Applying Molecular Modeling to the Design of Innovative, Non-Symmetrical CXCR4 Inhibitors with Potent Anticancer Activity

*Miquel Martínez-Asensio[1], Lluís Sàrrias[1], Gema Gorjón-de-Pablo[1,2], Miranda Fernández-Serrano[2], Judith Camaló-Vila[1], Albert Gibert[1], Raimon Puig de la Bellacasa[1], Jordi Teixidó[1], Gaël Roué[2], José I. Borrell[1], Roger Estrada-Tejedor [1]**

[1] Grup de Química Farmacèutica, IQS School of Engineering, Universitat Ramon Llull, Via Augusta 390, E-08017 Barcelona, Spain

[2] Lymphoma Translational Group, Josep Carreras Leukaemia Research Institute, 08916 Badalona, Spain

Corresponding author: roger.estrada@iqs.url.edu

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Table S1. List of molecular descriptors used in library selection

a_acc	b_1rotN	diameter	lip_don	PEOE_VSA_NEG	RPC+
a_acid	b_1rotR	FCharge	lip_druglike	PEOE_VSA_PNEG	rsynth
a_aro	b_ar	GCUT_PEOE [0-3]	lip_violation	PEOE_VSA_POL	SlogP
a_base	b_count	GCUT_SLOGP [0-3]	logP(o/w)	PEOE_VSA_POS	SlogP_VSA [0,9]
a_count	b_double	GCUT_SMR [0-3]	logS	PEOE_VSA_PPOS	SMR
a_don	b_heavy	h_ema	mr	petitjean	SMR_VSA [0,7]
a_donacc	b_max1len	h_emd	mutagenic	petitjeanSC	TPSA
a_heavy	b_rotN	h_emd_C	nmol	Q_PC-	VAdjEq
a_hyd	b_rotR	h_log_dbo	opr_brigid	Q_PC+	VAdjMa
a_IC	b_single	h_log_pbo	opr_leadlike	Q_RPC-	VDistEq
a_ICM	b_triple	h_logD	opr_nring	Q_RPC+	VDistMa
a_nB	balabanJ	h_logP	opr_nrot	Q_VSA_FHYD	vdw_area
a_nBr	BCUT_PEOE [0-3]	h_logS	opr_violation	Q_VSA_FNEG	vdw_vol
a_nC	BCUT_SLOGP [0-3]	h_mr	PC-	Q_VSA_FPNEG	vsa_acc
a_nCl	BCUT_SMR [0-3]	h_pavgQ	PC+	Q_VSA_FPOL	vsa_acid
a_nF	bpol	h_pKa	PEOE_PC-	Q_VSA_FPOS	vsa_base
a_nH	chi0	h_pKb	PEOE_PC+	Q_VSA_FPPOS	vsa_don
a_nI	chi0_C	h_pstates	PEOE_RPC-	Q_VSA_HYD	vsa_hyd
a_nN	chi0v	h_pstrain	PEOE_RPC+	Q_VSA_NEG	vsa_other
a_nO	chi0v_C	Kier1	PEOE_VSA [-6,+6]	Q_VSA_PNEG	vsa_pol
a_nP	chi1	Kier2	PEOE_VSA_FHYD	Q_VSA_POL	Weight
a_nS	chi1_C	Kier3	PEOE_VSA_FNEG	Q_VSA_POS	weinerPath
apol	chi1v	KierA1	PEOE_VSA_FPNEG	Q_VSA_PPOS	weinerPol
ast_fraglike	chi1v_C	KierA2	PEOE_VSA_FPOL	radius	zagreb
ast_fraglike_ext	chiral	KierA3	PEOE_VSA_FPOS	reactive	
ast_violation	chiral_u	KierFlex	PEOE_VSA_FPPOS	rings	
ast_violation_ext	density	lip_acc	PEOE_VSA_HYD	RPC-	

Table S2. List of 10 compounds with better docking score values.

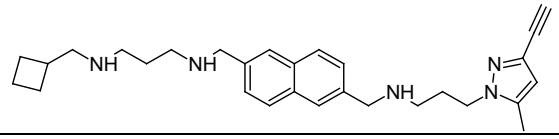
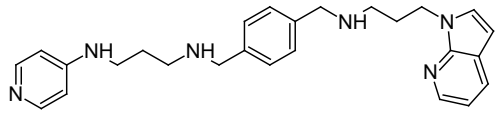
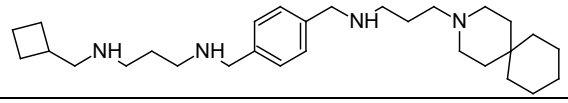
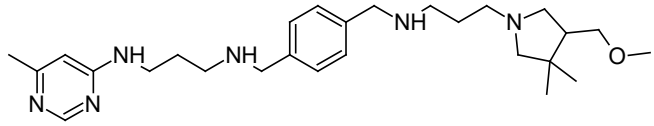
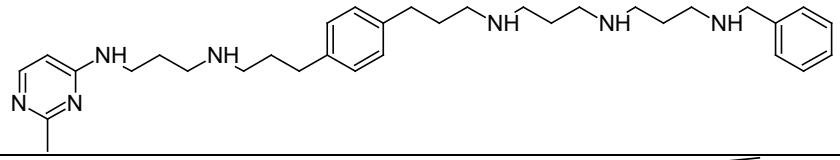
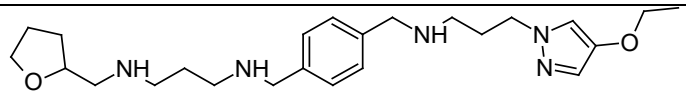
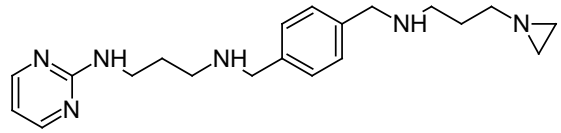
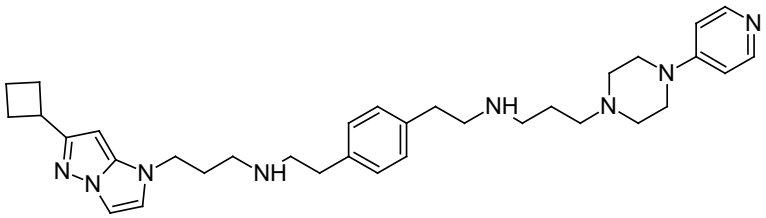
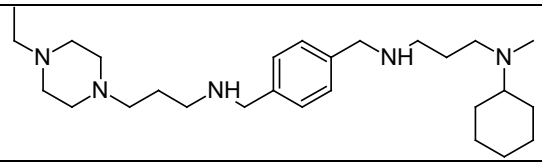
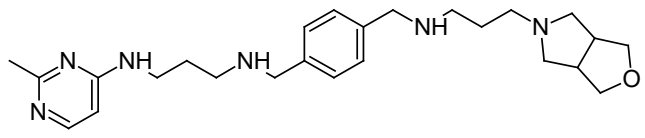
Compound	ID	S
	61	-6.3
	23	-6.3
	19	-6.1
	36	-6.1
	122	-6.0
	32	-6.0
	3	-6.0
	102	-5.9
	11	-5.7
	37	-5.6

Figure S1. Result of the validation docking. The IT1t structure obtained from the validation docking (green) was superposed with the conformation reported in the PDB (3ODU, red), showing an RMSD of 0.96.

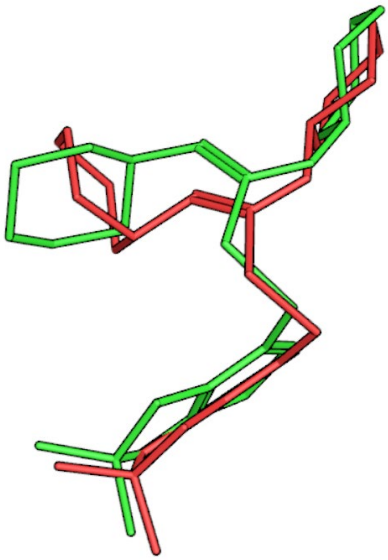
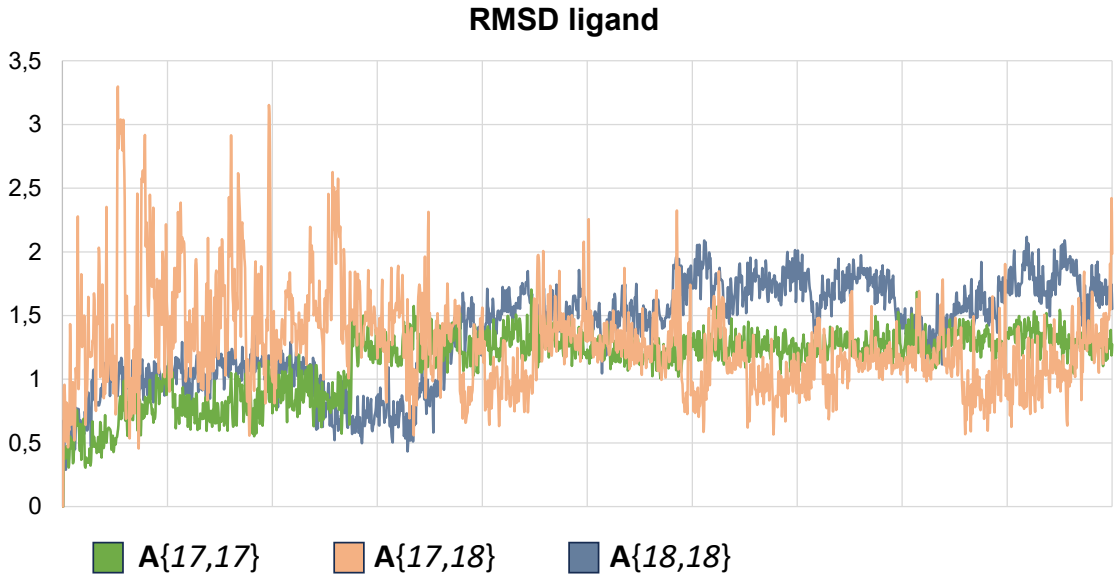


Figure S2. Root mean square deviation (RMSD) obtained in molecular dynamics simulations.

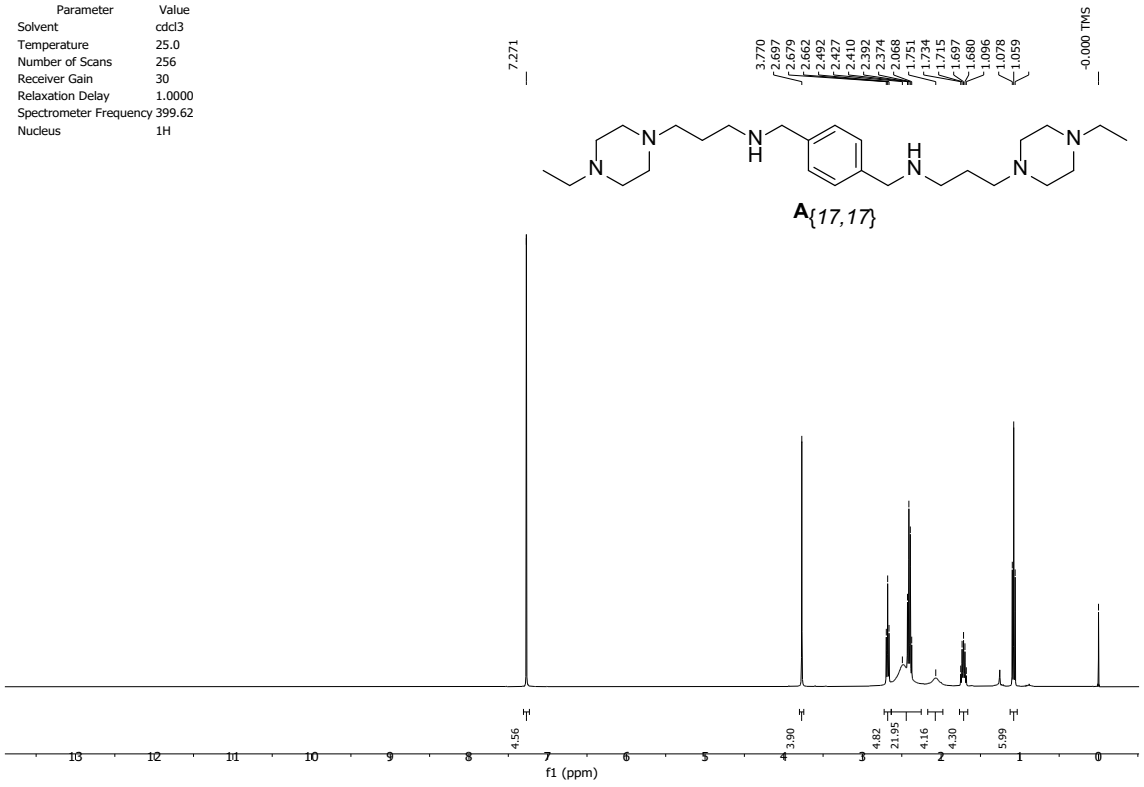
RMSD obtained for the ligands under study during the simulation. The RMSD (in Å) was calculated considering all non-hydrogen atoms in the ligand molecule.

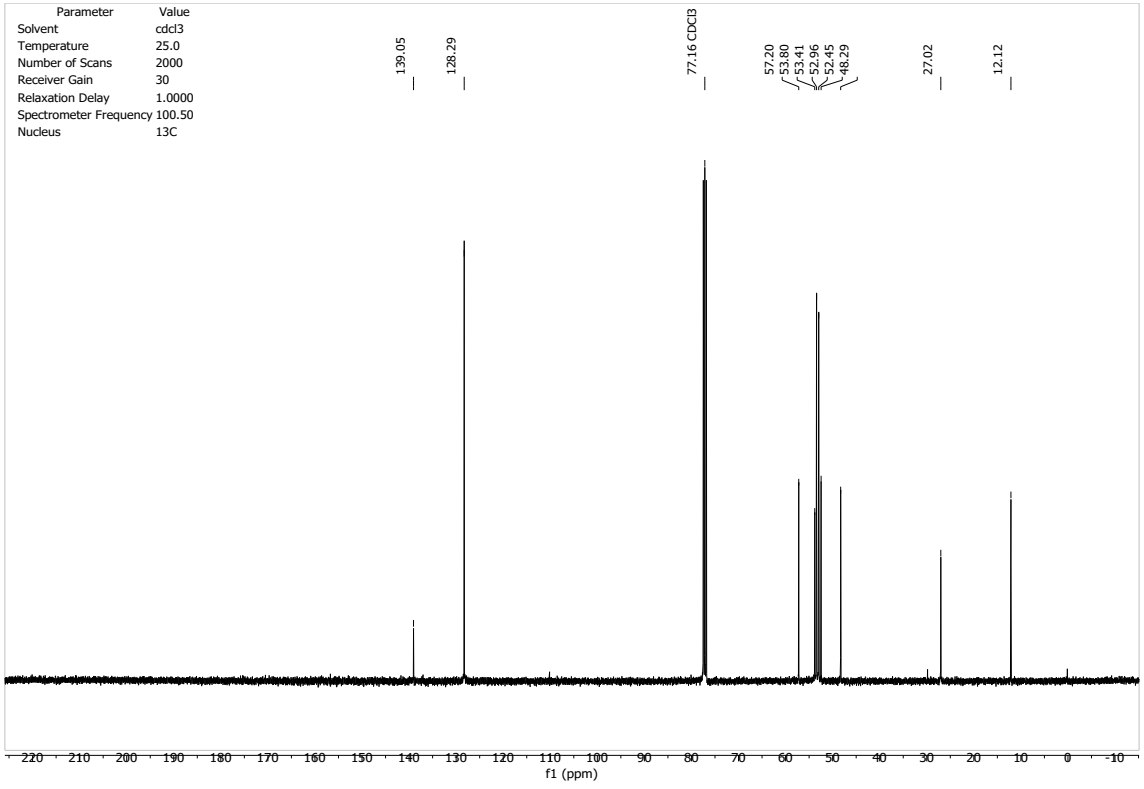
Ligands converge, in all simulations, to a metastable disposition with an RMSD < 1 Å difference.

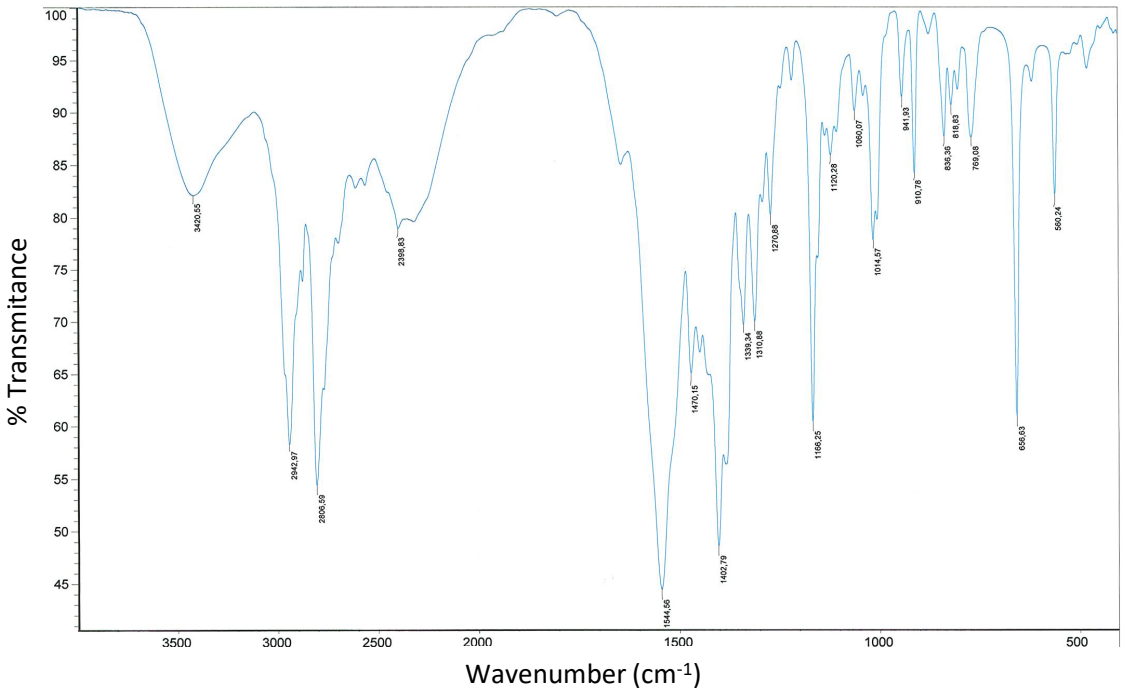


Appendix S1. NMR and IR Spectra

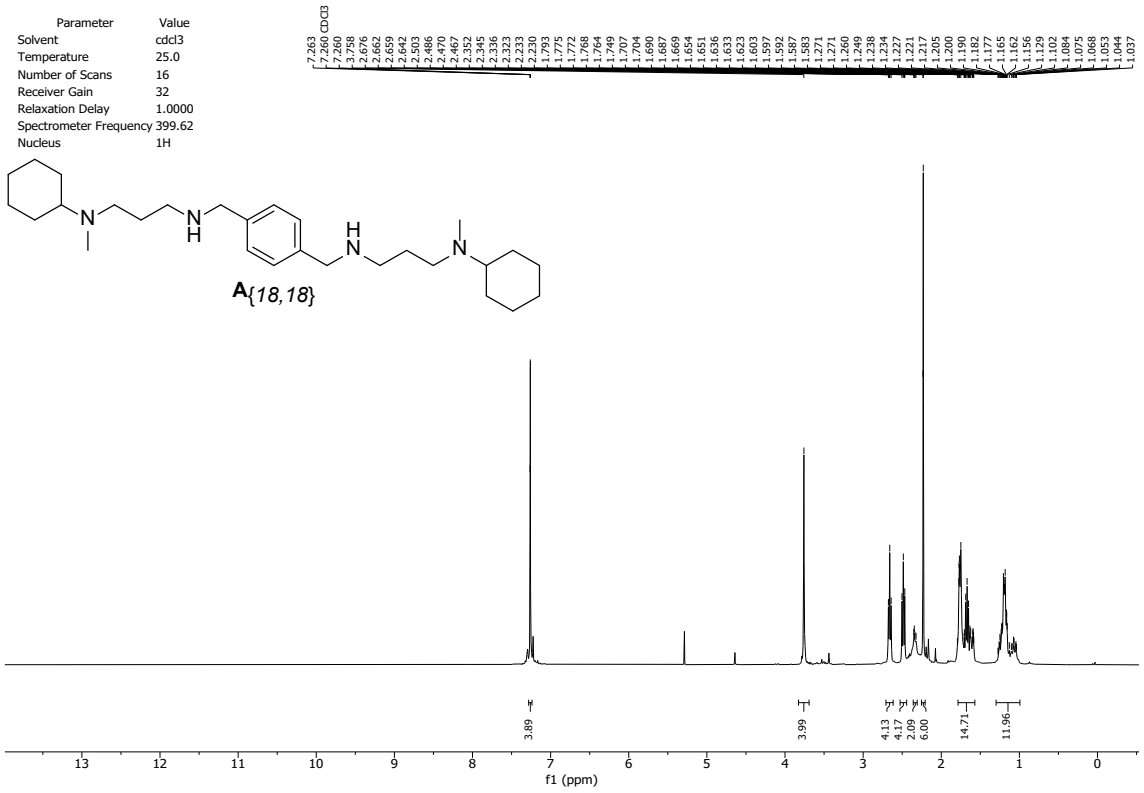
N,*N*'-(1,4-phenylenebis(methylene))bis(3-(4-ethylpiperazin-1-yl)propan-1-amine) (**A**{*17*,*17*})

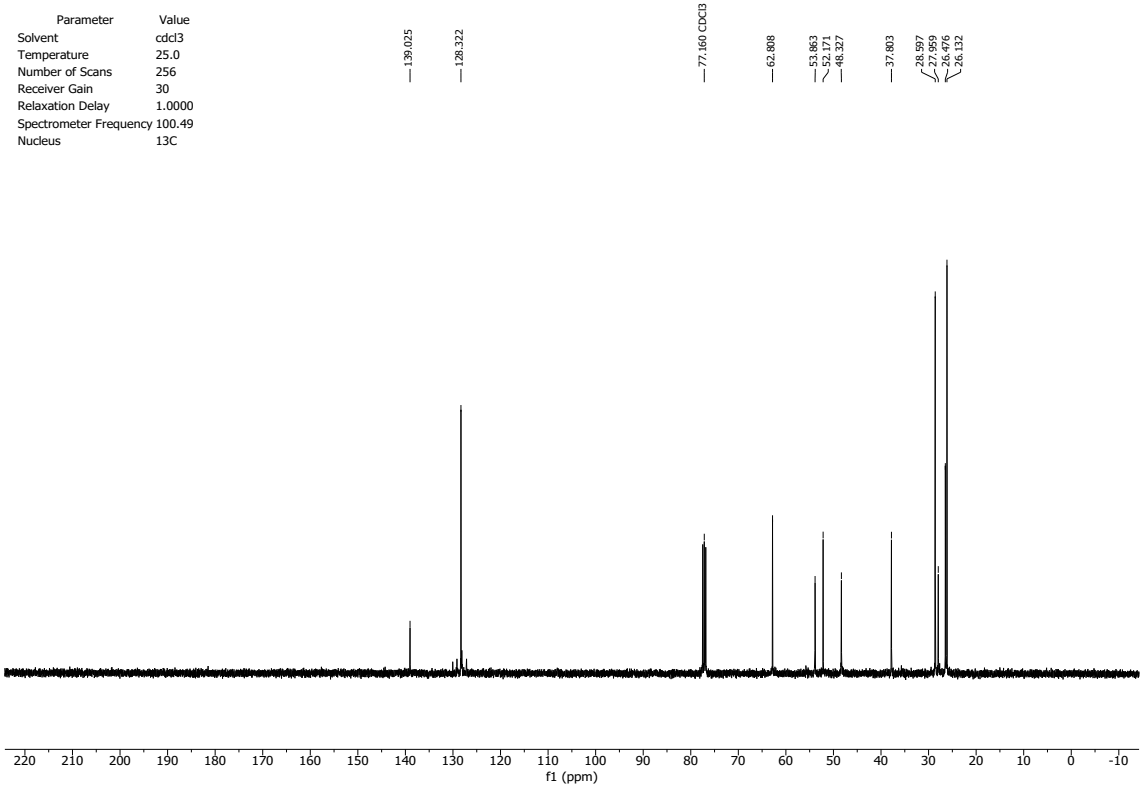


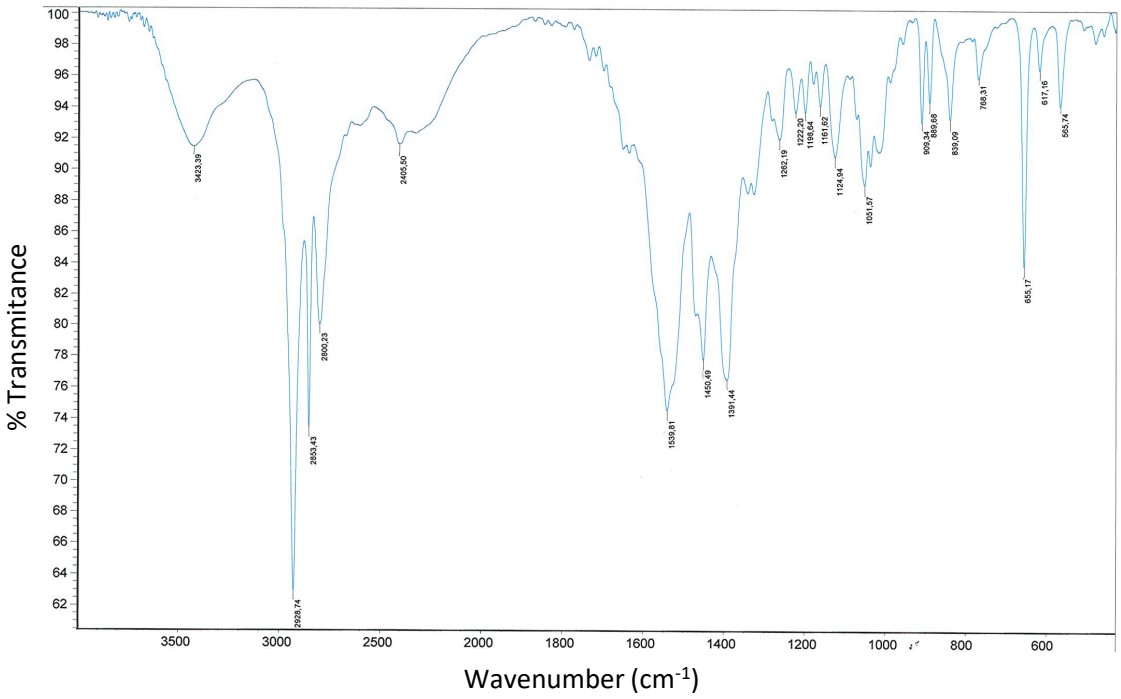



% Transmitance
100
95
90
85
80
75
70
65
60
55
50
45
3420.55
2942.97
2806.59
2398.83
1544.56
1470.15
1402.79
1339.34
1310.88
1270.88
1166.25
1120.28
1060.07
1014.57
941.93
910.76
836.36
818.83
769.08
656.03
560.24
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm-1)

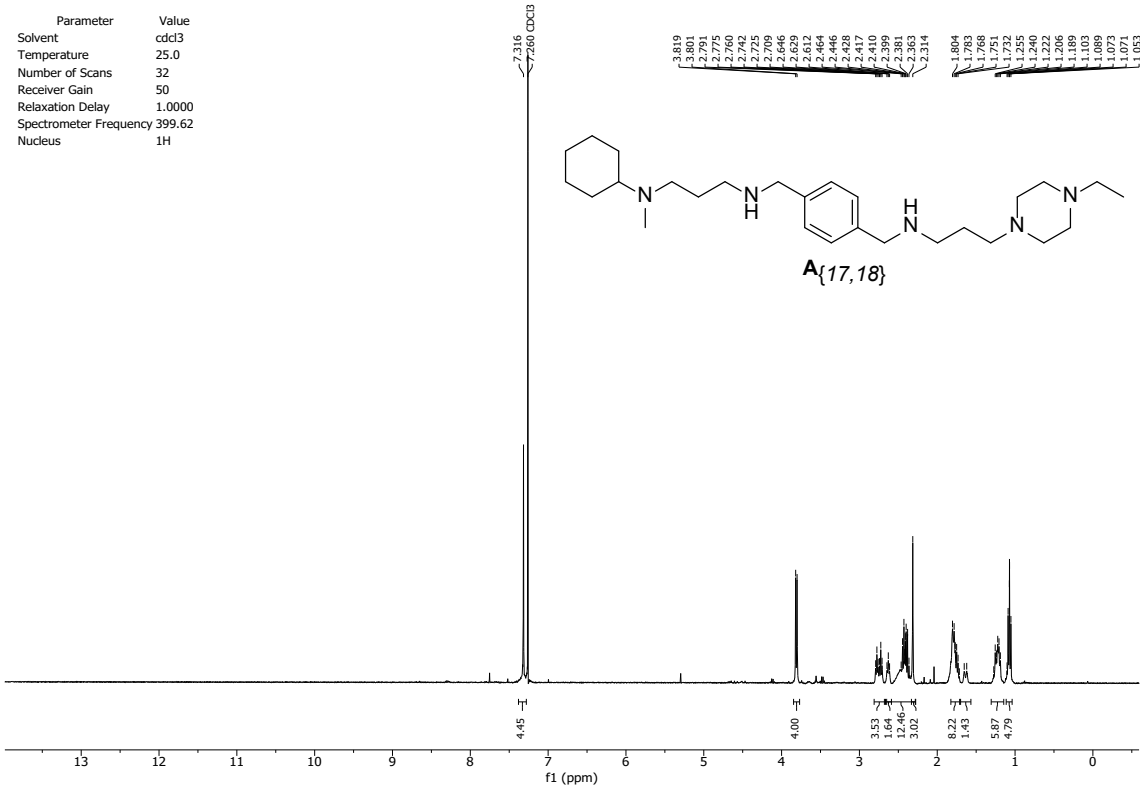
N^1,$N^{1'}$-(1,4-phenylenebis(methylene))bis(N^3-cyclohexyl-N^3-methylpropane-1,3-diamine) (**A**{*18*,*18*})

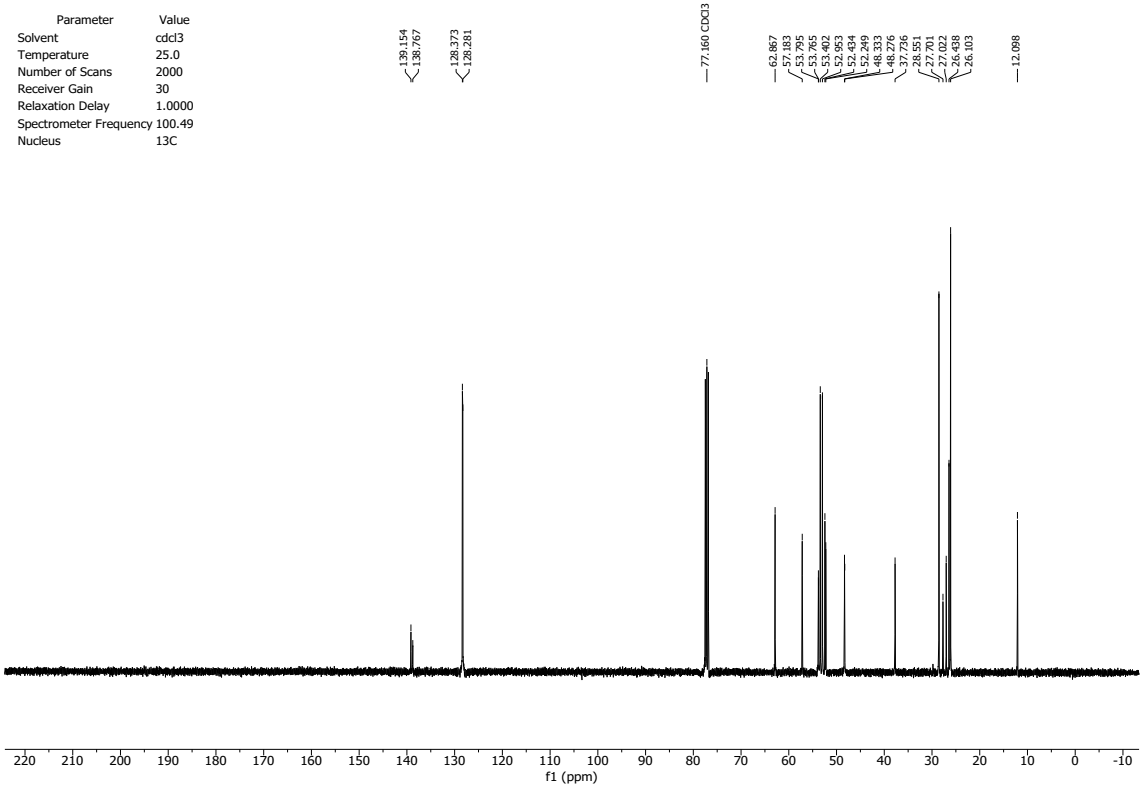


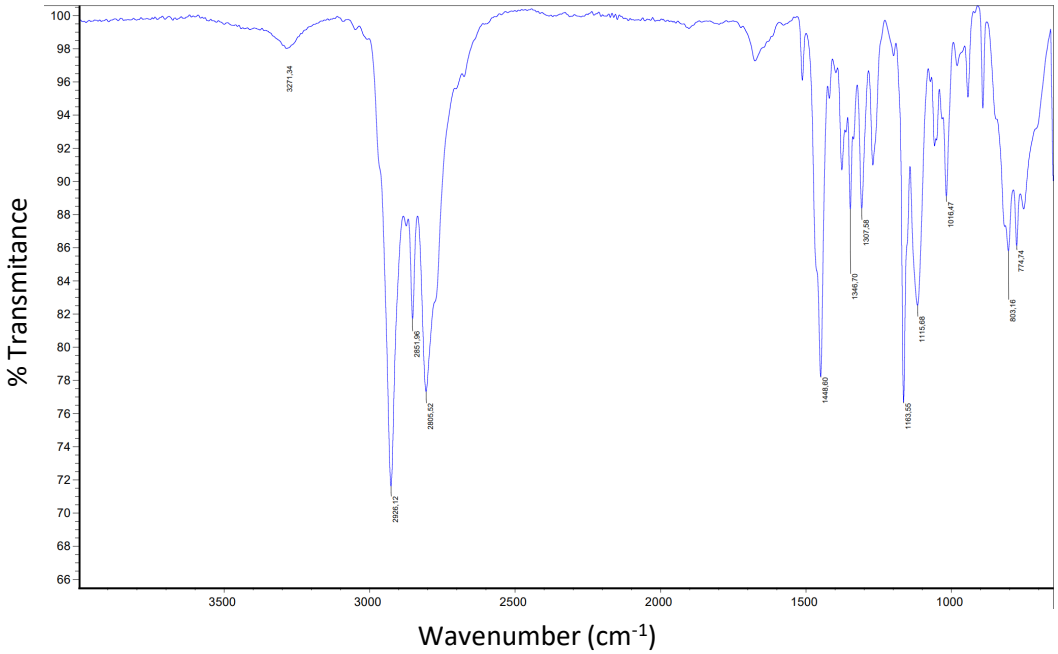



% Transmitance
Wavenumber (cm-1)
3423,39
2928,74
2853,43
2800,23
2405,90
1539,61
1450,49
1391,44
1282,19
1222,20
1161,62
1124,94
1051,57
909,34
889,68
839,09
788,31
655,17
617,16
565,74

N^1-cyclohexyl-N^3-(4-(((3-(4-ethylpiperazin-1-yl)propyl)amino)methyl)benzyl)-N^1-methylpropane-1,3-diamine (**A**{*17*,*18*})






% Transmitance
Wavenumber (cm-1)
3271.34
2926.12
2851.96
2805.52
1448.60
1340.70
1307.58
1163.55
1115.68
1016.47
803.16
774.74