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SYNTHESIS OF UNSYMMETRICAL HETEROBIARYLS WITH WINDING VINE-SHAPED MOLECULAR ASYMMETRY THROUGH A CONDENSATION PATHWAY‡

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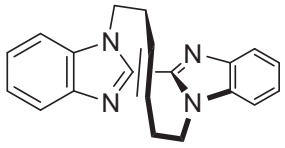
‡This paper is dedicated to Professor Masakatsu Shibasaki on celebration of his 70th birthday.

Abstract – Oxidative condensation of *N*-(3-buten-1-yl)-1,2-phenylenediamine with a formylated heteroarene bearing 3-buten-1-yl substituent gives unsymmetrical heterobiaryl in 42–86% yields. Ring-closing metathesis of the thus obtained product affords the cyclized product, which resulted in separation of each enantiomer by HPLC with a chiral column showing molecular asymmetry.

INTRODUCTION

Design of organic molecules involving molecular asymmetry attracts much interest in organic chemistry.[1] A wide range of chiral molecules have been developed to date and utilized in the field of asymmetric catalysis, advanced functional materials, etc.[2] We have recently revealed that a heterobiaryl derivative, whose aryl rings are connected by a certain number of alkenylene chain, shows chirality despite possessing no carbogenic stereocenter. We have been successful in affording bisimidazole and bithiophene derivatives **1** and **2** and transformation reactions, preparative resolution to enantiomers, and



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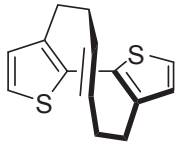

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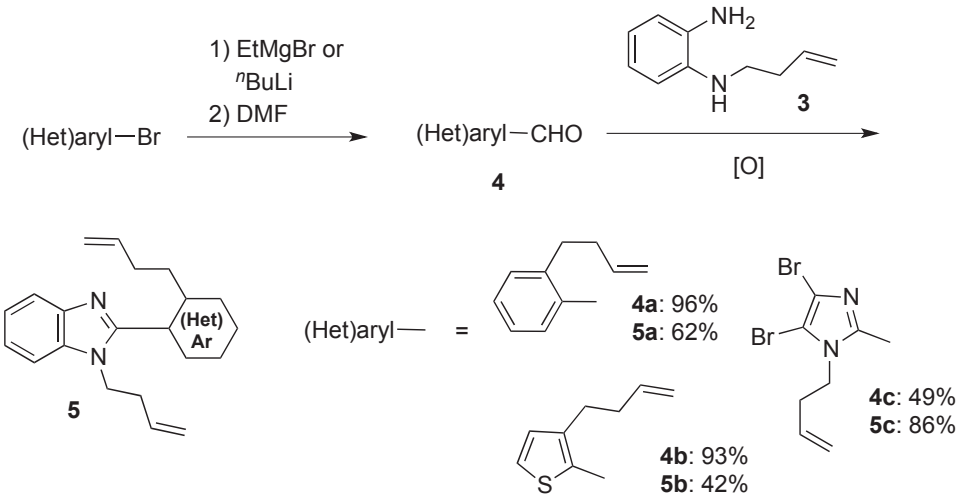
racemization behaviors of the thus resolved compound were also studied.[3] Such a unique chirality was named as winding vine-shaped molecular asymmetry, which showed axial, facial, and helical chiralities

in a single molecule.[1] The heterobiaryl was shown to be prepared by sequential dimerization of heteroaromatic compound by homocoupling at the carbon-hydrogen[4] or carbon-halogen bond by transition metal catalysis followed by ring-closing metathesis (RCM) with a ruthenium catalyst[5] leading to a large membered alkene. Our further concern turned to the preparation of such derivatives with molecular asymmetry bearing a different types of aromatic rings. We herein report that a pathway by condensation reaction is revealed practical for the preparation of the vine-shaped compounds with unsymmetrical heterobiaryls.[6]

RESULTS AND DISCUSSION

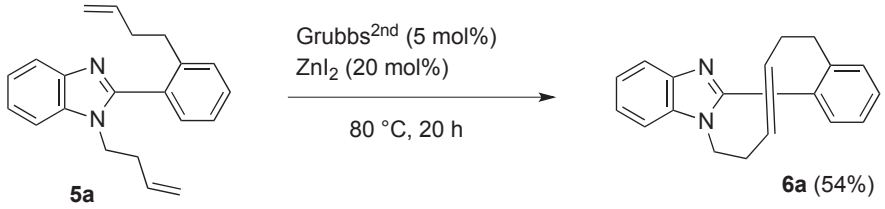
Preparation of heterobiaryl bearing 3-buten-1-yl substituent at each heteroaromatic ring was carried out by the oxidative condensation of formylated heteroaryl with *N*-(3-buten-1-yl)-1,2-phenylenediamine (**3**).[7] The corresponding aldehyde **4** was obtained by the reaction of bromide with a Grignard reagent or butyllithium to undergo halogen-metal exchange followed by treatment of DMF (49–96% yield). The reaction proceeded and aryl aldehydes **4** were obtained smoothly. The condensation reaction was then carried out with **3** and **4** in ethanol under aerobic conditions at 60 °C to give benzoimidazole **5** in 42–86% yield as shown in Scheme 1.



Scheme 1. Preparation of the metathesis precursors

The RCM reaction was carried out with Grubbs 2nd generation catalyst (5 mol%).[5] Considering our previous results on the metathesis of bisimidazole that the reaction proceeded smoothly in the presence of a Lewis acid,[3,8] the reaction was examined with Lewis acid as an additive. When heterobiaryl bearing a benzene ring **5a** was subjected to the reaction with ZnI_2 (20 mol%), the product was obtained in 54% yield (Scheme 2). Measurement of HRMS revealed to indicate M+H peak at 275.1561 which showed

agreement with the theoretical value 275.1548, suggesting that ring closure proceeded accompanied by formation of ethylene. Figure 1 shows ^{1}H NMR spectra of the metathesis precursor **5a** and the ring-closed product **6a**. By contrast that the spectrum of **5a** shows typical signals at ca. 4.8-5.0 ppm corresponding to the *exo*-methylenes, such signals disappeared in that of **6a** and four kinds of methylene signals changed to eight non-equivalent peaks by ring closure. Worthy of note is the shift of the vinyl protons at ca. 5.5 ppm to remarkably lower frequencies (ca. 4.1 and 4.5 ppm). The result suggests that these hydrogen atoms are located in shielded regions induced by the ring current of the benzoimidazole or benzene ring.



Scheme 2. Ring-closing metathesis of **5a**

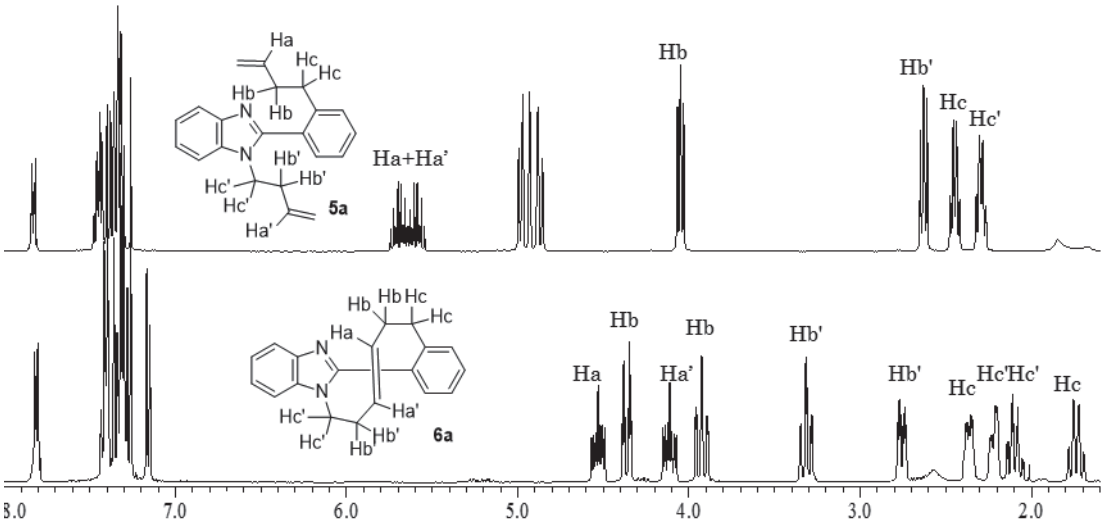


Figure 1. ^{1}H NMR spectra of **5a** and **6a**

Other heterobiaryls **5b** and **5c** were also subjected to the RCM reaction. As shown in Table 1, reactions of **5a**-**5c** were carried out under several conditions. In contrast with the case of bisimidazole,[3] it was found that metathesis of **5a** proceeded smoothly without additive to afford **6a** in 96% yield after stirring at 80 ºC for 4 h. The reaction of heterobiaryl bearing imidazole and thiophene rings **5b** also took place to give **6b** in a moderate yield (59%). It was found that the yield of **6b** was remarkably improved when the reaction was carried out under diluted conditions (0.025 M). The bisimidazole bearing 4,5-dibromo and

benzimidazole-fused ones **5c** was also subjected to the reaction. Although little reaction took place without additive under 0.1 M, the RCM reaction was found to proceed in the presence of 20 mol% $Ti(O^iPr)_4$ in excellent yield (>99%). By contrast, the reaction under diluted conditions (0.025 M) proceeded in 73% yield without additive.

Table 1. Ring-closing metathesis of heterobiaryls **5**[a]

Substrate	Additive (mol%)	Conc.[b] (M)	Time (h)	Yield[c] (%)
5a	ZnI_2 (20)	0.1	20	54
5a	none	0.1	4	96[d]
5b	none	0.1	23	59[d]
5b	none	0.025	23	>99[d]
5c	none	0.1	17	5[d]
5c	$Ti(O^iPr)_4$ (20)	0.1	17	>99
5c	none	0.025	19	73[d]

[a] The reaction was carried out with **5** (0.1-0.5 mmol) in 1,2-dichloroethane at 80 °C in the presence of Grubbs 2nd generation catalyst (5 mol%). [b] Substrate/solvent. [c] Unless noted, isolated yield of **6** was shown. [d] The yield was estimated by ^1H NMR using $(Me_3Si)_2O$ or 1,1,2,2-tetrachloroethane as an internal standard.

The obtained ring-closed products bearing different heteroaromatic groups **6a**-**6c** were subjected to HPLC analysis with a chiral column (DAICEL Chiralpak IC or IF). Figure 2 shows the chromatogram of **6a** using hexane/EtOH = 50:1 as an eluent (with Chiralpak IF, flow rate = 0.3 mL/min). Analysis of **6a** indicated clear separation at the retention times of 236.3 and 244.3 min. Other heterobiaryls **6b** and **6c** also showed clear separation under similar conditions.[9]

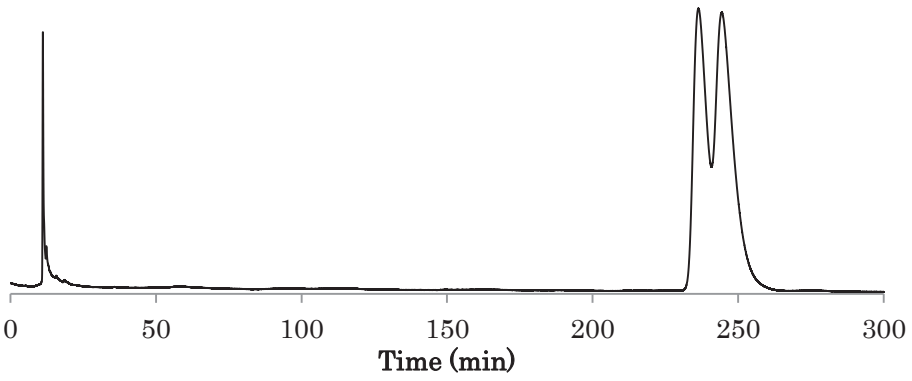


Figure 2. HPLC profile of **6a** with chiral column

In summary, we showed that metathesis precursors heterobiaryl **5** composed of different (hetero)aryl groups underwent RCM reaction to afford macrocyclic olefin **6**, which showed molecular asymmetry. The condensation pathway by the oxidative reaction of the corresponding diamine and aldehyde was found to occur successfully to afford **5**. Efforts on preparative resolution by HPLC with a chiral column or asymmetric RCM are under way to obtain enantioenriched **6** and the results is reported in due course, if successful.

EXPERIMENTAL

General. All the reactions were carried out under nitrogen atmosphere. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were measured on JEOL ECZ400 as a $CDCl_3$ solution. The chemical shifts were expressed in ppm with $CHCl_3$ (7.26 ppm for ^{1}H) or $CDCl_3$ (77.0 ppm for ^{13}C) as internal standards. IR spectra were recorded on Bruker Alpha with an ATR attachment (Ge). High resolution mass spectra (HRMS) were measured by JEOL JMS-T100LP AccuTOF LC-Plus (ESI) with a JEOL MS-5414 DART attachment. For thin layer chromatography (TLC) analyses throughout this work, Merck precoated TLC plates (silica gel 60 F_{254}) were used. Purification by HPLC with preparative SEC column (JAI-GEL-2H) was performed by JAI LC-9201. HPLC analysis with a chiral column was performed by HPLC analyses with a chiral column was carried out with JASCO LC-2000 Plus with chiral column Daicel Chiralpak IC or IF (0.46 cm I.D. x 25 cm) using UV (254 nm) detector. *N*-(3-Buten-1-yl)-1,2-phenylenediamine (**3**) was prepared in a manner shown in the literature.[7] Other chemicals were purchased and used without further purification.

2-(3-Buten-1-yl)benzaldehyde (4a): To a solution of 2-(3-buten-1-yl)bromobenzene (3.8 g, 18 mmol) in anhydrous THF (12 mL) was added a hexane solution of ^{n}BuLi (1.6 M, 12.4 mL, 20 mmol) dropwise at –78 °C and stirring was continued for 30 min followed by addition of DMF (3.34 mL, 43.2 mmol). The reaction temperature was gradually raised to room temperature. After stirring at room temperature for 18 h, the solution was poured into a mixture of 1 M sat. ammonium chloride and Et_2O to result in phase separation. The aqueous phase was extracted twice with Et_2O and the combined organic layer was dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure left a crude oil, which was purified by column chromatography on silica gel using hexane/isopropyl acetate = 4:1–1:1 as an eluent to afford 2.76 g of **4a** (96% yield). ^{1}H NMR (400 MHz) δ 2.38 (tddd, J = 7.8, 6.4, 1.4, 0.9 Hz, 2H), 3.14 (t, J = 7.8 Hz, 2H), 4.95-5.09 (m, 2H), 5.86 (ddt, J = 17.4, 10.5, 6.4 Hz, 1H), 7.28 (d, J = 7.8 Hz, 1H), 7.38 (ddd, J = 7.8, 7.3, 1.4 Hz, 1H), 7.51 (ddd, J = 7.8, 7.3, 1.4 Hz, 1H), 7.84 (dd, J = 7.8, 1.4 Hz, 1H), 10.27 (s, 1H); ^{13}C NMR δ 31.8, 35.8, 115.3, 126.4, 130.9, 131.9, 133.6x2, 137.2, 144.3, 192.2; IR (ATR) 3073,

2978, 2933, 1696, 1640, 1599, 913 cm^{-1}; HRMS (DART+) Calcd for $C_{11}H_{13}O$ $[M+H]^+$: 161.0966; found: *m/z* 161.0961.

3-(3-Buten-1-yl)-2-formylthiophene (4b): To 2-bromo-3-(3-buten-1-yl)thiophene (8.1 g, 37 mmol) was added a THF solution of EtMgCl (1.0 M, 41 mL, 39 mmol) dropwise at 0 °C and stirring was continued at 66 °C for 3 h followed by addition of excess DMF (43 mL). After stirring at room temperature for 1 h, the solution was poured into a mixture of 1 M hydrochloric acid and Et_2O to result in phase separation. The aqueous phase was extracted twice with Et_2O and the combined organic layer was dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure left a crude oil, which was purified by column chromatography on silica gel using hexane/isopropyl acetate = 100:0–91:9 to afford 5.8 g of **4b** (93% yield). ^{1}H NMR (400 MHz) δ 2.42 (td, *J* = 7.0, 6.8 Hz, 2H), 3.07 (t, *J* = 7.6 Hz, 2H), 5.00-5.08 (m, 2H), 5.82 (ddt, *J* = 17.4, 10.1, 6.8 Hz, 1H), 7.02 (d, *J* = 5.0 Hz, 1H), 7.65 (dd, *J* = 5.0, 0.9 Hz, 1H), 10.0 (d, *J* = 0.9 Hz, 1H); ^{13}C NMR (100 MHz) δ 27.9, 35.0, 116.0, 130.6, 134.4, 136.6, 137.7, 151.4, 182.1; IR (ATR): 3077, 2932, 2858, 1657, 1526, 1426, 1390, 1220, 1092, 997, 916, 841 cm^{-1}; HRMS (DART+) Calcd for $C_9H_{11}OS$ $[M+H]^+$: 167.0531; found: *m/z* 167.0529.

4,5-Dibromo-1-(3-buten-1-yl)-2-formylimidazole (4c): To a solution of 2,4,5-tribromo-*N*-(3-buten-1-yl)imidazole[3] (1.78 g, 5.0 mmol) in 5.0 mL of THF was added EtMgCl (1.0 M THF solution, 5.5 mL, 5.5 mmol) at 0 °C. Stirring was continued at 0 °C for 20 min followed by addition of DMF (2.71 mL, 35.0 mmol). After stirring at room temperature for 2 h, the reaction mixture was poured into a mixture of sat. NH_4Cl and isopropyl acetate to result in phase separation. Aqueous was extracted with isopropyl acetate twice and the combined organic layer was washed with aq. $NaHCO_3$ and dried over anhydrous sodium sulfate. Concentration of the solvent under reduced pressure left a crude oil, which was purified by column chromatography on silica gel using hexanes/isopropyl acetate = 100:1 to 10:1 as an eluent to afford 0.75 g of **4c** (49% yield) accompanied by an unidentified regioisomer as a byproduct. ^{1}H NMR (400 MHz) δ 2.49 (td, *J* = 7.3, 6.9 Hz, 2H), 4.52 (t, *J* = 7.3 Hz, 2H), 5.00-5.14 (m, 2H), 5.76 (ddt, *J* = 17.4, 10.5, 6.9 Hz, 1H), 9.57 (s, 1H); ^{13}C NMR (100 MHz) δ 34.3, 46.8, 114.1, 118.8, 120.1, 132.5, 143.2, 179.9; IR (ATR) 3081, 2980, 2957, 2915, 2840, 1689, 1459, 1410, 1220, 993, 923 cm^{-1}; HRMS (DART+) Calcd for $C_8H_9{}^{79}Br_2N_2O$ $[M+H]^+$: 306.9081; found: *m/z* 306.9090.

General procedure for the preparation of heterobiaryl 5 representative as the formation of *N*-(3-buten-1-yl)-2-(2-(3-buten-1-yl)phenyl)benzoimidazole (5a): To a 20 mL of round-bottomed flask equipped with a magnetic stirring bar were dissolved *N*-(3-buten-1-yl)-1,2-phenylenediamine (**3**, 81 mg,

0.50 mmol) and 2-(3-buten-1-yl)benzaldehyde (**4a**, 80 mg, 0.50 mmol) in EtOH (5.0 mL). $CuSO_4$ (0.8 mg, 0.005 mmol) was added to the solution and stirring was continued at 60 °C for 41 h. After cooling to room temperature, the mixture was poured into brine and the product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous sodium sulfate and removal of the solvent left a crude material, which was purified by column chromatography on silica gel using hexane/isopropyl acetate = 20:1 to 1:1 (gradient) as an eluent to afford 93 mg of **5b** (62% yield). ^{1}H NMR (400 MHz) δ 2.29 (td, *J* = 7.3, 6.9 Hz, 2H), 2.45 (td, *J* = 7.3, 7.3 Hz, 2H), 2.63 (t, *J* = 7.3 Hz, 2H), 4.05 (t, *J* = 7.3 Hz, 2H), 4.87 (dd, *J* = 10.1, 0.9 Hz, 1H), 4.91 (dd, *J* = 17.1, 0.9 Hz, 1H), 4.95 (dd, *J* = 17.1, 1.4 Hz, 1H), 4.98 (dd, *J* = 10.5, 1.4 Hz, 1H), 5.60 (ddt, *J* = 17.1, 10.1, 7.3 Hz, 1H), 5.69 (ddt, *J* = 17.1, 10.5, 6.9 Hz, 1H), 7.29-7.49 (m, 7H), 7.80-7.86 (m, 1H); ^{13}C NMR (100 MHz) δ 32.5, 33.6, 34.6, 43.6, 109.8, 114.9, 117.7, 119.9, 121.9, 122.4, 125.7, 129.3, 129.7x2, 130.2, 133.5, 134.3, 137.6, 141.6, 142.9, 152.9; IR (ATR) 3064, 2916, 2857, 1456, 1386, 995, 915 cm^{-1}; HRMS (DART+) Calcd for $C_{21}H_{23}N_2$ $[M+H]^+$: 303.1861; found: *m/z* 303.1850.

***N*-(3-Buten-1-yl)-2-(3-(3-buten-1-yl)thiophen-2-yl)benzoimidazole (5b):** The reaction was carried out in a similar manner for the synthesis of **5a** with **3** (85 mg, 0.52 mmol) and 3-(3-buten-1-yl)-2-formylthiophene (**4b**, 83 mg, 0.50 mmol) in EtOH (5 mL) at 60 °C for 72 h to afford 64.9 mg of **5b** (42% yield). ^{1}H NMR (400 MHz) δ 2.34 (td, *J* = 7.8, 6.9 Hz, 2H), 2.53 (td, *J* = 7.8, 7.8, Hz, 2H), 2.79 (t, *J* = 7.8 H, 2H), 4.23 (t, *J* = 7.8 Hz, 2H), 4.88-5.05 (m, 4H), 5.61-5.81 (m, 2H), 7.09 (d, *J* = 5.0 Hz, 1H), 7.28-7.36 (m, 2H), 7.40-7.44 (m, 1H), 7.46 (d, *J* = 5.0 Hz, 1H), 7.80-7.85 (m, 1H); ^{13}C NMR (100 MHz) δ 28.3, 33.7, 34.2, 43.8, 109.8, 115.0, 117.7, 119.9, 122.1, 122.7, 124.4, 126.9, 128.6, 133.3, 134.7, 137.4, 142.9, 144.1, 146.9; IR (ATR): 3076, 2977, 2930, 1640, 1454, 1416, 1280, 995, 915 cm^{-1}; HRMS (DART+) Calcd for $C_{19}H_{21}N_2S$ $[M+H]^+$: 309.1425; found: *m/z* 309.1421.

***N*-(3-Buten-1-yl)-2-(3,4-dibromo-1-(3-buten-1-yl)imidazol-2-yl)benzoimidazole (5c):** The reaction was carried out in a similar manner to that of **5a** with **4c** (364 mg, 1.1 mmol) and **3** (0.18 mL, 1.1 mmol) in EtOH (2 mL) at room temperature for 24 h to afford 0.43 g of **5c** (86% yield). ^{1}H NMR (400 MHz) δ 2.54 (td, *J* = 7.3, 6.9 Hz, 2H), 2.64 (td, *J* = 7.3, 7.3 Hz, 2H), 4.70 (t, *J* = 7.6 Hz, 2H), 4.84 (t, *J* = 7.6 Hz, 2H), 4.95-5.11 (m, 4H), 5.68 (ddt, *J* = 16.9, 10.1, 7.3 Hz, 1H), 5.80 (ddt, *J* = 16.9, 10.1, 6.9 Hz, 1H), 7.32-7.42 (m, 2H), 7.47 (d, *J* = 7.3 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz) δ 34.2, 34.4, 44.8, 47.5, 108.1, 110.4, 117.4, 117.7, 118.0, 119.9, 123.2, 124.1, 133.4, 134.0, 134.7, 137.5, 141.1x2; IR (ATR) 3073, 3005, 2950, 1742, 1478, 1340, 920 cm^{-1}; HRMS (DART+) Calcd for $C_{18}H_{19}{}^{79}Br_2N_4$ $[M+H]^+$: 448.9977; found: *m*/*z* 448.9986.

Benzo[1,2]-benzo[*d*]imidazo[4,3-*a*]-4-aza-7-(*E*)-cyclodecene (6a): To a solution of **5a** (41 mg, 0.14 mmol) in 1,2-dichloroethane (5.6 mL) was added ZnI_2 (8.9 mg, 0.03 mmol) at room temperature. After stirring for 30 min, Grubbs 2nd generation catalyst (5.9 mg, 0.007 mmol) was added and stirring was continued at 80 °C for 4 h. The resulting mixture was cooled to room temperature and poured into a mixture of CH_2Cl_2 and aqueous solution of sat. sodium bicarbonate to result in phase separation. The aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to leave a crude oil. Purification by column chromatography on silica gel using hexane/isopropyl acetate = 100:0–80:20 as an eluent afforded 121 mg of **6a** as a viscous liquid (>99% yield). ^{1}H NMR (400 MHz) δ 1.74 (dddd, *J* = 13.3, 10.6, 3.2, 2.7 Hz, 1H), 2.10 (dddd, *J* = 14.2, 10.1, 2.7, 2.3 Hz, 1H), 2.22 (dddd, *J* = 13.4, 5.3, 3.2, 2.7 Hz, 1H), 2.36 (dddd, *J* = 13.3, 4.8, 4.1, 2.7 Hz, 1H), 2.76 (ddd, *J* = 13.3, 4.1, 2.7 Hz, 1H), 3.32 (ddd, *J* = 13.3, 3.2, 2.7 Hz, 1H), 3.93 (ddd, *J* = 13.4, 2.7, 2.3 Hz, 1H), 4.11 (ddd, *J* = 15.4, 10.1, 5.3 Hz, 1H), 4.36 (ddd, *J* = 14.2, 3.2, 2.7 Hz, 1H), 4.53 (ddd, *J* = 15.4, 10.6, 4.8 Hz, 1H), 7.16 (d, *J* = 7.3 Hz, 1H), 7.28-7.43 (m, 6H), 7.79-7.84 (m, 1H); ^{13}C NMR (100 MHz) δ 31.5, 32.2, 34.9, 43.4, 109.6, 119.8, 122.1, 122.3, 125.6, 127.1, 128.8, 129.6, 131.5x2, 132.5, 134.1, 141.9, 142.7, 154.8; IR (ATR) 3061, 2934, 2852, 1456, 1379, 1279, 1243, 1155, 976 cm^{-1}; HRMS (DART+) Calcd for $C_{19}H_{19}N_2$ $[M+H]^+$: 275.1548; found: *m/z* 275.1561.

Benzo[*d*]imidazo[1,2-*a*]-thieno[3,4-*b*]-1-aza-7-(*E*)-cyclodecene (6b): The reaction was carried out in a similar manner to the synthesis of **6a** with **5b** (154 mg, 0.5 mmol), ZnI_2 (3 mg, 0.01 mmol), Grubbs 2nd generation catalyst (21 mg, 0.025 mmol) in 1,2-dichloroethane (20 mL) at 80 °C for 23 h to afford 121 mg of **6b** as a viscous liquid (86% yield). ^{1}H NMR (400 MHz) δ 1.72 (dddd, *J* = 12.4, 10.5, 8.7, 3.7 Hz, 1H), 2.09 (dddd, *J* = 10.5, 10.3, 10.1, 3.2 Hz, 1H), 2.32 (dt, *J* = 12.4, 3.7 Hz, 2H), 2.78-2.95 (m, 2H), 4.17 (ddd, *J* = 14.4, 12.8, 1.8 Hz, 1H), 4.26 (ddd, *J* = 15.3, 10.5, 4.8 Hz, 1H), 4.40 (dt, *J* = 14.2, 3.2 Hz, 1H), 4.57 (ddd, *J* = 15.6, 10.5, 5.0 Hz, 1H), 6.99 (d, *J* = 5.0 Hz, 1H), 7.28-7.36 (m, 2H), 7.28-7.36 (m, 2H), 7.78-7.83 (m, 1H); ^{13}C NMR (100 MHz) δ 27.4, 32.3, 33.7, 43.4, 109.4, 119.8, 122.1, 122.6, 125.9, 127.2, 128.4, 129.7, 131.0, 134.4, 142.9, 143.3, 148.8; IR (ATR) 2932, 2853, 1456, 1416, 1370, 1280, 1244, 1157, 974, 906 cm^{-1}; HRMS (DART+) Calcd for $C_{17}H_{17}N_2S$ $[M+H]^+$: 281.1112; found: *m/z* 281.1118.

Benzo[*d*]imidazo[1,2-*a*]-(4,5-dibromo)imidazo[3,4-*a*]-1,4-diaza-7-(*E*)-cyclodecene (6c): The reaction was carried out in a similar manner to that of **6a** with **5c** (45 mg, 0.1 mmol), Grubbs 2nd generation catalyst (4.2 mg, 0.005 mmol), and $Ti(O^iPr)_4$ (0.006 mL, 0.02 mmol) in 1.0 mL of 1,2-dichloroethane stirring at 80 °C for 17 h to afford 0.046 g of **6c** (99% yield). ^{1}H NMR (400 MHz) δ 1.92-2.11 (m, *J* = 7.3, 2H), 2.28 (dt, *J* = 13.3, 2.3 Hz, 1H), 2.39 (dt, *J* = 12.8, 2.3 Hz, 1H), 4.20 (ddd, *J* = 15.6, 10.3, 5.3 Hz, 1H),

4.31 (dt, *J* = 14.2, 3.2 Hz, 1H), 4.42-4.57 (m, 3H), 4.61 (ddd, *J* = 15.6, 10.5, 5.0 Hz, 1H), 7.36-7.45 (m, 2H), 7.48 (dd, *J* = 6.9, 2.3 Hz, 1H), 7.85 (dd, *J* = 6.6, 2.1 Hz, 1H); ^{13}C NMR (100 MHz) δ 32.7, 33.2, 42.9, 46.1, 106.2, 110.2, 117.2, 120.0, 123.7, 124.4, 129.1, 130.5, 133.6, 139.7, 140.8, 143.6; IR (ATR) 3015, 2960, 2929, 2855, 1405, 984, 908 cm^{-1}; HRMS (DART+) Calcd for $C_{16}H_{15}{}^{79}Br^{81}BrN_4$ $[M+H]^+$: 422.9643; found: *m*/*z* 422.9661.

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9. Compound **6b**: 22.9 min, 28.1 min (Chiralpak IC, hexane/EtOH = 10:1; flow rate = 0.5 mL/min) and **6c**: 6.9 min, 9.0 min (Chiralpak IF, hexane/EtOH = 1:1; flow rate = 1.0 mL/min).