Iodine-Catalyzed Chemoselective Hydroamination Reaction Using 5-Mercaptotetrazoles Derivatives

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Supporting Information

ABSTRACT: Metal-free chemoselective hydroamination of styrene derivatives has been achieved with high chemoselectivity over sulfenylation of 1H-tetrazole-5-thiol using a catalytic amount of iodine. The scope of this methodology has been extended for the hydroamination of α-substituted styrene derivatives. This reaction involves a single-step C−N bond formation under atom economical process. This eco-friendly method uses readily available and inexpensive iodine in a catalytic amount.

INTRODUCTION

Carbon−heteroatom bond-forming reactions have a great significance in synthetic organic chemistry as they provide avenues for synthesizing a variety of natural products. Among many sulfur-containing molecules, 1-phenyl-1H-tetrazole-5-thiol is a fascinating molecule, which provides a site for many sulfur-containing molecules, 1-phenyl-1H-tetrazole-5-thiol a promising pesticides and cytotoxic agents. Therefore, protocols for organic synthesis. As a consequence, iodine-reactions are attractive as they provide environmentally benign disubstituted tetrazolothione derivatives has received considerable attention.

In 2013, Wu and co-workers reported a remarkable Markovnikov-selective hydramination of 1-phenyl-1H-tetrazole-5-thiol with styrene using trifluoroacetic acid. In 2014, the same group reported another efficient hydramination of styrenyl substrates with 1-phenyl-1H-tetrazole-5-thiol using a catalytic amount of Ga(OTf)₃ (Scheme 1). Iodine-catalyzed reactions are attractive as they provide environmentally benign protocols for organic synthesis. As a consequence, iodine-catalyzed reactions for the formation of C−S bonds and heteroatom−heteroatom bonds have gained a great momentum. The oxidation of 1H-tetrazole-5-thiol to disulfides by iodine is a well-known reaction, and the corresponding disulfides have been extensively employed for the sulfenylation reaction with carbonyl compounds, imidazoheterocycles, enamines, and pyrazolones.

Despite the significant progress in C−S-bond-forming reactions of 1H-tetrazole-5-thiol using iodine, the chemoselective C−N-bond-forming reaction is in its infancy as 1H-tetrazole-5-thiols are highly prone to oxidation to form their corresponding disulfides in the presence of iodine. The sulfenylation of styrenes with thiols in the presence of iodine favors the formation of β-hydroxy sulfoxides as thiols are readily oxidized by iodine to form an S−I intermediate. Similarly, the hydroamination of styrenes in the presence of iodine is a challenging task as aminoiodination of styrene is facile under these conditions. In addition to the reactivity and compatibility, the most important aspect of the addition reaction of 1H-tetrazole-5-thiol to styrene derivatives is chemoselectivity. As our group is engaged in developing novel routes for building C−O, C−C, and C−S bonds under metal-free conditions, we became interested in designing a new synthetic strategy for an iodine-catalyzed hydramination of styrene with 1-phenyl-1H-tetrazole-5-thiol. Therefore, we investigated iodine-catalyzed and metal-free reactions employing 1H-tetrazole-5-thiol as a suitable N-nucleophile and describe the mild, user-friendly chemoselective hydramination of activated olefins.

RESULTS AND DISCUSSION

On the basis of our recent work on using 1H-tetrazole-5-thiol derivatives as a coupling partner for sulfenylation reactions, we envisioned that 1H-tetrazole-5-thiol might be employed to obtain iodothiolation of styrenyl derivatives. We started our investigations using 1-methyl-1H-tetrazole-5-thiol (1a) and styrene (2a) as model substrates in the presence of 20 mol % iodine as a Lewis acid and dichloroethane (DCE) as solvent at 25 °C. In this reaction, the corresponding sulfenylated product 3a' was obtained in 21% isolated yield (entry 1, Table 1). Increasing the temperature to 40 and 60 °C led to a significant increase in the yield of the hydraminated product along with sulfenylated products (entries 2 and 3). However, performing
the reaction at 80 °C furnished the corresponding hydroamminated product 3a, exclusively, in 96% yield (entry 4). These reactions (entries 2-4) indicate the formation of the stable thermodynamic control product 3a. Screening of solvent revealed that 1,2-dichloroethane would be an optimal solvent, as the reaction afforded the product 3a in 96% yield with
excellent chemoselectivity (entry 4, Table 1). However, the reactions in solvents such as acetonitrile, toluene, and dioxane also furnished the product 3a in 73, 90, and 76% yields, respectively (entries 5–7, Table 1), whereas other solvents such as dimethylformamide (DMF) and dimethylacetamide were not suitable under the reaction conditions (entries 7–9, Table 1). Further varying the equivalence of 1a, 2a, or iodine was not helpful (entries 10–14, Table 1). The same reaction did not furnish 3a in the absence of iodine under the optimal reaction conditions (entry 15, Table 1). With these screening studies, further investigation was carried out using 1a (1 equiv), 2a (1.2 equiv), and iodine (20 mol %) in solvent 1,2-dichloroethane (1 mL) at 80 °C.

After establishing the optimal reaction conditions, the scope of the reaction was explored using a variety of styrene derivatives (Scheme 2). A remarkably high selectivity was obtained with styrenes, α-substituted styrene derivatives, and vinyl ethers. From the reaction, it was found that styrene derivatives are most reactive, α-substituted styrene derivatives are moderately reactive, and vinyl ethers are poorly reactive under the reaction condition.

To probe the versatility of this catalytic system, the scope and limitation of the reaction have been evaluated using a variety of styrene derivatives with alkyl substitution at different positions on the phenyl ring. Alkyl groups, such as methyl or tert-butyl groups, present at different positions on the phenyl ring of styrene derivatives afforded the corresponding products in excellent yields (3b–f, Scheme 2). Further, the structures of these compounds were confirmed by the X-ray crystal structure of compound 3e (Figure 1).

Substrate scope was explored with aryl-substituted styrene, such as 4-vinyl-1,1′-biphenyl, which was found to be the most reactive substrate furnishing the product 3g in 94% yield (Scheme 2). Encouraged by these results, substrate scope was examined with various halogenated substrates, which are useful precursors for a variety of metal-catalyzed cross-coupling reactions. Thus, fluoro-, chloro-, and bromo-substituted styrene derivatives were well tolerated affording the corresponding hydroamination products 3h–j in 86, 91, and 81% yields, respectively. The reaction of 1-methyl-1H-tetrazole-5-thiol (1a) with 2-vinylthiophene and (E)-buta-1,3-dien-1-ylbenzene was facile, furnishing the corresponding aminated products 3k and 3l in 78 and 67% yields, respectively (Scheme 2). The reaction of 4-vinylphenyl acetate, a styrene derivative, with an electron-donating group on phenyl ring proceeded smoothly, furnishing the product 3m in 87% yield. Similar reactions with methoxy- and anilide-substituted derivatives were found to furnish the products 3n and 3o in moderate yields, respectively (Scheme 2). 4-Vinylaniline failed to furnish the desired product 3p under the reaction conditions. Heterocyclic-substituted derivatives, such as 2-vinylthiophene, afforded the aminated product 3q in moderate yield (69%). The scope of the reaction was extended by reacting styrene derivatives that contain electron-withdrawing substituents such as nitrile and nitro groups. 4-Vinylbenzonitrile failed to undergo the reaction, as initially it was intact under the reaction conditions, whereas 1-nitro-3-vinylbenzene surprisingly afforded the sulfonylated product 3s in poor yield (28%, Scheme 2).

We then examined the reaction of dihydronaphthalene, which underwent a chemoselective reaction affording the corresponding aminated product 3t in good yield (73%). The reaction of prop-1-en-2-ylbenzene, a styrene derivative that has methyl substitution at α-position of styrene, furnished the corresponding aminated product 3u in moderate yield (51%).

The scope of the reaction was further explored with vinyl ether derivatives, such as 5-methylfuran-2(3H)-one and 3,4-dihydro-2H-pyran. 5-Methylfuran-2(3H)-one delivered the desired product 3v in moderate yield (56%), whereas 3,4-
dihydro-2H-pyran afforded the product 3w in poor yield (20%). Even though the yields of the reactions were low, the high chemoselectivity obtained in these reactions to obtain hydroaminated products over hydrothiolation products is

**Scheme 2. Substrate Scope**

| Reaction conditions: | Isolated yield. nd = not detected. |
|----------------------|------------------------------------|
| 1 (0.86 mmol), 2 (1.03 mmol), and iodine (0.17 mmol) in 1 mL of DCE at 80 °C, 8−16 h. | |

**Table:**

| Compounds | Isolated Yield (%) |
|-----------|--------------------|
| 3a        | 96%                |
| 3b        | 91%                |
| 3c        | 99%                |
| 3d        | 85%                |
| 3e        | 90%                |
| 3f        | 81%                |
| 3g        | 94%                |
| 3h        | X = F, 86%         |
| 3i        | X = Cl, 91%        |
| 3j        | X = Br, 81%        |
| 3k        | 78%                |
| 3l        | 67%                |
| 3m        | 87%                |
| 3n        | 42%                |
| 3o        | R = COMe, 57%      |
| 3p        | R = H, 57%         |
| 3q        | 69%                |
| 3r        | nd                 |
| 3s        | 28%                |
| 3t        | 73%                |
| 3u        | 51%                |
| 3v        | 56%                |
| 3w        | 20%                |

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commendable. In these reactions, the decrease in the yields is due to the decomposition of the starting material thiol 1a. Upon changing from 1-methyl-1H-tetrazole-5-thiol to 1-phenyl-1H-tetrazole-5-thiol, no significant change in the reactivity was observed. Thus, 1-phenyl-1H-tetrazole-5-thiol successfully coupled with various styrene derivatives to form the corresponding hydroaminated products 4a–e in excellent yields (88, 92, 94, 89, and 78%, respectively; Scheme 2).

To get an insight into the reaction mechanism, a few control experiments were performed (Scheme 3). The reaction of 1a and 2a under the optimal conditions in the presence of 2,2,6,6-tetramethylpiperidine-1-oxyl furnished a trace amount of product 3a, whereas the same reaction in the presence of a radical inhibitor butylated hydroxytoluene proceeded well to form 3a in 91% yield, indicating that the reaction does not proceed through a radical pathway (Scheme 3a). The reaction of thiols with iodine is known to furnish the corresponding disulfide. Therefore, a reaction was performed with disulfide, 1,2-bis(1-methyl-1H-tetrazol-5-yl)disulfane, in the presence of iodine, in which the formation of the product 3a was not observed (Scheme 3b). The reaction of hydrothiolated product 3a′ under the optimal reaction conditions with iodine or HI failed to afford the corresponding hydroaminated product 3a (Scheme 3c). Similarly, the reactions of styrene 2a or thiol 1a with iodine, under the optimal reaction conditions, and the decomposition of the starting materials were observed (Scheme 3d). The reactions proceeded well with a catalytic amount of aqueous HI to form product 3a in 78% (Scheme 3e). Saito and Minakata independently reported a molecular iodine-catalyzed reaction involving HI and deiodination of the heteroatom. To find whether the present reaction also follows similar pathways, we performed reactions of 1a with (1-iodoethyl)benzene with iodine or HI and without iodine. However, these reactions furnished a mixture of 3a and 3a′ (3a as the major product and 3a′ as the minor product; Scheme 3f). As we obtain the hydroamination product exclusively, we believe that the reaction that we have developed proceeds through Lewis acid catalysis.

On the basis of literature reports and our observations, a plausible mechanism has been proposed (Scheme 4). Iodine acts as a Lewis acid to activate styrene to form carbocation (II). Further, N-atom of 1H-tetrazole-5-thiol acts as nucleophile to form electrophilic species (III). Intermediate (III) reacts further with styrene to form the desired product benzyl carbocation, and the cycles continues.

**CONCLUSIONS**

In summary, chemoselective hydroamination of styrene derivatives with 1-methyl-1H-tetrazole-5-thiol and 1-phenyl-1H-tetrazole-5-thiol has been described under metal-free reaction conditions using iodine in a catalytic amount. Interestingly, the reaction does not lead to either hydroxythiolation or iodoamination of styrene derivatives. A high selectivity obtained for the hydroamination over sulfenylation is remarkable as 1H-tetrazole-5-thiol is prone to oxidation by iodine to its disulfide. The salient feature of the reaction is that the reaction proceeds well in the absence of any metal catalyst, and the following reaction may be highly practical as it employs inexpensive, nontoxic, and eco-friendly iodine system and may find a good utility in organic chemistry.

**EXPERIMENTAL SECTION**

**General Experimental Procedure.** Deuterated solvents CDCl₃ or DMSO-d₆ were used as solvents for recording NMR spectra on a 400 MHz spectrometer. Tetramethylsilane for ¹H NMR in CDCl₃ and residual nondeuterated solvent peak (DMSO, δ = 2.50 ppm) in DMSO-d₆ served as internal standards. The solvent signals δ 77.00 for CDCl₃ and δ 39.5 for DMSO-d₆ were used as internal standards for ¹³C NMR experiments. IR spectra were recorded using an FT-IR spectrometer. A Q-TOF mass spectrometer (HRMS) was used for obtaining mass spectral data. Flash column chromatography was carried out by packing glass columns with commercial silica gel 230–400 mesh (commercial suppliers). Thin-layer chromatography (TLC) was carried out using silica gel GF-254. All catalysts, reagents, and reactants were procured from commercial suppliers. Dichloroethane was distilled over calcium hydride, stored over molecular sieves, and used for all procedures. Other solvents used for work up and chromatographic procedures were purchased from commercial suppliers.

**Typical Experimental Procedure for the Hydroamination of Styrene Derivatives.** Iodine (20 mol %) was added to a well-stirred solution of 1H-tetrazole-5-thiol (0.86 mmol, 1 equiv) and styrene (1.03 mmol, 1.2 equiv) in dichloroethane (1 mL). The reaction mixture was stirred at 80 °C for 12–16 h. After completion of the reaction (monitored by TLC), water (25 mL), and dilute sodium thiosulfate solution (5 mL) were added and extracted with ethyl acetate (3 × 20 mL). The organic layer was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude product was purified on a silica gel column using hexane/EtOAc to get the pure product.

**Caution:** Addition of iodine to thiols was highly exothermic and decomposition of 1H-tetrazole-5-thiol was observed. Iodine should be added to a well-stirred solution of thiol and styrene in solvent.

**Characterization Data.** 1-Methyl-4-((1-phenylethyl)-1,4-dihydro-5H-tetrazole-5-thione (3a). Pale yellow oily liquid; yield 96% (182 mg); Rₘ (5% EtOAc/hexane) 0.3; IR (neat, cm⁻¹) 3062, 3034, 2987, 2940, 2362, 1599; ¹H NMR (400 MHz, CDCl₃) δ 7.48–7.44 (m, 2H), 7.37–7.30 (m, 3H), 6.06 (q, J = 7.2 Hz, 1H), 3.87 (s, 3H), 1.93 (d, J = 7.2 Hz, 3H), 1.35 (s, 3H), 1.32 (s, 3H), 1.25 (s, 3H), 1.21 (s, 3H), 1.13 (s, 3H), 1.08 (s, 3H), 0.95 (s, 3H), 0.90 (s, 3H), 0.85 (s, 3H), 0.80 (s, 3H), 0.77 (s, 3H), 0.73 (s, 3H), 0.70 (s, 3H), 0.67 (s, 3H), 0.64 (s, 3H), 0.61 (s, 3H), 0.58 (s, 3H), 0.55 (s, 3H), 0.52 (s, 3H), 0.49 (s, 3H), 0.46 (s, 3H), 0.43 (s, 3H), 0.40 (s, 3H), 0.37 (s, 3H), 0.34 (s, 3H), 0.31 (s, 3H), 0.28 (s, 3H), 0.25 (s, 3H), 0.22 (s, 3H), 0.19 (s, 3H), 0.16 (s, 3H), 0.13 (s, 3H), 0.10 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H), 0.01 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 163.7, 138.3, 128.7, 128.5, 127.1, 57.7, 34.5, 20.0; HRMS (electrospray ionization time-of-flight (ESI-TOF)) m/z (M⁺ + Na) calc for C₁₉H₁₉N₅SNa 423.0680; found 423.0678.

1-Methyl-5-((1-phenylethyl)thio)-1H-tetrazole (3a'). Pale yellow oily liquid; yield 21% (40 mg); Rₘ (10% EtOAc/
Scheme 3. Control Experiments

hexane) 0.1; IR (neat, cm\(^{-1}\)) 3063, 3092, 2974, 2928, 2868, 1962, 1886, 1812, 1686, 1600, 1489, 1453; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.33–7.23 (m, 5H), 4.97 (q, \(J = 6.8\) Hz, 1H), 3.69 (s, 3H), 1.84 (d, \(J = 6.8\) Hz, 3H); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 152.8, 140.9, 128.8, 128.2, 127.0, 48.4, 33.3, 21.9; HRMS (ESI-TOF) \(m/z\) (M\(^+\) + Na) calcld for C\(_{10}\)H\(_{12}\)N\(_4\)SNa 243.0680; found 243.0679.

1-Methyl-4-(1-(m-tolyl)ethyl)-1,4-dihydro-5H-tetrazole-5-thione (3b). Colorless oily liquid; yield 91% (184 mg); \(R_l\) (5% EtOAc/hexane) 0.2; IR (neat, cm\(^{-1}\)) 3025, 2985, 2940, 2872, 1607, 1448, 1405; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.29–7.24 (m, 3H), 7.14 (d, \(J = 6.8\) Hz, 1H), 6.04 (q, \(J = 7.2\) Hz, 1H), 3.91 (d, \(J = 0.6\) Hz, 3H), 2.37 (s, 3H), 1.94 (d, \(J = 7.2\) Hz, 3H); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 163.7, 138.6, 138.3, 129.4,
128.7, 127.8, 124.2, 57.8, 34.6, 21.4, 20.2; HRMS (ESI-TOF) m/z (M⁺ + Na) calcd for C₁₁H₁₄N₄SNa 257.0837; found 257.0836.

1-Methyl-4-(1-(p-tolyl)ethyl)-1,4-dihydro-5H-tetrazole-5-thione (3e). Colorless oily liquid; yield 99% (200 mg); R₆ (5% EtOAc/hexane) 0.4; IR (neat, cm⁻¹) 3134, 3025, 2985, 2930, 2865, 2733, 1904, 1799, 1658, 1612; ¹H NMR (400 MHz, CDCl₃) δ 7.36 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 6.02 (q, J = 7.2 Hz, 1H), 3.87 (s, 3H), 2.32 (s, 3H), 1.91 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 163.7, 138.4, 135.4, 129.4, 127.1, 57.6, 34.5, 21.1, 20.0; HRMS (ESI-TOF) m/z (M⁺ + Na) calcd for C₁₁H₁₄N₄SNa 257.0837; found 257.0839.

1-(1,2,5-Dimethylphenyl)ethyl)-4-methyl-1,4-dihydro-5H-tetrazole-5-thione (3d). Colorless oily liquid; yield 85% (182 mg); R₆ (5% EtOAc/hexane) 0.2; IR (neat, cm⁻¹) 3029, 2958, 2930, 2870, 1616, 1504; ¹H NMR (400 MHz, CDCl₃) δ 7.19 (s, 1H), 7.09–7.03 (m, 2H), 6.18 (q, J = 7.2 Hz, 1H), 3.91 (s, 3H), 2.46 (s, 3H), 2.32 (s, 3H), 1.88 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 163.7, 136.5, 136.0, 132.7, 130.6, 129.1, 126.7, 54.6, 34.6, 21.1, 20.3, 19.2; HRMS (ESI-TOF) m/z (M⁺ + Na) calcd for C₁₄H₁₄N₄SNa 271.0993; found 271.0995.

1-(Mesityl)ethyl)-4-methyl-1,4-dihydro-5H-tetrazole-5-thione (3e). White solid (mp 144–146 °C); yield 90% (204 mg); R₆ (5% EtOAc/hexane) 0.2; IR (neat, cm⁻¹) 2958, 2861, 1607, 1447, 1403, 1352; ¹H NMR (400 MHz, CDCl₃) δ 6.88 (s, 2H), 5.98 (q, J = 7.2 Hz, 1H), 3.89 (d, J = 0.4 Hz, 3H), 2.31 (s, 6H), 2.26 (s, 3H), 1.99 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.1, 137.5, 136.1, 131.1, 130.6, 56.5, 34.5, 20.8, 18.0; HRMS (ESI-TOF) m/z (M⁺ + Na) calcd for C₁₃H₁₄N₄SNa 265.1100; found 265.1100.

1-(4-tert-Butyl)phenyl)ethyl)-4-methyl-1,4-dihydro-5H-tetrazole-5-thione (3f). Yellow solid (mp 78–80 °C); yield 81% (193 mg); R₆ (5% EtOAc/hexane) 0.2; IR (neat, cm⁻¹) 2960, 2869, 1661, 1613, 1512, 1450; ¹H NMR (400 MHz, CDCl₃) δ 7.45–7.37 (m, 4H), 6.07 (q, J = 7.2 Hz, 1H), 3.90 (d, J = 0.4 Hz, 3H), 1.94 (d, J = 7.2 Hz, 3H), 1.31 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 163.7, 151.6, 153.4, 126.5, 125.7, 57.5, 34.6, 31.2, 20.1; HRMS (ESI-TOF) m/z (M⁺ + Na) calcd for C₁₆H₂₀N₄SNa 293.1306; found 293.1305.

1-(1,1'-Biphenyl-4-yl)ethyl)-4-methyl-1,4-dihydro-5H-tetrazole-5-thione (3g). White solid (mp 98–100 °C); yield 94% (240 mg); R₆ (5% EtOAc/hexane) 0.2; IR (neat, cm⁻¹) 3029, 2986, 2924, 2437, 1895, 1806, 1735, 1678, 1620; ¹H NMR (400 MHz, CDCl₃) δ 7.57–7.50 (m, 6H), 7.42–7.38 (m, 2H), 7.32 (t, J = 7.2 Hz, 1H), 6.09 (q, J = 7.2 Hz, 1H), 3.90 (s, 3H), 1.95 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 163.7, 141.4, 140.3, 137.2, 128.7, 127.5, 127.4, 127.0, 57.4, 34.5, 20.0; HRMS (ESI-TOF) m/z (M⁺ + Na) calcd for C₁₈H₁₇N₄SNa 319.0993; found 319.0995.
4-(1-(4-Methyl-5-thiao-4,5-dihydro-1H-tetrazol-1-yl)ethyl)phenyl Acetate (3m). Yellow solid (mp 133–135 °C); yield 87% (206 mg); Rf (20% EtOAc/hexane) 0.2; IR (neat, cm⁻¹) 2996, 2940, 1739, 1603, 1549, 1402; ¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, J = 8.8 Hz, 2H), 7.09 (d, J = 8.4 Hz, 2H), 6.07 (q, J = 7.2 Hz, 1H), 3.89 (s, 3H), 2.39 (s, 3H), 1.94 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 169.2, 163.7, 153.8, 128.4, 121.9, 57.0, 34.5, 21.0, 20.0; HRMS (ESI-TOF) m/z (M⁺ + Na) calcd for C₁₉H₁₄N₄O₂Na 361.1463; found 361.1466.

1-(4-(4-Methoxyphenyl)ethyl)-4,4-dihydro-5H-tetrazole-5-thione (3n). Pale yellow oily liquid; yield 56% (103 mg); Rf (30% EtOAc/hexane) 0.3; IR (neat, cm⁻¹) 3745, 3676, 3620, 3565, 2944, 2853, 1795; ¹H NMR (400 MHz, CDCl₃) δ 3.87 (s, 3H), 3.51–3.43 (m, 1H), 3.08–2.99 (m, 1H), 2.82–2.74 (m, 1H), 2.51–2.74 (m, 1H), 2.21 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 174.2, 163.0, 96.4, 34.3, 31.3, 29.1, 26.6; HRMS (ESI-TOF) m/z (M⁺ + Na) calcd for C₁₆H₁₃N₄OSNa 257.0837; found 257.0840.

5-Methyl-5-(4-methyl-5-thiao-4,5-dihydro-1H-tetrazol-1-yl)dihydrofuran-2(3H)-one (3v). White solid (mp 82–84 °C); yield 56% (103 mg); Rf (30% EtOAc/hexane) 0.3; IR (neat, cm⁻¹) 3745, 3676, 3620, 3565, 2944, 2853, 1795; ¹H NMR (400 MHz, CDCl₃) δ 3.87 (s, 3H), 3.51–3.43 (m, 1H), 3.08–2.99 (m, 1H), 2.82–2.74 (m, 1H), 2.51–2.74 (m, 1H), 2.21 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 174.2, 163.0, 96.4, 34.3, 31.3, 29.1, 26.6; HRMS (ESI-TOF) m/z (M⁺ + Na) calcd for C₁₆H₁₃N₄OSNa 257.0837; found 257.0840.
HRMS (ESI-TOF) m/z (M⁺ + Na) calcd for C₁₇H₁₆N₄OSNa 331.0993; found 331.0994.

1-Phenyl-4-[(1,2,3,4-tetrahydrophenanthren-1-yl)-1,4-dihydro-5H-tetrazole-5-thione (46). White solid (mp 133–135 °C); yield 78% (206 mg); Rf (5% EtOAc/hexane) 0.2; IR ( neat, cm⁻¹) 3019, 2944, 2400, 2032, 1596, 1496, 1454, 1415; ¹H NMR (400 MHz, CDCl₃) δ 8.07–8.04 (m, 2H), 7.60–7.56 (m, 2H), 7.53–7.51 (m, 1H), 7.30–7.22 (m, 2H), 7.20–7.15 (m, 1H), 7.07 (d, J = 7.6 Hz, 1H), 6.34 (t, J = 6.4 Hz, 1H), 3.09–3.01 (m, 1H), 2.94–2.86 (m, 1H), 2.44–2.29 (m, 2H), 2.21–2.11 (m, 1H), 2.00–1.91 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 163.3, 137.9, 134.7, 132.2, 129.4, 129.0, 128.2, 128.1, 126.3, 56.3, 28.8, 28.6, 19.6; HRMS (ESI-TOF) m/z (M⁺ + Na) calcd for C₁₇H₁₆N₄OSNa 331.0993; found 331.0994.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.8b00499.

X-ray crystallographic structures and ¹H and ¹³C NMR spectral data of all compounds (PDF)

Crystallographic data (CIF)

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Notes

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