SYNTHESIS AND SOME REACTIONS OF 3-SUBSTITUTED 1,4-BIS-(4-HYDROXY-2-OXO-1,2-DIHYDROQUINOLIN-6-YLOXY)BUTANES*

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Received May 5, 1995
Accepted September 21, 1995

Condensations of 1,4-bis(4-aminophenoxy)butane *Ia* and its *N,N'*-dimethyl derivative *Ib* with substituted diethyl malonates gave 1,4-bis(4-hydroxy-2-oxo-1,2-dihydroquinolin-6-yloxy)butanes *IIa–IIf*. From these compounds, 1,4-bis(3-halogeno-2,4-dioxo-1,2,3,4-tetrahydroquinolin-6-yloxy)butanes *IIIa–IIIg* and 1,4-bis(3-hydroxy-2,4-dioxo-1,2,3,4-tetrahydroquinolin-6-yloxy)butanes *IIIh–IIIm* were prepared.

In our previous article[1], we have published the synthesis of some *N*-nitroso and *N*-(2-methyl-2-nitropropyl) derivatives of 1,4-bis(4-aminophenoxy)butane (*Ia*) and its *N,N'*-dimethyl derivative *Ib*, which act as improvers of dynamic properties of vulcanized rubber.

The amines *Ia* and *Ib* are readily available[1–4] and represent interesting starting material for the synthesis of bis(heteroaryl)alkane systems. From the literature data, however, only a few potential biologically active heterocycles on their basis were prepared: *N,N'*-bis(imidazolinylphenoxy)butanes[5,6] (lipoxygenase inhibiting antiallergics), bis(benzimidazolyloxy)butanes[7] (anthelmintics), and bis(pyrimidiniumaminophenoxy)-butanes[8] with trypanocidic activity.

In this article, we described the utilization of diamines *Ia* and *Ib* for the synthesis of bis(4-hydroxy-2-oxo-1,2-dihydroquinolinyloxy)butanes and some of their derivatives. Because many of simple derivatives of 4-hydroxy-2-quinolone are biologically active[9–15], the biological activity of presented compounds could be expected.

From diamines *I*, six 1,4-bis(4-hydroxy-2-oxo-1,2-dihydroquinolinyloxy)butanes (*IIa–IIf*) were prepared (Scheme 1) by the known condensation of anilines with sub-

* Presented at the *4th Blue Danube Symposium on Heterocyclic Chemistry, St. Polten, Austria, June 22–25, 1994*.

stituted diethyl malonates (e.g. refs[12,16,17]). Unsuccessful were condensations of diamines *I* with unsubstituted diethyl malonate, in which only polymeric substances were obtained. When diethyl phenylthiomalonate was used for the condensation, a polymer and almost theoretical amount of diphenyl disulfide were isolated.

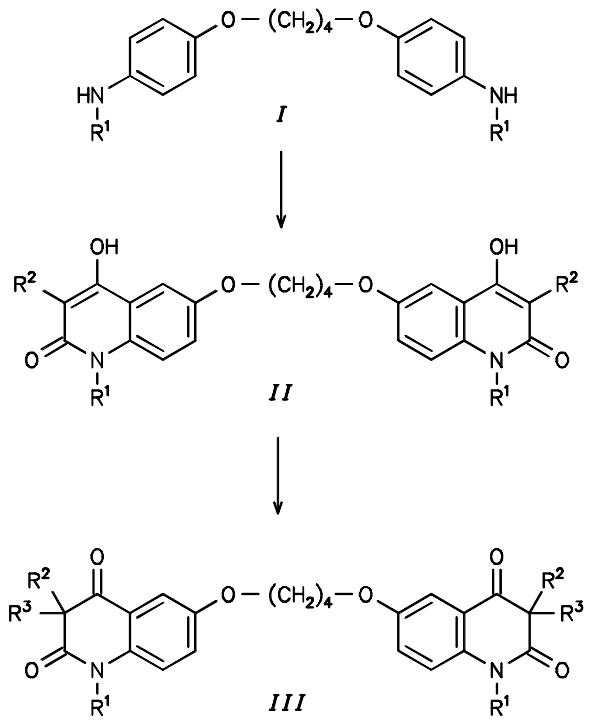
From compounds *IIa–IIf*, bis(3-halogeno-2,4-dioxo-1,2,3,4-tetrahydroquinolinyloxy)butanes *IIIa–IIIg* were obtained (Scheme 1) by their bromination in different reaction media or by chlorination with sulfuryl chloride in analogy with refs[12,17,18]. By the reduction of 3-bromo derivatives *IIIa* and *IIIb* with zinc in acetic acid or with hydrazine hydrate in ethanol, 4-hydroxyquinolones *IIa* and *IIb*, respectively, were obtained. Bis(3-hydroxy-2,4-dioxo-1,2,3,4-tetrahydroquinolinyloxy)butanes *IIIh–IIIm* were prepared by oxidation of compounds *IIa–IIf* with peroxyacetic acid according to ref.[18]. It was presented[18], that simple 3-hydroxy-2,4-quinolinediones can also be obtained by oxidation of 4-hydroxy-2-quinolones with nitric acid. However, the application of this method on our compounds of type *II* gave only mixtures of several compounds with minor content of the expected 3-hydroxy derivatives. Probably, nitration of the relatively active benzene nucleus takes place simultaneously with oxidation in position 3 of quinoline nucleus.

Some of the prepared compounds exhibit broad melting points and, in some cases, melting and a new crystallization can be observed during heating (Tables I and II). In the case of compounds *III*, this behavior could be due to the fact that these compounds are mixtures of racemate and mesoform. We assume approximately 1 : 1 ratio of these components; the preference of formation of one of both diastereoisomers is unlikely because of long distance between the positions 3 of quinolone moieties in their precursors *II*. Consequently, negligible stereospecific effect of one of new substituents on the introduction of the other could be expected. Due to long distance between the chiral centers in the molecules of substances *III* and, therefore, to a small probability of their interactions, only one spot on their thin-layer chromatograms (in several solvent systems) and the absence of any signal doubling in their NMR spectra are observed. All attempts to separate the diastereoisomers by means of recrystallization were unsuccessful. Because some compounds of the type *II*, which contain no chirality centers, exhibit also phase changes and oriented crystallization during further heating, the observed behavior of all substances under investigation can be connected with the shape of the molecule which principally enables the formation of the liquid-crystalline phase.

All elemental analyses were satisfactory (Tables I and II), the IR and ^{1}H NMR spectra of prepared compounds are presented in Table III.

EXPERIMENTAL

The melting points were determined on a Kofler block and are uncorrected. Infrared spectra were taken in potassium bromide pellets on a Perkin–Elmer 298 spectrophotometer. The ^{1}H NMR spectra were recorded on a Varian–Gemini 200 instrument using tetramethylsilane as an internal standard in



	R^1	R^2
Ia	H	–
Ib	CH_3	–
IIa	H	C_4H_9
IIb	H	$CH_2C_6H_5$
IIc	H	C_6H_5
IId	CH_3	C_4H_9
IIe	CH_3	$CH_2C_6H_5$
IIf	CH_3	C_6H_5

III	R^1	R^2	R^3
a	H	C_4H_9	Br
b	H	$CH_2C_6H_5$	Br
c	H	C_6H_5	Br
d	CH_3	C_4H_9	Br
e	CH_3	$CH_2C_6H_5$	Br
f	CH_3	C_6H_5	Br
g	CH_3	C_6H_5	Cl
h	H	C_4H_9	OH
i	H	$CH_2C_6H_5$	OH
j	H	C_6H_5	OH
k	CH_3	C_4H_9	OH
l	CH_3	$CH_2C_6H_5$	OH
m	CH_3	C_6H_5	OH

SCHEME 1

hexadeuteriodimethyl sulfoxide. All reactions were monitored by thin layer chromatography, carried out on 0.2 mm silica gel (Kavalier, Czech Republic) plates by using the solvent system chloroform–ethanol (9 : 1 and/or 19 : 1); for detection UV light and/or iodine vapours were used. Preparative column chromatography was carried out on silica gel 0.10/0.16 mm (Kavalier, Czech Republic).

General Procedure for the Synthesis of 1,4-Bis(4-hydroxy-2-oxo-1,2-dihydroquinolin-6-yloxy) butanes *II*

Method A. The mixture of respective diamine *I* (0.02 mol) and substituted diethyl malonate (0.044 mol) was heated on a metal bath at 180–200 °C for 0.5 h and then at 270–285 °C. Evolved ethanol was collected and weighed. When the near theoretical quantity of ethanol was obtained, the mixture was cooled, the solid product was crushed, washed several times with petroleum ether and/or diethyl ether and recrystallized. In the case of chromatographically impure product, purification by dissolving in

TABLE I
Characteristic data of substituted 1,4-bis(4-hydroxy-2-oxo-1,2-dihydroquinolin-6-yloxy)butanes *II*

Compound	Yield, % (Method)	M.p., °C (Solvent[a])	Formula (M.w.)	Calculated/Found		
				% C	% H	% N
IIa	87 (*A*)	302–307	$C_{30}H_{36}N_2O_6$	69.21	6.97	5.38
	74 (*B*)	(BuOH–DMF)	(520.6)	68.92	6.91	5.52
IIb	92 (*A*)	292–302	$C_{36}H_{32}N_2O_6$	73.45	5.48	4.76
	68 (*B*)	(DMF)	(588.7)	73.16	5.39	4.81
IIc	72 (*A*)	303–309	$C_{34}H_{28}N_2O_8$	72.85	5.03	5.00
		(DMSO)	(560.6)	72.87	4.82	5.30
IId	93 (*A*)	106–112,	$C_{32}H_{40}N_2O_6$	70.05	7.35	5.11
		204–209	(548.7)	69.68	7.47	4.79
		(BuOH–EtOH)				
IIe	96 (*A*)	158–162,	$C_{38}H_{36}N_2O_6$	74.01	5.88	4.54
	95 (*C*)	284–288	(616.7)	73.72	5.80	4.72
		(BuOH–DMF)				
IIf	83 (*A*)	300–312	$C_{36}H_{32}N_2O_6$	73.45	5.48	4.76
		(DMSO)	(588.7)	73.19	5.43	4.80

[a] BuOH 1-butanol, EtOH ethanol.

TABLE II
Characteristic data of 3-substituted 1,4-bis(2,4-dioxo-1,2,3,4-tetrahydroquinolin-6-yloxy)butanes *III*

Compound	Yield, % (Method)	M.p., °C (Solvent[a])	Formula (M.w.)	Calculated/Found		
				% C	% H	% N
IIIa	78 (*A*) 83 (*C*)	193–194 (EtOH)	$C_{30}H_{34}Br_2N_2O_6$ (678.4)	53.11 53.40	5.05 4.91	4.13 3.71
IIIb	74 (*D*)	207–209 (EtOH)	$C_{36}H_{30}Br_2N_2O_6$ (746.5)	57.93 57.70	4.05 3.91	3.75 4.02
IIIc	24[b](*D*)	289–308	$C_{34}H_{26}Br_2N_2O_6$ (718.4)	56.84 56.45	3.65 3.96	3.90 4.12
IIId	68 (*B*) 76 (*C*)	54–58 (MeOH)	$C_{32}H_{38}Br_2N_2O_6$ (706.5)	54.40 54.36	5.42 5.16	3.96 3.75
IIIe	88 (*D*)	128–129 (benzene)	$C_{38}H_{34}Br_2N_2O_6$ (774.5)	58.93 58.79	4.42 4.33	3.62 3.71
IIIf	57 (*E*)	97–100	$C_{36}H_{30}Br_2N_2O_6$ (746.5)	57.93 57.63	4.05 4.11	3.75 3.91
IIIg	96	150–160	$C_{36}H_{30}Cl_2N_2O_6$ (657.5)	65.76 65.23	4.60 4.69	4.26 4.26
IIIh	96	132–142, 218–226 (MeOH)	$C_{30}H_{36}N_2O_8$ (552.6)	65.20 65.25	6.57 6.44	5.07 4.69
IIIi	96	152–154, 276–281 (EtOH)	$C_{36}H_{32}N_2O_8$ (620.7)	69.67 69.51	5.20 5.17	4.51 4.38
IIIj	87	299–308 (BuOH–DMF)	$C_{34}H_{28}N_2O_8$ (592.6)	68.91 68.60	4.76 4.61	4.73 4.45
IIIk	78	73–76 (benzene)	$C_{32}H_{40}N_2O_8$ (580.7)	66.19 65.98	6.94 6.80	4.82 4.41
IIIl	98	86–90, 182–189 (benzene)	$C_{38}H_{36}N_2O_8$ (648.7)	70.36 70.19	5.59 5.50	4.32 4.18
IIIm	96	310–328 (MeOH–DMF)	$C_{36}H_{32}N_2O_8$ (620.7)	69.67 69.53	5.20 5.15	4.51 4.28

[a] MeOH methanol, EtOH ethanol, BuOH 1-butanol. [b] Purified by column chromatography on silica gel, eluent chloroform–ethanol 96 : 4.

TABLE III

Spectroscopic data for 1,4-bis(4-hydroxy-2-oxo-1,2-dihydroquinolin-6-yloxy)butanes *II* and 1,4-bis(2,4-dioxo-1,2,3,4-tetrahydroquinolin-6-yloxy)butanes *III*

Compound	IR ($\tilde{\nu}$, cm^{-1})	^1H NMR (δ, ppm)[a]
IIa	3 540–3 100 br, 2 952 m, 2 925 m, 2 862 m, 1 642 s, 1 620 sh, 1 603 s, 1 561 m, 1 507 s, 1 462 m, 1 428 m, 1 270 s, 1 234 s, 1 218 s, 1 195 sh, 1 165 m, 1 136 m	0.93 t, 3 H, *J* = 7.0 (CCH_3); 1.23–1.52 m, 4 H (H-2 and H-3 of butyl); 1.92 s, 2 H ($OCCH_2$); 2.59 t, 2 H, *J* = 7.0 (H-1 of butyl); 4.08 s, 2 H (OCH_2); 7.12 dd, 1 H, *J* = 8.0 and 2.0 (H-7); 7.21 d, 1 H, *J* = 8.0 (H-8); 7.40 d, 1 H, *J* = 2.0 (H-5); 9.93 s, 1 H (OH); 11.20 s, 1 H (NH)
IIb	3 600–2 800 br, 1 655 sh, 1 645 s, 1 620 s, 1 612 sh, 1 604 s, 1 557 m, 1 508 m, 1 453 m, 1 418 m, 1 382 m, 1 325 m, 1 271 m, 1 240 sh, 1 230 s, 1 215 m, 1 200 m	1.95 s, 2 H ($OCCH_2$); 3.95 s, 2 H ($ArCH_2$); 4.09 brs, 2 H (OCH_2); 7.16 dd, 1 H, *J* = 8.0 and 2.0 (H-7); 7.20–7.32 m, 6 H (H-8 and arom.); 7.48 d, 1 H, *J* = 2.0 (H-5); 10.31 brs, 1 H (OH); 11.30 s, 1 H (NH)
IIc	3 600–2 400 br, 1 648 s, 1 614 s, 1 601 s, 1 512 s, 1 477 m, 1 450 m, 1 370 m, 1 293 s, 1 234 s, 1 201 s, 1 050 m, 1 030 m, 821 m, 710 s, 660 m	1.88–2.02 m, 2 H ($OCCH_2$); 4.04–4.18 m, 2 H (OCH_2); 7.20 dd, 1 H, *J* = 9 and 2.6 (H-7); 7.23–7.46 m, 6 H (phenyl and H-8); 7.50 d, 1 H, *J* = 2.6 (H-5); 10.00 brs, 1 H (OH); 11.35 s, 1 H (NH)
IId	3 500–2 900 br, 2 955 m, 2 930 m, 2 875 m, 1 634 m, 1 611 s, 1 581 s, 1 509 m, 1 465 m, 1 345 m, 1 282 s, 1 225 m, 1 212 s, 1 193 s, 816 m	0.90 t, 3 H, *J* = 7.0 (CCH_3); 1.27–1.47 m, 4 H, (H-2 and H-3 of butyl); 1.96 brs, 2 H ($OCCH_2$); 2.63 t, 2 H, *J* = 7.0 (H-1 of butyl); 3.57 s, 3 H (NCH_3); 4.13 brs, 2 H (OCH_2); 7.22 dd, 1 H, *J* = 9.0 and 2.6 (H-7); 7.40 d, 1 H, *J* = 9.0 (H-8); 7.51 d, 1 H, *J* = 2.6 (H-5); 9.98 brs, 1 H (OH)
IIe	3 600–2 800 br, 1 640 sh, 1 612 s, 1 565 s, 1 510 s, 1 491 m, 1 420 m, 1 399 m, 1 351 m, 1 332 m, 1 269 m, 1 235 s, 1 218 s, 1 170 m, 971 m, 699 m	1.96 s, 2 H ($OCCH_2$); 3.58 s, 3 H (NCH_3); 4.00 s, 2 H ($ArCH_2$); 4.15 s, 2 H (OCH_2); 7.15–7.30 m, 6 H (H-7 and arom.); 7.43 d, 1 H, *J* = 8.0 (H-8); 7.58 d, 1 H, *J* = 2.0 (H-5); 10.35 brs, 1 H (OH)
IIf	3 400–2 700 br, 1 638 s, 1 618 s, 1 603 s, 1 580 s, 1 514 s, 1 458 m, 1 340 m, 1 300 m, 1 263 m, 1 229 m, 1 210 s, 1 118 m, 1 054 m, 1 023 m, 864 m, 807 m, 748 m, 696 m	1.94–2.04 m, 2 H ($OCCH_2$); 3.61 s, 3 H (CH_3); 4.16 t, 2 H, *J* = 7 (OCH_2); 7.31 dd, 1 H, *J* = 9 and 2.6 (H-7); 7.36–7.45 m, 5 H (phenyl); 7.51 d, 1 H, *J* = 9 (H-8); 7.59 d, 1 H, *J* = 2.6 (H-5)
IIIa	3 200–2 800 br, 1 705 s, 1 667 s, 1 658 sh, 1 502 s, 1 470 m, 1 425 m, 1 341 m, 1 262 m, 1 199 m, 824 m	0.85 t, 3 H, *J* = 7.0 (CCH_3); 1.15–1.22 m, 2 H (H-3 of butyl); 1.22–1.40 m, 2 H (H-2 of butyl); 1.90 s, 2 H ($OCCH_2$);2.43 t, 2 H, *J* = 8.0 (H-1 of butyl); 4.10 s, 2 H (OCH_2); 7.12 dd, 1 H, *J* = 8.0 and 2.0 (H-7); 7.30–7.40 m, 2 H (H-5, H-8); 11.19 s, 1 H (NH)

TABLE III
(*Continued*)

Compound	IR ($\tilde{\nu}$, cm^{-1})	^1H NMR (δ, ppm)[a]
IIIb	3 400–2 800 br, 1 702 s, 1 667 s, 1 658 sh, 1 619 m, 1 501 s, 1 428 m, 1 348 s, 1 278 m, 1 236 m, 1 190 m, 702 m	1.87 s, 2 H ($OCCH_2$); 3.87 s, 2 H ($ArCH_2$); 4.08 s, 2 H (OCH_2); 7.04 dd, 1 H, *J* = 8.0 and 2.0 (H-7); 7.15–7.37 m, 7 H (arom.); 11.25 s, 1 H (NH)
IIIc	1 708 s, 1 667 s, 1 615 m, 1 500 s, 1 469 m, 1 447 m, 1 420 m, 1 341 s, 1 271 m, 1 215 m, 1 182 m, 825 m, 735 m, 696 m, 659 m, 637 m	1.82–1.97 m, 2 H ($OCCH_2$); 4.00–4.16 m, 2 H (OCH_2); 7.05–7.55 m, 8 H (arom.); 11.34 s, 1 H (NH)
IIId	2 940 m, 2 868 m, 1 703 sh, 1 696 s, 1 664 s, 1 656 sh, 1 617 m, 1 587 m, 1 501 s, 1 468 s, 1 441 s, 1 348 s, 1 290 s, 1 235 m, 1 213 m, 1 172 m, 1 125 m, 1 087 m, 1 041 m, 819 m	0.86 t, 3 H, *J* = 7.5 (CCH_3); 1.08–1.26 m, 2 H (H-3 of butyl); 1.26–1.44 m, 2 H (H-2 of butyl); 1.93 s, 2 H ($OCCH_2$); 2.38–2.58 m, 2 H (H-1 of butyl); 3.45 s, 3 H (NCH_3); 4.17 s, 2 H (OCH_2); 7.42 brs, 3 H (arom.)
IIIe	3 100–2 800 br, 1 704 s, 1 693 s, 1 668 sh, 1 611 s, 1 500 s, 1 468 s, 1 441 s, 1 351 s, 1 292 m, 1 241 m, 1 212 m, 1 131 m, 819 m, 702 m	1.92 brs, 2 H ($OCCH_2$); 3.41 s, 3 H (NCH_3); 3.91 s, 2 H ($ArCH_2$); 4.15 brs, 2 H (OCH_2); 7.10–7.45 m, 8 H (arom.)
IIIf	1 705 s, 1 671 s, 1 620 m, 1 590 m, 1 505 s, 1 471 s, 1 443 s, 1 349 s, 1 299 s, 1 240 m, 1 225 m, 1 199 m, 1 135 m, 740 m	1.80–1.90 m, 2 H ($OCCH_2$); 3.47 s, 3 H (CH_3); 4.00–4.10 m, 2 H (OCH_2); 7.20–7.50 m, 8 H (arom.)
IIIg	1 710 s, 1 678 s, 1 582 m, 1 501 s, 1 468 s, 1 440 s, 1 341 m, 1 295 s, 1 286 sh, 1 238 m, 1 204 m, 1 129 m, 1 052 m, 1 036 m, 812 m, 760 m, 690 m	1.83–1.93 m, 2 H ($OCCH_2$); 3.49 s, 3 H (CH_3); 4.02–4.14 m, 2 H (OCH_2); 7.28–7.47 m, 8 H (arom.)
IIIh	3 500–3 200 br, 2 955 m, 2 925 m, 1 706 m, 1 670 s, 1 619 m, 1 500 s, 1 468 m, 1 420 m, 1 342 m, 1 269 m, 1 219 m, 1 192 m, 1 163 m, 824 m	0.78 t, 3 H, *J* = 7.0 (CCH_3); 1.08–1.40 m, 4 H (H-2 and H-3 of butyl); 1.62–1.80 m, 2 H (H-1 of butyl); 1.87 s, 2 H ($OCCH_2$); 4.06 s, 2 H (OCH_2); 5.63 s, 1 H (OH); 7.02 dd, 1 H, *J* = 7.0 and 2.0 (H-7); 7.20 d, 1 H, *J* = 2.0 (H-5); 7.25 d, 1 H, *J* = 7.0 (H-8); 10.61 s, 1 H (NH)
IIIi	3 600–2 800 br, 1 722 sh, 1 712 s, 1 671 s, 1 653 s, 1 618 s, 1 498 s, 1 471 m, 1 452 m, 1 420 m, 1 345 m, 1 270 m, 1 219 s, 1 179 m, 698 m	1.89 brs, 2 H ($OCCH_2$); 3.07 s, 2 H ($ArCH_2$); 4.07 brs, 2 H (OCH_2); 5.93 s, 1 H (OH); 6.90–7.33 m, 8 H (arom.); 10.68 s, 1 H (NH)
IIIj	3 640–3 000 br, 2 942 m, 1 640 s, 1 608 s, 1 595 s, 1 502 m, 1 468 m, 1 445 m, 1 430 m, 1 392 m, 1 364 m, 1 288 s, 1 228 s,1 194 s, 1 042 m, 1 022 m, 817 m, 782 m, 750 m, 705 s, 695 m, 653 m	1.88–2.02 m, 2 H ($OCCH_2$); 4.06–4.18 m, 2 H (OCH_2); 7.20–7.5 m, 8 H (Ar-H); 11.16 brs, 1 H (NH)

TABLE III
(*Continued*)

Compound	IR ($\tilde{\nu}$, cm^{-1})	^1H NMR (δ, ppm)[a]
IIIk	3 550–3 300 br, 2 960 m, 1 710 s, 1 661 s, 1 501 s, 1 468 s, 1 352 m, 1 305 m, 1 285 m, 1 225 s, 1 179 m, 1 114 m	0.76 t, 3 H, J = 6.6 (CCH_3); 1.06–1.28 m, 4 H (H-2 and H-3 of butyl); 1.62–1.77 m, 2 H (H-1 of butyl); 1.91 brs, 2 H ($OCCH_2$); 3.38 s, 3 H (NCH_3); 4.11 brs, 2 H (OCH_2); 5.70 s, 1 H (OH); 7.26–7.37 m, 3 H (arom.)
IIIl	3 600–3 100 br, 2 930 m, 2 870 m, 1 722 sh, 1 708 s, 1 662 s, 1 640 sh, 1 613 m, 1 585 m, 1 498 s, 1 469 s, 1 442 s, 1 351 m, 1 272 s, 1 223 s, 1 128 m, 1 103 s, 1 121 m, 700 m	1.94 brs, 2 H ($OCCH_2$); 3.03 s, 2 H ($ArCH_2$); 3.31 s, 3 H (NCH_3); 4.12 brs, 2 H (OCH_2); 5.96 s, 1 H (OH); 6.88–7.32 m, 8 H (arom.)
IIIm	3 300–3 100 br, 3 042 m, 2 940 m, 2 860 m, 1 631 s, 1 611 s, 1 598 s, 1 572 s, 1 508 s, 1 473 m, 1 450 m, 1 438 m, 1 335 m, 1 295 m, 1 259 m, 1 222 s, 1 205 s, 1 178 m, 1 112 m, 1 018 m, 800 s, 689 m	1.98 brs, 2 H ($OCCH_2$); 3.62 s, 3 H (CH_3); 4.16 brs, 2 H (OCH_2); 7.30–7.65 m, 8 H (arom.)

[a] According to the symmetry of the measured compounds, the numbers of hydrogen atoms are calculated for a half of the molecule.

0.5 M sodium hydroxide, filtration, precipitation with diluted hydrochloric acid and repeated crystallization was carried out.

Method B. The mixture of 3-bromo derivative *III* (1 mmol), acetic acid (30 ml) and zinc (0.5 g) was refluxed for 0.5 h. After cooling, the precipitate was filtered with suction, washed with diluted acetic acid and recrystallized from acetic acid.

Method C. To a stirred suspension of 3-bromo derivative *III* (1 mmol) in ethanol (30 ml), the solution of potassium hydroxide (0.4 g, 7 mmol) and hydrazine hydrate (0.2 g, 4 mmol) in ethanol (20 ml) was added within 10 min at 60 °C. After additional 15 min at this temperature, the mixture was taken down in vacuo to 15 ml, diluted with water (30 ml) and acidified with diluted (1 : 1) hydrochloric acid. The precipitate was filtered with suction and recrystallized.

General Procedure for the Synthesis of 1,4-Bis(3-bromo-2,4-dioxo-1,2,3,4-tetrahydroquinolin-6-yloxy)butanes *IIIa–IIIf*

Method A. To a stirred solution of the corresponding bis(quinolone) *II* (5 mmol) in acetic acid (from 60 to 150 ml), bromine (1.9 g, 12 mmol) was added at laboratory temperature within 10 min. After 15 min of stirring, the solution was filtered and the filtrate was diluted with water. Precipitated product was filtered with suction, washed with water and recrystallized.

Method B. The procedure is identical with that of method *A*, the mixture acetic acid–dioxan (9 : 1) was used as solvent.

Method C. The procedure is identical with that of method *A*, 0.25 M sodium hydroxide (120 ml) was used as solvent.

Method D. To a stirred suspension of the corresponding bis(quinolone) *II* (5 mmol) in chloroform (60 ml), bromine (1.9 g, 12 mmol) was added at laboratory temperature within 10 min. After 15 min of stirring the solution was filtered, the filtrate was evaporated in vacuo to dryness and the residue was recrystallized.

Method E. The procedure is identical with that of method *D*, tetrachloroethene was used as reaction medium. The reaction was carried out under cooling with ice bath, the product was precipitated from the reaction mixture with petroleum ether.

1,4-Bis(2-chloro-1-methyl-3-phenyl-2,4-dioxo-1,2,3,4-tetrahydroquinolin-6-yloxy)butane (*IIIg*)

To the stirred suspension of compound *IIf* (3.42 g, 5.81 mmol) in chloroform (116 ml), sulfuryl chloride (5.23 g, 39.1 mmol) was added. After 7 h boiling under stirring, the mixture was filtered under suction. The filtrate was taken down in vacuo and the residue was triturated with methanol. Yield 3.68 g (96%) yellow crystals of the compound *IIIg*.

General Procedure for the Synthesis of 1,4-Bis(3-hydroxy-2,4-dioxo-1,2,3,4-tetrahydroquinolin-6-yloxy)butanes *IIIh–IIIm*

To a stirred solution of respective bis(quinolone) *II* (5 mmol) in 0.25 M sodium hydroxide (120 ml), 30% peroxyacetic acid (20 ml) was added within 0.5 h at laboratory temperature. After additional 1 h stirring, the precipitated product was filtered with suction, washed with water, aqueous sodium bicarbonate and water till the filtrate was neutral, and recrystallized. All hydroxy derivatives show a characteristic light blue fluorescence on TLC plates.

The elemental analyses were performed in the Institute of Organic and Analytical Chemistry, Palacky University, Olomouc. This study was supported by the Grant Agency of the Czech Republic (Grant No. 104/94/0104).

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