Mechanistic Exploration of *N,N´*-Disubstituted Diamines as Promising Chagas Disease Treatments

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Supporting Information

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1. Compound´s SMILES.

Table S1. Compound´s SMILES.

ID	n	R	SMILES
3a	3	4-H	C(CNCc1ccccc1)CNCc1ccccc1
4a	4	4-H	C(CNCc1ccccc1)CCNCc1ccccc1
6a	6	4-H	C(CCNCc1ccccc1)CCCNCc1ccccc1
8a	8	4-H	C(CCCNCc1ccccc1)CCCCNCc1ccccc1
10a	10	4-H	C(CCCCNCc1ccccc1)CCCCCNCc1ccccc1
12a	12	4-H	C(CCCCCNCc1ccccc1)CCCCCCNCc1ccccc1
3b	3	4-OMe	COc1ccc(cc1)CNCCCNCc1ccc(cc1)OC
4b	4	4-OMe	COc1ccc(cc1)CNCCCCNCc1ccc(cc1)OC
6b	6	4-OMe	COc1ccc(cc1)CNCCCCCCNCc1ccc(cc1)OC
8b	8	4-OMe	COc1ccc(cc1)CNCCCCCCCCNCc1ccc(cc1)OC
10b	10	4-OMe	COc1ccc(cc1)CNCCCCCCCCCCNCc1ccc(cc1)OC
12b	12	4-OMe	COc1ccc(cc1)CNCCCCCCCCCCCCNCc1ccc(cc1)OC
3c	3	4-OBn	C(CNCc1ccc(cc1)OCc1ccccc1)CNCc1ccc(cc1)OCc1ccccc1
4c	4	4-OBn	C(CNCc1ccc(cc1)OCc1ccccc1)CCNCc1ccc(cc1)OCc1ccccc1
6c	6	4-OBn	C(CCNCc1ccc(cc1)OCc1ccccc1)CCCNCc1ccc(cc1)OCc1ccccc1
8c	8	4-OBn	C(CCCNCc1ccc(cc1)OCc1ccccc1)CCCCNCc1ccc(cc1)OCc1ccccc1
10c	10	4-OBn	C(CCCCNCc1ccc(cc1)OCc1ccccc1)CCCCCNCc1ccc(cc1)OCc1ccccc1
12c	12	4-OBn	C(CCCCCNCc1ccc(cc1)OCc1ccccc1)CCCCCCNCc1ccc(cc1)OCc1ccccc1
3d	3	3-OH 4-OMe	COc1ccc(cc1O)CNCCCNCc1ccc(c(c1)O)OC
4d	4	3-OH 4-OMe	COc1ccc(cc1O)CNCCCCNCc1ccc(c(c1)O)OC
6d	6	3-OH 4-OMe	COc1ccc(cc1O)CNCCCCCCNCc1ccc(c(c1)O)OC
8d	8	3-OH 4-OMe	COc1ccc(cc1O)CNCCCCCCCCNCc1ccc(c(c1)O)OC
10d	10	3-OH 4-OMe	COc1ccc(cc1O)CNCCCCCCCCCCNCc1ccc(c(c1)O)OC
12d	12	3-OH 4-OMe	COc1ccc(cc1O)CNCCCCCCCCCCCCNCc1ccc(c(c1)O)OC
3e	3	3-OMe 4-OBn	COc1cc(CNCCCNCc2ccc(c(c2)OC)OCc2ccccc2)ccc1OCc1ccccc1
4e	4	3-OMe 4-OBn	COc1cc(CNCCCCNCc2ccc(c(c2)OC)OCc2ccccc2)ccc1OCc1ccccc1
6e	6	3-OMe 4-OBn	COc1cc(CNCCCCCCNCc2ccc(c(c2)OC)OCc2ccccc2)ccc1OCc1ccccc1
8e	8	3-OMe 4-OBn	COc1cc(CNCCCCCCCCNCc2ccc(c(c2)OC)OCc2ccccc2)ccc1OCc1ccccc1
10e	10	3-OMe 4-OBn	COc1cc(CNCCCCCCCCCCNCc2ccc(c(c2)OC)OCc2ccccc2)ccc1OCc1ccccc1
12e	12	3-OMe 4-OBn	COc1cc(CNCCCCCCCCCCCCNCc2ccc(c(c2)OC)OCc2ccccc2)ccc1OCc1ccccc1

2. Compound´s LE and LLE

Table S2. Values of compound's ligand efficiency (LE) and ligand lipophilic efficiency (LLE).

ID	n	R	LE	LLE
3a	3	Benzyl	0.43323	3.6782
4a	4	Benzyl	0.32232	1.9228
6a	6	Benzyl	0.29302	1.014
8a	8	Benzyl	0.27746	0.26007
10a	10	Benzyl	0.24794	-0.80363
12a	12	Benzyl	0.23023	-1.7124
3b	3	4-Methoxy	0.28028	2.5172
4b	4	4-Methoxy	0.2686	2.0628
6b	6	4-Methoxy	0.35347	3.154
8b	8	4-Methoxy	-	-
10b	10	4-Methoxy	0.21488	-0.66363
12b	12	4-Methoxy	0.20145	-1.5724
3c	3	4-Benzyloxy	0.22945	0.83587
4c	4	4-Benzyloxy	0.23408	0.67027
6c	6	4-Benzyloxy	0.23263	0.062499
8c	8	4-Benzyloxy	0.16877	-2.3692
10c	10	4-Benzyloxy	0.15855	-3.3449
12c	12	4-Benzyloxy	0.14651	-4.4086
3d	3	3-OH,4OMe	0.25786	3.2086
4d	4	3-OH,4OMe	0.24794	2.7542
6d	6	3-OH,4OMe	0.26922	2.6412
8d	8	3-OH,4OMe	0.21488	0.93657
10d	10	3-OH,4OMe	0.20947	0.21486
12d	12	3-OH,4OMe	0.1896	-0.88103
3e	3	3-OMe.4-OBn	0.23726	1.8667
4e	4	3-OMe.4-OBn	0.17305	-0.28664
6e	6	3-OMe.4-OBn	0.15349	-1.5422
8e	8	3-OMe.4-OBn	0.14651	-2.451
10e	10	3-OMe.4-OBn	0.14014	-3.3598
12e	12	3-OMe.4-OBn	0.1343	-4.2686

3. NMR spectra of fluorescent analog and intermediates.

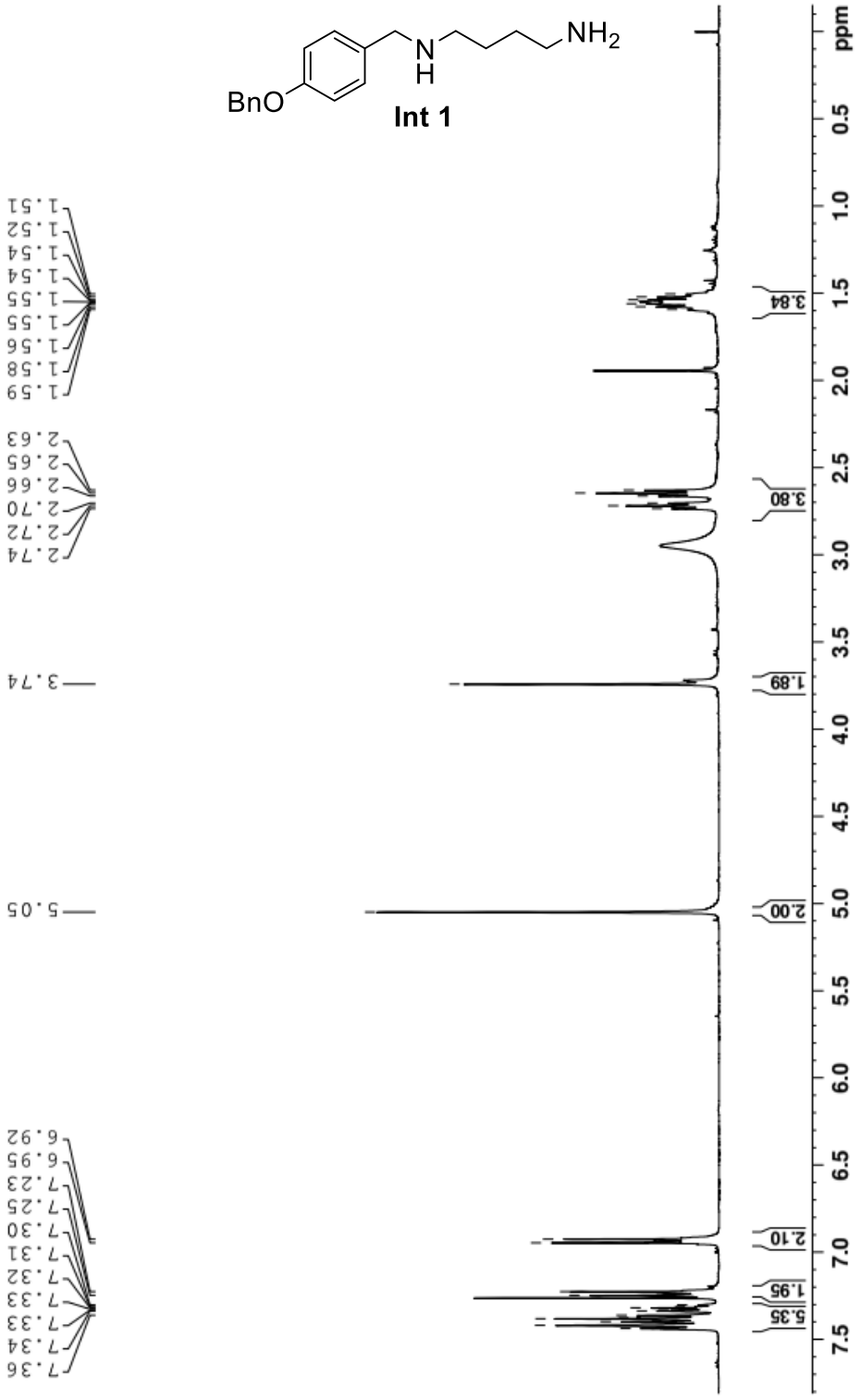


Figure S1. ^{1}H NMR of N^{1}-(4-(benzyloxy)benzyl)butane-1,4-diamine (**Int 1**)

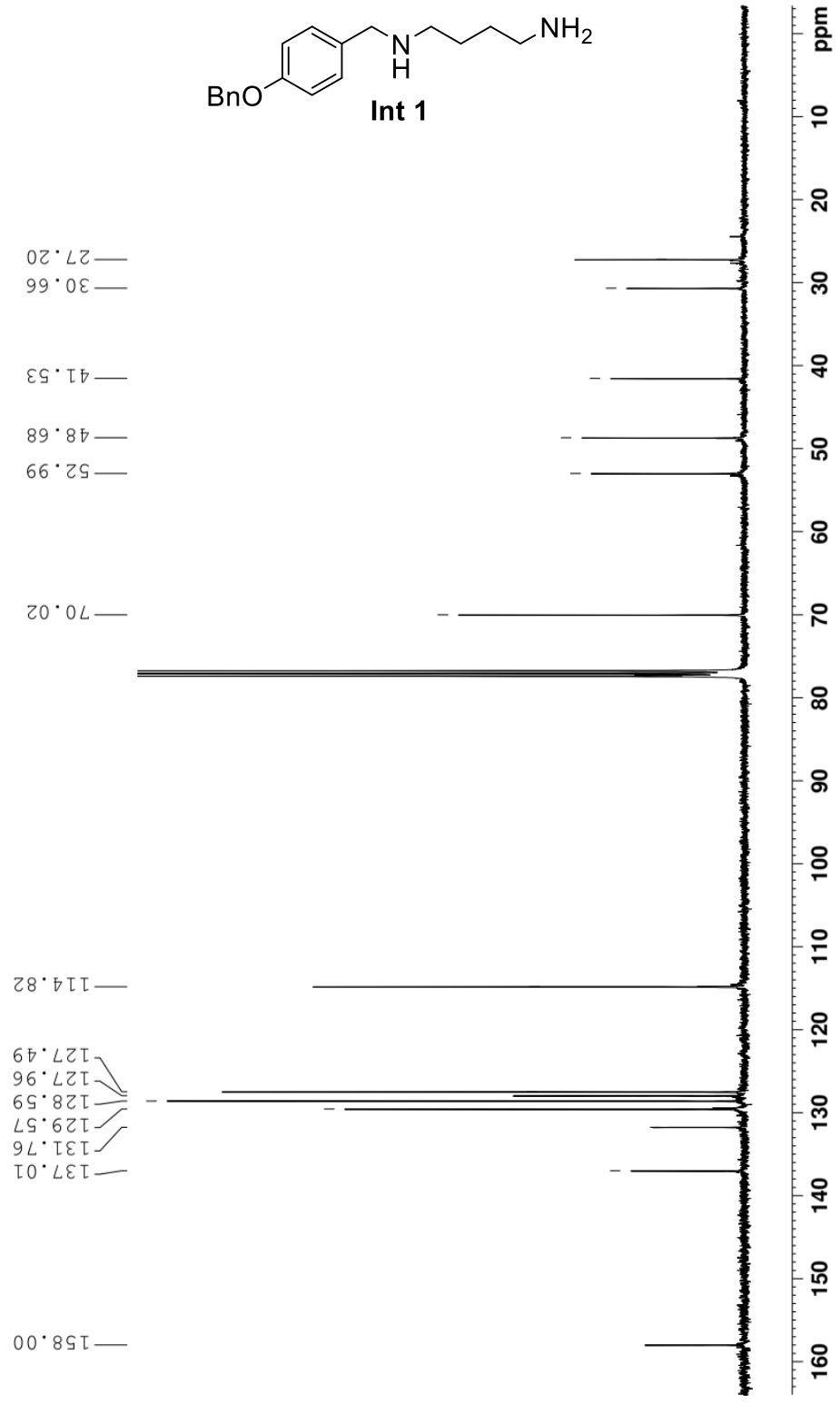
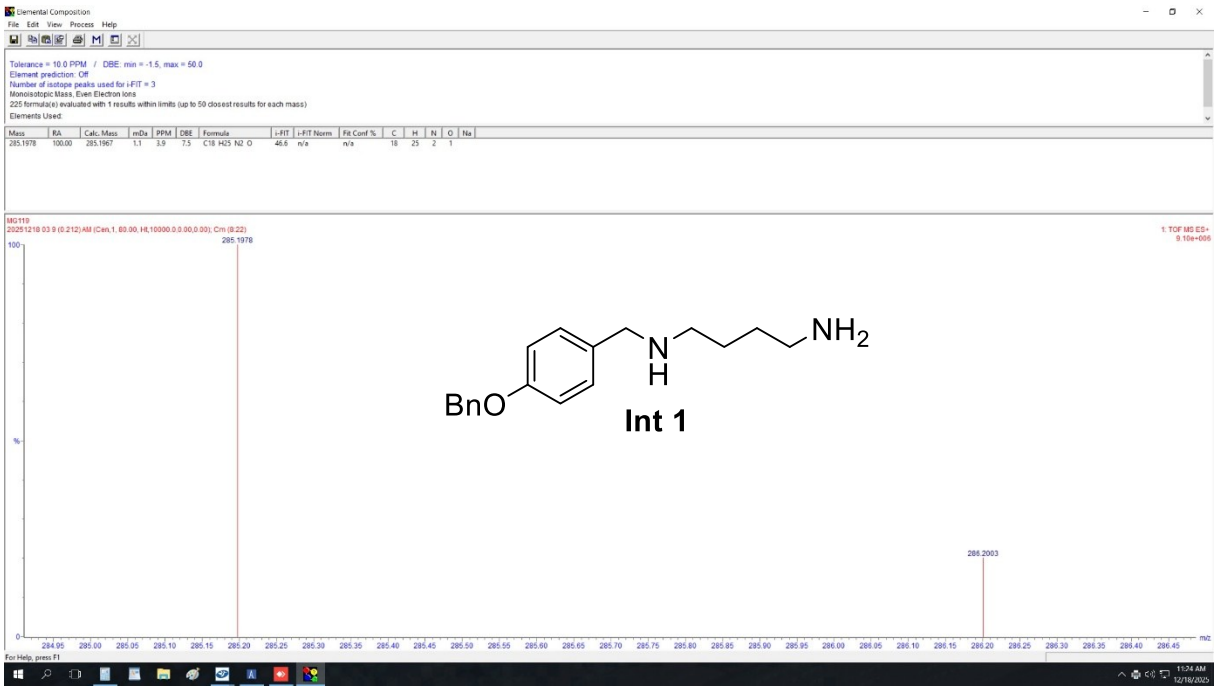


Figure S2. ^{13}C NMR of N^1-(4-(benzyloxy)benzyl)butane-1,4-diamine (**Int 1**)



Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
225 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 18-24 H: 20-26 N: 0-200 O: 1-8 Na: 0-1

MG119
20251218 03 9 (0.212) AM (Cen,1, 80.00, Ht,10000.0,0.00,0.00); Cm (8:22)

1: TOF MS ES+
9.10e+006

285.1978

286.2003

100
%
0
285.00 285.20 285.40 285.60 285.80 286.00 286.20 286.40
m/z

Minimum:	80.00				-1.5				
Maximum:	100.00		5.0	10.0	50.0				
Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
285.1978	100.00	285.1967	1.1	3.9	7.5	46.6	n/a	n/a	C18 H25 N2 O

Figure S3. ESI-HRMS of N[1]-(4-(benzyloxy)benzyl)butane-1,4-diamine (**Int 1**)

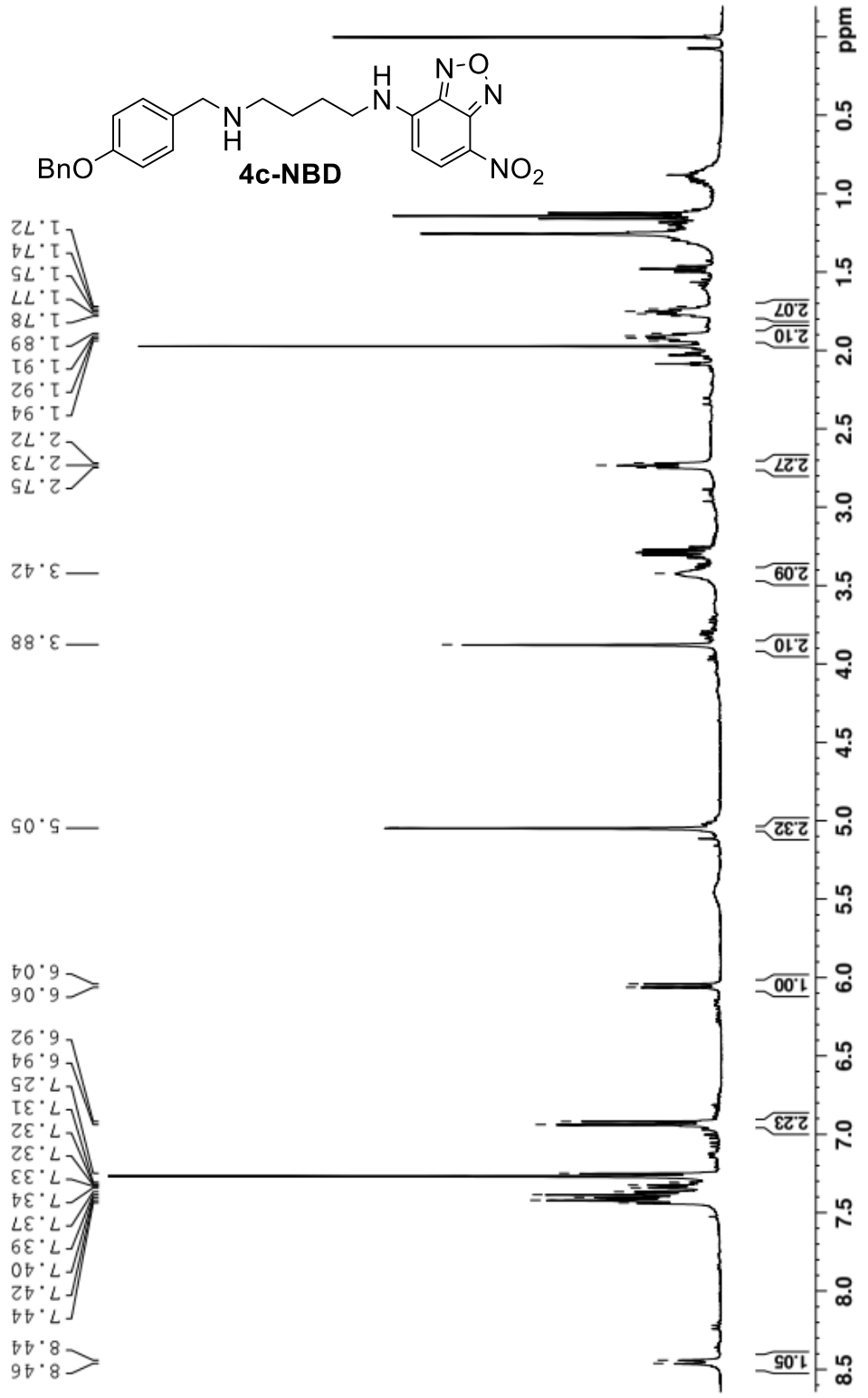


Figure S4. ^{1}H NMR of *N*-(4-(4-(benzyloxy)benzylamino)butyl)-7-nitrobenzo[c][1,2,5]oxadiazol-4-amine (**4c-NBD)**

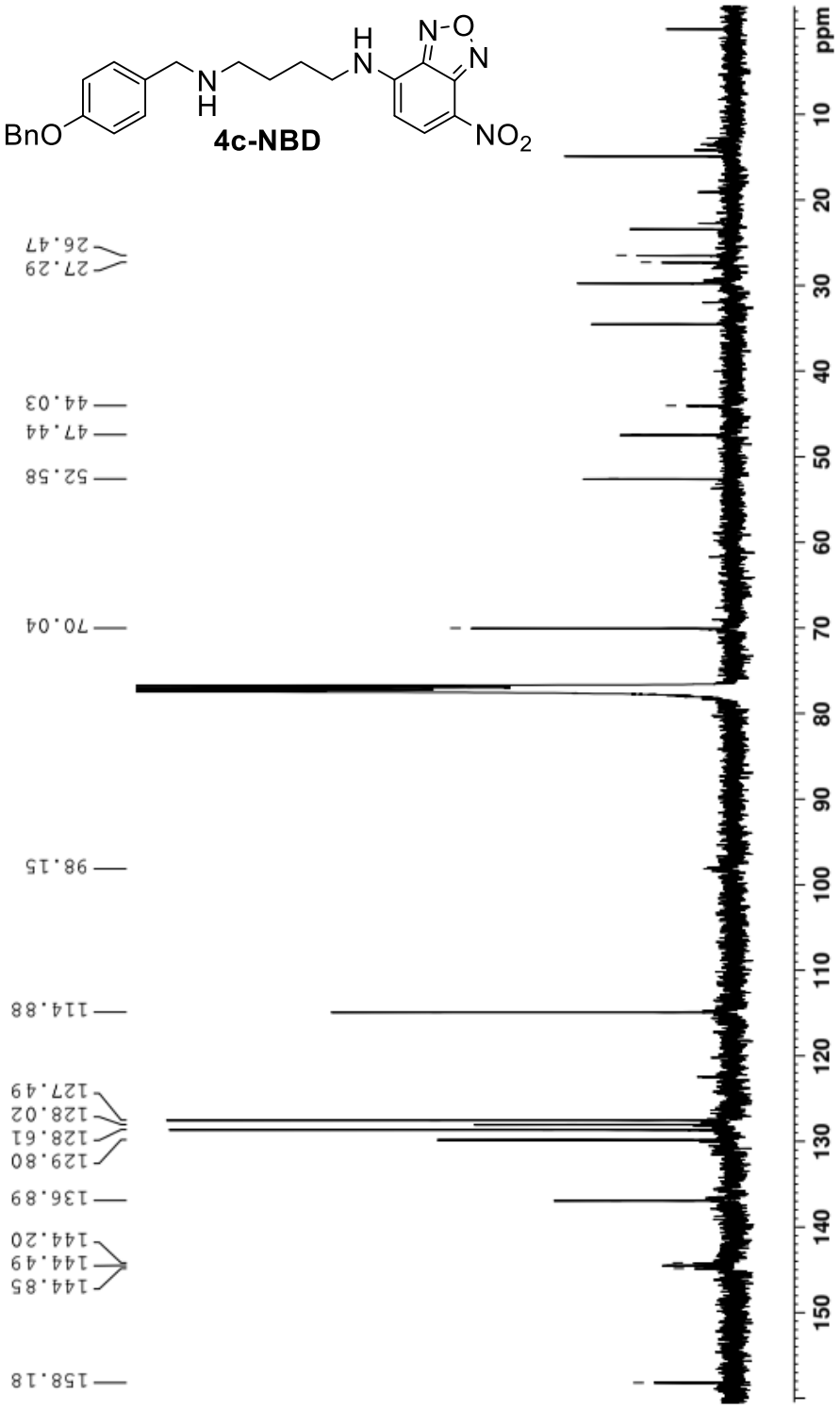
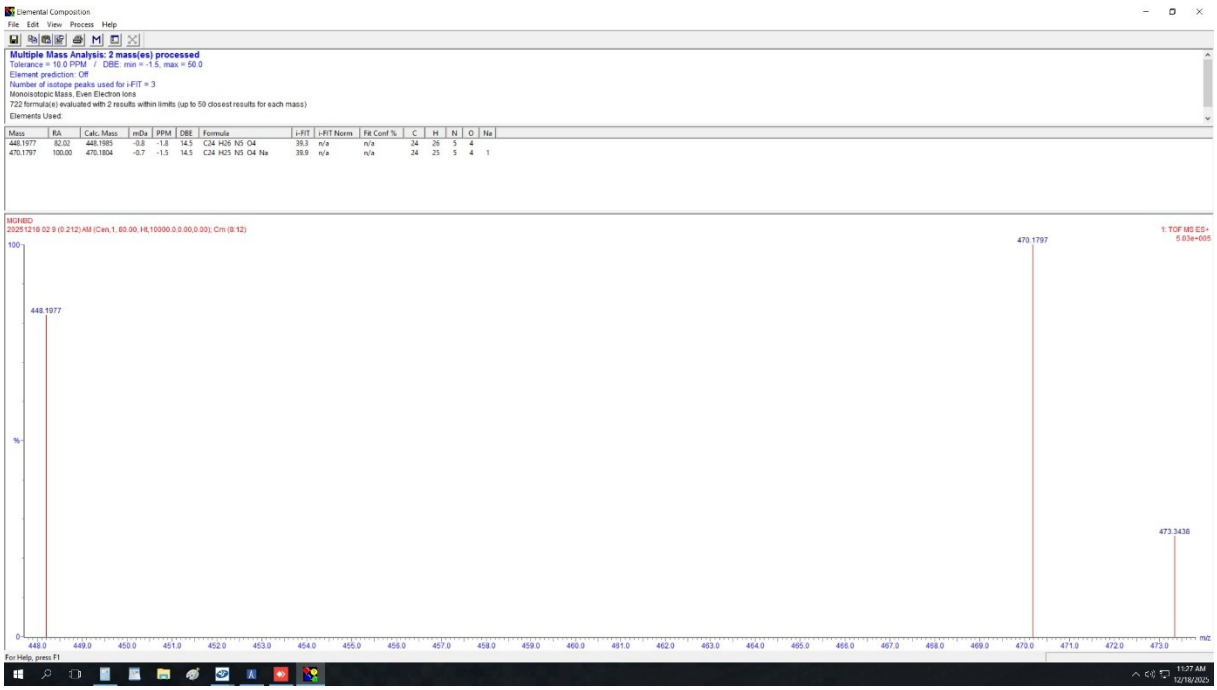


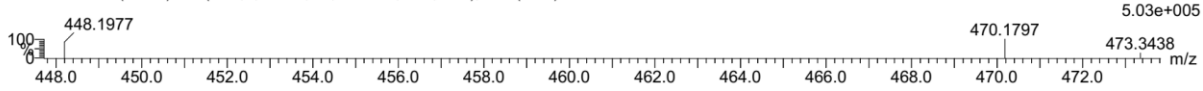
Figure S5. ^{13}C NMR of *N*-(4-(4-(benzyloxy)benzylamino)butyl)-7-nitrobenzo[c][1,2,5]oxadiazol-4-amine (**4c-NBD)**



Multiple Mass Analysis: 2 mass(es) processed
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
722 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 24-24 H: 20-26 N: 0-200 O: 1-8 Na: 0-1
MGNBD
20251218 02 9 (0.212) AM (Cen,1, 80.00, Ht,10000.0,0.00,0.00); Cm (8:12)

1: TOF MS ES+
5.03e+005



Minimum:	80.00				-1.5				
Maximum:	100.00		5.0	10.0	50.0				
Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
448.1977	82.02	448.1985	-0.8	-1.8	14.5	39.3	n/a	n/a	C24 H26 N5 O4
470.1797	100.00	470.1804	-0.7	-1.5	14.5	39.9	n/a	n/a	C24 H25 N5 O4 Na

Figure S6. ESI-HRMS of *N*-(4-(4-(benzyloxy)benzylamino)butyl)-7-nitrobenzo[c][1,2,5]oxadiazol-4-amine (**4c-NBD)**