SYNTHESIS OF 2(3*H*)-BENZOXA(THIA)ZOLONES CONTAINING A HETEROCYCLE IN THE ALKYL GROUP AT POSITION 3

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Numerous 3-alkylated 2(3*H*)-benzoxa(thia)zolones show various pharmacological and pesticidal activities[1 – 4]. On the other hand tetrazoles, predominantly 5-substituted derivatives, have been prepared and tested for biological activity[5 – 7]. Recently it has been established that the compound with a tetrazole moiety from a novel series of (2-quinolinylmethoxy)phenyl containing compounds represents the best combination of in vitro and in vivo activity as high-affinity leukotriene D_4 receptor antagonist[8]. It is known that some 5-substituted derivatives of 1,3,4-oxadiazoles are antituberculous agents[9].

The present paper deals with the synthesis of new compounds which combine two structures showing biological activities i. e. those of 3-alkylated 2(3*H*)-benzoxa(thia)-zolones and 5-substituted tetrazoles or 1,3,4-oxadiazoles.

EXPERIMENTAL

Melting points were determined on a Boetius block and are uncorrected. IR spectra of compounds *Ia – Ie* and *IIa* were recorded on a Specord 71 (Carl Zeiss) spectrophotometer and those of the other compounds – on a Perkin–Elmer 983G grating spectrometer (in Nujol, NaCl plate). ^{1}H NMR spectra of compounds *Ic*, *IIa – IIc*, *IIe*, *IIh*, *IIi* and *IIk* were measured on a Bruker (400 MHz) instrument and those of the other compounds on a Tesla BS 487C (80 MHz) spectrometer with tetramethylsilane as internal standard. The reaction paths and the purity of the compounds were checked by TLC on aluminium plates coated with silica gel 60 F_{254} (Merck) using dioxane–methanol (9 : 1) solvent system for compounds *I* and toluene–acetonitrile (2 : 1) for compounds *II*.

3-(2-Cyanoethyl)-2(3*H*)-benzoxa(thia)zolones were synthesized according to the known procedure[10 – 12].

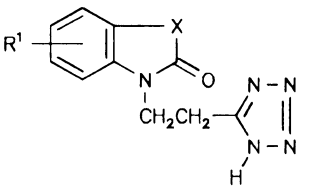
3-[2-(Tetrazol-5-yl)ethyl]-2(3*H*)-benzoxa(thia)zolones *Ia – Ic*; General Procedure

Sodium azide (40 mmol) and ammonium chloride (43 mmol) were added to a solution of the corresponding 3-(2-cyanoethyl)-2(3*H*)benzoxa(thia)zolone (30 mmol) in DMF (20 ml). The resulting mixture was refluxed for 15 h. The cooled reaction mixture was poured into 150 ml cold water and acidified with concentrated hydrochloric acid. The obtained precipitate of compound *I* was filtered, washed with water, dried and recrystallized from an appropriate solvent.

3-[2-(5-Phenyl-1,3,4-oxadiazol-2-yl)ethyl]-2(3*H*)-benzoxa(thia)zolones *IIa – IIo*; General Procedure

The corresponding freshly distilled benzoyl chloride (15 mmol) was added to a solution of benzoxa-(thia)zolone *I* (10 mmol) in 10 ml of dry pyridine and the mixture was heated at 100 °C for 2 – 4 h. After the reaction was completed (TLC) the mixture was cooled and the unreacted benzoyl chloride was hydrolyzed by addition of some water. After 15 min the mixture was poured into cold water (100 ml), allowed to stay at ambient temperature for few hours and the precipitated compound *II* was filtered, dried and recrystallized from an appropriate solvent.

The yields, melting points, analytical data and spectral characteristics of compounds *I* and *II* are listed in Tables I and II.



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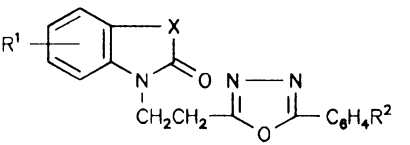

II

I	X	R^1
a	O	H
b	O	6-Br
c	O	5-Cl
d	S	H
e	S	6-Br

II	X	R^1	R^2
a	O	H	H
b	O	H	4-CH_3O
c	O	H	4-Cl
d	O	6-Br	H
e	O	6-Br	4-CH_3O
f	O	6-Br	4-Cl
g	O	5-Cl	H
h	O	5-Cl	4-CH_3O
i	O	5-Cl	4-Cl
j	S	H	H
k	S	H	4-CH_3O
l	S	H	4-Cl
m	S	6-Br	H
n	S	6-Br	4-CH_3O
o	S	6-Br	4-Cl

TABLE I
Characteristic data for compounds *Ia* – *Ic* and *IIa* – *IIo*

Compound	M. p., °C Yield, %	Formula (M. w.)	Calculated/Found		
			% C	% H	% N
Ia	208 – 209[a] 58	$C_{10}H_9N_5O_2$ (231.2)	51.95 52.04	3.92 4.16	30.28 30.30
Ib	223 – 225[a] 58	$C_{10}H_8BrN_5O_2$ (310.2)	38.73 39.09	2.60 2.51	22.57 22.90
Ic	196 – 197[a] 63	$C_{10}H_8ClN_5O_2$ (265.7)	45.21 45.55	3.04 3.29	26.36 26.30
Id	204 – 205.5[a] 68	$C_{10}H_9N_5OS$ (247.2)	48.58 48.40	3.67 3.86	28.32 28.10
Ie	258 – 260[a] 68	$C_{10}H_8BrN_5OS$ (326.2)	36.82 37.04	2.47 2.53	21.47 21.60
IIa	188 – 190[b] 67	$C_{17}H_{13}N_3O_3$ (307.3)	66.44 66.68	4.26 4.39	13.67 13.61
IIb	154 – 155[c] 72	$C_{18}H_{15}N_3O_4$ (337.3)	64.09 64.06	4.48 4.57	12.46 12.26
IIc	175 – 177[d] 68	$C_{17}H_{12}ClN_3O_3$ (341.8)	59.74 60.01	3.54 3.74	12.30 12.14
IId	199 – 201.5[d] 54	$C_{17}H_{12}BrN_3O_3$ (386.3)	52.86 52.41	3.13 3.48	10.88 10.92
IIe	188 – 189[d] 83	$C_{18}H_{14}BrN_3O_4$ (416.3)	51.94 52.11	3.39 3.66	10.09 10.37
IIf	209 – 211[d] 48	$C_{17}H_{11}BrClN_3O_3$ (420.7)	48.54 48.69	2.64 2.92	9.99 9.92
IIg	195 – 197[b] 47	$C_{17}H_{12}ClN_3O_3$ (341.8)	59.74 60.04	3.54 3.85	12.30 12.13
IIh	174 – 175.5[c] 59	$C_{18}H_{14}ClN_3O_4$ (371.8)	58.15 57.90	3.80 4.01	11.30 11.28
IIi	165 – 166.5[c] 50	$C_{17}H_{11}Cl_2N_3O_3$ (376.2)	54.27 54.62	2.95 3.20	11.17 11.33
IIj	164 – 165[b] 43	$C_{17}H_{13}N_3O_2S$ (323.4)	63.14 64.00	4.05 3.85	12.99 12.77
IIk	130 – 131.5[c] 75	$C_{18}H_{15}N_3O_3S$ (353.4)	61.18 61.25	4.28 4.41	11.89 11.94
IIl	117 – 118[c] 48	$C_{17}H_{12}ClN_3O_2S$ (357.8)	57.07 57.21	3.38 3.20	11.74 11.58
IIm	180 – 181[d] 45	$C_{17}H_{12}BrN_3O_2S$ (402.4)	50.74 50.54	3.01 2.86	10.44 10.12
IIn	177 – 178[d] 53	$C_{18}H_{14}BrN_3O_3S$ (432.4)	50.00 50.03	3.26 3.22	9.72 9.83
IIo	212 – 215[d] 50	$C_{17}H_{11}BrClN_3O_2S$ (436.8)	46.75 46.83	2.54 2.72	9.62 9.72

Crystallized from: [a] dioxane; [b] toluene; [c] ethanol; [d] acetonitrile.

TABLE II
Spectral characteristics of compounds *Ia – Ie* and *IIa – IIo*

Compound	IR spectrum $\tilde{\nu}$, cm^{-1}	^1H NMR spectrum δ, ppm
Ia[a]	3 150, 1 770	3.42 t, 2 H (CH_2); 4.28 t, 2 H (CH_2N); 6.85 – 7.35 m, 4 H (aromatic protons)
Ib[a]	3 160, 1 770, 1 780	3.42 t, 2 H (CH_2); 4.28 t, 2 H (CH_2N); 6.85 – 7.60 m, 3 H (arom.)
Ic[b]	3 130, 1 780	3.36 t, 2 H (CH_2); 4.17 t, 2 H (CH_2N); 7.10 – 7.19 m, 3 H (arom.)
Id[a]	3 150, 1 675	3.38 t, 2 H (CH_2); 4.38 t, 2 H (CH_2N); 6.95 – 7.70 m, 4 H (arom.)
Ie[c]	3 140, 1 670	3.32 t, 2 H (CH_2); 4.35 t, 2 H (CH_2N); 7.10 – 7.90 m, 3 H (arom.)
IIa[b]	1 770	3.43 t, 2 H (CH_2); 4.32 t, 2 H (CH_2N); 7.13 – 7.90 m, 9 H (arom.)
IIb[b]	1 770	3.40 t, 2 H (CH_2); 3.85 s, 3 H (CH_3); 4.30 t, 2 H (CH_2N); 7.11 – 7.83 m, 8 H (arom.)
IIc[b]	1 751	3.43 t, 2 H (CH_2); 4.32 t, 2 H (CH_2N); 7.13 – 7.91 m, 8 H (arom.)
IId[c]	1 783	3.50 t, 2 H (CH_2); 4.40 t, 2 H (CH_2N); 7.30 – 8.05 m, 8 H (arom.)
IIe[b]	1 767	3.39 t, 2 H (CH_2); 3.85 s, 3 H (CH_3); 4.29 t, 2 H (CH_2N); 7.11 – 7.83 m, 7 H (arom.)
IIf[b]	1 781	3.50 t, 2 H (CH_2); 4.40 t, 2 H (CH_2N); 7.30 – 8.10 m, 7 H (arom.)
IIg[c]	1 776	3.50 t, 2 H (CH_2); 4.42 t, 2 H (CH_2N); 7.0 – 8.05 m, 8 H (arom.)
IIh[b]	1 795	3.40 t, 2 H (CH_2); 3.85 s, 3 H (CH_3); 4.30 t, 2 H (CH_2N); 7.11 – 7.85 m, 7 H (arom.)
IIi[b]	1 773	3.42 t, 2 H (CH_2); 4.31 t, 2 H (CH_2N); 7.16 – 7.93 m, 7 H (arom.)
IIj[d]	1 659	3.40 t, 2 H (CH_2); 4.50 t, 2 H (CH_2N); 7.0 – 8.10 m, 9 H (arom.)
IIk[b]	1 676	3.34 t, 2 H (CH_2); 3.85 s, 3 H (CH_3); 4.41 t, 2 H (CH_2N); 7.11 – 7.83 m, 8 H (arom.)
IIl[c]	1 662	3.45 t, 2 H (CH_2); 4.52 t, 2 H (CH_2N); 7.05 – 8.10 m, 8 H (arom.)
IIm[b]	1 670	3.40 t, 2 H (CH_2); 4.48 t, 2 H (CH_2N); 7.35 – 8.60 m, 8 H (arom.)
IIn[d]	1 675	3.40 t, 2 H (CH_2); 3.90 s, 3 H (CH_3); 4.45 t, 2 H (CH_2N); 6.80 – 8.05 m, 7 H (arom.)
IIo[c]	1 659	3.45 t, 2 H (CH_2); 4.50 t, 2 H (CH_2N); 7.35 – 8.10 m, 7 H (arom.)

^1H NMR spectra are recorded in: [a] CD_3COCD_3–CD_3SOCD_3, [b] CD_3SOCD_3, [c] CD_3SOCD_3–CD_3COCD_3, [d] $CDCl_3$.

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