Res Chem Intermed (2016) 42:4341–4358
DOI 10.1007/s11164-015-2279-8

Efficient, microwave-mediated synthesis of benzothiazole- and benzimidazole-based heterocycles

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Received: 27 May 2015 / Accepted: 12 September 2015 / Published online: 24 September 2015

Abstract 1-(Benzothiazol-2-yl)-3-(*N*,*N*-dimethylamino)-2-(phenylsulfonyl)prop-2-en-1-one (**3**) and 1-(1-methylbenzimidazol-2-yl)-3-(*N*,*N*-dimethylamino)-2-(phenylsulfonyl)prop-2-en-1-one (**4**) were obtained from the reaction of 1-(benzothiazothiazol-2-yl)-2-phenylsulfonyl-1-ethanone (**1**) and 1-(1-methyl-1*H*-benzimidazol-2-yl)-2-(phenylsulfonyl)-1-ethanone (**2**) with *N*,*N*-dimethylformamide dimethyl acetal, respectively. The enaminosulfones **3** and **4** were used as versatile building blocks for the synthesis of novel pyrazolo[1,5-*a*]pyrimidine and [1,2,4]-triazolo[1,5-*a*]pyramidine derivatives via their reactions with the appropriate aminopyrazoles and aminotriazole under both microwave and thermal reaction conditions. They have been also utilized as reactive synthons for the construction of novel pyrimido[1,2-*a*]benzimidazole, pyrido[1,2-*a*]benzimidazole, pyrimidine, isoxazole and pyrazole heterocycles pendent to benzothiazole and benzimidazole ring systems.

Keywords Enaminosulfone · Benzimidazole · Benzothiazole · Pyrazolo[1,5-*a*]pyrimidine · [1,2,4]-Triazolo[1,5-*a*]pyramidine · Pyrimido[1,2-*a*]benzimidazole · Pyrido[1,2-*a*]benzimidazole

Introduction

Benzothiazole and benzimidazole ring systems are recognized as important heterocycles due to their diverse pharmacological properties [1, 2]. Their derivatives have attracted continued interest because of their varied biological activities [3–11].

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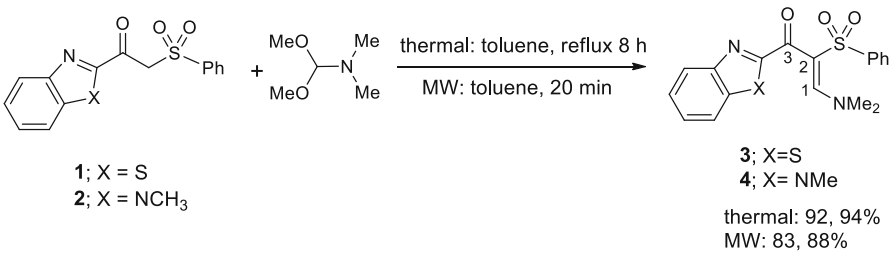
On the other hand, enaminones are considered reactive intermediates that are versatile for the synthesis of a great variety of heterocycles and aromatic compounds [12–15]. Their structural features constitute many compounds of anticonvulsive [16] and anti-histaminergic activities [17]. In addition, *β*-ketosulfones are readily available from a variety of precursors and display a broad range of synthetic versatility [18–21]. In addition, microwave irradiation assists in development and enhancement of organic synthesis [22–25]. In continuation of a research program directed towards the synthesis of a variety of heterocycles for biological evaluation [26–37], we report here on the utility of the enaminosulfone derivatives **3** and **4** as versatile intermediates, for the synthesis of new heterocyclic derivatives incorporating benzothiazole and benzimidazole moieties of biological and pharmacological importance.

Results and discussion

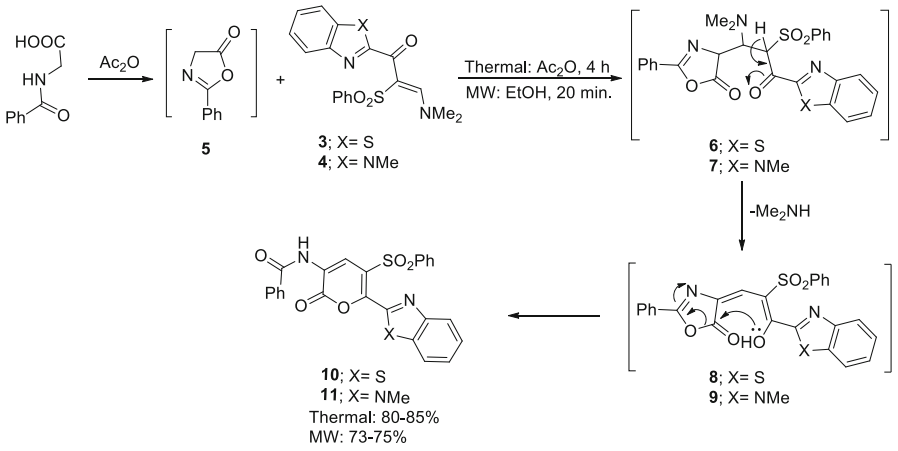
The enaminones **3** and **4** were readily obtained by the reaction of equimolar quantities of 1-(benzothiazothiazol-2-yl)-2-phenylsulfonyl-1-ethanone (**1**) or 1-(1-methyl-1*H*-benzimidazol-2-yl)-2-(phenylsulfonyl)-1-ethanone (**2**) with *N*,*N*-dimethylformamide dimethyl acetal in toluene at reflux or under microwave conditions (Scheme 1). The structures of compounds **3** and **4** were established from their elemental analyses and spectral data. For example, the proton nuclear magnetic resonance (^1H NMR) spectrum of compound **4** displayed a singlet signal at 3.05 ppm due to *N*,*N*-dimethyl protons, a singlet signal at 4.02 ppm due to an *N*-methyl group, a singlet at 7.87 ppm due to an olefinic proton, in addition to an aromatic multiplet in the region 7.35–8.03 ppm.

The reactivity of the enaminosulfones **3** and **4**, in general, can be attributed to the fact that they have two electron-poor centers at C-1 and C-3, in addition to one electron-rich center at C-2 due to the delocalization of the lone pair of electrons on the nitrogen atom beside conjugation with the sulfone group.

Thus, treatment of the enaminones **3** and **4** with *N*-benzoylglycine in acetic anhydride at reflux temperature or under microwave conditions, led to the formation of products identified as *N*-(6-(benzothiazol-2-yl)-2-oxo-5-(phenylsulfonyl)-2*H*-pyran-3-yl)benzamide (**10**) and *N*-(6-(1-methyl-1*H*-benzimidazol-2-yl)-2-oxo-5-(phenylsulfonyl)-2*H*-pyran-3-yl)benzamide (**11**), respectively (Scheme 2). The

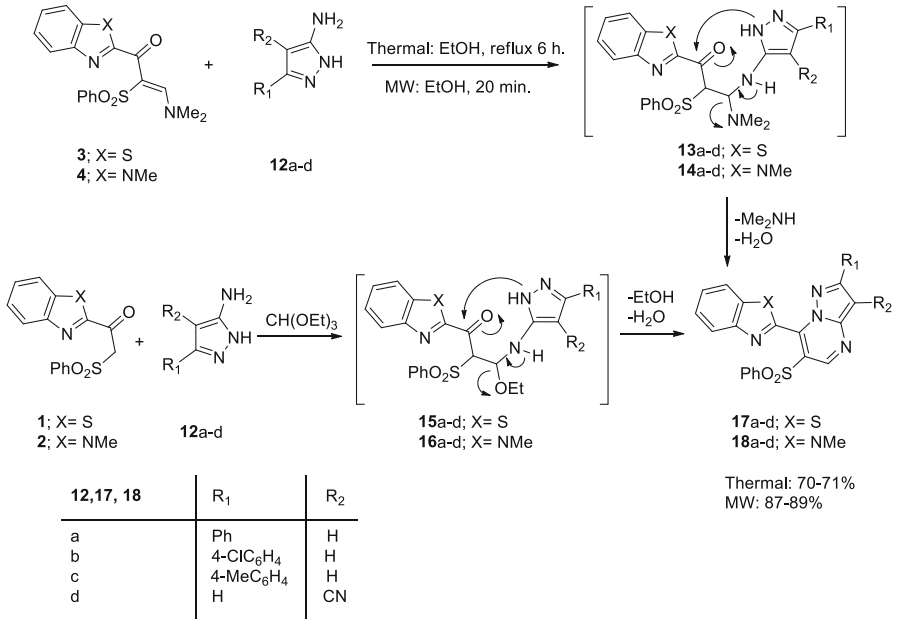


Scheme 1 Synthesis of the enaminones **3** and **4**



Scheme 2 Synthetic route to the compounds **10** and **11**

infrared (IR) spectra of the isolated products showed, in each case, two strong absorption bands at 1699 and 1672 cm^{-1}, due to two carbonyl groups and a strong absorption band at 3410 cm^{-1} due to the function of NH. Their mass spectra showed, in each case, a peak corresponding to the molecular ion. The ^{1}H NMR spectrum of compound **11** revealed a singlet signal at 4.02 ppm due to *N*-methyl



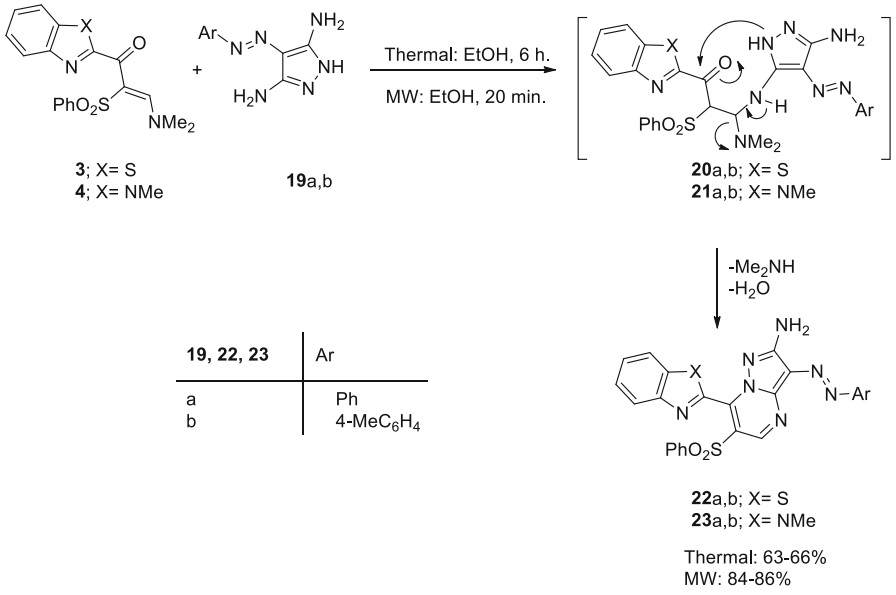
12,17, 18	R_1	R_2
a	Ph	H
b	4-ClC_6H_4	H
c	4-MeC_6H_4	H
d	H	CN

Scheme 3 Synthetic routes to pyrazolo[1,5-*a*]pyrimidine derivatives **17a–d** and **18a–d**

protons, a singlet signal at 6.30 ppm due a proton of the oxopyran ring and a multiplet signal in region of 7.51–8.14 ppm due to aromatic protons.

When the enaminone derivatives **3** and **4** were treated with substituted 5-amino-1*H*-pyrazole derivatives **12a–d** in ethanol (EtOH) in the presence of a catalytic amount of piperidine at reflux temperature or microwave conditions, they afforded the corresponding pyrazolo[1,5-*a*]pyrimidine derivatives **17a–d** and **18a–d**, respectively, in almost quantitative yields (Scheme 3). The ^{1}H NMR spectrum of compound **17a** showed a singlet signal at 9.25 ppm due to a pyrimidine CH-5 proton in addition to aromatic protons as a multiplet at 7.44–8.38 ppm. The IR spectrum of the same product revealed no peak due to carbonyl absorption. The IR spectrum of compounds **17d** and **18d** revealed, in each case, a band at 2194 cm^{-1} due to CN absorption (see "Experimental" section). The structures of compounds **17a–d** and **18a–d** were further supported by their independent synthesis from the reaction of compounds **1** and **2** with the heterocyclic amines **12a–d** and triethyl orthoformate in the presence of a catalytic amount of piperidine in a one pot reaction, which afforded products identical in all respects [melting point (m.p.), mixed m.p., and IR spectra)] with those obtained from the reaction of enaminones **3** and **4** with 5-amino-1*H*pyrazole derivatives (Scheme 3).

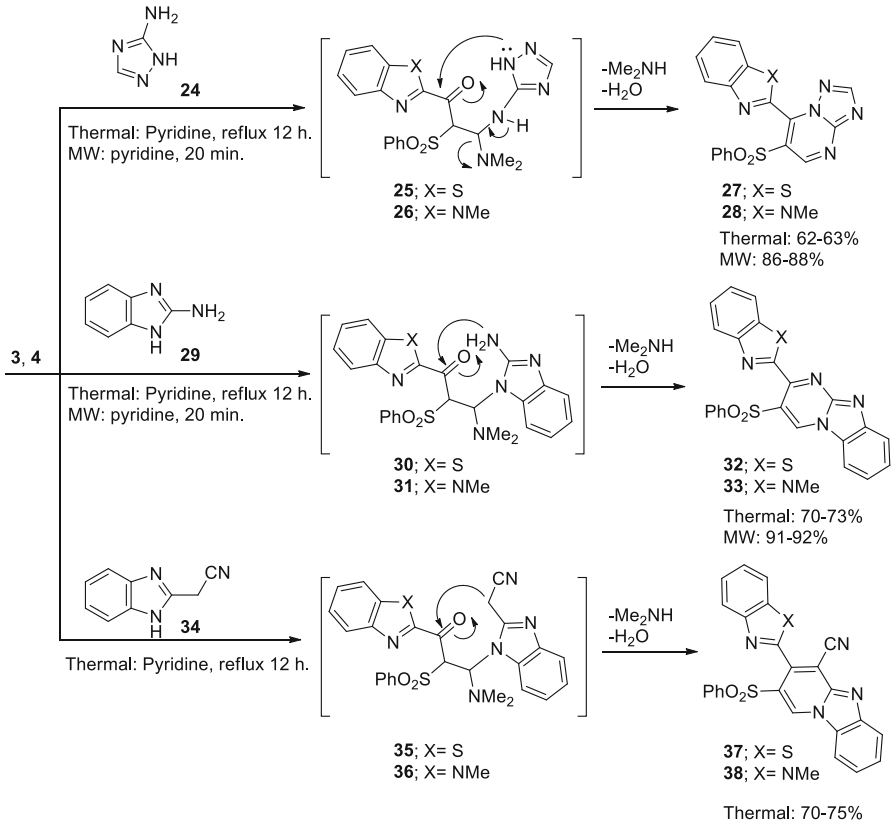
Similarly, the enaminosulfones **3** and **4** reacted with 4-arylazo-3,5-diaminopyrazoles **19a**,**b** under the same experimental conditions, to afford the corresponding polysubstituted pyrazolo[1,5-*a*]pyrimidines **22a**,**b** and **23a**,**b**, respectively (Scheme 4). The structures of products **22a**,**b** and **23a**,**b** were established on the basis of their elemental analyses and spectral data (see "Experimental" section).



Scheme 4 Synthesis of pyrazolo[1,5-*a*]pyrimidines **22a**,**b** and **23a**,**b**

The enaminones **3** and **4** reacted also with 3-amino-1,2,4-triazole (**24**) in refluxing pyridine to afford 2-(6-phenylsulfonyl-[1,2,4]-triazolo[1,5-*a*]pyrimidin-7-yl)benzothiazole (**27**) and 7-(1-methyl benzimidazol-2-yl)-6-(phenylsulfonyl)-[1,2,4]-triazolo[1,5-*a*]pyrimidine (**28**), respectively (Scheme 5). The ^{1}H NMR spectrum of compound **27** revealed a singlet signal at 9.11 ppm due to a pyrimidine CH-5 proton in addition to aromatic protons as a multiplet in the region of 7.21–8.13 ppm. The IR spectrum of the same compound revealed the absence of a band corresponding to a carbonyl group. A plausible mechanism for the formation of compounds **27** and **28** is outlined in (Scheme 5). Compounds **27** and **28** were assumed to be formed via an initial Michael-type addition of the amino group of 3-amino-1,2,4-triazole (**24**) to the activated double bond in enaminones **3** and **4** followed by elimination of dimethylamine and water molecules from the non-isolable intermediates **25** and **26** to afford the final products **27** and **28**, respectively (Scheme 5).

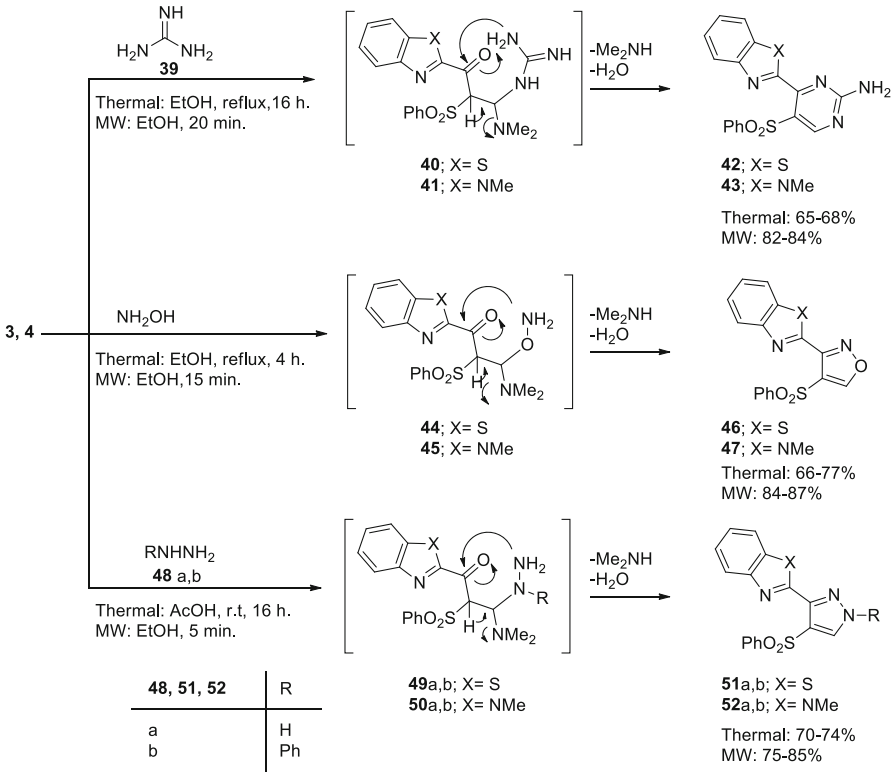
In contrast to its behavior towards the aminoheterocycles **12a**–**d**, **19a**,**b** and **24**, the enaminones **3** and **4** reacted with 2-aminobenzimidazole (**29**) in refluxing pyridine or under microwave conditions to afford, in each case, only one isolable



Scheme 5 Synthetic routes to fused ring heterocycles **27**, **28**, **32**, **33**, **37**, and **38**

product [as examined by thin-layer chromatography (TLC)]. The reaction products were identified as 3-(benzothiazol-2-yl)-2-(phenylsulfonyl)pyrimido[1,2-*a*]benzimidazole (**32**) and 3-(1-methylbenzimidazol-2-yl)-2-(phenylsulfonyl)pyrimido[1,2-*a*]benzimidazole (**33**), respectively (Scheme 5). The spectral data of the isolated products **32** and **33** were in complete agreement with the assigned structures. For example, the IR spectra of **32** and **33** revealed no absorption bands due to amino or carbonyl functions. Moreover, their ^{1}H NMR spectra revealed an aromatic multiplet in the region 7.45–8.75 ppm and a singlet signal at 9.21 ppm due to a pyrimidine proton. The formation of compounds **32** and **33** was assumed to take place via an initial Michael-type addition of the imino function (endocyclic nitrogen) [38, 39] in compound **29** to the double bond in the enaminones **3** and **4** to give the acyclic non-isolable intermediates **30** and **31**, respectively, which undergo intramolecular cyclization via the loss of dimethylamine and water molecules to afford the final products **32** and **33** (Scheme 5).

In a similar manner, the enaminones **3** and **4** reacted with 1*H*-benzimidazol-2-yl-acetonitrile (**34**) in refluxing pyridine to afford, in each case, only one isolable product (as examined by TLC). The reaction products were identified as 3-(benzothiazol-2-yl)-2-(phenylsulfonyl)pyrido[1,2-*a*]benzimidazole-4-carbonitrile



Scheme 6 Synthetic routes to the pyrimidines **42**, **43**, isoxazoles **46**, **47** and pyrazoles **51**, **52**

(**37**) and 3-(1-methylbenzimidazol-2-yl)-2-(phenylsulfonyl)pyrido-[1,2-*a*]benzimidazole-4-carbonitrile (**38**), respectively (Scheme 5). The IR spectra of the products **37** and **38** showed a characteristic absorption band at 2233 cm^{-1} due to the cyano function and revealed the absence of absorption bands corresponding to carbonyl groups.

The reaction of enaminones **3** and **4** with guanidine (**39**), liberated in situ from guanidine nitrate in the presence of two equivalents of sodium ethoxide, under refluxing or microwave conditions, resulted in the formation of high yields of 4-(benzthiazol-2-yl)-5-(phenylsulfonyl)pyrimidin-2-amine (**42**) and 4-(1-methyl-1*H*-benzimidazol-2-yl)-5-(phenylsulfonyl)pyrimidin-2-amine (**43**), respectively (Scheme 6). The IR spectra of the reaction products showed two absorption bands near 3367 and 3120 cm^{-1} due to an amino group. Plausible mechanisms for the formation of compounds **42** and **43** are outlined in Scheme 6. When the enaminones **3** and **4** were treated with hydroxylamine at reflux or under microwave conditions, they afforded, in each case, only one isolable product. The isolated products were identified as 3-(benzothiazol-2-yl)-4-(phenylsulfonyl)isoxazole (**46**) and 3-(1-methylbenzimiazol-2-yl)-4-(phenylsulfonyl)isoxazole (**47**), respectively (Scheme 6). The IR spectra of the isolated products revealed, in each case, no bands due to amino or carbonyl functions. Moreover, the ^{1}H NMR spectra of compounds **46** and **47** revealed, in each case, a singlet signal at 8.87 ppm due to an isoxazole proton, in addition to an aromatic multiplet in the region 7.38–8.14 ppm.

Similarly, the enaminones **3** and **4** underwent cyclocondensation upon treatment with hydrazine hydrate or phenylhydrazine in acetic acid at room temperature (rt), or under microwave conditions to afford 2-(1*H*-pyrazol-3-yl)-4-(phenysulfonyl)benzothiazole (**51a**), 2-(1*H*-pyrazol-3-yl)-4-(phenysulfonyl)-1-methylbenzimidazole (**51b**), 2-(1-phenylpyrazol-3-yl)-4-(phenylsulfonyl)-(benzothiazole) (**52a**) and 2-(1-phenylpyrazol-3-yl)-4-(phenylsulfonyl)-1-methylbenzimidazole (**52b**), respectively (Scheme 6). The IR spectra of the isolated products showed, in each case, an NH absorption band near 3132 cm^{-1}. The ^{1}H NMR spectra of the compounds **51a**,**b** and **52a**,**b** revealed, in each case, a singlet signal at 7.53 and 7.88 ppm due to pyrazole protons, and showed a D_2O-exchangeable signal at 12.22 ppm due to an NH proton in case of **51a**,**b,** in addition to an aromatic multiplet in the range 7.20–8.23 ppm.

Experimental

Melting points were determined in open glass capillaries with a Gallenkamp apparatus. The IR spectra were recorded using potassium bromide (KBr) disks on a Pye Unicam SP 3-300 or a Shimadzu Fourier transform-IR spectrophotometer (FTIR 8101 PC). The NMR spectra were recorded with a Varian Mercury VXR-300 NMR spectrometer at 300 and 75 MHz [^{1}H and carbon-13 (^{13}C) NMR spectra, respectively) using deuterated chloroform ($CDCl_3$) and deuterated dimethyl sulfoxide (DMSO-*d*6) as solvents. Chemical shifts were related to that of the solvent. Mass spectra [electron ionization (EI)] were obtained at 70 eV with a Shimadzu GCMQP 1000 EX spectrometer. TLC analyses were performed using

pre-coated silica gel 60,778 plates (Fluka), and the spots were visualized with ultraviolet (UV) light at 254 nm. Fluka silica gel 60,741 (70–230 mesh) was used for flash column chromatography. Microwave experiments were carried out using a CEM Discover LabMate microwave apparatus (300 W with ChemDriver Software). 1-(Benzothiazol-2-yl)-2-phenylsulfonyl-1-ethanone (**1**) and 1-(1-methyl-1*H*-benzimidazol-2-yl)-2-(phenylsulfonyl)-1-ethanone (**2**) [27], 5-aminopyrazole derivatives **12a–d** [40], 1,5-diamino-4-arylazo-pyrazoles (**19a**,**b**) [41], 2-cyanomethylbenzimidazole (**34**) [42] were prepared following procedures in the literature.

Reactions of 1-(benzothiazol-2-yl)-2-phenylsulfonyl-1-ethanone (1) and 1-(1-methyl-1*H*-benzimidazol-2-yl)-2-(phenylsulfonyl)-1-ethanone (2) with *N*,*N*-dimethylformamide dimethyl acetal

Method A (thermal)

General procedure To a solution of 1-(benzothiazothiazol-2-yl)-2-phenylsulfonyl-1-ethanone (**1**) or 1-(1-methyl-1*H*-benzimidazol-2-yl)-2-(phenylsulfonyl)-1-ethanone (**2**; 100 mmol), in dry toluene (150 mL), was added *N*,*N*-dimethylformamide dimethyl acetal (13.4 g, 100 mmol) and the mixture was refluxed for 8 h. The solvent was removed at reduced pressure and the residual reddish-brown viscous liquid was taken in petroleum ether (bp. 60–80 °C, 20 mL). The resulting golden-yellow crystal was collected by filtration, washed thoroughly with ether, dried and finally recrystallized from dry benzene to afford the 1-(benzothiazol-2-yl)-3-(*N*,*N*-dimethylamino)-2-(phenylsulphonyl)prop-2-en-1-one (**3**) and 1-(1-methylbenzimidazol-2-yl)-3-(*N*,*N*-dimethylamino)-2-(phenylsulphonyl)prop-2-en-1-one (**4**), respectively.

Method B (microwave)

General procedure To a solution of compound **1** or **2** (1 mmol) in dry toluene (1.5 mL) was added *N*,*N*-dimethylformamide dimethyl acetal (0.134 g, 1 mmol), followed by mixing in a process vial. The vial was capped properly and irradiated with a microwave under 17.2 bar, at 130 °C for 20 min. The solvent was evaporated in vacuo and the residual reddish-brown viscous liquid was taken in petroleum ether (bp 60–80 °C, 20 mL). The resulting golden-yellow crystals were collected by filtration, washed thoroughly with ether, dried and finally recrystallized from dry benzene to afford **3** and **4**, respectively.

1-(Benzothiazol-2-yl)-3-(N,N-dimethylamino)-2-(phenylsulfonyl)prop-2-en-1-one (**3**) Yield (A, 88 %); (B, 94 %); m.p.: 144–146 °C; IR (KBr): *v* 1645 (C=O), 1599 (C=N), 1325, 1160 SO_2 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.05 (s, 6H, $N(CH_3)_2$), 7.35–8.03 (m, 9H, Ar–H), 7.87 (s, 1H, =CH–N); ^{13}C NMR (75 MHz, DMSO-d_6): δ 43.17, 102.23, 121.59, 124.47, 125.26, 128.35, 129.71, 133.69, 136.19, 141.56, 149.46, 154.05, 156.96, 182.42; MS: *m/z* 372 [M^+] (100); Anal. calcd. for $C_{18}H_{16}N_2O_3S_2$, (%): C, 58.04; H, 4.33; N, 7.52; S 17.22; found, (%): C 57.96; H, 4.28; N, 7.49; S, 17.18.

1-(1-Methyl-1H-benzimidazol-2-yl)-3-(N,N-dimethylamino)-2-(phenylsulfonyl)prop-2-en-1-one (**4**) Yield (A, 83 %); (B, 92 %); m.p.: 150–152 °C; IR (KBr): *v* 1645 (C=O), 1599 (C=N), 1325,1160 SO_2 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 3.05 (s, 6H, $N(CH_3)_2$), 4.02 (s, 3H, NCH_3), 7.35–7.98 (m, 9H, Ar–H), 7.87 (s, 1H, =CH–N); ^{13}C NMR (75 MHz, DMSO-d_6): δ 32.37, 43.09, 101.23, 110.88, 115.2, 123.07, 128.3, 129.71. 133.69, 135.56, 138.69, 149.46, 141.46, 154.05, 186.42; MS: *m/z* 369 [M^+] (100); Anal. calcd. for $C_{19}H_{19}N_3O_3S$, (%): C, 61.77; H, 5.18; N, 11.37; S, 8.68; found, (%): C, 61.71; H, 5.19; N, 11.29; S, 8.61.

Reactions of enaminosulfone 3 and 4 with *N*-benzoylglycine

Method A (thermal)

General procedure A solution of the appropriate enaminones **3** or **4** (10 mmol) and *N*-benzoylglycine (1.7 g, 10 mmol) in acetic anhydride (20 mL) was refluxed for 4 h. The reaction mixture was concentrated in vacuo and the formed solid product upon cooling was filtered off, washed with EtOH, dried and finally recrystallized from dimethylformamide (DMF) to afford *N*-(6-(benzothiazol-2-yl)-2-oxo-5-(phenylsulfonyl)-2*H*-pyran-3-yl)benzamide **(10)** and *N*-(6-(1-metyl1*H*-benzoimidazol-2-yl)-2-oxo-5-(phenylsulfonyl)-2*H*-pyran-3-yl)benzamide **(11)**, respectively.

Method B (microwave)

General procedure An ethanolic solution of the appropriate enaminones **3** or **4** (10 mmol) and *N*-benzoylglycine (1.7 g, 10 mmol) was mixed in a process vial. The vial was capped properly and irradiated with microwave under 17.2 bar, at 80 °C for 20 min, The reaction mixture was concentrated in vacuo and the solid product, obtained upon cooling, was filtered off, washed with EtOH, dried and recrystallized from DMF to afford the corresponding 2*H*-pyran-3-yl-benzamide derivatives **10** and **11**, respectively.

N-(6-(benzothiazol-2-yl)-2-oxo-5-(phenylsulfonyl)-2H-pyran-3-yl-benzamide (**10**) Yield (A, 75 %); (B, 85 %); m.p.: 203–204 °C; IR (KBr): *v* 3410 (NH), 1699 (C=O), 1672 (C=O), 1591 (C=N), 1160 SO_2 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 6.30 (s, pyran-3-CH), 7.51–8.14 (m, 14H, ArH), 9.61 (s, 1H, NH, D_2O exchangable); MS: *m/z* 488 [M^+] (100); Anal. calcd. for $C_{25}H_{16}N_2O_5S_2$, (%): C, 61.46; H, 3.30; N, 5.73; S, 13.13; found, (%): C, 61.51; H, 3.27; N, 5.68; S, 13.08.

N-(6-(1-methyl-1H-benzimidazol-2-yl)-2-oxo-5-(phenylsulfonyl)-2H-pyran-3-yl-benzamide (**11**) Yield (A, 73 %); (B, 80 %); m.p.: >300 °C; IR (KBr): *v* 3410 (NH), 1710 (C=O), 1675 (C=O), 1585 (C=N), 1160 SO_2 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.02 (s, 3H, NCH_3), 6.30 (s, 1H, pyran-3-CH), 7.51–8.04 (m, 14H, ArH), 9.61 (s, 1H, NH, D_2O exchangeable); MS: *m/z* 485 [M^+] (100); Anal. calcd. for $C_{26}H_{19}N_3O_5S$, (%): C, 64.32; H, 3.94; N, 8.65; S, 6.60; found, (%): C, 64.29; H, 3.95; N, 8.67; S, 6.55.

Reactions of compounds 3 and 4 with 5-amino substituted pyrazoles 12a–d and 19a,b

Method A (thermal)

General procedure To a mixture of the appropriate enaminones **3** or **4** (10 mmol) and the appropriate aminopyrazole derivative **12** or **19** (10 mmol), in absolute EtOH (25 mL), a few drops of piperidine were added and the reaction mixture was refluxed for 6 h then allowed to cool. The solid product was filtered off, washed with EtOH, dried, and recrystallized from EtOH/DMF to afford the corresponding pyrazolo[1,5-*a*]pyrimidine derivatives **17a–d**, **18a**–**d**, **22a**,**b** and **23a**,**b**, respectively.

Method B (mi2crowave)

General procedure The appropriate enaminones **3** or **4** (1 mmol) and the appropriate aminopyrazole derivatives **12** or **19** (1 mmol), in absolute EtOH (2.5 mL), and a few drops of piperidine were mixed in a process vial. The vial was capped properly and irradiated with microwaves under conditions of 17.2 bars, at 80 °C for 20 min then left to cool. The solid product was filtered off, washed with EtOH and recrystallized from EtOH/DMF to afford the corresponding pyrazolo[1,5-*a*]pyrimidine derivatives **17a**, **18a**, **22a** and **23a**, respectively.

2-(2-Phenyl-6-(phenylsulfonyl)pyrozolo[1,5-a]pyrimidin-7-yl)benzothiazole (**17a**) Yield (A, 71 %); (B, 89 %); m.p.: 228–230 °C; IR (KBr): *v* 1596 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.07 (s, 1H, pyrazole-3-CH), 7.44–8.38 (m, 14H, ArH), 9.25 (s, pyrimidine-5-CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 93.31, 121.52, 121.78, 124.32, 125.98, 127.32, 128.53, 128.13, 129.48, 129.12, 131.31, 133.08, 133.21, 133.94, 141.54, 148.05, 153.65, 154.72, 156.31, 155.31, 162.81; MS: *m/z* 468 [M^+] (11); Anal. calcd. for $C_{25}H_{16}N_4O_2S_2$, (%): C, 64.08; H, 3.44; N, 11.96; S, 13.69; found, (%): C, 63.98; H, 3.52; N, 11.91; S, 13.61.

2-(2-(4-Chlorophenyl-6-(phenylsulfonyl)pyrozolo[1,5-a]pyrimidin-7-yl)benzothiazole (**17b**) Yield (A, 75 %); m.p.: 224–226 °C; IR (KBr): *v* 1595 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 6.71 (s, 1H, pyrazole-3-CH), 7.45–8.17 (m, 13H, ArH), 9.22 (s, pyrimidine-5-CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 95.72, 122.49, 122.68, 123.73, 126.86, 126.95, 127.65, 128.22, 129.02, 129.28, 129.97, 133.99, 134.66, 136.73, 140.13, 141.21, 148.41, 150.40, 151.46, 153.84, 157.37; MS: *m/z* 502 [M^+] (100); Anal. calcd. for $C_{25}H_{15}N_4ClO_2S_2$, (%): C, 59.70; H, 3.01; N, 11.14; S, 12.75; found, (%): C, 59.62; H, 3.12; N, 11.10; S, 12.69.

2-(6-Phenylsulfonyl)-2-(4-methylphenyl)pyrazolo[1,5-a]pyrimidin-7-yl)benzothiazole (**17c**) Yield (A, 72 %); m.p.: 190–192 °C; IR (KBr): *v* 1594 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 2.31 (s, 3H, CH_3), 6.69 (s, 1H, pyrazole-3-CH), 7.29–8.20 (m, 13H, ArH), 9.24 (s, pyrimidine-5-CH); MS: *m/z* 482 [M^+] (100); Anal. calcd. for $C_{26}H_{18}N_4O_2S_2$, (%): C, 64.71; H, 3.76; N, 11.61; S, 13.29; found, (%): C, 64.68; H, 3.72; N, 11.66; S, 13.31.

7-(Benzothiazol-2-yl)-6-(phenylsulfonyl)pyrozolo[1,5-a]pyrimidine-3-carbonitrile (**17d**) Yield (A, 73 %); m.p.: 128–130 °C; IR (KBr): *v* 1596 (C=N), 2194 (C≡N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 8.77 (s, 1H, pyrazole-2-CH), 7.43–8.20 (m, 9H, ArH), 9.25 (s, pyrimidine-5-CH); MS: *m/z* 417 [M^+] (100); Anal. calcd. for $C_{20}H_{11}N_5O_2S_2$, (%): C, 57.54; H, 2.66; N, 16.78; S, 15.36; found, (%): C, 57.52; H, 2.59; N, 16.79; S, 15.37.

7-(1-Methyl-1H-benzimidazol-2-yl)-2-phenyl-6-(phenylsulfonyl)pyrazolo[1,5-a]pyrimidine (**18a**) Yield (A, 68 %); (B, 85 %); m.p.: 260–262 °C; IR (KBr): *v* 1596 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.02 (s, 3H, NCH_3), 6.71 (s, 1H, pyrazole-3-CH), 7.21–8.07 (m, 14H, ArH), 9.23 (s, pyrimidine-5-CH); MS: *m/z* 465 [M^+] (100); Anal. calcd. for $C_{26}H_{19}N_5O_2S$, (%): C, 67.08; H, 4.11; N, 15.04; S, 6.89; found, (%): C, 66.99; H, 4.12; N, 15.11; S, 6.83.

2-(4-Chlorophenyl)-7-(1-methyl-1H-benzimidazol-2-yl)-6-(phenylsulfonyl)pyrazolo[1,5-a]pyrimidine (**18b**) Yield (A, 70 %); m.p.: 254–256 °C; IR (KBr): *v* 1596 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.01 (s, 3H, NCH_3), 6.69 (s, 1H, pyrazole-3-CH), 7.51–8.09 (m, 13H, ArH), 9.22 (s, pyrimidine-5-CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 32.05, 93.57, 110.50, 121.44, 122.28, 123.95, 126.45, 127.87, 127.96, 128.59, 128.98, 129.23, 130.11, 131.86, 134.03, 137.02, 140.66, 142.09, 147.33, 152.13, 153.74, 158.61; MS: *m/z* 499 [M^+] (100); Anal. calcd. for $C_{26}H_{18}N_5ClO_2S$, (%): C, 62.46; H, 3.63; N, 14.01; S, 6.41; found, (%): C, 62.52; H, 3.52; N, 14.10; S, 6.49.

2-(4-Methylphenyl)-7-(1-methyl-1H-benzimidazol-2-yl)-6-(phenylsulfonyl)pyrazolo[1,5-a]pyrimidine (**18c**) Yield (A, 77 %) (A); m.p.: 200–202 °C; IR (KBr): *v* 1595 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 2.31 (s, 3H, CH_3), 4.02 (s, 3H, NCH_3), 6.65 (s, 1H, pyrazole-3-CH), 7.21–8.06 (m, 13H, ArH), 9.21 (s, pyrimidine-5-CH); MS: *m/z* 479 [M^+] (100); Anal. calcd. for $C_{27}H_{21}N_5O_2S$, (%): C, 67.62; H, 4.41; N, 14.60; S, 6.69; found, (%): C, 67.68; H, 4.39; N, 14.62; S, 6.61.

7-(1-Methyl-1H-benzimidazol-2-yl)-6-(phenylsulfonyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile (**18d**) Yield (A, 70 %); m.p.: >300 °C; IR (KBr): *v* 1594 (C=N), 2194 (C≡N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.02 (s, 3H, NCH_3), 8.56 (s, 1H, pyrazole-2-CH), 7.21–8.05 (m, 9H, ArH), 9.22 (s, pyrimidine-5-CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 32.03, 62.62, 111.70, 120.61, 121.43, 123.94, 126.44, 127.95, 129.22, 134.01, 137.05, 139.42, 140.83, 142.32, 145.22, 150.89, 155.72, 162.36; MS: *m/z* 414 [M^+] (100); Anal. calcd. for $C_{21}H_{14}N_6O_2S$, (%): C, 60.86; H, 3.40; N, 20.28; S, 7.74; found, (%): C, 60.92; H, 3.32; N, 20.19; S, 7.73.

2-Amino-7-(benzothiazol-2-yl)-3-(phenylazo)-6-(phenylsulfonyl)pyrazolo[1,5-a]pyrimidine (**22a**) Yield (A, 66 %); (B, 86 %); m.p.: 268–270 °C; IR (KBr): *v* 3398, 3277 (NH_2), 1588 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 6.48 (s, 2H, NH_2, D_2O exchangeable), 7.44–8.22 (m, 14H, ArH), 9.23 (s, pyrimidine-5-CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 77.73, 119.00, 121.73, 123.25, 125.31, 126.85, 127.67, 128.02, 128.53, 128.96, 129.29, 134.17, 139.23, 149.31, 152.41, 152.50, 153.64, 155.17, 157.88; MS: *m/z* 511 [M^+] (100); Anal. calcd. for $C_{25}H_{17}N_7O_2S_2$,

(%): C, 58.69; H, 3.35; N, 19.17; S, 12.54; found, (%): C, 58.66; H, 3.28; N, 19.22; S, 12.42.

2-Amino-7-(benzothiazol-2-yl)-6-(phenylsulfonyl)-3-(4-methylphenylazo)pyrazolo[1,5-a]pyrimidine (**22b**) Yield (A, 68 %); m.p.: 224–226 °C; IR (KBr): *v* 3408, 3297 (NH_2), 1588 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 2.30 (s, 3H, CH_3), 6.68 (s, 2H, NH_2, D_2O exchangeable), 7.43–8.20 (m, 14H, ArH), 9.25 (s, pyrimidine-5-CH); MS: *m/z* 525 [M^+] (100); Anal. calcd. for $C_{26}H_{19}N_7O_2S_2$, (%): C, 59.41; H, 3.64; N, 18.65; S, 12.20; found, (%): C, 59.39; H, 3,62; N, 18.67; S, 12.23.

2-Amino-7-(1-methyl-1H-benzimidazol-2-yl)-3-(phenylazo)-6-(phenylsulfonyl)pyrazolo[1,5-a]pyrimidine (**23a**) Yield (A, 63 %); (B, 84 %); m.p.: 182–184 °C; IR (KBr): *v* 3391, 3276 (NH_2), 1584 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.02 (s, 3H, NCH_3), 6.48 (s, 2H, NH_2, D_2O exchangeable), 7.33–8.04 (m, 14H, ArH), 9.21 (s, pyrimidine-5-CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 32.06, 77.90, 111.74, 121.44, 123.95, 126.45, 127.96, 128.39, 129.24, 131.26, 134.03, 137.07, 139.42, 140.84, 145.24, 150.47, 152.91, 154.80, 157.01; MS: *m/z* 508 [M^+] (100); Anal. calcd. for $C_{26}H_{20}N_8O_2S$, (%): C, 61.41; H, 3.96; N, 22.03; S, 6.31; found, (%): C, 61.39; H, 3.88; N, 22.02; S, 6.29.

2-Amino-7-(1-methyl-1H-benzimidazol-2-yl)-6-(phenylsulfonyl)-3-(4-methylphenylazo)pyrazolo[1,5-a]pyrimidine (**23b**) Yield (A, 70 %); m.p.: 214–216 °C; IR (KBr): *v* 3408, 3297 (NH_2), 1585 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 2.33 (s, 3H, CH_3), 4.02 (s, 3H, NCH_3), 6.68 (s, 2H, NH_2, D_2O exchangeable), 7.34–8.04 (m, 14H, ArH), 9.20 (s, pyrimidine-5-CH); MS: *m/z* 522 [M^+] (100); Anal. calcd. for $C_{27}H_{22}N_8O_2S$, (%): C, 62.06; H, 4.24; N, 21.44; S, 6.14; found, (%): C, 61.98; H, 4.18; N, 21.51; S, 6.24.

Reactions of the enaminones 3 and 4 with 3-amino-1,2,4-triazole (24), 2-aminobenzimidazole (29) and with 2-cyanomethylbenzimidazole (34)

Method A (thermal)

General procedure A mixture of the appropriate enaminones **3** or **4** (10 mmol) and the appropriate heterocyclic amine **24**, **29** or **34** (10 mmol) in pyridine (25 mL) was refluxed for 12 h, then left to cool. The solvent was evaporated in vacuo and the residual solid was taken in EtOH then collected by filtration, washed with water, dried and finally recrystallized from DMF/H_2O to afford the corresponding triazolo[1,5-*a*]pyrimidine, pyrimido[1,2-*a*]benzimidazole, pyrido[1,2-*a*]benzimidazole derivatives **27**, **28**, **32**, **33**, **37** and **38**, respectively.

Method B (microwave)

General procedure The appropriate enaminones **3** or **4** (1 mmol) and the appropriate heterocyclic amine **24** or **29** (1 mmol) in pyridine (2.5 mL) were mixed in a process vial. The vial was capped properly and irradiated with

microwaves under conditions of 17.2 bars, at 130 °C for 20 min. The solvent was evaporated in vacuo and the residual solid was taken in EtOH then collected by filtration, washed with water, dried and finally recrystallized from DMF/H_2O to afford the corresponding triazolo[1,5-*a*]pyrimidine or pyrimido[1,2-*a*]benzimidazole derivatives **27**, **28**, **32** and **33**, respectively.

2-(6-(Phenylsulfonyl)-[1,2,4]triazolo[1,5-a]pyrimidin-7-yl)benzothiazole (**27**) Yield (A, 65 %); (B, 88 %); m.p.: 154–156 °C; IR (KBr): *v* 1611 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.21–8.13 (m, 9H, ArH), 8.60 (s, 1H, triazole-2-CH), 9.11 (s, pyrimidine-5-CH); MS: *m/z* 393 [M^+] (100); Anal. calcd. for $C_{18}H_{11}N_5O_2S_2$, (%): C, 54.95; H, 2.82; N, 17.80; S, 16.30; found, (%): C, 54.89; H, 2.86; N, 17.83; S, 16.26.

7-(1-Methyl-1H-benzimidazol-2-yl)-6-(phenylsulfonyl)-[1,2,4]triazolo[1,5-a]pyrimidine (**28**) Yield (A, 62 %); (B, 84 %); m.p.: 204–206 °C; IR (KBr): *v* 1611 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.02 (s, 3H, NCH_3), 7.21–7.95 (m, 9H, ArH), 8.60 (s, 1H, triazole-2-CH), 9.10 (s, pyrimidine-5-CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 32.06, 111.73, 120.41, 121.44, 123.95, 126.45, 127.96, 129.24, 134.03, 137.07, 139.43, 140.84, 145.24, 151.68, 153.53, 156.46, 159.22; MS: *m/z* 390 [M^+] (100), 196 (55), 77 (32); Anal. calcd. for $C_{19}H_{14}N_6O_2S$, (%): C, 58.45; H, 3.61; N, 21.53; S, 8.21; found, (%): C, 58.37; H, 3.66; N, 21.51; S, 8.24.

2-(Benzothiazol-2-yl)-3-(phenylsulfonyl)pyrimido[1,2-a]benzimidazole (**32**) Yield (A, 73 %); (B, 92 %); m.p.: 262–264 °C; IR (KBr): *v* 1620 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.57–8.75 (m, 13H, ArH), 9.21 (s, pyrimidine-1-CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 114.33, 118.72, 119.79, 120.60, 122.59, 123.52, 123.78, 126.93, 127.23, 127.37, 127.82, 128.64, 132.98, 135.55, 142.53, 143.74, 145.51, 151.11, 152.93, 163.95; MS: *m/z* 442 [M^+] (100); Anal. calcd. for $C_{23}H_{14}N_4O_2S_2$, (%): C, 62.43; H, 3.19; N, 12.66; S, 14.49; found, (%): C, 62.41; H, 3.25; N, 12.59; S, 14.52.

2-(1-Methylbenzimidazol-2-yl)-3-(phenylsulfonyl)pyrimido[1,2-a]benzimidazole (**33**) Yield (A, 70 %); (B, 86 %); m.p.: 244–246 °C; IR (KBr): *v* 1620 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.05 (s, 3H, NCH_3), 7.45–8.53 (m, 13H, ArH), 9.23 (s, pyrimidine-1-CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 31.55, 111.66, 114.62, 118.71, 120.58, 123.66, 126.44, 128.16, 129.09, 130.20, 133.22, 135.45, 141.21, 142.38, 142.51, 143.50, 150.56, 151.29, 155.34, 161.45; MS: *m/z* 439 [M^+] (100), 150 (12), 102 (13); Anal. calcd. for $C_{24}H_{17}N_5O_2S$, (%): C, 65.59; H, 3.90; N, 15.94; S, 7.30; found, (%): C, 65.54; H, 3.95; N, 15.88; S, 7.31.

3-(Benzothiazol-2-yl)-2-(phenylsulfonyl)pyrido[1,2-a]benzimidazole-4-carbonitrile (**37**) Yield (A, 75 %); m.p.: 214–216 °C; IR (KBr): *v* 2233 (C≡N), 1598 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.48–8.53 (m, 13H, ArH), 9.23 (s, 1H, pyridine-1-CH); MS: *m/z* 466 [M^+] (80), 263 (100), 161 (11); Anal. calcd. for $C_{25}H_{14}N_4O_2S_2$, (%): C, 64.36; H, 3.02; N, 12.01; S, 13.75; found, (%): C, 64.37; H, 3.05; N, 21.03; S, 13.69.

3-(1-Methylbenzimidazol-2-yl)-2-(phenylsulfonyl)pyrido[1,2-a]benzimidazole-4-carbonitrile (**38**) Yield (A, 70 %); m.p.: >300 °C; IR (KBr): *v* 2233 (C≡N), 1598 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.01 (s, 3H, NCH_3), 7.43–8.53 (m, 13H, ArH), 9.21 (s, 1H, pyridine-1-CH); MS: *m/z* 463 [M^+] (100); Anal. calcd. for $C_{26}H_{17}N_5O_2S$, (%): C, 67.37; H, 3.70; N, 15.11; S, 6.92; found, (%): C, 67.34; H, 3.66; N, 15.08; S, 6.88.

Reactions of compounds 3 and 4 with guanidine

Method A (thermal)

General procedure A solution of guanidine nitrate (1.73 g, 14.2 mmol) in absolute EtOH (15 mL) was added to a solution of the appropriate enaminones **3** or **4** (11.3 mmol) in boiling absolute EtOH (10 mL) with stirring for 20 min. To this mixture, was added sodium ethoxide solution (22.6 mmol) in absolute EtOH (10 mL) and the reaction mixture was refluxed for 16 h. The solution was allowed to cool to rt and the precipitated solid was removed by filtration. The filtrate was concentrated under reduced pressure. The solid product was collected by filtration, washed with water, dried and finally recrystallized from DMF to afford the 2-aminopyrimidine derivatives **42** and **43**, respectively.

Method B (microwave)

General procedure The appropriate enaminones **3** or **4** (2 mmol), guanidine nitrate (2.3 mmol) in EtOH (3 mL), and anhydrous potassium carbonate (4 mmol) were mixed in a process vial. The vial was capped properly and irradiated with microwaves under conditions of 17.2 bars, at 130 °C for 20 min. The reaction mixture was allowed to cool to rt then diluted with water (20 mL). The formed solid product was collected by filtration, washed with water and dried. Recrystallization from DMF afforded 2-aminopyrimidine derivative **42** and **43**, respectively.

2-Amino-4-(benzothiazol-2-yl)-5-(phenylsulfonyl)pyrimidine (**42**) Yield (A, 68 %); (B, 84 %); m.p.: 208–210 °C; IR (KBr): *v* 3367, 3120 (NH_2), 1583 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 6.97 (s, 2H, NH_2), 7.45–8.20 (m, 9H, ArH), 8.96 (s, pyrimidine-6-CH); MS: *m/z* 368 [M^+] (100); Anal. calcd. for $C_{17}H_{12}N_4O_2S_2$, (%): C, 55.42; H, 3.28; N, 15.21; S, 17.41; found, (%): C, 55.38; H, 3.30; N, 15.22; S, 17.36.

2-Amino-4-(1-methyl-1H-benzimidazol-2-yl)-5-(phenylsulfonyl)pyrimidine (**43**) Yield (A, 65 %); (B, 82 %); m.p.: >300 °C; IR (KBr): *v* 3362, 3130 (NH_2), 1583 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.02 (s, 3H, NCH_3), 6.97 (s, 2H, NH_2), 7.20–7.93 (m, 9H, ArH), 8.86 (s, pyrimidine-6-CH); MS: *m/z* 365 [M^+] (100); Anal. calcd. for $C_{18}H_{15}N_5O_2S$, (%): C, 59.16; H, 4.14; N, 19.17; S, 8.78; found, (%): C, 59.19; H, 4.11; N, 19.10; S, 8.70.

Reactions of compounds 3 and 4 with hydroxylamine

Method A (thermal)

General procedure A mixture of the appropriate enaminones **3** or **4** (10 mmol), hydroxylamine (10 mmol) and ammonium acetate (1.5 g) in EtOH (5 mL) was refluxed for 4 h. The reaction mixture was poured into ice cold water. The resulting solid product was filtered off, washed with water, dried and finally recrystallized from EtOH/DMF to afford the corresponding 3-(benzothiazol-2-yl)-4-(phenylsulfonyl)isoxazole (**46**) and 3-(1-methyl-1*H*-benzimidazol-2-yl)-4-(phenylsulfonyl) isoxazole (**47**), respectively.

Method B (microwave)

General procedure The appropriate enaminones **3** or **4** (1 mmol), hydroxylamine (1 mmol) in EtOH (0.5 mL) and ammonium acetate (0.15 g) were mixed in a process vial. The vial was capped properly and irradiated by microwaves using pressurized conditions at 17.2 bars, at 100 °C for 15 min. The reaction mixture was poured into ice cold water. The resulting solid product was filtered off, washed with EtOH, dried and finally recrystallized from EtOH/DMF to afford the corresponding isoxazole derivatives **46** and **47**, respectively.

3-(Benzothiazol-2-yl)-4-(phenylsulfonyl)isoxazole (**46**) Yield (A, 77 %); (B, 87 %); m.p.: 190–192 °C; IR (KBr): ν 1605 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 8.87 (s, 1H, isoxazole-3-CH), 7.57–8.14 (m, 9H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 94.22, 122.54, 122.94, 124.39, 125.31, 128.53, 129.27, 134.18, 135.48, 139.12, 149.16, 151.48, 155.47, 164.71; MS: *m/z* 342 [M^+] (100); Anal. calcd. for $C_{16}H_{10}N_2O_3S_2$, (%): C, 56.13; H, 2.94; N, 8.18; S, 18.73; found, (%): C, 56.09; H, 2.97; N, 8.22; S, 18.70.

3-(1-Methyl-1H-benzimidazol-2-yl)-4-(phenylsulfonyl)isoxazole (**47**) Yield (A, 66 %); (B, 84 %); m.p.: 256–258 °C; IR (KBr): ν 1605 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.10 (s, 3H, NCH_3), 8.87 (s, 1*H*, isoxazole-3-CH), 7.38–7.98 (m, 9H, ArH); MS: *m/z* 339 [M^+] (100); Anal. calcd. for $C_{17}H_{13}N_3O_3S$, (%): C, 60.17; H, 3.86; N, 12.38; S, 9.45; found, (%): C, 60.15; H, 3.89; N, 12.40; S, 9.43.

Reactions of the enaminones 3 and 4 with hydrazine and phenylhydrazine

Method A (thermal)

General procedure Hydrazine hydrate or phenylhydrazine (10.2 mmol) was added to a stirred solution of the enaminones **3** or **4** (10 mmol) in acetic acid (30 mL). Stirring was continued 16 h at rt and the solid product obtained was filtered off, washed with H_2O, dried and finally recrystallized from EtOH to afford 2-(4-

(phenysulfonyl)-*1H*-pyrazol-3-yl)benzothiazole (**51a**), 1-methyl-2-(4-(phenysulfonyl)-*1H*-pyrazol-3-yl)-1*H*-benzimidazole (**52a**) and derivatives **51b** and **52b**.

Method B (microwave)

General procedure An ethanolic solution of the enaminones **3** or **4** (1 mmol), and hydrazine (1.2 mmol) or phenylhydrazine (1.2 mmol) were mixed in a process vial. The vial was irradiated under conditions of 17.2 bar at 80 °C for 5 min, then left to cool. The solid product obtained was filtered off, washed with H_2O, dried and recrystallized from EtOH to afford the corresponding 2-(4-(phenysulfonyl)-*1H*-pyrazol-3-yl) derivatives **51a**,**b** and **52a**,**b** respectively.

2-(4-(Phenysulfonyl)-1H-pyrazol-3-yl)benzothiazole (**51a**) Yield (A, 74 %); (B, 82 %); m.p.: 198–200 °C; IR (KBr): *v* 3132 (NH), 1597 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.44–8.23 (m, 9H, ArH), 7.53 (s, 1H, pyrazole-5-CH), 12.22 (s, 1H, NH, D_2O-exchangeable); MS: *m/z* 341 [M^+] (100); Anal. calcd. for $C_{16}H_{11}N_3O_2S_2$, (%): C, 56.29; H, 3.25; N, 12.31; S, 18.78; found, (%): C, 56.34; H, 3.20; N, 12.25; S, 18.82.

2-(1-Phenyl-4-(phenysulfonyl)-1H-pyrazol-3-yl)benzothiazole (**51b**) Yield (A, 70 %); (B, 85 %); m.p.: 210–212 °C; IR (KBr): *v* 1597 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.44–8.23 (m, 14H, ArH), 7.88 (s, 1H, pyrazole-5-CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 120.20, 121.51, 121.99, 123.45, 124.77, 125.23, 125.70, 126.53, 128.01, 128.84, 129.43, 133.78, 139.18, 142.30, 150.49, 152.33, 155.34; MS: *m/z* 417 [M^+] (100); Anal. calcd. for $C_{22}H_{15}N_3O_2S_2$, (%): C, 63.29; H, 3.62; N, 10.06; S, 15.36; found, (%): C, 63.30; H, 3.58; N, 10.07; S, 15.38.

1-Methyl-2-(4-(phenylsulfonyl)-1H-pyrazol-3-yl)-1H-benzimidazole (**52a**) Yield (A, 72 %); (B, 79 %); m.p.: 276–278 °C; IR (KBr): *v* 3132 (NH), 1595 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.00 (s, 3H, NCH_3), 7.33–7.98 (m, 9H, ArH), 7.53 (s, 1H, Hz pyrazole-5-CH), 12.23 (s, 1H, NH, D_2O-exchangeable); MS: *m/z* 338 [M^+] (100); Anal. calcd. for $C_{17}H_{14}N_4O_2S$, (%): C, 60.34; H, 4.17; N, 16.56; S, 9.48; found, (%): C, 60.38; H, 4.22; N, 16.57; S, 9.42.

1-Methyl-2-(1-phenyl-4-(phenylsulfonyl)-1H-pyrazol-3-yl)-1H-benzimidazole (**52b**) Yield (A, 70 %); (B, 75 %); m.p.: 218–220 °C; IR (KBr): *v* 1594 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.02 (s, 3H, NCH_3), 7.20–8.08 (m, 14H, ArH), 7.88 (s, 1H pyrazole-5-CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 32.60, 109.90, 113.22, 118.68, 120.90, 121.74, 122.60, 123.53, 127.84, 128.62, 129.21, 129.90, 131.46, 133.59, 135.52, 138.88, 141.60, 155.34; MS: *m/z* 414 [M^+] (100); Anal. calcd. for $C_{23}H_{18}N_4O_2S$, (%): C, 66.65; H, 4.38; N, 13.52; S, 7.74; found, (%): C, 66.62; H, 4.33; N, 13.59; S, 7.70.

Conclusion

In the present study, we succeeded in synthesizing new heterocyclic derivatives attached to benzothiazole and benzimidazole ring systems of biological and pharmacological importance via reaction of 1-(benzothiazol-2-yl)-3-(*N*,*N*-dimethylamino)-2-(phenylsulfonyl)prop-2-en-1-one (**3**) and 1-(1-methylbenzimidazol-2-yl)-3-(*N*,*N*-dimethylamino)-2-(phenylsulfonyl)prop-2-en-1-one (**4**) with a variety of nucleophiles. Our synthetic routes involved both thermal and microwave techniques. We found that application of the microwave technique is an efficient and clean method which is superior to the traditional thermal heating and affords products in excellent yields and high purity after shorter reaction times.

Acknowledgments A. F. Darweesh is very thankful to Prof. Peter Metz [*Technische Universität* (TU)-Dresden] for giving him the chance to carry out spectral analysis at his laboratory during the Alexander von Humboldt fellowships: July 2012–July 2014. He also is deeply thankful to the Alexander von Humboldt Foundation (AvH) for granting him fellowships from July 2012–July 2014 at TU-Dresden. Amani A. Salman is very thankful to Prof. Kamal M. Dawood (Cairo University) for giving her the facilities for carrying out microwave experiments.

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