Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Syntheses of Sceptrins and Nakamuric Acid and Insights into the Biosyntheses of Pyrrole–Imidazole Dimers

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Supplementary Information

Computational details

All calculations were performed with the Gaussian 09 program. Density functional theory calculations using the (U)B3LYP method were used to locate all the minima and transition points involved. The 6-311G(d,p) basis set was applied for all elements Frequency calculations at the same level had been performed to confirm each stationary point to be either a minimum or a transition structure and to evaluate its zero-point energy and the thermal corrections at 298 K. The reported energies are Gibbs free energies in gas phase (ΔG) and enthalpies (ΔH) at 298 K.

Full Citation of Gaussian 09

Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian, Inc., Wallingford Connecticut, 2013.

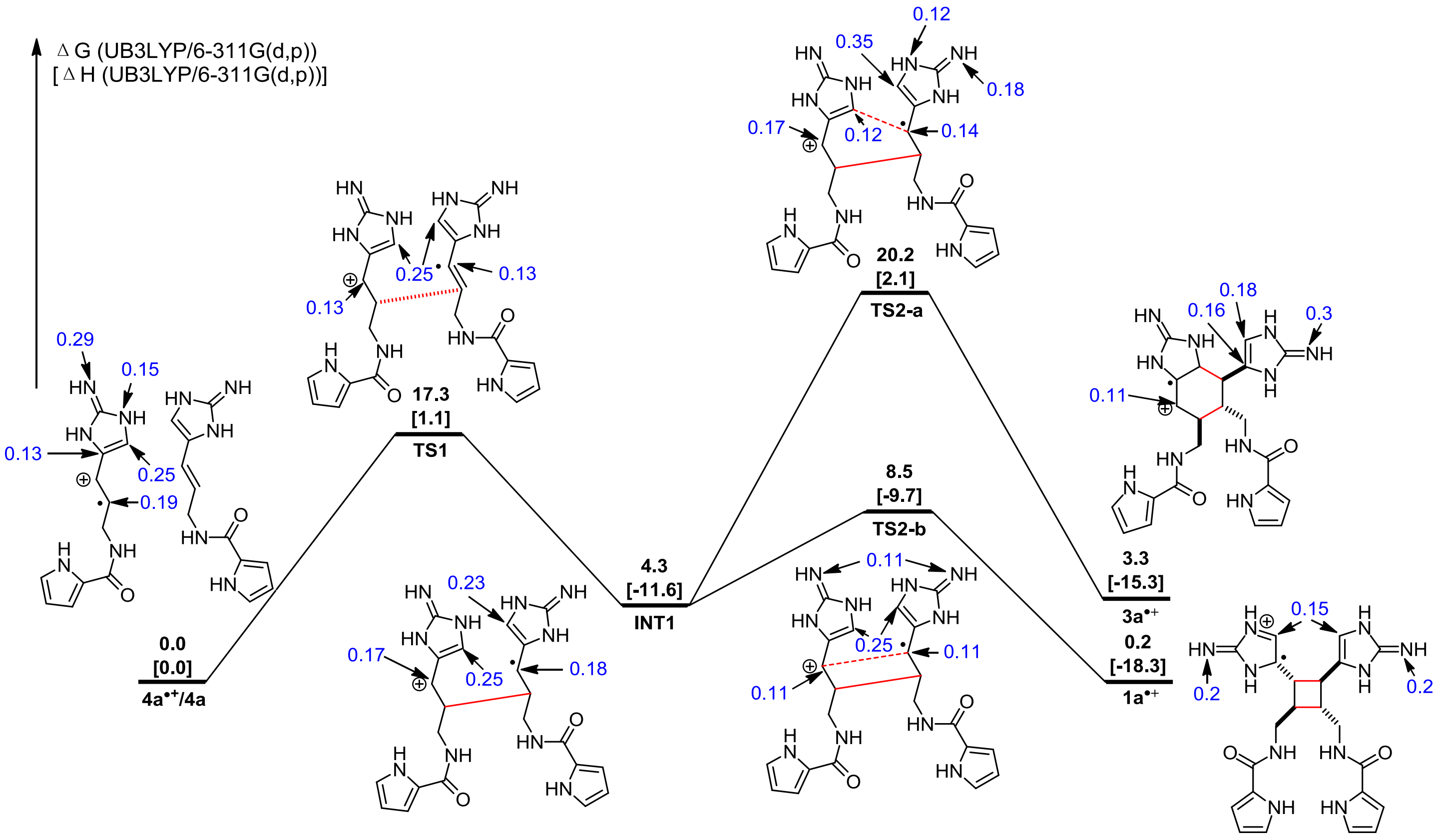
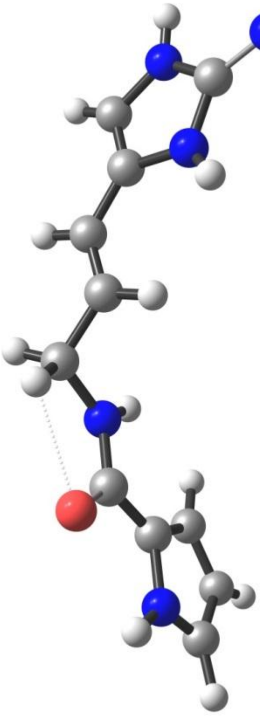


Figure S1. Computed spin distribution (blue numbers) in all radical species.

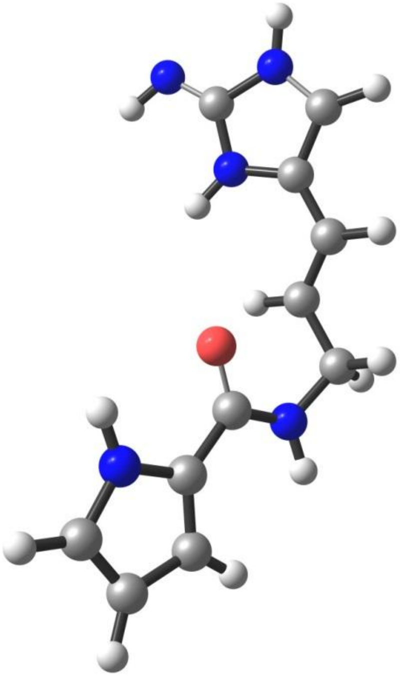
Table S1. Computed Energies of All Stationary Points

	TCGFE	***ZPE***	***H***	***G***
4c	0.192186	-775.931924	-775.914899	-775.978739
4c$^{\bullet+}$	0.194688	-775.692003	-775.675733	-775.737665
TS1	0.414075	-1551.621416	-1551.588824	-1551.688795
INT1	0.416044	-1551.641416	-1551.609124	-1551.709613
TS2a	0.418641	-1551.61857	-1551.587274	-1551.684267
TS2b	0.419071	-1551.637797	-1551.606163	-1551.702906
3d$^{\bullet+}$	0.422586	-1551.646052	-1551.614995	-1551.711090
1d$^{\bullet+}$	0.420751	-1551.650473	-1551.619795	-1551.716107

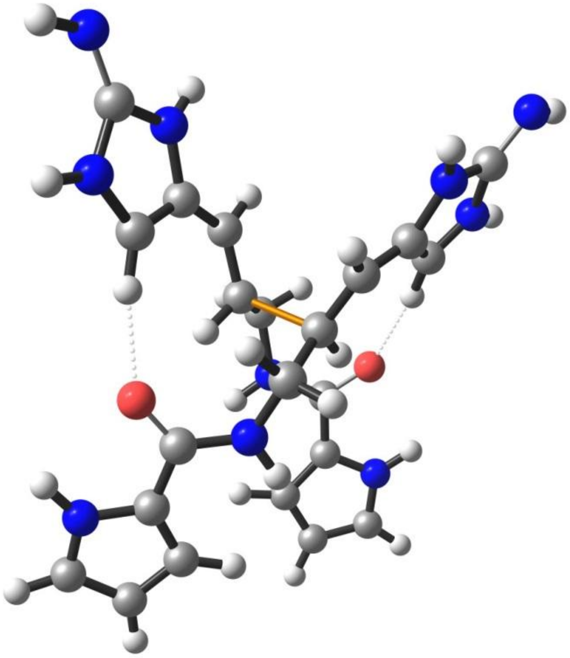
Thermal correction to Gibbs Free Energy (*TCGFE*, in Hartree)
Sum of electronic and zero-point Energies (*ZPE*, in Hartree)
Sum of electronic and thermal Enthalpies (*H*, in Hartree)
Sum of electronic and thermal Free Energies (*G*, in Hartree)



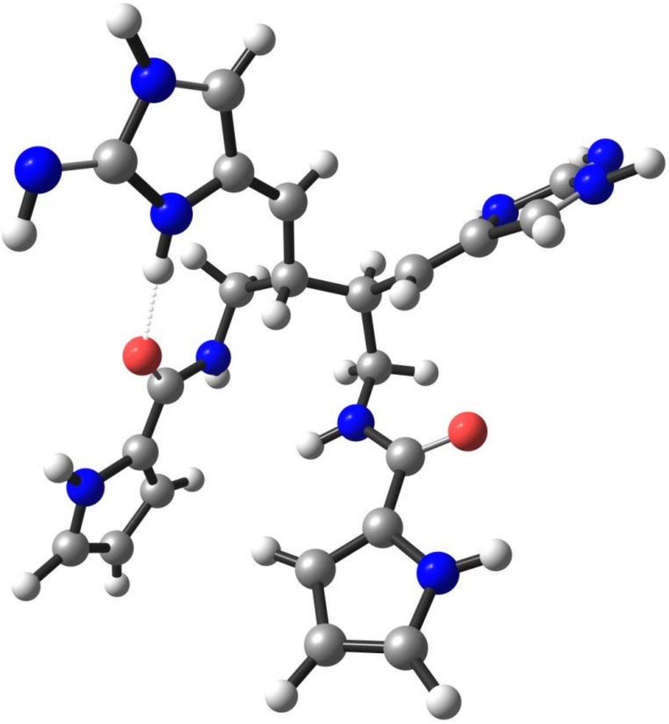
clathrodin (**4c**)



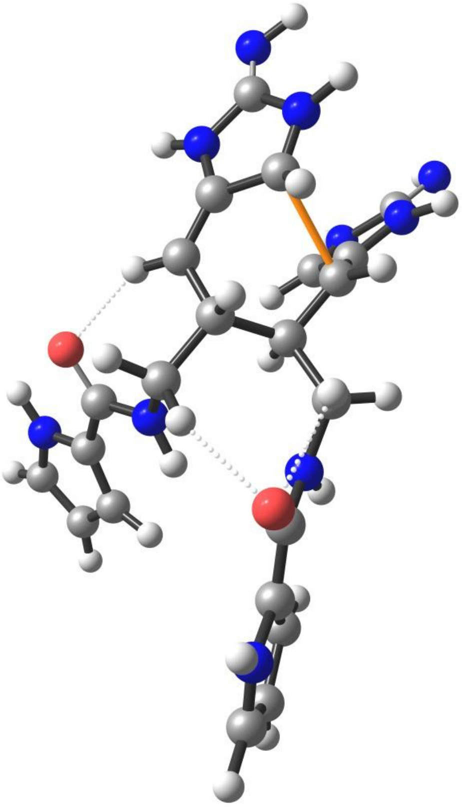
clathrodin radical cation (**4c$^{\bullet+}$**)



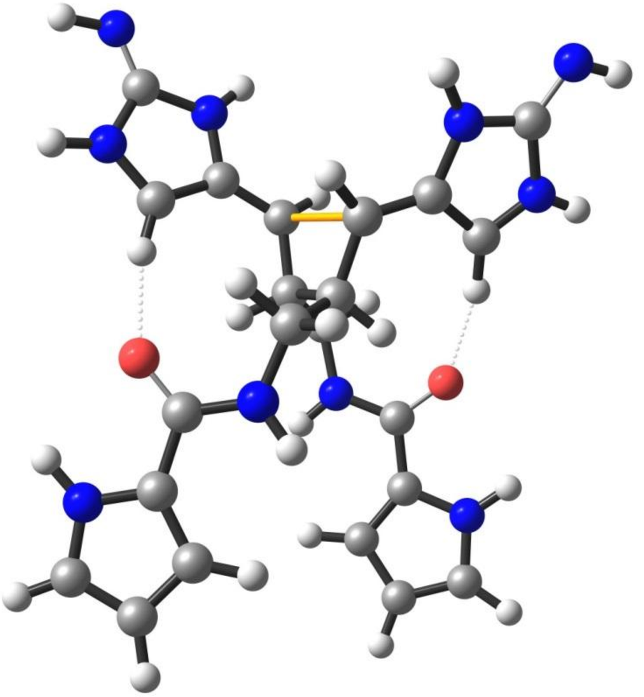
dimerization transition state (**TS1**)



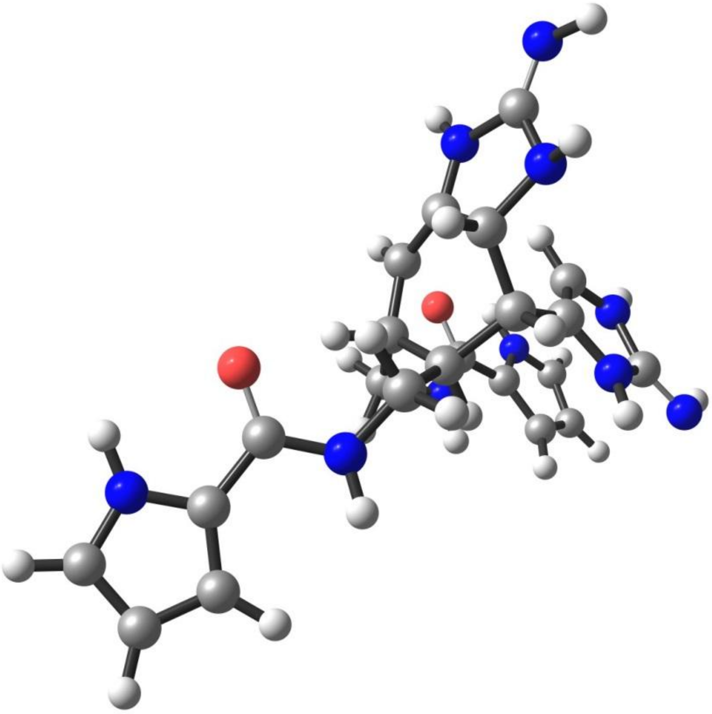
dimerization product (**INT1**)



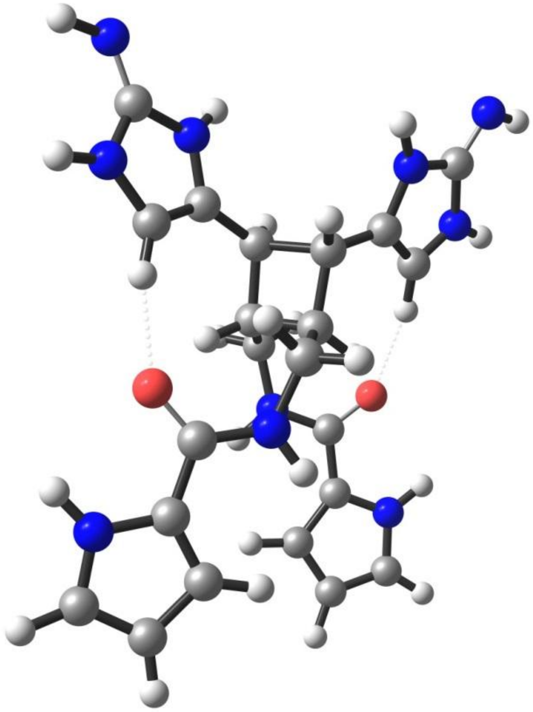
didebromoageliferin transition state (**TS2a**)



didebromosceptrin transition state (**TS2b**)



didebromoageliferin radical cation (**3d**$^{\bullet+}$)



didebromosceptrin radical cation (**1d**$^{\bullet+}$)

Coordinates of all stationary points in Figure 13

4c

Cartesian coordinates

ATOM	X	Y	Z
C	-3.28489700	0.42856100	0.41125300
C	-2.02493200	1.10254100	0.57810000
C	-0.91426600	0.92602100	-0.15600000
C	0.36148700	1.68524700	0.06304700
N	1.48161900	0.79854500	0.36282100
C	-4.41211700	0.52920000	1.16501800
N	-5.36306800	-0.32371600	0.63537000
C	-4.88244800	-0.97802400	-0.49724000
N	-3.56664600	-0.52133000	-0.58776400
C	2.64140100	0.80096600	-0.35741400
O	2.84651100	1.56328300	-1.29953900
C	3.66835600	-0.17332400	0.05131600
N	4.84742200	-0.17239900	-0.65053000
C	5.68859300	-1.12239300	-0.15854900
C	5.04429700	-1.75811900	0.88823500
C	3.76856200	-1.16027300	1.02252400
N	-5.57894700	-1.78599100	-1.20216500
H	-2.00723100	1.82969500	1.38680000
H	-0.88878700	0.19514800	-0.96112300
H	0.65835600	2.23444000	-0.83398400
H	0.23030900	2.41736300	0.86864200
H	1.37505300	0.13869200	1.11688600
H	-4.59420300	1.12363900	2.04378900
H	-6.31044300	-0.44818400	0.94718500
H	-2.99509600	-0.68322300	-1.39828900
H	5.00349500	0.46836700	-1.41467300
H	6.66913100	-1.27808600	-0.57837000
H	5.44873200	-2.56059100	1.48486600
H	3.01558800	-1.42874900	1.74806500
H	-5.04386900	-2.16295800	-1.97934400

4c$^{\bullet+}$

Cartesian coordinates

ATOM	X	Y	Z
C	-2.90525500	0.57974700	0.24941100
C	-1.79515800	1.45552400	0.35801700
C	-0.67338600	1.36257100	-0.40174700
C	0.48472000	2.30092600	-0.28467600
N	1.74296000	1.61108100	-0.51609300
C	-4.16030100	0.70907300	0.86866300
N	-4.91513700	-0.34052900	0.50317200
C	-4.21282200	-1.20720000	-0.34794900
N	-2.97049400	-0.58147700	-0.48392400
C	1.93777600	0.36990400	0.03207300
O	0.97534600	-0.25715900	0.49990000
C	3.28023800	-0.17884800	0.01829700
N	3.48944700	-1.43405800	0.54662800
C	4.80187500	-1.76276900	0.44818600
C	5.46794100	-0.70836500	-0.15890700
C	4.51351800	0.29060400	-0.42842100
N	-4.72187700	-2.27538700	-0.80538200
H	-1.86747700	2.21693400	1.12703900
H	-0.62354000	0.66044800	-1.22647700
H	0.38539200	3.07553900	-1.05514400
H	0.46316600	2.80295900	0.69086100
H	2.54242500	2.16294200	-0.78580700
H	-4.51276300	1.49448200	1.51699000
H	-5.87140800	-0.53133200	0.77329800
H	-2.18227900	-1.01864500	-0.93774700
H	2.75195700	-1.98655800	0.95676200
H	5.17343000	-2.70777000	0.81021600
H	6.52242400	-0.67191300	-0.37984800
H	4.70996400	1.24041500	-0.90245400
H	-4.10323300	-2.80464300	-1.41537300

TS1

Cartesian coordinates

ATOM	X	Y	Z
C	-0.71167800	0.44000600	0.93308200
C	-0.71167100	-0.44000000	-0.93308400
C	5.33719300	-2.56494500	0.70258000
C	4.24902300	-1.73220900	1.03942800
C	3.08479600	-2.47337700	0.85623900
C	1.65980100	-2.20242900	1.01986100
N	1.31081800	-0.96006300	1.46816900
C	-0.04882700	-0.60126100	1.83540500
N	3.46315000	-3.72155500	0.41793900
C	-2.00192600	0.85137200	1.33190700
C	-2.63138200	2.04490100	0.98024300
N	-3.94662500	2.38170900	1.29929800
C	-4.29157100	3.64604700	0.84756600
N	-3.10360700	4.07826300	0.20350900
C	-2.12365300	3.14931700	0.27895800
O	0.81283500	-3.06051700	0.73414100
N	-5.41834800	4.20292000	1.01031800
H	2.79510100	-4.45221200	0.22421000
H	5.31175400	-4.69433400	0.00475100
H	4.31817800	-0.70808700	1.37384400
H	2.05114900	-0.33173100	1.73947200
H	-0.03164100	-0.20413000	2.85632700
H	-0.63815800	-1.51970500	1.86289100
H	-0.04688400	1.23624800	0.61697900
H	-2.60143900	0.14741900	1.90569600
H	-4.59570600	1.82654700	1.83266700
H	-3.01065800	4.98355200	-0.23164700
H	-1.12980700	3.29297500	-0.12713200
H	-5.47413800	5.13147800	0.60271700
C	4.81615300	-3.79201000	0.32443600
C	-2.00191600	-0.85137200	-1.33191000
C	-0.04882300	0.60127200	-1.83540500
H	-0.04687300	-1.23623800	-0.61698200
C	-2.63137000	-2.04490200	-0.98024600
H	-2.60143100	-0.14742200	-1.90570000
N	1.31082300	0.96007000	-1.46817000
H	-0.03164000	0.20414800	-2.85632900
H	-0.63815600	1.51971600	-1.86288400
N	-3.94661200	-2.38171300	-1.29930400
C	-2.12364000	-3.14931700	-0.27896100
C	1.65980900	2.20243000	-1.01984600

H	2.05115200	0.33174200	-1.73948600
C	-4.29155500	-3.64605200	-0.84757400
H	-4.59569300	-1.82655100	-1.83267400
N	-3.10359100	-4.07826600	-0.20351600
H	-1.12979500	-3.29297400	0.12713300
C	3.08480500	2.47337800	-0.85623500
O	0.81284500	3.06051200	-0.73410400
N	-5.41833000	-4.20292800	-1.01032900
H	-3.01064100	-4.98355400	0.23164000
N	3.46316200	3.72154700	-0.41791400
C	4.24903300	1.73221700	-1.03945400
H	-5.47411900	-5.13148700	-0.60273000
C	4.81616500	3.79200500	-0.32442600
H	2.79511200	4.45219900	-0.22416200
C	5.33720400	2.56494800	-0.70260200
H	4.31818600	0.70810200	-1.37389200
H	5.31176800	4.69432300	-0.00472800
H	6.38360900	-2.30731700	0.73615000
H	6.38362100	2.30732400	-0.73619000

INT1

Cartesian coordinates

ATOM	X	Y	Z
C	1.02655000	3.17092500	0.48269700
C	1.45973000	2.19590300	-0.38527900
C	0.55975200	1.09921700	-0.88735300
C	-0.40725800	1.59386800	-2.00131600
N	-1.67354700	0.86410300	-2.03122800
C	1.76585700	4.25099000	1.01561300
N	0.95993400	4.93937100	1.83629400
C	-0.34263700	4.38024400	1.87889000
N	-0.24739000	3.27184200	1.05012100
C	-2.63296700	1.08904500	-1.08089700
O	-2.41737800	1.80678500	-0.09277000
C	-3.91435900	0.41796400	-1.25494100
N	-4.91042700	0.64893900	-0.33386100
C	-6.01875300	-0.06436300	-0.65997700
C	-5.74590300	-0.78173200	-1.81419800
C	-4.42130900	-0.48068000	-2.19110800
N	-1.26626200	4.90443200	2.57016900
H	2.45403000	2.30230300	-0.80084400
H	-0.07045200	0.77127100	-0.05368700
H	-0.60969800	2.65723200	-1.84856600
H	0.06015900	1.49301500	-2.98345800
H	-1.97427600	0.46932300	-2.90880800
H	2.79741400	4.51157500	0.84477300
H	1.18947900	5.76293300	2.37394000
H	-1.06093700	2.74829800	0.71387100
H	-4.79132300	1.26912000	0.45288700
H	-6.91478300	-0.01500900	-0.06271000
H	-6.42845600	-1.44385500	-2.32207100
H	-3.90285400	-0.88084800	-3.04962000
H	-2.14069800	4.38995200	2.50705300
C	3.70413400	-0.59591900	-0.11765300
C	2.36339200	-0.30698400	-0.07102200
C	1.46136800	-0.09741100	-1.25114900
C	0.69440900	-1.39597000	-1.64169300
N	-0.28030400	-1.83662100	-0.66508900
C	4.53213100	-0.91822900	0.97370900
N	5.77379400	-1.13748400	0.51703000
C	5.85197600	-0.99575800	-0.88842800
N	4.55431200	-0.62872400	-1.23829500
C	0.04592600	-2.73038300	0.32537200
O	1.21032500	-3.08079200	0.51823200

C	-1.05469000	-3.23350800	1.14671000
N	-0.76179800	-4.15750000	2.12189400
C	-1.89558600	-4.51565500	2.78003700
C	-2.95143600	-3.80768300	2.23013400
C	-2.42433600	-2.99899700	1.19959200
N	6.92986300	-1.18945100	-1.52188600
H	1.89369300	-0.38205400	0.90128300
H	2.06107900	0.18254100	-2.12968400
H	0.17884500	-1.23143400	-2.59051400
H	1.42021000	-2.19808200	-1.78911300
H	-1.25096300	-1.62461400	-0.83084700
H	4.26102900	-0.99924400	2.01328300
H	6.58563900	-1.40585800	1.05466800
H	4.24700600	-0.59492100	-2.19499000
H	0.17373100	-4.50503500	2.27002000
H	-1.87782200	-5.23940300	3.57867600
H	-3.98254500	-3.87286300	2.53876600
H	-2.98772000	-2.32266300	0.57420300
H	6.84345600	-1.05127900	-2.52468200

TS2a

Cartesian coordinates

ATOM	X	Y	Z
C	1.97223900	-1.58350300	-0.01872200
C	0.57428100	-1.06997500	0.25284500
C	0.42959500	-0.27883000	1.62938800
C	1.43092000	0.83301000	1.69359400
C	2.75122800	0.54880700	1.69277100
C	3.29290700	-0.78381900	1.73828600
N	-1.56773000	1.03515200	0.78980300
C	-1.00081900	0.25569000	1.88409700
N	-2.28070600	4.44116400	-0.33180400
C	-3.35921100	2.65593800	-1.10948400
C	-2.37490700	3.07392600	-0.22026200
N	3.84998600	1.38061100	1.47580000
C	5.03516100	0.67620200	1.35265200
N	4.62738700	-0.68223300	1.54878700
C	-1.49890200	2.40370100	0.74184400
O	-0.72336600	3.04918600	1.45146900
N	6.17102800	1.17395000	1.11908600
H	-1.65452100	4.98405500	0.24405100
H	-3.26024400	5.94722300	-1.47663000
H	-3.70084200	1.64338400	-1.26462500
H	-2.27233100	0.57856100	0.23206000
H	-1.66885900	-0.57647200	2.09843800
H	-0.96468000	0.88910500	2.77297500
H	0.62406000	-1.01126900	2.42440600
H	1.06521000	1.85400600	1.63245900
H	3.81975800	2.38075400	1.35884600
H	5.29288100	-1.42935100	1.67728400
H	2.87339700	-1.61571000	2.27925500
H	6.91593700	0.48712700	1.05084500
C	-3.17100300	4.89673400	-1.25188200
C	-3.85747800	3.80609600	-1.75988900
C	-0.39994600	-2.28857900	0.15954700
H	0.29229300	-0.36011900	-0.52844600
C	2.74791700	-1.13072700	-1.08937200
H	2.17660400	-2.60085500	0.30531100
N	-1.76055400	-1.95967400	-0.23872900
H	0.00568600	-3.00474500	-0.56093100
H	-0.46336000	-2.79285300	1.12620500
N	3.90899900	-1.73693300	-1.54905200
C	2.62996000	0.05350000	-1.84087900
C	-2.83951500	-2.32211300	0.55034700

H	-1.93494700	-1.90005700	-1.23109900
C	4.50781800	-1.02210600	-2.58347200
H	4.21128100	-2.67481100	-1.33744800
N	3.66972600	0.10574000	-2.71321200
H	1.88678600	0.82935000	-1.77549000
C	-4.15921500	-2.22722300	-0.06904200
O	-2.69853300	-2.65806400	1.72306200
N	5.55512400	-1.38576000	-3.19642500
H	3.84002600	0.84794200	-3.37507000
N	-5.25566000	-2.55236600	0.69381900
C	-4.62860500	-1.86757200	-1.33006200
H	5.84515600	-0.74554300	-3.93022400
C	-6.39074300	-2.41301800	-0.03805100
H	-5.17496800	-2.85361600	1.65398900
C	-6.03465900	-1.98533000	-1.30706200
H	-4.03493400	-1.55993100	-2.17815800
H	-7.36053800	-2.62402000	0.38249000
H	-4.63433600	3.84213600	-2.50685500
H	-6.71466200	-1.78568300	-2.11956600

TS2b

Cartesian coordinates

ATOM	X	Y	Z
C	0.65052300	-0.31310500	0.71024500
C	0.65052300	0.31310500	-0.71024500
C	2.12234900	-0.58979600	0.98639100
C	2.12234900	0.58979600	-0.98639000
C	-3.08231300	2.52349800	0.96995400
C	-1.65502300	2.23107600	1.06843400
N	-1.30624700	1.00513600	1.55872400
C	0.07297000	0.61693700	1.79836700
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$3d^{\bullet+}$

Cartesian coordinates

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1d$^{\bullet+}$

Cartesian coordinates

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H	0.06587500	-1.24565200	0.81291000
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H	-6.42847000	-2.45672100	-0.81050800
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Table S2. Comparison of the ^{1}H NMR data of sceptrin (**1a**) in D_2O

	Our synthetic **1a•TFA**	Baran's synthetic **1a•HCl**[5a]
H2/H2'	7.00 (d, *J* = 1.5 Hz, 2H)	7.00 (d, *J* = 1.6 Hz, 2 H)
H4/H4'	6.55 (d, *J* = 1.5 Hz, 2H)	6.56 (d, *J* = 1.6 Hz, 2 H)
H8/H8'	3.52 (dd, *J* = 14.0, 6.5 Hz, 2H)	3.52–3.40 (m, 4 H)
	3.44 (dd, *J* = 14.0, 6.5 Hz, 2H)	
H9/H9'	2.49–2.45 (m, 2H)	2.48–2.46 (m, 2 H)
H10/H10'	2.98 (A_2B_2, *J* = 9.5, 2.7 Hz, 2H)	2.98 (A_2B_2, *J* = 9.6, 2.4 Hz, 2H)
H15/H15'	6.52 (s, 2H)	6.53 (s, 2 H)

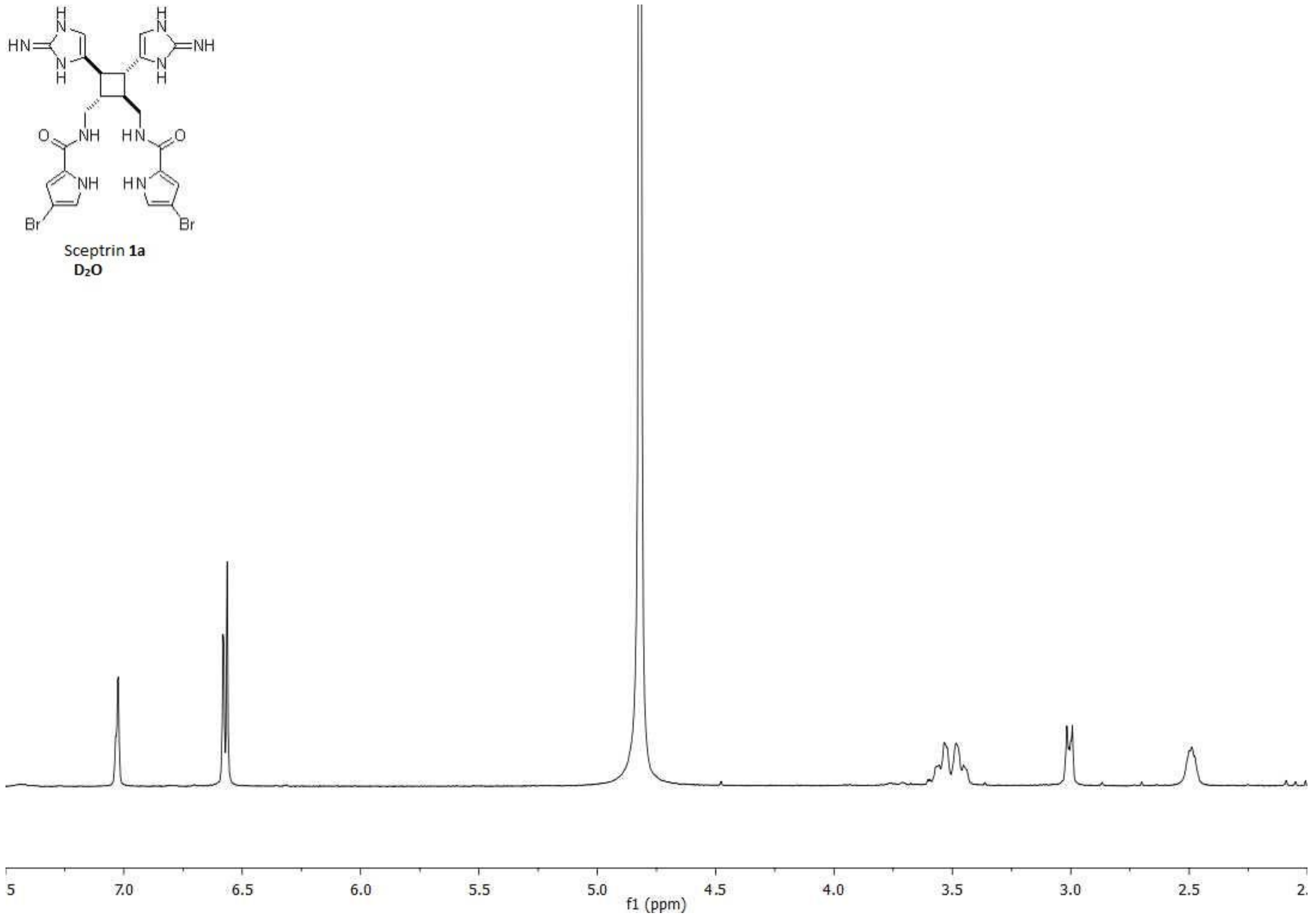


Table S3. Comparison of the ^{1}H NMR data of sceptrin (**1a**) in CD_3OD

	Our synthetic **1a•TFA**	Birman's synthetic **1a•TFA**[6]	Natural **1a•HOAc**[2b]
H2/H2'	6.92 (d, *J* = 1.4 Hz, 2H)	6.91 (d, *J* = 1.4 Hz, 2H)	6.91 (m, 2H)
H4/H4'	6.74 (d, *J* = 1.4 Hz, 2H)	6.75 (d, *J* = 1.4 Hz, 2H)	6.77 (d, *J* = 1.5 Hz, 2H)
H8/H8'	3.51–3.48 (m, 4H)	3.50–3.48 (m, 4H)	3.48 (br, 4H)
H9/H9'	2.37–2.34 (m, 2H)	2.37–2.34 (m, 2H)	2.33 (m, 2H)
H10/H10'	2.99 (A_2B_2, *J* = 9.4, 2.6 Hz, 2H)	2.99 (A_2B_2, *J* = 9.5, 2.5 Hz, 2H)	2.98 (m, 2H)
H15/H15'	6.57 (s, 2H)	6.56 (s, 2H)	6.50 (s, 2H)

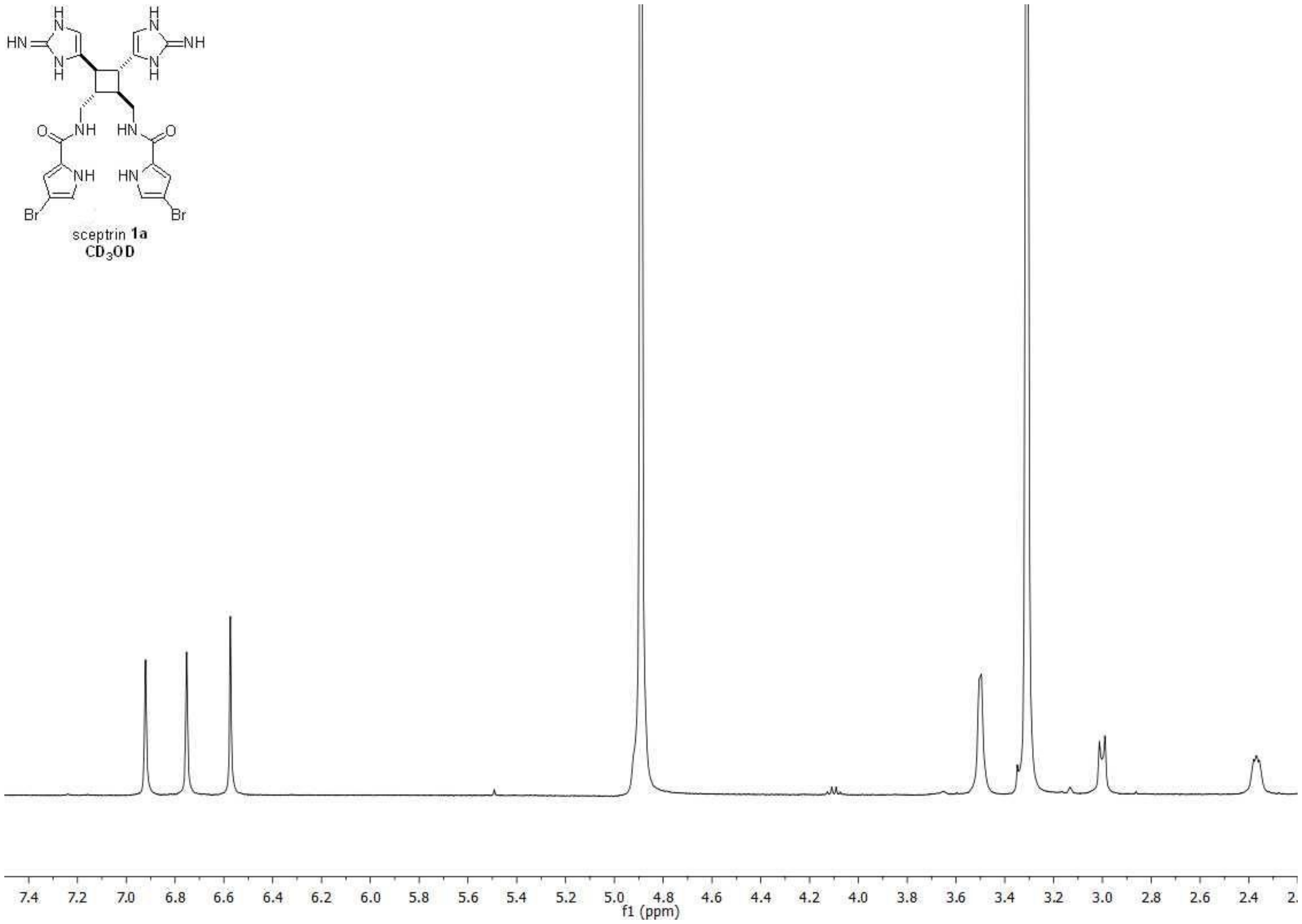


Table S4. Comparison of the ^{13}C NMR data of sceptrin (1a) in D_2O

	Our synthetic **1a•TFA**	Baran's synthetic **1a•HCl**[5a]	Natural **1a•HCl**[1a]	Natural **1a•HCl**[2b]
C2/C2'	121.5	121.5	121.6	121.6
C3/C3'	94.8	94.8	95.2	95.2
C4/C4'	111.0	111.0	111.6	111.6
C5/C5'	123.6	123.6	123.9	123.9
C6/C6'	160.8	160.8	160.8	160.8
C8/C8'	40.5	40.5	40.9	40.9
C9/C9'	37.2	37.2	36.9	36.9
C10/C10'	41.3	41.3	41.6	41.6
C11/C11'	125.2	125.3	(missing)	(missing)
C13/C13'	145.4	145.4	145.7	145.7
C15/C15'	108.0	108.0	108.3	108.3

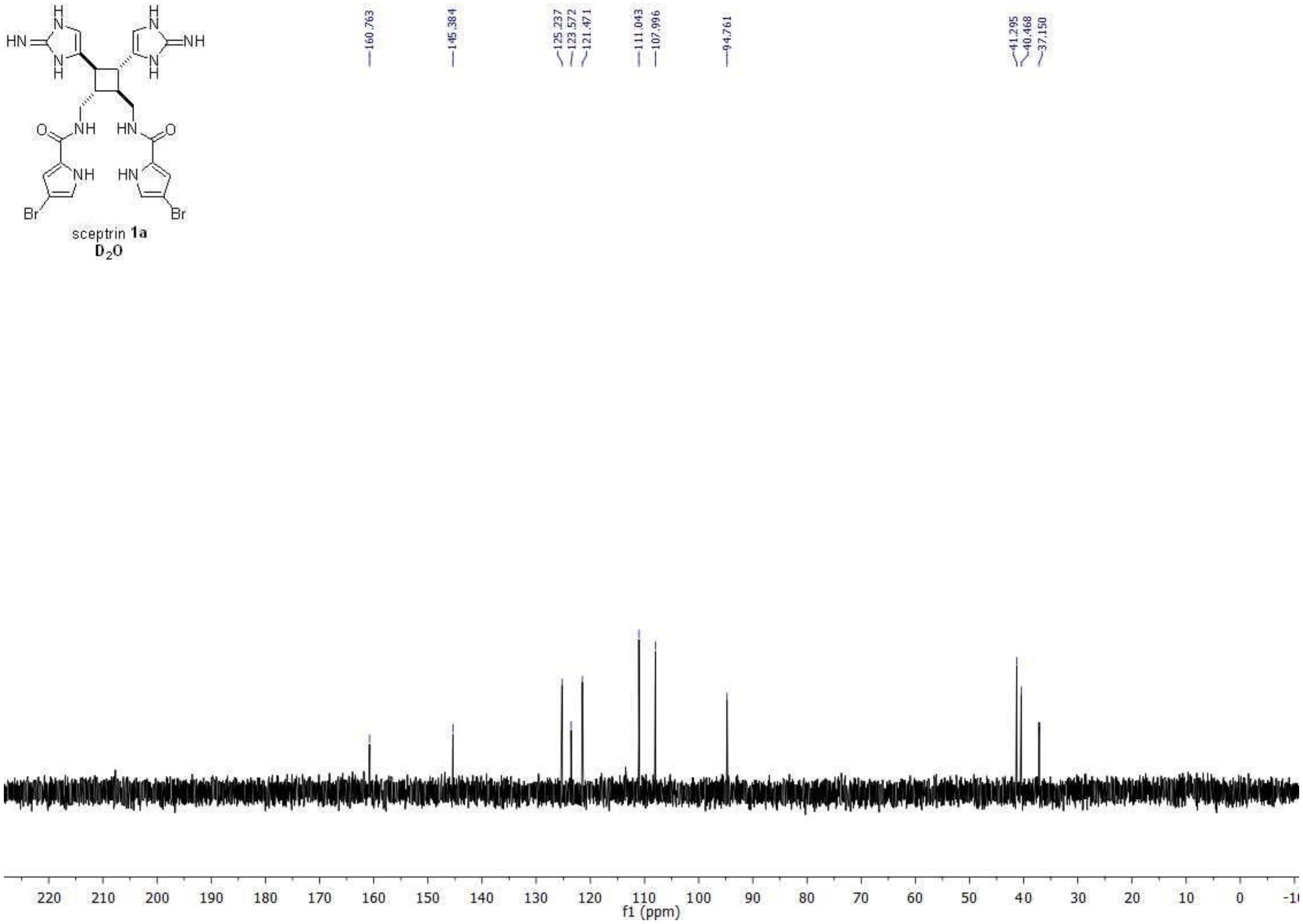


Table S5. Comparison of the ^{13}C NMR data of sceptrin (1a) in CD_3OD

	Our synthetic **1a•TFA**	Baran's synthetic **1a•TFA**[5b]	Birman's synthetic **1a•TFA**[6]	Natural **1a•HOAc**[2b]
C2/C2'	123.1	123.1	123.0	122.9
C3/C3'	97.6	97.6	97.5	97.5
C4/C4'	113.4	113.6	113.4	113.5
C5/C5'	127.2	127.3	127.2	127.4
C6/C6'	163.0	163.1	163.0	163
C8/C8'	42.3	42.4	42.3	42.4
C9/C9'	39.3	39.3	39.2	39.4
C10/C10'	44.3	44.3	44.2	44.3
C11/C11'	128.7	128.8	128.7	129.4
C13/C13'	149.0	149.1	148.9	149.4
C15/C15'	110.3	110.3	110.2	110.1

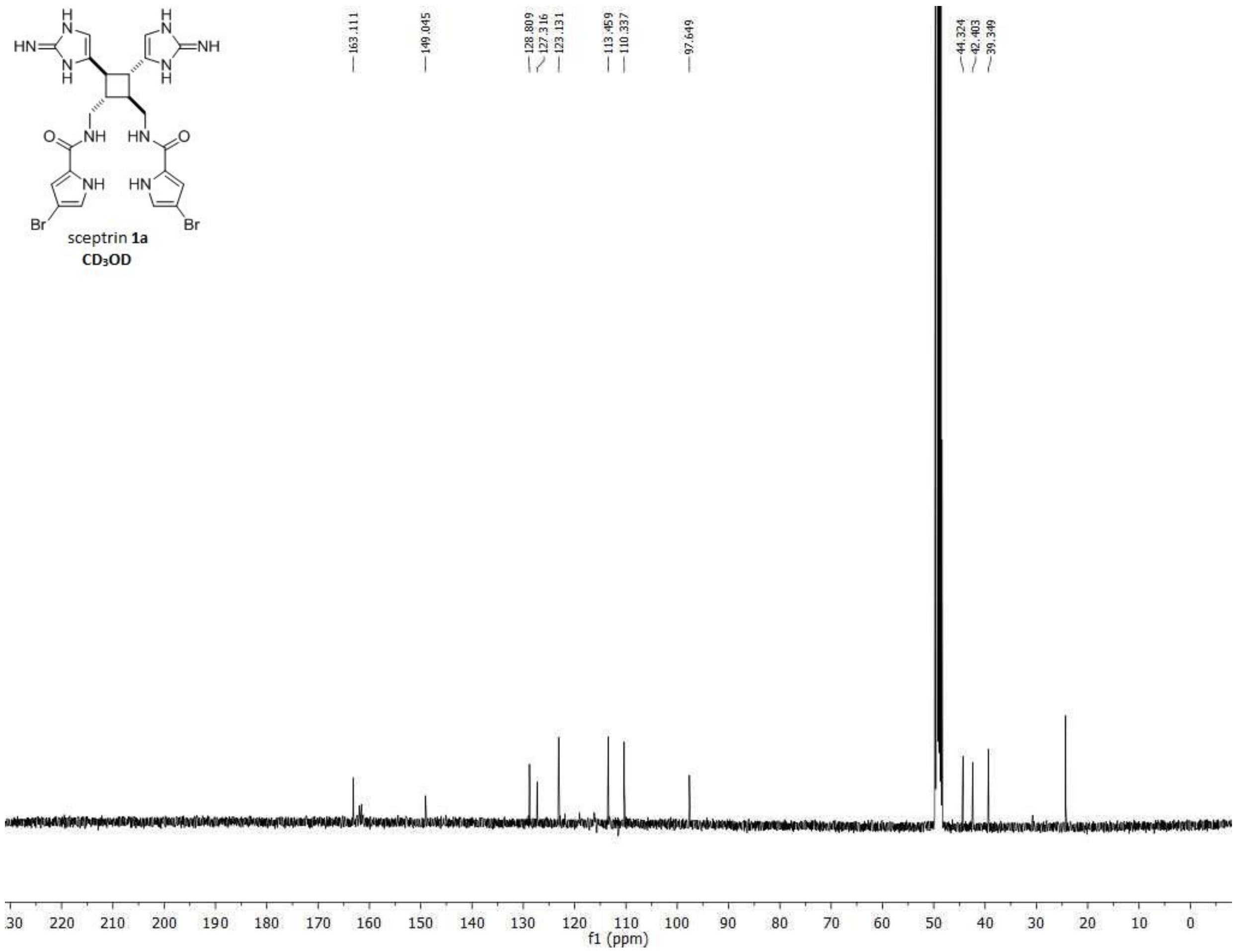


Table S6. Comparison of the ^{1}H NMR data of bromosceptrin (**1b**) in DMSO-d_6

	Our synthetic **1b•TFA**	Natural **1b•TFA**[1b]
H1/H1’	12.67/12.80	12.65/11.78
H2/H2'	6.98	6.98
H4/H4'	6.88/6.80	6.88/6.80
H7/H7’	8.21/8.18	8.20/8.16
H8/H8'	3.37	3.39
H9/H9'	2.27	2.27
H10/H10'	2.93	2.94
H12/H12’	12.29	12.20
H14/H14’	11.8	11.73
H15/H15'	6.60	6.60
H16/H16’	7.42	7.37

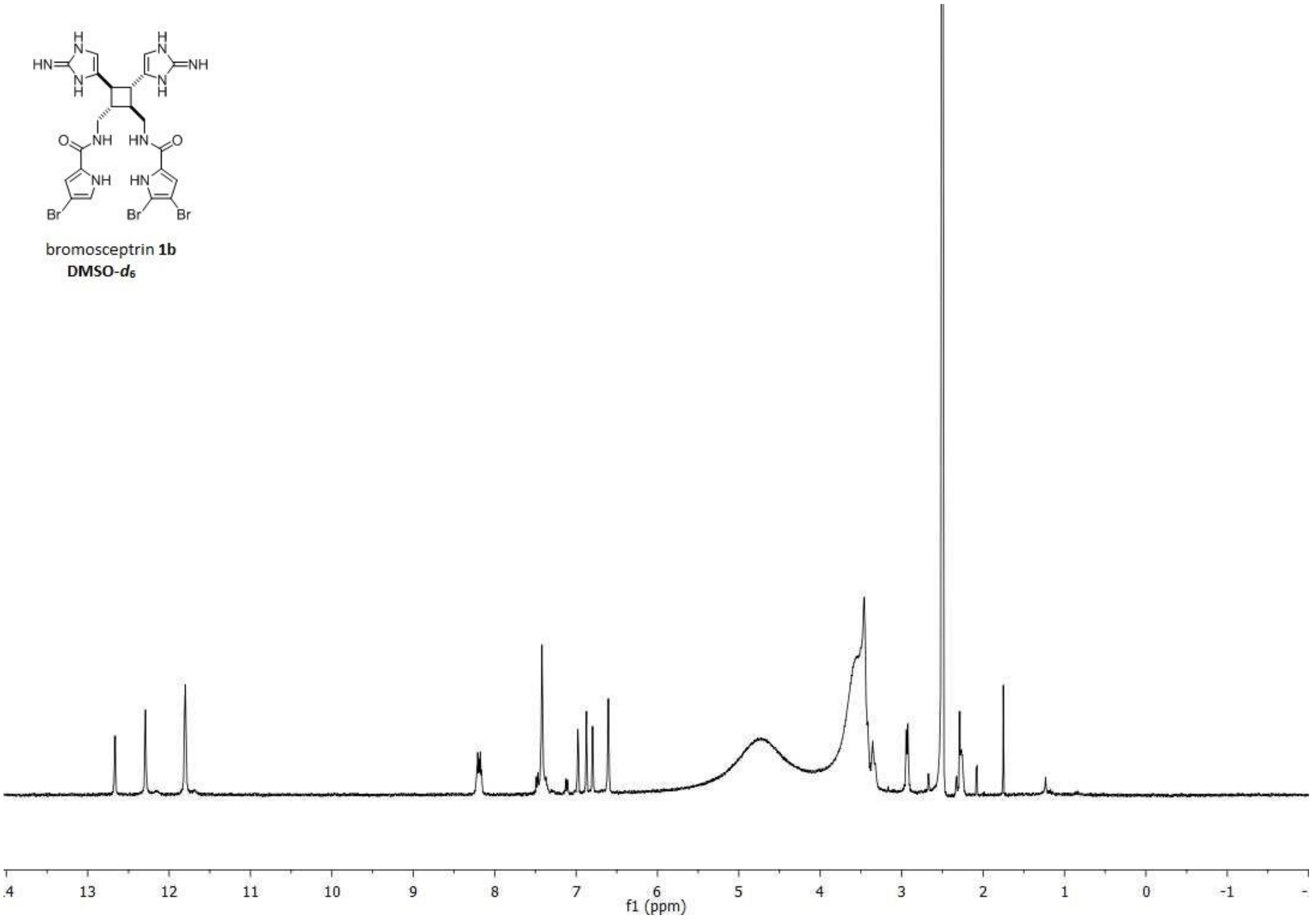


Table S7. Comparison of the ^{1}H NMR data of dibromosceptrin (**1c**) in CD_3OD

	Our synthetic **1c•TFA**	Birman's synthetic **1c•TFA**[6]	Natural **1c•HOAc**[2b]
H4/H4'	6.76 (s, 2H)	6.77 (s, 2 H)	6.81 (s, 2H)
H8/H8'	3.49–3.46 (m, 4H)	3.49 - 3.47 (m, 4H)	3.48 (m, 4H)
H9/H9'	2.37–2.33 (m, 2H)	2.37–2.34 (m, 2 H)	2.35 (m, 2H)
H10/H10'	2.98 (A_2B_2, *J* = 9.4, 2.6 Hz, 2H)	2.99 (A_2B_2, *J* = 9.6, 2.6 Hz, 2H)	3.00 (m, 2H)
H15/H15'	6.56 (s, 2H)	6.56 (s, 2 H)	6.52 (s, 2H)

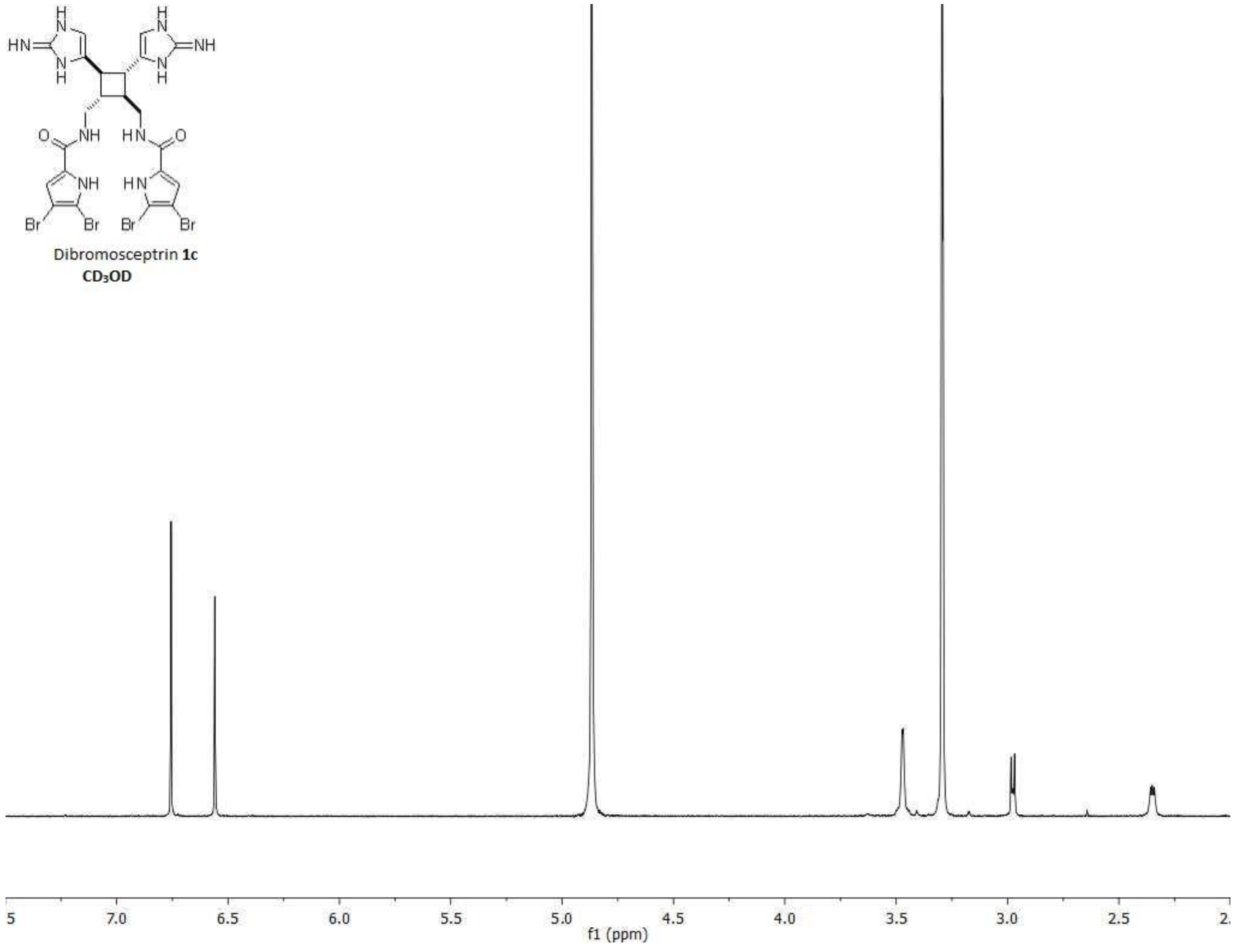


Table S8. Comparison of the ^{13}C NMR data of dibromosceptrin (**1c**) in CD$_3$OD

	Our synthetic **1c•TFA**	Birman's synthetic **1c•TFA**[6]	Natural **1c•HOAc**[2b]
C2/C2'	106.4	106.4	106.3
C3/C3'	100.1	100.1	100.1
C4/C4'	114.3	114.4	114.7
C5/C5'	128.5	128.5	128.5
C6/C6'	162.2	162.1	162.0
C8/C8'	42.4	42.4	42.5
C9/C9'	39.3	39.2	39.1
C10/C10'	44.2	44.1	44.2
C11/C11'	128.7	128.7	128.7
C13/C13'	149.0	149.0	149.2
C15/C15'	110.3	110.2	110.1

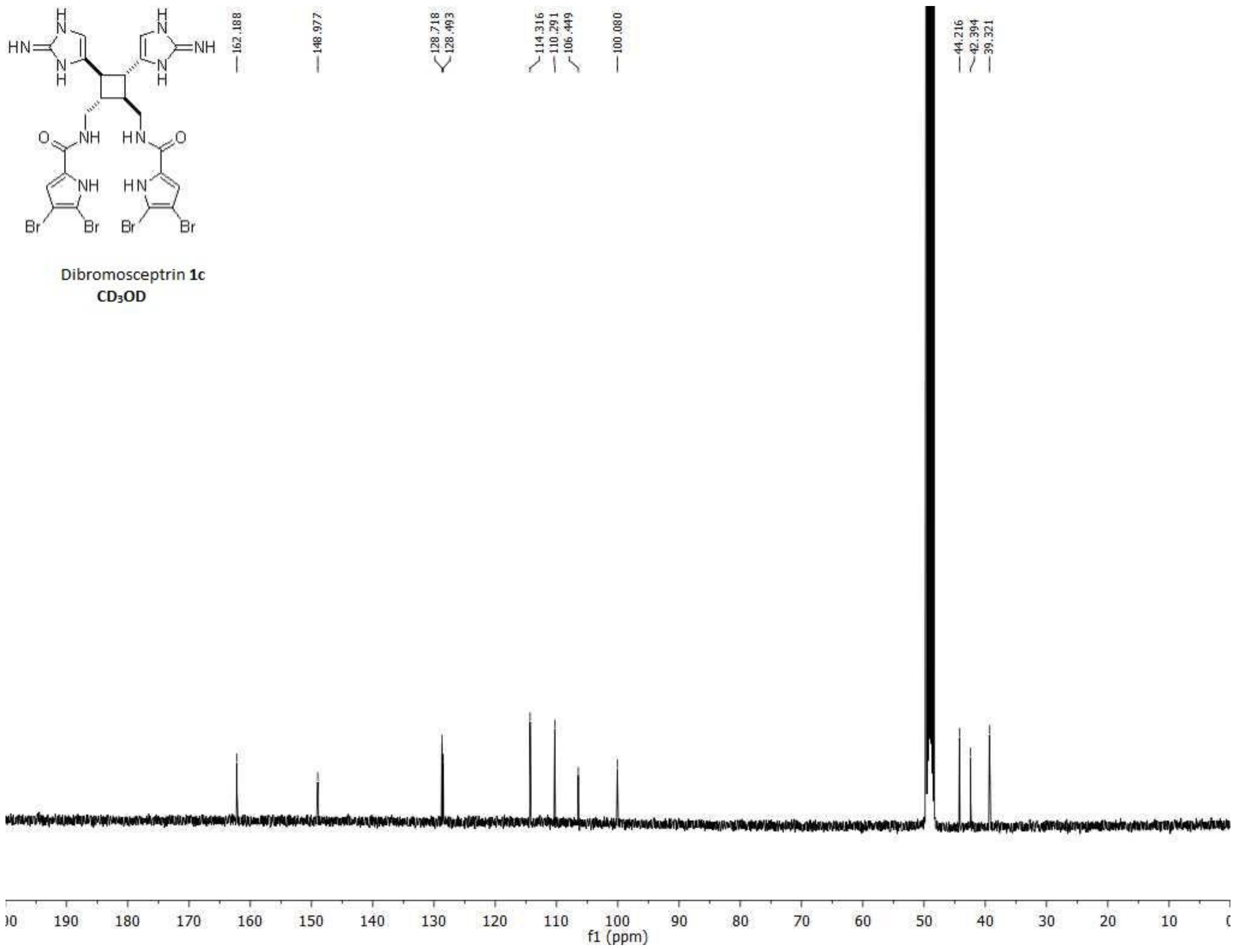
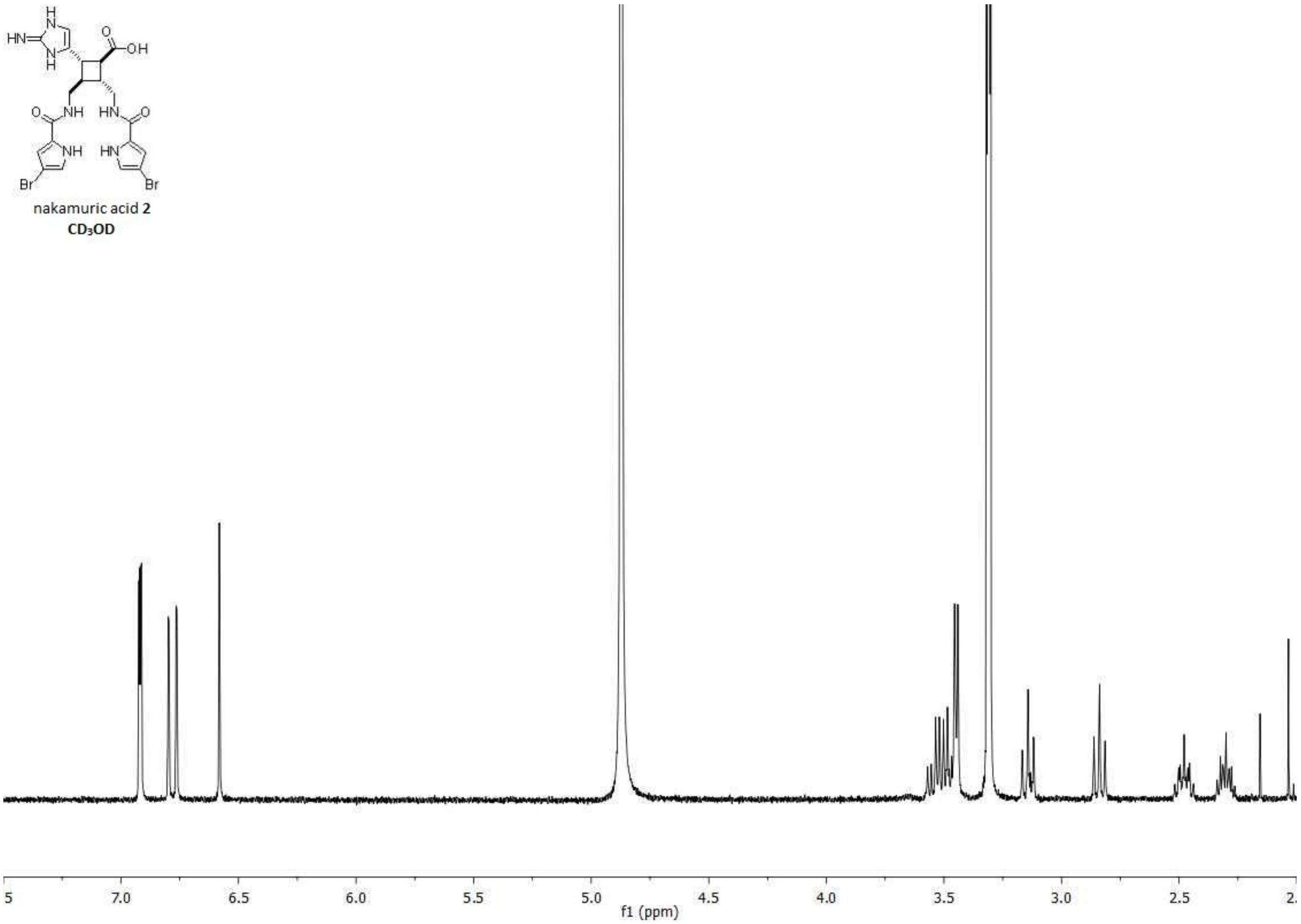


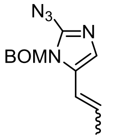
Table S9. Comparison of the ^{1}H NMR data of nakamuric acid (**2**) in D_2O

	Our synthetic **2•TFA**	Baran's synthetic **2•TFA**[5b]
H2/H2'	6.92 (d, *J* = 1.5 Hz, 1H)/6.91 (d, *J* = 1.5 Hz, 1H)	6.92 (m, 2 H)
H4/H4'	6.80 (d, *J* = 1.5, 1H)/6.76 (d, *J* = 1.5, Hz, 1H)	6.79 (d, *J* = 1.4 Hz, 1H)/6.76 (d, *J* = 1.4 Hz, 1H)
H8/H8'	3.52 (m, 2H)/ 3.45 (d, *J* = 5.4 Hz, 2H)	3.52 (m, 2H)/3.44 (d, *J* = 5.4 Hz, 2H)
H9/H9'	2.48 (m, 1H)/2.30 (m, 1H)	2.48 (m, 1H)/2.31 (m, 1H)
H10/H10'	2.84 (t, *J* = 9.6 Hz, 1H)/3.14 (t, *J* = 9.6 Hz, 1H)	2.84 (t, *J* = 9.5 Hz, 1H)/ 3.15 (t, *J* = 9.7 Hz, 1H)
H15/H15'	6.58 (s, 1H)	6.58 (s, 1H)



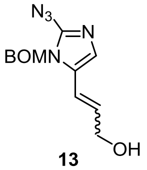
Experimental Procedures

General Experimental Procedures. All reactions were performed in glassware under a positive pressure of argon. The normal-phase flash column chromatography was performed as described by Still (Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925), employing EMD silica gel 60 (230–400 mesh ASTM). TLC analyses were performed on EMD 250 μm Silica Gel 60 F_{254} plates and visualized by quenching of UV fluorescence (λ_{max}= 254 nm), or by staining ceric ammonium molybdate. ^{1}H and ^{13}C NMR spectra were recorded on Varian Inova-600, Inova-500, or Inova-400. Chemical shifts for ^{1}H and ^{13}C NMR spectra are reported in ppm (δ) relative to the ^{1}H and ^{13}C signals in the solvent ($CDCl_3$: δ 7.26, 77.00 ppm; CD_3OD: δ 3.31, 49.00 ppm; DMSO-d_6: δ 2.50, 39.52 ppm; CD_3CN: δ 1.94, 118.2 ppm; C_6D_6: δ 7.16, 128.1; D_2O: 4.82) and the multiplicities are presented as follows: s = singlet, d = doublet, t = triplet, m = multiplet. Mass spectra were acquired on Agilent 6120 Single Quadrupole LC/MS. Preparative HPLC was performed using a Waters Atlantis dC18 OBD 5 μm column with dimension 19×150 mm or Eclipse XDB-C18 5 μm column with dimension 9.4×250 mm. The CD spectrum was recorded on a JACSO J-815 CD Spectrometer in water at 25 °C.



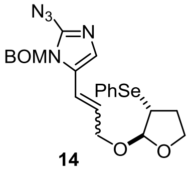
12

Azidoimidazole 12. To a solution of 2-azido-1-((benzyloxy)methyl)-1*H*-imidazole-5-carbaldehyde (**11**) (5.0 g, 19.4 mmol, 1.0 equiv) and 5-((2-(tert-butyldimethylsilyloxy)ethyl) sulfonyl)-2-phenyl-2*H*-tetrazole (7.50 g, 20.4 mmol, 1.05 equiv) in tetrahydrofuran (300 mL) was added potassium bis(trimethylsilyl)amide (0.5 M in toluene, 54.3 mL, 27.2 mmol, 1.4 equiv) at –78 °C slowly. The reaction mixture was warmed to –50 °C over 2 h. After stirring for an additional 30 min, the reaction was quenched with saturated ammonium chloride (100 mL). The solvents were then removed by rotary evaporation and the residue was diluted with 5% ethyl acetate/hexanes, washed successively with water and brine, dried over sodium sulfate, filtered, concentrated to afford crude **12**. (*E*)-**12:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.26 (m, 5H), 6.98 (s, 1H), 6.55–6.40 (dd, *J* = 16.0, 2.2 Hz, 1H), 6.21 (dt, *J* = 16.0, 4.6 Hz, 1H), 5.20 (s, 2H), 4.51 (s, 2H), 4.31 (dd, *J* = 4.6, 2.2 Hz, 2H), 0.93 (s, 9H), 0.10 (s, 6H); MS(ESI)+calcd for $C_{20}H_{30}N_5O_2Si$ (M+H)+ 400.2, found 400.2.



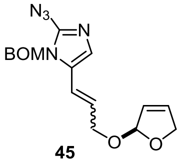
13

Alcohol 13. To a solution of the crude **12** obtained above in methanol (140 mL) was added hydrochloric acid (1.0 N, 9.7 mL, 9.7 mmol, 0.50 equiv) at 0 °C. After stirring for 2 h, the reaction was quenched with saturated sodium bicarbonate (10 mL). The solvent was then removed by rotary evaporation and the residue was diluted with ethyl acetate, washed successively with water and brine, dried over sodium sulfate, filtered, concentrated and purified by flash column chromatography over silica gel (50%→100% ethyl acetate/hexanes) to give **13** (3.55 g, 64% yield over two steps) as a pale yellow oil. (*E*)-**13**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.12 (m, 5H), 6.95 (s, 1H), 6.40 (d, *J* = 16.0 Hz, 1H), 6.21 (dt, *J* = 16.0, 5.4 Hz, 1H), 5.15 (s, 2H), 4.47 (s, 2H), 4.23 (dd, *J* = 5.3, 1.1 Hz, 2H); (*Z*)-**13**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.19 (m, 5H), 6.72 (s, 1H), 6.26 (d, *J* = 10.9 Hz, 1H), 5.90 (dt, *J* = 11.7, 5.9 Hz, 1H), 5.13 (s, 2H), 4.45 (s, 2H), 4.34 (dd, *J* = 5.9, 1.6 Hz, 2H); (*E*/*Z*)-**13**: ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 141.5, 136.6, 136.6, 133.0, 130.1, 130.0, 128.6, 128.6, 127.9, 127.9, 127.8, 127.7, 125.0, 71.4, 70.7, 70.6, 63.2, 60.2; MS(ESI)$^{+}$calcd for $C_{14}H_{16}N_5O_2$ (M+H)$^{+}$ 286.1, found 286.2.



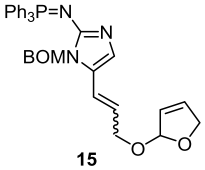
14

Selenide 14. To a solution of dihydrofuran (265 μL, 3.51 mmol, 2.0 equiv) in methylene chloride (30 mL) was added a solution of phenylselenyl chloride (672 mg, 3.51 mmol, 2.0 equiv) in methylene chloride (20 mL) at –78 °C slowly. After stirring for 10 min, a solution of alcohol **13** (500 mg, 1.75 mmol, 1.0 equiv), triethylamine (732 μL, 5.262 mmol, 3.0 equiv) in methylene chloride (20 mL) was added at –78 °C. After stirring at –50 °C for 1.5 h, the reaction was quenched with saturated sodium bicarbonate. The solvent was then removed by rotary evaporation and the residue was dissolved in ethyl acetate, washed successively with saturated sodium bicarbonate and brine, dried over sodium sulfate and concentrated to afford crude **14**.



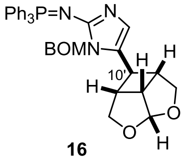
45

Dihydrofuran 45. To a solution of the crude **14** obtained above in 1,4-dioxane (30 mL) were added pyridine (1.4 mL, 17.54 mmol, 10.0 equiv) and aqueous hydrogen peroxide (10 wt. %, 1.8 mL, 5.26 mmol, 3.0 equiv) at 0 °C. After stirring for 10 h, the solvent was removed by rotary evaporation and the residue was partially purified by flash column chromatography over a short pack of C2-silica gel (0→20% ethyl acetate/hexanes). The resulting **45** (605 mg, 98% yield over two steps) is highly acid-sensitive and should be used immediately.



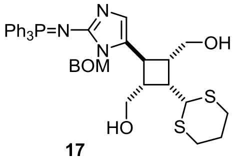
15

Dihydrofuran 15. To a solution of dihydrofuran **45** (605 mg, 1.71 mmol, 1.0 equiv) in tetrahydrofuran (20 mL) was added triphenylphosphine (494 mg, 1.885 mmol, 1.1 equiv) in small portions at 23 °C. After stirring for 10 min, the volatiles were removed by rotary evaporation to afford crude **15**, which is highly acid-sensitive and should be used directly without purification.

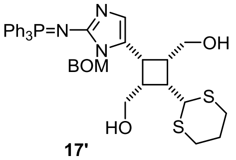


16

Cyclobutane 16. The crude **15** obtained above and tris[2-phenylpyridinato-C^2,*N*]iridium(III) (Ir(ppy)$_3$) (34 mg, 0.052 mmol, 0.03 equiv) in *N*,*N*-dimethylformamide (17 mL) was degassed by three freeze-pump-thaw cycles. After stirring with CFL-irradiation at 23 °C for 60 h, the reaction was diluted with ethyl acetate (300 mL), washed successively with water (×10) and brine, dried over sodium sulfate and concentrated to give crude **16**. A portion of this material was purified by HPLC to give pure **16** for characterization purposes. Attempts to isolate the minor diastereomeric reaction product with various HPLC columns (reverse and normal phase) to provide analytically pure samples were not successful. **16**: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.78–7.48 (m, 15H), 7.38–7.20 (m, 3H), 7.20–7.07 (m, 2H), 6.55 (s, 1H), 5.89 (d, *J* = 3.7 Hz, 1H), 5.41 (s, 2H), 4.50 (s, 2H), 4.16 (d, *J* = 9.0 Hz, 2H), 4.03–3.97 (m, 2H), 3.45–3.37 (m, 1H), 3.13–3.06(m, 1H), 2.80–2.72 (m, 2H); MS(ESI)$^+$calcd for $C_{36}H_{35}N_3O_3P$ $(M+H)^+$ 588.2, found 588.2.



17

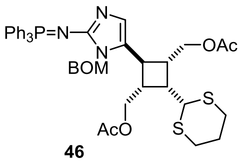


17'

Diol 17 and diol 17'. To a solution of crude **16** (1.71 mmol) in dichloromethene (100 mL) were added 1,3-propanedithiol (1.37 mL, 13.71 mmol, 8.0 equiv) and boron trifluoride diethyl etherate (1.48 mL, 12.0 mmol, 7.0 equiv) at –78 °C. After keeping –20 °C for 16 h, the reaction was quenched with 10% KOH (35 mL). The volatiles were then removed by rotary evaporation. The residue was dissolved in ethyl acetate, washed successively with water and brine, dried over sodium sulfate, concentrated, and purified by preparative HPLC (Waters Atlantis dC18 OBD, 19×150 mm, 5 μm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: acetonitrile with 0.1% trifluoroacetic acid, gradient: T = 0 min: 45% B, T = 30 min: 65% B, 5.0 mL/min, retention time: 22.2 and 23.4 min) to give **17•TFA** (494 mg, 35% yield over 5 step) and **17'•TFA** (246 mg, 14% yield over 5 steps). Washing the ethyl acetate solution of **17•TFA** with saturated sodium bicarbonate followed by brine gave **17** as a free base.

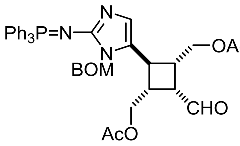
17: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.77–7.41 (m, 15H), 7.30–7.19 (m, 3H), 7.14 (d, *J* = 6.5 Hz, 2H), 6.58 (s, 1H), 5.51 (s, 2H), 4.56 (s, 2H), 4.33 (d, *J* = 12.5 Hz, 1H), 4.03 (dd, *J* = 11.8, 6.2 Hz, 2H), 3.88 (dd, *J* = 11.8, 6.2 Hz, 2H), 3.21–3.08 (m, 2H), 2.97–2.78 (m, 4H), 2.58–2.67 (m, 2H), 2.15–2.04 (m, 1H), 1.96–1.84 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 136.4, 133.8, 133.7, 132.5, 132.4, 130.0, 129.6, 129.5, 128.6, 128.1, 127.5, 126.2, 125.2, 100.0, 109.7, 70.6, 70.4, 61.6, 44.2, 43.8, 39.2, 31.3, 29.1, 25.2; MS(ES)$^+$ calcd for $C_{39}H_{43}N_3O_3PS_2$ $(M+H)^+$ 696.2, found 696.2.

17': ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89–7.40 (m, 15H), 7.38–7.05 (m, 5H), 6.82 (s, 1H), 5.43 (s, 2H), 4.52 (s, 2H), 4.40 (d, *J* = 12.2 Hz, 1H), 4.19 (dd, *J* = 11.6, 5.5 Hz, 2H), 4.04–3.85 (m, 2H), 3.32–2.72 (m, 8H), 2.24–2.07 (m, 1H), 1.95–1.77 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 136.4, 133.9, 132.3, 132.2, 129.7, 129.6, 128.9, 128.6, 128.2, 127.5, 126.0, 125.0, 123.4, 112.3, 71.0, 70.5, 59.6, 44.7, 43.5, 40.3, 30.5, 29.7, 25.2; MS(ES)$^+$ calcd for $C_{39}H_{43}N_3O_3PS_2$ $(M+H)^+$ 696.2, found 696.2.



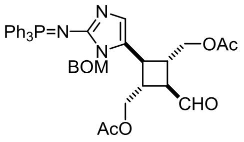
46

Bisacetate 46. To the solution of **17** (free base, 353 mg, 0.508 mmol, 1.0 equiv) in dichloromethene (15 mL) was added pyridine (820 μL, 10.2 mmol, 20.0 equiv) followed by acetic anhydride (311 μL, 3.05 mmol, 6.0 equiv) at 0 °C. After stirring for 10 h, the volatiles were removed by rotary evaporation. The residue was then dissolved in ethyl acetate, washed successively with saturated sodium bicarbonate and brine, dried over sodium sulfate, and concentrated to give crude **46**. MS(ES)$^+$ calcd for $C_{43}H_{47}N_{35}O_3PS_2$ (M+H)$^+$ 780.3, found 780.2.



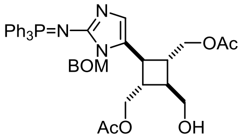
18

Aldehyde 18. To a solution of crude **46** (0.508 mmol, 1.0 equiv) in tetrahydrofuran (8.0 mL) was added a solution of calcium carbonate (508 mg, 5.08 mmol, 10.0 equiv) and mercury(II) perchlorate trihydrate (608 mg, 1.34 mmol, 2.6 equiv) in water (2.0 mL) at 23 °C. After stirring for 10 min, the reaction was quenched with water, filtered through celite, extracted with ethyl acetate, washed successively with water and brine, dried over sodium sulfate, filtered, and concentrated to give crude **18**. MS(ES)$^+$ calcd for $C_{40}H_{41}N_3O_6P$ (M+H)$^+$ 690.3, found 690.3.



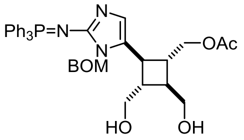
47

Aldehyde 47. To a solution of crude **18** obtained above in dichloromethene (5.0 mL) was added 20% trifluoroacetic acid in dichloromethene (5.0 mL) at 23 °C. After stirring for 36 h, the reaction was quenched by saturated sodium bicarbonate, extracted with ethyl acetate, washed successively with water and brine, dried over sodium sulfate, filtered, and concentrated to give crude **47**.



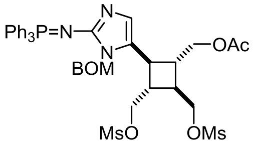
19

Alcohol 19. To a solution of crude **47** obtained above in methanol-dichloromethene (1:1, 8.0 mL) was added sodium borohydride (96 mg, 2.54 mmol, 5.0 equiv) in methanol (0.5 mL) at 0 °C. After stirring for 10 min, the volatiles were removed by rotary evaporation. The residue was extracted with ethyl acetate, washed successively with water and brine, dried over sodium sulfate, filtered, and concentrated to give crude **19**. MS(ES)$^+$ calcd for $C_{40}H_{43}N_3O_6P$ (M+H)$^+$ 692.3, found 692.2.



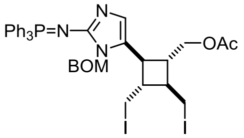
48

Diol 48. To a solution of crude **19** obtained above in toluene (11 mL) was added diisobutylaluminium hydride (1.0 N in tetrahydrofuran, 2.3 mL, 2.3 mmol, 4.5 equiv) at –78 °C. After stirring for 3 d, the reaction was quenched by 10% aqueous Rochelle salt, extracted with ethyl acetate, washed successively with water and brine, dried over sodium sulfate, filtered, and concentrated to give crude **48**. ^{1}H NMR (400 MHz, CD_3OD) δ 7.94–7.53 (m, 15H), 7.39–6.98 (m, 5H), 6.56 (s, 1H), 5.61 (s, 2H), 4.63 (s, 2H), 4.17 (d, *J* = 5.4 Hz, 2H), 3.63 (dd, *J* = 5.6, 2.4 Hz, 2H), 3.60–3.54 (dd, *J* = 5.1, 3.4 Hz, 2H), 3.10 (t, *J* = 9.0 Hz, 1H), 2.46–2.34 (m, 1H), 2.26–2.16 (m, 1H), 2.15-2.05 (m, 1H), 1.97 (s, 3H). $C_{38}H_{41}N_3O_5P$ (M+H)$^+$ 650.3, found 650.3.



20

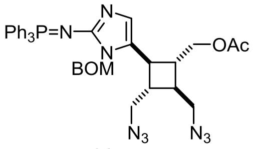
Mesylate 20. To a solution of crude **48** obtained above in dichloromethene (10.0 mL) were added pyridine (410 μL, 5.08 mmol, 10.0 equiv) and methanesulfonyl chloride (236 μL, 3.05 mmol, 6.0 equiv) at 0 °C. After stirring for 3 h, the solvent was removed by rotary evaporation. The residue was dissolved in ethyl acetate, washed successively with water and brine, dried over sodium sulfate, filtered, and concentrated to give crude **20**. $C_{40}H_{45}N_3O_9PS_2$ (M+H)$^+$ 806.2, found 806.2.



49

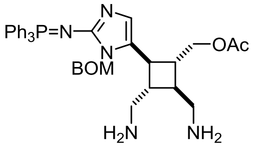
Diiodide 49. To a solution of crude **20** obtained above in acetone (12 mL) was added sodium iodide (3.81 g, 25.4 mmol, 50 equiv). After stirring at 60 °C for 2 h, the solvent was removed by rotary evaporation. The residue was dissolved in ethyl acetate-water, washed successively with 10% sodium thiosulfate/saturated sodium bicarbonate (1:1) and brine, dried over sodium sulfate, filtered, and concentrated to give crude **49**.

$C_{38}H_{39}I_2N_3O_3P$ $(M+H)^+$ 870.1, found 870.1.



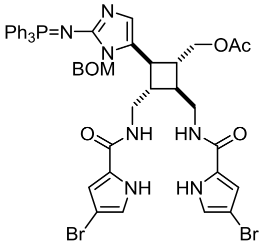
21

Bisazide 21. To a solution of crude **49** obtained above in anhydrous *N*,*N*-dimethylformamide (4.0 mL) was added sodium azide (330 mg, 5.08 mmol, 10.0 equiv) at 23 °C. After stirring for 2 h, the reaction was diluted with ethyl acetate, washed successively with water and brine, dried over sodium sulfate, filtered, concentrated, and purified by preparative HPLC (Waters Atlantis dC18 OBD, 19×150 mm, 5 μm, eluent A: water, eluent B: acetonitrile, gradient: T = 0 min: 57% B, T = 30 min: 70% B, 5.0 mL/min, retention time: 23.2 min) to give **21•TFA** as a pale yellow oil (165 mg, 40% yield for eight steps). ^{1}H NMR (400 MHz, CD_3OD) δ 7.80–7.66 (m, 9H), 7.66–7.55 (m, 6H), 7.31–7.22 (m, 3H), 7.15-7.20 (m, 2H), 6.65 (d, *J* = 0.8 Hz, 1H), 5.62–5.54 (m, 2H), 4.63 (s, 2H), 4.17 (d, *J* = 5.2 Hz, 2H), 3.49 (ddd, *J* = 7.1, 5.7, 2.5 Hz, 5H), 3.11 (t, *J* = 9.1 Hz, 1H), 2.39 (ddd, *J* = 14.1, 9.1, 5.2 Hz, 1H), 2.33–2.24 (m, 1H), 2.23–2.13 (m, 1H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 172.7, 138.5, 135.0, 135.0, 133.7, 133.6, 131.8, 130.8, 130.7, 129.6, 129.1, 128.5, 127. 9, 126.8, 110.7, 72.38, 71.9, 65.8, 54.8, 54.2, 44.0, 43.1, 38.6, 33.4, 20.7; MS(ES)$^+$ calcd for $C_{38}H_{39}N_9O_3P$ $(M+H)^+$ 700.3, found 700.3.



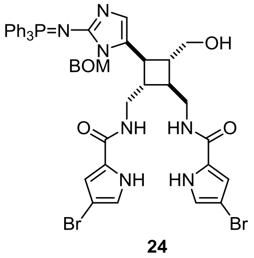
22

Diamine 22. To a solution of **21•TFA** (23 mg, 23.2 μmol, 1.0 equiv) in ethyl acetate (2.0 mL) was added platinum(IV) oxide (1.9 mg, 8.37 μmol, 0.35 equiv) at 23 °C. The reaction vessel was then filled with hydrogen by three pump-fill cycles. After stirring for 16 h, the catalyst was removed by filtration and the filtrate was concentrated to give crude **22**. ^{1}H NMR (400 MHz, CD_3OD) δ 7.91–7.47 (m, 15H), 7.39–6.96 (m, 5H), 6.77 (d, *J* = 0.8 Hz, 1H), 5.62 (d, *J* = 11.1 Hz, 1H), 5.55 (d, *J* = 11.2 Hz, 1H), 4.66 (s, 2H), 4.31 (dd, *J* = 11.8, 4.3 Hz, 1H), 4.15 (dd, *J* = 11.8, 5.9 Hz, 1H), 3.27–3.14 (m, 4H), 3.11 (dd, *J* = 13.2, 8.0 Hz, 1H), 2.65–2.49 (m, 1H), 2.47–2.37 (m, 1H), 2.35–2.25 (m, 1H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 172.6, 138.2, 135.0, 133.7, 133.6, 130.8, 130.7, 129.7, 129.2, 128.6, 127.7, 126.7, 111.4, 72.0, 71.9, 65.6, 45.0, 43.3, 43.2, 41.0, 37.6, 33.9, 20.8; MS(ES)$^+$ calcd for $C_{38}H_{43}N_5O_3P$ $(M+H)^+$ 648.3, found 648.3.



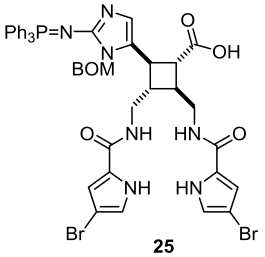
23

Bispyrrole 23. To a solution of crude **22** obtained above in anhydrous *N*,*N*-dimethylformamide (0.15 mL) were added pyridine (19 μL, 0.232 mmol, 10.0 equiv), *N*-(3-dimethylaminopropyl)-*N′*-ethylcarbodiimide hydrochloride (13.3 mg, 70 μmol, 3.0 equiv), 1-hydroxybenzotriazole hydrate (9.4 mg, 70 μmol, 3.0 equiv), and 4-bromo-1*H*-pyrrole-2-carboxylic acid (13.2 mg, 70 μmol, 3.0 equiv) in *N*,*N*-dimethylformamide (0.2 mL) at 23 °C. After stirring in dark for 16 h, the reaction mixture was directly purified by preparative HPLC (Waters Atlantis dC18 OBD, 19×150 mm, 5 μm, eluent A: water, eluent B: acetonitrile, gradient: T = 0 min: 70% B, T = 40 min: 100% B, 5.0 mL/min) to give **23•TFA** (13.3 mg, 51% yield over two steps, retention time: 27.5 min). MS(ES)$^+$ calcd for $C_{48}H_{47}Br_2N_7O_5P$ $(M+H)^+$ 990.2, found 990.1.



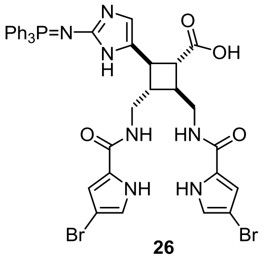
24

Alcohol 24. To a solution of **23•TFA** (3.1 mg, 2.8 μmol, 1.0 equiv) in anhydrous methanol (0.2 mL), was added sodium methoxide (5.4 M in methanol, 16 μL, 0.084 mmol, 30 equiv). After stirring at 0 °C for 3 h, the reaction was diluted with ethyl acetate, washed successively with water and brine, dried over sodium sulfate, filtered, concentrated, and purified by preparative HPLC (Waters Atlantis dC18 OBD, 19×150 mm, 5 μm, eluent A: water, eluent B: acetonitrile, gradient: T = 0 min: 40% B, T = 10 min: 60% B, T = 25 min: 70% B, 5.0 mL/min, retention time: 20.2 min) to give **24•TFA** (2.7 mg, 90% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.76–7.55 (m, 15H), 7.28–7.19 (m, 3H), 7.13-7.18 (m, 2H), 6.91 (d, *J* = 1.6 Hz, 1H), 6.89 (d, *J* = 1.6 Hz, 1H), 6.76 (d, *J* = 1.6 Hz, 1H), 6.71 (d, *J* = 1.6 Hz, 1H), 6.50 (s, 1H), 5.92–5.35 (m, 2H), 4.57–4.67 (m, 1H), 3.71–3.55 (m, 2H), 3.53–3.34 (m, 4H), 3.05–2.92 (m, 1H), 2.39–2.27 (m, 1H), 2.16–2.06 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 162.77, 162.72, 138.5, 134.93, 134.90, 133.6, 133.5, 133.0, 130.8, 130.6, 129.6, 129.0, 128.5, 127.9, 127.44, 127.40, 126.9, 122.9, 113.2, 110.1, 97.5, 72.2, 71.7, 64.0, 48.1, 43.9, 43.2, 43.1, 40.0, 34.0; MS(ES)$^+$ calcd for $C_{46}H_{45}Br_2N_7O_4P$ (M+H)$^+$ 948.2, found 948.1.



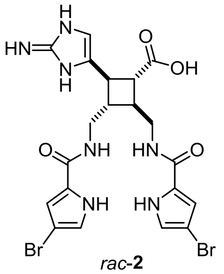
25

Acid 25. To a solution of **24** (2.5 mg, 2.35 µmol, 1.0 equiv) in dichloromethene (0.2 mL) were added sodium bicarbonate (1.2 mg, 14.1 µmol, 6.0 equiv), Dess–Martin periodinane (2.0 mg, 4.7 µmol, 2.0 equiv) and water (0.04 µL, 2.35 µmol, 1.0 equiv) at 23 °C. After stirring for 30 min, methanol (0.1 mL) and pH 3.5 buffer (0.1 mL) was added followed by 2-methyl-2-butene (50 µL) at 0 °C. A freshly prepared sodium chlorite solution (10 mg/mL in water, 21 µL, 2.35 µmol, 1.0 equiv) was then added. After stirring for 10 min, the volatiles were removed by rotary evaporation at 0 °C and the residual was purified by preparative HPLC (Eclipse XDB–C18, 9.4×250 mm, 5 µm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: acetonitrile with 0.1% trifluoroacetic acid, gradient: T = 0 min: 40% B, T = 15 min: 70% B, 4.8 mL/min, retention time: 12.2 min) to give **25•TFA**. (2.2 mg, 87% yield over two steps). ^{1}H NMR (400 MHz, CD_3OD) δ 7.81–7.53 (m, 15H), 7.28–7.08 (m, 5H), 6.91 (d, *J* = 1.5 Hz, 1H), 6.90 (d, *J* = 1.5 Hz, 1H), 6.78 (d, *J* = 1.5 Hz, 1H), 6.71 (d, *J* = 1.5 Hz, 1H), 6.52 (s, 1H), 5.61 (d, *J* = 10.5 Hz, 1H), 5.50 (d, *J* = 10.5 Hz, 1H), 4.56 (d, *J* = 2.4 Hz, 2H), 3.52–3.43 (m, 5H), 2.78 (t, *J* = 8.9 Hz, 1H), 2.52– 2.44 (m, 2H); MS(ES)$^+$ calcd for $C_{46}H_{43}Br_2N_7O_5P$ (M+H)$^+$ 962.1, found 962.0.



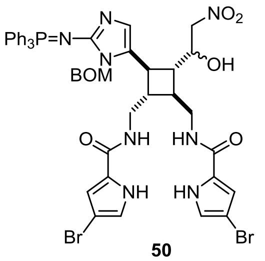
26

Acid 26. To a solution of **25** (2.2 mg, 2.04 µmol, 1.0 equiv) in methylene chloride (0.20 mL) was added boron trichloride (1.0 M in methylene chloride, 61 µL, 0.0612 mmol, 30 equiv) at –50 °C. After stirring at –10 °C for 30 min, an acetonitrile solution of concentrated aqueous ammonium hydroxide (200 µL, 1:4 v/v) was added. After stirring at 23 °C for another 20 min, the volatiles were removed by rotary evaporation and the residue was purified by HPLC (Eclipse XDB–C18, 9.4×250 mm, 5 µm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: methanol with 0.1% trifluoroacetic acid, gradient: T = 0 min: 45% B, T = 20 min: 80% B, 4.0 mL/min, retention time: 17.7 min) to give **26•TFA** (1.6 mg, 83% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.89–7.50 (m, 15H), 6.91 (d, *J* = 1.5 Hz, 1H), 6.90 (d, *J* = 1.5 Hz, 1H), 6.79 (d, *J* = 1.5 Hz, 1H), 6.73 (d, *J* = 1.5 Hz, 1H), 6.43 (s, 1H), 3.60–3.35 (m, 4H), 3.08 (t, *J* = 9.8 Hz, 1H), 2.81 (t, *J* = 9.6 Hz, 1H), 2.47–2.39 (m, 1H), 2.31–2.15 (m, 1H); MS(ES)$^+$ calcd for $C_{38}H_{35}Br_2N_7O_4P$ (M+H)$^+$ 842.1, found 842.0.



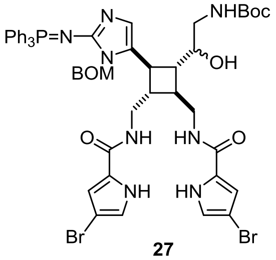
rac-**2**

***rac*-Nakamuric acid (*rac*-2).** To a solution of **26•TFA** (1.6 mg, 1.69 µmol, 1.0 equiv) in 1,4-dioxane (70 µL) was added hydrochloric acid (0.20 N in water, 70 µL). After stirring at 40 °C for 2 h, the reaction mixture was purified directly by HPLC (Eclipse XDB–C18, 9.4×250 mm, 5 µm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: acetonitrile with 0.1% trifluoroacetic acid, gradient: T = 0 min: 25% B, T = 10 min: 35% B, 4.2 mL/min, retention time: 9.33 min) to give *rac*-nakamuric acid (**2•TFA**) (1.0 mg, 88% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 6.92 (d, *J* = 1.5 Hz, 1H), 6.91 (d, *J* = 1.5 Hz, 1H), 6.80 (d, *J* = 1.5, 1H), 6.76 (d, *J* = 1.5, Hz, 1H), 6.58 (s, 1H), 3.59–3.46 (m, 2H), 3.45 (d, *J* = 5.5 Hz, 2H), 3.14 (t, *J* = 9.6 Hz, 1H), 2.84 (t, *J* = 9.6 Hz, 1H), 2.52–2.43 (m, 1H), 2.34–2.25 (m, 1H). MS(ES)$^+$ calcd for $C_{20}H_{22}Br_2N_7O_4$ (M+H)$^+$ 582.0, found 581.9.

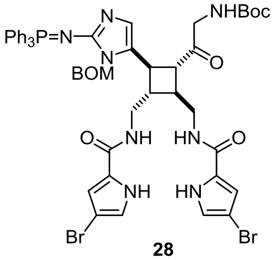


50

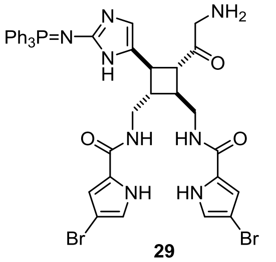
Alcohol 50. To a solution of **24•TFA** (3.5 mg, 3.3 µmol, 1.0 equiv) in dichloromethene (0.2 mL) were added sodium bicarbonate (1.6 mg, 20 µmol, 6.0 equiv), Dess–Martin periodinane (2.8mg, 6.6 µmol, 2.0 equiv), and water (0.06 µL, 3.3 µmol, 1.0 equiv) at 23 °C. After stirring for 30 min, the solvent was removed. The residue was dissolved in ethyl acetate, washed successively with 10% sodium thiosulfate/saturated sodium bicarbonate solution (1:1), water and brine, dried over sodium sulfate, filtered, and concentrated. The residue was then dissolved in nitromethane (1 mL) before adding triethylamine (50 µL) at 0 °C. After stirring for 30 min, the solvent was removed with rotary evaporation to give crude **50**. MS(ES)$^+$ calcd for $C_{47}H_{46}Br_2N_8O_6P$ (M+H)$^+$ 1007.2, found 1007.1.


27

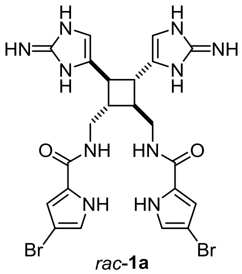
Alcohol 27. To a solution of the crude **50** obtained above in methanol (2.5 mL) and saturated ammonium chloride solution (2.5 mL) was added zinc (21 mg, 0.329 mmol, 100 equiv) at 0 °C. After stirring for 1 h, the reaction solution was basicified with saturated sodium bicarbonate to > pH 7 and di-*tert*-butyl dicarbonate (15 μL, 0.0658 mmol, 20.0 equiv) was added. After stirring for another 2 h at 23 °C, the volatiles were removed. The residue was dissolved in ethyl acetate, washed successively with saturated sodium bicarbonate and brine, dried over sodium sulfate, filtered and concentrated, purified on HPLC (Eclipse XDB–C18, 9.4×250 mm, 5 μm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: acetonitrile with 0.1% trifluoroacetic acid, gradient: T = 0 min: 40% B, T = 15 min: 70% B, 4.5 mL/min, retention time: 13.40 min) to give **27•TFA** (ca. 80% pure). MS(ES)$^+$ calcd for $C_{52}H_{56}Br_2N_8O_6P$ $(M+H)^+$ 1077.2, found 1077.1.


28

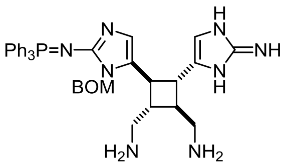
Ketone 28. To the **27•TFA** obtained in dichloromethene (0.2 mL) were added Dess–Martin periodinane (2.8 mg, 6.6 μmol, 2.0 equiv) and water (0.06 μL, 3.3 μmol, 1.0 equiv) at 23 °C. After stirring at 40 °C for 2 h, the solvent was removed. The residue was diluted with ethyl acetate, washed successively with 10% sodium thiosulfate/saturated sodium bicarbonate solution (1:1), water and brine, dried over sodium sulfate, filtered, concentrated and purified by preparative HPLC (Eclipse XDB–C18, 9.4×250 mm, 5 μm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: acetonitrile with 0.1% trifluoroacetic acid, gradient: T = 0 min: 40% B, T = 15 min: 75% B, 4.5 mL/min, retention time: 14.4 min) to give **28•TFA**. (1.2 mg, 32% yield over four steps). ^{1}H NMR (400 MHz, CD_3OD) δ 7.90–7.48 (m, 15H), 7.28–7.17 (m, 3H), 7.13 (d, *J* = 7.3 Hz, 2H), 6.93 (d, *J* = 1.5 Hz, 1H), 6.90 (d, *J* = 1.5 Hz, 1H), 6.80 (s, 1H), 6.69 (s, 1H), 6.51 (s, 1H), 5.50 (d, *J* = 11.0 Hz, 1H), 5.33 (d, *J* = 11.0 Hz, 1H), 4.69–4.38 (m, 2H), 3.89 (d, *J* = 18.8 Hz, 1H), 3.67 (d, *J* = 18.8 Hz, 1H), 3.61–3.51 (m, 2H), 3.52–3.40 (m, 3H), 3.00 (t, *J* = 8.8 Hz, 1H), 2.58–2.51 (m, 1H), 2.35–2.28 (m, 1H), 1.40 (s, 9H). MS(ES)$^+$ calcd for $C_{52}H_{54}Br_2N_8O_6P$ $(M+H)^+$ 1075.2, found 1075.1.


29

Amine 29. To a solution of **28•TFA** (0.8 mg, 0.67 μmol, 1.0 equiv) in methylene chloride (0.15 mL) was added boron trichloride (1.0 M in methylene chloride, 20 μL, 0.0202 mmol, 30 equiv) at –50 °C. After stirring at –10 °C for 30 min, an acetonitrile solution of concentrated aqueous ammonium hydroxide (1:4 v/v, 100 μL) was added at 23 °C. After stirring for 30 min, the volatiles were removed by rotary evaporation and the residue was purified by HPLC (Eclipse XDB–C18, 9.4×250 mm, 5 μm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: methanol with 0.1% trifluoroacetic acid, gradient: T = 0 min: 20% B, T = 20 min: 50% B, 4.0 mL/min, retention time: 10.68 min) to give **29•TFA** (0.5 mg, 77% yield). MS(ES)$^+$ calcd for $C_{39}H_{38}Br_2N_8O_3P$ $(M+H)^+$ 855.2, found 855.1.

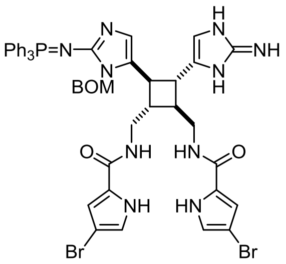

rac-**1a**

***rac*-Sceptrin (*rac*-1a).** To a solution of **29•TFA** (0.5 mg, 0.515 μmol, 1.0 equiv) in ethanol (0.20 mL) was added cyanamide (6.5 mg, 0.154 mmol, 300 equiv) at 23 °C. After stirring at 85 °C in dark for 3 h, the volatiles were removed by rotary evaporation and the residue was purified by HPLC (Eclipse XDB–C18, 9.4×250 mm, 5 μm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: methanol with 0.1% trifluoroacetic acid, gradient: T = 0 min: 10% B, T = 10 min: 40% B, 4.0 mL/min, retention time: 11.09 min) to give *rac*-**1a•2TFA** (0.4 mg, 85% yield). ^{1}H NMR (600 MHz, CD_3OD) δ 6.92 (d, *J* = 1.4 Hz, 2H), 6.74 (d, *J* = 1.4 Hz, 2H), 6.57 (s, 2H), 3.51–3.48 (m, 4H), 2.99 (d, *J* = 9.4 Hz, 2H), 2.37–2.34 (m, 2H); MS(ES)$^+$ calcd for $C_{22}H_{25}Br_2N_{10}O_2$ $(M+H)^+$ 619.0, found 618.9.



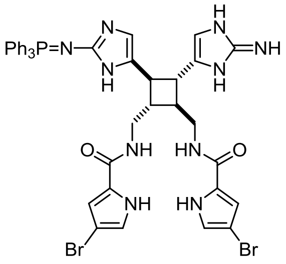
43

Diamine 43. To a solution of **42** that was prepared from D-glutamic acid[8e] (17.3 mg, 0.021 mmol, 1.0 equiv) in *tert*-butanol (3.0 mL) was added added platinum(IV) oxide (2.4 mg, 0.0105 mmol, 0.50 equiv) at 23 °C. The reaction vessel was then filled with hydrogen by three pump-fill cycles. After stirring for 14 h, the catalyst was removed by filtration and the filtrate was concentrated and purified by HPLC (Waters Atlantis dC18 OBD, 19×150 mm, 5 μm, eluent A: water, eluent B: acetonitrile, gradient: T = 0 min: 25% B, T = 25 min: 50% B, 5.0 mL/min, retention time: 18.2 min) to give **43•3TFA** (10.4 mg, 50% yield). ^{1}H NMR (400 MHz, CD$_3$OD) δ 7.90–7.47 (m, 15H), 7.30–7.20 (m, 3H), 7.10 (d, *J* = 7.0 Hz, 2H), 6.84 (s, 1H), 6.64 (s, 1H), 5.46 (dd, *J* = 11.1 Hz, 1H), 5.38 (d, J = 11.1 Hz, 1H), 4.46 (q, *J* = 12.7 Hz, 2H), 3.59 (t, *J* = 9.3 Hz, 1H), 3.27 – 3.10 (m, 5H), 2.74–2.60 (m, 2H); ^{13}C NMR (100 MHz, CD$_3$OD) δ 149.5, 138.2, 135.0, 133.7, 133.6, 130.82, 130.7, 130.0, 129.7, 129.2, 128.4, 127.7, 127.2, 126.7, 111.7, 72.3, 71.7, 42.8, 42.2, 41.6, 41.0, 40.6, 38.1. MS(ESI)$^+$calcd for $C_{38}H_{42}N_8O_1P$ (M+H)$^+$657.3, found 657.2.



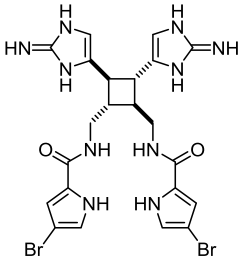
44a

Pyrrole 44a. To a solution of **43•3TFA** (10.4 mg, 0.0104 mmol, 1.0 equiv) in *N*,*N*-dimethylformamide (150 μL) were added 2,6-lutidine (6.0 μL, 0.052 mmol, 5.0 equiv), *N*-(3-dimethylaminopropyl)-*N′*-ethylcarbodiimide hydrochloride (EDCI) (10.0 mg, 0.052 mmol, 5.0 equiv), 1-hydroxybenzotriazole hydrate (HOBt) (7.0 mg, 0.052 mmol, 5.0 equiv) and a solution of 4-bromo-1*H*-pyrrole-2-carboxylicacid (9.8 mg, 0.052 mmol, 5.0 equiv) in *N*,*N*-dimethylformamide (150 μL) at 23 °C. After stirring at 23 °C in dark for 12 h, the reaction mixture was directly purified by HPLC (Eclipse XDB–C18, 9.4×250 mm, 5 μm, eluent A: water, eluent B: acetonitrile, gradient: T = 0 min: 30% B, T = 15 min: 55% B, 4.5 mL/min, retention time: 14.5 min) to give **44a•TFA** (5.8 mg, 50% yield, 90% pure).



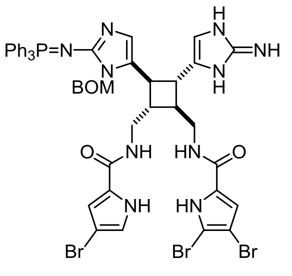
51

Iminophosphoran 51. To a solution of ***ent*-43a•TFA** (5.8 mg, 5.2 μmol, 1.0 equiv) in methylene chloride (0.3 mL) was added boron trichloride (1.0 M in methylene chloride, 156 μL, 0.156 mmol, 30 equiv) at –50 °C. After stirring at –10 °C for 30 min, an acetonitrile solution of concentrated aqueous ammonium hydroxide (1:4 v/v, 100 μL) was added. After stirring at 23 °C for another 20 min, the volatiles were removed by rotary evaporation and the residue was purified by HPLC (Eclipse XDB–C18, 9.4×250 mm, 5 μm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: acetonitrile with 0.1% trifluoroacetic acid, gradient: T = 0 min: 35% B, T = 17 min: 60% B, 4.5 mL/min, retention time: 10.0 min) to give **51•TFA** (4.3 mg, 83% yield). ^{1}H NMR (400 MHz, CD$_3$OD) δ 7.78–7.52 (m, 15H), 6.91 (d, *J* = 1.5 Hz, 1H), 6.89 (d, *J* = 1.5 Hz, 1H), 6.73 (d, *J* = 1.5 Hz, 1H), 6.72 (d, *J* = 1.5 Hz, 1H), 6.54 (s, 1H), 6.41 (s, 1H), 3.52–3.38 (m, 4H), 3.01–2.89 (m, 2H), 2.38–2.28 (m, 2H); MS(ESI)$^+$calcd for $C_{40}H_{38}Br_2N_{10}O_2P$ (M+H)$^+$879.1, found 879.0.



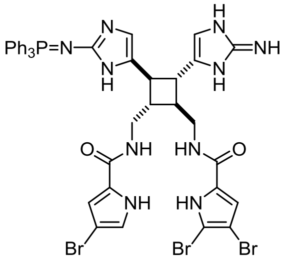
nat-**1a**

***nat*-Sceptrin (*nat*-1a)**. To a solution of **51•TFA** (4.3 mg, 4.3 μmol, 1.0 equiv) in 1,4-dioxane (0.2 mL) was added hydrochloric acid (0.20 N, 0.2 mL). After stirring at 35 °C for 1.5 h, the reaction mixture was purified directly by HPLC (Eclipse XDB–C18, 9.4×250 mm, 5 μm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: acetonitrile with 0.1% trifluoroacetic acid, gradient: T = 0 min: 25% B, T = 10 min: 35% B, 4.5 mL/min; retention time: 10.4 min) to give *nat*-**1a•2TFA** (2.8 mg, 78% yield). ^{1}H NMR (600 MHz, D$_2$O) δ 7.00 (d, *J* = 1.5 Hz, 2H), 6.55 (d, *J* = 1.5 Hz, 2H), 6.52 (s, 2H), 3.52 (dd, *J* = 14.0, 6.5 Hz, 2H), 3.44 (dd, *J* = 14.0, 6.5 Hz, 2H), 2.98 (A$_2$B$_2$, *J* = 9.5, 2.7 Hz, 2H), 2.49–2.45 (m, 2H); ^{1}H NMR (600 MHz, CD$_3$OD) δ 6.92 (d, *J* = 1.4 Hz, 2H), 6.74 (d, *J* = 1.4 Hz, 2H), 6.57 (s, 2H), 3.51–3.48 (m, 4H), 2.99 (d, *J* = 9.4 Hz, 2H), 2.37–2.34 (m, 2H); ^{13}C NMR (100 MHz, CD$_3$OD) δ 163.0, 149.0, 128.7, 127.2, 123.1, 113.4, 110.3, 97.6, 44.3, 42.3, 39.3. ^{13}C NMR (100 MHz, D$_2$O) δ 160.8, 145.4, 125.2, 123.6, 121.5, 111.0, 108.0, 94.8, 41.3, 40.5, 37.2; MS(ESI)$^+$calcd for $C_{22}H_{25}Br_2N_{10}O_2$ [M+H]$^+$: 619.0; found: 618.9.



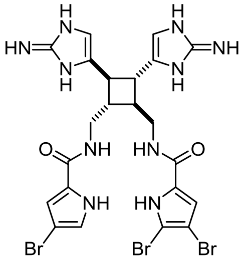
44b

Pyrrole 44b. To a solution of **43•3TFA** (2.5 mg, 2.5 μmol, 1.0 equiv) in *N*,*N*-dimethylformamide (50 μL) were added 2,6-lutidine (1.0 μL, 10 μmol, 4.0 equiv), *N*-(3-dimethylaminopropyl)-*N′*-ethylcarbodiimide hydrochloride (EDCI) (1.9 mg, 10 μmol, 4.0 equiv), 1-hydroxybenzotriazole hydrate (HOBt) (1.4 mg, 10 μmol, 4.0 equiv) and a solution of 4-bromo-1*H*-pyrrole-2-carboxylicacid (0.3 mg, 1.62 mmol, 0.65 equiv) in *N*,*N*-dimethylformamide (0.1 mL) at 23 °C. After stirring at 23 °C in dark for 12 h, 3,4-dibromo-1*H*-pyrrole-2-carboxylic acid (1.0 mg, 3.75 μmol, 1.5 equiv) in *N*,*N*-dimethylformamide (50 μL) was added. After stirring for another 12 h, the reaction mixture was directly purified by HPLC (Eclipse XDB–C18, 4.6×150 mm, 5 μm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: acetonitrile with 0.1% trifluoroacetic acid, gradient: T = 0 min: 10% B, T = 7 min: 95% B, T = 10 min: 95% B, T = 10.1 min: 100% B, 0.8 mL/min; retention time: 14.5 min) to give **44b•TFA** (1.1 mg, 37% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.81–7.50 (m, 15H), 7.21 (dt, *J* = 14.7, 7.1 Hz, 3H), 7.03 (d, *J* = 7.2 Hz, 2H), 6.90 (dd, *J* = 12.7, 1.6 Hz, 1H), 6.74 (d, *J* = 6.3 Hz, 1H), 6.71 (dd, *J* = 7.4, 1.6 Hz, 1H), 6.58 (d, *J* = 2.4 Hz, 1H), 6.54 (d, *J* = 1.6 Hz, 1H), 5.51 (d, *J* = 11.1 Hz, 1H), 5.41 (d, *J* = 11.1 Hz, 1H), 4.44 (d, *J* = 12.7 Hz, 1H), 4.34 (dd, *J* = 12.7, 4.8 Hz, 1H), 3.70–3.54 (m, 2H), 3.53–3.40 (m, 4H), 2.96 (t, *J* = 9.4 Hz, 1H), 2.65–2.27 (m, 2H).



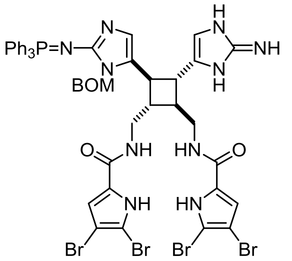
52

Iminophosphorane 52. To a solution of **44b•TFA** (1.1 mg, 0.92 μmol, 1.0 equiv) in methylene chloride (0.3 mL) was added boron trichloride (1.0 M in methylene chloride, 28 μL, 0.028 mmol, 30 equiv) at –50 °C. After stirring at –10 °C for 30 min, an acetonitrile solution of concentrated aqueous ammonium hydroxide (1:4 v/v, 100 μL) was added. After stirring at 23 °C for another 20 min, the volatiles were removed by rotary evaporation and the residue was purified by HPLC (Eclipse XDB–C18, 9.4×250 mm, 5 μm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: methanol with 0.1% trifluoroacetic acid, gradient: T = 0 min: 45% B, T = 20 min: 80% B, 4.0 mL/min, retention time: 14.4 min) to give **52•TFA** (0.7 mg, 71% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.82–7.68 (m, 8H), 7.61 (td, *J* = 7.8, 3.1 Hz, 7H), 6.91 (dd, *J* = 8.8, 1.5 Hz, 1H), 6.77 (dd, *J* = 8.6, 1.5 Hz, 1H), 6.74 (dd, *J* = 6.6, 1.5 Hz, 1H), 6.56 (d, *J* = 2.3 Hz, 1H), 6.42 (d, *J* = 4.8 Hz, 1H), 3.53–3.42 (m, 4H), 3.13 (t, *J* = 1.6 Hz, 1H), 3.00–2.96 (m, 1H), 2.40–2.30 (m, 2H). MS(ESI)$^+$calcd for $C_{40}H_{37}Br_3N_{10}O_2P$ $(M+H)^+$ 957.0, found 957.0.



nat-**1b**

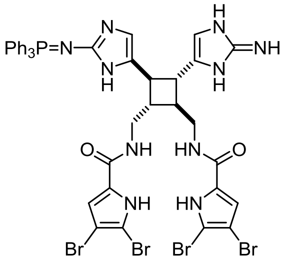
***nat*-Bromosceptrin (*nat*-1b)**. To a solution of **52•TFA** (0.7 mg, 0. 65 μmol, 1.0 equiv) in 1,4-dioxane (75 μL) was added hydrochloric acid (0.20 N, 75 μL). After stirring at 35 °C for 1.5 h, the reaction mixture was purified directly by HPLC (Eclipse XDB–C18, 9.4 × 250 mm, 5 μm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: acetonitrile with 0.1% trifluoroacetic acid, gradient: T = 0 min: 25% B, T = 10 min: 35% B, 4.2 mL/min; retention time: 10.4 min) to give *nat*-**1b•2TFA** (0.5 mg, 90% yield). ^{1}H NMR (400 MHz, DMSO-d6) δ 12.67 (d, *J* = 2.3 Hz, 1H), 12.29 (bs, 2H), 11.80 (bs, 3H), 8.19 (dt, *J* = 12.6, 5.8 Hz, 2H), 7.42 (bs, 2H), 6.98 (dd, *J* = 3.0, 1.6 Hz, 2H), 6.88 (d, *J* = 2.8 Hz, 1H), 6.81–6.78 (m, 1H), 6.63–6.58 (m, 2H), 3.38–3.29 (m, 2H), 2.99–2.85 (m, 2H), 2.31–2.18 (m, 2H). MS(ESI)$^+$calcd for $C_{22}H_{24}Br_3N_{10}O_2$ $(M+H)^+$ 697.0, found 696.9.



44c

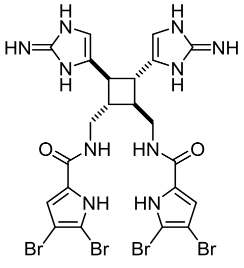
Pyrrole 44c. To a solution of **43•3TFA** (8.1 mg, 7.28 μmol, 1.0 equiv) in *N*,*N*-dimethylformamide (100 μL) were added 2,6-lutidine (3.8 μL, 0.0437 mmol, 6.0 equiv), *N*-(3-dimethylaminopropyl)-*N′*-ethylcarbodiimide hydrochloride (EDCI) (7.0 mg, 0.0364 mmol, 5.0 equiv), 1-hydroxybenzotriazole hydrate (HOBt) (4.7 mg, 0.0364 mmol, 5.0 equiv) and a solution of 4,5-dibromo-1*H*-pyrrole-2-carboxylic acid (9.8 mg, 0.0364 mmol, 5.0 equiv) in *N*,*N*-dimethylformamide (100 μL) at 23 °C. After stirring at 23 °C in dark for 16 h, the reaction mixture was directly purified by HPLC (Waters Atlantis dC18 OBD, 19×150 mm, 5 μm, eluent A: water, eluent B: acetonitrile, gradient:

T = 0 min: 35% B, T = 30 min: 65% B, 5.0 mL/min, retention time: 29.7 min) to give **44c•TFA** (7.1 mg, 70% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.84–7.52 (m, 15H), 7.28 –7.14 (m, 3H), 7.03 (d, *J* = 7.0 Hz, 2H), 6.77 (s, 1H), 6.75 (s, 1H), 6.58 (s, 1H), 6.53 (s, 1H), 5.50 (d, *J* = 11.1 Hz, 1H), 5.40 (d, *J* = 11.1 Hz, 1H), 4.44 (d, *J* = 12.7 Hz, 1H), 4.34 (d, *J* = 12.7 Hz, 1H), 3.58 (dd, *J* = 13.8, 7.3 Hz, 1H), 3.53–3.41 (m, 3H), 3.32–3.30 (m, 1H overlap with solvent), 2.97 (t, *J* = 9.4 Hz, 1H), 2.56–2.23 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 162.2, 161.9, 148.9, 148.0, 135.0, 133.6, 133.5, 131.5, 130.8, 130.7, 129.1, 128.7, 128.6, 128.5, 128.3, 128.0, 127.7, 126.7, 114.2, 110.6, 106.4, 100.1, 72.3, 71.4, 44.7, 43.7, 43.0, 42.0, 41.2, 38.7. MS(ESI)$^+$calcd for $C_{48}H_{44}Br_4N_{10}O_3P(M+H)^+$ 1155.0, found 1154.9.



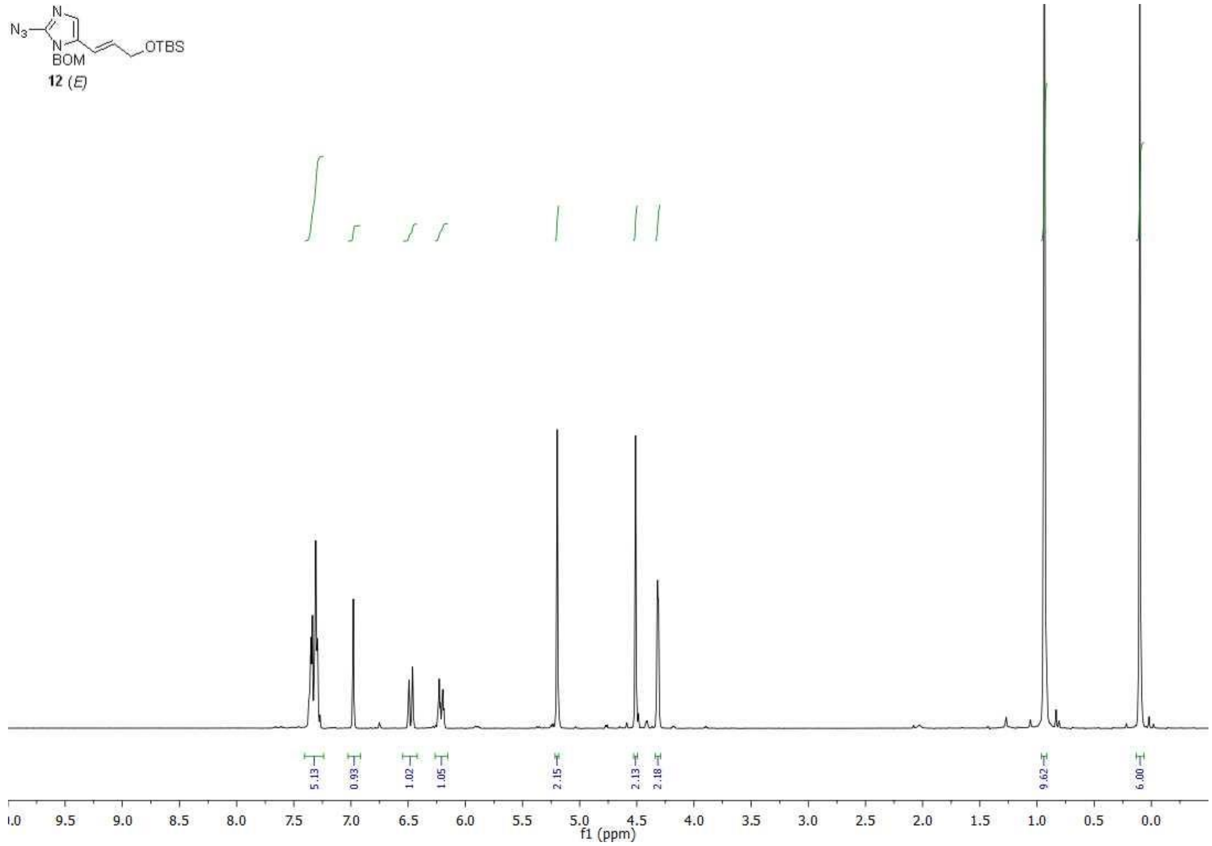
53

Iminophosphoran 53. To a solution of **44c•TFA** (7.1 mg, 5.1 μmol, 1.0 equiv) in methylene chloride (0.3 mL) was added boron trichloride (1.0 M in methylene chloride, 153 μL, 0.153 mmol, 30 equiv) at –50 °C. After stirring at –10 °C for 30 min, an acetonitrile solution of concentrated aqueous ammonium hydroxide (1:4 v/v, 100 μL) was added. After stirring at 23 °C for another 20 min, the volatiles were removed by rotary evaporation and the residue was purified by HPLC (Eclipse XDB–C18, 9.4×250 mm, 5 μm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: methanol with 0.1% trifluoroacetic acid, gradient: T = 0 min: 45% B, T = 20 min: 80% B, 4.0 mL/min, retention time: 10.0 min) to give **53•TFA** (5.3 mg, 90% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.86–7.66 (m, 8H), 7.60 (td, *J* = 7.7, 3.2 Hz, 7H), 6.77 (s, 1H), 6.75 (s, 1H), 6.55 (s, 1H), 6.41 (s, 1H), 3.51–3.39 (m, 4H), 3.05–2.91 (m, 2H), 2.44–2.25 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 162.2, 162.0, 149.0, 148.4, 134.7, 134.7, 133.6, 133.5, 130.6, 130.5, 129.1, 128.8, 128.6, 128.5, 127.5, 114.3, 110.3, 106.4, 100.1, 44.3, 44.1, 42.7, 42.3, 39.7, 39.2. MS(ESI)$^+$calcd for $C_{40}H_{36}Br_4N_{10}O_2P(M+H)^+$ 1034.9.0, found 1034.9.



nat-1c

***nat*-Dibromosceptrin (*nat*-1c).** To a solution of **53•TFA** (5.3 mg, 4.6 μmol, 1.0 equiv) in 1,4-dioxane (100 μL) was added hydrochloric acid (0.20 N, 100 μL). After stirring at 35 °C for 1.5 h, the reaction mixture was purified directly by HPLC (Eclipse XDB–C18, 9.4 × 250 mm, 5 μm, eluent A: water with 0.1% trifluoroacetic acid, eluent B: acetonitrile with 0.1% trifluoroacetic acid, gradient: T = 0 min: 25% B, T = 10 min: 35% B, 4.2 mL/min; retention time: 11.9 min) to give *nat*-**1c•2TFA** (1.9 mg, 40% yield). ^{1}H NMR (600 MHz, CD_3OD) δ 6.76 (s, 2H), 6.56 (s, 2H), 3.49–3.46 (m, 4H), 2.98 (A_2B_2, *J* = 9.4, 2.6 Hz, 2H), 2.37–2.33 (m, 2H).^{13}C NMR (100 MHz, CD_3OD) δ 162.2, 149.0, 128.7, 128.5, 114.3, 110.3, 106.4, 100.1, 44.2, 42.4, 39.3.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OTBS
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1.02
1.05
2.15
2.13
2.18
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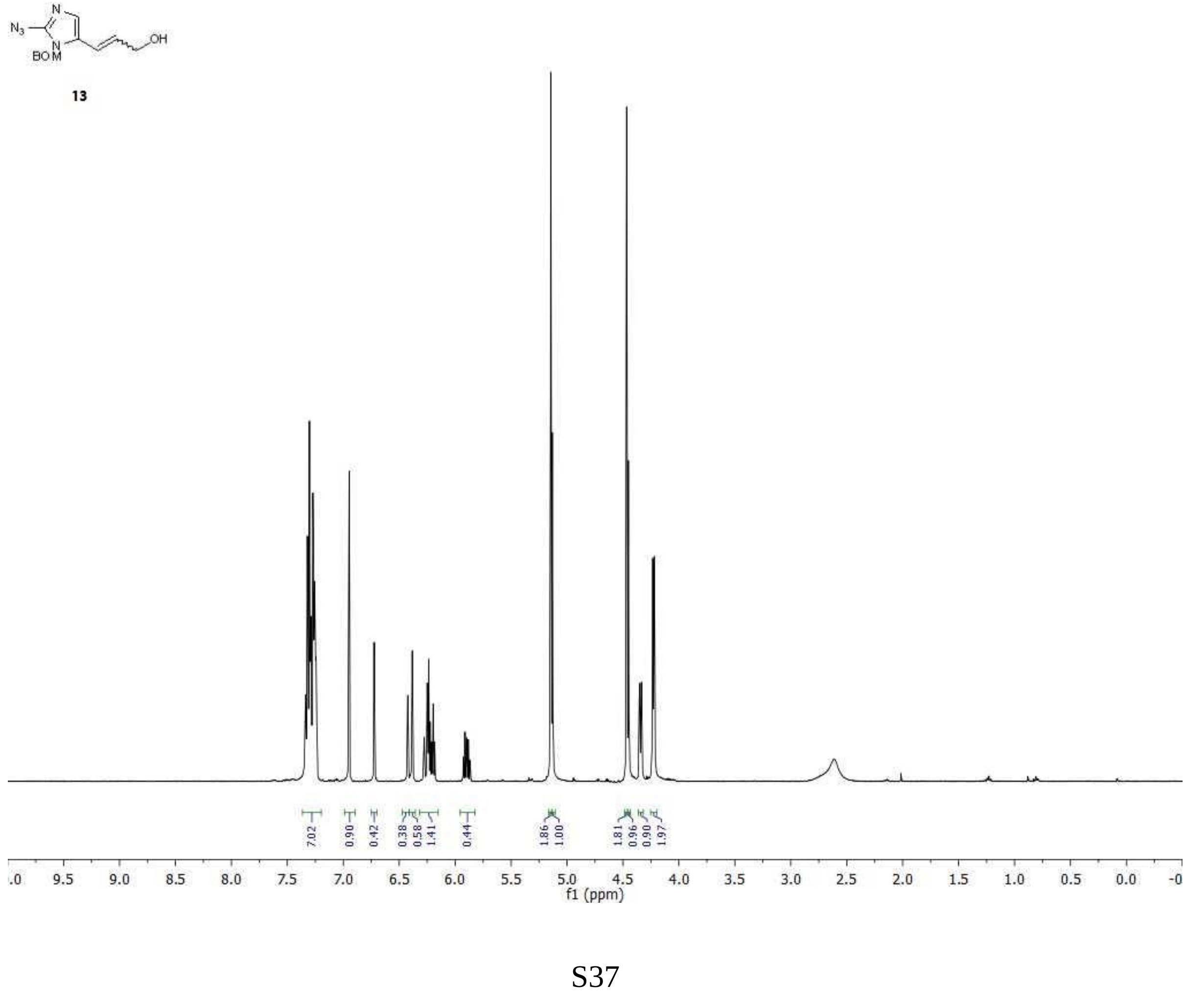
6.00
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

12 (*E*)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0.58
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1.00
1.81
0.96
0.90
1.97
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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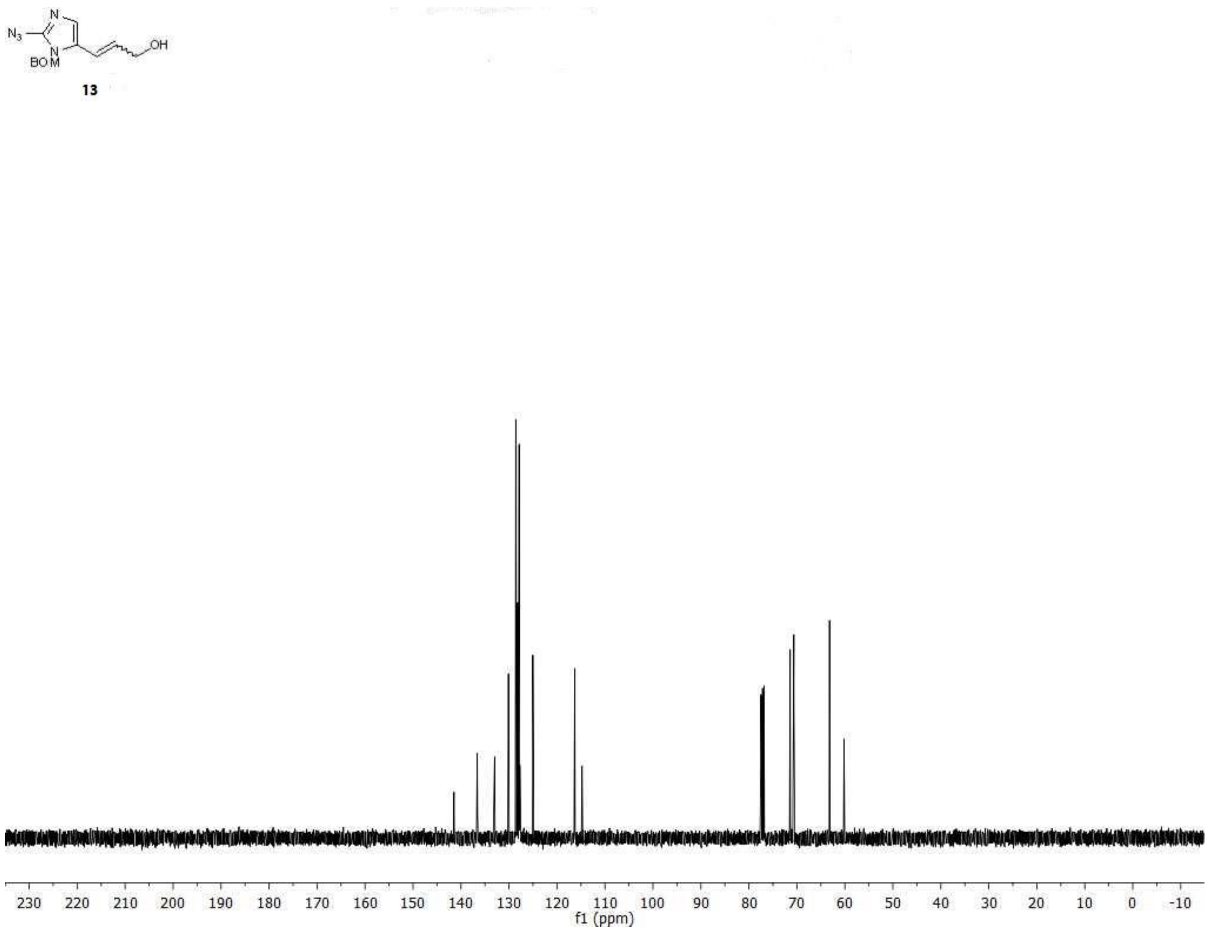
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

13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N
BOM
OH
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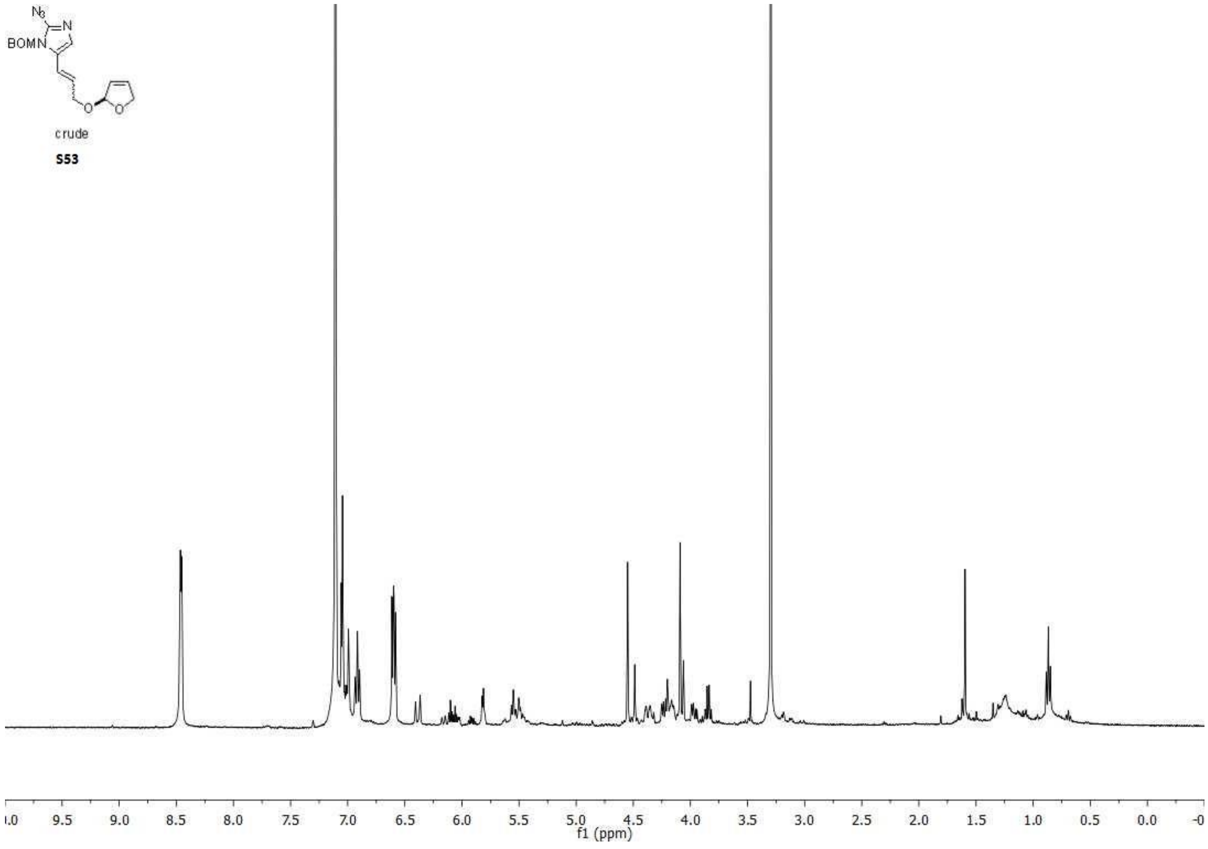
f1 (ppm)

13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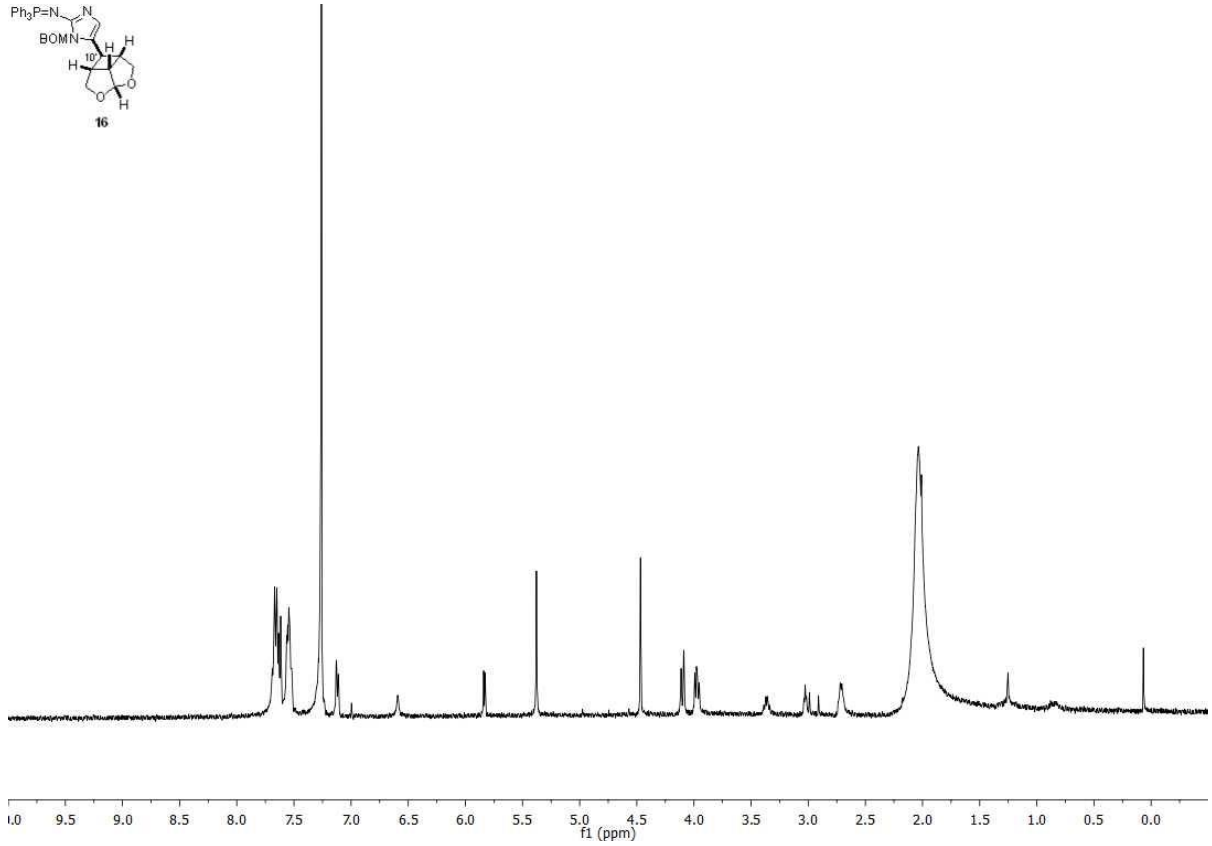
N
BOMN
O
O
.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

crude

S53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H
O
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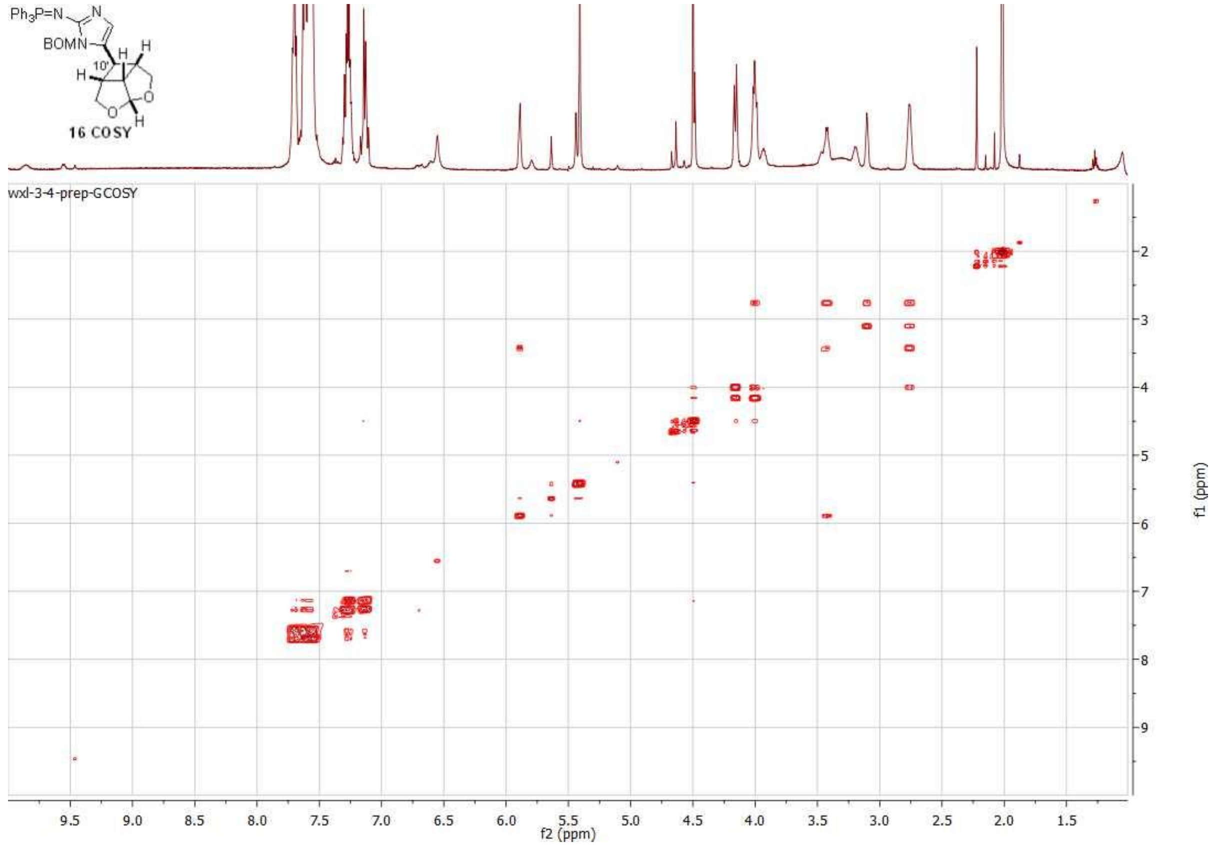
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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O
16 COSY
wxl-3-4-prep-GCOSY
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5.5
5.0
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4.0
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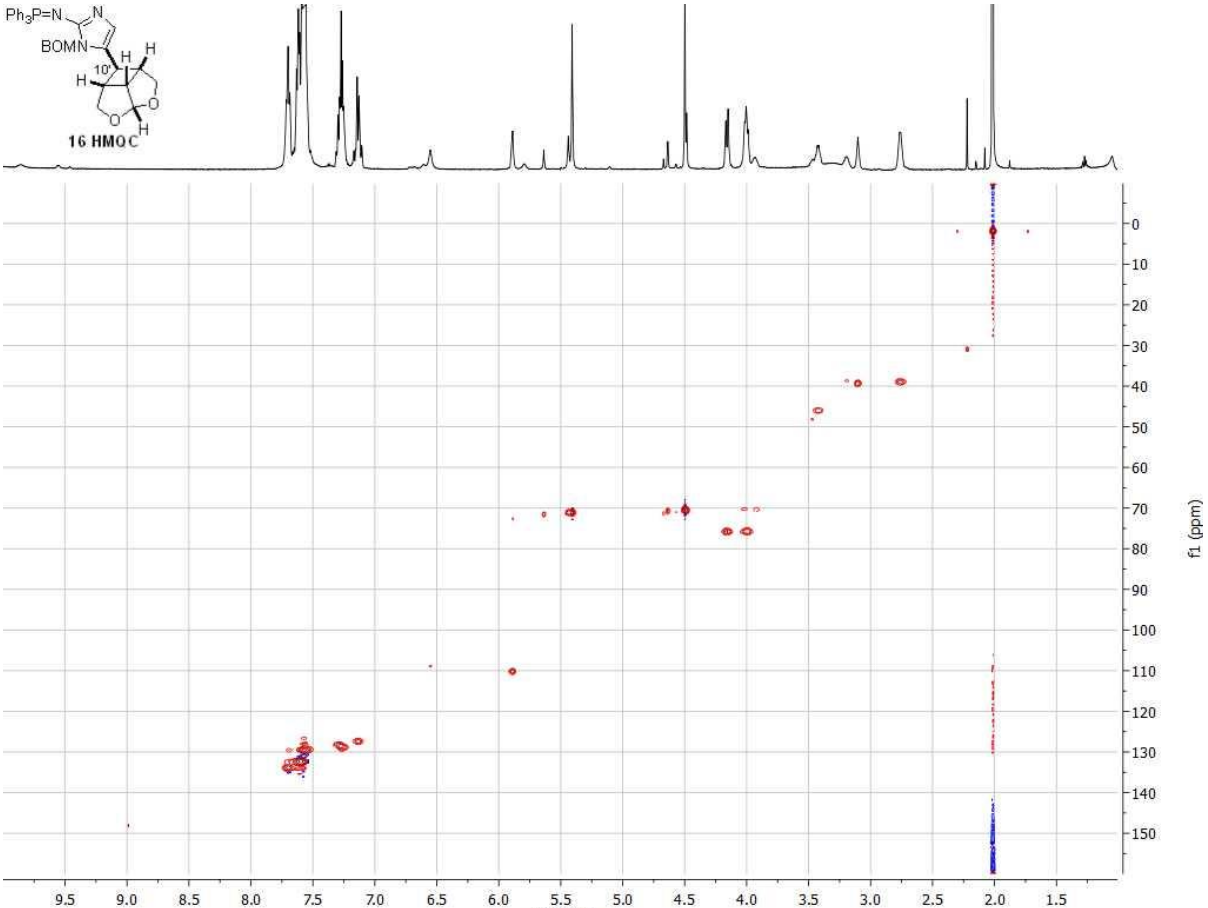
6
7
8
9
f1 (ppm)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N
BOMN
10'
H
H
H
O
O
H
16 HMQC
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f2 (ppm)
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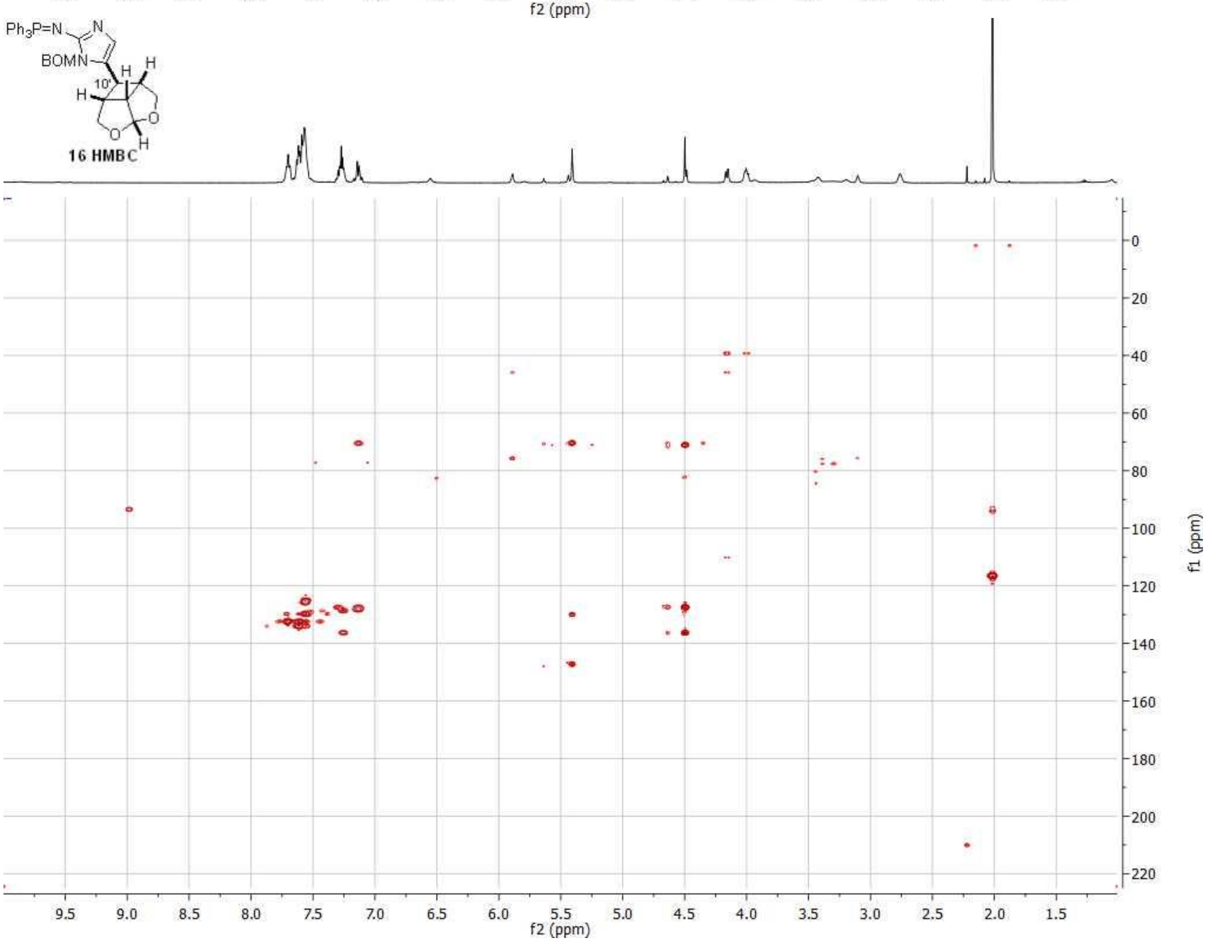
f1 (ppm)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N
BOMN
10'
H
H
H
O
O
H
16 HMBC
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f2 (ppm)
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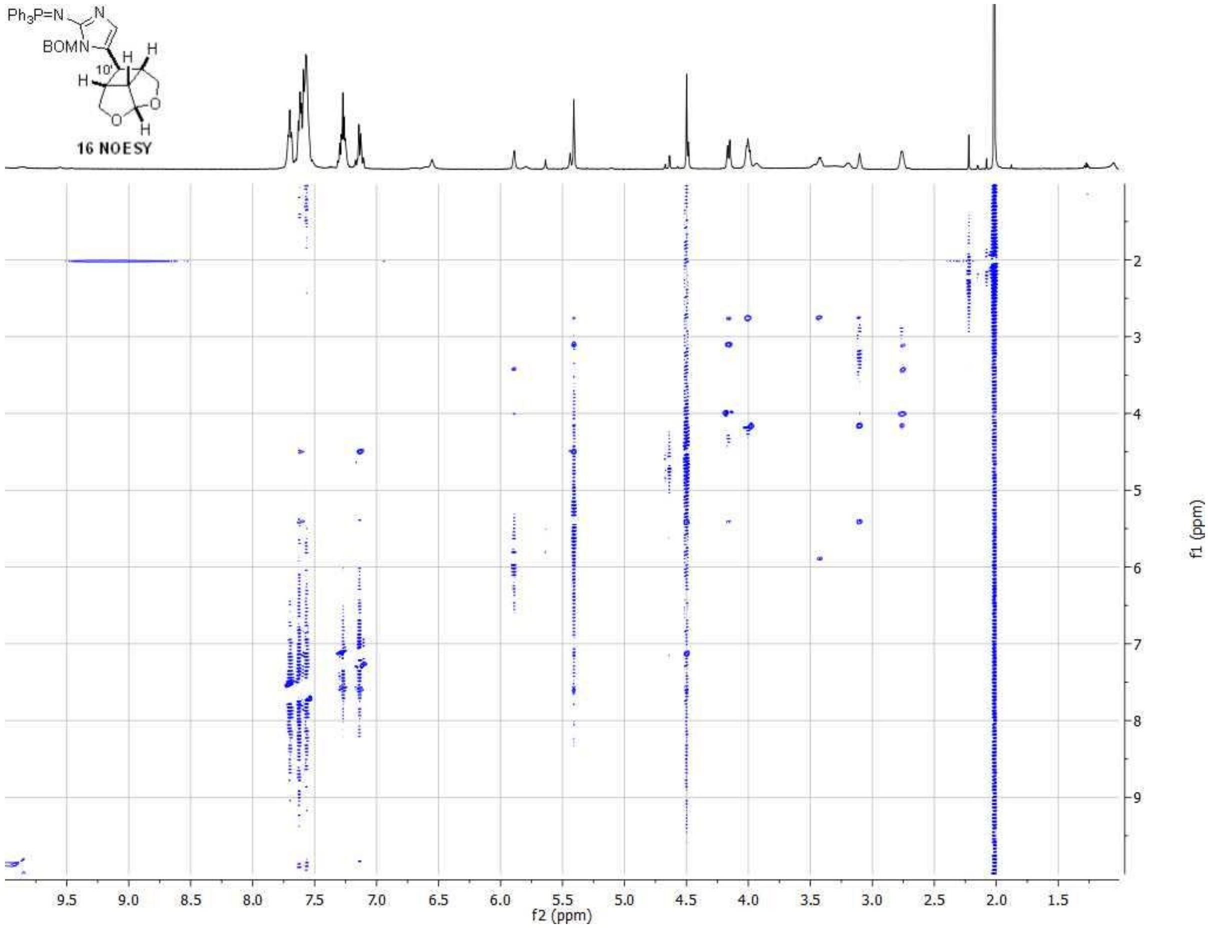
f1 (ppm)


16 NOESY

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BOMN
N
10'
H
H
H
O
O
H
f2 (ppm)
f1 (ppm)
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9.0
8.5
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7.5
7.0
6.5
6.0
5.5
5.0
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3.5
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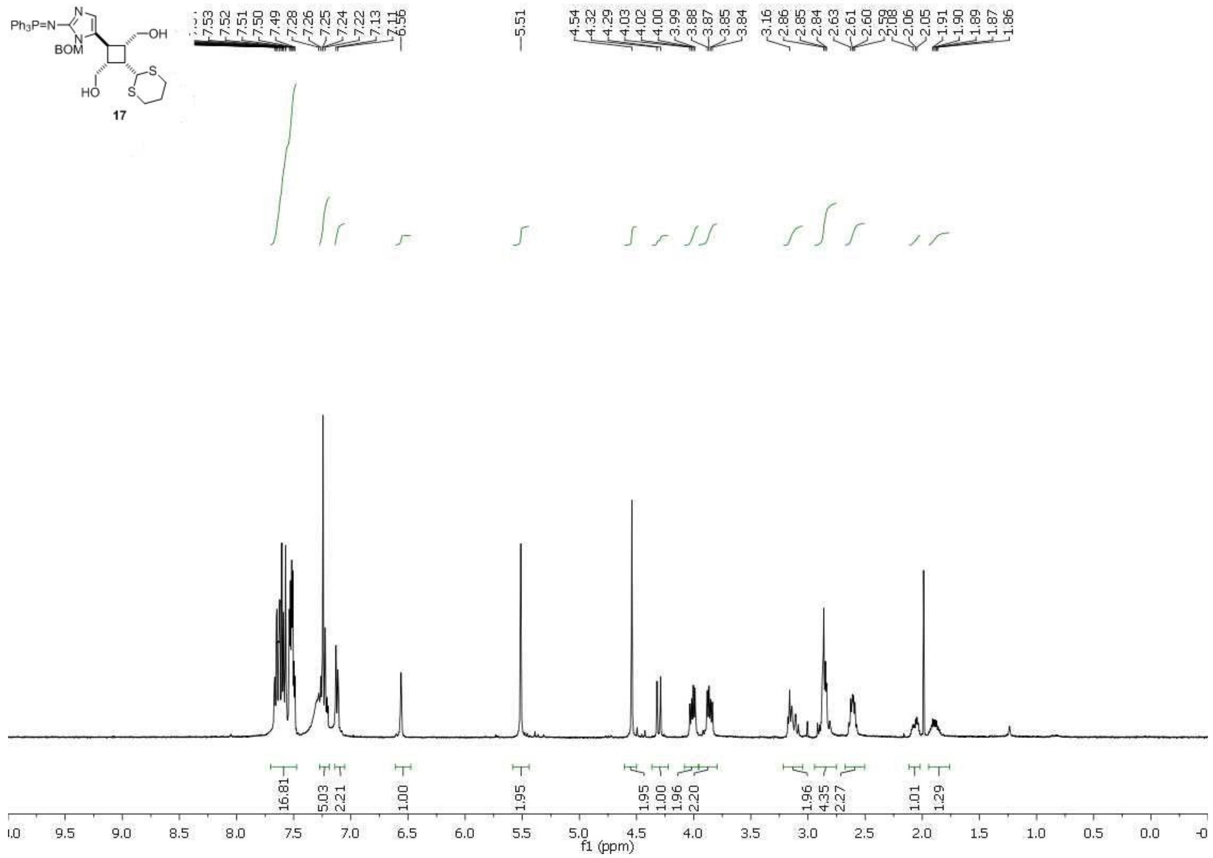
4
5
6
7
8
9


17

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BOM
OH
HO
S
S
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7.52
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7.50
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7.26
7.25
7.24
7.22
7.13
7.11
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4.54
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4.29
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4.02
4.00
3.99
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3.87
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3.84
3.16
2.86
2.85
2.84
2.63
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1.90
1.89
1.87
1.86
16.81
5.03
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1.95
1.95
1.00
1.96
2.20
1.96
4.35
2.27
1.01
1.29
f1 (ppm)
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9.0
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8.0
7.5
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6.5
6.0
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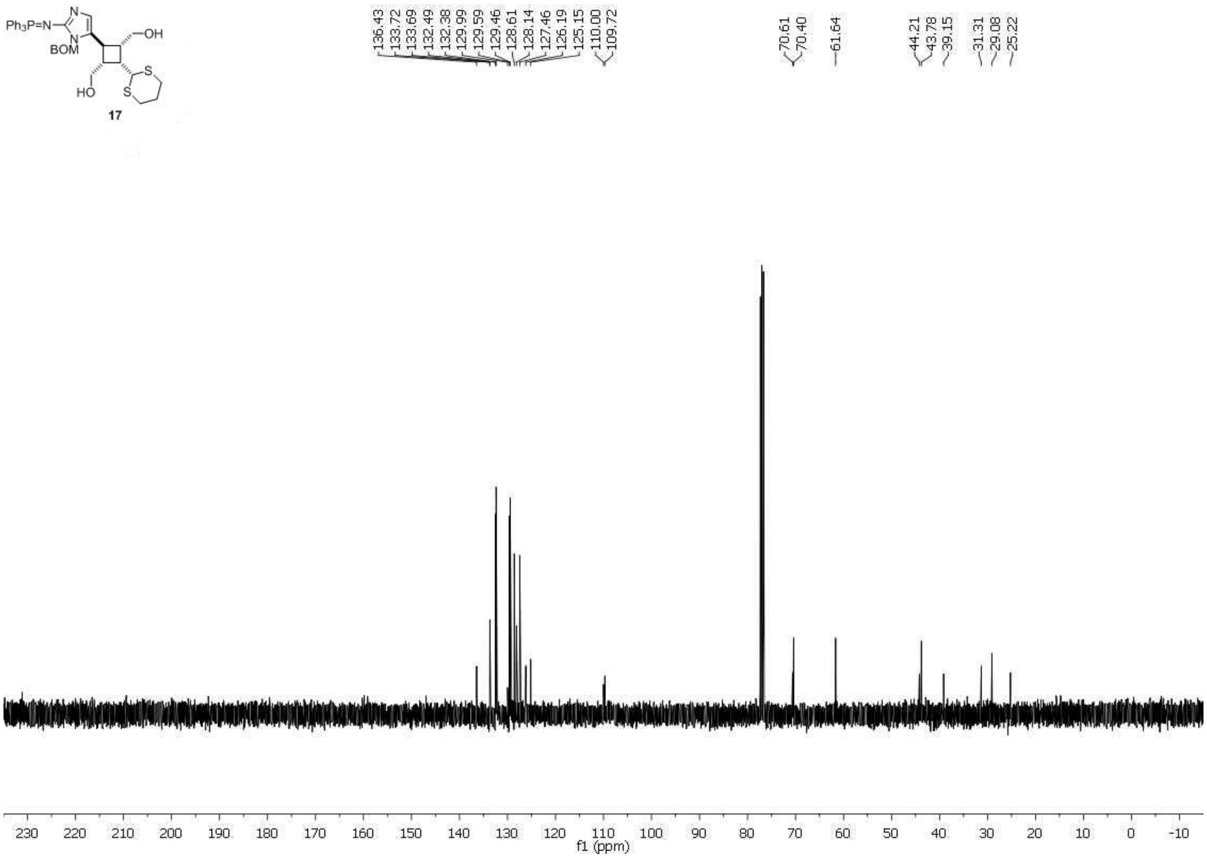
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128.14
127.46
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109.72
70.61
70.40
61.64
44.21
43.78
39.15
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29.08
25.22
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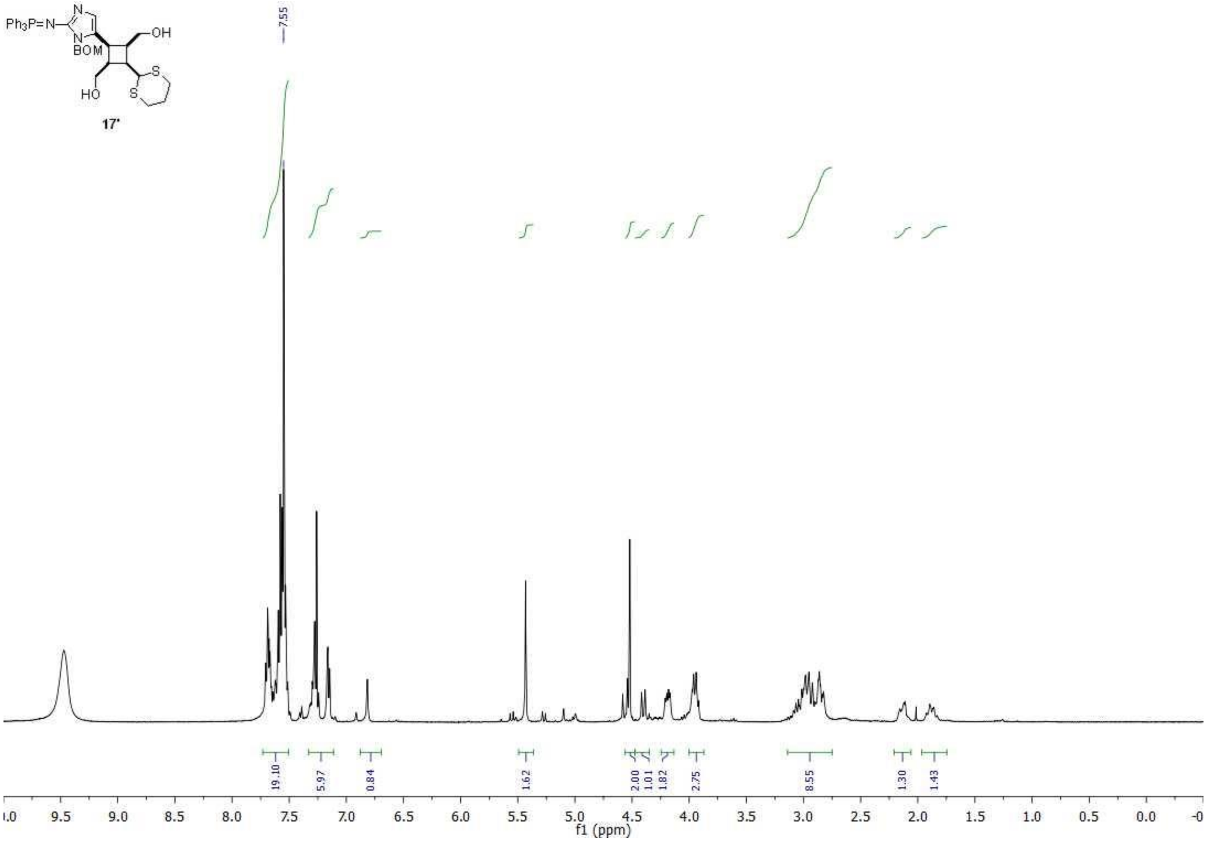
f1 (ppm)

17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2.75
8.55
1.30
1.43
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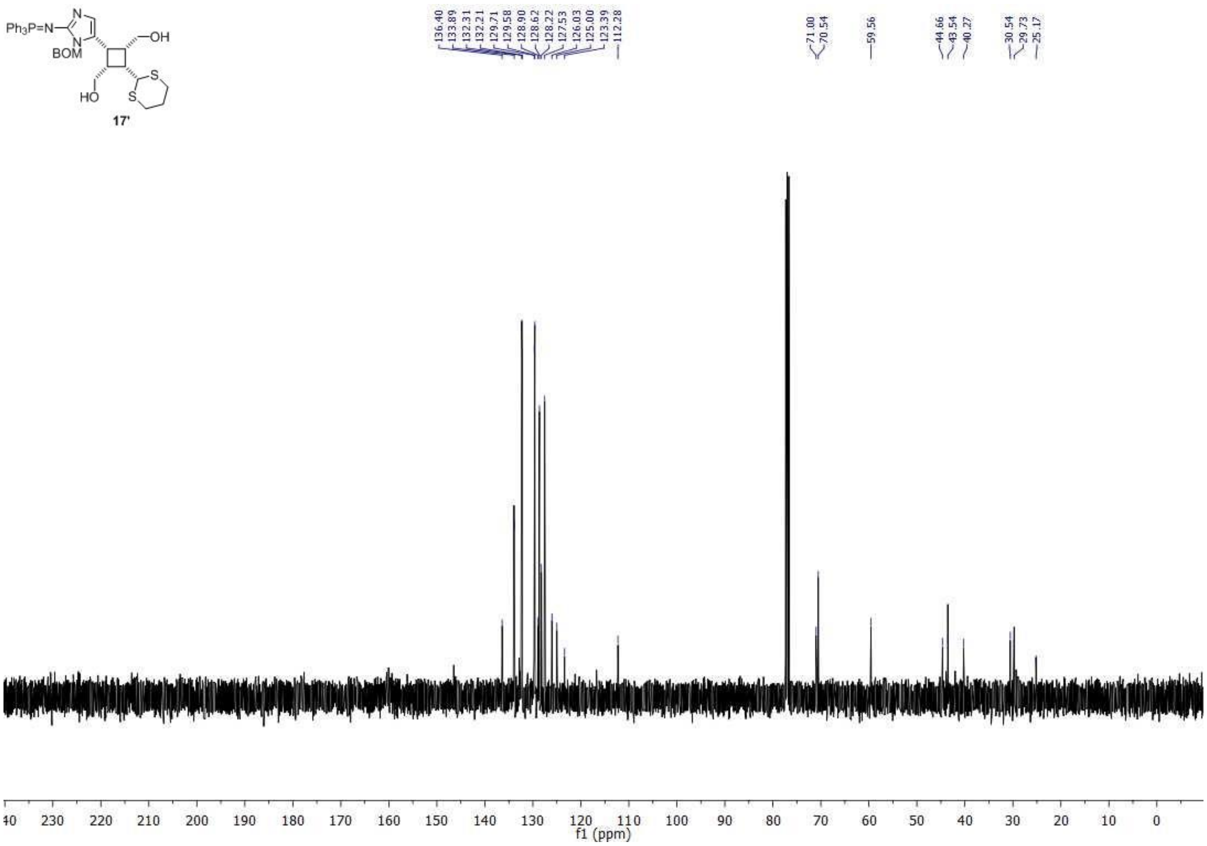
f1 (ppm)

17'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17'
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30.54
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200
190
180
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110
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50
40
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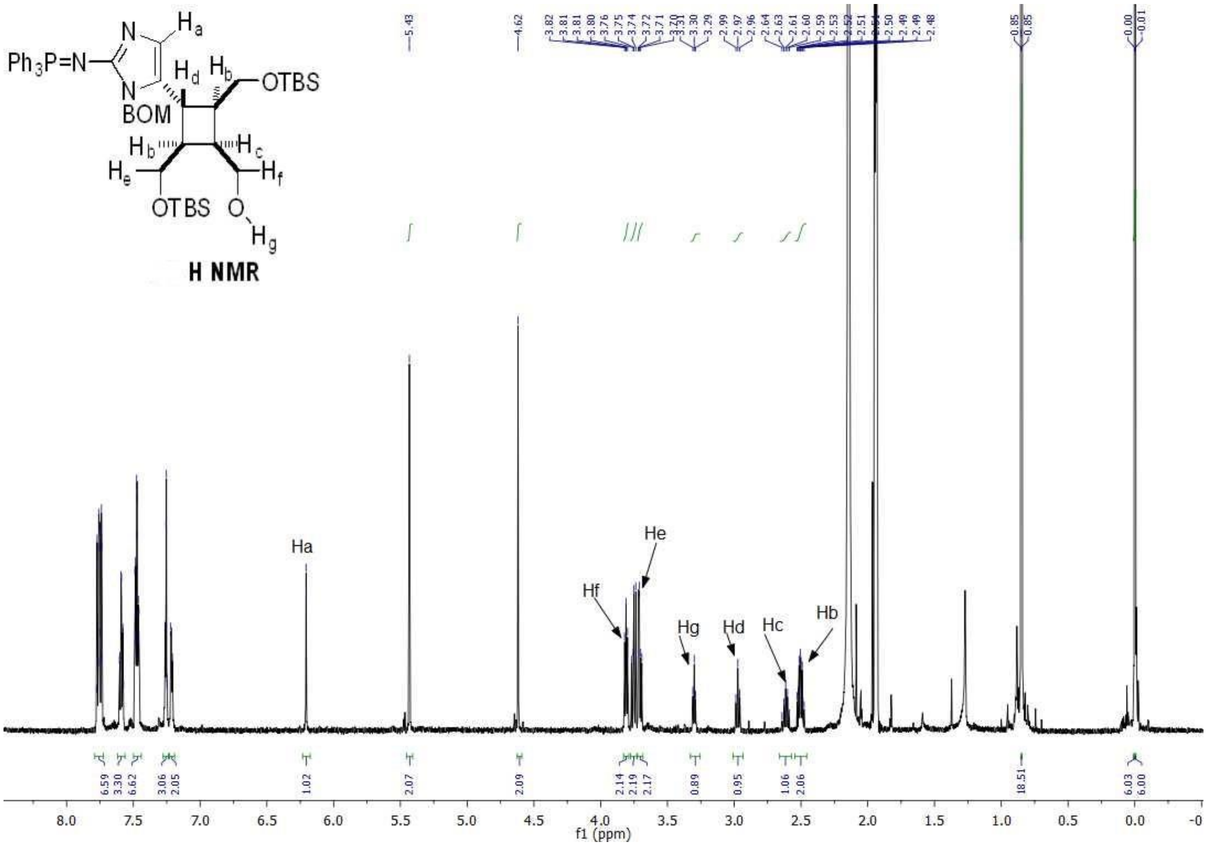
f1 (ppm)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Hb
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Hb
Hc
He
Hf
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3.80
3.76
3.75
3.74
3.72
3.71
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2.64
2.63
2.61
2.60
2.59
2.53
2.52
2.51
2.50
2.49
2.49
2.48
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0.85
0.00
-0.01
Ha
Hf
He
Hg
Hd
Hc
Hb
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3.30
6.62
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2.05
1.02
2.07
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2.19
2.17
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0.95
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2.06
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7.5
7.0
6.5
6.0
5.5
5.0
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4.0
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3.0
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2.0
1.5
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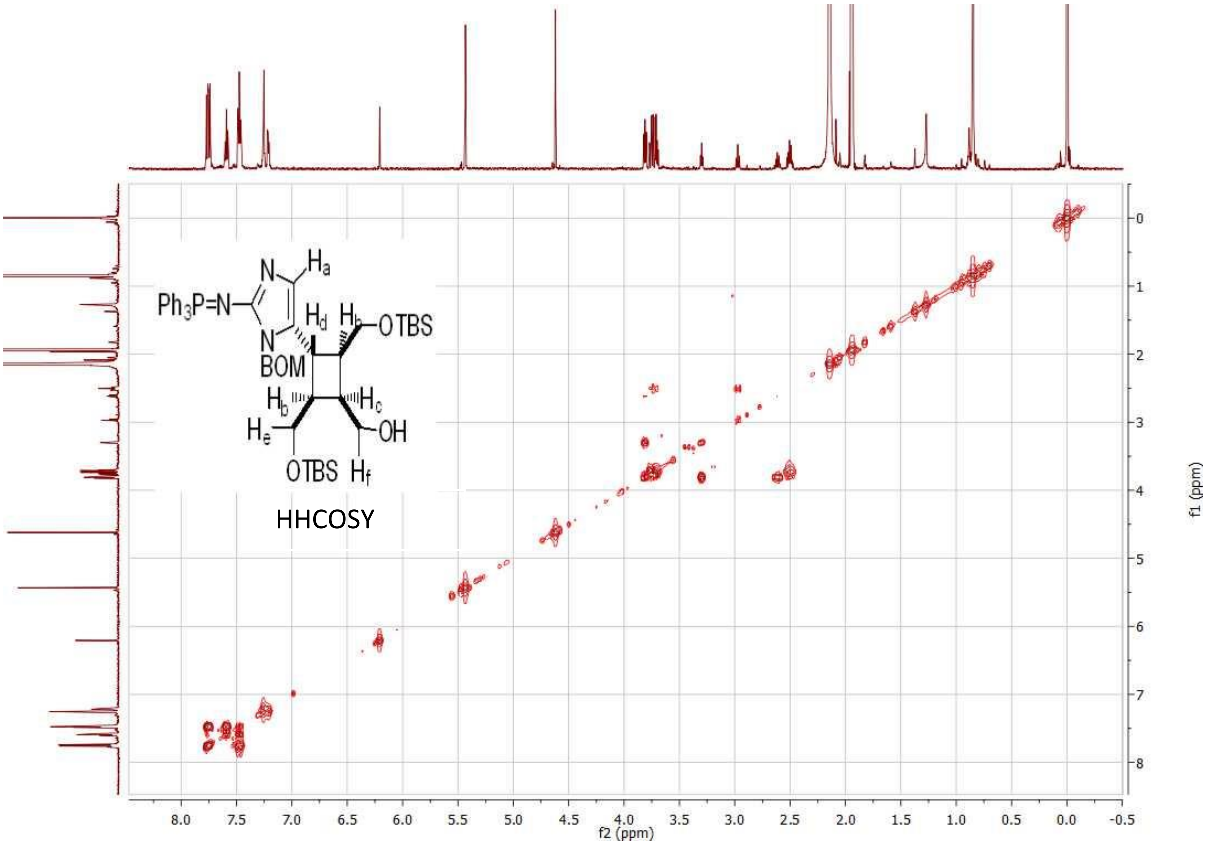
0.0
-0
f1 (ppm)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He
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f2 (ppm)
f1 (ppm)
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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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0.5
0.0
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0
1
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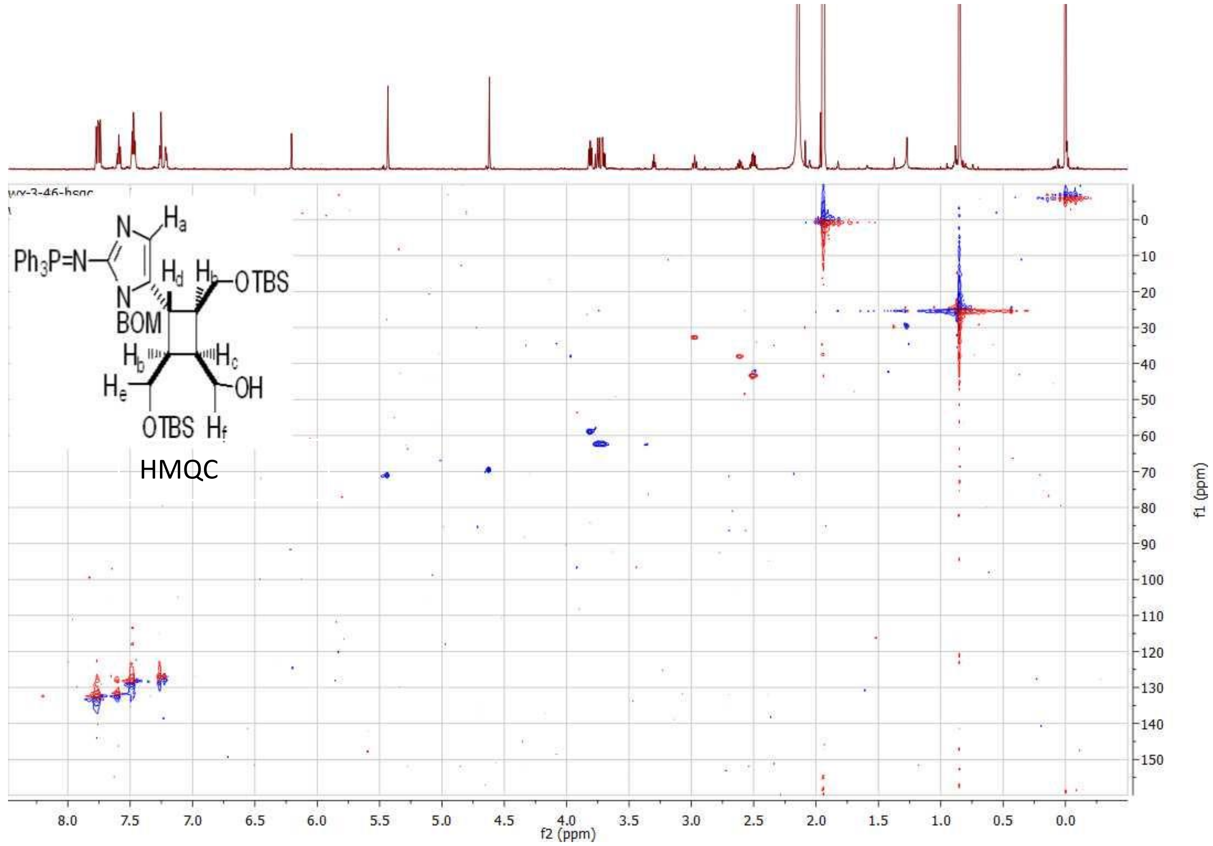
3
4
5
6
7
8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Hd
Hb
OTBS
Hb
Hc
He
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OTBS
Hf
HMQC
f2 (ppm)
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
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40
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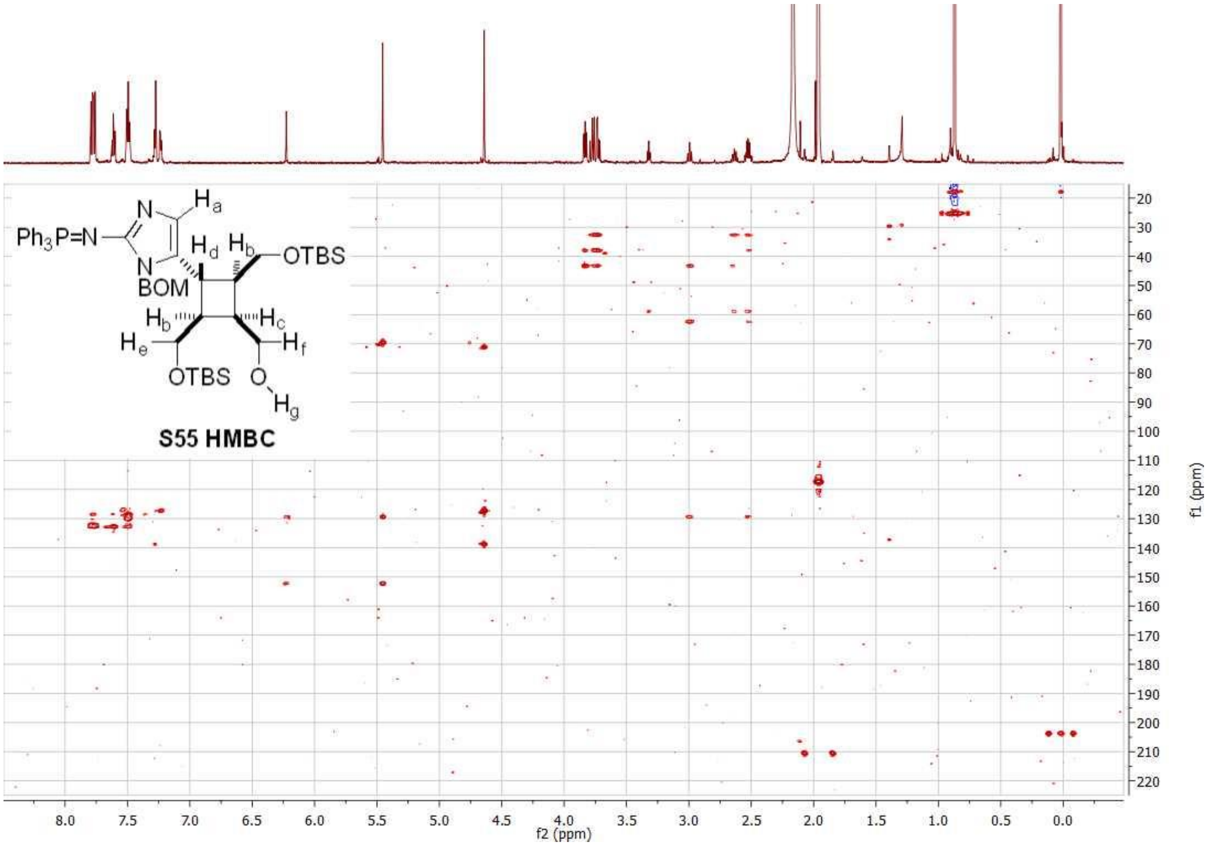

Ph$_3$P=N
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N
BOM
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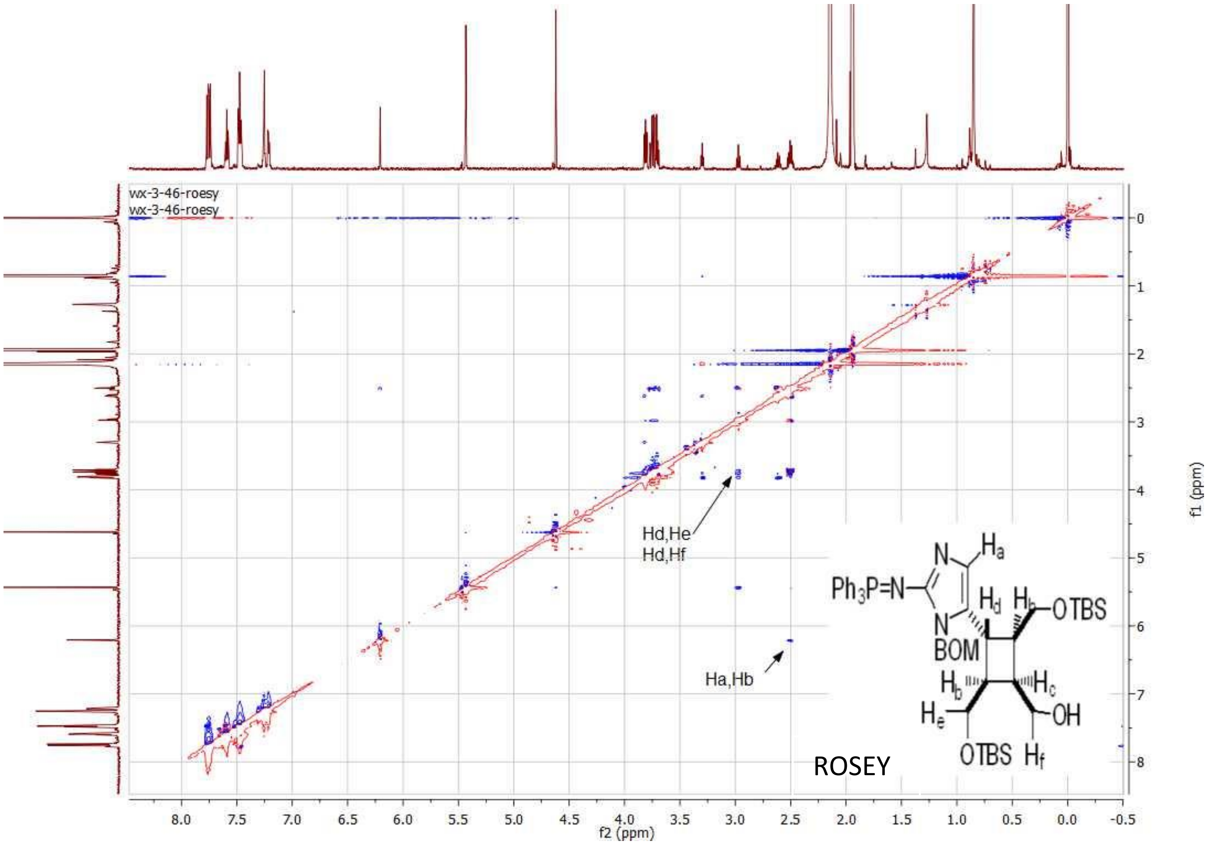
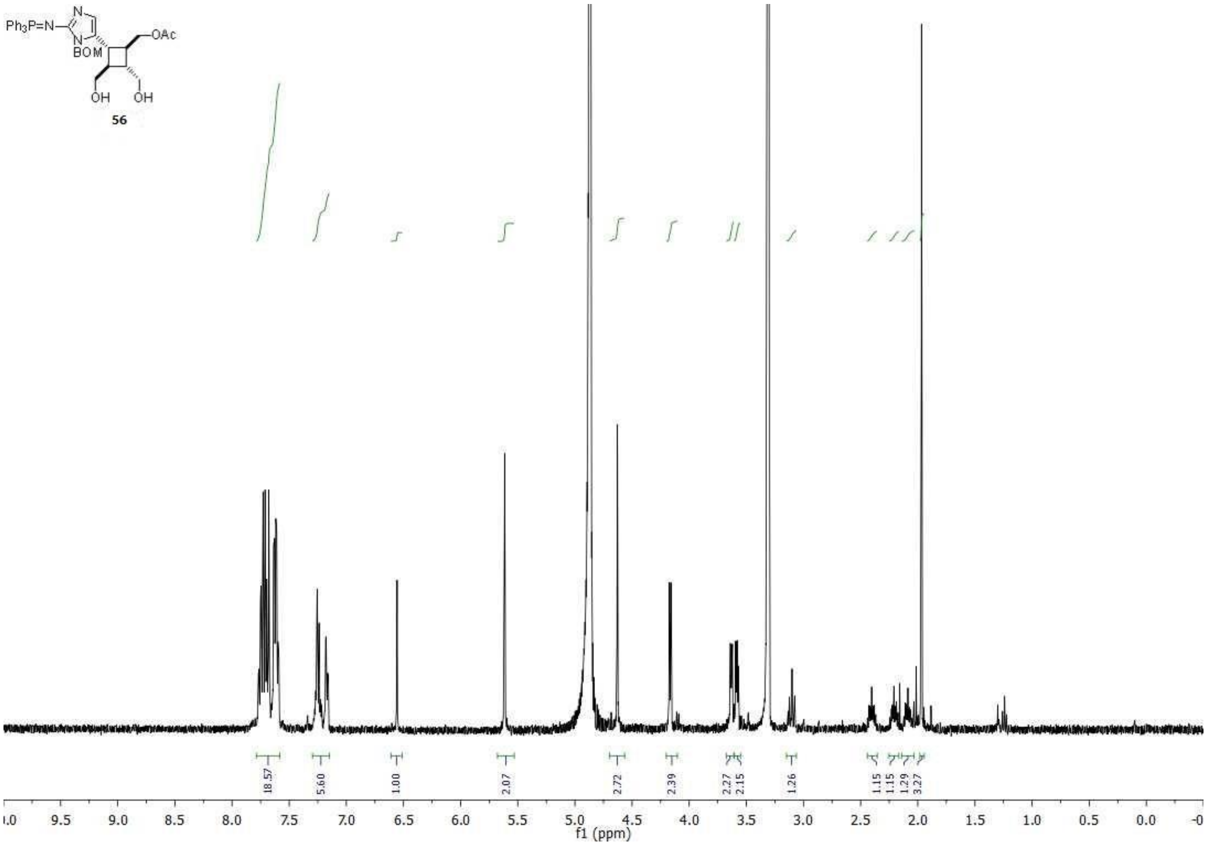
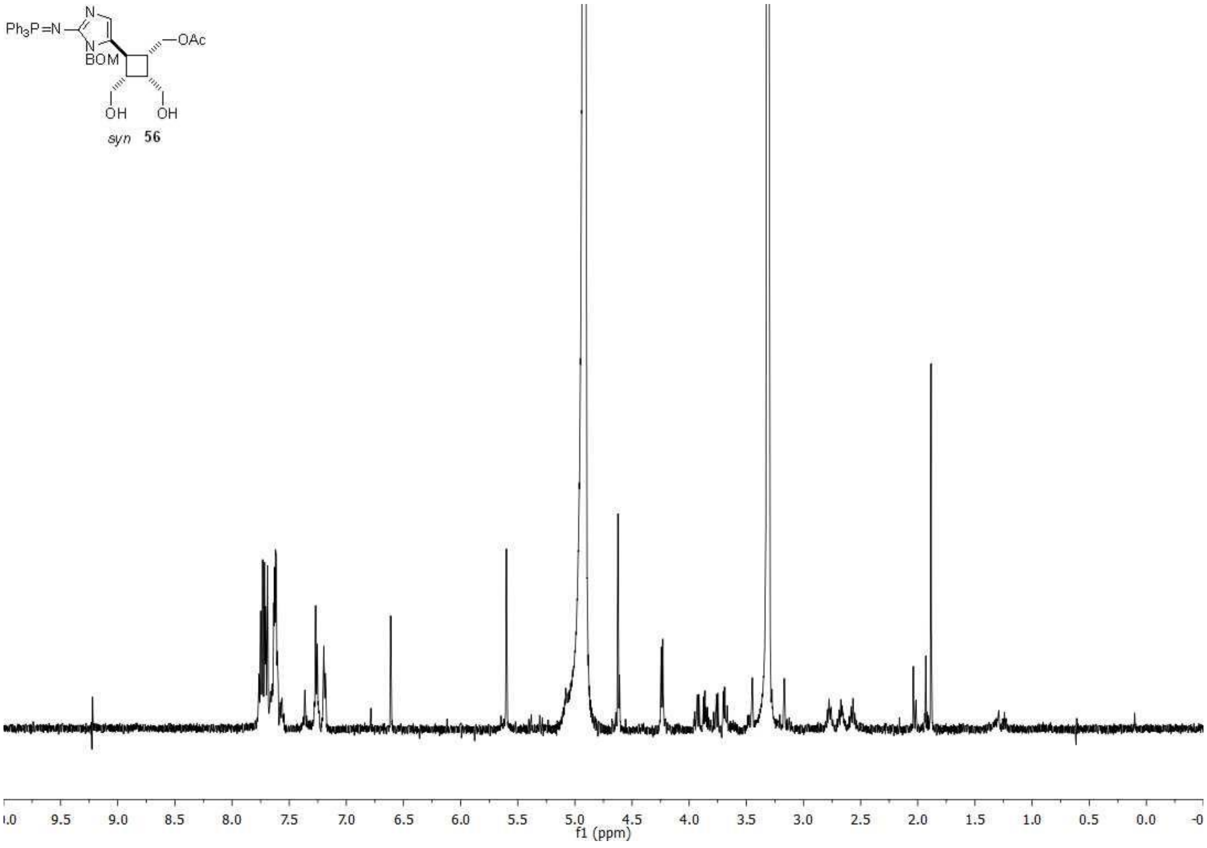
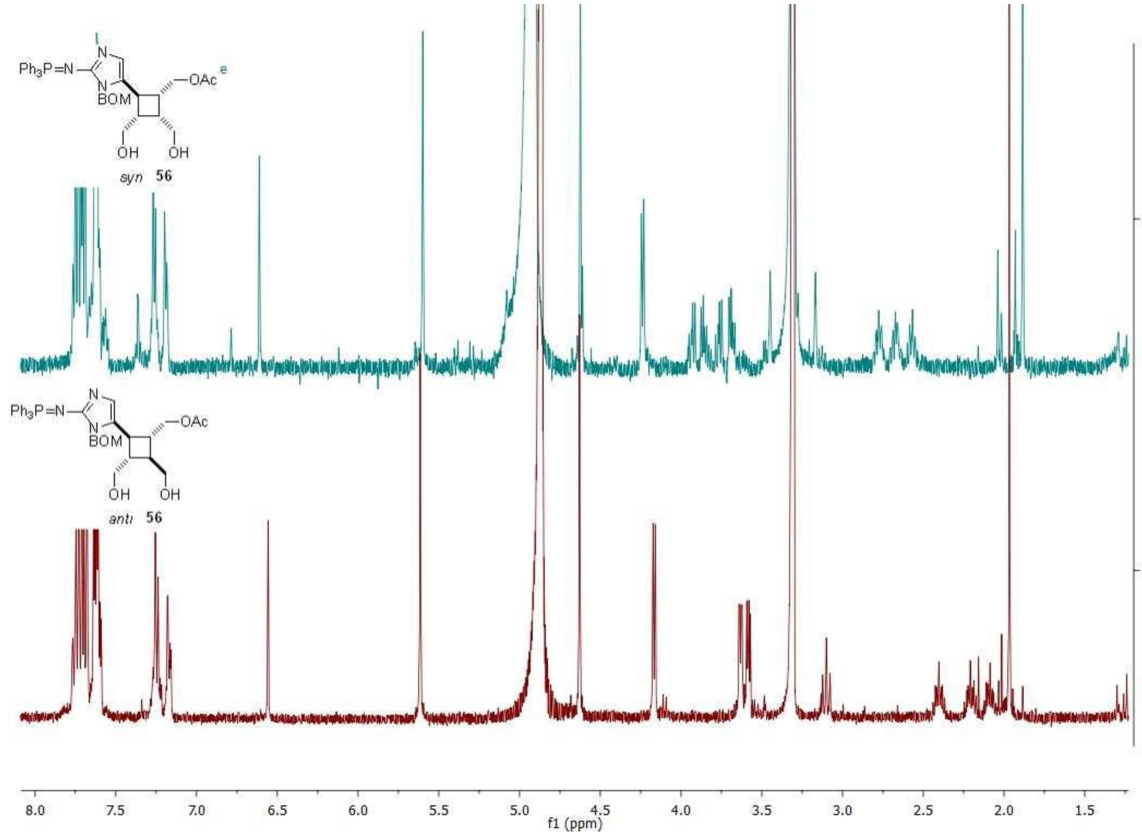
H$_d$
H$_b$
OTBS
H$_b$
H$_c$
H$_e$
H$_f$
OTBS
O
H$_g$
S55 HMBC
f1 (ppm)
f2 (ppm)
20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

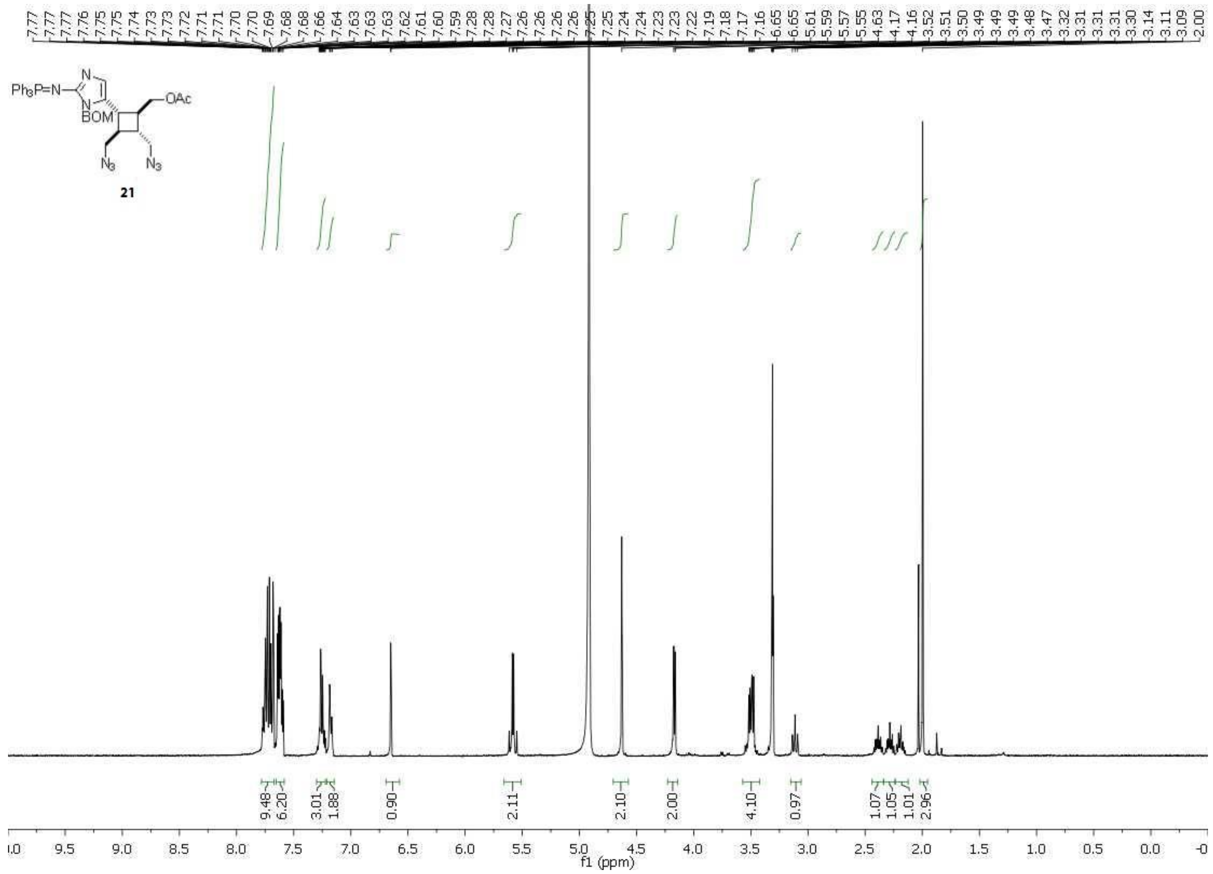


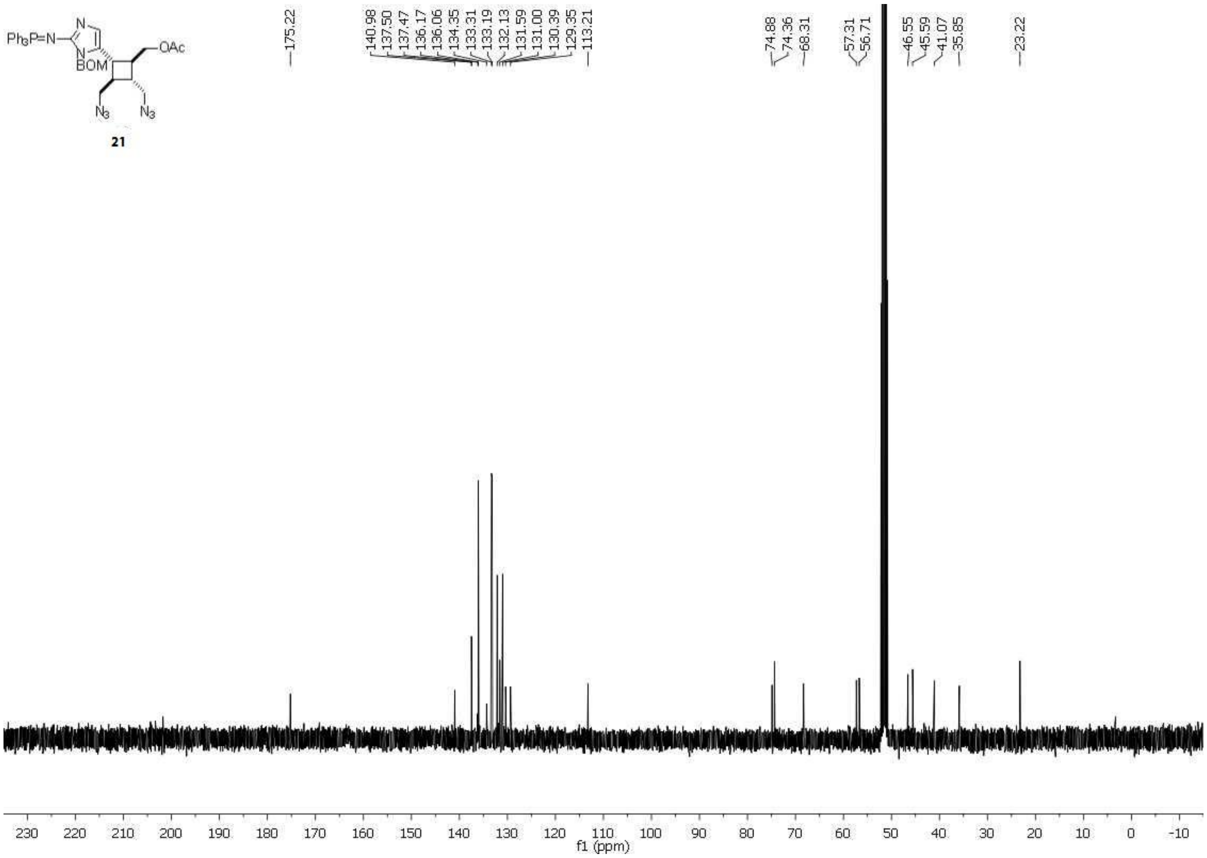
wx-3-46-roesy
wx-3-46-roesy
Hd,He
Hd,Hf
Ha,Hb
Ph$_3$P=N
N
N
BOM
H$_a$
H$_d$
H$_b$
OTBS
H$_b$
H$_c$
H$_e$
OH
OTBS
H$_f$
ROSEY
f1 (ppm)
f2 (ppm)
0 1 2 3 4 5 6 7 8
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5


Ph3P=N
N
BOM
OAc
OH
OH
56
18.57
5.60
1.00
2.07
2.72
2.39
2.27
2.15
1.26
1.15
1.15
1.29
3.27
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

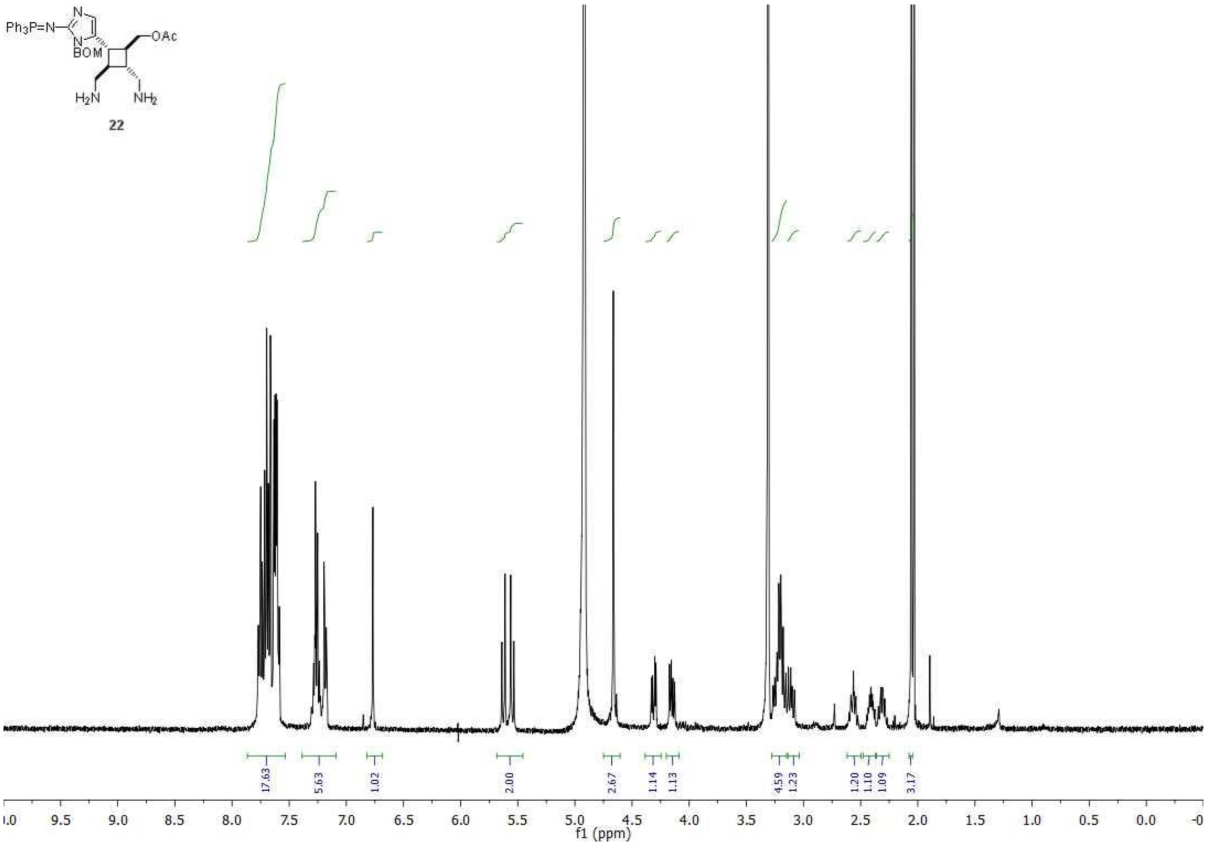

Ph3P=N
N
BOM
OAc
OH
OH
syn 56
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)


Ph$_3$P=N
N
N
BOM
OAc
e
OH
OH
syn **56**
Ph$_3$P=N
N
N
BOM
OAc
OH
OH
anti **56**
2
1
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

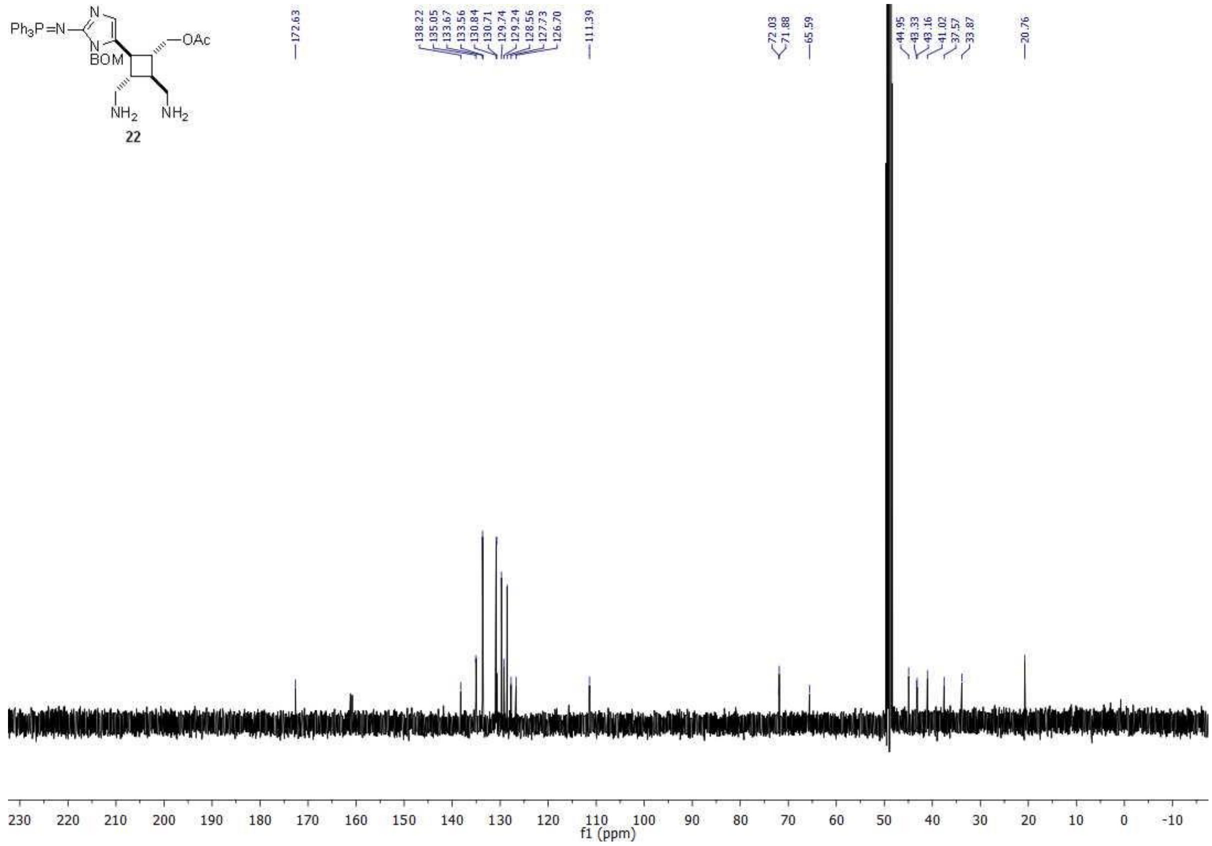

7.77
7.77
7.76
7.75
7.75
7.74
7.73
7.73
7.72
7.71
7.71
7.70
7.70
7.69
7.68
7.66
7.64
7.63
7.63
7.62
7.61
7.60
7.59
7.28
7.27
7.26
7.26
7.26
7.25
7.25
7.24
7.24
7.23
7.23
7.22
7.19
7.18
7.17
7.16
6.65
6.65
5.61
5.59
5.57
5.55
4.63
4.17
4.16
3.52
3.51
3.50
3.49
3.49
3.48
3.47
3.32
3.31
3.31
3.30
3.14
3.11
3.09
2.00
Ph$_3$P=N
N
N
BOM
OAc
N$_3$
N$_3$
21
9.48
6.20
3.01
1.88
0.90
2.11
2.10
2.00
4.10
0.97
1.07
1.05
1.01
2.96
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

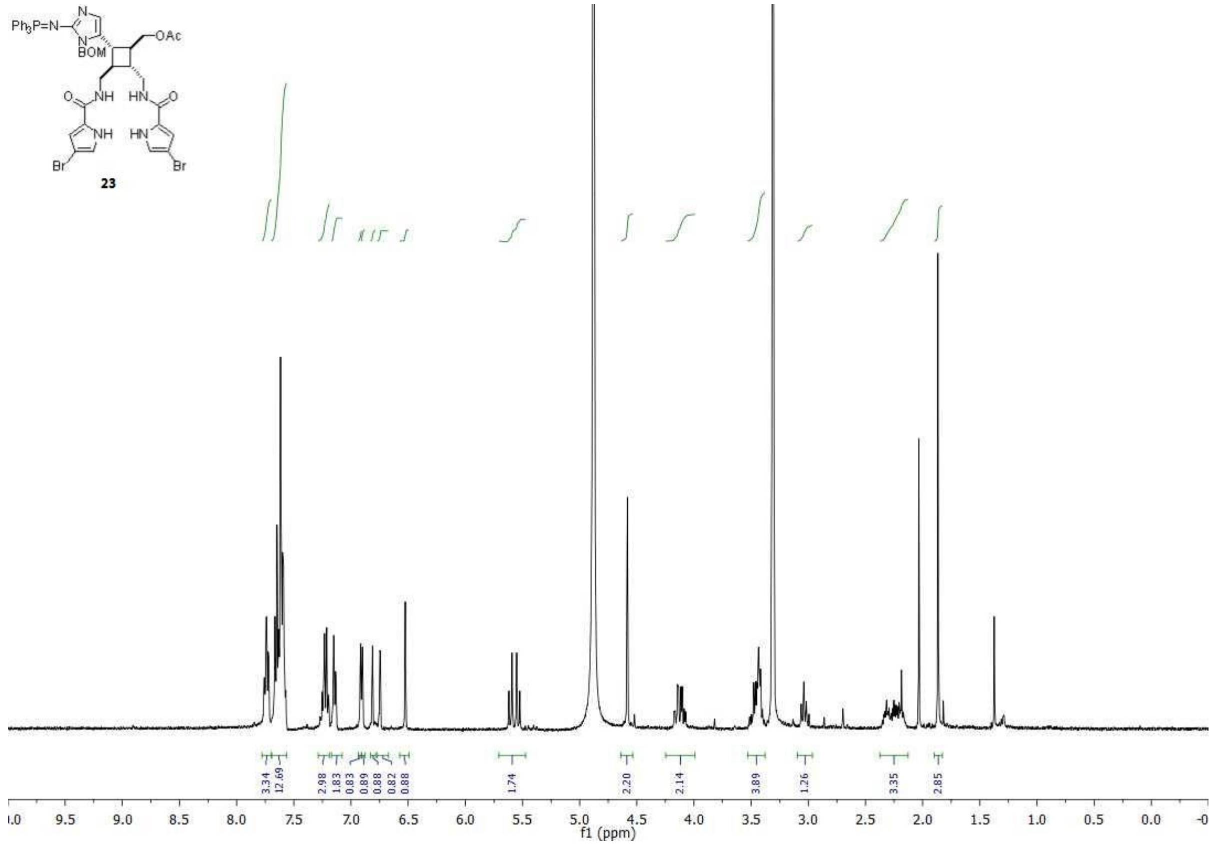

Ph3P=N
N
BOM
OAc
N3
N3
175.22
140.98
137.50
137.47
136.17
136.06
134.35
133.31
133.19
132.13
131.59
131.00
130.39
129.35
113.21
74.88
74.36
68.31
57.31
56.71
46.55
45.59
41.07
35.85
23.22
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

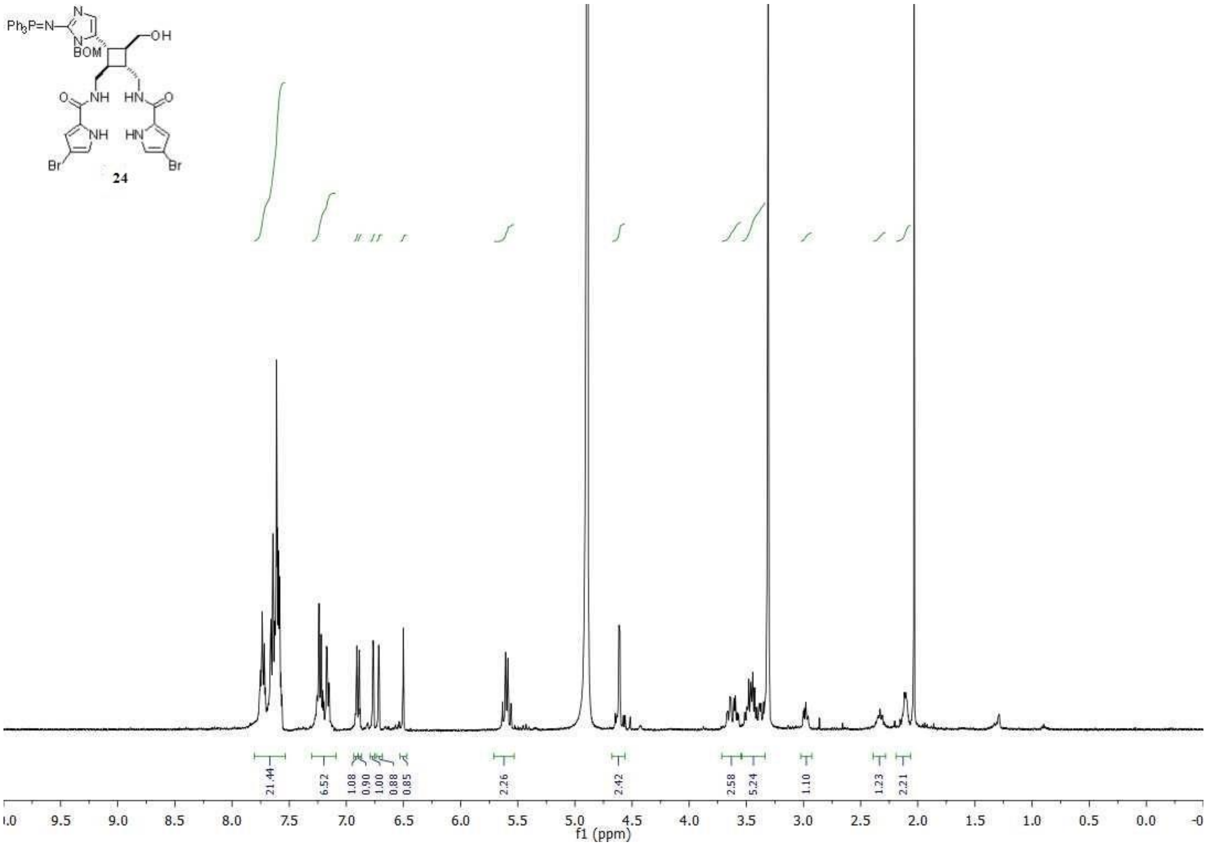
21

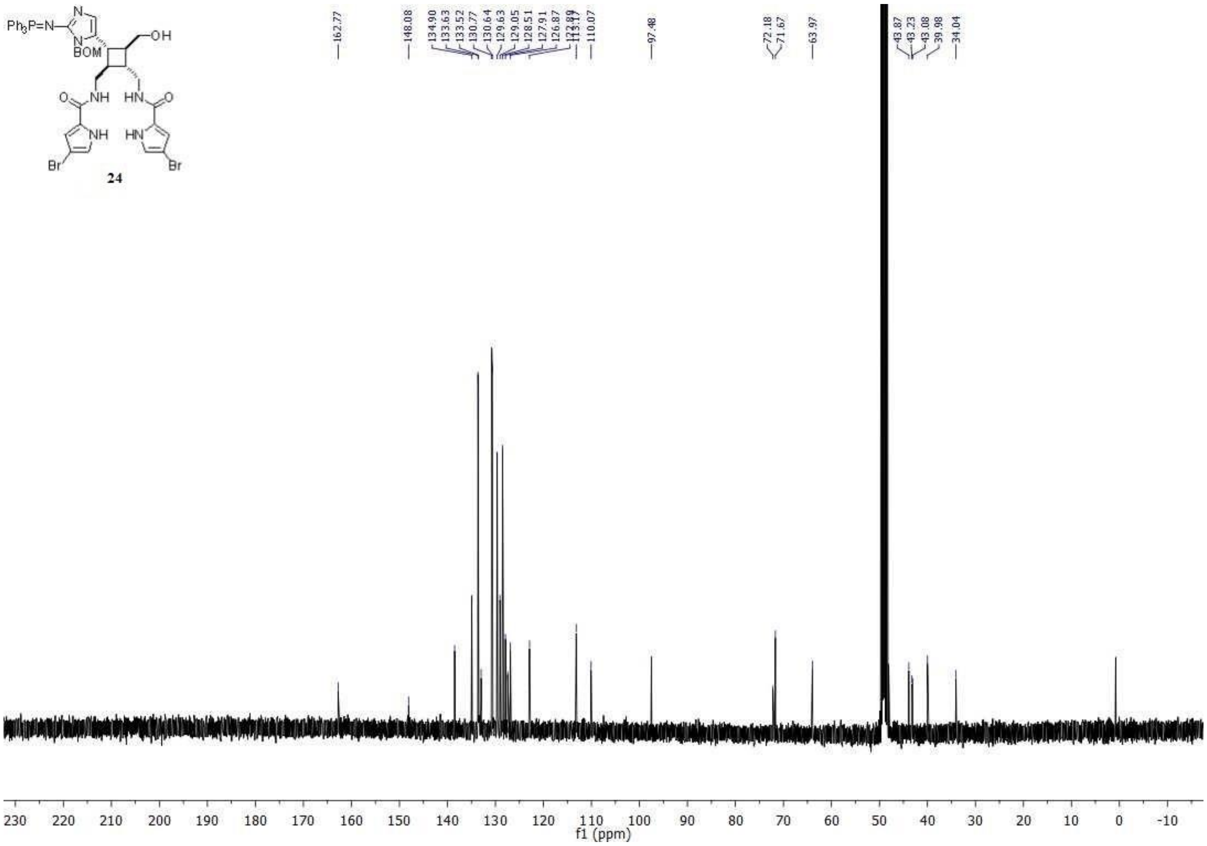

Ph3P=N
N
BOM
OAc
H2N
NH2
17.63
5.63
1.02
2.00
2.67
1.14
1.13
4.59
1.23
1.20
1.10
1.09
3.17
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

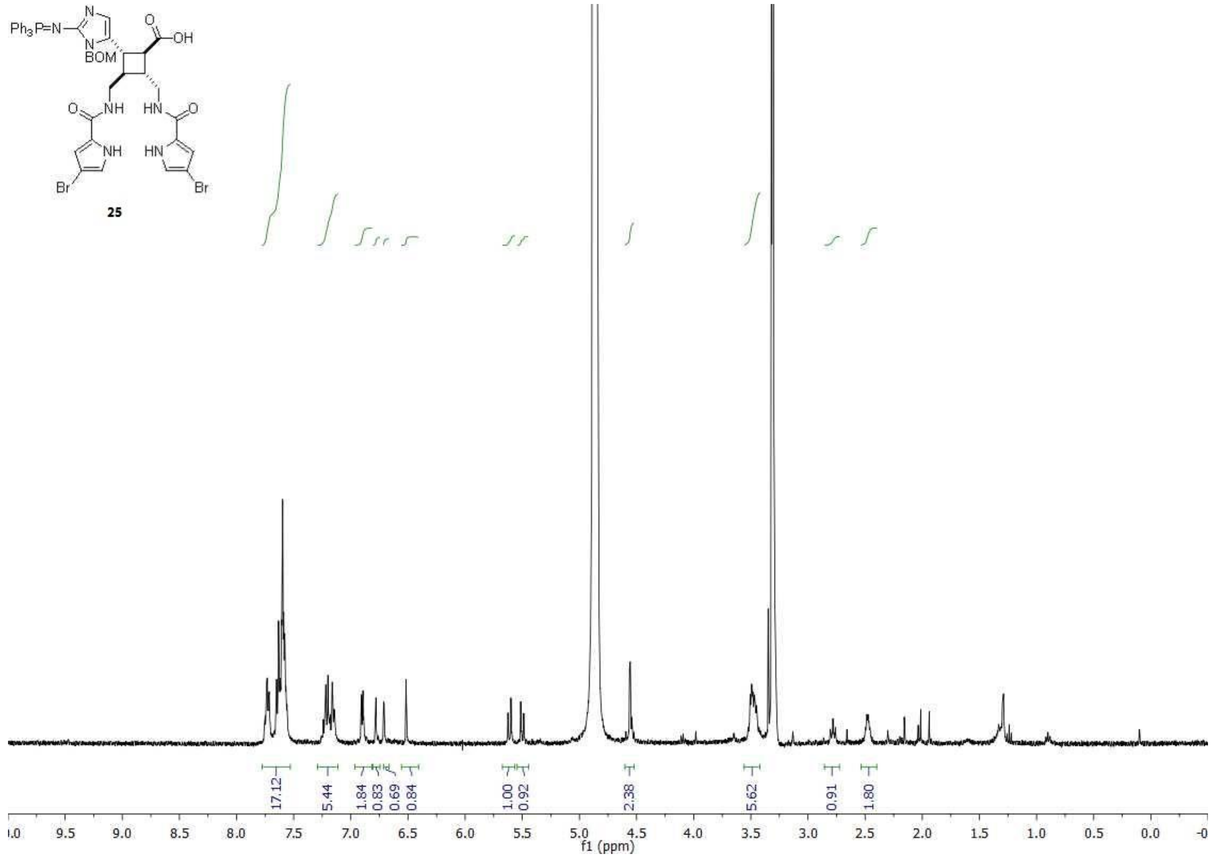
22


Ph$_3$P=N
N
N
BOM
OAc
NH$_2$
NH$_2$
22
172.63
138.22
135.05
133.67
133.56
130.84
130.71
129.74
129.24
128.56
127.73
126.70
111.39
72.03
71.88
65.59
44.95
43.33
43.16
41.02
37.57
33.87
20.76
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph$_3$P=N
N
N
BOM
OAc
NH
HN
O
O
NH
HN
Br
Br
23
3.34
12.69
2.98
1.83
0.83
0.89
0.88
0.82
0.88
1.74
2.20
2.14
3.89
1.26
3.35
2.85
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

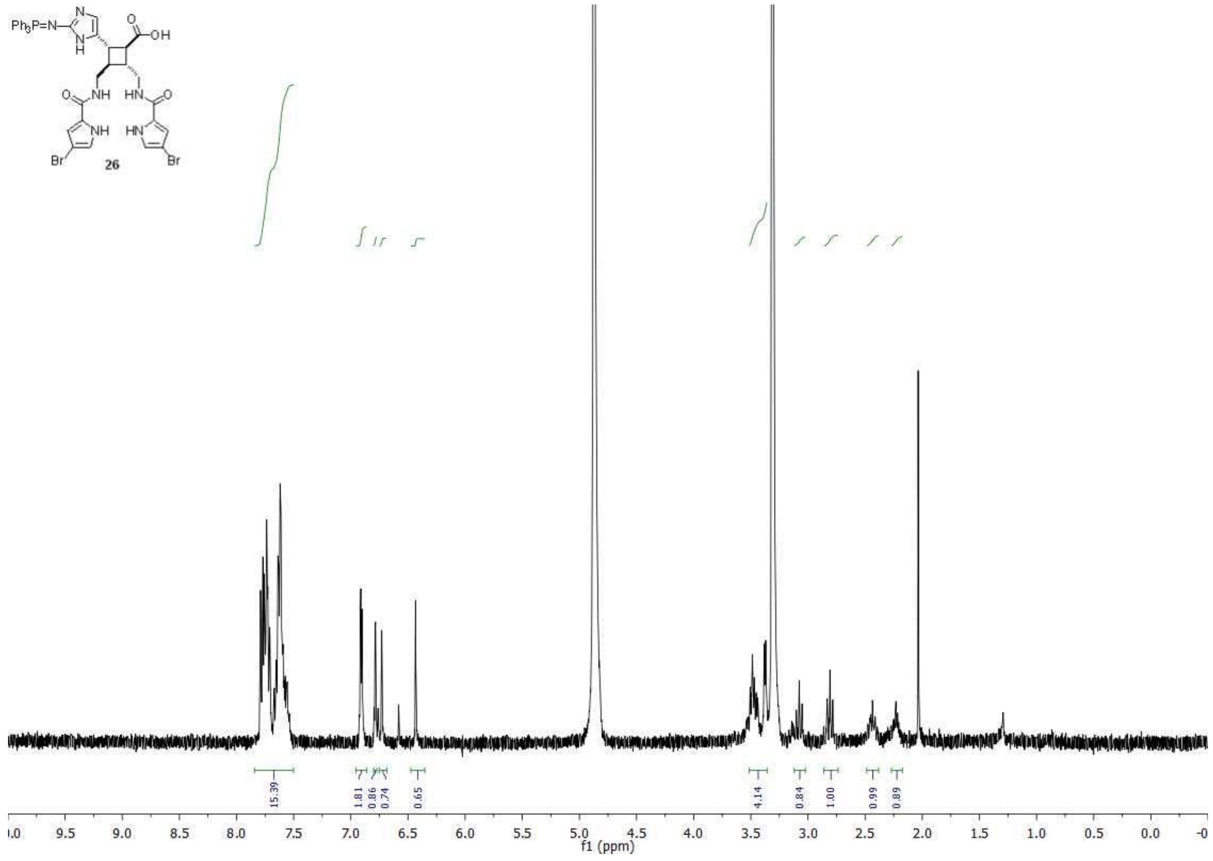

Ph3P=N
N
N
BOM
OH
O
NH
HN
O
NH
HN
Br
Br
24
21.44
6.52
1.08
0.90
1.00
0.88
0.85
2.26
2.42
2.58
5.24
1.10
1.23
2.21
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)


Ph3P=N
N
N
BOM
OH
O
NH
HN
O
NH
HN
Br
Br
24
162.77
148.08
134.90
133.63
133.52
130.77
130.64
129.63
129.05
128.51
127.91
126.87
122.89
113.17
110.07
97.48
72.18
71.67
63.97
43.87
43.23
43.08
39.98
34.04
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



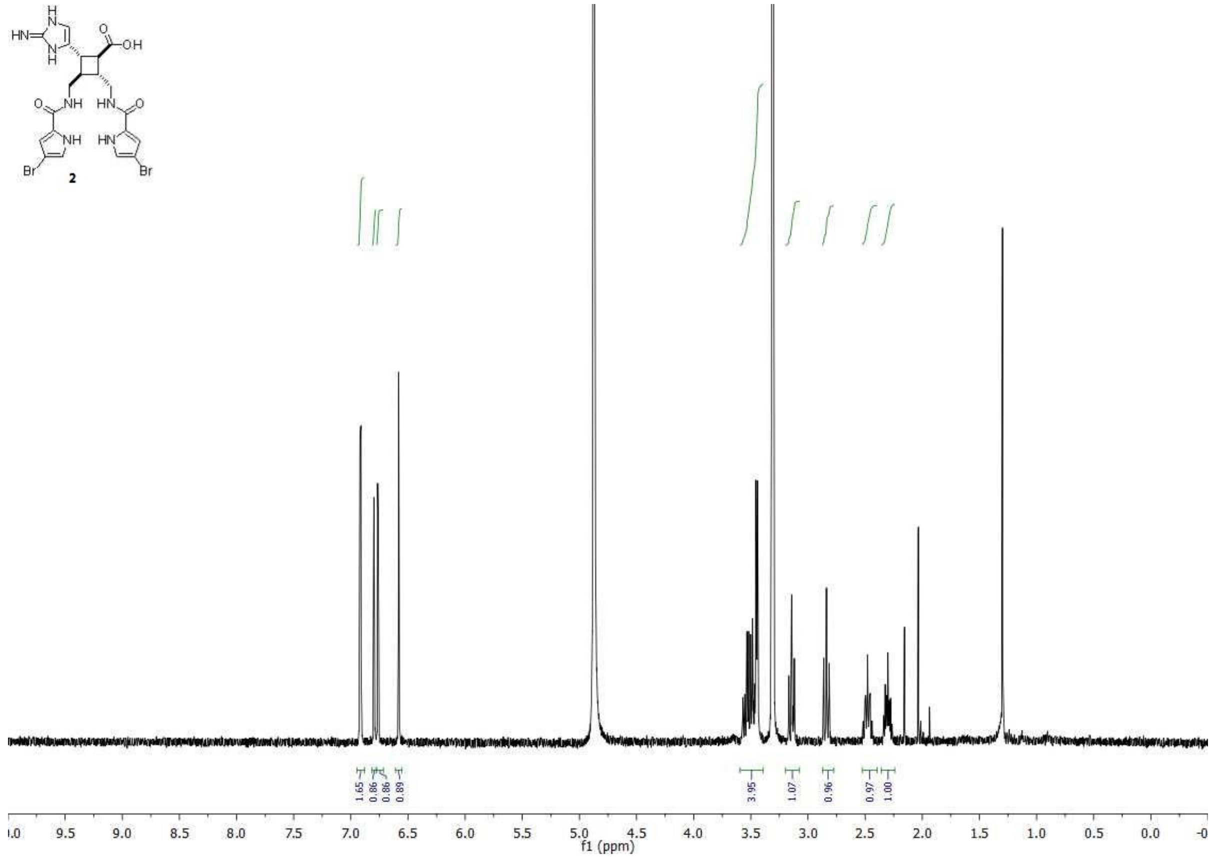
Ph3P=N
N
BOM
O
OH
O
NH
HN
O
NH
HN
Br
Br
17.12
5.44
1.84
0.83
0.69
0.84
1.00
0.92
2.38
5.62
0.91
1.80
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

25

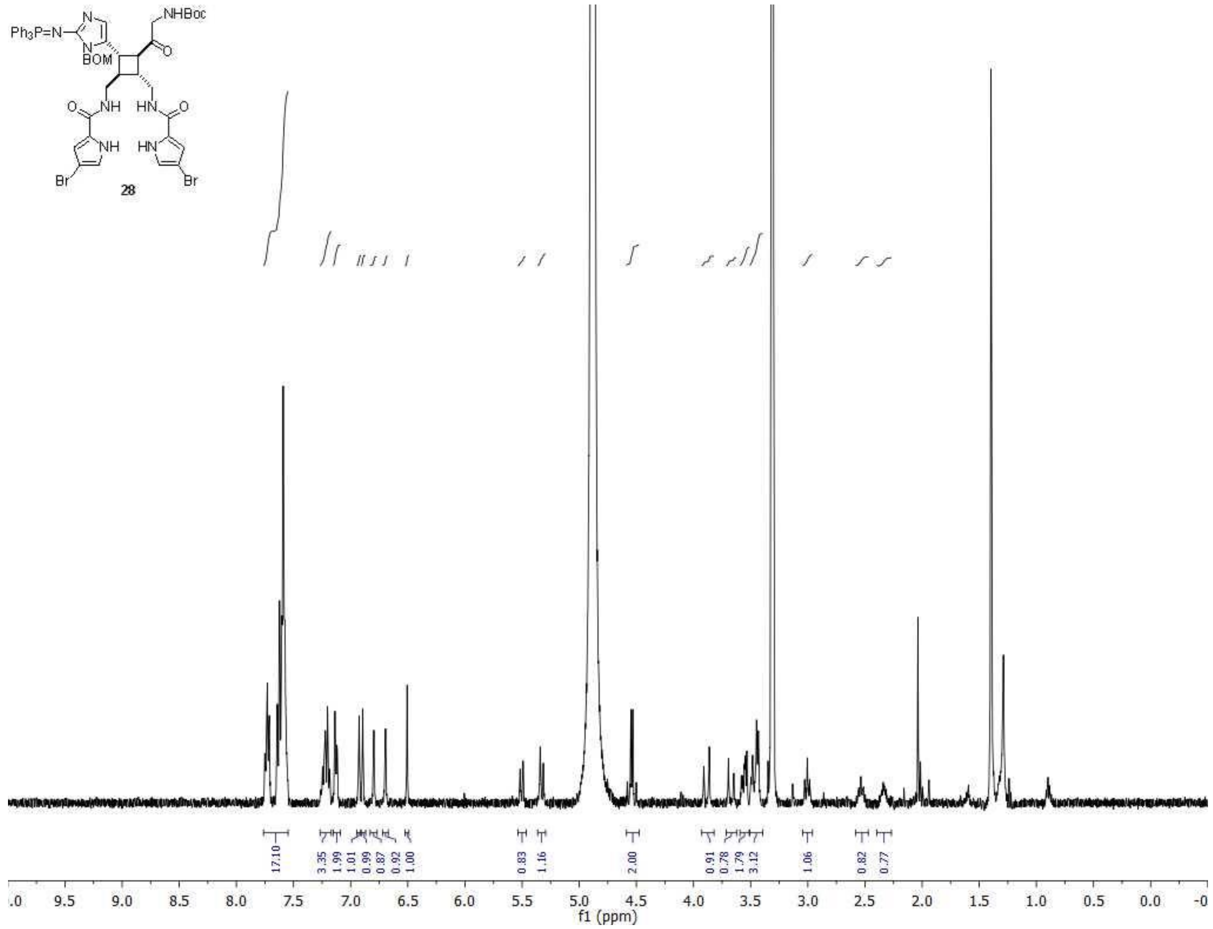


Ph3P=N
N
H
O
OH
O
NH
HN
O
NH
HN
Br
Br
15.39
1.81
0.86
0.74
0.65
4.14
0.84
1.00
0.99
0.89
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

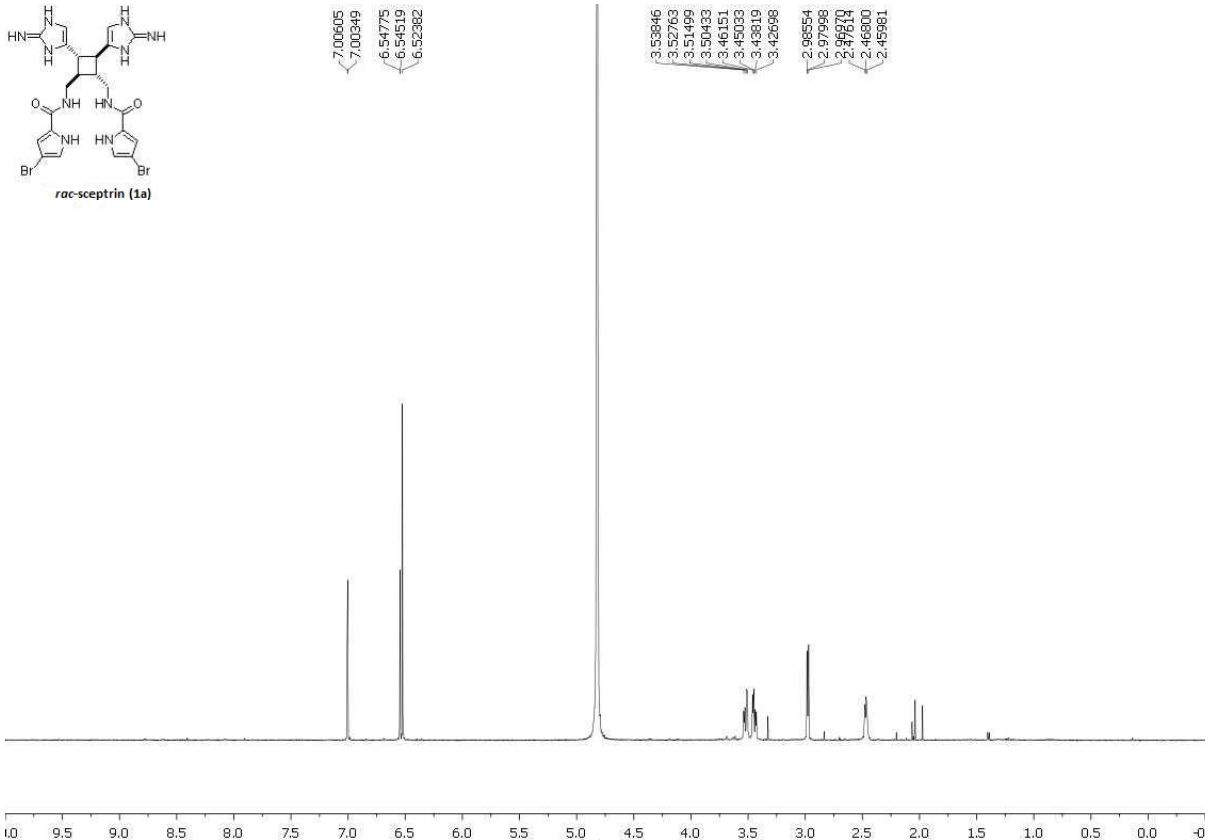
26


2

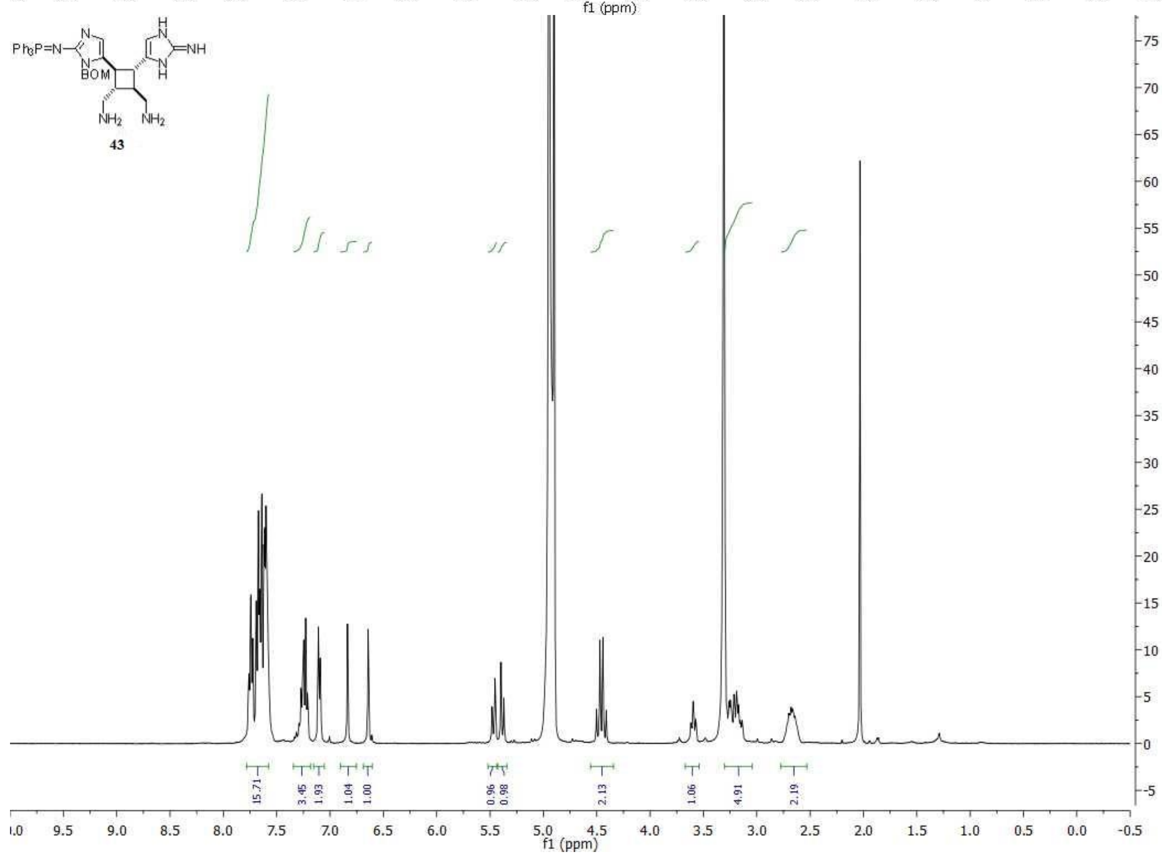
HN
NH
OH
Br
1.65
0.86
0.86
0.89
3.95
1.07
0.96
0.97
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)


28

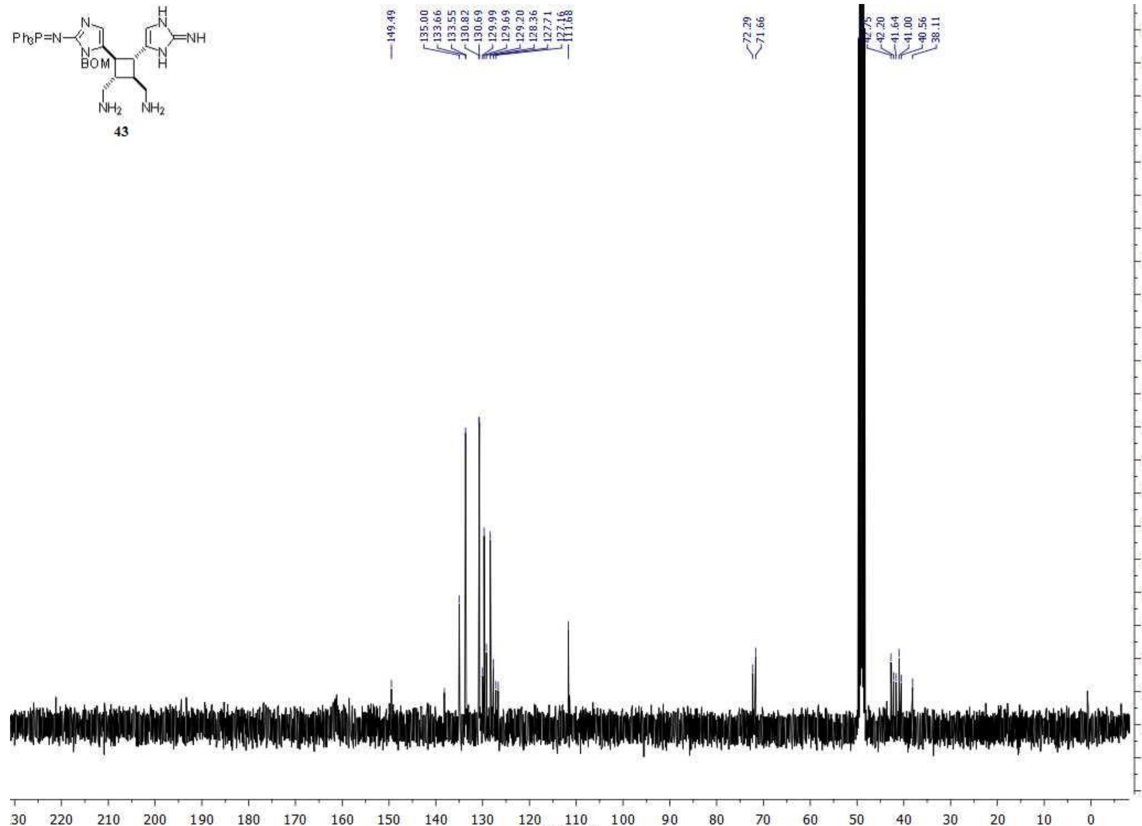
Ph3P=N
N
BOM
NHBoc
O
NH
HN
Br
17.10
3.35
1.99
1.01
0.99
0.87
0.92
1.00
0.83
1.16
2.00
0.91
0.78
1.79
3.12
1.06
0.82
0.77
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)



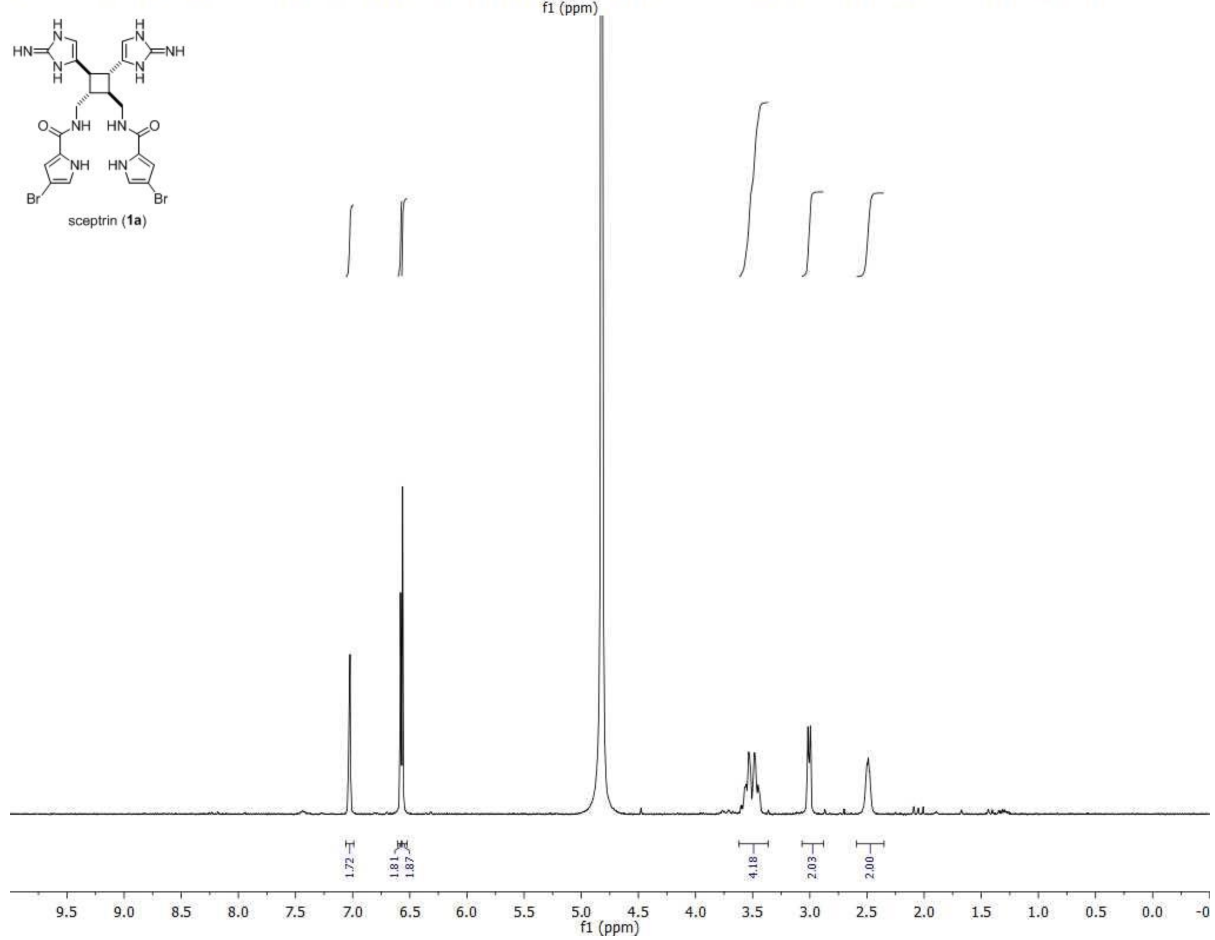
rac-sceptrin (1a)



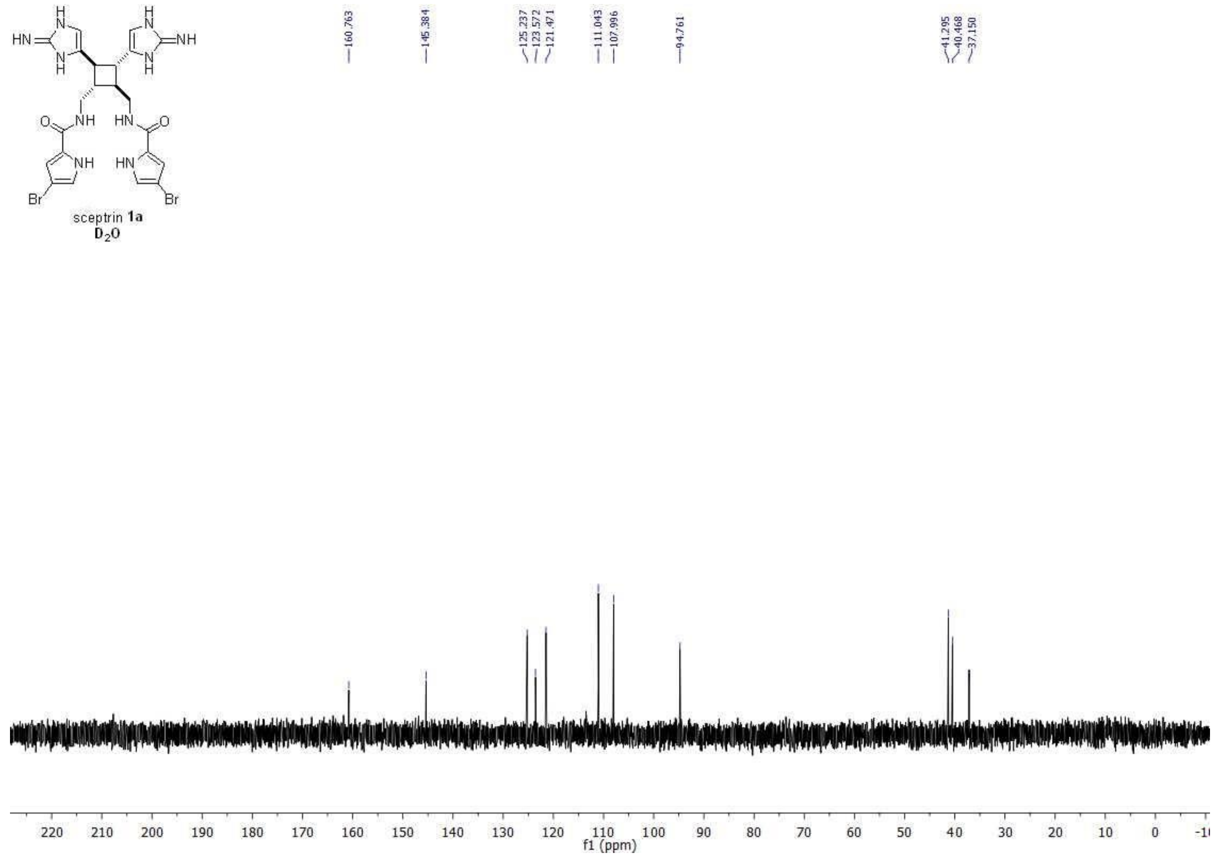
43



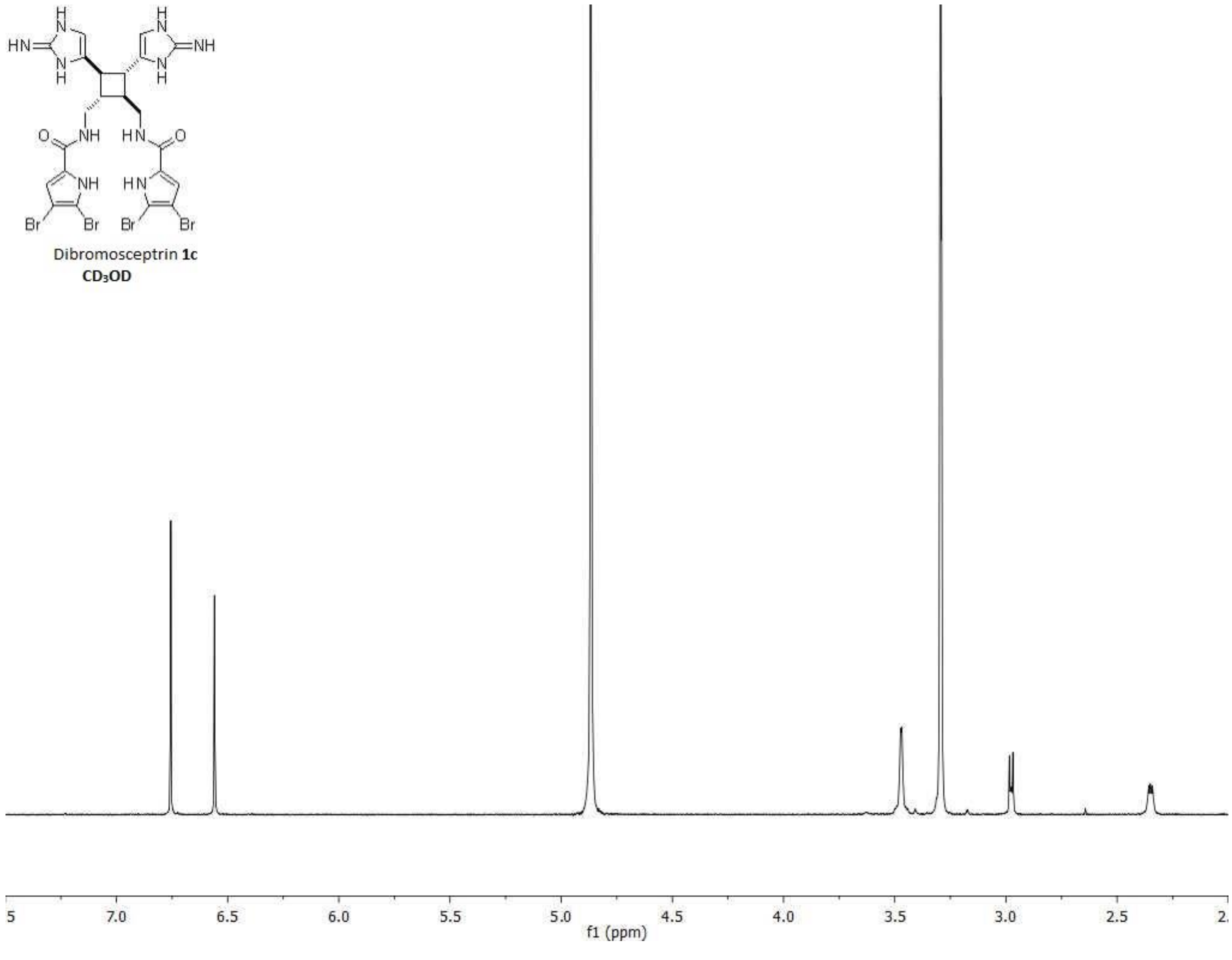
43



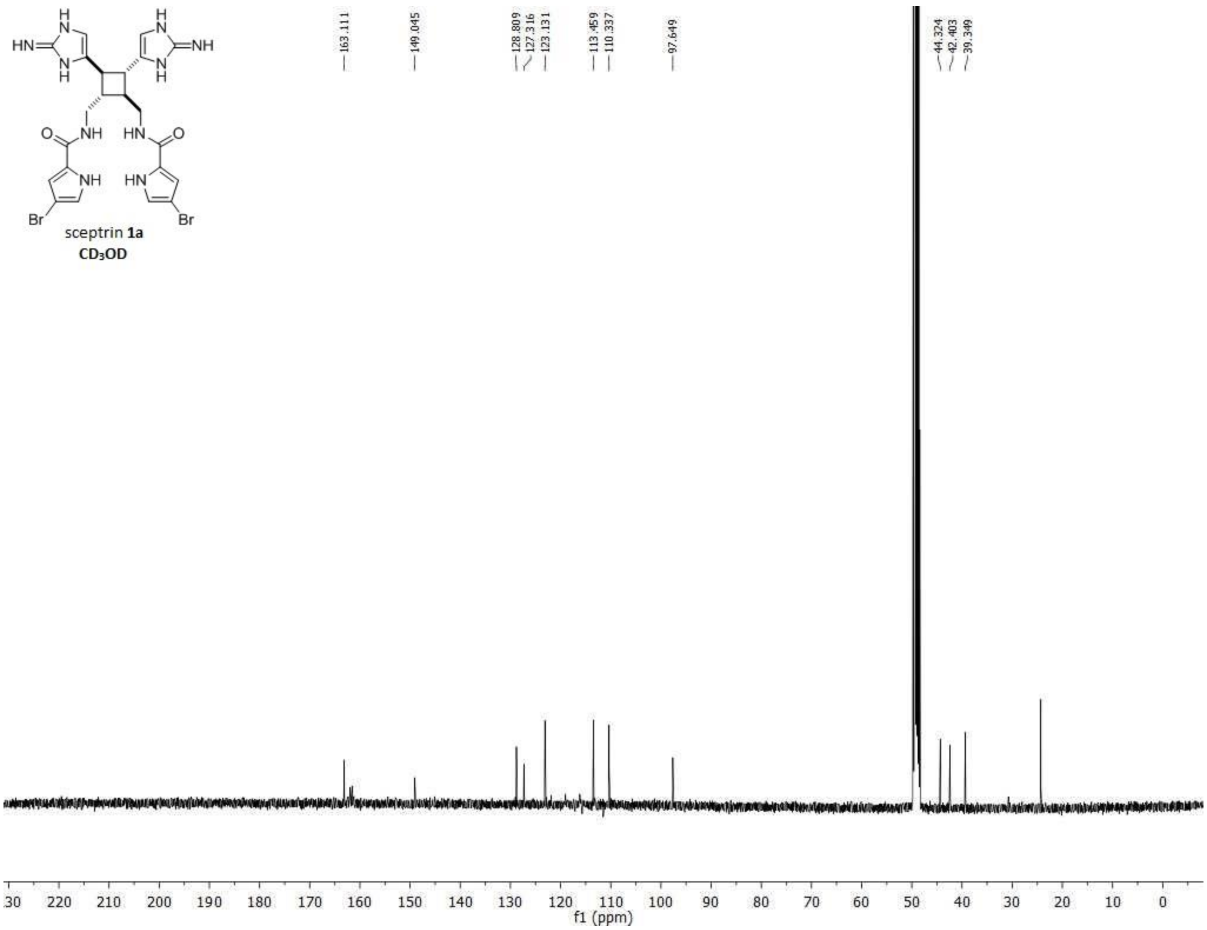
sceptrin (**1a**)


sceptrin **1a**

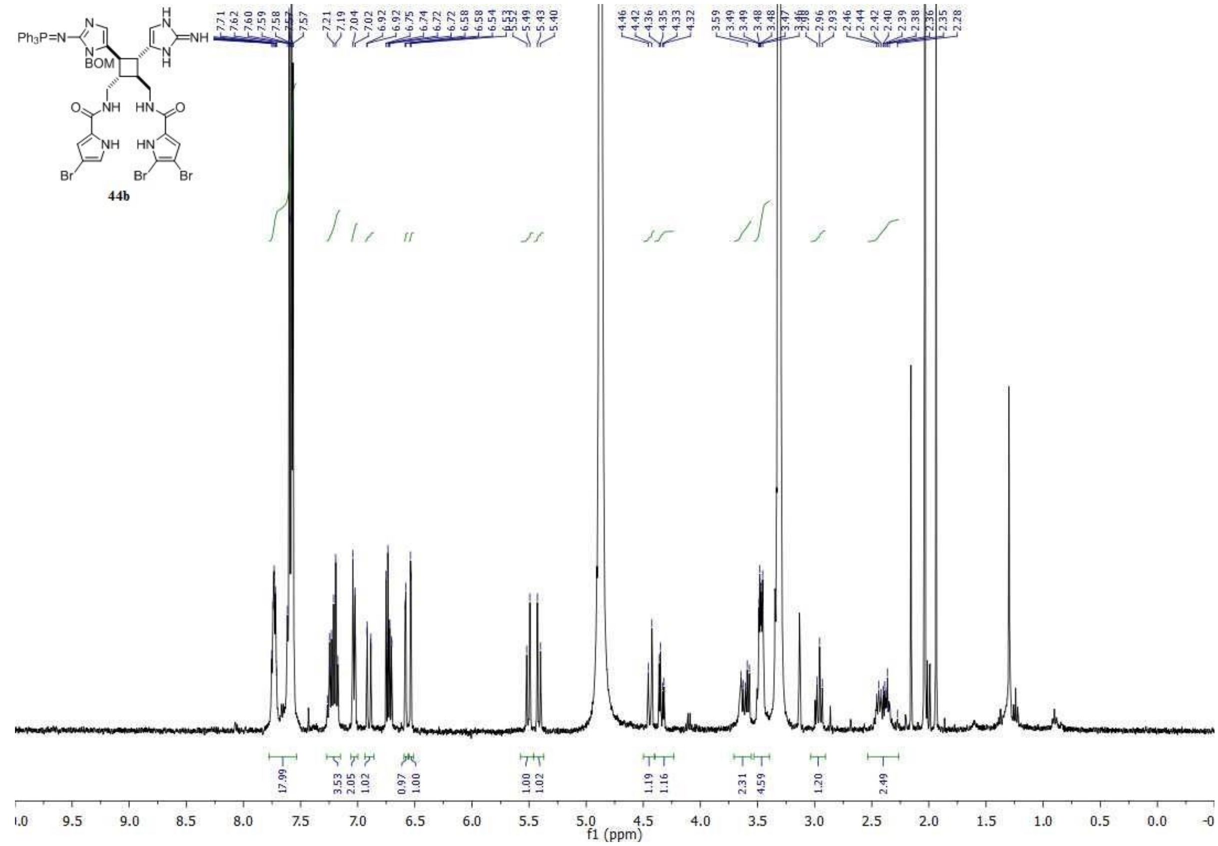
D_2O

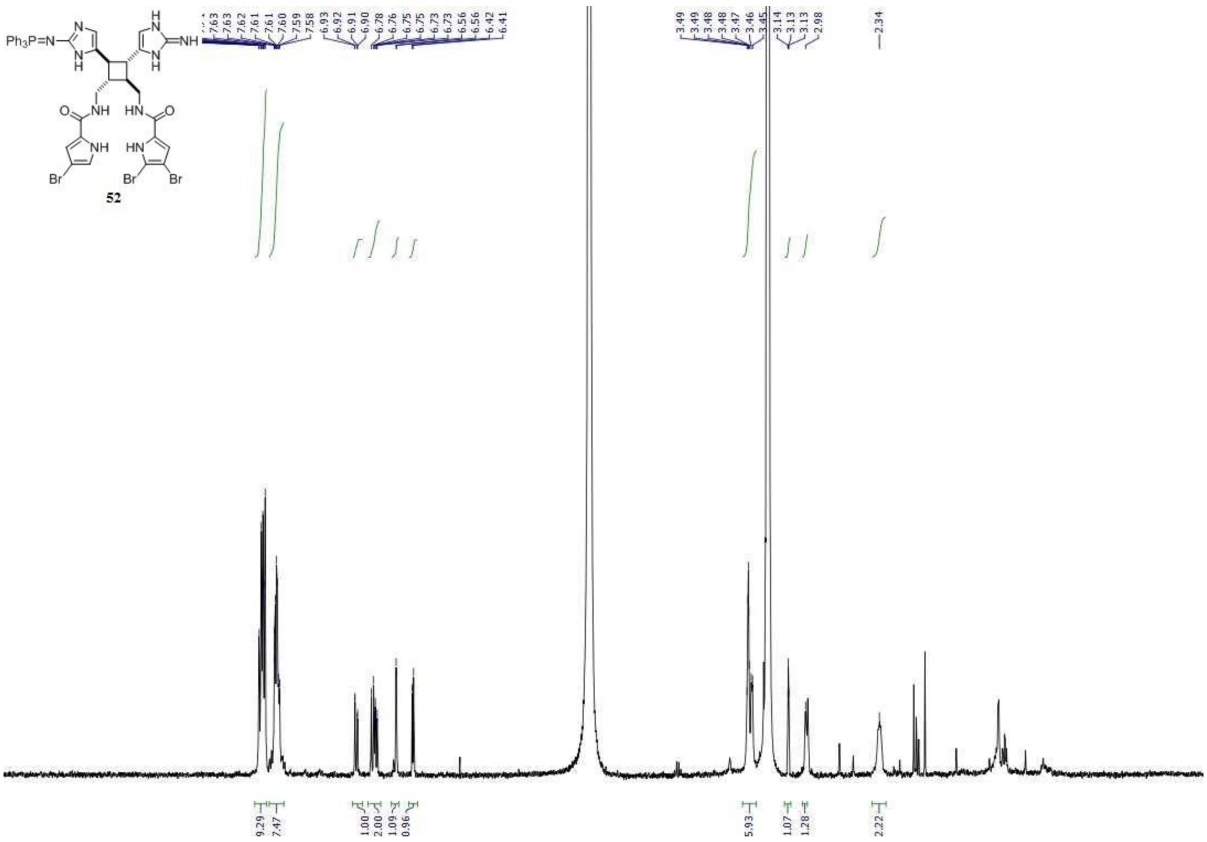

Dibromosceptrin **1c**

CD_3OD

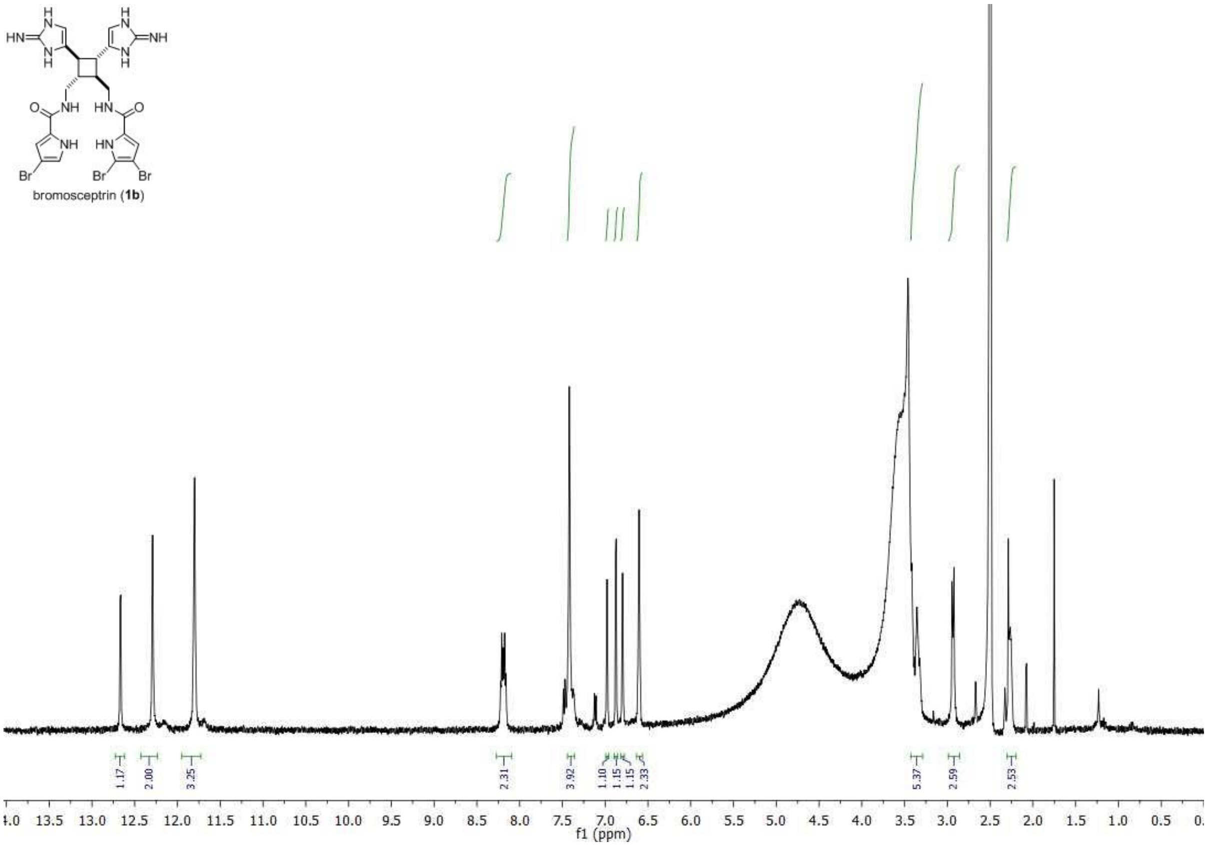

sceptrin **1a**

CD₃OD

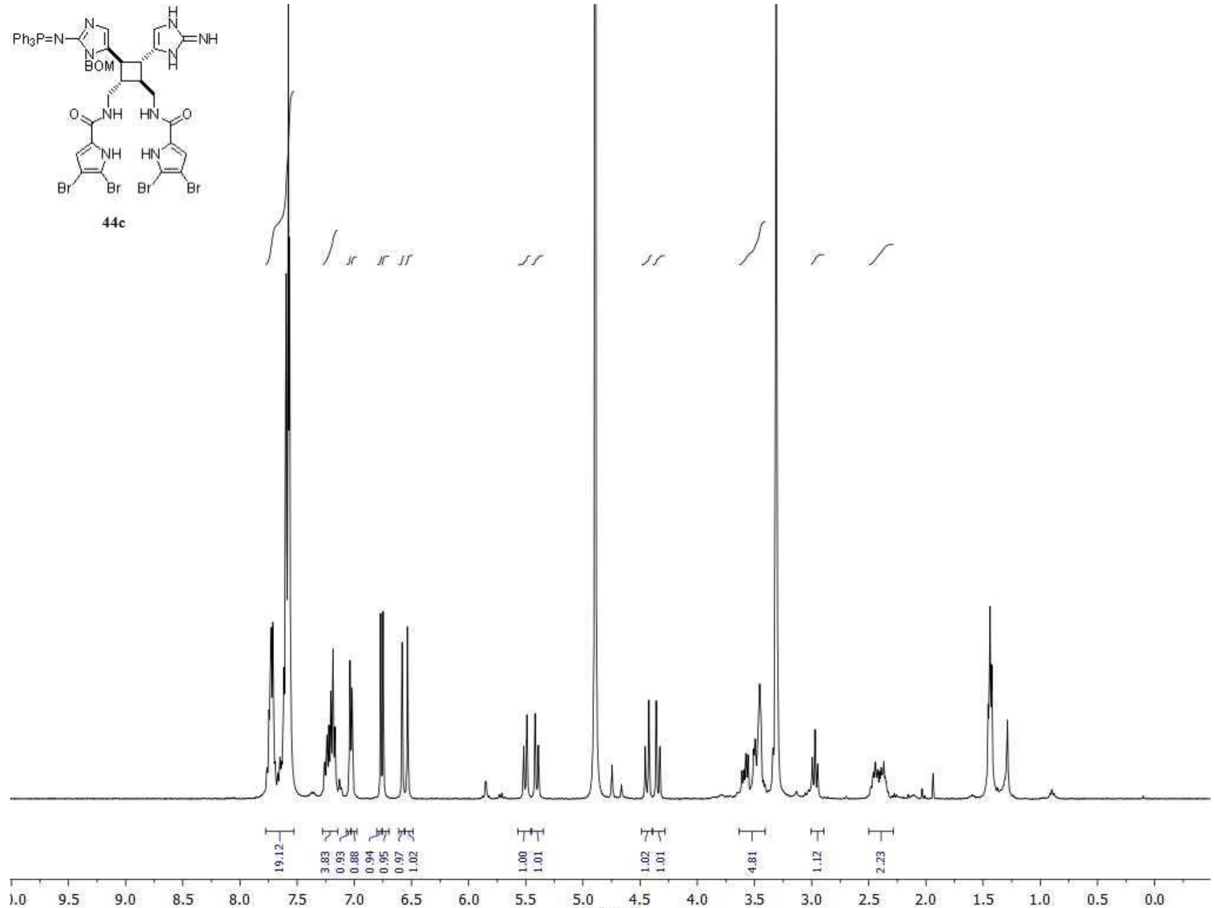

44b



52

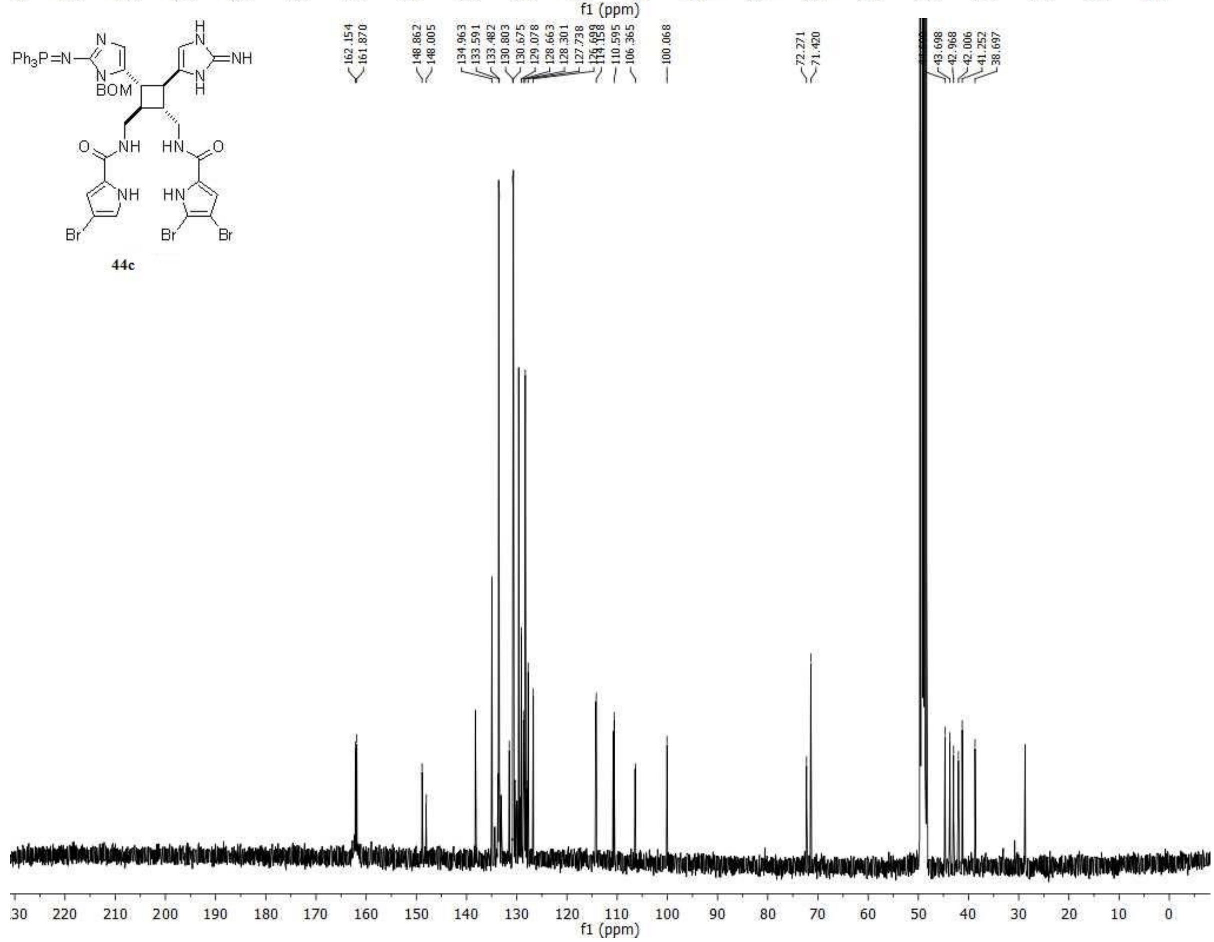


bromosceptrin (**1b**)



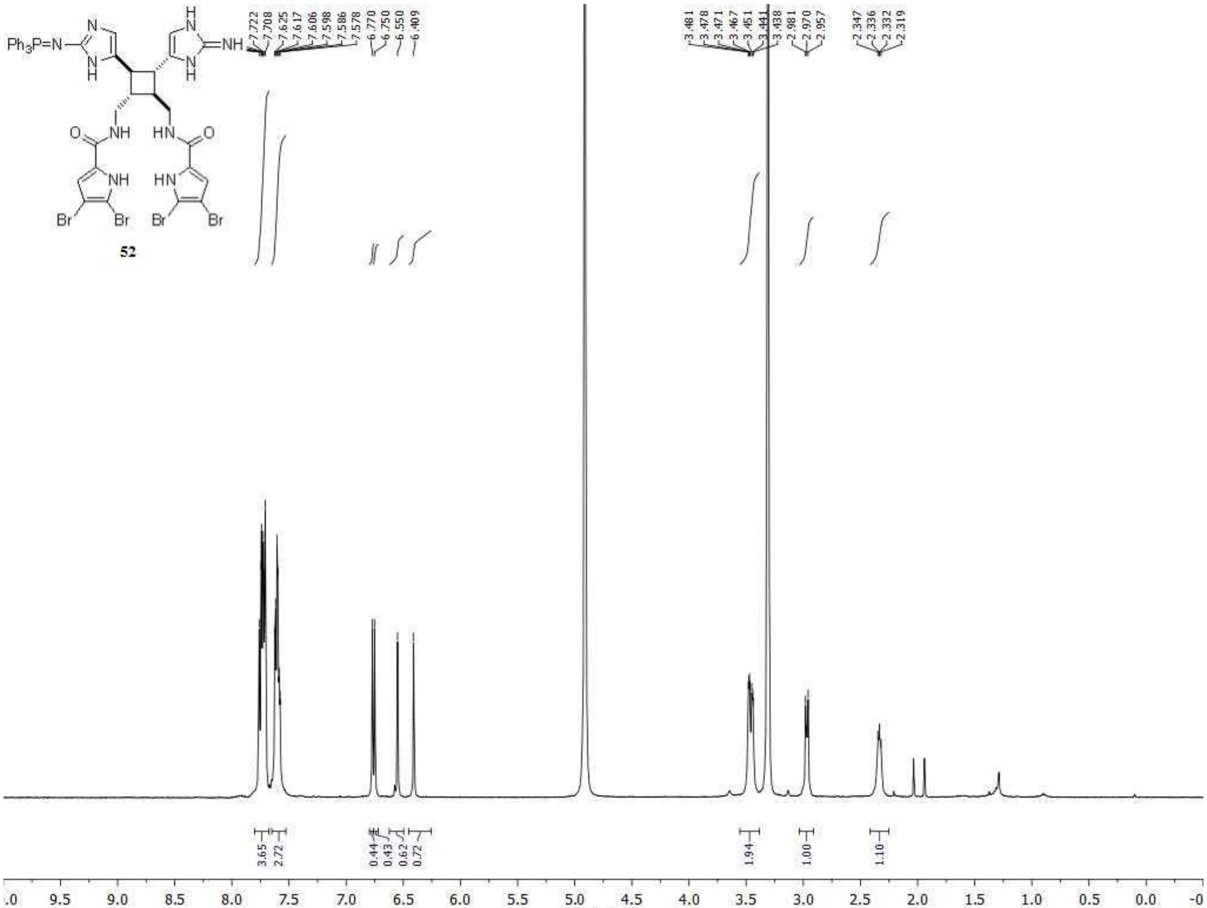
44c

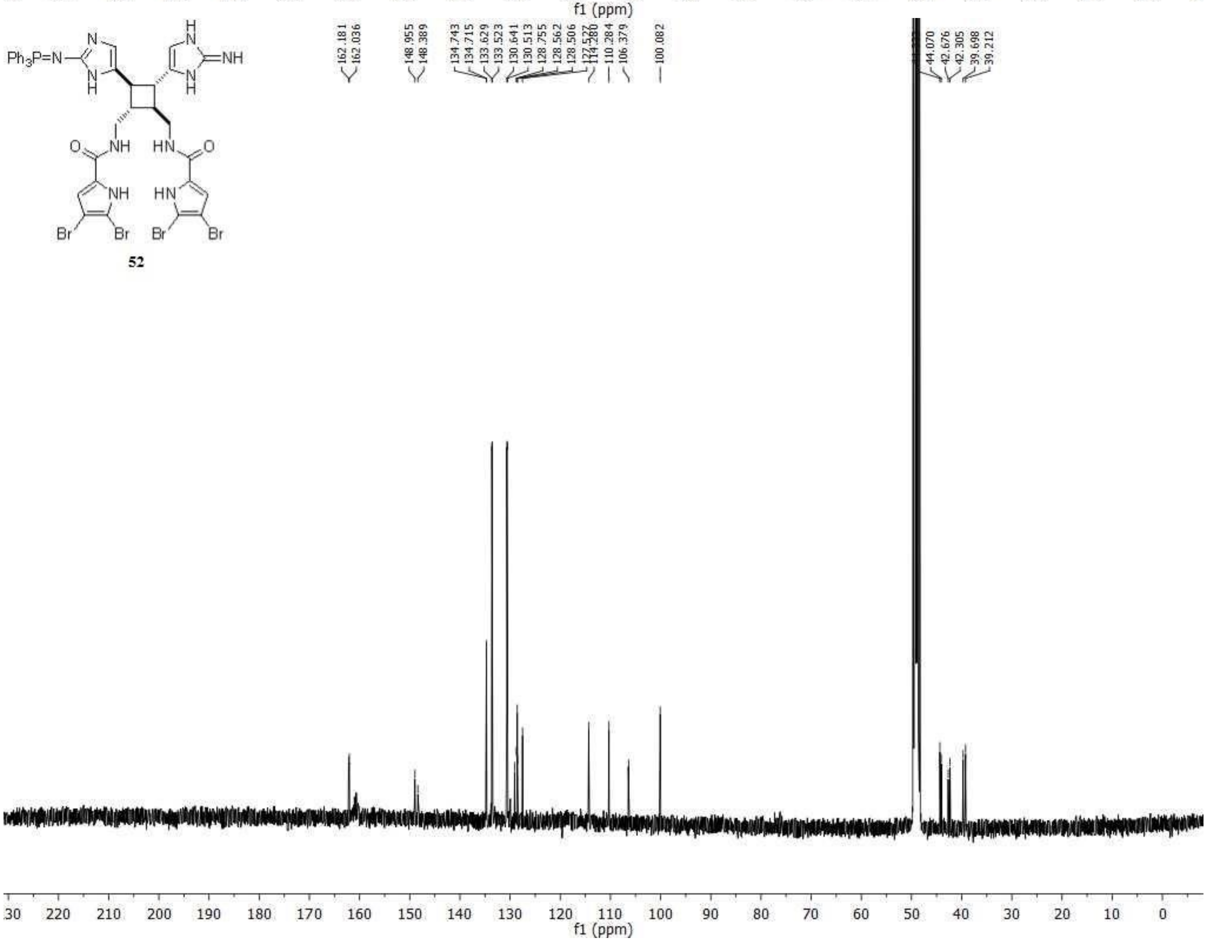
19.12
3.83
0.93
0.88
0.94
0.95
0.97
1.02
1.00
1.01
1.02
1.01
4.81
1.12
2.23
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

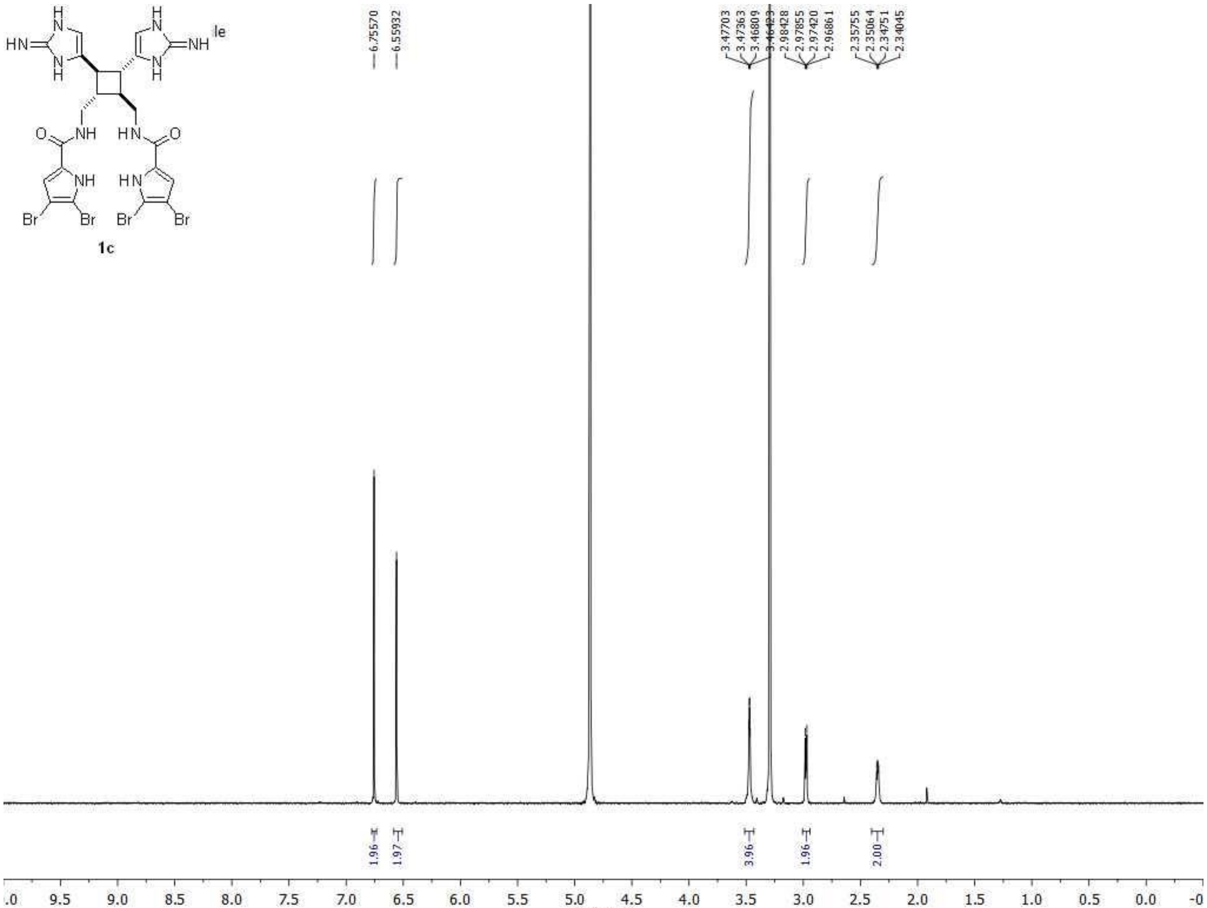


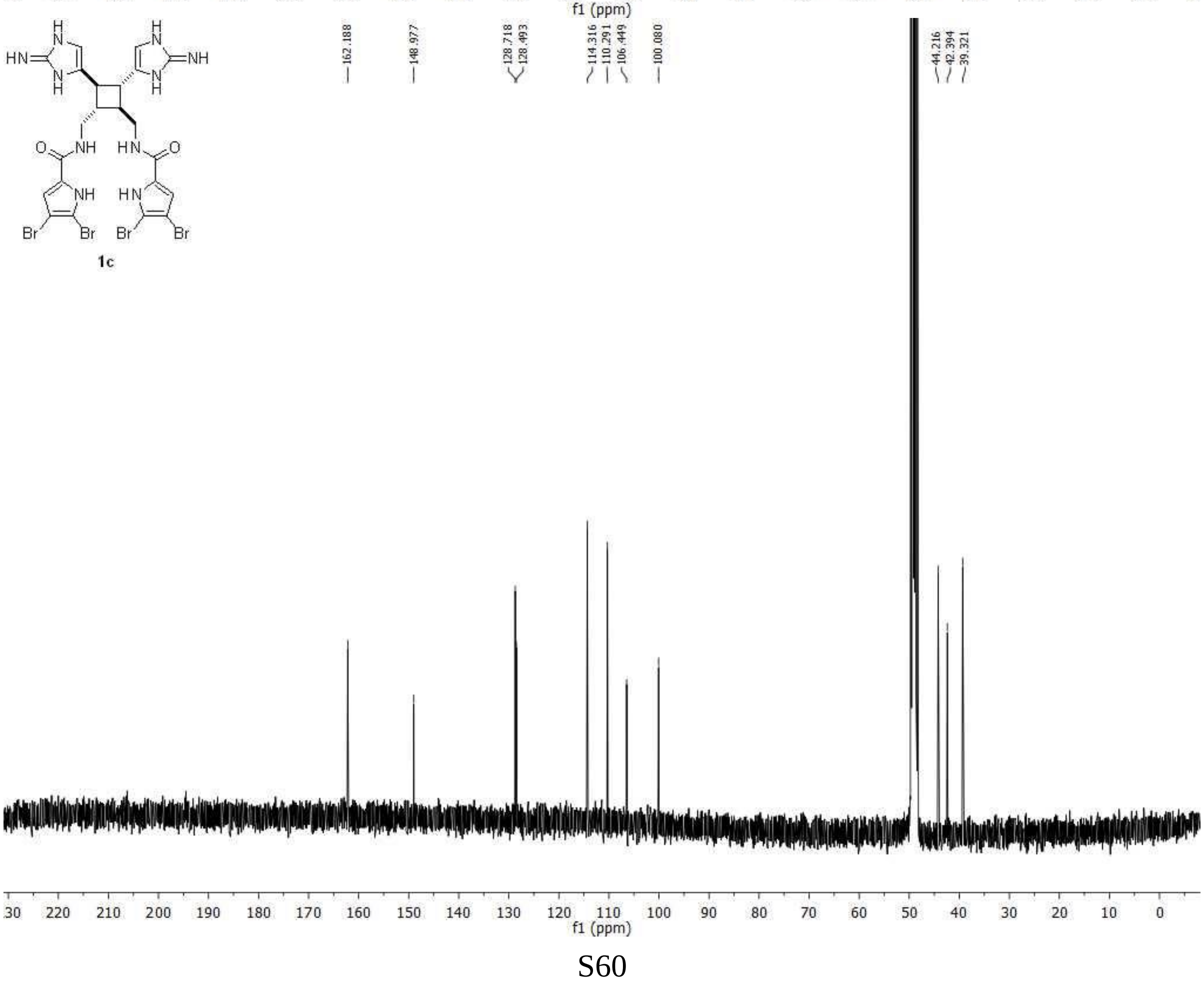
44c

162.154
161.870
148.862
148.005
134.963
133.591
133.482
130.803
130.675
129.078
128.663
128.301
127.738
126.699
114.158
110.595
106.365
100.068
72.271
71.420
43.698
42.968
42.006
41.252
38.697
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Ph3P=N
N
H
H
N
N
H
=NH
NH
HN
O
O
NH
HN
Br
Br
Br
Br
52
7.722
7.708
7.625
7.617
7.606
7.598
7.586
7.578
6.770
6.750
6.550
6.409
3.481
3.478
3.471
3.467
3.451
3.441
3.438
2.981
2.970
2.957
2.347
2.336
2.332
2.319
3.65
2.72
0.44
0.43
0.62
0.72
1.94
1.00
1.10
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)


Ph3P=N
N
H
H
N
N
H
=NH
NH
HN
O
O
NH
HN
Br
Br
Br
Br
52
162.181
162.036
148.955
148.389
134.743
134.715
133.629
133.523
130.641
130.513
128.755
128.562
128.506
127.527
114.280
110.284
106.379
100.082
44.070
42.676
42.305
39.698
39.212
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


HN
NH
H
N
O
Br
1c
6.75570
6.55932
3.47703
3.47363
3.46809
3.46423
2.98428
2.97855
2.97420
2.96861
2.35755
2.35064
2.34751
2.34045
1.96
1.97
3.96
1.96
2.00
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)


HN
NH
H
N
O
Br
1c
162.188
148.977
128.718
128.493
114.316
110.291
106.449
100.080
44.216
42.394
39.321
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)