Facile Preparation of Thiazoles from 1*H*-1-(1′-Alkynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-Dioxide with Thioamides

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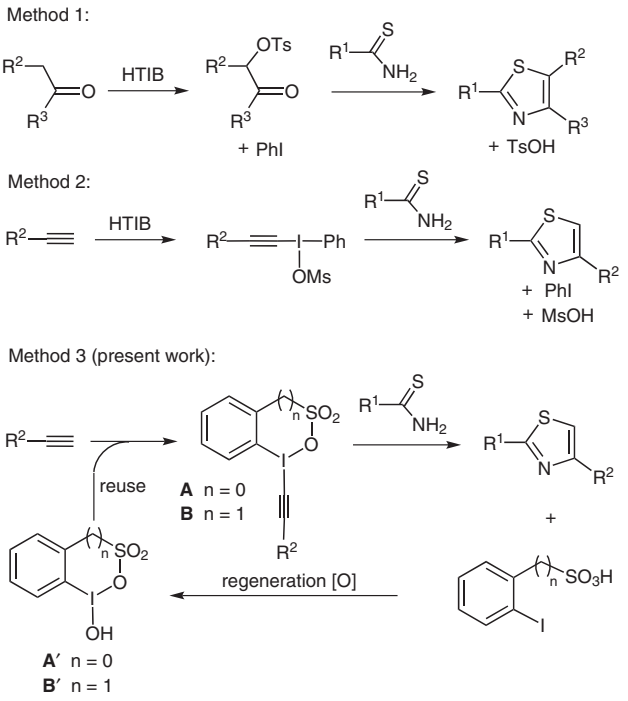
Received 27 June 2008

Abstract: Thiazoles were obtained in high yields by the reaction of 1*H*-1-(1′-alkynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxides, which were easily prepared from the reaction of 1*H*-1-hydroxy-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide and 1-alkynes, with thioamides. Here, the co-product, potassium 2-iodo-5-methylbenzenesulfonate, was recovered quantitatively by simple filtration of the reaction mixture, and was regenerated to 1*H*-1-(1′-alkynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxides to be reused for the same preparation of thiazoles, keeping good yields.

Key words: thiazole, 1*H*-1-(1′-alkynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide, 1-alkyne, thioamide

The thiazole unit is a very important moiety in medicinal chemistry, because certain pharmaceuticals containing the thiazole unit[1] possess such biological activities as anti-inflammatory,[2a] antihypertensive,[2b] antibacterial,[2c] and anti-HIV.[2d] Examples are meloxicam (anti-inflammatory), arotinolol (antihypertensive), nizatidine (gastric antisecretory). Many methods for the preparation of the thiazole moiety are available,[1] and among them, the Hantzsch thiazole synthesis[3] using α-haloketones with thioamides is one of the most excellent methods. On the other hand, thiazoles can also be prepared in two steps without using α-haloketones. The reaction of ketones with Koser's reagent [(hydroxy)(tosyloxy)iodobenzene] (HTIB) to form α-tosyloxyketones, and the subsequent treatment of α-tosyloxyketones with thioamides provide corresponding thiazoles in moderate yields (Scheme 1, method 1).[4] However, in method 1, iodobenzene and *p*-toluenesulfonic acid are formed as co-products. Recently, another preparation method of thiazoles using hypervalent iodine, that is, cyclocondensation of thioamides and alkynyl(aryl)iodoniums, was reported (method 2).[5] This is very interesting since 1-alkynes can be used as the starting material, instead of ketones. However, the yields of thiazoles were not so good. And iodobenzene and methanesulfonic acid, which are difficult to recover, are formed as co-products. Moreover, in the preparation of alkynyl(aryl)iodonium mesylates or tosylates, the addition products of mesylate or tosylate anion to the triple bond of the alkynyl(aryl)iodoniums are formed partly, and it is not easy to restrain the addition reaction.



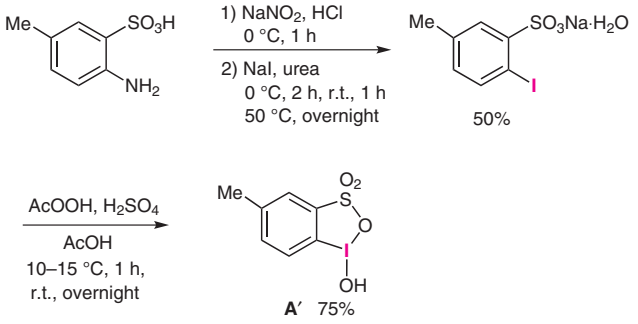
Scheme 1 Synthetic approach to thiazoles with hypervalent iodines

As part of our study for the preparation of heterocyclic compounds using hypervalent iodines,[4g,h,6] we would like to report herein the preparation of thiazoles using cyclic 1-alkynyliodonium hypervalent iodine, as shown in method 3, that is, 1*H*-1-(1′-alkynyl)-1,2,3-benziodoxathiole 3,3-dioxides (**A**: n = 0, five-membered ring).

As a five-membered ring, we selected and prepared 1*H*-1-(1′-phenylethynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide (**A-1**) from 2-amino-5-methylbenzenesulfonic acid. Thus, we employed the Griess reaction of 2-amino-5-methylbenzenesulfonic acid to form sodium 2-iodo-5-methylbenzenesulfonate, followed by oxidation with peroxyacetic acid to 1*H*-1-hydroxy-5-methyl-1,2,3-benziodoxazole (**A′**) based on the literature,[7] as shown in Scheme 2.

Treatment of cyclic hypervalent iodine **A′** with 1-phenylacetylene provided 1*H*-1-(1′-phenylethynyl)-5-methyl-1,2,3-benziodoxazole (**A-1**) in 50–60% yields. Using the same method, 1*H*-1-(1′-hexynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide (**A-2**) and 1*H*-1-(1′-octynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide (**A-3**) were prepared in almost the same yields. However, as a six-

SYNLETT 2008, No. 17, pp 2637–2641
Advanced online publication: 01.10.2008
DOI: 10.1055/s-0028-1083439; Art ID: U06808ST



Scheme 2 Preparation of 1*H*-1-hydroxy-5-methyl-1,2,3-benziodoxazole **A′**

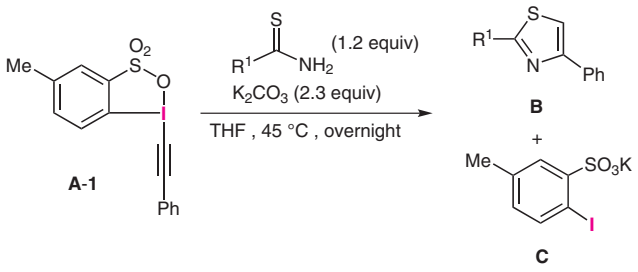
membered ring, 1*H*-1-(1′-alkynyl)-1,2,3-benziodoxathioine 3,3-dioxide (**B**) could not be obtained in pure state by the reaction of 1-alkyne with 1*H*-1-hydroxy-1,2,3-benziodoxathioine 3,3-dioxide (**B′**), which was prepared from the oxidation of *o*-iodophenylmethanesulfonic acid with peroxyacetic acid. Therefore, we decided to use 1*H*-1-(1′-phenylethynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide (**A-1**) with various thioamides, such as thiobenzamide, thioacetamide, 4-methylthiobenzamide, 4-methoxythiobenzamide, 4-nitrothiobenzamide, and thiourea, in the presence of potassium carbonate under THF warming conditions, and corresponding thiazoles **B** were obtained in better yields than those with method 2, as shown in Table 1.[8] Among diethyl ether, THF, and dichloromethane solvent, THF showed the best result.

When 1*H*-1-(1′-hexynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide (**A-2**) and 1*H*-1-(1′-octynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide (**A-3**) were treated with the same thioamides and thiourea, the reactions proceeded smoothly at room temperature to provide corresponding thiazoles **B** again in good yields. The results are shown in Table 2.[8] After these reactions, potassium 2-iodo-5-methylbenzenesulfonate (**C**) was recovered quantitatively by simple filtration of the reaction mixture. Oxidation of potassium salt **C** with peroxyacetic acid in the presence of sulfuric acid gave 1*H*-1-hydroxy-5-methyl-1,2,3-benziodoxathiole (**A′**), and subsequent treatment with 1-alkynes gave 1*H*-1-(1′-alkynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxides (**A**) in 50–60% yields.

The reaction mechanism is proposed in Scheme 3. The initial I–S bond formation between iodine atom of 1*H*-1-(1′-alkynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide (**A**) and sulfur atom of thioamide occurs to form intermediate **a**, followed by [3,3] sigmatropic rearrangement to provide intermediates **b** and **b′**. Then, α-cleavage of intermediate **b′** occurs to generate vinyl carbene **c**, and cyclization ensures to give thiazole **B**, as proposed in method 2. In supporting of initial I–S bond formation, the DIB-mediated N-acylation of 1,3-disubstituted thiourea was reported recently to proceed through the initial I–S bond formation.[9]

In conclusion, 1*H*-1-(1′-alkynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxides (**A**), which can be smoothly prepared from the reaction of 2-iodo-5-methylbenzenesulfonic acid and 1-alkynes, reacted smoothly with thioamides to give the corresponding thiazoles **B** in good yields. Here, co-products, such as iodobenzene and *p*-toluenesulfonic acid are not formed, and the formed potassium 2-iodo-5-methylbenzenesulfonate (**C**) can be recovered quantitatively, and regenerated to 1*H*-1-(1′-alkynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxides (**A**) in moderate yields. Regenerated 1*H*-1-(1′-alkynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxides (**A**) could be

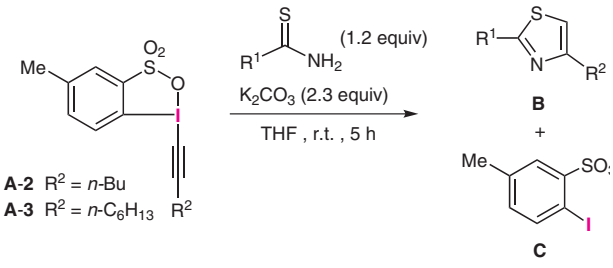
Table 1 Reaction of 1*H*-1-(1′-Phenylethynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-Dioxide (**A-1**) with Thioamides



Entry	R^1	Yield of **B** (%)
1	Ph	65 (78)[a]
2	Me	61
3	Tol	78
4	PMP	82 (80)[a]
5[b]	4-$O_2NC_6H_4$	46
6	NH_2	66

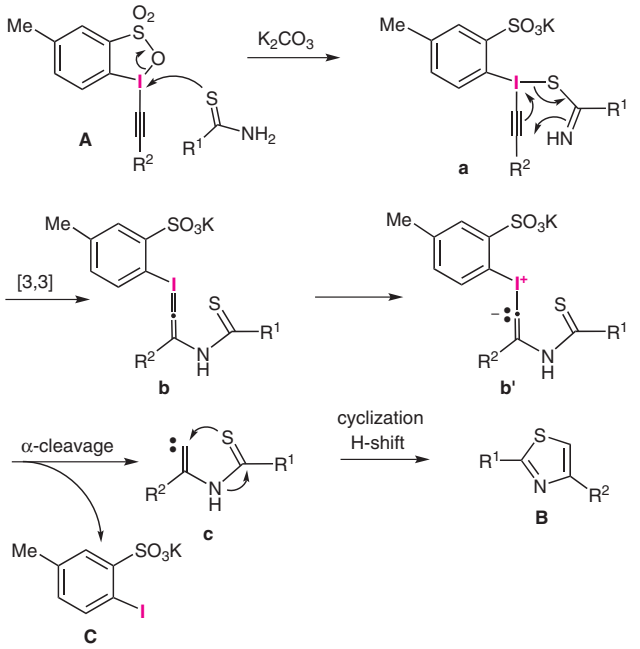
[a] Regenerated **A-1** from recovered **C** was used.
[b] Reaction temperature was 60 °C.

Table 2 Reaction of 1*H*-1-(1′-Alkynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-Dioxides **A-2** and **A-3** with Thioamides



Entry	R^1	Yield of **B** (%)	
		A-2	**A-3**
1	Ph	67 (74)[a]	76 (80)[a]
2	Me	63	76
3	Tol	80 (76)[a]	84
4	PMP	70	72
5	4-$O_2NC_6H_4$	56	69
6	NH_2	66	73

[a] Regenerated **A-2** or **A-3** from recovered **C** was used.



Scheme 3 Possible reaction pathway

reused for the same preparation of thiazoles **B** (entries 1 and 4 in Table 1, and entries 1 and 3 in Table 2).

Acknowledgment

Financial support in the form of a Grant-in-Aid for Scientific Research on Priority Area (20031007) from the Ministry of Education, Culture, Sports, Science, and Technology is gratefully acknowledged.

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(8) **Typical Procedure for Preparation of 1*H*-1-(1′-Hexynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-Dioxide**
A mixture of 1*H*-1-hydroxy-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide (5 mmol), PTSA·H_2O (5 mmol), and 1-hexyne (25 mmol) in MeCN (40 mL) was refluxed for 20 h. After removal of the solvent to obtain an oil, a solution of the oil in $CHCl_3$ (200 mL) was washed with 5% $NaHCO_3$ (80 mL) and H_2O (3 × 50 mL), and was concentrated to a solid. Recrystallization of the solid with a mixture of CH_2Cl_2 (30 mL), Et_2O (100 mL), and hexane (60 mL) gave 1*H*-1-(1′-hexynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide in 53% yield.
1*H*-1-(1′-Hexynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-Dioxide (R = *n*-Bu)
Mp 164–166 °C (dec.); lit.[7] 179–181 °C (dec.). IR (Nujol): 2166 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.01(s, 1 H), 7.92 (d, *J* = 8.5 Hz, 1 H), 7.47 (d, *J* = 8.7 Hz, 1 H), 2.73 (t, *J* = 7.2 Hz, 2 H), 2.50 (s, 3 H), 1.61–1.74 (m, 2 H), 1.43–1.55 (m, 2 H), 0.98 (t, *J* = 7.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 143.7, 141.6, 135.1, 130.8, 126.8, 115.5, 105.8, 29.9, 28.5, 22.1, 20.8, 20.6, 13.5.
1*H*-1-(1′-Octynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-Dioxide (R = *n*-C_6H_{13})
Mp 150 °C (dec.); lit.[7] 152–154 °C (dec.). IR (Nujol): 2168 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.04 (s, 1 H), 7.90 (d, *J* = 8.7 Hz, 1 H), 7.48 (dd, *J* = 1.6, 8.6 Hz, 1 H), 2.73 (t, *J* = 7.1 Hz, 2 H), 2.51 (s, 3 H), 1.64–1.74 (m, 2 H), 1.42–1.52 (m, 2 H), 1.30–1.40 (m, 4 H), 0.92 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 143.8, 141.5, 135.0, 130.8, 126.6, 115.5, 105.8, 31.1, 28.5, 28.4, 27.8, 22.4, 20.9, 20.7, 14.0.
1*H*-1-(1′-Phenylethynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-Dioxide (R = Ph)
Mp 217–219 °C (dec.); lit.[7] 221–223 °C (dec.). IR (Nujol): 2160 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6, TMS): δ = 8.12 (d, *J* = 8.4, 1 H), 7.76–7.81(m, 3 H), 7.53–7.67 (m, 4 H), 2.45 (s, 3 H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ = 142.6, 142.4, 135.0, 133.0, 131.6, 129.1, 129.1, 128.9, 119.4, 107.7, 107.2, 41.3, 20.2.
Typical Procedure for Preparation of Thiazoles
To a solution of thiobenzamide (0.48 mmol) in THF (2 mL)

were added K_2CO_3 (0.92 mmol) and 1*H*-1-(1′-phenylethynyl)-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide (0.4 mmol). The obtained mixture was stirred at 45 °C overnight under argon atmosphere. After the reaction, the mixture was filtered to remove potassium 2-iodo-5-methyl-benzenesulfonate quantitatively. After evaporation of the filtrate, the residue was chromatographed on SiO_2 (eluent: hexane–$CHCl_3$, 1:1) to afford pure 1,4-diphenylthiazole in 65% yield.

2,4-Diphenylthiazole

Mp 91–92 °C; lit.[10] 91–92 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.98–8.09 (m, 4 H), 7.41–7.51 (m, 6 H), 7.35 (t, *J* = 7.4 Hz, 1 H).

Regeneration of Potassium 2-Iodo-5-methylbenzenesulfonate to 1*H*-1-Hydroxy-5-methyl-1,2,3-benziodoxathiole 3,3-Dioxide

Hydrogen peroxide (33%, 1.3 mL) was added dropwise to a solution of acetic anhydride (1.2 mL) at 0 °C. The obtained mixture was stirred overnight. After the reaction, the mixture was added dropwise to a stirred mixture of potassium 2-iodo-5-methylbenzenesulfonate (2.4 mmol) in AcOH (4 mL) and concd H_2SO_4 (1.2 mL) while keeping the temperature at 10–15 °C. The mixture was stirred at this temperature for 1 h and overnight at r.t. After the reaction, the precipitate was filtered to give 1*H*-1-hydroxy-5-methyl-1,2,3-benziodoxathiole 3,3-dioxide in 50–60% yield.

2-Phenyl-4-butylthiazole

Oil. IR(neat): 2956, 2929, 2859, 1516, 1498, 1460, 1436, 1244, 1004, 763, 689 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.93 (dd, *J* = 1.4, 8.0 Hz, 2 H), 7.38–7.45 (m, 3 H), 6.86 (s, 1 H), 2.83 (t, *J* = 7.8 Hz, 2 H), 1.70–1.80 (m, 2 H), 1.37–1.49 (m, 2 H), 0.96 (t, *J* = 7.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 167.4, 158.9, 133.9, 129.7, 128.8, 126.5, 112.6, 31.4, 31.3, 22.4, 13.9. HRMS–FAB: *m/z* calcd for $C_{13}H_{16}NS$ [M + H]: 218.1003; found: 218.1006.

2-Methyl-4-butylthiazole

Oil. IR(neat): 3427, 2956, 2929, 2859, 1637, 1523, 1457, 1183, 1133, 730, 560, 526 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 6.69 (s, 1 H), 2.67–2.76 (m, 5 H), 1.62–1.73 (m, 2 H), 1.32–1.44 (m, 2 H), 0.93 (t, *J* = 7.4 Hz, 3 H).^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 165.2, 157.3, 111.9, 31.4, 31.2, 22.4, 19.1, 13.9. HRMS–FAB: *m/z* calcd for $C_8H_{14}NS$ [M + H]: 156.0847; found: 156.0837.

2-(4-Methylphenyl)-4-butylthiazole

Oil. IR(neat): 2955, 2928, 2859, 1509, 1457, 1246, 1007, 818, 735, 711 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.82 (d, *J* = 8.2 Hz, 2 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 6.82 (s, 1 H), 2.81 (t, *J* = 7.7 Hz, 2 H), 2.38 (s, 3 H), 1.69–1.79 (m, 2 H), 1.36–1.48 (m, 2 H), 0.96 (t, *J* = 7.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 167.6, 158.7, 139.8, 131.3, 129.5, 126.4, 112.1, 31.4, 31.3, 22.4, 21.4, 13.9. HRMS–FAB: *m/z* calcd for $C_{14}H_{18}NS$ [M + H]: 232.1160; found: 232.1161.

2-(4-Methoxyphenyl)-4-butylthiazole

Oil. IR(neat): 2859 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.87 (d, *J* = 8.9 Hz, 2 H), 6.94 (d, *J* = 9.0 Hz, 2 H), 6.79 (s, 1 H), 3.85 (s, 3 H), 2.81 (t, *J* = 7.7 Hz, 2 H), 1.68–1.80 (m, 2 H), 1.36–1.48 (m, 2 H), 0.96 (t, *J* = 7.3 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 167.5, 161.0, 158.7, 128.1, 127.1, 114.3, 111.8, 55.5, 31.6, 31.5, 22.6, 14.1. HRMS–FAB: *m/z* calcd for $C_{14}H_{18}NOS$ [M + H]: 248.1109; found: 248.1119.

2-(4-Nitrophenyl)-4-butylthiazole

Mp 47–48 °C. IR (Nujol): 1522, 1345, 851 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.29 (d, *J* = 8.9 Hz, 2 H), 8.11 (d, *J* = 9.2 Hz, 2 H), 7.03 (s, 1 H), 2.85 (t, *J* = 7.7 Hz, 2 H), 1.71–1.81 (m, 2 H), 1.38–1.49 (m, 2 H), 0.97 (t, *J* = 7.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 164.2, 160.1, 148.2, 139.4, 127.0, 124.2, 115.0, 31.3, 22.3, 13.9. HRMS–FAB: *m/z* calcd for $C_{13}H_{15}N_2O_2S$ [M + H]: 263.0854; found: 263.0838.

2-Amino-4-butylthiazole

Oil. IR (Nujol): 3436, 1607, 1521, 1113, 696 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 6.08 (s, 1 H), 4.91 (s, 2 H), 2.53 (t, *J* = 7.8 Hz, 2 H), 1.56–1.68 (m, 2 H), 1.30–1.43 (m, 2 H), 0.92 (t, *J* = 7.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 167.3, 102.5, 102.5, 31.7, 31.2, 22.7, 14.2. HRMS–FAB: *m/z* calcd for $C_7H_{13}N_2S$ [M + H]: 157.0799; found: 157.0811.

2-Phenyl-4-hexylthiazole

Oil. IR(neat): 2926, 2856, 1517, 1458, 1239, 1003, 763, 689 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.94 (dd, *J* = 1.7, 7.8 Hz, 2 H), 7.36–7.47 (m, 3 H), 6.87 (s, 1 H), 1.70–1.82 (m, 2 H), 1.27–1.47 (m, 6 H), 0.89 (t, *J* = 7.1 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 167.4, 158.9, 133.9, 129.7, 128.8, 126.5, 112.6, 31.7, 31.7, 29.2, 29.0, 22.6, 14.1. HRMS–FAB: *m/z* calcd for $C_{15}H_{20}NS$ [M + H]: 246.1316; found: 246.1315.

2-Methyl-4-hexylthiazole

Oil. IR(neat): 2955, 2926, 2856, 1523, 1457, 1183, 728 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 6.69 (s, 1 H), 2.67–2.75 (m, 5 H), 1.62–1.75 (m, 2 H), 1.23–1.45 (m, 6 H), 0.88 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 165.2, 157.4, 111.9, 31.6, 31.6, 29.2, 29.0, 22.6, 19.1, 14.1. HRMS–FAB: *m/z* calcd for $C_{10}H_{18}NS$ [M + H]: 184.1160; found: 184.1167.

2-(4-Methylphenyl)-4-hexylthiazole

Oil. IR(neat): 2926, 2856, 1509, 1457, 1247, 1005, 817, 711 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.82 (d, *J* = 8.3 Hz, 2 H), 7.22 (d, *J* = 7.8 Hz, 2 H), 6.82 (s, 1 H), 2.80 (t, *J* = 7.6 Hz, 2 H), 2.38 (s, 3 H), 1.70–1.81 (m, 2 H), 1.27–1.46 (m, 6 H), 0.89 (t, *J* = 7.1 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 167.6, 158.7, 139.9, 131.3, 129.5, 126.4, 112.1, 31.7, 31.7, 29.2, 29.0, 22.6, 21.4, 14.1. HRMS–FAB: *m/z* calcd for $C_{16}H_{22}NS$ [M + H]: 260.1473; found: 260.1493.

2-(4-Methoxyphenyl)-4-hexylthiazole

Oil. IR(neat): 2855 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.87 (d, *J* = 9.0 Hz, 2 H), 6.94 (d, *J* = 8.8 Hz, 2 H), 6.79 (s, 1 H), 3.85 (s, 3 H), 2.80 (t, *J* = 7.8 Hz, 2 H), 1.69–1.80 (m, 2 H), 1.25–1.45 (m, 6 H), 0.89 (t, *J* = 6.9 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 160.8, 158.6, 134.0, 127.9, 126.9, 114.1, 111.7, 55.4, 31.7, 31.7, 29.2, 29.0, 22.6, 14.1. HRMS–FAB: *m/z* calcd for $C_{16}H_{22}NOS$ [M + H]: 276.1422; found: 276.1401.

2-(4-Nitrophenyl)-4-hexylthiazole

Mp 45–46 °C. IR (Nujol): 1523, 1339, 852 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.28 (d, *J* = 8.8 Hz, 2 H), 8.10 (d, *J* = 9.1 Hz, 2 H), 7.03 (s, 1 H), 2.84 (t, *J* = 7.8 Hz, 2 H), 1.72–1.81 (m, 2 H), 1.30–1.45 (m, 6 H), 0.90 (t, *J* = 7.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 164.2, 160.1, 148.2, 139.4, 127.0, 124.2, 115.0, 31.6, 31.6, 29.1, 28.9, 22.6, 14.1. HRMS–FAB: *m/z* calcd for $C_{15}H_{19}N_2O_2S$ [M + H]: 291.1167; found: 291.1169.

2-Amino-4-hexylthiazole

Mp 45–46 °C. IR (Nujol): 3432, 3235, 1606, 1508, 1103, 706 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 6.08 (s, 1 H), 4.92 (s, 2 H), 2.52 (t, *J* = 6.9 Hz, 2 H), 1.56–1.68 (m, 2 H), 1.24–1.39 (m, 6 H), 0.88 (t, *J* = 6.9 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 167.0, 153.7, 102.2, 31.7, 31.6, 29.0, 28.7, 22.6, 14.1. HRMS–FAB: *m/z* calcd for $C_9H_{17}N_2S$ [M + H]: 185.1112; found: 185.1106.

2-Phenyl-4-butylthiazole

Oil. IR(neat): 2956, 2929, 2859, 1516, 1498, 1460, 1436, 1244, 1004, 763, 689 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$,

TMS): δ = 7.93 (dd, *J* = 1.4, 8.0 Hz, 2 H), 7.38–7.45 (m, 3 H), 6.86 (s, 1 H).

2-Methyl-4-phenylthiazole

Mp 60 °C; lit.[4h] 64 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.87 (d, *J* = 8.3 Hz, 2 H), 7.41 (t, *J* = 7.5 Hz, 2 H), 7.32 (t, *J* = 7.5 Hz, 1 H), 7.31 (s, 1 H), 2.78 (s, 3 H).

2-(4-Methylphenyl)-4-phenylthiazole

Mp 126 °C. IR (Nujol): 974, 815, 741, 690, 676 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.00 (d, *J* = 8.2 Hz, 2 H), 7.94 (d, *J* = 8.2 Hz, 2 H), 7.41–7.48 (m, 3 H), 7.35 (t, *J* = 7.3 Hz, 1 H), 7.26 (d, *J* = 6.5 Hz, 2 H), 2.41 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 168.0, 156.1, 140.3, 134.6, 131.1, 129.6, 128.7, 128.1, 126.5, 126.4, 112.1, 21.4. HRMS–FAB: *m/z* calcd for $C_{16}H_{14}NS$ [M + H]: 252.0847; found: 252.0851.

2-(4-Methoxyphenyl)-4-phenylthiazole

Mp 97–98 °C. IR (Nujol): 1256, 1173, 979, 833, 738 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.96–8.02 (m, 4 H), 7.40–7.48 (m, 3 H), 7.34 (t, *J* = 7.4 Hz, 1 H), 6.98 (d, *J* = 8.9 Hz, 2 H), 3.88 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 177.6, 161.4, 134.9, 133.6, 128.9, 128.3, 127.0, 126.6, 115.0, 114.5, 111.9, 55.7. HRMS–FAB: *m/z* calcd for $C_{16}H_{14}NOS$ [M + H]: 268.0796; found: 268.0802.

2-(4-Nitrophenyl)-4-phenylthiazole

Mp 164–165 °C. IR (Nujol): 1514, 1339, 849 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.33 (d, *J* = 8.9 Hz, 2 H), 8.22 (d, *J* = 8.9 Hz, 2 H), 8.00 (d, *J* = 8.2 Hz, 2 H), 7.63 (s, 1 H), 7.48 (t, *J* = 7.4 Hz, 2 H), 7.40 (t, *J* = 7.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 164.8, 157.3, 148.4, 139.1, 133.9, 128.9, 128.7, 127.1, 126.5, 124.3, 114.6. HRMS–FAB: *m/z* calcd for $C_{15}H_{11}N_2O_2S$ [M + H]: 283.0541; found: 283.0547.

2-Amino-4-phenylthiazole

Mp 145–147 °C. IR (Nujol): 3433, 1595, 1518, 1038, 714 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.78 (d, *J* = 8.0 Hz, 2 H), 7.38 (t, *J* = 7.6 Hz, 2 H), 7.29 (t, *J* = 7.4 Hz, 1 H), 6.73 (s, 1 H), 5.03 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 167.0, 151.3, 134.6, 128.6, 127.7, 126.0, 102.9. HRMS–FAB: *m/z* calcd for $C_9H_9N_2S$ [M + H]: 177.0486; found: 177.0485.

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