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N-Aryl-2-dialkylaminosuccinimides

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Abstract—Reaction of *N*-arylmaleimides with an equimolar amount of diethylamine, piperidine, and morpholine afforded the corresponding *N*-aryl-2-dialkylaminosuccinimides as mixtures of stereoisomers.

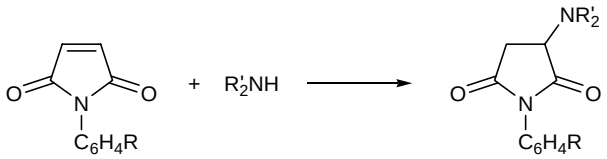
Some *N*-aryl-2-(4-alkyl-1-piperazinyl)- and *N*-aryl-2-(2-benzimidazolyl)succinimides were found to exhibit somnific, anticonvulsant, antiarrythmic, and other kinds of biological activity [1–3]. On the other hand, the number of known compounds of this series is relatively small. Therefore, synthesis of new 2-amino-substituted *N*-arylsuccinimides is important. Taking into account the above stated, we have synthesized new *N*-aryl-2-dialkylaminosuccinimides and exaimed their properties. The syntheses were performed by heating mixtures of equimolar amounts of *N*-aryl-maleimides **Ia**–**Il** and diethylamine (**IIa**), piperidine (**IIb**), or morpholine (**IIc**) in dioxane at 45–100°C (Scheme 1).

Succinimides **IIIa–IIIi** and **IVa–IVj** (Table 1) are crystalline or amorphous powders with different colors (from colorless to bright orange). Their purity was checked by TLC, and the structure was confirmed by elemental analysis and IR and ^{1}H NMR spectroscopy (Table 2). In the IR spectra of succinimides **III** and **IV**, stretching vibrations of the carbonyl groups give rise to one or two strong bands in the region 1710–1655 cm^{-1} and a medium-intensity band 1775–1730 cm^{-1}; also, a weak but characteristic overtone is observed at 3470–3440 cm^{-1}. The ^{1}H NMR spectra of the products (except for **IIIa**, **IIId**, **IVa**, **IVd**, **Va**, and **Vd**) contained signals from protons of the endocyclic CH_2 group as a doublet of doublets at δ 2.58–2.87 ppm ($^3J_{HH}$ = 4, 12 Hz) and a quartet at δ 2.87–3.03 ppm ($^3J_{HH}$ = 8 Hz). The 2-H proton in **IIIb** and **IIIe**–**IIIi** appeared as a quartet at δ 4.13–4.30 ppm, and the corresponding signal of compounds **IVb**, **IVc**, **IVg**, **IVi**, **Vb**, **Vc**, and **Vg** was located at δ 3.94–4.06 ppm (q, $^3J_{HH}$ = 4 Hz). The presence of a methyl group in the *ortho* position of the aromatic ring in compounds **IIId**, **IVd**, and **Vd** leads to additional splitting of the CH_2 and CH signals, and the latter appear as octets in the corresponding spectral region, the above given coupling constants remaining unchanged. The observed pattern indicates that these compounds are mixtures of stereoisomers.

EXPERIMENTAL

The IR spectra were recorded on a Specord IR-75 spectrometer, and the ^{1}H NMR spectra were obtained on a Bruker DRX-500 instrument (500.13 MHz) in DMSO-d_6 using TMS as internal reference. TLC

Scheme 1.



Ia–Il **IIa–IIc** **IIIa–IIIi**, **IVa–IVj**, **Va–Vg**

I, R = *o*-NO_2 (**a**), *m*-NO_2 (**b**), *p*-NO_2 (**c**), *o*-Me (**d**), *m*-Me (**e**), *p*-Me (**f**), *p*-PhN=N (**g**), *o*-piperidino (**h**), *p*-piperidino (**i**), *o*-BuO (**j**), *p*-BuO (**k**), *m*-PhCONH (**l**); **II**, R' = Et (**a**), R'$_2$ = $(CH_2)_5$ (**b**), R'$_2$ = $(CH_2)_2O(CH_2)_2$ (**c**); **III**, R' = Et, R = *o*-NO_2 (**a**), *m*-NO_2 (**b**), *p*-NO_2 (**c**), *o*-Me (**d**), *m*-Me (**e**), *p*-Me (**f**), *p*-PhN=N (**g**), *p*-piperidino (**h**), *m*-PhCONH (**i**); **IV**, R'$_2$ =$(CH_2)_5$, R = *o*-NO_2 (**a**), *m*-NO_2 (**b**), *p*-NO_2 (**c**), *o*-Me (**d**), *m*-Me (**e**), *p*-Me (**f**), *p*-PhN=N (**g**), *p*-piperidino (**g**), *o*-BuO (**i**), *p*-BuO (**j**); **V**, R'$_2$ = $(CH_2)_2O(CH_2)_2$, R = *o*-NO_2 (**a**), *m*-NO_2 (**b**), *p*-NO_2 (**c**), *o*-Me (**d**), *m*-Me (**e**),*p*-Me (**f**), *p*-PhN=N (**g**).

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Table 1. Yields, melting points, R_f values, and elemental analyses of *N*-aryl-2-dialkylaminosuccinimides **III**–**V**

Comp. no.	Yield, %	mp, °C (solvent)	R_f	Found, %			Formula	Calculated, %		
				C	H	N		C	H	N
IIIa	80.9	92–94 (*i*-PrOH)[a]	0.66	57.60	5.80	14.31	$C_{14}H_{17}N_3O_4$	57.73	5.88	14.43
IIIb	62.5	106–108 (aq. *i*-PrOH)[a]	0.65	57.78	5.85	14.50	$C_{14}H_{17}N_3O_4$	57.73	5.88	14.43
IIIc	80.8	114–115 (*i*-PrOH)	0.67	57.69	5.81	14.37	$C_{14}H_{17}N_3O_4$	57.73	5.88	14.43
IIId	80.4	96–98 (*i*-PrOH)[a]	0.74	69.10	7.68	10.70	$C_{15}H_{20}N_2O_2$	69.21	7.74	10.76
IIIe	55.0	60–62 (Et_2O)	0.65	69.08	7.70	10.67	$C_{15}H_{20}N_2O_2$	69.21	7.74	10.76
IIIf	82.6	110–112 (*i*-PrOH)	0.71	69.09	7.63	10.68	$C_{15}H_{20}N_2O_2$	69.21	7.74	10.76
IIIg	85.7	143.5–145 (*i*-PrOH)[a]	0.74	68.43	12.53	15.87	$C_{20}H_{22}N_4O_2$	68.55	12.61	15.99
IIIh	93.3	96–97.5 (*i*-PrOH)[a]	0.71	69.15	8.15	12.62	$C_{19}H_{27}N_3O_2$	69.27	8.26	12.75
IIIi	74.5	156–157 (*i*-PrOH)[a]	0.68	68.98	6.39	11.42	$C_{21}H_{23}N_3O_2$	69.03	6.34	11.50
IVa	89.5	95–96 (Et_2O)	0.58	59.28	5.56	13.74	$C_{15}H_{17}N_3O_4$	59.40	5.65	13.85
IVb	60.4	147–149 (EtOH)	0.57	59.21	5.54	13.76	$C_{17}H_{17}N_3O_4$	59.40	5.65	13.85
IVc	83.6	151–152 (EtOH)[a]	0.61	59.26	5.72	13.77	$C_{17}H_{17}N_3O_4$	59.40	5.65	13.85
IVd	98.3	99–101 (*i*-PrOH)[a]	0.65	70.46	7.33	10.16	$C_{16}H_{20}N_2O_2$	70.57	7.40	10.29
IVe	41.6	130–132 (EtOH)	0.66	70.65	7.31	10.17	$C_{16}H_{20}N_2O_2$	70.57	7.40	10.29
IVf	63.3	170–172 (AcOEt)	0.67	70.38	7.35	10.38	$C_{16}H_{20}N_2O_2$	70.57	7.40	10.29
IVg	35.9	188–190 (*i*-PrOH)	0.67	69.47	8.18	15.37	$C_{21}H_{22}N_4O_2$	69.60	8.26	15.46
IVh	85.9	152–154 (*i*-PrOH)	0.70	70.23	7.16	12.40	$C_{20}H_{27}N_3O_2$	70.35	7.97	12.31
IVi	84.5	74–75 (*i*-PrOH)[a]	0.72	69.15	7.99	8.36	$C_{19}H_{26}N_2O_3$	69.06	7.93	8.48
IVj	88.3	127–128 (*i*-PrOH)[a]	0.68	68.97	7.82	8.39	$C_{19}H_{26}N_2O_3$	69.06	7.93	8.48
Va	89.5	156–158 (*i*-PrOH)	0.40	54.97	4.87	13.65	$C_{14}H_{15}N_3O_5$	55.09	4.95	13.77
Vb	75.1	146–148 (EtOH)[a]	0.45	54.98	4.88	13.66	$C_{14}H_{15}N_3O_5$	55.09	4.95	13.77
Vc	84.2	150–154 (EtOH)	0.54	55.17	4.98	13.70	$C_{14}H_{15}N_3O_5$	55.09	4.95	13.77
Vd	37.4	114–116 (PhMe)[a]	0.46	65.57	6.50	10.11	$C_{15}H_{18}N_2O_3$	65.68	6.61	10.21
Ve	86.3	99–101 (Et_2O)	0.53	65.55	6.52	10.10	$C_{15}H_{18}N_2O_3$	65.68	6.61	10.21
Vf	41.9	159–161 (AcOEt)	0.53	65.56	6.54	10.13	$C_{15}H_{18}N_2O_3$	65.68	6.61	10.21
Vg	61.8	206–208 (dioxane)	0.70	65.81	5.49	15.28	$C_{20}H_{22}N_4O_2$	65.92	5.53	15.37

[a] Double recrystallization.

Table 2. IR and ^{1}H NMR spectra of N-aryl-2-dialkylaminosuccinimides **III**–**V**

Comp. no.	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm (*J*, Hz)
IIIa	3460, 1770, 1700 (C=O); 1500, 1325 (NO_2)	1.12 t (6H, $2CH_3$, $^3J_{HH}$ = 8); 2.65–2.75 m (4H, CH_2N; 1H, CH_2); 2.95–3.05 m (1H, CH_2); 4.28 s (1H, CH); 7.49 d, 7.69 t, 7.84 t, and 8.13 d (4H, H_{arom}, $^3J_{HH}$ = 8)
IIIb	3470, 1750, 1695, 1680 (C=O); 1520, 1330 (NO_2)	1.06 t (6H, CH_3, $^3J_{HH}$ = 8); 2.62–2.72 (4H, CH_2N); 2.78 d and 2.97 q (2H, CH_2); 4.30 q (1H, CH, $^3J_{HH}$ = 8); 7.80 m, 8.22 s, and 8.27 d (4H, H_{arom}, $^3J_{HH}$ = 8)
IIIc	3460, 1760, 1700, 1680 (C=O); 1525, 1310 (NO_2)	–
IIId	3460, 1760, 1700, 1690 (C=O)	1.10 t (6H, CH_3, $^3J_{HH}$ = 8); 2.12 s (3H, CH_3); 2.62–2.75 m (4H, CH_2N; 1H, CH_2); 3.00 oct (1H, CH_2,); 4.23 oct (1H, CH); 7.02 d and 7.07 d (1H, H_{arom}, $^3J_{HH}$ = 8); 7.24–7.28 m and 7.29–7.33 m (3H, H_{arom})

Table 2. (Contd.)

Comp. no.	IR spectrum, ν, cm^{-1}	^1H NMR spectrum, δ, ppm (*J*, Hz)
IIIe	3470, 1775, 1700 (C=O)	1.12 t (6H, CH_3, $^3J_{HH}$ = 8); 2.40 s (3H, CH_3); 2.63–2.74 m (4H, CH_2N); 2,58 d.d and 2.95 q (2H, CH_2); 4.15 q (1H, CH); 7.00 d, 7.02 s, 7.18 d, and 7.32 t (4H, H_{arom}, $^3J_{HH}$ = 8)
IIIf	3470, 1760, 1690 (C=O)	1.10 t (6H, CH_3, $^3J_{HH}$ = 8); 2.40 s (3H, CH_3); 2.56–2.62 m (4H, CH_2N); 2.58 d.d and 2.94 q (1H, CH_2); 4.13 q (1H, CH); 7.08 d and 7.21 d (4H, H_{arom}, $^3J_{HH}$ = 8)
IIIg	3460, 1685 (C=O)	1.12 t (6H, CH_3, $^3J_{HH}$ = 8); 2.63–2.77 s (4H, CH_2N; 1H, CH_2); 3.00 q (1H, CH_2, $^3J_{HH}$ = 8); 4.22 q (1H, CH); 7.43–7.57 m (5H, C_6H_5); 7.90 d and 7.98 d (4H, C_6H_4, $^3J_{HH}$ = 8)
IIIh	3440, 1750, 1650 (C=O)	1.05 s (6H, CH_3); 1.60 s (2H, CH_2N); 1.65 s (4H, CH_2N); 2.65 s (4H, CH_2N; 1H, CH_2); 2.92 q (1H, CH_2); 3.20 s (4H, CH_2N); 4.18 s (1H, CH); 6.94 d and 7.04 d (4H, H_{arom}, $^3J_{HH}$ = 8)
IIIi	3340 (NH); 3440, 1750, 1660 (C=O); 1630 (CONH)	1.12 t (6H, CH_3, $^3J_{HH}$ = 7); 2.62–2.76 m (4H, CH_2N; 1H, CH_2); 2.98 q (1H, CH_2, $^3J_{HH}$ = 8); 4.21 q (1H, CH); 6.92 d (1H, H_{arom}, C_6H_4, $^3J_{HH}$ = 8); 7.38 t and 7.47 t (3H, H_{arom}, C_6H_5, $^3J_{HH}$ = 8); 7.52 t, 7.76 s, and 7.88 d (3H, H_{arom}, C_6H_4, $^3J_{HH}$ = 8); 7.99 d (2H, H_{arom}, C_6H_5, $^3J_{HH}$ = 8); 10.20 s (1H, NH)
IVa	3470, 1775, 1710, 1700 (C=O); 1515, 1340 (NO_2)	1.47 m (2H, CH_2N); 1.57 s (4H, CH_2N); 2.53 m and 2.87 m (4H, CH_2N); 2.72 m and 3.00 m (2H, CH_2); 4.03 s (1H, CH_2); 7.48 d, 7.20 s, 7.83 t, and 8.13 s (4H, H_{arom}, $^3J_{HH}$ = 8)
IVb	3450, 1775, 1690 (C=O); 1500, 1330 (NO_2)	–
IVc	3460, 1750, 1690 (C=O); 1500, 1320 (NO_2)	1.47 m (2H, CH_2N); 1.58 s (4H, CH_2N); 2.52 m and 2.85 m (4H, CH_2N); 2.72 d.d and 3.02 q (2H, CH_2); 3.95 q (1H, CH); 7.60 d and 8.30 d (4H, H_{arom}, $^3J_{HH}$ = 8)
IVd	3440, 1750, 1670 (C=O)	1.47 m (2H, CH_2N); 1.57 s (4H, CH_2N); 2.12 s (3H, CH_3); 2.53 m and 2.85 m (4H, CH_2N); 2.70 oct and 3.02 oct (2H, CH_2); 3.96 oct (1H, CH); 7.00 d, 7.07 d, 7.26 t, and 7.30 m (3H, H_{arom}, $^3J_{HH}$ = 8)
IVe	3460, 1750, 1670 (C=O)	–
IVf	3470, 1770, 1700, 1690 (C=O)	–
IVg	3470, 1700 (C=O)	1.47 m (2H, CH_2N); 1.57 s (4H, CH_2N); 2.53 m and 2.87 m (4H, CH_2N); 2.68 d.d and 3.03 q (2H, CH_2); 3.94 q (1H, CH); 7.45–7.57 m (5H, H_{arom}, C_6H_5); 7.88 d and 7.98 d (4H, H_{arom}, C_6H_4, $^3J_{HH}$ = 8)
IVh	3440, 1730, 1670, 1655 (C=O)	–
IVi	3460, 1750, 1675 (C=O); 1180, 1040 (COC)	0.93 t (3H, CH_3, $^3J_{HH}$ = 7); 1.38 m (2H, CH_2, Bu); 1.43 s (2H, CH_2N); 1.56 s (4H, CH_2N); 1.62 m (2H, CH_2, Bu); 2.55 m and 2.75 m (4H, CH_2N); 2.67 d.d and 2.95 q (2H, CH_2); 3.95 m (1H, CH; 2H, CH_2, Bu); 6.98 t, 7.10 m, and 7.38 t (4H, H_{arom})
IVj	3470, 1755, 1675, 1660 (C=O); 1160, 1050 (COC)	–
Va	3450, 1760, 1705, 1695 (C=O); 1500, 1330 (NO_2); 1160 (COC)	2.58 m and 2.88 m (4H, CH_2N); 2.82 d.d and 3.02 q (2H, CH_2); 3.62 t (4H, CH_2O); 4.06 q (1H, CH); 7.52 d, 7.70 t, 7.85 t, and 8.15 d (4H, H_{arom}, $^3J_{HH}$ = 8)
Vb	3460, 1775, 1700, 1680 (C=O); 1510, 1340 (NO_2); 1145 (COC)	2.57 m and 2.92 m (4H, CH_2N); 2.78 d.d and 3.03 q (2H, CH_2); 3.63 t (4H, CH_2O); 3.98 q (2H, CH_2); 7.75 m and 8.25 m (4H, H_{arom})

Table 2. (Contd.)

Comp. no.	IR spectrum, ν, cm^{-1}	^1H NMR spectrum, δ, ppm (*J*, Hz)
Vc	3450, 1770, 1695 (C=O); 1510, 1315 (NO_2); 1125 (COC)	–
Vd	3440, 1760, 1680 (C=O); 1130 (COC)	2.12 s (3H, CH_3); 2.58 m and 2.92 m (4H, CH_2N); 2.77 oct and 3.05 oct (2H, CH_2); 3.65 t (4H, CH_2O); 3.97 oct (1H, CH); 7.04 d, 7.07 d, 7.27 t, and 7.32 m (4H, H_{arom}, $^3J_{HH}$ = 8)
Ve	3460, 1770, 1690, 1680 (C=O); 1170 (COC)	–
Vf	3460, 1760, 1690 (C=O); 1140 (COC)	–
Vg	3450, 1690, 1680 (C=O); 1150 (COC)	2.58 m and 2.93 m (4H, CH_2N); 2.87 d.d and 3.03 q (2H, CH_2); 3.65 s (4H, CH_2O); 3.95 q (1H, CH); 7.48–7.58 m (5H, H_{arom}, C_6H_5); 7.87 d and 7.98 d (4H, H_{arom}, C_6H_4, $^3J_{HH}$ = 8)

analysis was performed on Sorbfil PTSKh-P-V plates using ethanol–hexane (3:1) as eluent and iodine vapor as developer. The elemental compositions were determined on a Perkin–Elmer 2400 CHN analyzer. Maleimides **Ia**–**Il** were synthesized as described in [4–8].

N-Aryl-2-dialkylaminosuccinimides III–V. A solution of 0.01 mol of secondary amine **IIa**–**IIc** in 2–5 ml of dioxane was slowly added to a solution or suspension of 0.01 mol of maleimide **Ia**–**Il** in 4–10 ml of dioxane. The mixture was stirred for 2–4 h at room temperature and was then heated for 1 h at 45–50°C (with diethylamine) or for 1 h at 80–100°C (with piperidine and morpholine). The mixture was cooled to room temperature, and the products were isolated by evaporation of the resulting solution under reduced pressure (**IIIa**, **IIId**, **IIIh**, **IIIi**, **IVd**, **Vd**, and **Ve**) or by stirring the mixture with water (**IIIb**, **IIIc**, **IIIe**, **IIIf**, **IIIg**, **IVa**, **IVc**, **IVh**, **IVj**, **Vb**, and **Vc**). Succinimides **IVb**, **IVe**, **IVf**, **IVg**, **Va**, **Vf**, and **Vg** precipitated directly from the reaction mixture. All compounds **III**–**V** were additionally purified by recrystallization.

REFERENCES

1. JPN Patent no. 30313, 1968; *Ref. Zh., Khim.*, 1970, no. 7N375P.
2. JPN Patent no. 21433, 1968; *Ref. Zh., Khim.*, 1969, no. 23N310P.
3. Swiss Patent no. 583226, 1976; *Ref. Zh., Khim.*, 1977, no. 14O131P.
4. Lifits, A.L., Veitsman, A.A., and Distanova, L.Ya., *Metody polucheniya khimicheskikh reaktivov i preparatov* (Methods of Preparation of Chemical Reagents), Moscow: IREA, 1970, vol. 22, p. 118.
5. Kolyamshin, O.A., Vasil'eva, S.Yu., and Kol'tsov, N.I., *Russ. J. Org. Chem.*, 2001, vol. 37, p. 1614.
6. Nayler, P. and Whiting, M.C., *J. Chem. Soc.*, 1955, p. 2970.
7. Kolyamshin, O.A., Sokolova, T.V., and Kol'tsov, N.I., Available from VINITI, no. 1699-V 2002; *Ref. Zh., Khim.*, 2003, no. 19Zh217DEP.
8. Vasil'eva, S.Yu., Kolyamshin, O.A., and Kol'tsov, N.I., *Vestn. Chuvash. Univ.*, 2000, nos. 3–4, p. 69.