Supplementary Material

Convergent synthesis and biological evaluation of 3-[2-(benzylidenehydrazinyl)thiazol-4-yl]-4-hydroxycoumarins

Meloddy H. Manyeruke,[a] Tendamudzimu Tshiwawa,[a] Heinrich C.Hoppe,[b,c] Michelle Isaacs,[c] Ronnett Seldon,[d] Digby F. Warner,[e] Rui W.M. Krause,*[a,c] and Perry T. Kaye*[a,c]

[a]Department of Chemistry, [b] Department of Biochemistry and Microbiology and [c]Centre for Chemico- and Biomedicinal Research (CCBR), Rhodes University, Makhanda/Grahamstown, 6140, South Africa

[d]Drug Discovery and Development Centre (H3-D), Department of Chemistry, University of Cape Town, Rondebosch 7701, South Africa

[e]Molecular Mycobacteriology Research Unit, Department of Pathology and Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, South Africa

Email: P.Kaye@ru.ac.za, R.Krause@ru.ac.za

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1. Bioassay and *in silico* docking protocols and data.

1.1. Antimalarial and anti-trypanosomal assays

To assess antimalarial activity, percentage viability of *Plasmodium falciparum* (3D7 strain) parasites incubated for 48 hours with 20 µM of the test compounds was determined by detecting plasmodium lactate dehydrogenase (pLDH) activity as described previously by Lunga *et al.*(*ChemMedChem* **2018**, *13*, 1352-1362). For anti-trypanosomal and cytotoxicity evaluation, percentage viability of *Trypanosoma brucei brucei* (427 strain) parasites or HeLa cells incubated with 20 µM of the test compounds for 48 hours was determined using resazurin, as previously described by Veale and Hoppe (*Med. Chem. Commun.* **2018**, *9*, 2037).

Table 1. Anti-bacterial and cytotoxicity data for compounds **14a,c-e,g** at a concentration of 50 mg/mL

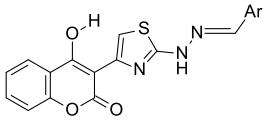
Compd,	E. coli Activity	% growth	S. aureus Activity	% growth [a]	Cytotoxicity Status
14a	*not active*	114	*active*	37-47	*not toxic*
14c	*not active*	97	*active*	46	*toxic*
14d	*not active*	120	*active*	31	*not toxic*
14e	*not active*	106	*active*	43	*not toxic*
14g	*not active*	109	*active*	50	*not toxic*

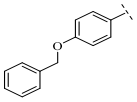
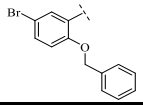
[a] As % metabolic activity

2.2. In silico docking protocols and data.

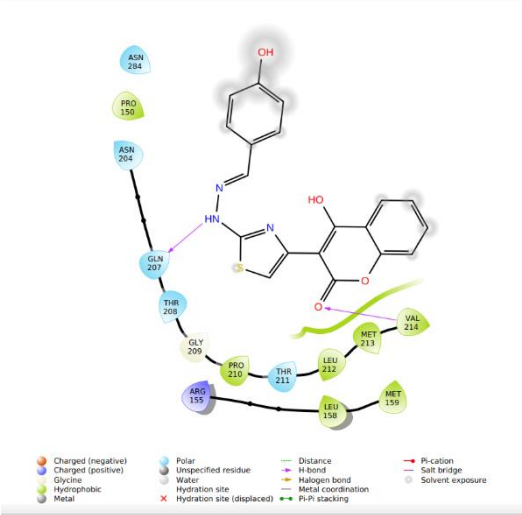
In silico docking was performed using Schrödinger software (Maestro 11.4, Schrödinger 2017-4). The reported ligands were built in Maestro and prepared for docking using the LigPrep module (Schrodinger, LLC, NY, USA, 2009). The OPLS_2005 force field was selected in LigPrep for the energy minimization of the ligands to generate low-energy ligand isomers. The protein structures were obtained from Protein Data Bank (http://www.rscb.org) and prepared for docking using the protein preparation wizard as implemented in Maestro. The receptor grid generations were achieved using "Glide Grid Generation" module and the active site was selected with the radius of 20 Å around the crystal ligand. Glide module (Schrodinger, LLC, NY, USA, 2009) was used for docking protocol using Standard precision (SP) approach. The results obtained were visualized using Maestro interface (Schrödinger Suite, LLC, NY).

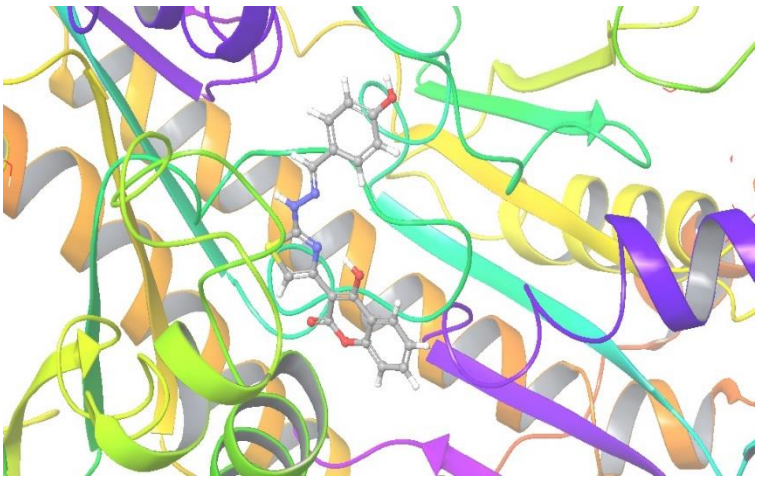
Table 2. *In silico* binding affinities in Kcal/mol for the ligands **14a-g** in selected enzyme receptor sites.



Ligand	Ar	HIV-1 IN 5FRN	HIV-1 PR 1YT9	HIV-1 PR 1ZP8	*Pf* 1T2C	*Pf* 1V0O	*T.b. brucei* 4FWN	*M.tb* 4BFW
14a		-5.981	-6.933	-5.935	-7.961	-3.219	-4.668	-7.479
14b		-5.666	-7,257	-6.306	-8.294	-4.460	-5.337	-5.899
14c		-7.558	-7,341	-6.169	-8.849	-3.750	-4.906	-5.714
14d		-5.531	-7.127	-5.666	-7.823	-3.439	-3.240	-4.774
14e		-6.845	-7,191	-5.985	-8.118	-4.075	-4.325	-6.197
14f		-6.138	-6.960	-5.183	-6.701	-3.554	-4.521	-5.841
14g		-6.085	-6,092	-5.439	-5.226	-3.296	-3.630	-5.913

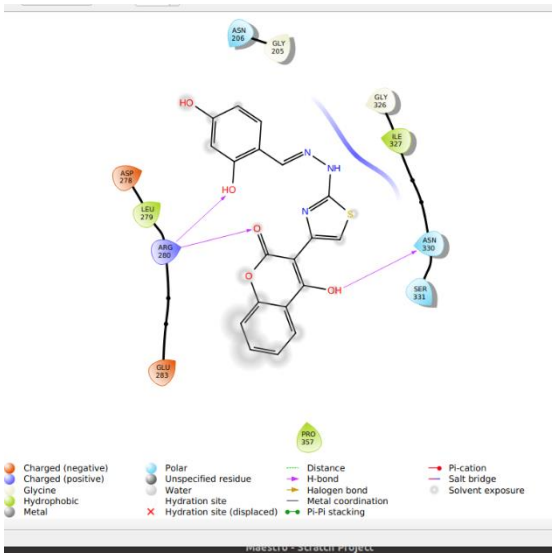
4FBW_14a **4FBW_14a**

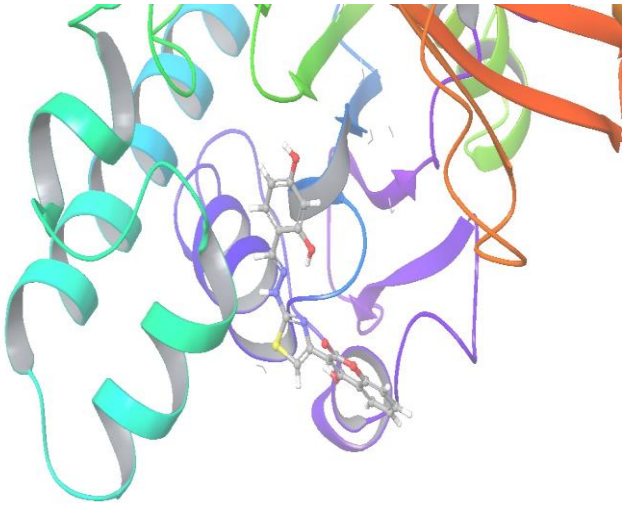




Docking and receptor-site interactions of ligand **14a** in the *M.tb* enzyme 4FBW**.**

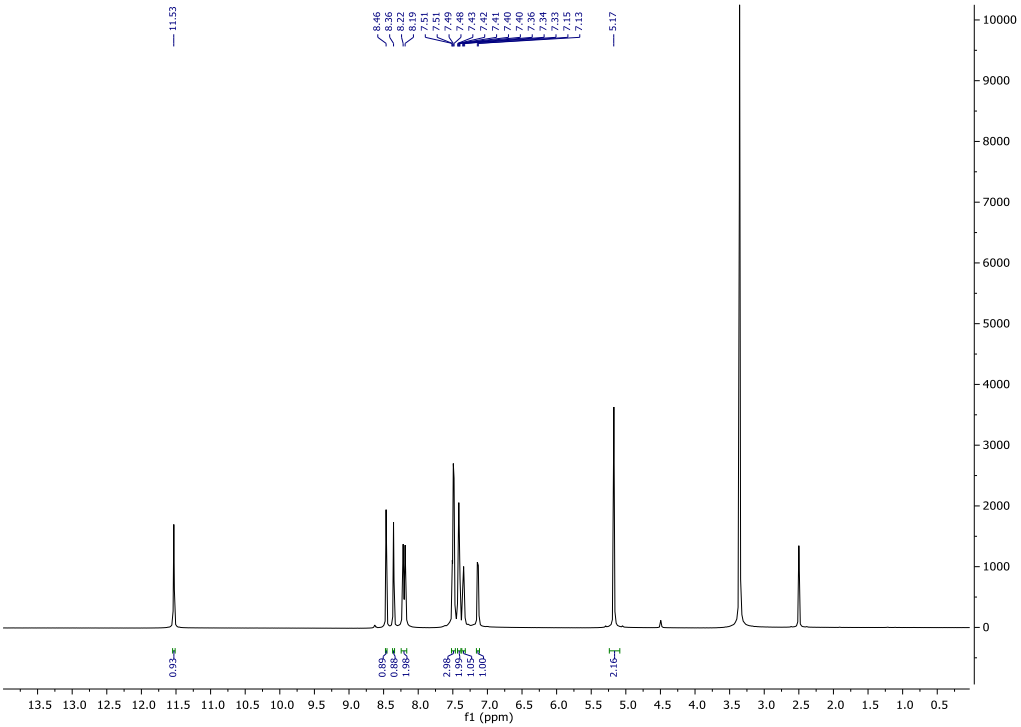
4FWN_14b **4FWN_14b**



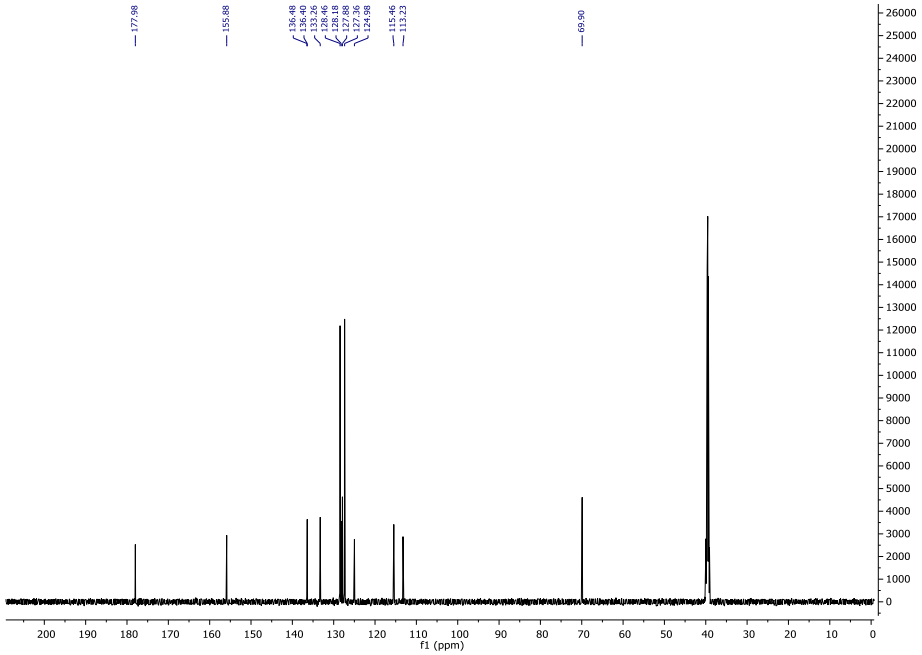


Docking and receptor-site interactions of ligand **14b** in the *T.b.brucei* enzyme 4FWN**.**

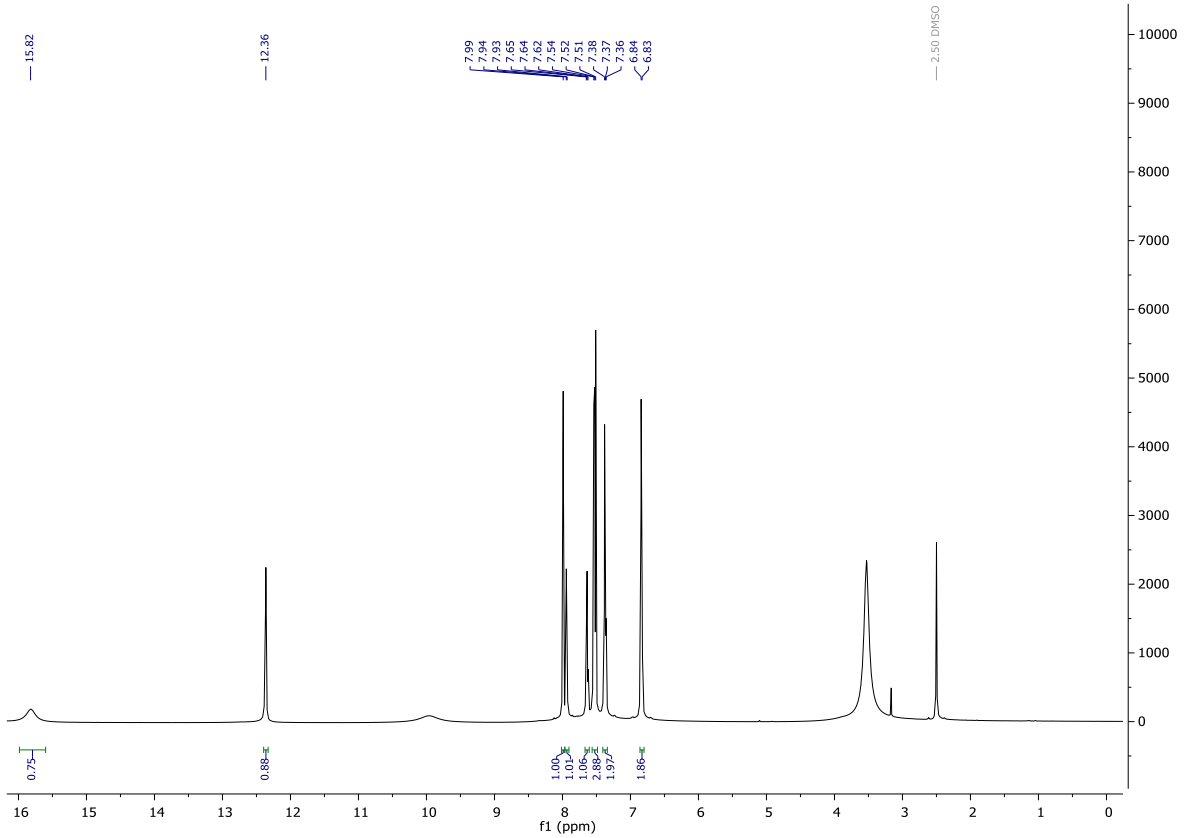
2. NMR Spectra.



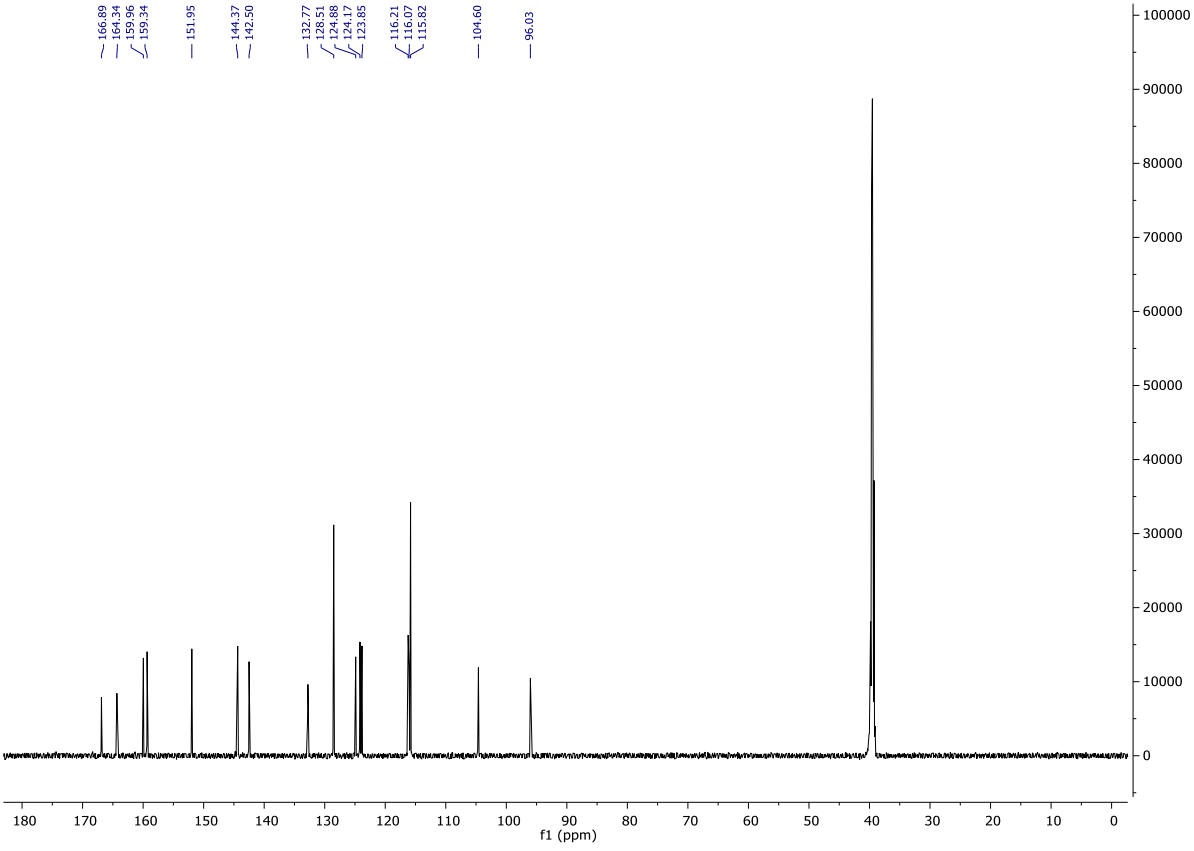
600 MHz ^{1}H NMR spectrum of compound **13g** in DMSO-d_6.



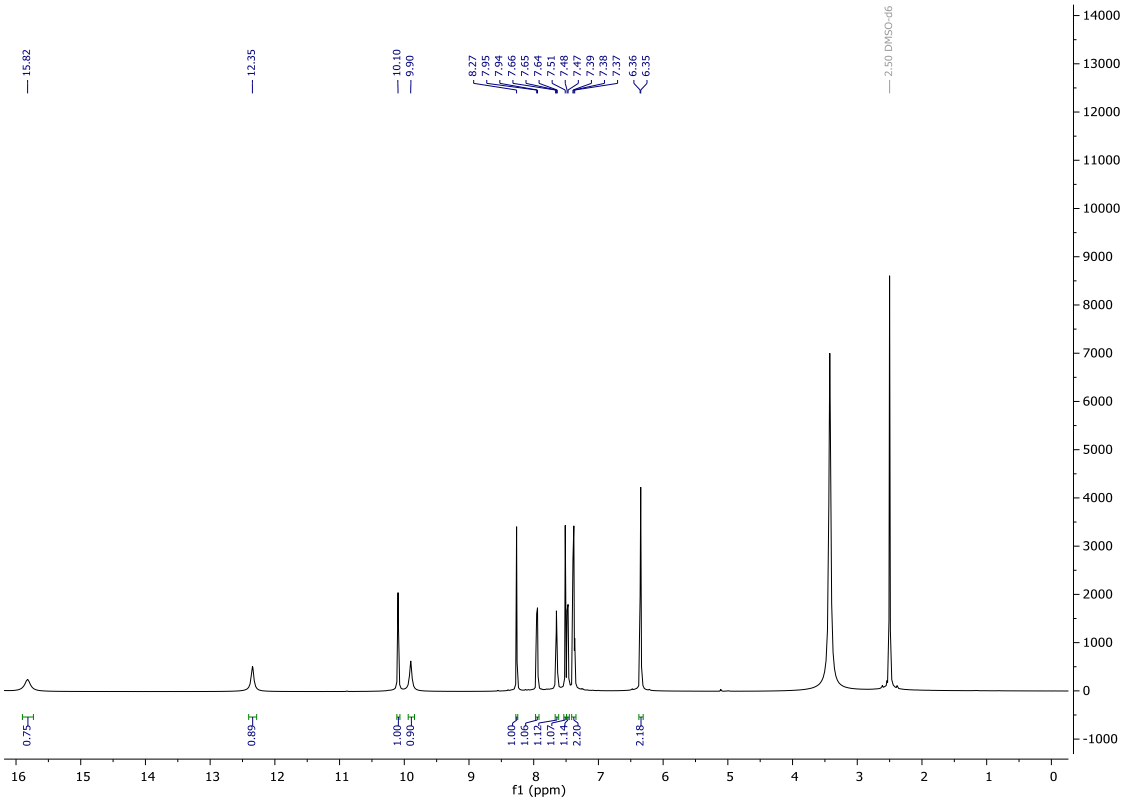
150 MHz ^{13}C NMR spectrum of compound **13g** in DMSO-d_6



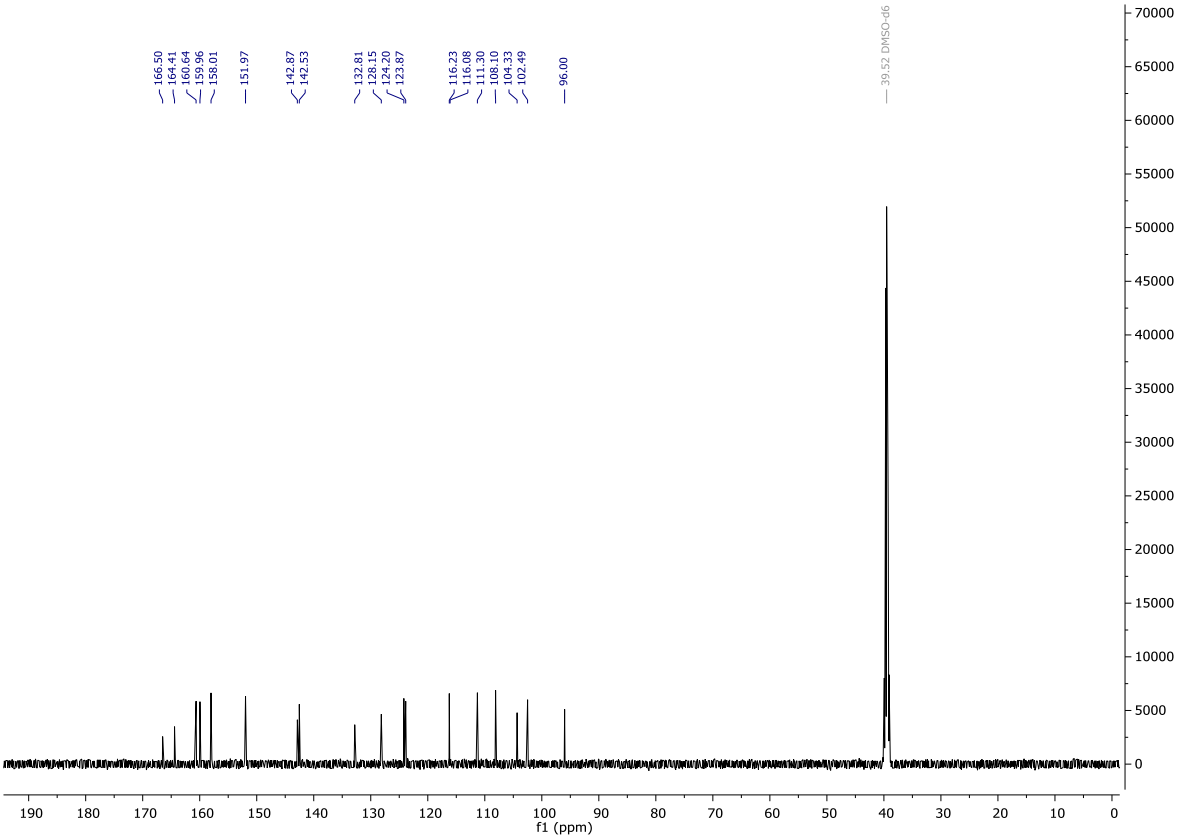
600 MHz ^{1}H NMR spectrum of compound **14a** in DMSO-d_6.



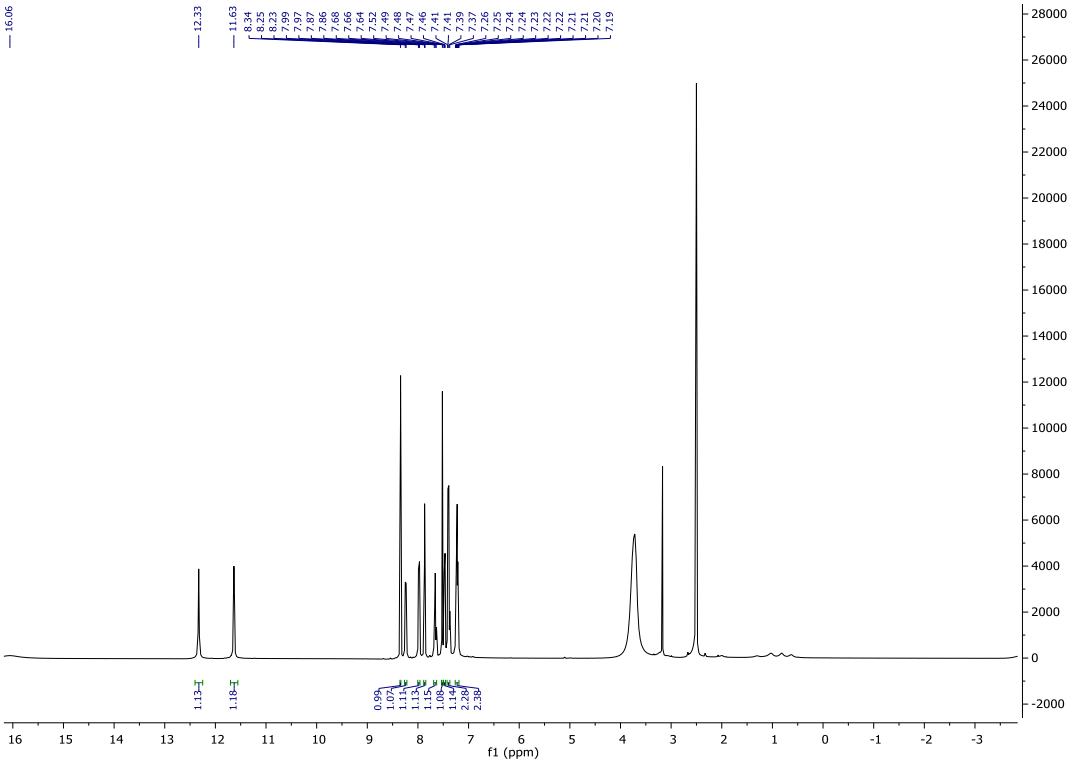
150 MHz ^{13}C NMR spectrum of compound **14a** in DMSO-d_6.



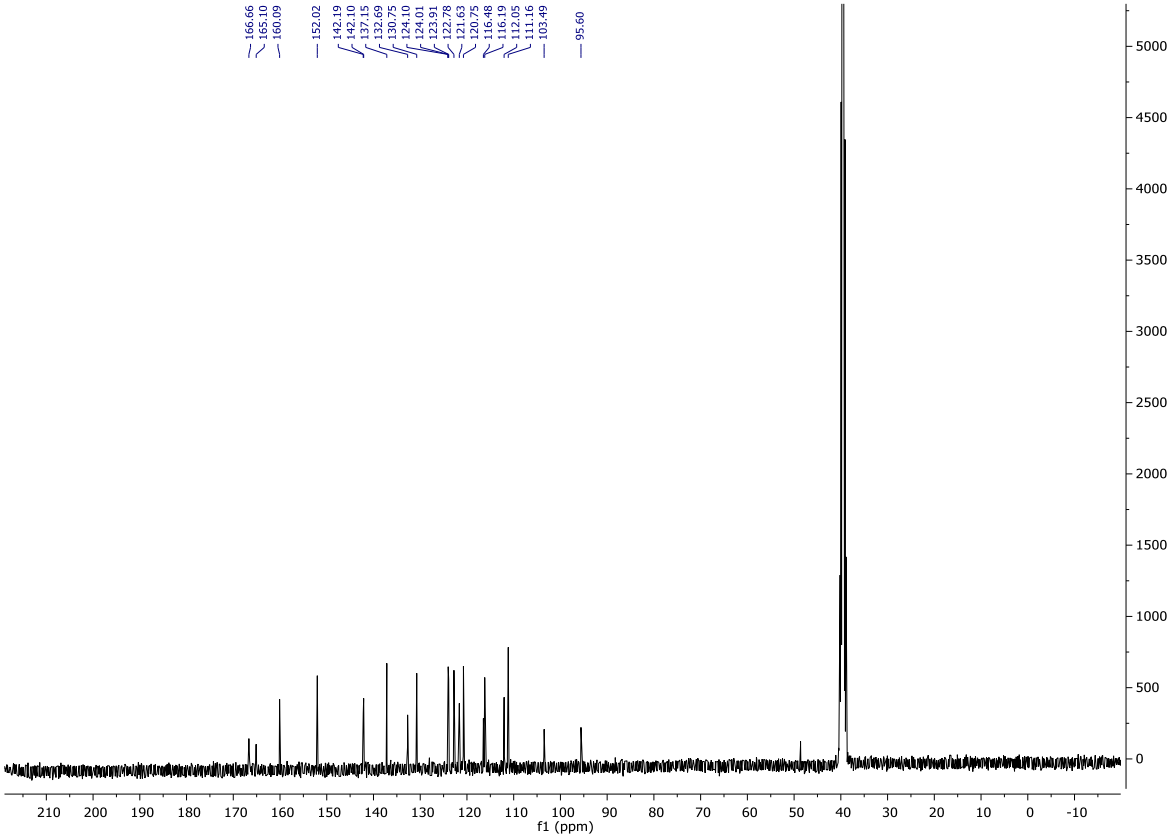
600 MHz ^{1}H NMR spectrum of compound **14b** in DMSO-d_6.



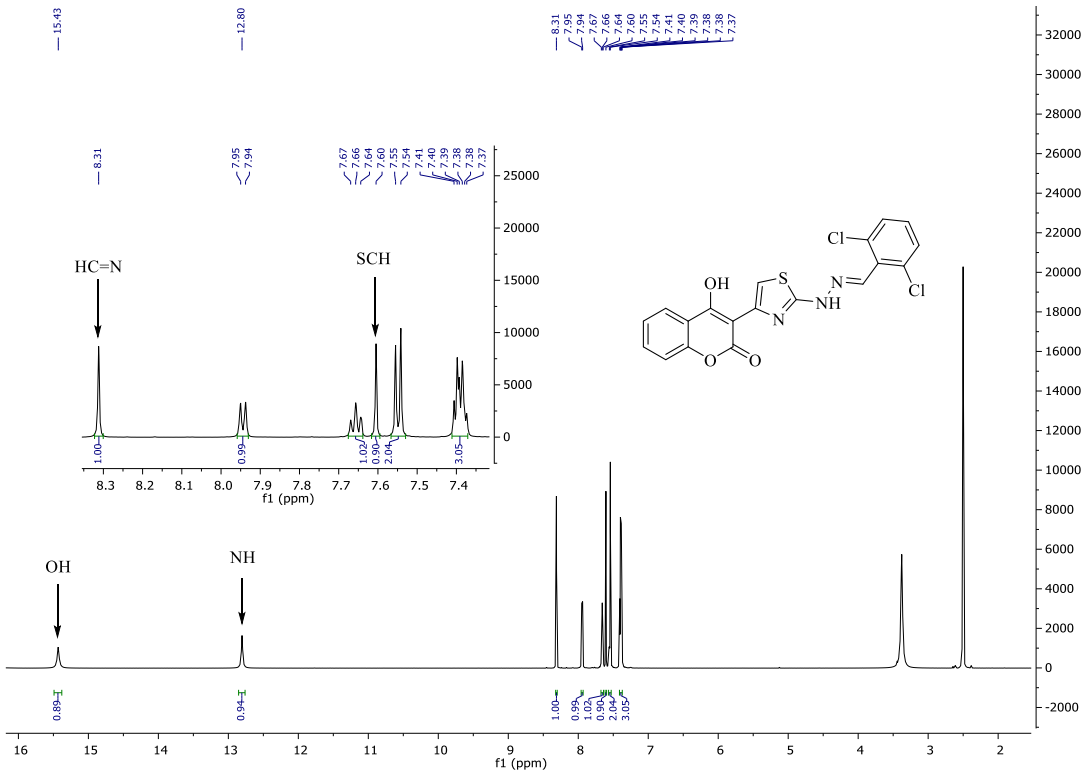
150 MHz ^{13}C NMR spectrum of compound **14b** in DMSO-d_6.



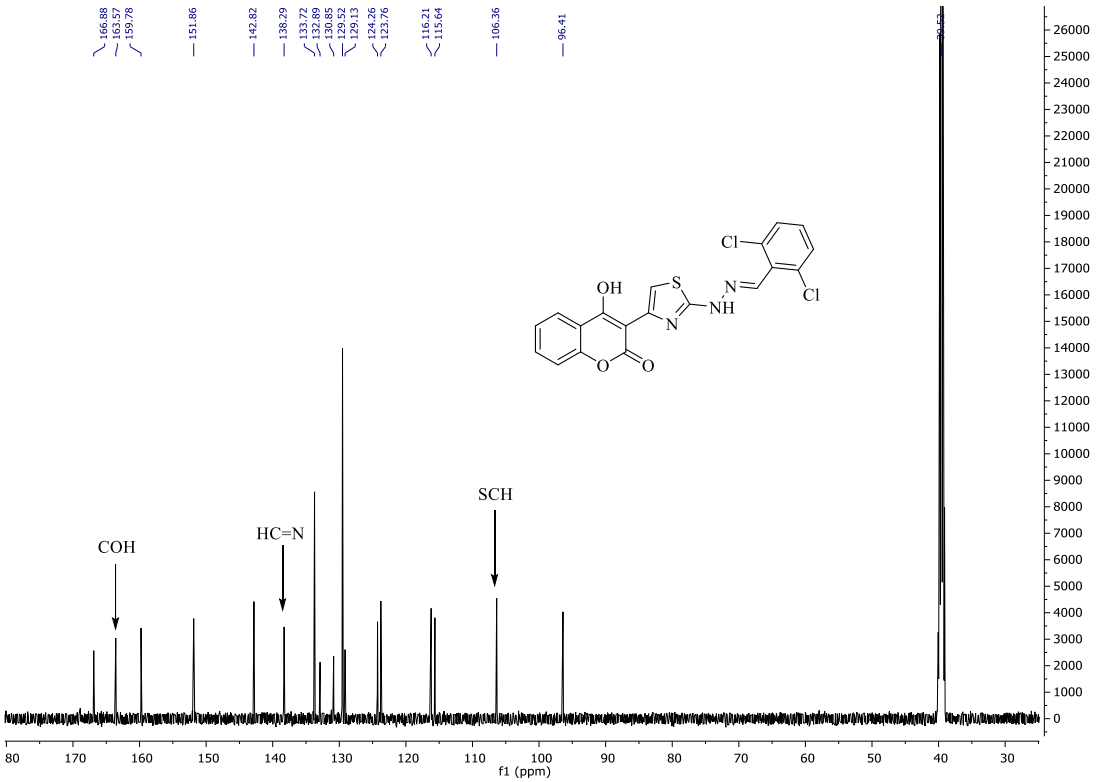
400 MHz ^{1}H NMR spectrum of compound **14c** in DMSO-d_6.



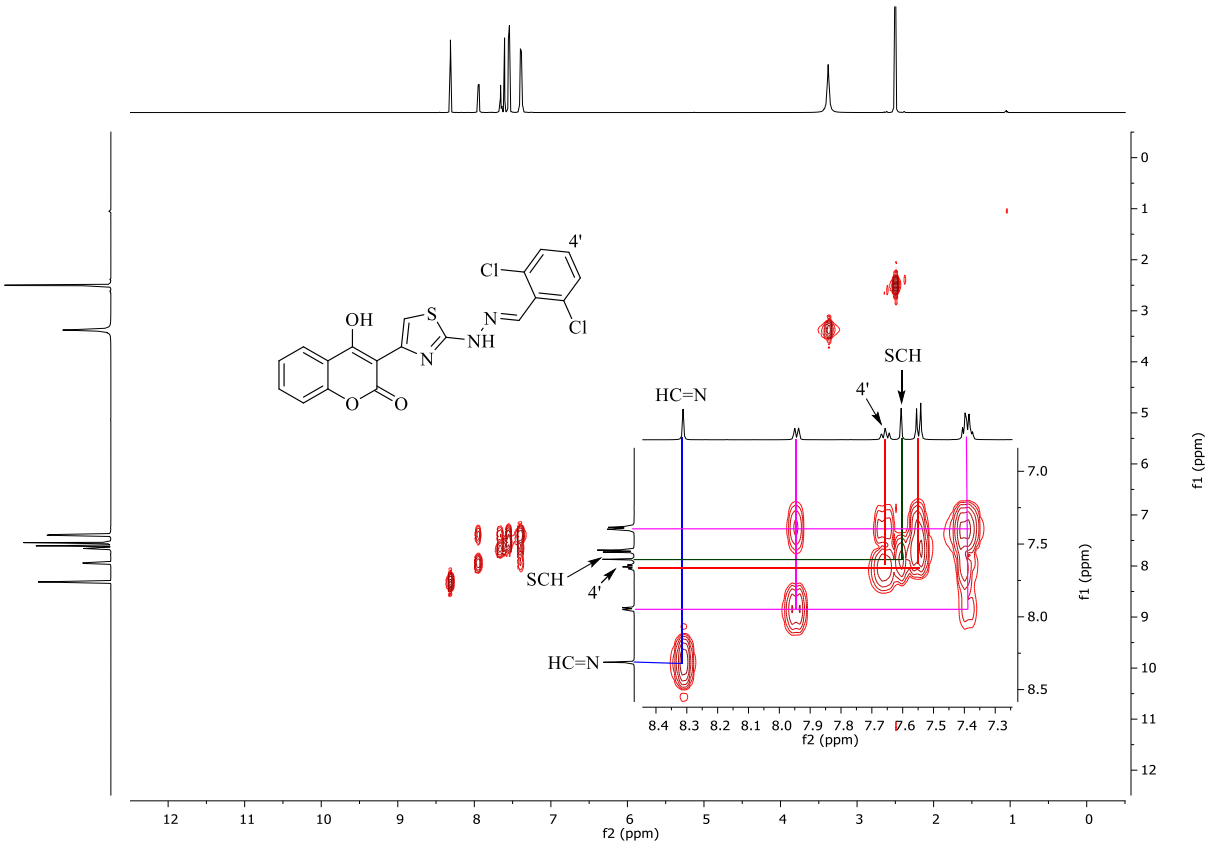
100 MHz ^{13}C NMR spectrum of compound **14c** in DMSO-d_6.



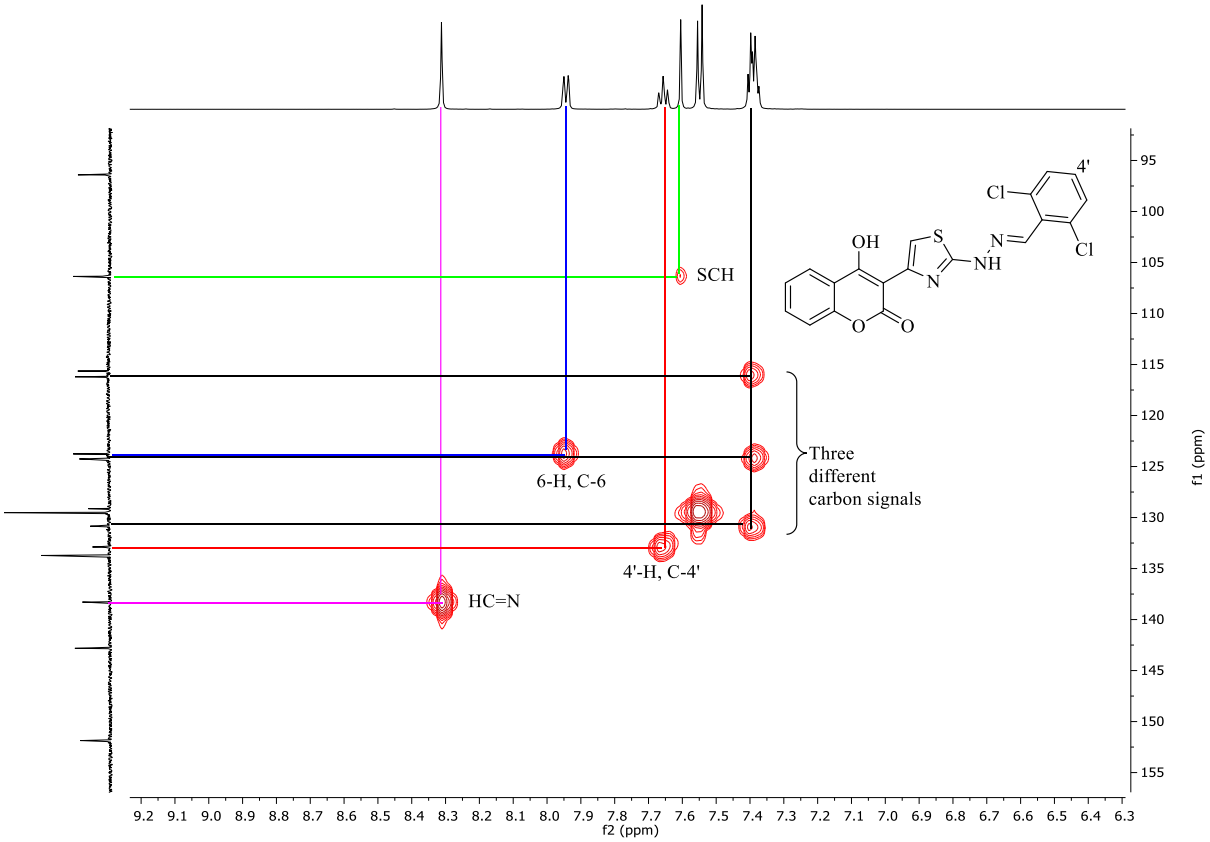
600 MHz ^{1}H NMR spectrum of compound **14d** in DMSO-d_6.



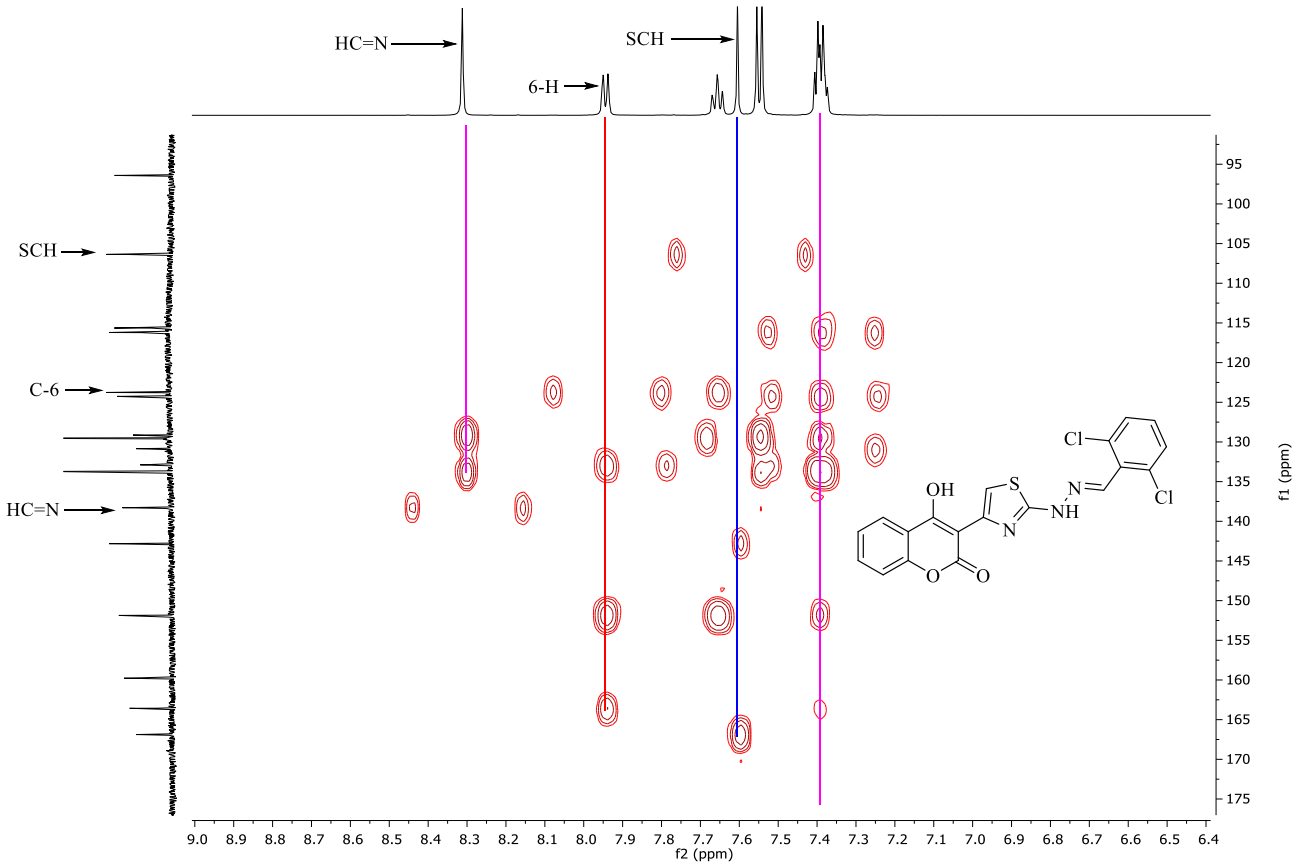
150 MHz ^{13}C NMR spectrum of compound **14d** in DMSO-d_6.



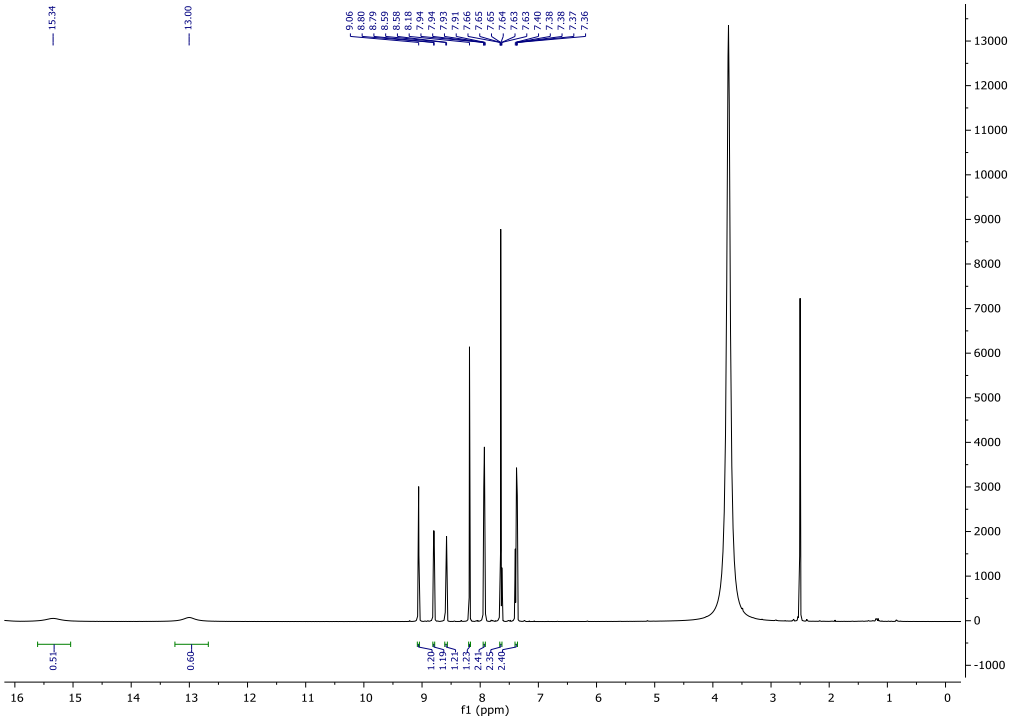
600 MHz COSY NMR spectrum of compound **14d** in DMSO-d_6.



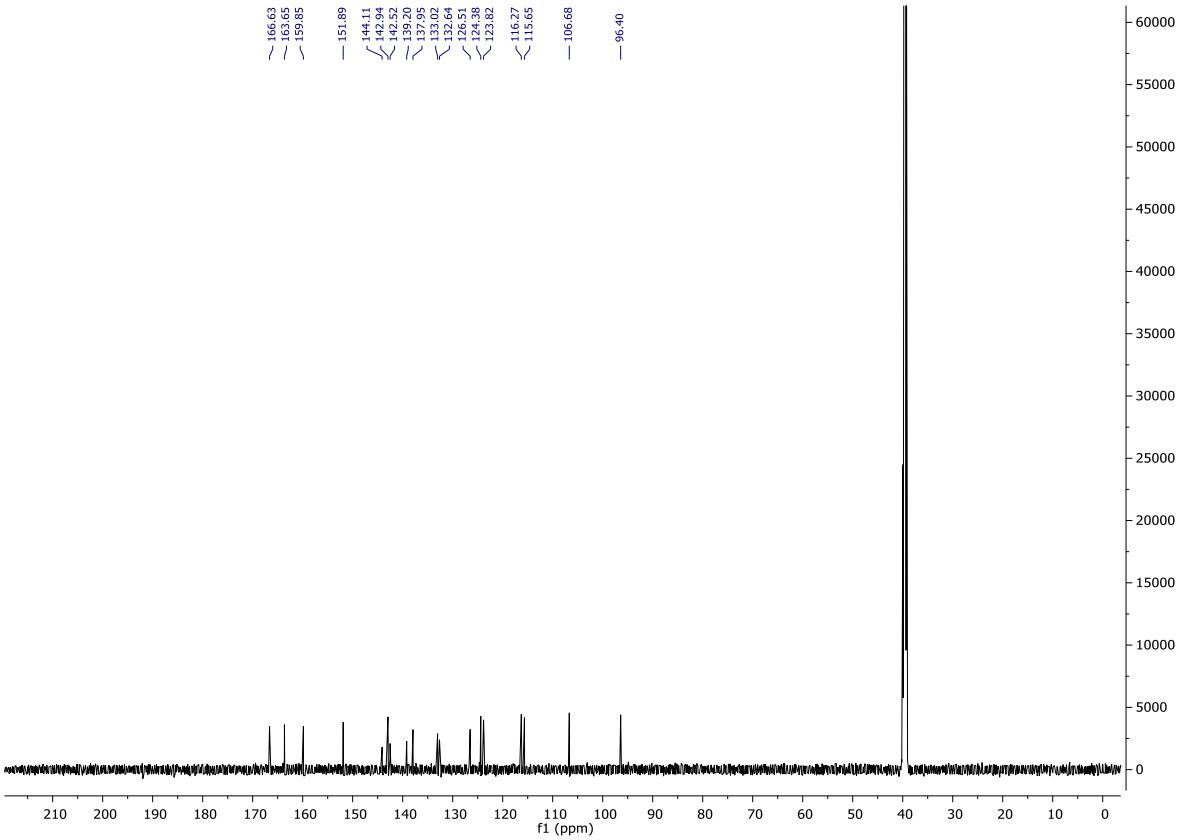
Partial HSQC NMR spectrum of compound **14d** in DMSO-d_6.



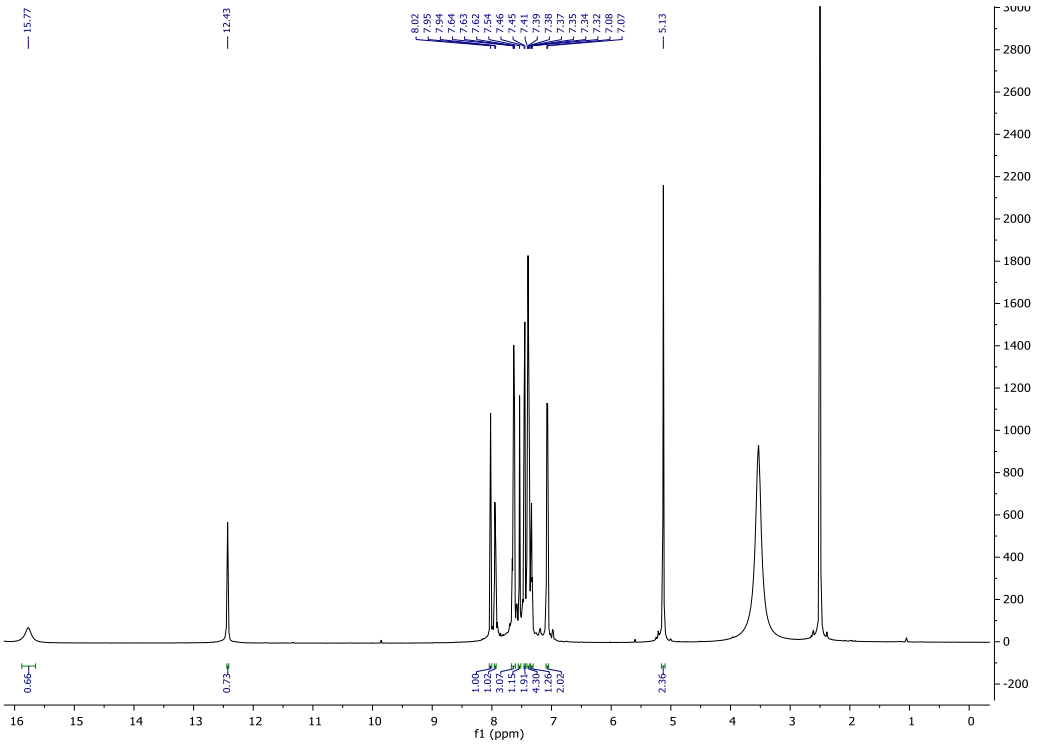
HMBC NMR spectrum of compound **14d** in DMSO-d_6.



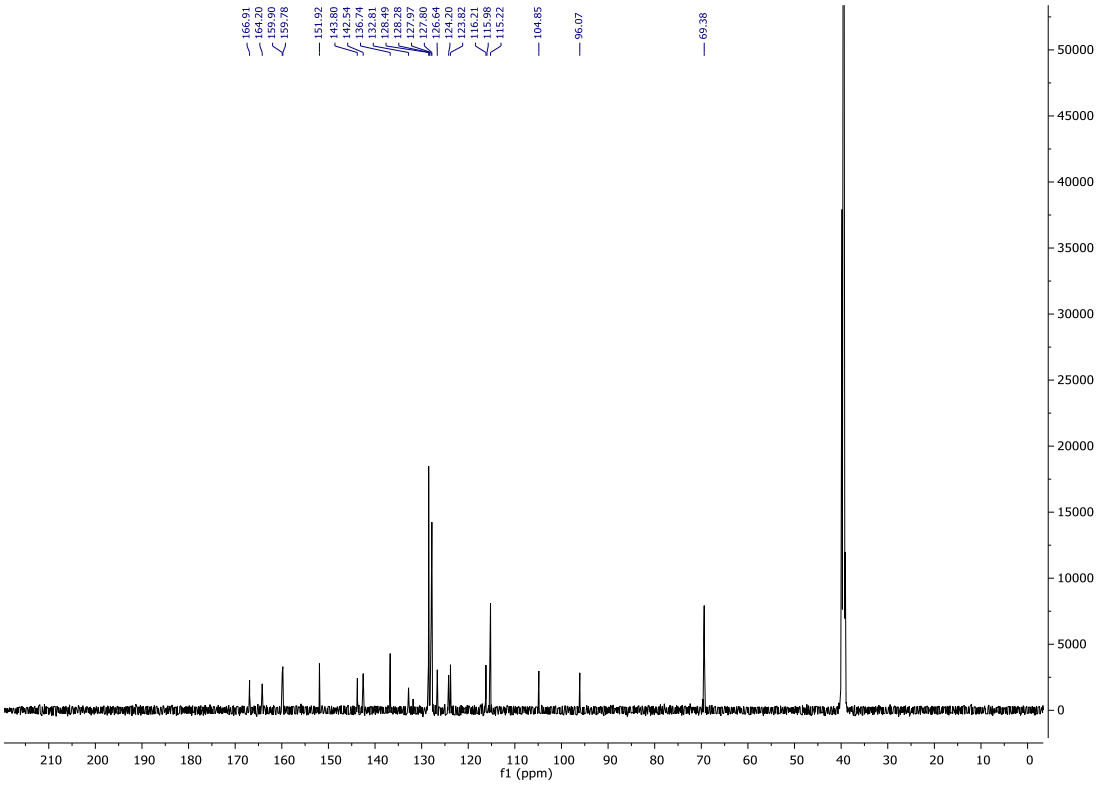
600 MHz ^{1}H NMR spectrum of compound **14e** in DMSO-d_6.



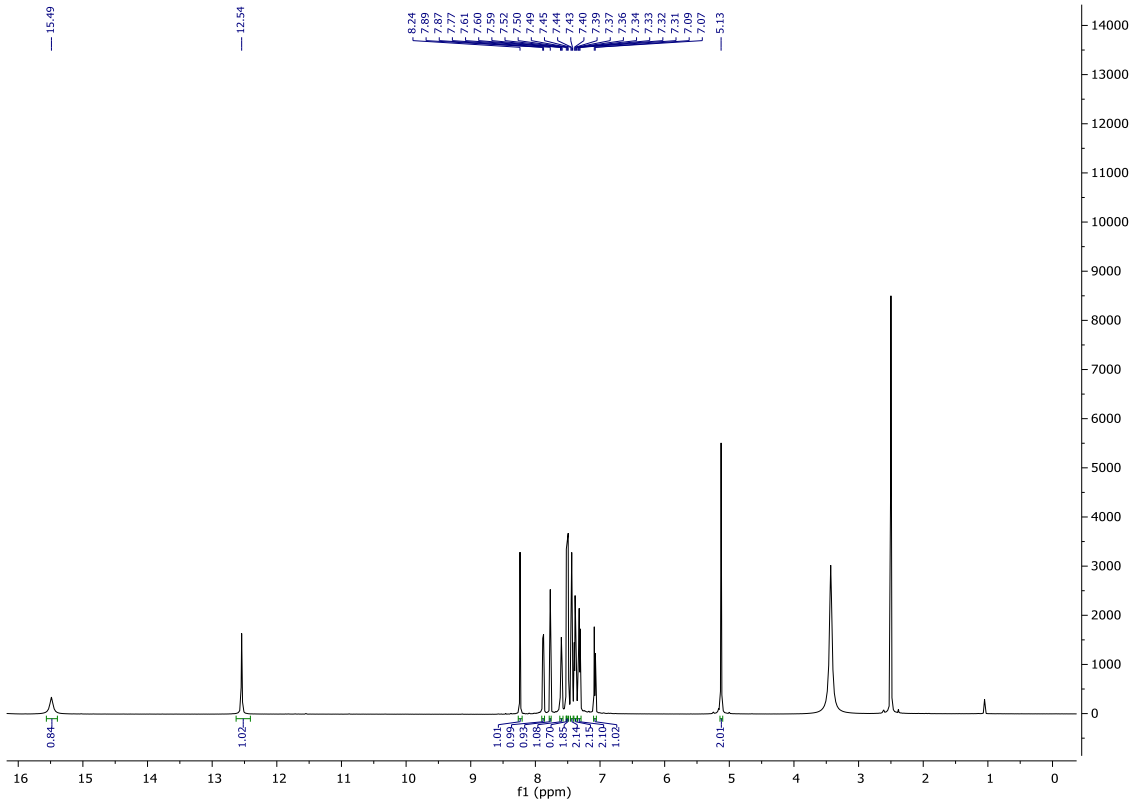
150 MHz ^{13}C NMR spectrum of compound **14e** in DMSO-d_6.



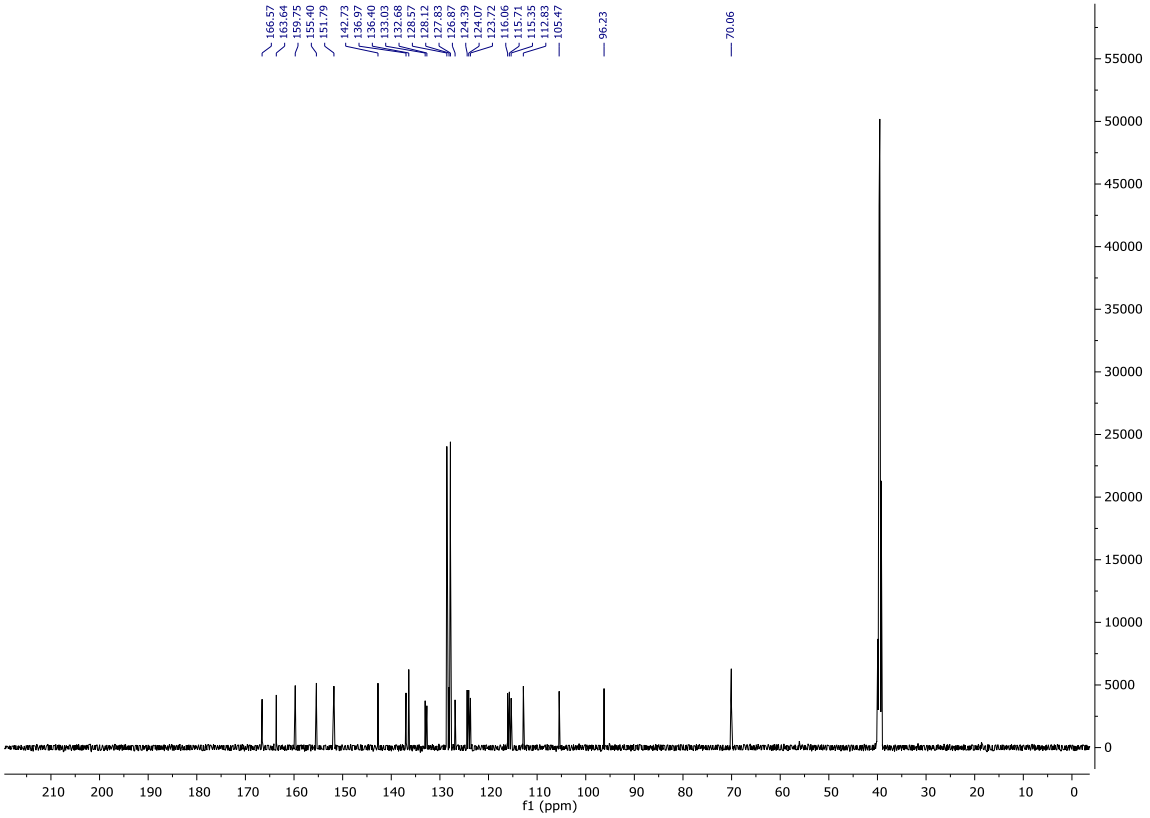
600 MHz ^{1}H NMR spectrum of compound **14f** in DMSO-d_6.



150 MHz ^{13}C NMR spectrum of compound **14f** in DMSO-d_6.



600 MHz ^{1}H NMR spectrum of compound **14g** in DMSO-d_6.



150 MHz ^{13}C NMR spectrum of compound **14g** in DMSO-d_6.