Synthesis and antifungal activity of 2*H*-1,4-benzoxazin-3(4*H*)-one derivatives

Małgorzata Śmist ¹, Halina Kwiecień ^{1*} and Maria Krawczyk ²

¹ *Institute of Organic Technology, West Pomeranian University of Technology, Szczecin
Al. Piastów 42, 71-065 Szczecin, Poland*

² *Institute of Industrial Organic Chemistry, Department of Applications and Formulation of
Pesticides, Annopol 6, 03-236 Warsaw, Poland*

* Corresponding author. E-mail: halina.kwiecien@zut.edu.pl

SUPPORTING INFORMATION

(for online publication only)

Methyl 2-(2-nitrophenoxy)butanoate (3a). Yield: 91%; colorless solid, mp. 39-41 °C; GC/MS (τ = 17,12 min.), MS m/z (%) = 239 (M^+ , 17), 193 (69), 180 (30), 139 (60), 122 (100), 101 (46), 78 (23), 59 (63). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 7.84 (dd, $J=8.1, 1.6$, 1H, Ar), 7.53-7.40 (m, 1H, Ar), 7.12-7.01 (m, 1H, Ar), 6.89 (d, $J=8.5$, 1H, Ar), 4.70 (t, $J=5.9$, 1H, CH), 3.75 (s, 3H, OCH_3), 2.14-1.98 (m, 2H, CH_2), 1.10 (t, $J=7.4$, 3H, CH_3); ^{13}C NMR δ 170.9, 151.2, 140.4, 133.9, 125.8, 121.3, 115.1, 79.0, 52.4, 26.1, 9.5. Anal. Calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_5$: C, 55.23; H, 5.48; N, 5.86. Found: C, 55.29; H, 5.57; N, 5.91.

Methyl 2-(2-nitrophenoxy)pentanoate (3b). Yield: 93%; colorless solid, mp. 37-38 °C.

GC/MS (τ = 17,87 min.), MS m/z (%) = 253 (M^+ , 15), 207 (61), 194 (27), 139 (37), 122 (100), 92 (17), 73 (41), 55 (48). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 7.83 (dd, J =1.6, 6.5, 1H, Ar), 7.47-7.45 (m, 1H, Ar), 7.08-7.04 (m, 1H, Ar), 6.90 (d, J =8.4, 1H, Ar), 4.75 (dd, J =4.7, 3.0, 1H, CH), 3.75 (s, 3H, OCH_3), 2.03-1.97 (m, 2H, CH_2), 1.56-1.54 (m, 2H, CH_2), 0.98 (t, J =7.4, 3H, CH_3); ^{13}C NMR δ 171.1, 151.2, 140.4, 133.9, 125.7, 121.2, 115.0, 77.7, 52.5, 34.6, 18.3, 13.6. Anal. Calcd for $\text{C}_{12}\text{H}_{15}\text{NO}_5$: C, 56.91; H, 5.97; N, 5.53. Found: C, 56.87; H, 6.02; N, 5.49.

Metyl (2-nitrophenoxy)hexanoate (3c). Yield: 89%; colorless solid, mp. 45-47 °C.

GC/MS (τ = 18,84 min.), MS m/z (%) = 267 (M^+ , 16), 221 (60), 208 (29), 139 (23), 122 (100), 97 (54), 69 (73), 55 (25). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 7.84 (dd, $J=8.1$, 1.7, 1H, Ar), 7.54-7.42 (m, 1H, Ar), 7.09-7.03 (m, 1H, Ar), 6.93-6.86 (m, 1H, Ar), 4.73 (dd, 7.3, 5.0, 1H, CH), 3.75 (s, 3H, OCH_3), 2.10-1.90 (m, 2H, CH_2), 1.57-1.47 (m, 2H, CH_2), 1.43-1.32 (m, 2H, CH_2), 0.93 (t, $J=7.3$, 3H, CH_3); ^{13}C NMR δ 171.1, 151.2, 140.4, 133.9, 125.8, 121.2, 115.0, 78.0, 52.5, 32.3, 27.1, 22.2, 13.8. Anal. Calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_5$: C, 58.42; H, 6.41; N, 5.24. Found: C, 58.35; H, 6.46; N, 5.21.

Methyl 2-(5-methyl-2-nitrophenoxy)butanoate (3d). Yield: 81%; colorless solid, mp. 28-29 °C. GC/MS (τ = 17,84 min.), MS m/z (%) = 253 (M^+ , 13), 207 (100), 194 (21), 153 (97), 136 (83), 123 (31), 101 (32), 78 (21), 59 (56). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 7.76 (d, $J=8.2$, 1H, Ar), 6.85 (d, $J=8.2$, 1H, Ar), 6.71 (s, 1H, Ar), 4.72 (t, $J=5.8$, 1H, CH), 3.76 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3), 2.07-2.02 (m, 2H, CH_2), 1.10 (t, $J=7.4$, 3H, CH_3); ^{13}C NMR δ 171.0, 151.4, 145.7, 138.0, 125.9, 122.0, 115.7, 78.8, 52.4, 26.1, 21.8, 9.4. Anal. Calcd for $\text{C}_{12}\text{H}_{15}\text{NO}_5$: C, 56.91; H, 5.97; N, 5.53. Found: C, 56.87; H, 6.01; N, 5.51.

Methyl 2-(5-methyl-2-nitrophenoxy)pentanoate (3e). Yield: 86%; colorless solid, mp. 61-63 °C. GC/MS (τ = 18,61 min.), MS m/z (%) = 267 (M^+ , 14), 221 (100), 208 (21), 153 (96), 136 (88), 115 (63), 92 (7), 73 (39), 55 (46). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 7.77 (d, $J=8.3$, 1H, Ar), 6.85 (dq, $J=6.2$, 0.7, 1H, Ar), 6.68 (s, 1H, Ar), 4.75 (dd, $J=4.6$, 3.0, 1H, CH), 3.76 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3), 2.03-1.94 (m, 2H, CH_2), 1.62-1.55 (m, 2H, CH_2), 0.97 (t, $J=7.4$, 3H, CH_3); ^{13}C NMR δ 171.2, 151.4, 145.6, 138.0, 125.9, 122.0, 115.5, 77.6, 52.4, 34.6, 21.9, 18.3, 13.6. Anal. Calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_5$: C, 58.42; H, 6.41; N, 5.24. Found: C, 58.46; H, 6.48; N, 5.21.

Methyl 2-(5-methyl-2-nitrophenoxy)hexanoate (3f). Yield: 93%; colorless solid, mp. 44-45 °C. GC/MS (τ = 19,48 min.), MS m/z (%) = 281 (M^+ , 13), 235 (100), 222 (20), 153 (65), 136 (86), 120 (21), 97 (47), 69 (69), 55 (24). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 7.78 (d, $J=8.3$, 1H, Ar), 6.85 (dd, $J=7.6$, 0.7, 1H, Ar), 6.67 (s, 1H, Ar), 4.72 (dd, $J=5.0$, 2.3, 1H, CH), 3.76 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3), 2.03-1.99 (m, 2H, CH_2), 1.56-1.48 (m, 2H, CH_2), 1.42-1.35 (m, 2H, CH_2), 0.93 (t, $J=7.3$, 3H, CH_3); ^{13}C NMR δ 171.2, 151.4, 145.6, 138.0, 126.0, 122.0, 115.5, 77.9, 52.5, 32.4, 27.1, 22.3, 21.9, 13.8. Anal. Calcd for $\text{C}_{14}\text{H}_{19}\text{NO}_5$: C, 59.78; H, 6.81; N, 4.98. Found: C, 59.69; H, 6.90; N, 4.95.

Methyl 2-(5-fluoro-2-nitrophenoxy)butanoate (3g). Yield 91%; colorless solid, mp. 56-58 °C. GC/MS (τ = 16,24 min.), MS m/z (%) = 257 (M^+ , 5), 211 (99), 198 (25), 157 (17), 140 (100), 124 (22), 101 (44), 76 (20), 59 (84). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 7.96 (dd, $J=5.9, 3.1$, 1H, Ar), 6.79-6.74 (m, 1H, Ar), 6.60 (dd, $J=7.6, 2.5$, 1H, Ar), 4.68 (t, $J=5.9$, 1H, CH), 3.78 (s, 3H, OCH_3), 2.08 (p, $J=7.0$, 2H, CH_2), 1.11 (t, $J=7.4$, 3H, CH_3); ^{13}C NMR δ 170.3, 166.6, 164.1, 153.4, 128.2, 108.3, 102.9, 79.1, 52.6, 26.0, 9.4. Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{FNO}_5$: C, 51.36; H, 4.70; F, 7.39; N, 5.45. Found: C, 51.32; H, 4.79; F, 7.15; N, 5.48.

Methyl 2-(5-fluoro-2-nitrophenoxy)pentanoate (3h). Yield: 90%; colorless solid mp. 40-41 °C. GC/MS (τ = 17,03 min.), MS m/z (%) = 271 (M^+ , 4), 225 (79), 212 (22), 157 (7), 140 (100), 115 (61), 96 (19), 73 (48), 55 (56). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 7.95 (dd, J =5.9, 3.1, 1H, Ar), 6.79-6.74 (m, 1H, Ar), 6.59 (dd, J = 7.6, 2.5, 1H, Ar), 4.72 (dd, J =4.6, 3.1, 1H, CH), 3.78 (s, 3H, OCH_3), 2.05-1.99 (m, 2H, CH_2), 1.61-1.53 (m, 2H, CH_2), 0.98 (t, J =7.4, CH_3); ^{13}C NMR δ 170.5, 166.6, 164.1, 153.4, 128.2, 108.2, 102.8, 77.9, 52.7, 34.4, 18.3, 13.6. Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{FNO}_5$: C, 53.14; H, 5.20; F, 7.00; N, 5.16. Found: C, 53.10; H, 5.28; F, 6.79; N, 5.14.

Methyl 2-(5-fluoro-2-nitrophenoxy)hexanoate (3i). Yield: 88%; colorless solid, mp. 42-43 °C. GC/MS ($\tau = 17.93$ min.), MS m/z (%) = 285 (M^+ , 4), 239 (82), 226 (23), 157 (5), 140 (100), 124 (17), 97 (60), 82 (11), 69 (83), 55 (28). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 7.95 (dd, $J=5.9, 3.1$, 1H, Ar), 6.79-6.74 (m, 1H, Ar), 6.59 (dd, $J=7.6, 2.5$, 1H, Ar), 4.70 (dd, $J=5.0, 2.2$, 1H, CH), 3.78 (s, 3H, OCH_3), 2.05-2.01 (m, 2H, CH_2), 1.52 (p, $J=7.6$, 2H, CH_2), 1.43-1.34 (m, 2H, CH_2), 0.94 (t, $J=7.3$, CH_3); ^{13}C NMR δ 170.5, 166.6, 164.1, 153.4, 128.2, 108.2, 102.8, 78.2, 52.7, 32.2, 27.0, 22.2, 13.8. Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{FNO}_5$: C, 54.73; H, 5.65; F, 6.66; N, 4.91. Found: C, 54.76; H, 5.75; F, 6.44; N, 4.87.

Methyl 2-(2,4-dichloro-6-nitrophenoxy)butanoate (3j). Yield: 80%; a pale yellow solid, mp. 60-62 °C. GC/MS (τ = 18,56 min.), MS m/z (%) = 307 (M^+ -1, 13), 261 (4), 248 (7), 207 (64), 190 (29), 162 (28), 149 (7), 132 (10), 101 (95), 73 (6), 59 (100). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 7.71 (d, J =2.6, 1H, Ar), 7.59 (d, J =2.6, 1H, Ar), 4.94 (t, J =5.6, 1H, CH), 3.67 (s, 3H, OCH_3), 2.12-2.06 (m, 2H, CH_2), 1.09 (t, J =7.4, 3H, CH_3); ^{13}C NMR δ 170.1, 146.3, 146.0, 134.3, 130.0, 129.4, 123.9, 82.2, 52.4, 25.9, 8.9. Anal. Calcd for $\text{C}_{11}\text{H}_{11}\text{Cl}_2\text{NO}_5$: C, 42.88; H, 3.60; Cl, 23.01; N, 4.55. Found: C, 43.01; H, 3.70; Cl, 22.71; N, 4.61.

Methyl 2-(2,4-dichloro-6-nitrophenoxy)pentanoate (3k). Yield: 79%; a pale yellow solid, mp. 37-38 °C. GC/MS (τ = 19,33 min.), MS m/z (%) = 321 (M^+ -1, 7), 275 (2), 262 (5), 207 (27), 190 (19), 162 (18), 149 (4), 132 (9), 115 (100), 97 (19), 73 (47), 55 (47). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 7.71 (d, J =2.6, 1H, Ar), 7.58 (d, J =2.6, 1H, Ar), 4.97 (t, J =5.7, 1H, CH), 3.68 (s, 3H, OCH_3), 2.05-1.99 (m, 2H, CH_2), 1.67-1.58 (m, 1H, CH_2), 1.55-1.47 (m, 1H, CH_2), 0.99 (t, J =7.4, 3H, CH_3); ^{13}C NMR δ 170.3, 146.3, 146.0, 134.3, 130.0, 129.4, 123.9, 81.2, 52.4, 34.7, 17.9, 13.8. Anal. Calcd for $\text{C}_{12}\text{H}_{13}\text{Cl}_2\text{NO}_5$: C, 44.74; H, 4.07; Cl, 22.01; N, 4.35. Found: C, 44.82; H, 4.18; Cl, 21.75; N, 4.43.

Metyl 2-(2,4-dichloro-6-nitrofenoksy)hexanoate (3I). Yield: 79%; a pale yellow solid, 42-44 °C. GC/MS ($\tau = 20,18$ min.), MS m/z (%) = 335 (M^+ , 6), 289 (1), 276 (5), 207 (20), 190 (19), 162 (18), 149 (5), 129 (100), 113 (6), 97 (85), 69 (83), 55 (25). 1H NMR ($CDCl_3$), δ (ppm), J (Hz): 7.71 (d, $J=2.6$, 1H, Ar), 7.58 (d, $J=2.5$, 1H, Ar), 4.96 (t, $J=5.7$, 1H, CH), 3.68 (s, 3H, OCH_3), 2.05-2.02 (m, 2H, CH_2), 1.58-1.54 (m, 1H, CH_2), 1.46-1.36 (m, 3H, 2 CH_2), 0.94 (t, $J=7.2$, 3H, CH_3); ^{13}C NMR δ 170.3, 146.3, 146.0, 134.3, 130.0, 129.4, 123.9, 81.4, 52.4, 32.4, 26.6, 22.5, 13.9. Anal. Calcd for $C_{13}H_{15}Cl_2NO_5$: C, 46.45; H, 4.50; Cl, 21.09; N, 4.17. Found: C, 46.53; H, 4.59; Cl, 20.86; N, 4.23.

2-Ethyl-2H-1,4-benzoxazin-3(4H)-one (4a). Yield: 86%; colorless solid, mp. 103-104 °C (Lit. 103.5-104 °C). ^[1] GC/MS (τ = 15,97 min.), MS m/z (%) = 177 (M^+ , 95), 149 (39), 135 (8), 120 (100), 93 (11), 69 (13), 52 (9¹H NMR (CDCl₃), δ (ppm), J (Hz): 10.04 (s, 1H, NH), 7.00-6.87 (m, 4H, Ar), 4.52 (dd, J =4.6, 3.6, 1H, CH), 1.99-1.89 (m, 2H, CH₂), 1.10 (t, J =7.4, 3H, CH₃); ¹³C NMR δ 168.8, 142.9, 126.3, 124.1, 122.4, 117.0, 115.9, 78.0, 23.9, 9.4. ^[2,3] Anal. Calcd for C₁₀H₁₁NO₂: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.74; H, 6.31; N, 7.88.

2-Propyl-2H-1,4-benzoxazin-3(4H)-on (4b). Yield: 85%; colorless solid, mp. 85-86 °C (Lit. 85-85.5 °C). ^[1] GC/MS (τ = 16,86 min.), MS m/z (%) = 191 (M^+ , 70), 149 (100), 135 (5), 120 (60), 93 (14), 55 (11). ¹H NMR (CDCl₃), δ (ppm), J (Hz): 10.01 (s, 1H, NH), 6.96-6.92 (m, 3H, Ar), 6.89-6.86 (m, 1H, Ar), 4.61-4.58 (m, 1H, CH), 1.90-1.84 (m, 2H, CH₂), 1.65-1.53 (m, 2H, CH₂), 1.00-0.95 (m, 3H, CH₃); ¹³C NMR δ 169.0, 142.8, 126.4, 124.1, 122.4, 117.0, 115.9, 77.4, 32.4, 18.3, 13.7. ^[2,3] Anal. Calcd for C₁₁H₁₃NO₂: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.06; H, 6.88; N, 7.27.

2-Butyl-2H-1,4-benzoxazin-3(4H)-on (4c). Yield: 82%; colorless solid, mp. 101-102 °C (Lit. 100.5-101.5 °C). ^[1] GC/MS (τ = 17,85 min.), MS m/z (%) = 205 (M^+ , 63), 162 (15), 149 (100), 135 (5), 120 (49), 93 (14), 50 (12). ¹H NMR (CDCl₃), δ (ppm), J (Hz): 9.61 (s, 1H, NH), 6.98-6.93 (m, 3H, Ar), 6.87-6.85 (m, 1H, Ar), 4.59-4.55 (m, 1H, CH), 1.89-1.81 (m, 2H, CH₂), 1.50-1.41 (m, 2H, CH₂), 1.39-1.36 (m, 2H, CH₂), 0.92 (t, J =7.4, 3H, CH₃); ¹³C NMR δ 168.7, 142.8, 126.3, 124.1, 122.4, 117.1, 115.8, 77.4, 30.1, 27.1, 22.3, 13.9. Anal. Calcd for C₁₂H₁₅NO₂: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.25; H, 7.40; N, 6.78.

-
- (1) Wheeler, K. W. Some 2-substituted 2H-1,4-benzoxazin-3(4H)-ones. *J. Med. Chem.*, **1962**, 5, 1378-1383.
 - (2) Dai, W.-M.; Wang, X.; Ma, C. Microwave-assisted one-pot regioselective synthesis of 2-alkyl-3,4-dihydro-3-oxo-2H-1,4-benzoxazines. *Tetrahedron*, **2005**, 61, 6879-6885.
 - (3) Ramesh, C.; Raju, B.R.; Kavala, V.; Kuo, C.-W; Yao, C.-F. A simple and facile route for the synthesis of 2H-1,4-benzoxazin-3-(4H)-ones *via* reductive cyclization of 2-(2-nitrophenoxy)acetonitrile adducts in the presence of Fe/acetic acid. *Tetrahedron*, **2011**, 67, 1187-1192.

2-Ethyl-7-methyl-2*H*-1,4-benzoxazin-3(4*H*)-on (4d). Yield: 80%; colorless solid, mp. 144-145 °C. GC/MS (τ = 16,86 min.), MS m/z (%) = 191 (M^+ , 100), 162 (38), 149 (5), 134 (94), 107 (8), 93 (5), 77 (12), 51 (4). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 9.63 (s, 1H, NH), 6.79 (s, 1H, Ar), 6.74 (s, 2H, Ar), 4.50-4.47 (m, 1H, CH), 2.28 (s, 3H, CH_3), 1.98-1.87 (m, 2H, CH_2), 1.09 (t, $J=7.4$, 3H, CH_3); ^{13}C NMR δ 168.4, 142.6, 134.2, 123.8, 122.9, 117.6, 115.5, 78.1, 23.8, 20.9, 9.4. Anal. Calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.02; H, 6.92; N, 7.35.

7-Methyl-2-propyl-2*H*-1,4-benzoxazin-3(4*H*)-one (4e). Yield: 88%; colorless solid, mp. 135-136 °C. GC/MS (τ = 17,92 min.), MS m/z (%) = 205 (M^+ , 85), 163 (100), 149 (4), 134 (71), 107 (13), 94 (5), 77 (12), 55 (9). ^1H NMR (CDCl_3 , $\text{DMSO-}d_6$), δ (ppm), J (Hz): 9.67 (s, 1H, NH), 6.78-6.71 (m, 4H, Ar), 4.57-4.54 (m, 1H, CH), 2.30-2.26 (m, 3H, CH_3), 1.84-1.83 (m, 2H, CH_2), 1.63-1.48 (m, 2H, CH_2) 0.99-0.95 (m, 3H, CH_3); ^{13}C NMR δ 168.6, 142.5, 134.1, 123.8, 122.9, 117.6, 115.5, 77.4, 32.4, 20.9, 18.3, 13.7. Anal. Calcd for $\text{C}_{12}\text{H}_{15}\text{NO}_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.26; H, 7.43; N, 6.79.

2-Butyl-7-methyl-2*H*-1,4-benzoxazin-3(4*H*)-one (4f). Yield: 91%; colorless solid, mp. 127-128 °C. GC/MS (τ = 18,82 min.), MS m/z (%) = 219 (M^+ , 79), 176 (14), 163 (100), 148 (5), 134 (55), 107 (13), 94 (4), 77 (10), 55 (10). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 9.65 (s, 1H, NH), 6.78 (s, 1H, Ar), 6.74 (d, J =1.0, 2H, Ar), 4.54 (dd, J =4.6, 3.9, 1H, CH), 2.30 (s, 3H, CH_3), 1.89-1.85 (m, 2H, CH_2), 1.59-1.32 (m, 4H, 2CH_2), 0.92 (t, J =7.3, 3H, CH_3); ^{13}C NMR δ 168.6, 142.6, 134.1, 123.8, 122.9, 117.6, 115.5, 77.4, 30.1, 27.1, 22.3, 21.0, 14.0. Anal. Calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.18; H, 7.87; N, 6.35.

2-Ethyl-7-fluoro-2*H*-1,4-benzoxazin-3(4*H*)-one (4g). Yield: 95%; colorless solid, mp. 134-135 °C. GC/MS (τ = 15,91 min.), MS m/z (%) = 195 (M^+ , 98), 167 (36), 153 (8), 138 (100), 111 (13), 97 (7), 83 (10), 69 (20), 55 (6). ^1H NMR (CDCl_3 , $\text{DMSO-}d_6$), δ (ppm), J (Hz): 10.29 (s, 1H, NH), 6.84-6.82 (m, 1H, Ar), 6.81-6.59 (m, 2H, Ar), 4.47-4.42 (m, H, CH), 1.91-1.88 (m, 2H, CH_2), 1.08-1.02 (m, 3H, CH_3); ^{13}C NMR δ 166.8, 159.8, 143.6, 123.4, 116.1, 108.6, 104.5, 78.1, 23.9, 9.3. Anal. Calcd for $\text{C}_{10}\text{H}_{10}\text{FNO}_2$: C, 61.53; H, 5.16; F, 9.73; N, 7.18. Found: C, 61.55; H, 5.23; F, 9.45; N, 7.15.

7-Fluoro-2-propyl-2H-1,4-benzoxazin-3(4H)-one (4h). Yield: 92%; colorless solid, mp. 120-121 °C. GC/MS (τ = 16,85 min.), MS m/z (%) = 209 (M^+ , 66), 167 (100), 153 (5), 138 (61), 111 (15), 98 (5), 83 (20), 70 (5), 55 (17). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 10.03 (s, 1H, NH), 6.81 (dd, $J=5.4, 3.2$, 1H, Ar), 6.73-6.64 (m, 2H, Ar), 4.61-4.57 (m, H, CH), 1.89-1.83 (m, 2H, CH_2), 1.63-1.50 (m, 2H, CH_2), 0.98 (t, $J=7.4$, 3H, CH_3); ^{13}C NMR δ 168.4, 160.4, 143.6, 122.6, 116.2, 108.6, 105.1, 77.4, 32.4, 18.2, 13.6. Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{FNO}_2$: C, 63.15; H, 5.78; F, 9.08; N, 6.69. Found: C, 63.09; H, 5.81; F, 8.85; N, 6.65.

2-Butyl-7-fluoro-2*H*-1,4-benzoxazin-3(4*H*)-one (4i). Yield: 83%; colorless solid, mp. 113-114 °C. GC/MS (τ = 17.97 min.), MS m/z (%) = 223 (M^+ , 63), 180 (15), 167 (100), 153 (85), 138 (51), 111 (15), 97 (7), 83 (8), 70 (4), 55 (13). ^1H NMR (CDCl_3), δ (ppm), J (Hz): 10.06 (s, 1H, NH), 6.83-6.80 (m, 1H, Ar), 6.73-6.64 (m, 2H, Ar), 4.57 (t, J = 4.2, H, CH), 1.90-1.86 (m, 2H, CH_2), 1.56-1.47 (m, 2H, CH_2), 1.38-1.37 (m, 2H, CH_2), 0.95 (t, J = 7.1, 3H, CH_3); ^{13}C NMR δ 168.4, 160.4, 143.6, 122.6, 116.2, 109.0, 105.1, 77.4, 30.2, 27.0, 22.3, 13.9. Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{FNO}_2$: C, 64.56; H, 6.32; F, 8.51; N, 6.27. Found: C, 64.51; H, 6.39; F, 8.22; N, 6.23.

6,8-Dichloro-2-ethyl-2H-1,4-benzoxazin-3(4H)-one (4j). Yield: 89%; a pale yellow solid, mp. 130-131 °C. GC/MS (τ = 19,64 min.), MS m/z (%) = 245 (M^+ -1, 100), 217 (29), 203 (21), 188 (77), 161 (7), 148 (7), 133 (8), 112 (15), 69 (65), 55 (13). ^1H NMR (CDCl_3 , $\text{DMSO-}d_6$), δ (ppm), J (Hz): 10.79 (s, 1H, NH), 7.22-7.18 (m, 1H, Ar), 7.06-7.02 (m, 1H, Ar), 4.71-4.67 (m, 1H, CH), 1.97-1.87 (m, 2H, CH_2), 1.11-1.10 (m, 3H, CH_3); ^{13}C NMR δ 161.8, 137.4, 131.2, 127.1, 123.6, 122.0, 111.9, 79.6, 24.1, 9.3. Anal. Calcd for $\text{C}_{10}\text{H}_9\text{Cl}_2\text{NO}_2$: C, 48.81; H, 3.69; Cl, 28.81; N, 5.69. Found: C, 48.84; H, 3.78; Cl, 28.64; N, 5.71.

6,8-Dichloro-2-propyl-2H-1,4-benzoxazin-3(4H)-one (4k). Yield: 90%; a pale yellow solid mp. 141-142 °C. GC/MS (τ = 20,42 min.), MS m/z (%) = 259 (M^+ -1, 69), 230 (9), 217 (100), 203 (11), 188 (42), 161 (13), 148 (6), 133 (7), 112 (11), 83 (40), 55 (38). ^1H NMR (CDCl_3 , $\text{DMSO}-d_6$), δ (ppm), J (Hz): 10.70 (s, 1H, NH), 7.24-7.20 (m, 1H, Ar), 7.04-7.01 (m, 1H, Ar), 4.79-4.74 (m, 1H, CH), 1.92-1.78 (m, 2H, CH_2), 1.49-1.67 (m, 2H, CH_2), 1.01-0.96 (m, 3H, CH_3); ^{13}C NMR δ 161.8, 137.4, 131.2, 127.1, 123.6, 122.0, 111.9, 79.6, 24.1, 9.3. Anal. Calcd for $\text{C}_{11}\text{H}_{11}\text{Cl}_2\text{NO}_2$: C, 50.79; H, 4.26; Cl, 27.26; N, 5.38. Found: C, 50.83; H, 4.37; Cl, 27.03; N, 5.40.

2-Butyl-6,8-dichloro-2H-1,4-benzoxazin-3(4H)-one (4I). Yield: 93%; a pale yellow solid, mp. 120-121 °C. GC/MS (τ = 21,29 min.), MS m/z (%) = 273 (M^+ -1, 63), 230 (13), 217 (100), 203 (8), 188 (36), 161 (14), 148 (5), 133 (6), 112 (8), 97 (19), 69 (13), 55 (33). ^1H NMR (CDCl_3 , $\text{DMSO-}d_6$), δ (ppm), J (Hz): 10.03 (s, 1H, NH), 7.30 (d, $J=2.3$, 1H, Ar), 7.12 (d, $J=2.3$, 1H, Ar), 4.78 (dd, $J=4.4$, 4.3, 1H, CH), 1.88-1.81 (m, 2H, CH_2), 1.48-1.32 (m, 4H, 2CH_2), 0.90 (t, $J=7.3$, 3H, CH_3); ^{13}C NMR δ 162.8, 137.5, 129.2, 127.8, 125.2, 122.7, 112.5, 78.3, 30.3, 26.9, 22.1, 13.8. Anal. Calcd for $\text{C}_{12}\text{H}_{13}\text{Cl}_2\text{NO}_2$: C, 52.57; H, 4.78; Cl, 25.86; N, 5.11. Found: C, 52.51; H, 4.84; Cl, 25.59; N, 5.06.

6,7-Dibromo-2-ethyl-2H-1,4-benzoxazin-3(4H)-one (5a). Yield: 99 %; colorless solid, mp. 226-227 °C. GC/MS (τ = 22,11 min.), MS m/z (%) = 335 (M^+ , 100), 307 (25), 293 (9), 278 (71), 265 (13), 238 (5), 197 (5), 158 (9), 143 (4), 118 (9), 69 (40), 55 (11). ^1H NMR (CDCl_3 , $\text{DMSO}-d_6$), δ (ppm), J (Hz): 10.74 (s, 1H, NH), 7.21-7.13 (m, 2H, Ar), 4.47-4.43 (m, 1H, CH), 1.90-1.85 (m, 2H, CH_2), 1.08-1.03 (m, 3H, CH_3); ^{13}C NMR δ 166.1, 142.6, 128.1, 121.1, 119.5, 116.3, 116.0, 77.7, 23.8, 9.2. Anal. Calcd for $\text{C}_{10}\text{H}_9\text{Br}_2\text{NO}_2$: C, 35.85; H, 2.71; Br, 47.71; N, 4.18. Found: C, 35.81; H, 2.78; Br, 47.41; N, 4.16.

6,7-Dibromo-2-propyl-2H-1,4-benzoxazin-3(4H)-one (5b). Yield: 87%; colorless solid, mp. 186-187 °C. GC/MS (τ = 22,83 min.), MS m/z (%) = 349 (M^+ , 73), 307 (100), 293 (6), 278 (43), 265 (13), 226 (9), 197 (4), 158 (8), 143 (4), 118 (6), 83 (18), 55 (21). ^1H NMR (CDCl_3 , $\text{DMSO}-d_6$), δ (ppm), J (Hz): 10.84 (s, 1H, NH), 7.27 (s, 1H, Ar), 7.16 (s, 1H, Ar), 4.58 (dd, J =5.0, 2.8, 1H, CH), 1.78-1.73 (m, 2H, CH_2), 1.52-1.44 (m, 2H, CH_2), 0.93 (t, J =7.4, 3H, CH_3); ^{13}C NMR δ 166.6, 142.5, 128.0, 121.2, 119.6, 116.6, 116.2, 76.7, 32.4, 18.0, 13.6. Anal. Calcd for $\text{C}_{11}\text{H}_{11}\text{Br}_2\text{NO}_2$: C, 37.85; H, 3.18; Br, 45.79; N, 4.01. Found: C, 37.82; H, 3.22; Br, 45.56; N, 3.99.

6,7-Dibromo-2-butyl-2H-1,4-benzoxazin-3(4H)-one (5c). Yield: 53%; colorless solid, mp. 152-153 °C. GC/MS (τ = 23,62 min.), MS m/z (%) = 363 (M^+ , 74), 320 (13), 307 (100), 293 (6), 278 (37), 265 (14), 226 (9), 197 (4), 158 (7), 143 (3), 118 (7), 97 (7), 76 (6), 55 (20). 1H NMR ($CDCl_3$, $DMSO-d_6$), δ (ppm), J (Hz): 10.69 (s, 1H, NH), 7.20 (m, 2H, Ar), 4.50 (s, 1H, CH), 1.87-1.82 (m, 2H, CH_2), 1.51-1.38 (m, 4H, $2CH_2$), 0.93 (t, $J=7.4$, 3H, CH_3); ^{13}C NMR δ 166.5, 142.5, 128.1, 121.1, 119.6, 116.5, 116.1, 76.9, 32.1, 26.8, 22.1, 13.8. Anal. Calcd for $C_{12}H_{13}Br_2NO_2$: C, 39.70; H, 3.61; Br, 44.02; N, 3.86. Found: C, 39.73; H, 3.71; Br, 43.82; N, 3.89.

4-Acetyl-2-ethyl-2*H*-1,4-benzoxazin-3(4*H*)-one (6). Yield: 97%; a pale yellow solid, mp. 52-54 °C. GC/MS (τ = 15,72 min.), MS m/z (%) = 219 (8), 177 (100), 148 (49), 135 (7), 120 (56), 106 (3), 90 (5), 69 (9), 52 (5). ^1H NMR (CDCl_3 , $\text{DMSO-}d_6$) δ (ppm), J (Hz): 7.61-7.59 (m, 1H, Ar), 7.17-7.12 (m, 1H, Ar), 7.08-7.04 (m, 2H, Ar), 4.39 (dd, $J=4.5$, $J=8.4$, 1H, CH), 2.69 (s, 3H, CH_3), 1.98-1.89 (m, 1H, CH_2), 1.87-1.83 (m, 1H, CH_2), 1.10 (t, $J=7.4$, 3H, CH_3); ^{13}C NMR δ 162.3, 161.5, 137.0, 117.1, 116.5, 113.5, 113.2, 108.5, 70.8, 19.0, 13.8. Anal. Calcd for $\text{C}_{12}\text{H}_{13}\text{NO}_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.69; H, 6.07; N, 6.35.