# Kinetic and Thermodynamic Evaluation of the Reversible N-Heterocyclic Carbene−Isothiocyanate Coupling Reaction: Applications in Latent Catalysis

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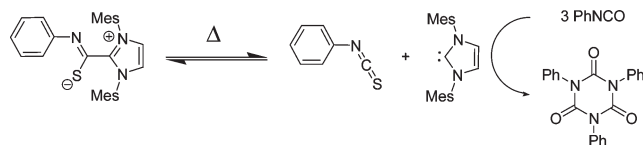
Using stopped flow and other spectroscopic techniques, the thermodynamic parameters of the coupling reaction between 1,3-dimesitylimidazolylidene and phenyl isothiocyanate were determined ($H^o = -96.1$ kJ mol^{-1} and $\Delta S^o = -39.6$ J mol^{-1} K^{-1}). On the basis of these data which indicated that the reaction was reversible ($K_{eq} = 5.94 \times 10^{14}$ M^{-1} at 25 °C; $k_f = 252$ M^{-1} s^{-1}; $k_r = 4.24 \times 10^{-13}$ s^{-1}), the adduct formed from the two aforementioned coupling partners was used as a latent catalyst to facilitate the [2 + 2 + 2] cyclotrimerization of phenyl isocyanate and the polymerization of DL-lactide.

Latent catalysts are generally inert under ambient conditions but become activated upon the application of an external stimulus, such as heat or light. They have found utility in a broad range of applications, including adhesives, photoresists (i.e., Novolac), and packaging for "flip chip" circuits.[1]

Contemporary efforts have been directed toward the development of latent catalysts that generate N-heterocyclic carbenes (NHCs).[2] NHCs are a diverse class of reactive species that are known to catalyze numerous reactions,[3] including the [2 + 2 + 2] cyclotrimerization of isocyanates[4] and the polymerization of lactide and other monomers.[5] Previous reports of using NHC adducts as latent catalysts generally contain either transition metals or carbon dioxide.[6,7] While these adducts are effective, only the NHC component may be altered to tune the activation temperature, which can influence the reactivity of the carbene catalyst generated. To expand the utilities of latent catalysts involving NHCs and to access adducts which do not involve transition metals, there is a need to develop other organic coupling partners that reversibly react with NHCs.

Recently, we discovered[8] that the reaction[9,10] between NHCs and isothiocyanates is thermally reversible and demonstrated that appropriately functionalized ditopic derivatives may be used to prepare structurally dynamic polymers. Moreover, we found that the reversibility of the reaction depended on the structure and electronic properties of the coupling partners. Building on these results, we reasoned that NHC−isothiocyanate adducts may find utility as latent catalysts, and we describe our efforts toward achieving that goal herein.

Since the thermodynamic parameters of the NHC−isothiocyanate coupling reaction are essential to predicting the concentration of the carbene catalyst that may ultimately be generated upon activation, initial efforts were directed toward studying a reaction involving two prototypical substrates: 1,3-dimesitylimidazolylidene (**1**) and phenyl isothiocyanate (**2**).

(1) (a) Smith, J. D. B. In *Epoxy Resin Chemistry*; Bauer, R. S., Ed.; American Chemical Society: Washington, DC, 1978; Chapter 3. (b) Pappas, S. P.; Hill, L. W. *J. Coat. Technol.* **1981**, *53*, 43–51. (c) Muizebelt, M. J. *J. Coat. Technol.* **1985**, *57*, 43–44. (d) Endo, T.; Sanda, F. *Macromol. Symp.* **1996**, *107*, 237–238.

(2) (a) Nyce, G. W.; Glauser, T.; Connor, E. F.; Möck, A.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 3046–3056. (b) Nyce, G. W.; Csihony, S.; Waymouth, R. M.; Hedrick, J. L. *Chem.—Eur. J.* **2004**, *10*, 4073–4079. (c) Csihony, S.; Culkin, D. A.; Sentman, A. C.; Dove, A. P.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 9079–9084. (d) Coulembier, O.; Dove, A. P.; Pratt, R. C.; Sentman, A. C.; Culkin, D. A.; Mespouille, L.; Dubois, P.; Waymouth, R. M.; Hedrick, J. L. *Angew. Chem., Int. Ed.* **2005**, *44*, 4964–4968. (e) Coulembier, O.; Lohmeijer, B. G. G.; Dove, A. P.; Pratt, R. C.; Mespouille, L.; Culkin, D. A.; Benight, S. J.; Dubois, P.; Waymouth, R. M.; Hedrick, J. L. *Macromolecules* **2006**, *39*, 5617–5628. (f) Arnold, P. L.; Casely, I. J.; Turner, Z. R.; Bellabarba, R.; Tooze, R. B. *Dalton Trans.* **2009**, 7236–7247. (g) Bantu, B.; Pawar, G. M.; Wurst, K.; Decker, U.; Schmidt, A. M.; Buchmeiser, M. R. *Eur. J. Inorg. Chem.* **2009**, 1970–1976. (h) Bantu, B.; Pawar, G. M.; Decker, W.; Wurst, K.; Schmidt, A. M.; Buchmeiser, M. R. *Chem.—Eur. J.* **2009**, *15*, 3103–3109.

(3) For excellent reviews on the utilities of NHCs as organocatalysts, see: (a) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606–5655. (b) Marion, N.; Díez-González, S.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2988–3000.

(4) Duong, H. A.; Cross, M. J.; Louie, J. *Org. Lett.* **2004**, *6*, 4679–4681.

(5) (a) Connor, E. F.; Nyce, G. W.; Myers, M.; Möck, A.; Hedrick, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 914–915. (b) Culkin, D. A.; Jeong, W.; Csihony, S.; Gomez, E. D.; Hedrick, J. L.; Balsara, N. P.; Waymouth, R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 2627–2630. (c) Raynaud, J.; Absalon, C.; Gnanou, Y.; Taton, D. *J. Am. Chem. Soc.* **2009**, *131*, 3201–3209. (d) Lohmeijer, B. G. G.; Dubois, G.; Leibfarth, F.; Pratt, R. C.; Nederberg, F.; Nelson, A.; Waymouth, R. M.; Wade, C.; Hedrick, J. L. *Org. Lett.* **2006**, *8*, 4683–4686.

(6) (a) Van Ausdall, B. R.; Glass, J. L.; Wiggins, K. M.; Aarif, A. M.; Louie, J. *J. Org. Chem.* **2009**, *74*, 7935–7942. (b) Duong, H. A.; Tekavec, T. N.; Arif, A. M.; Louie, J. *Chem. Commun.* **2004**, 112–113.

(7) For examples of using NHC−CO$_2$ adducts as precursors to metal complexes, see: (a) Voutchkova, A. M.; Appelhans, L. N.; Chianese, A. R.; Crabtree, R. H. *J. Am. Chem. Soc.* **2005**, *127*, 17624–17625. (b) Tudose, A.; Demonceau, A.; Delaude, L. *J. Organomet. Chem.* **2006**, *691*, 5356–5365. (c) Sauvage, X.; Demonceau, A.; Delaude, L. *Adv. Synth. Catal.* **2009**, *351*, 2031–2038. For examples of using NHC−CO$_2$ adducts as latent catalysts for the synthesis of cyclic carbonates, see: (d) Zhou, H.; Zhang, W.-Z.; Liu, C.-H.; Qu, J.-P.; Lu, X.-B. *J. Org. Chem.* **2008**, *73*, 8039–8044.

(8) Norris, B. C.; Bielawski, C. W. *Macromolecules* **2010**, *43*, 3591–3593.

(9) The products obtained from NHC−isothiocyanate coupling have been shown to engage in 1,3-dipolar additions with alkynes and arynes, see: (a) Liu, M.-F.; Wang, B.; Cheng, Y. *Chem Commun.* **2006**, 1215–1217. (b) Zhu, Q.; Liu, M.-F.; Bo, W.; Cheng, Y. *Org. Biomol. Chem.* **2007**, *5*, 1282–1286. (c) Li, J.-Q.; Liao, R.-Z.; Ding, W.-J.; Cheng, Y. *J. Org. Chem.* **2007**, *72*, 6266–6269. (d) Cheng, Y.; Liu, M.-F.; Fang, D.-C.; Lei, X.-M. *Chem.—Eur. J.* **2007**, *13*, 4282–4292. (e) Xue, J.; Yang, Y.; Huang, X. *Synlett* **2007**, 1533–1536.

(10) For early examples of using NHC−isothiocyanate adducts in 1,3-dipolar cycloaddition reactions, see: (a) Winberg, H. E.; Coffman, D. D. *J. Am. Chem. Soc.* **1965**, 2776–2777. (b) Regitz, M.; Hocker, J.; Schössler, W.; Weber, B.; Liedhegener, A. *Liebigs Ann. Chem.* **1971**, *748*, 1–19.
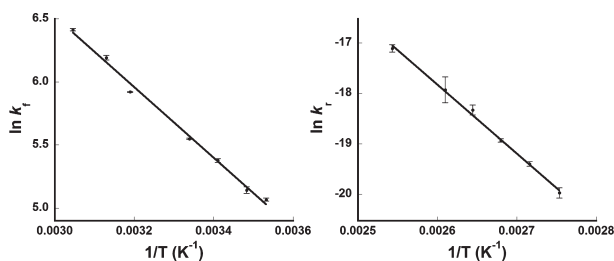
FIGURE 1. (Left) Plot of ln k_f versus $1/T$ for the reaction shown in eq 1. The best-fit line can be described by the equation: $y = -2795.2x + 14.903$ ($R^2 = 0.995$). (Right) Plot of ln k_r versus $1/T$ for the reaction shown in eq 2. The best-fit line can be described by the equation: $y = -14356x + 19.661$ ($R^2 = 0.997$). The data shown are the average of three separate experiments performed for each temperature analyzed.

Preliminary efforts attempted to measure the equilibrium constant (K_{eq}) between these reagents and their respective adduct (**3**) using ^{1}H NMR spectroscopy. However, analysis of a dilute DMF-d_7 solution of **3** ([**3**]$_0$ = 70 mM) did not show the presence of **1** or **2**, even at elevated temperatures (120 °C), which suggested to us that the reaction between **1** and **2** is highly favored. As such, the equilibrium constant (K_{eq}) was determined by measuring the rates of the forward (k_f) and reverse (k_r) reactions over a range of temperatures and using the equation $K_{eq} = k_f/k_r$.

The forward rate k_f was measured by combining toluene solutions **1** and **2** in a stopped flow reactor, and the concentration of the product **3** was measured by continuously monitoring the absorbance signal at $\lambda_{max} = 350$ nm over time. By varying the initial concentrations of the starting materials, the reaction was determined to be first order with respect to both the free NHC as well as the isothiocyanate (Figures S1 and S2, Supporting Information). Under pseudo-first-order kinetics conditions, where an excess of **1** (22 equiv) was employed, the k_f was measured over a range of temperatures (9.9−55 °C); a summary of the data is shown in Figure 1 (left).

The reverse rate k_r was also determined over a range of temperatures (90−120 °C)[11] by monitoring toluene solutions of **3** in the presence of excess sulfur (2.0 equiv), which reacts irreversibly with **1**[12] to form a known[12a] thiourea. Aliquots were periodically removed from the aforementioned solutions, separated via high performance liquid chromatography (HPLC; conditions: methanol as eluent, 25 °C), and then analyzed by UV/vis spectroscopy (λ = 350 nm); a summary of the data are shown in Figure 1 (right). The reaction was determined to be first order with respect to the starting material **3** and zero order with respect to sulfur (Figures S3 and S4, Supporting Information). These results suggested to us that the dissociation of NHC−isothiocyanate adduct was the rate-determining step and that the sulfur effectively trapped the NHC generated in situ without facilitating dissociation.

As shown in Figure 1, linear correlations between the ln k and the inverse temperature were observed for the forward

FIGURE 2. NHC−PhNCS adduct **3** facilitated the (top) [2 + 2 + 2] cyclotrimerization of phenyl isocyanate and the (bottom) ring-opening polymerization of DL-lactide.

and reverse reactions described above. From these data, the activation energies (E_a) were determined for eqs 1 and 2 using the Arrhenius equation: E_a (eq 1) = 23 kJ mol^{-1} K^{-1} and E_a (eq 2) = 119 kJ mol^{-1} K^{-1}. The kinetics data also facilitated the determination of the K_{eq} for the reaction of **1** with **2**. For example, at 25 °C, the K_{eq} = 5.94 × 10^{14} M^{-1} (k_f = 252 M^{-1} s^{-1}, k_r = 4.24 × 10^{-13} s^{-1}). Using these data, the thermodynamic parameters of the reaction were also calculated: ΔH^o = −96.1 kJ mol^{-1} and ΔS^o = −39.6 J mol^{-1} K^{-1}. The experimentally measured ΔH^o was in reasonable agreement with the ΔH^o predicted from DFT calculations (−111 kJ mol^{-1}) (see ESI).[13]
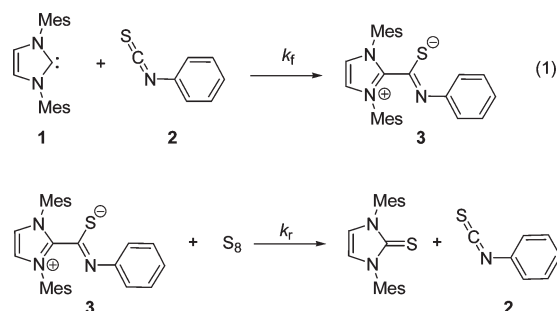
Once the kinetic and thermodynamic parameters for aforementioned NHC−isothiocyanate coupling reaction were determined, our efforts shifted toward exploring the potential of using **3** as a latent catalyst to facilitate [2 + 2 + 2] cyclotrimerization reactions. As summarized in Figure 2 (top), heating a toluene solution of phenyl isocyanate (initial concentration = 0.42 M) and **3** (20 mol %) at 120 °C for 24 h afforded phenyl isocyanurate in 82% isolated yield after purification via column chromatography.[14] To support the notion that a catalytically active NHC (i.e., **1**) was generated during the aforementioned reaction, a series of control

(11) The forward reaction (i.e., eq 1) was measured at the full temperature range of the stopped flow detector (9.9−55 °C). However, the reverse reaction (i.e., eq 2) was found to be too slow to achieve good kinetic data at these temperatures, and therefore was studied over the range of 90−120 °C.

(12) (a) Huang, J.; Schanz, H.-J.; Stevens, E. D.; Nolan, S. P.; Capps, K. B.; Bauer, A.; Hoff, C. D. *Inorg. Chem.* **2000**, *39*, 1042–1045. (b) Ramnial, T.; Taylor, S. A.; Bender, M. L.; Gorodetsky, B.; Lee, P. T. K.; Dickie, D. A.; McCollum, B. M.; Pye, C. C.; Walsby, C. J.; Clyburne, J. A. C. *J. Org. Chem.* **2008**, *73*, 801–812.
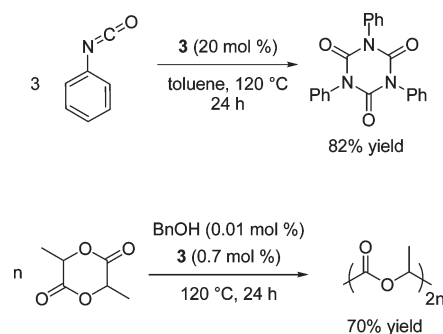
(13) DFT calculations were performed using the Perdew−Wang-91 generalized-gradient approximation functional. Valence electrons were described with a plane wave basis set up to a cutoff energy of 250 eV. Frozen core states were described by pseudopotentials using the projector-augmented wave framework, as implemented in the VASP code. See: (a) Kresse, G.; Hafner, J. *Phys. Rev. B* **1993**, *47*, 558–561. (b) Kresse, G.; Hafner, J. *Phys. Rev. B* **1994**, *49*, 14251–14269. (f) Perdew, J. P. In *Electronic Structure of Solids*; Ziesche, P., Eschrig, H., Eds.; Akademie Verlag: Berlin, 1991. (c) Blochl, P. E. *Phys. Rev. B* **1994**, *50*, 17953–17979. (d) Kresse, G.; Furthmuller, J. *Comput. Mater. Sci.* **1996**, *6*, 1–50. (e) Kresse, G.; Furthmuller, , J. *Phys. Rev. B* **1996**, *54*, 11169–11186.

(14) Using the data shown in Figure 1, the concentration of **1** at 120 °C (K_{eq} = 5.09 × 10^{10} M^{-1}; k_f = 2.43 × 10^3 M^{-1} s^{-1}, k_r = 4.79 × 10^{-8} s^{-1}) was calculated to be approximately 2 orders of magnitude higher than at 25 °C.
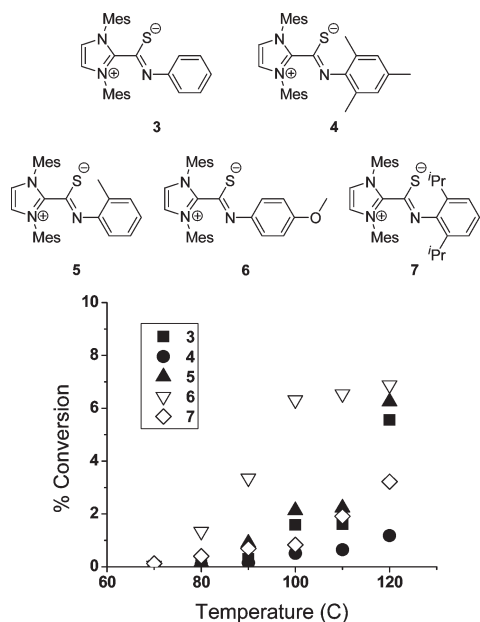
FIGURE 3. (Top) Structures of **3**–**7**. (Bottom) Plot of percent conversion of phenyl isocyanate to phenyl isocyanuranate versus temperature. Each data point was taken after the respective reaction was heated for 2 h at the indicated temperature followed by 8 h at ambient temperature. Conditions: 2:1 phenyl isocyanate/cyclooctane (as an internal standard), 0.05 mol % catalyst. The cycloaddition reactions were monitored by IR spectroscopy (see text).

experiments were performed. Heating a toluene solution of phenyl isocyanate in the presence of **2** (20 mol %) to 120 °C did not afford the isocyanurate product. Likewise, a toluene solution of phenyl isocyanate did not undergo spontaneous cyclotrimerization upon heating to 120 °C for 24 h.

In a separate experiment, neat DL-lactide was treated with **3** (0.7 mol %) and benzyl alcohol (BnOH) as an initiator ([lactide]$_0$/[BnOH]$_0$ = 10,000) at 120 °C (Figure 3, bottom). After 24 h, 80% of the lactide had been consumed, as determined by gas chromatography (GC),[15] and the resulting polymer was collected in 70% isolated yield after dissolution in tetrahydrofuran followed by precipitation from methanol. The number average molecular weight (M_n) of the polymer was determined by gel permeation chromatography[16] to be 2.1 kDa, which was lower than expected based on the initial monomer to initiator ratio and monomer conversion. This discrepancy suggested to us that the polymerization reaction experienced premature termination.[17] Regardless, heating a solution of DL-lactide with BnOH at 120 °C for 24 h did not afford polymer, which supported the notion that **3** effectively catalyzed the polymerization reaction (via the in situ generation of **1**). To probe catalyst latency, a solution of DL-lactide, **3** (20 mol %), and benzyl alcohol ([lactide]$_0$/[BnOH]$_0$ = 10,000) was stirred at room temperature for 7 d. Although no monomer consumption was observed, as determined by GC, subsequent heating of the reaction mixture to 120 °C for 24 h afforded

a polymeric material of comparable molecular weight (M_n = 3.1 kDa) as described above.

Finally, efforts were directed toward determining if the identity of the isothiocyanate component of a NHC–isothiocyanate adduct would influence its activation temperature. Adducts **3**–**7** (Figure 3, top) were selected for study because they feature a range of electron-rich and/or bulky aryl isothiocyanate moieties. These differences were expected to effect the adduct dissociation process and facilitate catalyst activation at different temperatures. After the synthesis of **3**–**7**, toluene solutions of these adducts (0.05 mol %) with phenyl isocyanate and cyclooctane as an internal standard were independently prepared and divided into several ampules. Following heating at various temperatures for 2 h to facilitate catalyst activation, the ampules were allowed to stand at ambient temperature for 8 h to enable the [2+2+2] cyclotrimerization reaction to proceed. Afterward, the ampules were opened, and the conversion of phenyl isocyanate to phenyl isocyanurate was measured via IR spectroscopy (CH$_2$Cl$_2$) by comparing the integrated signal attributed to product (v_{CO} = 1700 cm^{-1}) to that assigned to cyclooctane (v_{CH} = 2845 and 2915 cm^{-1}).

As summarized in Figure 3 (bottom), the activation temperature of the adducts studied appeared to be more dependent on the electronic properties of the isothiocyanate component than sterics. The methoxy derivative **6**, for example, consistently afforded higher percent conversions of phenyl isocyanate to phenyl isocyanurate over the range of temperatures and reaction times studied.[18] Surprisingly, **5** appeared to activate more readily than **3** or **4**, which suggested to us that the NHC–isothiocyanate adducts may require the adoption of a specific conformation that is aided by electron-donating groups to dissociate. Although other trends were not apparent, the data obtained indicated that the catalyst activation process was dependent on the identity of the isothiocyanate component of the respective adducts.

In summary, the kinetic and thermodynamic parameters of the coupling reaction between 1,3-dimesitylimidazolylidene and phenyl isothiocyanate were evaluated. The reaction was determined to be reversible, and the adduct formed from the two aforementioned coupling partners was used as a latent catalyst to facilitate the [2 + 2 + 2] cyclotrimerization of phenyl isocyanate and the polymerization of DL-lactide. Furthermore, it was found that the catalyst activation temperature may be modified by varying the structure and electronic properties of the isothiocyanate component of the NHC–isothiocyanate adduct. These results effectively expand the range of organic latent catalysts that generate NHCs upon thermal activation and provides a method for tuning the temperature at which catalyst activation occurs without modifying the NHC component.

Experimental Section

Determination of k_f. Toluene solutions of **1** (λ = 350 nm; ε = 6790 M^{-1} cm^{-1}) were prepared in a nitrogen filled glovebox and

(15) A predetermined quantity of diglyme (100 mg) was added as an external standard to each aliquot (100 mg) removed from the reaction mixture prior to GC analysis.

(16) The molecular weight data are reported relative to polystyrene standards in DMF.

(17) In support of this conclusion, the polydispersity of the isolated polymer was broad (PDI = 2.8).

(18) This result is consistent with previous studies which demonstrated that NHCs react relatively slowly with electron-rich electrophiles, see: (a) Khramov, D. M.; Bielawski, C. W. *Chem. Commun.* **2005**, 4958–4960. (b) Khramov, D. M.; Bielawski, C. W. *J. Org. Chem.* **2007**, *72*, 9407–9417. (c) Tennyson, A. G.; Khramov, D. M.; Varnado, C. D., Jr.; Creswell, P. T.; Kamplain, J. W.; Lynch, V. M.; Bielawski, C. W. *Organometallics* **2009**, *28*, 5142–5147. (d) Coady, D. J.; Khramov, D. M.; Norris, B. C.; Tennyson, A. G.; Bielawski, C. W. *Angew. Chem., Int. Ed.* **2009**, 5187–5190.

transferred to a stopped flow reactor via nitrogen-flushed syringes. Separate injections were made with excess **1** ($[\mathbf{1}]_0 = 2.16$ mM; $[\mathbf{2}]_0 = 0.100$ mM) as well as excess phenyl isothiocyanate ($[\mathbf{2}]_0 = 1.00$ mM; $[\mathbf{1}]_0 = 0.100$ mM) to determine the order of the reaction (Figures S1 and S2, Supporting Information). Under pseudo-first-order kinetics conditions ($[\mathbf{1}]_0 = 2.16$ mM; $[\mathbf{2}]_0 = 0.100$ mM), the reaction was monitored at various temperatures (9.9, 14, 20, 40, 46, and 55 °C), and the k_f were calculated by plotting ln [**1**] vs time. The error was calculated by standard deviation from the average of three, separate 100 μL injections.

Determination of k_r. In a nitrogen-filled glovebox, a series of 5-mL vials containing 3 Å molecular sieves was charged with various quantities of **1**, elemental sulfur, anthracene (as an internal standard) (400 mM), and toluene. The vials were then placed in an oil bath and heated to 120 °C. Aliquots (100 μL) were removed periodically over time and diluted to a total volume of 1 mL with methanol. The aliquots were then separated via HPLC and analyzed by UV–vis spectroscopy ($\lambda = 350$ nm). The residual concentration of **1** was determined by calculating the integral of the signal attributed to this compound ($\lambda = 350$ nm; $\varepsilon = 6790$ M^{-1} cm^{-1}) with respect to the internal standard ($\lambda = 350$ nm; $\varepsilon = 3938$ M^{-1} cm^{-1}). The order of the reaction was determined by varying the initial concentrations of **1** and sulfur (Figures S3 and S4, Supporting Information). Next, a stock solution of **1** (175.6 mg, 0.400 mmol), sulfur (25.6 mg, 0.800 mmol), anthracene (71.3 mg, 0.400 mmol), and toluene (100 mL) was prepared in a 100-mL volumetric flask, and kinetic experiments analogous to those described above were performed using 2-mL portions of this stock solution at 90, 95, 100, 105, 110, and 120 °C.

General Procedure for the Synthesis of 3–7. In a nitrogen-filled glovebox, a 5-mL vial was charged with **1** (263 mg, 0.866 mmol), tetrahydrofuran (2 mL), and a stir bar. A solution of aryl isothiocyanate (1 equiv) in tetrahydrofuran (2 mL) was added at ambient temperature, and the solvent was immediately removed under vacuum. The residual solid was purified by silica column chromatography using acetone/hexanes (0:1 → 1:1 v/v) as the mobile phase which yielded the desired compound. Isolated yields and spectroscopic data are reported below.

Compound 3: obtained as a yellow solid (368 mg, 97% yield); mp 241–242 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.09 (t, $J = 7.3$ Hz, 2H), 7.03 (s, 2H), 7.00 (s, 4H), 6.85 (t, $J = 7.2$ Hz, 1H), 6.64 (d, $J = 3$ Hz, 2H), 2.33 (m, 18H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 164.8, 151.6, 146.6, 140.3, 135.7, 131.3, 129.2, 128.1, 122.2, 121.3, 120.1, 21.1, 18.3. HRMS: [M+H$^+$] Calcd for C$_{28}$H$_{30}$N$_3$S: 440.2155; Found: 440.2156. Anal. Calcd (%) for C$_{28}$H$_{29}$N$_3$S: C, 76.50; H, 6.65; N, 9.56; S, 7.29; Found: C, 76.42; H, 6.67; N, 9.55; S, 7.13.

Compound 4: obtained as tan solid (297 mg, 94% yield); mp 259–260 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.00 (s, 2H), 6.96 (s, 4H), 6.6 (s, 2H), 2.4 (s, 12H), 2.3 (s, 6H), 2.1 (s, 3H), 1.3 (s, 6H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 164.7, 147.0, 146.9, 140.3, 136.1, 131.3, 130.6, 129.1, 128.0, 126.8, 120.4, 20.5, 18.5, 17.0. HRMS: [M + H$^+$] Calcd for C$_{31}$H$_{36}$N$_3$S: 482.2625; Found: 482.2626. Anal. Calcd. (%) for C$_{31}$H$_{35}$N$_3$S: C, 77.30; H, 7.32; N, 8.72; S, 6.66; Found: C, 77.08; H, 7.24 ; N, 8.70; S, 6.66.

Compound 5: obtained as tan solid (272 mg, 84% yield); mp 258–260 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.01 (s,2H), 6.97 (s, 4H), 6.8 (m, 2H), 6.21 (t, $J = 7.8$ Hz), 2.36 (m, 18H), 1.45 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 165.2, 151.3, 146.7, 140.4, 136.0, 131.4, 129.8, 129.3, 128.3, 126.0, 122.1, 120.6, 119.7, 21.2, 18.5, 17.1. HRMS: [M + H$^+$] Calcd for C$_{29}$H$_{32}$N$_3$S: 454.2317; Found: 454.2309. Anal. Calcd (%) for C$_{29}$H$_{31}$N$_3$S: C, 76.78; H, 6.89; N, 9.26; S, 7.07; Found: C, 76.57; H, 6.60; N, 9.33; S, 7.15.

Compound 6: obtained as yellow solid (276 mg, 88% yield); mp 244–246 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.02 (s, 2H), 6.94 (s, 4H), 6.91 (d, $J = 8.8$ Hz, 2H), 6.68 (d, $J = 8.8$ Hz, 2H), 3.68 (s, 3H), 2.3 (m, 18H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 163.5, 155.2, 136.7, 144.7, 140.3, 135.7, 131.5, 129.3, 123.1, 113.43, 55.4, 21.2, 18.4. HRMS: [M + H$^+$] Calcd for C$_{29}$H$_{32}$N$_3$OS: 470.2266; Found: 470.2273. Anal. Calcd (%) for C$_{29}$H$_{31}$N$_3$OS: C, 74.17; H, 6.65; N, 8.95; S, 6.83; Found: C, 74.26; H, 6.90; N, 8.61; S, 6.63.

Compound 7: obtained as white solid (282 mg, 81% yield); mp 282–284 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.05 (s, 4H), 6.98 (s, 2H), 6.9 (m, 3H), 2.4 (m, 18H), 1.85 (m, 2H), 0.87 (d, $J = 6.9$ Hz, 6H), 0.67 (d, 6.9 Hz, 6H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 167.4, 147.5, 140.7, 138.2, 136.5, 131.7, 129.6, 123.0, 123.0, 120.8, 27.6, 24.7, 24.2, 21.5, 18.8. HRMS: [M + H$^+$] Calcd for C$_{34}$H$_{42}$N$_3$S: 524.3099; Found: 524.3101. Anal. Calcd (%) for C$_{34}$H$_{41}$N$_3$S: C, 77.97; H, 7.89; N, 8.02; S, 6.12; Found: C, 78.24; H, 7.70; N, 8.12; S, 6.03.

Supporting Information Available: Additional experimental procedures, integrated UV–vis data, IR spectra, NMR spectra, and Cartesian coordinates used for the DFT calculations are available free of charge via the Internet at http://pubs.acs.org.