Heterocycles of biological importance: Part 7[1]. Synthesis of biologically active pyrimido[2,1-*b*]benzothiazoles from acetylenic acids and 2-aminobenzothiazoles

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Abstract

Conjugate addition of the imino nitrogen of 2-aminobenzothiazoles **1** to the alkyne β-carbon atom of acetylenic acids **2** followed by ring closure gives rise to novel 2*H*-pyrimido[2,1-*b*]-benzothiazol-2-ones in good yield.

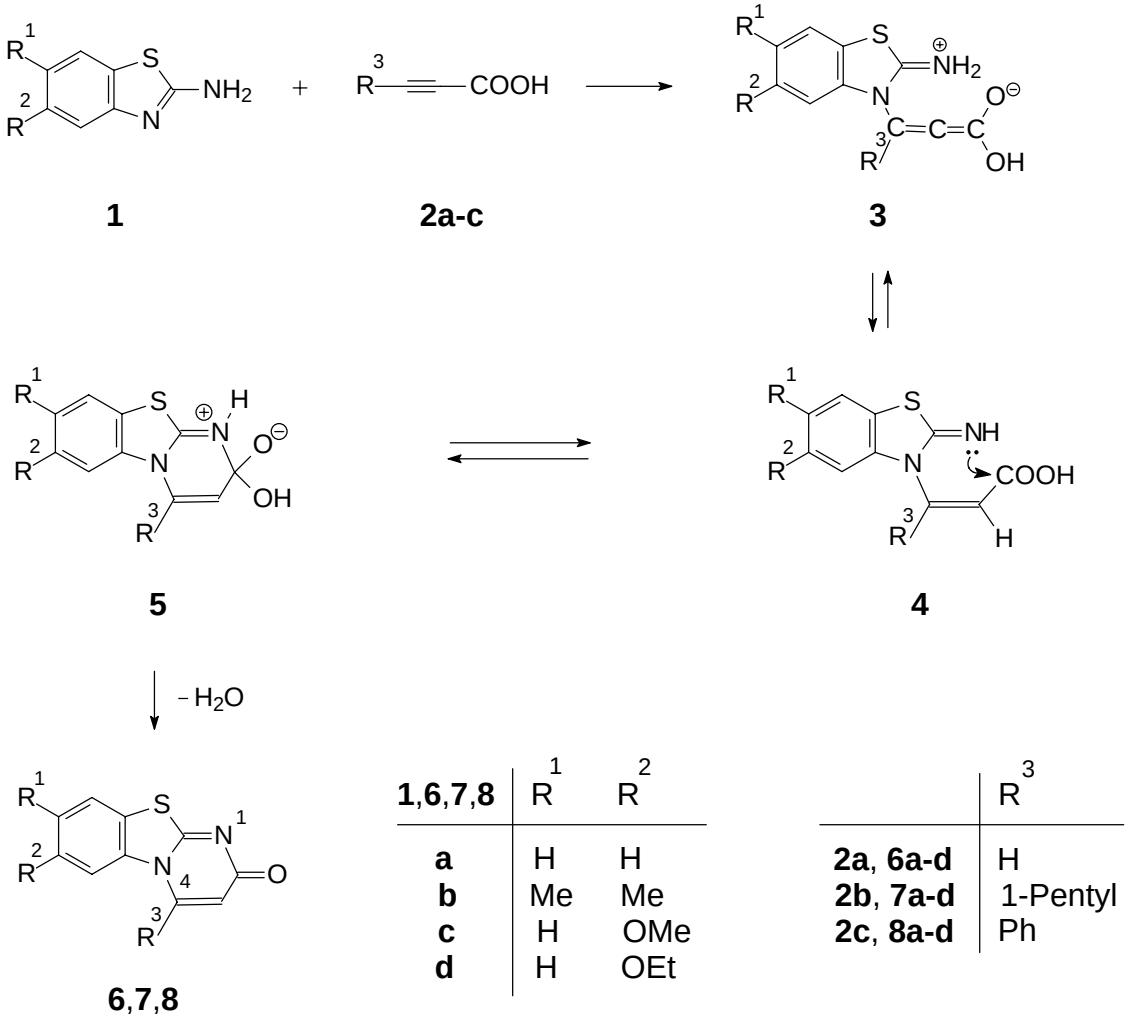
Keywords: Michael addition, amidines, fused nitrogen heterocycles, cyclocondensation

Introduction

Condensed pyrimidine compounds have been shown to exhibit interesting pharmacological properties[2] and a number of synthetic methods[3-11] has been reported for their preparation. As a part of an ongoing study of the syntheses of heterocyclic compounds of potential biological activity from allenic and acetylenic compounds,[12-13] we have shown recently[14] that substituted and unsubstituted 2*H*-pyrimido[2,1-*b*]benzothiazol-2-ones are a new group of $GABA_A$/ benzodiazepine receptor ligands. In this paper we wish to present the preparation of these compounds.

Results and Discussion

The conjugate addition of 2-aminobenzothiazole **1** to the acetylenic acids **2** in butanol, followed by cyclocondensation, gave the corresponding 2*H*-pyrimido[2,1-*b*]benzothiazol-2-ones **6-8** in 68–86% yield (Scheme 1).



1,6,7,8	R1	R2
a	H	H
b	Me	Me
c	H	OMe
d	H	OEt

	R3
2a, **6a-d**	H
2b, **7a-d**	1-Pentyl
2c, **8a-d**	Ph

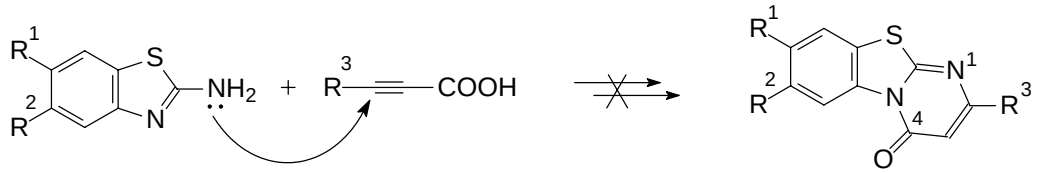
Scheme 1

The structures of these compounds were established beyond any doubt by their ^{1}H-NMR and ^{13}C-NMR spectra and by additional COSY, HMQC (Heteronuclear Multiple-Quantum Correlation) and HMBC (Heteronuclear Multiple-Bond Correlation) experiments.

When 2-aminobenzothiazoles **1a–1d** were allowed to react with phenyl propiolic acid (**2c**), 4-phenyl-2*H*-pyrimido[2,1-*b*]benzothiazol-2-ones **8a-8d** were obtained. The NMR spectra of the 8-methoxy compound **8c** and the 8-ethoxy compound **8d** showed singlets at δ 6.20 ppm and δ 6.15 ppm, respectively, attributed to 3-H, and doublets at δ 6.01 ppm and δ 5.96 ppm, respectively, for 6-H. The shielding effects observed for the 6-H in the compounds **8a-8d** is due to the diamagnetic effect of the phenyl group attached to C-4.

The above data exclude the formation of the isomeric 2-phenyl-4*H*-pyrimido[2,1-*b*]benzothiazole-4-ones **9** which should exhibit a deshielded proton (6-H) near δ 9 ppm resulting from the anisotropic effect of the carbonyl group[5]. Further evidence for the formation of the 2-one derivatives was obtained from the fact that no shielding effect was noticed in compounds **6a-d** and **7a-d** where the phenyl group was replaced by H or 1-pentyl, respectively.

The reaction of 2-aminobenzothiazoles **1** with acetylenic acids **2** is rationalized as shown (Scheme 1), whereby the alkynoic acid is first attacked at the β-carbon atom by the ring nitrogen atom of the benzothiazole. An attack of the 2-amino group of **1** on the β-carbon of **2** which eventually would generate the isomeric product **9** definitely does not occur[15, 16] (Scheme 2).



1 **2** **9**

Scheme 2

Experimental Section

General Procedures. All the melting points were determined with a Reichert Thermovar microscope and are uncorrected. Electron impact mass spectra (direct inlet, 70 eV) were recorded with a Jeol JMS-SX102 spectrometer. The Ultraviolet (UV) spectra were determined in an ethanol-chloroform mixture (1:1) on a Perkin – Elmer 554 instrument and the Infrared (IR) spectra were recorded with a Varian Cary 2290 and Perkin Elmer 298 spectrometers. ^{1}H-NMR (500 MHz) and ^{13}C-NMR spectra (125 MHz) were recorded at room temperature with a Bruker instrument using an inverse 5 mm probe equipped with a shielded gradient coil. Chemical shifts (δ) are given in ppm and coupling constants (in brackets) are reported in Hz. COSY, HMQC and HMBC experiments were performed with gradient enhancements using sine shaped gradient pulses, and for the 2D heteronuclear correlation spectroscopy, the refocusing delays were optimised for $^{1}J_{CH}$ = 145 Hz and $^{2}J_{CH}$ = 10 Hz. The raw data were transformed and the spectra were evaluated with the standard Bruker UXNMR software (rev. 941001). Combustion analyses were performed with CHN + O/S elemental analyser "CARLO ERBA" model 1106. The purity of the samples was checked routinely by TLC.

Synthesis of 2*H*-pyrimido[2,1-*b*]benzothiazol-2-ones 6a-d, 7a-d and 8a-d

The alkynoic acid **2a-c** (20 mmol) and the appropriate 2-aminobenzothiazole (**1a-d,** 10 mmol) were heated to reflux in 1-butanol (50 mL) for 48 hours. Evaporation of solvent under reduced pressure gave the crude product which was crystallized from hexane/ethyl acetate to give the 2*H*-pyrimido[2,1-*b*]benzothiazol-2-ones.

2*H*-Pyrimido[2,1-*b*]benzothiazol-2-one (6a). From **1a** and **2a,** Yield: 68 %; colourless crystals mp 272 – 275 °C [Lit[4]: mp 272 – 275 °C]; IR: ν/cm^{-1} 1630 (C=O), 1583 (C=N), 1533 (C=C). UV (EtOH/$CHCl_3$ 1:1) λ_{max} (nm), (log ε): 260 (4.03), 300 (4.11). NMR data: δ_H ($CDCl_3$) 6.32 (1H, d, $J_{3,4}$ 7.7 Hz, 3-H), 7.46 (1H, dd, $J_{7,6} = J_{7,8}$ 8.0 Hz, 7-H), 7.58 (1H, dd, $J_{8,7} = J_{8,9}$ 8.0 Hz, 8-H), 7.98 (1H, d, $J_{9,8}$ 7.9 Hz, 9-H), 8.03 (1H, d, $J_{6,7}$ 8.2 Hz, 6-H), 8.86 (1H, d, $J_{4,3}$ 7.7 Hz, 4-H). δ_C ($CDCl_3$) 110.8 (C-3), 122.9 (C-9a), 123.7 (C-6), 126.1 (C-9), 127.2 (C-7), 128.8 (C-8), 134.8 (C-4), 135.0 (C-5a), 163.6 (C-10a), 166.9 (C-2). MS (EI): *m/z* 202.0213 (M^+, 100 %, $C_{10}H_6N_2OS$ requires 202.0201) 176 (32), 174 (64), 150 (15), 148 (13); Anal. Calcd. for $C_{10}H_6N_2OS$: C, 59.41; H, 2.97; N, 13.86; O, 7.92; S, 15.84. Found: C, 59.49; H, 3.03; N, 13.78; S, 15.70.

7,8-Dimethyl-2*H*-pyrimido[2,1-*b*]benzothiazol-2-one (6b). From **1b** and **2a,** Yield: 75%; colourless crystals, no melt below 300°C. IR: ν/cm^{-1} 1640 (C=O), 1617 (C=N), 1570 (C=C). UV (EtOH/$CHCl_3$ 1:1) λ_{max} (nm), (log ε): 265 (4.16), 276 (4.12), 307 (4.26). NMR data: δ_H ($CDCl_3$) 2.30 (3H, s, 8-CH_3), 2.35 (3H, s, 7-CH_3), 6.41 (1H, d, $J_{3,4}$ 7.7 Hz, 3-H), 7.35 (1H, s, 9-H), 7.37 (1H, s, 6-H), 8.24 (1H, d, $J_{4,3}$ 7.7 Hz, 4-H); δ_C ($CDCl_3$) 19.7 (7-CH_3), 20.1 (8-CH_3), 111.5 (C-3), 112.1 (C-6), 120.6 (C-9a), 123.5 (C-9), 132.2 (C-5a), 133.1 (C-4), 136.3 (C-8), 137.0 (C-7), 164.3 (C-10a), 168.5 (C-2). MS (EI): *m/z* 230.0513 (M^+, 100 %, $C_{12}H_{10}N_2OS$ requires 230.0514) 204 (20), 202 (52), 189 (18), 187 (15). Anal. Calcd. for $C_{12}H_{10}N_2OS$: C, 62.61; H, 4.35; N, 12.17; O, 6.96; S, 13.91. Found: C, 62.72; H, 4.39; N, 12.11; S, 13.83.

8-Methoxy-2*H*-pyrimido[2,1-*b*]benzothiazol-2-one (6c). From **1c** and **2a,** Yield: 80%; colourless crystals; no melt below 300°C (Lit[4]: > 300 °C). IR: ν/cm^{-1} 1636 (C=O), 1492 (C=N), 1472 (C=C). UV (EtOH/$CHCl_3$ 1:1) λ_{max} (nm), (log ε): 242 (4.27), 277 (4.12), 311 (4.21). NMR data: δ_H ($CDCl_3$) 3.82 (3H, s, 8-OCH_3), 6.29 (1H, d, $J_{3,4}$ 7.7 Hz, 3-H), 7.16 (1H, dd, $J_{7,6}$ 9.1 Hz and $J_{7,9}$ 2.6 Hz, 7-H), 7.64 (1H, d, $J_{9,7}$ 2.6 Hz, 9-H), 7.95 (1H, d, $J_{6,7}$ 9.1 Hz, 6-H), 8.81 (1H, d, $J_{4,3}$ 7.7 Hz, 4-H); δ_C ($CDCl_3$) 55.9 (8-OCH_3), 108.0 (C-9), 110.6 (C-3), 113.5 (C-7), 114.4 (C-6), 124.3 (C-9a), 128.6 (C-5a), 135.0 (C-4), 157.6 (C-8), 163.2 (C-10a), 166.7 (C-2). MS (EI): *m/z* 232.0319 (M^+, 100 %, $C_{11}H_8N_2O_2S$ requires 232.0306) 206 (18), 204 (33), 191 (20), 189 (27). Anal. Calcd. for $C_{11}H_8N_2O_2S$: C, 56.90; H, 3.45; N, 12.07; O, 13.79; S, 13.79. Found: C, 56.85; H, 3.51; N, 12.07; S, 13.88.

8-Ethoxy-2*H*-pyrimido[2,1-*b*]benzothiazol-2-one (6d). From **1d** and **2a,** Yield: 83%; colourless crystals (83 %); no melt below 300°C. IR: ν/cm^{-1} 1640 (C=O), 1585 (C=N), 1500 (C=C). UV (EtOH/$CHCl_3$ 1:1) λ_{max} (nm), (log ε): 240 (4.30), 278 (4.12), 313 (4.23). NMR data: δ_H ($CDCl_3$) 1.35 (3H, t, *J* 6.9 Hz, 8-OCH_2CH_3), 4.09 (2H, q, *J* 6.9 Hz, 8-OCH_2CH_3), 6.29 (1H, d, $J_{3,4}$ 7.7 Hz, 3-H), 7.15 (1H, dd, $J_{7,6}$ 9.0 Hz and $J_{7,9}$ 2.4 Hz, 7-H), 7.61 (1H, d, $J_{9,7}$ 2.4 Hz, 9-H), 7.92 (1H, d, $J_{6,7}$ 9.0 Hz, 6-H), 8.80 (1H, d, $J_{4,3}$ 7.7 Hz, 4-H). δ_C ($CDCl_3$) 14.5 (8-OCH_2CH_3), 64.0 (8-OCH_2CH_3), 108.4 (C-9), 110.6 (C-3), 113.5 (C-7), 114.8 (C-6), 124.3 (C-9a), 128.5 (C-5a), 135.0 (C-4), 156.8 (C-8), 163.2 (C-10a), 166.7 (C-2). MS (EI): *m/z* 246.0461 (M^+, 100 %, $C_{12}H_{10}N_2O_2S$ requires 246.0463) 218 (32), 192 (21), 190 (55), 165 (10). Anal. Calcd. for $C_{12}H_{10}N_2O_2S$: C, 58.54; H, 4.06; N, 11.38; O, 13.01; S, 13.01. Found: C, 58.65; H, 4.04; N, 11.28; S, 13.01.

4-Pentyl- 2*H*-pyrimido[2,1-*b*]benzothiazol-2-one (7a). From **1a** and **2b,** Yield 75%; colourless crystals, mp 138-140°C. IR: ν/cm^{-1} 1634 (C=O), 1576 (C=N), 1500 (C=C). UV (EtOH/$CHCl_3$ 1:1) λ_{max} (nm), (log ε): 225 (4.47), 262 (4.13), 293 (4.06), 301 (4.08). NMR data: δ_H ($CDCl_3$) 0.86 (3H, t, $J_{5',4'}$ 7.2 Hz, 5'-H), 1.33 (2H, m, 4'-H), 1.43 (2H, m, 3'-H), 1.70 (2H, tt, $J_{2',1'}$ 8 Hz and $J_{2',3'}$ 8 Hz, 2'-H), 3.02 (2H, t, $J_{1',2'}$ 7.5 Hz, 1'-H), 6.13 (1H, s, 3-H), 7.36 (1H, dd, $J_{8,7}$ 9 Hz and $J_{8,9}$ 8 Hz, 8-H), 7.42 (1H, dd, $J_{7,6}$ 9.0 Hz and $J_{7,8}$ 8 Hz 7-H), 7.61 (1H, d, $J_{9,8}$ 7.8 Hz, 9-H), 7.74 (1H, d, $J_{6,7}$ 8.6 Hz, 6-H). δ_C ($CDCl_3$) 13.7 (C-5'), 22.1 (C-4'), 26.5 (C-2'), 30.7 (C-3'), 33.5 (C-1'), 110.7 (C-3), 116.0 (C-6), 123.1 (C-9), 124.1 (C-9a), 126 (C-7), 126.9 (C-8), 135.6 (C-5a), 151.5 (C-4), 164.8 (C-10a), 167.1 (C-2). MS (EI): *m/z* 272.0986 (M^+, 97 %, $C_{15}H_{16}N_2OS$ requires 272.0983) 230 (39), 216 (54), 188 (43), 187 (42), 176 (100), 146 (16). Anal. Calcd. for $C_{15}H_{16}N_2OS$: C, 66.18; H, 5.88; N, 10.29; O, 5.88; S, 11.76. Found: C, 66.01; H, 5.83; N, 10.25; S, 11.76.

7,8-Dimethyl-4-pentyl-2*H*-pyrimido[2,1-*b*]benzothiazol-2-one (7b). From **1b** and **2b,** Yield: 77%, Colourless needles; mp 178-181°C. IR: ν/cm^{-1} 1640 (C=O), 1570 (C=N), 1500 (C=C). UV (EtOH/$CHCl_3$ 1:1) λ_{max} (nm), (log ε): 232 (4.43), 274 (4.06), 307 (4.14); NMR data: δ_H ($CDCl_3$) 0.87 (3H, t, $J_{5',4'}$ 7.3 Hz, 5'-H), 1.35 (2H, tq, $J_{4',3'}$ 8.0 Hz and $J_{4',5'}$ 7.0 Hz, 4'-H), 1.44 (2H, m, 3'-H), 1.70 (2H, tt, $J_{2',1'}$ 8.0 Hz and $J_{2',3'}$ 8.0 Hz, 2'-H), 2.28 (3H, s, 7-CH_3), 2.32 (3H, s, 8-CH_3), 2.98 (2H, t, $J_{1',2'}$ 7.6 Hz, 1'-H), 6.10 (1H, s, 3-H), 7.32 (1H, s, 9-H), 7.46 (1H, s, 6-H). δ_C ($CDCl_3$) 13.7 (C-5'), 19.4 (8-CH_3), 20.6 (7-CH_3), 22.1 (C-4'), 26.7 (C-2'), 30.8 (C-3'), 33.5 (C-1'), 110.6 (C-3), 116.8 (C-6), 121.1 (C-9a), 123.2 (C-9), 133.9 (C-5a), 135.5 (C-7), 136.0 (C-8), 151.3 (C-4), 165.0 (C-10a), 167.3 (C-2). MS (EI): *m/z* 300.1279 (M^+, 100 %, $C_{17}H_{20}N_2OS$ requires 300.1296) 258 (36), 244 (39), 216 (36), 204 (85), 189 (13), 174 (11). Anal. Calcd. for $C_{17}H_{20}N_2OS$: C, 68.00; H, 6.67; N, 9.33; O, 5.33; S, 10.67. Found: C, 68.00; H, 6.70; N, 9.26; S, 10.55.

8-Methoxy-4-pentyl-2*H*-pyrimido[2,1-*b*]benzothiazol-2-one (7c). From **1b** and **2c,** yield: 80%; colourless crystals; mp 174-175 °C. IR: ν/cm^{-1} 1630 (C=O), 1574 (C=N), 1507 (C=C). UV (EtOH/$CHCl_3$ 1:1) λ_{max} (nm), (log ε): 231 (4.42), 285 (4.10), 308 (4.23). NMR data: δ_H ($CDCl_3$) 0.90 (3H, t, $J_{5',4'}$ 7.3 Hz, 5'-H), 1.37 (2H, tq, $J_{4',3'}$ 8.0 Hz and $J_{4',5'}$ 7.0 Hz, 4'-H), 1.45 (2H, m, 3'H), 1.73 (2H, tt, $J_{2',1'}$ 8.0 Hz and $J_{2',3'}$ 8.0 Hz, 2'-H), 3.01 (2H, t, $J_{1',2'}$ 7.6 Hz, 1'-H), 3.85 (3H, s, 8-OCH_3), 6.15 (1H, s, 3-H), 6.97 (1H, dd, $J_{7,6}$ 9.4 Hz and $J_{7,9}$ 2.7 Hz, 7-H), 7.12 (1H, d, $J_{9,7}$ 2.7 Hz, 9-H), 7.65 (1H, d, $J_{6,7}$ 9.4 Hz, 6-H). δ_C ($CDCl_3$) 13.8 (C-5') 22.2 (C-4'), 26.5 (C-2'), 30.9 (C-3'), 33.5 (C-1'), 55.8 (8-OCH_3), 107.2 (C-9), 110.6 (C-3), 114.0 (C-7), 117.0 (C-6), 125.9 (C-9a), 129.6 (C-5a), 151.2 (C-4), 157.5 (C-8), 164.5 (C-10a), 167.3 (C-2). MS (EI): *m/z* 302.1071 (M^+, 100 %, $C_{16}H_{18}N_2O_2S$ requires 302.1089) 274 (6), 260 (21), 246 (32), 218 (20), 206 (81), 191 (12). Anal. Calcd. for $C_{16}H_{18}N_2O_2S$: C, 63.57; H, 5.96; N, 9.27; O, 10.60; S, 10.60. Found: C, 63.55; H, 5.95; N, 9.27; S, 10.60.

8-Ethoxy-4-pentyl-2*H*-pyrimido[2,1-*b*]benzothiazol-2-one (7d). From **1b** and **2b,** yield 84%; colourless crystals; mp 153-154°C. IR: ν/cm^{-1} 1640 (C=O), 1605 (C=N), 1580 (C=C); UV (EtOH/$CHCl_3$ 1:1) λ_{max} (nm), (log ε) : 219 (4.52), 231 (4.53), 287 (4.19), 310 (4.31). NMR data: δ_H ($CDCl_3$) 0.90 (3H, t, $J_{5',4'}$ 7.3 Hz, 5'-H), 1.36 (2H, tq, $J_{4',3'}$ 8.0 Hz and $J_{4',5'}$ 7.0 Hz, 4'-H), 1.42

(3H, t, *J* 7.0 Hz, 8-OCH$_2$C*H*$_3$), 1.45 (2H, m, 3'-H), 1.73 (2H, tt, $J_{2',1'}$ 8.0 Hz and $J_{2',3'}$ 8.0 Hz 2'-H), 3.00 (2H, t, $J_{1',2'}$ 7.6 Hz, 1'-H), 4.05 (2H, q, *J* 7.0 Hz, 8-OC*H*$_2$CH$_3$), 6.15 (1H, s, 3-H), 6.95 (1H, dd, $J_{7,6}$ 9.4 Hz and $J_{7,9}$ 2.6 Hz, 7-H), 7.09 (1H, d, $J_{9,7}$ 2.6 Hz, 9-H), 7.63 (1H, d, $J_{6,7}$ 9.4 Hz, 6-H). δ_C ($CDCl_3$) 13.8 (C-5'), 14.6 (8-OCH$_2$*C*H$_3$), 22.2 (C-4'), 26.5 (C-2'), 30.9 (C-3'), 33.5 (C-1'), 64.2 (8-O*C*H$_2$CH$_3$), 107.6 (C-9), 110.5 (C-3), 114.0 (C-7), 117.0 (C-6), 125.9 (C-9a), 129.4 (C-5a), 151.2 (C-4), 156.9 (C-8), 164.5 (C-10a), 167.3 (C-2). MS (EI): *m/z* 316.1256 (M^+, 100%, $C_{17}H_{20}N_2O_2S$ requires 316.1245) 287 (9), 274 (23), 260 (28), 232 (20), 220 (55), 192 (18). Anal. Calcd. for $C_{17}H_{20}N_2O_2S$: C, 64.56; H, 6.32; N, 8.86; O, 10.13; S, 10.13. Found: C, 64.29; H, 6.39; N, 8.75; S, 10.05.

4-Phenyl-2*H*-pyrimido[2,1-*b*]benzothiazol-2-one (8a). From **1a** and **2c**, yield: 76%, colourless needles; mp 236-238°C (Lit[4]: 237 - 238 °C). IR: ν/cm^{-1} 1640 (C=O), 1600 (C=N), 1585 (C=C); UV (EtOH/$CHCl_3$ 1:1) λ_{max} (nm), (log ε): 220 (4.52), 243 (4.39), 300 (4.12). NMR data: δ_H ($CDCl_3$) 6.10 (1H, d, $J_{6,7}$ 8.6 Hz, 6-H), 6.16 (1H, s, 3-H), 6.95 (1H, dd, $J_{7,6}$ 8.0 Hz and $J_{7,8}$ 8.0 Hz 7-H), 7.21 (1H, dd, $J_{8,7}$ 8.0 Hz and $J_{8,9}$ 8.0 Hz, 8-H), 7.38 (2H, d, $J_{2',3'}$ 7.4 Hz, 2'-H, 6'-H), 7.51 (2H, dd, $J_{3',2'}$ 7.0 Hz and $J_{3',4'}$ 8.0 Hz 3'-H, 5'-H), 7.56 (1H, d, $J_{9,8}$ 8.0 Hz, 9-H), 7.58 (1H, t, $J_{4',3'}$ 8.0 Hz, 4'-H). δ_C ($CDCl_3$) 112.9 (C-3), 116.2 (C-6), 122.8 (C-9), 123.9 (C-9a), 125.9 (C-7), 126.0 (C-8), 128.0 (C-2', C-6'), 129.2 (C-3', C-5'), 130.7 (C-4'), 131.8 (C-1'), 135.0 (C-5a), 148.9 (C-4), 164.6 (C-10a), 166.8 (C-2). MS (EI): *m/z* 278.0529 (M^+, 100 %, $C_{16}H_{10}N_2OS$ requires 278.0514) 250 (67), 237 (7), 176 (64), 150 (12), 148 (8), 102 (13). Anal. Calcd. for $C_{16}H_{10}N_2OS$: C, 69.06; H, 3.60; N, 10.07; O, 5.76; S, 11.51. Found: C, 69; H, 3.60; N, 10.02; S, 11.56.

7,8-Dimethyl-4-phenyl-2*H*-pyrimido[2,1-*b*]benzothiazol-2-one (8b). From **1b** and **2c,** yield 78%, colourless crystals; mp 228-230°C. IR: ν/cm^{-1} 1635 (C=O), 1600 (C=N), 1565 (C=C). UV (EtOH/$CHCl_3$ 1:1) λ_{max} (nm), (log ε): 221 (4.53), 249 (4.38), 308 (4.22). NMR data: δ_H ($CDCl_3$) 1.89 (3H, s, 7-CH_3), 2.18 (3H, s, 8-CH_3), 5.79 (1H, s, 6-H), 6.18 (1H, s, 3-H), 7.29 (1H, s, 9-H), 7.38 (2H, d, $J_{2',3'}$ 7.3 Hz, 2'-H, 6'-H), 7.53 (2H, dd, $J_{3',2'}$ 7.0 Hz and $J_{3',4'}$ 8.0 Hz , 3'-H, 5'-H), 7.61 (1H, t, $J_{4',3'}$ 7.5 Hz, 4'-H). δ_C ($CDCl_3$) 19.4 (8-CH_3), 20.2 (7-CH_3), 112.6 (C-3), 117.3 (C-6), 120.9 (C-9a), 122.9 (C-9), 128.3 (C-2', C-6'), 129.1 (C-3', C-5'), 130.6 (C-4'), 132.0 (C-1'), 133.3 (C-5a), 135.2 (C-7), 135.4 (C-8), 148.9 (C-4), 164.9 (C-10a), 167.0 (C-2). MS (EI): *m/z* 306.0834 (M^+, 100 %, $C_{18}H_{14}N_2OS$ requires 306.0827) 278 (53), 265 (7), 204 (50), 189 (12), 129 (6), 102 (7). Anal. Calcd. for $C_{18}H_{14}N_2OS$: C, 70.59; H, 4.57; N, 9.15; O, 5.23; S, 10.46. Found: C, 70.46; H, 4.56; N, 9.27; S, 10.46.

8-Methoxy-4-phenyl-2*H*-pyrimido[2,1-*b*]benzothiazol-2-one (8c). From **1c** and **2c**, yield 81%, colourless crystals; mp 254-256°C. IR: ν/cm^{-1} 1635 (C=O), 1600 (C=N), 1580 (C=C). UV (EtOH/$CHCl_3$ 1:1) λ_{max} (nm), (log ε) : 216 (4.48), 230 (4.48), 247 (4.35) 275 (4.12), 312 (4.19). NMR data: δ_H ($CDCl_3$) 3.76 (3H, s, 8-OCH_3), 6.01 (1H, d, $J_{6,7}$ 9.4 Hz, 6-H), 6.20 (1H, s, 3-H), 6.52 (1H, dd, $J_{7,6}$ 9.4 Hz and $J_{7,9}$ 2.6 Hz, 7-H), 7.07 (1H, d, $J_{9,7}$ 2.6 Hz, 9-H), 7.41 (2H, d, $J_{2',3'}$ 7.3 Hz, 2'-H, 6'-H), 7.54 (2H, dd, $J_{3',4'}$ 8 Hz and $J_{3',2'}$ 7.0 Hz, 3'-H, 5'-H), 7.61 (1H, t, $J_{4',3'}$ 7.6 Hz, 4'-H). δ_C ($CDCl_3$) 55.7 (8-OCH_3), 107.0 (C-9), 112.8 (C-3), 113.5 (C-7), 117.2 (C-6), 125.6 (C-9a), 128.2 (C-2', C-6'), 129 (C-5a), 129.3 (C-3', C-5'), 130.8 (C-4'), 131.9 (C-1'), 148.8 (C-

4), 157.5 (C-8), 164.3 (C-10a), 167.0 (C-2). MS (EI): *m/z* 308.0629 (M^+, 100 %, $C_{17}H_{12}N_2O_2S$ requires 308.0619) 280 (32), 265 (8), 206 (54), 191 (25), 191 (25), 138 (13), 137 (13). Anal. Calcd. for $C_{17}H_{12}N_2O_2S$: C, 66.23; H, 3.90; N, 9.09; O, 10.39; S, 10.39. Found: C, 66.10; H, 3.97; N, 9.14; S, 10.50.

8-Ethoxy-4-phenyl-2*H*-pyrimido[2,1-*b*]benzothiazol-2-one (8d). From **1d** and **2c,** Yield 86%, colourless crystals; mp 211-213°C. IR: ν/cm^{-1} 1640 (C=O), 1600 (C=N), 1580 (C=C). UV (EtOH/$CHCl_3$ 1:1) λ_{max} (nm), (log ε): 214 (4.44), 230 (4.43), 246 (4.31), 274 (4.06), 312 (4.16). NMR data: δ_H ($CDCl_3$) 1.31 (3H, t, *J* 7 Hz, 8-OCH_2CH_3), 3.93 (2H, q, *J* 7 Hz, 8-OCH_2CH_3), 5.96 (1H, d, $J_{6,7}$ 9.4 Hz, 6-H), 6.15 (1H, s, 3-H), 6.47 (1H, dd, $J_{7,6}$ 9.4 Hz and $J_{7,9}$ 2.5 Hz, 7-H), 7.02 (1H, d, $J_{9,7}$ 2.5 Hz, 9-H), 7.38 (2H, d, $J_{2',3'}$ 7.4 Hz, 2'-H, 6'-H), 7.51 (2H, dd, $J_{3',4'}$ 8.0 Hz and $J_{3',2'}$ 7.0 Hz, 3'-H, 5'-H), 7.58 (1H, d, $J_{4',3'}$ 7.5 Hz, 4'-H). δ_C ($CDCl_3$) 14.4 (8-OCH_2CH_3), 64.0 (8-OCH_2CH_3), 107.4 (C-9), 112.6 (C-3), 113.5 (C-7), 117.1 (C-6), 125.4 (C-9a), 128.1 (C-2', C-6'), 128.6 (C-5a), 129.2 (C-3', C-5'), 130.8 (C-4'), 131.8 (C-1'), 148.7 (C-4), 156.8 (C-8), 164.3 (C-10a), 166.9 (C-2). MS (EI): *m/z* 322.0777 (M^+, 100 %, $C_{18}H_{14}N_2O_2S$ requires 322.0776) 294 (22), 266 (18), 220 (28), 192 (37), 191 (29), 129 (9). Anal. Calcd. for $C_{18}H_{14}N_2O_2S$: C, 67.08; H, 4.35; N, 8.69; O, 9.94; S, 9.94. Found: C, 67.02; H, 4.43; N, 8.61; S, 9.92.

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