

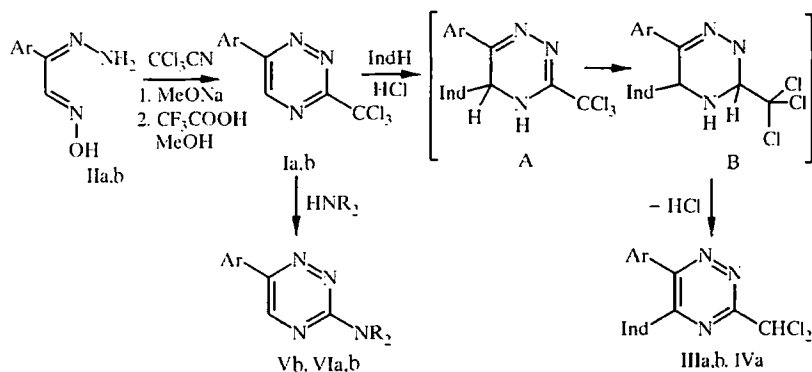
NUCLEOPHILIC *tele*-SUBSTITUTION REACTIONS IN 3-TRICHLOROMETHYL-1,2,4-TRIAZINES

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In electrophilic arenes bearing a halogen atom (chlorine) in the α -position of side chain, the aromatization of σ^H -adducts in nucleophilic substitution reactions of hydrogen (S_N^H) is possible on elimination of this atom. However *tele*-substitution of halogen (addition of nucleophile at the unoccupied position of the heterocycle with subsequent elimination of hydrogen together with halogen from the side chain) has been observed only on reaction with strongly anionic nucleophiles (alkoxide or hydroxide anions) [1,2].

With the aim of studying the *tele*-substitution of chlorine in 6-aryl-3-trichloromethyl-1,2,4-triazines I we have developed a simple method of synthesis of the latter based on the reaction of hydrazones of α -oximinoacetophenones II with trichloroacetonitrile in methanol in the presence of sodium methylate, with subsequent acidification with trifluoroacetic acid.

While studying the reaction of compounds Ia,b with nucleophiles it was established that interaction with indole or 1-methylindole in the presence of catalytic amounts of HCl formed 6-aryl-3-dichloromethyl-5-(3-indolyl)-1,2,4-triazines IIIa,b and IVb in 65-85% yield.



I-VI a Ar = Ph, b Ar = 4-Cl-C₆H₄; III Ind = 3-indolyl;
IV Ind = 1-methyl-3-indolyl; V NR₂ = NH₂; VI NR₂ = pyrrolidino

In view of the 5,3-sigmatropic shift of hydrogen frequently observed in 1,2,4-triazines [3,4] it can be assumed that in the first stage addition of indole occurs at the unsubstituted position 5 of the 1,2,4-triazine I activated by protonation, with the formation of the intermediate σ^H -adduct A. Subsequent hydride shift leads to 3,4-dihydro-1,2,4-triazine B, which is readily aromatized by β -elimination of molecule of HCl.

The reaction being considered is the first example of a *tele*-substitution reaction of halogen atom on reacting a neutral nucleophile with substrate activated by protonation. Such reaction conditions enable the range of nucleophiles to be broadened and previously inaccessible aromatic and heteroaromatic C-nucleophiles to be used.

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On the other hand, on reacting compounds Ia,b with ammonia and pyrrolidine *ipso* substitution of the trichloromethyl group occurs with the formation of 3-amino-6-(4-chlorophenyl)-1,2,4-triazine Vb and 6-phenyl-3-pyrrolidino-1,2,4-triazine VIa.

The structures of the compounds obtained were confirmed by data of ^1H NMR spectroscopy and mass spectrometry. The physicochemical characteristics of compound VIa agreed with literature data [5].

EXPERIMENTAL

3-Dichloromethyl-5-(1-methyl-3-indolyl)-6-phenyl-1,2,4-triazine (IVa) Hydrochloric acid (1 drop) was added to solution of 6-phenyl-3-trichloromethyl-1,2,4-triazine Ia (550 mg; 2 mmol) and 1-methylindole (0.26 ml; 2 mmol) in THF (2 ml) and the mixture was left at room temperature overnight. The precipitate was filtered off and recrystallized from ethanol. Product IVa (680 mg, 80%) was obtained; mp 256-258°C (decomp.). ^1H NMR spectrum (DMSO- d_6): 3.66 (3H, s, N-CH $_3$); 6.78 (1H, s); 7.25 (2H, m); 7.4 (1H, m); 7.43 (1H, s, CHCl $_2$); 7.5-7.7 (5H, m); 8.6 ppm (1H, m). Mass spectrum, m/z (%): 372 (5), 370 (30), 368 (46) (M^+). Found, %: C 61.66; H 3.70; N 15.05. C $_{19}$ H $_{14}$ Cl $_2$ N $_4$. Calculated, %: C 61.80; H 3.82; N 15.17.

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