SYNTHESIS OF SYMMETRICAL 1,2-DIHYDROTRIAZINES BY THE REACTION OF 1,1,1-TRIFLUORO-2-PHENYL-2,4,6,6-TETRACHLORO-3,5-DIAZAHEXA-3,5-DIENE WITH PRIMARY AMINES

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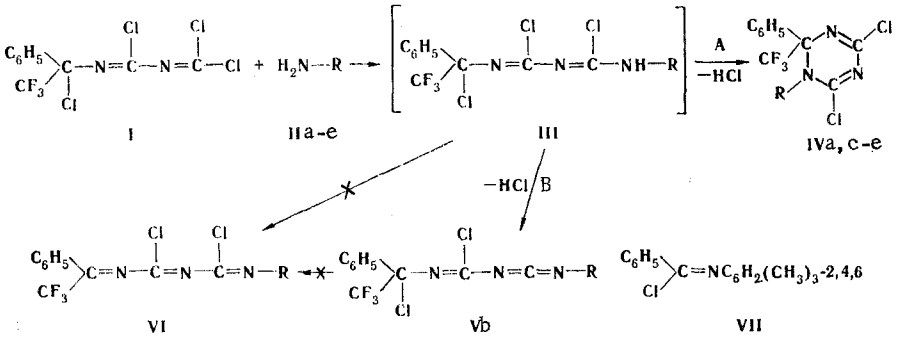
The reaction of 1,1,1-trifluoro-2-phenyl-2,4,6,6-tetrachloro-3,5-diazahexa-3,5-diene with primary amines proceeds via two pathways and leads to 1,2-dihydro-1,3,5-triazines or the corresponding carbodiimides. The reaction pathway is determined by the steric characteristics of the amines.

It is known that 1,2-dihydro-1,3,5-triazines are obtained by the condensation of amidines with aldehydes or imino compounds [1, 2].

We have found a new method for the synthesis of substituted 1,2-dihydro-1,3,5-triazines by heterocyclization of 1,1,1-trifluoro-2-phenyl-2,4,6,6-tetrachloro-3,5-diazahexa-3,5-diene (I) upon reaction with primary amines. The reaction of diazadiene I with amines IIa-e is realized at 0°C in ether in the presence of a base and evidently commences with replacement of one of the chlorine atoms of the $N{=}CCl_2$ group by the amine to give compounds of the III type, which are unstable and immediately undergo further transformations. Two pathways for stabilization of III are possible: formation of 1,2-dihydro-1,3,5-triazines IVa, c-e (pathway A) or formation of carbodiimide Vb (pathway B).



When amines IIa, c-e are used, stabilization of compounds of the III type proceeds as intramolecular nucleophilic substitution (pathway A) and leads to cyclic products IVa, c-e. The formation of a triazine ring in these cases is so favorable that cyclization takes place regardless of the reagent ratios and the reaction conditions (see [3]).

In the reaction of diazadiene I with tert-butylamine stabilization of III is realized by splitting out of hydrogen chloride (pathway B). In this case the bulky tert-butyl group attached to the nitrogen atom evidently hinders its participation in nucleophilic substitution and thus promotes the formation of carbodiimide Vb.

In addition to a multiplet of a benzene ring at 7.62-7.96 ppm, the PMR spectrum of IVa contains two septets of a methylidyne proton with an intensity of 1H at 3.85 and 3.80 ppm and two doublets of methyl groups with intensities of 3H each at 1.80 and 1.33 ppm, respectively. A double set of signals of 3-H and 5-H protons and protons of the $2\text{-}CH_3$ and $6\text{-}CH_3$ groups of the mesityl grouping is also observed in the PMR spectrum of triazine IVa. The presence of phenyl and trifluoromethyl groups, as well as a chlorine atom, in vicinal positions creates considerable steric hindrance for substituent R, and this evidently leads to its retarded rotation relative to the C–N bond and is manifested by doubling of the signals

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TABLE 1. 1,2-Dihydro-1,3,5-triazines (IVa, c-e)

Compound	R	mp, °C (hexane)	Found, %				Empirical formula	Calc., %				Yield, %
			C	H	Cl	N		C	H	Cl	N	
IVa	i-C_3H_7	95—97	45,9	3,8	—	12,5	$C_{13}H_{12}Cl_2F_3N_3$	46,2	3,6	—	12,4	72
IVc	C_6H_5	146—147	51,6	2,6	19,0	11,4	$C_{16}H_{10}Cl_2F_3N_3$	51,5	2,7	19,0	11,3	80
IVd	4-ClC_6H_4	130—132	47,1	2,2	25,8	10,3	$C_{16}H_9Cl_3F_3N_3$	47,3	2,2	26,2	10,3	73
IVe	2,4,6-$(CH_3)_3C_6H_2$	118—119	55,0	3,9	16,9	10,2	$C_{19}H_{16}Cl_2F_3N_3$	55,1	3,9	17,1	10,1	76

TABLE 2. Spectral Data for 1,2-Dihydro-1,3,5-triazines (IVa, c-e)

Compound	IR spectrum (CCl_4), cm^{-1}	PMR spectrum (CCl_4), ppm	^{19}F NMR spectrum (CCl_4), δ, ppm	UV spectrum, λ_{max}, nm (hexane)	M^+
IVa	1635	7,62—7,96 (5H, m, C_6H_5); 3,85, 3,80 (1H, sept., CH, J=7 Hz); 1,80 (3H, d, 1-CH_3, J=7 Hz); 1,33 (3H, d, 1-CH_3, J=7 Hz)	2,82	302	338
IVc	1640	7,50—7,78 (10H, m, 1- and 2-C_6H_5)	4,05	295	372
IVd	1625	7,42—7,72 (9H, m, C_6H_5 and C_6H_4)	4,35	296	406
IVe	1630	7,43—7,73 (5H, m, C_6H_5); 7,22 (1H, s, 3′-CH); 6,73 (1H, s, 3′-CH); 2,75 (3H, s, CH_3); 2,53 (3H, s, CH_3); 1,70 (3H, s, CH_3)	1,1	294	414

indicated above. The activation barriers to rotation of the isopropyl group in IVa ($\Delta G^{\neq}$ = 17.55 kcal/mole, T_{coal} = 100°C) and of the mesityl group in IVe ($\Delta G^{\neq}$ = 18.36 kcal/mole, T_{coal} = 82°C) at the coalescence temperatures (T_{coal}) were calculated.

However, it should be noted that, in connection with the presence of a chiral center in the 2 position of the triazine ring, doubling of the corresponding signals in the PMR spectra of IVa, e is possible also as a consequence of the anisochronicity of the methyl groups in the isopropyl grouping and of 2-CH_3, 6-CH_3, 3-H, and 5-H in the mesityl group.

The PMR spectrum of model compound VII, which was obtained by a method similar to that in [4], contains only lone signals of 2-CH_3 and 6-CH_3 groups and 3-H and 5-H protons of the mesityl grouping; this indicates the absence of retarded rotation in this sort of system, and on the basis of this one may disregard the possibility of the formation of compounds of the linear VI type that are isomers of triazines IV.

EXPERIMENTAL

The IR spectra were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Tesla BS-467 spectrometer (60 MHz) at 25°C with hexamethyldisiloxane as the external standard. The ^{19}F NMR spectra were recorded with a Tesla BS-487B spectrometer (80 MHz) at 25°C with CF_3COOH as the external standard. The molecular masses were determined with an MS-1302 mass spectrometer at an ionizing-electron energy of 70 eV. All of the reactions were carried out in anhydrous solvents.

1-Alkyl(aryl)-2-phenyl-2-trifluoromethyl-4,6-dichloro-1,2-dihydro-1,3,5-triazines (IVa, c-e). A solution of 0.01 mole of amine IIa, c-e and 0.02 mole of triethylamine in 20 ml of ether was added dropwise with cooling (ice water) and stirring to a solution of 0.01 mole of diene I in 20 ml of ether, and the mixture was stirred at 25°C for 2 h. The triethylamine hydrochloride was removed by filtration, the filtrate was evaporated, and the residue was purified by crystallization from hexane. Triazines IV are colorless crystalline substances that are quite soluble in all organic solvents (see Tables 1 and 2).

N-tert-Butyl-N′-1,3-dichloro-3-phenyl-4,4,4-trifluoro-2-azabuten-1-ylcarbodiimide (Vb). This compound was similarly obtained by the action of tert-butylamine on diazadiene I. The product was purified by three reprecipitations from ether solution by means of hexane at 5°C. This procedure gave 2.57 g (71%) of product. IR spectrum (CCl_4): 2190 (N=C=N) and 1650 cm^{-1} (C=N). PMR spectrum (CCl_4): 7.48-7.87 (5H, m, C_6H_5) and 1.72 ppm (9H, s, C_4H_9).

^{19}F NMR spectrum (CCl_4): 1.00 ppm (s, CF_3). Found: C 47.2; H 4.3; N 11.7%. $C_{14}H_{14}Cl_2F_3N_3$. Calculated: C 47.8; H 4.0; N 11.9%.

N-Mesitylbenzimidoyl Chloride (VII). In analogy with [4], a mixture of 3.6 g (0.015 mole) of N-mesitylbenzamide and 4.16 g (0.02 mole) of PCl_5 in 30 ml of benzene was refluxed for 1 h until HCl evolution ceased, after which the mixture was cooled and SO_2 was passed through it to remove the excess PCl_5. The solvent was evaporated, and the residue was distilled *in vacuo* to give 2.78 g (72%) of a product with bp 122-123°C (0.06 mm) and n_D^{20} 1.6021. IR spectrum (CCl_4): 1670 cm^{-1} (C=N). PMR spectrum (CCl_4): 7.43-8.30 (5H, m, C_6H_5), 6.97 (2H, s, CH), 2.43 (3H, s, CH_3), and 2.20 ppm (6H, s, CH_3). Found: C 74.3; H 6.0; N 5.5%. $C_{16}H_{16}ClN$. Calculated: C 74.6; H 6.3; N 5.4%.

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SYNTHESIS AND REACTIVITIES OF 5-HYDROXYPYRIMIDINE 1-OXIDES IN ELECTROPHILIC SUBSTITUTION

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1-Oxides of a series of 5-hydroxypyrimidine derivatives were synthesized, and their reactivities in electrophilic-substitution reactions (aminomethylation) as compared with 3-hydroxypyridine 1-oxides were investigated. It is shown that the activity of the 5-hydroxypyrimidine ring in the case of ring substitution increases as a result of N-oxidation, whereas methyl groups become less active.

Until recently, 5-hydroxypyrimidine 1-oxides were an uninvestigated class of nitrogen-containing heteroaromatic compounds, and their direct synthesis by N-oxidation of the pyrimidine ring had not been described. Data on the N-oxidation of other pyrimidine derivatives by the action on them of hydrogen peroxide and acetic acid [1, 2] (sometimes in the presence of a catalyst [3]) and permaleic and m-chloroperbenzoic acids [4] have been presented in the literature; tert-amyl hydroperoxide in the presence of molybdenum salts also serves as a good reagent for these purposes [5]. N-Oxidation, like protonation, of one of the nitrogen atoms of the pyrimidine ring significantly decreases the basicity of the second nitrogen atom. The preparation of N,N'-dioxides of the pyrimidine ring without introducing electron-donor substituents into the molecule is apparently impossible for this reason — the presence of two amino groups makes this reaction possible [6]. We noted that steric factors sometimes hinder the N-oxidation of pyrimidine derivatives. The oxidation of a substituted 2-phenylpyrimidine did not lead to the production of the corresponding N-oxide, 4-phenylpyrimidine gave only the 1-oxide, and a mixture of 1- and 3-oxides was obtained from 4-methylpyrimidine [4, 7].

We have synthesized a number of N-oxides that are derivatives of 5-hydroxypyrimidine (see Table 1), including 2-phenyl- and 2-tert-butyl-4,6-dimethyl-5-hydroxypyrimidine 1-oxides, which constitutes evidence for the possibility of overcoming the steric hindrance created by the 2-phenyl group and the even bulkier 2-tert-butyl group in N-oxidation. In

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