Preparation of Aryl Isothiocyanates via Protected Phenylthiocarbamates and Application to the Synthesis of Caffeic Acid (4-Isothiocyanato)phenyl Ester

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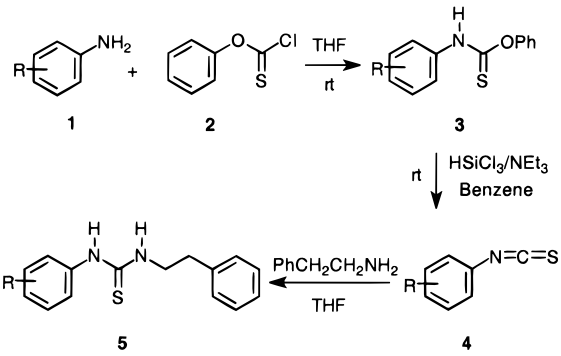
Introduction

Isothiocyanates have been widely used in organic synthesis, especially in the synthesis of heterocycles,[1,2] and they have also been isolated from natural products, including marine sesquiterpenes.[3,4] Additionally, synthetic isothiocyanates have been reported to exhibit interesting biological effects, among which are antitumor and antiparasitic activities[5,6] and the preparation of irreversible inhibitors.[7] There are currently several methods of preparing isothiocyanates from amines,[8−14] isocyanides,[15,16] organic halides,[17,18] and olefins.[19,20] For amines, the most widely used methods involve reaction of the amine with an activated thiocarbonyl species such as thiophosgene,[7,21] thiocarbonyl diimidazole,[22] or di-2-pyridyl thiocarbonate,[23] with product isothiocyanate being isolated directly from the reaction mixture. A potential disadvantage of such "direct" approaches is the use of highly reactive species, which may not be compatible with functionality found elsewhere in the molecule. One means of overcoming these difficulties could rely on an "indirect approach," whereby latent isothiocyanate functionality could be introduced early in a synthesis and carried forward through subsequent steps prior to liberation of the isothiocyanate group in a penultimate step. The advantage of this approach would be that introduction of the latent isothiocyanate could be achieved either prior to introduction of contraindicating functionality, or while such secondary functionality was masked. In this regard, thiocarbamates could serve as stable, "protected isothiocyanates" which could be liberated to free isothiocyanates when desired. In so doing, side reactions normally associated with direct isothiocyanate formation using standard protocols, could be avoided. Accordingly, we have examined the applicability of this method to the preparation of isothiocyanates and have taken note of the recent reports of isocyanates being prepared from carbamate intermediates.[24] We report herein that this approach is broadly applicable for the synthesis of a variety of aryl isothiocyanates and include, as exemplary of the potential utility of the method, the preparation of the 4-isothiocyanato derivative of caffeic acid phenethyl ester (CAPE) as a potential irreversible acylating variant of this biologically important compound.

Scheme 1



Results and Discussion:

Synthesis of aryl isothiocyanates were performed as shown in Scheme 1. Intermediate *N*-aryl thiocarbamates (**3**) were prepared by reaction of appropriate arylamines (**1**) with phenyl chlorothioformate. Subsequent treatment of resulting *N*-aryl thiocarbamates (**3**) with trichlorosilane in the presence of triethylamine produced the desired isothiocyanates (**4**) in moderate to high yield. Isothiocyanate products (**4**) were confirmed both on the basis of NMR, MS, and combustion analysis (or HRMS) as well as by conversion to their thiourea adducts (**5**) by reacting with phenylethylamine.

Steric and electrical properties of ancillary aryl substituents had little effect on either reaction rates or product yields, as shown in Table 1.

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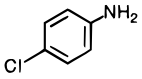
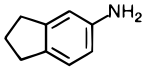
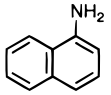
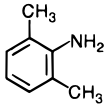
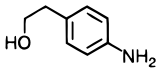
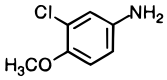
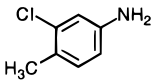
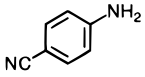
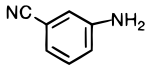
Table 1. Yields of Thiocarbamates 3, Isothiocyanates 4, and Thioureas 5

No.	Arylamine	Thiocarbamates (% yield)	Isothiocyanates (% yield)	Thioureas (% yield)
1a		**3a** (80)	**4a** (80)	**5a** (86)
1b		**3b** (98)	**4b** (68)	**5b** (75)
1c		**3c** (49)	**4c** (98)	**5c** (81)
1d		**3d** (66)	**4d** (70)	**5d** (58)
1e		**3e** (75)	**4e** (100)	**5e** (77)
1f		**3f** (78)	**4f** (93)	**5f** (35)
1g		**3g** (98)	**4g** (51)	**5g** (98)
1h		**3h** (97)	**4h** (60)	**5h** (97)
1i		**3i** (98)	**4i** (73)	**5i** (86)

Appending isothiocyanate functionality onto biologically active molecules so as to render them as site-directed acylating agents, has been of demonstrated value in several instances,[25] including the preparation of both radiolableled[26] and unlabeled irreversible opiate ligands[7,27] which have proven useful in the isolation of opiate receptors.[28] Caffeic acid phenethyl ester (CAPE) is an active constituent of "propolis," derived from honeybee hives, which has been shown to exhibit a variety of biological properties, including differential cytotoxicity against several tumor cell lines.[29,30] Interestingly, CAPE has also been shown to be a moderately potent inhibitor of HIV-1 integrase[31] with its structure being prototypical example of an entire family of bisaryl catechol-containing inhibitors of this enzyme.[32] To exemplify the application of our current methodology to the preparation of potentially relevant biological targets, we successfully utilized this new method for the synthesis of CAPE 4-isothiocyanate analogue **9**.

As shown in Scheme 2, reaction of phenyl chlorothionoformate (**2**) with 2-(4-aminophenyl)ethanol (**1e**) resulted in selective acylation of the amino functionality to provide the phenyl thiocarbamate **3e** in 75% yield. Reaction with TBS-protected caffeoyl chloride[33] **6** gave CAPE intermediate **7** bearing the isothiocyanate group in its latent, "protected" form. It proved advantageous to liberate the free isothiocyanate group prior to deprotection of the catechol functionality. Accordingly, treatment of **7** with trichlorosilane in the presence of NEt_3 provided the corresponding isothiocyanate **8** in nearly quantitative yield. Presumably, the trichlorosilane-induced cleavage reaction involves initial nitrogen silation followed by elimination akin to that of the Wittig or Pederson reactions.[34] Subsequent removal of catechol

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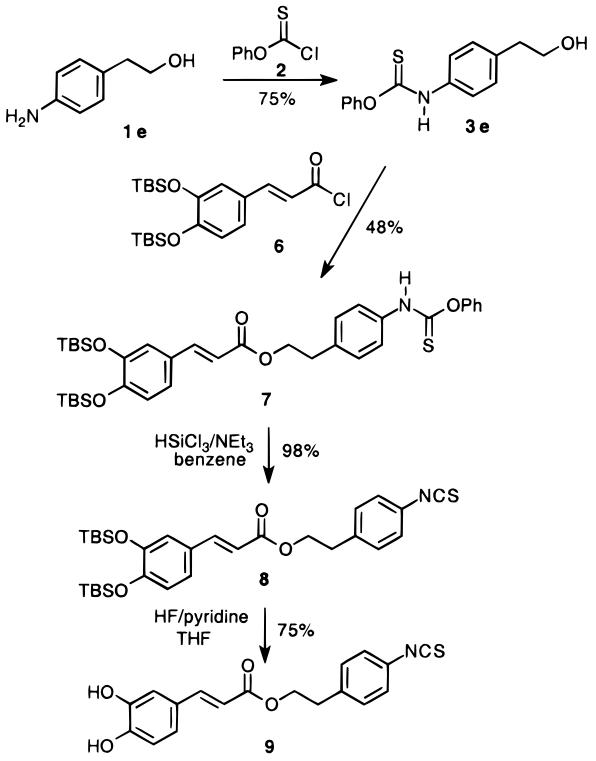
Scheme 2



protection (HF in pyridine) gave the desired CAPE 4-isothiocyanate **9** in 75% yield.

In conclusion, we have developed a new procedure for the synthesis of aryl isothiocyanates under mild conditions. An advantage of this method is its utilization of stable thiocarbamate intermediates which may be introduced as a protected isothiocyanates early in a synthetic sequence with subsequent liberation to free isothiocyanates then undertaken in later steps. In this fashion, potential side reactions normally associated with direct formation of isothiocyanates using standard protocols may be avoided.

Experimental Section

General Methods. All commercial reagents were used as supplied. Products solutions were dried over Na_2SO_4 prior to evaporation of the solvent under reduced pressure by using a rotary evaporator. Column chromatograph was performed on silica gel 60 (40−60 μm, E. Merck Darmstadt). Combustion analysis were obtained from Atlantic Microlab Inc., Norcross, GA. Mass spectra were obtained using fast atom bombardment ionization with the sample in a 3-nitrobenzyl alcohol matrix, except where noted.

General Procedure for Synthesis of Phenyl Thiocarbamates from Arylamines.

((4-Chlorophenyl)amino)phenoxymethane-1-thione (3a). A mixture of 4-chloroaniline (**1a**) (255 mg, 2 mmol) and phenyl chlorothionoformate (173 mg, 1 mmol) in THF (5 mL) was stirred at room temperature (30 min), the mixture was filtered through Celite 521 to remove precipitate, and the resulting solution was evaporated under reduced pressure. Residue was chromatographed [EtOAc:hexane (1:5)] to afford product thiocarbamate **3a** (210 mg, 80%). ^{1}H NMR ($CDCl_3$) δ 7.55−7.34 (m, 7H), 7.24−7.19 (m, 2H); FABMS *m*/*z* 264 (MH^+, 100). Anal. Calcd for $C_{13}H_{10}ClNOS$: C, 59.20; H, 3.82: N, 5.31; Cl, 13.44; s, 12.15. Found: C, 58.98; H, 4.00; N, 5.30; Cl, 13.68; S, 12.04.

(Indan-5-ylamino)phenoxymethane-1-thione (3b). ^{1}H NMR ($CDCl_3$) δ 7.61−7.13 (m, 8H), 2.92 (t, J = 7 Hz, 4H), 2.12-(m, 2H); FABMS *m*/*z*: 270 (MH^+, 100). Anal. Calcd for $C_{16}H_{15}NOS$: C, 71.34; H, 5.61; N, 5.20. Found: C, 71.06; H, 5.93; N, 4.97.

(Naphth-1-ylamino)phenoxymethane-1-thione (3c). ^{1}H NMR ($CDCl_3$) δ 8.31−7.85 (m, 3H), 7.72−7.05 (m, 9H); FABMS *m*/*z* 280 (MH^+, 100). Anal. Calcd for $C_{17}H_{13}NOS$: C, 73.09; H, 4.68; N, 5.01; S, 11.48. Found: C, 73.06; H, 4.78; N, 5.02; S, 11.40.

((2,6-Dimethophenyl)amino)phenoxymethane-1-thione (3d). ^{1}H NMR ($CDCl_3$) δ 7.47−7.03 (m, 8H), 2.42 (s, 3H), 2.38 (s, 3H); FABMS *m*/*z* 258 (MH^+, 100). Anal. Calcd for $C_{15}H_{15}NOS$: C, 70.00; H, 5.87; N, 5.44; S, 12.46. Found: C, 70.11; H, 5.89; N, 5.45; S, 12.38.

2-(4-((Phenoxythioxomethyl)amino)phenyl)ethan-1-ol (3e). ^{1}H NMR ($CDCl_3$) δ 7.75−7.08 (m, 9H), 3.88 (t, J = 6.5 Hz, 2H), 2.88 (t, J = 6.5 Hz, 2H); CI-MS (NH_3) *m*/*z* 291 ($M + NH_4 +$ 98). Anal. Calcd for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.53; N, 5.12. Found: C, 65.70; H, 5.68; N, 5.16.

((3-Chloro-4-methoxyphenyl)amino)phenoxymethane-1-thione (3f). ^{1}H NMR ($CDCl_3$) δ 7.47−6.87 (m, 8H), 3.92 (s, 3H); FABMS *m*/*z* 294 (MH^+, 100). Anal. Calcd for $C_{14}H_{12}ClNO_2S$: C, 57.24; H, 4.11; N, 4.76; Cl, 12.06; S, 10.91. Found: C, 57.02; H, 4.20; N, 4.83; Cl, 12.22; S, 10.77.

((3-Chloro-4-methylphenyl)amino)phenoxymethane-1-thione (3g). ^{1}H NMR ($CDCl_3$) δ 7.47−7.11 (m, 8H), 2.37 (s, 3H); FABMS *m*/*z* 278 (MH^+, 100), 110 (63), 95 (46). FABMS (exact mass) MH^+: Calcd *m*/*z* 278.0406; Found: 278.0416. Anal. Calcd for $C_{14}H_{12}ClNOS$: C, 60.53; H, 4.35; N. 5.04. Found: C, 60.25; H, 4.36; N, 5.02.

((4-Cyanophenyl)amino)phenoxymethane-1-thione (3h). ^{1}H NMR ($CDCl_3$) δ 7.70−7.30 (m, 7H), 7.15 (d, J = 6.8 Hz, 2H); FABMS *m*/*z* 255 (MH^+, 100). Anal. Calcd for $C_{14}H_{10}N_2OS$: C, 66.12; H, 3.96; N, 11.01; S, 12.61. Found: C, 66.19; H, 4.10; N, 10.92; S, 12.53.

((3-Cyanophenyl)amino)phenoxymethane-1-thione (3i). ^{1}H NMR ($CDCl_3$) δ 7.52−7.13 (m, 9H); FABMS *m*/*z* 255 (MH^+, 100), 161 (5), 110 (34), 95 (24), 77 (12). Anal. Calcd for $C_{14}H_{10}N_2OS$: C, 66.12; H, 3.96; N, 11.01. Found: C, 66.26; H, 4.11; N, 10.95.

General Procedure for Conversion of Phenyl Thiocarbamates to Isothiocyanates.

4-Chlorophenyl Isothiocyanate (4a). To a stirred solution of **3a** (150 mg, 0.57 mmol) in benzene (5 mL) was added triethylamine (92 mg, 0.91 mmol) and trichlorosilane (123 mg, 0.91 mmol) and the mixture was stirred at room temperature (1 h) then filtered through Celite 521. The resulting solution was evaporated under reduced pressure and purified by silica gel chromatography [EtOAc: hexane (1:8)] to provide 4-chlorobenzoisothiocyanate **4a**[35] (77 mg, 80%).^{1}H NMR ($CDCl_3$) δ 7.33 (d, J = 9 Hz, 2H), 7.16 (9 Hz, 2H).

Indan-5-yl Isothiocyanate (4b). ^{1}H NMR ($CDCl_3$) δ 7.25 (d, J = 8 Hz, 1H), 7.16 (s, 1H), 7.07 (dd, J = 8 Hz, 2 Hz,1H), 2.97 (t, J = 7.4 Hz, 4H), 2.17 (m, 2H); FABMS *m*/*z* 175 (MH^+, 100).

1-Naphthalenyl Isothiocyanate (4c). Previously prepared.[23] ^{1}H NMR ($CDCl_3$) δ 8.14 (d, J = 8 Hz, 1H), 7.91−7.87 (m, 1H), 7.82−7.76 (m,1H), 7.67−7.54 (m, 2H), 7.46−7.42 (m, 2H); FABMS *m*/*z* 185 (M^+, 100).

2,6-Dimethylphenyl Isothiocyanate (4d). Previously reported.[36] ^{1}H NMR ($CDCl_3$) δ 7.08−7.02 (m, 3H), 2.38 (s, 6H); EI-MS *m*/*z* 163 ($M^{+\bullet}$, 100).

4-(2-Hydroxyethyl)phenyl Isothiocyanate (4e). ^{1}H NMR ($CDCl_3$) δ 7.23−7.14 (m, 4H), 3.84 (t, J = 6.5 Hz, 2H), 2.85 (t, J = 6.5 Hz, 2H); FABMS *m*/*z* 179 (M^+, 100). Anal. Calcd for C_9H_9NOS: C, 60.31; H, 5.06; N, 7.81; S, 17.89. Found: C, 60.48; H, 5.22; N, 7.67; S, 17.61.

3-Chloro-4-methoxyphenyl Isothiocyanate (4f). Previously reported.[37] ^{1}H NMR ($CDCl_3$) δ 7.29−6.85 (m, 3H), 3.91 (s, 3H); FABMS *m*/*z* 199 (M^+, 100). Anal. Calcd for C_8H_6ClNOS:

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C, 48.12; H, 3.03; N, 7.01; Cl, 17.75; S, 16.06. Found: C, 48.17; H, 3.18; N, 6.97; Cl, 17.86; S, 15.98.

3-Chloro-4-methylphenyl Isothiocyanate (4g). Previously reported.[37] ^{1}H NMR ($CDCl_3$) δ 7.24−7.18 (m, 2H), 7.05−7.01 (dd, J = 8 Hz, 2 Hz, 1H), 2.37 (s, 3H); EI-MS m/z 183 ($M^{+\bullet}$, 100).

4-Cyanophenyl Isothiocyanate (4h). ^{1}H NMR ($CDCl_3$) δ 7.67 (d, J = 8 Hz, 2H), 7.31 (d, J = 8 Hz, 2H); FABMS m/z 161 (MH^+, 100). Anal. Calcd for $C_8H_4N_2S$: C, 59.98, H, 2.51; N, 17.48; S, 20.01. Found: C, 59.79; H, 2.60; N, 17.27; S, 19.73.

3-Cyanophenyl Isothiocyanate (4i). ^{1}H NMR ($CDCl_3$) δ 7.59−7.43 (m, 4H); EI-MS m/z 160 (M^+, 100). Anal. Calcd for $C_8H_4N_2S$: C, 59.98; H, 2.51; N, 17.48; S, 20.01. Found: C, 60.09; H, 2.48; N, 17.38; S, 19.97.

General Procedure for the Reaction of Isothiocyanates with Phenylethylamine.

((4-Chlorophenyl)amino)((2-phenylethyl)amino)methane-1-thione (5a). To a solution of 4-chlorophenyl isothiocyanate (**4a**) (21 mg, 0.124 mmol) in THF (5 mL) was added phenylethylamine (16.5 mg, 0.136 mmol), and the mixture was stirred at room temperature (1 h). Solvent was evaporated under reduced pressure, and the residue was purified by silica gel flash chromatography [EtOAc:hexanes (1:2)] to provide product **5a** (31 mg, 86%).^{1}H NMR ($CDCl_3$) δ 7.28−7.13 (m, 7H), 6.91 (d, J = 8 Hz, 2H), 3.89 (t, J = 6.6 Hz, 2H), 2.93 (t, J = 6.6 Hz, 2H); FABMS m/z 291 (MH^+, 100). Anal. Calcd for $C_{15}H_{15}ClN_2S$: C, 61.95; H, 5.20; N, 9.63; S, 11.02. Found: C, 62.06; H, 5.32; N, 9.45; S, 10.92

(Indan-5-ylamino)((2-phenylethyl)amino)methane-1-thione (5b). ^{1}H NMR ($CDCl_3$) δ 7.26−6.74 (m, 8H), 3.88 (m, 2H), 2.87 (m, 6H), 2.08 (m, 2H); FABMS m/z 297 (MH^+, 100), 263 (8), 176 (5), 105 (57). Anal. Calcd for $C_{18}H_{20}N_2S\cdot{}^1/_5H_2O$: C, 72.06; H, 6.85; N, 9.34; S, 10.69. Found: C, 72.39; H, 6.97; N, 9.13; S, 10.42. FABMS (exact mass) MH^+: Calcd for $C_{18}H_{21}N_2S$; 297.1425. Found 297.1408.

(Naphth-1-ylamino)((2-phenylethyl)amino)methane-1-thione (5c). ^{1}H NMR ($CDCl_3$) δ 8.10−7.82 (m, 3H), 7.58−7.54 (m, 2H), 7.43−7.37 (t, J = 8 Hz, 1H), 7.26−7.21 (m, 1H), 7.10−7.08 (m, 3H), 6.92−6.90 (m, 2H), 3.82 (t, J = 6.6 Hz, 2H), 2.78 (t, J = 6.6 Hz, 2H); FABMS m/z 307 (MH^+, 100). Anal. Calcd for $C_{19}H_{18}N_2S$: C, 74.47; H, 5.91; N, 9.14. Found: C, 73.98; H, 6.06; N, 8.90. HR−FABMS Calcd for $C_{18}H_{21}N_2S$; 307.1269. Found 307.1237.

((2,6-Dimethylphenyl)amino)((2-phenylethyl)amino)-methane-1-thione (5d). ^{1}H NMR ($CDCl_3$) δ 7.71−7.08 (m, 8H), 3.87 (m, 2H), 2.90 (t, J = 7 Hz, 2H), 2.21 (s, 6H); FABMS m/z 285 (MH^+, 100). Anal. Calcd for $C_{17}H_{20}N_2S$: C, 71.79; H, 7.08; N, 9.84; S, 11.27. Found: C, 71.85; H, 7.12; N, 9.68; S, 11.11

2-(4-((((2-Phenylethyl)amino)thioxomethyl)amino)-phenyl)ethan-1-ol (5e). ^{1}H NMR ($CDCl_3$) δ 7.51−7.12 (m, 7H), 7.0 (d, J = 8 Hz, 2H), 3.93 (m, 4H), 3.01−2.89 (m, 4H); FABMS m/z 301 (MH^+, 49). Anal. Calcd for $C_{17}H_{20}N_2OS$: C, 67.97; H, 6.71; N, 9.32; S, 10.67. Found: C, 67.75; H, 6.69; N, 9.15; S, 10.43.

((3-Chloro-4-methoxyphenyl)amino)((2-phenylethyl)-amino)methane-1-thione (5f). ^{1}H NMR ($CDCl_3$) δ 7.28−6.85 (m, 8H), 3.90 (m, 5H), 2.91 (m, 2H); FABMS m/z 321 (MH^+, 100). Anal. Calcd for $C_{16}H_{17}ClN_2OS$: C, 59.90; H, 5.33; N, 8.73; Cl, 11.04. Found: C, 59.62; H, 5.55; N, 8.23; Cl, 10.92. FABMS (exact mass) MH^+: Calcd for $C_{16}H_{17}ClN_2OS$; 321.0828. Found 321.0776.

((3-Chloro-4-methylphenyl)amino)((2-phenylethyl)amino)methane-1-thione (5g). ^{1}H NMR ($CDCl_3$) δ 7.33−6.78 (m, 8H), 3.89 (t, J = 6.8 Hz, 2H), 2.93 (t, J = 6.8 Hz, 2H), 2.35 (s, 3H); FABMS m/z: 305 (MH^+, 100). Anal. Calcd for $C_{16}H_{17}ClN_2S$: C, 63.04; H, 5.61; N, 9.18; Cl;, 11.62; S, 10.52. Found: C, 63.20; H, 5.76; N, 9.05; Cl, 11.60;, S, 10.37.

((4-Cyanophenyl)amino)((2-phenylethyl)amino)methane-1-thione (5h). ^{1}H NMR ($CDCl_3$) δ 7.54 (d, J = 8 Hz, 2H), 7.34−7.19 (m, 5H), 7.04 (d, J = 8 Hz, 2H), 3.94 (t, J = 6.5 Hz, 2H), 2.99 (t, J = 6.5 Hz, 2H); FABMS m/z 282 (MH^+, 98). Anal. Calcd for $C_{16}H_{15}N_3S$: C, 68.30; H, 5.37; N, 14.93; S, 11.39. Found: C, 68.48; H, 5.53; N, 14.69; S, 11.26.

((3-Cyanophenyl)amino)((2-phenylethyl)amino)methane-1-thione (5i). ^{1}H NMR ($CDCl_3$) δ 7.45−7.15 (m, 9H), 3.86 (m, 2H), 2.94 (t, J = 7 Hz, 2H); FABMS m/z 282 (MH^+, 100). Anal. Calcd for $C_{16}H_{15}N_3S$: C, 68.30; H, 5.37; N, 14.93. Found: C, 68.42; H, 5.63; N, 14.54.

Silyl-Protected CAPE Thiocarbamate (7). To a stirred solution of freshly prepared TBS-protected caffeoyl chloride (**6**) (0.807 mmol) in toluene (8 mL) were added **3e** (221 mg, 0.807 mmol) and pyridine (1.2 mL), and the mixture was stirred at room temperature (overnight) and then filtered through Celite 521 and solvent removed under reduced pressure. The residue was chromatographed [EtOAc:hexane (1:4)] to afford **7** (256 mg, 48%). ^{1}H NMR ($CDCl_3$) δ 7.56 (d, J = 16 Hz, 1H), 7.46−6.80 (m, 12H), 6.23 (d, J = 16 Hz, 1H), 4.41 (t, J = 7.3 Hz, 2H), 3.02 (t, J = 7.3 Hz, 2H), 0.99 (s, 18H), 0.22 (s,12H); CI-MS (NH_3) m/z 665 (MH^+, 100). Anal. Calcd for $C_{36}H_{49}NO_5SSi_2$: C, 65.11; H, 7.43; N, 2.10. Found: C, 65.05; H, 7.45; N, 2.08.

Silyl-Protected CAPE 4-Isothiocyanate (8). To a stirred solution of silyl-protected CAPE thiocarbamate **7** (80 mg, 0.12 mmol) in benzene (5 mL) was added triethylamine (19 mg, 0.19 mmol) followed by trichlorosilane (26 mg, 0.19 mmol), and the mixture was stirred at room temperature (1 h) and then filtered through Celite 521. The resulting solution was evaporated under reduced pressure and purified by silica gel chromatography [EtOAc:hexane (1:10)] to provide **8** (69 mg, 98%). ^{1}H NMR ($CDCl_3$) δ 7.57 (d, J = 16 Hz, 1H), 7.29−7.19 (m, 4H), 7.05−7.02 (m, 2H), 6.85 (d, J = 8.8 Hz, 1H), 6.23 (d, J = 16 Hz, 1H), 4.42 (t, J = 6.8 Hz, 2H), 3.04 (t, J = 6.8 Hz, 2H), 1.02 (s, 18H), 0.25 (s, 12 H). FABMS m/z 570 (MH^+, 2). Anal. Calcd for $C_{30}H_{43}NO_4SSi$: C, 63.22; H, 7.60; N, 2.45. Found: C, 63.13; H, 7.63; N, 2.43.

CAPE 4-Isothiocyanate (9). To a stirred solution of silyl-protected CAPE 4-isothiocyanate **8** (72 mg, 0.126 mmol) in THF (3 mL) was added pyridinium hydrogen fluoride (0.1 mL), and the mixture was stirred at room temperature (4h) then filtered through Celite 521. The resulting solution was evaporated under reduced pressure and purified by silica gel chromatography [EtOAc: Hexane (1:2)] to give the desired CAPE 4-isothiocyanate **9** (34 mg, 75%). ^{1}H NMR (CD_3OD) δ 7.50 (d, J = 16 Hz, 1H), 7.34−7.20 (m, 4H), 7.01−6.90 (m, 2H), 6.77 (d, J = 7 Hz, 1H), 6.21 (d, J = 16 Hz, 1H), 4.36 (t, J = 6.5 Hz, 2H), 3.01 (t, J = 6.5 Hz, 2H); FABMS m/z 342 (MH^+, 100). Anal. Calcd for $C_{18}H_{15}NO_4S$: C, 63.33; H, 4.42; N, 4.10; S, 9.39. Found: C, 63.50; H, 4.56; N, 4.16; S, 9.28.

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