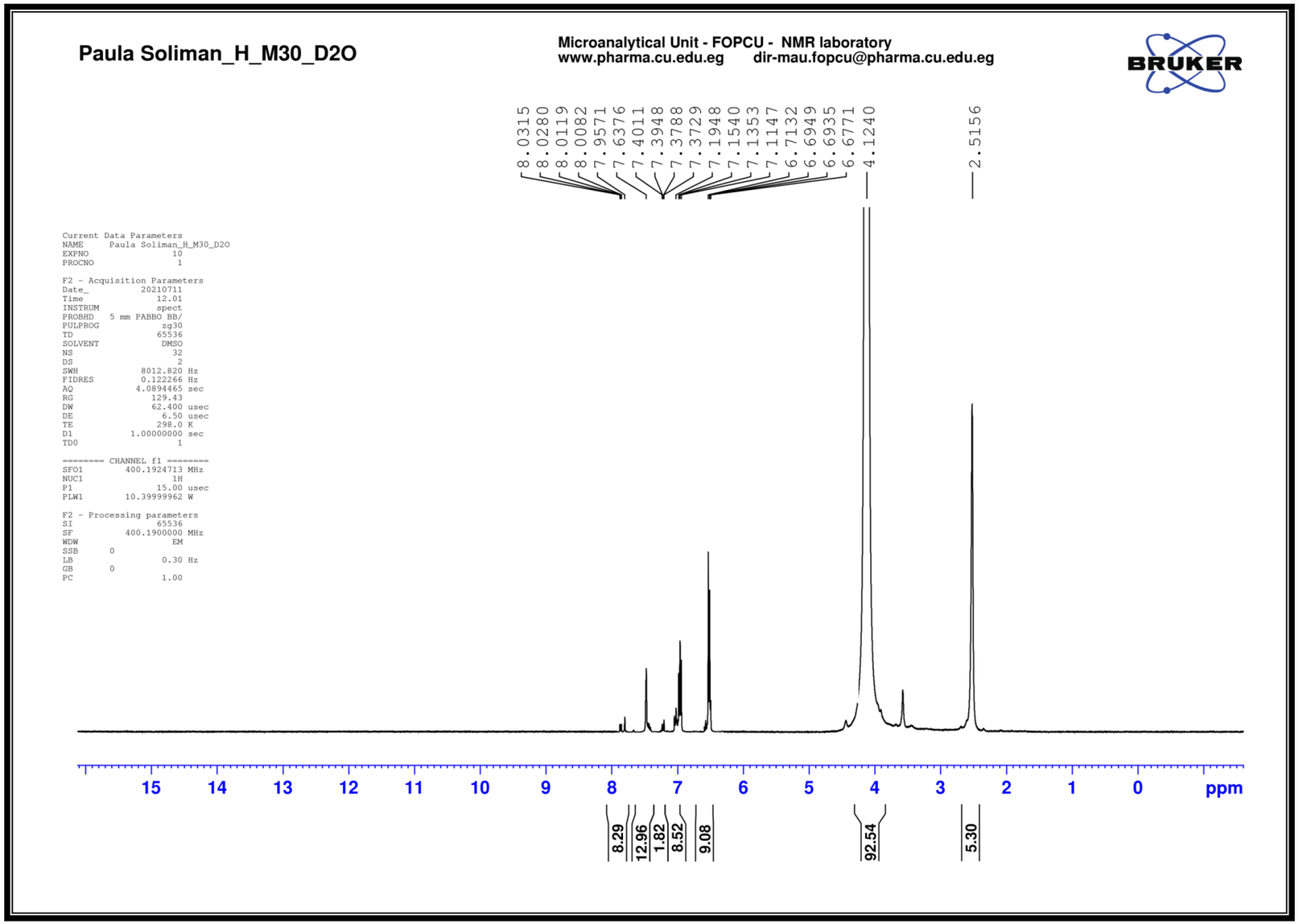
^{13}C-NMR of *N*-(4-(4-chlorophenyl)-6-thioxo-6,7-dihydro-5H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (2).



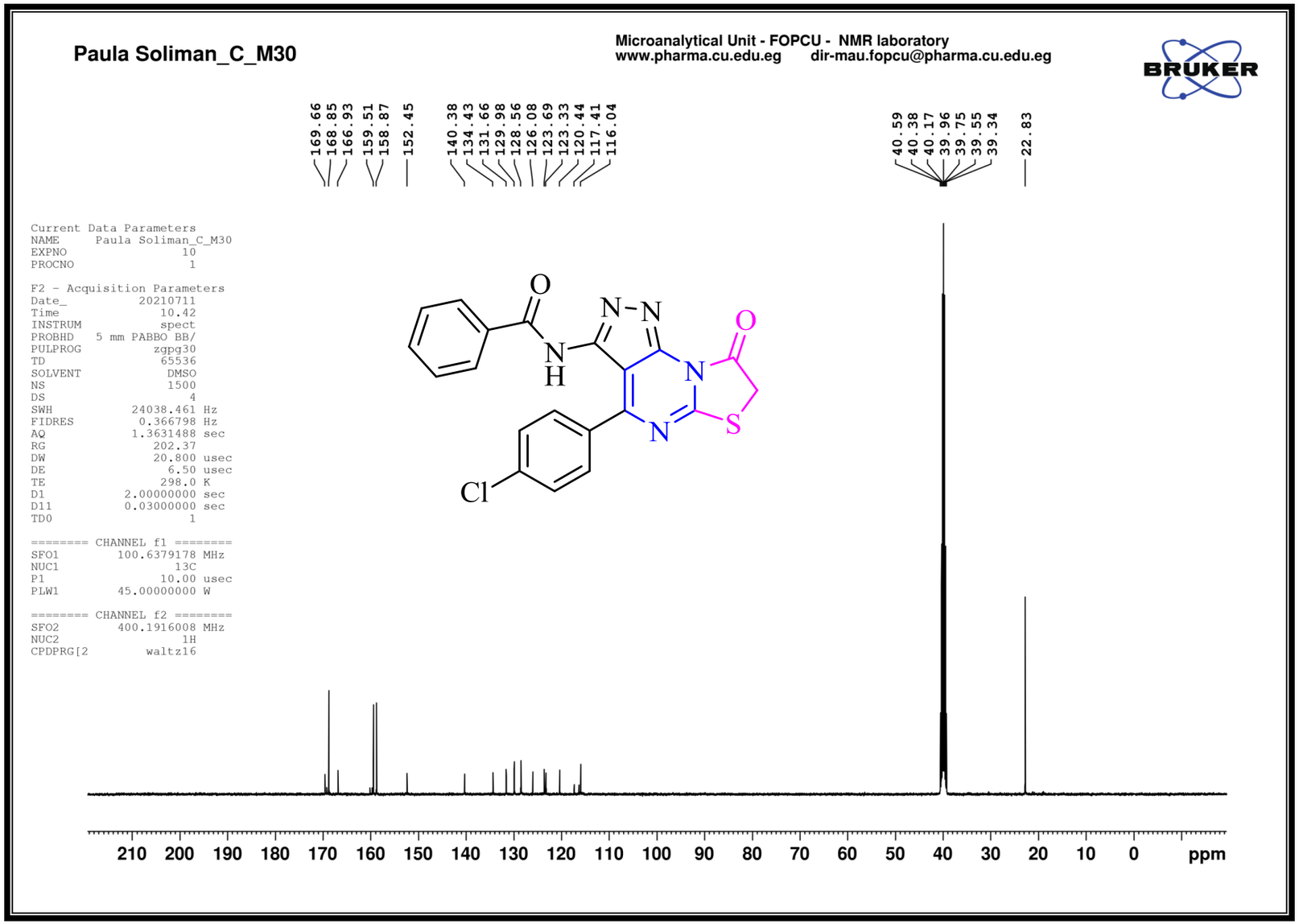
IR of *N*-(4-(4-chlorophenyl)-8-oxo-7,8-dihydropyrazolo[4,3-e]thiazolo[3,2-a]pyrimidin-3-yl)benzamide (3).



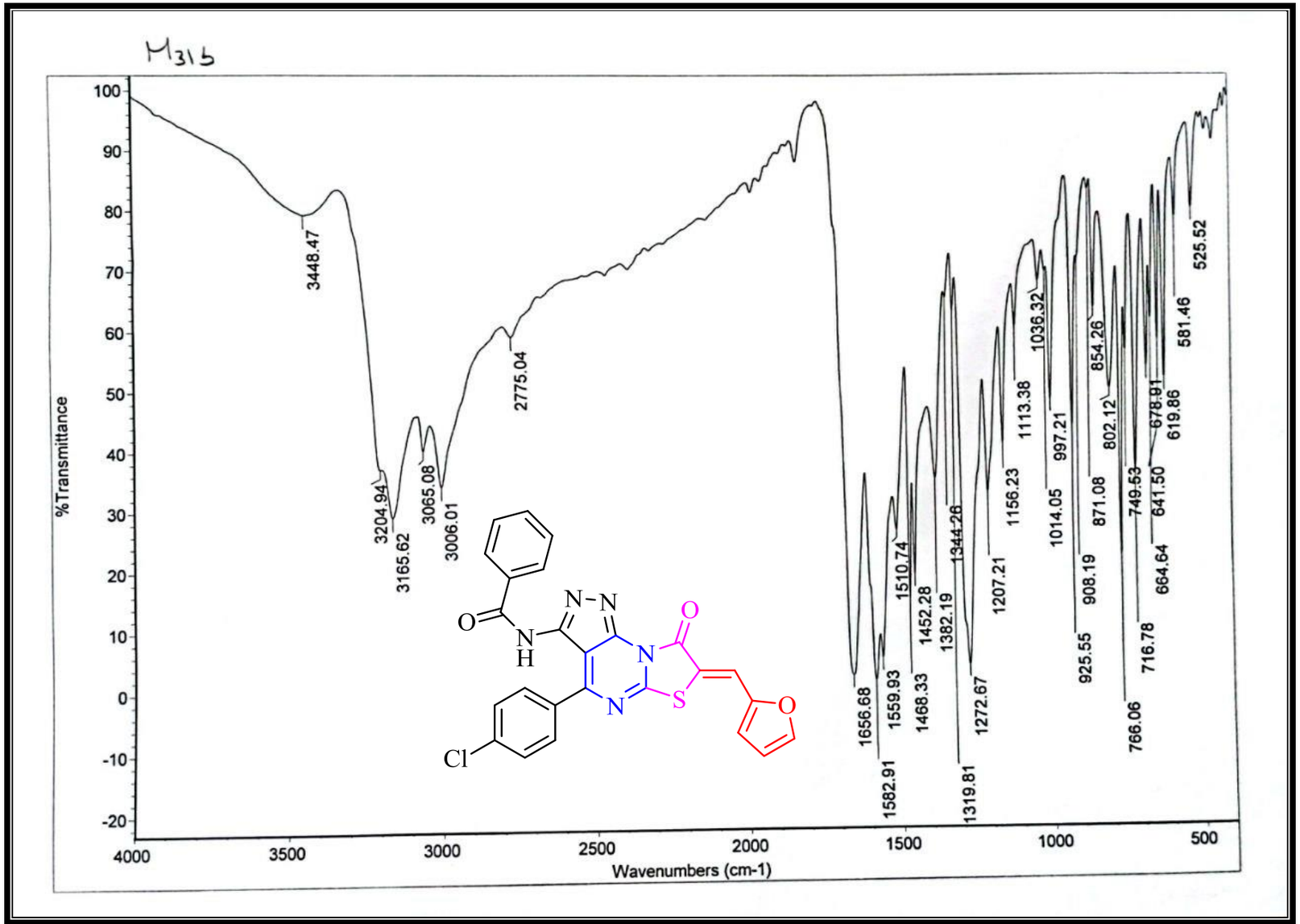
^{1}H-NMR of *N*-(4-(4-chlorophenyl)-8-oxo-7,8-dihydropyrazolo[4,3-e]thiazolo[3,2-a]pyrimidin-3-yl)benzamide (3).



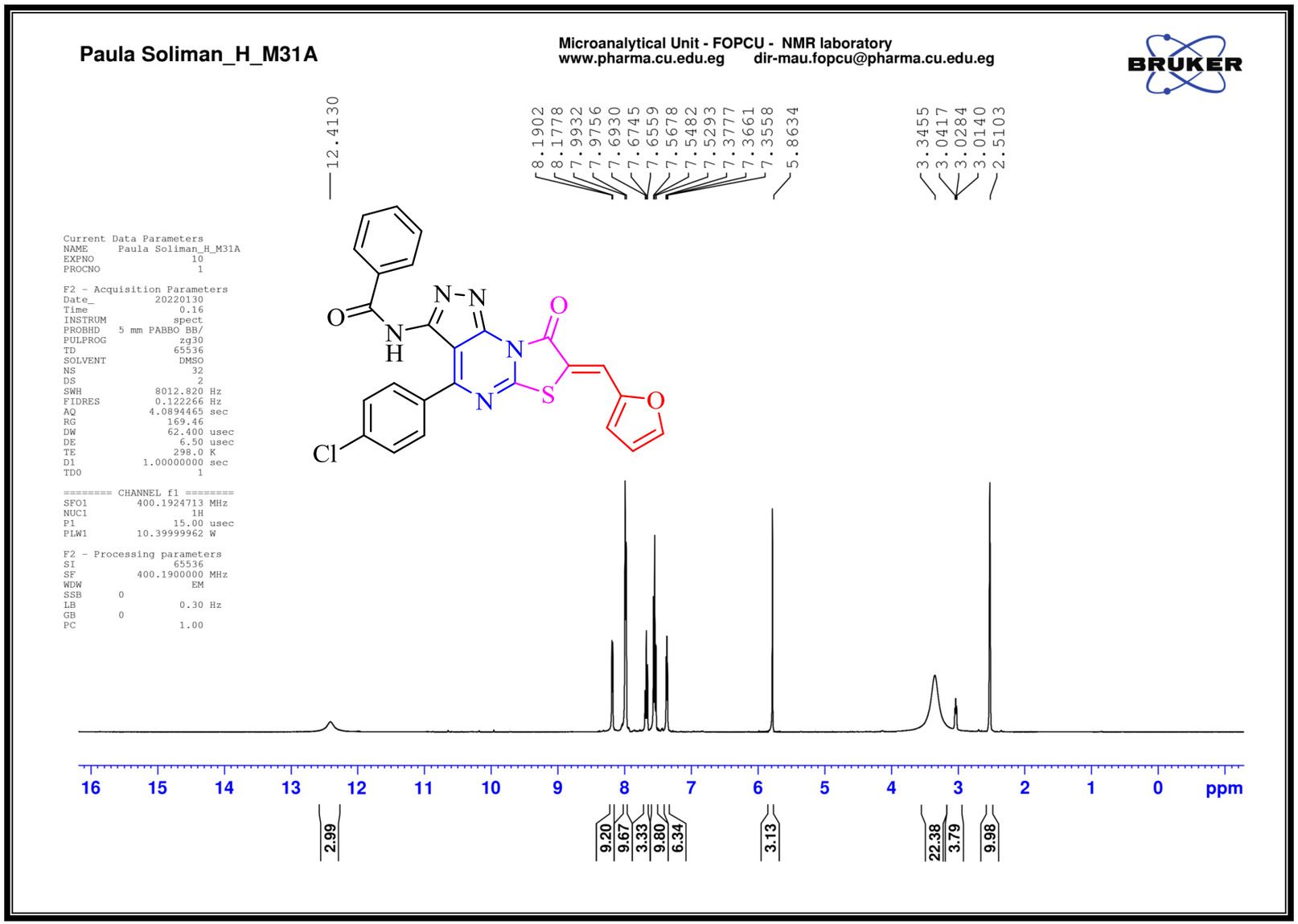
D_2O of *N*-(4-(4-chlorophenyl)-8-oxo-7,8-dihydropyrazolo[4,3-e]thiazolo[3,2-a]pyrimidin-3-yl)benzamide (3).



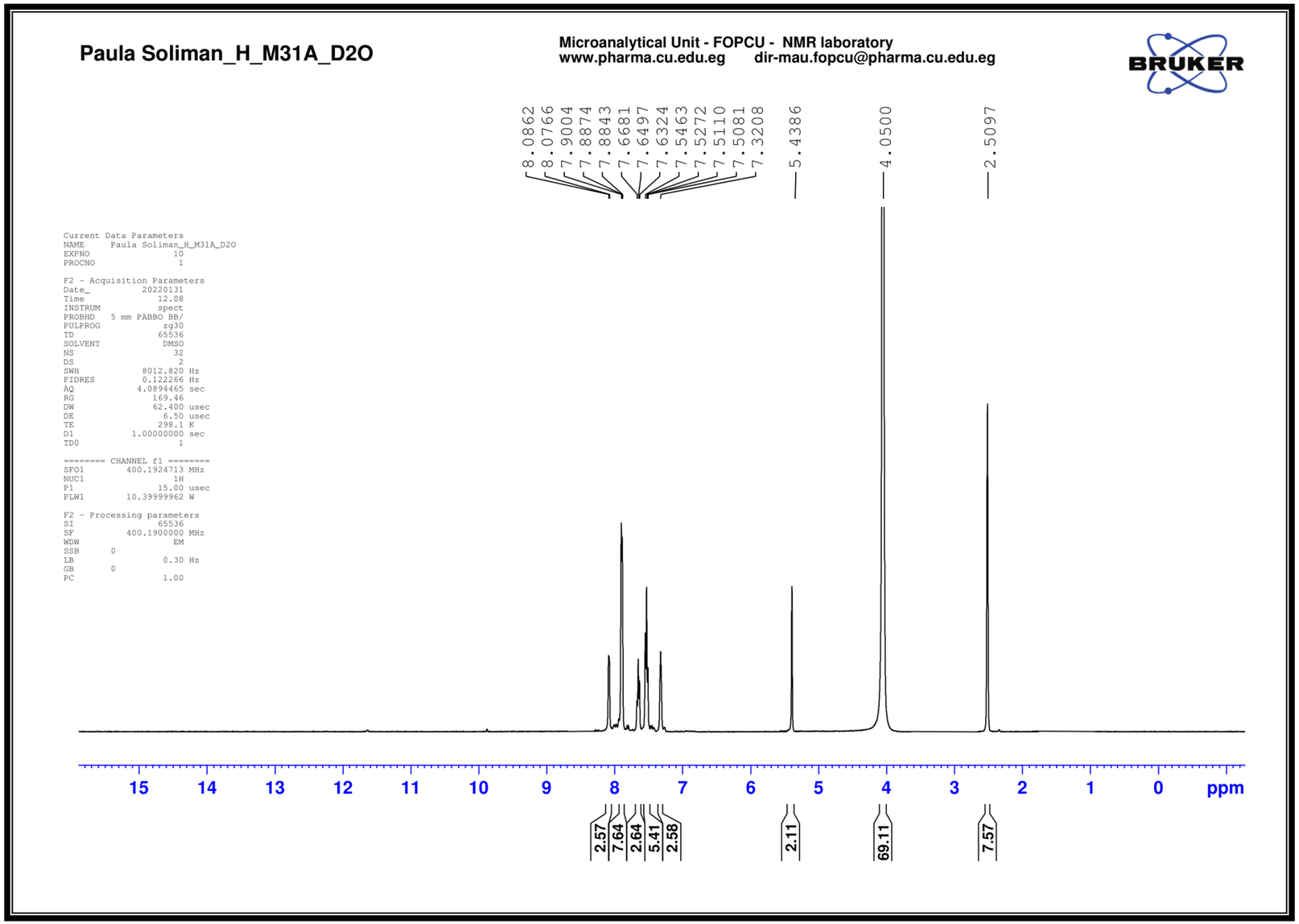
^{13}C-NMR of *N*-(4-(4-chlorophenyl)-8-oxo-7,8-dihydropyrazolo[4,3-e]thiazolo[3,2-a]pyrimidin-3-yl)benzamide (3).



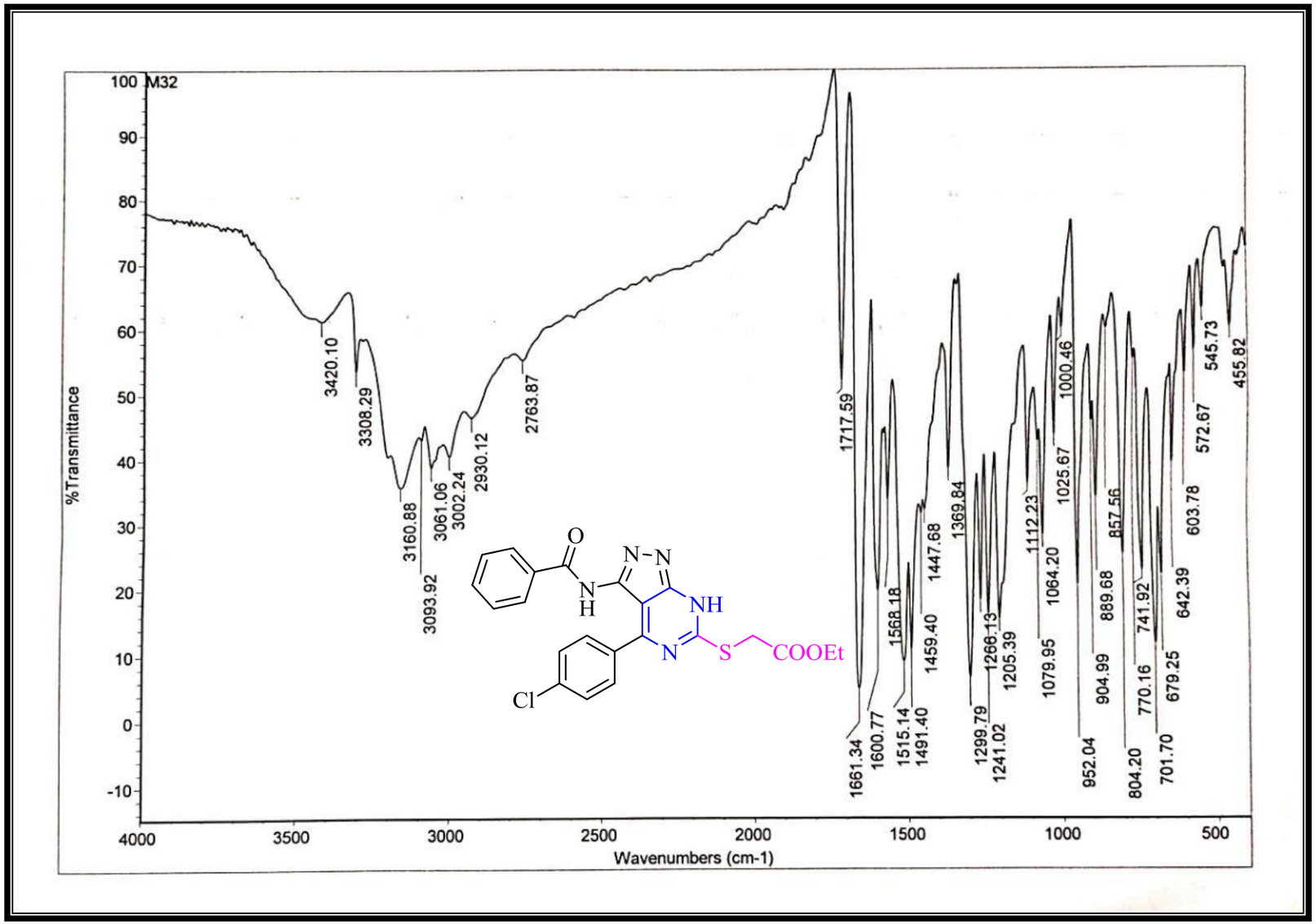
IR of (*E*,*Z*)-*N*-(4-(4-chlorophenyl)-7-(furan-2-ylmethylene)-8-oxo-7,8-dihydropyrazolo[4,3-e]thiazolo[3,2-a]pyrimidin-3-yl)benzamide (4).



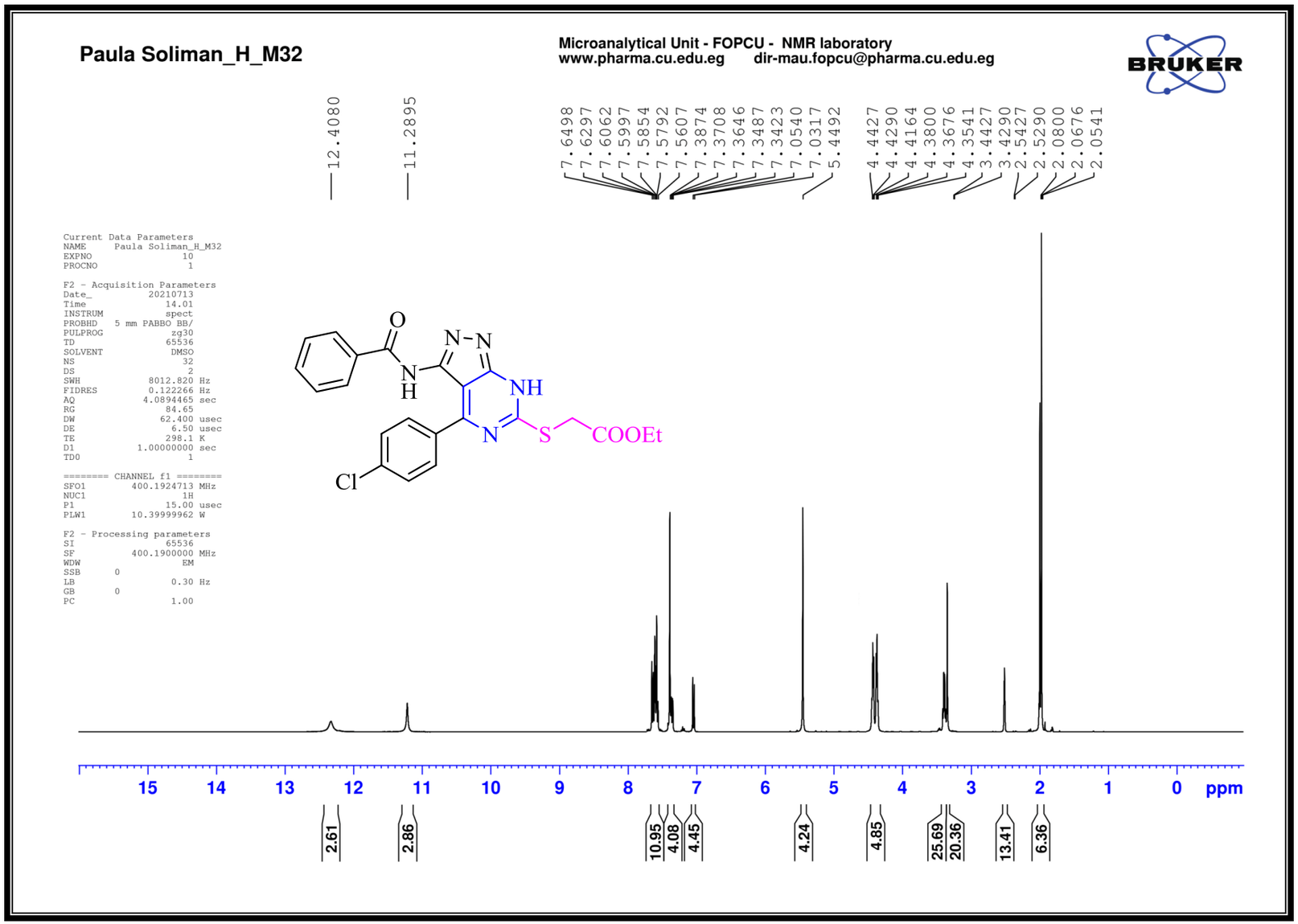
^{1}H-NMR of (*E*,*Z*)-*N*-(4-(4-chlorophenyl)-7-(furan-2-ylmethylene)-8-oxo-7,8-dihydropyrazolo[4,3-e]thiazolo[3,2-a]pyrimidin-3-yl)benzamide (4).



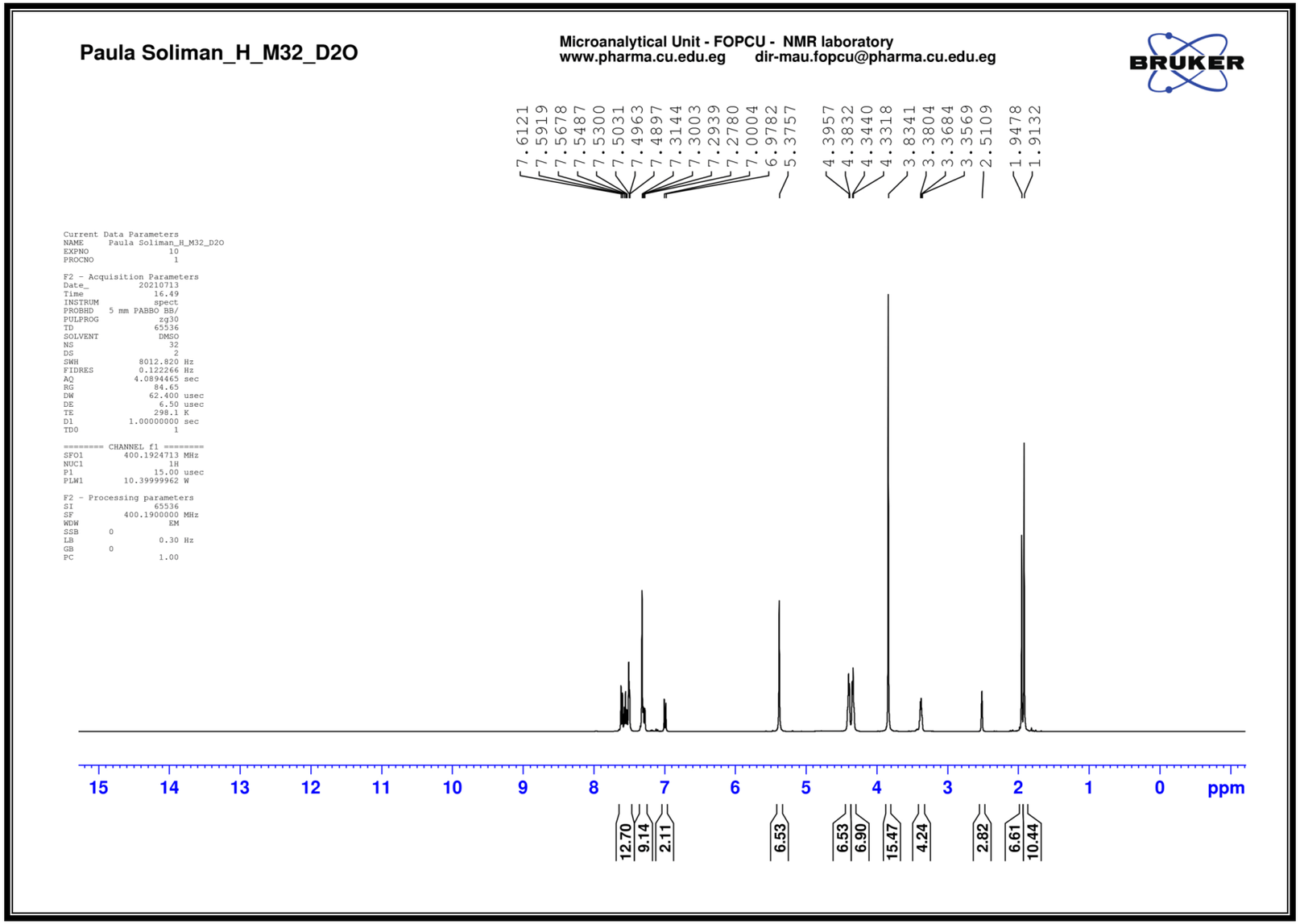
D_2O of (*E,Z*)-*N*-(4-(4-chlorophenyl)-7-(furan-2-ylmethylene)-8-oxo-7,8-dihydropyrazolo[4,3-e]thiazolo[3,2-a]pyrimidin-3-yl)benzamide (4).



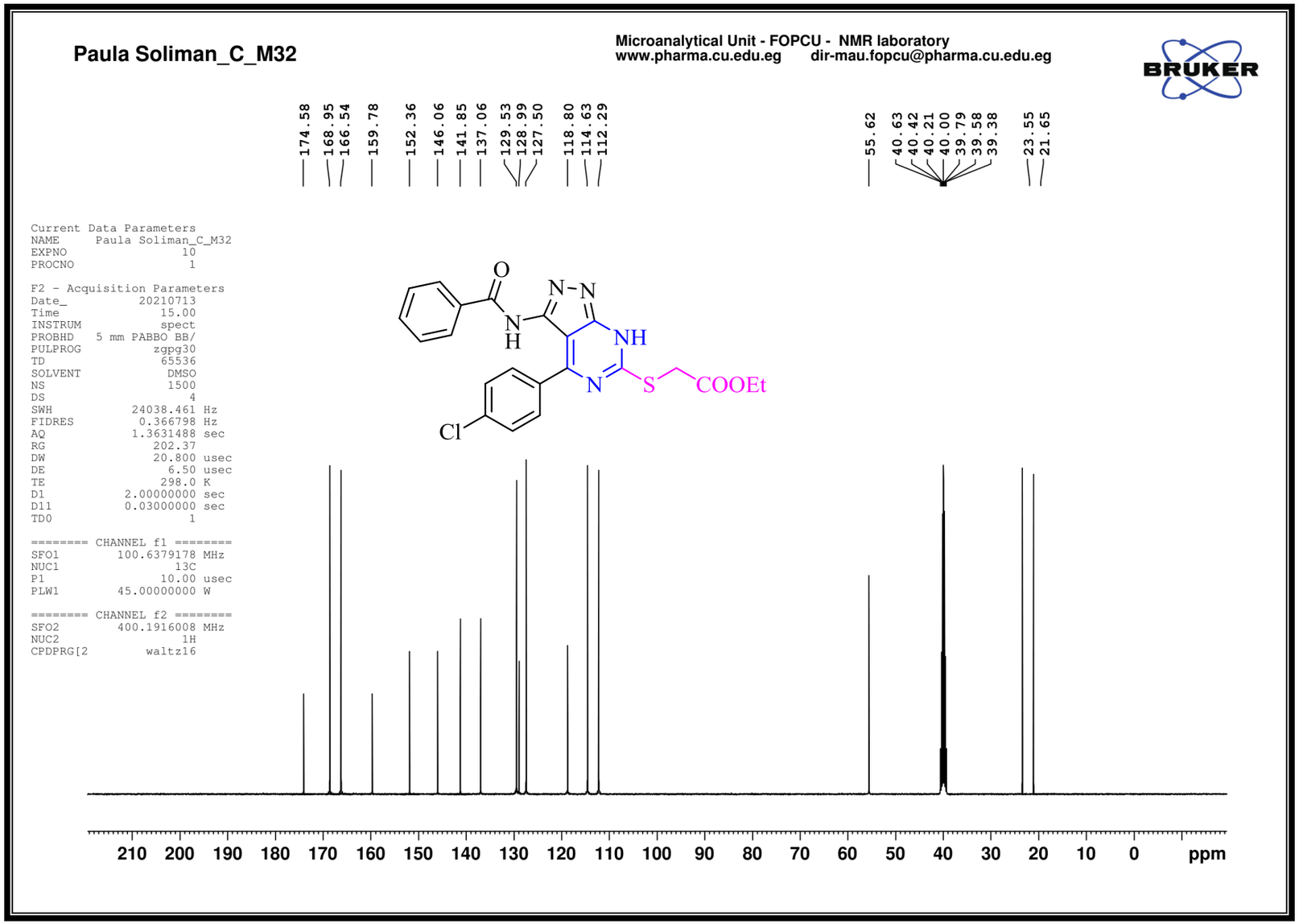
IR of Ethyl 2-((3-benzamido-4-(4-chlorophenyl)-7H-pyrazolo[3,4-d]pyrimidin-6-yl)thio)acetate (5).



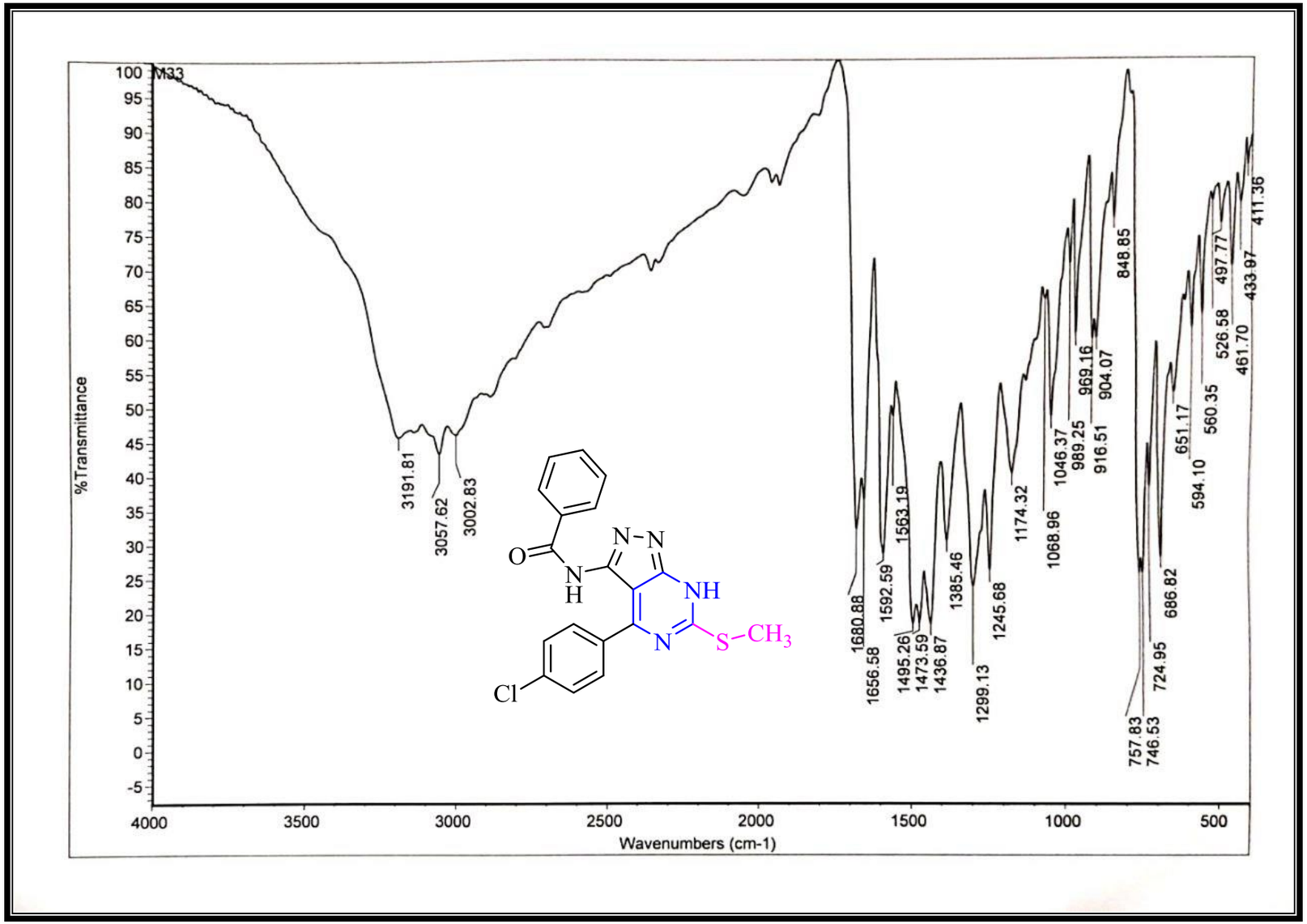
^{1}H-NMR of Ethyl 2-((3-benzamido-4-(4-chlorophenyl)-7H-pyrazolo[3,4-d]pyrimidin-6-yl)thio)acetate (5).



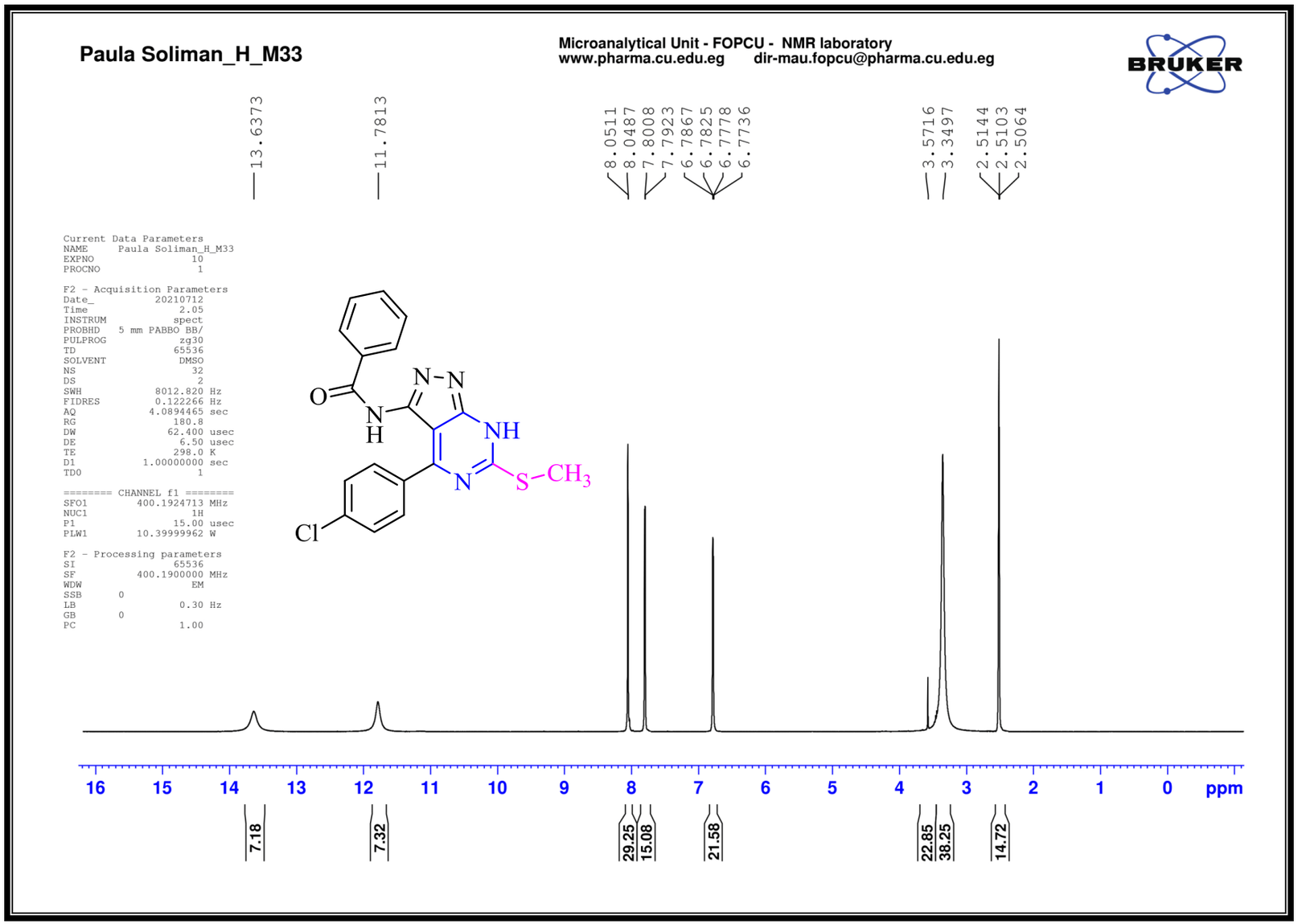
D_2O of Ethyl 2-((3-benzamido-4-(4-chlorophenyl)-7H-pyrazolo[3,4-d]pyrimidin-6-yl)thio)acetate (5).



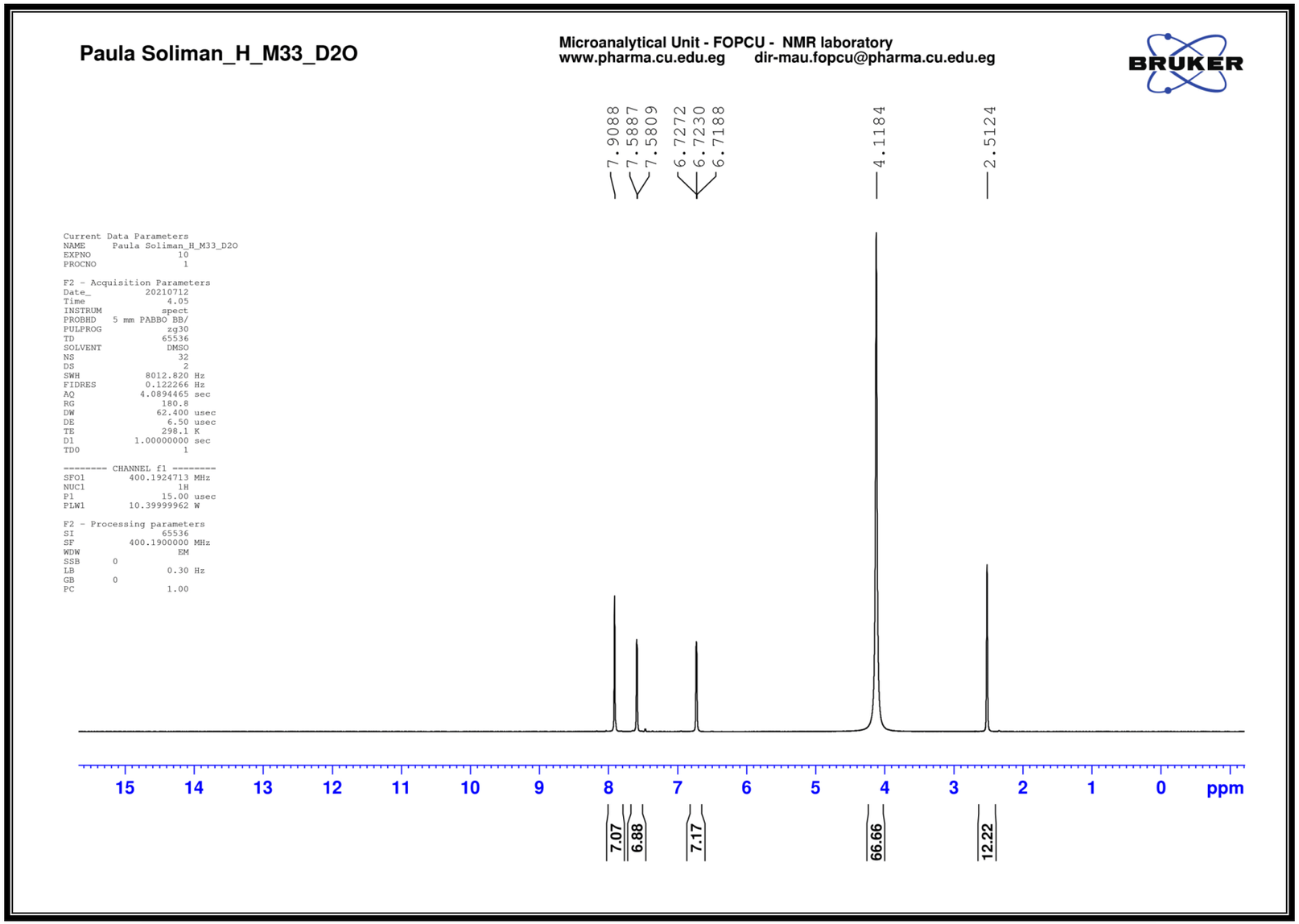
^{13}C-NMR of Ethyl 2-((3-benzamido-4-(4-chlorophenyl)-7H-pyrazolo[3,4-d]pyrimidin-6-yl)thio)acetate (5).



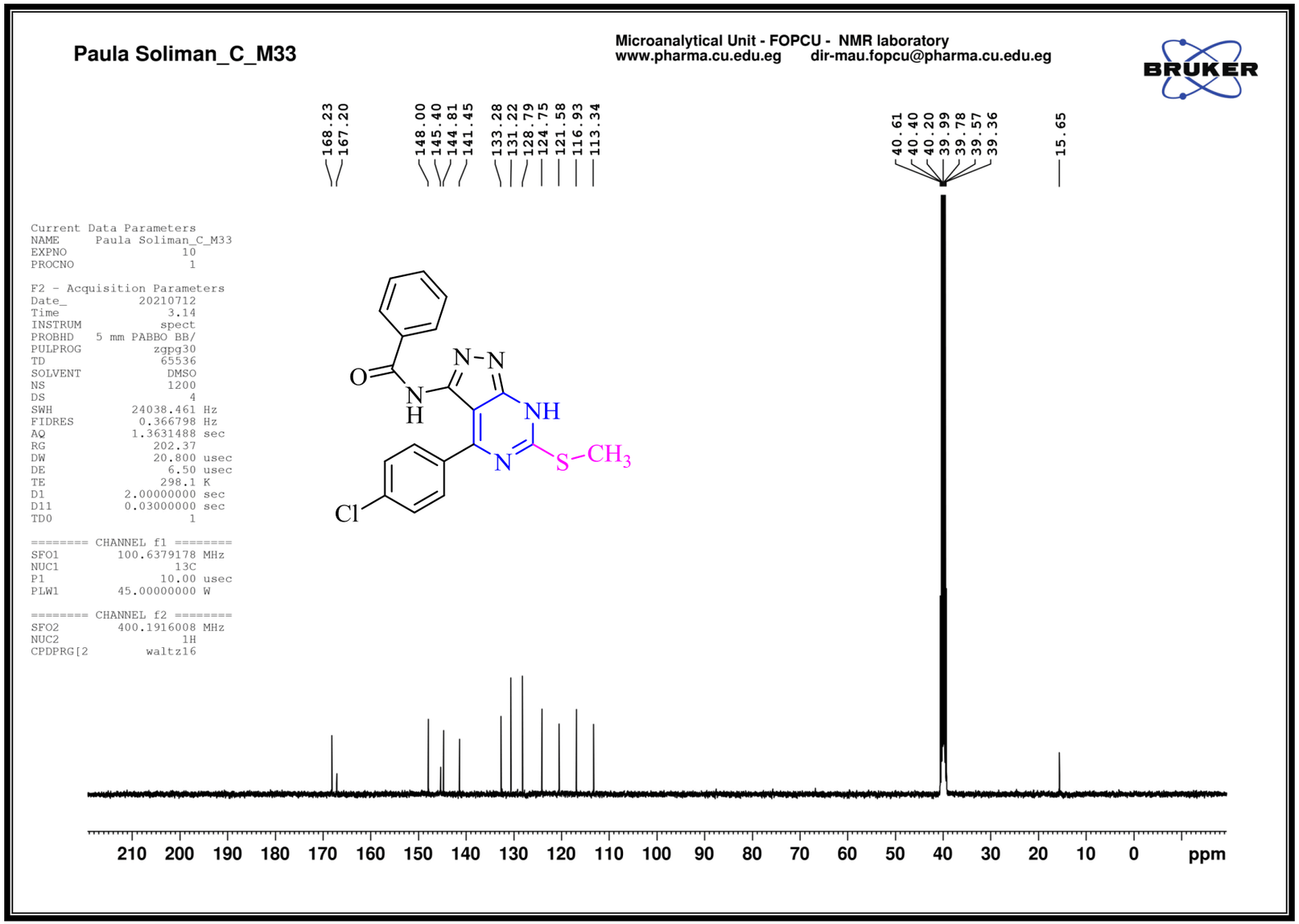
IR of *N*-(4-(4-chlorophenyl)-6-(methylthio)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (6).



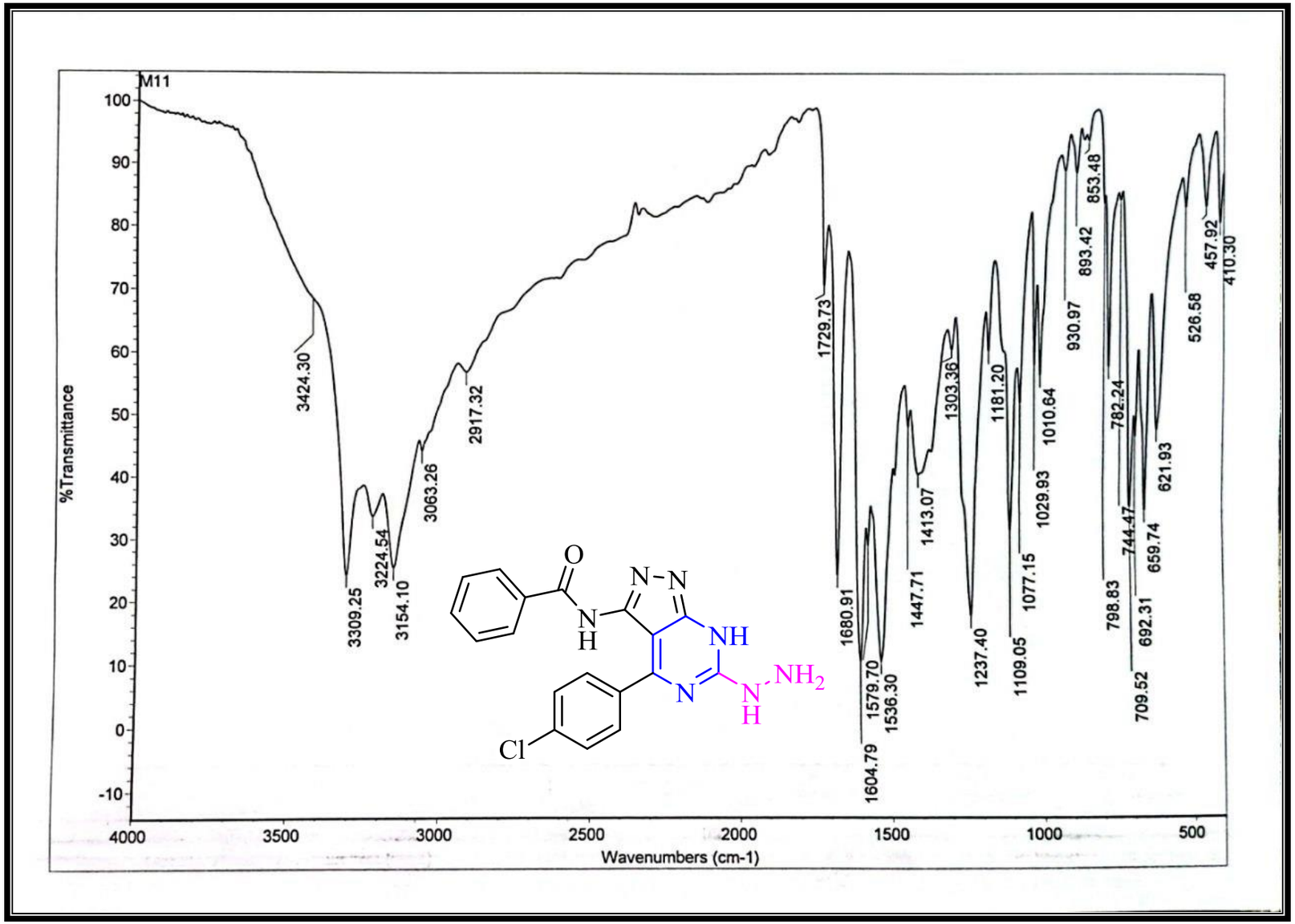
^{1}H-NMR of *N*-(4-(4-chlorophenyl)-6-(methylthio)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (6).



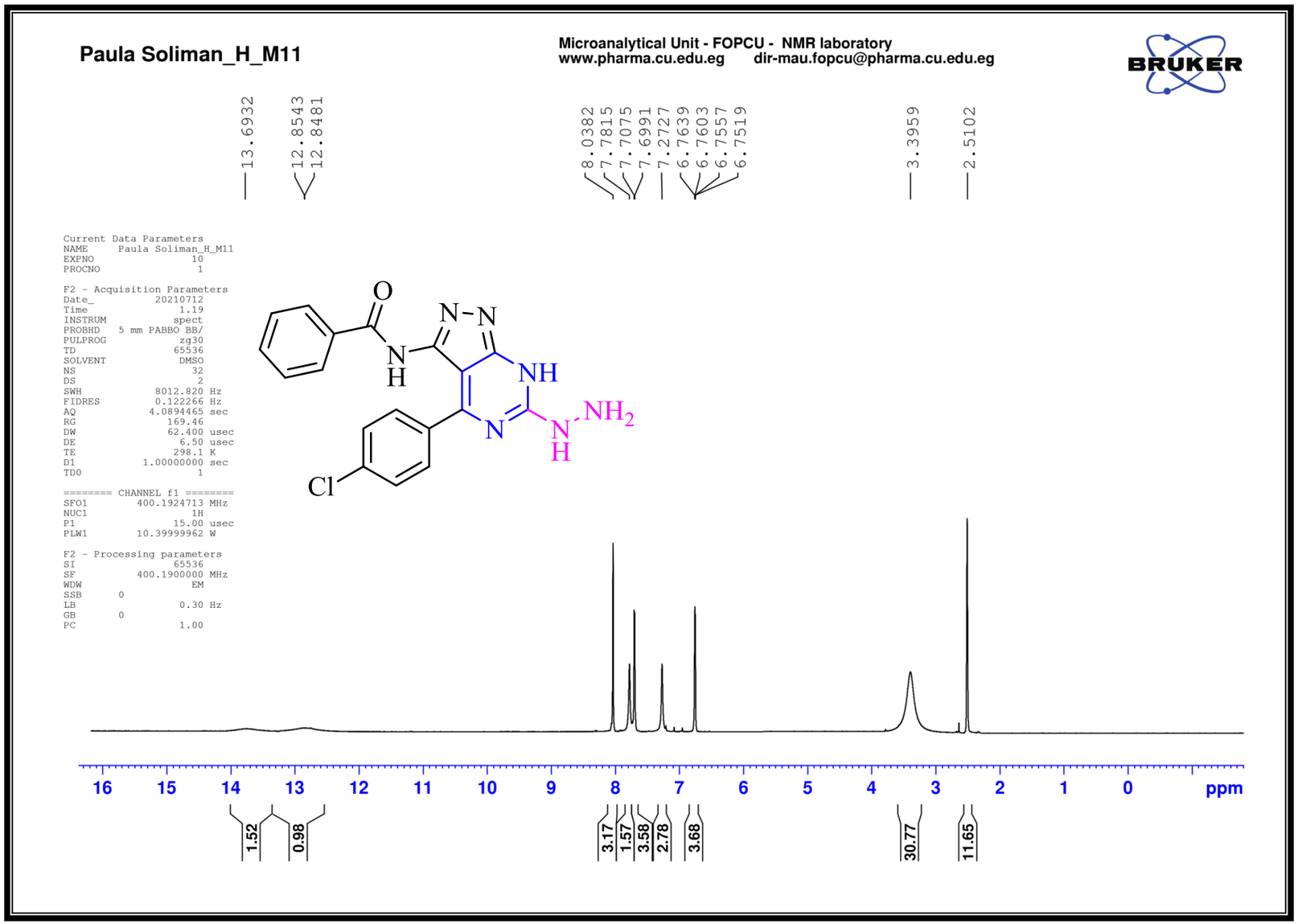
D_2O of *N*-(4-(4-chlorophenyl)-6-(methylthio)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (6).



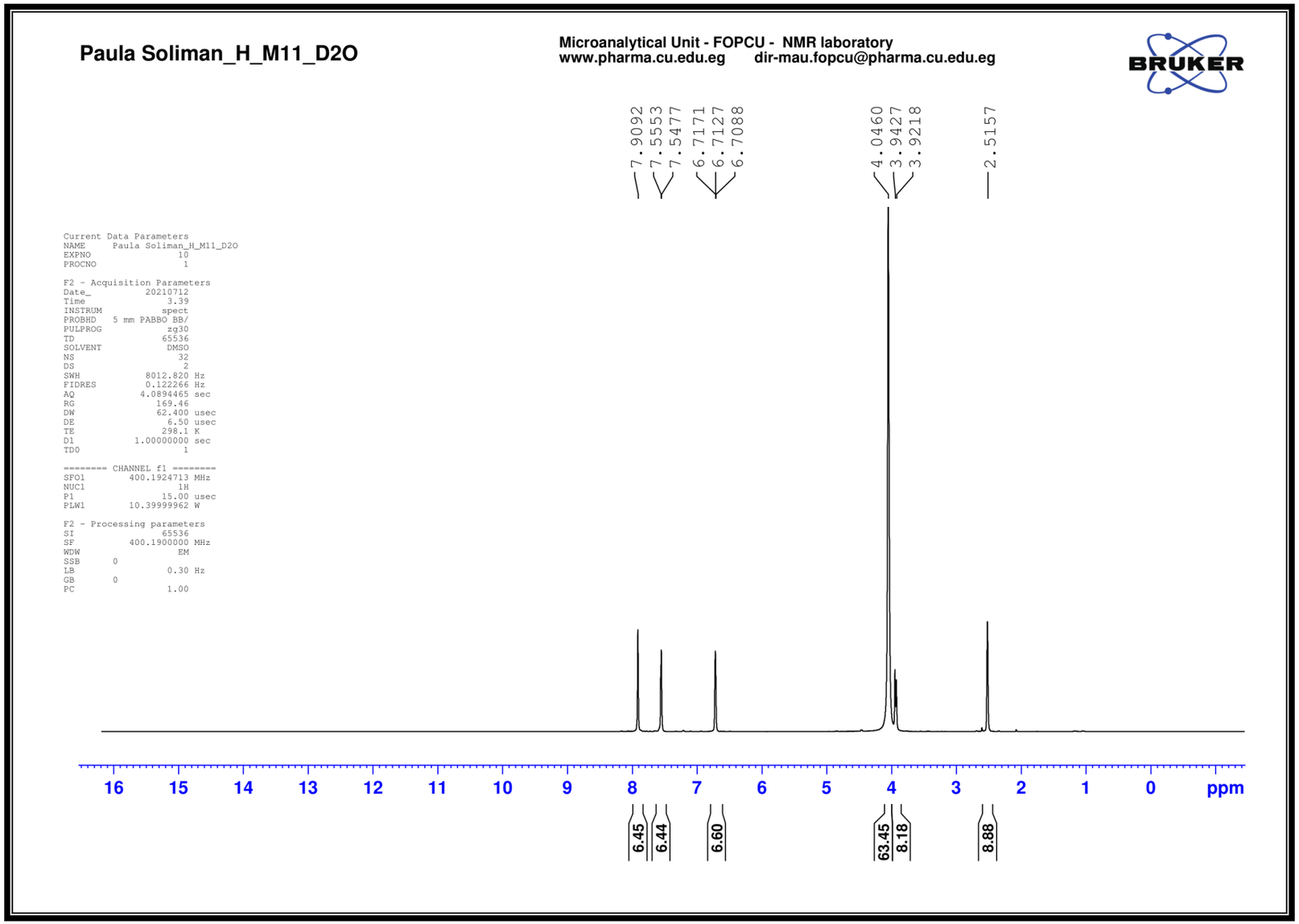
^{13}C-NMR of *N*-(4-(4-chlorophenyl)-6-(methylthio)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (6).



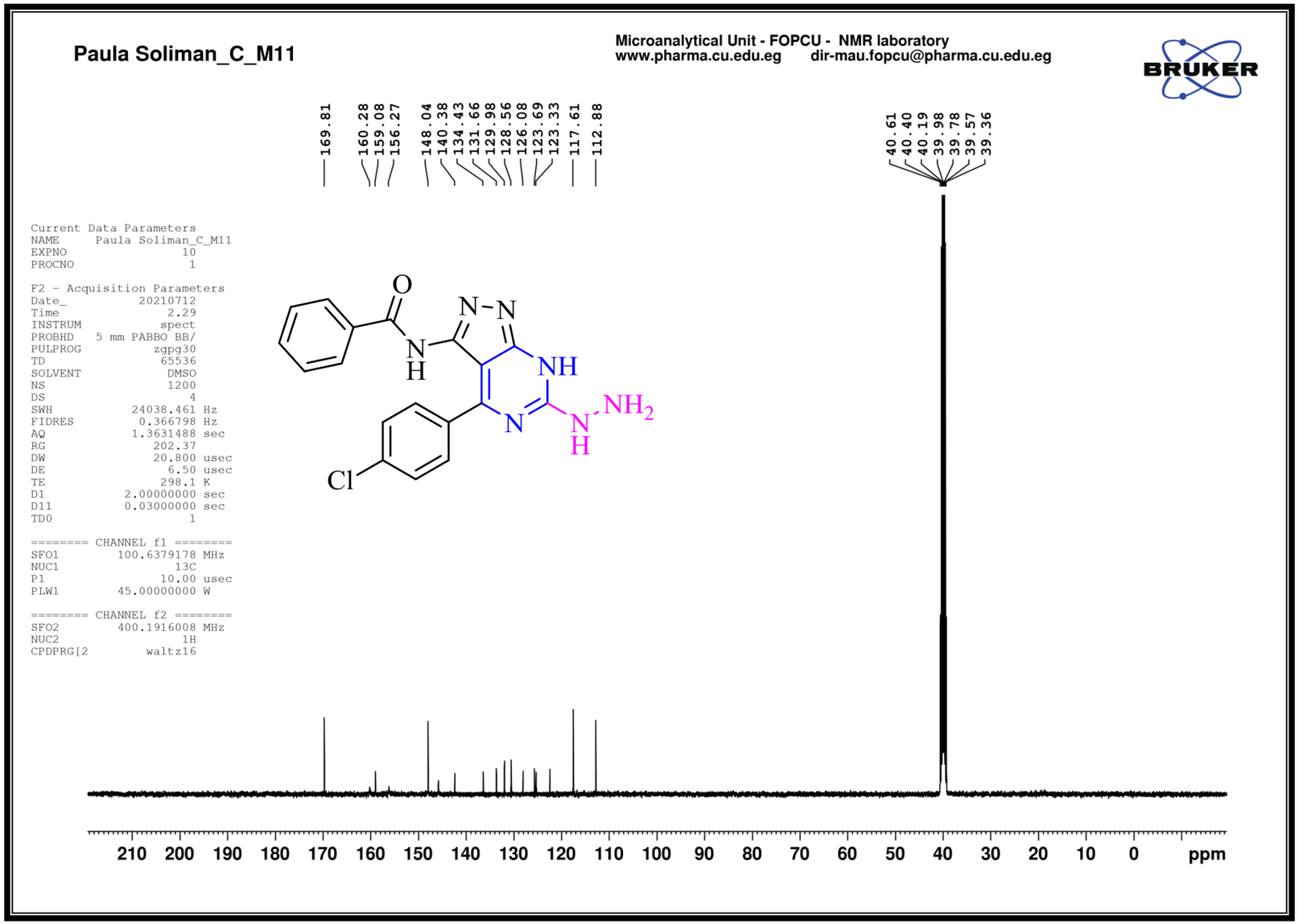
IR of *N*-(4-(4-chlorophenyl)-6-hydrazineyl-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (7).



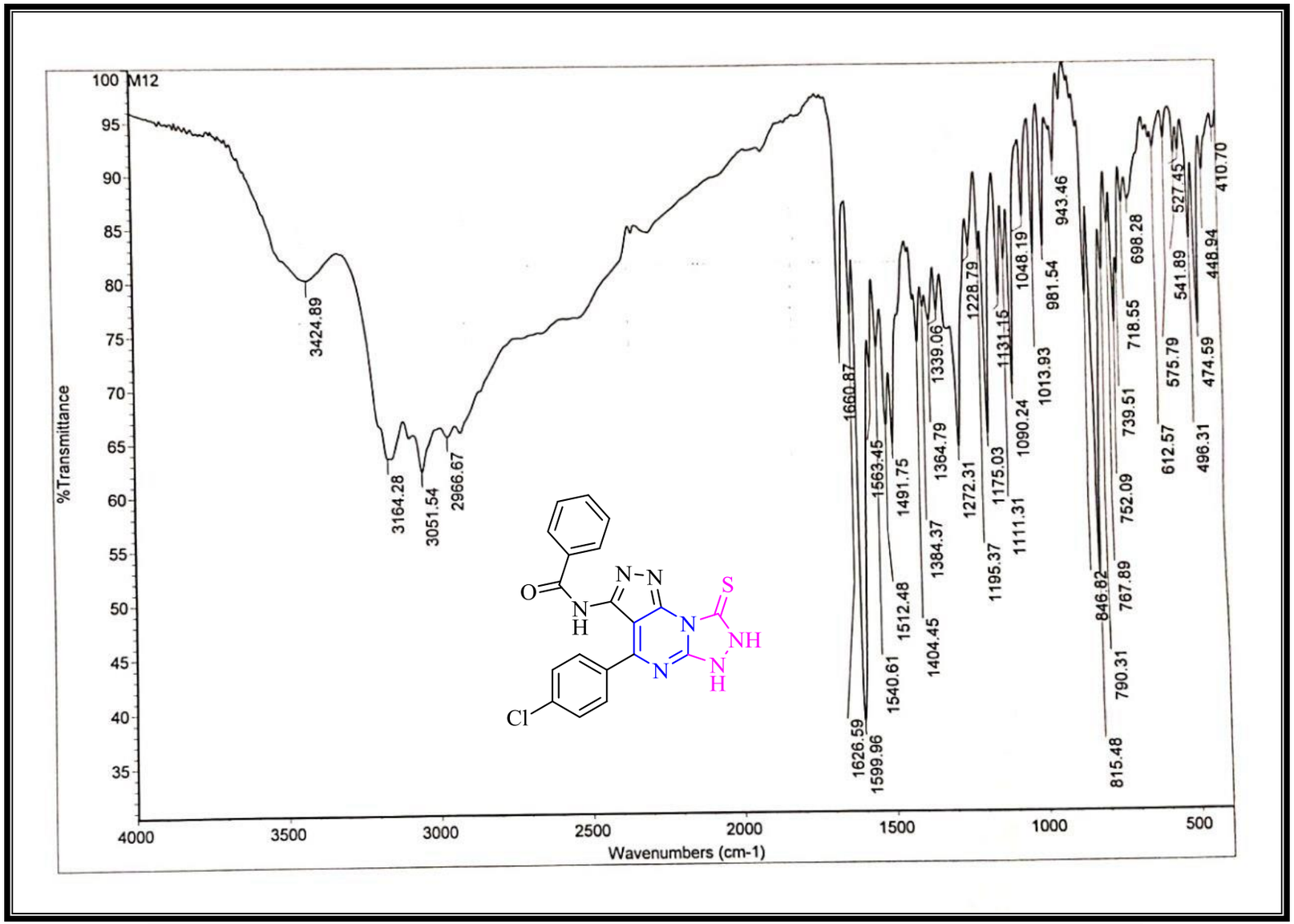
^{1}H-NMR of *N*-(4-(4-chlorophenyl)-6-hydrazineyl-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (7).



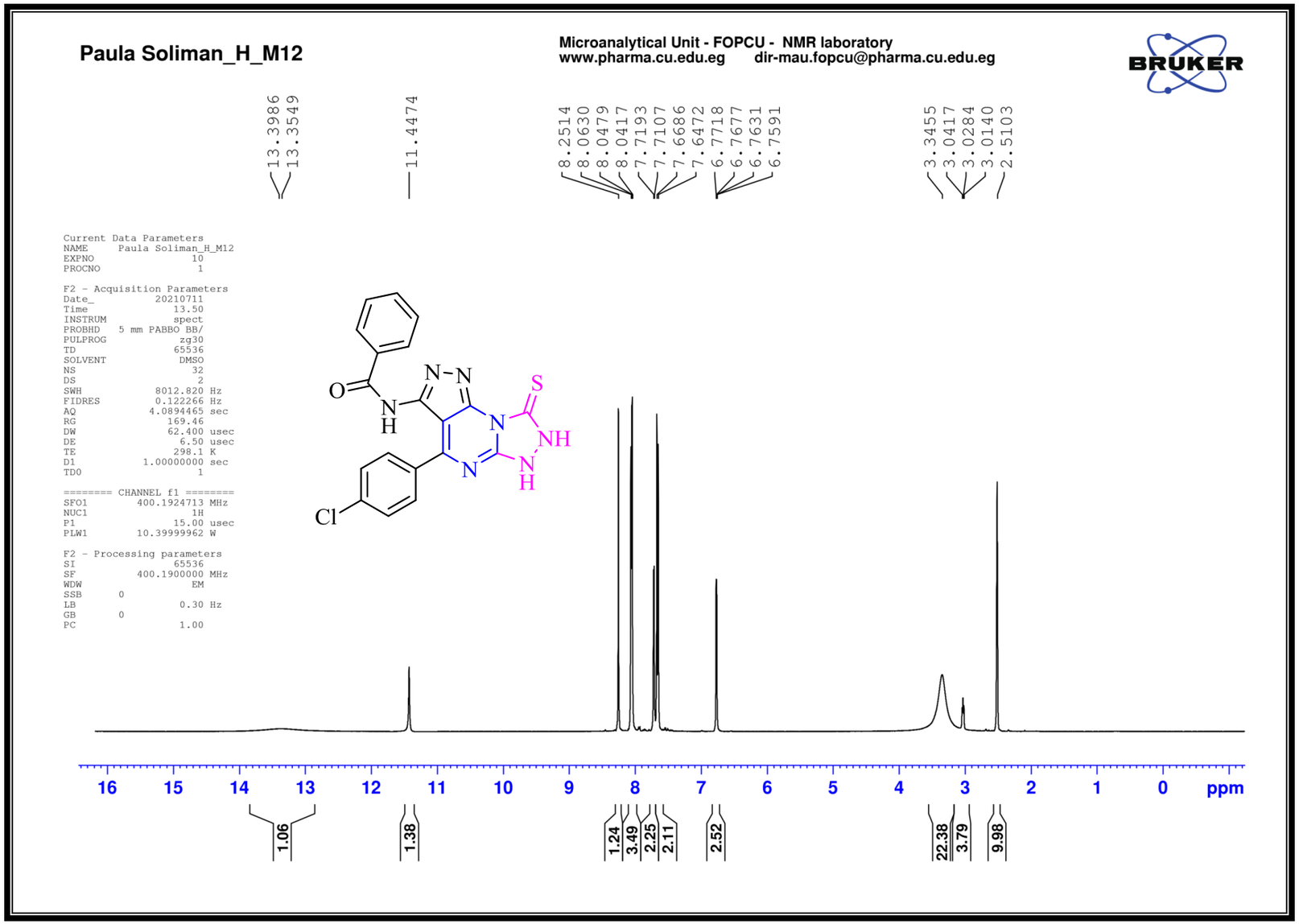
D_2O of *N*-(4-(4-chlorophenyl)-6-hydrazineyl-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (7).



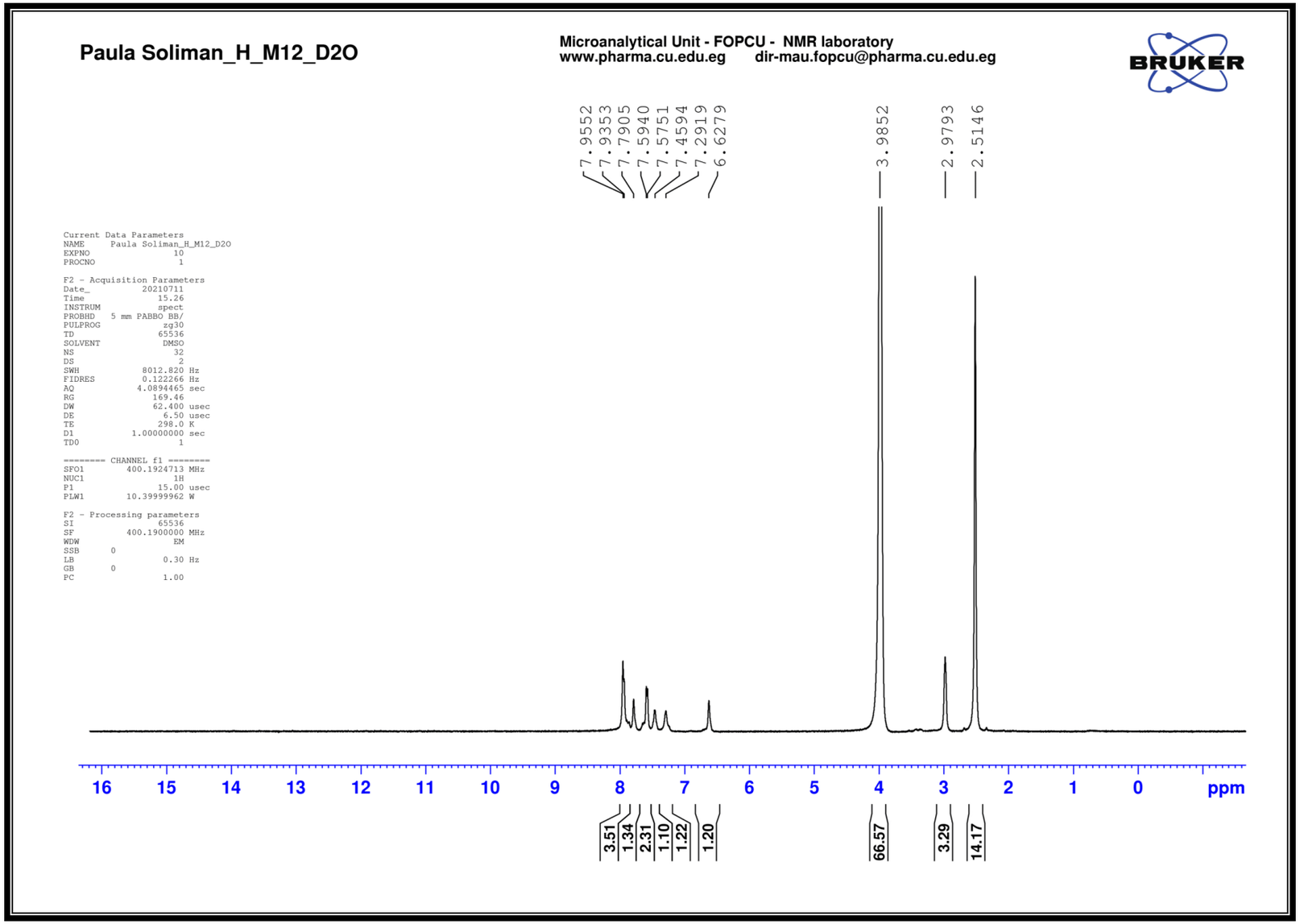
^{13}C-NMR of *N*-(4-(4-chlorophenyl)-6-hydrazineyl-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (7).



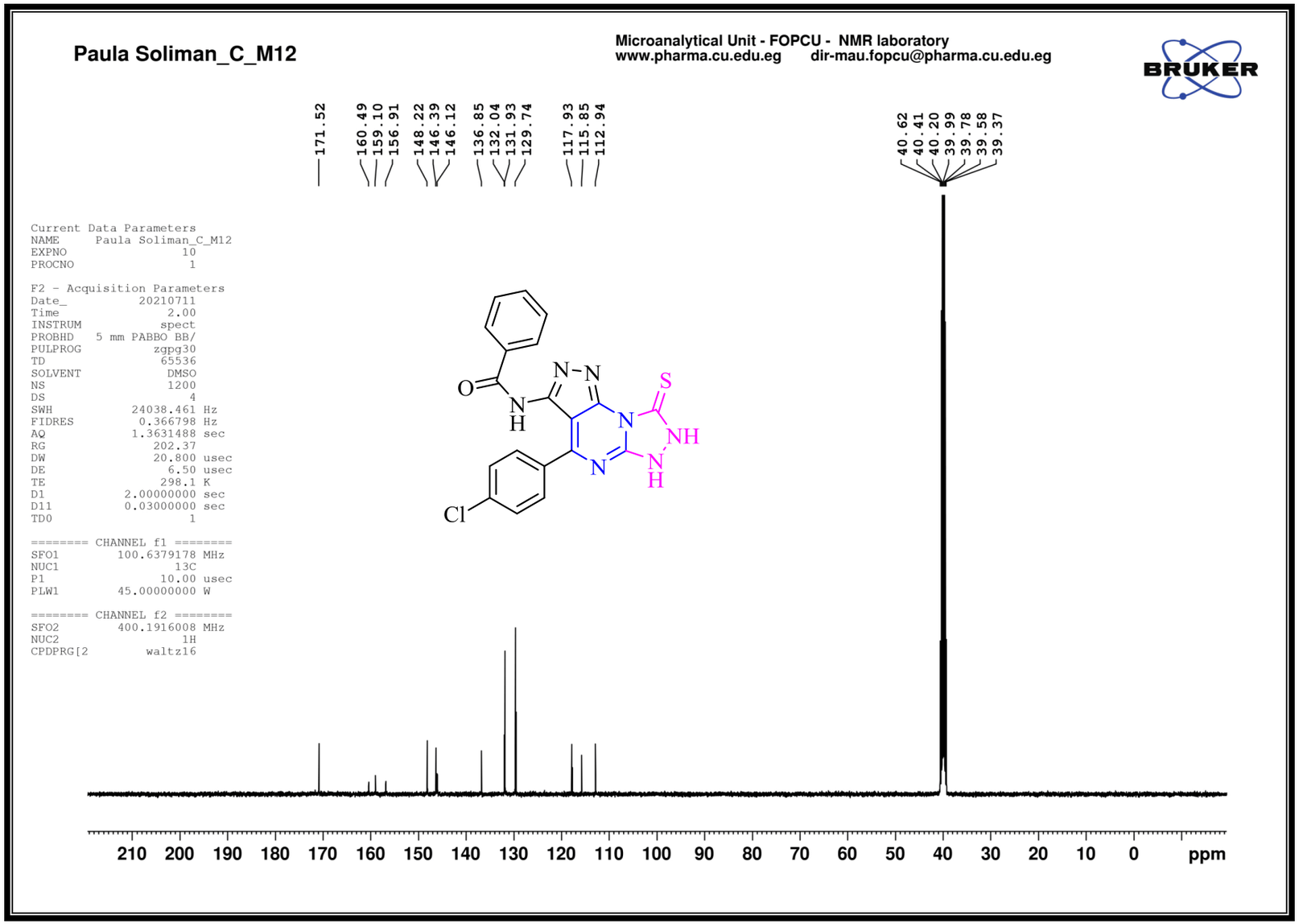
IR of *N*-(4-(4-chlorophenyl)-8-thioxo-7,8-dihydro-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (8).



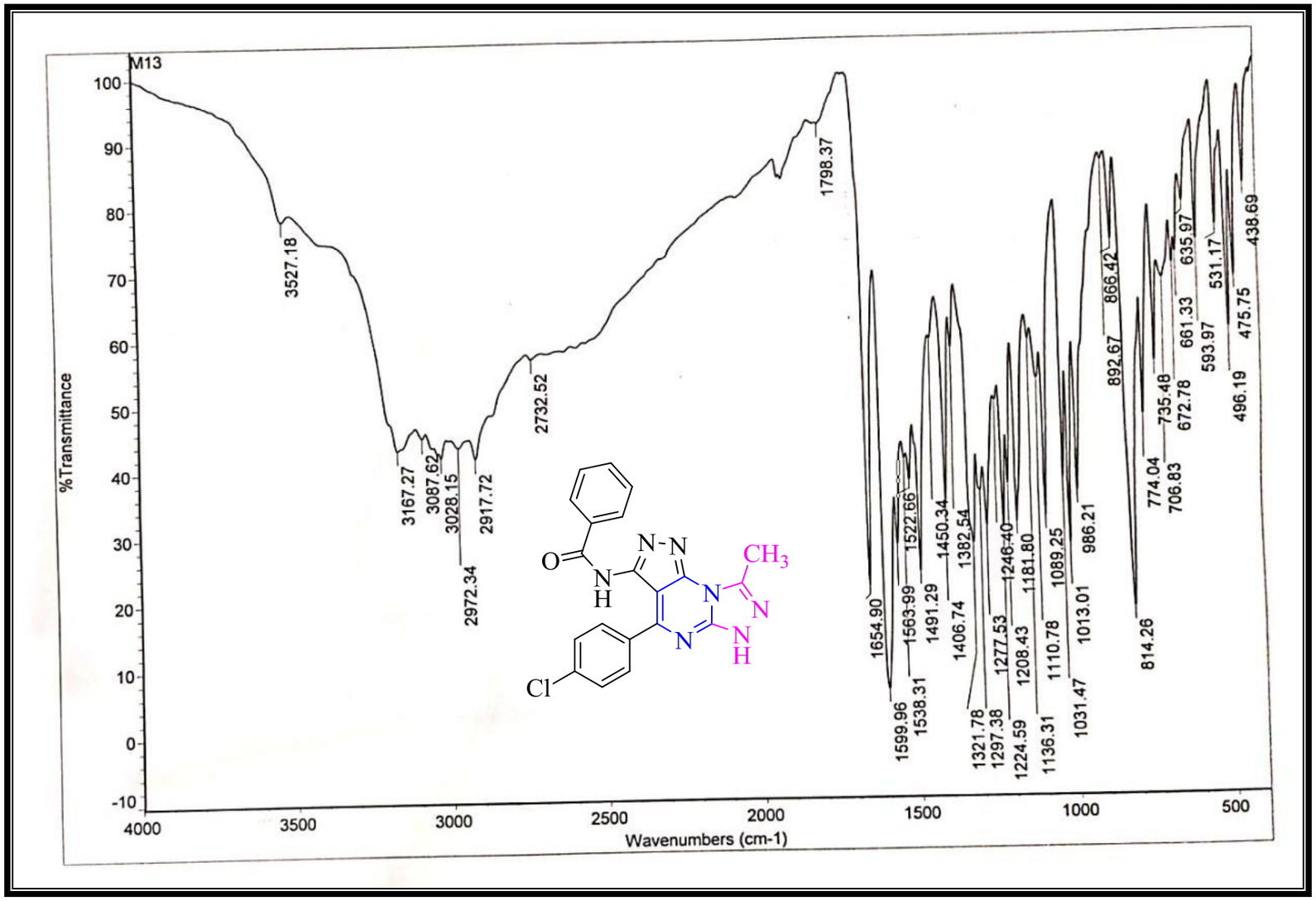
^{1}H-NMR of *N*-(4-(4-chlorophenyl)-8-thioxo-7,8-dihydro-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (8).



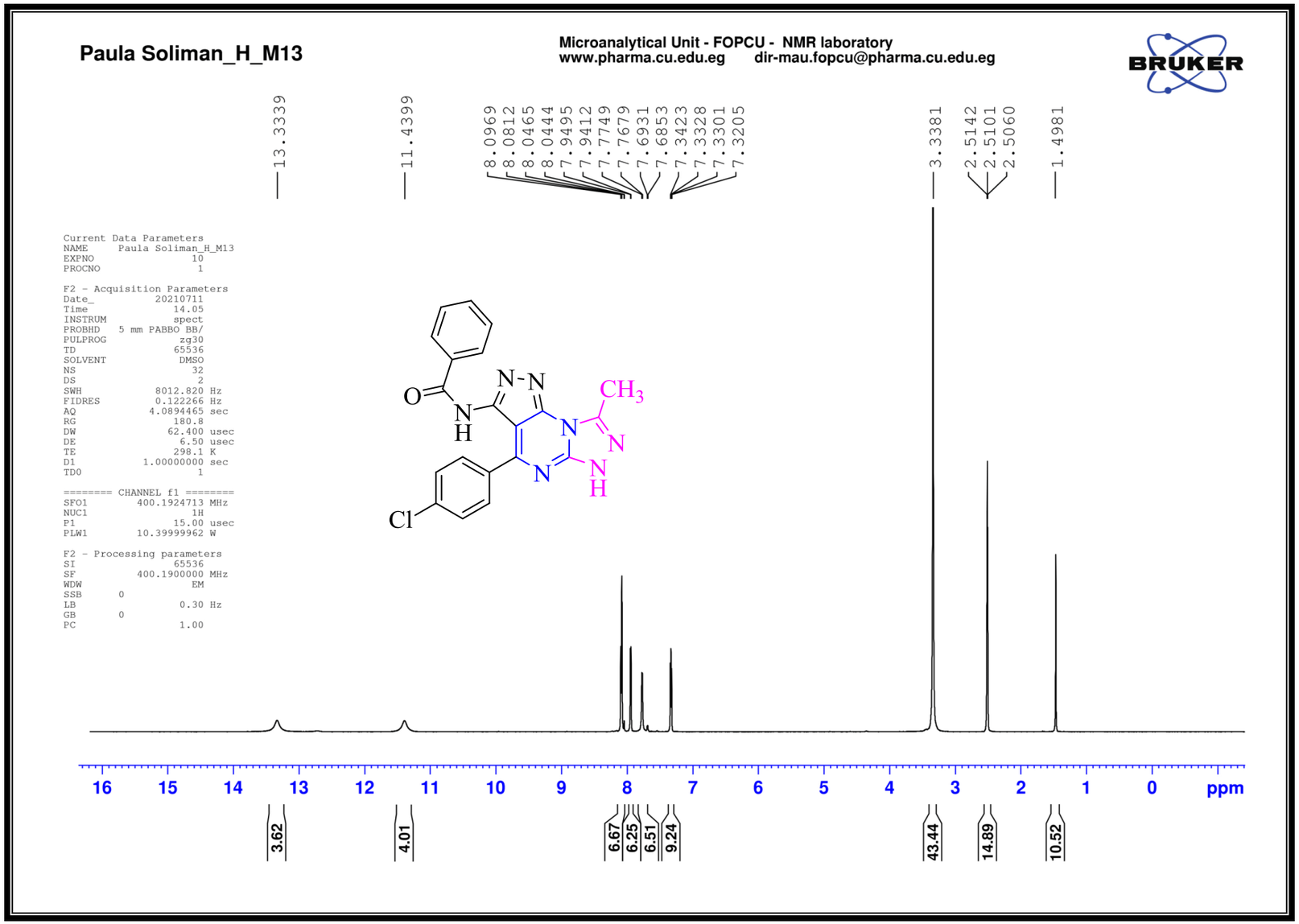
D_2O of *N*-(4-(4-chlorophenyl)-8-thioxo-7,8-dihydro-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (8).



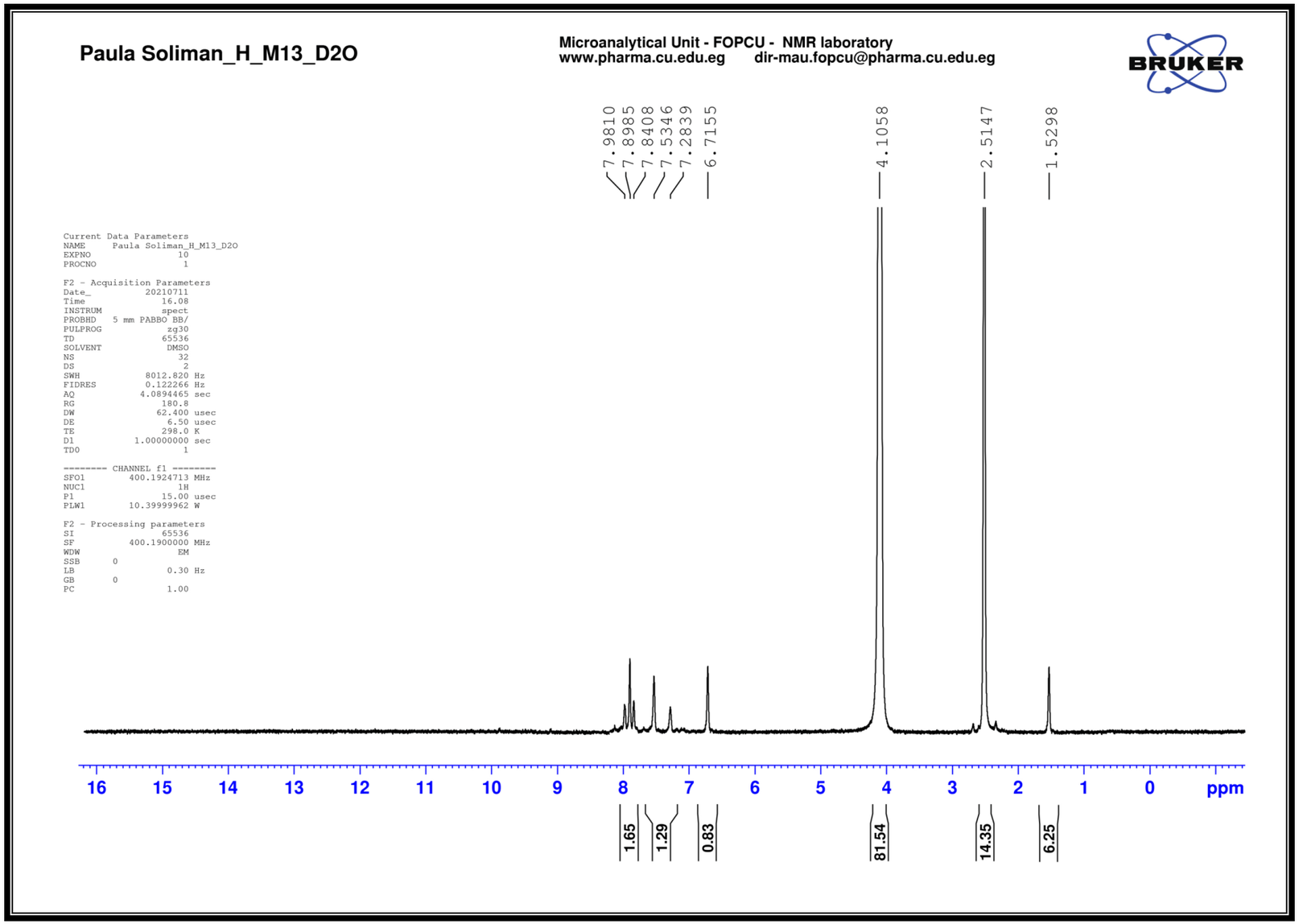
^{13}C-NMR of *N*-(4-(4-chlorophenyl)-8-thioxo-7,8-dihydro-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (8).



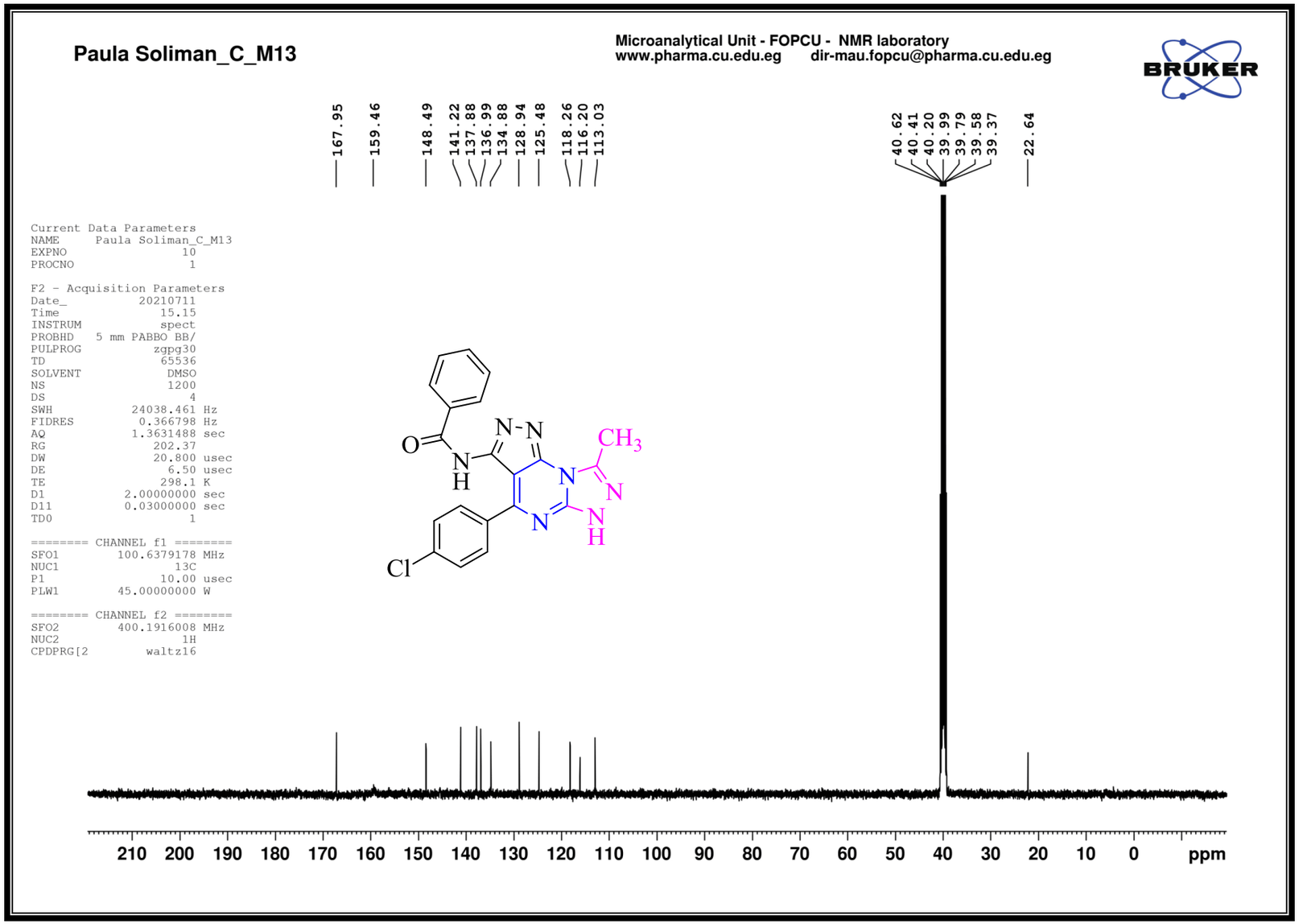
IR of *N*-(4-(4-chlorophenyl)-8-methyl-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (9).



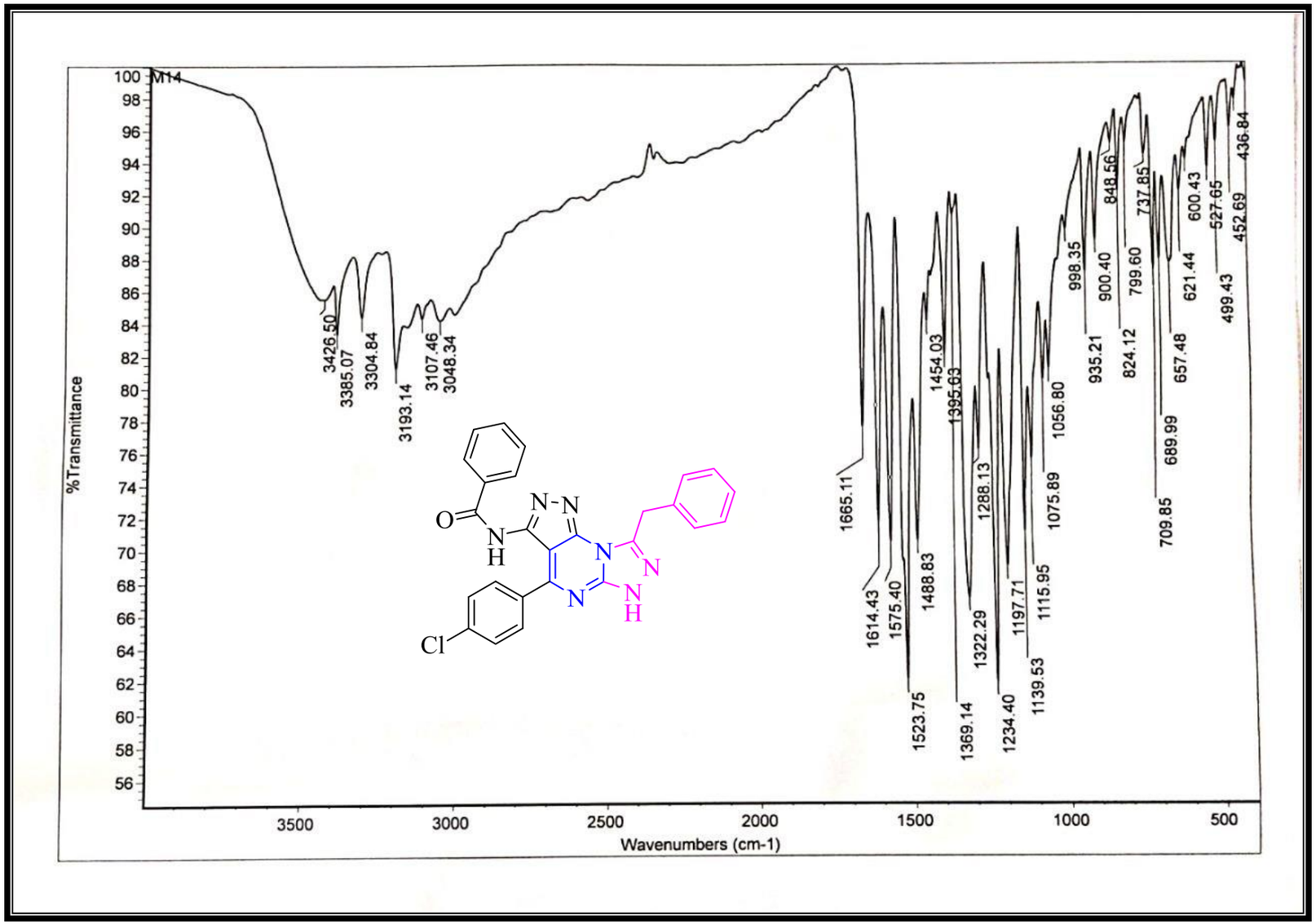
^{1}H-NMR of *N*-(4-(4-chlorophenyl)-8-methyl-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (9).



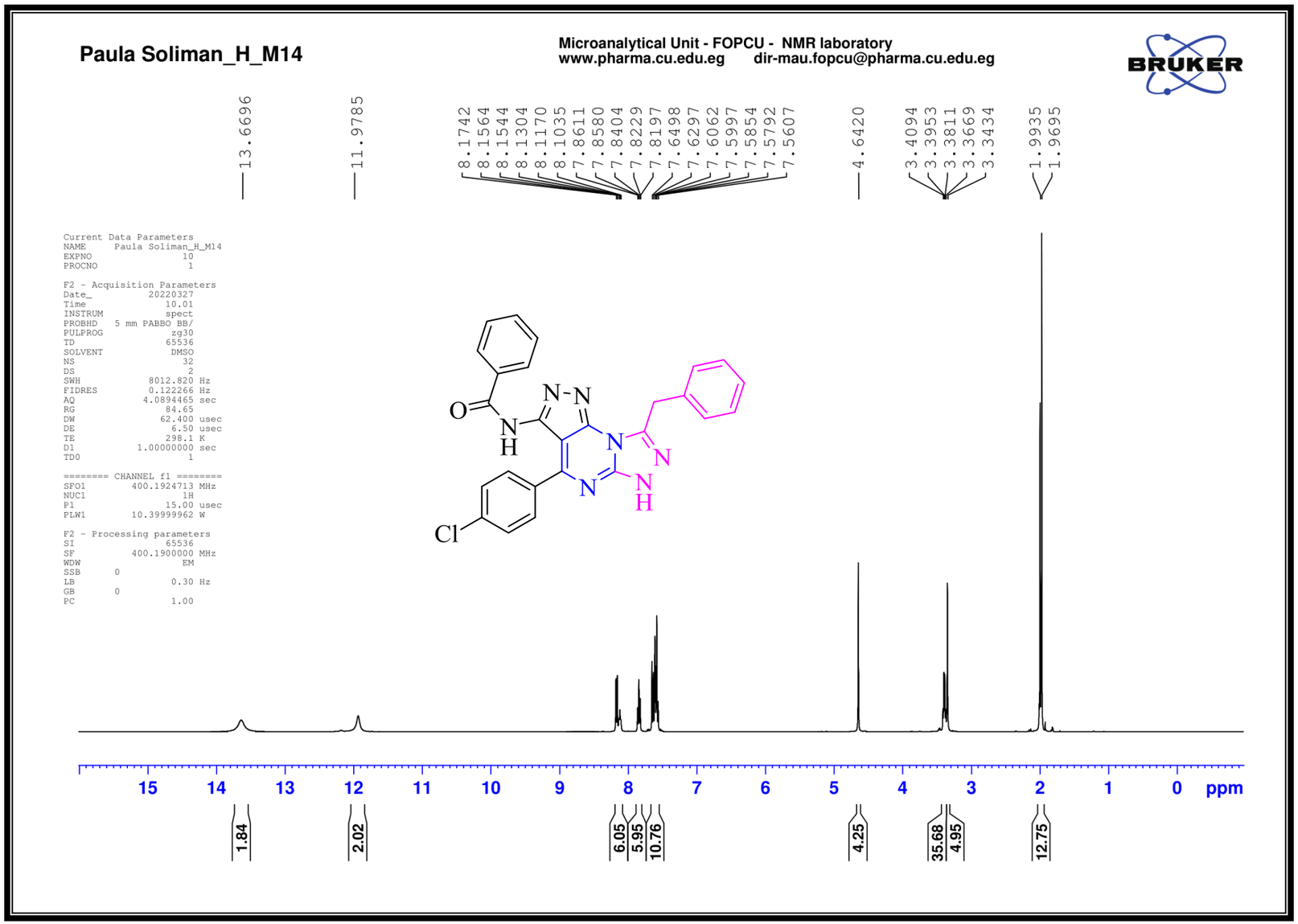
D_2O of *N*-(4-(4-chlorophenyl)-8-methyl-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (9).



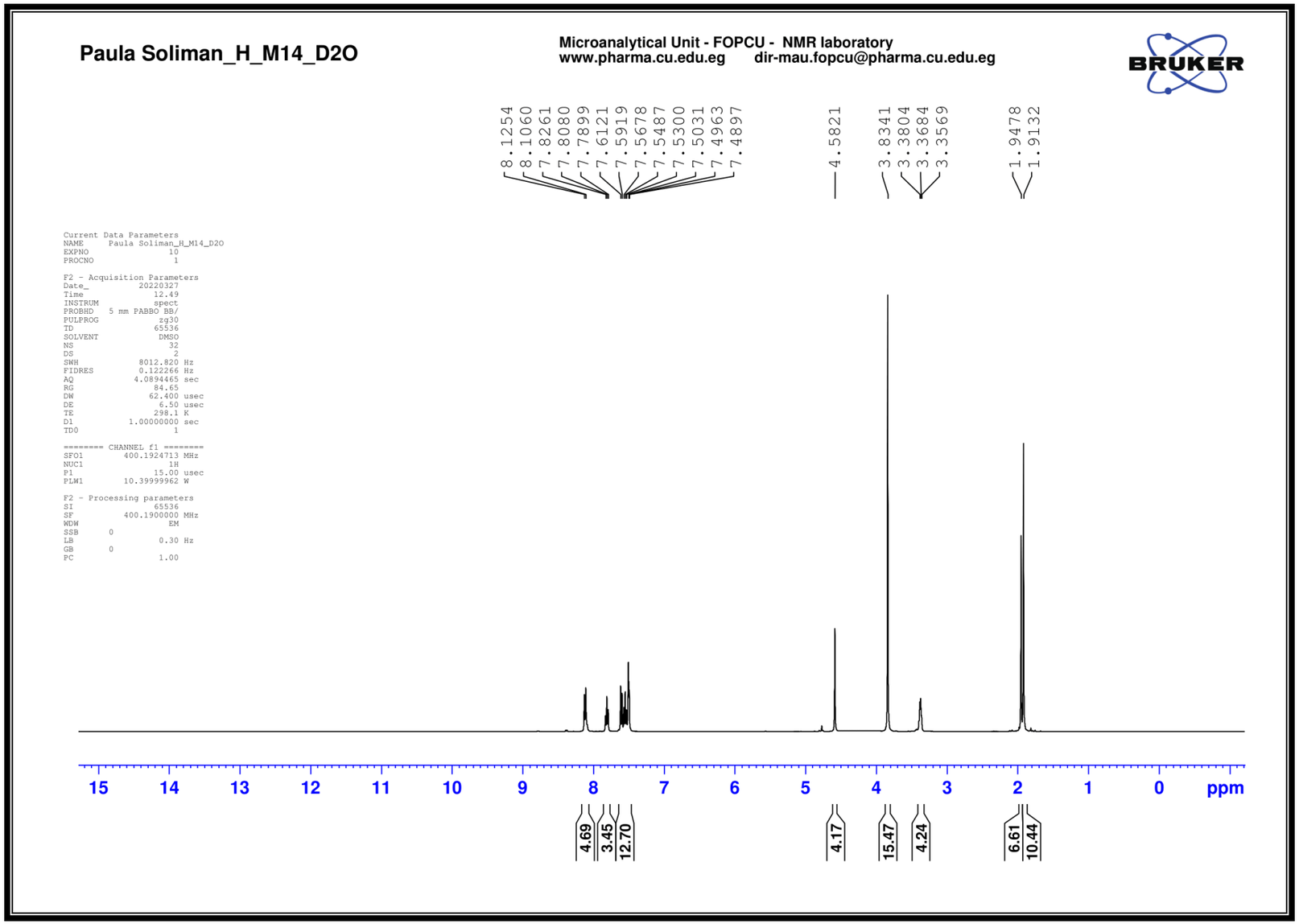
^{13}C-NMR of *N*-(4-(4-chlorophenyl)-8-methyl-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (9).



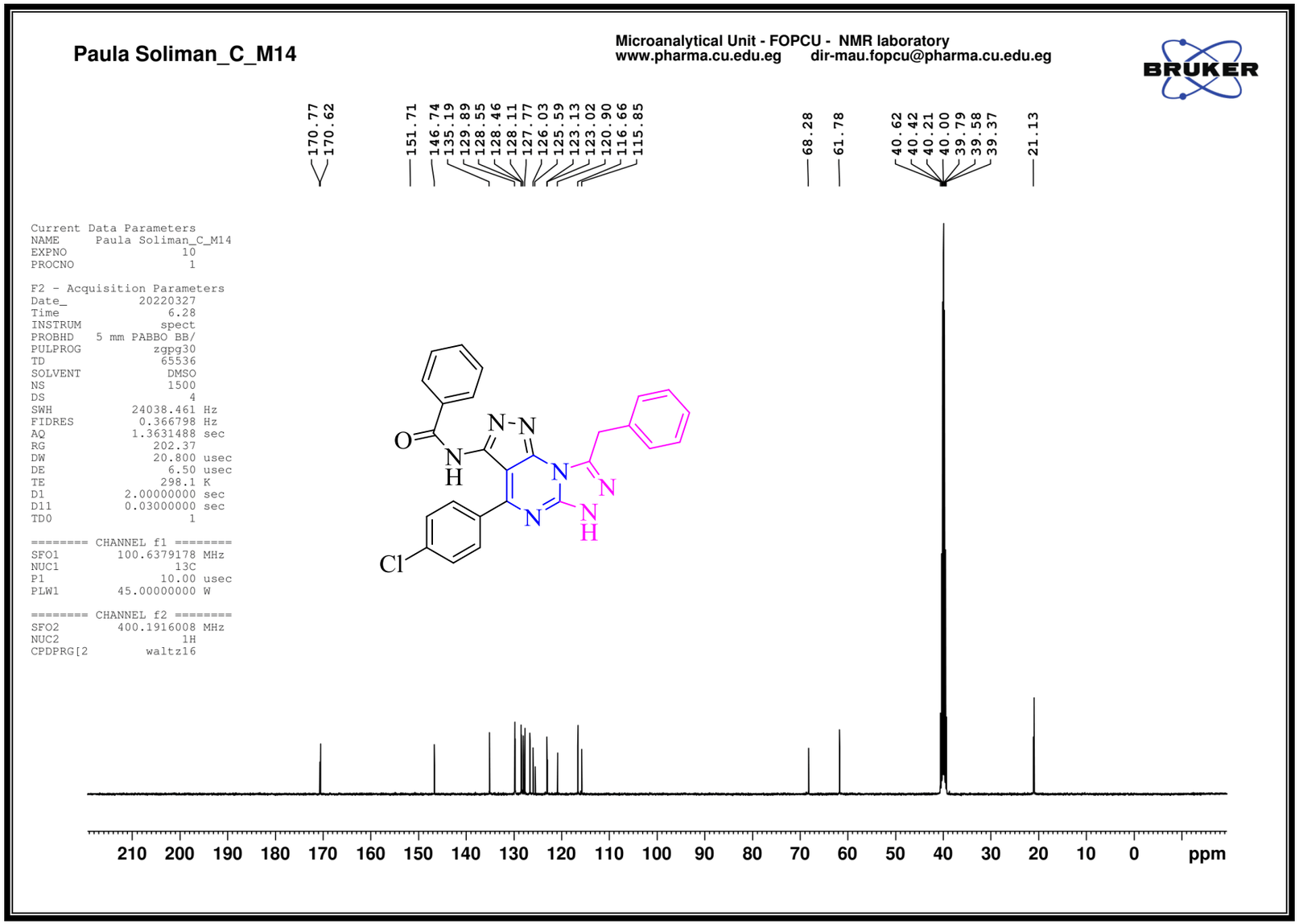
IR of *N*-(4-(4-chlorophenyl)-8-phenyl-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (10).



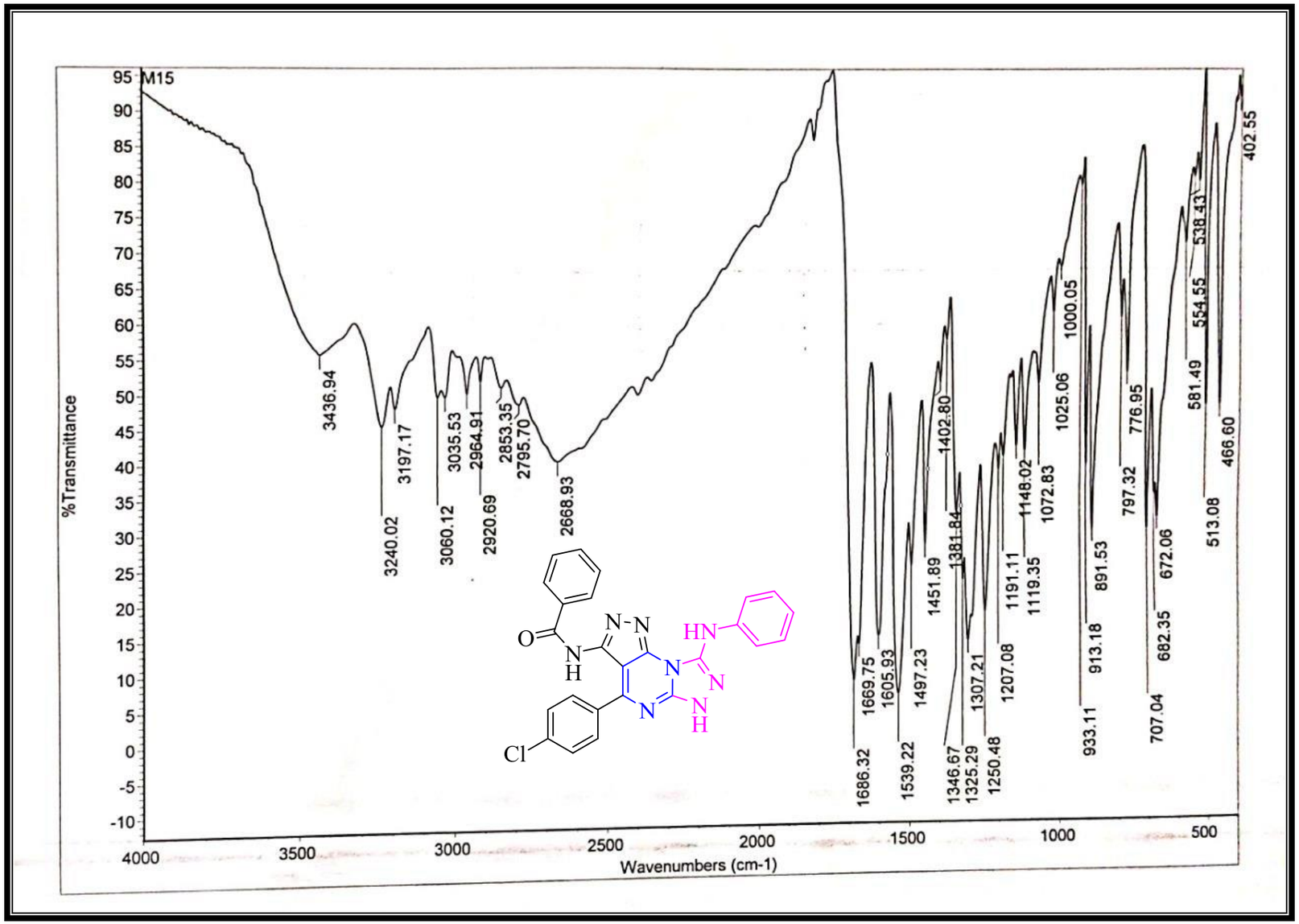
^{1}H-NMR of *N*-(4-(4-chlorophenyl)-8-phenyl-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (10).



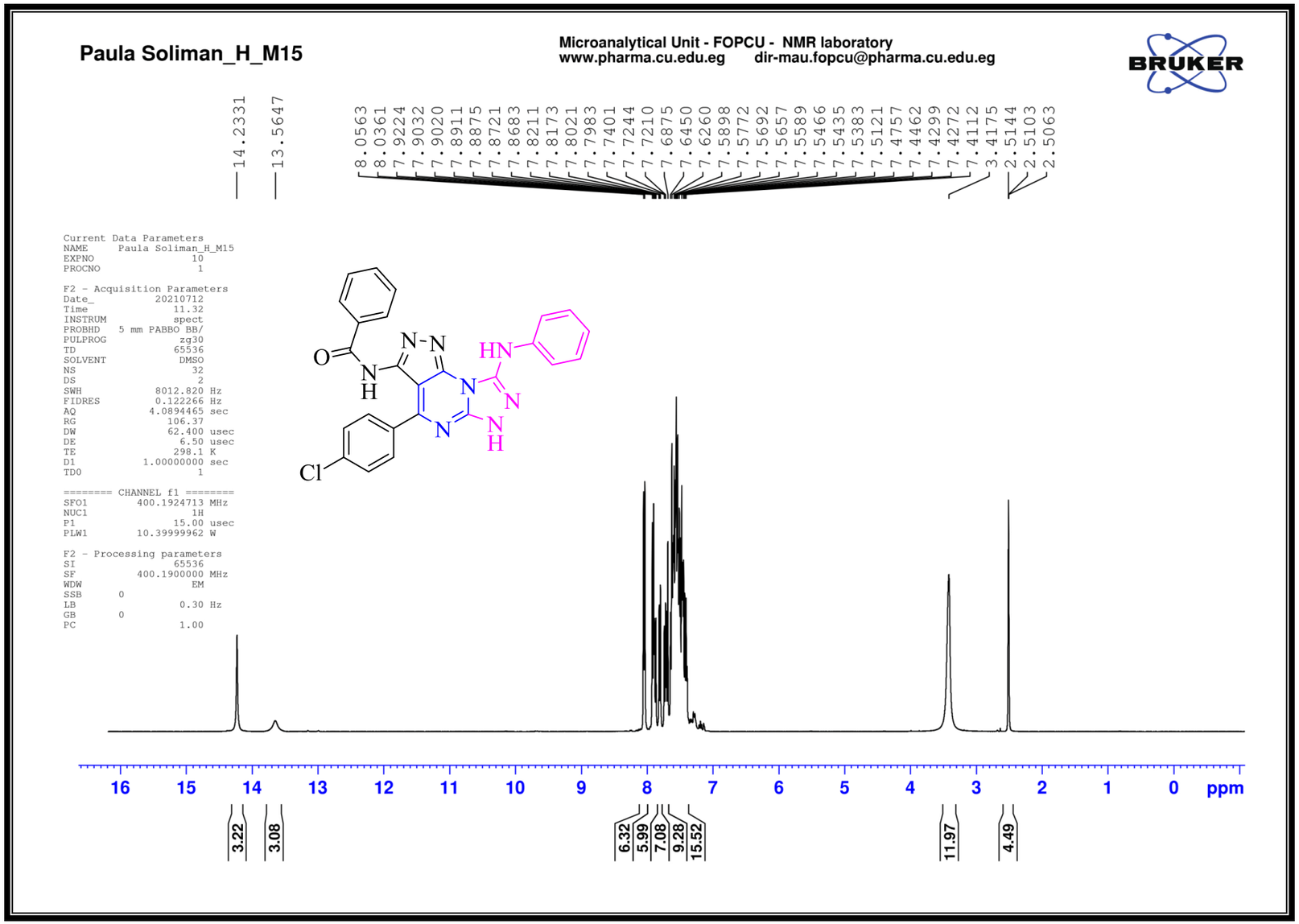
D_2O of *N*-(4-(4-chlorophenyl)-8-phenyl-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (10).



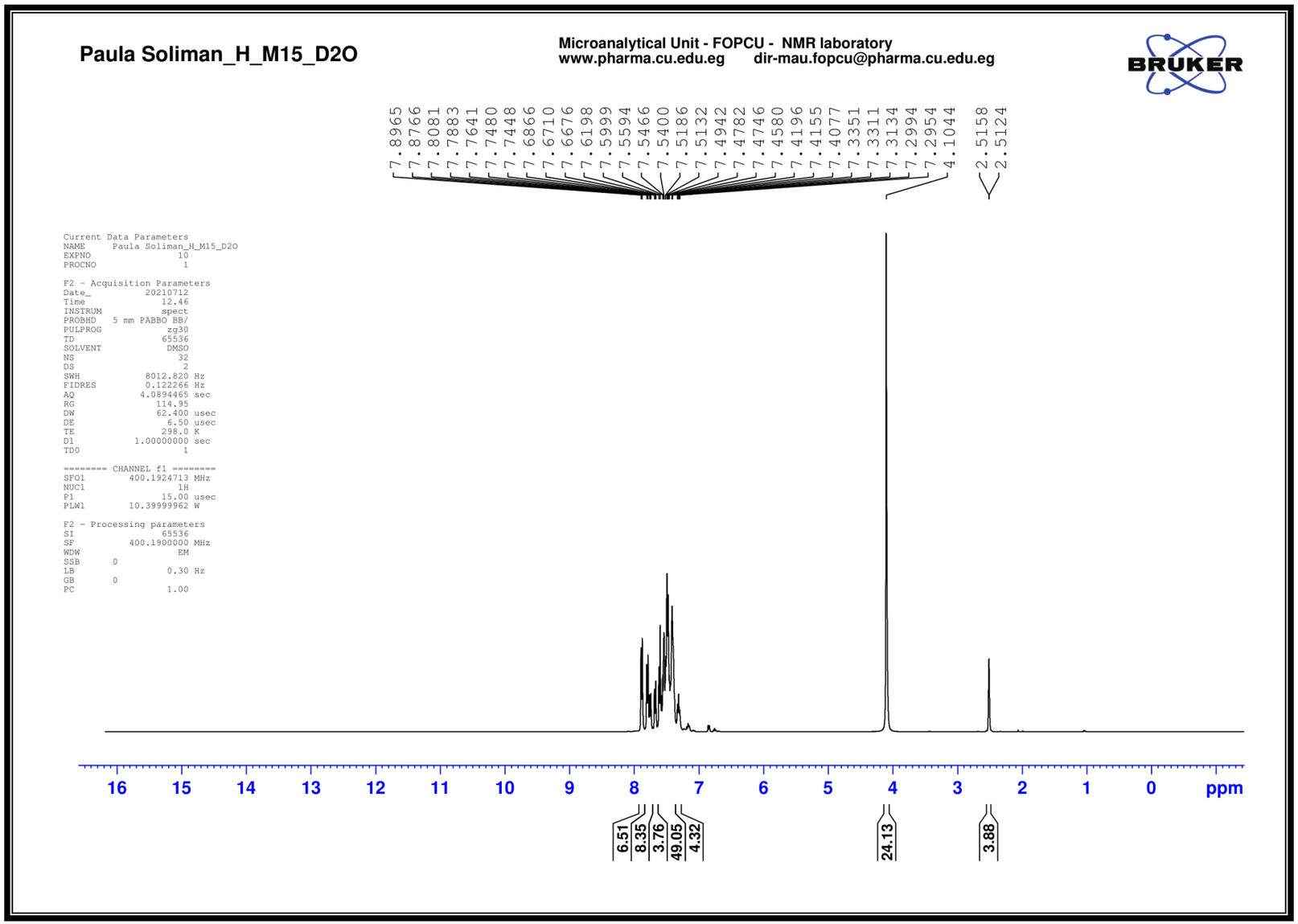
^{13}C-NMR of *N*-(4-(4-chlorophenyl)-8-phenyl-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (10).



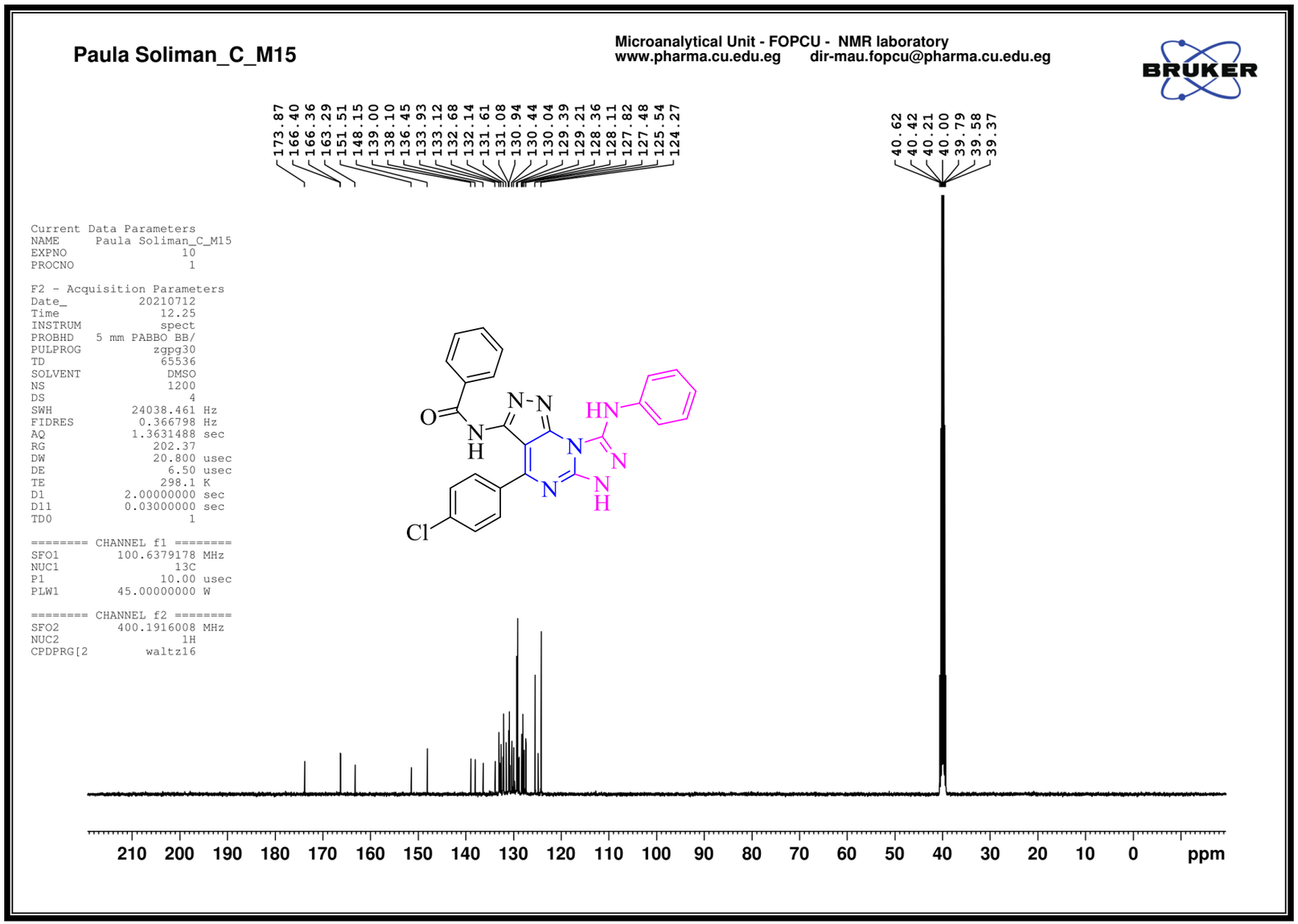
IR of *N*-(4-(4-chlorophenyl)-8-(phenylamino)-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (12).



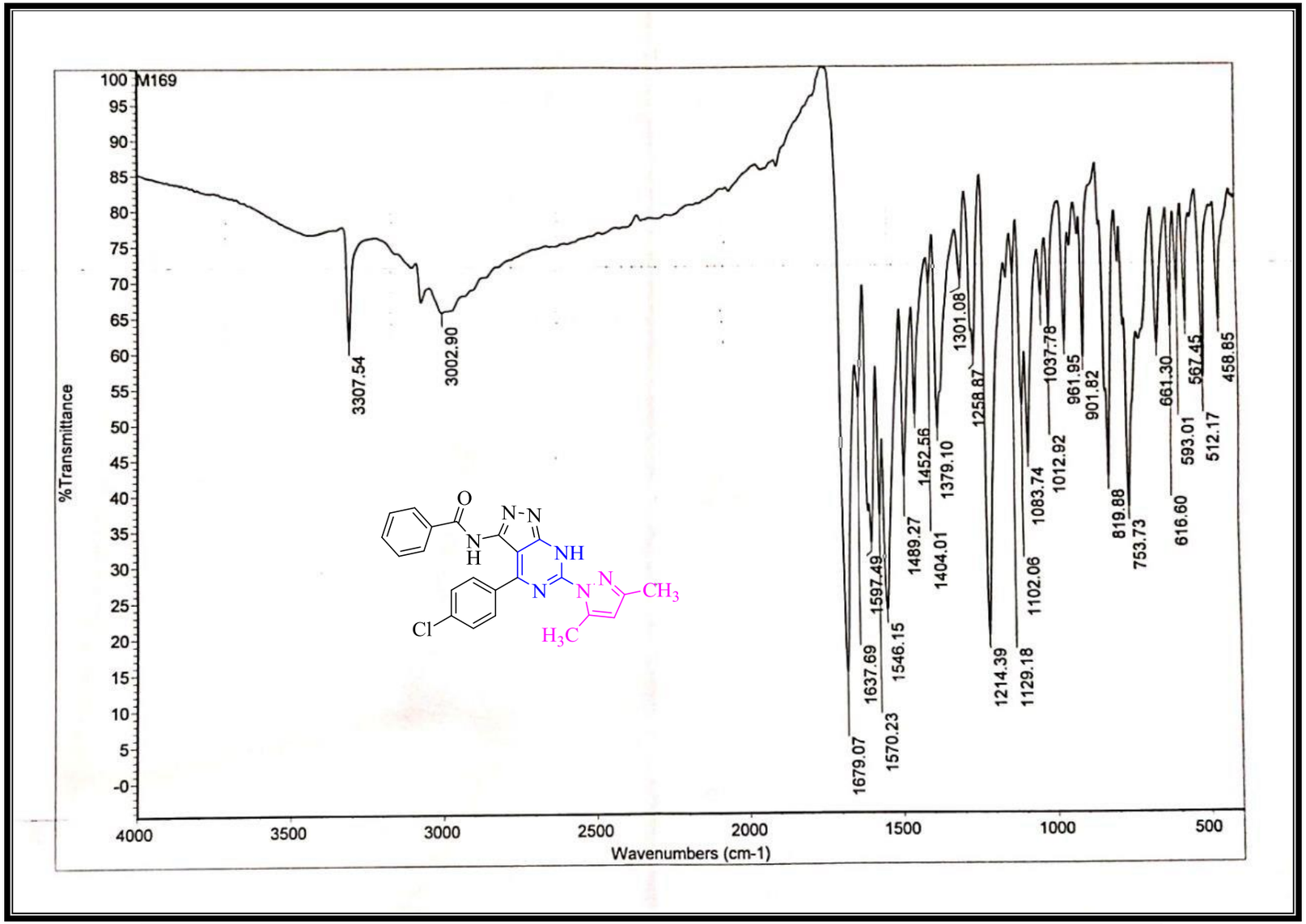
^{1}H-NMR of *N*-(4-(4-chlorophenyl)-8-(phenylamino)-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (12).



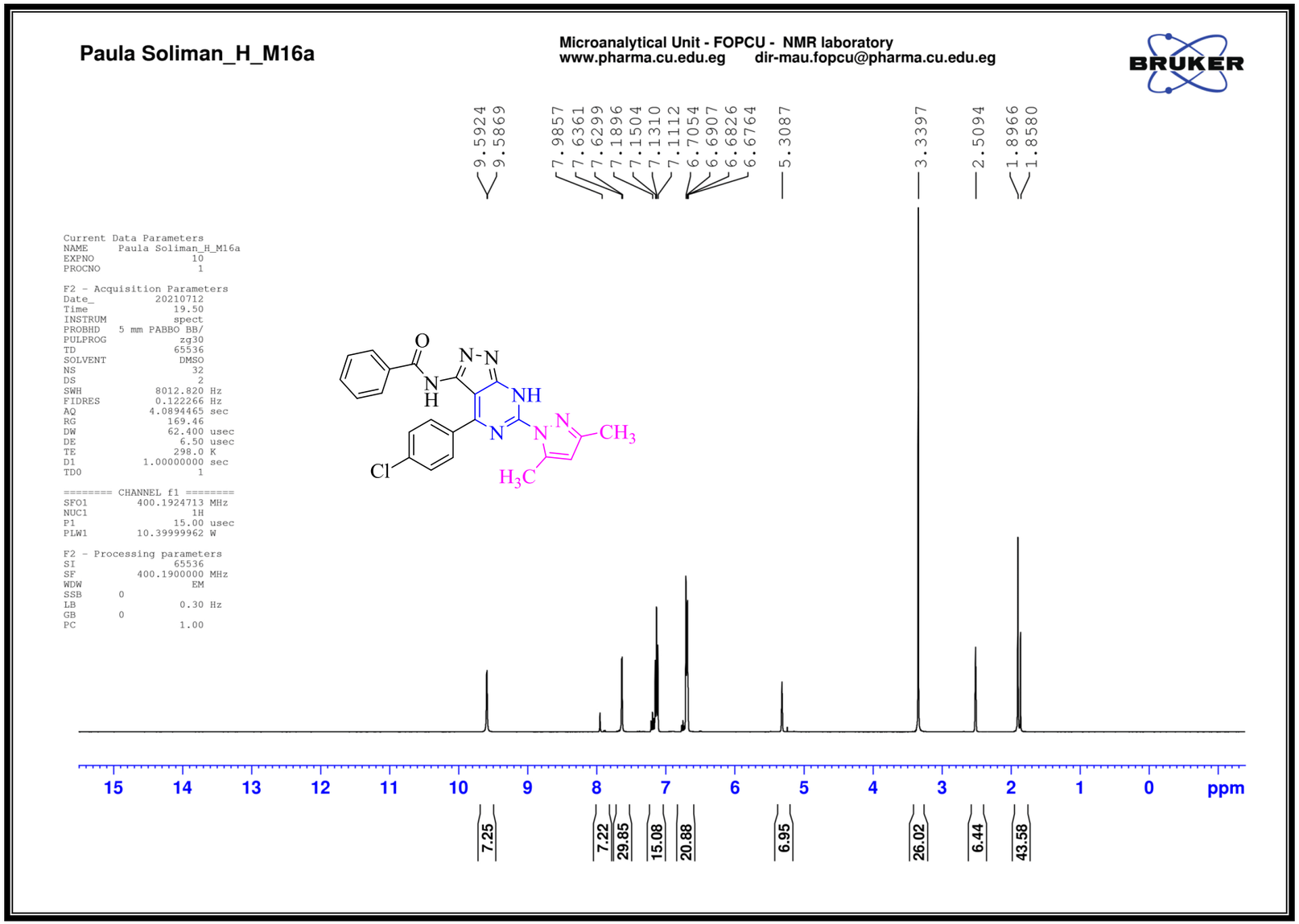
D_2O of *N*-(4-(4-chlorophenyl)-8-(phenylamino)-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (12).



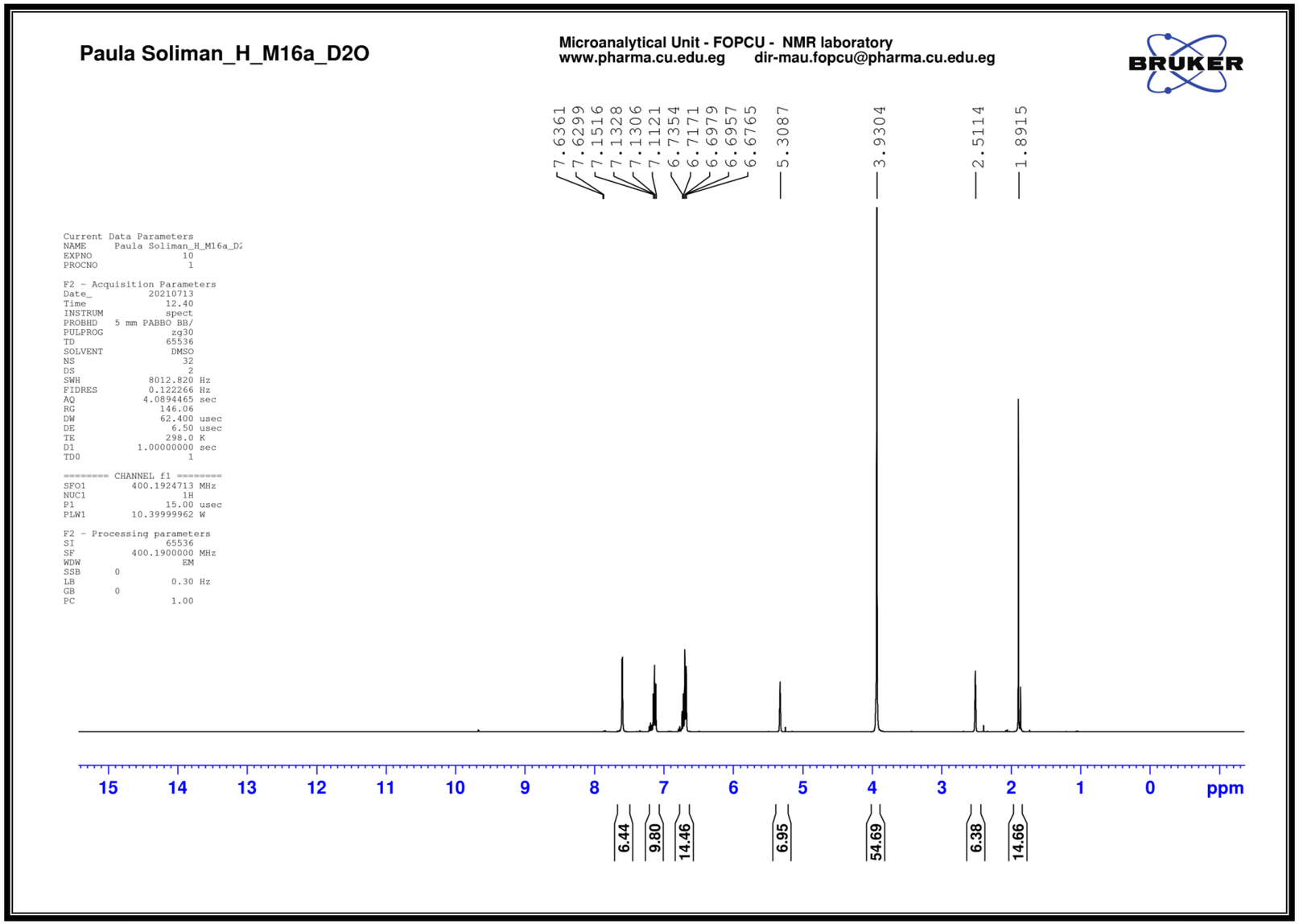
^{13}C-NMR of *N*-(4-(4-chlorophenyl)-8-(phenylamino)-6H-pyrazolo[4,3-e][1,2,4]triazolo[4,3-a]pyrimidin-3-yl)benzamide (12).



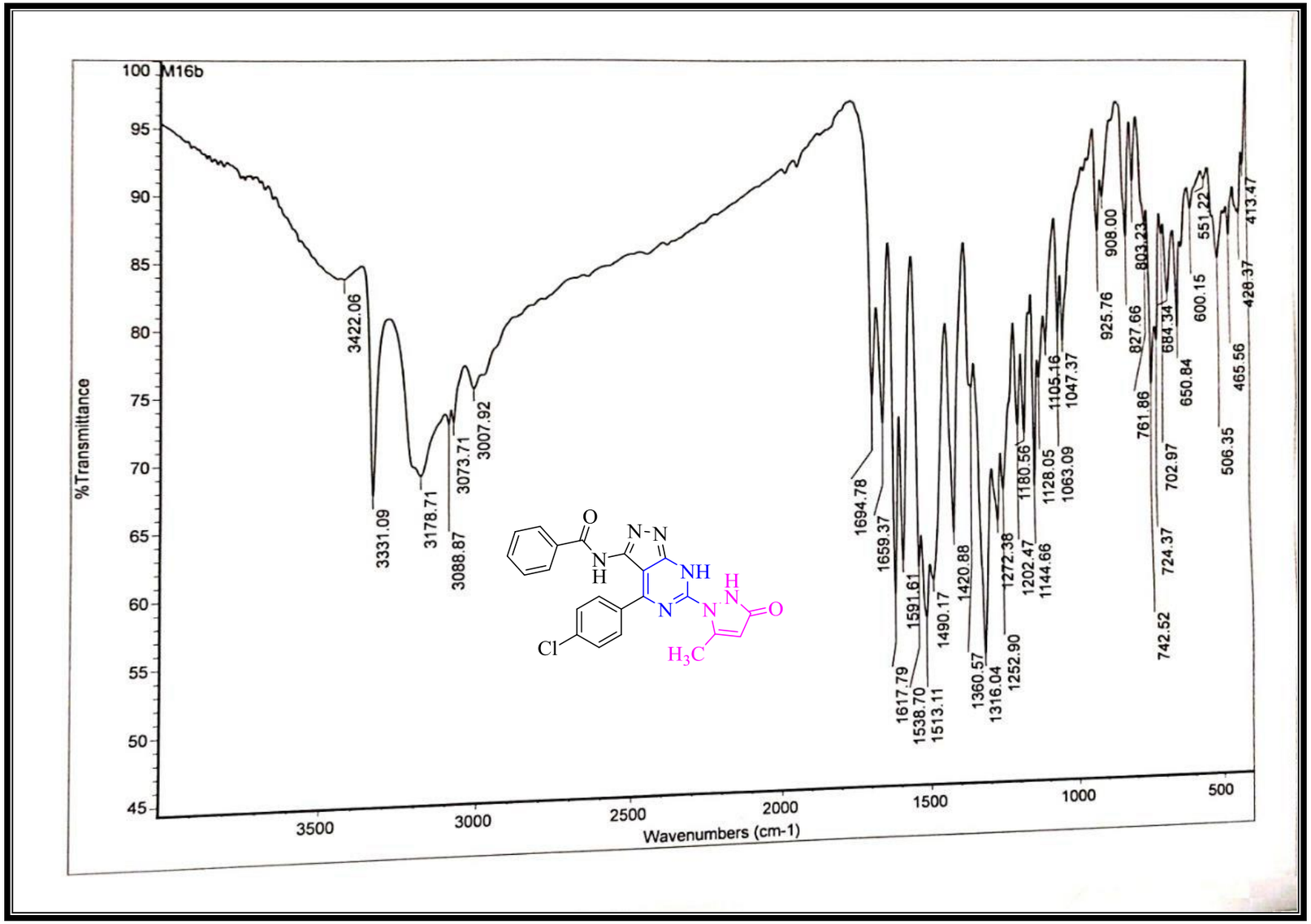
IR of *N*-(4-(4-chlorophenyl)-6-(3,5-dimethyl-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (13a).



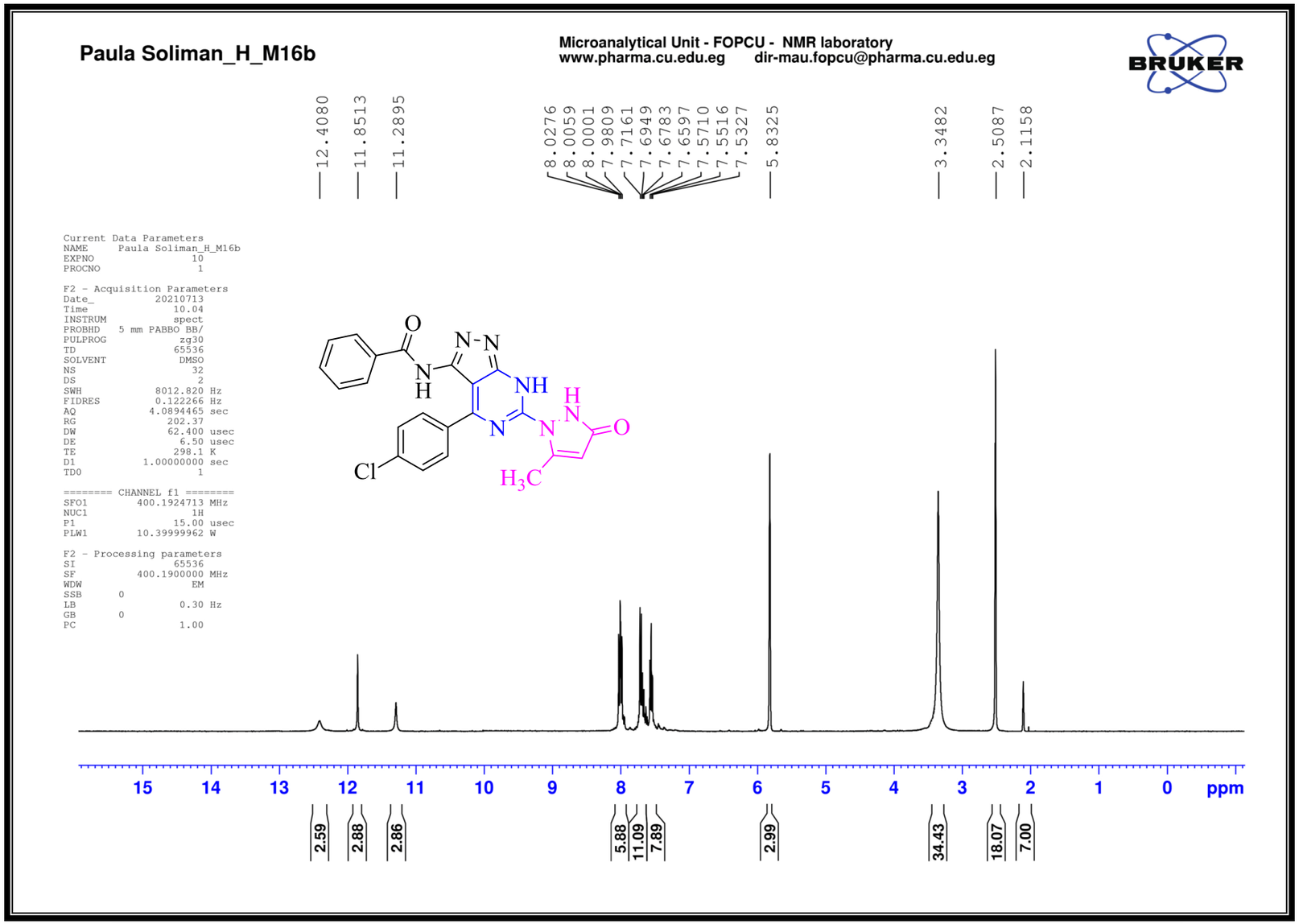
^{1}H-NMR of *N*-(4-(4-chlorophenyl)-6-(3,5-dimethyl-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (13a).



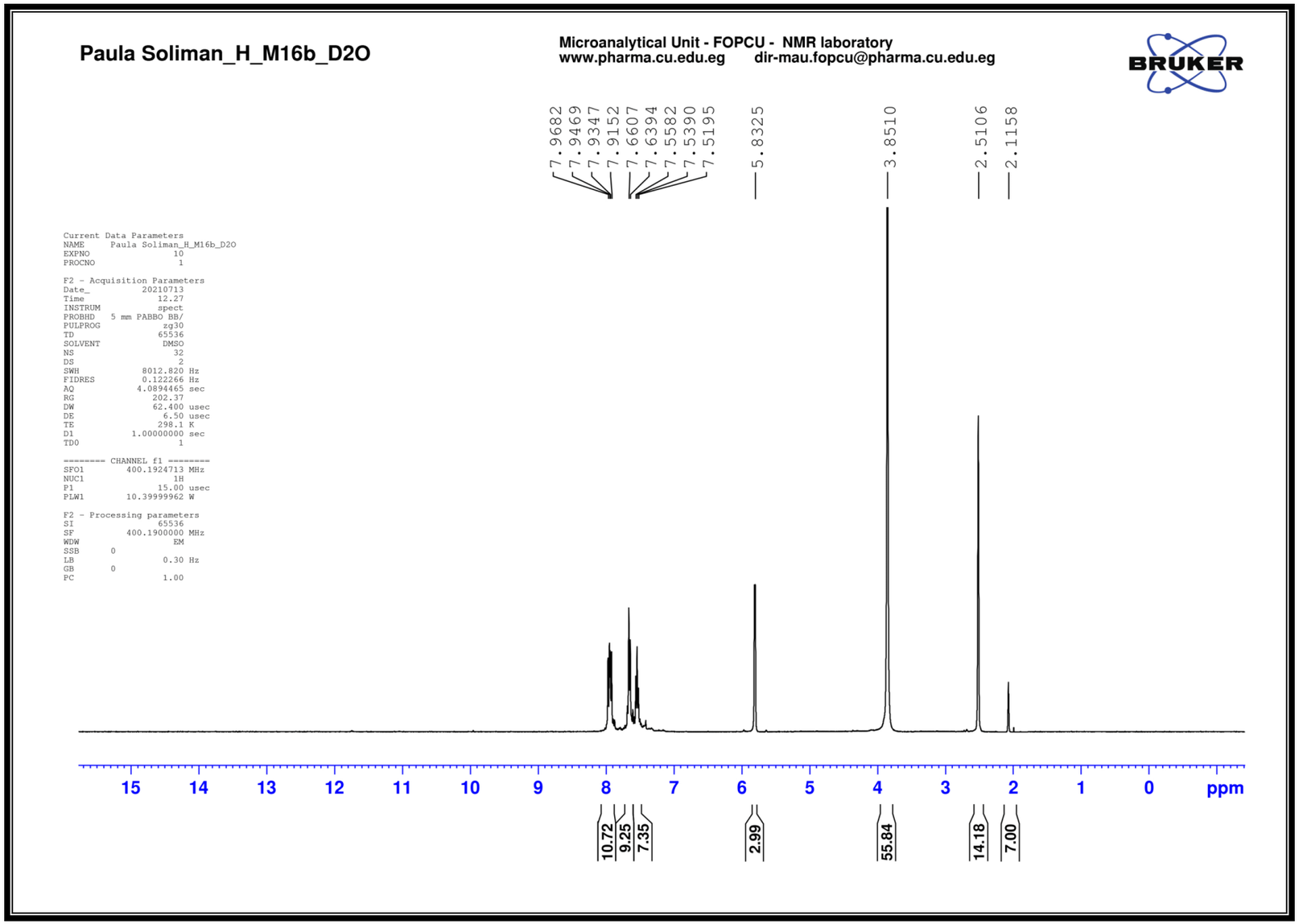
D_2O of *N*-(4-(4-chlorophenyl)-6-(3,5-dimethyl-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (13a).



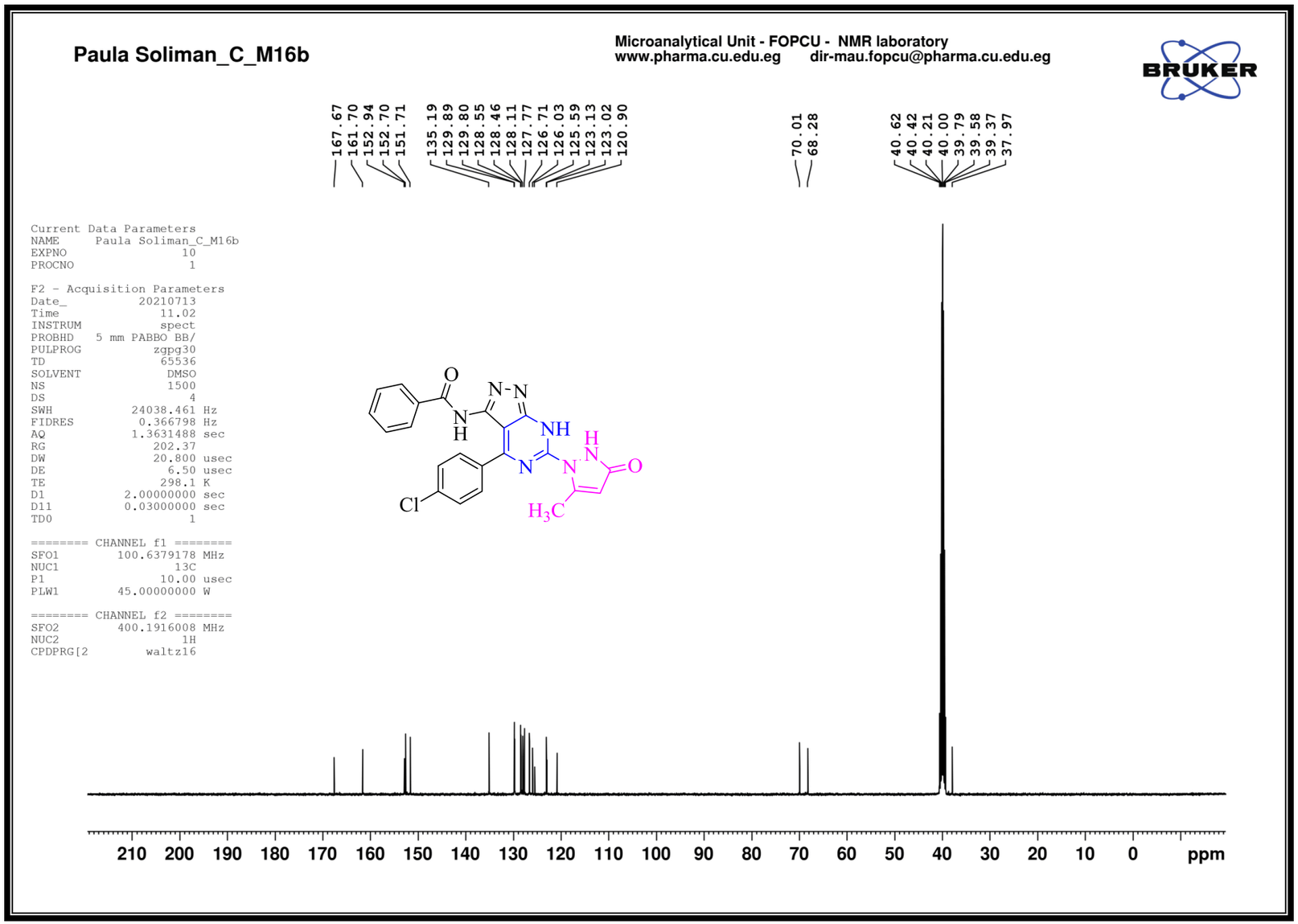
IR of *N-(4-(4-chlorophenyl)-6-(5-methyl-3-oxo-2,3-dihydro-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide* (13b).



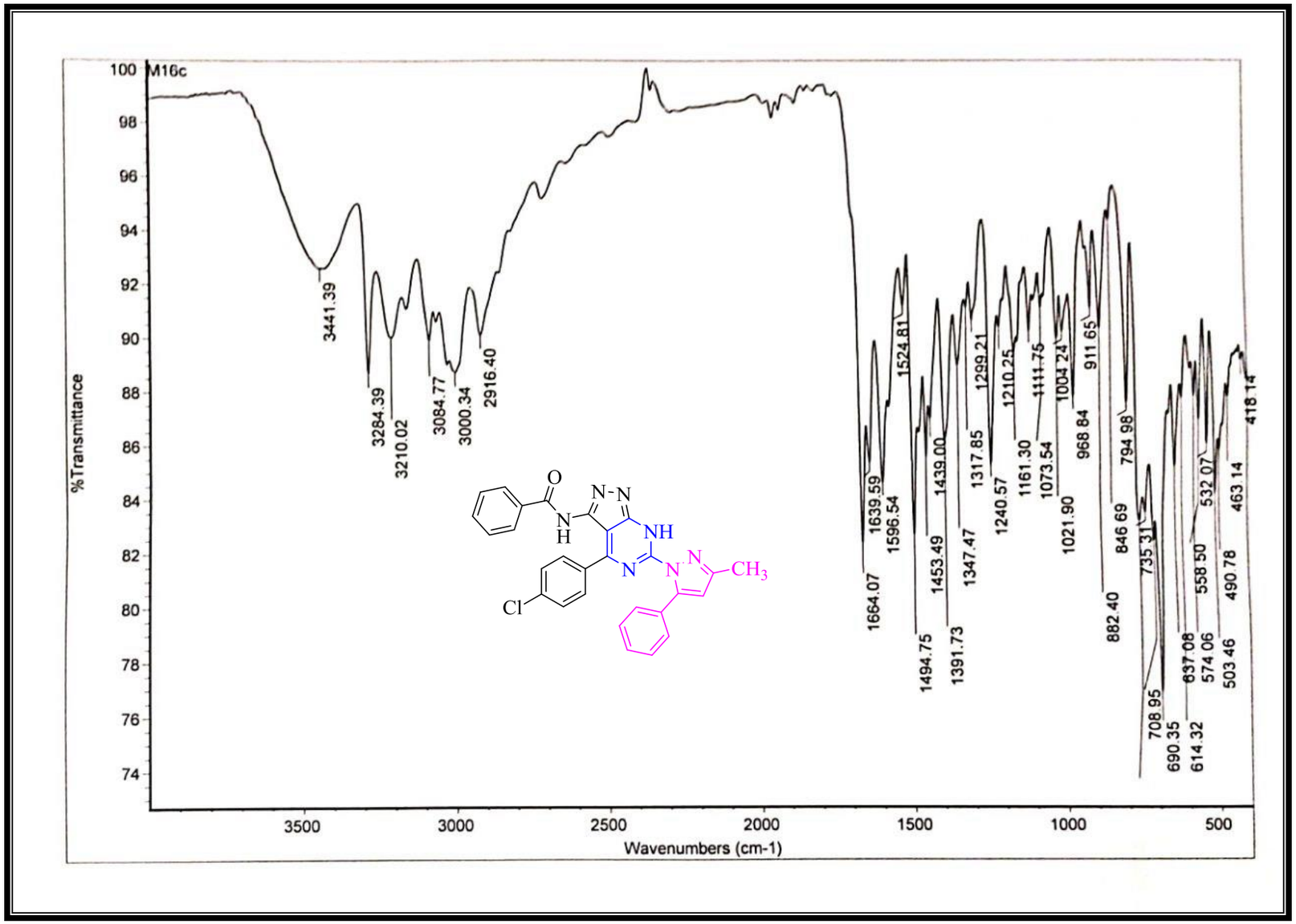
^{1}H-NMR of *N-(4-(4-chlorophenyl)-6-(5-methyl-3-oxo-2,3-dihydro-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide* (13b).



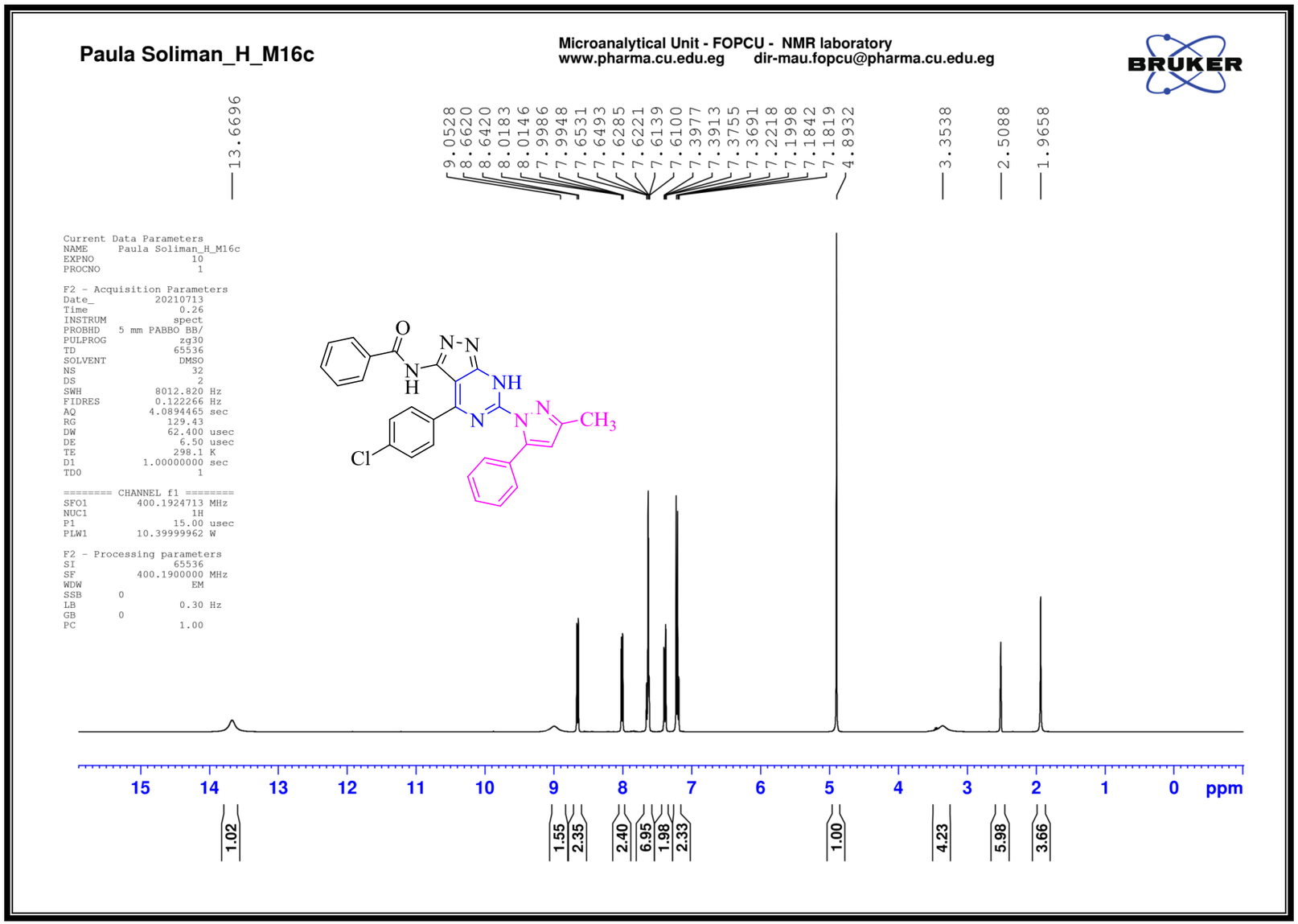
D_2O of *N-(4-(4-chlorophenyl)-6-(5-methyl-3-oxo-2,3-dihydro-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide* (13b).



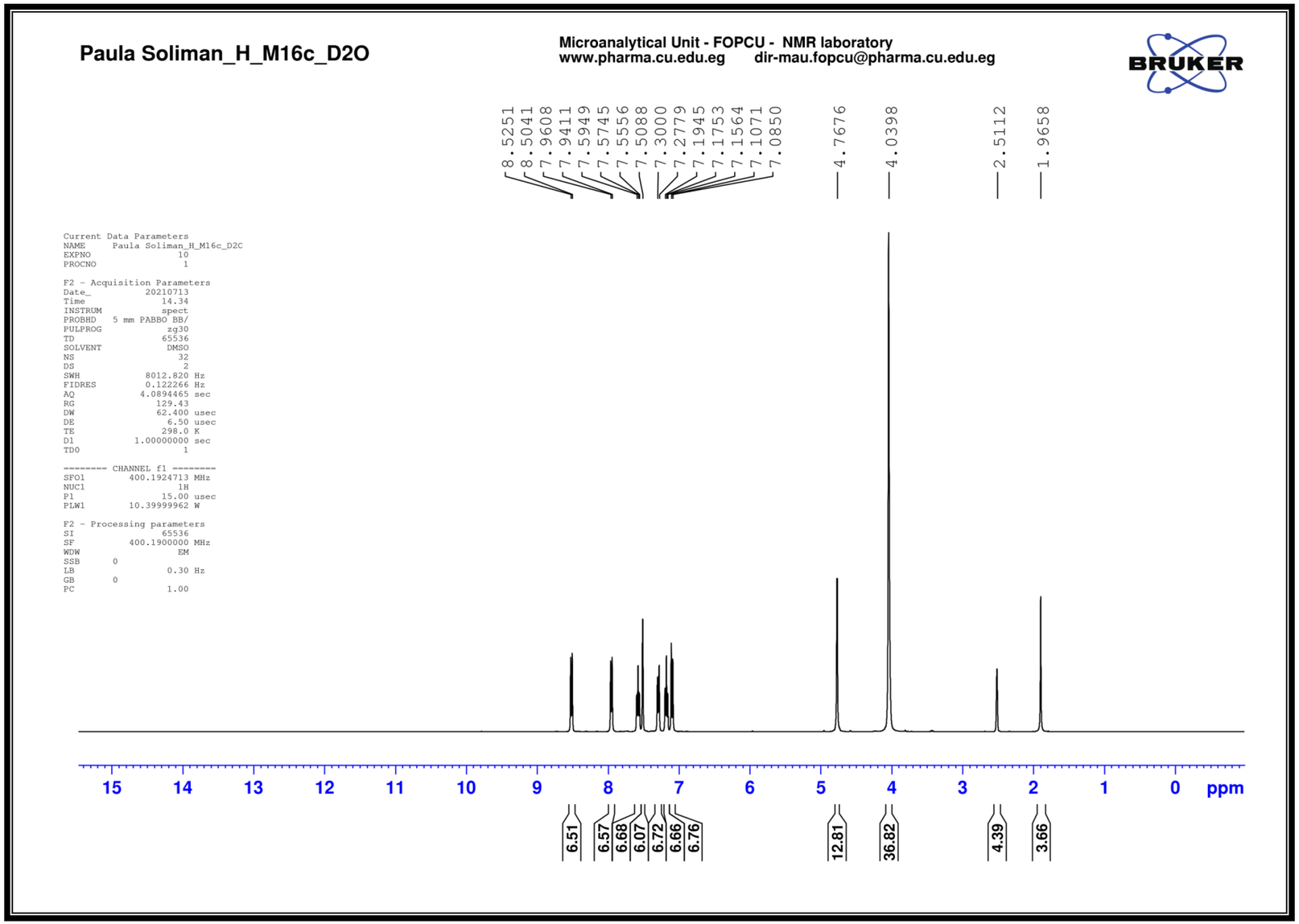
^{13}C-NMR of *N-(4-(4-chlorophenyl)-6-(5-methyl-3-oxo-2,3-dihydro-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide* (13b).



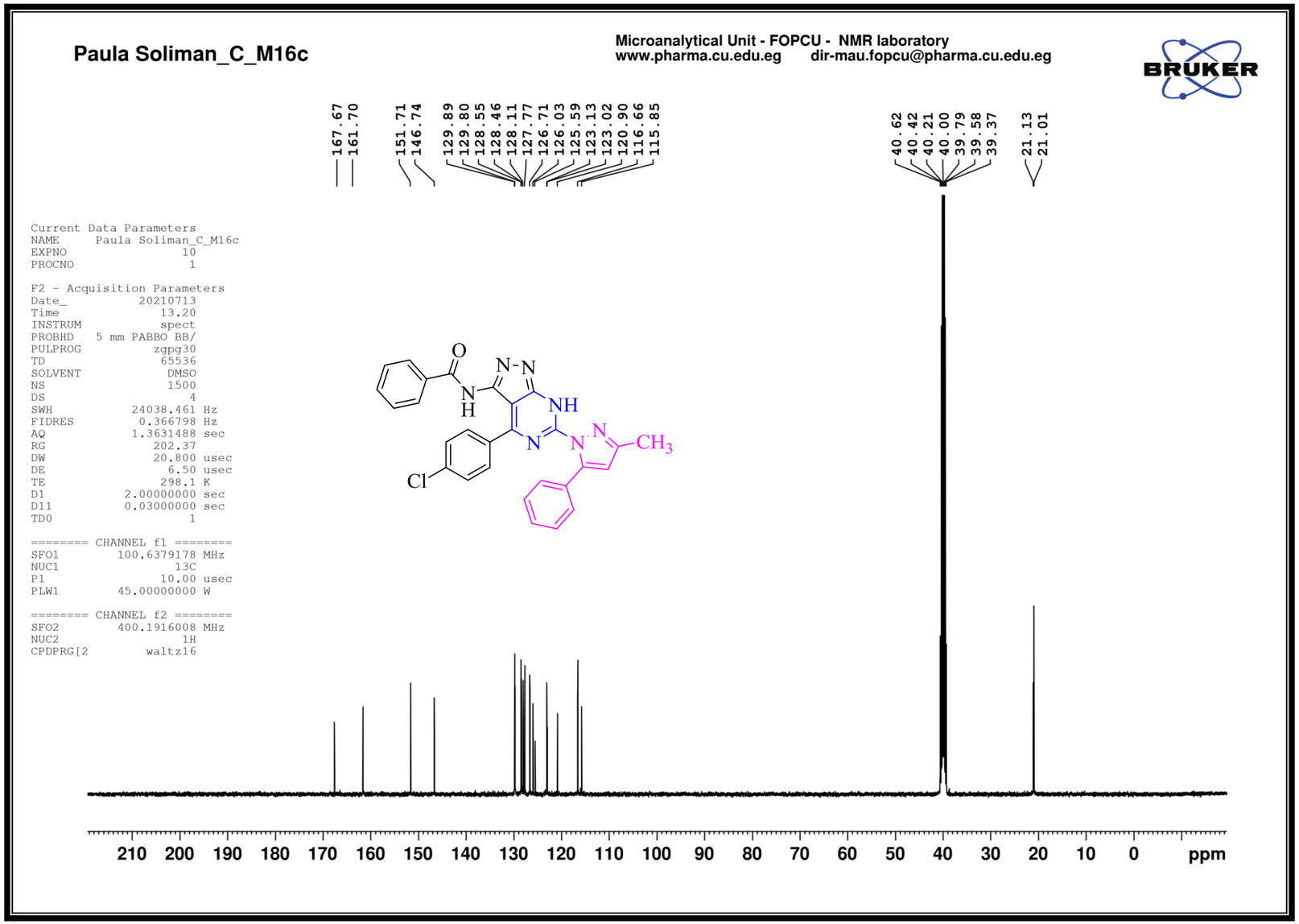
IR of *N*-(4-(4-chlorophenyl)-6-(3-methyl-5-phenyl-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (13c).



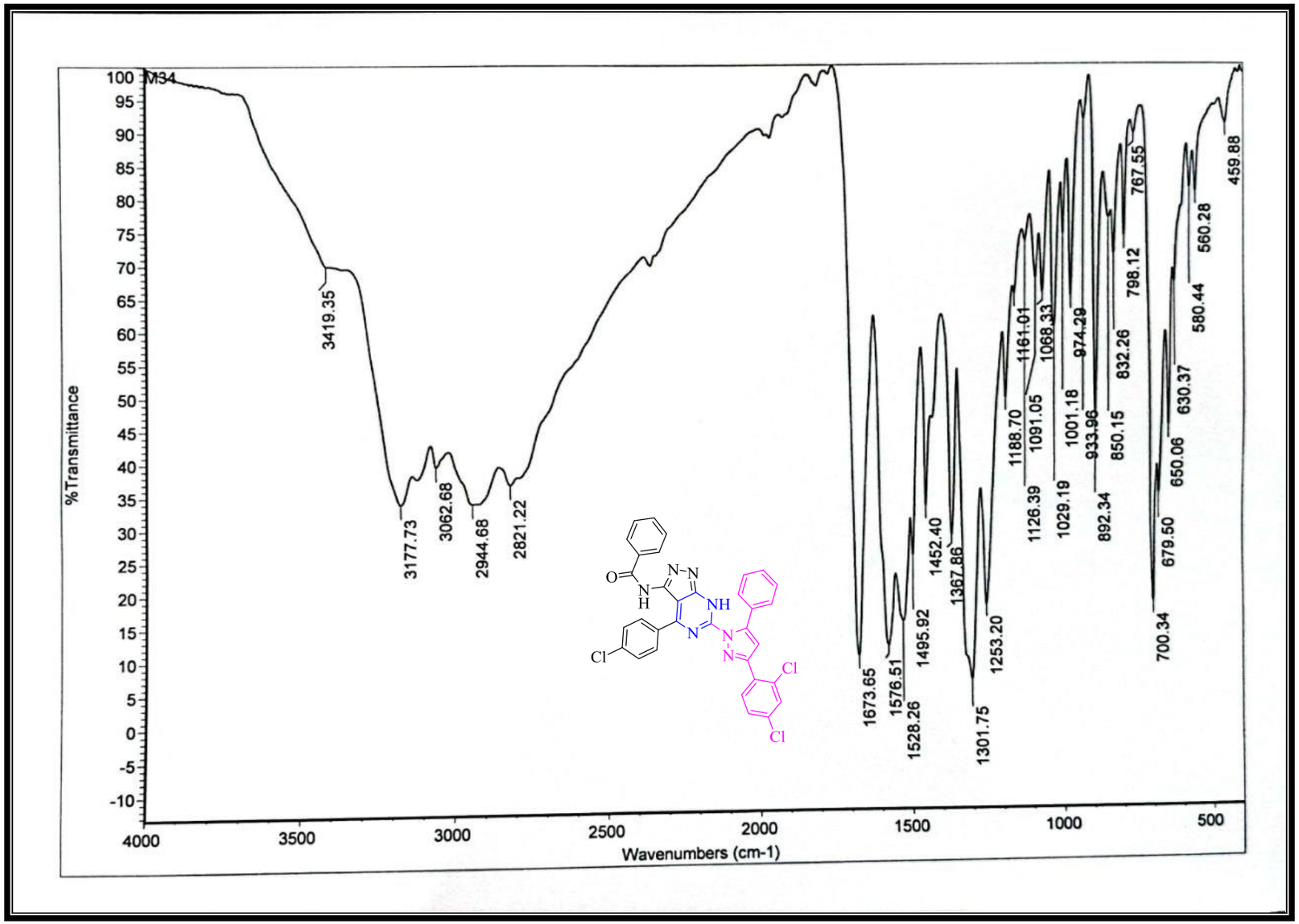
^{1}H-NMR of *N*-(4-(4-chlorophenyl)-6-(3-methyl-5-phenyl-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (13c).



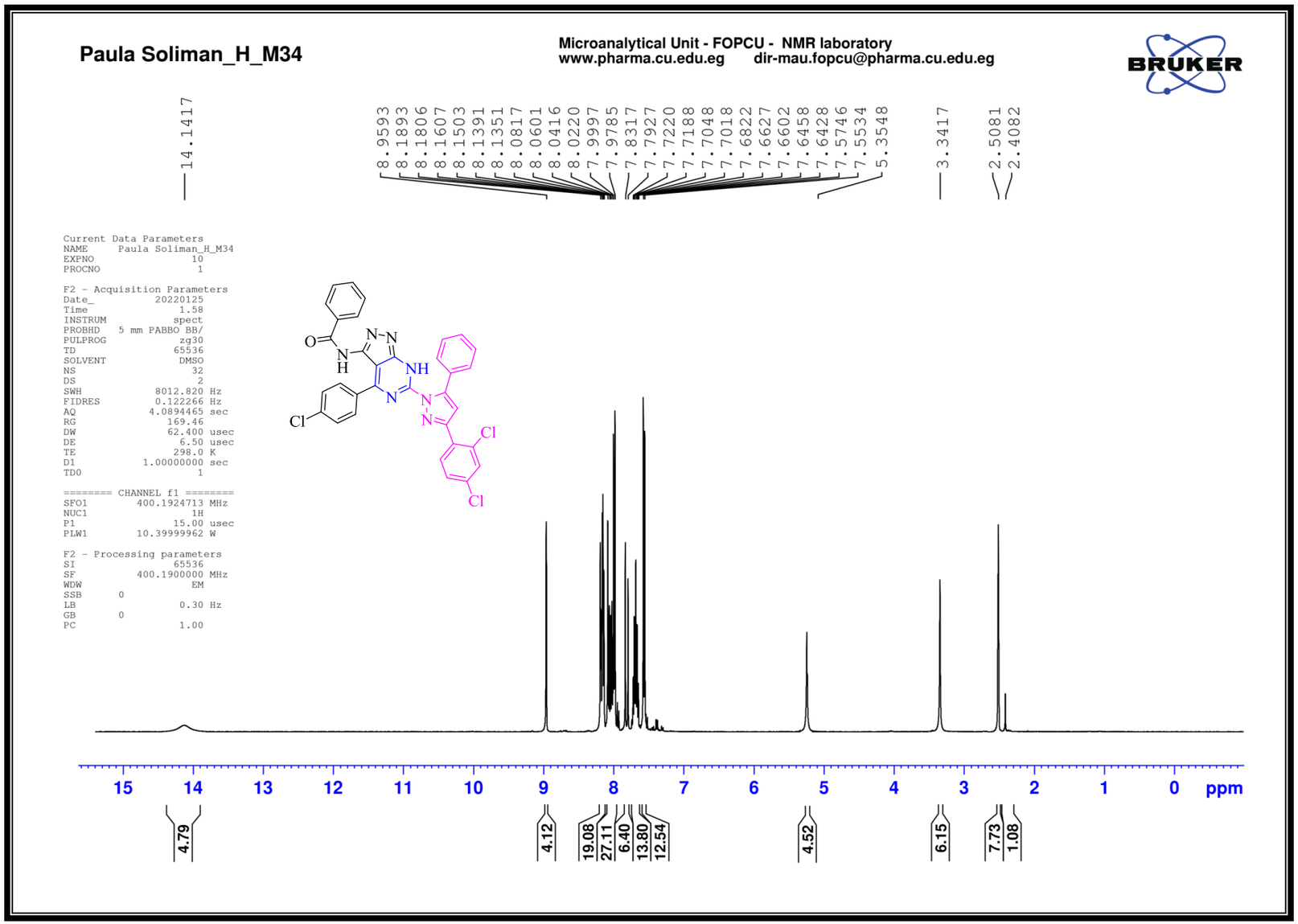
D_2O of *N*-(4-(4-chlorophenyl)-6-(3-methyl-5-phenyl-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (13c).



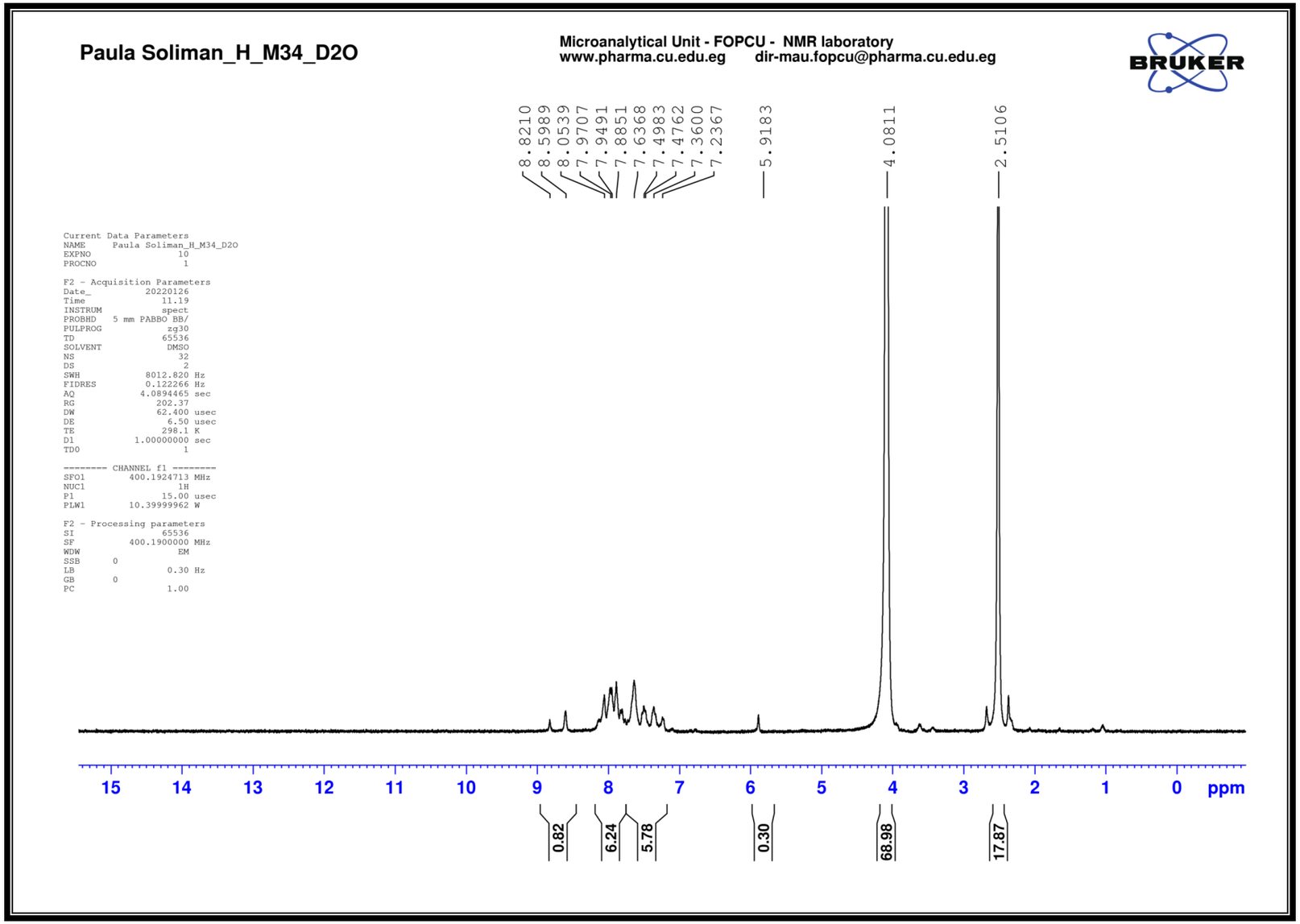
^{13}C-NMR of *N*-(4-(4-chlorophenyl)-6-(3-methyl-5-phenyl-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (13c).



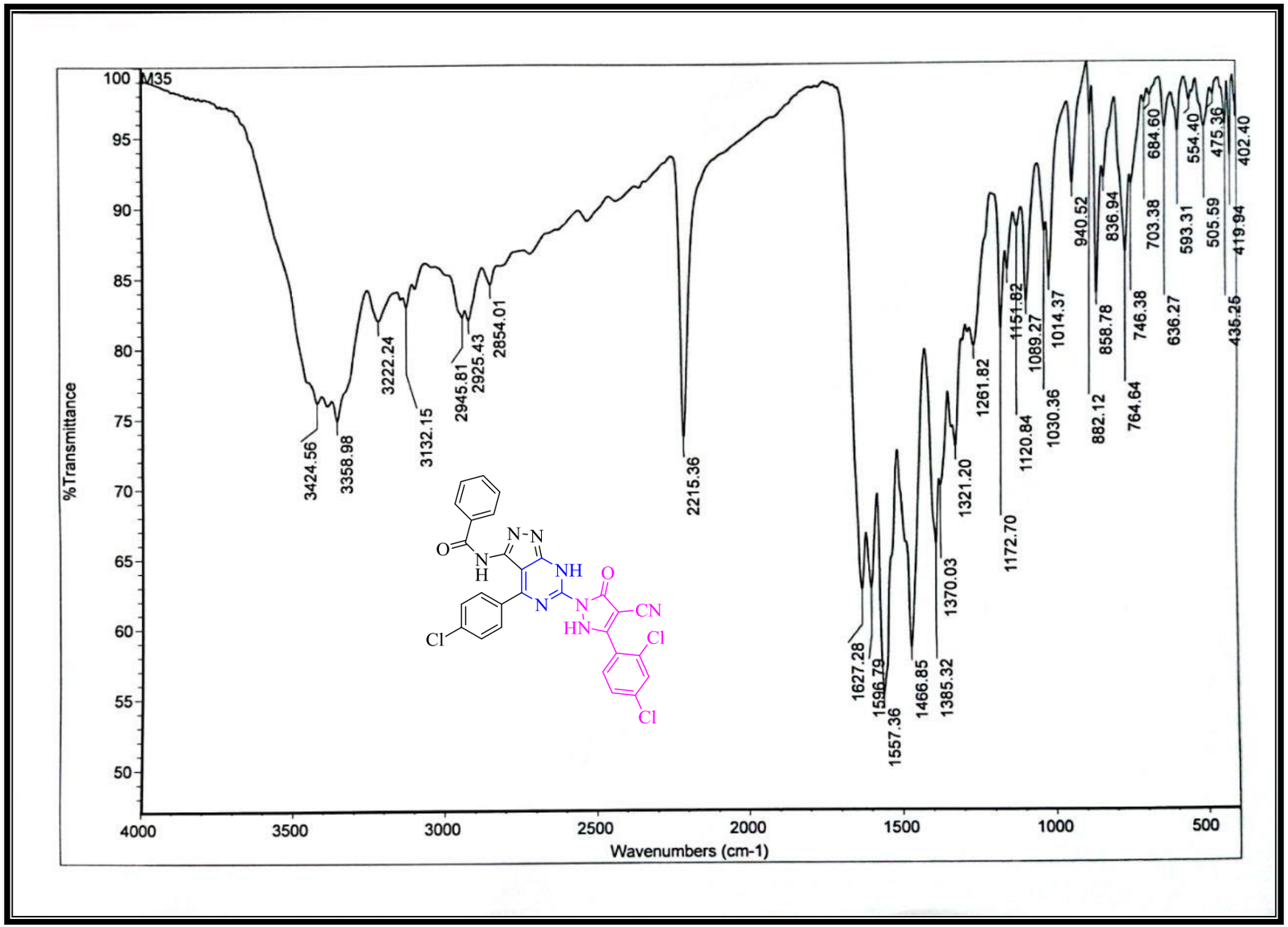
IR of *N-(4-(4-chlorophenyl)-6-(5-(2,4-dichlorophenyl)-3-phenyl-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide* (14).



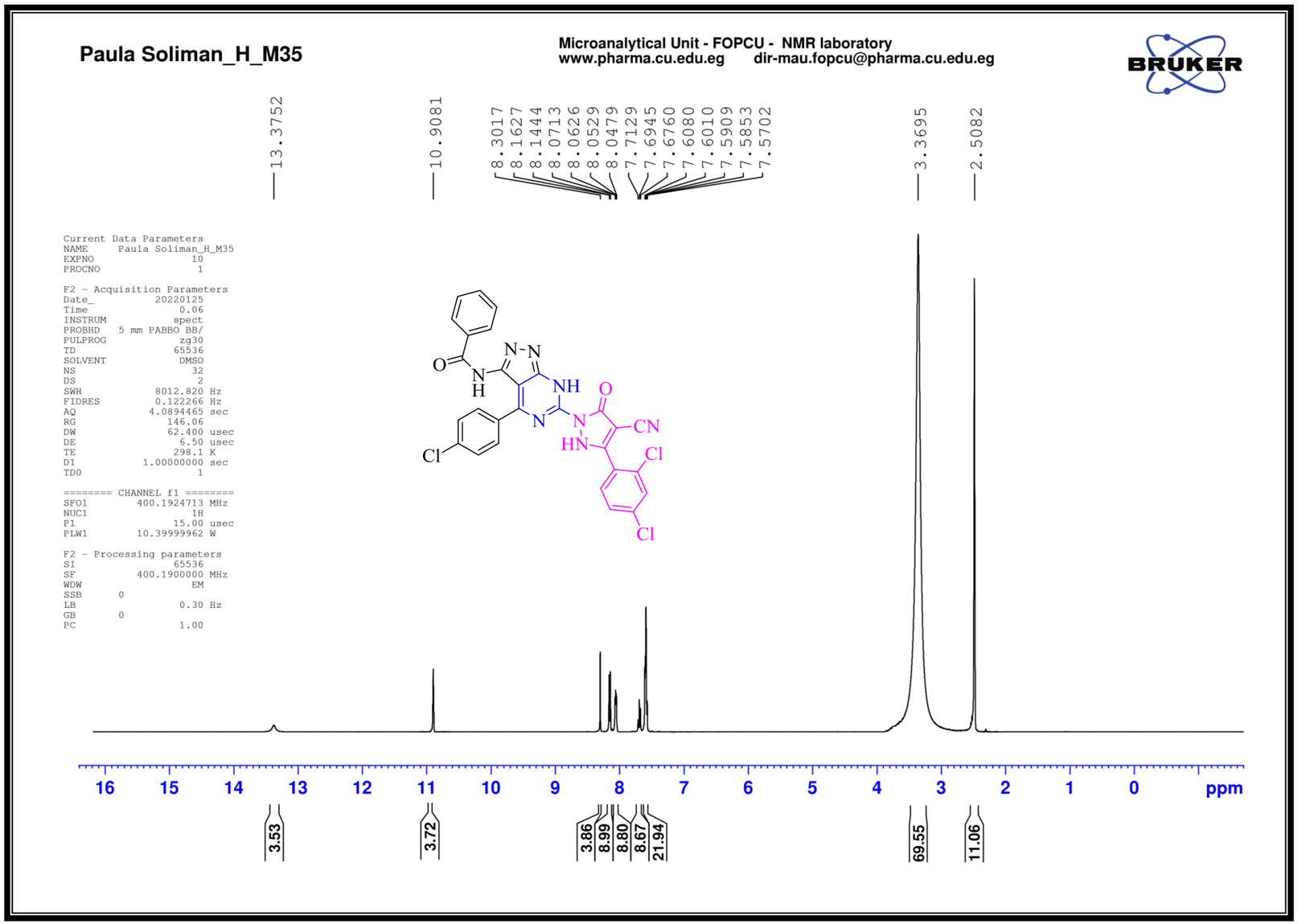
^{1}H-NMR of *N-(4-(4-chlorophenyl)-6-(5-(2,4-dichlorophenyl)-3-phenyl-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide* (14).



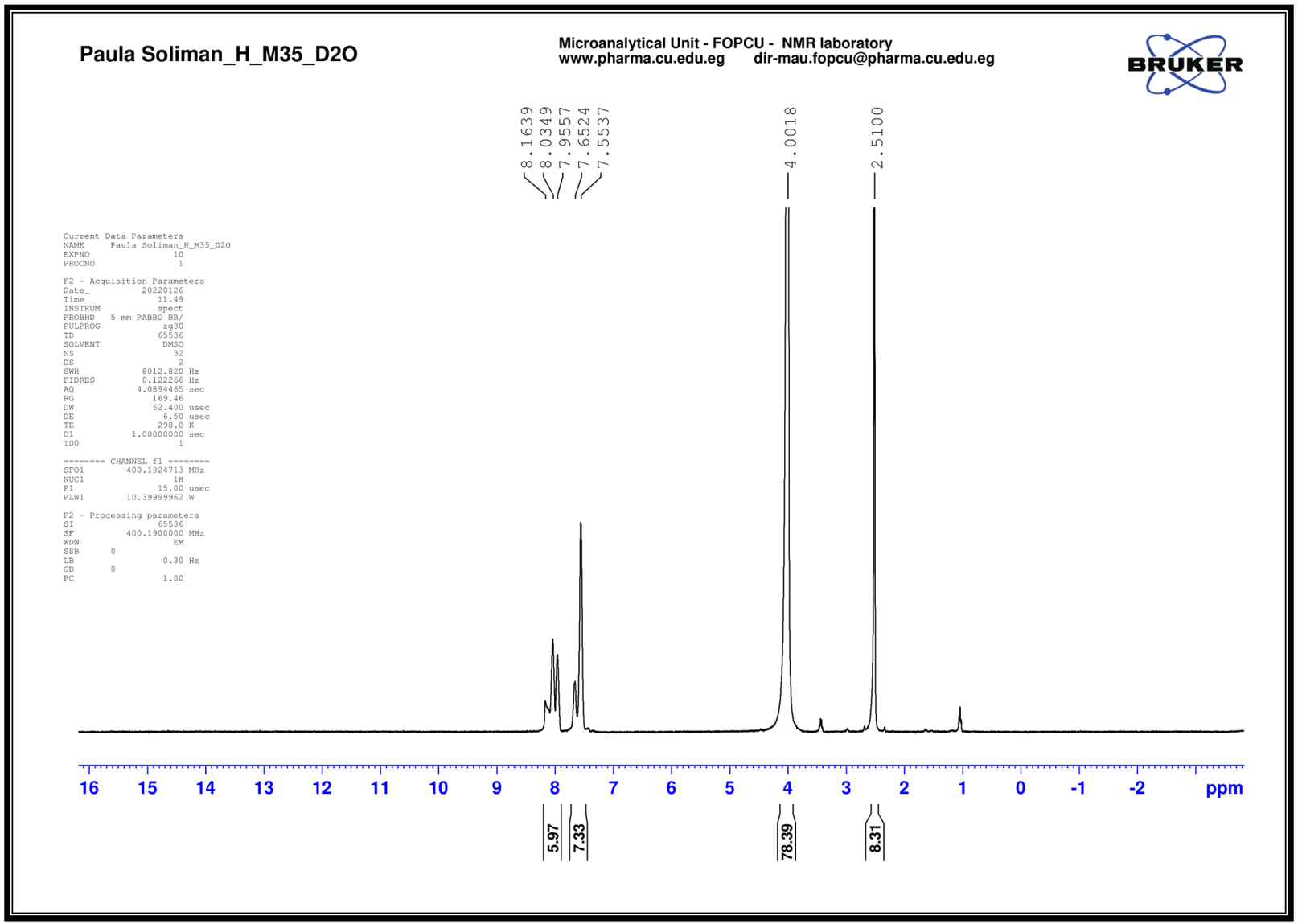
D_2O of *N-(4-(4-chlorophenyl)-6-(5-(2,4-dichlorophenyl)-3-phenyl-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide* (14).



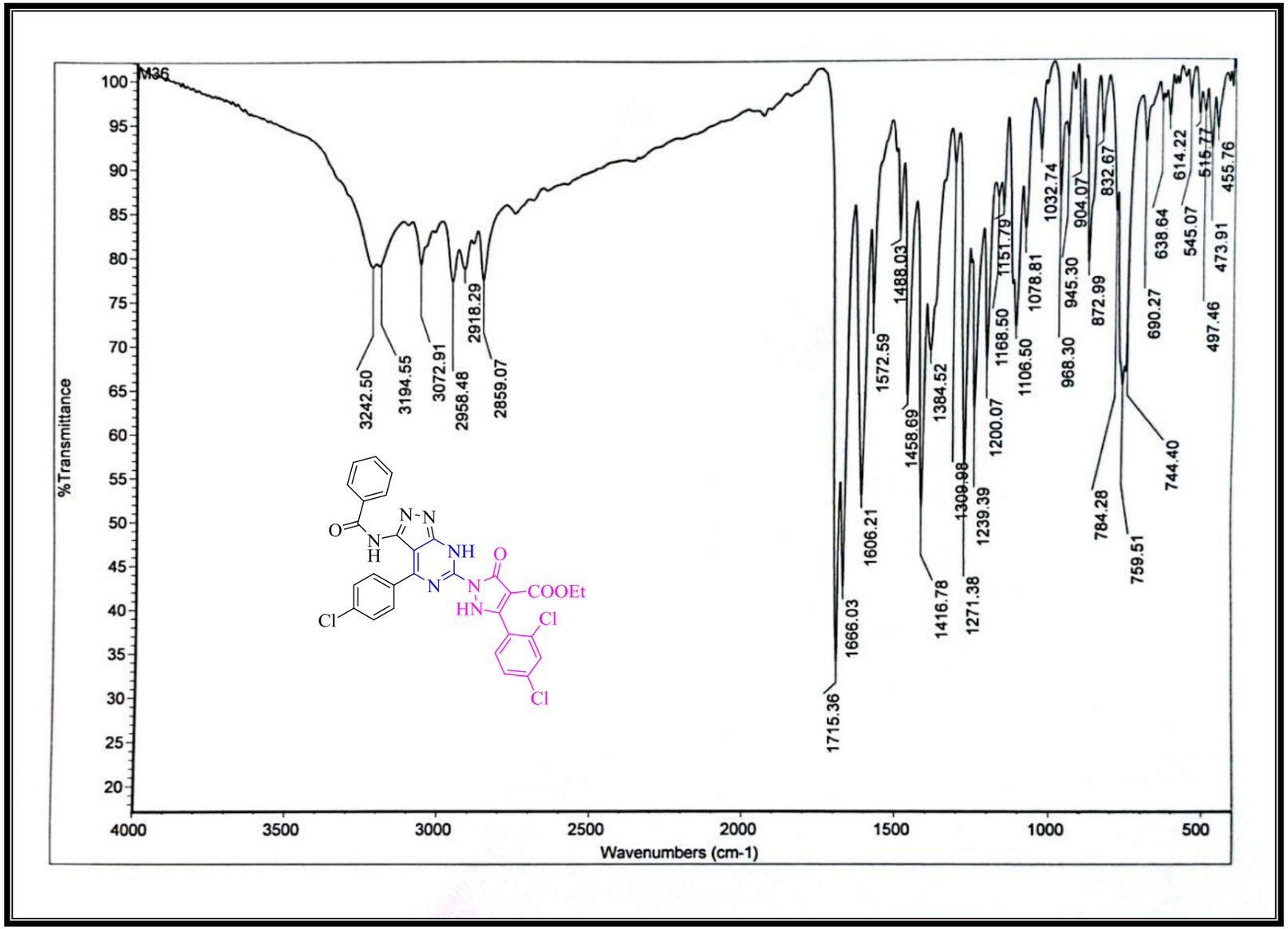
IR of *N-(4-(4-chlorophenyl)-6-(4-cyano-5-(2,4-dichlorophenyl)-3-oxo-2,3-dihydro-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (15).*



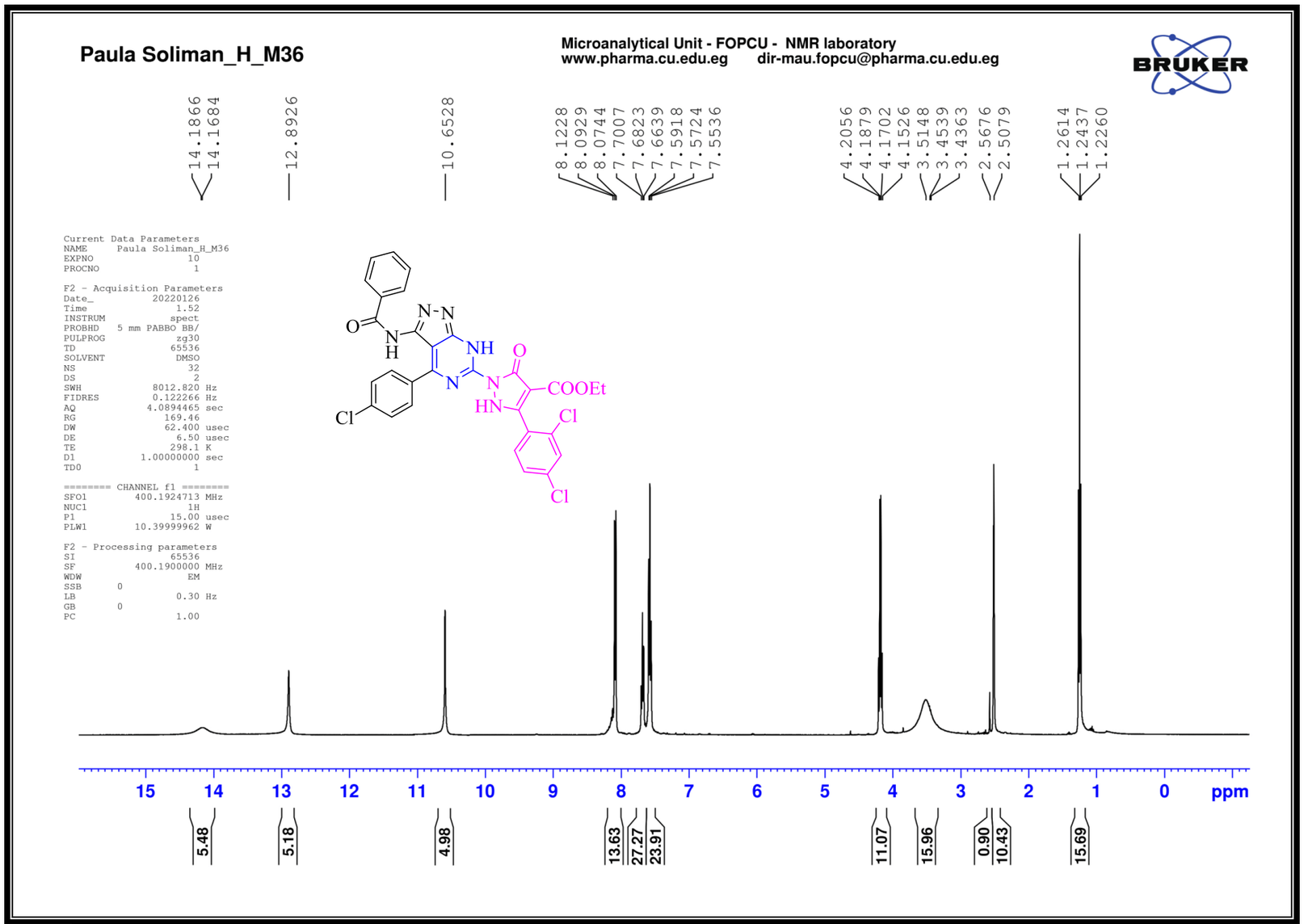
^{1}H-NMR of *N-(4-(4-chlorophenyl)-6-(4-cyano-5-(2,4-dichlorophenyl)-3-oxo-2,3-dihydro-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (15).*



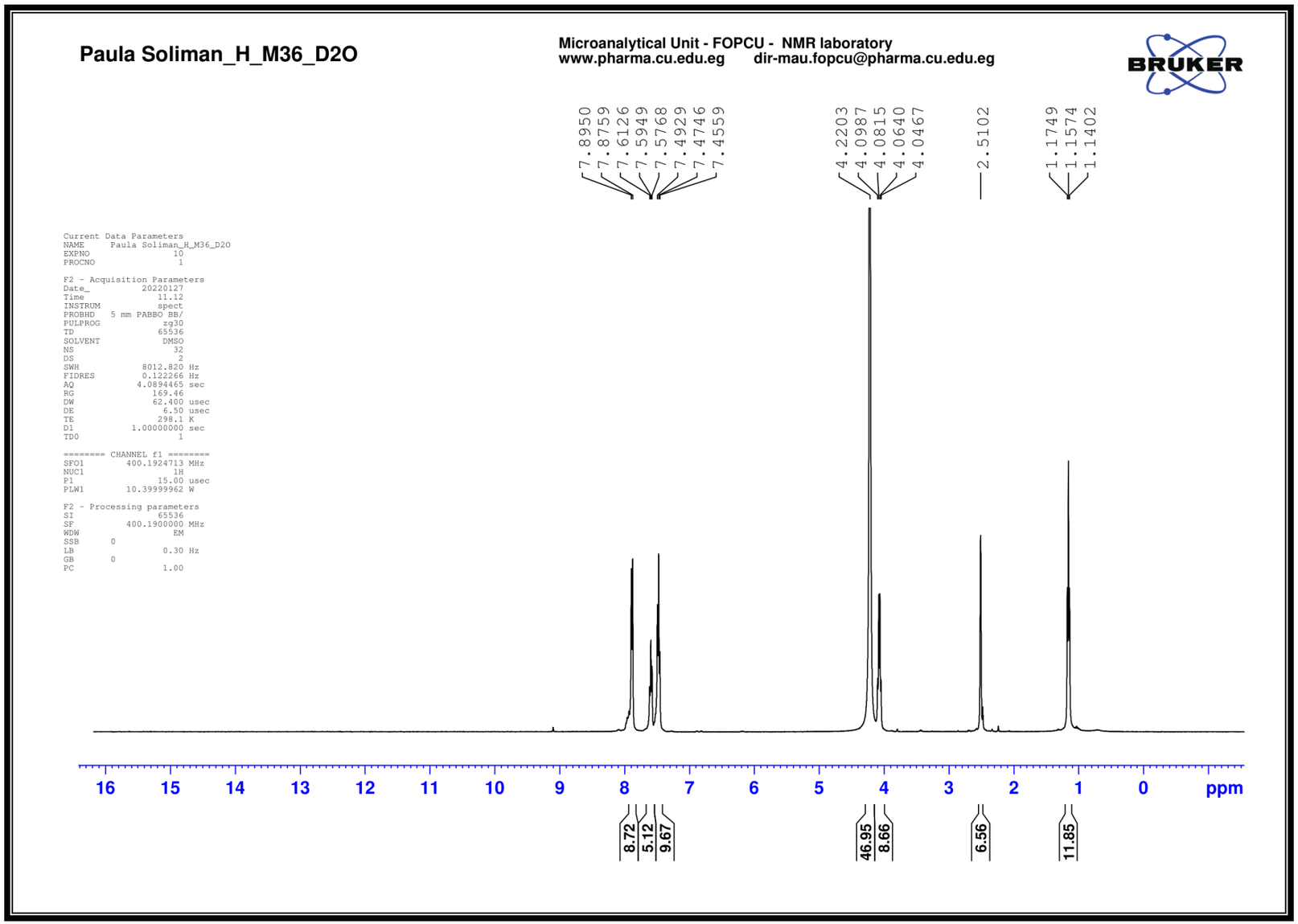
D_2O of *N-(4-(4-chlorophenyl)-6-(4-cyano-5-(2,4-dichlorophenyl)-3-oxo-2,3-dihydro-1H-pyrazol-1-yl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (15).*



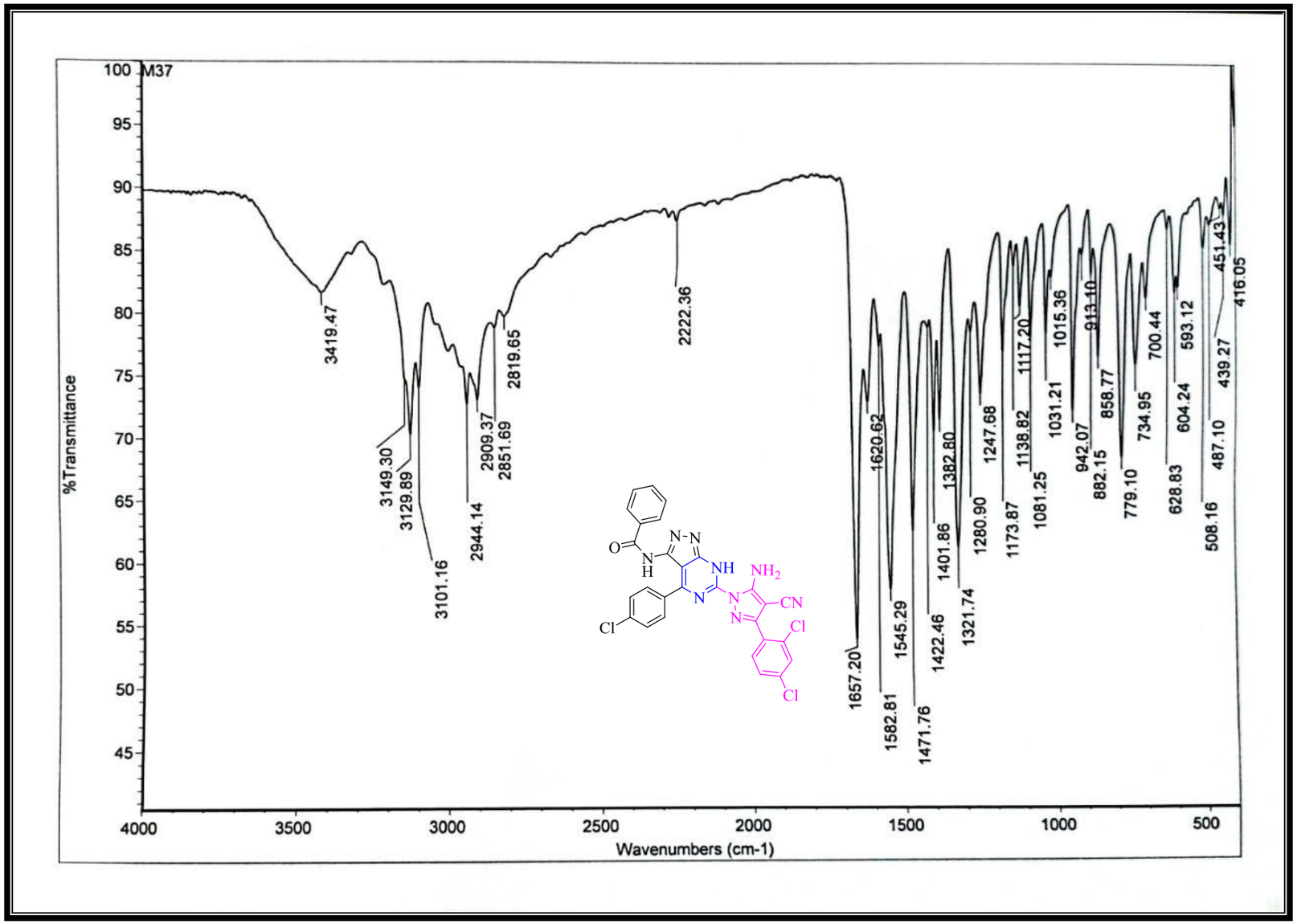
IR of *Ethyl 1-(3-benzamido-4-(4-chlorophenyl)-7H-pyrazolo[3,4-d]pyrimidin-6-yl)-5-(2,4-dichlorophenyl)-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxylate (16).*



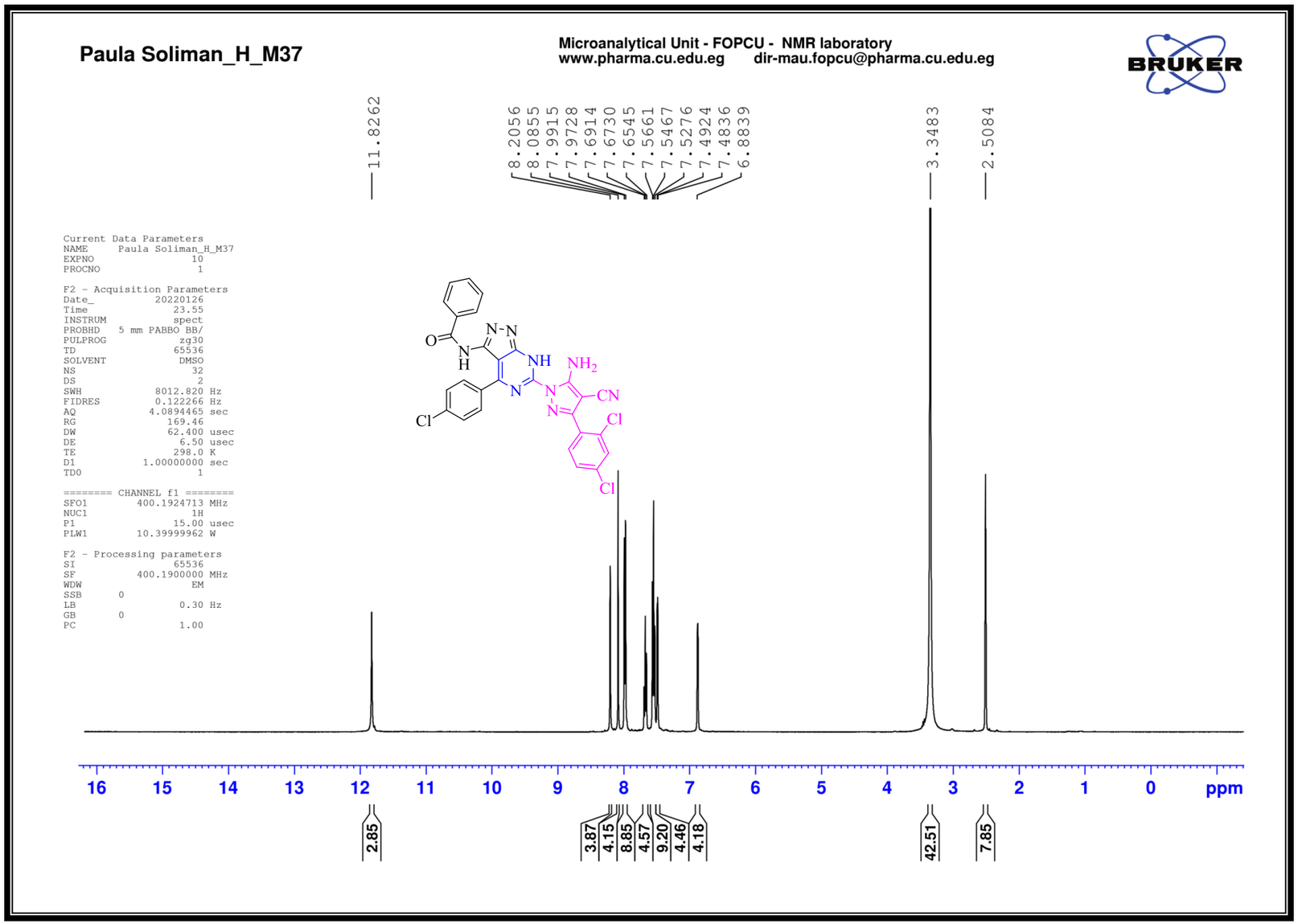
^{1}H-NMR of *Ethyl 1-(3-benzamido-4-(4-chlorophenyl)-7H-pyrazolo[3,4-d]pyrimidin-6-yl)-5-(2,4-dichlorophenyl)-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxylate (16).*



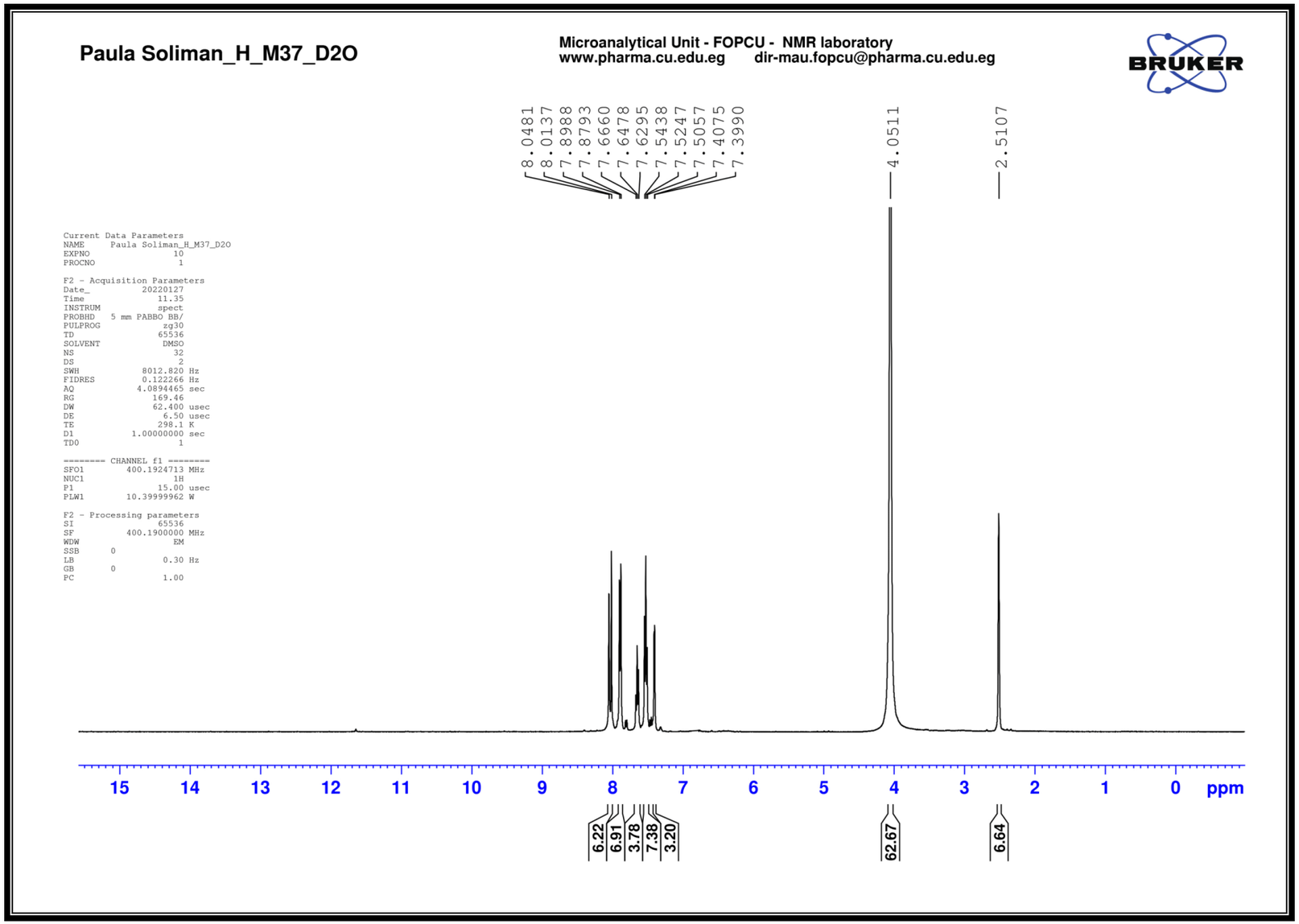
D_2O of *Ethyl 1-(3-benzamido-4-(4-chlorophenyl)-7H-pyrazolo[3,4-d]pyrimidin-6-yl)-5-(2,4-dichlorophenyl)-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxylate (16).*



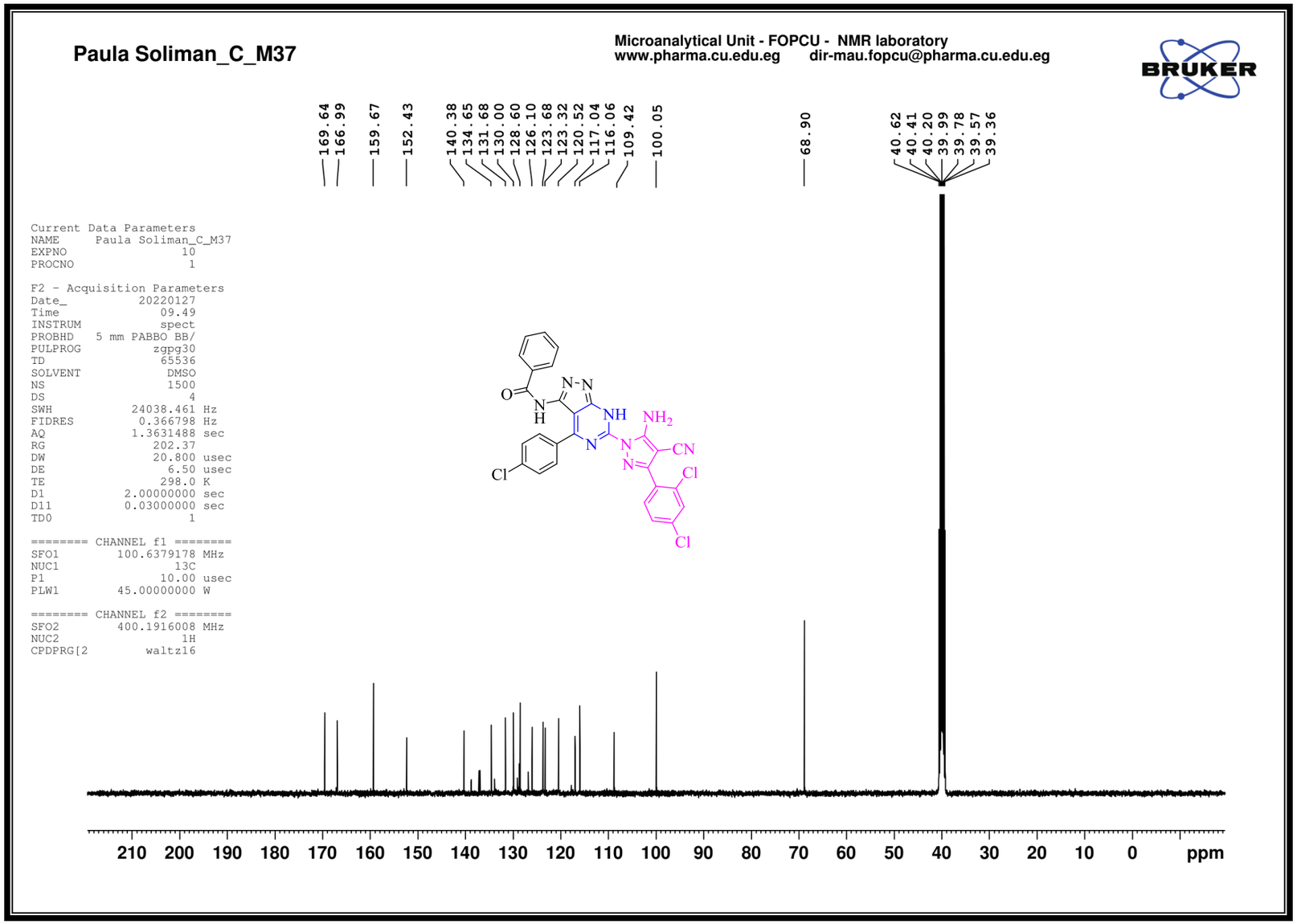
IR of *N-(6-(3-amino-4-cyano-5-(2,4-dichlorophenyl)-1H-pyrazol-1-yl)-4-(4-chlorophenyl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (17).*



D_2O of *N-(6-(3-amino-4-cyano-5-(2,4-dichlorophenyl)-1H-pyrazol-1-yl)-4-(4-chlorophenyl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (17).*

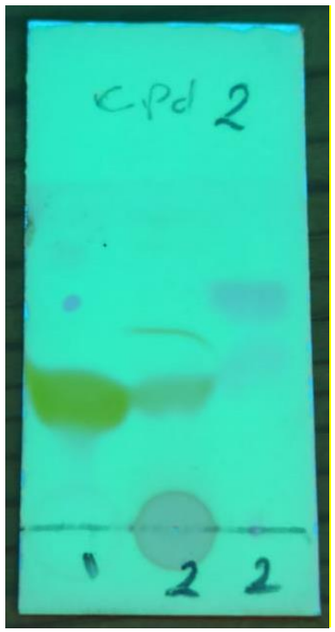


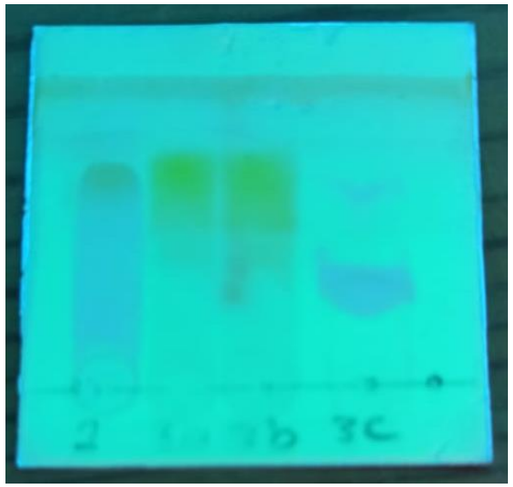
D_2O of *N-(6-(3-amino-4-cyano-5-(2,4-dichlorophenyl)-1H-pyrazol-1-yl)-4-(4-chlorophenyl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (17).*

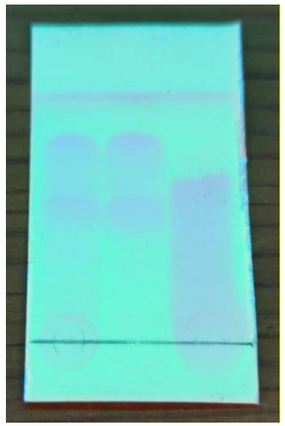
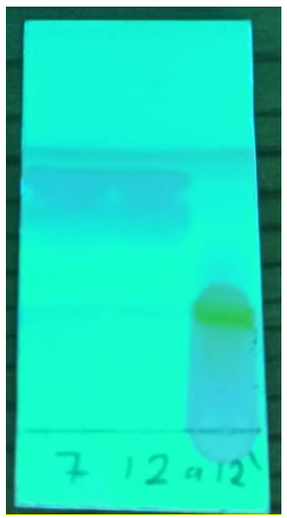


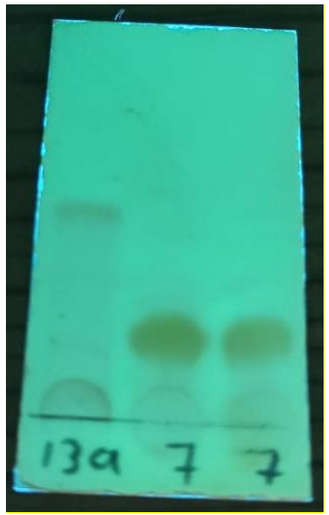
^{13}C-NMR of *N-(6-(3-amino-4-cyano-5-(2,4-dichlorophenyl)-1H-pyrazol-1-yl)-4-(4-chlorophenyl)-7H-pyrazolo[3,4-d]pyrimidin-3-yl)benzamide (17).*

1.2. Impurity Profile

	**TLC following up for synthesizing compound 2.** TLC (Thin Layer Chromatography) monitoring process for the synthesis of Compound **2**. TLC is a common technique used in organic chemistry to monitor the progress of a reaction and to check the purity of reaction mixtures. **Spot (1): Compound 1 reactant.** This is the starting material, Compound 1, before any reaction has taken place. It serves as a reference point to compare with subsequent spots. **Spot (2): After 1hr.** After 1 hour, we have a new spot on the TLC plate. This indicates the presence of a new compound formed during the reaction or a change in the starting material. **Spot (3): After reaction completion 3hr.** After 3 hours, we have another spot. This could indicate the formation of the desired Compound **2** or possibly other by-products. The movement of this spot on the TLC plate was provide information about the progress of the reaction and the purity of the final product.

	**TLC following up for synthesizing compound 3.** TLC (Thin Layer Chromatography) monitoring process for the synthesis of Compound **3**. **Spot (1): Compound 2 reactant.** This is the starting material, Compound **2**, before any reaction has taken place. It serves as a reference point to compare with subsequent spots. **Spot (2): After 1hr.** **After 1hr, there is no changing in reaction, but the color was changed.** it suggested that there might be a transformation or reaction occurring in the mixture. The change in color could indicate the formation of an intermediate or a by-product that is not separated well on the TLC plate. **Spot (3): After 2.5hr.** After 2.5 hour, we have a new spot on the TLC plate. This indicates the presence of a new compound formed during the reaction or a change in the starting material. **Spot (4): After reaction completion 5hr.** After 5 hours, we have another spot. This could indicate the formation of the desired Compound **3** or possibly other by-products. The movement of this spot on the TLC plate was provide information about the progress of the reaction and the purity of the final product.

	**TLC following up for synthesizing compound 10.** TLC (Thin Layer Chromatography) monitoring process for the synthesis of Compound **10**. **Spot (1): Compound 7 reactant.** This is the starting material, Compound **7**, before any reaction has taken place. It serves as a reference point to compare with subsequent spots. **Spot (2): After 30 min.** After 0.5 hour, we have not any new spot on the TLC plate. **Spot (3): After reaction completion 1.5hr.** After 3 hours, we have another spot. This could indicate the formation of the desired Compound **10** or possibly other by-products. The movement of this spot on the TLC plate was provide information about the progress of the reaction and the purity of the final product.
	**TLC following up for synthesizing compound 12.** TLC (Thin Layer Chromatography) monitoring process for the synthesis of Compound **12**. **Spot (1): Compound 7 reactant.** This is the starting material, Compound **7**, before any reaction has taken place. It serves as a reference point to compare with subsequent spots. **Spot (2): After 4hr.** After 4 hours, we have not any new spot on the TLC plate. **Spot (3): After reaction completion 15hr.** After 15 hours, we have another spot and changing in color. This could indicate the formation of the desired Compound **12** or possibly other by-products. The movement of this spot on the TLC plate was provide information about the progress of the reaction and the purity of the final product.

	**TLC following up for synthesizing compound 13a.** TLC (Thin Layer Chromatography) monitoring process for the synthesis of Compound **13a**. **Spot (1): Compound 7 reactant.** This is the starting material, Compound **7**, before any reaction has taken place. It serves as a reference point to compare with subsequent spots. **Spot (2): After 1hr.** **After 1hr, there is no changing in reaction, but the color was changed.** it suggested that there might be a transformation or reaction occurring in the mixture. The change in color could indicate the formation of an intermediate or a by-product that is not separated well on the TLC plate. **Spot (3): After reaction completion 3hr.** After 3 hours, we have another spot and changing in color. This could indicate the formation of the desired Compound **13a** or possibly other by-products. The movement of this spot on the TLC plate was provide information about the progress of the reaction and the purity of the final product.

2. *Biological Evaluation*

2.1. Results of in-vitro primary single dose (10 µM) full NCI 60 cell panel assay

Table S1: *In vitro* NCI 60 cell line anticancer screening results of compounds (2-17) at single dose of10 µM presented as percent cell growth promotion.

Panel/Cell Line	2	3	4	5	6	7	8	9	10	12	13a	13b	13c	14	15	16	17
Leukemia																	
CCRF-CEM	94.83	98.69	23.29	98.53	93.09	92.90	91.31	90.33	96.13	101.27	97.83	87.17	96.28	88.09	30.10	22.60	106.80
HL-60(TB)	96.07	100.71	31.92	93.69	94.10	92.51	93.19	101.91	98.02	116.88	101.08	101.67	111.51	86.24	**7.37**	**5.63**	124.44
K-562	97.62	99.49	26.48	82.62	87.33	98.76	87.44	90.78	100.26	100.16	104.53	89.52	93.99	96.74	12.36	11.14	95.51
MOLT-4	99.99	105.81	32.81	99.48	99.11	106.99	100.82	105.01	107.09	103.25	107.67	94.76	97.39	95.53	20.53	**2.13**	102.78
RPMI-8226	96.30	93.31	44.42	82.25	91.81	96.54	92.04	84.29	93.25	102.22	95.01	89.10	96.03	89.71	33.50	18.74	89.84
SR	91.60	86.05	18.16	84.90	83.15	90.92	75.24	87.02	89.30	101.38	67.82	85.36	94.11	88.85	25.67	**7.20**	85.43
Non-Small Cell Lung Cancer																	
A549/ATCC	96.74	107.60	57.21	105.81	103.64	102.29	96.48	109.95	102.91	100.71	104.21	103.13	93.11	82.97	24.58	7.56	96.54
EKVX	92.70	88.97	53.79	100.14	93.30	104.04	98.39	101.98	94.95	97.94	93.87	98.49	95.31	84.89	33.37	10.76	95.23
HOP-62	94.66	85.55	31.12	89.52	81.17	95.54	64.56	101.37	97.03	101.85	96.74	85.54	98.05	100.72	3.58	18.76	102.92
HOP-92	90.41	85.52	57.19	109.22	**-95.03**	94.90	86.33	119.49	98.20	101.99	75.56	106.45	93.70	91.32	56.77	32.34	131.97
NCI-H226	85.25	79.08	23.77	91.05	100.46	108.85	105.79	106.79	94.00	93.67	91.42	94.47	93.79	88.56	19.84	32.16	100.40
NCI-H23	96.86	97.22	58.58	94.27	97.18	99.99	88.54	100.09	94.95	102.42	94.01	101.05	102.17	90.23	**1.50**	**-7.61**	100.05
NCI-H322M	101.11	98.93	40.04	96.60	98.84	98.93	98.62	108.20	100.81	95.94	106.85	91.73	80.29	89.01	29.53	24.98	90.32
NCI-H460	99.15	99.35	15.80	97.54	114.75	99.95	111.61	110.25	107.98	104.77	83.25	91.98	98.32	93.32	6.93	**4.04**	93.04
NCI-H522	104.48	92.01	13.23	73.34	92.57	95.30	94.71	47.89	105.75	90.58	76.48	93.50	88.74	82.72	**-9.93**	**-30.52**	99.02
Colon Cancer																	
COLO 205	122.30	126.57	115.51	99.18	N/A	N/A	N/A	N/A	N/A	11.12	N/A	119.94	124.17	103.43	**-36.06**	**-62.28**	126.27
HCC-2998	98.77	87.10	54.12	94.24	107.34	107.13	109.22	115.43	108.45	102.64	92.99	112.81	102.70	96.22	**3.16**	**-5.78**	108.53
HCT-116	99.08	98.77	38.32	99.26	97.35	98.83	92.71	101.24	94.82	98.26	84.77	88.28	100.11	100.33	**9.09**	**-19.42**	114.28
HCT-15	97.81	100.90	31.74	89.18	99.99	101.83	95.72	90.85	101.89	100.02	96.02	81.15	89.80	69.26	16.72	**-29.73**	87.90
HT29	104.66	99.79	49.25	109.24	112.25	105.22	117.20	118.60	110.67	101.75	75.73	108.21	113.56	86.65	13.25	**0.19**	104.59
KM12	98.46	99.34	39.89	100.26	100.10	100.33	97.87	104.51	99.12	105.35	96.53	99.97	101.77	82.91	27.56	**-6.67**	91.89
	102.58	100.91	48.91	96.40	105.09	106.80	106.16	105.66	101.45	101.55	95.15	96.99	101.44	96.95	22.91	**4.14**	115.86

SW-620																	
CNS Cancer																	
SF-268	92.78	92.82	42.17	97.39	101.14	109.39	102.95	115.73	100.95	95.36	98.10	92.69	93.17	89.88	38.66	23.77	95.90
SF-295	101.73	91.93	50.97	94.77	96.18	102.91	79.18	102.28	101.57	92.09	77.21	94.46	91.01	86.43	**-13.87**	16.19	98.58
SF-539	94.69	96.21	46.40	93.99	91.46	96.38	85.37	101.85	96.76	92.70	87.68	92.91	94.70	93.28	**-63.68**	**-4.38**	92.81
SNB-19	95.31	94.30	32.65	91.18	85.25	93.80	75.64	89.33	92.11	94.16	86.94	91.59	90.49	93.83	31.06	N/A	93.68
SNB-75	68.54	63.79	50.42	84.72	95.26	92.24	89.00	110.12	82.92	N/A	48.37	N/A	N/A	N/A	N/A	29.18	N/A
U251	106.76	108.54	48.70	102.25	96.68	96.84	72.78	103.09	101.00	98.14	87.92	81.65	93.06	92.89	**6.80**	**2.68**	98.32
Prostate Cancer																	
PC-3	92.80	100.67	64.50	104.19	76.29	91.66	94.23	101.31	100.60	96.44	93.79	104.03	96.90	88.28	**6.40**	**-11.29**	110.58
DU-145	100.21	101.08	57.23	99.76	106.08	103.18	100.37	105.62	102.59	110.21	106.16	103.32	102.74	88.08	**7.01**	25.71	102.24
Melanoma																	
LOX IMVI	103.64	109.00	42.53	86.93	104.68	113.53	111.35	118.10	120.02	102.68	102.28	86.82	99.19	64.62	**5.24**	**-98.48**	100.58
MALME-3M	89.06	92.15	77.76	85.07	92.71	98.52	98.52	96.01	93.51	99.02	77.76	90.10	97.01	78.85	13.66	**-26.04**	101.81
M14	100.84	104.34	58.48	98.30	96.79	101.63	106.98	101.24	99.56	106.99	68.24	91.77	103.38	99.11	**-3.96**	**-43.66**	110.64
MDA-MB-435	100.22	101.16	56.43	98.75	102.63	103.18	103.14	103.52	100.51	99.74	60.00	99.03	97.31	91.58	**-44.38**	**-19.82**	98.92
SK-MEL-2	107.90	104.91	68.94	106.88	107.49	114.78	107.52	114.65	112.83	N/A	86.36	N/A	N/A	N/A	N/A	N/A	N/A
SK-MEL-28	104.18	109.73	48.12	101.54	105.62	105.67	117.02	110.59	111.47	108.39	104.33	92.56	96.21	101.18	53.82	14.35	111.46
SK-MEL-5	96.17	96.28	45.80	97.12	98.91	101.48	97.35	100.14	97.72	98.29	87.86	97.39	78.50	85.74	**0.62**	**-98.61**	99.78
UACC-257	106.34	104.22	92.43	105.68	98.82	103.24	104.92	106.74	101.95	101.90	85.19	98.17	98.83	95.90	69.66	20.20	101.52
UACC-62	101.15	99.07	34.05	92.36	94.17	102.03	93.48	105.00	102.19	92.41	76.79	81.08	77.80	66.26	30.11	14.34	82.10
Ovarian Cancer																	
IGROV1	107.22	94.63	40.42	92.51	103.69	100.11	97.46	108.76	118.34	107.33	114.60	109.70	98.36	105.25	26.52	21.89	79.48
OVCAR-3	103.53	104.06	43.93	100.18	112.27	116.73	118.44	117.20	109.37	99.52	119.45	88.82	83.64	92.11	13.52	22.67	86.29
OVCAR-4	100.29	99.72	50.29	94.24	94.57	99.87	96.78	95.36	96.94	95.85	107.35	105.40	103.92	110.87	24.85	11.33	124.63
OVCAR-5	108.44	101.17	66.28	101.03	108.97	103.51	116.32	124.46	121.99	107.66	119.50	98.34	99.65	95.47	11.08	16.48	104.56
OVCAR-8	103.71	99.82	44.43	101.87	98.76	106.16	91.58	105.53	107.40	106.60	102.37	77.28	102.05	89.60	**-23.25**	**-29.69**	109.59
SK-OV-3	105.38	94.69	53.65	94.55	82.59	108.44	99.27	108.33	103.02	98.01	110.38	108.15	97.84	100.62	**-5.94**	19.95	122.91
Renal Cancer																	
786-0	99.74	98.38	53.59	100.76	95.31	98.47	72.41	103.37	96.85	103.31	96.19	101.95	97.92	9187	**2.33**	**7.00**	108.46
A498	97.35	107.99	78.80	108.37	117.20	114.49	100.97	106.14	110.45	107.21	119.30	114.54	92.09	90.13	79.21	72.50	121.58
ACHN	96.67	98.73	40.45	100.60	95.15	108.39	78.81	107.17	104.39	100.49	99.37	98.74	91.99	86.67	30.39	12.53	103.15
CAKI-1	91.05	83.81	42.20	90.47	73.15	93.81	74.07	89.09	89.14	90.66	73.94	90.95	97.65	67.05	23.90	13.72	92.68
RXF 393	90.88	99.21	60.61	119.24	101.47	99.66	87.59	105.02	97.16	101.35	102.77	99.76	84.07	96.81	**-35.47**	**-13.52**	101.96
SN12C	100.19	96.56	41.15	97.91	92.38	92.59	97.13	103.53	104.12	95.28	92.42	91.64	87.09	85.07	32.54	**-17.37**	95.19
TK-10	111.70	153.37	51.69	125.43	117.29	138.75	119.03	111.54	120.34	103.45	115.33	108.56	101.92	106.30	56.23	64.00	115.88
UO-31	90.47	89.92	29.60	83.88	64.68	87.99	91.27	82.24	88.29	94.00	75.46	87.58	80.19	76.65	24.46	17.31	95.86

Breast Cancer																	
MCF7	91.49	76.58	52.11	92.64	96.19	96.76	84.28	89.01	91.37	91.32	88.21	88.85	58.32	82.43	16.66	**067**	16.51
MDA-MB 231/ATCC	91.26	86.07	53.75	93.92	80.10	77.04	67.92	94.26	96.33	101.89	74.22	106.69	94.23	72.00	**-20.77**	**-4.05**	86.28
HS 578T	96.37	89.15	58.21	92.60	86.73	95.88	74.01	101.05	97.55	93.77	79.95	93.59	70.46	90.47	**-0.63**	17.55	90.40
BT-549	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	104.29	N/A	99.47	100.35	118.95.	33.47	27.07	120.88
T-47D	98.15	76.23	48.83	89.21	82.52	97.21	89.56	97.61	100.40	95.87	82.28	102.42	84.32	79.14	24.07	**7.66**	74.02
MDA-MBA-468	91.65	97.02	46.12	96.77	100.38	118.11	106.25	120.31	100.53	96.49	101.68	92.87	72.00	99.03	**-36.27**	**-21.38**	**-12.76**
Mean	98.21	97.40	47.92	96.62	93.18	101.29	94.86	102.81	101.25	100.27	92.06	96.21	93.96	90.12	**13.44**	**2.30**	98.35

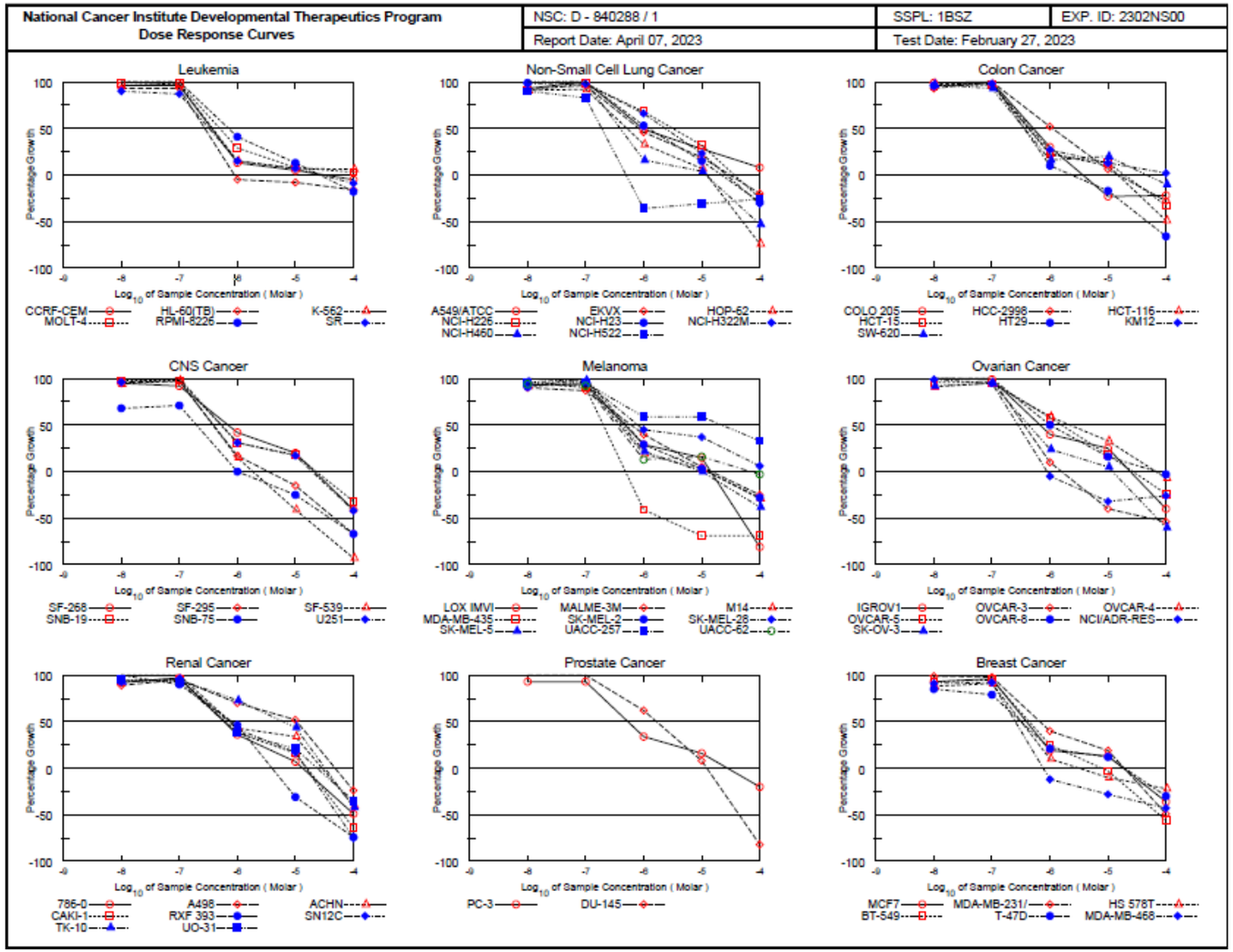
* Results are presented as percent cell growth promotion.
* Values less than 10% growth promotion are presented in bold.

2.2. Five Doses

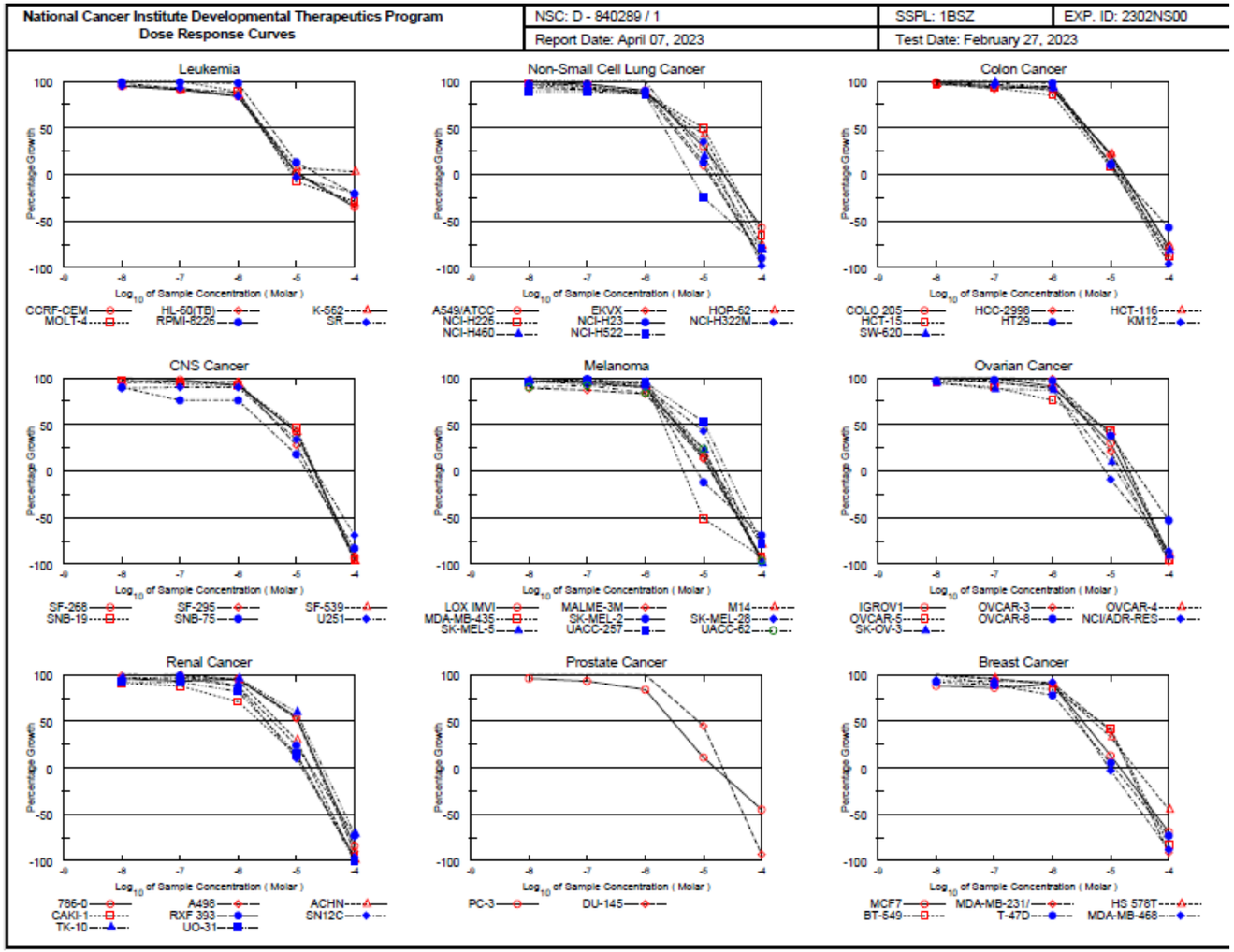
Table S2: ***In vitro*** **NCI 5 log dose results for compounds (15 and 16) in μM against 60 cell panel.**

Panel	Cell Line	Compound 15			Compound 16		
		GI_{50}	TGI	LC_{50}	GI_{50}	TGI	LC_{50}
Leukemia	**CCRF-CEM**	3.58	3.28	>100	2.60	1.09	>100
	HL-60(TB)	2.74	8.88	>100	2.76	1.12	>100
	K-562	3.79	>100	>100	2.76	>100	>100
	MOLT-4	5.03	>100	>100	2.54	8.36	>100
	RPMI-8226	7.20	2.69	>100	3.65	2.40	>100
	SR	3.26	2.80	>100	2.47	9.23	>100
Non-Small Cell Lung Cancer	**A549/ATCC**	**9.63**	>100	>100	4.62	2.20	8.29
	EKVX	**8.44**	3.06	>1005.	3.01	1.24	3.97
	HOP-62	**5.14**	1.21	00	6.99	2.29	5.96
	HOP-92	**ND**	ND	ND	ND	ND	ND
	NCI-H226	**3.17**	3.58	>100	9.98	2.71	7.36
	NCI-H23	**1.18**	2.18	>100	3.27	1.33	4.10
	NCI-H322M	**2.40**	2.71	>100	5.30	1.83	4.35
	NCI-H460	**3.92**	1.16	8.76	4.54	1.59	4.91
	NCI-H522	**1.89**	4.97	>100	2.12	5.99	2.88
Colon Cancer	**COLO 205**	5.251.	3.69	>100	4.02	1.67	5.25
	HCC-2998	11	1.53	>100	3.97	1.52	4.33
	HCT-116	4.30	1.50	>100	3.92	1.68	5.30
	HCT-15	4.18	1.95	>100	2.86	1.21	4.09
	HT29	3.83	2.38	4.75	3.48	1.40	7.79
	KM12	4.72	>100	>100	3.40	1.29	3.73
	SW-620	3.63	4.62	>100	3.33	1.31	4.50
CNS Cancer	**SF-268**	6.95	2.16	>100	6.98	2.07	4.88
	SF-295	3.88	3.43	4.80	4.77	1.70	4.37
	SF-539	3.82	1.86	1.47	6.85	2.00	4.60
	SNB-19	5.19	2.27	>100	8.31	2.12	4.79
	SNB-75	2.00	1.01	3.85	2.77	1.50	4.68
	U251	5.38	1.97	>100	5.20	2.15	6.60

Melanoma	**LOX IMVI**	4.79	1.42	4.70	3.43	1.39	4.03
	MALME-3M	6.06	1.50	>100	2.93	1.31	3.81
	M14	3.88	1.26	>100	3.61	1.53	5.03
	MDA-MB-435	2.03	4.88	2.13	2.06	4.52	9.91
	SK-MEL-2	5.05	1.26	>100	2.58	7.75	4.69
	SK-MEL-28	7.99	>100	>100	7.01	2.02	4.58
	SK-MEL-5	4.24	9.51	>100	4.21	1.54	3.97
	UACC-257	2.18	>100	>100	1.05	2.53	6.10
	UACC-62	3.39	7.29	>100	3.72	1.59	4.13
Ovarian Cancer	**IGROV1**	6.87	2.44	>100	4.77	1.79	4.69
	OVCAR-3	3.94	1.57	4.91	4.25	1.51	4.01
	OVCAR-4	2.28	6.79	>100	6.67	2.09	5.05
	OVCAR-5	1.59	2.68	>100	6.52	2.06	4.68
	OVCAR-8	1.03	7.13	>100	6.34	2.62	9.19
	NCI/ADR-RES	2.82	8.87	>100	2.52	8.13	3.42
	SK-OV-3	4.30	1.19	7.10	3.00	1.25	3.91
Renal Cancer	**786-0**	5.90	1.32	>100	1.08	2.48	5.70
	A498	1.07	4.83	>100	1.05	2.35	5.25
	ACHN	7.68	2.88	>100	4.86	1.71	4.15
	CAKI-1	6.27	1.58	6.68	2.33	1.35	3.89
	RXF 393	8.10	3.93	2.71	3.96	1.78	5.84
	SN12C	7.20	1.53	5.31	3.05	1.25	3.69
	TK-10	6.32	3.24	>100	1.20	2.88	6.90
	UO-31	6.11	2.39	>100	2.98	1.35	3.68
Prostate Cancer	**PC-3**	**5.36**	2.80	>100	2.92	1.58	>100
	DU-145	**1.65**	1.22	4.39	8.09	2.11	4.88



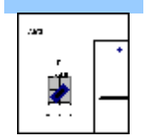
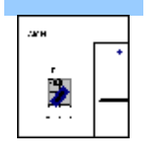
Dose response curve for compound 15.

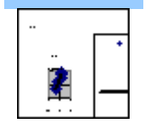


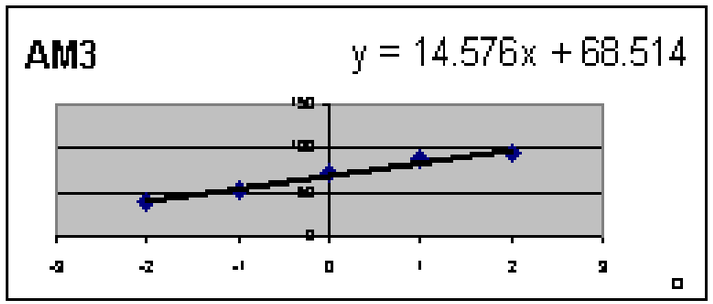
Dose response curve for compound 16.

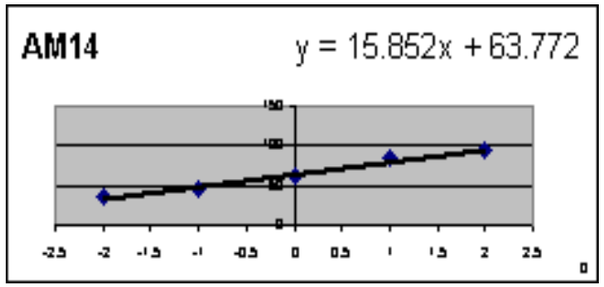
2.3. In vitro EGFR tyrosine kinase inhibitory activity

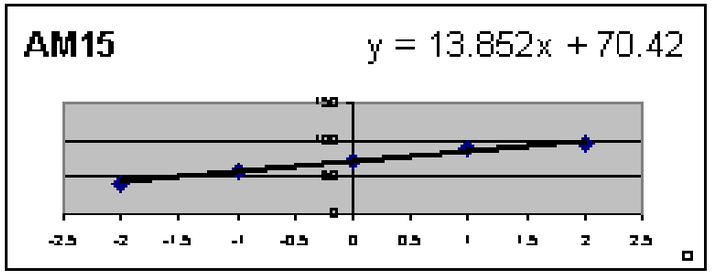
Table 3S: Epidermal growth factor receptor biological activity of compounds (4, 15 and 16).

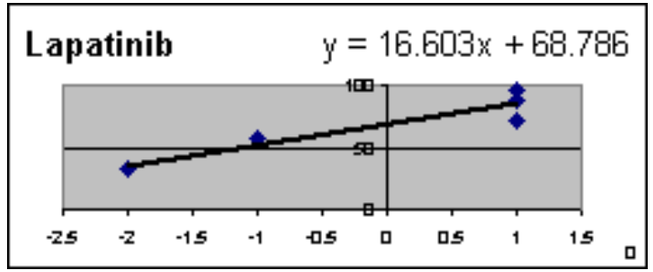
EGFR											
code	IC50	conc	log	%inh	T2	T1	ΔT	RFU2	RFU1	slope	K.Activity
4		100	2	94	30	0	30	6.18	0	3.33333	7.416007
		10	1	87	30	0	30	13.44	0	3.33333	16.12802
		1	0	71	30	0	30	28.57	0	3.33333	34.28403
		0.1	-1	53	30	0	30	46.92	0	3.33333	56.30406
		0.01	-2	38	30	0	30	62.32	0	3.33333	74.78407
EC				0	30	0	30	100	0	3.33333	120
code	IC50	conc	log	%inh	T2	T1	ΔT	RFU2	RFU1	slope	K.Activity
15		100	2	94	30	0	30	6.22	0	3.33333	7.464007
		10	1	85	30	0	30	15.28	0	3.33333	18.33602
		1	0	61	30	0	30	39.11	0	3.33333	46.93205
		0.1	-1	45	30	0	30	54.82	0	3.33333	65.78407
		0.01	-2	34	30	0	30	65.71	0	3.33333	78.85208

EC				0	30	0	30	100	0	3.33333	120
		[redacted]		[redacted]			[redacted]		[redacted]		
code	IC50	conc	log	%inh	T2	T1	ΔT	RFU2	RFU1	slope	K.Activity
16		100	2	94	30	0	30	5.59	0	3.33333	6.708007
		10	1	88	30	0	30	12.03	0	3.33333	14.43601
		1	0	72	30	0	30	27.66	0	3.33333	33.19203
		0.1	-1	56	30	0	30	43.51	0	3.33333	52.21205
		0.01	-2	41	30	0	30	59.11	0	3.33333	70.93207
EC				0	30	0	30	100	0	3.33333	120
		[redacted]		[redacted]			[redacted]		[redacted]		
code	IC50	conc	log	%inh	T2	T1	ΔT	RFU2	RFU1	slope	K.Activity
Lapatinib		10	1	95	30	0	30	5.07	0	3.33333	6.084006
		10	1	88	30	0	30	11.61	0	3.33333	13.93201
		10	1	71	30	0	30	28.91	0	3.33333	34.69203
		0.1	-1	57	30	0	30	42.55	0	3.33333	51.06005
		0.01	-2	32	30	0	30	67.93	0	3.33333	81.51608
EC				0	30	0	30	100	0	3.33333	120
		[redacted]		[redacted]			[redacted]		[redacted]		









Curves for compounds **4, 15, 16, and Lapatinib**