

Supplementary Material

Pyrimidine-2,4-diamines as antiplasmodial antifolates

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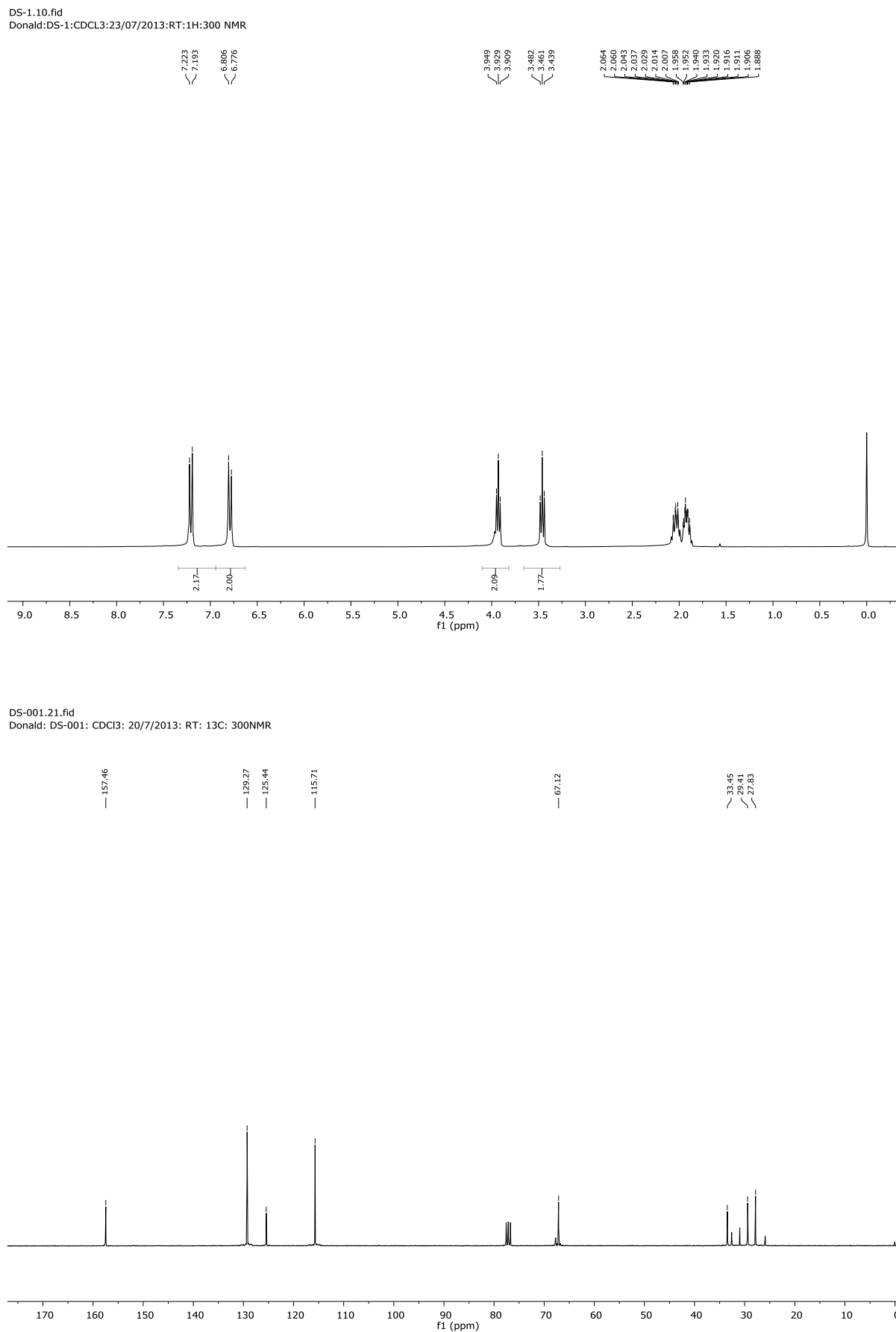
Figure S1. ^1H and ^{13}C NMR spectra of 1-(4-bromobutoxy)-4-chlorobenzene (**9a**).

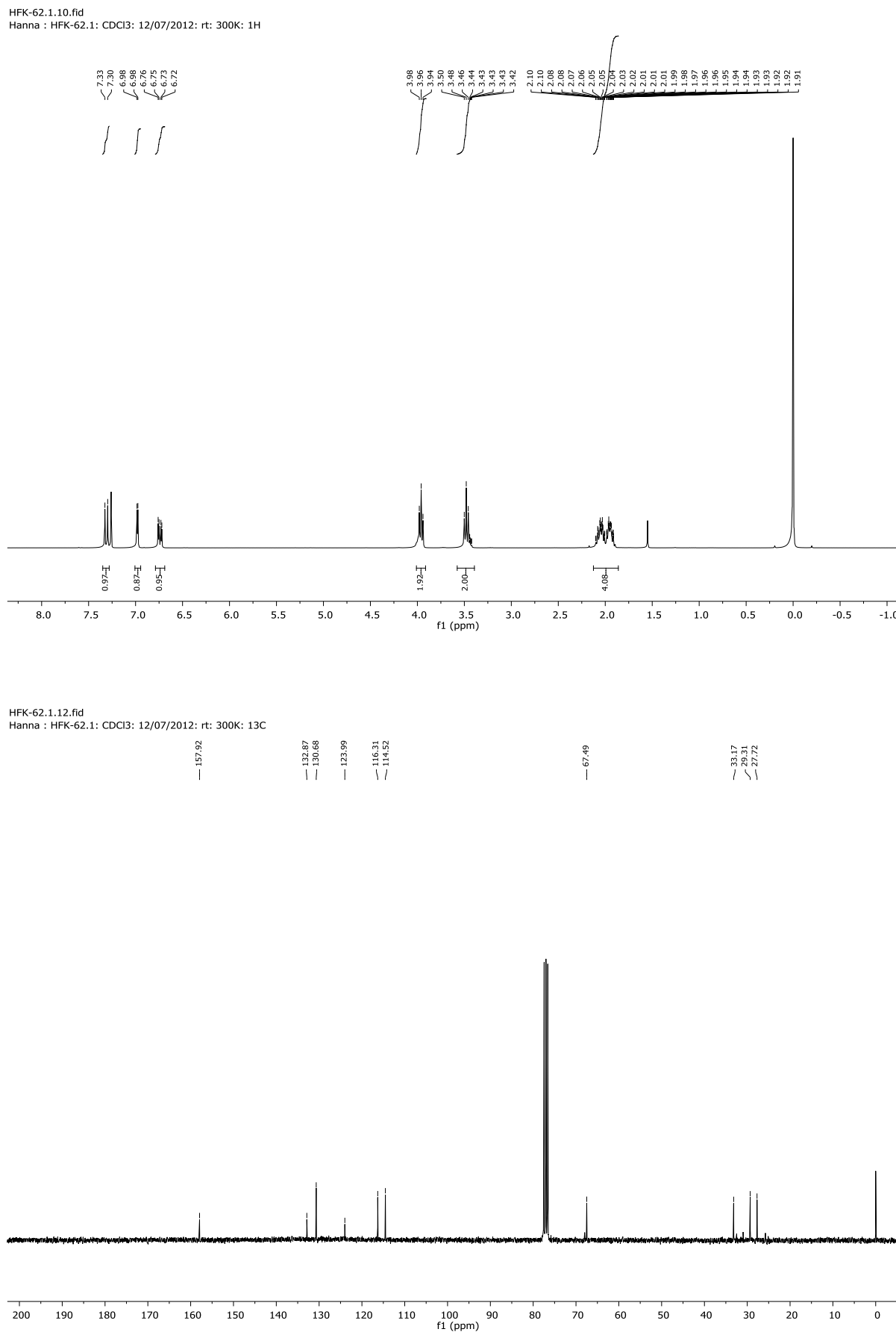
Figure S2. ^1H and ^{13}C NMR spectra of 1-(4-bromobutoxy)-3,4-dichlorobenzene (**9b**).

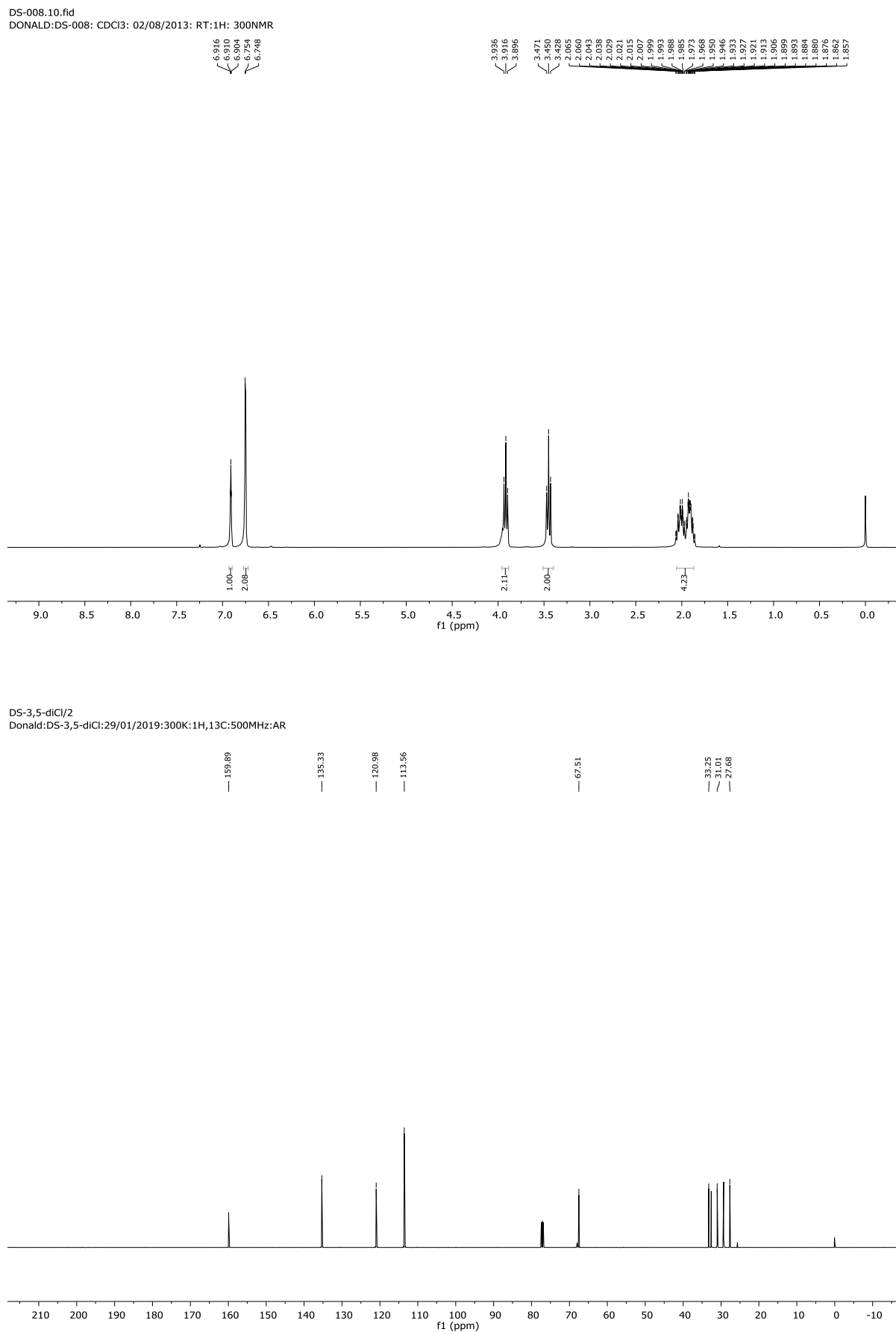
Figure S3. ^1H and ^{13}C NMR spectra of 1-(4-bromobutoxy)-3,5-dichlorobenzene (**9c**).

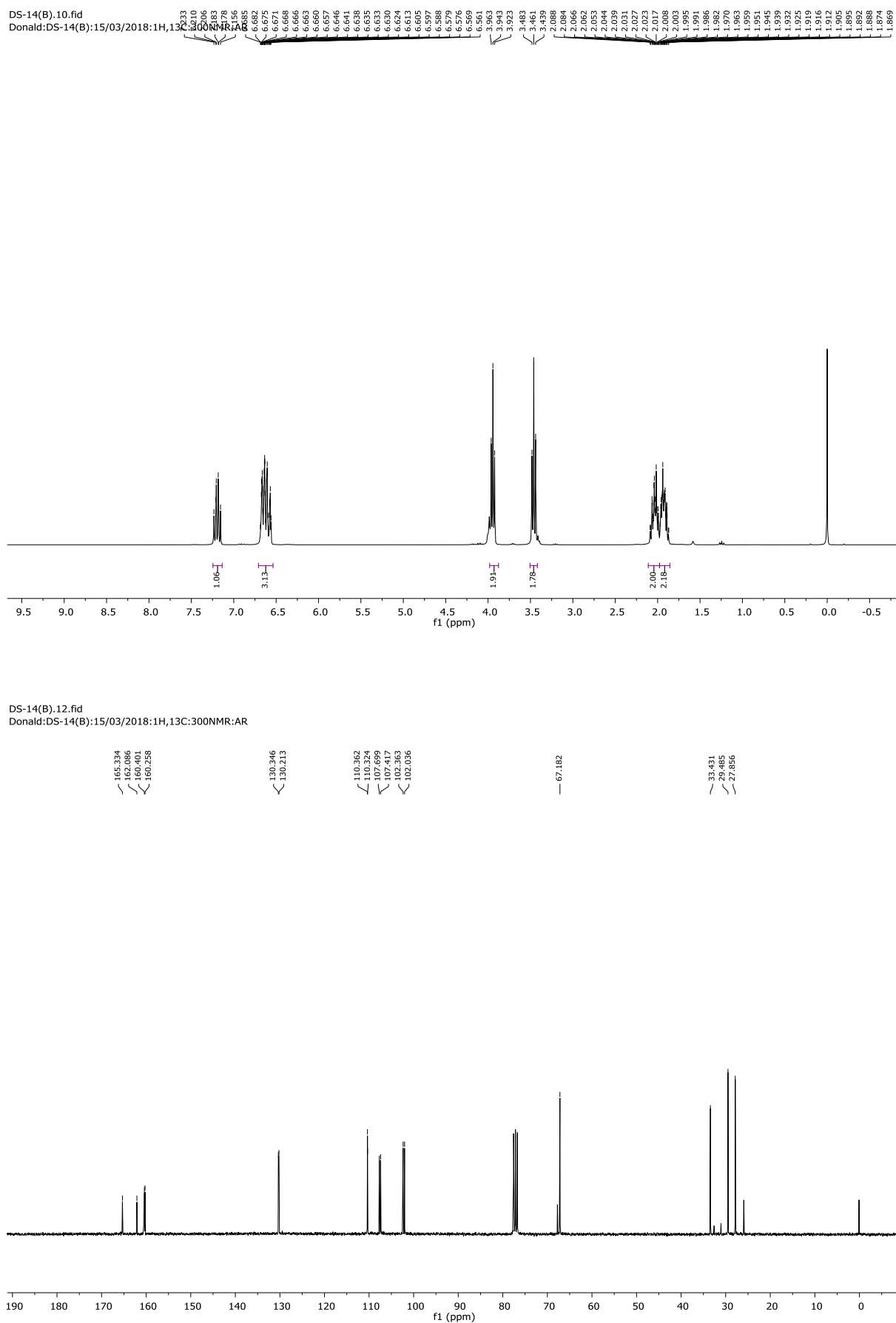
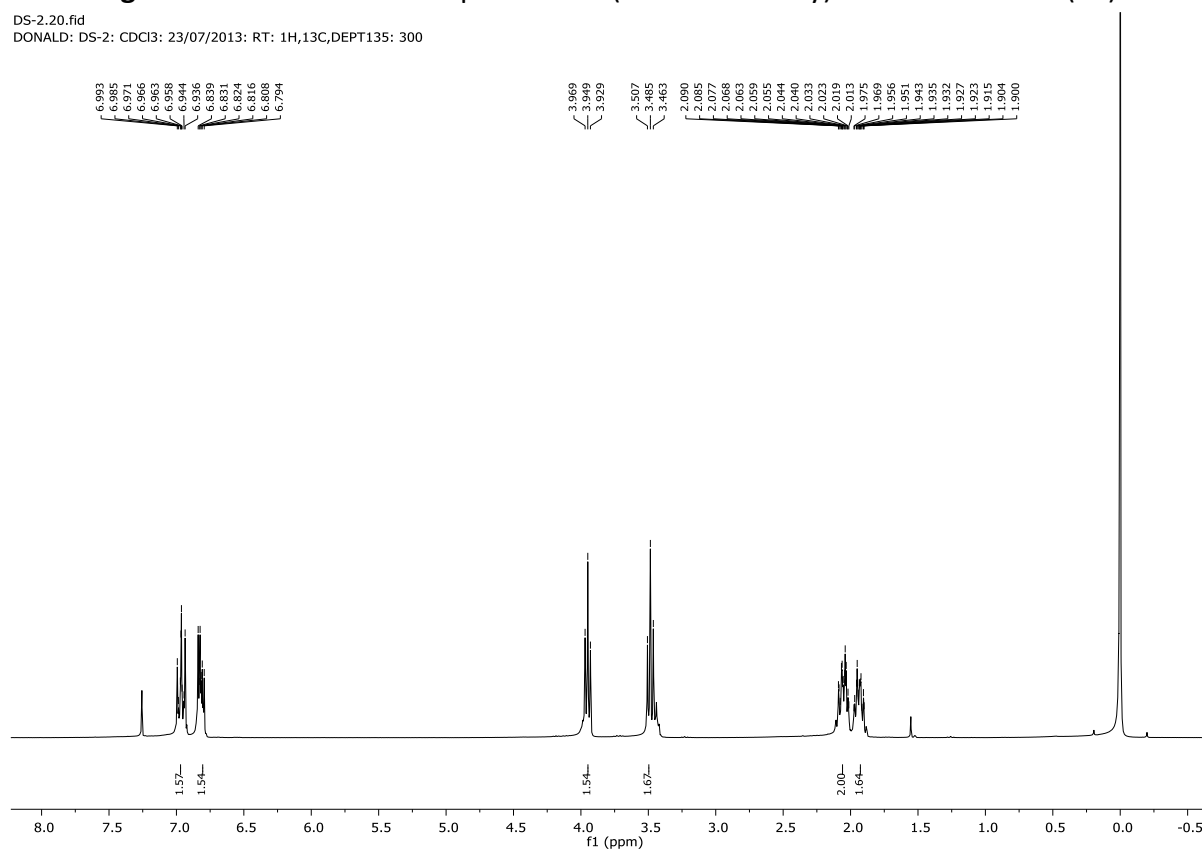
Figure S4. ^1H and ^{13}C NMR spectra of 1-(4-bromobutoxy)-3-fluorobenzene (**9d**).

Figure S5. ^1H and ^{13}C NMR spectra of 1-(4-bromobutoxy)-4-fluorobenzene (**9e**).

DS-2.20.fid

DONALD: DS-2; CDCl₃; 23/07/2013; RT: ^1H , ^{13}C ,DEPT135: 300

DS-2.21.fid

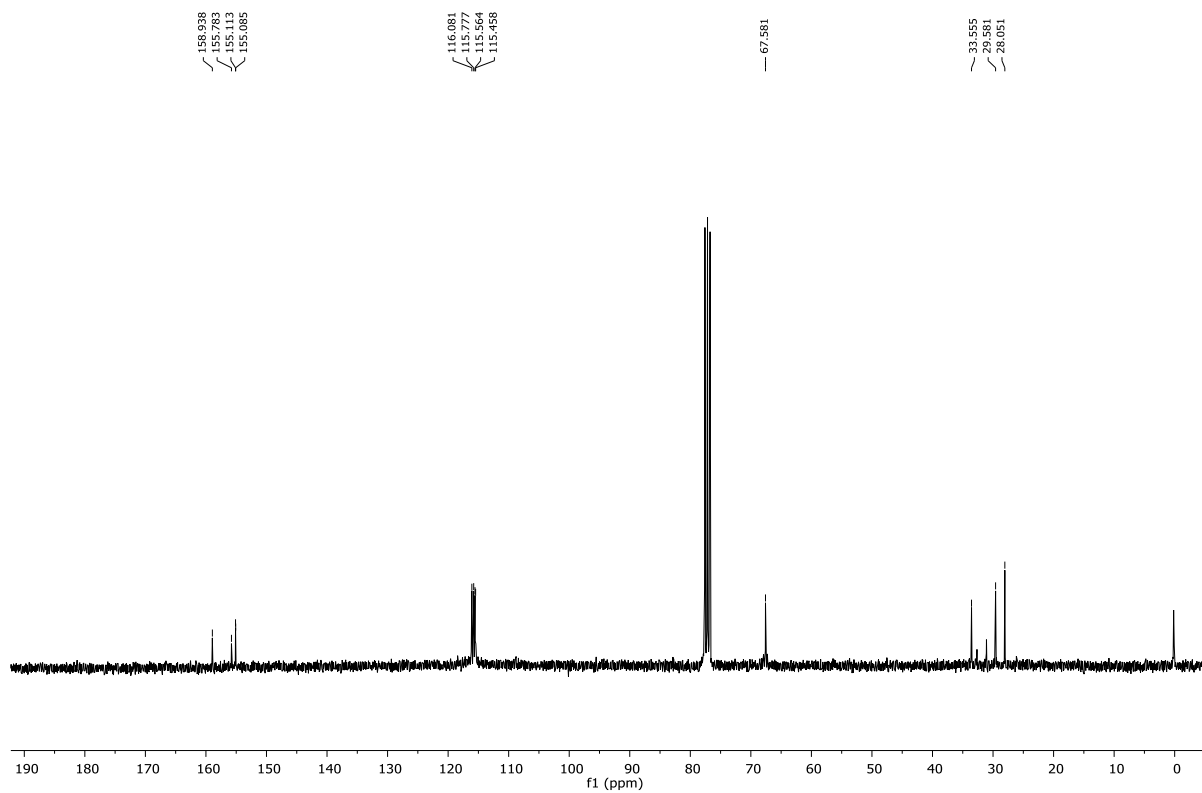
DONALD: DS-2; CDCl₃; 23/07/2013; RT: ^1H , ^{13}C ,DEPT135: 300

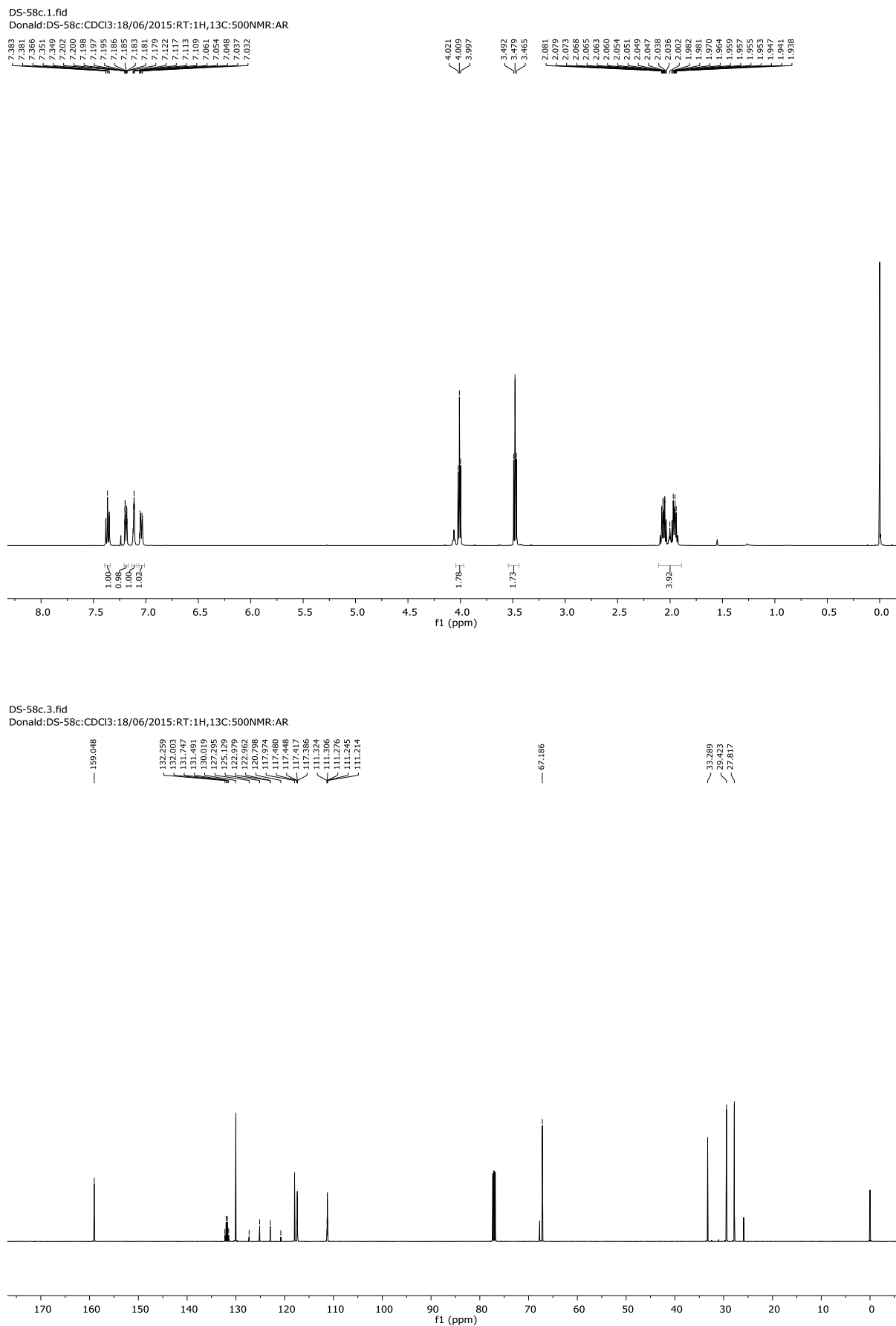
Figure S6. ^1H and ^{13}C NMR spectra of 1-(4-bromobutoxy)-3-(trifluoromethyl)benzene (**9f**).

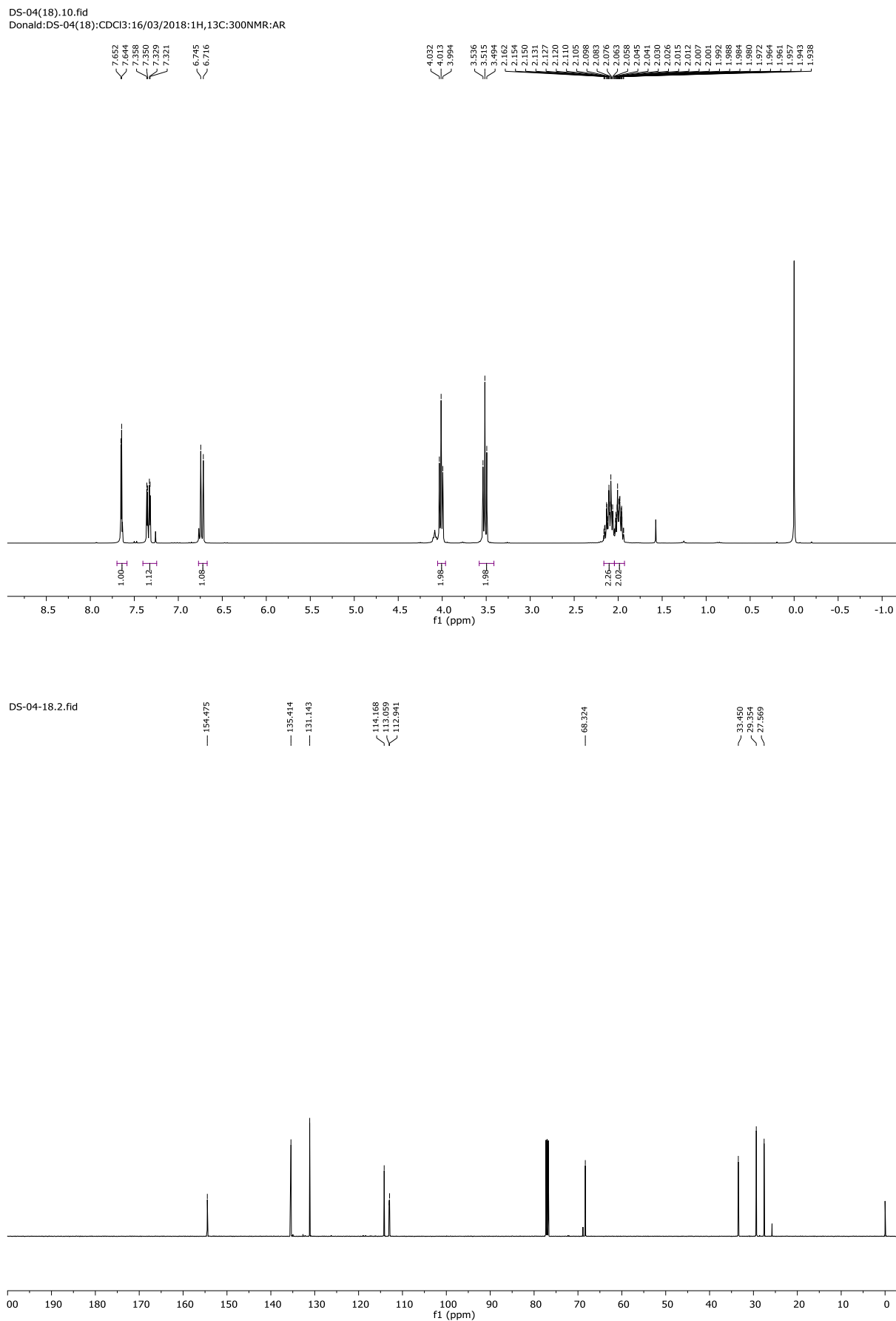
Figure S7. ^1H and ^{13}C NMR spectra of 2,4-dibromo-1-(4-bromobutoxy)benzene (**9g**).

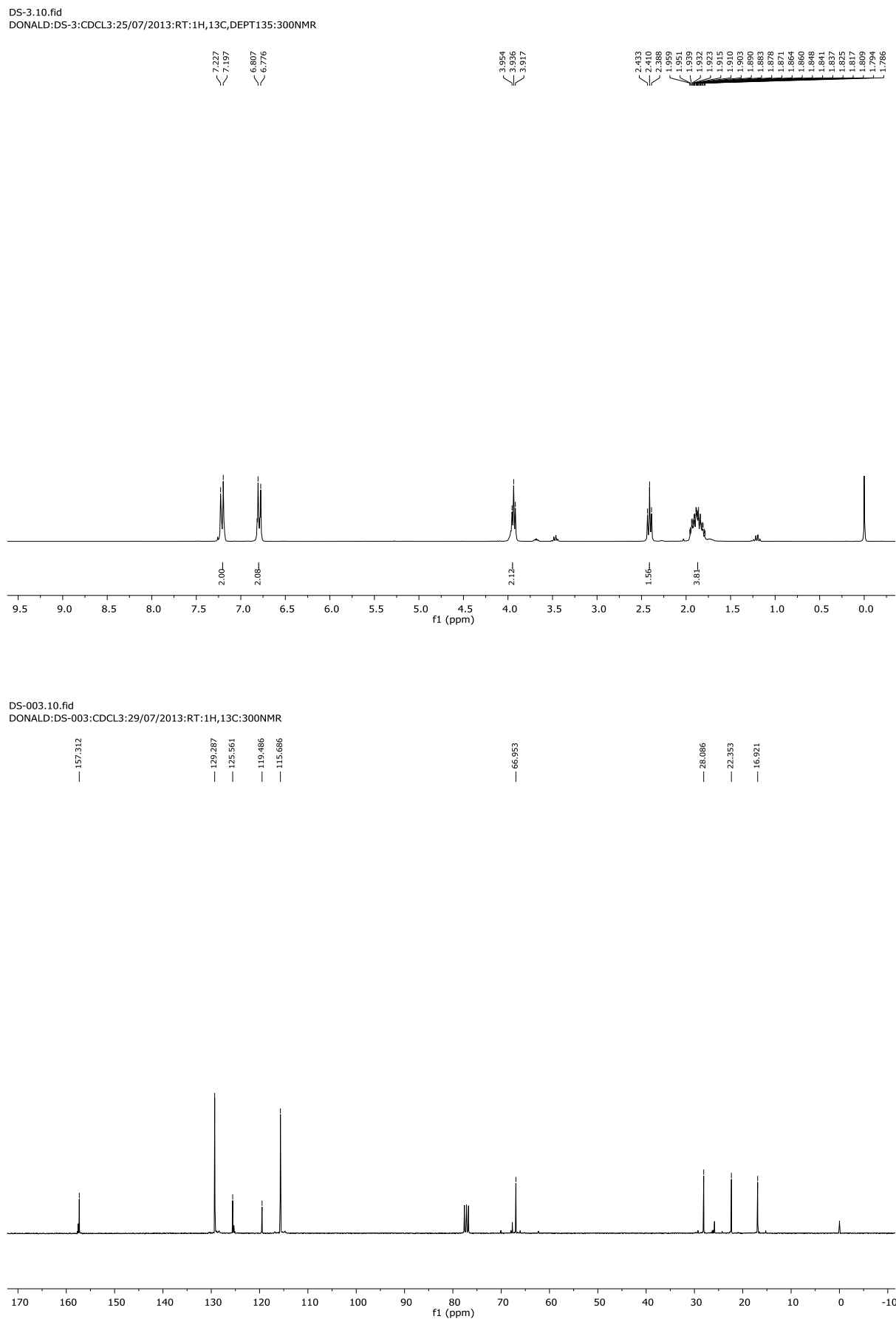
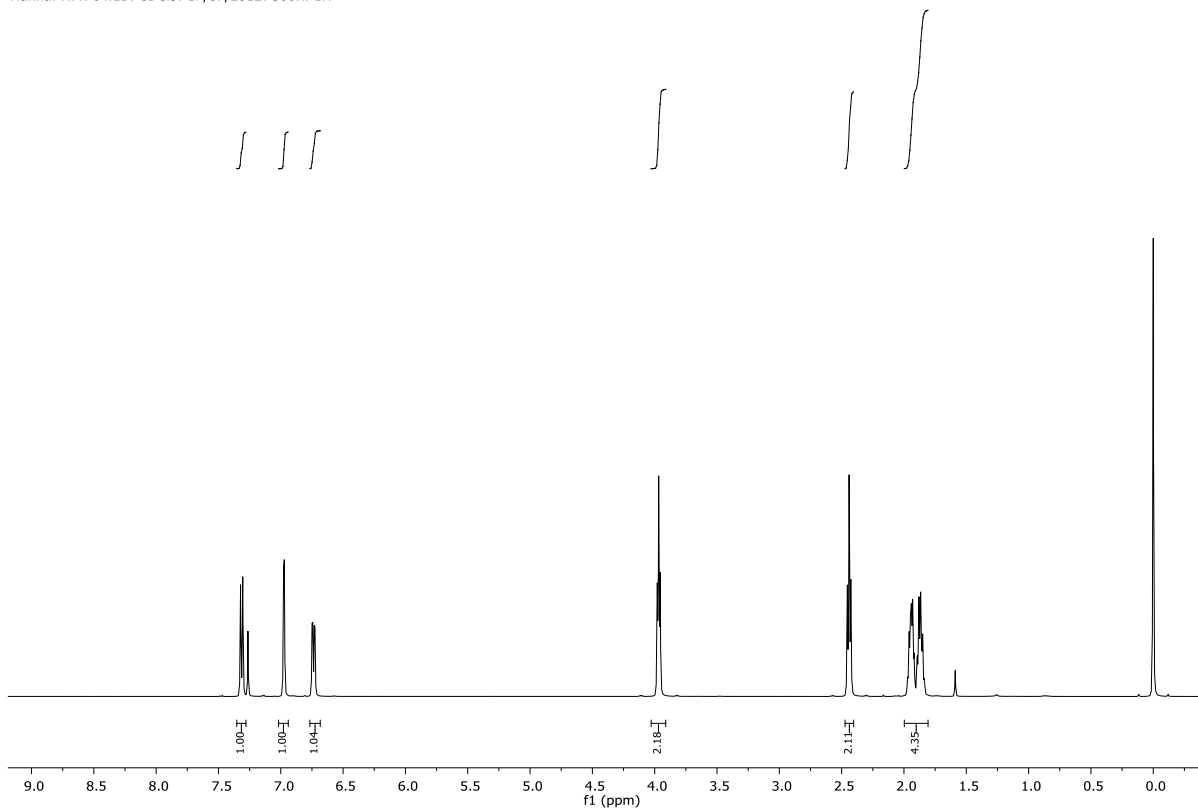
Figure S8. ^1H and ^{13}C NMR spectra of 5-(4-chlorophenoxy)pentanenitrile (**10a**).

Figure S9. ^1H and ^{13}C NMR spectra of 5-(3,4-dichlorophenoxy)pentanenitrile (**10b**).

HFK-64.1B.1.fid
Hanna: HFK-64.1B: CDCl₃: 17/07/2012: 500K: ^1H



HFK-64.1B.2.fid
Hanna: HFK-64.1B: CDCl₃: 17/07/2012: 500K: ^{13}C

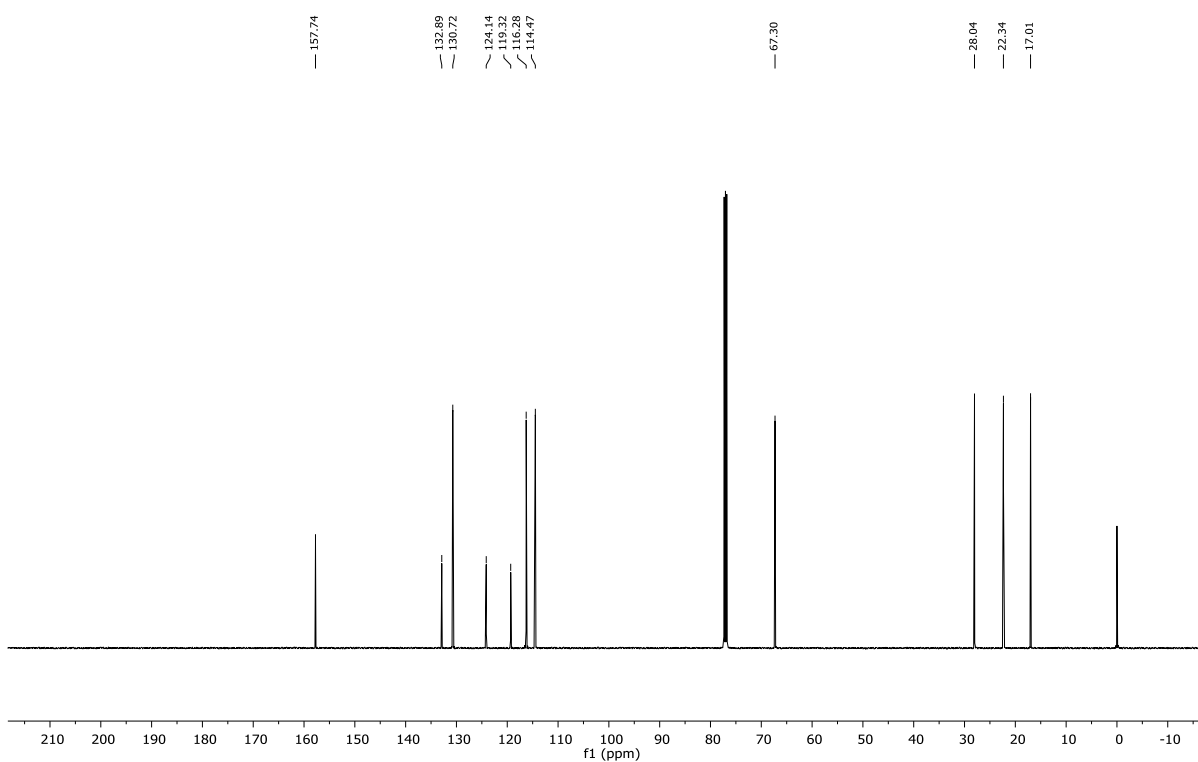


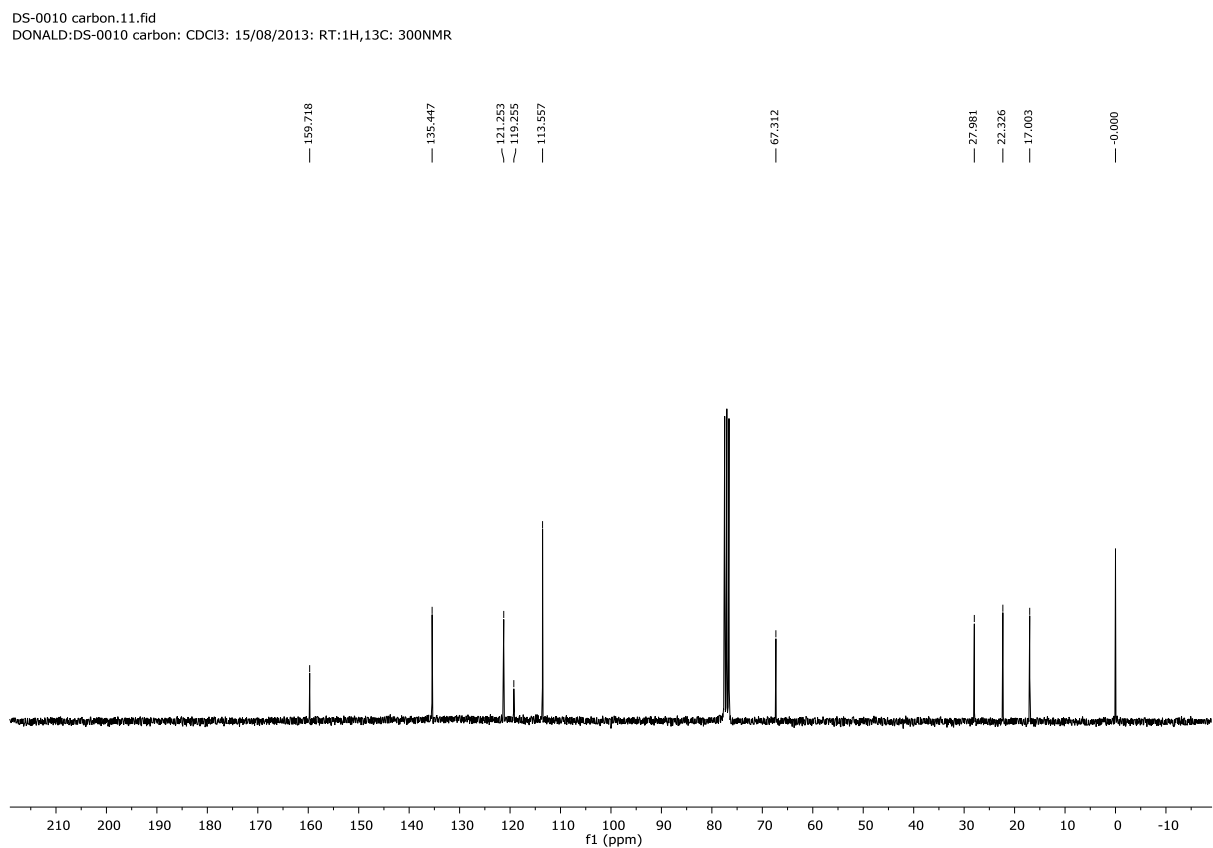
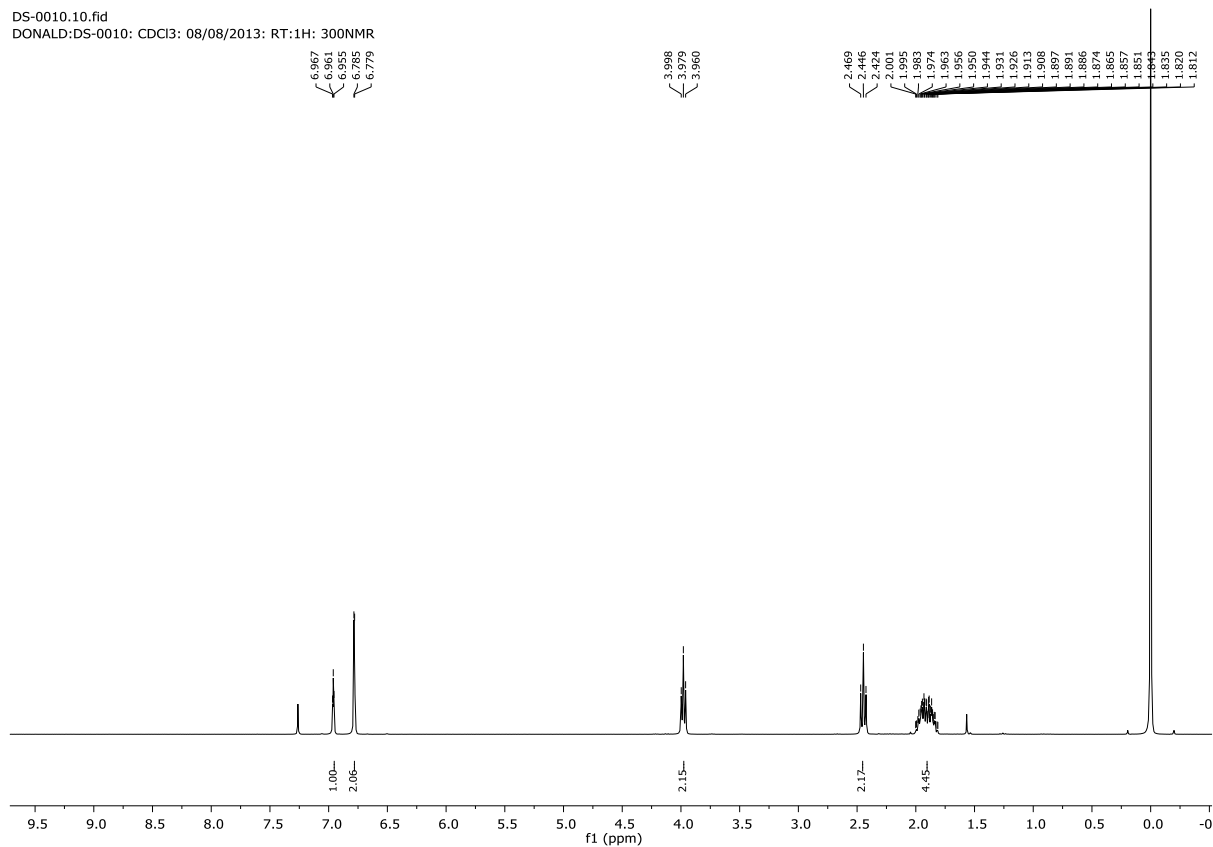
Figure S10. ^1H and ^{13}C NMR spectra of (5-(3,5-dichlorophenoxy)pentanenitrile (**10c**).

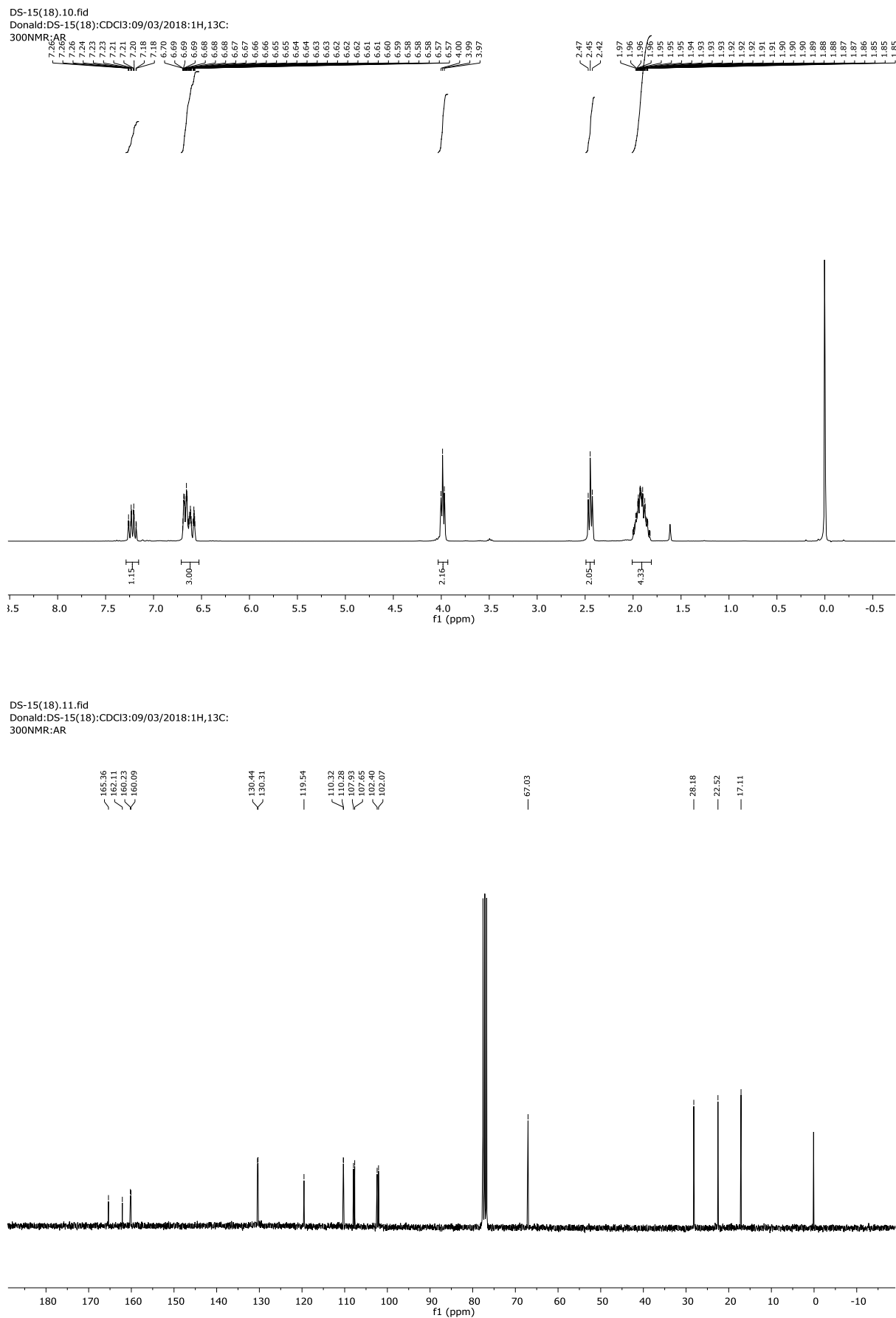
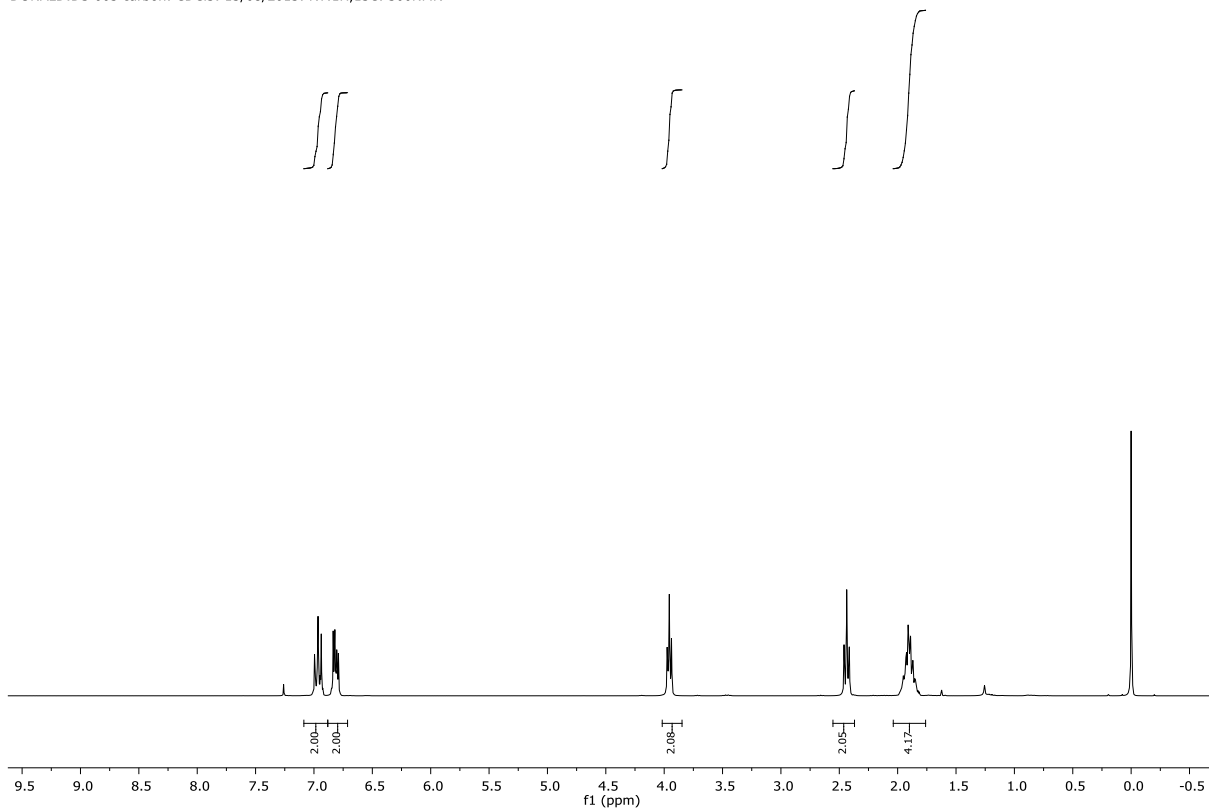
Figure S11. ^1H and ^{13}C NMR spectra of 5-(3-fluorophenoxy)pentanenitrile (**10d**).

Figure S12. ^1H and ^{13}C NMR spectra of 5-(4-fluorophenoxy)pentanenitrile (**10e**).

DS-005 carbon.10.fid

DONALD:DS-005 carbon: CDCl₃: 15/08/2013: RT:1H,13C: 300NMR

DS-005 carbon.11.fid

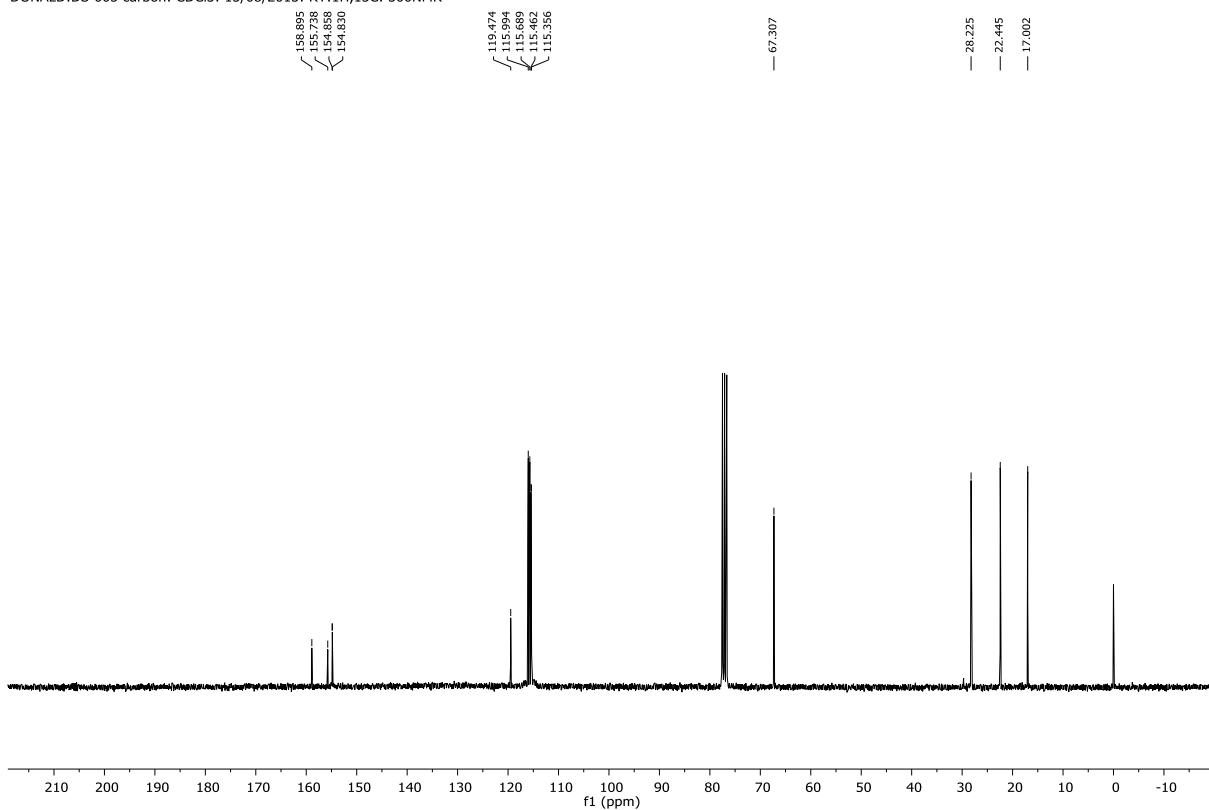
DONALD:DS-005 carbon: CDCl₃: 15/08/2013: RT:1H,13C: 300NMR

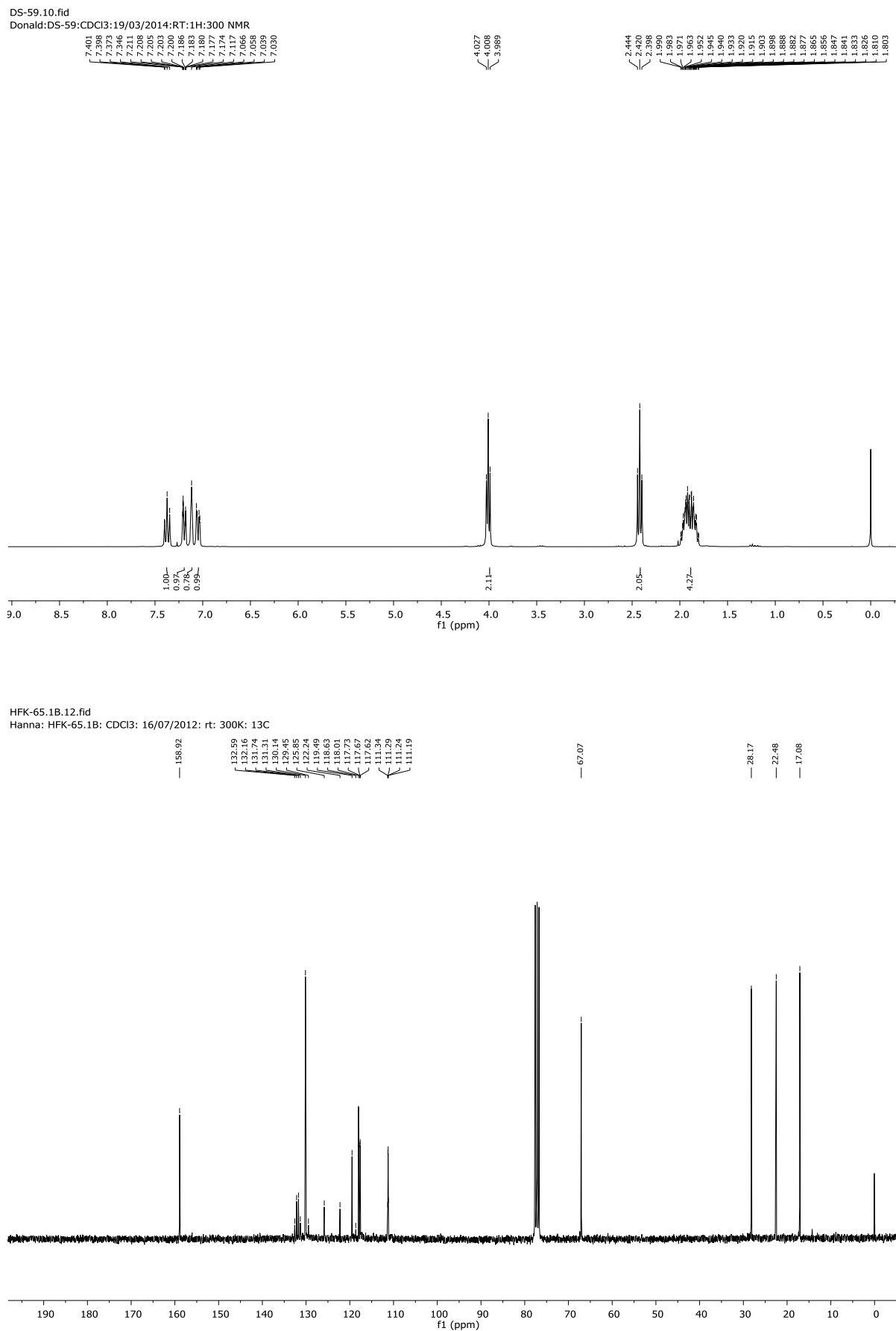
Figure S13. ^1H and ^{13}C NMR spectra of 5-(3-(trifluoromethyl)phenoxy)pentanenitrile (**10f**).

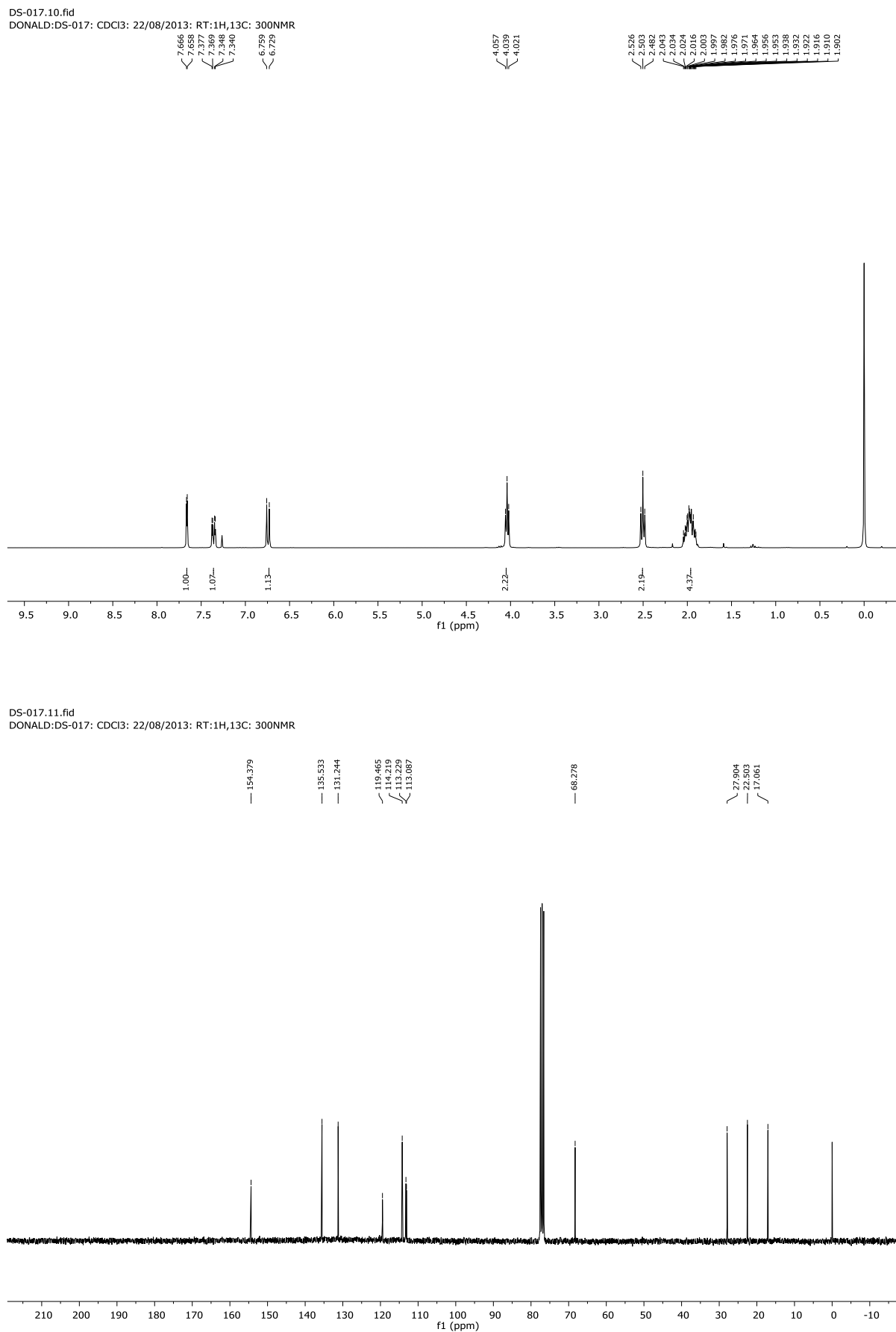
Figure S14. ^1H and ^{13}C NMR spectra of 5-(2,4-dibromophenoxy)pentanenitrile (**10g**).

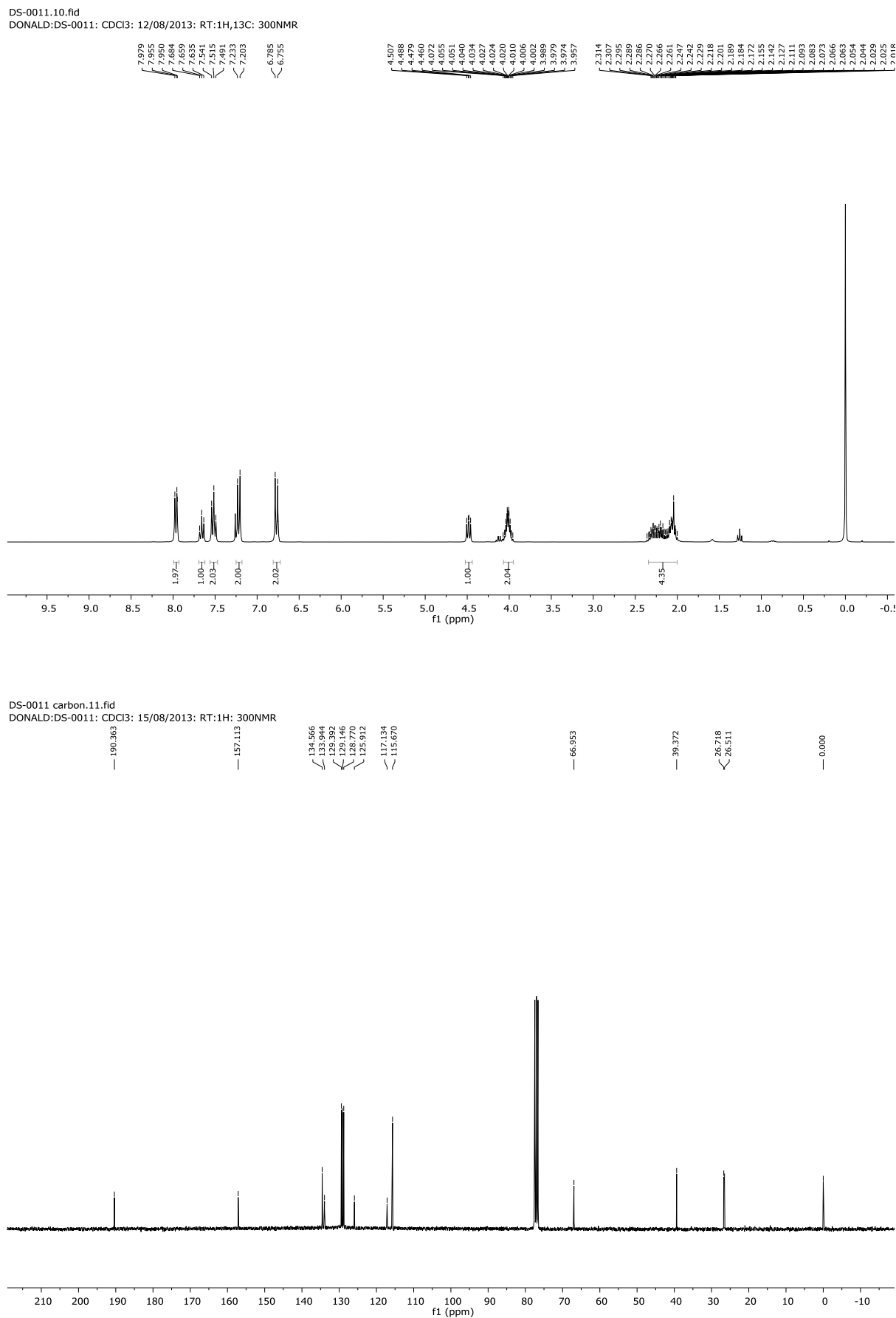
Figure S15. ^1H and ^{13}C NMR spectra of 2-benzoyl-5-(4-chlorophenoxy)pentanenitrile (**11a**).

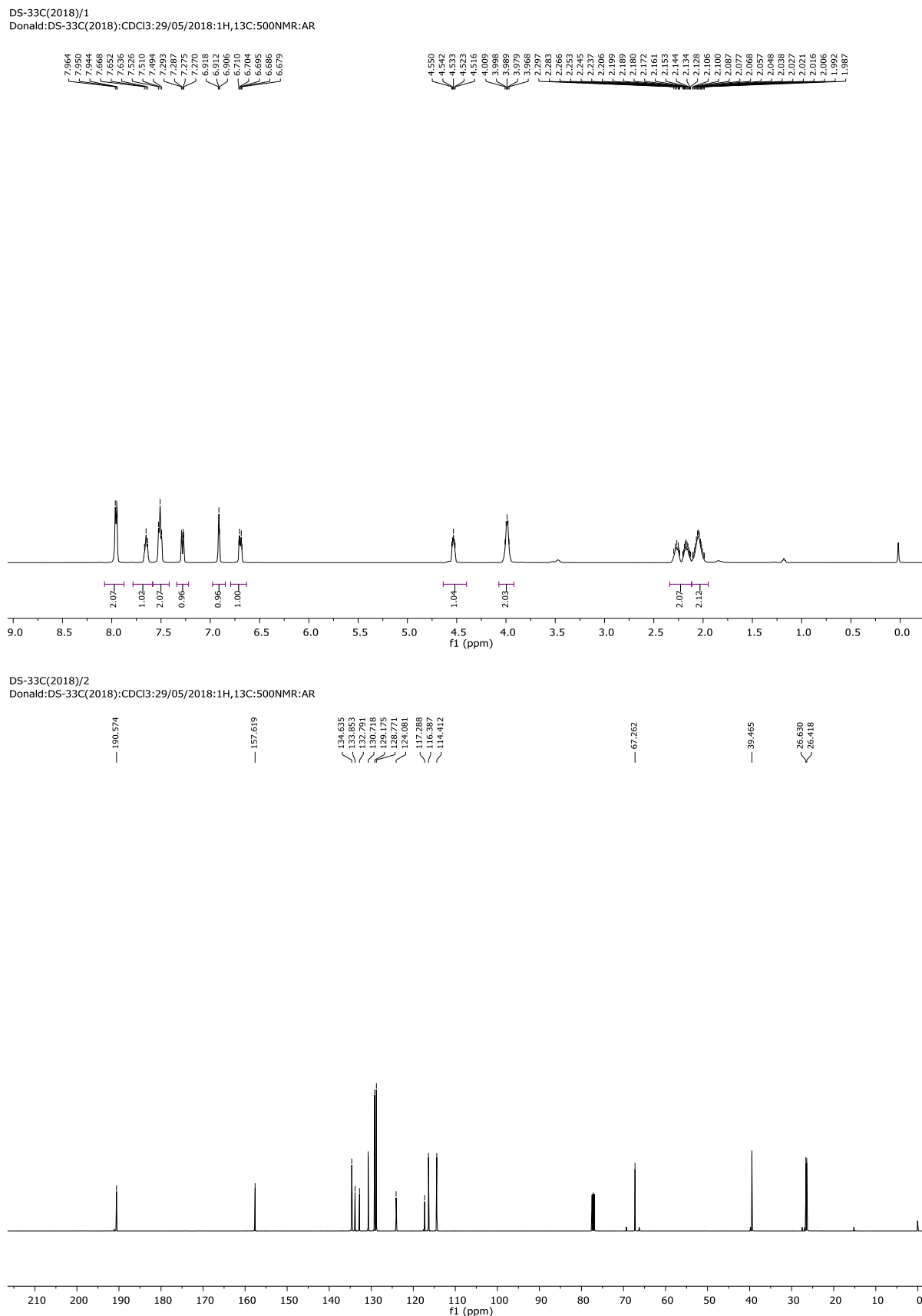
Figure S16. ^1H and ^{13}C NMR spectra of 2-benzoyl-5-(3,4-dichlorophenoxy)pentanenitrile (**11b**).

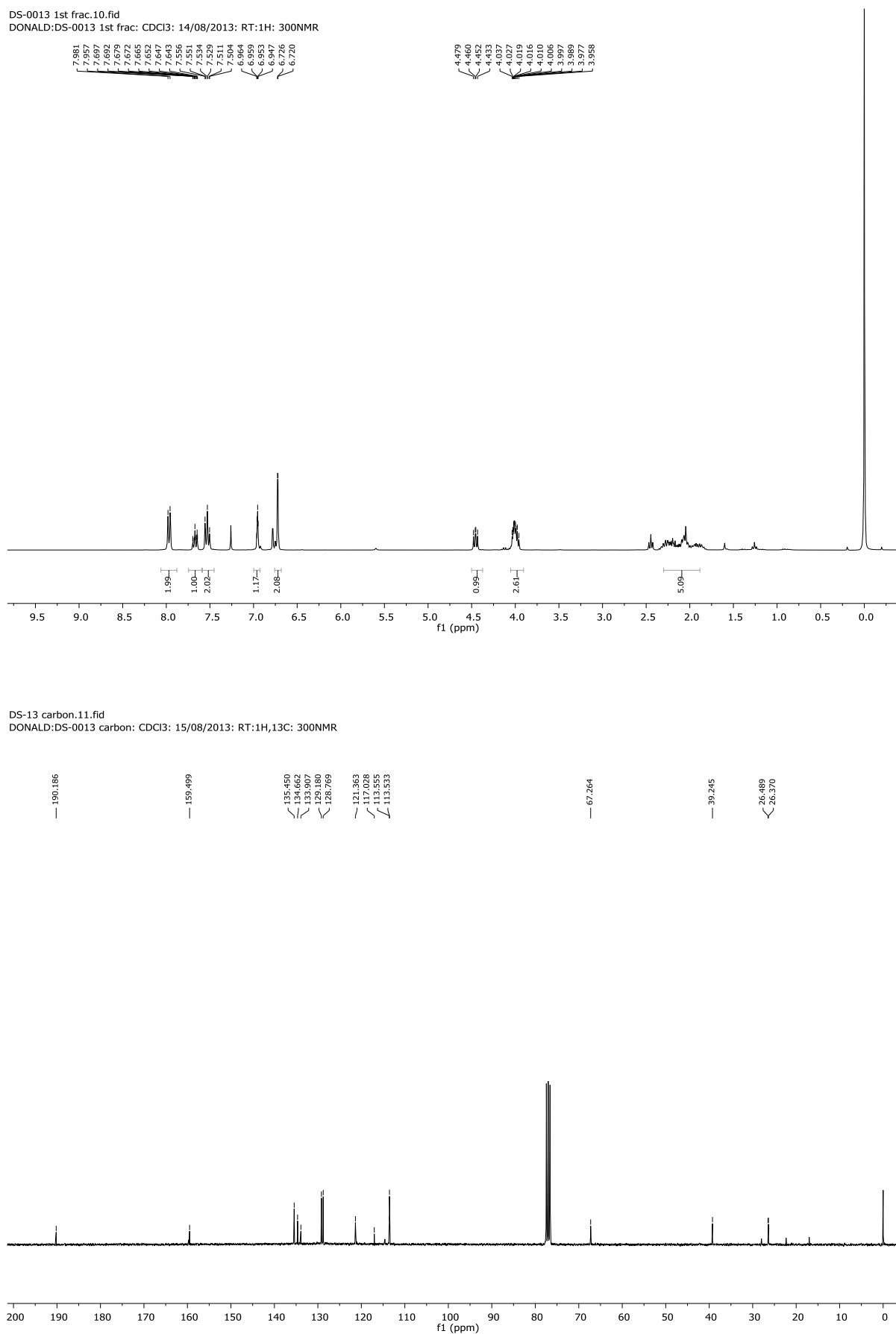
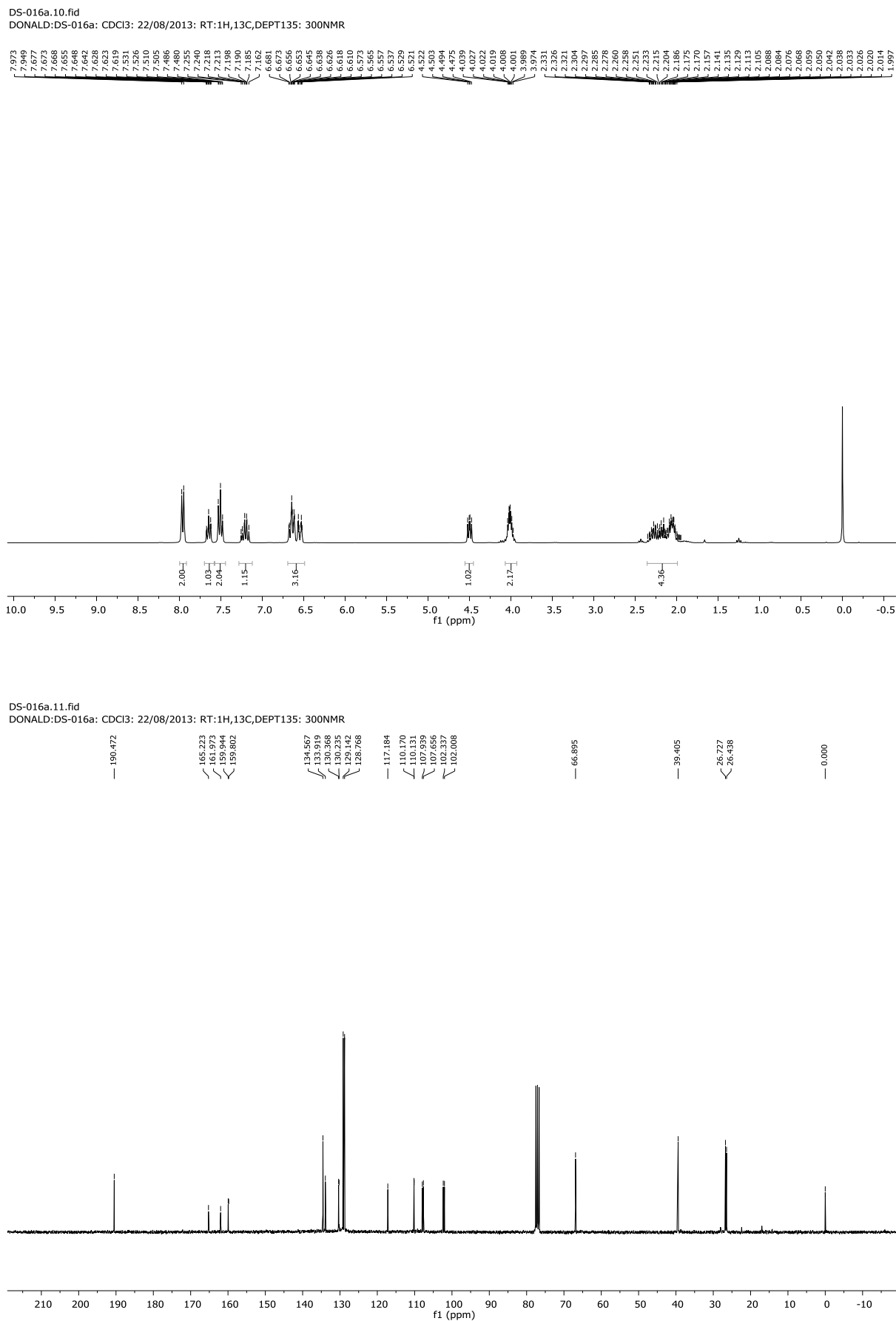
Figure S17. ^1H and ^{13}C NMR spectra of 2-benzoyl-5-(3,5-dichlorophenoxy)pentanenitrile (**11c**).

Figure S18. ^1H and ^{13}C NMR spectra of 2-benzoyl-5-(3-fluorophenoxy)pentanenitrile (**11d**).

DS-009.10.fid
DONALD:DS-009: CDCl3: 14/08/2013: RT:1H: 300NMNR

Chemical shifts (ppm): 7.985, 7.982, 7.976, 7.964, 7.958, 7.952, 7.680, 7.675, 7.663, 7.656, 7.649, 7.635, 7.631, 7.626, 7.539, 7.535, 7.532, 7.517, 7.512, 7.494, 7.487, 6.997, 6.987, 6.982, 6.966, 6.959, 6.956, 6.951, 6.951, 6.929, 6.929, 6.877, 6.872, 6.822, 6.815, 6.803, 6.794, 6.788, 6.780, 6.772, 6.766, 6.758, 4.519, 4.500, 4.491, 4.472, 4.452, 4.406, 4.018, 4.015, 4.011, 4.001, 3.997, 3.984, 3.960, 3.962, 3.943, 2.318, 2.299, 2.292, 2.275, 2.272, 2.266, 2.247, 2.230, 2.219, 2.211, 2.202, 2.191, 2.173, 2.156, 2.152, 2.104, 2.088, 2.084, 2.077, 2.071, 2.066, 2.059, 2.049, 2.042, 2.037, 2.037, 2.025, 2.019, 1.936, 1.930, 1.917, 1.909, 1.900, 1.895.

Integration values: 2.00, 0.96, 1.99, 2.55, 2.55, 0.96, 2.60, 4.44.

13C NMR spectrum (CDCl₃) of compound 10a. The x-axis is labeled f1 (ppm) and ranges from -10 to 210. The spectrum shows several peaks, with the most prominent one at approximately 77 ppm, which is the solvent peak (CDCl₃). Other significant peaks are labeled with their chemical shifts: 190.434, 158.964, 155.803, 154.648, 154.620, 134.551, 133.965, 129.143, 128.781, 117.177, 116.036, 115.720, 115.699, 115.444, 115.338, 67.273, 39.414, 26.797, and 26.590. The peaks are grouped with brackets and lines indicating their assignment to specific carbon environments in the molecule.

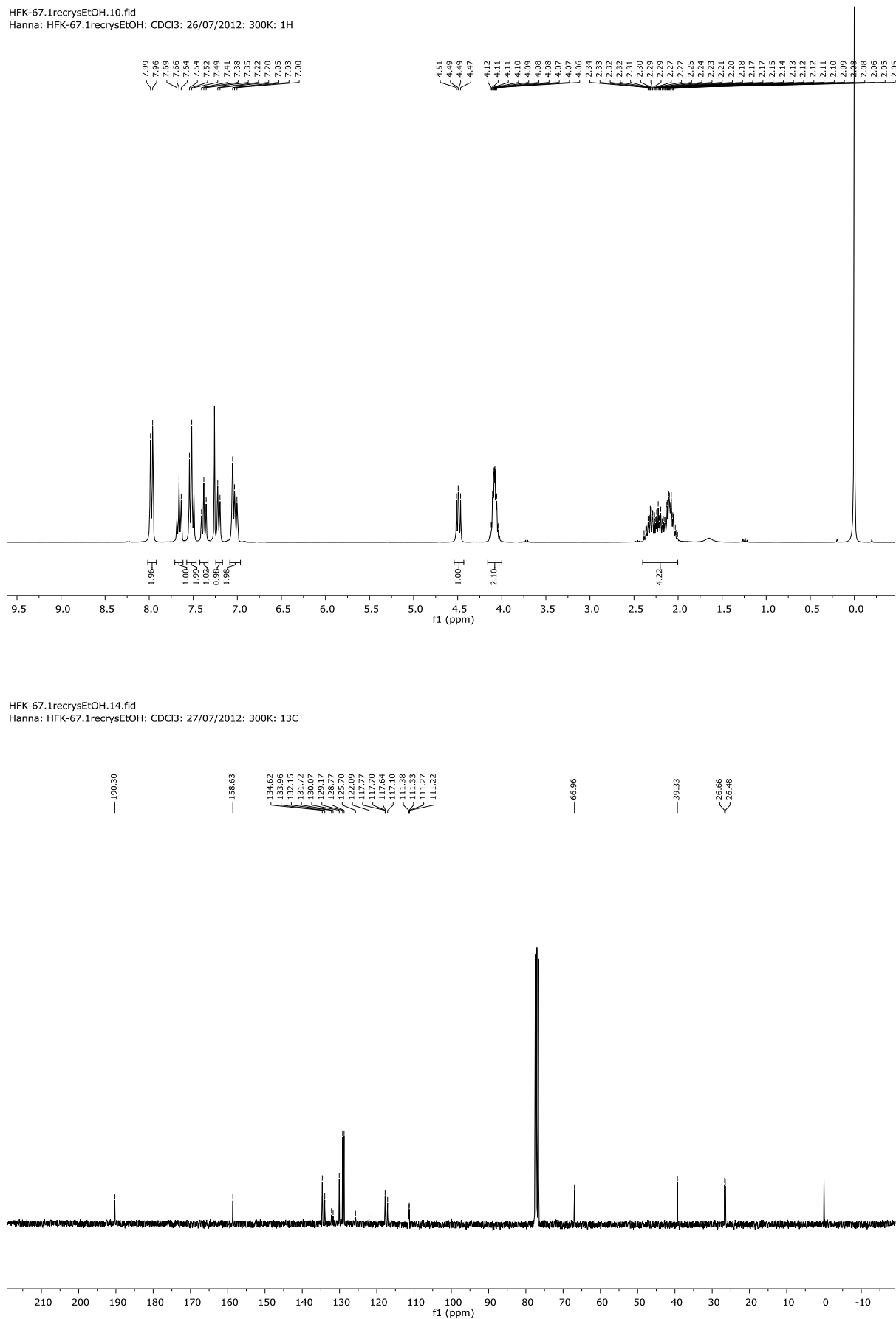
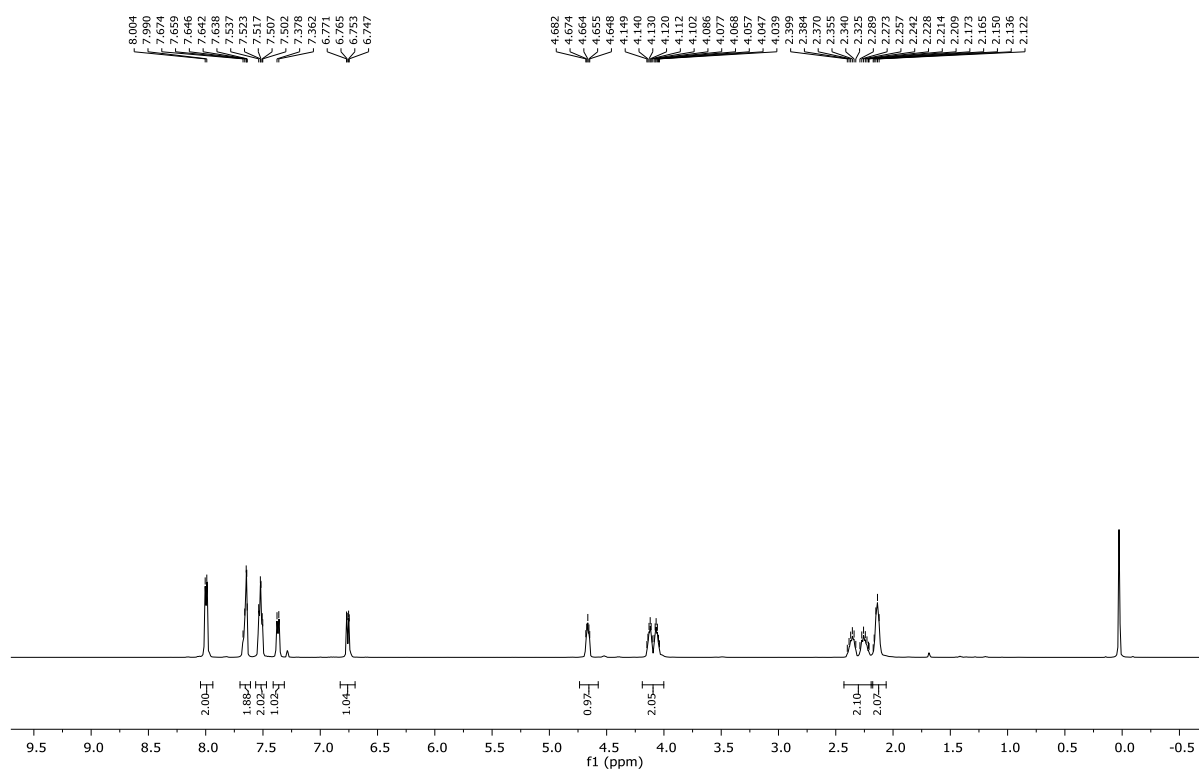
Figure S20. ^1H and ^{13}C NMR spectra of 2-benzoyl-5-(3-(trifluoromethyl)phenoxy)pentanenitrile (**11f**).

Figure S21. ^1H and ^{13}C NMR spectra of 2-benzoyl-5-(2,4-dibromophenoxy)pentanenitrile (**11g**).

DS-18C(2018)/1
Donald:DS-18C(2018):CDCl₃:29/05/2018:1H,13C:500NMR:AR



DS-18C(2018)/2
Donald:DS-18C(2018):CDCl₃:29/05/2018:1H,13C:500NMR:AR

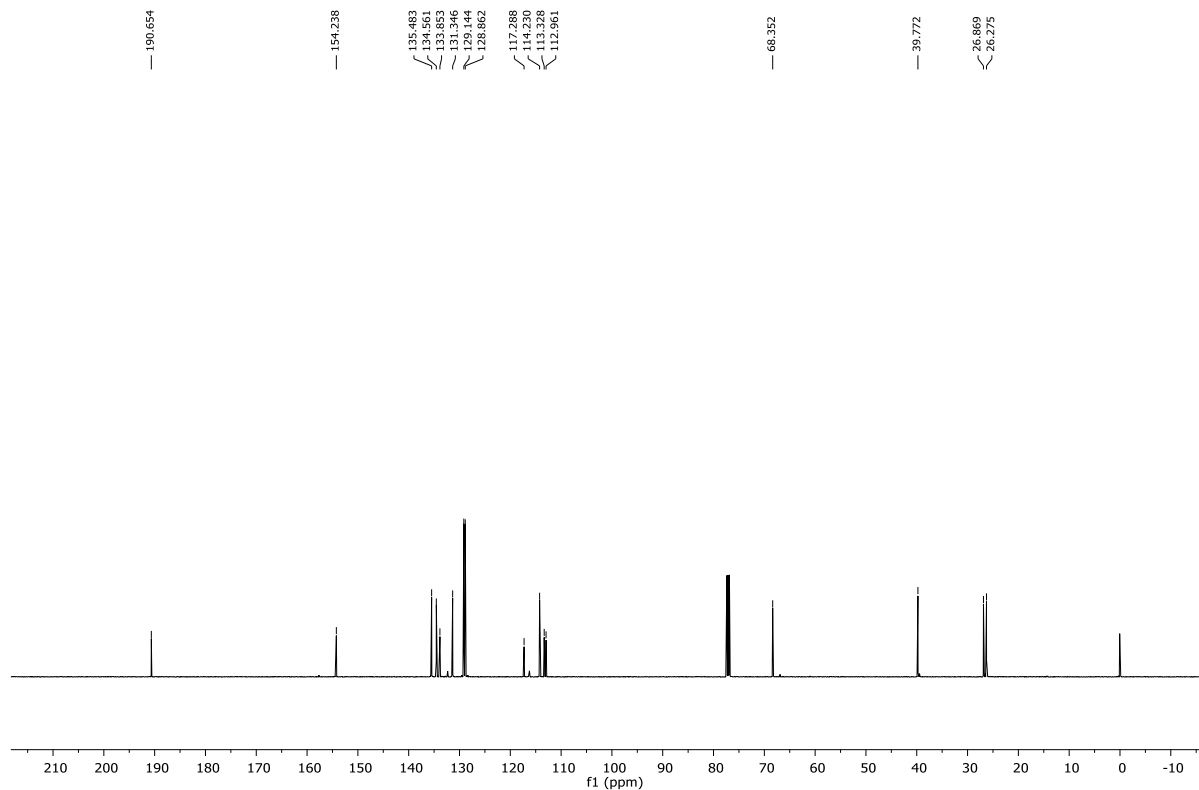
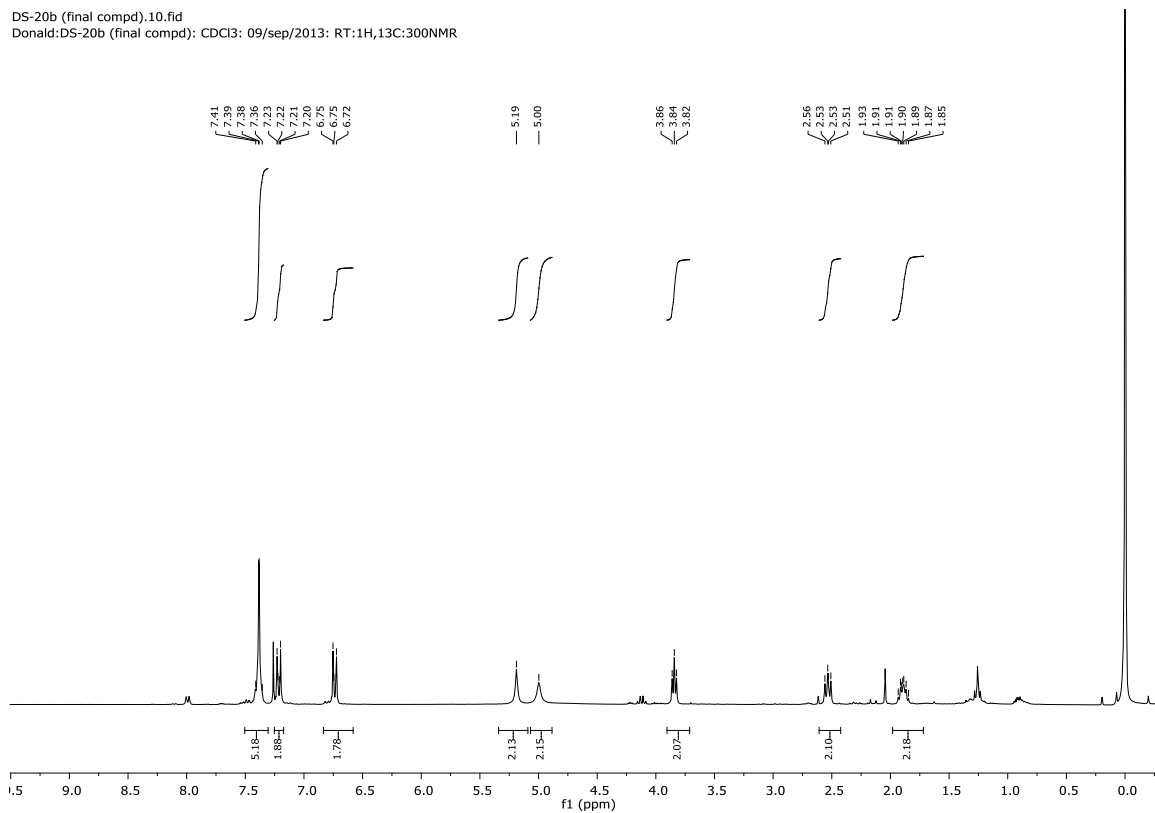


Figure S22. ^1H and ^{13}C NMR spectra of 5-(3-(4-chlorophenoxy)propyl)-6-phenylpyrimidine-2,4-diamine (**6a**).

DS-20b (final compd).10.fid

Donald:DS-20b (final compd): CDCl₃: 09/sep/2013: RT:1H,13C:300NMR

DS-20b (final compd).11.fid

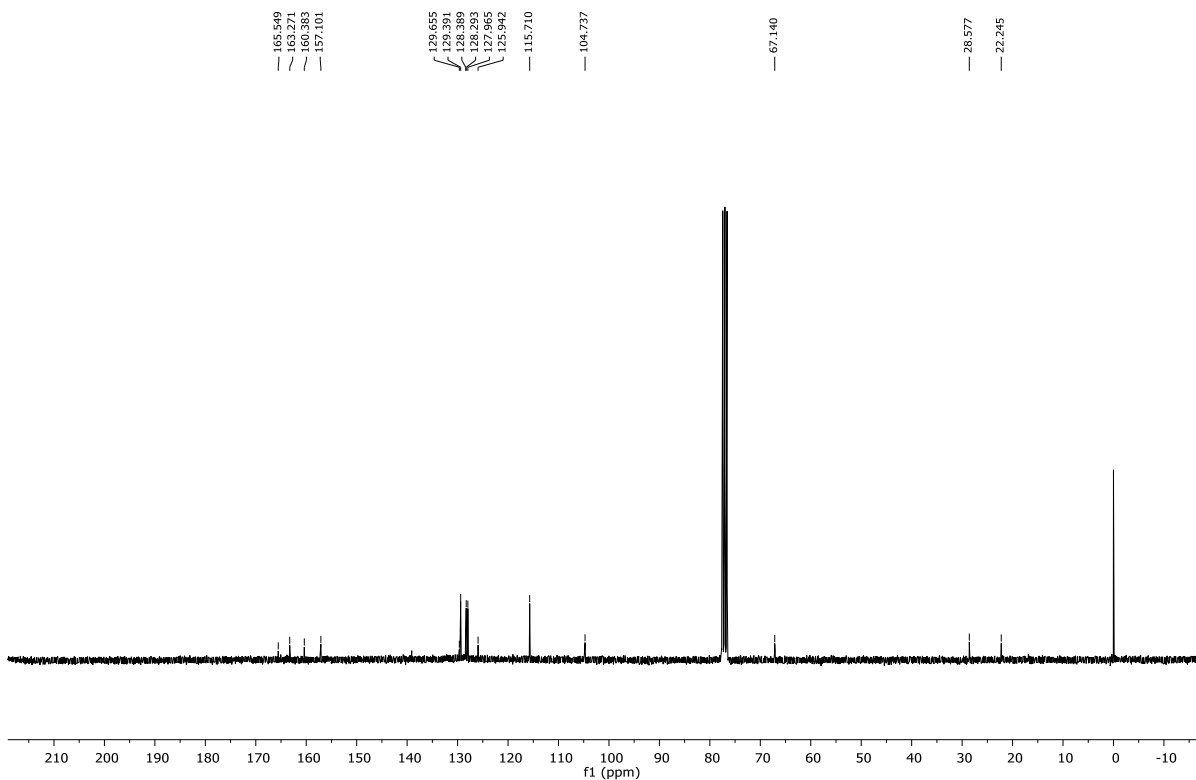
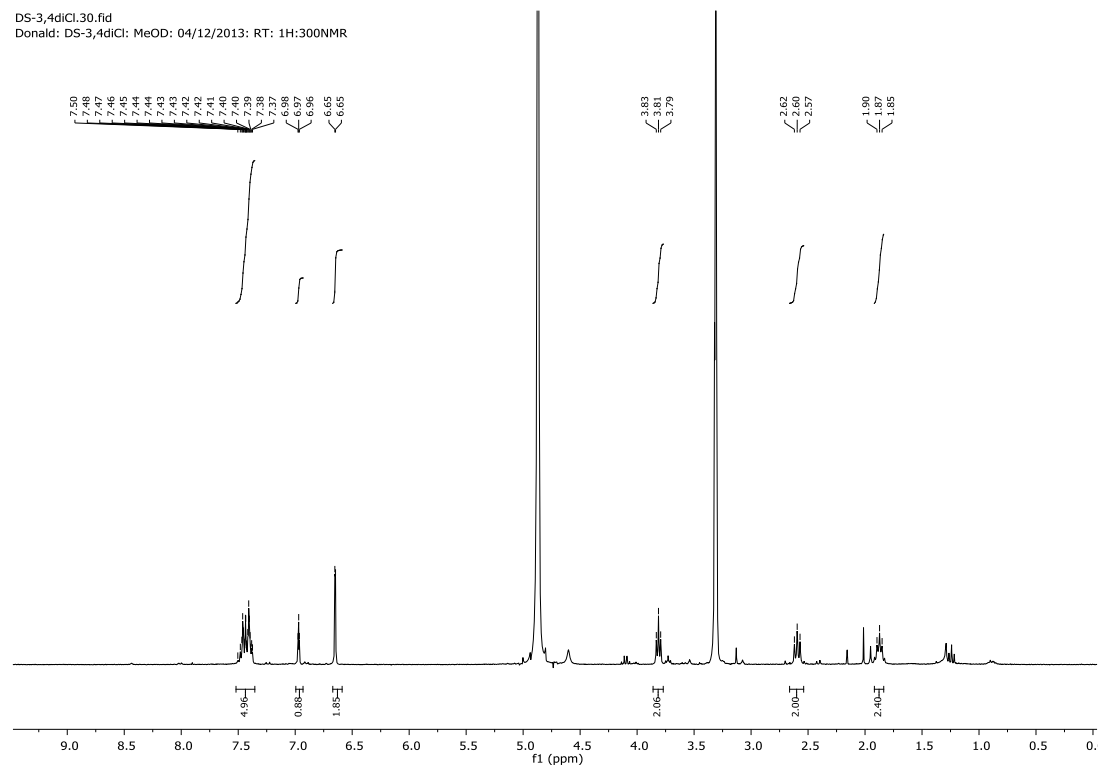
Donald:DS-20b (final compd): CDCl₃: 09/sep/2013: RT:1H,13C:300NMR

Figure S23. ^1H and ^{13}C NMR spectra of 5-(3-(3,4-dichlorophenoxy)propyl)-6-phenylpyrimidine-2,4-diamine (**6b**).

DS-026.4.fid
Donald: DS 026: MeOD: 10/03/2014: 300K: 1H, 13C: 500NMR

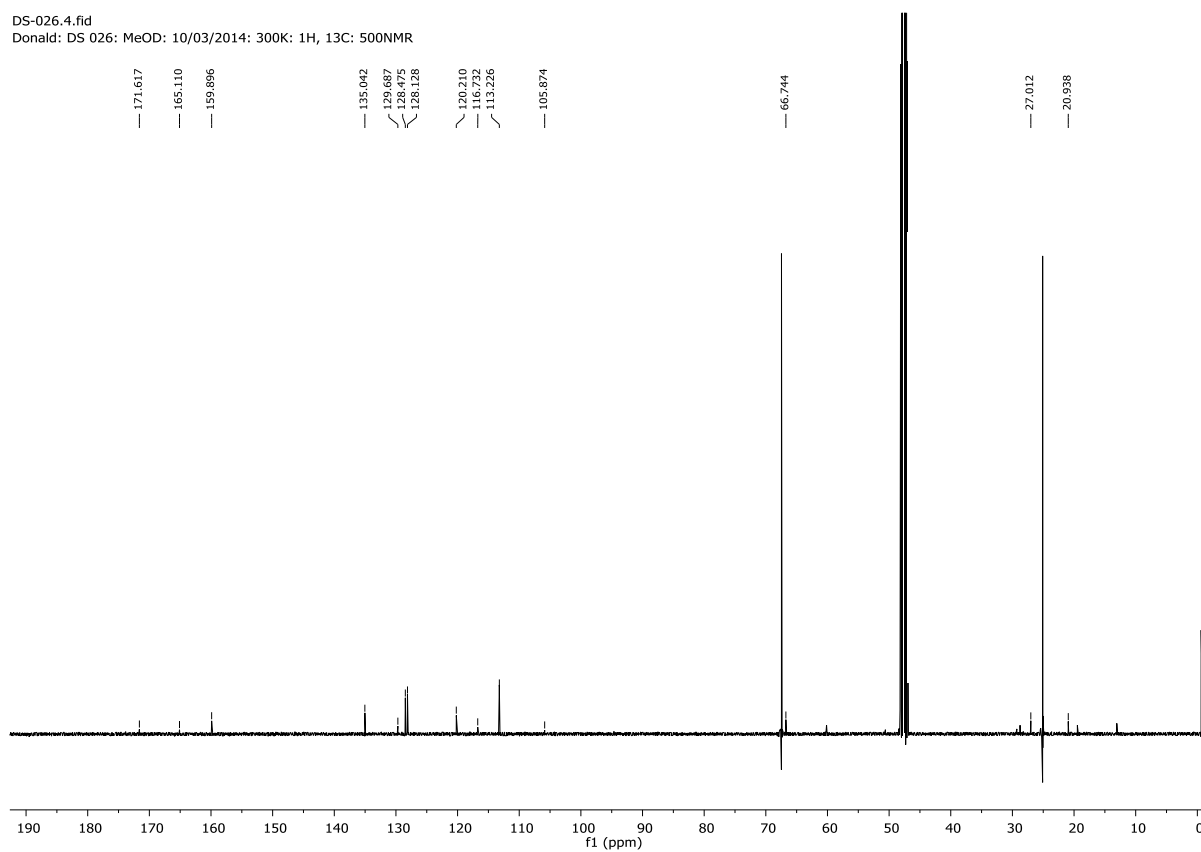
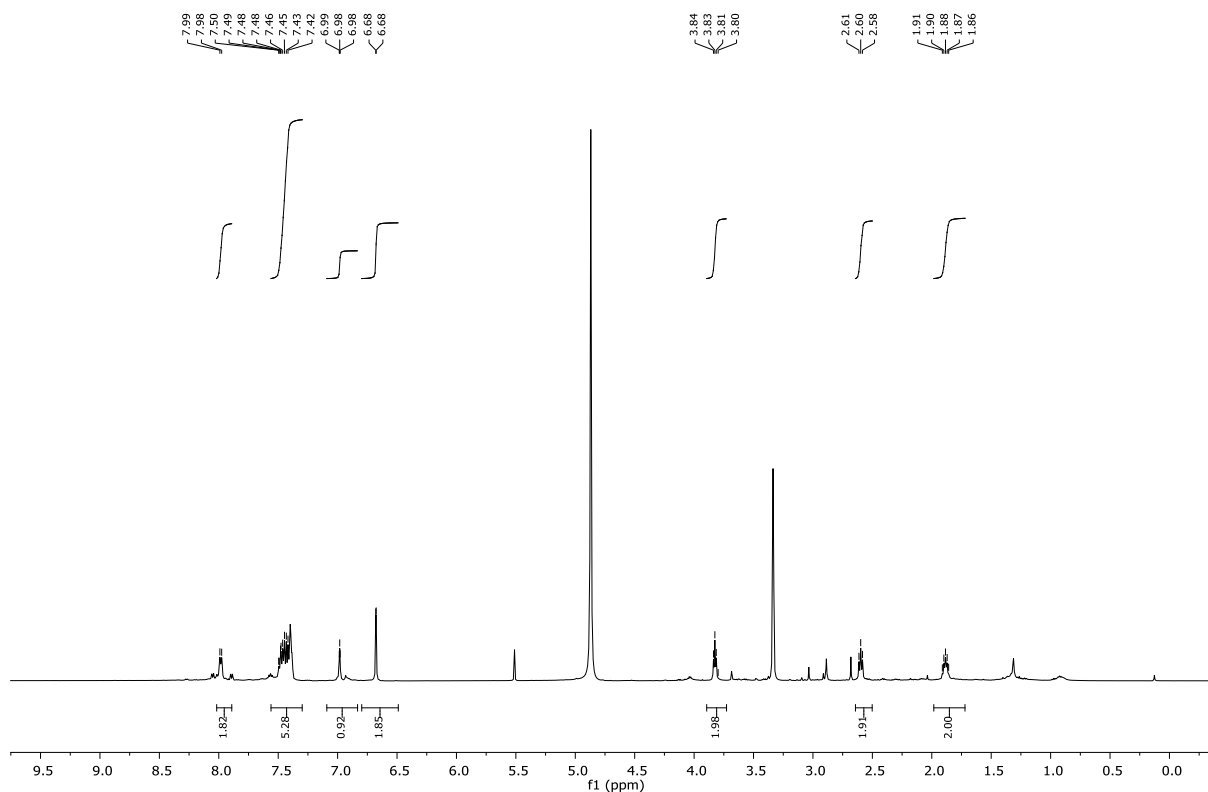


Figure S24. ^1H and ^{13}C NMR spectra of 5-(3-(3,5-dichlorophenoxy)propyl)-6-phenylpyrimidine-2,4-diamine (**6c**).

DS-24(FP).1.fid

Donald-24(FP): MeOD:30/09/2013:RT:1H,13C:500NMR



DS-24(FP).2.fid

Donald-24(FP): MeOD:30/09/2013:RT:1H,13C:500NMR

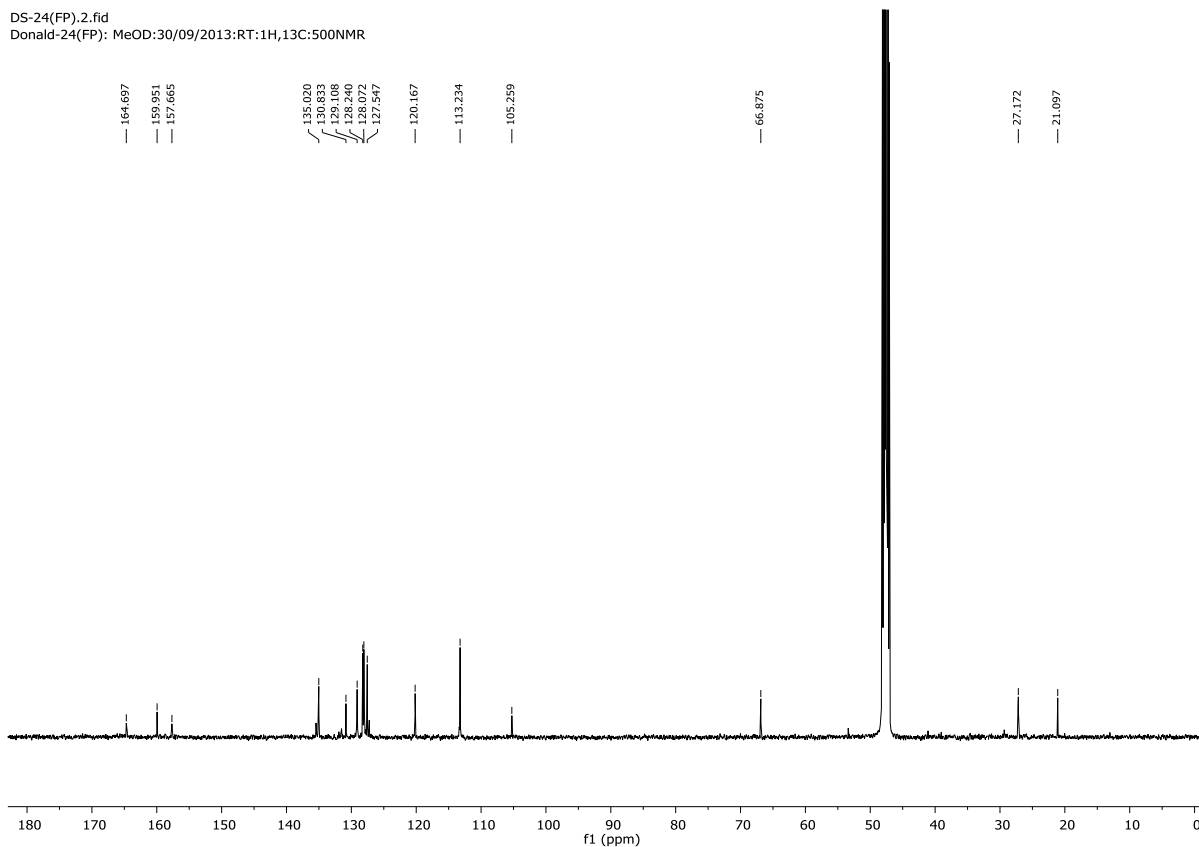


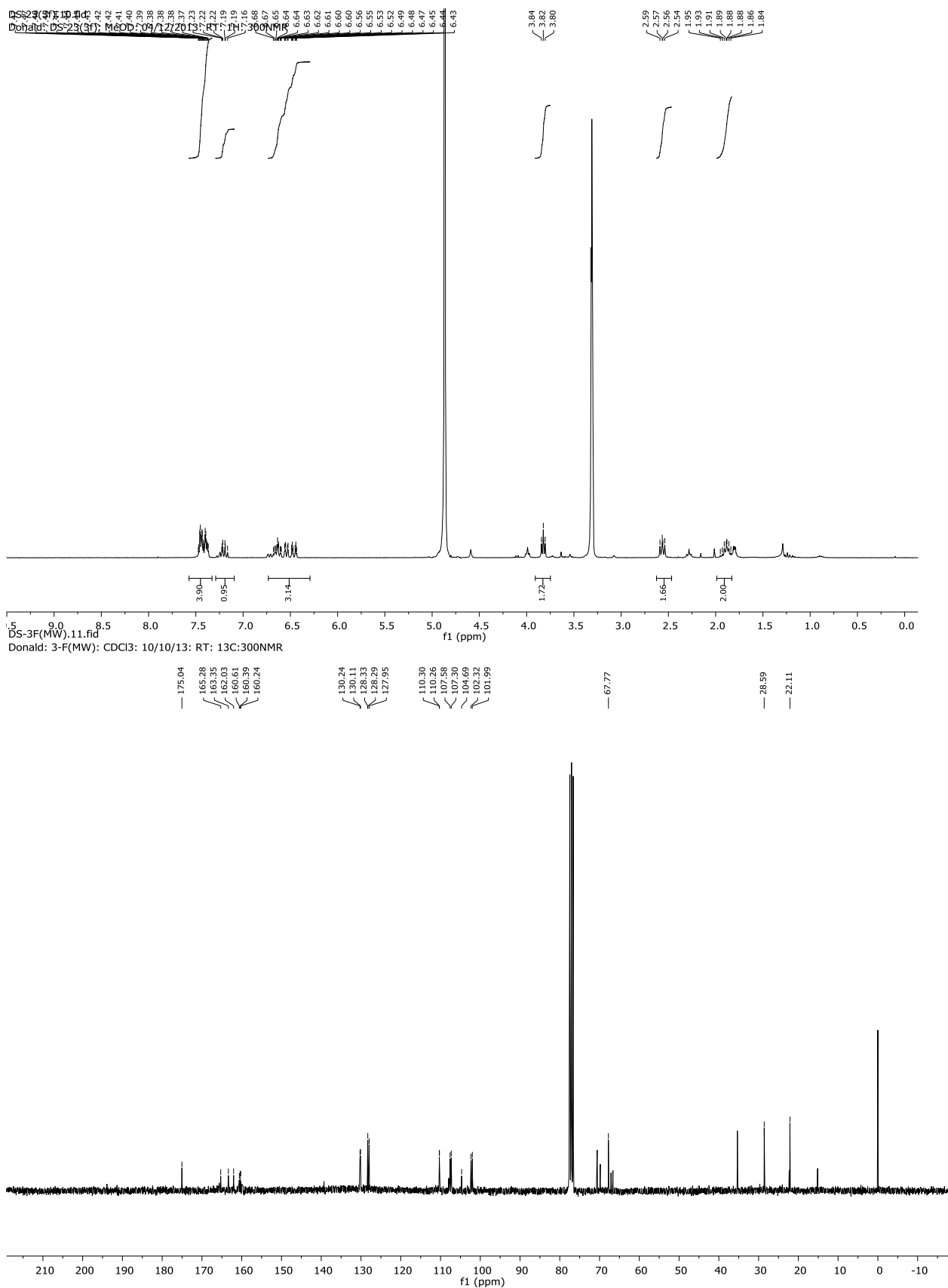
Figure S25. ^1H and ^{13}C NMR spectra of 5-(3-(3-fluorophenoxy)propyl)-6-phenylpyrimidine-2,4-diamine (**6d**).

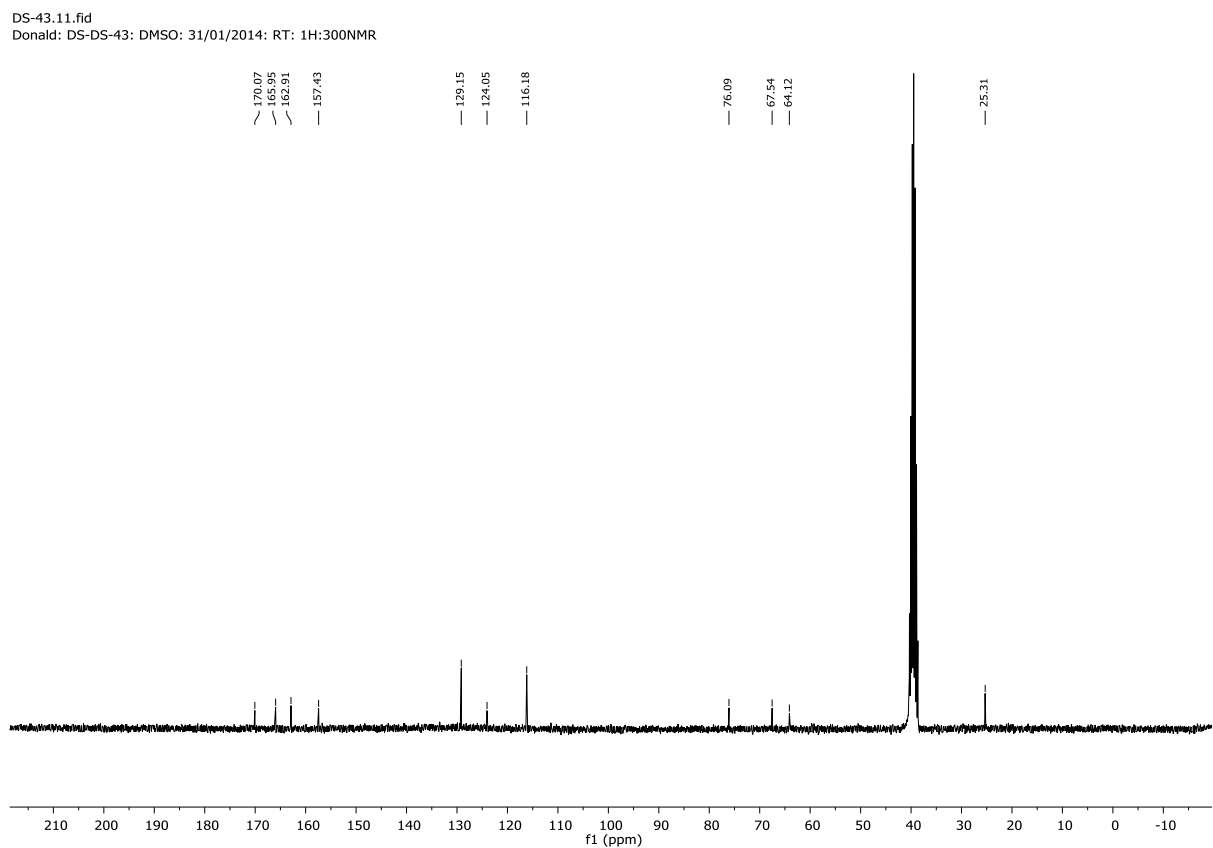
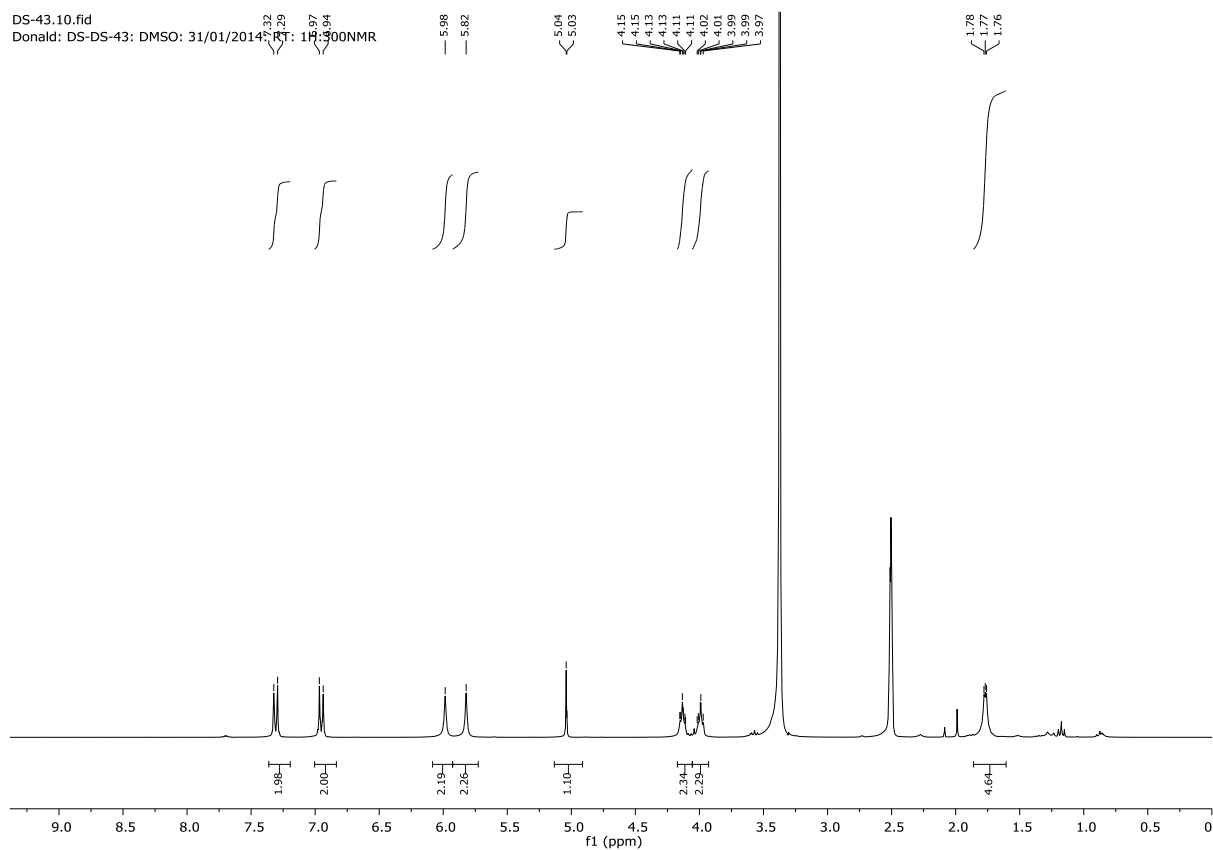
Figure S26. ^1H and ^{13}C NMR spectra of 6-(4-(4-chlorophenoxy)butoxy)pyrimidine-2,4-diamine (**7a**).

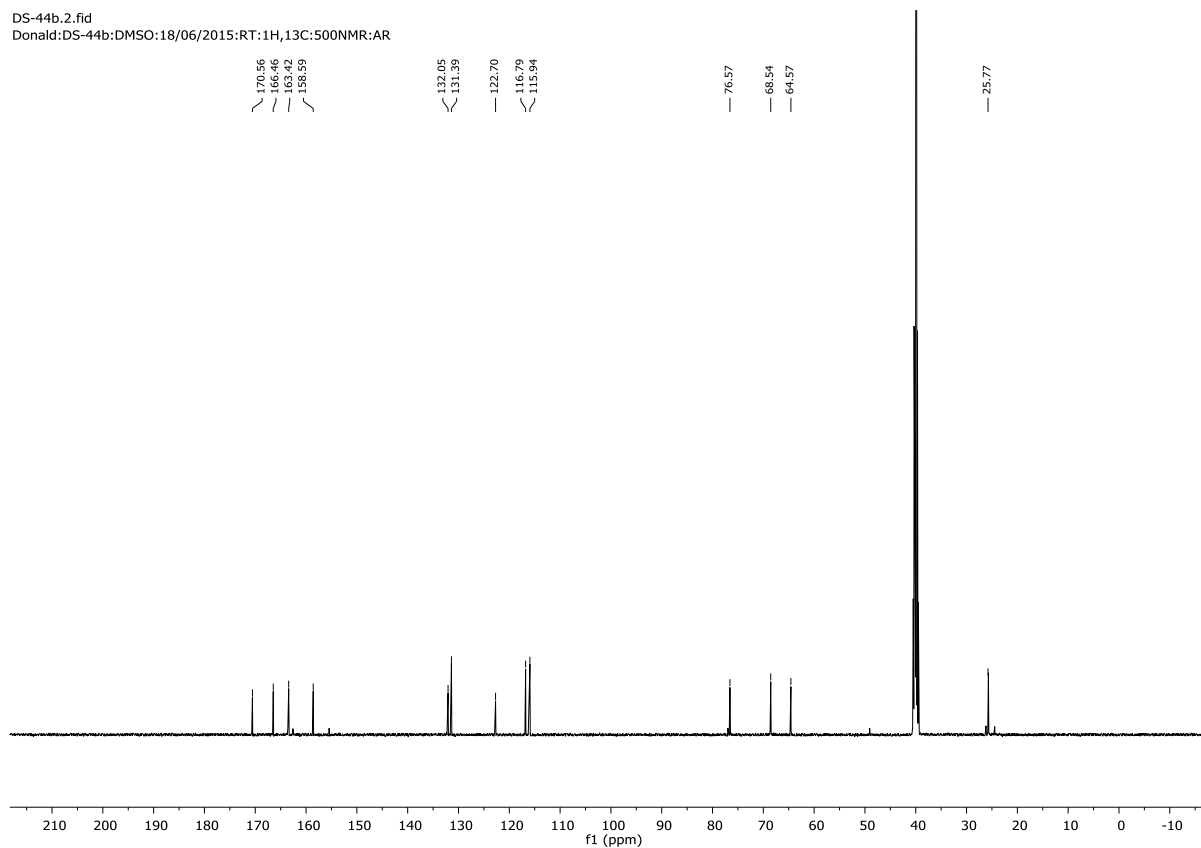
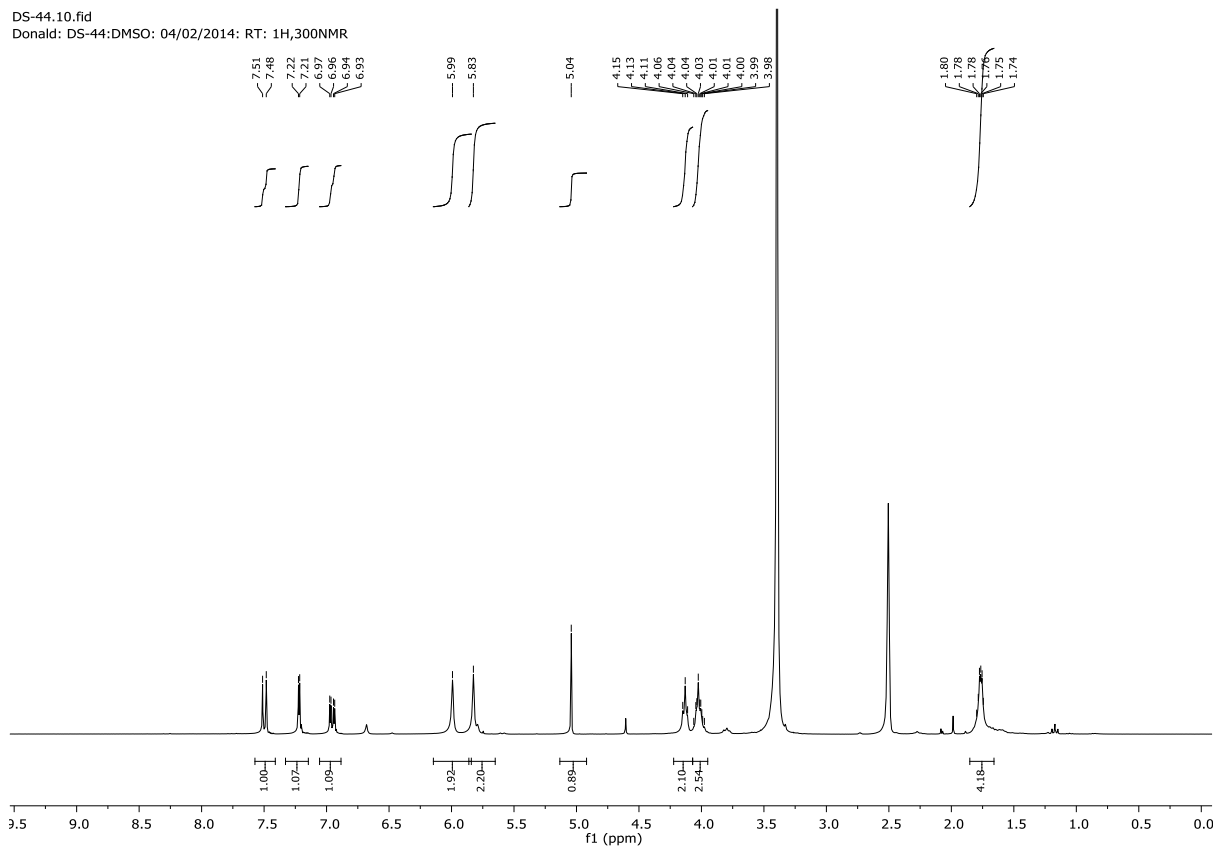
Figure S27. ^1H and ^{13}C NMR spectra of 6-(4-(3,4-dichlorophenoxy)butoxy)pyrimidine-2,4-diamine (**7b**).

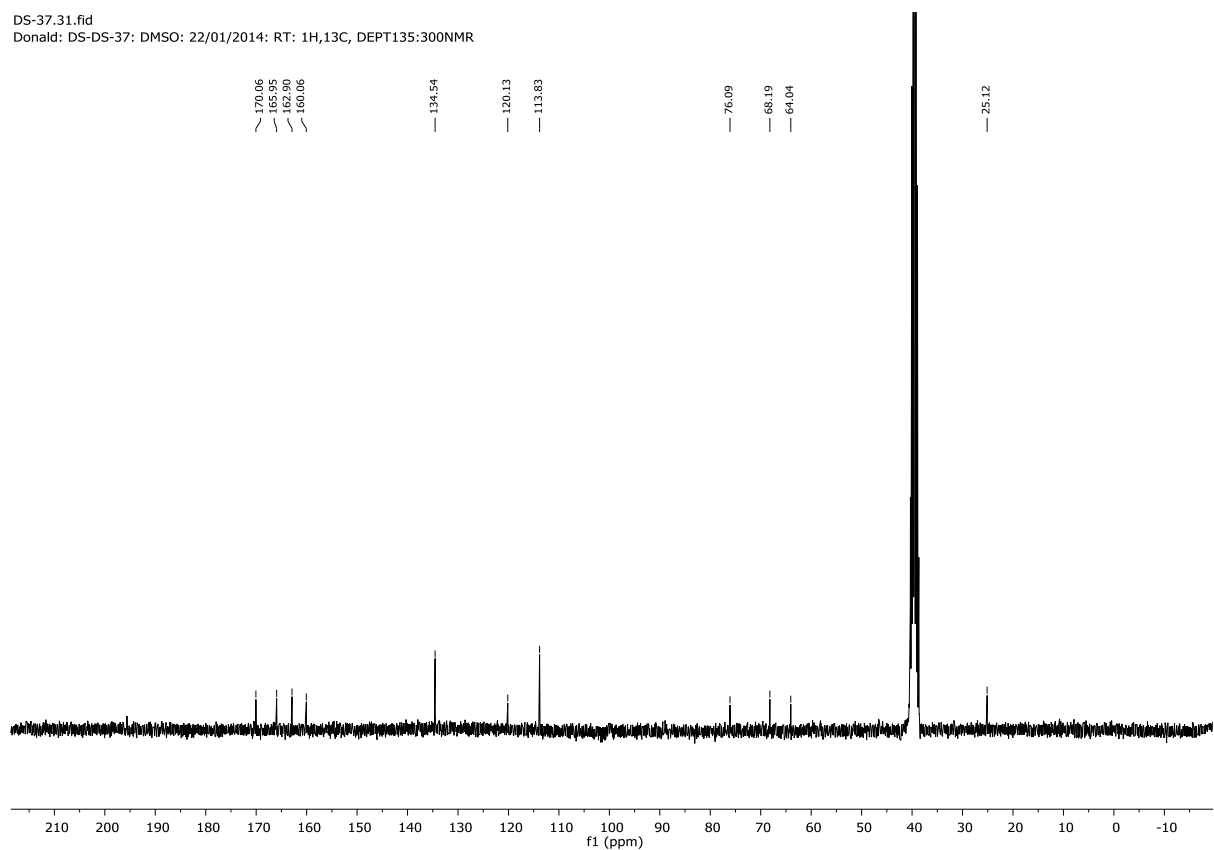
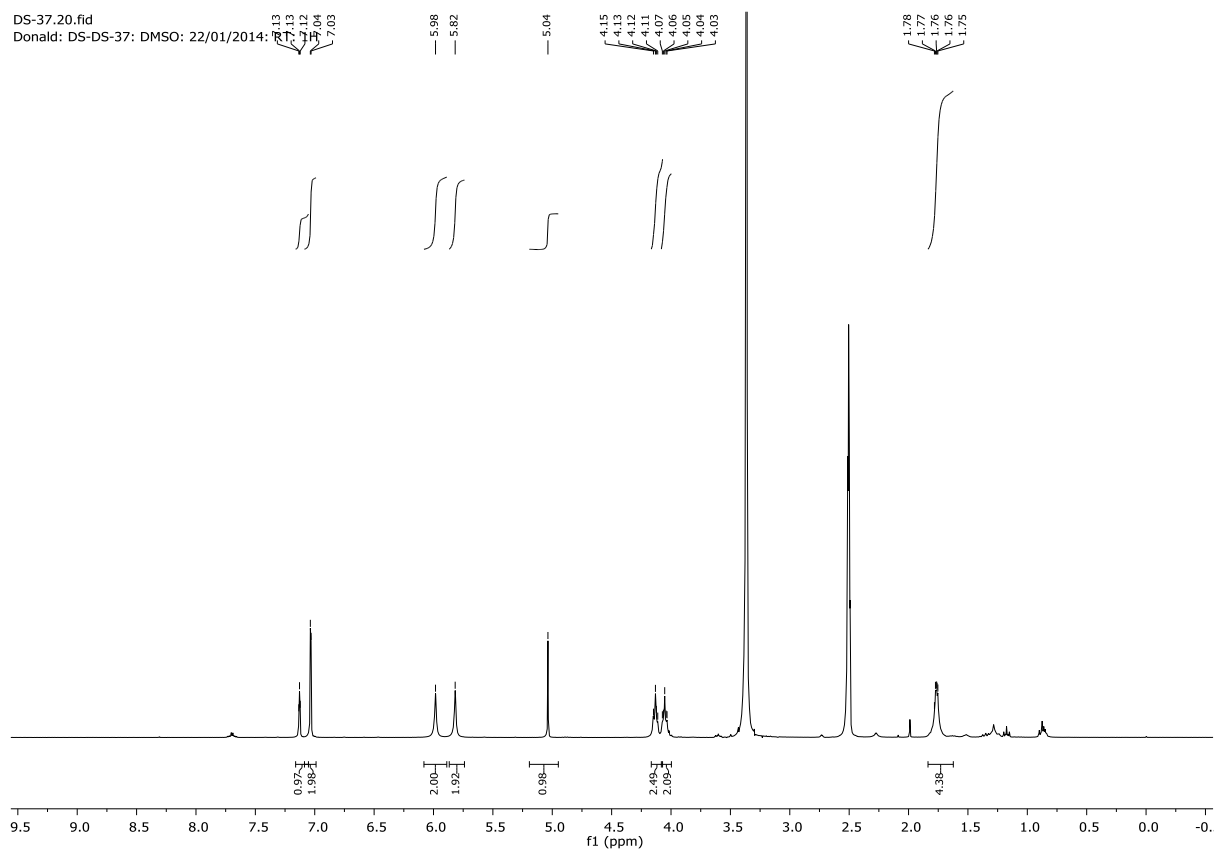
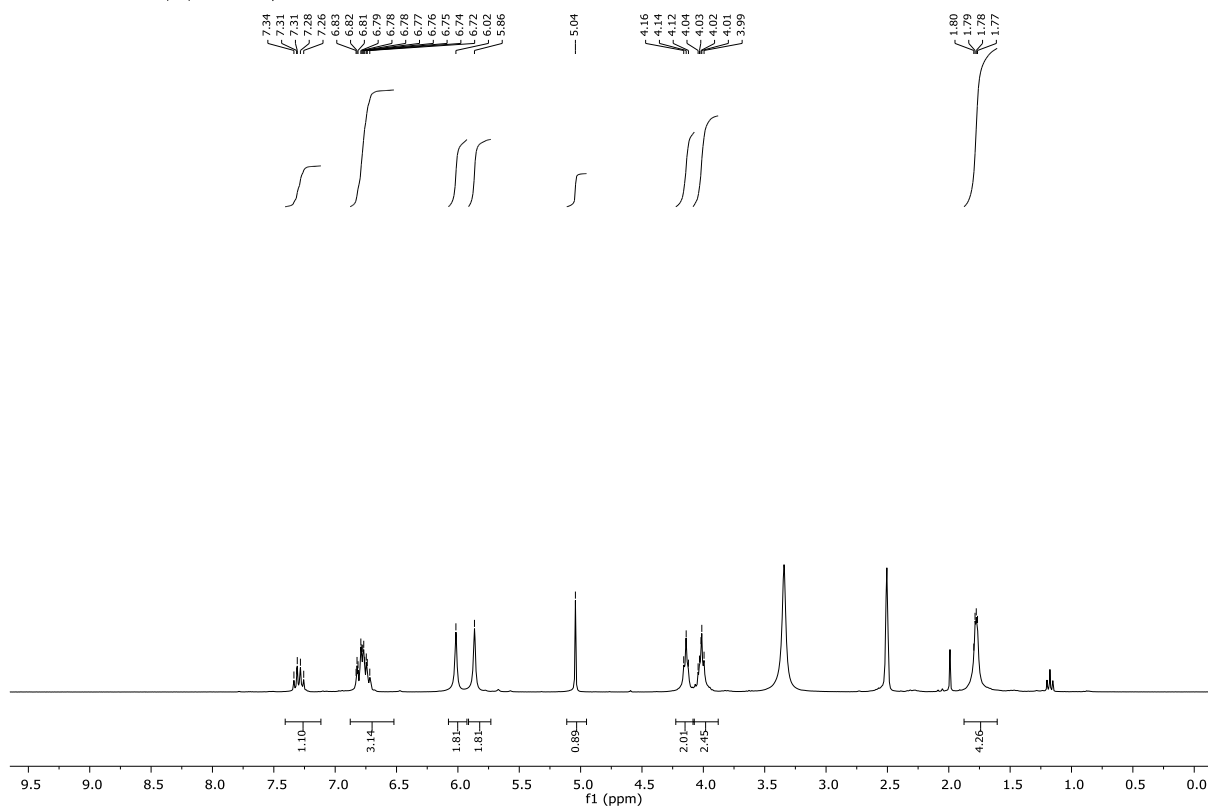
Figure S28. ^1H and ^{13}C NMR spectra of 6-(4-(3,5-dichlorophenoxy)butoxy)pyrimidine-2,4-diamine (**7c**).

Figure S29. ^1H and ^{13}C NMR spectra of 6-(4-(3-fluorophenoxy)butoxy)pyrimidine-2,4-diamine (**7d**).

DS-45.10.fid

Donald:DS-45:DMSO:26/04/2014:RT:1H,13C:300NMR



DS-45.11.fid

Donald:DS-45:DMSO:26/04/2014:RT:1H,13C:300NMR

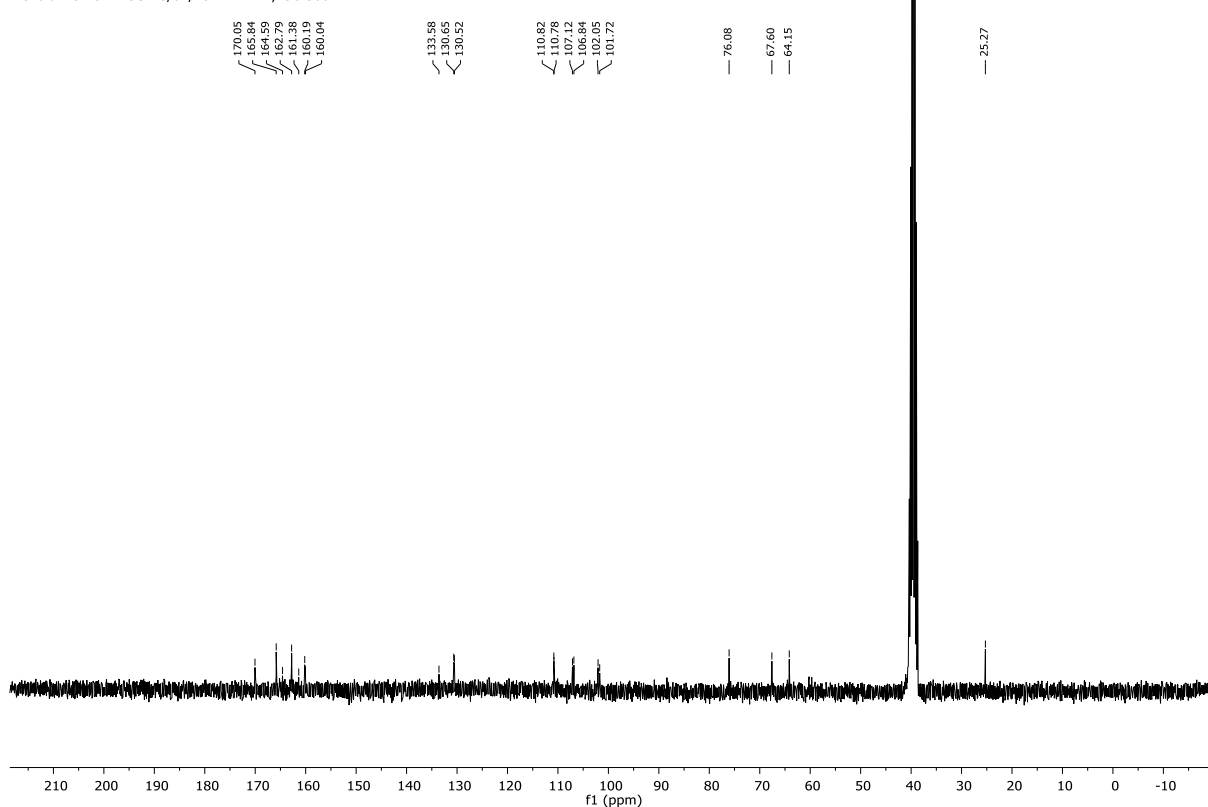


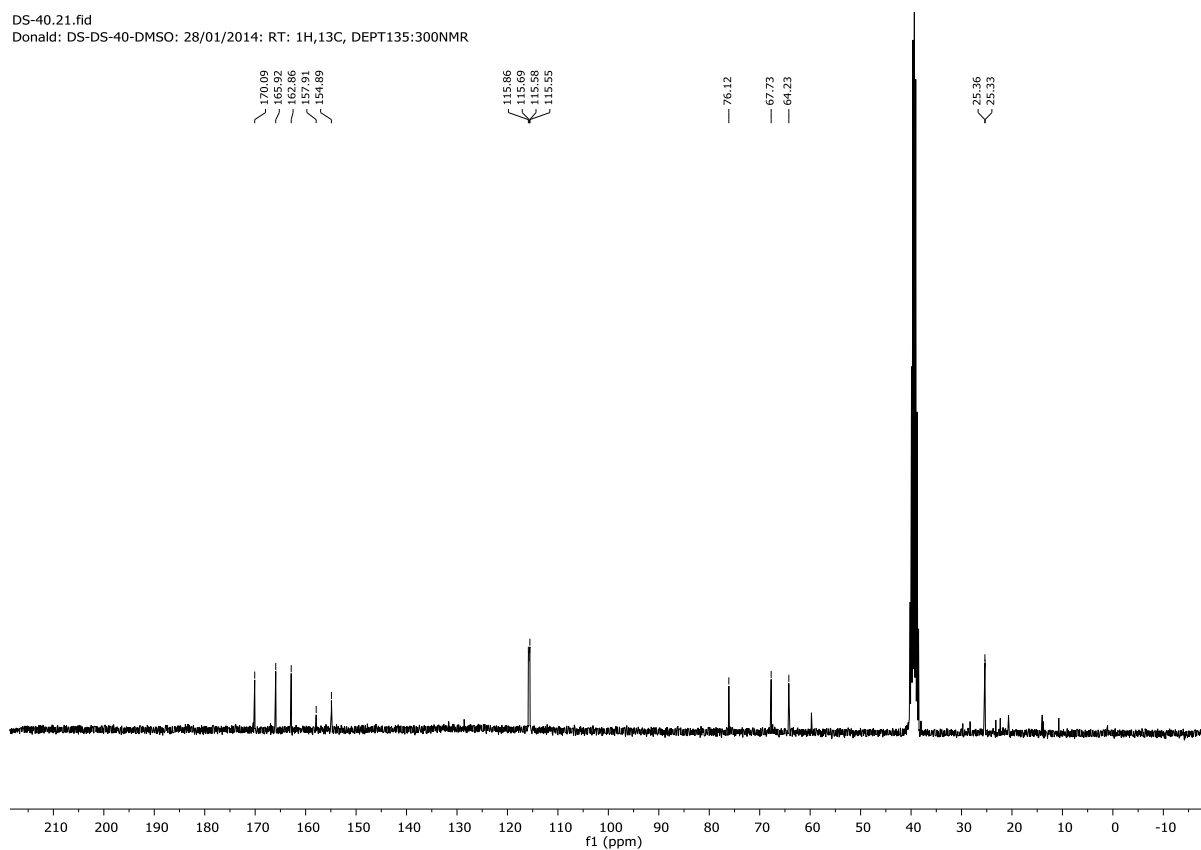
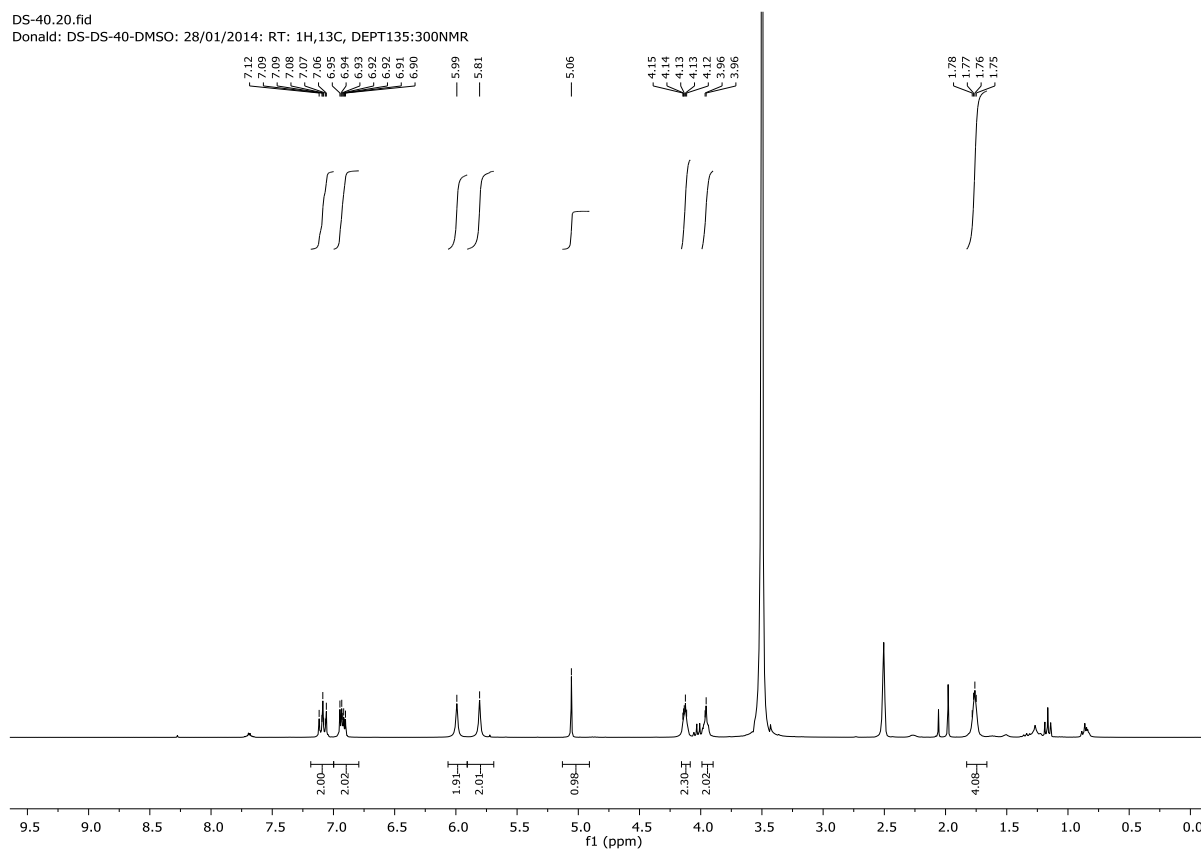
Figure S30. ^1H and ^{13}C NMR spectra of 6-(4-(4-fluorophenoxy)butoxy)pyrimidine-2,4-diamine (**7e**).

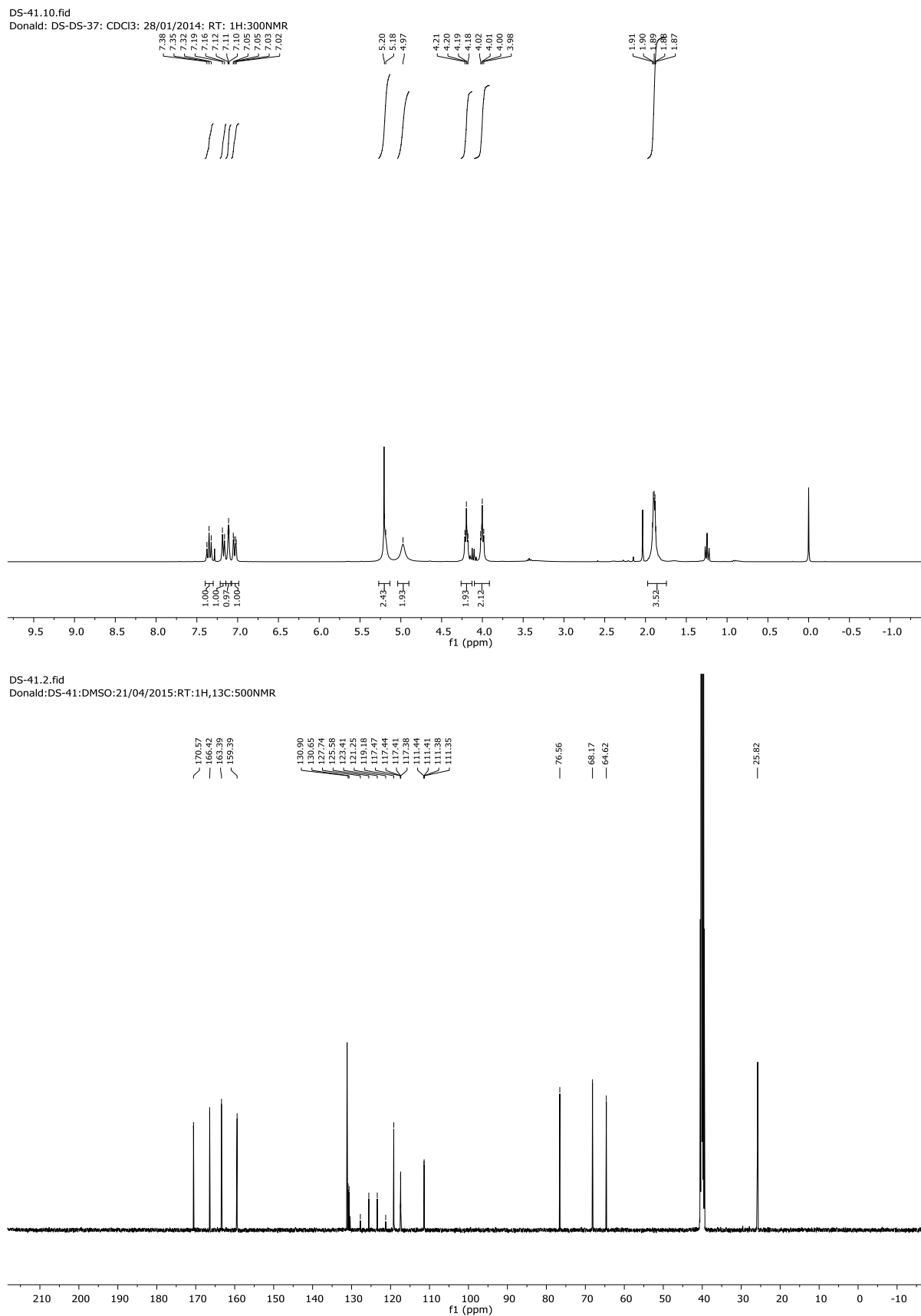
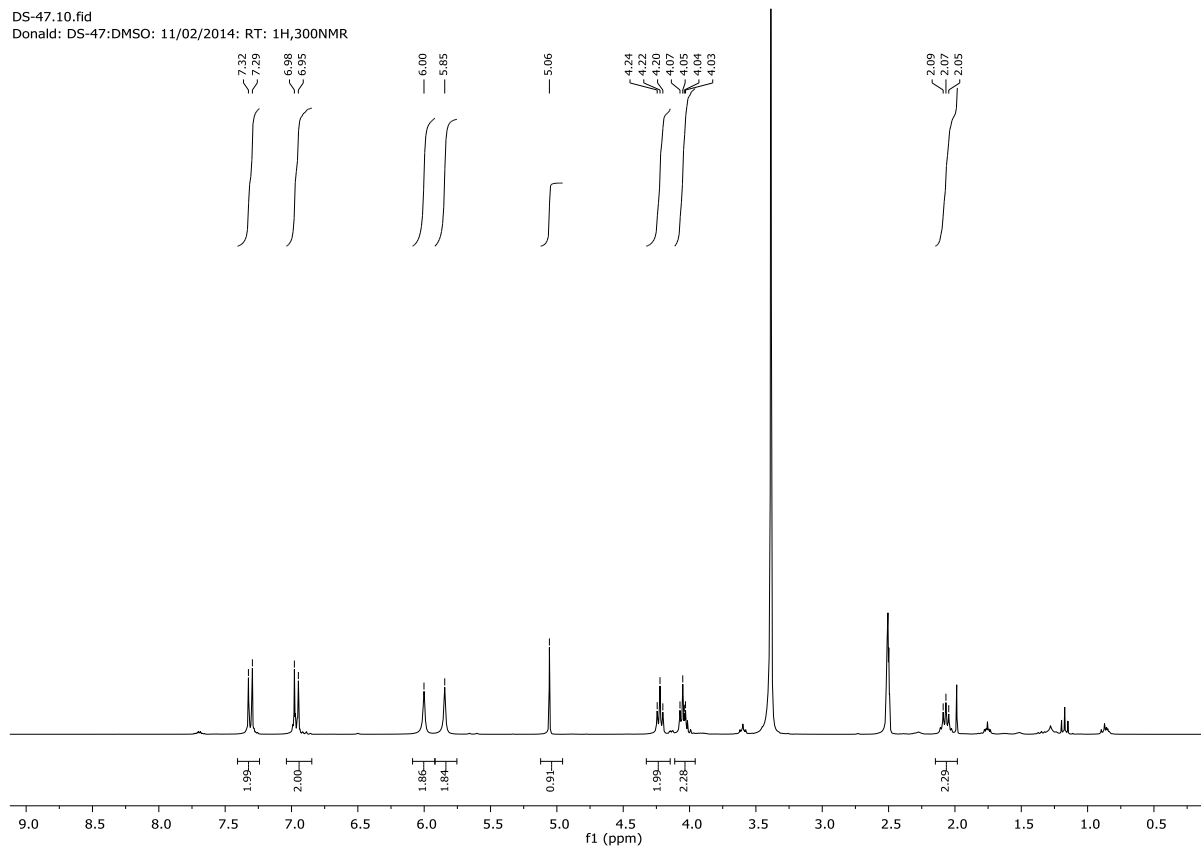
Figure S31. ^1H and ^{13}C NMR spectra of 6-(4-(3-(trifluoromethyl)phenoxy)butoxy)pyrimidine-2,4-diamine (**7f**).

Figure S32. ^1H and ^{13}C NMR spectra of 6-(3-(chlorophenoxy)propoxy)pyrimidine-2,4-diamine (**7g**).

DS-47.11.fid
Kamogelo (Donald): DS-47: DMSO: 23/07/2020: 1H, 13C: 300K, 200MNR

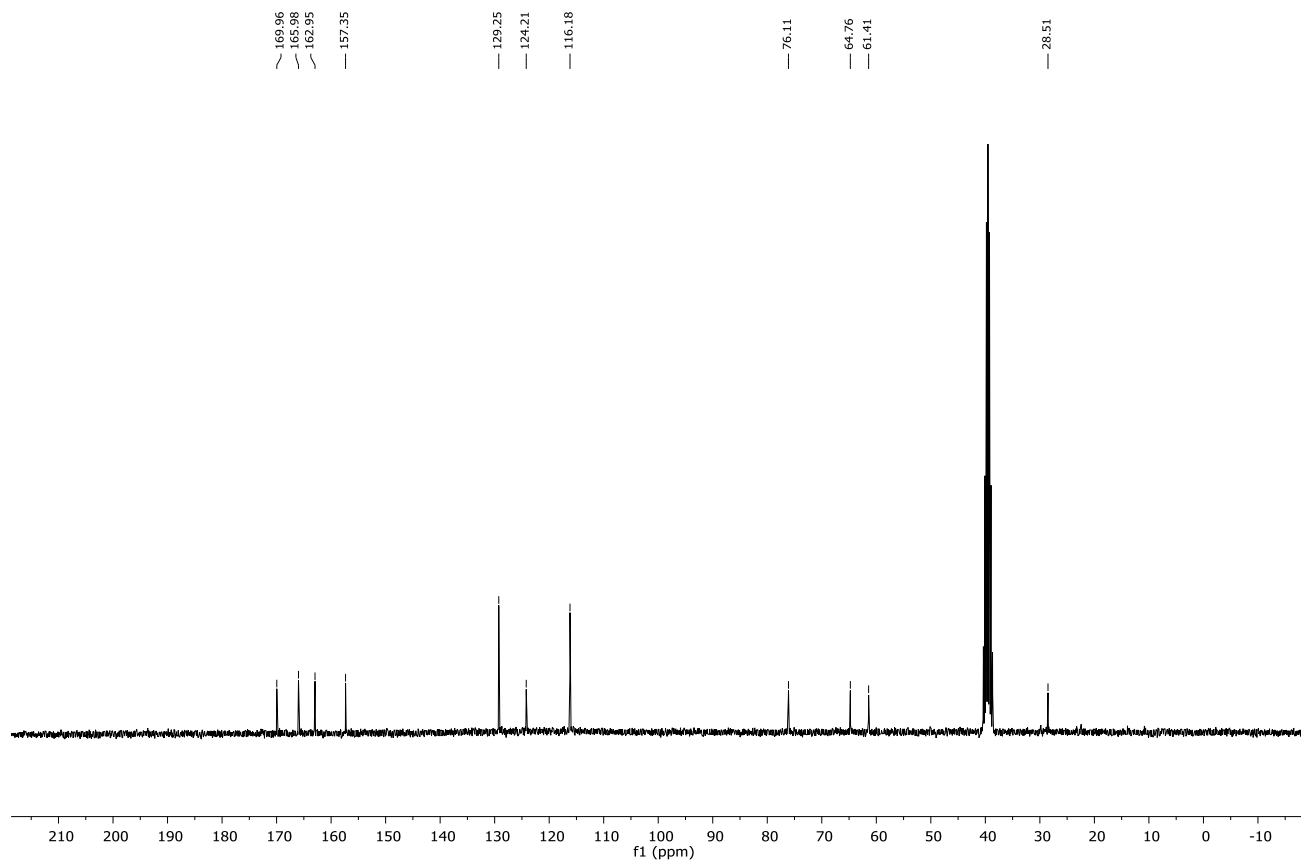


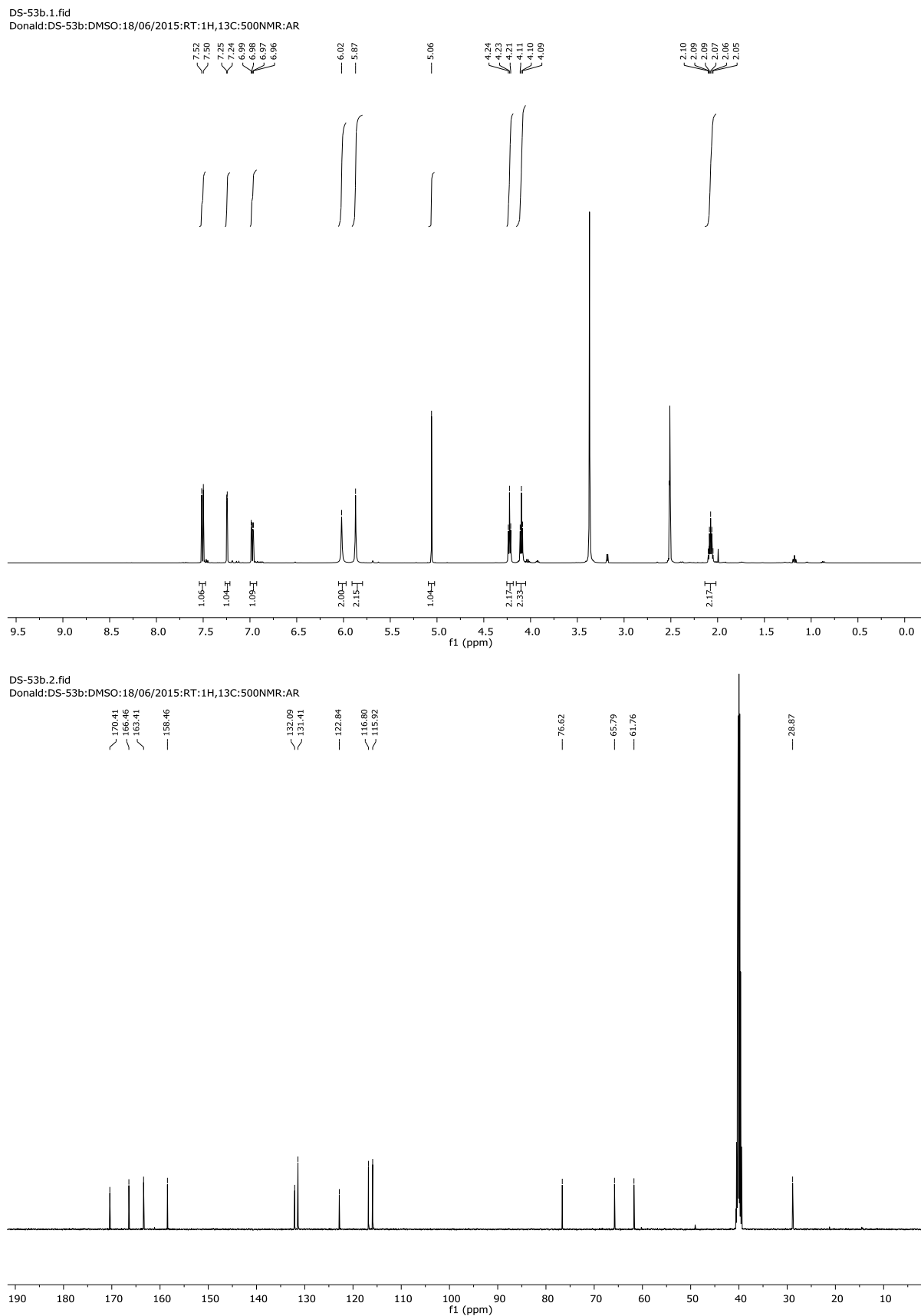
Figure S33. ^1H and ^{13}C NMR spectra of 6-(3-(3,4-dichlorophenoxy)propoxy)pyrimidine-2,4-diamine (**7h**).

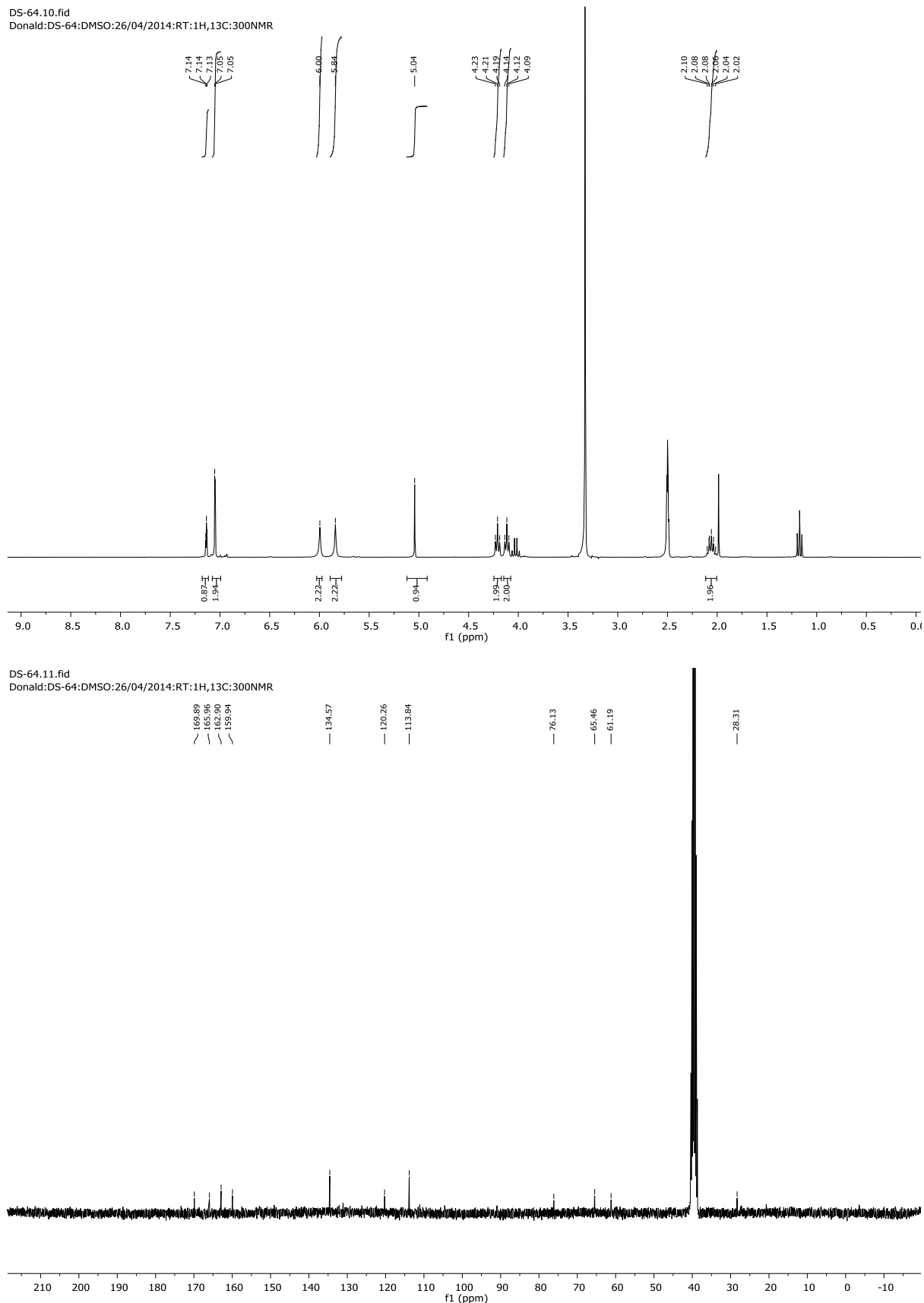
Figure S34. ^1H and ^{13}C NMR spectra of 6-(3-(3,5-dichlorophenoxy)propoxy)pyrimidine-2,4-diamine (**7i**).

Figure S35. ^1H and ^{13}C NMR spectra of 6-(3-(4-fluorophenoxy)propoxy)pyrimidine-2,4-diamine (**7j**).