A Simple, Rapid and Efficient One-pot Protocol for the Synthesis of 2-substituted Benzothiazole Derivatives and their Antimicrobial Screening

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ABSTRACT

A rapid and efficient condensation reaction of 2-aminothiophenol with various fatty acids in solvent-free conditions with or without microwave irradiation was carried out to afford the corresponding 2-substituted benzothiazole derivatives in good to excellent yields. The structures of the new products were established by elemental analyses, IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. All the title compounds were screened for their antibacterial and antifungal activity. Most of the compounds exhibited good antimicrobial activity.

KEYWORDS

Fatty acids, 2-substituted benzothiazole, 2-aminothiophenol, antimicrobial activity, microwave irradiation.

1. Introduction

2-Substituted benzothiazoles are an important group of heterocyclic compounds that have widespread applications in pharmaceutical and industrial research. The benzothiazoyl moiety is a structural element of compounds with potent and selective antitumour activity,[1] antiviral,[2] anticonvulsant,[3] neuroprotective[4] and immunosuppressive properties.[5] The benzothiazole nucleus is a key element in some thermally stable rigid-rod polymers possessing high tensile strength and in modulus manufacturing.[6] The availability of 2-substituted benzothiazoles depends on the preparative routes in which the fused thiazole ring is constructed from acyclic reactants. Methods for the preparation of 2-substituted benzothiazoles have been extensively studied. The most common direct method is the condensation of 2-aminothiophenol with the substituted aromatic aldehydes[7] and carboxylic acids or their derivatives in polyphosphoric acid (PPA),[8] polyphosphate ester,[9] or a mixture of methane sulphonic acid and phosphorus pentoxide.[10] Other methods include potassium ferricyanide cyclization of thiobenzanilides,[11] the reaction of α,α,α-trihalomethyl aromatic compounds with 2-aminothiophenol in PPA,[12] palladium-catalyzed reaction of aryl halides with *o*-aminothiophenol in presence of carbon monoxide,[13] the reaction of 2-aminothiophenol with acid chlorides,[14] and the ceric ammonium nitrate mediated reaction of thiophenols and aromatic nitriles.[15] However, some of these methods suffer from one or more of the disadvantages such as high thermal conditions and long reaction times, while sometimes excess reagents are required and the use of toxic metallic compounds results in waste stream problems.

Microwave-assisted reactions in solvent or solvent-free conditions have gained popularity because of rapid reaction rate and ease of manipulation.[16] Recently, some methods use microwave heating for the synthesis of 2-substituted benzothiazoles such as condensation of aromatic or aliphatic aldehydes with 2-aminothiophenol on SiO_2,[17] aromatic aldehydes with 2-aminothiophenol in the presence of nitrobenzene/SiO_2, or nitrobenzene/montmorillonite K10,[18] or carboxylic acids.[19]

To the best of our knowledge 2-substituted benzothiazole derivatives of fatty acids have not yet been reported. The present work is a continuation of our study on the derivatization of fatty acids. Tetrazoles,[20,21] pyrazolines,[22] tetrazine,[23,24] spiro[oxathiolane-2,2'-dihydrotetrazoles][25] and aziridines[26] have been previously prepared in our laboratory. Cyanoethoxy and morpholine derivatives of hydroxy fatty acids[27] and fatty esters[28] showed significant antifungal and antibacterial activity, respectively. Thus, keeping in view the practical synthetic applications of fatty acid derivatives, we have synthesized 2-substituted benzothiazoles from saturated and olefinic (internal and terminal) fatty acids and the new compounds were screened for antibacterial and antifungal activity.

2. Results and Discussion

The reactions described in this paper have a remarkable synthetic utility because they make compounds available in one step from fatty acids in a short time with or without microwave irradiation.

We now report the synthesis of 2-substituted benzothiazoles by the condensation of 2-aminothiophenol with various fatty acid chlorides (Scheme 1) (method 1). At first we focused on the reaction of fatty acids with thionyl chloride. Since fatty acid chlorides are not commercially available we planned to synthesize the latter *in situ.* In a typical procedure, the fatty acid (2.5 mmol) **1a–f** was treated with thionyl chloride (3 mmol) under neat conditions at 80 °C for 2 h, to yield the corresponding fatty acid chloride **2a–f**. The complete conversion of the fatty acid chloride **2a–f** was monitored by taking an aliquot portion of the reaction mixture with a few drops of methanol followed by TLC analysis. The appearance of a new spot of methyl ester and the disappearance of the fatty acid spot showed the complete conversion to the corresponding acid chloride, otherwise formation of acid chloride would not be observed on the TLC plate due

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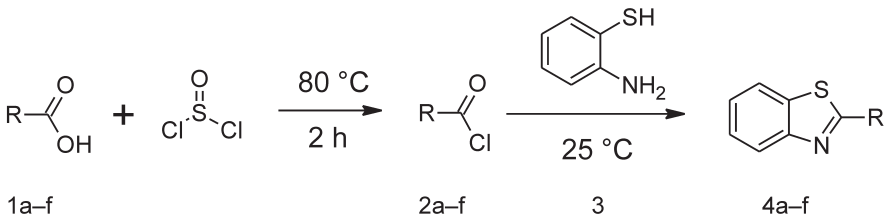


Scheme 1
Synthesis of 2-substituted benzothiazoles from fatty acids.

to the trailing effect of acid chloride. Acid chlorides of saturated, olefinic and hydroxy fatty acids were formed with sufficient ease. In the next step excess of thionyl chloride was distilled off and 2-aminothiophenol (3 mmol) was added. Since the addition of **3** with acid chloride is an exothermic reaction, mixing was carried out at 0–5 °C. Excellent yields were obtained in all cases (see Table 1).

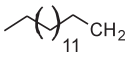
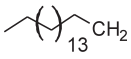
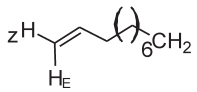
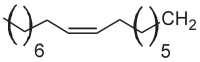
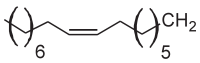
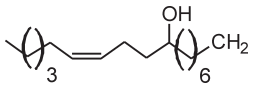
Our investigations showed that 2-aminothiophenol reacts smoothly with various saturated, olefinic and hydroxy fatty acid chlorides in a short time. The corresponding 2-substituted benzothiazoles were obtained in excellent yields. Double bonds, hydroxy groups or chain length do not affect the yield of the 2-substituted benzothiazoles.

We have also prepared the title compounds under microwave-assisted, solvent-free conditions by the reaction of 2-aminothiophenol **3** with fatty acids (Scheme 2) (method 2). Multimode microwave irradiation at full power was used. The optimization results are summarized in Table 2.

As shown in Table 2, 1 eq of fatty acid reacts with 1.2 eq of 2-aminothiophenol to yield the corresponding 2-substituted benzothiazoles. When the reactions were performed below 50 % power, no reaction took place. To carry out the reaction power was increased up to 80 % as a result of which 2-substituted benzothiazoles were obtained but the yield was low at about 35–40 %. In order to increase the yield full power was used. Our results also indicate that the yields were significantly improved when the title compounds **4a–f** were prepared by method 1 rather than method 2.

The title compounds were identified on the basis of IR, ^{1}H NMR and mass spectra. ^{1}H NMR spectra of 2-(dec-9-enyl)-benzothiazole **4c** showed characteristic signals of two sets of doublets at δ 7.96 and 7.84 ppm and two sets of triplets at δ 7.44 and 7.34 ppm for a total of four aromatic protons. A triplet for two hydrogen atoms was observed at δ 3.11 ppm for methylene protons alpha to the thiazole moiety. A methine proton of C-10 appeared at δ 5.82 ppm. The C-11 methylene protons designated as H_E and H_Z displayed two distinct δ-values due to coupling with the adjacent C-10 methine proton. Thus, the ^{1}H NMR spectrum showed two doublets of doublets at δ 5.02 and 4.90 ppm for H_Z and H_E protons, respectively. The structure of **4c** was further supported by its mass spectral results, which showed a molecular ion peak at *m*/*z* 273 consistent with its molecular formula $C_{17}H_{23}NS$. The base peak appears at *m*/*z* 134. ^{13}C NMR values are summarized in Table 4. Detailed spectra of the title compounds are given in Tables 3 and 4.

Table 1 2-Substituted benzothiazoles.

Compound	R	Product yield/% **4a–f** [b]
1a [a], **2a, 4a**		98
1b [a], **2b, 4b**		98
1c [a], **2c, 4c**		97
1d [a], **2d, 4d**		98
1e [a], **2e, 4e**		95
1f [a], **2f, 4a**		90

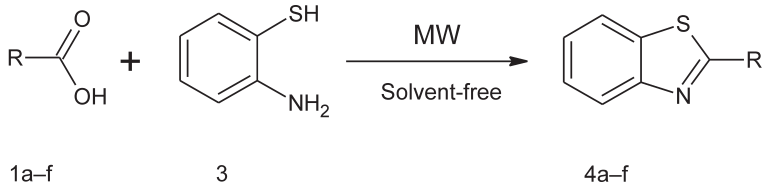
[a] The fatty acid (2.5 mmol) was treated with thionyl chloride (3 mmol) at 80 °C for 2 h, followed by the addition of **3** (2.5 mmol) at room temperature in toluene for 1.5 h.
[b] All compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR, MS and elemental analysis.

3. Experimental

Undec-10-enoic, (Z)-octadec-9-enoic, stearic and palmitic acids were obtained commercially from Fluka chemicals (Switzerland). (9Z,12R)-12-Hydroxyoctadec-9-enoic (ricinoleic) and (9R,12Z)-9-hydroxyoctadec-12-enoic (isoricinoleic) acids were isolated from the natural sources, i.e. from *Ricinus communis* and *Wrightia tinctoria* seed oils, respectively, following Gunstone's partition method.[29] 2-Aminothiophenol (99+ %) was purchased from Sigma-Aldrich (Germany). Thionyl chloride was obtained from Merck (Mumbai, India) and was further distilled off before use. General (GR) grade solvents were employed for the extraction purposes and when required solvents were dried and distilled before use. Homogeneity of the products was confirmed using TLC. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker DRX-300 instrument. The chemical shifts (δ) were measured relative to internal TMS. Coupling constants were expressed in Hz. Mass spectra were obtained on a Jeol SX-102 (FAB) spectrometer. IR spectra were obtained on a Shimadzu 8201 PC FT-IR using KBr pellets. The micromave irradiations were carried out using an unmodified domestic oven (LG, Model MC-808WAR, 1.35 kW, 2450 MHz).

3.1. General Procedure for the Preparation of 2-Substituted Benzothiazoles (Method 1)

Thionyl chloride (3 mmol) was added to the fatty acid (2.5 mmol) at 80 °C for about 2 h to form the corresponding acid chloride. The progress of the reaction was monitored by TLC. The excess of thionyl chloride was distilled off and 2-aminothiophenol (2.5 mmol) was added to the cooled reaction



1a–f 3 4a–f

Scheme 2
Synthesis of 2-substituted benzothiazoles under microwave-assisted, solvent-free conditions.

Table 2 Optimization of the reaction of 2-aminothiophenol with fatty acid to synthesize 2-substituted benzothiazoles under microwave-assisted, solvent-free conditions.

No.	**1/3** [a]	Microwave equipment [b]	Power [c]	Time/min [d]	Yield/% [e]
1	1.0/1.2	Multimode	Full	28	65
2	1.0/1.2	Multimode	Full	28	63
3	1.0/1.2	Multimode	Full	30	61
4	1.0/1.2	Multimode	Full	30	62
5	1.0/1.2	Multimode	Full	30	60
6	1.0/1.2	Multimode	Full	30	60

[a] All reactions were carried out using fatty acid (1 eq) and 2-aminothiophenol (1.2 eq) under microwave irradiation.
[b] Microwave equipment multimode was used.
[c] Full power means 100% at 1.35 kW.
[d] Monitored by TLC.
[e] All yields refer to isolated products and the products were characterized by IR, ^{1}H NMR, MS and elemental analysis.

Table 3 ^{13}C NMR chemical shifts of compounds [a] **4a, 4b, 4c, 4d, 4e** and **4f.**

Compound	Chemical shift/ppm
4a	172.20(C-2), 153.20(C-4), 135.12(C-5), 122.51(C-6), 124.62(C-7), 125.89(C-8), 121.49(C-9), 34.39(C-10), 31.94(C-11), 29.52(C-12),-(C-21), 31.54(C-22), 22.65(C-23), 14.12(C-24).
4b	172.15(C-2), 153.22(C-4), 135.24(C-5), 122.55(C-6), 124.60(C-7), 125.77 (C-8), 121.44(C-9), 34.40(C-10), 31.84(C-11), 29.59(C-12), -(C-23), 31.52(C-24), 22.56(C-25), 14.21(C-26).
4c	172.43(C-2), 153.30(C-4), 135.18(C-5), 122.54(C-6), 125.88(C-7), 125.20(C-8), 121.50(C-9), 33.82(C-10 & C-11), 29.27(C-12),-(C-16), 34.39(C-17), 139.19(C-18), 114.20(C-19).
4d	172.66(C-2), 153.19(C-4), 135.11(C-5), 122.51(C-6), 125.92(C-7), 124.68(C-8), 121.51(C-9), 33.56(C-10 & C-11), 31.95(C-12),-(C-15), 34.39(C-16 & C-19), 130.06(C-17 & C-18), 29.37(C-20),-(C-24), 22.73(C-25), 14.17(C-26).
4e	172.43(C-2), 153.30(C-4), 135.20(C-5), 122.67(C-6), 125.90(C-7), 125.10(C-8), 121.45(C-9), 31.76(C-10 & C-11), 29.64(C-12),-(C-15), 34.39(C-16 & C-19), 130.14(C-17 & C-18), 71.54(C-20), 39.12(C-21), 25.38(C-22), 31.54(C-23 & C-24), 22.65(C-25),14.17(C-26).
4f	172.42(C-2), 153.30(C-4), 135.18(C-5), 122.65(C-6), 125.45(C-7), 125.15(C-8), 121.52(C-9), 31.54(C-10 & C-11), 29.24(C-12),-(C-15), 37.24(C-16 & C-18), 72.14(C-17), 34.39(C-19 & C-22), 130.52(C-20 & C-21), 30.96(C-23& C-24), 22.32(C-25), 14.15(C-26).

[a] Recorded in $CDCl_3$ at 100 MHz.

mixture (0–5 °C) in toluene (10 mL) followed by stirring at room temperature for 2 h. The reaction mixture was diluted with ethyl acetate (15 mL) and a saturated solution of $NaHCO_3$ (10 mL). The organic layer was washed with H_2O (3 × 15 mL), dried over anhydrous Na_2SO_4 and solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/diethyl ether).

3.1.1. 2-*(Pentadecyl)-benzothiazole* **4a**

Compound **4a** was purified through columtn chromatography with hexane/diethyl ether (99:1, v/v) as the solvent. Purification gave a light yellow-coloured liquid. $\bar{\nu}$ (KBr): 2928, 2857, 1588, 1459, 728, 672 cm^{-1}; δ_H ($CDCl_3$, 400 MHz): 7.97 (1H, d, *J* 8.1 Hz, Ar-*H*), 7.84 (1H, d, *J* 7.8 Hz, Ar-*H*), 7.45 (1H, t, *J* 8.1 Hz, Ar-*H*), 7.34 (1H, t, *J* 8.0 Hz, Ar-*H*), 3.11 (2H, t, *J* 7.6 Hz, CH_2 α to thiazole ring), 1.92–1.83 (2H, m, -CH_2 β to thiazole ring), 1.29 (24H, br. s, chain CH_2), 0.88 ppm (3H, dist. t, CH_3); (Found: C, 76.54; H, 10.19; N, 4.01; S, 9.26 %. Calc. for $C_{22}H_{35}NS$ (345.65): C, 76.52; H, 10.14; N, 4.06; S, 9.28 %).

Table 4 FAB mass spectral data of compounds **4a, 4b, 4c, 4d, 4e** and **4f**.

Compound	m/z/%
4a	345 [(11.5), M$^+$], 244 (4.6), 188 (4.9), 174 (3.9), 162 (8.6), 148 (12.5), 134 (100), 101 (2.6).
4b	373 [(11.2), M$^+$], 244 (4.5), 188 (5.6), 174 (3.4), 162 (9.2), 148 (12.6), 134 (100), 129 (6.5).
4c	273 [(10.8), M$^{+]}$, 246 (23.6), 174 (3.5), 188 (5.9), 162 (12.5), 148 (12.8), 139 (10.1), 134 (100), 127 (3.6), 113(3.8).
4d	371 [(6.9), M$^+$], 270 (6.4), 284 (4.9), 258 (10.8), 216(5.1), 188(5.2), 174 (3.8), 162 (12.5), 148 (13.5), 134 (100), 155 (4.2).
4e	387 [(10.8), M$^+$], 314 (3.7), 302 (16.8), 256 (6.6), 188 (5.3), 174 (3.9), 162 (12.5), 148 (13.2), 134 (100).
4f	387 [(9.2), M$^+$], 328 (4.7), 314 (5.7), 262 (58.33), 188 (5.9), 174 (3.9), 162 (22.22), 148 (19.44), 134 (100).

Table 5 Antimicrobial activity [a] of compounds **4a, 4b, 4c, 4d, 4e and 4f.**

Compound	Bacteria				Fungi			
	E. coli (K 12)	*B. subtilis* (ATCC 6051)	*S. aureus* (MSSA 22)	*S. typhimurium* (MTCC 98)	*C. albicans* (IOA-109)	*Penicillium* sp. Laboratory isolate	*A. niger* Laboratory isolate	*H. oryzae* (2537)
4a	+	+	+	-	+ +	+ +	+ +	+ +
4b	+	+	++	-	+ ++	+ +	+ +	+ +
4c	+	+	++	-	+ + +	+ +	+ +	++
4d	+	+	++	-	+ ++	+ +	+ ++	++
4e	+	+	++	-	+ +	+ +	+ +	+
4f	+	+	++	-	+ +	+ +	+ +	+
Control DMF	---	---	**---**	-	---	---	---	---
Chloramphenicol	+ + +	+ + +	+ + +	-	---	---	---	---
Nystatin	---	---	**---**	---	+ + +	+ + +	+ + +	+ + +

[a] Zone of diameter of growth inhibition; <10 mm (-), 10–12 mm (+), 13–15 mm (++), 16–20 mm (+++).

3.1.2. *2-(Heptadecyl)-benzothiazole* **4b**

Purification of the crude product by column chromatography with hexane/diethyl ether (99:1, v/v) as the eluent gave a pale yellow liquid. $\bar{\nu}$ (KBr): 2928, 2857, 1588, 1459, 728, 672 cm^{-1}; δ_H ($CDCl_3$, 400 MHz): 7.96 (1H, d, *J* 8.1 Hz, Ar-*H*), 7.84 (1H, d, *J* 7.8 Hz, Ar-*H*), 7.45 (1H, t, *J* 8.1 Hz, Ar-*H*), 7.34 (1H, t, *J* 8.0 Hz, Ar-*H*), 3.11 (2H, t, *J* 7.6 Hz, C$H_2\alpha$ to thiazole ring), 1.92–1.84 (2H, m, -C$H_2\beta$ to thiazole ring), 1.38 (28H, br. s, chain CH_2), 0.88 ppm (3H, dist. t, CH_3); (Found: C, 77.18; H, 10.49; N, 3.70; S, 8.63 %. Calc. for $C_{24}H_{39}NS$ (373.71): C, 77.21; H, 10.46; N, 3.75; S, 8.58 %).

3.1.3. *2-(Dec-9-enyl)-benzothiazole* **4c**

Purification of the crude product over a column of silica gel using hexane/diethyl ether (98:2, v/v) as the eluting solvent gave a colourless liquid. $\bar{\nu}$ (KBr): 2927, 2855, 1592, 1439, 728, 672 cm^{-1}; δ_H ($CDCl_3$, 400 MHz): 7.96 (1H, d, *J* 8.0 Hz, Ar-*H*), 7.84 (1H, d, *J* 7.6 Hz, Ar-*H*), 7.44 (1H, t, *J* 8.4 Hz, Ar-*H*), 7.34 (1H, t, *J* 8.0 Hz, Ar-*H*), 5.85–5.75 (1H, tdd, $J_{H\text{-}^8CH_2}$ 6.6 Hz, $J_{H\text{-}H_Z}$ 10.2 Hz, $J_{H\text{-}H_E}$ 17.1 Hz, CH_2=C*H*-), 5.01–4.91 (1H, dd, $J_{H_Z\text{-}H}$ 10.2 Hz, $J_{H_Z\text{-}H_E}$ 1.2 Hz, H_ZC=CH-), 4.90 (1H, dd, $J_{H_E\text{-}H}$ 17.1 Hz, $J_{H_E\text{-}H_Z}$ 1.2 Hz, H_EC=CH-), 3.11 (2H, t, *J* 7.6 Hz, C$H_2\alpha$ to thiazole ring), 2.06–2.01 (2H, m, -CH_2-CH=CH_2), 1.92–1.84 (2H, m, -C$H_2\beta$ to thiazole ring), 1.33 (10H, br. s, chain CH_2); (Found: C, 74.62; H, 8.38; N, 5.20; S, 11.80 %. Calc. for $C_{17}H_{23}NS$ (273.48): C, 74.73; H, 8.42; N, 5.13; S, 11.72 %).

3.1.4. *2-(Heptadec-8-enyl)-benzothiazole* **4d**

Compound **4d** was purified through column chromatography with hexane/diethyl ether (97:3, v/v) as the solvent. Purification gave a light yellow-coloured liquid. $\bar{\nu}$ (KBr): 2927, 2856, 1592, 1458, 728, 674 cm^{-1}; δ_H ($CDCl_3$, 400 MHz): 7.96 (1H, d, *J* 8.4 Hz, Ar-*H*), 7.83 (1H, d, *J* 7.6 Hz, Ar-*H*), 7.40 (1H, t, *J* 8.4 Hz, Ar-*H*), 7.31 (1H, t, *J* 8.4 Hz, Ar-*H*), 5.36–5.33 (2H, m, -C*H*=C*H*-), 3.11 (2H, t, *J* 7.6 Hz, -C$H_2\alpha$ to thiazole ring), 2.05–2.01 (4H, m, -CH_2-CH=CH-CH_2-), 1.92–1.84 (2H, m, -C$H_2\beta$ to thiazole ring), 1.29 (20H, br. s, chain CH_2), 0.88 (3H, dist. t, CH_3); (Found: C, 77.57; H, 10.01; N, 3.71; S, 8.71 %. Calc. for $C_{24}H_{37}NS$ (371.69): C, 77.63; H, 9.97; N, 3.77; S, 8.63 %).

3.1.5. *2-[(8Z, 11R)–11-Hydroxyheptadec-8-enyl]-benzothiazole* **4e**

Purification of the crude product by column chromatography with hexane/diethyl ether (94:6, v/v) as the eluent gave a light brown-coloured liquid. $\bar{\nu}$ (KBr): 2928, 2857, 1588, 1459, 728, 672 cm^{-1}; δ_H ($CDCl_3$, 400 MHz): 7.96 (1H, d, *J* 8.0 Hz, Ar-*H*), 7.84 (1H, d, *J* 8.0 Hz, Ar-*H*), 7.44 (1H, t, *J* 7.2 Hz, Ar-*H*), 7.34 (1H, t, *J* 7.2 Hz, Ar-*H*), 5.49–5.44 (2H, m, -C*H*=C*H*-), 3.89–3.87 (1H, m, -C*H*-OH), 3.11 (2H, t, *J* 7.6 Hz, -C$H_2\alpha$ to thiazole ring), 2.43–2.41 (1H, m, -CH-O*H*), 2.04–1.98 (4H, m, -CH_2-CH=CH-CH_2-), 1.92–1.84 (2H, m, -C$H_2\beta$ to thiazole ring), 1.29 (18H, br. s, chain CH_2), 0.88 ppm (3H, dist. t, CH_3); (Found: C, 74.34; H, 9.50; N, 3.66; S, 8.32 %. Calc. for $C_{24}H_{37}ONS$ (387.68): C, 74.42; H, 9.56; N, 3.62; S, 8.27 %.)

3.1.6. *2-[(8R, 11Z)-8-Hydroxyheptadec-11-enyl]-benzothiazole* **4f**

Compound **4f** when purified by column chromatography with hexane/diethyl ether (90:10, v/v) as the solvent gave a brown-coloured liquid. $\bar{\nu}$ (KBr): 2929, 2857, 1586, 1458, 728, 674 cm^{-1}; δ_H ($CDCl_3$, 400 MHz): 7.96 (1H, d, *J* 8.4 Hz, Ar-*H*), 7.84 (1H, d, *J* 8.4 Hz, Ar-*H*), 7.44 (1H, t, *J* 7.2 Hz, Ar-*H*), 7.34 (1H, t, *J* 7.2 Hz, Ar-*H*), 5.49–5.44 (2H, m, -C*H*=C*H*-), 4.08–4.01 (1H, m, -C*H*-OH), 3.11 (2H, t, *J* 7.2 Hz -C$H_2\alpha$ to thiazole ring), 2.33–2.26 (1H, m, -CH-O*H*), 2.07–2.00 (4H, m, -CH_2-CH=CH-CH_2-), 1.89–1.84 (2H, m, -C$H_2\beta$ to thiazole ring), 1.44 (18H, br. s, chain CH_2), 0.98 ppm (3H, dist. t, CH_3); (Found: C, 74.38; H, 9.47; N, 3.65; S, 8.30 %. Calc. for $C_{24}H_{37}ONS$ (387.68): C, 74.42; H, 9.56; N, 3.62; S, 8.27 %).

3.2. General Procedure for the Preparation of 2-Substituted Benzothiazoles in Microwave-assisted, Solvent-free Conditions (Method 2)

A mixture of fatty acid (2.5 mmol) and 2-aminothiophenol (3 mmol) was placed in a beaker and subjected to microwave irradiation using a domestic microwave oven and irradiated (multimode, full power) for the specified time (see Table 2). After cooling, the product was extracted with diethyl ether (2 × 30 mL). The combined organic layers were washed with a saturated solution of $NaHCO_3$ (2 × 10 mL), dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to leave the crude product. The product was purified by column chromatography on silica gel (hexane/diethyl ether). The compounds **4a–f** obtained by this method were compared on the basis of elemental analysis, IR, ^{1}H NMR, ^{13}C NMR and mass spectra with the spectral data as described above.

3.3. Antimicrobial Activity

To determine the biological activity of the compounds, the series of compounds **4a–f** was screened for antimicrobial activity against bacteria (e.g. *Escherichia coli, Staphylococcus aureus, Bacillus subtilis* and *Salmonella typhimurium*), filamentous fungi (*Helminthosporum oryzae, Aspergillus niger, Penicillium* sp.) and *Candida albicans* (Table 5).

The disc diffusion method[30] with little modification was used. Briefly 0.1 mL of diluted inoculum (10^5 CFU mL^{-1}) of test

organism was spread on nutrient agar (NA) and sabouraud dextrose (SD) agar plates. Sterile filter paper (Hi-Media Pvt. Ltd., Mumbai, India) disc (8 mm) impregnated with 50 μg of each compound and a disc without compound was used as a negative control. The NA was incubated for 18 h at 37 °C for test bacteria and *Candida albicans.* The SD plates for filamentous fungi were incubated for 5–6 days at 25 °C. The antimicrobial activity was evaluated by measuring the zone of growth inhibition of the test organism. Antibiotics, chloramphenicol and nystatin (Hi-Media Pvt. Ltd., Mumbai, India) were used in the test system as positive controls. The compounds were dissolved in DMF. The results are shown in Table 5, which revealed that the compounds showed good activity against *C. albicans, A. niger, H. oryzae* and *Penicillium* sp. and moderate activity against *E. coli, S. aureus* and *Bacillus subtilis*. However the title compounds showed no activity against *Salmonella typhimurium.*

4. Conclusion

In conclusion, two efficient methods for the synthesis of novel benzothiazole derivatives of saturated and olefinic (internal and terminal) fatty acids have been developed. The fact that readily available reagents are used along with short reaction time, no additives, simple work-up and isolation of the product make the current approach a feasible and attractive protocol for the generation of 2-substituted benzothiazoles from fatty acids. The present method has also solved the problem of non-availability of both types of fatty acid chlorides by *in situ* preparation of the latter. Most of the compounds exhibited good activity against fungi and moderate activity against bacteria.

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