

Electronic Supplementary Information

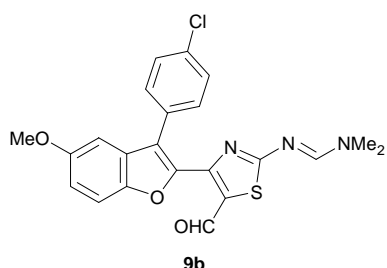
Preparation of 3-(4-chlorophenyl)-2-(2-aminothiazol-4-yl)-5-methoxybenzo[*b*]furan derivatives and their leukotriene B₄ inhibitory activity

General Experimental

Melting point was measured with a Yanaco MP micro-melting-point apparatus and uncorrected. ¹H-NMR spectra were measured on JEOL JNM-ECP500 (500 MHz) or JEOL JNM-ECP400 (400MHz) and the chemical shifts were expressed in parts per million (ppm) downfield from tetramethylsilane as the internal standard. Mass spectra were measured on JJEOL JMS DX-303 EIMS spectrometer. Elemental analyses were performed on a CHN CORDER MT-3 (Yanako).

Preparation of

3-(4-chlorophenyl)-2-[5-formyl-2-[(dimethylamino)methyleneamino]thiazol-4-yl]-5-methoxybenzo[*b*]furan **9b**

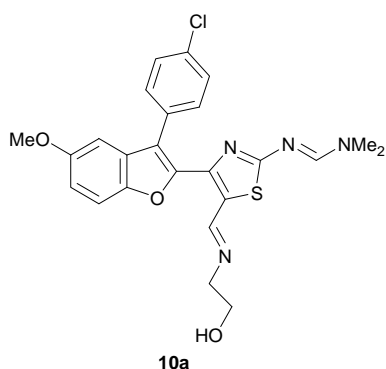


A solution of the compound **6** (1.65 g, 4.62 mmol) in DMF (38 mL) was added to a stirred solution of POCl₃ (2.58 mL, 27.8 mmol) in DMF (15 mL) at 0°C under N₂. After stirring for 48 h at rt, the reaction mixture was poured into a 5% NaOH aqueous solution, and the resulting precipitate was collected by filtration and washed with H₂O to give an orange solid, which was recrystallized from MeOH-AcOEt to give **9b** (1.22 g, 60%) as red crystals; mp, 196-198°C; δ_H (CDCl₃, 400 MHz) 3.07 (6H, s, N(CH₃)₂), 3.82 (3H, s, OCH₃), 6.94 (1H, d, *J* = 2.8 Hz, 4-H), 7.03 (1H, dd, *J* = 9.0, 2.6 Hz, 6-H), 7.42-7.55 (5H, m, 7- and Ar-H), 7.96 (1H, s, CH=N), 10.4 (1H, s, CHO); *m/z* 441 (40), 439 (M⁺, 100), 410 (17), 395 (18), 380 (18), 283 (14), 235 (16), 208 (16), 115 (20), 98 (15); *Anal.* Calcd for C₂₂H₁₈ClN₃O₃S: C, 60.07; H, 4.12; N, 9.55 found: C, 59.99; H, 3.99; N, 9.57.

Preparation of

3-(4-chlorophenyl)-2-[5-(2-hydroxyethyl)iminomethyl-2-[(dimethylamino)methyleneamino]-

thiazol-4-yl]-5- methoxybenzo[*b*]furan **10a**

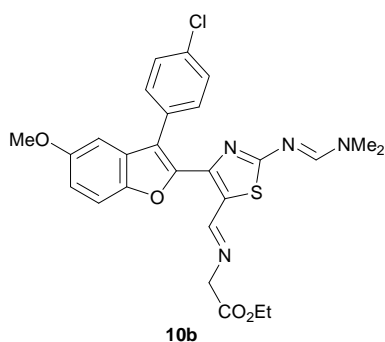


A solution of **9b** (0.30 g, 0.68 mmol) and ethanolamine (0.06 mL, 1.03 mmol) in EtOH (5 mL) was refluxed for 0.5 h. The solvent was evaporated to give a yellow residue, which was dissolved in AcOEt, washed with H₂O and saturated NaCl aqueous solution. The organic layer was dried over anhydrous magnesium sulfate and evaporated to give an orange solid, which was recrystallized from AcOEt to give **10a** (0.24 g, 72%) as red crystals; mp, 168-169°C; δ_{H} (CDCl₃, 400 MHz) 3.06 (6H, s, N (CH₃)₂), 3.60-3.62 (2H, m, OCH₂CH₂N), 3.80-3.83 (2H, m, OCH₂CH₂N), 3.83 (3H, s, OCH₃), 6.98 (1H, d, *J* = 1.8 Hz, 4-H), 6.99 (1H, dd, *J* = 8.7, 2.3 Hz, 6-H), 7.41 (2H, d, *J* = 8.7 Hz, Ar-H), 7.45 (2H, d, *J* = 8.7 Hz, Ar-H), 7.46 (1H, d, *J* = 8.7 Hz, 7-H), 8.03 (1H, s, N=CH) 8.64 (1H, s, N=CH); *m/z* 484 (6), 482 (M⁺, 14), 385 (17), 371 (100); *Anal.* Calcd for C₂₄H₂₃ClN₄O₃S: C, 59.68; H, 4.80; N, 11.60 found: C, 59.49; H, 4.77; N, 11.35.

Preparation

of

3-(4-chlorophenyl)-2-[ethoxycarbonylmethyliminomethyl-2-[(dimethylamino)methyleneamino]thiazol-4-yl]-5- methoxybenzo[*b*]furan **10b**



A mixture of **9b** (0.50 g, 1.13 mmol), glycine ethyl ester hydrochloride (0.18 g, 1.36 mmol), Et₃N (0.31 mL, 2.28 mmol) and molecular sieves (3A, 0.1 g) in EtOH (10 mL) was refluxed for 1 h. The solvent was evaporated to give a yellow residue, which was dissolved in AcOEt, washed with H₂O and saturated NaCl aqueous solution. The organic layer was dried over anhydrous magnesium sulfate and evaporated to give an orange solid, which was recrystallized from AcOEt to give **10b** (0.10 g, 17%) as red crystals; mp, 162-165°C; δ_{H} (CDCl₃, 500 MHz) 1.29 (3H, t, *J* = 7.4, CH₂CH₃), 3.05 (3H, s, NCH₃), 3.06 (3H, s, NCH₃), 3.82 (3H, s, OCH₃), 4.21 (2H, q, *J* = 7.4 Hz, CH₂CH₃), 4.23 (2H, s, NCH₂CO), 6.97-7.00 (2H, m, 4- and 6-H), 7.41 (2H, d, *J* = 8.7 Hz, Ar-H), 7.41 (2H, d, *J* = 8.7 Hz, Ar-H), 7.45 (2H, d, *J* = 8.7 Hz, Ar-H), 8.01 (H, s, N=CH), 8.62 (H, s, N=CH); *m/z* 526 (10), 524 (M⁺, 25), 427 (23), 413 (100), 356 (12), 354 (31); *Anal.* Calcd for C₂₆H₂₅ClN₄O₄S·0.2H₂O: C, 59.07; H, 4.84; N, 10.60 found: C, 59.25; H, 4.80; N, 11.34.