# CONDENSED IMIDAZO-1,2,4-AZINES.

# 14.[*] SYNTHESIS AND REACTIVITY OF 3-CHLORINE-SUBSTITUTED IMIDAZO[1,2-b]-1,2,4-TRIAZINES

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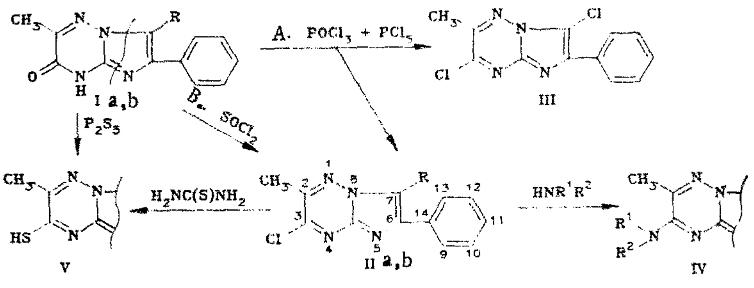
When boiled with phosphorus pentachloride in phosphorus oxychloride, 2-methyl-6-phenyl-imidazo[1,2-b]1,2,4-triazin-4H-3-one gives a mixture of mono- and dichloro derivatives, whereas the action of thionyl chloride in chloroform with a catalytic amount of DMFA gives only the monosubstituted product 2-methyl-3-chloro-6-phenylimidazo[1,2-b]-1,2,4-triazine. The reactivity of the 3-chloro derivatives of imidazo[1,2-b]-1,2,4-triazine in reactions with diethylamine, piperidine, morpholine, aniline, hydrazine hydrate and thiourea was investigated.

According to the data from spectral analysis of imidazo[1,2-b]-1,2,4-triazines (imitrines) [2,3], their laser characteristics are due to the electronic characteristics of the substituents in the imidazole fragment of the molecule (at positions 6 and 7). While continuing a series of researches into the chemical and laser characteristics of substituted imidazo[1,2-b]-1,2,4-triazines, we realized the synthesis of new imitrines with a variable substitutent in the triazine part of the molecule.

Earlier we reported on the synthesis of 2-methyl-3-chloro-6-phenylimidazo[1,2-b]-1,2,4-triazine (IIa) by the action of a mixture of phosphorus oxychloride and phosphorus pentachloride on 2-methyl-6-phenylimidazo[1,2-b]-1,2,4-triazin-4H-3-one (Ia) [4].



a R=H; b R=Ph

Chromatographic analysis of the reaction mixture obtained by this method (method A) by GLC showed that the previously described reaction does not take place in a well-defined manner but leads to the formation of two final products. In order to established the structures of the individual components of the mixture we used chromato-mass spectrometry (CMS) with a high-resolution mass spectrometer. The individual components of the mixture were identified on the basis of an analysis of the mass spectra, recorded repeatedly at the maxima of the chromatographic peaks. By CMS it was established that the first chromatographic peak ($\tau_{min}$ = 10'20", yield 87%), corresponds to the monochloro derivative (IIa). In its mass spectrum (Table 1) the molecular ion peaks (M$^+$) 244/246[†] were recorded with an intensity ratio of 3:1. This indicates the presence of one chlorine atom in the molecule. According to high-resolution mass spectrometry, the peak of the M$^+$ ion for (IIa) corresponds to the

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[*] For Communication 13, see [1].

[†] The numbers characterizing the ions denote the m/z values.

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TABLE 1. The Mass Spectra* of Compounds (IIa, b, IVc, d)

| Compound | m/z values (relative intensity, %) |
|---|---|
| IIa | 246 (33), 245 (12), 244 (100), 205 (9), 203 (29), 169 (7), 168 (67), 141 (18), 129 (7), 116 (15), 115 (22), 114 (14), 104 (13), 103 (18), 102 (10), 89 (49), 88 (14), 78 (9), 77 (18), 76 (15), 63 (25), 62 (12), 51 (23), 50 (16) |
| IIb | 322 (36), 321 (20), 320 (100), 319 (16), 245 (9), 243 (26), 219 (5), 217 (15), 192 (14), 178 (13), 166 (7), 165 (32), 141 (11), 115 (19), 114 (14), 103 (10), 89 (26), 77 (17), 76 (14), 63 (8), 51 (5) |
| III | 282 (10), 280 (57), 278 (100), 241 (4), 239 (25), 237 (36), 204 (8), 202 (27), 177 (5), 175 (15), 152 (4), 150 (20), 148 (16), 138 (7), 136 (21), 115 (12), 102 (10), 101 (18), 88 (13), 77 (10), 63 (13), 51 (18), 50 (13) |
| IVc | 370 (32), 369 (100), 368 (13), 329 (13), 328 (59), 260 (19), 259 (12), 244 (10), 178 (6), 165 (14), 129 (15), 104 (13), 103 (32), 89 (13), 84 (9), 77 (10), 66 (12) |
| IVd | 372 (33), 371 (100), 331 (8), 330 (35), 260 (15), 259 (18), 244 (10), 178 (9), 165 (17), 129 (12), 104 (10), 103 (31), 89 (14), 86 (8), 77 (15), 66 (23) |

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*The peaks of ions with intensities of $\geqslant$ 3% of the maximum are given.

molecular formula $C_{12}H_9N_4{}^{35}Cl$ (found 244.0513; calculated 244.0515). The initial stage in the fragmentation of $M^+$ for compound (IIa) under electron impact coincides with the general scheme for the dissociation of $M^+$ in imidazo[1,2-b]-1,2,4-triazines [3] and involves destruction of the triazine fragment with the elimination of the $CH_3CH$ particle (the $\Phi$ ion, found 203.0205; $C_{10}H_6N_3{}^{35}Cl$; calculated 203.0250) and subsequent elimination of a chlorine atom (the $\Phi_1$ ion, 168). The $\Phi_1$ ion subsequently loses two HCN molecules (for the $[\Phi_1{-}HCN]^+$ ion, found 141.0495, calculated 141.0452; for the $[\Phi_1{-}HCN, {-}HCN]^+$ ion, found 114.0389, calculated 114.0343). The appearance of the 116 and 115 ions is due to the cleavage of the imidazole ring of the molecule. The fragments which form probably have azarine radical-cation and cation structures (found 116.0498 and 115.0391, $C_8H_6N$ and $C_8H_5N$, calculated 116.0500 and 115.0421 respectively) and, together with the $[C_6H_5C{\equiv}CH]^+$ ion (found 102.0469, calculated 102.0471), demonstrate the absence of a chlorine atom at position 7 in compound (IIa).

At the maximum of the second chromatographic peak ($\tau_{min}$ = 13'10", yield 13%) we obtained the mass spectrum of (III); the intensity ratios of the $M^+$278/280/282 peaks were 9:6:1, which indicates the presence of two chlorine atoms in the molecule, i.e., the product (III) is dichloro-substituted 2-methyl-6-phenylimidazo[1,2-b]-1,2,4-triazine. This is confirmed by high-resolution mass spectrometry, according to which the 278 ion corresponds to the molecular formula $C_{12}H_8N_4{}^{35}Cl_2$ (found 278.0184, calculated 278.0126). The fragmentation path of $M^+$ in compound (III) is similar to that examined above for the monochloro-substituted compound (IIa) (Table 1); the elimination of the $CH_3CN$ particle from $M^+$ is observed (the $\Phi$ ion, 237/239/241) with subsequent removal of the chlorine atom ($\Phi_1$ ion, 202/204). Then as in the case of compound (IIa), successive elimination of two molecules of HCN takes place from the $\Phi_1$ ion (175/177 and 148/150). Such an analogy in the dissociative ionization path indicates that one of the chlorine atoms is at position 3 of the bicyclic compound. The appearance of the $[C_6H_5C{\equiv}CCl]^+$ (136/138) and $[C_6H_5C{=}CCl{-}N]^+$ (150/152) ions in the mass spectrum indicates that the second chlorine atom is at position 7 (found 136.0066 and 152.0069, $C_6H_5{}^{35}Cl$ and $C_8H_5N^{37}Cl$, 136.0079 and 152.0081 respectively).

The PMR spectrum of the isolated mixture of chlorination products (IIa, III) contains signals for the following protons: 2.19 (3H, s, $CH_3$); 7.38-7.91 (5H, m, arom.); 8.28 ppm (1H, s, CH of imidazole) and does not contain signals for the protons of an AB system; this rules out the presence of the product chlorinated at the $C_{(11)}$ atom in the mixture [5].

The IR spectra of the bicyclic compounds (IIa, III), unlike those of the initial compound, do not contain absorption bands for the carbonyl ($\nu_{C=O}$ 1700-1700 $cm^{-1}$) and imino ($\nu_{NH}$ 3110-3180 $cm^{-1}$) groups.

It is interesting to note that brief boiling of the imidazotriazin-3-one (Ia) with thionyl chloride in chloroform in the presence of catalytic amounts of DMFA (method B) leads to the exclusive formation of the monochloro derivative (IIa).

TABLE 2. The Characteristics of the Synthesized Substances

| Compound[*] | $R^1$ | $R^2$ | Tmp, °C[†] | $R_f$[‡] | Found, % |  |  | Molecular formula | Calculated, % |  |  | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  | C | H | N |  | C | H | N |  |
| Ib | — | — | 307—308 | 0,15 | 71,8 | 4,4 | 18,7 | $C_{18}H_{14}N_4O$ | 71,5 | 4,7 | 18,5 | 94 |
| IIb | — | — | 246—248 | 0,74 | 67,3 | 4,0 | 17,4 | $C_{18}H_{13}ClN_4$ | 67,4 | 4,1 | 17,5 | 93 |
| IVa | $C_2H_5$ | $C_2H_5$ | 161—163 | 0,70 | 73,9 | 6,3 | 19,6 | $C_{22}H_{23}N_5$ | 73,9 | 6,5 | 19,6 | 60 |
| IVb | $—CH_2(CH_2)_3CH_2—$ |  | 156—157 | 0,41 | 69,2 | 6,4 | 23,7 | $C_{17}H_{19}N_5$ | 69,6 | 6,5 | 23,9 | 79 |
| IVc | $—CH_2(CH_2)_3CH_2—$ |  | 219—220 | 0,71 | 74,7 | 6,5 | 19,1 | $C_{23}H_{23}N_5$ | 74,8 | 6,3 | 19,0 | 58 |
| IVd | $—CH_2CH_2—O—CH_2CH_2—$ |  | 239—240 | 0,68 | 71,3 | 6,2 | 18,9 | $C_{22}H_{21}N_5O$ | 71,1 | 5,7 | 18,9 | 61 |
| IVe | $C_6H_5$ | H | 231—232 | 0,63 | 71,4 | 4,7 | 23,1 | $C_{18}H_{15}N_5$ | 71,7 | 5,0 | 23,2 | 56 |
| IVf | $NH_2$ | H | 227—229 | 0,17 | 60,0 | 5,1 | 34,8 | $C_{12}H_{12}N_6$ | 60,0 | 5,0 | 35,0 | 62 |
| IVg | $NH_2$ | H | 247—248 | 0,31 | 68,5 | 4,8 | 26,5 | $C_{18}H_{16}N_6$ | 68,3 | 5,1 | 26,6 | 48 |
| Va | — | — | 288—290 | 0,74 | 59,1 | 4,5 | 22,9 | $C_{12}H_{10}N_4S$ | 59,5 | 4,2 | 23,1 | 75 |
| Vb | — | — | 286—287 | 0,64 | 67,7 | 4,9 | 17,6 | $C_{18}H_{14}N_4S$ | 67,9 | 4,4 | 17,6 | 69 |

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[*] Compounds (Ib, IIb, IVa, c, d, g, Vb) R = $C_6H_5$; (IVb, e, f, Va), R = H.

[†] The compounds were recrystallized: (Ib, Va, b) from DMFA; (IIb, IVc, d) from methanol; (IVa) from aqueous methanol; (Vb, f, g) from dioxane; (IVe) from aqueous DMFA.

[‡] Silufol UV-54 plates, eluat isopropanol for (IVb, e) and a 2:1 mixture of toluene and isopropanol for the remaining compounds.

During the chlorination of 2-methyl-6,7-diphenylimidazo[1,2-b]-1,2,4-triazinone (Ib) by method A only the monochloro derivative (IIb) was isolated. In the mass spectrum of (IIb) we detected a doublet of strong peaks for $M^+$ 320/322 (signal ratio 3:1), corresponding to its molecular mass with the allowance for the chlorine isotopes. With the introduction of a second bulky substituent ($R = C_6C_5$) the fragmentation path for $M^+$ of compound (IIb) changes greatly in connection with the preference for the dissociation processes due to the ortho effect [6]. Thus, the appearance of peaks 243/245 (3:1) in the mass spectrum is due to the elimination of the phenyl group, while the peaks for the 217/219 ions are due to the elimination of the benzonitrile fragment (Table 1). The ions of the 1,2-diphenylacetylene (178) and fluorene (165) structures confirm the ortho arrangement of the phenyl groups and indicate that the chlorine atom is not present in these substituents.

In connection with the electron deficiency at the $C_{(3)}$ atom in the imidazotriazines (IIa, b)[*] the chlorine atom at this position can be expected to have significant mobility. In order to confirm this conclusion experimentally we studied the behavior of compounds (IIa, b) in reactions with nucleophilic reagents. It was found that the boiling of 3-chloroimidazotriazines (IIa, b) in an excess of diethylamine, piperidine, morpholine, aniline, and hydrazine hydrate leads to the formation of the corresponding derivatives of imidazo[1,2-b]-1,2,4-triazine (IVa-g) (Table 2).

In the mass spectra of compunds (IVc, d) we recorded the peaks for $M^+$ 369 and 371, respectively (Table 1). At the first stage of the dissociation of $M^+$ the $CH_3CN$ particle is eliminated (the Φ ion). At the same time the other nitrile residue is eliminated from the triazine part of the molecule (with the formation of the common $[M - R^1R^2N{-}CN]$ (259) ion). Most of the remaining fragment ions in the mass spectra of the imidazotriazines (IVc, d) are due to the dissociation of the imidazole part of the molecule (the 178, 165, 129, 103, 77).

In the IR spectra of the bicyclic compounds (IVf) and (IVg) the hydrazine group is characterized by two broad absorption bands in the region of 3230—3310 $cm^{-1}$.

When the 3-chlorine-substituted compounds (IIa, b) were heated with thiourea in dioxane, the corresponding thio analogs (Va, b) were obtained. The latter are formed readily during the direct thionylation of the initial imidazotriazin-3-ones (Ia, b) by the action of phosphorus pentasulfide in pyridine (see the scheme).

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[*] The charge at the $C_{(3)}$ atom, calculated by the Hückel method, amounts to +0.102 and +0.189 respectively.

The obtained compounds (II-V) exhibit luminescence ($\lambda_{max}$ 475–532 nm) and are capable of generating laser radiation during excitation by the third and fourth harmonics of the neodymium laser in the 485–593 nm band.* The imidazotriazines (IVa) exhibit the highest generating efficiency (22%).

## EXPERIMENTAL

The IR spectra of the compounds were measured in dioxane and in tablets with potassium bromide on a UR-20 spectrophotometer. The PMR spectra of 10% solutions of the reaction mixture of (IIa) and (III) in DMSO-$d_6$ were obtained on a Bruker WH-90 instrument with TMS as internal standard.

The GLC and mass-spectral investigations were carried out on LKB-2091 instrument at 70 eV with a cathode emission current of 300 µA and an accelerating potential of 3 kV. A packed column was used for the separation of the reaction products (IIa, III) ($l$ = 2 m, d = 2 mm, liquid phase OV-101). The chromatograph injector temperature was 300°C, and the column temperature was 250°C (isothermal). The high-resolution mass spectra were obtained on a Varian MAT-311 instrument with resolution $M/\Delta M$ = 15,000 and with PPA as standard.

The quantum-chemical calculations for compounds (IIa, b) were performed out in the Hückel approximation. The coulomb and resonance integrals were taken from [9]. Compound (Ia) was obtained by the method in [10], and imidazotriazin-3-one (Ib) was obtained for the first time by a similar method.

The characteristics of the synthesized compounds are given in Table 2.

Chlorination of Compounds (Ia, b). A. The chlorination of (Ia, b) was realized by the method in [4]. Starting from imidazotriazin-3-one (Ia), we obtained a mixture of compounds (IIa) and (III). From compound (Ib) we obtained the individual 2-methyl-3-chloro-6,7-diphenylimidazo[1,2-b]-1,2,4-triazine (IIb).

B. A mixture of 0.01 mole of the respective imidazotriazin-3-one (Ia, b), 11.9 g (0.1 mole) of thionyl chloride, and 5–7 drops of DMFA in 100 ml of chloroform was boiled for 2 h. The mixture was filtered out, and the precipitate was washed with cold ethyl acetate and dried. The yields of (IIa, b)were 65 and 73% respectively.

Synthesis of Compounds (IVa-g). A mixture of 0.1 mole of 3-chloroimidazo-1,2,4-triazine (IIa) or (IIb) and 1 mole of the corresponding amine or hydrazine hydrate was boiled for 4–6 h. The mixture was cooled, and the precipitate was filtered off, washed with ether, and dried.

3-Mercapto-Substituted Imidazo[1,2-b]-1,2,4-triazine (Va, b) A. Amixture of 0.005 mole of 3-chloro-imidazotriazine (IIa) or (IIb) and 0.015 mole of thiourea in 50 ml of propyl alcohol was boiled for 6 h. The reaction mass was cooled, and the precipitate was filtered off and washed with water. The yields of (Va, b) were 63 and 58% respectively.

B. A mixture of 0.01 mole of (Ia) or (Ib) and 0.02 mole of phosphorus pentasulfide was boiled for 4 h. The mixture was cooled, poured onto ice, and left at 0°C for 4 h. The precipitate was filtered off, washed with water, and dried.

## LITERATURE CITED

1. V. P. Kruglenko, V. P. Gnidets, N. A. Klyuev, E. V. Logachev, M. A. Klykov, and M. V. Povstyanoi, Kh. Geterotsikl. Soedin., No. 10, 1402 (1985).
2. V. S. Zuev, L. A. Komel'kova, V. P. Kruglenko, O. A. Logunov, M. V. Povstyanoi, A. V. Startsev, Yu. Yu. Stoilov, and A. A. Timoshin, Kvantovaya Élektron., 11, 393 (1984).
3. M. V. Povstyanoi, V. P. Kruglenko, A. A. Timoshin, N. A. Klyuev, I. I. Grandberg, and Yu. Yu. Stoilov, Izv. Timiryazevsk. S-kh-Akad., No. 5, 155 (1984).
4. M. V. Povstyanoi, V. A. Grin', V. P. Kruglenko, and S. S. Stoyanovich, Zh. Org. Khim., 15, 1991 (1979).
5. Yu. V. Strokin, B. A. Priimenko, A. K. Sheinkman, and N. A. Klyuev, Khim. Geterotsikl. Soedin., No. 10, 1404 (1979).
6. R. A. Khmel'nitskii, Khim. Geterotsikl. Soedin., No. 3, 291 (1974).

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*The lasar characteristics of compounds (II-V) are discussed in detail in [7, 8].

7. L. A. Komel'kova, V. P. Kruglenko, O. A. Logunov, M. V. Povstyanoi, A. V. Startsev, Yu. Yu. Stoilov, and A. A. Timoshin, Kvantovaya Élektron., 10, 876 (1983).
8. V. S. Zuev, V. P. Kruglenko, O. A. Logunov, A. V. Startsev, and Yu. Yu. Stoilov, Kvantovaya Élektron., 8, 1567 (1981).
9. A. Streitwieser, Molecular Orbital Theory for Organic Chemists, Wiley, New York (1961).
10. J. Lalezari and Y. Levy, J. Heterocycl. Chem., 11, 327 (1974).

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# REACTION OF 2-ALKYLAMINOBENZOTHIAZOLES WITH ACRYLIC ACID

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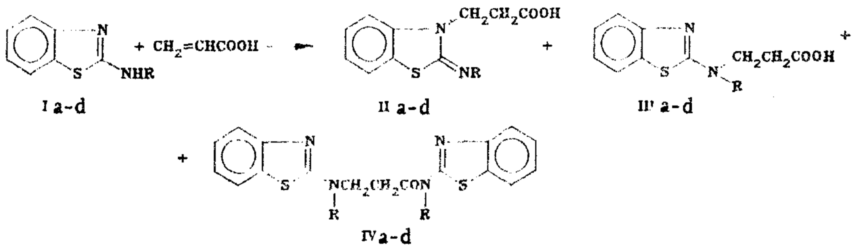
The behavior of 2-alkylaminobenzothiazoles in the reaction with acrylic acid was studied and it was shown that under kinetically controlled conditions, the reaction proceeds at the endocyclic nitrogen atom of the ambifunctional system. The formation of amino-isomers is controlled thermodynamically.

The addition of 2-alkylaminobenzothiazoles to reagents containing carbon—carbon multiple bonds has not yet been investigated. There are only a few reports on the reaction of unsubstituted 2-aminobenzothiazole with acetylenecarboxylic acid esters [1-5], leading to the formation of condensed addition products at the endocyclic nitrogen atom of the hetero-system. At the same time, in addition to pyrimidobenzothiazoles, the authors of [3] isolated an adduct with an amino structure, i.e., an addition product at the exocyclic nitrogen atom.

To synthesize potential pesticides, and to examine the paths and conditions of the reaction of 2-aminobenzothiazoles with activated alkenes, we studied the reaction of compounds Ia-d with acrylic acid. The reaction was carried out in aprotic solvents (acetone, toluene) in the temperature range from 30 to 110°C.



I–IV a R=$CH_3$, b R=$C_2H_5$, c R=$C_3H_7$, d R=$C_4H_9$

The ratio of yields of compounds IIa-d–IVa-d depends on the temperature (Table 1). At 30 and 56°C, 2-alkylimino-3-(2-carboxyethyl)benzothiazolines (IIa-d), products of addition of acrylic acid to the endocyclic nitrogen of the heterocycle, become predominant. The isomeric amino analogs IIIa-d are not formed in appreciable amounts. Increase in the temperature to 110°C leads to a sharp increase in the yield of 2-[N-alkyl-N-(2-carboxyethyl)amino]benzothiazoles (IIIa-d). Under the same conditions, benzothiazolylamides of 3-(2-benzothiazolyl)propionic acids (IVa-d) are formed in low yields. The alkyl substituent in compounds Ia-d does not influence the path of the reaction, but the overall yield of the products somewhat decreases with the elongation of the chain. The predominant formation of compounds IIIa-d at 110°C (Table 1) is probably the result of isomerization of the imino analogs IIa-d under the reaction conditions. We shall discuss this fact in a future article.

The structure of the synthesized compunds was established by using IR, UV, and PMR spectroscopy methods (Table 4), and mass spectrometry (Tables 2 and 3), and was also confirmed by elemental analysis data (Table 5) and alternative synthesis.

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