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SYNTHESIS AND THERMAL REARRANGEMENT OF 2-(2-CHLOROETHOXY)-4,6-DISUBSTITUTED *sym*-TRIAZINES

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On thermolysis of 4-methoxy- and 4-alkylamino-2-(2-chloroethoxy)-6-morpholino(piperidino)-sym-triazines, the corresponding oxazolo- or imidazo-sym-triazinones are formed by elimination of methyl chloride or hydrogen chloride, and 4,6-disubstituted 3-(2-chloroethyl)-sym-triazin-2-ones are formed from 4,6-dimorpholino(dipiperidino) derivatives.

Keywords: condensed heterocycles, oxazolo-, imidazo-*sym*-triazines, rearrangement, thermolysis.

We recently described the rearrangement of chloroalkoxy(chloroalkylthio, chloroalkylamino)-*sym*-triazines with the formation of condensed heterocyclic systems [1]. Results are presented in this paper on an investigation of the indicated reaction using examples of chloroethoxy derivatives of morpholino(piperidino)-*sym*-triazines. It might be assumed that the physiological activity of the obtained compounds will be caused not only by their basic triazine fragment, embedded in the base of many known triazine herbicide molecules [2-4], but also by the presence of the residue of morpholine and piperidine, individual derivatives of which are used as pesticides [5, 6].

The quaternary salts **1a-j** were synthesized by the procedure developed previously in [7] for the corresponding alkyl- or dialkylamino derivatives of *sym*-triazine. It turned out that the indicated method of synthesis, the gist of which comprises the action of trimethylamine on the corresponding chlorotriazines in absolute benzene at room temperature, was also applied by us on replacing these groups by piperidine and morpholine substituents. The chloroethoxy-*sym*-triazines **2a-j** were obtained by the action of ethylene chlorohydrin in the presence of alkali at low temperature on the quaternary ammonium salts **1a-j**.

It was established that compounds **2a-h** on brief heating in an inert medium at 115-120°C were subject to thermolysis-rearrangement with elimination of either methyl chloride (**2a**,**b**) or hydrogen chloride (**2c-f**), forming respectively oxazolo- (**3a**,**b**) or imidazo-*sym*-triazinones **4a-d**. Compounds **4a**,**b** were also obtained as a result of elimination of methyl chloride from triazinones **2g**,**h**.

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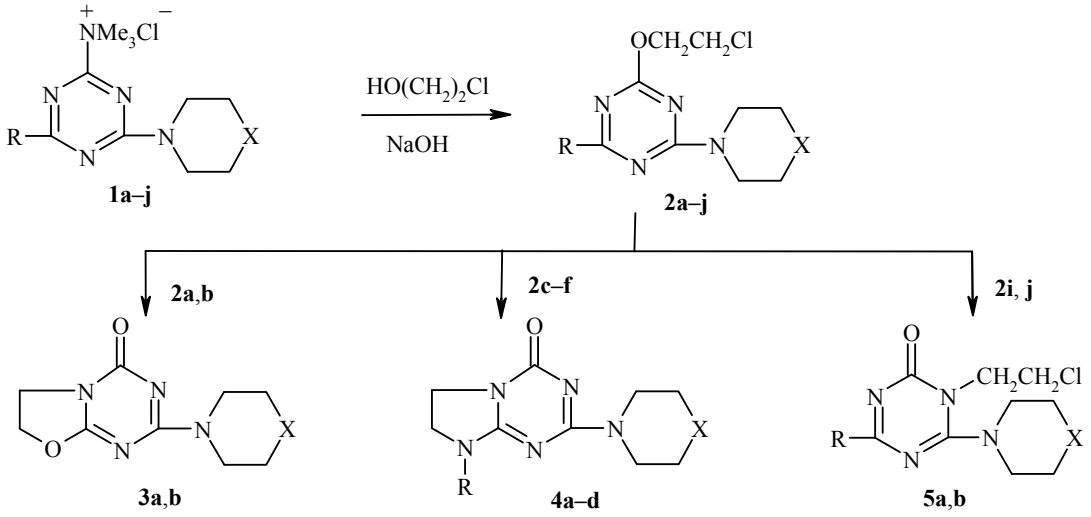

1,**2 a**,**b** R = OMe, **c**,**d** R = NHMe, **e**,**f** R = NHEt, **g**,**h** R = NMe_2; **1i**, **2i**, **5a** R = $N(CH_2)_4O$, **1j**, **2j**, **5b** R = $N(CH_2)_5$; **4a**,**b** R = Me, **c**,**d** R = Et; **1a–5a**, **1c**,**e**,**g**,**i**, **2c**,**e**,**g**,**i**, **4c** X = O; **1b–5b**, **1d**,**f**,**h**,**j**, **2d**,**f**,**h**,**j**, **4d** X = CH_2

TABLE 1. Characteristics of Compounds **1a-j**, **2a-j**

Compound	Empirical formula	Found, % / Calculated, %		mp, °C	Yield, %
		Cl	N		
1a	$C_{11}H_{22}ClN_5O_2$	12.57 / 12.26	24.45 / 24.18	153-154	86
1b	$C_{12}H_{22}ClN_5O$	12.28 / 12.35	24.69 / 24.35	150-151	90
1c	$C_{11}H_{21}ClN_6O$	12.88 / 12.30	28.95 / 29.12	168-170	90
1d	$C_{12}H_{23}ClN_6$	12.74 / 12.39	29.00 / 29.32	144-146	84
1e	$C_{12}H_{23}ClN_6O$	12.08 / 11.74	28.12 / 27.77	156-158	80
1f	$C_{13}H_{25}ClN_6$	11.61 / 11.81	28.22 / 27.95	147-148	83
1g	$C_{12}H_{23}ClN_6O$	11.39 / 11.74	27.46 / 27.77	160-162	80
1h	$C_{13}H_{25}ClN_6$	11.41 / 11.81	28.26 / 27.95	130-132	75
1i	$C_{14}H_{25}ClN_6O_2$	10.65 / 10.30	24.59 / 24.38	193-195	84
1j	$C_{16}H_{29}ClN_6$	10.71 / 10.43	25.00 / 24.67	126-128	78
2a	$C_{10}H_{15}ClN_4O_3$	12.38 / 12.93	20.64 / 20.40	102-103	84
2b	$C_{11}H_{17}ClN_4O_2$	12.84 / 13.03	20.86 / 20.55	56-57	90
2c	$C_{10}H_{16}ClN_5O_2$	13.25 / 12.98	26.00 / 25.59	120-122	94
2d	$C_{11}H_{18}ClN_5O$	12.80 / 13.07	25.45 / 25.78	136-138	90
2e	$C_{11}H_{18}ClN_5O_2$	12.61 / 12.34	24.52 / 24.34	126-128	96
2f	$C_{12}H_{20}ClN_5O$	12.10 / 12.43	24.18 / 24.52	112-114	82
2g	$C_{11}H_{18}ClN_5O_2$	12.59 / 12.34	24.60 / 24.34	96-98	90
2h	$C_{12}H_{20}ClN_5O$	12.65 / 12.43	24.82 / 24.52	60-62	88
2i	$C_{13}H_{20}ClN_5O_3$	11.05 / 10.77	21.47 / 21.24	140-142	83
2j	$C_{15}H_{24}ClN_5O$	11.33 / 10.91	21.18 / 21.51	88-90	83

TABLE 2. Characteristics of Compounds **3-5**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
3a	$C_9H_{12}N_4O_3$	48.57 / 48.21	5.61 / 5.36	25.23 / 25.00	208-210	83
3b	$C_{10}H_{14}N_4O_2$	53.83 / 54.05	6.50 / 6.31	25.51 / 25.23	184-186	90
4a	$C_{10}H_{14}N_4O_2$	51.00 / 50.63	6.49 / 6.33	29.11 / 29.54	177-178	77
4b	$C_{11}H_{17}N_5O$	56.52 / 56.17	7.43 / 7.23	30.04 / 29.79	138-140	86
4c	$C_{11}H_{17}N_5O_2$	52.11 / 52.59	6.55 / 6.77	28.12 / 27.89	172-174	79
4d	$C_{12}H_{19}N_5O$	57.56 / 57.83	7.85 / 7.63	27.76 / 28.11	128-130	72
5a	$C_{13}H_{20}N_5O_3$	47.62 / 47.34	6.39 / 6.07	21.49 / 21.24	72-74	80
5b	$C_{15}H_{24}ClN_5O$	54.90 / 55.30	7.01 / 7.37	21.83 / 21.51	112–114	90

TABLE 3. ^{1}H NMR Spectra of Compounds **3-5**

Compound	Chemical shifts, δ, ppm (*J*, Hz)*
2a	3.60-3.85 (10H, m, CH_2Cl and morpholine); 3.90 (3H, s, OCH_3); 4.52 (2H, t, *J* = 6.7, OCH_2)
2b	1.55-1.75 (6H, m, $(CH_2)_3$); 3.72-3.85 (6H, m, $N(CH_2)_2$ and CH_2Cl); 3.90 (3H, s, OCH_3); 4.50 (2H, t, *J* = 6.6, OCH_2)
2c	2.90 (3H, s, NCH_3); 3.60-3.82 (10H, m, CH_2Cl and morpholine); 4.40-4.52 (2H, m, OCH_2); 6.7, 6.9 and 7.62 (in total 1H, br. s, NH)
2d	1.50-1.70 (6H, m, $(CH_2)_3$); 2.92 (3H, s, NCH_3); 3.70-3.83 (6H, m, $N(CH_2)_2$ and CH_2Cl); 4.43 (2H, t, *J* = 6.6, OCH_2); 6.75, 7.00 and 7.70 (in total 1H, br. s, NH)
2e	1.22 (3H, t, *J* = 7.0, CH_3); 3.40 (2H, q, *J* = 7.0, $NC\underline{H}_2CH_3$); 3.72-3.85 (10H, m, morpholine and CH_2Cl); 4.45 (2H, t, *J* = 6.7, OCH_2); 6.80, 6.90 and 7.65 (in total 1H, br. s, NH)
2f	1.20 (3H, t, *J* = 7.0, CH_3); 1.50-1.70 (6H, m, $(CH_2)_3$); 3.42 (2H, q, *J* = 7.0, $NC\underline{H}_2CH_3$); 3.70-3.85 (6H, m, $N(CH_2)_2$ and CH_2Cl); 4.42 (2H, t, *J* = 6.5, OCH_2); 6.90, 7.00 and 7.80 (in total 1H, br. s, NH)
2g	3.10 (6H, s, $N(CH_3)_2$); 3.60-3.77 (8H, m, morpholine); 3.79 (2H, t, *J* = 6.7, CH_2Cl); 4.43 (2H, t, *J* = 6.7, OCH_2)
2h	1.50-1.70 (6H, m, $(CH_2)_3$); 3.08 (6H, s, $N(CH_3)_2$); 3.70-3.83 (6H, m, $N(CH_2)_2$ and CH_2Cl); 4.40 (2H, t, *J* = 6.6, OCH_2);
2i	3.60-3.76 (16H, m, morpholine); 3.79 (2H, t, *J* = 6.7, CH_2Cl); 4.43 (2H, t, *J* = 6.7, OCH_2)
2j	1.50-1.70 (12H, m, $(CH_2)_6$ piperidine); 3.70-3.82 (10H, m, $N(CH_2)_4$ piperidine and CH_2Cl); 4.45 (2H, t, *J* = 6.6, OCH_2)
3a	3.58-3.82 (8H, m, morpholine); 4.10 (2H, t, *J* = 7.5, NCH_2); 4.70 (2H, t, *J* = 7.5, OCH_2)
3b	1.50-1.75 (6H, m, $(CH_2)_3$); 3.75 (4H, m, $(NCH_2)_2$); 4.07 (2H, t, *J* = 7.4, NCH_2); 4.70 (2H, t, *J* = 7.4, OCH_2)
4a	2.95 (3H, s, NCH_3); 3.58-3.80 (8H, m, morpholine); 3.67 (2H, t, *J* = 7.5, NCH_2); 3.90 (2H, t, *J* = 7.5, NCH_2)
4b	1.50-1.72 (6H, m, $(CH_2)_3$); 3.62 (2H, t, *J* = 7.3, NCH_2); 3.72 (4H, m, $N(CH_2)_2$); 3.90 (2H, t, *J* = 7.3, NCH_2)
4c	1.20 (3H, t, *J* = 7.2, CH_3); 3.42 (2H, q, *J* = 7.2, $NC\underline{H}_2CH_3$); 3.57-3.80 (8H, m, morpholine); 3.70 (2H, t, *J* = 7.5, NCH_2); 3.90 (2H, t, *J* = 7.5, NCH_2)
4d	1.22 (3H, t, *J* = 7.0, CH_3); 1.50-1.75 (6H, m, $(CH_2)_3$ piperidine); 3.42 (2H, q, *J* = 7.0, $NC\underline{H}_2CH_3$); 3.60 (2H, t, *J* = 7.3, NCH_2); 3.72 (4H, m, $N(CH_2)_2$ piperidine); 3.88 (2H, t, *J* = 7.3, NCH_2)
5a	3.50-3.97 (m, CH_2Cl, NCH_2 and morpholine)
5b	1.50-1.70 (12H, m, $(CH_2)_6$ piperidine); 3.65-3.82 (10H, m, $N(CH_2)_4$ piperidine and CH_2Cl); 3.95 (2H, t, *J* = 6.8, NCH_2)

*In the ^{1}H NMR spectra of compounds **2c-f** signals were observed for various conformers which is linked with the inhibition of rotation around the of N–heterocycle bond. This process is studied in detail in [8].

The rearrangement under consideration was confirmed by spectral data. In the IR spectra of compounds **3a**,**b**, **4a-d** the absorption bands for the C–O–C groups (1065-1185 cm^{-1}), characteristic of compounds **2a-h**, disappeared, and an intense absorption appeared at 1685-1695 cm^{-1} corresponding to a conjugated C=O group. In the ^1H NMR spectra, in place of the signals of the $ClCH_2CH_2O$ grouping of compounds **2a-h**, signals were observed for the methylene groups of the oxazole or imidazole rings of compounds **3a**,**b**, **4a-d** (Table 3).

Under analogous conditions bispiperidino- and bismorpholino derivatives **2i**,**j**, the structure of which excludes the possibility of eliminating hydrogen chloride and methyl chloride, are rearranged into 3-(2-chloroethyl)-*sym*-triazinones **5a**,**b**, which was also confirmed by data of ^1H NMR spectra (Table 3).

EXPERIMENTAL

The IR spectra were taken on a Nicolet Nexus spectrometer in nujol, and the ^1H NMR spectra on a Mercury 300 NMR spectrometer (300 MHz) in DMSO-d_6, internal standard was TMS. A check on the progress of reactions and the homogeneity of substances obtained was effected by TLC on Silufol UV-254 plates in the system acetone–hexane, 1:1.

The characteristics of the synthesized compounds **1-5** are given in Tables 1-3.

4-Methoxy-6-morpholino-2-trimethylammonio-*sym*-triazine Chloride (1a). Trimethylamine (2.4 g, 0.04 mol) in absolute benzene (15 ml) was added with stirring and cooling to 2-chloro-4-methoxy-6-morpholino-*sym*-triazine (9.2 g, 0.04 mol) in absolute benzene (30 ml). The mixture was left overnight, the precipitated solid was filtered off, washed with absolute ether, and dried over sulfuric acid in a vacuum desiccator. Product **1a** (10.0 g, 86%) was obtained with mp 153-154°C (decomp.).

Compounds 1b-j were obtained analogously.

2-(2-Chloroethoxy)-4-dimethylamino-6-piperidino-*sym*-triazine (2h). A 10% aqueous solution of NaOH (0.8 g, 0.02 mol) was added slowly dropwise with stirring to a mixture of compound **1h** (6.0 g, 0.02 mol) and ethylene chlorohydrin (6.4 g, 0.08 mol) at 0-5°C. The mixture was maintained under these conditions for 1.5 h. Ice-water (15 ml) was added and the precipitated solid filtered off. Product **2h** (5.0 g, 88%) was obtained with mp 60-62°C (ether).

Compounds 2a-g,i,j were obtained analogously.

2-Morpholino-6,7-dihydrooxazolo[3,2-*a*]-1,3,5-triazin-4(4H)-one (3a). A solution of compound **2a** (2.75 g, 0.01 mol) in absolute toluene (10 ml) was boiled for 6 h. The reaction mixture was cooled, the precipitated solid was filtered off, and washed with ether (10 ml) on the filter. Product **3a** (2.0 g, 83%) with mp 208-210°C was obtained.

Compound 3b was obtained analogously.

8-Methyl-4-morpholino-6,7-dihydroimidazo[1,2-*a*]-1,3,5-triazin-4(4H)-one (4a). A solution of compound **2c** (2.73 g, 0.01 mol) in absolute toluene (10 ml) was boiled for 4 h. The precipitated solid was filtered off, the filter washed with ether (10 ml), and **4a** hydrochloride (2.5 g, 91%) was obtained with mp 224-226°C (decomp.), which was neutralized with NaOH solution to pH 6-7. The solution was evaporated to dryness, and compound **4a** was extracted with acetone. Product **4a** (2.0 g, 77%) was obtained with mp 177-178°C (C_6H_6).

Compounds 4b-d were obtained analogously.

1-(2-Chloroethyl)-4,6-dimorpholino-1,2-dihydro-*sym*-triazin-2-one (5a). A solution of compound **2i** (3.3 g, 0.01 mol) in absolute toluene (10 ml) was boiled for 5 h. The reaction mixture was cooled, filtered from turbidity, the filtrate evaporated, the solid was thoroughly triturated with hexane, then with petroleum ether, and filtered. Product **5a** (2.65 g, 80%) was obtained with mp 72-74°C (decomp.).

Compound 5b was obtained analogously.

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