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Desulfurization Mediated by Hypervalent Iodine(III): A Novel Strategy for the Construction of Heterocycles

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Dedicated to Professor G. B. Behera on the occasion of his 70th birthday

Keywords: Iodine / Desulfurization / Oxidation / Isothiocyanates / Heterocycles / Hypervalent compounds

The desulfurization ability of diacetoxyiodobenzene (DIB) has been explored in the preparation of isothiocyanates from the corresponding dithiocarbamate salts. The in situ generated isothiocyanates reacted with *o*-phenylenediamine and *o*-aminophenol to form monothioureas, which, on treatment with a further equivalent of DIB in one pot, gave benzimidazoles and aminobenzoxazoles, respectively. Aliphatic 1,2-diamines on reaction with 2 equiv. of isothiocyanate followed by treatment with DIB gave imidazolidenecarbothioamides, whereas the treatment of aromatic 1,2-diaminebis(thioureas) yielded benzimidazoles with the concurrent formation of isothiocyanate. The driving force for the formation of the latter is the aromatization of the product. The use of DIB makes these methods simpler and more efficient, giving high yields of the desired products in one pot.

Introduction

The upsurge in the use of hypervalent iodine reagents in recent years is reflected in the growing number of related publications and reviews. The advantage of these nonmetallic oxidizing agents is their nontoxicity, which contrasts toxicity of heavy metal oxidants such as lead-, mercury-, and thallium-based reagents.[1] In addition to serving as a useful oxidizing agent, derivatives of hypervalent iodine reagents occupy an important place in the realm of natural and synthetic organic chemistry because they have potential applications in the construction of carbon–heteroatom and carbon–carbon bonds.[2] From an environmental point of view, they are interesting reagents for the development of new synthetic organic transformations. We have recently demonstrated the regioselective *N*-acylation of thiourea to *N*-acylurea using diacetoxyiodobenzene (DIB).[3a] Taking cues from this and other[3b–3e] work, we sought to explore the thiophilic property of diacetoxyiodobenzene (DIB) in the preparation of isothiocyanates and the construction of various heterocycles in one pot from the in situ generated isothiocyanates.

In synthetic organic chemistry, isothiocyanates are an important class of molecule that are frequently encountered in many natural products and are key intermediates in the preparation of both sulfur- and nitrogen-containing organic compounds, especially heterocycles.[4] They are prepared conventionally by treating amines with thiophosgene.[5] Owing to difficulties in handling thiophosgene, its equivalents have been prepared and employed for this purpose.[6] The reactions of amines with "thiocarbonyl transfer" reagents afford the corresponding isothiocyanates.[7] An alternative approach relies on the decomposition of dithiocarbamic acid salts into isothiocyanates promoted by various reagents. The reagents used are uranium- and phosphonium-based coupling agents,[8,9] tosyl chloride,[10] di-*tert*-butyl dicarbonate,[11] hydrogen peroxide,[12] and ethyl chlorocarbonate.[13] The drawbacks of this process mainly result from the use of environmentally unsafe halogenated solvents, longer reaction times, and hazardous and toxic reagents.

Results and Discussion

The use of diacetoxyiodobenzene (DIB) overcomes many of the problems associated with the preparation of isothiocyanates. When the dithiocarbamate salt[14] **1** (1 equiv.) was treated with DIB (1 equiv.) in the presence of triethylamine (1.5 equiv.) in acetonitrile, isothiocyanate **1a** was obtained in nearly quantitative yield. The proposed mechanism is shown in Scheme 1. The formation of phenyl iodide and the precipitation of elemental sulfur from the reaction mixture support the mechanism.

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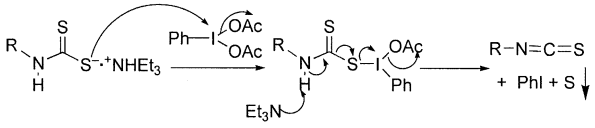
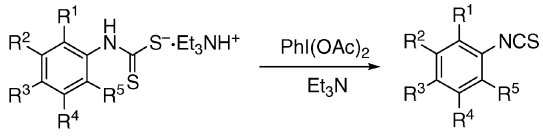
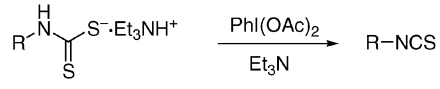


Scheme 1. Mechanism of the formation of isothiocyanate from the dithiocarbamate salt.

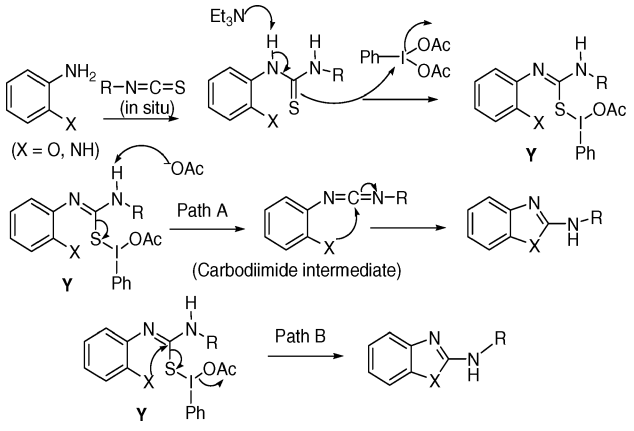
Several isothiocyanates (Table 1) were successfully prepared in good to excellent yields by utilizing this protocol. As can be seen from Table 1, aromatic substrates containing *ortho*, *meta*, and *para* substituents all gave isothiocyanates in good yields. Recently, we found that regioselective *N*-acylation of unsymmetrical 1,3-disubstituted thiourea is dependent on the pK_a of the amine attached to the thioureas.[3a] Based on this observation and the mechanism proposed in Scheme 1, we have reason to believe that an amine with a lower pK_a should yield the isothiocyanate faster because of its easy deprotonation. Triethylamine, the base employed for this purpose is sufficiently basic (pK_a = 10.78) compared with the aromatic amines used (pK_a = 2.46–5.63). The pK_a of the NH proton upon formation of the dithiocarbamate salt is expected to decrease further. Hence all the dithiocarbamic acid salts (**1**–**10**) gave the corresponding isothiocyanates (**1a**–**10a**) in excellent yields when triethylamine was used as the base along with DIB. Alkylamines such as *n*-butyl- (pK_a = 10.77), cyclohexyl- (pK_a = 10.66), and benzylamine (pK_a = 9.33), which have comparable basicity to that of triethylamine (10.78), yielded isothiocyanates **11a**–**13a** in good yields in shorter reaction times. The attachment of hypervalent iodine to sulfur makes it a much better leaving group and is probably the rate-limiting step in this reaction (Scheme 1). Further, the NH protons of the alkylamines are expected to become more acidic due to the presence of a C=S moiety leading to facile deprotonation by the base triethylamine.

Table 1. Preparation of isothiocyanates from dithiocarbamate salts and DIB.[a]

Substrate	Product[b]	Yield (%)[c]
		
1, R^1 = H, R^2 = H, R^3 = H, R^4 = H, R^5 = H;	**1a**	96%
2, R^1 = Cl, R^2 = H, R^3 = H, R^4 = H, R^5 = H;	**2a**	94%
3, R^1 = H, R^2 = Cl, R^3 =H, R^4 = H, R^5 = H;	**3a**	91%
4, R^1 = H, R^2 = H, R^3 = Cl, R^4 = H, R^5 = H;	**4a**	93%
5, R^1 = H, R^2 = NO_2, R^3 = H, R^4 = H, R^5 = H;	**5a**	78%
6, R^1 = H, R^2 = H, R^3 = Br, R^4 = H, R^5 = H;	**6a**	93%
7, R^1 = H, R^2 = H, R^3 = Me, R^4 = H, R^5 = H;	**7a**	92%
8, R^1 = H, R^2 = H, R^3 = OMe, R^4 = H, R^5 = H;	**8a**	97%
9, R^1 = Me, R^2 = H, R^3 = Me, R^4 = H, R^5 = H;	**9a**	90%
10, R^1 = Me, R^2 = H, R^3 = H, R^4 = H, R^5 = Me;	**10a**	95%
		
11, *n*-Butyl	**11a**	63%
12, Cyclohexyl	**12a**	81%
13, Benzyl	**13a**	93%

[a] Reactions were monitored by TLC. [b] Confirmed by IR, ^{1}H, and ^{13}C NMR spectroscopy. [c] Isolated yield.

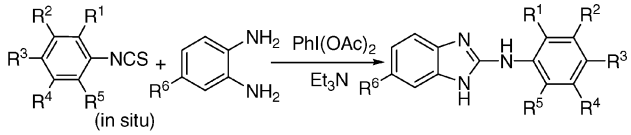
After successfully synthesizing various isothiocyanates, we focused our attention on the synthesis of 2-aminobenzimidazole. Benzimidazoles are widely used structural motifs in drug discovery and can be found in a number of biologically active molecules.[15] The most commonly adopted method for the synthesis involves the cyclodesulfurization of preformed monothioureas. The reported desulfurization agents include carbodiimides,[16] tosyl chloride,[17] methyl iodide,[18] mercury(II) oxide,[19] mercury(II) chloride,[20] and copper(I) salts.[21] Because isothiocyanate can be generated from a dithiocarbamate salt by using DIB, which also has desulfurization ability,[3] we decided to develop a one-pot procedure for the synthesis of 2-aminobenzimidazole by treating *o*-phenylenediamine with the in situ generated isothiocyanates (Scheme 1). The resultant monothiourea was treated with another equivalent of DIB to give the desired benzimidazole in good yield. The sulfur atom of the thiourea attacks the thiophilic iodine of $PhI(OAc)_2$ displacing one of its acetate groups to give intermediate **Y** (Scheme 2). Reductive β-elimination of the λ^3-iodane intermediate (path A, Scheme 2) with the expulsion of sulfur produced a carbodiimide intermediate, which reacted intramolecularly with the *o*-amino group to yield the desired product, as shown in Scheme 2. The precipitation of elemental sulfur and formation of phenyl iodide support the proposed mechanism. Alternatively, a mechanism involving direct intramolecular cyclization at the iminium carbon atom (path B) cannot be ruled out.



Scheme 2. Mechanism for the formation of benzimidazole/benzoxazole.

This strategy has successfully been applied to the preparation of various benzimidazoles (**1b**, **2b**, **3b′**, **4b**, **6b**, **7b**, **8b**, and **8b′**), as shown in Table 2. The structure of the product **1b** was confirmed by X-ray crystallography (Figure 1).[22]

Table 2. One-pot preparation of benzimidazole.[a]

Substrate	Product[b]	Yield (%)[c]
 (in situ)		
1a, R^1 = H, R^2 = H, R^3 = H, R^4 = H, R^5 = H; (R^6 = H);	**1b**	71%
2a, R^1 = Cl, R^2 = H, R^3 = H, R^4 = H, R^5 = H; (R^6 = H);	**2b**	70%
3a, R^1 = H, R^2 = Cl, R^3 =H, R^4 = H, R^5 = H; (R^6 = Me);	**3b'**	64%
4a, R^1 = H, R^2 = H, R^3 = Cl, R^4 = H, R^5 = H; (R^6 = H);	**4b**	69%
6a, R^1 = H, R^2 = H, R^3 = Br, R^4 = H, R^5 = H; (R^6 = H);	**6b**	65%
7a, R^1 = H, R^2 = H, R^3 = Me, R^4 = H, R^5 = H; (R^6 = H);	**7b**	75%
8a, R^1 = H, R^2 = H, R^3 = OMe, R^4 = H, R^5 = H; (R^6 = H);	**8b**	69%
8a, R^1 = H, R^2 = H, R^3 = OMe, R^4 = H, R^5 = H; (R^6 = Me);	**8b'**	68%

[a] Reactions were monitored by TLC. [b] Confirmed by IR, ^{1}H, and ^{13}C NMR spectroscopy. [c] Isolated yield.

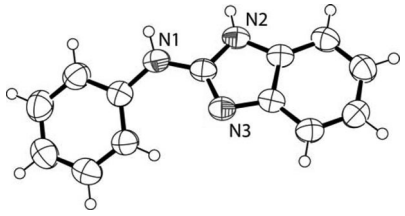
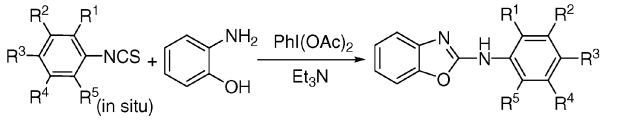
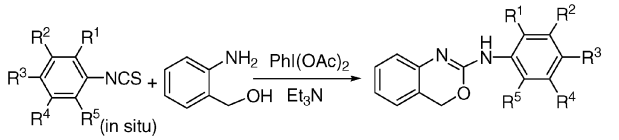


Figure 1. ORTEP view of **1b** with the atomic numbering scheme.

The success of this strategy lies in the selective formation of monothiourea from *o*-phenylenediamine in the presence of 1 equiv. of the in situ generated isothiocyanate.

The successful synthesis of benzimidazole prompted us to apply this strategy to the synthesis of aminobenzoxazoles. This class of compounds has great potential as drug candidates, and its use is currently under investigation in the treatment of a wide variety of disorders, such as HIV, neurogeneration, and inflammatory diseases.[23] The general method used for the synthesis of aminobenzoxazoles is the cyclodesulfurization of *N*-substituted 2-hydroxyphenylthioureas. The cyclodesulfurization reagents include NiO,[24a] HgO,[24b–24d] $AgNO_3$,[24e,24f] KO_2,[24g,24h] salts of transition metals,[24i] and dicyclohexylcarbodiimide (DCC).[24j] Oxidative cyclodesulfurization by using aqueous hydrogen peroxide and LiOH has recently been reported to give excellent yields of the products.[25] However, these reported methods have several limitations and cannot be applied to large-scale reactions. Thus, the strategy applied to the synthesis of 2-aminobenzimidazole was also applied to the synthesis of aminobenzoxazoles. The in situ generated isothiocyanate (Scheme 1) was treated with *o*-aminophenol to yield the monothiourea. The resultant monothiourea, on treatment with another equivalent of DIB, produced the desired aminobenzoxazoles. The mechanism is expected to be similar to the one proposed in Scheme 2. Several aminobenzoxazole derivatives (**1c**–**3c**, **6c**, and **8c**) were successfully prepared in excellent yields in shorter reaction times. Another important class of compounds, benzoxazines, has also been prepared by using DCC as the desulfurization agent[24j] and by the arduous tandem aza-Wittig/heterocumulene-mediated annulation strategy.[26] Thus, this one-pot strategy has been applied successfully to the synthesis of benzoxazine derivatives **6d** and **8d**, as shown in Table 3.

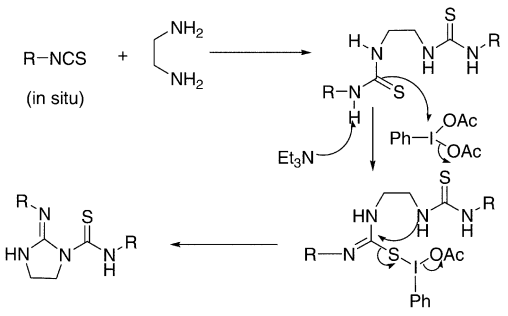
Table 3. One-pot preparation of aminobenzoxazole.[a]

Substrate	Product[b]	Yield (%)[c]
 (in situ)		
1a, R^1 = H, R^2 = H, R^3 = H, R^4 = H, R^5 = H;	**1c**	70%
2a, R^1 = Cl, R^2 = H, R^3 = H, R^4 = H, R^5 = H;	**2c**	67%
3a, R^1 = H, R^2 = Cl, R^3 =H, R^4 = H, R^5 = H;	**3c**	73%
6a, R^1 = H, R^2 = H, R^3 = Br, R^4 = H, R^5 = H;	**6c**	69%
8a, R^1 = H, R^2 = H, R^3 = OMe, R^4 = H, R^5 = H;	**8c**	65%
 (in situ)		
6a, R^1 = H, R^2 = H, R^3 = Br, R^4 = H, R^5 = H;	**6d**	68%
8a, R^1 = H, R^2 = H, R^3 = OMe, R^4 = H, R^5 = H;	**8d**	71%

[a] Reactions were monitored by TLC. [b] Confirmed by IR, ^{1}H, and ^{13}C NMR spectroscopy. [c] Isolated yield.

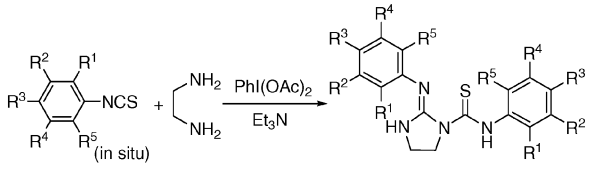
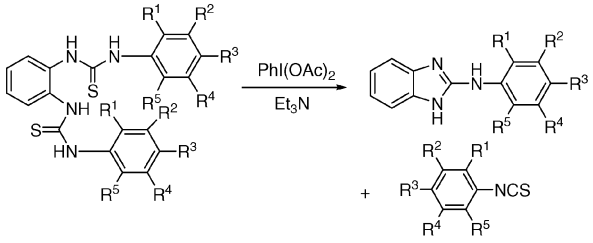
The most interesting aspect of this investigation is the synthesis of 1-imidazolidinecarbothioamides. These compounds are useful as insecticides, particularly for the control of *Epilachna varivestis*.[27] Only two methods have been reported for their synthesis. One involves the use of a toxic mercury salt from bis(urea) and the other the treatment of 2-methylamino-2-imidazoline with isothiocyanate.[28] The in situ generated isothiocyanate **1a** (2 equiv.), when treated with ethylenediamine (1 equiv.), gave bis(urea), which, on reaction with DIB, gave an excellent yield of imidazolidinecarbothioamide (**1e**) (Scheme 3). The mechanism for the formation of imidazolidinecarbothioamide is shown in Scheme 3.

As a result of this success, the strategy was applied to the synthesis of other imidazolidinecarbothioamides (**2e**, **3e**, and **6e**–**8e**) in good yields, as shown in Table 4. The structure of **8e** was confirmed by X-ray crystallography (Figure 2).[22]



Scheme 3. Mechanism for the formation of 1-imidazolidinecarbothioamide.

Table 4. Synthesis of imidazolidenecarbothioamides and benzimidazole.[a]

Substrate	Product[b]	Yield (%)[c]
		
1a, R^1 = H, R^2 = H, R^3 = H, R^4 = H, R^5 = H;	**1e**	73%
2a, R^1 = Cl, R^2 = H, R^3 = H, R^4 = H, R^5 = H;	**2e**	76%
3a, R^1 = H, R^2 = Cl, R^3 =H, R^4 = H, R^5 = H;	**3e**	68%
6a, R^1 = H, R^2 = H, R^3 = Br, R^4 = H, R^5 = H;	**6e**	70%
7a, R^1 = H, R^2 = H, R^3 = Me, R^4 = H, R^5 = H;	**7e**	67%
8a, R^1 = H, R^2 = H, R^3 = OMe, R^4 = H, R^5 = H;	**8e**	75%
		
1a', R^1 = H, R^2 = H, R^3 = H, R^4 = H, R^5 = H;	**1b**	93%
3a', R^1 = H, R^2 = Cl, R^3 = H, R^4 = H, R^5 = H;	**3b**	92%
8a', R^1 = H, R^2 = H, R^3 = OMe, R^4 = H, R^5 = H;	**8b**	94%

[a] Reactions were monitored by TLC. [b] Confirmed by IR, ^{1}H, and ^{13}C NMR spectroscopy. [c] Isolated yield.

When the flexible ethylenediamine was replaced by a rigid aromatic system such as *o*-phenylenediamine, the reactivity changed completely to give benzimidazole and isothiocyanate instead of imidazolidinecarbothioamide. The bis(ureas) of *o*-phenylenediamine (**1a′**, **3a′**, and **8a′**) were prepared according to a modified literature procedure, and the reaction was performed by starting from the isolated bis(ureas) (**1a′**, **3a′**, and **8a′**). In this case the intermediate imidazolidinecarbothioamide rapidly lost 1 equiv. of isothiocyanate to give benzimidazole. The driving force for this reaction is the gain in the aromatic character of the product

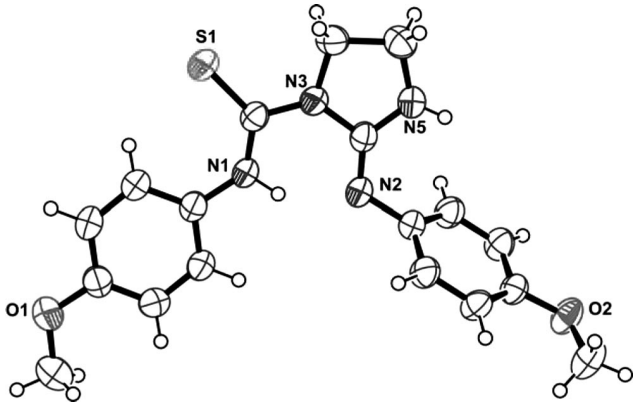
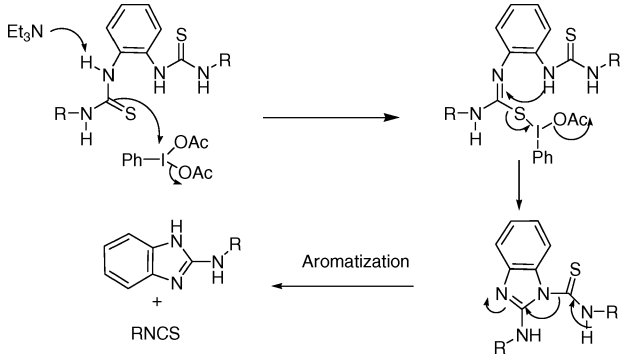


Figure 2. ORTEP view of **8e** with the atomic numbering scheme.

benzimidazole as a result of the loss of isothiocyanate (Scheme 4), which was not observed with the analogous aliphatic ethylenediaminebis(ureas) (Scheme 3).



Scheme 4. Reaction of aromatic 1,2-bis(thiourea) with DIB.

Conclusions

We have demonstrated the multifaceted use of diacetoxyiodobenzene for various synthetically useful organic transformations. In the past most of these reactions were carried out in several steps by using toxic heavy metals or expensive reagents. It has been demonstrated here that the reactions can be carried out under mild conditions by using the hypervalent iodine reagent DIB. Although the overall isolated yields look moderate, considering that the reactions are multistep processes, the yields are in fact good to excellent. An interesting difference in reactivity was observed for the bis(thioureas) of aliphatic and aromatic 1,2-diamines, the former giving 1-imidazolidinecarbothioamide and the latter benzimidazole and isothiocyanate.

Experimental Section

General Remarks: All reagents were of commercial grade and purified according to established procedures. Organic extracts were dried with anhydrous sodium sulfate. Solvents were removed in a rotary evaporator under reduced pressure. Silica gel (60–120 mesh) was used for column chromatography. Reactions were monitored by TLC on silica gel 60 F_{254} (0.25 mm). NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard

for ^{1}H (400 MHz) and $CDCl_3$ as the internal standard for ^{13}C (100 MHz). HR mass spectra were recorded by using Waters MS system Q-tof according to the MS–MS method, and data were analyzed with Mass Lynx 4.1 software (Waters Corporation, USA, **2005**). IR spectra were recorded neat or in KBr with a Nicolet Impact 410 spectrophotometer. Melting points were recorded with a Büchi B-545 melting point apparatus and are uncorrected.

Crystallographic Analysis: Crystal data were collected with a Bruker Smart Apex-II CCD diffractometer by using graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å) at 298 K. Cell parameters were retrieved by using SMART[29] software and refined with SAINT[29] for all observed reflections. Data reduction was performed with the SAINT software and corrected for Lorentzian and polarization effects. Absorption corrections were applied with the SADABS program.[30] The structures were solved by direct methods implemented in the SHELX-97[31] program and refined by full-matrix least-squares methods on F^2. All non-hydrogen atom positions were located in difference Fourier maps and refined anisotropically. The hydrogen atoms were placed in their geometrically generated positions. The crystals were isolated in rectangular shape from a chloroform/methanol mixture at room temperature.

General Procedure 1. Preparation of Phenyl Isothiocyanate (1a) from Dithiocarbamate Salt 1: Triethylamine (417 μL, 3 mmol) was added to a stirred and ice-cooled suspension of dithiocarbamate **1** (540 mg, 2 mmol) in acetonitrile (5 mL). DIB (644 mg, 2 mmol) was added portionwise over a period of 30 min. A light-yellow precipitate of sulfur started to separate during this period. After the complete addition of DIB, the stirring was stopped to allow complete precipitation of the sulfur. The precipitated sulfur was filtered, and the organic layer was concentrated and admixed with hexane (15 mL). The hexane layer was washed with 1 N HCl (2 × 5 mL) and water (1 × 5 mL). The organic layer was dried with anhydrous Na_2SO_4, concentrated under reduced pressure, and purified through a short column of silica gel (100% hexane) to give **1a**[10] (259 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21–7.37 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 125.8, 127.4, 129.6, 131.3, 135.3 ppm. IR (KBr): $\tilde{\nu}$ = 3064.6, 2164.83, 2063.3, 1591.9, 1489.6, 1474.1, 1451.6, 1070.29, 927.6, 905.9, 749.6, 684.3 cm^{-1}.

General Procedure 2. One-Pot Preparation of Benzimidazole (1b) Starting from the Corresponding Dithiocarbamate Salt 1: Phenyl isothiocyanate was prepared in situ from the corresponding dithiocarbamate salt (540 mg, 2 mmol) according to the standard procedure described above and was used as such without any further purification. *o*-Phenylenediamine (216 mg, 2 mmol) was added to the above in situ generated phenyl isothiocyanate. Complete conversion to the corresponding monothiourea was confirmed by TLC (30–60 min). Triethylamine (278 μL, 2 mmol) was added to this reaction mixture followed by the portionwise addition of DIB (644 mg, 2 mmol) over a period of 10–15 min. The conversion of the thiourea to benzimidazole was observed within 5–10 min with concomitant precipitation of sulfur. The reaction mixture was allowed to stand, and the precipitated sulfur was filtered. The organic layer was concentrated and admixed with ethyl acetate (15 mL). The ethyl acetate layer was washed with water (2 × 5 mL). The organic layer was dried with anhydrous Na_2SO_4, concentrated under reduced pressure, and purified through a short column of silica gel to give the pure product **1b**[17] (296 mg, 71%). M.p. 150–152 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 6.29 (br. s, 1 H), 6.92 (t, J = 7.6 Hz, 1 H), 7.04 (m, 2 H), 7.23 (m, 2 H), 7.30 (m, 2 H), 7.49 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 112.7, 118.4, 120.7, 122.0, 129.1, 137.4, 140.0, 151.4 ppm. IR (KBr): $\tilde{\nu}$ = 3053, 2917, 1635, 1603, 1573, 1531, 1498, 1456, 1270, 1233, 1184, 1045, 898, 754, 743, 693, 497 cm^{-1}.

General Procedure 3. One-Pot Preparation of *N*-Phenyl-1,3-benzoxazol-2-amine (1c) Starting from the Dithiocarbamate Salt 1: Phenyl isothiocyanate was prepared in situ from the corresponding dithiocarbamate salt (540 mg, 2 mmol) according to the standard procedure described above and was used as such without any further purification. *o*-Aminophenol (218 mg, 2 mmol) was added to the above in situ generated phenyl isothiocyanate. Complete conversion to the corresponding thiourea was confirmed by TLC (30–60 min). Triethylamine (278 μL, 2 mmol) was added to this reaction mixture followed by the portionwise addition of DIB (644 mg, 2 mmol) over a period of 10–15 min. The conversion of the thiourea to benzoxazole was observed within 5–10 min with concomitant precipitation of sulfur. The reaction mixture was allowed to stand, and the precipitated sulfur was filtered. The organic layer was concentrated and admixed with ethyl acetate (15 mL). The ethyl acetate layer was washed with water (2 × 5 mL). The organic layer was dried with anhydrous Na_2SO_4, concentrated under reduced pressure, and purified through a short column of silica gel to give the pure product **1c**[17] (294 mg, 70%). M.p. 176–178 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 7.05 (m, 2 H), 7.19 (t, J = 7.6 Hz, 1 H), 7.32 (m, 3 H), 7.46 (d, J = 7.8 Hz, 1 H), 7.71 (m, 2 H), 9.64 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 108.6, 116.7, 118.1, 121.4, 122.4, 123.8, 128.9, 138.4, 142.5, 147.4, 158.4 ppm. IR (KBr): $\tilde{\nu}$ = 3162, 2922, 1659, 1601, 1574, 1502, 1459, 1375, 1249, 1225, 1164, 1003, 972, 892, 739, 686, 636, 504 cm^{-1}.

General Procedure 4. One-Pot Preparation of *N*-(4-Bromophenyl)-4*H*-3,1-benzoxazin-2-amine (6d) Starting from Dithiocarbamate Salt 6: Similar to General Procedure 3, except 2-aminobenzyl alcohol was used instead of *o*-aminophenol to give product **6d**.[32] M.p. 182–184 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 5.20 (s, 2 H), 6.99 (m, 3 H), 7.22 (m, 1 H), 7.29–7.38 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 67.7, 115.3, 120.7, 122.2, 123.1, 123.9, 129.1, 131.8, 139.6, 140.6, 151.4 ppm. IR (KBr): $\tilde{\nu}$ = 3166, 3053, 2992, 2872, 1695, 1682, 1600, 1496, 1480, 1456, 1408, 1394, 1315, 1267, 1245, 1206, 1169, 1069, 1025, 1007, 885, 839, 754, 692, 663 cm^{-1}.

General Procedure 5. One-Pot Preparation of *N*-Phenyl-2-(phenylimino)imidazolidine-1-carbothioamide (1e) Starting from the Corresponding Dithiocarbamate Salt 1: Phenyl isothiocyanate was prepared in situ from the corresponding dithiocarbamate salt (540 mg, 2 mmol) according to General Procedure 1 described above and was used as such without any further purification. Ethylenediamine (1 mmol, 68 μL) was added to the above reaction mixture. Complete conversion to the bis(thiourea) was observed (30 min). Triethylamine (139 μL, 1 mmol) was added to this reaction mixture followed by the portionwise addition of DIB (322 mg, 1 mmol) over a period of 10–15 min. Conversion of the bis(thiourea) to *N*-phenyl-2-(phenylimino)imidazolidine-1-carbothioamide (**1e**) was observed with concomitant precipitation of sulfur (5 min). The reaction mixture was allowed to stand for 5 min, and the precipitated sulfur was filtered. The organic layer was concentrated and admixed with ethyl acetate (15 mL). The ethyl acetate layer was washed with water (2 × 5 mL). The organic layer was dried with anhydrous Na_2SO_4, concentrated under reduced pressure, and purified through a short column of silica gel to give the pure product **1e** (216 mg, 73%). M.p. 190–192 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 3.46 (t, J = 7.9 Hz, 2 H), 4.45 (t, J = 8.0 Hz, 2 H), 5.39 (s, 1 H), 7.02 (m, 2 H), 7.08 (t, J = 6.4 Hz, 1 H), 7.19 (t, J = 7.2 Hz, 1 H), 7.35 (m, 4 H), 7.61 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 38.4, 48.4, 122.6, 123.7, 124.4, 125.7, 128.6, 129.5, 139.1, 146.5, 151.9, 178.8 ppm. IR (KBr): $\tilde{\nu}$ = 3290, 3061, 2900, 1662, 1620, 1574, 1591, 1480, 1426, 1404, 1378,

1323, 1289, 1212, 1129, 1069, 821, 785, 761, 731, 695, 577, 502 cm^{-1}.

Characterization of Compounds: Compounds **1a**, **2a**, **4a**, **6a**, **8a**, **12a**, **13a**,[10] **11a**,[12] **3a**,[32] **5a**, **7a**, **9a**,[33] **10a**,[34] **1b**,[17] **3b**,[35] **4b**,[21a] **6b**, **8b**, **6c**,[16a] **7b**,[36] **1c**,[17] **6d**, and **8d**[32] are known compounds. The new compounds were fully characterized.

Spectral Data for Selected Compounds

***N*-(2-Chlorophenyl)-1*H*-benzo[*d*]imidazol-2-amine (2b):** M.p. 152–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 6.70 (br. s, 1 H), 6.89 (t, J = 7.2 Hz, 1 H), 7.07 (m, 2 H), 7.25–7.38 (m, 4 H), 8.66 (d, J = 6.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]-DMSO): δ = 112.6, 118.9, 120.5, 121.6, 127.5, 128.8, 136.4, 150.2 ppm. IR (KBr): $\tilde{\nu}$ = 3056, 2926, 1625, 1600, 1557, 1461, 1448, 1319, 1267, 1233, 1034, 738, 617 cm^{-1}. $C_{13}H_{10}ClN_3$ (243.70): calcd. C 64.07, H 4.14, N 17.24; found C 64.11, H 4.19, N 17.18.

***N*-(3-Chlorophenyl)-6-methyl-1*H*-benzo[*d*]imidazol-2-amine (3b′):** M.p. 95–97 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 2.41 (s, 3 H), 4.62 (br. s, 1 H), 6.92 (t, J = 8.0 Hz, 2 H), 7.21 (m, 3 H), 7.44 (m, 1 H), 7.62 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 21.6, 112.5, 112.8, 116.4, 118.0, 121.8, 122.4, 130.2, 130.9, 134.4, 134.6, 136.1, 141.2, 150.1 ppm. IR (KBr): $\tilde{\nu}$ = 2921, 1648, 1594, 1558, 1478, 1275, 1094, 912, 856, 798, 770, 678, 594 cm^{-1}. $C_{14}H_{12}ClN_3$ (257.72): calcd. C 65.25, H 4.69, N 16.30; found C 65.11, H 4.73, N 16.22. MS (ESI): calcd. for $C_{14}H_{13}N_3Cl$ [MH]$^+$ 258.73; found 258.08.

***N*-(4-Methoxyphenyl)-6-methyl-1*H*-benzo[*d*]imidazol-2-amine (8b′):** M.p. 114–116 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 2.42 (s, 3 H), 3.77 (s, 3 H), 4.80 (br. s, 1 H), 6.85 (d, J = 9.2 Hz, 2 H), 6.90 (d, J = 8.0 Hz, 1 H), 7.12 (s, 1 H), 7.20 (d, J = 8.0 Hz, 1 H), 7.40 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 21.5, 55.5, 112.0, 112.5, 114.5, 121.5, 121.9, 130.5, 132.6, 134.4, 136.3, 151.9, 155.6 ppm. IR (KBr): $\tilde{\nu}$ = 3053, 2924, 2850, 1663, 1573, 1509, 1458, 1405, 1276, 1239, 1178, 1031, 826, 800, 740, 652, 596, 519 cm^{-1}. $C_{15}H_{15}N_3O$ (253.30): calcd. C 71.13, H 5.97, N 16.59; found C 71.18, H 6.03, N 16.52.

***N*-(2-Chlorophenyl)-1,3-benzoxazol-2-amine (2c):** M.p. 109–111 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 7.09 (m, 1 H), 7.22 (m, 1 H), 7.31 (m, 1 H), 7.43 (m, 3 H), 7.58 (d, J = 8.0 Hz, 1 H), 7.84 (s, 1 H), 8.57 (d, J = 8.4 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 109.1, 117.6, 119.4, 121.9, 122.3, 123.5, 124.2, 127.9, 129.2, 134.5, 142.2, 147.6, 157.1 ppm. IR (KBr): $\tilde{\nu}$ = 3230, 3029, 1661, 1589, 1571, 1531, 1458, 1339, 1317, 1245, 1229, 1166, 1055, 1003, 969, 920, 743, 707, 630, 494 cm^{-1}. $C_{13}H_9ClN_2O$ (244.68): calcd. C 63.82, H 3.71, N 11.45; found C 63.87, H 3.67, N 11.37.

***N*-(3-Chlorophenyl)-1,3-benzoxazol-2-amine (3c):** M.p. 184–186 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 6.99 (d, J = 8.0 Hz, 1 H), 7.12 (t, J = 7.6 Hz, 1 H), 7.22 (t, J = 7.6 Hz, 1 H), 7.28 (t, J = 8.4 Hz, 1 H), 7.35 (d, J = 8.0 Hz, 1 H), 7.46 (d, J = 7.6 Hz, 1 H), 7.63 (d, J = 7.4 Hz, 1 H), 7.92 (s, 1 H), 10.35 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 108.2, 115.5, 116.4, 117.0, 121.2, 121.4, 123.4, 129.4, 133.6, 139.6, 141.8, 146.8, 157.3 ppm. IR (KBr): $\tilde{\nu}$ = 3022, 2920, 1687, 1600, 1579, 1461, 1483, 1350, 1246, 1170, 1080, 882, 776, 737, 676 cm^{-1}. $C_{13}H_9ClN_2O$ (244.68): calcd. C 63.82, H 3.71, N 11.45; found C 63.85, H 3.76, N 11.39.

***N*-(4-Methoxyphenyl)-1,3-benzoxazol-2-amine (8c):** M.p. 136–138 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 3.80 (s, 3 H), 6.90 (d, J = 8.8 Hz, 2 H), 7.06 (t, J = 7.6 Hz, 1 H), 7.18 (t, J = 7.6 Hz, 1 H), 7.29 (d, J = 8.0 Hz, 1 H), 7.42 (d, J = 7.6 Hz, 1 H), 7.59 (d, J = 8.8 Hz, 2 H), 9.22 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 55.5, 108.7, 114.3, 116.6, 120.4, 121.2, 123.9, 131.6, 142.6, 147.7, 155.5, 159.2 ppm. IR (KBr): $\tilde{\nu}$ = 3154, 3043, 2838, 1681, 1590, 1580, 1554, 1505, 1484, 1369, 1347, 1231, 1174, 1006, 1031, 967, 821, 742, 626, 600, 515 cm^{-1}. $C_{14}H_{12}N_2O_2$ (240.26): calcd. C 69.99, H 5.03, N 11.66; found C 70.08, H 5.09, N 11.57.

***N*-Phenyl-2-(phenylimino)imidazolidine-1-carbothioamide (1e):** M.p. 190–192 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 3.46 (t, J = 7.9 Hz, 2 H), 4.45 (t, J = 8.0 Hz, 2 H), 5.39 (s, 1 H), 7.02 (m, 2 H), 7.08 (t, J = 6.4 Hz, 1 H), 7.19 (t, J = 7.2 Hz, 1 H), 7.35 (m, 4 H), 7.61 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]-DMSO): δ = 38.4, 48.4, 122.6, 123.7, 124.4, 125.7, 128.6, 129.5, 139.1, 146.5, 151.9, 178.8 ppm. IR (KBr): $\tilde{\nu}$ = 3290, 3061, 2900, 1662, 1620, 1574, 1591, 1480, 1426, 1404, 1378, 1323, 1289, 1212, 1129, 1069, 821, 785, 761, 731, 695, 577, 502 cm^{-1}. $C_{16}H_{16}N_4S$ (296.40): calcd. C 64.84, H 5.44, N 18.90, S 10.82; found C 64.78, H 5.36, N 18.79, S 10.73.

2-(2-Chlorophenylimino)-*N*-(2-chlorophenyl)imidazolidine-1-carbothioamide (2e): M.p. 147–149 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 3.48 (t, J = 8.0 Hz, 2 H), 4.42 (t, J = 8.4 Hz, 2 H), 6.24 (s, 1 H), 7.02 (m, 1 H), 7.15 (m, 2 H), 7.21–7.30 (m, 2 H), 7.39 (m, 2 H), 8.02 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 38.1, 48.3, 123.6, 124.1, 126.2, 126.6, 127.3, 127.4, 127.8, 128.8, 129.1, 129.6, 136.3, 143.3, 151.2, 179.1 ppm. IR (KBr): $\tilde{\nu}$ = 3230, 2889, 1689, 1600, 1581, 1556, 1470, 1415, 1395, 1364, 1322, 1294, 1123, 1067, 1048, 779, 742, 684 cm^{-1}. $C_{16}H_{14}Cl_2N_4S$ (365.28): calcd. C 52.61, H 3.86, N 15.34, S 8.78; found C 52.66, H 3.83, N 15.29, S 8.73.

2-(3-Chlorophenylimino)-*N*-(2-chlorophenyl)imidazolidine-1-carbothioamide (3e): M.p. 138–140 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 3.46 (t, J = 7.6 Hz, 2 H), 4.41 (t, J = 7.6 Hz, 2 H), 5.82 (s, 1 H), 6.92 (m, 1 H), 7.04–7.08 (m, 2 H), 7.14 (m, 1 H), 7.27 (m, 2 H), 7.47 (m, 1 H), 7.76 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 38.3, 48.4, 121.2, 122.4, 122.9, 123.7, 124.1, 125.6, 129.5, 130.5, 133.9, 134.7, 140.2, 147.8, 152.1, 178.6 ppm. IR (KBr): $\tilde{\nu}$ = 2894, 1667, 1586, 1560, 1474, 1403, 1376, 1322, 1294, 1133, 1078, 898, 828, 791, 679, 581 cm^{-1}. $C_{16}H_{14}Cl_2N_4S$ (365.28): calcd. C 52.61, H 3.86, N 15.34, S 8.78; found C 52.68, H 3.87, N 15.28, S 8.74.

2-(4-Bromophenylimino)-*N*-(4-bromophenyl)imidazolidine-1-carbothioamide (6e): M.p. 180–182 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 3.47 (t, J = 7.6 Hz, 2 H), 4.44 (t, J = 8.4 Hz, 2 H), 4.78 (s, 1 H), 6.89 (d, J = 8.4 Hz, 2 H), 7.45 (m, 4 H), 7.52 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 38.6, 48.7, 117.2, 119.0, 124.6, 126.1, 131.9, 132.9, 138.3, 145.6, 152.1, 178.9 ppm. IR (KBr): $\tilde{\nu}$ = 3230, 2813, 1658, 1589, 1572, 1530, 1458, 1365, 1338, 1246, 1230, 1165, 1056, 1033, 1003, 970, 919, 836, 742, 710, 631 cm^{-1}. $C_{16}H_{14}Br_2N_4S$ (454.19): calcd. C 42.31, H 3.11, N 12.34, S 7.06; found C 42.35, H 3.08, N 12.27, S 7.00.

2-(*p*-Tolylimino)-*N*-(*p*-tolyl)imidazolidine-1-carbothioamide (7e): M.p. 142–144 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 2.32 (s, 3 H), 2.33 (s, 3 H), 3.43 (t, J = 8.0 Hz, 2 H), 4.42 (t, J = 7.6 Hz, 2 H), 5.34 (s, 1 H), 6.90 (d, J = 8.0 Hz, 2 H), 7.14 (m, 4 H), 7.45 (d, J = 8.4 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D$_6$]DMSO): δ = 20.8, 21.0, 38.4, 48.4, 122.4, 124.5, 129.1, 130.0, 133.0, 135.4, 136.6, 143.8, 152.0, 178.9 ppm. IR (KBr): $\tilde{\nu}$ = 3017, 2918, 2850, 1670, 1624, 1565, 1507, 1471, 1408, 1364, 1315, 1285, 1262, 1127, 1076, 822, 807, 765, 690, 509 cm^{-1}. $C_{18}H_{20}N_4S$ (324.45): calcd. C 66.64, H 6.21, N 17.27, S 9.88; found C 66.69, H 6.25, N 17.19, S 9.83.

2-(4-Methoxyphenylimino)-*N*-(4-methoxyphenyl)imidazolidine-1-carbothioamide (8e): M.p. 126–128 °C. ^{1}H NMR (400 MHz, $CDCl_3$, [D_6]DMSO): δ = 3.44 (t, J = 7.6 Hz, 2 H), 3.78 (s, 3 H), 3.80 (s, 3 H), 4.42 (t, J = 8.0 Hz, 2 H), 5.48 (s, 1 H), 6.80–6.96 (m, 6 H), 7.45 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, [D_6]DMSO): δ = 29.4, 38.3, 48.3, 55.3, 113.6, 114.5, 123.3, 126.0, 132.1, 139.5, 152.2, 155.7, 157.2, 179.0 ppm. IR (KBr): $\tilde{\nu}$ = 2956, 2917, 2835, 1660, 1633, 1573, 1505, 1446, 1429, 1401, 1374, 1324, 1293, 1238, 1178, 1129, 1030, 827, 765, 712, 545, 519 cm^{-1}. $C_{18}H_{20}N_4O_2S$ (356.45): calcd. C 60.65, H 5.66, N 15.72, S 9.00; found C 60.69, H 5.71, N 15.67, S 8.93.

Supporting Information (see footnote on the first page of this article): Full characterization data of compounds; IR, ^{1}H and ^{13} C NMR spectra.

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[22] CCDC-635623 (**1b**) and -635622 (**8e**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Crystal data for **1b**: $C_{26}H_{22}N_6$, M_r = 418.50, orthorhombic, space group *Pbca*, a = 8.5445(4), b = 10.9972(6) (2), c = 22.4895(12) Å, 0.30 × 0.28 × 0.23 mm, V = 2113.24(19) Å^3, Z = 4, $\rho_{calcd.}$ = 1.315 mg/m^3, μ = 0.081 mm^{-1}, F(000) = 880, reflections collected/unique = 24797/2602, refinement method = full-matrix least squares on F^2, final R indices [$I > 2\sigma(I)$]: R_1 = 0.0421, wR_2 = 0.1175, R indices (all data): R_1 = 0.0745, wR_2 = 0.1481, goodness of fit = 0.768. Crystal data for **8e**: $C_{18}H_{20}N_4O_2S$, M_r = 356.44, monoclinic, space group $P2_1/c$, a = 8.5759(3), b = 23.5834(9), c = 9.2172(4) Å, β = 104.572(2), 0.52 × 0.34 × 0.18 mm, V = 1804.20(12) Å^3, Z = 4, $\rho_{calcd.}$ = 1.312 mg/m^3, μ = 0.198 mm^{-1}, F(000) = 752, reflections collected/unique = 16995/4004, refinement method = full-matrix least squares on F^2, final R indices [$I > 2\sigma(I)$]: R_1 = 0.0379, wR_2 = 0.0961, R indices (all data): R_1 = 0.0531, wR_2 = 0.1046, goodness of fit = 1.041.

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