ors [10] ascertained the presence of a maximum of M-cholinolytic activity in compounds also with an octyl radical for another class of substances.

Thus, on the examples of two homologous series of organophosphorus M-cholinolytics, containing an ammonium or sulfonium atom, we demonstrated the pattern of variation of their activity as a function of the length of the aliphatic radical at the onium atom. The results obtained can be used in the targeted search for new M-cholinolytics and the search for ways of modifying already known compounds in order to increase their activity.

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SYNTHESIS AND BIOLOGICAL ACTIVITY OF 4-SUBSTITUTED 1,2-NAPHTHOQUINONES, 1,2-NAPHTHALENEDIOLS, AND THEIR DERIVATIVES

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It has already been shown [1-3] that different 1,2-naphthoquinones, in particular, 6-halo-1,2-naphthoquinones [1-2], exhibit antiviral activity. Research on this series of compounds led to finding an original preparation for systemic application, bonaphthone (6-bromo-1,2-naphthoquinone) [4, 7]. It was therefore of interest to synthesize and study antiviral compounds structurally similar to bonaphthone, i.e., halo-1,2-naphthoquinones substituted at the 4-position.

In the present work, we studied the reactions of 3-chloro- (Ia), 6-bromo-3-chloro (Ib), 3,6-dibromo- (Ic), and 6-bromo-3-nitro-1,2-naphthoquinones (Id) with malonic and cyanoacetic esters and MeOH, and also the antiviral and antimicrobial activity of the compounds obtained.

The reaction of malonic and cyanoacetic esters with quinones Ia-c in an alcoholic–dioxane medium in the presence of EtONa led to the formation of 1,2-naphthalenediols (IIa-c, e,

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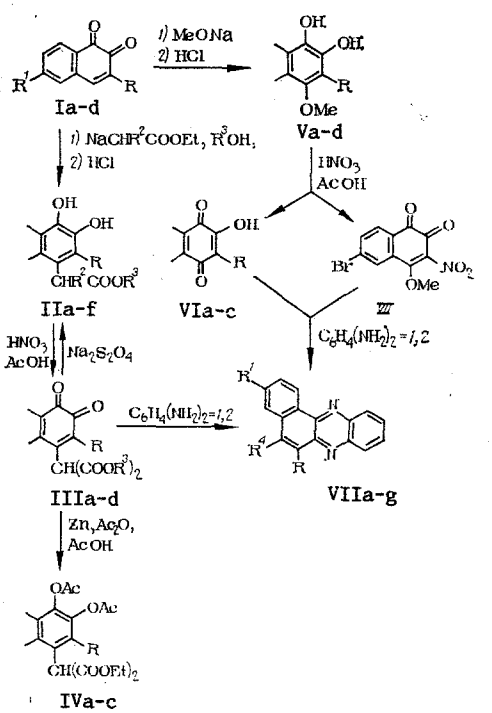
f). During oxidation, compounds IIa-c converted into the corresponding derivatives of 1,2-naphthoquinone (IIIa-c). Diols IIe, f underwent polymerization during oxidation. Reduction of 1,2-naphthoquinones IIIa-c by sodium hydrosulfite gave the 1,2-naphthalenediols II-a-c again. When sodium methylate in MeOH was used in the condensation of quinone Ic with malonic ester, a transesterification of the malonic ester residue was observed. After the oxidation of the intermediate 1,2-naphthalenediol (IId), identified mass-spectrometrically, the dimethyl ester of naphthoquinolylmalonic acid (IIId) was obtained.

The individual products of the addition of malonic and cyanoacetic esters to nitroquinone Id could not be isolated.

In the reaction with o-phenylenediamine, quinones IIIa-c were converted into phenazine derivatives (VIIIa-c), and in a reductive acetylation, into diacetates (IVa-c). During the reductive acetylation, quinone IIIc underwent also debromination with the formation of diacetate IVc, whose structure was confirmed by the PMR spectral data.

The reaction of quinones Ia-d with MeONa led initially to 6-methoxy-1,2-naphthalenediols (Va-d), whose formation in all cases was confirmed mass spectrometrically, while compound Vc was isolated and characterized. Depending on the character of the substituent at the 3-position, the oxidation of compounds Va-d led to the formation of either 2-hydroxy-1,4-naphthoquinones (VIa-c), or 3-nitro-4-methoxy-6-bromo-1,2-naphthoquinone (VII). Two of these compounds (VIa, c) were previously obtained by other methods [8, 9]. Compounds VIa-c and VII were converted into derivatives of phenazine (VIIId-g), one of which, VIIId, was described previously in [11, 12].

The structure of compounds obtained was confirmed by the data of IR, PMR, and mass spectroscopy.



I, IV-VI:a—R = Cl, R^1 = H; b—R = Cl, R^1 = Br;
I, V, VIc:R = R^1 = Br; I, Vd:R = NO_2, R^1 = Br;
IVc R = H, R^1 = Br; II, III:a—R = Cl, R^1 = H,
R^2 = COOEt, R^3 = Et; b—R = Cl, R^1 = Br,
R^2 = COOEt, R^3 = Et; c—R = R^1 = Br, R^2 = COOEt,
R^3 = Et; d—R = R^1 = Br, R^2 = COOMe, R^3 = Me;
II: e—R = Cl, R^1 = H, R^2 = CN, R^3 = Et; f—R = R^1 = Br,
R^2 = CN, R^2 = Et; VIII: a—R = Cl, R^1 = H, R^4 = $CH(COOEt)_2$;
b—R = Cl, R^1 = Br, R^4 = $CH(COOEt)_2$; c—R = R^1 = Br,
R^4 = $CH(COOEt)_2$; d—R = Cl, R^1 = H, R^4 = OH;
e—R = Cl, R^1 = Br, R^4 = OH; f—R = R^1 = Br, R^4 = OH;
g—R = NO_2, R^1 = Br, R^4 = OMe.

TABLE 1. Diethyl(3,4-diacetoxy-1-naphthyl)malonates IIa-c, Ethyl(3,4-dihydroxy-1-naphthyl)cyanoacetates IIe, f, Dialkyl(3,4-dihydro-3,4-dioxo-1-naphthyl)malonates IIIa-d, and Diethyl(3,4-dihydroxy-1-naphthyl)-malonates IVa-c

Compound	Yield, %	mp, °C	Found, %			Empirical formula	Calc., %			M		IR spectrum, ν_{max}, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)
			C	H	Br (Cl)		C	H	Br (Cl)	found[c]	calc.		
IIa	96	139—40	57,76	4,76	(10,09)	$C_{17}H_{17}ClO_6$	57,88	4,86	(10,05)	352	352,8	3430—3415 (OH), 1740—1720 (C=O)	242 (4,74), 297 (3,65), 306 (3,68), 340 (3,51)
IIb	97	155—6	47,40	3,80	18,54 (8,22)	$C_{17}H_{16}BrClO_6$	47,30	3,74	18,51 (8,21)	430	431,7	3400 (OH), 1740—1730 (C=O)	250 (4,78), 303 (3,66), 331 (3,65), 348 (3,51)
IIc	97	162—4	42,87	3,32	33,50	$C_{17}H_{16}Br_2O_6$	42,88	3,38	33,56	474	476,1	3390 (OH), 1735, 1710 (C=O)	251 (4,77), 302 (3,64), 310 (3,63), 347 (3,53)
IId	80[a]	99—101	58,76	3,95	(11,61)	$C_{15}H_{13}ClNO_4$	58,93	3,96	(11,60)	305	305,7	3320 (OH), 2260 (C≡N), 1740 (C=O)	244 (4,59), 298 (3,60), 308 (3,62), 342 (3,51)
IIe	82[b]	203—5	42,22	2,65	37,36	$C_{15}H_{11}Br_2NO_4$	41,99	2,58	37,25	427	429,1	3320 (OH), 2025 (C≡N), 1740 (C=O)	222 (4,32), 253 (4,67), 303 (3,52), 349 (3,46)
IIIf	60	132—3	47,57	3,28	18,53 (8,29)	$C_{17}H_{14}BrClO_6$	47,52	3,28	18,60 (8,25)	428	429,7	1745—1735, 1690 (C=O)	209 (4,32), 254 (4,42), 352 (3,61)
IIIb*	70	127—8	43,02	2,86	33,85	$C_{17}H_{14}Br_2O_6$	43,07	2,98	33,71	472	474,1	1750—1730, 1690 (C=O)	207 (4,60), 262 (4,65), 358 (3,88)
IIIc†	76	182—4	40,62	2,30	35,81	$C_{15}H_{10}Br_2O_6$	40,39	2,26	35,83	444	446,1	1775—1730, 1690 (C=O)	215 (4,58), 267 (4,69), 354 (3,91)
IVa	96	147—8	57,67	5,18	(8,33)	$C_{21}H_{21}ClO_8$	57,73	4,84	(8,11)	436	436,9	1770, 1740 (C=O)	233 (4,84), 270 (3,70), 279 (3,85), 289 (3,92), 300 (3,79) sh
IVb	90	152—3	49,13	3,99	15,46 (6,86)	$C_{21}H_{20}BrClO_8$	48,90	3,90	15,50 (6,87)	514	515,8	1780, 1745—1725 (C=O)	241 (4,93) sh 284 (3,47), 292 (3,81), 300 (3,71), 333 (2,95)
IVc‡	94	125	52,18	4,31	16,59	$C_{21}H_{21}BrO_8$	52,40	4,40	16,60	480	481,3	1770, 1745—1725 (C=O)	238 (4,85), 286 (3,90), плечо 297 (3,84), 317 (3,08), 332 (3,07)

[a]Found, %: N 4.59. Calculated, %: N 4.58.

[b]Found, %: N 3.00. Calculated, %: N 3.26.

[c]Mass-spectrometrically, peaks of molecular monoisotopic (^{79}Br, ^{35}Cl) ions.

*PMR spectrum ($CDCl_3$ + CD_3OD), δ, ppm: 1.29 t ($COOCH_2CH_3$), 4.31 q ($COOCH_2CH_3$), 5.65 s ($\underline{H}C(COOC_2H_5)_2$), 7.66-8.02 m (5-H, 7-H, 8-H).

†PMR spectrum, δ, ppm: 3.85 s ($COOCH_3$), 5.67 s ($\underline{H}C(COOCH_3)_2$), 7.72-7.98 m (5-H, 7-H, 8-H). Integral intensities 6:1:3.

‡PMR spectrum, δ, ppm: 1.28 t ($COOCH_2\underline{CH_3}$), 2.32 s, 2.45 s ($OCOCH_3$), 4.26 q ($COO\underline{CH_2}CH_3$), 5.28 s ($\underline{H}C(COOC_2H_5)_2$), 7.58-7.81 m (5-H, 7-H, 8-H), 8.14 (3-H).

Note. Compounds IIa-c, e, III, IV-a-c were recrystallized from alcohol, IIf from AcOH, IIId from ethyl acetate.

CHEMICAL EXPERIMENTAL

The IR spectra were run on Perkin-Elmer 599 and Perkin-Elmer 457 spectrophotometers (Sweden) in a suspension in mineral oil; the UV spectra were measured on Hitachi EPS-3T (Japan) and Perkin-Elmer 575 (Sweden) spectrometers in alcohol. The PMR spectra were obtained on a Varian XL-100 spectrometer (Switzerland) (100 MHz) in $CDCl_3$ and d_6-acetone solutions, using TMS as internal standard. The mass spectra were run on a Varian-Mat-112 mass spectrometer (GFR) (70 eV) with a direct introduction of the sample to the ionic source. The melting points were measured on a PTP-1 apparatus, at a heating rate of 1-3°C/min near the melting point. The individual state of the compounds was controlled by TLC on Silufol UV-254 plates (from the firm Kavalier ChSSR), using as eluents $CHCl_3$ or a benzene–methanol mixture, 9:1, and developing in UV light.

3-Chloro-6-bromo-1,2-naphthoquinone (Ib). A strong current of chlorine is passed through a suspension of 23.7 g of 6-bromo-1,2-napthoquinone in 300 ml glacial acetic acid up to the formation of a solution, which is immediately poured into 900 ml of hot (80-85°C) water. The reaction mixture is cooled, an orange precipitate is filtered, washed with water, and dried. The yield of Ib is 22 g (81%), mp 165-167°C ($CHCl_3$). IR spectra ν_{max}, cm^{-1}: 1685 (C=O). Found, %: C 44.08; H 1.71; Br 29.28; Cl 13.02. M^+ 270 (^{79}Br, ^{35}Cl). $C_{10}H_4BrClO_2$. Calculated, %: C 44.24; H 1.48, Br 29.43; Cl 13.06. M 271.5.

Ethyl(3,4-dihydroxy-1-naphthyl)cyanoacetates (IIe, f) (Table 1). A solution of 0.01 mole of quinone Ia or Ic in 30 ml of anhydrous dioxane is added in one portion, with stirring, to a solution containing 0.02 mole of EtONa and 2.3 ml (0.02 mole) of cyanoacetic ester in 50 ml of absolute ethanol. The mixture is stirred for 2 min, then 5 ml of concentrated HCl, 20 ml of water, and 5 ml of a freshly distilled 10% solution of $Na_2S_2O_4$ are added, and the mixture is poured into 170 g of crushed ice. The mixture is left to stand in a refrigerator for 4 days. The precipitate is filtered, washed with water, dried in a vacuum desiccator over P_2O_5, ground with 5 ml of ether, filtered, and filtrate washed with 5 ml of ether. Colorless crystalline compounds which become blue on contact with aqueous solutions of bases.

Compounds Ia-c were obtained under similar conditions by the action of malonic ester on quinones IIa-c.

Diethyl(2-chloro-3,4-dihydro-3,4-dioxo-1-naphthyl)malonate (IIIa). A solution of sodium-malonic ester obtained from 3.2 ml (0.02 mole) of malonic ester and 0.46 g (0.02 mole) of Na in 20 ml of absolute ethanol is added in one portion to a solution of 1.9 g (0.01 mole) of quinone Ia in a mixture of 30 ml of anhydrous dioxane and 50 ml of anhydrous alcohol. After 3 min, the reaction mixture is acidified with 4 ml of concentrated HCl. The NaCl precipitate is filtered, and the filtrate is evaporated in a rotary evaporator. The residue is dissolved in 10 ml of AcOH and oxidized with 5 ml of HNO_3 (d 1.35). After the dark coloration changes into orange, the reaction mixture is diluted with water and extracted with $CHCl_3$. The organic layer is separated, washed twice with water, dried, and evaporated in a rotary evaporator. The residue is ground with ether with ice cooling, and the precipitate is filtered, and washed with 2 ml of ether. The yield of IIIa is 1.82 g (52%), mp 97-98°C (alcohol IR spectrum, ν_{max}, cm^{-1}: 1755-1730, 1680 (C=O). UV spectrum, λ_{max}, nm (log ε): 208 (4.51), 245 (4.55), 260 (4.48), 344 (3.67). Literature data [10]: mp 97°C (alcohol).

Compounds IIIb, c were obtained in a similar way (see Table 1). Orange-red crystalline substances.

Dimethyl(2,7-dibromo-3,4-dihydro-3,4-dioxo-1-naphthyl)malonate (IIId). A solution of 0.01 mole of MeONa and 1.6 ml (0.01 mole) of malonic ester in 20 ml of MeOH is added to a solution of 1.58 g (0.005 mole) of quinone IIIc in 15 ml of anhydrous dioxane and 35 ml of MeOH. The reaction solution is treated under the conditions of the isolation of compound IIIa. Dark-red crystals; for other data on compound IIId, see Table 1.

Diethyl(3,4-dihydroxyl-1-naphthyl)malonates (IIa-c). A freshly prepared 10% solution of $Na_2S_2O_4$ is added dropwise to a hot solution of 0.01 mole of quinone IIIa-c in 40 ml of alcohol, up to decoloration. The reaction mixture is cooled, poured into a mixture of 100 ml of water and 50 g of crushed ice, the precipitate is filtered, washed with water, and dried in a vacuum desiccator over P_2O_5. Colorless crystalline compounds. Data on IIa-c are given in Table 1.

Diethyl(3,4-diacetoxy-1-naphthyl)malonates (Ia-c). A 3 g portion of zinc dust and 3 g of anhydrous AcONa are added with stirring to a solution of 0.01 mole of quinone IIIa-c in a

TABLE 2. Benzo[a]phenazines VIIIa-h

Compound	Yield, %	mp, °C	Found, %				Empirical formula	Calc., %				M		IR spectrum, ν_{max}, cm^{-1}
			C	H	Br (Cl)	N		C	H	Br (Cl)	N	found[b]	calc.	
VIIIa	91	167	65,35	4,55	(8,10)	6,40	$C_{23}H_{19}ClN_2O_4$	65,33	4,53	(8,38)	6,63	422	422,9	1740—1720 (C=O)
VIIIb	75	171—2	55,00	3,78	15,72 (6,97)	5,62	$C_{23}H_{18}BrClN_2O_4$	55,05	3,62	15,93 (7,07)	5,58	500	501,8	1750—1735(C=O)
VIIIc	86	181—2	50,34	3,60	29,24	5,10	$C_{23}H_{18}Br_2N_2O_4$	50,57	3,32	29,26	5,13	544	546,2	1750—1735 (C=O)
VIIId	94	288 (dec.)[a]	68,45	3,57	(12,69)	10,44	$C_{16}H_9ClN_2O$	68,46	3,23	(12,63)	9,98	280	280,7	3240—3060 (OH)
VIIIe	87	>350 (dec.)	53,01	2,22	22,30 (9,80)	7,58	$C_{16}H_8BrClN_2O$	53,44	2,24	22,22 (9,86)	7,79	358	359,6	3270—3070 (OH)
VIIIf	90	>360 (dec.)	47,31	1,92	39,82	6,87	$C_{16}H_8Br_2N_2O$	47,56	2,00	39,55	6,93	402	404,1	3240—3060 (OH)
VIIIg	48	235	52,73	2,57	20,84	10,75	$C_{17}H_{10}BrN_3O_3$	53,15	2,62	20,80	10,94	383	384,2	1560—1550 1350—1330(NO_2)
VIIIh	54	230	56,01	2,25	23,20 (10,29)	7,91	$C_{16}H_8BrClN_2$	55,93	2,35	23,25 (10,32)	8,15	342	343,6	...

[a]Literature data [11]: decomposes without melting at a temperature above 280°C.
[b]Mass-spectroscopically, peaks of molecular monoisotopic (^{79}Br and ^{35}Cl) ions.
Note. Compounds VIIIa-c were recrystallized from ethyl acetate, compounds VIIId-h from $CHCl_3$.

mixture of 30 ml of AcOH and 30 ml of Ac_2O. The mixture is stirred for 10 min at 60-70°C, filtered with suction, and the tarry residue on the filter is washed with 10 ml of hot AcOH. The combined filtrate is cooled, mixed with a fivefold amount of ice water, and left to stand in a refrigerator for 2 h. The precipitate is filtered, washed with water, and dried. Colorless crystalline compounds. Data on IVa-c are given in Table 1.

4-Methoxy-3,6-dibromo-1,2-naphthalenediol (Vc). A solution of 1.58 g (0.005 mole) of quinone Ic in 15 ml of anhydrous dioxane is added with stirring to a solution of 0.01 mole of MeONa in 20 ml of MeOH. After 2 min, 3 ml of concentrated HCl and 5 ml of 10% $Na_2S_2O_4$ solution are added to the reaction mixture. The mixture is poured onto 100 g of crushed ice, and the precipitate is filtered, washed with water, and dried. After reprecipitation by high-boiling petroleum ether from a benzene solution, the yield of Vc is 0.9 g (52%), mp 151-153°C (benzene). IR spectrum, ν_{max}, cm^{-1}: 3500, 3350 (ν OH), 1310 (δ OH). Found, %: C 37.77; H 2.26; Br 45.89. M^+ 346 (^{79}Br). $C_{11}H_8Br_2O_3$. Calculated, %: C 37.96; H 2.32; Br 45.92. M 348.0.

2-Hydroxy-3-chloro-6-bromo-1,4-naphthoquinone (IVb). A solution of 2.72 g (0.01 mole) of quinone Ib in 30 ml of anhydrous dioxane is added in one portion, with stirring to a solution of 0.02 mole of MeONa in 60 ml of MeOH. The stirring is continued for 5 min. The reaction mixture is acidified by 5 ml of concentrated HCl, and filtered from the NaCl precipitate. The filtrate is evaporated in a rotary evaporator, and to the residue, 10 ml of AcOH, 5 ml of HNO_3 (d 1.35) are added, followed, after 5 min, by 5 ml of water. The precipitate is filtered, washed with AcOH, water, AcOH, and recrystallized from 10 ml of AcOH. The yield of VIb is 1.78 g (62%). Compound VIb can be also obtained as a by-product during a half-hour chlorination of 6-bromo-1,2-naphthoquinone and treatment of the primary adduct with boiling water (see preparation of quinone Ib). Bright-yellow crystals, mp 236-237°C (from $CHCl_3$). IR spectrum, ν_{max}, cm^{-1}: 3380 (OH), 1660-1640 (C=O). UV spectrum, λ_{max}, nm (log ε): 204 (4.24, 250 (4.14), 264 (4.17), 285 (4.37), 294 (4.39), 380 (3.13). Found, %: C 41.39; H 1.61; Br 27.57, Cl 12.23. M^+ 286 (^{79}Br, ^{35}Cl). $C_{10}H_4BrClO_3$. Calculated, %: C 41.78, H 1.40, Br 27.80, Cl 12.33. M 287.5. Quinones VIa, c were obtained similarly in a yield of 68 and 53%, respectively, from quinones Ia, c. Quinone VIa: mp 224°C (AcOH), IR spectrum, ν_{max}, cm^{-1}: 3270 (OH), 1675 (C=O). UV spectrum, λ_{max}, nm (log ε): 208 (4.12), 255 (4.40), 280 (4.15), 332 (3.41), shoulder at 383 (3.09). Literature data [8]: mp 215°C (alcohol). Quinone VIc: mp 220-221°C (AcOH). IR spectrum, ν_{max}, cm^{-1}: 3350 (OH), 1660 (C=O). Literature data [9]: mp 219°C (benzene).

3-Nitro-4-methoxy-6-bromo-1,2-naphthoquinone (VII). A solution of 0.02 mole of MeONa in 60 ml of MeOH is added, with stirring, to a solution of 2.82 g (0.01 mole) of quinone I in 40 ml of anhydrous dioxane. Further treatment up to the oxidation stage is carried out under the conditions of the preparation of quinone VIb. The oxidation is carried out by adding 7 ml of HNO_3 (d 1.35) and then another 3 ml of HNO_3 (d 1.5). The reaction mixture is cooled with cold water, the precipitate is filtered, washed with HNO_3 (d 1.35) and water, and dried. The yield of VII is 1.56 g (50%). Bright-yellow crystals, mp 196°C (AcOH). IR spectrum, ν_{max}, cm^{-1}: 1705, 1670 (C=O), 1550, 1330 (NO_2). PMR spectrum, δ, ppm: 4.31 s (Me), 8.02-8.25 m (5-H, 7-H, 8-H). Found, %: C 42.31, H 2.23, Br 25.62, N 4.46, M 311 (^{79}Br). $C_{11}H_6BrNO_5$. Calculated, %: C 42.33; H 1.94; Br 25.60; N 4.49, M 312.1.

Diethyl(6-chloro-5-benzo[a]phenazinyl)malonate (VIIIa) (Table 2). A solution of 1.19 g (0.011 mole) of o-phenylenediamine in 10 ml of AcOH is added, with stirring, to a solution of 3.5 g (0.01 mole) of quinone IIIa in 30 ml of hot AcOH. The mixture is stirred for 10 min, cooled, the crystals are filtered, and washed with AcOH and ether. The yield of VIIIa is 3.85 g (91%). Yellow crystals. UV spectrum, λ_{max}, nm (log ε): shoulder at 217 (4.53), 231 (4.64), shoulder at 240 (4.54), 257 (4.41), 2.84 (4.74), shoulder at 295 (4.58), shoulder at 367 (3.95), 385 (4.11), 4.06 (4.11). Similarly, from the corresponding quinones, the following compounds were obtained: diethyl(5-benzo[a]phenazinyl)malonates VIIIb, c, yellow crystals; 5-hydroxybenzo[a]phenazines VIIId, f, dark-red crystals with a bronze tint; 3-bromo-5-methoxy-6-nitrobenzo[a]phenazine VIIIg, apple-green-yellow compound; and 3-bromo-6-chlorobenzo[a]phenazine VIIIh, greyish-yellow compound.

BIOLOGICAL EXPERIMENTAL

The cytotoxic and virus-inhibiting action of compounds II, IV, VIa-c, IIe, f, IIIa-d, VII, and VIIIa were studied in relation to the influenza virus A/FPV(HavlN1) in a cell culture of chick embryo fibroblasts (CEF) and virucidal action on the influenza virus A/PR-8 A/PR-8(HON1) by the method previously described in [5]. It was found that compounds IIe and VIb exhibit a pronounced virucidal action, lowering the infection titer of the virus by 2.0

log TCD_{50}, compared with control, while compound VII has a weak virucidal action, lowering the infection titer of the virus by 1.0 log TCD_{50}. All the compounds studied have cytotoxic activity with respect to CEF. The maximum endurable concentration (MEC) is 5-10 μg/ml. Compound IIe exhibits a high cytotoxicity (MEC 2 μg/ml), which possibly causes its virucidal action.

The antimicrobial activity of all the synthesized compounds was studied by the method of double serial dilutions in a liquid culture medium by the methods described in [6] with respect to four strains of gram-positive, five strains of gram-negative bacteria, and five strains of pathogenic fungi. Compounds IIc, f and IVc are characterized by a fairly high activity with respect to gram-positive bacteria, their minimal suppressing concentration varying within 3.9 to 31.2 mg/ml. Compounds IIe, IIIa-d exhibited a moderate activity with respect to the gram-positive bacteria (the minimum suppressing concentration is from 31.2 to 125 mg/ml). Compound II is characterized by a weak activity with respect to gram-positive and certain strains of gram-negative (*E. coli, S. typhi, Sh. flexneri*) bacteria. Its minimal suppressing concentration is 125-250 μg/ml. Compounds IIe, f have a similar activity with respect to gram-negative bacteria.

Compounds IIa, c, e, f, IIIa-d, IVc, which suppress the growth of gram-positive bacteria in experiments *in vitro*, also exhibit a weak activity with respect to pathogenic fungi.

The results obtained show that the antimicrobial activity in the series of compounds studied decreases on transition from o-quinoid structures to p-quinoid ones. The phenazine derivatives (VIIIa-c, e, g) of the biologically active quinones IIIa-c, IVb, VII, completely lose all types of activity on the subjects used. The absence of bromine at the 6-position of 1,2-naphthoquinone IIIa and related structures IIa and IVa leads to decrease or disappearance of the antiviral and, to a lesser extent, of the antimicrobial activity. The character and degree of expression of the biological activity change little in the series of compounds II-IV with the same substituents, which are capable of undergoing mutual transformations in the living systems, but substantially depend on the character of the substituent, introduced into the 4-position of the initial 1,2-naphthoquinone.

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