

Synthesis of thieno[2,3-*d*]thiazole-6-carboxylic acid derivatives as potential inducers of systemic resistance in plants

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Dedicated to Prof. Fritz Sauter on the occasion of his 70th birthday

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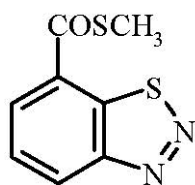
Abstract

Reduction of nitrothiocyanatothiophene **2**, available *via* nucleophilic substitution from the corresponding bromo compound **1**, gave thienothiazole **3** in excellent yield. Conversion of the amino functionality under Sandmeyer conditions gave access to halo compounds **4** as key intermediates for the subsequent introduction of sulfur, nitrogen, and oxygen nucleophiles. An unexpected side-reaction was observed when DMF was used as solvent and a mechanism for the introduction of a dimethylamino group is proposed.

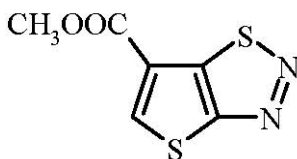
Keywords: Thiazoles, thienothiazoles, plant activators, nucleophilic substitution

Introduction

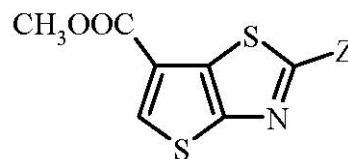
Treatment of crop plants with plant activators – a recently developed group of synthetic compounds – triggers their own defense system giving them the ability to resist the attack of naturally occurring pathogens ("systemic acquired resistance", SAR).¹ Recently, *acibenzolar-S-methyl* (Bion[®], **I**) was introduced to the market as the first commercial product in this field of research. After succeeding in the synthesis of similar thienothiadiazole derivatives (**II**)² we focused on various derivatives of thieno[2,3-*d*]thiazoles **III**.



I *Acibenzolar-S-methyl*;
Bion[®]



II



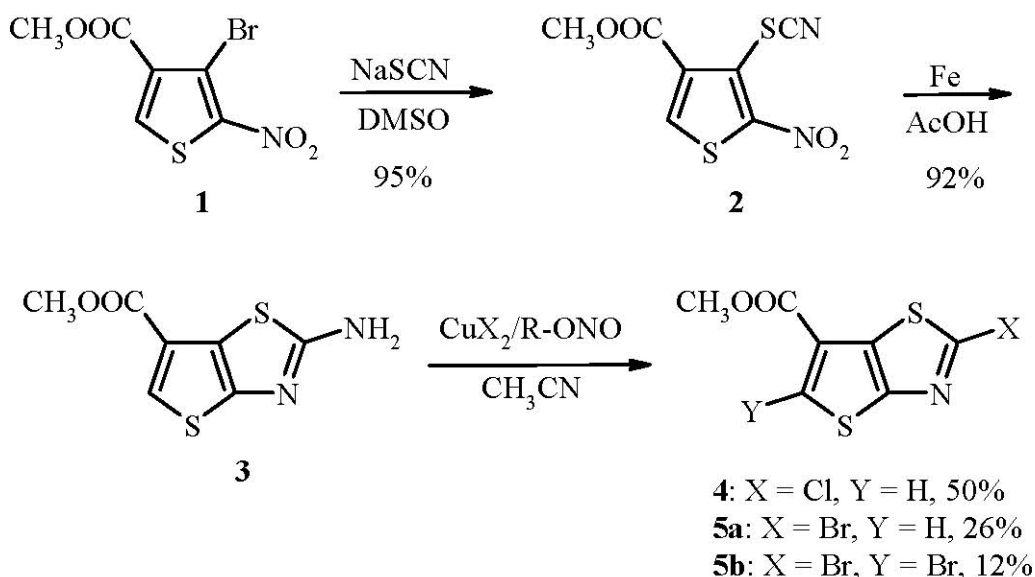
III

Z = Hal, OR, SR, NRR'

Results and Discussion

Starting from **1**, available *via* a recently optimized protocol,³ nucleophilic displacement of the bromo substituent by sodium thiocyanate led to intermediate **2** in excellent yield (Scheme 1). The nitro group in **2** was reduced with Fe/AcOH to the corresponding thiophenamine **3** which spontaneously cyclized *via* intramolecular nucleophilic attack at the carbon of the SCN-group yielding the amino compound **3**.

Our goal was the development of a highly flexible route to compounds **III** with a variety of substituents Z. Hence the corresponding halo products (Z = Hal, Scheme 1) represent valuable intermediates. Introduction of chlorine and formation of the chloro derivative **4** was achieved by diazotization under non-aqueous conditions followed by treatment of the diazonium salt with CuCl₂.⁴ However, the reaction of **3** with CuBr₂ under comparable conditions gave a mixture of the desired **5a** accompanied by substantial amounts of the dibromo compound **5b** as a by-product.



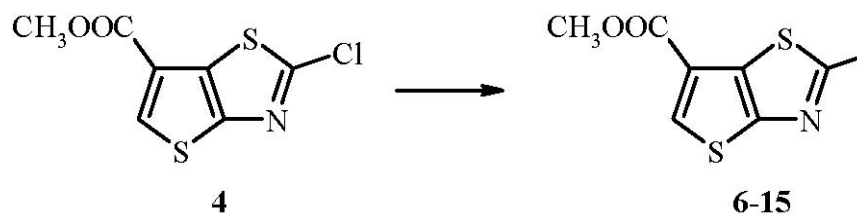
Scheme 1

A series of 2-substituted thienothiazoles **6-15** was available *via* nucleophilic substitution of the chloro atom in compound **4** applying various sulfur, nitrogen, and oxygen nucleophiles. As expected, sulfur nucleophiles (Scheme 2, entries 1–4) gave excellent conversions to the desired products **6-9**. Formation of amines **10-14** (Scheme 2, entries 5–9) required more drastic reaction conditions. A similar behavior was encountered with an oxygen nucleophile (**15**, Scheme 2, entry 10).

A noteworthy side-reaction was observed when using diethanolamine as nucleophile in DMF as solvent. The formation of the expected **12** (yield 34%) was accompanied by the dimethylamino product **13** (15%). This can be explained by a transamidation reaction of the

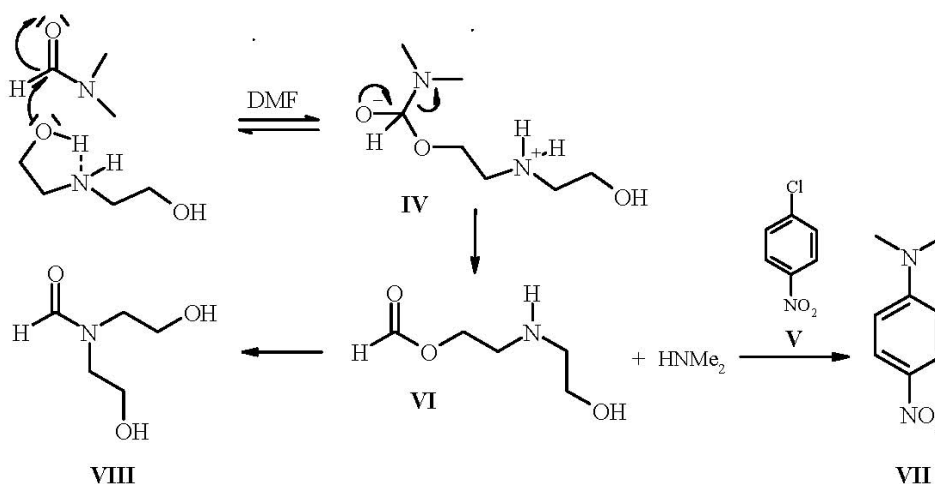
diethanolamine and DMF leading to dimethylamine as a competing nucleophile. A similar reaction was observed by Cho et al.⁵ for the conversion of **V** to **VII** via the following mechanism (Scheme 3).

Essential for the formation of the dimethylamino derivative is the lower reactivity of the amino alcohol towards direct substitution, which can be explained by intramolecular hydrogen bonding. The activated hydroxy group attacks DMF assisted by the adjacent basic amino function to produce an intermediate, which can introduce the dimethylamino group into the substrate while a formate is formed. Subsequent intramolecular transfer of the formyl group occurs under the reaction condition finally to produce formamide **VIII**.



Entry	R	Product	Yield [%]
1	SPh	6	85
2	SCH ₂ Ph	7	67
3	SCH ₂ CH ₂ CH ₃	8	84
4	SCH ₂ COOCH ₃	9	85
5		10	55
6		11	25
7		12	34
8	N(Me) ₂	13	15
9		14	47
10	OMe	15	40

Scheme 2



Scheme 3

Experimental Section

General Procedures. All reactions were carried out with commercially available chemicals, solvents were distilled prior to use. Flash column chromatography (FCC) was performed on Merck Kieselgel 60 (40–63 μm). Melting points were determined on a Galen III Kofler type hot-stage apparatus. NMR spectra were recorded with a Bruker AC 200 FT spectrometer (¹H NMR at 200 MHz) with CDCl₃ or DMSO-*d*₆ as solvents and (CH₃)₄Si as internal standard. Signals, which could not be assigned unambiguously are marked (*). Elemental analyses were carried out at Microanalytical Laboratory, University of Vienna.

Methyl 5-nitro-4-thiocyanatothiophene-3-carboxylate (2). A solution of methyl 4-bromo-5-nitrothiophene-3-carboxylate (**1**) (5.00 g, 18.79 mmol) and dry NaSCN (4.60 g, 56.38 mmol) in dry DMSO (50 mL) was stirred at 60 °C for 2 h. The reaction mixture was poured into water, the precipitate formed was filtered off, washed with water, and dried in vacuo to give **1** as beige crystals (4.36 g, 95%); mp 99–100 °C; ¹H NMR (CDCl₃): δ 3.99 (s, 3H, OCH₃), 8.32 (s, 1H, H-2); ¹³C NMR (CDCl₃): δ 53.0 (q, OCH₃), 107.6 (s, SCN), 122.9 (s, C-4), 133.0 (s, C-3), 136.5 (d, C-2), 150.6 (s, C-5), 160.3 (s, CO₂). Anal. Calcd. for C₇H₄N₂O₄S₂ (244.25): C, 34.42; H, 1.65; N, 11.47. Found: C, 34.58; H, 1.66; N, 11.45.

Methyl 2-aminothieno[2,3-*d*]thiazole-6-carboxylate (3). A solution of methyl 5-nitro-4-thiocyanatothiophene-3-carboxylate (**2**) (4.00 g, 16.38 mmol) in AcOH (120 mL) was treated with Fe powder (3.66 g, 65.51 mmol) in small portions so that the temperature of the reaction mixture was kept below 30 °C. After stirring at room temperature for 1 h the reaction mixture was poured into a saturated NaHCO₃ solution and extracted with diethyl ether. The organic layer was separated and washed with saturated NaHCO₃ solution, dried over Na₂SO₄ and evaporated to dryness. The crude product was purified by column chromatography (100 g silica gel PE/EtOAc 5:1) to give **3** as orange crystals (3.22 g, 92%); mp 214–216 °C; ¹H NMR (DMSO-*d*₆): δ 3.83 (s, 3H, OCH₃), 7.49 (broad s, 2H, NH₂), 7.89 (s, 1H, H-5); ¹³C NMR (DMSO-*d*₆): δ 52.0 (q, OCH₃),

120.9 (s, C-6a*), 123.6 (s, C-6*), 125.5 (d, C-5), 152.6 (s, C-3a), 161.7 (s, CO₂), 172.5 (s, C-2).

General procedure for the diazotization of 3

3-Methylbutylnitrite (1.5 equiv.) was added to a suspension of copper(II) chloride or copper(II) bromide (1.2 equiv.) in dry acetonitrile. The reaction mixture was stirred at room temperature for 10 min, and methyl 2-aminothieno[2,3-*d*]thiazole-6-carboxylate **3** (1 equiv.) was added at 15 °C within 1 h. The reaction mixture was stirred at room temperature for 30 min and then filtered. Some silica gel was added, the filtrate was evaporated, and the crude product was purified by column chromatography (silica gel, PE/EtOAc 50:1).

Methyl 2-chlorothieno[2,3-*d*]thiazole-6-carboxylate (4). Treatment of **3** (0.20 g, 0.94 mmol) with CuCl₂ gave **4** as yellow crystals (0.11 g, 50%); mp 155–157 °C; ¹H NMR (CDCl₃): δ 3.96 (s, 3H, OCH₃), 8.20 (s, 1H, H-2); ¹³C NMR (CDCl₃): δ 52.3 (q, OCH₃), 124.0 (s, C-6), 132.2 (s, C-6a), 132.5 (d, C-5), 151.7 (s, C-2), 154.8 (s, C-3a), 161.3 (s, CO₂). Anal. Calcd. for C₇H₄ClNO₂S (233.70): C, 35.98; H, 1.73; N, 5.99;. Found: C, 36.18; H, 1.66; N, 5.89.

Methyl 2-bromothieno[2,3-*d*]thiazole-6-carboxylate (5a). Treatment of **3** (0.30 g, 1.41 mmol) with CuBr₂ gave **5a** as colorless crystals (0.10 g, 26%); mp 161–164 °C; ¹H NMR (CDCl₃): δ 3.95 (s, 3H, OCH₃), 8.21 (s, 1H, H-2); ¹³C NMR (CDCl₃): δ 52.4 (q, OCH₃), 123.8 (s, C-6), 132.9 (d, C-5), 134.0 (s, C-6a), 139.5 (s, C-2), 153.2 (s, C-3a), 161.4 (s, CO₂). Anal. Calcd. for C₇H₄BrNO₂S₂ (278.15): C, 30.23; H, 1.45; N, 5.04). Found: C, 30.33; H, 1.36; N, 4.86.

Methyl 2,5-dibromothieno[2,3-*d*]thiazole-6-carboxylate (5b). By-product from the synthesis of compound **5a**: Colorless crystals **5b** (0.06g, 12%); mp 165–167 °C; ¹H NMR (CDCl₃): δ 3.99 (s, 3H, OCH₃); ¹³C NMR (CDCl₃): δ 52.4 (q, OCH₃), 121.4 (s, C-5), 122.0 (s, C-6), 133.7 (s, C-6a), 139.7 (s, C-2), 150.7 (s, C-3a), 160.5 (s, CO₂).

General procedure for the substitution of 4 with sulfur nucleophiles

The nucleophile (1.1 equiv.) was added to a solution of methyl 2-chlorothieno[2,3-*d*]thiazole-6-carboxylate **4** (1 equiv.) and K₂CO₃ (1.1 equiv.) in dry DMF or DMSO. When the reaction was complete the mixture was poured into water. The precipitate formed was filtered off, washed with water, and dried in vacuo. Alternatively, the aqueous solution was repeatedly extracted with diethyl ether, the combined organic layers were washed with saturated aqueous NaHCO₃ solution, dried over Na₂SO₄, and evaporated to dryness.

Methyl 2-(phenylsulfanyl)thieno[2,3-*d*]thiazole-6-carboxylate (6). Compound **4** (0.10 g, 0.43 mmol) reacted with benzenethiol in DMF at room temperature for 1 h and afforded after purification by column chromatography (silica gel/crude product 100:1, PE/EtOAc 10:1) yellow crystals **6** (0.11g, 85%); mp 93–95 °C. ¹H NMR (CDCl₃): δ 3.76 (s, 3H, OCH₃), 7.25–7.40 (m, 3H, H_{Ph}-2,4,6), 7.47–7.62 (m, 2H, H_{Ph}-3,5), 7.94 (s, 1H, H-5); ¹³C NMR (CDCl₃): δ 52.2 (q, OCH₃), 123.8 (s, C-6), 129.9 (d, C_{Ph}-2,6), 130.0 (d, C_{Ph}-4), 130.3 (s, C_{Ph}-1), 131.7 (d, C-5), 132.1 (s, C-6a), 134.3 (d, C_{Ph}-3,5), 155.1 (s, C-3a), 161.6 (s, CO₂), 170.8 (s, C-2). Anal. Calcd. for C₁₃H₉NO₂S₃ (307.42): C, 50.79; H, 2.95; N 4.56. Found: C, 50.87; H, 3.11; N 4.46.

Methyl 2-(benzylsulfanyl)thieno[2,3-*d*]thiazole-6-carboxylate (7). Compound **4** (1.20 g,

5.13 mmol), nucleophile: benzylthiol, solvent: DMSO, reaction conditions: 60 °C, 4 h, purification by column chromatography: (silica gel/crude product 50:1, PE/EtOAc 10:1): light yellow crystals **7** (1.10 g, 67%); mp 71–74 °C; ¹H NMR (CDCl₃): δ 3.91 (s, 3H, OCH₃), 4.50 (s, 2H, SCH₂), 7.23–7.44 (m, 5H, C₆H₅), 8.07 (s, 1H, H-5); ¹³C NMR (CDCl₃): δ 38.8 (t, SCH₂), 52.2 (q, OCH₃), 123.8 (s, C-6), 127.7 (d, C_{Ph}-4), 128.6 (2×d, C_{Ph}-3,5), 128.9 (2×d, C_{Ph}-2,6), 129.1 (s, C-6a), 131.3 (d, C-5), 135.8 (s, C_{Ph}-1), 154.7 (s, C-3a), 161.6 (s, CO₂), 168.8 (s, C-2). Anal. Calcd. for C₁₄H₁₁NO₂S₃ (321.44): C, 52.31; H, 3.45; N, 4.36. Found: C, 52.60; H, 3.47; N, 4.09.

Methyl 2-(propylsulfanyl)thieno[2,3-d]thiazole-6-carboxylate (8). Compound **4** (2.00 g, 8.56 mmol), nucleophile: propane-1-thiol, solvent: DMSO, reaction conditions: 50 °C, 4 h, room temperature, overnight, purification by column chromatography (silica gel/product 50:1, PE/EtOAc 10:1): light yellow crystals **8** (1.96 g, 84%); mp 37–39 °C. ¹H NMR (CDCl₃): δ 1.06 (t, *J*_{3',2'} = 6 Hz, 3H, 3'-CH₃), 1.83 (sext, *J*_{2',1'} = 6 Hz, *J*_{2',3'} = 6 Hz, 2H, 2'-CH₂), 3.25 (t, *J*_{1',2'} = 6 Hz, 2H, 1'-CH₂), 3.93 (s, 3H, OCH₃), 8.04 (s, 1H, H-5); ¹³C NMR (CDCl₃): δ 13.2 (q, CH₃), 22.6 (t, CH₂), 36.5 (t, SCH₂), 52.2 (q, OCH₃), 123.8 (s, C-6), 130.9 (s, C-6a), 131.1 (d, C-5), 154.8 (s, C-3a), 161.7 (s, CO₂), 170.1 (s, C-2). Anal. Calcd. for C₁₀H₁₁NO₂S₃ (273.40): C, 43.93; H, 4.06; N, 5.12. Found: C, 44.23; H, 3.87; N, 5.10.

Methyl 2-[(methoxy-2-oxoethyl)sulfanyl]thieno[2,3-d]thiazole-6-carboxylate (9). Compound **4** (2.00 g, 8.56 mmol), nucleophile: methyl 2-sulfanylacetate, solvent: DMSO, reaction conditions: 70 °C, 3 h, purification by column chromatography (silica gel/product 50:1, PE/EtOAc 10:1): colorless crystals **9** (2.22 g, 85%); mp 80–82 °C. ¹H NMR (CDCl₃): δ 3.74 (s, 3H, CH₂COOCH₃), 3.90 (s, 3H, OCH₃), 4.07 (s, 2H, SCH₂), 8.05 (s, 1H, H-5); ¹³C NMR (CDCl₃): δ 35.6 (t, SCH₂), 52.2 (q, CH₂CO₂CH₃), 52.8 (q, OCH₃), 123.7 (s, C-6a), 131.5 (s, C-6), 131.6 (d, C-5), 154.4 (s, C-3a), 161.5 (s, 6-CO₂), 167.1 (s, C-2), 168.5 (s, CH₂COO). Anal. Calcd. for C₁₀H₉NO₄S₃ (303.38): C, 39.59; H, 2.99; N, 4.62. Found: C, 39.39; H, 2.80; N, 4.45.

Methyl 2-pyrrolidinothieno[2,3-d]thiazole-6-carboxylate (10). A solution of **4** (0.10 g, 0.43 mmol) in dry DMF (5 mL) was added to a solution of pyrrolidine (0.06 g, 0.43 mmol) in DMF (5 mL). After stirring at room temperature for 2 h pyrrolidine (0.06 g, 0.43 mmol) was added, and the reaction mixture was stirred at room temperature for 1 hour. The solution was then poured into water, and the mixture was extracted with CH₂Cl₂. The combined organic layers were washed with 2 N HCl and with saturated NaHCO₃ solution, dried over Na₂SO₄ and evaporated to dryness. The product was purified by column chromatography (silica gel/product 30:1, PE/EtOAc 10:1) to give yellow crystals **10** (0.06 g, 55%); mp 130–132 °C; ¹H NMR (CDCl₃): δ 1.95–2.12 (m, 4H, 2 CH₂), 3.43–3.56 (m, 4H, 2 CH₂N), 3.88 (s, 3H, OCH₃), 7.62 (s, 1H, H-5); ¹³C NMR (CDCl₃): δ 25.5 (t, 2 CH₂), 49.2 (t, 2 CH₂N), 51.9 (q, OCH₃), 121.1 (s, C-6), 124.0 (s, C-6a), 124.4 (d, C-5), 154.0 (s, C-3a), 162.3 (s, CO₂), 170.7 (s, C-2). Anal. Calcd. for C₁₃H₉NO₂S₃ (307.42): C, 49.23; H, 4.51; N, 10.44. Found: C, 49.30; H, 4.31; N, 10.36.

Methyl 2-[(3-hydroxypropyl)amino]thieno[2,3-d]thiazole-6-carboxylate (11). A mixture of **4** (0.30 g, 1.28 mmol), 3-aminopropanol (0.12 g, 1.54 mmol) and K₂CO₃ (0.35 g, 2.57 mmol) was heated in dry dioxane (10 mL) at 100 °C for 4 h. Upon addition of dry DMSO (8 mL) the solution was stirred at 110 °C for 2 h. The solution was poured into water (100 mL), and the

mixture was extracted with EtOAc. The combined organic layers were washed twice with water, and the combined aqueous layers were extracted with EtOAc. The combined organic layers were dried over Na₂SO₄, some silica gel was added, and the solvent was removed in vacuo. The crude product was purified by column chromatography (silica gel/product 30:1, PE/EtOAc 5:1) to give brown crystals **11** (0.09 g, 25%); mp 118–120 °C (EtOAc); ¹H NMR (DMSO-*d*₆): δ 1.76 (quint., 2H, CH₂CH₂CH₂, *3J* = 7 Hz), 3.38 (broad q, 2H, NCH₂, *3J* = 7 Hz), 3.50 (t, 2H, CH₂OH), 3.83 (s, 3H, OCH₃), 4.50 (broad s, 1H, OH), 7.90 (s, 1H, H-5), 8.07 (t, 1H, NH, *3J* = 5 Hz); ¹³C NMR (DMSO-*d*₆): δ 31.8 (t, CH₂CH₂CH₂), 41.4 (t, NCH₂), 52.1 (q, OCH₃), 58.2 (t, CH₂OH), 120.0 (s, C-6), 123.5 (s, C-6a*), 125.3 (d, C-5*), 152.8 (s, C-3a), 161.6 (s, CO₂), 172.3 (s, C-2). Anal. Calcd. for C₁₀H₁₂N₂O₃S₂ (272.35): C, 44.10; H, 4.44; N, 10.29. Found: C, 44.12; H, 4.35; N, 10.09.

Methyl 2-[bis(2-hydroxyethyl)amino]thieno[2,3-*d*]thiazole-6-carboxylate (12). A solution of **4** (0.50 g, 2.13 mmol) in dry DMF (10 mL) was heated to 100 °C. Diethanolamine (0.56 g, 5.35 mmol) was added dropwise, and the reaction mixture was stirred at 100 °C for 7 h and subsequently at room temperature for 16 h. The solution was poured into water (500 mL), and the mixture was extracted with EtOAc. The combined organic layers were washed with water, dried over Na₂SO₄, some silica gel was added, and the suspension was evaporated. The crude product was purified by column chromatography (silica gel/product 30:1, PE/EtOAc 5:1, increasing EtOAc content) to give **12** as brown crystals (0.22 g, 34%); mp 121–124 °C (EtOAc); ¹H NMR (DMSO-*d*₆): δ 3.50–3.75 [m, 8H, N(CH₂CH₂OH)₂], 3.84 (s, 3H, OCH₃), 4.90 (t, 2H, 2 × OH, *3J* = 5.5 Hz), 7.97 (s, 1H, H-5); ¹³C NMR (DMSO-*d*₆): δ 52.2 (q, OCH₃), 54.3 (t, 2 NCH₂), 62.8 (t, 2 OCH₂), 120.3 (s, C-6), 123.5 (s, C-6a*), 125.6 (d, C-5*), 153.3 (s, C-3a), 161.6 (s, CO₂), 173.1 (s, C-2). Anal. Calcd. for C₁₁H₁₄N₂O₄S₂ (302.37): C, 43.70; H, 4.67; N, 9.26. Found: C, 43.84; H, 4.69; N, 9.04.

Methyl 2-(dimethylamino)thieno[2,3-*d*]thiazole-6-carboxylate (13). This compound is a by-product in the synthesis of **12** and was isolated as the first fraction eluted from column chromatography (silica gel/product 30:1, PE:EtOAc 5:1, gradient elution to PE/EtOAc 1:1): yellow crystals **13** (0.08 g, 15%); mp 96–98 °C (diisopropyl ether); ¹H NMR (CDCl₃): δ 3.12 [s, 6H, N(CH₃)₂], 3.89 (s, 3H, OCH₃), 7.64 (s, 1H, H-5); ¹³C NMR (CDCl₃): δ 39.8 [q, N(CH₃)₂], 51.8 (q, OCH₃), 121.7 (s, C-6*), 124.0 (s, C-6a*), 124.7 (d, C-5), 153.7 (s, C-3a), 162.2 (s, CO₂), 174.2 (s, C-2). Anal. Calcd. for C₉H₁₀N₂O₂S₂ (242.32): C, 44.61; H, 4.16; N, 11.56. Found: C, 44.67; H, 3.98; N, 11.34.

Methyl 2-[[3-(dimethylamino)propyl]amino]thieno[2,3-*d*]thiazole-6-carboxylate (14). Methyl 2-chlorothieno[2,3-*d*]thiazole-6-carboxylate **4** (2.00 g, 8.56 mmol), 3-(dimethylamino)propylamine (1.31 g, 12.82 mmol) and K₂CO₃ (2.37 g, 17.15 mmol) were heated in dry DMSO (25 mL) at 100 °C for 1 h. The reaction mixture was poured into water (500 mL) and extracted with EtOAc. The combined organic layers were washed with water, dried over Na₂SO₄, and the solvent was removed in vacuo. The product was purified by flash column chromatography (silica gel/product 30:1, methanol) to give **14** as brown crystals (1.20 g, 47%); mp 91–94 °C (EtOAc); ¹H NMR (DMSO-*d*₆): δ 1.73 (quint., 2H, CH₂CH₂CH₂, *3J* = 6 Hz), 2.16

(s, 6H, N(CH₃)₂), 2.28 (t, 2H, CH₂N(CH₃)₂, ${}^3J = 6$ Hz), 3.31 (q, 2H, NHCH₂, ${}^3J = 6$ Hz), 3.84 (s, 3H, OCH₃), 7.90 (s, 1H, H-5), 8.10 (t, 1H, NH, ${}^3J = 3$ Hz); ¹³C NMR (DMSO-*d*₆): δ 26.5 (t, CH₂CH₂CH₂), 42.5 (t, CH₂N(CH₃)₂), 45.1 [q, N(CH₃)₂], 52.0 (q, OCH₃), 56.4 (t, NHCH₂), 120.0 (s, C-6), 123.5 (s, C-6a*), 125.3 (d, C-5*), 152.8 (s, C-3a), 161.6 (s, CO₂), 172.2 (s, C-2). Anal. Calcd. for C₁₂H₁₇N₃O₂S₂ (299.42): C, 48.14; H, 5.72; N, 14.03. Found: C 47.93, H 5.48, N 13.76.

Methyl 2-methoxythieno[2,3-*d*]thiazole-6-carboxylate (15). Methyl 2-chlorothieno-[2,3-*d*]thiazole-6-carboxylate **4** (0.10 g, 0.43 mmol) was slowly added to a solution obtained from sodium (0.02 g, 0.64 mmol) and dry MeOH (10 mL). After stirring at 50 °C for 4 h and thereafter at room temperature overnight, the reaction mixture was evaporated to dryness. The residue was dissolved in water and extracted with CH₂Cl₂. The organic layer was dried over Na₂SO₄, and the solvent was removed in vacuo. The product was purified by column chromatography (silica gel/product 30:1, PE/EtOAc 10:1) to give **15** as yellow crystals (0.04 g, 40%); mp 78–80 °C; ¹H NMR (CDCl₃): δ 3.93 (s, 3H, CO₂CH₃), 4.16 (s, 3H, OCH₃), 7.92 (s, 1H, H-5); ¹³C NMR (CDCl₃): δ 52.2 (q, CO₂CH₃), 58.9 (q, OCH₃), 124.5 (s, C-6), 128.0 (C-5, C-6a), 148.6 (s, C-3a), 161.9 (s, CO₂), 177.9 (s, C-2).

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