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DERIVATIVES OF IMIDAZO-*sym*-TRIAZINE

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2-Dimethylamino-4,6,7,8-tetrahydroimidazo[1,2-a]-sym-triazin-4-one synthesized by us previously is converted by the action of aryl isocyanates and arenesulfonyl chlorides into the corresponding derivatives of urea and N-arenesulfonyl-substituted imidazo-sym-triazinones. It was shown that 6-(2-chloroethoxy)-2-dimethylamino-4-(methoxycarbonylmethylamino)-sym-triazine is converted by thermolysis into 2-dimethylamino-8-methoxycarbonylmethyl-4,6,7,8-tetrahydroimidazo[1,2-a]-1,3,5-triazin-4-one, which is also obtained by the action of methyl bromoacetate on the imidazo-sym-triazinone.

Keywords: imidazo-*sym*-triazines, rearrangement-cyclization.

Within the framework of investigations of the rearrangement-cyclization reaction, discovered recently by us, of chloroethoxy-*sym*-triazines into annelated *sym*-triazinones [1] it was found that on thermolysis 4-alkyl-2-(2-chloroethoxy)-6-dialkylamino-*sym*-triazines split off hydrogen chloride or are subject to dechloro-alkylation with the formation of 8-alkyl-4,6,7,8-tetrahydroimidazo[1,2-*a*]-1,3,5-triazin-4-ones [2]. The high phyto and fungal activity of oxazole derivatives [3-5] directed the search for new pesticides towards the series of 8-substituted derivatives of imidazo-*sym*-triazinones. Using the basic approaches of the indicated procedure the corresponding chloroethoxy derivative **2** was obtained from the quaternary ammonium salt **1**. On thermolysis and subsequent alkaline treatment compound **2** is converted into the methyl ester of (2-dimethylamino-4-oxo-6,7-dihydro-4H-imidazo[1,2-*a*]-1,3,5-triazin-8-yl)acetic acid (**3**) and then into the corresponding hydrazide **4** (Table 1). In place of the triplet signals of the chloroethoxy group of compound **2** a multiplet is observed characteristic of the methylene groups of the imidazole ring of compounds **3** and **4** (Table 2).

In addition, a simpler and more effective procedure for the synthesis of a series of 8-alkyl-substituted imidazo-*sym*-triazinones was, in our opinion, the use of 2-substituted 7,8-dihydro-6H-imidazo[1,2-*a*]-1,3,5-triazin-4-one as starting material. As an example, 2-dimethylamino-7,8-dihydro-6H-imidazo[1,2-*a*]-*sym*-triazin-4-one **5** was synthesized by a similar cyclization procedure from 6-chloroethylamino-4-dimethylamino-2-methoxy-*sym*-triazine [6]. It was shown that compound **3** is also formed on alkylation of compound **5** with methyl bromoacetate in DMF and in the presence of potassium hydroxide (Tables 1, 2).

Urea derivatives **6a-d** were formed on boiling a toluene solution of compound **5** with aryl isocyanates. N-Acetyl (**7**) and N-arenesulfonyl (**8a-c**) derivatives were obtained by acetylation and arenesulfonylation of compound **5**.

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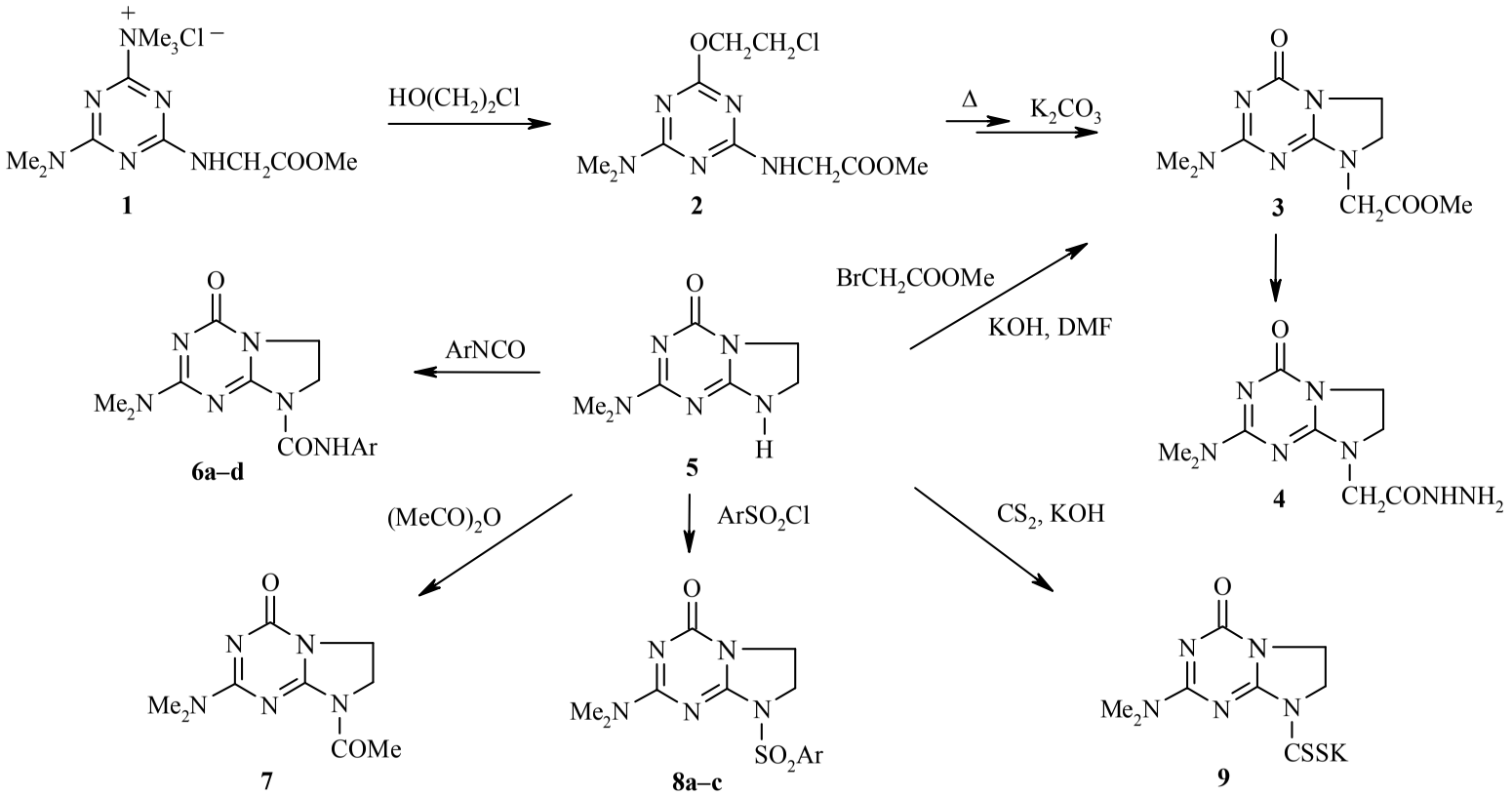
+
NMe3Cl −
Me2N
NHCH2COOMe
1
HO(CH2)2Cl
OCH2CH2Cl
2
Δ
K2CO3
O
3
CH2COOMe
BrCH2COOMe
KOH, DMF
4
CH2CONHNH2
ArNCO
CONHAr
6a–d
5
H
(MeCO)2O
7
COMe
ArSO2Cl
8a–c
SO2Ar
CS2, KOH
9
CSSK

TABLE 1. Physicochemical Characteristics of Compounds **1-9**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		Cl	N	S		
1	$C_{11}H_{21}ClN_6O_2$	12.03 / 11.66	27.83 / 27.58	—	155-156	92
2	$C_{10}H_{16}ClN_5O_3$	12.41 / 12.26	24.49 / 24.18	—	118-119	89
3	$C_{10}H_{15}N_5O_3$	—	27.36 / 27.67	—	Viscous liquid	90
4	$C_9H_{15}N_7O_2$	—	35.00 / 38.74	—	239–241	79
6a	$C_{14}H_{16}N_6O_2$	—	27.53 / 28.00	—	220-222	89
6b	$C_{14}H_{15}ClN_6O_2$	11.00 / 10.61	25.53 / 25.11	—	205-207	83
6c	$C_{14}H_{15}ClN_6O_2$	10.22 / 10.61	24.79 / 25.11	—	240-242	90
6d	$C_{14}H_{14}Cl_2N_6O_2$	19.58 / 19.24	23.11 / 22.76	—	236-238	83
7	$C_9H_{13}N_5O_2$	—	31.65 / 31.39	—	210-212	94
8a	$C_{14}H_{17}N_5O_3S$	—	21.27 / 20.90	10.00 / 9.55	226-228	70
8b	$C_{13}H_{14}ClN_5O_3S$	—	10.32 / 9.99	19.31 / 19.69	223-225	73
8c	$C_{15}H_{18}N_6O_4S$	—	21.95 / 22.22	8.11 / 8.47	228-229	70
9	$C_8H_{10}KN_5OS_2$	—	23.30 / 23.73	22.00 / 21.69	>300	88

TABLE 2. ^{1}H NMR Spectra of Compounds **1-9**

Compound	Chemical shifts, δ, ppm (*J*, Hz)
1	3.35 [6H, s, $N(CH_3)_2$]; 3.65 [9H, s, $N^+(CH_3)_3$]; 3.82 (3H, s, OCH_3); 4.08 (2H, s, NCH_2CO); 9.78 (1H, br. s, NH)
2	3.16 and 3.20 [both 3H, s, $N(CH_3)_2$]; 3.65 (2H, t, *J* = 6.7, CH_2Cl); 3.78 (3H, s, OCH_3); 4.05 (2H, s, NCH_2CO); 4.27 (2H, t, *J* = 6.7, OCH_2); 9.62 (1H, br. s, NH)
3	3.22 and 3.24 [both 3H, s, $N(CH_3)_2$]; 3.75 (3H, s, OCH_3); 3.90-4.12 (4H, m, NCH_2CH_2N); 4.37 (2H, s, NCH_2CO)
4	3.10 and 3.15 [both 3H, s, $N(CH_3)_2$]; 3.63-3.95 (4H, m, NCH_2CH_2N); 3.98 (2H, s, NCH_2CO); 4.10 (2H, v. br. s, NH_2); 9.28 (1H, br. s, NH)
6a	3.20 and 3.28 [both 3H, s, $N(CH_3)_2$]; 3.90-4.12 (4H, m, NCH_2CH_2N); 7.13-7.50 (5H, m, C_6H_5); 10.52 (1H, s, NH)
6b	3.22 and 3.28 [both 3H, s, $N(CH_3)_2$]; 3.92-4.13 (4H, m, NCH_2CH_2N); 7.27-7.54 (4H, m, C_6H_4); 10.58 (1H, s, NH)
6c	3.16 and 3.18 [both 3H, s, $N(CH_3)_2$]; 3.70-4.08 (4H, m, NCH_2CH_2N); 7.25-7.50 (4H, m, C_6H_4); 9.38 (1H, br. s, NH)
6d	3.18 and 3.22 [both 3H, s, $N(CH_3)_2$]; 3.90-4.05 (4H, m, NCH_2CH_2N); 7.30-7.58 (4H, m, C_6H_3); 10.12 (1H, s, NH)
7	2.58 (3H, s, $COCH_3$); 3.15 and 3.17 [both 3H, s, $N(CH_3)_2$]; 3.85-4.00 (4H, m, NCH_2CH_2N)
8a	2.47 (3H, s, CH_3); 3.08 and 3.17 [both 3H, s, $N(CH_3)_2$]; 3.85-4.18 (4H, m, NCH_2CH_2N); 7.35-7.97 (4H, m, C_6H_4)
8b	3.12 and 3.18 [both 3H, s, $N(CH_3)_2$]; 3.82-4.15 (4H, m, NCH_2CH_2N); 7.40-8.00 (4H, m, C_6H_4)
8c	2.27 (3H, s, $COCH_3$); 3.15 and 3.20 [both 3H, s, $N(CH_3)_2$]; 3.80-4.12 (4H, m, NCH_2CH_2N); 7.48-8.10 (4H, m, C_6H_4)
9	3.12 and 3.17 [both 3H, s, $N(CH_3)_2$]; 3.80-4.05 (4H, m, NCH_2CH_2N)

The corresponding potassium dithiocarbamate **9** was synthesized as a compound with potential fungicidal activity.

In the ^{1}H NMR spectra of the synthesized compounds **6-9** signals were displayed corresponding to the protons of the 8-substituent, in place of the signal of the NH group proton in compound **5** (Table 2).

EXPERIMENTAL

The ^{1}H NMR spectra were taken on a Mercury-300 (300 MHz) NMR spectrometer in DMSO-d_6, internal standard was TMS. TLC was carried out on Silufol UV-254 plates in the system acetone–hexane, 1:2.

(2-Dimethylamino-6-methoxycarbonylmethylamino-*sym*-triazin-4-yl)trimethylammonium Chloride (1) was obtained by the procedure described in [2]. Yield was 92%; mp 155-156°C. Found, %: Cl 11.37; N 27.80. $C_{11}H_{21}ClN_6O_2$. Calculated, %: Cl 11.65; N 27.58.

6-(2-Chloroethoxy)-2-dimethylamino-4-methoxycarbonylmethylamino-*sym*-triazine (2). Ethylene chlorohydrin (3.2 g, 40 mmol) was added to a suspension of 84% KOH (powder) (0.7 g, 10 mmol) in dry $CHCl_3$ (10 ml) at 0°C, then compound **1** (3.0 g, 10 mmol) was added in portions. The reaction mixture was stirred for 30 min at 0°C, then for 4 h at 20°C. The mixture was filtered, the filtrate evaporated, the residue was treated with water (10 ml), and compound **2** was filtered off.

(2-Dimethylamino-4-oxo-6,7-dihydro-4H-imidazo[1,2-*a*]-1,3,5-triazin-8-yl)acetic Acid Methyl Ester (3). A. A solution of compound **2** (1.45 g, 5 mmol) in absolute benzene (15 ml) was boiled for 10 h. The benzene was decanted, and the glassy mass was triturated sequentially with hexane and with petroleum ether, filtered, and rapidly transferred to a desiccator over H_2SO_4. Compound **3** hydrochloride (1.0 g, 69%) was obtained of decomposition point 96-97°C. A suspension of the latter in dry acetone (10 ml) was then neutralized with K_2CO_3 powder (0.24 g, 1.7 mmol). After 3 h the KCl was filtered off, and compound **3** was isolated (0.6 g, 69%) from the filtrate as a readily water-soluble viscous liquid.

B. Compound **5** (0.9 g, 5 mmol) was added to a suspension of 84% KOH powder (0.35 g, 5 mmol) in DMF (10 ml) and the mixture was stirred for 2 h at 20°C. Methyl bromoacetate (0.8 g, 5 mmol) was added and the mixture heated for 6 h at 75-80°C, cooled, the KBr filtered off, and DMF was distilled from the filtrate at 68-70°C (40 mm Hg), the residue was triturated with hexane, and the latter decanted. Compound **3** (1.1 g, 88%) was obtained in the residue as a viscous liquid, readily soluble in water.

(2-Dimethylamino-4-oxo-6,7-dihydro-4H-imidazo[1,2-*a*]-1,3,5-triazin-8-yl)acetic Acid Hydrazide (4). Hydrazine hydrate (63%, 2 ml) was added to a solution of compound **3** (0.76 g, 3 mmol) in water (2 ml) and the mixture maintained at 20°C during 3 h. Compound **4** was filtered off and dried in the air.

2-Dimethylamino-7,8-dihydro-6H-imidazo[1,2-*a*]-1,3,5-triazin-4-one (5) was obtained by the method described in [6]. ^{1}H NMR spectrum, δ, ppm: 3.08 [6H, s, $N(CH_3)_2$]; 3.57-3.95 (4H, m, NCH_2CH_2N); 8.10 (1H, br. s, NH).

(2-Dimethylamino-4-oxo-6,7-dihydro-4H-imidazo[1,2-*a*]-1,3,5-triazin-8-yl)carboxylic Acid Phenyl-amide (6a). A mixture of compound **1** (1.8 g, 10 mmol) and freshly distilled phenyl isocyanate (1.19 g, 10 mmol) in absolute toluene (10 ml) was boiled in the presence of catalytic quantities of pyridine for 5 h. The precipitate of compound **6a** was filtered off and washed on the filter with benzene (10 ml).

Compounds 6b-d were obtained analogously.

8-Acetyl-2-dimethylamino-7,8-dihydro-6H-imidazo[1,2-*a*]-1,3,5-triazin-4-one (7). A mixture of compound **5** (1.8 g, 10 mmol) in acetic anhydride (10 ml) was boiled for 8 h. The solution was evaporated, the solid triturated under hexane, then boiled with petroleum ether, and solid compound **7**, which dissolved well in water, was filtered off.

2-Dimethylamino-8-tosyl-7,8-dihydro-6H-imidazo[1,2-*a*]-1,3,5-triazin-4-one (8a). A suspension of compound **5** (1.8 g, 10 mmol) and 84% KOH powder (0.7 g, 10 mmol) in DMF (10 ml) was stirred for 2 h at

20°C. *p*-Toluenesulfonyl chloride (1.9 g, 10 mmol) was then added and the reaction mixture heated at 70-80°C for 4 h. The KCl was filtered off, DMF was distilled from the filtrate at 70-72°C (40 mm Hg), the residue was boiled with benzene, and compound **8a** was filtered off.

Compounds 8b,c were obtained analogously.

Potassium Salt of 2-Dimethylamino-4-oxo-6,7-dihydro-4H-imidazo[1,2-*a*]-1,3,5-triazine-8-dithiocarbonic Acid (9). 84% KOH powder (0.7 g, 10 mmol) was added to compound **5** (1.8 g, 10 mmol) in absolute ethanol (10 ml) and the mixture was stirred for 30 min. Carbon disulfide (0.8 g, 10 mmol) was added dropwise at 0°C and the reaction mixture was maintained at 20°C for 24 h. The solid compound **9** was filtered off, and washed on the filter with absolute ether (10 ml).

REFERENCES

1. V. V. Dovlatyan, *Khim. Geterotsikl. Soedin.*, 435 (1996). [*Chem. Heterocycl. Comp.*, **32**, 375 (1996)].
2. V. V. Dovlatyan, K. A. Eliazyan, and L. G. Agadzhanyan, *Khim. Geterotsikl. Soedin.*, 262 (1977). [*Chem. Heterocycl. Comp.*, **13**, 210 (1977)].
3. N. N. Mel′nikov, *Chemistry and Technology of Pesticides* [in Russian], Khimiya, Moscow (1974), 665 pp.
4. R. K. Robins, J. B. Allen, G. R. Rewenkaz, US Patent 246408 (1980); *Chem. Abs.*, **95**, 25544 (1981).
5. J. B. Holtwick and N. J. Leonard, *J. Org. Chem.*, **46,** 3681 (1981).
6. K. A. Eliazyan, A. M. Akopyan, V. A. Pivazyan, A. G. Akopyan, and V. V. Dovlatyan, *Khim. Geterotsikl. Soedin.*, 228 (1992). [*Chem. Heterocycl. Comp.*, **28**, 188 (1992)].