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Synthesis of 2,3-dihydro-1*H*-isoindole-1-thiones via the bromine–lithium exchange between 1-bromo-2-(1-isothiocyanatoalkyl)benzenes and butyllithium

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ABSTRACT

The reaction of 1-bromo-2-(1-isothiocyanatoalkyl)benzenes, which are easily derived from 2-bromophenyl ketones or (2-bromophenyl)methanamine, with butyllithium generates 1-(1-isothio cyanatoalkyl)-2-lithiobenzenes, which immediately underwent intramolecular cyclization to give rise to the corresponding 3-substituted and 3,3-disubstituted 2,3-dihydro-1*H*-isoindole-1-thiones in good yields.

1. Introduction

2,3-Dihydro-1*H*-isoindole-1-thiones have been of interest as they are efficient building blocks in the synthesis of structurally more complex and/or medicinally important molecules.[1] The reaction of 2,3-dihydro-1*H*-isoindol-1-ones with P_4S_{10} or Lawesson's reagent has commonly been used for the preparation of 2,3-dihydro-1*H*-isoindole-1-thiones.[2] However, a major drawback of this method is the tedious reaction conditions. We envisaged that the generation of 1-(1-isothiocyanatoalkyl)-2-lithiobenzenes **8** by the bromine–lithium exchange between 1-bromo-2-(1-isothio cyanatoalkyl)benzenes **4**, followed by cyclization through the intramolecular attack of the carbanion on the isothiocyanato carbon, would give the desired 2,3-dihydro-1*H*-isoindole-1-thiones **10**. We, herein, wish to describe the results of our study, which provides a new and efficient synthetic route to substituted 2,3-dihydro-1*H*-isoindole-1-thiones.

2. Results and discussion

First, we carried out the preparation of the precursor isothiocyanates **4a**–**h** for the present 2,3-dihydro-1*H*-isoindole-1-thione synthesis, as illustrated in Scheme 1. Thus, *N*-[1-(2-bromophenyl)alkyl]formamides **2** were prepared in fair-to-good yields by the reaction of 2-bromophenyl ketones **1** with formamide and formic acid under heating. Their dehydration with phosphorous chloride in the presence of triethylamine in THF at 0 °C afforded the corresponding isocyanides **3a**–**d** in good yields. We then investigate possibility of the alkylation of the carbon α to the isocyano function of these compounds and were pleased to find that the successive treatment of **3a**–**c** with LDA and haloalkanes provided the α,α-disubstituted 2-bromobenzyl isocyanides **3e**–**h** in fair-to-good yields. Treatment of compounds **3a**–**h** with sulfur in the presence of a catalytic amount of selenium under Fujiwara's conditions[3] gave the requisite precursors **4a**–**h** in reasonable yields.

We also prepared 1-bromo-2-(1-isothiocyanatoalkyl)benzenes **4j** and **k** from commercially available (2-bromophenyl)methanamine **5**, as shown in Scheme 2. Treatment of **5** with formic acid in the presence of acetic anhydride gave *N*-[(2-bromophenyl)methyl] formamide (**6**), which was dehydrated as described above for the preparation of **3a**–**d** to afford 1-bromo-2-(isocyanomethyl) benzene (**7**). Conversion of **7** to **4j** and **k**, via the isocyanides **3j** and **k**, was performed as described above.

With the precursor isothiocyanates **4** in hands, we next conducted the transformation of **4** into substituted 2,3-dihydro-1*H*-isoindole-1-thiones **10**. When these precursor isothiocyanates **4** were treated with butyllithium in THF at −78 °C, the

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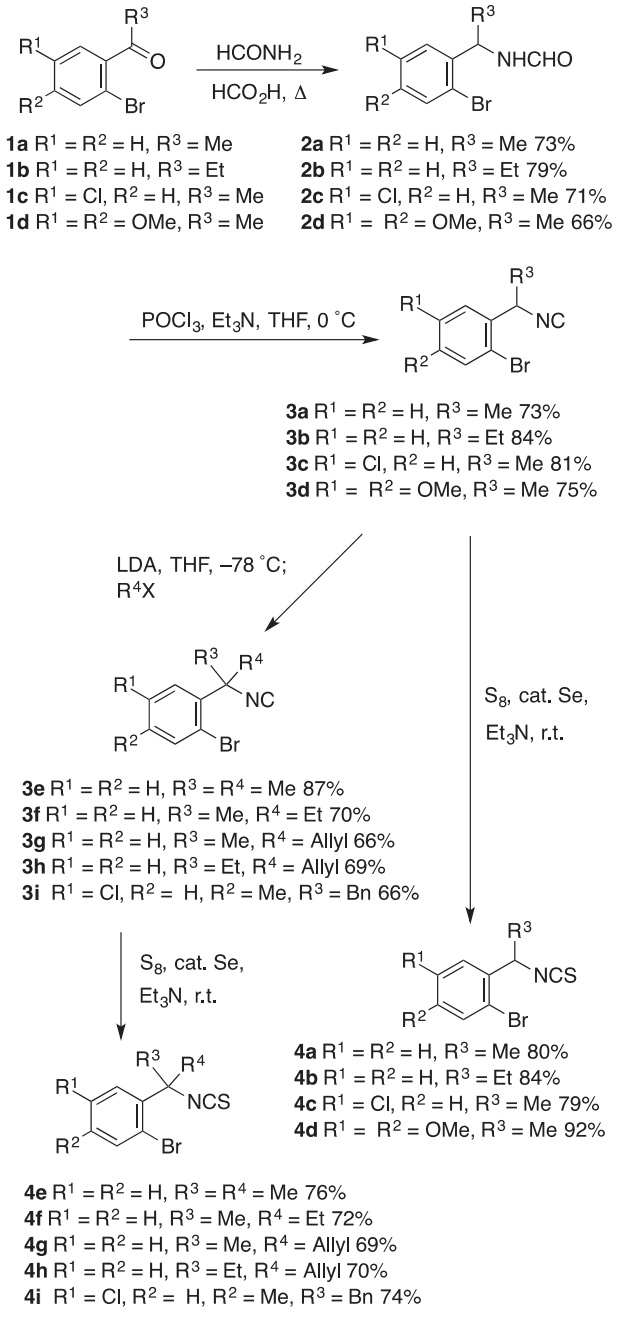
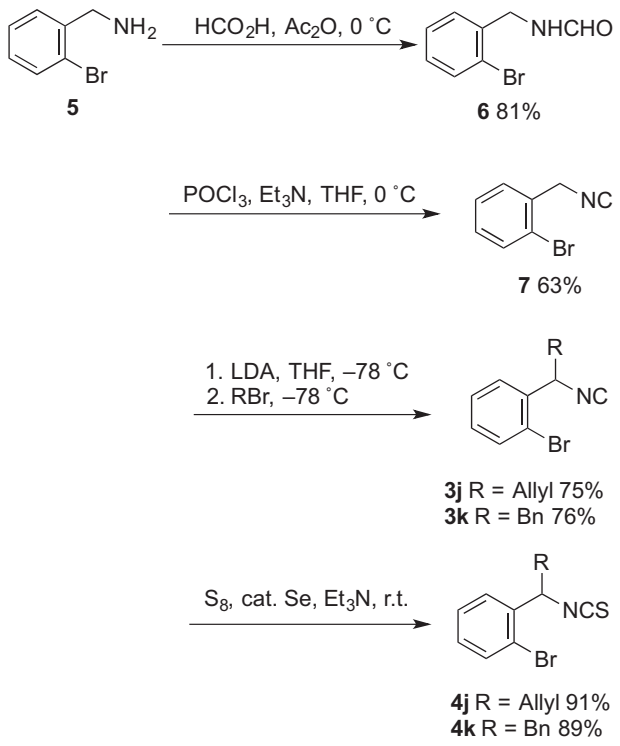
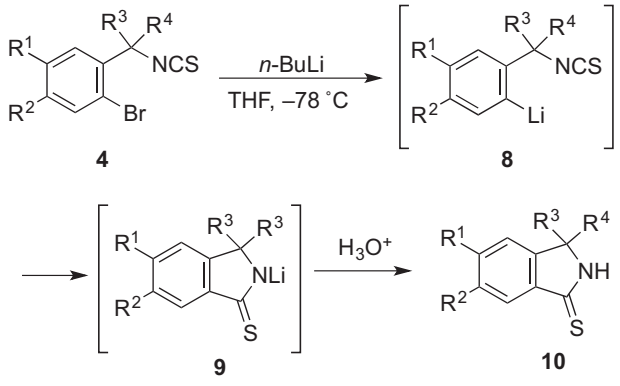


Scheme 1.



Scheme 2.



Scheme 3.

bromine–lithium exchange occurred to generate the lithium compounds **8**, which underwent cyclization to give the lithium thiolactamides **9**. This sequence proceeded quickly and cleanly, and after aqueous work up and the subsequent purification by recrystallization the desired products **10** were obtained, as illustrated in Scheme 3. The yields of the products are good as summarized in Table 1. It should be noted that the reaction of 1-bromo-2-(isothiocyanatomethyl)benzene, derived from 1-bromo-2-(isocyanomethyl)benzene (**7**), with butyllithium under the same conditions, expecting the production of 2,3-dihydro-1*H*-isoindole-1-thione, resulted in the formation of an intractable mixture of products.

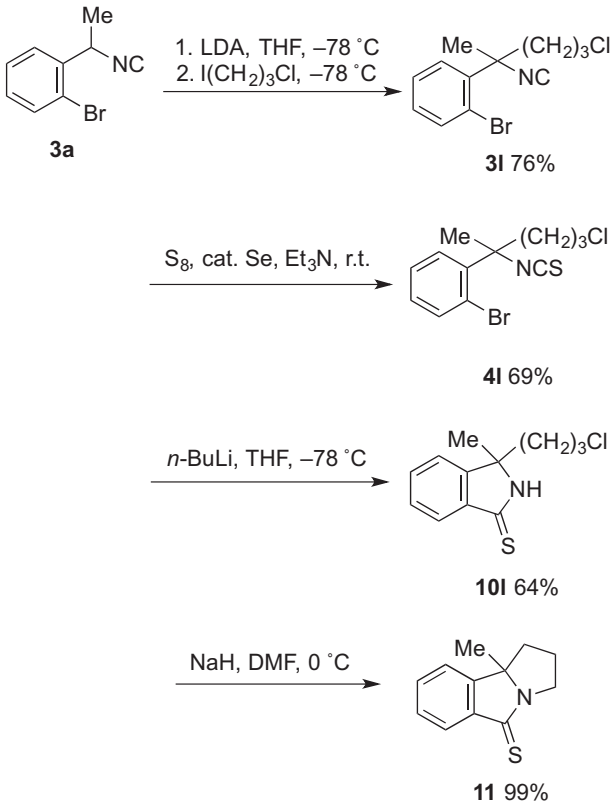
Finally, we tried to synthesize 9b-methyl-1,2,3,9b-tetrahydropyrrolo[2,1-*a*]isoindole-5-thione (**11**), which involves the pyrrolizidine structure, in order to demonstrate utility of the present

Table 1
Preparation of 2,3-dihydro-1*H*-isoindole-1-thiones **10**

Entry	**4**	**10**	Yield/%[a]
1	**4a** (R^1=H, R^2=H, R^3=Me, R^4=H)	**10a**	79
2	**4b** (R^1=H, R^2=H, R^3=Et, R^4=H)	**10b**	94
3	**4c** (R^1=Cl, R^2=H, R^3=Me, R^4=H)	**10c**	84
4	**4d** (R^1=OMe, R^2=OMe, R^3=Me, R^4=H)	**10d**	77
5	**4e** (R^1=H, R^2=H, R^3=Me, R^4=Me)	**10e**	87
6	**4f** (R^1=H, R^2=H, R^3=Me, R^4=Et)	**10f**	89
7	**4g** (R^1=H, R^2=H, R^3=Me, R^4=Allyl)	**10g**	75
8	**4h** (R^1=H, R^2=H, R^3=Et, R^4=Allyl)	**10h**	84
9	**4i** (R^1=Cl, R^2=H, R^3=Me, R^4=Bn)	**10i**	94
10	**4j** (R^1=H, R^2=H, R^3=Allyl, R^4=H)	**10j**	94
11	**4k** (R^1=H, R^2=H, R^3=Bn, R^4=H)	**10k**	83

[a] Yields of isolated products.

method. As illustrated in Scheme 4, 1-bromo-2-(4-chloro-1-isocyano-1-methylbutyl)benzene (**3l**) was prepared in relatively good yield by the successive treatment of 1-bromo-2-(1-isocyanoethyl)benzene (**3a**) with LDA and 1-chloro-3-iodopropane and converted into 1-bromo-2-(4-chloro-1-isocyanato-1-methylbutyl)benzene (**4l**) in fair yield under the same conditions as mentioned above. Treatment of **4l** with butyllithium gave the corresponding 2,3-dihydro-1*H*-isoindole-1-thione derivative **10l** in a reasonable yield, cyclization of which with sodium hydride in DMF at 0 °C proceeded very cleanly and smoothly to give the desired product **11** in excellent yield.



Scheme 4.

In summary, a convenient route for the preparation of substituted 2,3-dihydro-1*H*-isoindole-1-thiones has been developed, which relied on the butyllithium-mediated cyclization of 1-bromo-2-(1-isothiocyanatoalkyl)benzenes, derived from 2-bromophenyl ketones or (2-bromophenyl)methanamine by using easy sequences. This method may find some value in organic synthesis because of its simplicity and the readily availability of the starting materials.

3. Experimental

3.1. General

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded with a Perkin–Elmer Spectrum65 FTIR spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz or JEOL LA400FTNMR spectrometer operating at 400 MHz. ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 125 MHz. Low-resolution MS spectra (EI, 70 eV) were measured by a JEOL JMS AX505 HA spectrometer. High-resolution MS spectra (DART, positive) were measured by a Thermo Scientific Exactive spectrometer. TLC was carried out on Merck Kieselgel 60 PF_{254}. Column chromatography was performed using WAKO GEL C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

3.2. Starting materials

1-(2-Bromophenyl)propan-1-one (**1b**)[4] and 1-(2-bromo-4,5-dimethoxyphenyl)ethanone (**1d**)[5] were prepared according to the appropriate reported procedures. Butyllithium was supplied by Asia Lithium Corporation. All other chemicals used in this study were commercially available.

*3.2.1. 1-(2-Bromo-5-chlorophenyl)ethanone (**1c**).* This compound was prepared by the acetylation of 1-bromo-2-chlorobenzene with AcCl according to the reported procedure.[6] A colorless liquid; R_f 0.23 (AcOEt/hexane 1:20); IR (neat) 1703 cm^{-1}; ^{1}H NMR (500 MHz) δ 2.63 (s, 3H), 7.27 (dd, J=8.6, 2.3 Hz, 1H), 7.43 (d, J=2.3 Hz, 1H), 7.54 (d, J=8.6 Hz, 1H). Anal. Calcd for C_8H_6BrClO: C, 41.15; H, 2.59. Found: C, 40.94; H, 2.68.

3.3. Typical procedure for the preparation of formamides 2

*3.3.1. N-[1-(2-Bromophenyl)ethyl]formamide (**2a**).* A mixture of 1-(2-bromophenyl)ethanone (**1a**) (4.0 g, 20 mmol), $HCONH_2$ (9.3 mL), and HCO_2H (6.2 mL) was heated at 180 °C for 33 h. After cooling to room temperature, water (50 mL) was added and the mixture was extracted with AcOEt (3×30 mL). The combined extracts were washed with water (20 mL), satd aq $NaHCO_3$ (3×20 mL), and then brine (20 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on silica gel to afford **2a** (2.9 g, 73%); a yellow oil; R_f 0.10 (AcOEt/hexane 1:2); IR (neat) 3280, 1660 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.53 and 1.55 (2d, J=6.9 Hz each, combined 3H), 5.07–5.13 and 5.42–5.48 (2m, combined 1H), 5.97 (br 1H), 7.14 and 7.17 (2t, J=7.4 Hz each, combined 1H), 7.29–7.35 (m, 2H), 7.56 and 7.58 (2d, J=7.4 Hz each, combined 1H), 8.18 and 8.20 (2s, combined 1H); ^{13}C NMR δ 21.00, 22.42, 47.97, 51.04, 122.43, 122.82, 126.89, 127.78, 128.17, 128.90, 129.20, 133.27, 133.40, 141.49, 141.89, 160.16, 164.29. Anal. Calcd for $C_9H_{10}BrNO$: C, 47.39; H, 4.42; N, 6.14. Found: C, 47.27; H, 4.68; N, 6.01.

*3.3.2. N-[1-(2-Bromophenyl)propyl]formamide (**2b**).* White needles; mp 70–72 °C (hexane/Et_2O); IR (neat) 3281, 1661 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.96 and 1.00 (2t, J=7.4 Hz, each, combined 3H), 1.74–1.97 (m, 2H), 4.80–4.95 and 5.26–5.31 (2m, combined 1H), 6.03–8.22 (m, 6H). Anal. Calcd for $C_{10}H_{12}BrNO$: C, 49.61; H, 5.00; N, 5.79. Found: C, 49.50; H, 5.04; N, 5.70.

*3.3.3. N-[1-(2-Bromo-5-chlorophenyl)ethyl]formamide (**2c**).* A yellow solid; mp 110–113 °C (hexane/$CHCl_3$); IR (KBr) 3310, 1658 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.50 and 1.55 (2d, J=6.9 Hz each, combined 3H), 5.02–5.08 and 5.35–5.41 (2m, combined 1H), 5.90 (br s, 1H), 7.12 and 7.16 (2dd, J=8.6, 2.9 Hz each, combined 1H), 7.29 and 7.31 (2d, J=2.9 Hz each, combined 1H), 7.48 and 7.50 (2d, J=8.6 Hz, each, combined 1H), 8.17 and 8.20 (2s, combined 1H). Anal. Calcd for $C_9H_9BrClNO$: C, 41.17; H, 3.46; N, 5.34. Found: C, 41.04; H, 3.59; N, 5.34.

*3.3.4. N-[1-(2-Bromo-4,5-dimethoxyphenyl)ethyl]formamide (**2d**).* A light-brown amorphous; R_f 0.13 (AcOEt/hexane 2:1); IR (KBr) 3279, 1662, 1604 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.53 (d, J=6.9 Hz, 3H), 3.86 (s, 3H), 3.88 (s, 3H), 5.04 and 5.35 (2quint, J=7.4 and

6.9 Hz, respectively, combined 1H), 5.96 and 6.19 (2br s, combined 1H), 6.79 and 6.82 (2s, combined 1H), 7.01 and 7.02 (2s, combined 1H), 8.17 and 8.19 (2s, combined 1H). Anal. Calcd for $C_{11}H_{14}BrNO_3$: C, 45.85; H, 4.90; N, 4.86. Found: C, 45.51; H, 4.90; N, 4.63.

3.4. 1-Bromo-2-(1-isocyanoethyl)benzenes 3

These compounds were prepared by dehydration of **2** with $POCl_3$/Et_3N under conditions reported previously.[7]

*3.4.1. 1-Bromo-2-(1-isocyanoethyl)benzene (**3a**).* A pale-yellow liquid; R_f 0.59 (Et_2O/hexane 1:5); IR (neat) 2141 cm^{-1}; ^1H NMR (400 MHz) δ 1.67 (d, J=6.8 Hz, 3H), 5.22 (q, J=6.8 Hz, 1H), 7.21 (t, J=7.8 Hz, 1H), 7.42 (t, J=7.8 Hz, 1H), 7.56 (d, J=7.8 Hz, 1H), 7.65 (d, J=7.8 Hz, 1H); ^{13}C NMR δ 23.79, 53.57 (t, J=6.0 Hz), 121.29, 126.90, 128.37, 129.83, 133.07, 137.74, 156.96 (t, J=4.8 Hz). HRMS calcd for C_9H_9BrN: M+H, 209.9918. Found: m/z 209.9908.

*3.4.2. 1-Bromo-2-(1-isocyanopropyl)benzene (**3b**).* A yellow liquid; R_f 0.83 (AcOEt/hexane 1:10); IR (neat) 2140 cm^{-1}; ^1H NMR (500 MHz) δ 1.11 (t, J=7.4 Hz, 3H), 1.80–1.84 (m, 1H), 1.95–2.01 (m, 1H), 5.05–5.08 (m, 1H), 7.21 (ddd, J=8.0, 7.4, 1.7 Hz, 1H), 7.40 (dd, J=8.0, 7.4, 1.1 Hz, 1H), 7.56 (dd, J=8.0, 1.1 Hz, 1H), 7.59 (dd, J=8.0, 1.7 Hz, 1H). HRMS calcd for $C_{10}H_{11}BrN$: M+H, 224.0075. Found: m/z 224.0059.

*3.4.3. 1-Bromo-4-chloro-2-(1-isocyanoethyl)benzene (**3c**).* A yellow liquid; R_f 0.53 (Et_2O/hexane 1:10); IR (neat) 2141 cm^{-1}; ^1H NMR (500 MHz) δ 1.67 (d, J=6.9 Hz, 3H), 5.17 (q, J=6.9 Hz, 1H), 7.20 (dd, J=8.6, 1.3 Hz, 1H), 7.49 (d, J=8.6 Hz, 1H), 7.63 (d, J=2.3 Hz, 1H). HRMS calcd for C_9H_8BrClN: M+H, 243.9528. Found: m/z 243.9509.

*3.4.4. 1-Bromo-2-(1-isocyanoethyl)-4,5-dimethoxy benzene (**3d**).* A white solid; mp 68–70 °C (hexane); IR (neat) 2145, 1603 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.64 (d, J=6.3 Hz, 3H), 3.88 (s, 3H), 3.93 (s, 3H), 5.15 (q, J=6.3 Hz, 1H), 6.99 (s, 1H), 7.08 (s, 1H). Anal. Calcd for $C_{11}H_{12}BrNO_2$: C, 48.91; H, 4.48; N, 5.19. Found: C, 48.81; H, 4.56; N, 5.10.

3.5. Typical procedure for the preparation of 1-bromo-2-(1-isocyanoalkyl)benzenes 3e–i and l

*3.5.1. 1-Bromo-2-(1-isocyano-1-methylethyl)benzene (**3e**).* To a stirred solution of LDA (2.0 mmol), generated from *i*-Pr_2NH and *n*-BuLi by the standard method, in THF (5 mL) at −78 °C was added a solution of **3a** (0.29 g, 1.4 mmol) in THF (2 mL) dropwise. After 20 min, MeI (0.29 g, 2.0 mmol) was added and stirring was continued an additional 20 min before satd aq NH_4Cl and water (10 mL each) was added. The mixture was warmed to room temperature and extracted with AcOEt (3×10 mL). The combined extract was washed with brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on silica gel to afford **3d** (2.7 g, 87%); a pale-yellow liquid; R_f 0.43 (AcOEt/hexane 1:5); IR (neat) 2133 cm^{-1}; ^1H NMR (500 MHz) δ 2.01 (s, 6H), 7.19 (dd, J=8.0, 7.4 Hz, 1H), 7.36 (dd, J=8.0, 7.4 Hz, 1H), 7.65 (d, J=8.0 Hz, 1H), 7.71 (d, J=8.0 Hz, 1H); ^{13}C NMR δ 29.63, 61.88 (t, J=6.0 Hz), 120.29, 127.38, 127.83, 129.58, 135.99, 138.89, 156.72 (t, J=4.8 Hz). HRMS calcd for $C_{10}H_{11}BrN$: M+H, 224.0075. Found: m/z 224.0065.

*3.5.2. 1-Bromo-2-(1-isocyano-1-methylpropyl)benzene (**3f**).* A pale-yellow liquid; R_f 0.47 (Et_2O/hexane 1:15); IR (neat) 2129 cm^{-1}; ^1H NMR (500 MHz) δ 0.88 (t, J=7.4 Hz, 3H), 2.00 (s, 3H), 2.08–2.13 (m, 1H), 2.61–2.69 (m, 1H), 7.18 (ddd, J=8.0, 7.4, 1.7 Hz, 1H), 7.36 (ddd, J=8.0, 7.4, 1.7 Hz, 1H), 7.63 (dd, J=8.0, 1.7 Hz, 1H), 7.76 (dd, J=8.0, 1.7 Hz, 1H). HRMS calcd for $C_{11}H_{13}BrN$: M+H, 238.0231. Found: m/z 238.0231.

*3.5.3. 1-Bromo-2-(1-isocyano-1-methylbut-3-enyl)benzene (**3g**).* A colorless liquid; R_f 0.46 (Et_2O/hexane 1:10); IR (neat) 2130, 1642 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.00 (s, 3H), 2.87 (dd, J=14.3, 7.3 Hz, 1H), 3.30 (ddd, J=14.3, 6.9, 1.1 Hz, 1H), 5.12 (dd, J=10.3, 1.1 Hz, 1H), 5.18 (ddd, J=16.8, 2.8, 1.7 Hz, 1H), 5.60–5.69 (m, 1H), 7.18 (ddd, J=8.0, 7.4, 1.7 Hz, 1H), 7.36 (ddd, J=8.0, 7.4, 1.7 Hz, 1H), 7.64 (dd, J=8.0, 1.7 Hz, 1H), 7.72 (dd, J=8.0, 1.7 Hz, 1H). HRMS calcd for $C_{12}H_{13}BrN$: M+H, 250.0231. Found: m/z 250.0215.

*3.5.4. 1-Bromo-2-(1-ethyl-1-isocyanobut-3-enyl)benzene (**3h**).* A pale-yellow liquid; R_f 0.51 (Et_2O/hexane 1:10); IR (neat) 2129, 1642 cm^{-1}; ^1H NMR (500 MHz) δ 0.85 (t, J=7.4 Hz, 3H), 2.03–2.10 (m, 1H), 2.73–2.82 (m, 2H), 3.41 (dd, J=14.3, 7.4 Hz, 1H), 5.07 (d, J=10.3 Hz, 1H), 5.16 (d, J=16.6 Hz, 1H), 5.56–5.64 (m, 1H), 7.17 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.36 (t, J=7.4 Hz, 1H), 7.62 (d, J=7.4 Hz, 1H), 7.72 (dd, J=8.0, 1.1 Hz, 1H). HRMS calcd for $C_{13}H_{15}BrN$: M+H, 264.0388. Found: m/z 250.0391.

*3.5.5. 1-Bromo-4-chloro-2-(1-isocyano-1-methyl-2-phenylethyl) benzene (**3i**).* A beige oil; R_f 0.34 (Et_2O/hexane 1:30); IR (neat) 2128 cm^{-1}; ^1H NMR (500 MHz) δ 2.02 (s, 3H), 3.39 (d, J=14.3 Hz, 1H), 3.73 (d, J=14.3 Hz, 1H), 7.13 (dd, J=6.9, 2.3 Hz, 2H), 7.17 (dd, J=8.6, 2.3 Hz, 1H), 7.24–7.25 (m, 3H), 7.50 (d, J=2.3 Hz, 1H), 7.61 (d, J=8.6 Hz, 1H). HRMS calcd for $C_{16}H_{14}BrClN$: M+H, 333.9998. Found: m/z 333.9976.

*3.5.6. 1-Bromo-2-(4-chloro-1-isocyano-1-methylbutyl)benzene (**3l**).* A pale-yellow liquid; R_f 0.31 (Et_2O/hexane 1:15); IR (neat) 2129 cm^{-1}; ^1H NMR (500 MHz) δ 1.50–1.59 (m, 1H), 1.85–1.94 (m, 1H), 2.03 (s, 3H), 2.16–2.22 (m, 1H), 2.87–2.92 (m, 1H), 3.52 (t, J=6.9 Hz, 2H), 7.20 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.39 (dd, J=8.0, 7.4 Hz, 1H), 7.64 (d, J=8.0 Hz, 1H), 7.78 (d, J=8.0 Hz, 1H). HRMS calcd for $C_{12}H_{14}BrClN$: M+H, 285.9998. Found: m/z 286.0002.

3.6. Bromophenyl isothiocyanates 4

These compounds were prepared by treatment with S_8 in the presence of a catalytic amount of Se under Fujiwara's conditions.[3]

*3.6.1. 1-Bromo-2-(1-isothiocyanatoethyl)benzene (**4a**).* A pale-yellow liquid; R_f 0.88 (hexane); IR (neat) 2093 cm^{-1}; ^1H NMR (500 MHz) δ 1.66 (d, J=6.9 Hz, 3H), 5.36 (q, J=6.9 Hz, 1H), 7.19 (td, J=7.6, 1.5 Hz, 1H), 7.39 (td, J=7.6, 1.5 Hz, 1H), 7.53 (dd, J=7.6, 1.5 Hz, 1H), 7.55 (dd, J=7.6, 1.5 Hz, 1H); ^{13}C NMR δ 23.65, 56.51, 121.33, 126.89, 128.22, 129.64, 133.08 (2C), 139.22. Anal. Calcd for C_9H_8BrNS: C, 44.64; H, 3.33; N, 5.78. Found: C, 44.61; H, 3.39; N, 5.71.

*3.6.2. 1-Bromo-2-(1-isothiocyanatopropyl)benzene (**4b**).* A colorless liquid; R_f 0.50 (hexane); IR (neat) 2082 cm^{-1}; ^1H NMR (500 MHz) δ 1.09 (t, J=7.4 Hz, 3H), 1.85–1.92 (m, 1H), 1.97–2.02 (m, 1H), 5.19 (dd, J=8.6, 4.0 Hz, 1H), 7.19 (ddd, J=8.0, 7.4, 1.7 Hz, 1H), 7.38 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.48 (dd, J=8.0, 1.7 Hz, 1H), 7.55 (dd, J=8.0, 1.1 Hz, 1H). Anal. Calcd for $C_{10}H_{10}BrNS$: C, 46.89; H, 3.93; N, 5.47. Found: C, 46.87; H, 4.01; N, 5.26.

*3.6.3. 1-Bromo-4-chloro-2-(1-isothiocyanatoethyl)benzene (**4c**).* A pale-yellow liquid; R_f 0.50 (hexane); IR (neat) 2084, 2049 cm^{-1}; ^1H NMR (500 MHz) δ 1.66 (d, J=6.3 Hz, 3H), 5.33 (q, J=6.3 Hz, 1H), 7.18 (dd, J=8.6, 2.9 Hz, 1H), 7.48 (d, J=8.6 Hz, 1H), 7.50 (d, J=2.9 Hz, 1H).

Anal. Calcd for $C_9H_7BrClNS$: C, 39.08; H, 2.55; N, 5.06. Found: C, 38.72; H, 2.73; N, 5.02.

*3.6.4. 1-Bromo-2-(1-isothiocyanatoethyl)-4,5-dimethoxy benzene (**4d**).* A pale-yellow oil; R_f 0.30 (AcOEt/hexane 1:5); IR (neat) 2100, 1603 cm^{-1}; ^1H NMR (500 MHz) δ 1.63 (d, J=6.9 Hz, 3H), 3.88 (s, 3H), 3.93 (s, 3H), 5.27 (q, J=6.9 Hz, 1H), 6.97 (s, 1H), 6.98 (s, 1H). Anal. Calcd for $C_{11}H_{12}BrNO_2S$: C, 43.72; H, 4.00; N, 4.64. Found: C, 43.48; H, 4.03; N, 4.37.

*3.6.5. 1-Bromo-2-(1-isothiocyanato-1-methylethyl)benzene (**4e**).* A pale-yellow liquid; R_f 0.30 (hexane); IR (neat) 2077 cm^{-1}; ^1H NMR (400 MHz) δ 1.98 (s, 6H), 7.16 (td, J=7.8, 2.0 Hz, 1H), 7.32 (t, J=7.8 Hz, 1H), 7.54 (dd, J=7.8, 2.0 Hz, 1H), 7.64 (dd, J=7.8, 2.0 Hz, 1H); ^{13}C NMR δ 29.86, 64.14, 120.83, 127.12, 127.64, 129.41, 132.67, 135.86, 140.57. Anal. Calcd for $C_{10}H_{10}BrNS$: C, 46.89; H, 3.93; N, 5.47. Found: C, 46.81; H, 4.03; N, 5.46.

*3.6.6. 1-Bromo-2-(1-isothiocyanato-1-methylpropyl)benzene (**4f**).* A pale-yellow liquid; R_f 0.47 (hexane); IR (neat) 2083 cm^{-1}; ^1H NMR (500 MHz) δ 0.89 (t, J=7.4 Hz, 3H), 1.98 (s, 3H), 2.12–2.19 (m, 1H), 2.59–2.66 (m, 1H), 7.15 (dd, J=8.0, 7.4 Hz, 1H), 7.33 (dd, J=8.0, 7.4 Hz, 1H), 7.58 (d, J=8.0 Hz, 1H); 762 (d, J=8.0 Hz, 1H). Anal. Calcd for $C_{11}H_{12}BrNS$: C, 48.90; H, 4.48, N, 5.18. Found: C, 48.83; H, 4.58; N, 5.09.

*3.6.7. 1-Bromo-2-(1-isothiocyanato-1-methylbut-3-enyl)benzene (**4g**).* A colorless liquid; R_f 0.48 (hexane); IR (neat) 2086, 1641 cm^{-1}; ^1H NMR (500 MHz) δ 1.98 (s, 3H), 2.91 (dd, J=14.3, 7.4 Hz, 1H), 3.28 (dd, J=14.3, 6.9 Hz, 1H), 5.14 (d, J=10.3 Hz, 1H), 5.20 (d, J=17.2 Hz, 1H), 5.60–5.69 (m, 1H), 7.16 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.33 (td, J=7.4, 1.1 Hz, 1H), 7.55 (dd, J=8.0, 1.1 Hz, 1H), 7.63 (d, J=7.4 Hz, 1H). Anal. Calcd for $C_{12}H_{12}BrNS$: C, 51.07; H, 4.29; N, 4.96. Found: C, 50.75; H, 4.34; N, 5.24.

*3.6.8. 1-Bromo-2-(1-ethyl-1-isothiocyanatobut-3-enyl)benzene (**4h**).* A pale-yellow liquid; R_f 0.45 (hexane); IR (neat) 2082, 1639 cm^{-1}; ^1H NMR (500 MHz) δ 0.84 (t, J=7.4 Hz, 3H), 2.11–2.16 (m, 1H), 2.72–2.77 (m, 1H), 2.86–2.90 (m, 1H), 3.41 (dd, J=14.3, 7.4 Hz, 1H), 5.10 (d, J=9.7 Hz, 1H), 5.18 (dd, J=16.6 Hz, 1H), 5.54–5.63 (m, 1H), 7.15 (ddd, J=8.0, 7.4, 1.7 Hz, 1H), 7.33 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.57 (dd, J=8.0, 1.7 Hz, 1H), 7.61 (dd, J=8.0, 1.1 Hz, 1H). Anal. Calcd for $C_{13}H_{14}BrNS$: C, 52.71; H, 4.76; N, 4.73. Found: C, 52.77; H, 4.80; N, 4.72.

*3.6.9. 1-Bromo-4-chloro-2-(1-isocyano-1-methyl-2-phenylethyl) benzene (**4i**).* A colorless oil; R_f 0.32 (hexane); IR (neat) 2074 cm^{-1}; ^1H NMR (500 MHz) δ 1.99 (s, 3H), 3.38 (d, J=13.7 Hz, 1H), 3.72 (d, J=13.7 Hz, 1H), 7.08 (dd, J=7.4, 2.3 Hz, 2H), 7.14 (dd, J=8.6, 2.3 Hz, 1H), 7.24–7.26 (m, 3H), 7.35 (d, J=2.3 Hz, 1H), 7.60 (d, J=8.6 Hz, 1H). Anal. Calcd for $C_{16}H_{13}BrClNS$: C, 52.41; H, 3.57; N, 3.82. Found: C, 52.34; H, 3.74; N, 3.70.

*3.6.10. 1-Bromo-2-(4-chloro-1-isothiocyanato-1-methylbutyl)benzene (**4l**).* A colorless liquid; R_f 0.31 (hexane); IR (neat) 2070 cm^{-1}; ^1H NMR (500 MHz) δ 1.58–1.65 (m, 1H), 1.79–1.87 (m, 1H), 2.02 (s, 3H), 2.20–2.27 (m, 1H), 2.82–2.88 (m, 1H), 3.53 (t, J=6.3 Hz, 2H), 7.17 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.35 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.60 (dd, J=8.0, 1.1 Hz, 1H), 7.63 (dd, J=8.0, 1.1 Hz, 1H). Anal. Calcd for $C_{12}H_{13}BrClNS$: C, 45.23; H, 4.11; N, 4.40. Found: C, 45.18; H, 4.12; N, 4.30.

3.7. *N*-[(2-Bromophenyl)methyl]formamide (6)

A mixture of (2-bromophenyl)methanamine hydrochloride (2.2 g, 10 mmol) and Et_3N (1.2 g, 12 mmol) in Et_2O (30 mL) was stirred at room temperature for 2 h. The precipitate was filtered off and the filtrate was concentrated by evaporation. The residue was dissolved in Ac_2O (4.7 mL) and the solution was cooled to 0 °C. To this solution was added HCO_2H (7.6 mL) and the mixture was stirred for 20 min at the same temperature. Excess Ac_2O and HCO_2H were removed under reduced pressure and the resulting residual solid was triturated with hexane to give, after filtration, **6** (1.7 g, 81%); a white solid; mp 77–79 °C (hexane/$CHCl_3$); IR (KBr) 3261, 1677, 1657 cm^{-1}; ^1H NMR (400 MHz) δ 4.48 and 4.57 (2d, J=6.1 and 6.9 Hz, respectively, combined 2H), 6.09 (br 1H), 7.17 and 7.20 (t and dd, J=7.6 Hz and J=8.4, 7.6 Hz, respectively, combined 1H), 7.26–7.34 (m, 2H), 7.56 and 7.59 (2d, J=7.6 and 8.4 Hz, respectively, combined 1H), 8.18 and 8.21 (2s, combined 1H). Anal. Calcd for C_8H_8BrNO: C, 44.89; H, 3.77; N, 6.54. Found: C, 44.80; H, 3.89; N, 6.29.

3.8. 1-Bromo-2-(1-isocyanomethyl)benzene (7)

This compound was prepared by dehydration of **6** with $POCl_3$ under conditions reported previously;[7] a pale-yellow oil; R_f 0.78 (Et_2O/hexane 1:1); IR (neat) 2152 $cm^{-1}cm^{-1}$; ^1H NMR (500 MHz) δ 4.74 (s, 2H), 7.26 (t, J=7.6 Hz, 1H), 7.42 (t, J=7.6 Hz, 1H), 7.58 (d, J=7.6 Hz, 1H), 7.60 (d, J=7.6 Hz, 1H). HRMS calcd for C_8H_7BrN: M+H, 195.9762. Found: m/z 195.9753.

3.9. 1-Bromo-2-(1-isocyanobut-3-enyl)benzene (3j)

This compound was prepared from **7** and 3-bromopropene by the procedure as described for the preparation of **3e**; a colorless liquid; R_f 0.42 (Et_2O/hexane 1:10); IR (neat) 2139, 1643 cm^{-1}; ^1H NMR (500 MHz) δ 2.48–2.54 (m, 1H), 2.66–2.69 (m, 1H), 5.16–5.24 (m, 3H), 5.80–5.88 (m, 1H), 7.22 (ddd, J=8.0, 7.4, 1.7 Hz, 1H), 7.41 (td, J=7.4, 1.1 Hz, 1H), 7.57 (dd, J=8.0, 1.1 Hz, 1H), 7.59 (dd, J=7.4, 1.7 Hz, 1H). HRMS calcd for $C_{11}H_{11}BrN$: M+H, 236.0075. Found: m/z 236.0072.

3.10. 1-Bromo-2-(1-isocyano-2-phenylethyl)benzene (3k)

This compound was prepared from **7** and (bromomethyl)benzene by the procedure as described for the preparation of **3e**; a colorless oil; R_f 0.35 (AcOEt/hexane 1:15); IR (neat) 2139 cm^{-1}; ^1H NMR (500 MHz) δ 2.94 (dd, J=13.7, 9.2 Hz, 1H), 3.24 (dd, J=13.7, 3.8 Hz, 1H), 5.32 (dd, J=9.2, 3.8 Hz, 1H), 7.21–7.26 (m, 3H), 7.28–7.35 (m, 3H), 7.38 (t, J=7.6 Hz, 1H), 7.53 (dd, J=7.6, 1.5 Hz, 1H), 7.59 (dd, J=7.6, 1.5 Hz, 1H). HRMS calcd for $C_{15}H_{13}BrN$: M+H, 286.0231. Found: m/z 286.0219.

3.11. 1-Bromo-2-(1-isothiocyanatobut-3-enyl)benzene (4j)

This compound was prepared by treatment of **3j** with S_8 in the presence of a catalytic amount of Se under Fujiwara's conditions;[3] a colorless liquid; R_f 0.30 (hexane); IR (neat) 2078, 1642 cm^{-1}; ^1H NMR (500 MHz) δ 2.55–2.61 (m, 1H), 2.69–2.74 (m, 1H), 5.23–5.31 (m, 3H), 5.81–5.89 (m, 1H), 7.20 (ddd, J=8.0, 7.4, 1.7 Hz, 1H), 7.39 (dd, J=8.0, 7.4 Hz, 1H), 7.49 (dd, J=8.0, 1.1 Hz, 1H), 7.56 (d, J=8.0 Hz, 1H). Anal. Calcd for $C_{11}H_{10}BrNS$: C, 49.27; H, 3.76; N, 5.22. Found: C, 49.25; H, 3.77; N, 5.11.

3.12. 1-Bromo-2-(1-isothiocyanato-2-phenylethyl)benzene (4k)

This compound was prepared by treatment of **3k** with S_8 in the presence of a catalytic amount of Se under Fujiwara's conditions;[3] a colorless oil; R_f 0.23 (hexane); IR (neat) 2080 cm^{-1}; ^1H NMR (500 MHz) δ 2.98 (dd, J=13.7, 9.2 Hz, 1H), 3.28 (dd, J=13.7, 3.8 Hz, 1H), 5.45 (dd, J=9.2, 3.8 Hz, 1H), 7.21 (td, J=7.6, 1.5 Hz, 1H), 7.25 (d,

J=7.6 Hz, 2H), 7.28–7.38 (m, 4H), 7.45 (dd, J=7.6, 1.5 Hz, 1H), 7.58 (dd, J=7.6, 1.5 Hz, 1H). Anal. Calcd for $C_{15}H_{12}BrNS$: C, 56.61; H, 3.80; N, 4.40. Found: C, 56.47; H, 3.81; N, 4.30.

3.13. Typical procedure for the preparation of 2,3-dihydro-1*H*-isoindole-1-thiones 10

*3.13.1. 3-Methyl-2,3-dihydro-1H-isoindole-1-thione (**10a**).* To a stirred solution of **4a** (0.18 g, 0.76 mmol) in THF (4 mL) −78 °C was added *n*-BuLi (1.6 M in hexane; 0.76 mL). After 10 min, the mixture was worked up as described for the preparation of **3e**. The residual solid was recrystallized from hexane/CH_2Cl_2 to give **10a** (97 mg, 79%); a beige solid; mp 139–141 °C; IR (KBr) 3140, 1612, 1512, 1253 cm^{-1}; ^1H NMR (500 MHz) δ 1.56 (d, J=6.9 Hz, 3H), 4.88 (q, J=6.9 Hz, 1H), 7.44 (d, J=7.6 Hz, 1H), 7.51 (t, J=7.6 Hz, 1H), 7.61 (t, J=7.6 Hz, 1H), 8.07 (d, J=7.6 Hz, 1H), 8.62 (br s, 1H); ^{13}C NMR δ 18.79, 59.85, 121.51, 125.53, 128.49, 132.01, 137.96, 146.73, 195.04; MS m/z 163 (M^+, 100). Anal. Calcd for C_9H_9NS: C, 66.22; H, 5.56; N, 8.58. Found: C, 66.03; H, 5.67; N, 8.46.

*3.13.2. 3-Ethyl-2,3-dihydro-1H-isoindole-1-thione (**10b**).* A gray solid; mp 105–107 °C (hexane/CH_2Cl_2); IR (KBr) 3163, 1613, 1507, 1243 cm^{-1}; ^1H NMR (500 MHz) δ 0.99 (t, J=7.4 Hz, 3H), 1.76–1.84 (m, 1H), 2.03–2.12 (m, 1H), 4.78 (t, J=6.3 Hz, 1H), 7.44 (d, J=7.4 Hz, 1H), 7.51 (t, J=7.4 Hz, 1H), 7.60 (t, J=7.4 Hz, 1H), 8.07 (d, J=7.4 Hz, 1H), 8.60 (br s, 1H); ^{13}C NMR δ 9.66, 26.47, 65.42, 121.74, 125.54, 128.50, 131.92, 138.49, 145.29, 195.44; MS m/z 177 (M^+, 100). Anal. Calcd for $C_{10}H_{11}NS$: C, 67.76; H, 6.25; N, 7.90. Found: C, 67.61; H, 6.29; N, 7.84.

*3.13.3. 5-Chloro-3-methyl-2,3-dihydro-1H-isoindole-1-thione (**10c**).* A beige solid; mp 171–173 °C (hexane/CH_2Cl_2); IR (KBr) 3142, 1611, 1515, 1277 cm^{-1}; ^1H NMR (500 MHz) δ 1.56 (d, J=6.9 Hz, 3H), 4.86 (q, J=6.9 Hz, 1H), 7.42 (d, J=1.7 Hz, 1H), 7.48 (dd, J=8.0, 1.7 Hz, 1H), 7.98 (d, J=8.0 Hz, 1H), 8.40 (br s, 1H); ^{13}C NMR δ 18.78, 59.51, 122.07, 126.82, 129.17, 136.49, 138.70, 148.14, 193.93; MS m/z 197 (M^+, 100). Anal. Calcd for C_9H_8ClNS: C, 54.68; H, 4.08; N, 7.09. Found: C, 54.60; H, 4.18; N, 7.00.

*3.13.4. 5,6-Dimethoxy-3-methyl-2,3-dihydro-1H-isoindole-1-thione (**10d**).* A pale-yellow solid; mp 192–196 °C (decomp.) (hexane/CH_2Cl_2); IR (KBr) 3211, 1614, 1506, 1276 cm^{-1}; ^1H NMR (500 MHz) δ 1.53 (d, J=6.9 Hz, 3H), 3.98 (s, 3H), 3.99 (s, 3H), 4.79 (q, J=6.9 Hz, 1H), 6.86 (s, 1H), 7.49 (s, 1H), 8.65 (br s, 1H); ^{13}C NMR δ 18.97, 56.28, 56.31, 59.37, 103.21, 106.80, 130.97, 140.93, 149.94, 153.36, 194.78; MS m/z 223 (M^+, 100). Anal. Calcd for $C_{11}H_{13}NO_2S$: C, 59.17; H, 5.87; N, 6.27. Found: C, 59.15; H, 5.90; N, 6.23.

*3.13.5. 3,3-Dimethyl-2,3-dihydro-1H-isoindole-1-thione (**10e**).* Colorless needles; mp 138–139 °C (hexane/CH_2Cl_2); IR (KBr) 3158, 1612, 1515, 1303 cm^{-1}; ^1H NMR (500 MHz) δ 1.60 (s, 6H), 7.38 (d, J=7.4 Hz, 1H), 7.49 (t, J=7.4 Hz, 1H), 7.59 (t, J=7.4 Hz, 1H), 8.03 (d, J=7.4 Hz, 1H), 9.02 (br s, 1H); ^{13}C NMR δ 26.35, 66.82, 120.34, 125.75, 128.47, 132.20, 136.74, 150.81, 193.46. HRMS calcd for $C_{10}H_{12}NS$: M+H, 178.0687. Found: m/z 178.0683. Anal. Calcd for $C_{10}H_{11}NS$: C, 67.76; H, 6.25; N, 7.90. Found: C, 67.70; H, 6.17; N, 7.87.

*3.13.6. 3-Ethyl-3-methyl-2,3-dihydro-1H-isoindole-1-thione (**10f**).* A white solid; mp 125–128 °C (hexane/CH_2Cl_2); IR (KBr) 3143, 1612, 1504, 1343 cm^{-1}; ^1H NMR (500 MHz) δ 0.71 (t, J=7.6 Hz, 3H), 1.57 (s, 3H), 1.90–1.99 (m, 2H), 7.32 (dd, J=7.6, 0.8 Hz, 1H), 7.48 (t, J=7.6 Hz, 1H), 7.58 (td, J=7.6, 0.8 Hz, 1H), 8.04 (d, J=7.6 Hz, 1H), 8.25 (br s, 1H); ^{13}C NMR δ 8.32, 24.67, 32.52, 70.29, 120.54, 125.68, 128.41, 132.10, 137.67, 149.53, 194.08. HRMS calcd for $C_{11}H_{14}NS$: M+H, 192.0847. Found: m/z 192.0842. Anal. Calcd for $C_{11}H_{13}NS$: C, 69.07; H, 6.85; N, 7.32. Found: C, 69.77; H, 8.03; N, 7.25.

*3.13.7. 3-Methyl-3-(prop-2-enyl)-2,3-dihydro-1H-isoindole-1-thione (**10g**).* A white solid; mp 119–120 °C (hexane/CH_2Cl_2); IR (KBr) 3147, 1643, 1612, 1501, 1340 cm^{-1}; ^1H NMR (500 MHz) δ 1.58 (s, 3H), 2.52 (d, J=14.3, 7.4 Hz, 1H), 2.65 (dd, J=14.3, 6.9 Hz, 1H), 5.11 (d, J=16.7 Hz, 1H), 5.12 (d, J=10.9 Hz, 1H), 5.58–5.66 (m, 1H), 7.36 (d, J=7.4 Hz, 1H), 7.49 (t, J=7.4 Hz, 1H), 7.59 (t, J=7.4 Hz, 1H), 8.03 (d, J=7.4 Hz, 1H), 8.46 (br s, 1H); ^{13}C NMR δ 24.18, 43.75, 69.16, 120.43, 120.73, 125.73, 128.56, 131.35, 132.08, 137.37, 149.43, 194.01. HRMS calcd for $C_{12}H_{14}NS$: M+H, 204.0847. Found: m/z 204.0845. Anal. Calcd for $C_{12}H_{13}NS$: C, 70.89; H, 6.45; N, 6.89. Found: C, 70.62; H, 6.46; N, 6.60.

*3.13.8. 3-Ethyl-3-(prop-2-enyl)-2,3-dihydro-1H-isoindole-1-thione (**10h**).* A white solid; mp 144–146 °C (hexane/CH_2Cl_2); IR (KBr) 3140, 1643, 1612, 1504, 1343 cm^{-1}; ^1H NMR (500 MHz) δ 0.67 (t, J=7.4 Hz, 3H), 1.94–1.99 (m, 1H), 2.02–2.07 (m, 1H), 2.59 (dd, J=13.7, 7.4 Hz, 1H), 2.69 (dd, J=13.7, 7.4 Hz, 1H), 5.05–5.10 (m, 2H), 5.51–5.59 (m, 1H), 7.33 (d, J=8.0 Hz, 1H), 7.49 (dd, J=8.0, 7.4 Hz, 1H), 7.59 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 8.04 (d, J=8.0 Hz, 1H), 8.83 (br s, 1H); ^{13}C NMR δ 7.83, 30.53, 42.52, 72.88, 120.24, 120.94, 125.67, 128.53, 131.20, 132.00, 138.52, 147.76, 194.98. HRMS calcd for $C_{13}H_{16}NS$: M+H, 218.1003. Found: m/z 218.0995. Anal. Calcd for $C_{13}H_{15}NS$: C, 71.84; H, 6.96; N, 6.44. Found: C, 71.75; H, 7.04; N, 6.42.

*3.13.9. 5-Chloro-3-methyl-3-phenylmethyl-2,3-dihydro-1H-isoindole-1-thione (**10i**).* A white solid; mp 154–156 °C (hexane/CH_2Cl_2); IR (KBr) 3124, 1609, 1521, 1328 cm^{-1}; ^1H NMR (500 MHz) δ 1.61 (s, 3H), 3.00 (d, J=13.7 Hz, 1H), 3.14 (d, J=13.7 Hz, 1H), 7.10 (dd, J=7.4, 1.7 Hz, 2H), 7.26–7.28 (m, 3H), 7.34 (d, J=1.1 Hz, 1H), 7.44 (dd, J=8.6, 1.1 Hz, 1H), 7.89 (d, J=8.6 Hz, 1H), 8.47 (br s, 1H); ^{13}C NMR δ 23.84, 45.70, 69.20, 121.51, 127.08, 127.49, 128.58, 129.22, 130.20, 134.69, 135.76, 138.59, 151.06, 192.80. HRMS calcd for $C_{16}H_{15}ClNS$: M+H, 288.0613. Found: m/z 288.0597. Anal. Calcd for $C_{16}H_{14}ClNS$: C, 66.77; H, 4.90; N, 4.87. Found: C, 66.73; H, 4.95; N, 4.84.

*3.13.10. 3-(Prop-2-enyl)-2,3-dihydro-1H-isoindole-1-thione (**10j**).* A beige solid; mp 90–91 °C (hexane/CH_2Cl_2); IR (KBr) 3153, 1642, 1612, 1501, 1333 cm^{-1}; ^1H NMR (500 MHz) δ 2.38–2.44 (m, 1H), 2.75–2.80 (m, 1H), 4.84 (dd, J=8.7, 5.2 Hz, 1H), 5.21–5.24 (m, 2H), 5.79–5.87 (m, 1H), 7.46 (dd, J=7.4, 1.1 Hz, 1H), 7.52 (t, J=7.4 Hz, 1H), 7.60 (td, J=7.4, 1.1 Hz, 1H), 8.07 (d, J=7.4 Hz, 1H), 8.72 (br s, 1H); ^{13}C NMR δ 37.84, 63.24, 119.83, 121.83, 125.66, 128.71, 131.94, 132.39, 138.36, 144.77, 195.61; MS m/z 189 (M^+, 100). Anal. Calcd for $C_{11}H_{11}NS$: C, 69.80; H, 5.86; N, 7.40. Found: C, 69.90; H, 6.01; N, 7.21.

*3.13.11. 3-Phenylmethyl-2,3-dihydro-1H-isoindole-1-thione (**10k**).* A pale-yellow solid; mp 138–139 °C (hexane/CH_2Cl_2); IR (KBr) 3140, 1613, 1503, 1346 cm^{-1}; ^1H NMR (500 MHz) δ 2.85 (dd, J=13.7, 9.2 Hz, 1H), 3.28 (dd, J=13.7, 5.4 Hz, 1H), 4.99 (dd, J=9.2, 5.4 Hz, 1H), 7.26 (d, J=6.9 Hz, 2H), 7.30–7.38 (m, 4H), 7.51 (dd, J=7.6, 6.9 Hz, 1H), 7.57 (dd, J=7.6, 6.9 Hz, 1H), 8.06 (d, J=7.6 Hz, 1H), 8.31 (br s, 1H); ^{13}C NMR δ 40.11, 65.12, 121.96, 125.74, 127.46, 128.79, 129.06, 131.86, 141.87, 136.28, 138.30, 144.73, 195.54; MS m/z 239 (M^+, 100). Anal. Calcd for $C_{15}H_{13}NS$: C, 75.28; H, 5.47; N, 5.85. Found: C, 75.34; H, 5.54; N, 5.94.

*3.13.12. 3-(3-Chloropropyl)-3-methyl-2,3-dihydro-1H-isoindole-1-thione (**10l**).* A pale-yellow solid; mp 107–109 °C (hexane/CH_2Cl_2); IR (KBr) 3153, 1611, 1497, 1341 cm^{-1}; ^1H NMR (500 MHz) δ 1.23–1.32 (m, 1H), 1.59–1.67 (m including s at 1.61, 4H), 2.13 (t, J=8.0 Hz, 2H), 3.38–3.43 (m, 2H), 7.36 (d, J=7.4 Hz, 1H), 7.50 (dd,

J=8.0, 7.4 Hz, 1H), 7.61 (t, J=7.4 Hz, 1H), 8.04 (d, J=7.4 Hz, 1H), 8.33 (br s, 1H); ^{13}C NMR δ 25.49, 26.80, 36.66, 44.56, 69.41, 120.54, 125.78, 128.71, 132.41, 137.51, 148.97, 194.14; MS m/z 239 (M^+, 100). Anal. Calcd for $C_{12}H_{14}ClNS$: C, 60.11; H, 5.89; N, 5.84. Found: C, 60.08; H, 5.91; N, 5.75.

3.14. 9b-Methyl-1,2,3,9b-tetrahydropyrrolo[2,1-*a*]isoindole-5-thione (11)

To a stirred suspension of NaH (60% in mineral oil; 10 mg, 0.25 mmol) in DMF (1.6 mL) at room temperature was added a solution of **10k** (55 mg, 0.23 mmol) in DMF (1 mL) dropwise. After 10 min, the mixture was worked up as described for the preparation of **3d**. The residue was purified by column chromatography on silica gel to give **11** (46 mg, 99%); a yellow oil; R_f 0.36 (AcOEt/hexane 1:1); IR (KBr) 1611, 1473, 1410, 1317 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.51–1.57 (m including s at 1.55, 4H), 2.05–2.11 (m, 1H), 2.43–2.50 (m, 1H), 2.53–2.64 (m, 1H), 3.68–3.73 (m, 1H), 4.17–4.23 (m, 1H), 7.38 (d, J=7.4 Hz, 1H), 7.46 (dd, J=8.0, 7.4 Hz, 1H), 7.54 (t, J=7.4 Hz, 1H), 7.97 (d, J=8.0 Hz, 1H); ^{13}C NMR δ 22.86, 27.73, 32.96, 44.05, 77.04, 120.95, 125.55, 128.60, 131.63, 139.46, 149.14, 193.71; MS m/z 203 (M^+, 100). Anal. Calcd for $C_{12}H_{13}NS$: C, 70.89; H, 6.45; N, 6.89. Found: C, 70.80; H, 6.71; N, 6.82.

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