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GREEN AND EXPEDITIOUS SYNTHESIS OF SOME 2-AMINO/ ARYLAMINO-4-(1-NAPHTHYL)THIAZOLE DERIVATIVES USING [HYDROXY(TOSYLOXY)IODO]BENZENE

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ABSTRACT The synthesis of a series of 2-amino/arylamino-4-(1-naphthyl)thiazole **4** under solvent-free and eco-friendly conditions by applying 'Grindstone Chemistry Technique' using [hydroxy(tosyloxy)iodo]benzene is described practicing the modified Hantzsch thiazole synthesis of α-tosyloxyacetonaphthone **2** and thiourea/ substituted thioureas **3**.

KEYWORDS 2-Amino/arylamino-4-(1-naphthyl)thiazole, [Hydroxy(tosyloxy)iodo]benzene, Thioureas, Solvent-free, 1-(α-Tosyloxy)acetonaphthone.

INTRODUCTION

In recent years, the green chemical methodologies have evolved as one of the most influential tools in the development of organic syntheses. The rise in the domain of solvent-free reactions has offered organic chemists with efficient synthetic methods of great promise. Reactions under solvent-free conditions (SFC) are of tremendous importance for providing eco-friendly systems and are fascinating in offering reduced pollution.[1-3] The reactions offer low cost together with simplicity in processing and handling. In view of the pharmacological applications of naphthalene[4-7] and thiazoles,[8-10] an efficient method for the solvent-free synthesis of 2-amino/arylamino-4-(1-naphthyl)thiazoles under clean, safe and mild conditions is offered. In the present study, the title compounds have been synthesized by the cyclocondensation of 1-(α-tosyloxy) acetonaphthone with substituted thioureas. The tosyloxy compound is, in turn, prepared by treating 1-acetylnaphthalene with the organoiodine(III) reagent, [hydroxyl (tosyloxy) iodo] benzene (HTIB, Koser's reagent). HTIB is corroborated to be a versatile reagent for the synthesis of a large variety of heterocyclic compounds via α-tosyloxylation of enolizable carbonyl compounds.[11-17] Some work on the HTIB mediated synthesis of heterocyclic compounds has also been done in our laboratory.[18-20] The present research work focuses to further explore the potential of HTIB in the synthesis of a library of several new 2-amino/arylamino-4-(1-naphthyl)thiazole derivatives by using the Grindstone Technique.

RESULTS AND DISCUSSION

Herein, the reaction of 1-(α-tosyloxy)acetonaphthone (**2**) with thioureas **3** to synthesize the potentially biologically active aminothiazoles containing naphthalene moiety was examined. To begin with, equimolar amounts of **2** and thiourea (**3a**) was ground at room temperature in the presence of catalytic amounts of K_2CO_3 and then heated. Usual workup of the reaction mixture afforded a single product in excellent yield (93%) which was characterized to be the expected cycloadduct, 2-amino-4-(1-naphthyl)thiazole **(4a)** (**Scheme 1, Table 1**).

The productive outcome of the process prompted us to generalize the reaction for the synthesis of variously substituted 2-arylamino-4-(1-naphthyl)thiazoles (**4b-h**). The expected 4-naphthylthiazoles were obtained in all the cases as summarized in **Table 1.**

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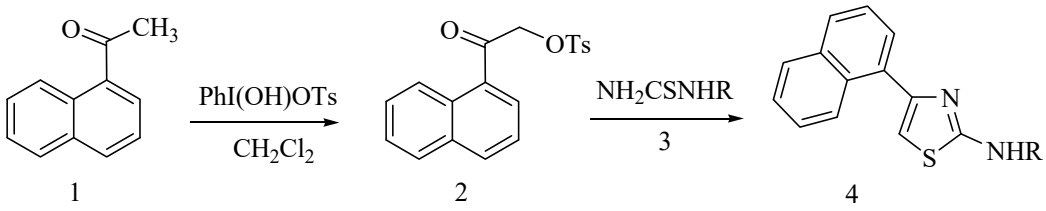

Scheme 1

Table 1: Physical data of the title compounds 4

Product (4)	R	Mp (lit. mp) (°C)	Yield[a] (%)
a	H	161-162 (164-166)[21]	93
b	C_6H_5	188-190	86
c	4-$CH_3C_6H_4$	176-178	88
d	4-$OCH_3C_6H_4$	162-164	87
e	4-FC_6H_4	208-210	89
f	4-ClC_6H_4	201-203	90
g	4-BrC_6H_4	197-198	86
h	4-$NO_2C_6H_4$	214-216	91

[a]The yields of the isolated pure products **4** were calculated w.r.t. **3**

The structure of the thiazole derivatives **4,** synthesized during the study, were confirmed by combined application of spectral (IR, ^1H and ^{13}C NMR) and elemental data. The IR spectrum of **4a** showed the disappearance of the C=O stretch at 1690 cm^{-1} originally present in the tosyloxy compound **2**. Two new bands appeared at 3427 and 3364 cm^{-1}, indicating the presence of NH_2. The presence of NH_2 was also confirmed by the ^1H NMR spectrum of the product **4a**. A broad band appeared at δ 5.78 in the ^1H NMR spectrum which disappeared after D_2O shake, as expected. A characteristic singlet appeared at ä 8.61 due to thiazolyl proton. Also, the peaks at ä 2.42 (due to three protons of tolyl) and at ä 5.28 (due to two protons of methylene), present in the tosylate **2** were absent in the ^1H NMR spectrum of **4a.**

The tosylate **2,** needed for the present study, was prepared from the tosyloxylation of 1-acetonaphtone with HTIB in dichloromethane while stirring. It is to mention that the compound **2** has been obtained as a solid while it is reported to be an oil in literature.[22] The spectral data of our product matched with the reported data. The arylthioureas (**3)** were prepared from the reaction of aniline/p-substituted anilines with aminothiocyanate under acidic conditions.[23] Products **4a, 4f-g** are reported in literature but their characterization data is not available. So all of these products were fully characterized by spectral and elemental analytical data.

EXPERIMENTAL SECTION

Melting points were taken in open capillaries in an electrical apparatus and are uncorrected. IR spectra in KBr were recorded on Perkin-Elmer 1800 FT-IR spectrophotometer. The ^1H NMR and ^{13}C spectra were recorded on Bruker instrument at 300 MHz and 75 MHz respectively. The chemical shifts were expressed in ppm units downfield from an internal TMS standard. Purity of the compounds was checked by thin layer chromatography (TLC) using silica gel aluminium sheets of Merck and UV lamp was used for the visualization of the compounds. Elemental analyses were carried out in Perkin-Elmer 2400 instrument. All the chemicals were purchased from commercial suppliers and were used without further purification.

Preparation of 1-(α-tosyloxy)acetonaphthone (2)

To a solution of 1-acetonaphthone (**1**, 1.70 g, 10 mmol) in DCM (40 mL) was added HTIB (4.31 g, 10 mmol) and the mixture was allowed to stir at 40-50 °C temperature. HTIB was initially insoluble in DCM, but gradually disappeared as the reaction proceeded and the stirring was allowed to continue for about 4 h. The solvent was evaporated under vacuum and the gummy mass so obtained, was triturated with pet ether (60-80 °C) to remove iodobenzene. The resulting colourless solid was thoroughly washed with water and recrystallized from ethanol to yield the pure tosyloxy compound **2**, mp 168-170 °C, yield 85%.

IR (ν_{max}, in KBr): 1690 cm^{-1};

^{1}H NMR ($CDCl_3$, 300 MHz, ä): 2.42 (s, 3H, CH_3), 5.28 (s, 2H, CH_2), 7.31-7.91 (m, 7H), 8.04 (d, 2H, J = 7.8 Hz), 8.48 (d, 2H, J = 7.8 Hz);

^{13}C NMR ($CDCl_3$, 75.5 MHz ä): 21.16, 71.01, 124.15, 125.40, 126.83, 128.10, 128.32, 128.43, 128.51, 129.87, 130.22, 131.43, 132.79, 134.00, 145.21, 193.95.

Preparation of 4-(1-naphthyl)-2-amino/ arylaminothiazoles (4)

General Procedure

A mixture of 1-(α-tosyloxy)acetonaphthone (**2**, 3.28 g, 10 mmol) and thiourea/substituted thiourea (10 mmol) was ground in a pestle mortar in the presence of pinch of K_2CO_3 and heated at 50-60 °C. The resulting solid was filtered, washed with water (2-3 times) and recrystallized from ethanol to give pure **4**.

2-Amino-4-(1-naphthyl)thiazole (4a)

IR (ν_{max}, in KBr): 3427, 3364 cm^{-1};

^{1}H NMR ($CDCl_3$, 300 MHz, ä): 6.90 (s, 1H), 7.30-7.37 (m, 2H), 7.41-7.45 (m, 4H), 8.61 (s, 1H), 5.78 (s, 2H, exchangeable with D_2O);

^{13}C NMR ($CDCl_3$, 75.5 MHz, ä): 102.41, 117.15, 117.39, 123.86, 125.24, 126.57, 127.70, 129.13, 130.32, 131.29, 133.88, 140.26, 168.63;

4-(1-Naphthyl)-2-phenylaminothiazole (4b)

IR (ν_{max}, in KBr): 3327 cm^{-1};

^{1}H NMR ($CDCl_3$, 300 MHz, ä): 6.86 (s, 1H), 7.29-7.48 (m, 4H), 7.51-7.59 (m, 5H), 7.68-7.71 (m, 2H), 8.59 (s, 1H), 11.82 (s, 1H, exchangeable with D_2O);

^{13}C NMR ($CDCl_3$, 75.5 MHz ä): 104.41, 117.85, 119.69, 122.86, 124.27, 125.04, 125.84, 126.68, 127.65, 128.64, 129.28, 130.56, 131.39, 133.64, 138.47, 140.22, 167.58;

Elemental analysis: Calculated for $C_{19}H_{14}N_2S$: C 75.47, H 4.67, N 9.26; Found: C 75.31, H 4.80, N 9.43.

4-(1-Naphthyl)-2-(4-tolyl)aminothiazole (4c)

IR (ν_{max}, in KBr): 3304 cm^{-1};

^{1}H NMR ($CDCl_3$, 300 MHz, ä): 2.38 (s, 3H, CH_3), 6.86 (s, 1H), 7.30-7.47 (m, 6H), 7.53-7.65 (m, 4H), 8.59 (s, 1H), 11.85 (s, 1H, exchangeable with D_2O);

^{13}C NMR ($CDCl_3$, 75.5 MHz ä): 18.58, 105.48, 117.81, 119.29, 122.59, 124.37, 125.18,

125.90, 126.88, 127.46, 128.73, 129.38, 130.64, 131.41, 133.84, 138.42, 140.35, 167.88;

Elemental analysis: Calculated for $C_{20}H_{16}N_2S$: C 75.92, H 5.10, N 8.85; Found: C 75.73, H 5.19, N 8.63.

2-(4-Methoxyphenyl)-4-(1-naphthyl)aminothiazole (4d)

IR (ν_{max}, in KBr): 3298 cm^{-1};

^{1}H NMR ($CDCl_3$, 300 MHz, ä): 3.64 (s, 3H, OCH_3), 6.87 (s, H), 7.41-7.48 (m, 4H), 7.53-7.57(m, 4H), 7.68-7.71 (m, 2H), 8.47 (s, 1H, 11.72 (s, 1H, exchangeable with D_2O);

^{13}C NMR ($CDCl_3$, 75.5 MHz ä): 52.68, 106.37, 118.15, 119.71, 122.99, 124.46, 125.28, 125.83, 126.72, 127.87, 128.93, 129.37, 130.75, 131.41, 133.72, 138.52, 140.49, 167.81;

Elemental analysis: Calculated for $C_{20}H_{16}N_2OS$: C 72.26, H 4.85, N 8.43; Found: C 75.11, H 4.74, N 8.58.

2-(4-Fluorophenyl)-4-(1-naphthyl)aminothiazole (4e)

IR (ν_{max}, in KBr): 3286 cm^{-1};

^{1}H NMR ($CDCl_3$, 300 MHz, ä): 7.06 (s, H), 7.23 (d, 2H), 7.31-7.40 (m, 6H), 7.53-7.64 (d, 2H), 8.60 (s, 1H), 11.82 (s, 1H, exchangeable with D_2O);

^{13}C NMR ($CDCl_3$, 75.5 MHz ä): 102.35, 117.13, 117.44, 123.96, 124.08, 125.38, 125.94, 126.82, 127.84, 128.04, 129.00, 130.44, 131.24, 133.91, 138.47, 140.14, 162.36, 168.59;

Elemental analysis: Calculated for $C_{19}H_{13}FN_2S$: C 71.23, H 4.09, N 8.74; Found: 71.40, H 4.14, N 8.53.

2-(4-Chlorophenyl)-4-(1-naphthyl)aminothiazole (4f)

IR (ν_{max}, in KBr): 3304 cm^{-1};

^{1}H NMR ($CDCl_3$, 300 MHz, ä): 6.90 (s, 1H), 7.40-7.61 (m, 4H,), 7.79-7.96 (m, 4H), 8.15-8.26 (m, 2H), 8.74 (s, 1H), 11.92 (s, 1H, exchangeable with D_2O);

^{13}C NMR ($CDCl_3$, 75.5 MHz ä): 104.54, 119.97, 122.76, 124.35, 125.19, 125.90, 126.37, 127.53, 128.67, 129.41, 130.38, 131.80, 133.59, 136.00, 138.51, 140.28, 167.37;

Elemental analysis: Calculated for $C_{19}H_{13}ClN_2S$: C 67.75, H 3.89, N 8.32; Found: C67.61, H 3.80, N 8.53.

2-(4-Bromophenyl)-4-(1-naphthyl)aminothiazole (4g)

IR (ν_{max}, in KBr): 3294 cm^{-1};

^{1}H NMR ($CDCl_3$, 300 MHz, ä): 7.02 (s, 1H), 7.44-7.67 (m, 4H), 7.78-7.89 (m, 4H), 8.10-8.28 (m, 2H), 8.63 (s, 1H), 11.76 (s, 1H, exchangeable with D_2O);

^{13}C NMR ($CDCl_3$, 75.5 MHz ä): 105.32, 119.85, 122.58, 124.87, 125.24, 125.93, 126.37, 126.88, 127.56, 128.49, 129.52, 130.38, 131.42, 133.64, 138.58, 140.12, 168.04;

Elemental analysis: Calculated for $C_{19}H_{13}BrN_2S$: C 59.85, H 3.44, N 7.35; Found: C 59.71, H 3.35, N 7.52.

2-(4-Nitrophenyl)-4-(1-naphthyl)aminothiazole (4h)

IR (ν_{max}, in KBr): 3314 cm^{-1};

^{1}H NMR ($CDCl_3$, 300 MHz, ä): 6.92 (s, 1H), 7.34-7.43 (m, 4H), 7.50-7.72 (m, 4H), 7.90-8.18 (m, 2H), 8.51 (s, 1H), 11.86 (s, 1H, exchangeable with D_2O);

^{13}C NMR ($CDCl_3$, 75.5 MHz ä): 104.82, 117.87, 119.74, 122.89, 124.37, 125.28, 125.93, 126.75, 127.78, 128.64, 129.24, 130.63, 131.48, 133.74, 138.40, 140.18, 167.83;

Elemental analysis: Calculated for $C_{18}H_{11}NO_2S$: C 65.69, H 3.77, N 12.10; Found: C 65.86, H 3.66, N 12.27.

CONCLUSION

The present study elaborates the synthetic utility of the organoiodine(III) reagent, HTIB, in the green synthesis of several 2-amino/arylamino-4-(1-naphthyl)thiazole compounds (**4a-h**) under solvent-free conditions.

LIST OF ABBREVIATIONS

HTIB = [Hydoxy(tosyloxy)iodo]benzene
SFC = Solvent-free conditions
DCM = Dichloromethane

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