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An efficient green synthesis of new benzothiazoles containing sulfonamide or cyclic imide moieties

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Abstract

An efficient and convenient protocol for the one-pot synthesis of new benzothiazoles bearing sulfonamide or cyclic imide moieties using Cesium salt of Wells-Dawson heteropolyacid ($Cs_5HP_2W_{18}O_{62}$) as solid catalyst and water as solvent under ultrasound irradiation was reported. The reaction speed was remarkably catalyzed with the aid of ultrasound irradiation. Moreover, this approach prepares multiple other benefits such as operational ease, higher yields, and energy performance.

1 | INTRODUCTION

Benzothiazole derivatives containing scaffolds have been rated as one of the new emerging areas in heterocyclic chemistry because of their various biological and pharmacological properties. These compounds have enormous applications in organic and medicinal chemistry.

They possess a wide range of bioactivities including antimicrobial,[1] anticancer,[2] anti-inflammatory,[3] anticonvulsant,[4] antidiabetic,[5] anti-Alzheimer,[6] antipsychotic,[7] protein tyrosine inhibitor,[8] and diuretic[9] activities.

Several drugs are developed from benzothiazole derivatives. For example, riluzole (**1**) is a glutamate receptor antagonist, used to treat amyotrophic lateral sclerosis and anxiety disorders,[10] Zopolrestat (**2**) demonstrates antidiabetic effects,[11] and Frentizole (**3**), the urea derivative of benzothiazole is used as antiviral agent.[12]

The introduction of the sulfonamide group with some rings such as oxazolidinone,[13] phthalimide,[14] and quinolone,[15] could be very interesting due to its high biological activities.[16–19]

Also, this combination is found with benzothiazole scaffold such as: Ethoxzolomide (**4**), the sulfonamide drug serving as diuretic and molecules (**5**) as antitubercular.[20] Moreover, new benzothiazole-6-sulfonamides (**6**) were described by Ibrahim *et al* as highly potent inhibitors of carbonic anhydrase isoforms I, II, IX, and XII[21] (Figure 1).

Several methods have been reported for the synthesis of benzothiazole compounds from different starting materials, still remains a great demand for the introduction of efficient, simple and more practical methods.

Recently, the application of ultrasound as a powerful technique in synthetic organic chemistry has become extremely efficient and attractive. Prominent features of the ultrasound approach are enhanced organic reaction rates, formation of purer products in high yields and under mildes reaction conditions. Further, it is considered a processing aid in terms of energy conservation and waste minimization compared to traditional methods.

Prompted by the aforementioned biological and pharmaceutical activities of benzothiazole derivatives, and as a part of an ongoing program aiming at the synthesis of new heterocyclic compounds.[22–24] We describe herein an efficient procedure for the synthesis of a novel series of new benzothiazole derivatives, using ultrasound irradiation in the presence of Cesium salt of Wells-Dawson heteropolyacid ($Cs_5HP_2W_{18}O_{62}$) as catalyst.

This latter catalyst has been reported in our recent work[24] for the synthesis of substituted *N*-acylsulfonamides and cyclic imides containing sulfonyl group. It not only

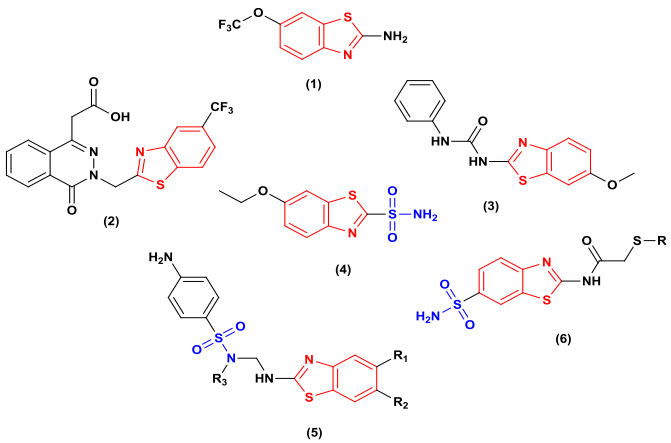


FIGURE 1 Some molecules with both sulfonamide and benzothiazole moieties

afforded the products in good to excellent yields, but also addresses challenges associated with catalysts such as ease of handling, recovery, safety and pollution.

1.1 | Experimental section

All the chemicals were commercially available and used as received. Cesium salt of Wells-Dawson heteropolyacid ($Cs_5HP_2W_{18}O_{62}$) was prepared according to the literature,[25] and characterized in our previous work[24] by spectroscopic methods (IR, ^{31}PNMR). All the reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light (254 nm) as the visualizing agent and ninhydrine solution and heat as developing agents. Melting points were determined in open capillary tubes on Buchi B-540. Proton nuclear magnetic resonance was determined with a 400-MHz Brucker spectrometer using $CDCl_3$ or MeOD as solvent and TMS as an internal standard. Chemical shifts are reported in d units (ppm). All coupling constants J are reported in Hertz. Multiplicity is indicated as s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet), and combination of these signals. The mass spectra were recorded on a DSQ Thermoelectron apparatus (70 eV) by chemical ionization (gaseous ammonia) by direct introduction. Elemental analysis was performed with a Perkin-Elmer 2400 C, H, N analyzer and determined values were within the acceptable limits of the calculated values. Sonication was performed in a Fischerbrand FB11020 ultrasonic bath with a frequency of 35 kHz.

1.2 | Preparation of benzothiazole derivatives containing sulfonamide moiety (2a-2u)

One millimole of sulfonamide were added to a mixture of cyclic anhydride (2 mmol) and $Cs_5HP_2W_{18}O_{62}$ (10 mmol %) in 2 mL of water. Then reaction mixture was subjected to ultrasonication by an ultrasonic bath with a frequency of 35 kHz for appropriate time (3-6 min) at 25°C. Then, 1 mmol of 2-amino benzothiazole derivative were added with additional irradiation (<10 min). Reaction was monitored by TLC. After completion of the reaction, the catalyst was removed by filtration. The filtrate was washed by water (10 mL) and extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4 then the solvent was evaporated in vacuum and the crude compound was purified by flash chromatography (Merck silica gel 60 H, CH_2Cl_2/MeOH, 9:1) to afford the corresponding products.

N^1-(Benzo[d]thiazol-2-yl)-N^4-tosylsuccinamide (2a). Yield: 77%, mp 171°C, Rf = 0.46 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.38 (s, 3H, CH_3-Ph), 2.62(s, 4H, (CH_2)-CO_{amide}), 7.23 (d, J = 8.1 Hz, 2H, Ar-H), 7.40 (d, J = 8.2 Hz, 2H, Ar-H), 7.60 (d, J = 8.2 Hz, 1H, Ar-H), 7.65 (d, J = 8.2 Hz, 1H, Ar-H), 7.70 (d, J = 8.2 Hz, 1H, Ar-H), 7.85(d, J = 8.2 Hz, 2H, Ar-H), 8.08(s, 1H, NH), 9.10 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 21.6, 30.9, 118.9, 120.6, 124.6, 125.1, 127.1, 130.0, 131.2, 136.9, 143.9, 153.1, 172.6, 173.9, 174.5. MS (ESI$^+$ 70 eV m/z): 404.07([M + 1]$^+$, 70%). Elemental anal. (%), calculated: C, 53.58; H, 4.25; N, 10.41; found: C, 53.62; H, 4.28; N, 1037.

N^1-(Benzo[d]thiazol-2-yl)-N^4-tosylfumaramide (2b). Yield: 64%, mp 166°C, Rf = 0.47 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.51 (s, 3H, CH_3), 6.48 (s, 2H, CH = CH), 7.65(d, J = 8.1 Hz, 2H, Ar-H), 7.75(d,

J = 8.2 Hz, 2H, Ar-H), 8.09(d, J = 8.6 Hz, 2H, Ar-H), 8.30(d, J = 8.7 Hz, 2H, Ar-H), 9.00(s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 23.3, 118.8, 120.6, 124.6, 125.2, 127.3, 129.5, 131.2, 135.8, 136.5, 141.3, 153.2, 166.4, 175.1. Elemental anal. (%), calculated: C, 53.85; H, 3.77; N, 10.47; found: C, 53.81; H, 3.79; N, 10.51.

N^1-(Benzo[d]thiazol-2-yl)-2,3-dichloro-N^4-tosylmaleamide (2c). Yield: 60%, mp 166°C, Rf = 0.47 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.51 (s, 3H, CH_3), 6.90(d, J = 6.7 Hz, 1H, Ar-H), 7.15(t, J = 7.6 Hz, 1H, Ar-H), 7.32(d, J = 7.8 Hz, 2H, Ar-H), 7.55(d, J = 8.2 Hz, 2H, Ar-H), 7.69(d, J = 8.4 Hz, 2H, Ar-H), 8.25(s, 1H, NH), 9.00(s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 23.3, 118.8, 120.6, 124.6, 125.2, 127.3, 129.5, 131.2, 135.8, 136.5, 141.3, 153.2, 166.4, 174.8. Elemental anal. (%), calculated: C, 52.72; H, 3.58; N, 9.34; found: C, 52.75; H, 3.60; N, 9.30.

N^1-(Benzo[d]thiazol-2-yl)-N^5-tosylglutaramide (2d). Yield: 67%, mp 173°C, Rf = 0.49(CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 1.25 (m, 2H, CH_2-CH_2-CH_2, 2.45(t, J = 7.5, 4H, CH_2-CO), 2.46 (s, 3H, CH_3), 7.28 (d, J = 8.1 Hz, 2H, Ar-H), 7.57 (d, J = 8.2 Hz, 2H, Ar-H), 7.67 (d, J = 8.2 Hz, 2H, Ar-H), 7.95(s, 1H, NH), 9.02(s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 20.9, 21.6, 32.5, 34.9, 118.8, 120.6, 124.6, 125.2, 127.1, 129.2, 131.8, 137.3, 142.9, 153.7, 172.7, 173.7, 174.7. Elemental anal. (%), calculated: C, 54.66; H, 4.59; N, 10.06; found: C, 54.64; H, 4.62; N, 10.03.

N^1-(Benzo[d]thiazol-2-yl)-N- tosylphthalamide (2e). Yield: 49%, mp 176°C, Rf = 0.49 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.45 (s, 3H, CH_3-Ph), 7.38 (d, J = 8.1 Hz, 2H, Ar-H), 7.84 (d, J = 8.2 Hz, 2H, Ar-H), 7.94 (d, J = 8.2 Hz, 2H, Ar-H), 8.05 (m, 4H, Ar-H), 8.09 (d, 1H, Ar-H), 8.09(s, 1H, NH), 9.08(s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 21.6, 118.7, 120.5, 123.8, 124.6, 125.3, 127.7, 128.3, 130.0, 131.4, 131.9, 132.1, 134.5, 137.2, 137.9, 153.1, 172.9, 173.7, 174.8. Elemental anal. (%), calculated: C, 58.52; H, 3.79; N, 9.31; found: C, 58.55; H, 3.82; N, 9.28.

N^1-(6-Methylbenzo[d]thiazol-2-yl)-N^4-tosylsuccinamide (2f). Yield: 76%, mp 172°C, Rf = 0.48 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.38 (s, 6H, CH_3-Ph), 2.64(s, 4H, (CH_2)-CO_{amide}), 7.30 (d, J = 8.1 Hz, 2H, Ar-H), 7.60 (s, 1H, Ar-H), 7.63 (d, J = 8.2 Hz, 1H, Ar-H), 7.78 (d, J = 8.2 Hz, 2H, Ar-H), 8.08 (s, 1H, Ar-H), 8.08 (s, 1H, NH), 9.10 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 21.6, 21.9, 30.9, 118.9, 121.6, 127.1, 128.2, 128.7, 130.0, 131.2, 131.8, 134.1, 136.9, 143.9, 153.1, 153.6, 172.6, 173.9, 174.5, 174.8. MS (ESI$^+$ 70 eV m/z): 418.20($[M + 1]^+$, 100%). Elemental anal. (%), calculated: C, 54.66; H, 4.59; N, 10.06; found: C, 54.62; H, 4.56; N, 10.13.

N^1-(6-Methylbenzo[d]thiazol-2-yl)-N^4-tosylfumaramide (2 g). Yield: 63%, mp 169°C, Rf = 0.49 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.38 (s, 6H, CH_3), 6.50 (s, 2H, CH=CH), 7.40(d, J = 7.5 Hz, 2H, Ar-H), 7.60(s, 1H, Ar-H), 7.65(d, J = 8.2 Hz, 1H, Ar-H), 7.75(d, J = 8.4 Hz, 2H, Ar-H), 8.10(d, J = 8.5, 2H, Ar-H), 9.00(s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 23.3, 118.5, 120.7, 124.9, 125.4, 127.9, 129.3, 131.2, 134.8, 135.8, 137.2, 150.3, 166.9, 167.4, 175.2. Elemental anal. (%), calculated: C, 54.92; H, 4.12; N, 10.11; found: C, 54.95; H, 4.10; N, 10.14.

N^1-(6-Methyl benzo[d]thiazol-2-yl)-2,3-dichloro-N^4-tosylmaleamide (2 h). Yield: 59%, mp 168°C, Rf = 0.48 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.37 (s, 6H, CH_3), 7.34(d, J = 7.8 Hz, 2H, Ar-H), 7.62(d, J = 8.1 Hz, 2H, Ar-H), 7.76(d, J = 8.3 Hz, 2H, Ar-H), 8.01(s, 1H, NH), 9.00(s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 21.4, 22.9, 118.5, 120.6, 124.6, 127.2, 128.5, 131.2, 135.8, 136.5, 137.3, 141.3, 151.2, 166.4, 168.3, 174.8. Elemental anal. (%), calculated: C, 47.11; H, 3.12; N, 8.68; found: C, 47.16; H, 3.09; N, 8.70.

N^1-(6-Methyl benzo[d]thiazol-2-yl)- N^5-tosylglutaramide (2i). Yield: 68%, mp 174°C, Rf = 0.50 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 1.25 (m, 2H, CH_2-CH_2-CH_2, 2.45(t, J = 6.5 Hz, 4H, CH_2-CO), 2.46 (s, 6H, CH_3), 7.30(d, J = 7.5 Hz, 1H, Ar-H), 7.35 (d, J = 8.1 Hz, 2H, Ar-H), 7.71 (d, J = 8.2 Hz, 2H, Ar-H), 7.75 (s, 1H, Ar-H), 7.85 (d, J = 8.4 Hz, 1H, Ar-H), 8.02(s, 1H, NH), 9.04(s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 20.9, 21.6, 21.9, 32.5, 34.9, 118.8, 121.6, 128.1, 128.7, 129.2, 131.8, 135.3, 138.9, 152.4, 173.8, 174.6, 174.9. Elemental anal. (%), calculated: C, 55.67; H, 4.91; N, 9.74; found: C, 55.64; H, 4.92; N, 9.80.

N^1-(6-Methyl benzo[d]thiazol-2-yl)-N^2- tosylphthalamide (2j). Yield: 48%, mp 178°C, Rf = 0.47 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.45 (s, 6H, CH_3-Ph), 7.38 (d, J = 8.1 Hz, 1H, Ar-H), 7.44 (d, J = 8.1 Hz, 2H, CH_{arom}), 7.72 (d, J = 8.2 Hz, 2H, Ar-H), 7.75 (s, 1H, Ar-H), 7.94(m, 4H, Ar-H), 8.02 (d, J = 8.5 Hz, 1H, Ar-H), 8.07(s, 1H, NH), 9.05(s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 21.6, 22.2, 118.7, 120.5, 123.8, 124.6, 125.3, 127.7, 128.3, 130.0, 131.4, 131.9, 132.1, 134.6, 137.2, 137.9, 153.1, 172.9, 173.7, 174.2, 174.8. Elemental anal. (%), calculated: C, 59.34; H, 4.11; N, 9.03; found: C, 59.36; H, 4.14; N, 9.01.

N^1-(6-Nitrobenzo[d]thiazol- 2-yl)-N^4-tosylsuccinamide (2 k). Yield: 43%, mp 175°C, Rf = 0.43 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.33 (s, 3H, CH_3-Ph), 2.67(s, 4H, (CH_2)-CO_{amide}), 7.32 (d, J = 8.1 Hz, 2H, Ar-H), 7.40 (s, 1H, Ar-H), 7.76 (d, J = 8.2 Hz, 2H, Ar-H), 8.08(s, 1H, NH), 8.20 (d, J = 8.2 Hz, 1H, Ar-H), 8.78 (s, 1H, Ar-H), 9.00 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 21.6, 21.9, 30.9, 117.8, 119.2, 121.9, 128.2, 131.2, 137.3, 137.7, 144.9, 159.5, 173.9, 174.5, 174.8. MS (ESI$^+$ 70 eV m/z): 448.07($[M]^+$, 100%). Elemental anal. (%),

calculated: C, 48.21; H, 3.60; N, 12.49; found: C, 48.26; H, 3.63; N, 12.43.

N^1-(Benzo[d]thiazol-2-yl)-N^4-(*N*-butylsulfamoyl)succinamide (2 l). Yield: 89%, mp 137°C, Rf = 0.48 (CH_2Cl_2/MeOH, 9/1). ^{1}HNMR ($CDCl_3$,δppm): 0.75 (t, 3H, *J* = 5.8 Hz, CH_3), 1.22 (m, 2H, CH_2), 1.33 (m, 2H, CH_2), 2.65(s, 4H, CH_2-CO_{amide}), 2.85 (m, 2H, CH_2-N), 7.36(d, *J* = 7.8 Hz, 2H, Ar-H), 7.70(d, *J* = 8.5 Hz, 1H, Ar-H), 7.80(d, *J* = 8.5 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 13.5, 19.8, 29.6, 29.7, 30.9, 43.5, 118.6, 121.8, 124.9, 125.7, 130.8, 153.4, 173.5, 174.4, 175.1. Ms (ESI$^+$ 70 eVm/s): 385.13($[M + 1]^+$, 100%). Elemental anal. (%), calculated: C, 46.86; H, 5.24; N, 14.57; found: 46.89; H, 5.28; N, 14.59.

N^1-(Benzo[d]thiazol-2-yl)-N^4-(*N*-tert-butylsulfamoyl) succinamide (2 m). Yield: 92%, mp 139°C, Rf = 0.50 (CH_2Cl_2/MeOH, 9/1). ^{1}HNMR ($CDCl_3$,δppm): 1.28(s, 9H, 3(CH_3), 2.46(s, 4H, CH_2-CO_{amide}), 7.65(d, *J* = 7.5 Hz, 2H, Ar-H), 7.75(d, *J* = 7.7 Hz, 1H, Ar-H), 8.02(d, *J* = 8.2 Hz, 1H, Ar-H), 9.02(s, 1H, NH), 9.08(s, 1H, NH). ^{13}CNMR (CDl_3, δppm): 29.4, 29.7, 44.6, 118.6, 121.8, 124.9, 125.7, 130.8, 153.4, 173.5, 174.4, 175.1. Ms (ESI$^+$ 70 eVm/s): 155.03(67%), 255.02(14%), 407.13 ($[M + Na]^+$, 100%). Elemental anal. (%), calculated: C, 46.86; H, 5.24; N, 14.57; found: C, 46.90; H, 5.22; N, 14.60.

N^1-(Benzo[d]thiazol-2-yl)-N^4-(*N*- phenylsulfamoyl) succinamide (2n). Yield: 84%, mp 148°C, Rf = 0.48 (CH_2Cl_2/MeOH, 9/1), ^{1}H NMR ($CDCl_3$, δ ppm): 2.67(s, 4H, CH_2-CO_{amide}), 4.05(s, 1H, NH), 6.79(m, 5H, Ar-H), 7.74(d, *J* = 7.5 Hz, 2H, Ar-H), 7.92(d, *J* = 7.8 Hz, 1H, Ar-H), 8.04(d, *J* = 8.2 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 29.8, 29.9, 118.6, 121.2, 121.8, 124.3, 124.9, 125.7, 126.1, 130.8, 140.4, 153.4, 173.6, 174.6, 175.8. MS (ESI$^+$ 70 eV m/z): 406 ($[M]^+$, 100%). Elemental anal. (%), calculated: C, 50.48; H, 3.99; N, 13.85; found: C, 50.45; H, 3.98; N, 13.89.

N^1-(Benzo[d]thiazol-2-yl)-N^4-((3,4-dihydroisoquinolin-2(1H)yl)sulfonyl)succinamide (2o). Yield: 90%, mp 143°C, Rf = 0.39 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.69(s, 4H, CH_2-CO amide), 2.88(t, 2H, *J* = 5.8 Hz, CH_2-Ar), 3.60(t, 2H, *J* = 5.7 Hz, CH_2N), 4.51(s, 2H, Ar-CH_2N), 7.05(m, 1H, Ar-H), 7.09(m, 1H, Ar-H), 7.17(m, 2H, Ar-H), 7.56(d, *J* = 7.8 Hz, 2H, Ar-H), 7.92(d, *J* = 8.3 Hz, 1H, Ar-H), 8.07(s, 1H, NH_{amide}), 8.04(d, *J* = 8.5 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 22.4, 20.0, 32.3, 52.1, 53.2, 119.8, 122.6, 124.3, 125.7, 126.2, 127.1, 128.4, 129.6, 132.4, 135.4, 152.5, 168.4, 171.2, 172.5. MS (ESI$^+$ 70 eV m/z): 445.07($[M + 1]^+$, 68%). Elemental anal. (%), calculated: C, 54.04; H, 4.53; N, 12.60; found: C, 54.06; H, 4.50; N, 12.64.

N^1-(Benzo[d]thiazol-2-yl)-N^4-((4-phenylpiperazin-1-yl) sulfonyl)succinamide (2p).

Yield: 88%, mp 148°C, Rf = 0.51 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.80(s, 4H, CH_2-CO_{amide}), 3.30(t, *J* = 6.8 Hz, 4H, CH_2-N), 3.75(t, *J* = 6.8 Hz, 4H, CH_2-N), 7.05(m, 3H, Ar-H), 7.30(t, 2 *J* = 7.5 Hz, H, Ar-H), 7.75(d, *J* = 7.7 Hz, 2H, Ar-H), 8.25 (d, *J* = 8.1, 1H, Ar-H), 8.04(d, *J* = 8.4, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 29.6, 31.1, 46.5, 49.1, 117.1, 118.7, 121.1, 121.9, 124.9, 125.7, 129.5, 130.8, 150.6, 153.4, 173.5, 174.4, 175.1. MS (ESI$^+$ 70 eV m/z): 474.10 ($[M + H]^+$, 100%). Elemental anal. (%), calculated: C, 53.26; H, 4.90; N, 14.79; found: C, 53.30; H, 4.92; N, 14.77.

N^1-(Benzo[d]thiazol-2-yl)-N^4-(*N*- phenylsulfamoyl) fumaramide (2q). Yield: 89%, mp 141°C, Rf = 0.51 (CH_2Cl_2/MeOH, 9/1), ^{1}H NMR ($CDCl_3$, δ ppm): 6.70(s, 2H, CH=CH), 7.25(m, 5H, Ar-H), 7.45(d, *J* = 7.5 Hz, 2H, Ar-H), 7.64(d, *J* = 7.8 Hz, 2H, Ar-H), 8.04(s, 1H, N-H), 9.00(s, 1H, N-H). ^{13}C NMR ($CDCl_3$, δ ppm): 118.6, 119.5, 121.2, 121.8, 124.3, 124.9, 125.7, 126.1, 135.8, 138.7, 153.4, 168.2, 169.6, 175.8. MS (ESI$^+$ 70 eV m/z): 402 ($[M]^+$, 100%). Elemental anal. (%), calculated: C, 50.74; H, 3.51; N, 13.92; found: C, 50.75; H, 3.54; N, 13.90.

N^1-(Benzo[d]thiazol-2-yl)-2,3-dichloro-N^4-((4-methoxy phenyl)sulfonyl)maleamide (2r). Yield: 82%, mp 169°C, Rf = 0.45 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR (DMSO, δ ppm): 3.72 (s, 3H, CH_3), 6.92(d, *J* = 7.6 Hz, 2H, Ar-H), 7.20(d, *J* = 7.9 Hz, 2H, Ar-H), 7.60–7.73(2d, *J* = 7.9, 4H, Ar-H), 7.74(s, 1H, N-H), 8.80(s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 55.7, 112.8, 115.2, 117.7, 121.6, 124.6, 130.8, 133.8, 135.9, 140.8, 150.1, 157.9. MS (ESI$^+$ 70 eV m/z): 485.10 ($[M]^+$, 100%). Elemental anal. (%), calculated: C, 44.45; H, 2.69; N, 8.64; found: C, 44.47; H, 2.67; N, 8.67.

N^1-(Benzo[d]thiazol-2-yl)-2,3-dichloro-N^4-((4-chlorophenyl) sulfonyl)maleamide (2 s). Yield: 80%, mp 169°C, Rf = 0.47 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR (DMSO, δ ppm): 7.32(d, *J* = 7.8 Hz, 2H, Ar-H), 7.43(d, *J* = 8.1 Hz, 2H, Ar-H), 7.64 (d, *J* = 8.3 Hz, 2H, Ar-H), 7.66 (d, *J* = 8.4 Hz, 2H, Ar-H), 8.20(s, 1H, NH), 9.10(s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 118.8, 121.6, 124.6, 125.2, 128.8, 129.2, 131.2, 137.8, 138.5, 153.2, 163.4, 168.7, 174.8. MS (ESI$^+$ 70 eV m/z): 489.08 ($[M]^+$, 100%). Elemental anal. (%), calculated: C, 41.60; H, 2.05; N, 8.56; found: C, 41.63; H, 2.06; N, 8.54.

N^1-(6-Methoxybenzo[d]thiazol-2-yl)-2,3-dichloro-N^4-tosylmaleamide (2 t). Yield: 83%, mp 166°C, Rf = 0.48(CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.41 (s, 3H, CH_3), 3.76 (s, 3H, CH_3), 7.35(d, *J* = 6.7 Hz, 1H, Ar-H), 7.63(d, *J* = 7.8, 2H, Ar-H), 7.75–7.80(2d, 4H, Ar-H), 7.78(d, *J* = 8.2 Hz, 1H, NH), 8.15(s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 21.3, 56.8, 104.9, 114.8, 118.8, 128.6, 129.6, 131.2, 136.8, 137.3, 145.3, 156.8, 163.4, 168.4,

174.8. MS (ESI$^+$ 70 eV m/z): 499.05 ([M]$^+$, 100%). Elemental anal. (%), calculated: C, 45.61; H, 3.02; N, 8.40; found: C, 45.64; H, 3.06; N, 8.42.

N^1-(6-Methylbenzo[d]thiazol-2-yl)-2,3-dimethyl-*N*^{4}-tosyl maleamide (2u). Yield: 86%, mp 160°C, Rf = 0.53 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.35 (s, 6H, CH_3), 2.62 (s, 6H, CH_3), 7.35(d, *J* = 6.7, 2H, Ar-H), 7.60(d, *J* = 7.9 Hz, 1H, Ar-H), 7.65(d, *J* = 6.9 Hz, 2H, Ar-H), 7.78(d, *J* = 8.2 Hz, 2H, Ar-H), 8.12(s, 1H, NH), 8.98(s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 7.8, 8.1, 19.2, 19.6, 116.8, 119.5, 125.6, 128.6, 129.5, 131.8, 133.4, 138.4, 138.9, 150.1, 164.8, 169.2, 175.2. MS (ESI$^+$ 70 eV m/z): 443.10 ([M]$^+$, 100%). Elemental anal. (%), calculated: C, 56.87; H, 4.77; N, 9.47; found: C, 56.90; H, 4.78; N, 9.44.

1-Tosylpyrrolidine-2,5-dione (3a). Yield: 30%, mp 126°C, Rf = 0.88 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.45 (s, 3H, CH_3-Ph), 2.65(s, 4H, (CH_2)-CO_{amide}), 7.40 (d, *J* = 8.1 Hz, 2H, Ar-H), 7.75 (d, *J* = 8.2 Hz, 2H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 21.5, 26.9, 128.5, 129.3, 137.6, 137.9, 175.8. MS (ESI$^+$ 70 eV m/z): 254.09 ([M + 1]$^+$, 40%), 271.02 ([M + NH_4]$^+$, 100%). Elemental anal. (%), calculated: C, 52.16; H, 4.38; N, 5.53; found: C, 52.19; H, 4.29; N, 5.59.

1-(Benzo[d]thiazol-2-yl) pyrrolidine-2,5-dione (4a). Yield: 94%, mp 121°C, Rf = 0.86 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.82(s, 4H, (CH_2)-CO), 7.50 (d, *J* = 8.2 Hz, 2H, Ar-H), 8.10 (d, *J* = 8.1 Hz, 1H, Ar-H), 8.22 (d, *J* = 8.2 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 30.8, 124.1, 125.6, 128.1, 129.7, 136.8, 139.7, 161.8, 176.2. MS (ESI$^+$ 70 eV m/z): 233.13 ([M + 1]$^+$, 35%), 250.10 ([M + NH_4]$^+$, 100%). Elemental anal. (%), calculated: C, 56.88; H, 3.47; N, 12.06; found: C, 56.82; H, 3.53; N, 12.12.

1-(Benzo[d]thiazol-2-yl)-1*H*-pyrrole-2,5-dione (4b). Yield: 92%, mp 115°C, Rf = 0.69 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 6.85 (s, 2H, CH=CH), 7.65 (t, *J* = 6.8 Hz, 1H, Ar-H), 7.75 (t, *J* = 6.9 Hz, 1H, Ar-H), 8.15 (d, *J* = 8.2 Hz, 1H, Ar-H), 8.30 (d, *J* = 8.2 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 118.4, 121.6, 124.3, 125.7, 135.4, 136.3, 139.9, 160.9, 167.2. MS (ESI$^+$ 70 eV m/z): 231.13 ([M + 1]$^+$, 28%), 248.10 ([M + NH_4]$^+$, 100%). Elemental anal. (%), calculated: C, 57.38; H, 2.63; N, 12.17; found: C, 57.40; H, 2.62; N, 12.12.

1-(Benzo[d]thiazol-2-yl) -3,4-dichloro-1*H*- pyrrole −2,5-dione (4c). Yield: 89%, mp 123°C, Rf = 0.66 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 7.55 (d, *J* = 7.6 Hz, 2H, Ar-H), 7.90 (d, *J* = 8.2 Hz, 1H, Ar-H), 8.10 (d, *J* = 8.2 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 118.5, 121.5, 125.6, 127.8, 136.8, 137.5, 139.7, 161.2, 162.2. MS (ESI$^+$ 70 eV m/z): 299.1 ([M]$^+$, 100%), 322.2 (M + Na)$^+$, 67%). Elemental anal. (%), calculated: C, 44.17; H, 1.35; N, 9.36; found: C, 44.21; H, 1.32; N, 9.40.

1-(Benzo[d]thiazol-2-yl) piperidine-2,6-dione (4d). Yield: 86%, mp 121°C, Rf = 0.64 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.12(m, 2H, CH_2-CH_2), 2.24(t, *J* = 6.5, 4H, CH_2-CO), 7.50 (d, *J* = 8.2 Hz, 2H, Ar-H), 8.10 (d, *J* = 8.4 Hz, 1H, Ar-H), 8.22 (d, *J* = 8.2 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 18.1, 32.3, 118.2, 122.3, 125.9, 126.2, 135.1, 138.9, 158.2, 170.0. MS (ESI$^+$ 70 eV m/z): 247.10 ([M + 1]$^+$, 90%), 264.14 ([M + NH_4]$^+$, 25%). Elemental anal. (%), calculated: C, 58.52; H, 4.09; N, 11.37; found: C, 58.55; H, 4.07; N, 11.36.

2-(Benzo[d]thiazol-2-yl) isoindoline-1,3-dione (4e). Yield: 75%, mp 133°C, Rf = 0.66 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 7.45 (d, *J* = 8.2 Hz, 2H, Ar-H), 7.80 (m, 4H, Ar-H), 7.86 (d, *J* = 8.1 Hz, 1H, Ar-H), 8.15 (d, *J* = 8.3 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 118.5, 121.5, 123.8, 124.6, 125.3, 132.4, 133.1, 136.1, 139.8, 161.2, 169.2. MS (ESI$^+$ 70 eV m/z): 281.08 ([M + 1]$^+$, 35%), 298.10 ([M + NH_4]$^+$, 100%). Elemental anal. (%), calculated: C, 64.27; H, 2.88; N, 9.99; found: C, 64.29; H, 2.85; N, 9.98.

1-(6-Methylbenzo[d]thiazol-2-yl) pyrrolidine-2,5-dione (4f). Yield: 90%, mp 118°C, Rf = 0.69 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.35(s, 3H, CH_3), 2.86(s, 4H, (CH_2)-CO), 7.60 (s, 1H, Ar-H), 7.73 (d, *J* = 8.2 Hz, 1H, Ar-H), 8.02 (s, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 20.2, 30.8, 117.4, 121.1, 126.7, 130.7, 135.3, 150.4, 161.1, 174.2. MS (ESI$^+$ 70 eV m/z): 247.10 ([M + 1]$^+$, 100%). Elemental anal. (%), calculated: C, 58.52; H, 4.09; N, 11.37; found: C, 58.56; H, 4.07; N, 11.40.

1-(6-Methylbenzo[d]thiazol-2-yl)-1*H*-pyrrole-2,5-dione (4 g). Yield: 89%, mp 115°C, Rf = 0.57 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.39(s, 3H, CH_3), 6.85 (s, 2H, CH=CH), 7.40 (d, *J* = 8.2 Hz, 1H, Ar-H), 7.75 (s, 1H, Ar-H), 7.81 (d, *J* = 8.2 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 21.5, 118.1, 122.3; 125.2, 126.5, 132.1, 135.1, 151.7, 159.8, 161.3. MS (ESI$^+$ 70 eV m/z): 245.07 ([M + 1]$^+$, 85%), 262.14 ([M + NH_4]$^+$, 100%). Elemental anal. (%), calculated: C, 59.00; H, 3.30; N, 11.47; found: C, 59.03; H, 3.32; N, 11.45.

1-(6-Methylbenzo[d]thiazol-2-yl) -3,4-dichloro-1*H*-pyrrole −2,5-dione (4h). Yield: 80%, mp 125°C, Rf = 0.64 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.39(s, 3H, CH_3), 7.32 (d, *J* = 8.1 Hz, 1H, Ar-H), 7.70 (s, 1H, Ar-H), 7.85 (d, *J* = 8.2 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 20.3, 118.5, 121.5, 125.6, 130.8, 134.8, 137.7, 150.7, 161.2, 162.2. MS (ESI$^+$ 70 eV m/z): 314.13 ([M + 1]$^+$, 100%). Elemental anal. (%), calculated: C, 46.02; H, 1.93; N, 8.95; found: C, 46.00; H, 1.96; N, 8.92.

1-(6-Methylbenzo[d]thiazol-2-yl) piperidine-2,6-dione (4i). Yield: 78%, mp 124°C, Rf = 0.60 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.12(m, 2H, CH_2-CH_2), 2.24(t, 4H, CH_2-CO), 2.33(s, 3H, CH_3), 7.60 (s, 1H, Ar-H),

7.73 (d, J = 8.2 Hz, 1H, Ar-H), 8.02 (s, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 18.2, 22.4, 31.9, 118.2, 121.9, 125.9, 130.0, 132.4, 152.1, 162.9, 168.2. MS (ESI$^+$ 70 eV m/z): 261.11 ($[M + 1]^+$, 55%), 278.10 ($[M + NH_4]^+$, 100%). Elemental anal. (%), calculated: C, 59.98; H, 4.65; N, 10.76; found: C, 59.96; H, 4.68; N, 10.79.

2-(6-Methylbenzo[d]thiazol-2-yl) isoindoline-1,3-dione (4j). Yield: 72%, mp 136°C, Rf = 0.61 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.38(s, 3H, CH_3), 7.35 (s, 1H, Ar-H), 7.76–7.93 (m, 6H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 20.9, 117.5, 121.5, 123.9, 126.5, 130.8, 132.6, 134.3, 150.4, 161.1, 169.2. MS (ESI$^+$ 70 eV m/z): 317.1 [M + Na^+, 15%). Elemental anal. (%), calculated: C, 65.29; H, 3.42; N, 9.52; found: C, 65.30; H, 3.46; N, 9.50.

1-(6-Nitrobenzo[d]thiazol-2-yl) pyrrolidine-2,5-dione (4 k). Yield: 70%, mp 128°C, Rf = 0.48 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.94(s, 4H, CH_2-CO), 8.00 (d, J = 8.2 Hz, 1H, Ar-H), 8.25 (d, J = 8.2 Hz, 1H, Ar-H), 8.75 (s, 1H, Ar-H).. ^{13}C NMR ($CDCl_3$, δ ppm): 30.8, 117.8, 119.3, 122.1, 130.7, 144.8, 159.9, 161.8, 176.2. MS (ESI$^+$ 70 eV m/z): 277.10 ($[M]^+$, 100%). Elemental anal. (%), calculated: C, 47.65; H, 2.54; N, 15.16; found: C, 47.63; H, 2.56; N, 15.13.

1-(6-Nitrobenzo[d]thiazol-2-yl)-1*H*-pyrrole-2,5-dione (4 l). Yield: 68%, mp 125°C, Rf = 0.46 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 6.90 (s, 2H, CH=CH), 7.70 (d, J = 8.2 Hz, 1H, Ar-H), 7.85 (d, J = 8.2 Hz, 1H, Ar-H), 8.05 (s, 1H, Ar-H),. ^{13}C NMR ($CDCl_3$, δ ppm): 118.1, 120.3; 123.2, 132.1, 135.1, 145.7, 159.8, 161.3. MS (ESI$^+$ 70 eV m/z): 276.08 ($[M + 1]^+$, 85%), 294.14 ($[M + NH_4]^+$, 100%). Elemental anal. (%), calculated: C, 48.00; H, 1.83; N, 15.27; found: C, 48.03; H, 1.82; N, 15.25.

1-(6-Nitrobenzo[d]thiazol-2-yl) -3,4-dichloro-1*H*- pyrrole −2,5-dione (4 m). Yield: 67%, mp 125°C, Rf = 0.54 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 8.01 (d, J = 8.1 Hz, 1H, Ar-H), 8.25 (d, J = 8.2 Hz, 1H, Ar-H), 8.75 (s, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 118.5, 121.1, 123.6, 131.8, 137.8, 146.7, 161.2, 162.2. MS (ESI$^+$ 70 eV m/z): 344.3 ($[M + 1]^+$. Elemental anal. (%), calculated: C, 38.39; H, 0.88; N, 12.21; found: C, 38.37; H, 0.89; N, 12.24.

1-(6-Methoxybenzo[d]thiazol-2-yl) pyrrolidine-2,-5-dione (4n). Yield: 74%, mp 117°C, Rf = 0.65 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.82(s, 4H, (CH_2)-CO), 3.82(s, 3H, CH_3), 7.13 (d, J = 8.2 Hz, 1H, Ar-H), 7.51 (d, J = 8.3 Hz, 1H, Ar-H), 7.82 (s, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 30.8, 55.2, 117.4, 122.2, 126.2, 130.1, 143.5, 157.4, 162.7, 168.5. MS (ESI$^+$ 70 eV m/z): 263.10 ($[M + 1]^+$, 100%). Elemental anal. (%), calculated: C, 54.95; H, 3.84; N, 10.68; found: C, 54.98; H, 3.82; N, 10.67.

1-(6-Methoxybenzo[d]thiazol-2-yl)-1*H*-pyrrole-2,5-dione (4o). Yield: 72%, mp 119°C, Rf = 0.60 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 3.84(s, 3H, CH_3), 6.85 (s, 2H, CH=CH), 7.40 (d, J = 8.2 Hz, 1H, Ar-H), 7.76 (s, 1H, Ar-H), 7.82 (d, J = 8.3 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 56.7, 106.6, 117.4, 118.8, 131.5, 143.5, 157.4, 161.1, 174.4. MS (ESI$^+$ 70 eV m/z): 261.07 ($[M + 1]^+$, 80%), 278.14 ($[M + NH_4]^+$, 100%). Elemental anal. (%), calculated: C, 55.38; H, 3.10; N, 10.76; found: C, 55.40; H, 3.12; N, 10.73.

1-(6-Methoxybenzo[d]thiazol-2-yl) -3,4-dichloro-1*H*-pyrrole −2,5-dione (4p). Yield: 67%, mp 129°C, Rf = 0.60 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 3.82(s, 3H, CH_3), 7.58 (d, J = 8.1 Hz, 1H, Ar-H), 7.80 (s, 1H, Ar-H), 7.85 (d, J = 8.2 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 57.3, 105.3, 115.5, 119.5, 130.8, 136.8, 143.8, 156.7, 161.2, 163.2. MS (ESI$^+$ 70 eV m/z): 329.13 ($[M + 1]^+$. Elemental anal. (%), calculated: C, 43.79; H, 1.84; N, 8.51; found: C, 43.77; H, 1.86; N, 8.49.

2-(6-Methoxybenzo[d]thiazol-2-yl) isoindoline-1,-3-dione (4q). Yield: 74%, mp 140°C, Rf = 0.59 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 3.78(s, 3H, CH_3), 7.32 (d, J = 8.1 Hz, 1H, Ar-H), 7.53 (s, 1H, Ar-H), 7.59 (d, J = 8.2 Hz, 1H, Ar-H), 7.76–7.93 (m, 4H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 56.9, 105.5, 117.7, 119.5, 123.9, 131.8, 146.6, 157.4, 161.1, 169.7. MS (ESI$^+$ 70 eV m/z): 311.1 [M + H^+, 100%),. Elemental anal. (%), calculated: C, 61.93; H, 3.25; N, 9.03; found: C, 61.90; H, 3.29; N, 9.01.

1-(Benzo[d]thiazol-2-yl) -3,4-dimethyl-1*H*- pyrrole −2,5-dione (4r). Yield: 82%, mp 127°C, Rf = 0.68 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.45(s, 6H, CH_3), 7.55 (d, J = 7.6 Hz, 2H, Ar-H), 7.90 (d, J = 8.2 Hz, 1H, Ar-H), 8.10 (d, J = 8.2 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm):9.5, 118.5, 121.5, 125.6, 126.2, 136.8, 139.7, 140.1, 161.2, 172.1. MS (ESI$^+$ 70 eV m/z): 258.1 ($[M]^+$, 100%). Elemental anal. (%), calculated: C, 60.45; H, 3.90; N, 10.85; found: C, 60.44; H, 3.92; N, 10.82.

1-(6-Methylbenzo[d]thiazol-2-yl) -3,4- dimethyl--1*H*-pyrrole −2,5-dione (4s). Yield: 80%, mp 120°C, Rf = 0.66 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.22(s, 3H, CH_3), 2.38(s, 6H, CH_3), 7.75 (d, J = 8.1 Hz, 1H, Ar-H), 7.79 (s, 1H, Ar-H), 8.01 (d, J = 8.2 Hz, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm):9.8, 20.3, 118.5, 121.5, 126.3, 130.8, 134.8, 138.5, 150.7, 161.2, 172.2. MS (ESI$^+$ 70 eV m/z): 272.99 ($[M + 1]^+$, 60%), 290.07 ($[M + NH_4]^+$, 100%). Elemental anal. (%), calculated: C, 61.75; H, 4.44; N, 10.29; found: C, 61.77; H, 4.48; N, 10.27.

1-(6-Nitrobenzo[d]thiazol-2-yl) -3,4-dimethyl-1*H*- pyrrole −2,5-dione (4t). Yield: 65%, mp 135°C, Rf = 0.52 (CH_2Cl_2/MeOH, 9/1). ^{1}H NMR ($CDCl_3$, δ ppm): 2.40(s, 6H, CH_3), 8.10 (d, J = 8.1 Hz, 1H, Ar-H), 8.30 (d,

J = 8.2 Hz, 1H, Ar-H), 8.60 (s, 1H, Ar-H). ^{13}C NMR ($CDCl_3$, δ ppm): 9.8, 118.5, 120.5, 121.5, 130.9, 138.8, 143.4, 161.2, 171.2. MS (ESI$^+$ 70 eV m/z): 304.13 ($[M + 1]^+$. Elemental anal. (%), calculated: C, 51.48; H, 2.99; N, 13.85; found: C, 51.45; H, 2.97; N, 13.88.

2 | RESULTS AND DISCUSSION

From the point of synthetic simplicity, one-pot reaction could provide a far more efficient and straightforward access to the target molecules. In the connection with our recent work,[24] we envisioned that carboxylic acid (2′) produced in situ from sulfonamide (a) and cyclic anhydride may react with 2-amino benzothiazole to form new product (b) containing both scaffolds: sulfonamide and benzothiazole (Scheme 1). Initially, a one-pot, one-step protocol at room temperature was examined, using the same already optimized conditions in previous report[24] (5 mmol% $Cs_5HP_2W_{18}O_{62}$ as catalyst and water as solvent) for the preparation of (**2a**) from sulfonamide (**1a**), succinic anhydride and 2-amino benzothiazole as the model reaction (Scheme 1).

The formation of the desired compound (**2a**) containing benzothiazole and sulfonamide moieties was observed with the investigated solid at room temperature, but the yield was very unsatisfactory (<10%) (Scheme 1).

The low yield is due to the concomitant formation of by-products, since $Cs_5HP_2W_{18}O_{62}$ promotes the condensation of succinic anhydride once with sulfonamide (**1a**) to afford cyclic imide (**3a**), and then with 2-amino benzothiazole to give other cyclic imide (**4a**).

In order to improve the performance of this one-pot reaction, it was carried out with another protocol using two steps.

This protocol involving the reaction of sulfonamide (**1a**) with succinic anhydride and $Cs_5HP_2W_{18}O_{62}$ in water, followed by the in situ coupling reaction with 2-amino benzothiazole at room temperature.

It was noted that the one-pot, two-step reaction was more effective and afforded only the desired product (**2a**) with a slight improvement in the reaction yield (25%) within 4 hours. To further improve the yield and decrease the reaction time, the above reaction was carried out under many conditions.

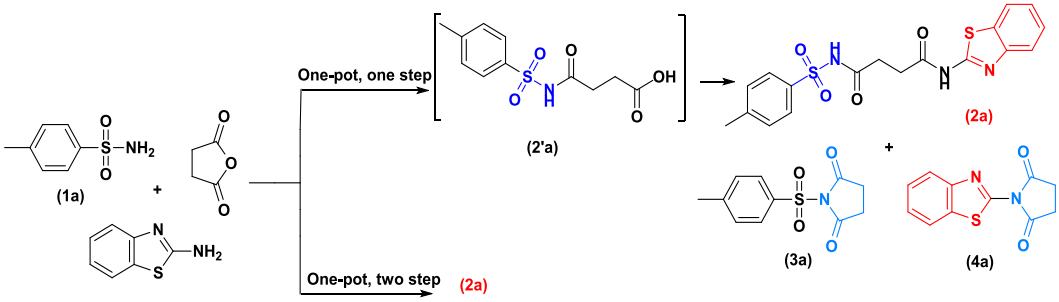
The corresponding results are listed in Table 1.

The use of ultrasound assisted one-pot, two-step protocol was found to be more advantageous in terms of rate-accelerations, loadings and reaction time (92% in 6 minutes; Table 1, entry 15) in comparison to microwave irradiation and room temperature methods (76% in 25 minutes and 35% in 240 minutes, respectively; Table 1, entries 19 and 20). Also, we observed that when the one-pot, two step reaction was accelerated under ultrasound irradiation in a shorter reaction time (6 minutes; Table 1, entry 15) lead to a higher yield (92%) of compound (**2a**), compared to a longer reaction times (Table 1, entries 5 and 14).

When the influence of solvents was investigated, we found that only H_2O was critical for the reaction efficiency (Table 1, entry 5). The use of other solvents, such as acetonitrile, tetrahydrofuran, toluene, and chloroforme led to a lower yield of product (**2a**) (Table 1, entries 7-10). As we all know, water is very green and environmental, and using water as the solvent for the organic synthesis could avoid the employment of some toxic solvents, such as acetonitrile, toluene, etc.

In order to find the minimum amount of H_2O required to get maximum yield in short duration, the reaction was carried out in different volumes of H_2O and it was found that, the minimum amount of H_2O required to get the maximum yield of the product is 2 mL. (Table 1, entry 14).

The benzothiazole containing sulfonamide moiety (**2a**) (Scheme 1) is obtained in high yields (50%–86% yield; Table 1, entries 2-5) using a catalytic amount from 5 to 12 mmol% of $Cs_5HP_2W_{18}O_{62}$. The results show a significant effect of the amount of the catalyst. It is found that the increase of the catalytic amount of $Cs_5HP_2W_{18}O_{62}$ leads to a considerably increased reaction rate, from 45 minutes with 5 mmol% to 15 minutes using 10 mmol% of this catalyst (Table 1, entries 2-5). For quantities of catalyst between 5 and 8 mmol%, the reaction



SCHEME 1 Model reaction

TABLE 1 Optimization of the one-pot, two-step reaction conditions

Entry[a]	Catalyst (mmol%)	Solvent (mL)	Conditions	Time (min)/yield (%)[b]
1	Without	H_2O (2)	))))	45/traces
2	$Cs_5HP_2W_{18}O_{62}$(5)	H_2O (2)	))))	30/50
3	$Cs_5HP_2W_{18}O_{62}$(6)	H_2O (2)	))))	25/61
4	$Cs_5HP_2W_{18}O_{62}$(8)	H_2O (2)	))))	20/69
5	$Cs_5HP_2W_{18}O_{62}$(10)	H_2O (2)	))))	15/86
6	$Cs_5HP_2W_{18}O_{62}$(12)	H_2O (2)	))))	15/86
7	$Cs_5HP_2W_{18}O_{62}$(10)	CH_3CN (2)	))))	15/48
8	$Cs_5HP_2W_{18}O_{62}$(10)	THF (2)	))))	15/54
9	$Cs_5HP_2W_{18}O_{62}$(10)	Toluene (2)	))))	15/58
10	$Cs_5HP_2W_{18}O_{62}$(10)	$CHCl_3$ (2)	))))	15/40
11	$Cs_5HP_2W_{18}O_{62}$(10)	H_2O (0.5)	))))	15/60
12	$Cs_5HP_2W_{18}O_{62}$(10)	H_2O (1)	))))	15/69
13	$Cs_5HP_2W_{18}O_{62}$(10)	H_2O (1.5)	))))	15/80
14	$Cs_5HP_2W_{18}O_{62}$(10)	H_2O (2)	))))	10/89
15	**$Cs_5HP_2W_{18}O_{62}$(10)**	**H_2O (2)**	**))))**	**06/92**
16	$Cs_5HP_2W_{18}O_{62}$(10)	H_2O (2.5)	))))	10/85
17	$Cs_5HP_2W_{18}O_{62}$(10)	H_2O (3)	))))	10/75
18	$Cs_5HP_2W_{18}O_{62}$(10)	H_2O (4)	))))	10/64
19	$Cs_5HP_2W_{18}O_{62}$(10)	H_2O (2)	RT	240/35
20	$Cs_5HP_2W_{18}O_{62}$(10)	H_2O (2)	MW	30/76

Note. The bold values indicate the best result.

[a]Reaction conditions: sulfonamide 1a (1 mmol), succinic anhydride (2 mmol) and 2-aminobenzothiazole (1 mmol) in the presence of the indicated conditions.

[b]Isolated yield after workup and chromatographic purification of compound 2a.

time is 30 minutes and the yields range from 50% to 69% yield (Table 1, entries 2-4). Furthermore, without a catalyst, only traces of (**2a**) are detected (Table 1, entry 1).

The utility of this catalyst to achieve the one-pot, two step reaction was affirmed not only by these results, but with another test carried out on step 2 of the reaction.

Herein, the intermediate carboxylic acid (**2′a**) was isolated and reacted with 2-amino benzothiazole in the presence and without catalyst.

It should be noted that the intermediate carboxylic acid (**2′a**) was already obtained in our recent work[24] in the presence of 5 mmol% $Cs_5HP_2W_{18}O_{62}$ as catalyst and water as solvent. Also, we found that the second step does take place only in the presence of this catalyst, hence its high efficiency.

Thus, reacting all the components in the presence of 10 mmol% of $Cs_5HP_2W_{18}O_{62}$ in 2 mL of water under ultrasound irradiation proved to be the optimum conditions for the one-pot, two-step reaction.

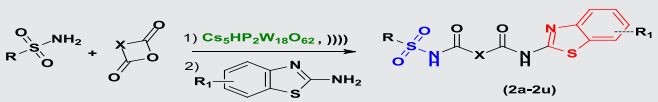
To extend the use of Cesium salt of Wells-Dawson heteropolyacid ($Cs_5HP_2W_{18}O_{62}$) and its catalytic reactivity, the reaction conditions were applied on a series of variously substituted sulfonamides prepared according to the literature,[26,27] coupled to diverse cyclic anhydrides and some 2-amino benzothiazole derivatives in the presence of 10 mmol% of $Cs_5HP_2W_{18}O_{62}$ in 2 mL of water as green solvent under ultrasound irradiation.

The benzothiazole derivatives containing sulfonamide moiety (**2a-2u**) were obtained in 48% to 92% yield within 6 to 15 minutes, depending on the structures of the cyclic anhydride and the amine (Table 2).

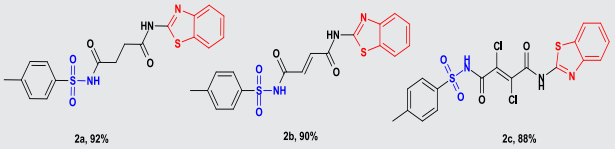
The use of different cyclic anhydrides: Maleic anhydride (MA), 2,3-Dichloro maleic anhydride (DCMA) and Glutaric anhydride (GA) leads, respectively to the new benzothiazoles containing sulfonamide moiety (**2a-2d**) with 88% to 92% yield when using the 2-amino benzothiazole and sulfonamide (**1a**). In the case of phthalic anhydride (PA), the condensation was much slower because of its steric effects and resulting product (**2e**) was obtained with lower yield (58%; Table 2).

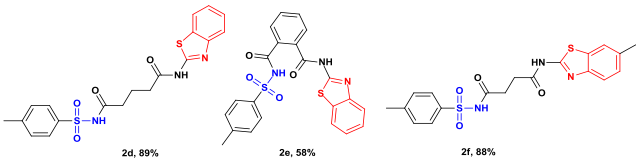
Similarly, in the presence of substituted 2-amino benzothiazole such as 2-Amino-6-methylbenzothiazole with the above series of cyclic anhydrides, the benzothiazoles containing sulfonamide moiety (**2f-2j**) were obtained in 59%-88% yield.

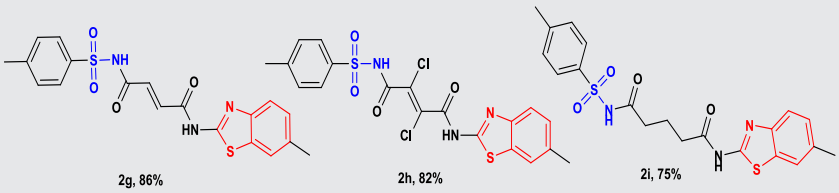
TABLE 2 $Cs_5HP_2W_{18}O_{62}$ catalyzed one-pot synthesis of new benzothiazoles containing sulfonamide moiety (**2a-2u**)

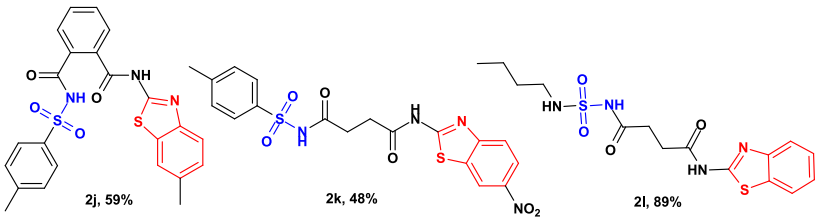


Benzothiazoles containing sulfonamide moiety (2a-2u)[a], yield%









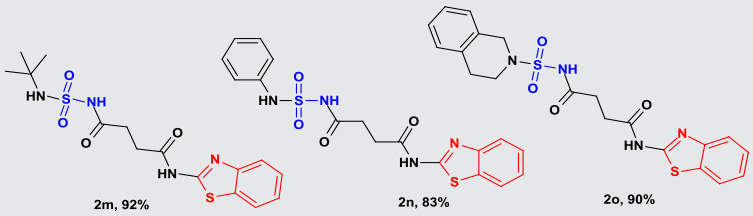


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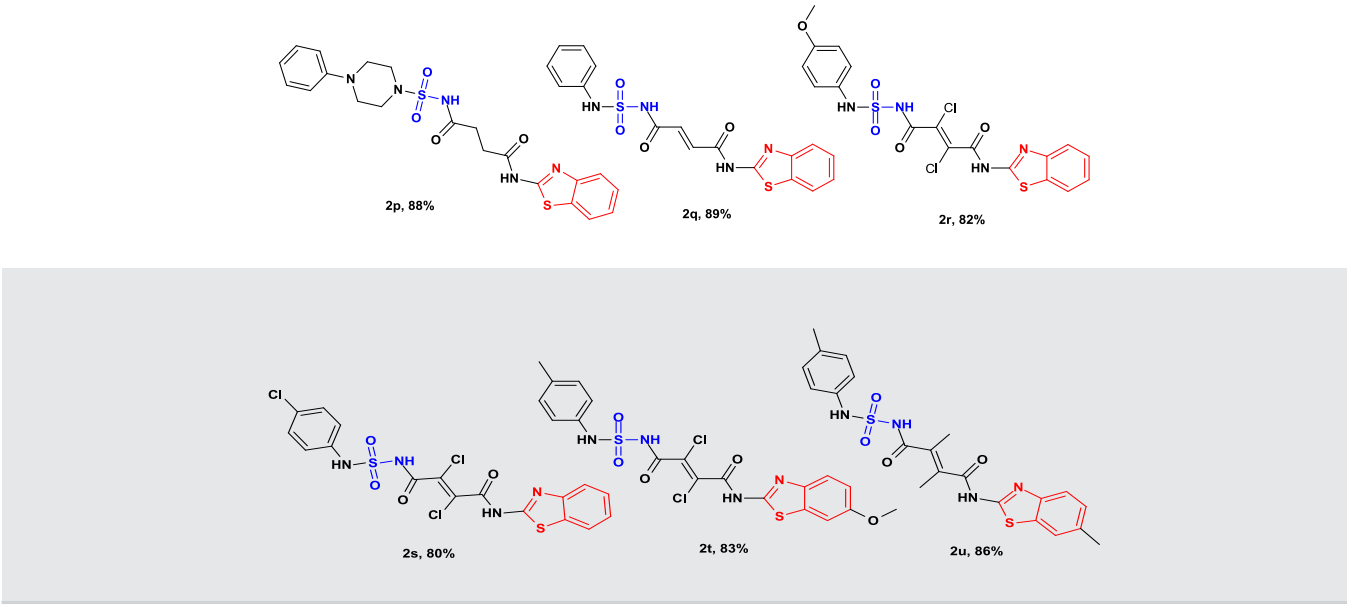
TABLE 2 (Continued)



[a]Reaction conditions: sulfonamide (1 mmol), cyclic anhydride (2 mmol) in the presence of $Cs_5HP_2W_{18}O_{62}$ (10 mmol%) as catalyst and water (2 mL) as solvent, then 2-aminobenzothiazole derivatives (1 mmol) was added under ultrasound irradiation for both steps.

The employment of 2-amino-6-nitrobenzothiazole gives moderate yield of product (**2k**) (48%), due to the presence of the nitro group **(**Table 2**)**.

Indeed, reaction of various sulfonamides (derivatives of primary and secondary, aromatic and aliphatic or cyclic and acyclic amines) with succinic anhydride and 2-aminobenzothiazole leads to original benzothiazole derivatives containing sulfonamide moiety (**2l-2u**) with excellent yields in the range 83%-92%.

The structures of new benzothizoles containing sulfonamide moiety presented in Table 2 were determined by proton, carbon NMR and mass spectroscopy, as well as elemental analysis.

As shown in scheme 1, when using only one-pot, one-step protocol for the synthesis of benzothiazole containing sulfonamide moiety (**2a**), we had noticed the formation of compounds (**3a**) and (**4a**). Although these latter compounds are considered as by-products but of great importance, since they contain cyclic imide moiety known by their potential bioactivities.[28–32]

Similar structures to compound (**3a**) have been already obtained in our previous works,[22,24] but compound (**4a**) is never mentioned in the literature.

For this purpose, we have seen that it is interesting to synthesize such as this type of new molecule (**4a**), especially that it contains the benzothiazole fragment (the title compound).

Indeed, carrying out the reaction of substituted 2-amino benzothiazole and cyclic anhydrides under the same conditions (10 mmol% of $Cs_5HP_2W_{18}O_{62}$ in 2 mL of water under ultrasound irradiation) had led to the preparation of new benzothiazole derivatives containing cyclic imide fragment (**4a-4t**) with good to excellent yields (65%-94%) (Table 3).

The structure of compounds (**4a-4t**) was established from the spectral data and the elemental analysis. (see Supporting Information).

3 | CONCLUSION

The described procedure for the synthesis of new benzothiazoles, which proceeds efficiently under ultrasound irradiation results in a clean and useful alternative.

The results show that the one-pot reaction using Cesium salt of Wells-Dawson heteropolyacid ($Cs_5HP_2W_{18}O_{62}$) as catalyst in water as green solvent, was effective and afforded the desired benzothiazoles containing sulfonamide or cyclic imide moieties with good to excellent yields. The described approach was simple and environmentally friendly.

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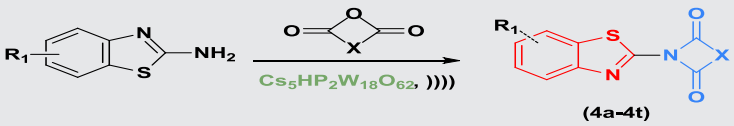
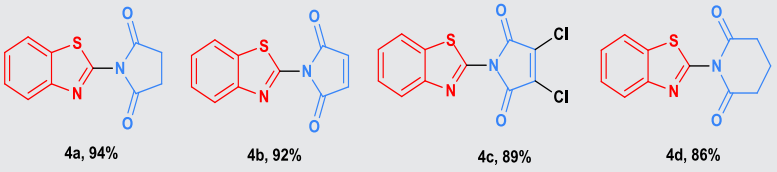
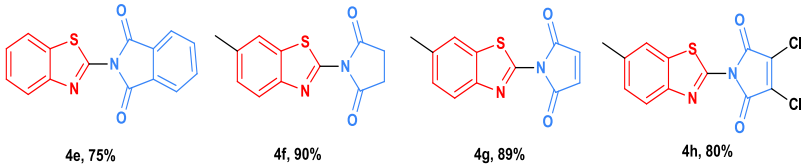
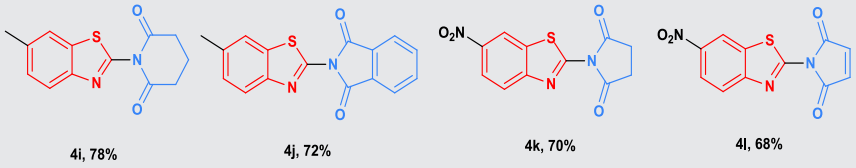
TABLE 3 Synthesis of benzothiazole derivatives containing cyclic imide

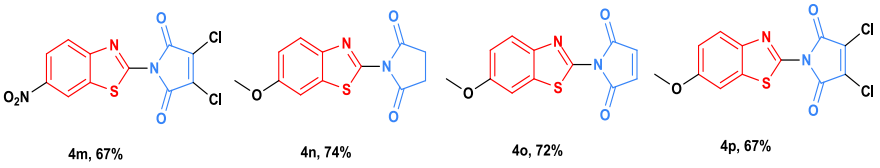


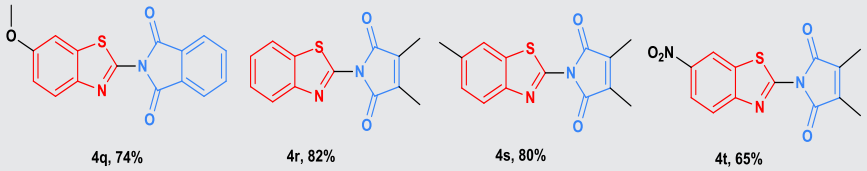
Benzothiazoles containing cyclic imide moiety (4a-4t)[a], yield%











[a]Reaction conditions: 2-aminobenzothiazole derivatives (1 mmol), cyclic anhydride (2 mmol) in the presence of $Cs_5HP_2W_{18}O_{62}$ (10 mmol%) as catalyst and water (2 mL) as solvent under ultrasound irradiation.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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