Molecules **2000**, *5*, 714-726

molecules

ISSN 1420-3049
http://www.mdpi.org

Synthesis of N,N'-Diarylalkanediamides and Their Antimycobacterial and Antialgal Activity

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Received: 2 November 1999 / Accepted: 13 December 1999 / Published: 14 May 2000

Abstract: A set of N,N'-diarylalkanediamides was synthesized. The compounds were tested for their antimycobacterial and antialgal activity. The antimycobacterial activity of N,N'-diarylalkanediamides depends on the lipophilicity of the respective acid. Antimycobacterially active substances were found only in the series of N,N'-diarylethanediamides and N,N'-diarylbutanediamides. Other compounds (derivatives of pentane-, hexane-, octane- and nonanediamide) were inactive against various strains of mycobacteria. The compounds inhibited growth and chlorophyll production in *Chlorella vulgaris*. Their relatively low antialgal activity is probably connected with their lowered aqueous solubility, and hence by a restricted passage of the inhibitor through the hydrophilic regions of thylakoid membranes.

Keywords: N,N'-diarylalkanediamides, antimycobacterial activity, antialgal activity.

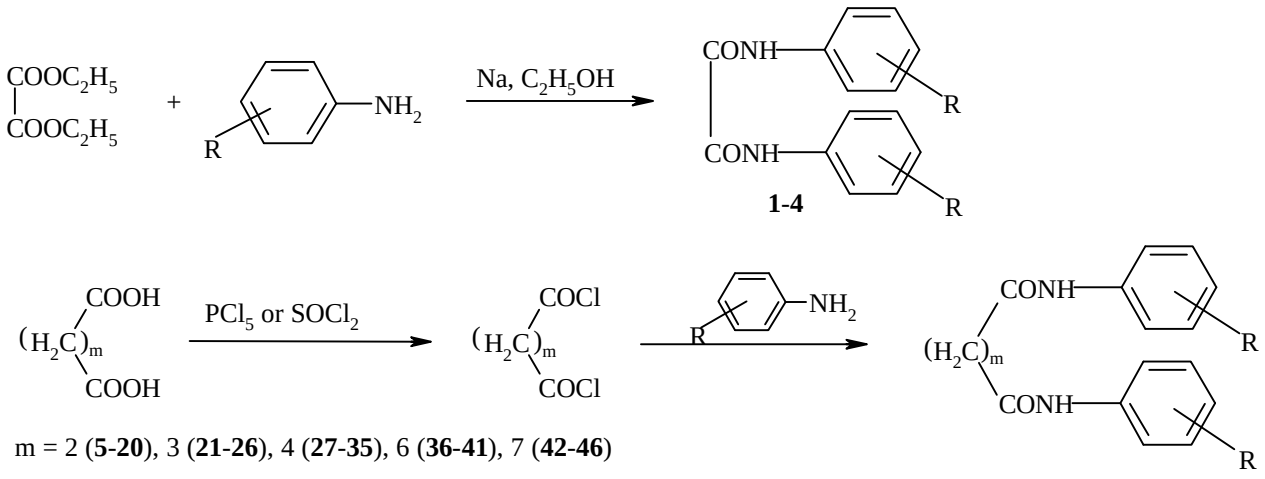
Introduction

As the end of the 20th century witnesses a sharp rise in the incidence of mycobacterial infections, the development of new antimycobacterial drugs is presently of utmost importance and should proceed at a rapid pace. When exploring a possible link between antituberculous activity and the ability to form chelates with heavy metals, we prepared a set of N,N'-diarylethane- and -propanediamides, which were evaluated *in vitro* against *Mycobacterium tuberculosis*, and some of them showed significant activity [1]. Other authors have described various kinds of biological activity of alkanediamide derivatives as well. For example, some 2-methylcarbonylbutanediamides are active against *M. tuberculosis* [2], 2,3-diarylpentanediamides display activity against Gram-positive bacteria [3], and N,N'-substituted 2-halobutanediamides act as herbicides [4]. Raynes et al. studied the influence of the length of the connecting chain on the antimalarial activity of bisquinolines; the derivative of butanediamide was the most efficient [5]. In our previous study [6] we found that N,N'-bis(3,4-dichlorophenyl)butanediamide effectively inhibited oxygen evolution rate (OER) in spinach chloroplasts and that this compound interacted with the pigment-protein complexes in photosystem 2. The increase of the length of the connecting chain in the series of N,N'-bis(3,4-dichlorophenyl)alkanediamides led to the decrease of OER-inhibiting activity in spinach chloroplast [7]. The decrease in biological activity with increasing lipophilicity of the compounds is probably linked to their lowered aqueous solubility, and hence to a restricted passage of the inhibitor through the hydrophilic regions of thylakoid membranes.

This study is focused on the synthesis of a large set of N,N'-diarylalkanediamides and on the study of antimycobacterial and antialgal activity of these compounds.

Results and Discussion

N,N'-Diarylalkanediamides, with the exception of N,N'-diarylethanediamides, were prepared from the corresponding anilines by treatment with the appropriate alkanedioyl dichlorides in pyridine at 0°C. The reaction mixtures were allowed to stand at room temperature and after 24 hours they were poured into water. The products were filtered off, washed with water and crystallized from ethanol. The alkanedioyl dichlorides were prepared from the corresponding acids by the reaction with phosphorus pentachloride (butanedioyl dichloride) or thionyl chloride (all other alkanedioyl dichlorides). N,N'-Diarylethanediamides were prepared from diethyl oxalate by the reaction with the corresponding aniline in the presence of sodium ethanolate. All syntheses are outlined in Scheme 1. The yields, physical properties and analytical data for compounds **1**-**46** are given in Table 1 and Table 2.



Scheme 1.

Compounds **1**-**46** were tested for their *in vitro* antimycobacterial activity against *Mycobacterium tuberculosis*, *M. avium*, *M. fortuitum*, and *M. kansasii*. We found that the antimycobacterial activity of N,N'-diarylalkanediamides depends on the lipophilicity of the respective acid. Active substances were found only in the series of N,N'-diarylethanediamides and N,N'-diarylbutanediamides, but their antimycobacterial activity was mostly low. The MIC values of the active compounds are given in Table 3. All derivatives of pentane-, hexane-, octane- and nonanediamide were inactive against the studied mycobacteria strains.

The inhibition of chlorophyll production in statically cultivated algae *Chlorella vulgaris* by selected derivatives was investigated at a constant inhibitor concentration of 75 μmol dm^{-3}. The antialgal activity of the compounds was generally low, and the observed inhibition of algal chlorophyll production varied in the range of 14.2 (**10**) to 57.9% (**40**) (Table 4 and Table 5). The antialgal activity of N,N'-diarylbutanediamides was relatively low, varying in the range of 14.2 (**10**) to 43.6% (**15**) (Table 5). The most effective inhibitor from the series of N,N'-diarylalkanediamides was N,N'-bis(4-methoxyphenyl)octanediamide (**40**), causing 57.9% inhibition of chlorophyll production (Table 4). Antialgal activity of substituted N,N'-diarylalkanediamides with the same substituent R was proportional to the number of methylene groups in the connecting chain of the molecule (m = 2-4, 6, 7) for derivatives with R = H and 4-Cl, respectively. For derivatives with R = 4-CH_3, 4-OCH_3 and 3,4-Cl_2, a quasi-parabolic dependence of the inhibitory activity on m was found, with maximum inhibition for N,N'-diaryloctanediamides (m = 6; R = 4-CH_3 (**39**) and 4-OCH_3 (**40**)) and N,N'-bis(3,4-dichlorophenyl)hexanediamide (m = 4; **31**). The relatively low biological activity of the compounds is probably a consequence of their low aqueous solubility, and hence a restricted passage of the inhibitor through the hydrophilic regions of thylakoid membranes. An efficient inhibition of photosynthetic electron transport in spinach chloroplasts by N,N'-bis(3,4-dichlorophenyl)butanediamide has been observed previously [6,7].

Table 1. Physical properties and analytical data of compounds **1**-**46**.

Compd.	Formula (M. w.)	m	R	M.p. (°C) (Yield, %)	% Calc. % Found		
					C	H	N
1[a]	$C_{16}H_{16}N_2O_2$ (268.3)	0	2-CH_3	211-212 (65)	-	-	-
2[a]	$C_{16}H_{16}N_2O_2$ (268.3)	0	3-CH_3	135-137 (60)	-	-	-
3[a]	$C_{14}H_{10}N_4O_6$ (330.3)	0	4-NO_2	357-358 (61)	-	-	-
4[a]	$C_{14}H_{10}Br_2N_2O_2$ (398.1)	0	4-Br	329-331 (58)	-	-	-
5[a]	$C_{16}H_{14}Br_2N_2O_2$ (426.1)	2	4-Br	281-282 (92)	-	-	-
6[b]	$C_{16}H_{12}Cl_4N_2O_2$ (406.1)	2	3,4-Cl_2	258-259 (93)	-	-	-
7[a]	$C_{16}H_{16}N_2O_2$ (268.3)	2	H	231-233 (95)	-	-	-
8[a]	$C_{18}H_{20}N_2O_4$ (328.4)	2	4-OCH_3	256-257 (90)	-	-	-
9	$C_{16}H_{14}Cl_2N_2O_2$ (337.2)	2	4-Cl	288-290 (90)	56.99 57.24	4.18 4.15	8.31 8.38
10	$C_{18}H_{20}N_2O_2$ (296.4)	2	4-CH_3	273-275 (91)	72.95 72.87	6.80 6.79	9.45 9.59
11[b]	$C_{16}H_{14}F_2N_2O_2$ (304.3)	2	3-F	206-207 (89)	-	-	-
12[b]	$C_{16}H_{14}F_2N_2O_2$ (304.3)	2	4-F	244-245 (92)	-	-	-
13[b]	$C_{16}H_{14}N_4O_6$ (358.3)	2	3-NO_2	228-230 (88)	-	-	-
14[b]	$C_{20}H_{24}N_2O_2$ (324.4)	2	3,4-$(CH_3)_2$	231-232 (85)	-	-	-
15[a]	$C_{16}H_{14}Cl_2N_2O_2$ (337.2)	2	3-Cl	233-235 (92)	-	-	-
16[b]	$C_{24}H_{32}N_2O_2$ (380.5)	2	4-C_4H_9	232-234 (81)	-	-	-

Continuation of the Table 1.

Compd.	Formula (M. w.)	m	R	M.p. (°C) (Yield, %)	% Calc. % Found		
					C	H	N
17[b]	$C_{22}H_{28}N_2O_2$ (352.5)	2	4-isoC_3H_7	234-236 (83)	-	-	-
18[b]	$C_{24}H_{32}N_2O_2$ (380.5)	2	4-*sec*-C_4H_9	178-179 (81)	-	-	-
19[a]	$C_{20}H_{26}N_4O_2$ (354.5)	2	4-$N(CH_3)_2$	282.5-283.5 (88)	-	-	-
20	$C_{18}H_{14}N_4O_2S_2$ (382.5)	2	[c]	282-285 (92)	56.53 56.55	3.69 3.87	14.65 14.88
21	$C_{17}H_{16}Cl_2N_2O_2$ (351.2)	3	4-Cl	242-243 (70)	58.13 58.13	4.59 4.59	7.98 7.98
22	$C_{19}H_{22}N_2O_4$ (342.4)	3	4-OCH_3	222.5-224 (62)	66.65 66.93	6.48 6.45	8.18 8.24
23[a]	$C_{17}H_{18}N_2O_2$ (282.3)	3	H	224-225 (84)	-	-	-
24[a]	$C_{19}H_{22}N_2O_2$ (310.4)	3	4-CH_3	220-2211 (54)	-	-	-
25[b]	$C_{17}H_{14}Cl_4N_2O_2$ (420.1)	3	3,4-Cl_2	266-267 (63)	-	-	-
26[a]	$C_{17}H_{16}Br_2N_2O_2$ (440.1)	3	4-Br	256-257 (58)	-	-	-
27	$C_{20}H_{24}N_2O_2$ (324.4)	4	4-CH_3	258-259 (67)	74.05 74.21	7.46 7.52	8.63 8.66
28[a]	$C_{18}H_{20}N_2O_2$ (296.4)	4	H	237-238 (75)	-	-	-
29	$C_{18}H_{18}N_4O_6$ (386.4)	4	3-NO_2	238-239 (58)	55.96 55.80	4.70 4.73	14.50 14.67
30	$C_{18}H_{18}Cl_2N_2O_2$ (365.3)	4	3-Cl	197-198 (60)	59.19 59.14	4.97 4.97	7.67 7.90
31[b]	$C_{18}H_{16}Cl_4N_2O_2$ (434.2)	4	3,4-Cl_2	276-277 (59)	-	-	-
32	$C_{20}H_{24}N_2O_4$ (356.4)	4	2-OCH_3	151-152 (40)	67.40 67.49	6.79 6.68	7.86 7.79

Continuation of the Table 1.

Compd.	Formula (M. w.)	m	R	M.p. (°C) (Yield, %)	% Calc. % Found		
					C	H	N
33	$C_{20}H_{24}N_2O_4$ (356.4)	4	4-OCH_3	233-234 (65)	67.40 67.62	6.79 6.78	7.86 7.88
34	$C_{18}H_{18}Cl_2N_2O_2$ (356.3)	4	4-Cl	238-239 (67)	59.19 58.91	4.97 4.82	7.67 7.79
35	$C_{24}H_{28}N_2O_6$ (440.5)	4	4-$COOC_2H_5$	216-217 (54)	65.44 65.70	6.41 6.33	6.36 6.17
36[b]	$C_{20}H_{20}Cl_4N_2O_2$ (462.2)	6	3,4-Cl_2	167-168 (35)	-	-	-
37	$C_{20}H_{22}Cl_2N_2O_2$ (393.3)	6	4-Cl	197-198 (81)	61.11 61.08	5.60 5.64	7.12 7.12
38[a]	$C_{20}H_{24}N_2O_2$ (324.4)	6	H	186-188 (57)	-	-	-
39[a]	$C_{22}H_{28}N_2O_2$ (352.5)	6	4-CH_3	224-226 (55)	-	-	-
40	$C_{22}H_{28}N_2O_4$ (384.5)	6	4-OCH_3	220-221 (63)	68.78 68.60	7.24 7.15	7.29 7.19
41[a]	$C_{20}H_{22}Br_2N_2O_2$ (482.2)	6	4-Br	251-253 (54)	-	-	-
42[b]	$C_{21}H_{22}Cl_4N_2O_2$ (476.2)	7	3,4-Cl_2	170-171 (52)	-	-	-
43	$C_{21}H_{24}Cl_2N_2O_2$ (407.3)	7	4-Cl	196-197 (61)	61.92 62.06	5.94 5.85	6.88 6.99
44[a]	$C_{21}H_{26}N_2O_2$ (338.5)	7	H	180-181 (63)	-	-	-
45[a]	$C_{23}H_{30}N_2O_2$ (366.5)	7	4-CH_3	197-198 (61)	-	-	-
46	$C_{23}H_{30}N_2O_4$ (398.5)	7	4-OCH_3	194-196 (44)	69.32 69.61	7.59 7.73	7.03 7.07

[a]M. p. values from literature: Compound, value (°C) [ref.]: **1**, 209 [8]; **2**, 133 [8]; **3**, 359 [9]; **4**, 321-322 [10]; **5**, 284 [11]; **7**, 230,5 [12]; **8**, 256 [13]; **15**, 232 [14]; **19**, 277-280 [15]; **23**, 223 [11]; **24**, 218 [11]; **26**, 256 [11]; **28**, 235 [11]; **38**, 186-7 [16]; **39**, 219 [11]; **41**, 248 [11]; **44**, 186-7 [16]; **45**, 198 [11].

[b]The data of the compound were taken from [7].

[c]The compound is N,N'-bis(2-benzothiazolyl)butanediamide.

Table 2. ^{1}H NMR and IR spectroscopic data.

Compd.	^{1}H NMR δ (ppm)	IR ν(C=O) (cm^{-1})
1	-	1668
2	-	1666
3	-	1706
4	-	1666
5	-	1652
6	-	1659
7	-	1663
8	-	1648
9	2.63 (s, 4H), 7.35-7.28 (m, 4H) , 7.63-7.56 (m, 4H), 10.14 (s, 2H)	1652
10	2.21 (s, 6H), 2.60 (s, 4H), 7.11-7.03 (m, 4H) , 7.48-7.40 (m, 4H), 9.89 (s, 2H)	1655
11	-	1663
12	-	1651
13	-	1675
14	-	1651
15	-	1668
16	-	1659
17	-	1656
18	-	1655
19	-	1645
20	2.88 (s, 4H), 7.32-7.23 (m, 2H) , 7.46-7.37 (m, 2H), 7.76-7.69 (m, 2H), 7.97-7.90 (m, 2H)	1694
21	1.95-1.81 (m, 2H), 2.36 (t, J=7.4 Hz, 4H), 7.35-7.29 (m, 4H) , 7.64-7.57 (m, 4H), 10.05 (s, 2H)	1664
22	1.93-1.81 (m, 2H), 2.31 (t, J=7.4 Hz, 4H), 3.69 (s, 6H), 6.89-6.79 (m, 4H) , 7.53-7.43 (m, 4H), 9.76 (s, 2H)	1659
23	-	1673
24	-	1664
25	-	1679
26	-	1664
27	1.63-1.55 (m, 4H),2.21 (s, 6H), 2.33-2.24 (m, 4H), 7.10-7.03 (m, 4H) , 7.48-7.41 (m, 4H), 9.79 (s, 2H)	1659
28	-	1660

Continuation of the Table 2.

Compd.	^{1}H NMR δ (ppm)	IR ν(C=O) (cm^{-1})
29	1.70-1.60 (m, 4H), 2.43-2.33 (m, 4H), 7.57 (t, J=8.1, 2H), 7.91-7.83 (m, 4H), 8.63 (t, J=2.1 Hz, 2H), 10.41 (s, 2H)	1667
30	1.65-1.55 (m, 4H), 2.38-2.27 (m, 4H), 7.10-7.03 (m, 2H) , 7.30 (t, J=8.1, 2H), 7.45-7.38 (m, 2H), 7.80 (t, J=1.9, 2H), 10.09 (s, 2H)	1663
31	-	1670
32	1.65-1.54 (m, 4H), 2.44-2.33 (m, 4H), 3.79 (s, 6H), 6.93-6.82 (m, 2H), 7.10-6.96 (m, 4H), 7.97-7.84 (m, 2H), 9.03 (s, 2H)	1659
33	1.64-1.52 (m, 4H), 2.33-2.20 (m, 4H), 3.69 (s, 6H), 6.89-6.79 (m, 4H), 7.52-7.42 (m, 4H), 9.74 (s, 2H)	1648
34	1.65-1.55 (m, 4H), 2.37-2.26 (m, 4H), 7.35-7.29 (m, 4H), 7.63-7.56 (m, 4H), 10.03 (s, 2H)	1656
35	1.28 (t, J=7.1 Hz, 6H), 1.68-1.57 (m, 4H), 2.42-2.31 (m, 4H), 4.25 (q, J=14.2, J=7.1 Hz, 4H), 7.74-7.67 (m, 4H), 7.91-7.84 (m, 4H), 10.25 (s, 2H)	1708, 1693
36	-	1671
37	1.36-1.25 (m, 4H), 1.64-1.49 (m, 4H), 2.27 (t, J=7.4, 4H), 7.35-7.27 (m, 4H), 7.63-7.55 (m, 4H), 10.00 (s, 2H)	1659
38	-	1659
39	-	1656
40	1.34-1.24 (m, 4H), 1.64-1.48 (m, 4H), 2.24 (t, J=7.4, 4H), 3.68 (s, 6H), 6.87-6.79 (m, 4H), 7.50-7.42 (m, 4H), 9.72 (s, 2H)	1652
41	-	1664
42	-	1680
43	1.32-1.22 (m, 6H), 1.63-1.48 (m, 4H), 2.27 (t, J=7.3 Hz, 4H), 7.34-7.28 (m, 4H), 7.62-7.55 (m, 4H), 10.00 (s, 2H)	1660
44	-	1671
45	-	1662
46	1.35-1.20 (m, 6H), 1.63-1.47 (m, 4H), 2.23 (t, J=7.3 Hz, 4H), 3.68 (s, 6H), 6.88-6.80 (m, 4H), 7.50-7.42 (m, 4H), 9.71 (s, 2H)	1655

Table 3. Antimycobacterial activity of the active compounds expressed as MIC (μmol dm^{-3}). (m = number of methylene groups in the connecting chain of the compounds).

Compound	m	R	MIC (μmol dm^{-3})			
			M. tuberculosis	*M. avium*	*M. kansasii*	*M. fortuitum*
3	0	4-NO_2	37	-[a)]	-[a)]	-[a)]
4	0	4-Br	4.1	-[a)]	-[a)]	-[a)]
6	2	3,4-Cl_2	250	250	500	500
7	2	H	500	500	500	500
12	2	4-F	250	1000	1000	1000
14	2	3,4-$(CH_3)_2$	500	>1000	>1000	>1000
15	2	3-Cl	500	>1000	>1000	>1000
16	2	4-C_4H_9	500	63	>1000	>1000
17	2	4-isoC_3H_7	>1000	63	>1000	>1000
18	2	4-*sec*-C_4H_9	500	63	>1000	>1000

[a)]not tested

Table 4. Inhibition of chlorophyll production in *Chlorella vulgaris* by N,N'-diarylalkanediamides (m = number of methylene groups in the connecting chain of the compounds; concentrations of compounds were constant, 75 μmol dm^{-3}).

m	Compound % of inhibition				
	R= H	4-CH_3	4-OCH_3	4-Cl	3,4-Cl_2
2	**7**	**10**	**8**	**9**	**6**
	22.8	14.2	30.8	33.2	19.8
3	**23**	**24**	**22**	**21**	**25**
	41.8	26.2	41.6	34.3	28.7
4	**28**	**27**	**33**	**34**	**31**
	41.0	37.7	46.0	41.4	33.5
6	**38**	**39**	**40**	**37**	**36**
	44.2	41.4	57.9	45.4	22.6
7	**44**	**45**	**46**	**43**	**42**
	48.5	37.9	53.9	45.5	15.1

Table 5. Inhibition of chlorophyll production in *Chlorella vulgaris* by N,N'-diarylbutanediamides (m = 2; concentrations of compounds were constant, 75 μmol dm^{-3}).

Compound	R	% of inhibition	Compound	R	% of inhibition
7	H	22.8	**5**	4-Br	27.1
11	3-F	25.2	**17**	4-isoC_3H_7	36.5
15	3-Cl	43.6	**16**	4-C_4H_9	32.6
13	3-NO_2	25.4	**18**	4-*sec*-C_4H_9	36.5
12	4-F	35.4	**19**	4-$N(CH_3)_2$	28.8
9	4-Cl	33.2	**6**	3,4-Cl_2	19.8
10	4-CH_3	14.2	**14**	3,4-$(CH_3)_2$	26.7
8	4-OCH_3	30.8			

Experimental

General

The melting points were determined on a Kofler block and are uncorrected. The samples for elemental analyses and biological tests were dried over P_2O_5 at 61°C and 66 Pa for 24 h. Elemental analyses were performed on a C,H,N,S analyzer (FISONS AE 1110, Milano). The IR spectra were measured in KBr on a Nicolet Impact 400 apparatus. The purity of the compounds was checked by TLC, using petroleum ether:ethyl acetate (1:1) and chloroform:acetone (9:1) as the mobile phases. ^{1}H NMR spectra of new compounds were recorded for DMSO-d_6 solutions at ambient temperature on a Varian Mercury-Vx BB 300 spectrometer (operating at 300 MHz). Chemical shifts were recorded as δ values in ppm, and were indirectly referenced to tetramethylsilane via the solvent signal (2.49 for ^{1}H).

Synthesis of alkanedioyl dichlorides

Butanedioyl dichloride

Phosphorus pentachloride (0.328 mol) was added to a finely powdered succinic acid (0.400 mol), and the mixture was heated at 120°C for 5 hours. Phosphorus oxychloride was then distilled off, and the crude product was purified by vacuum distillation (yield 75%, b.p. 104-105°C / 3.33 kPa, lit. [17] b.p. 103-104°C / 3.33 kPa).

Octanedioyl dichloride

Suberic acid (0.287 mol) was heated with thionyl chloride (1.260 mol) at 120°C for 4 hours. After

the removal of the excess reagent by distillation, the crude product was purified by distillation at reduced pressure (yield 69.20%, b. p. 145°C / 1.33 kPa, lit. [18] b.p. 149-150°C / 1.60 kPa). The same protocol was used for the preparation of the other alkanedioyl dichlorides (yield; b.p.; b.p. [ref]): pentanedioyl dichloride (90.7%; 104°C / 2.53 kPa; 100°C / 2.00 kPa [19]); hexanedioyl dichloride (81.2%; 130-132°C / 2.40 kPa; 126°C / 1.60 kPa [19]); nonanedioyl dichloride (71.4%; 162°C / 1.20 kPa; 158-159°C / 1.60 kPa [20]).

Synthesis of N,N'-diarylalkanediamides

*N,N'-Diarylethanediamides (***1**-**4***)*

Sodium (1 g) was dissolved in absolute ethanol (100 ml), a substituted aniline (0.300 mol) followed by diethyl oxalate (0.150 mol) were added to the solution, and the reaction mixture was heated at reflux for 1 hour. After cooling, the crude product was filtered off, washed with water, and crystallized from ethanol. The experimental data of compounds **1-4** are given in Table 1.

*Other N,N'-diarylalkanediamides (***5**-**46***)*

Butanedioyl dichloride (0.016 mol) was added dropwise to a stirred solution of an appropriate aniline (0.032 mol) in pyridine (20 ml) at 0°C. The reaction mixture was allowed to stand at ambient temperature for 24 hours, and then poured into water (100 ml). The product was filtered off and crystallized from ethanol. The yields, melting points, IR and NMR spectral data as well as elemental analyses are summarized in Table 1 and Table 2.

Biological assays

Antimycobacterial activity

Antimycobacterial evaluation of N,N'-diarylalkanediamides (m = 0, 3, 4, 6, 7) was carried out in a semisynthetic liquid protein-containing Sula medium (IMUNA, Sarisske Michalany), buffered to pH=7.2. The following mycobacterial strains were used: *Mycobacterium tuberculosis* H_{37}*Rv*, *M. kansasii PKG8*, *M. avium No. 80/72* and *M. fortuitum 1021*. The MICs were determined after 14 days of incubation at 37°C. The compounds were added to the medium in dimethyl sulfoxide (DMSO) solutions. The final concentrations were 1000; 333; 111; 37; 12.3; and 4.1 μmol dm^{-3}.

Antimycobacterial activity of N,N'-diarylbutanediamides (m = 2) was determined in Sula semisynthetic medium (SEVAC, Prague). For evaluation of their *in vitro* antimycobacterial activity, the following strains were used: *M. tuberculosis* CNCTC My 1/47, *M. kansasii* CNCTC My 235/80, *M. avium* CNCTC My 80/72 and *M. fortuitum* CNCTC My 187/73 from the National Institute of Public Health, Prague. The compounds were added to the medium in DMSO solutions. The final concentra-

tions were 1000; 500; 250; 125; 62; 31; 16; 8; 4 μmol dm^{-3}. The minimum inhibitory concentrations were determined after incubation at 37°C for 21 days.

MIC was the lowest concentration of a substance (on the above-stated concentration scale), at which inhibition of the growth of mycobacteria occurred. The compound is considered as active, when its MIC is lower than 1000 μmol dm^{-3}. DMSO concentration in the medium was maximum for concentration 1000 μmol dm^{-3} of the tested compound and the control samples contained the same DMSO amount (10 v/v %). The applied DMSO content did not affect the antimycobacterial activity.

Antialgal activity

The inhibitory effect of selected N,N'-diarylalkanediamides on algal chlorophyll (Chl) production has been investigated in statically cultivated *Chlorella vulgaris* (96 hours; photoperiod 16 h light / 8 h dark; illumination: 5 000 lx; pH = 7.2; Chl content at the beginning of cultivation: 0.5 mg dm^{-3}) at room temperature and a constant inhibitor concentration 75 μmol dm^{-3} according to Kralova et al. [21]. Chl content of algal suspensions was determined spectrophotometrically following its extraction into N,N-dimethylformamide according to Inskeep and Bloom [22]. The compounds were dissolved in DMSO as their solubility in water was insufficient. DMSO concentration in the algal suspensions did not exceed 0.75 v/v % and the control samples contained the same DMSO amount as the suspensions treated with the tested compounds. The antialgal activity was expressed as the percentage of inhibition of the untreated control.

Acknowledgements: The authors wish to thank Mrs. J. Zizkova from the Department of Inorganic and Organic Chemistry for measurements of the IR spectra and Mrs. D. Karlickova from the Department of Pharmaceutical Chemistry and Drug Control, Faculty of Pharmacy, Charles University, for elemental analyses. This study was supported by the Ministry of Education of the Czech Republic (CEZ J 13/98: 11600001), and by the Scientific Grant Agency of the Ministry of Education of the Slovak Republic (grant No. 1/4013/97).

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Samples Availability: available from the authors.