HETEROCYCLIC ANALOGS OF PLEIADIENE.

55.* 2-AZIDOPERIMIDINES: STABILITY OF THE TETRAZOLE FORM

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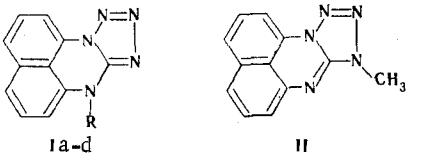
2-Azidoperimidine and its 1-methyl, 1-benzyl, and 1-phenyl derivatives were synthesized by the action of sodium azide on the corresponding 2-chloroperimidines. The IR spectra constitute evidence for the existence of all of these compounds in both the solid state and in solution in exclusively the tetrazolo[1,5-a]perimidine form.

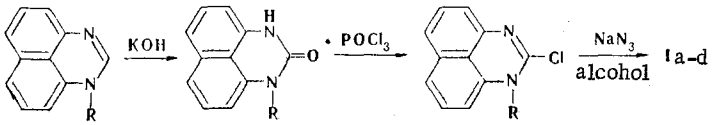
It was recently [2] reported that 2-azido- and 1-methyl-2-azidoperimidines exist exclusively in the tetrazolo[1,5-a]perimidine form (Ia, b). Although there was no doubt about this conclusion for the first compound in view of the unambiguous character of the method used to synthesize it (from 2-chloroperimidine and sodium azide), this was not the case for the N-methyl compound (Ib). The fact is that Ib was obtained by methylation of Ia in an alkaline medium, and the reaction theoretically could also take place in the tetrazole ring of the ambident anion, which would lead to II. The II structure could not be completely excluded on the basis of the data in [2]. The situation was also complicated by the fact that previously one of us and several co-workers reported that the IR spectrum of Ib contains a ν_{N_3} band at 2135 cm^{-1}, on the basis of which an azido form was ascribed to it [3].



Ia-d II

I a R=H; b R=CH_3; c R=$C_6H_5CH_2$; d R=C_6H_5

In this connection, the aim of the present research was to synthesize a series of N-substituted 2-azidoperimidines by reaction of the corresponding 2-chloroperimidines with sodium azide. In addition to a methyl group, we also selected benzyl and phenyl groups as the substituents in the 1 position. Compounds Ib-d were obtained via the following scheme:



IIIb-d IVb-d Vb-d

The hydroxylation of 1-benzylperimidine (IIIc) with alkali proceeded just as readily as in the case of IIIb [4], and purified 1-benzylperimidone (IVc) was obtained in 76% yield. However, in an attempt to obtain 1-phenylperimidone (IVd) by this method we found that it is formed in only 13% yield under the hydroxylation conditions. In addition to resinification under the influence of alkali, the heteroring in starting IIId was cleaved to give the previously unknown [5] 1-anilino-8-aminonaphthalene (VII). The possibility of the side transformation is undoubtedly associated with the decrease in the hydride lability of the hydrogen atom in σ complex VIa under the influence of the N-phenyl group [6]. As a result, deformylation under the influence of alkali of the acyclic form of the σ complex (VIb),

*See [1] for Communication 54.

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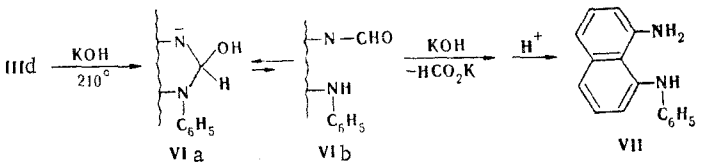
which evidently exists in equilibrium with the cyclic form, became the dominant process. Similar types of transformations are known in the perimidine series [7, 8].



In view of the complication noted above we developed another more convenient method for the preparation of 1-phenylperimidone, which consisted in heating the hydrochloride of VII with urea at 200°C. Compound IVd was obtained in 84% yield in this case.

The conversion of perimidones IV to 2-chloroperimidines V under the influence of phosphorus oxychloride proceeds without difficulty. N-Substituted 2-azidoperimidines Ib-d, as well as 2-azidoperimidine (Ia), were obtained by heating 2-chloroperimidines with a 1.5-fold to twofold excess of sodium azide in absolute alcohol. Work with V under absolute conditions is extremely important, since they have a very labile chlorine atom and are hydrolyzed to perimidones even by traces of moisture. This is particularly true of N-phenyl-substituted Vd.

2-Azidoperimidines are virtually colorless crystalline substances that differ from the bright-yellow perimidines such as III or V, and this constitutes evidence that they exist in cyclic tetrazole form I in the crystalline state. This conclusion is completely confirmed by the IR spectroscopic data. The IR spectra of Ia-d at 1500-1650 cm^{-1} are very similar to one another both in solution and in the solid form: They contain an extremely intense band at 1645 cm^{-1}, which can be ascribed to the stretching vibrations of the C=N bond, two intense bands at 1590-1600 cm^{-1}, and an intense band at 1510 cm^{-1}. However, the important thing is the absence of the absorption band of an azido group at 2130 cm^{-1}. All of these data constitute evidence for the monotypic character of the molecular structures of 2-azidoperimidines, which, in agreement with the conclusions in [2], exist in solutions in nonpolar solvents (we recorded the spectra of Ib-d in chloroform and carbon tetrachloride) and in the crystalline form in cyclic tetrazole form I. We were unable to record the IR spectrum in solution only in the case of Ia because of its low solubility.

We also obtained Ib in 38% yield by methylation of Ia with methyl iodide in an alcohol solution of alkali. With respect to all of its physicochemical parameters it proved to be identical to the sample obtained from 1-methyl-2-chloroperimidine and sodium azide, and its melting point was in agreement with the melting point in [2]. From this it may be concluded that the methylation of the anion of Ia in both alcohol and in DMSO [2] takes place at the nitrogen atom of the diazine ring rather than at the nitrogen atom of the tetrazole ring.

Since the data on the presence of a ν_{N_3} band in the IR spectrum of 1-methyl-2-azidoperimidine [3] were not reproducible, it may be assumed that the previously investigated sample contained admixed sodium azide, which is found together with the reaction product in the precipitate when the synthesis of I is carried out in alcohol solution.

EXPERIMENTAL

The IR spectra were recorded with a UR-20 spectrometer.

1-Benzylperimidone (IVc). A mixture of 4 g (0.015 mole) of 1-benzylperimidine [9] and 4 g (0.071 mole) of freshly fused powdered potassium hydroxide was heated at 205°C for 1.5 h, after which it was cooled and treated with a 5% solution of hydrochloric acid (75 ml). The mixture was filtered, and the precipitate was washed thoroughly with water and recrystallized from acetic acid to give 3.2 g (76%) of colorless crystals with mp 271-272°C, in agreement with the data in [10] (the compound was obtained previously by debenzylation of 1,3-dibenzylperimidone). IR spectrum (mineral oil): 1680 cm^{-1} (C=O).

1-Phenylperimidone (IVd). A) A mixture of 4 g (0.015 mole) of 1-anilino-8-aminonaphthalene hydrochloride and 6 g (0.083 mole) of urea was heated at 200°C for 1 h, after which it was cooled and treated with 100 ml of water, and the precipitate was separated and dried at 100°C to give 3.2 g (84%) of colorless crystals with mp 269-270°C (from o-xylene). IR spectrum (mineral oil): 1680 (C=O); 3130, 3200 cm^{-1} (N—H). Found: C 78.8; H 4.6; N 11.0%. $C_{17}H_{12}N_2O$. Calculated: C 78.5; H 4.6; N 10.8%.

B) A mixture of 5 g (0.02 mole) of perimidine IIId [11] and 5 g (0.089 mole) of freshly fused potassium hydroxide was heated at 210°C for 1 h, after which it was cooled and treated with 100 ml of 5% hydrochloric acid solution. The resinous mass was removed by filtration and triturated with 100 ml of benzene. The benzene-insoluble component was 1-phenylperimidone, which was identical to the sample obtained by method A. The yield was 0.68 g (13%). The benzene solution was evaporated, and the concentrate was passed through a column filled with aluminum oxide (elution with benzene). The first fraction was collected and evaporated, and the residue was recrystallized twice from alcohol to give 0.13 g (16%) of 1-anilino-8-aminonaphthalene in the form of colorless plates with mp 124-125°C [5]. The IR spectrum was identical to the spectrum of a genuine sample.

1-Benzyl-2-chloroperimidine (Va). A 3-g (0.011 mole) sample of 1-benzylperimidone was refluxed for 3 h with 20 ml of phosphorus oxychloride, after which the mixture was poured over 100 g of ice mixed with 45 ml of chloroform and 50 ml of 22% ammonium hydroxide. The resulting suspension was neutralized to pH 8 with ammonia, and the chloroform extract was separated and dried with calcium chloride. The chloroform was removed by distillation, and the residue was recrystallized twice from heptane to give 2.2 g (70%) of bright-yellow crystals with mp 146-147°C. Found: C 73.0; H 4.0; Cl 12.6; N 10.0%. $C_{17}H_{11}ClN_2$. Calculated: C 73.5; H 4.0; Cl 12.7; N 10.0%.

2-Chloroperimidine and 1-methyl-2-chloroperimidine were obtained by the methods described in [4].

Tetrazolo[1,5-a]perimidines (I). A mixture of 0.01 mole of the corresponding 2-chloroperimidine and 0.02 mole of sodium amide in 75 ml of absolute ethanol was refluxed with stirring for 5 h, after which it was cooled, and the precipitate was removed by filtration, washed thoroughly with water, and recrystallized from butanol (in the case of Ib-d) or xylene (in the case of Ia). In the preparation of tetrazoloperimidine Ia some of the substance after the reaction was found in the alcohol mother liquor, from which it was isolated separately by removal of the alcohol by distillation.

Tetrazolo[1,5-a]perimidine (Ia). This compound, with mp 240°C [2], was obtained in 50% yield. IR spectrum (mineral oil): 1640, 1610, 1595, and 1510 cm^{-1}.

11-Methyltetrazolo[1,5-a]perimidine (Ib). This compound, with mp 219-220°C [2], was obtained in 95% yield. IR spectrum (in mineral oil): 1642, 1610, 1595, and 1510 cm^{-1}. IR spectrum (in CCl_4): 1642, 1610, 1595, and 1515 cm^{-1}.

11-Benzyltetrazolo[1,5-a]perimidine (Ic). This compound was obtained in 85% yield as colorless platelets with mp 179-180°C. IR spectrum (in mineral oil): 1640, 1605, 1590, and 1510 cm^{-1}. IR spectrum (in $CHCl_3$): 1645, 1610, 1592, and 1515 cm^{-1}. Found: C 72.2; H 4.5; N 23.3%. $C_{18}H_{13}N_5$. Calculated: C 72.2; H 4.4; N 23.4%.

11-Phenyltetrazolo[1,5-a]perimidine (Ia). This compound, with mp 220-221°C, was obtained in 78% yield. IR spectrum (in mineral oil): 1642, 1605, 1595, 1580, and 1510 cm^{-1}. IR spectrum (in $CHCl_3$): 1642, 1603, 1595, 1580, and 1510 cm^{-1}. Found: C 71.8; H 4.0; N 24.0%. $C_{17}H_{11}N_5$. Calculated: C 71.6; H 3.9; N 24.6%.

Methylation of Tetrazolo[1,5-a]perimidine. A 0.17-g (3.2 mmole) sample of potassium hydroxide was added with stirring and heating in a stream of nitrogen to a solution of 0.5 g (2.5 mmole) of Ia in 15 ml of alcohol. After 5 min, a solution of 0.2 ml (3.2 mmole) of methyl iodide in 3 ml of alcohol was added, and the mixture was stirred in an inert atmosphere, initially at ∿20°C for 1 h, after which it was refluxed for another 4 h. It was then cooled, and the precipitate was removed by filtration and recrystallized from butanol to give 0.2 g (38%) of colorless crystals with mp 219-220°C. This product was identical to a sample obtained from 1-methyl-2-chloroperimidine and sodium azide with respect to its IR spectrum and melting point.

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MASS-SPECTROMETRIC BEHAVIOR OF 2-METHYL-3-OXO-3,4-DIHYDROQUINOXALINE DERIVATIVES

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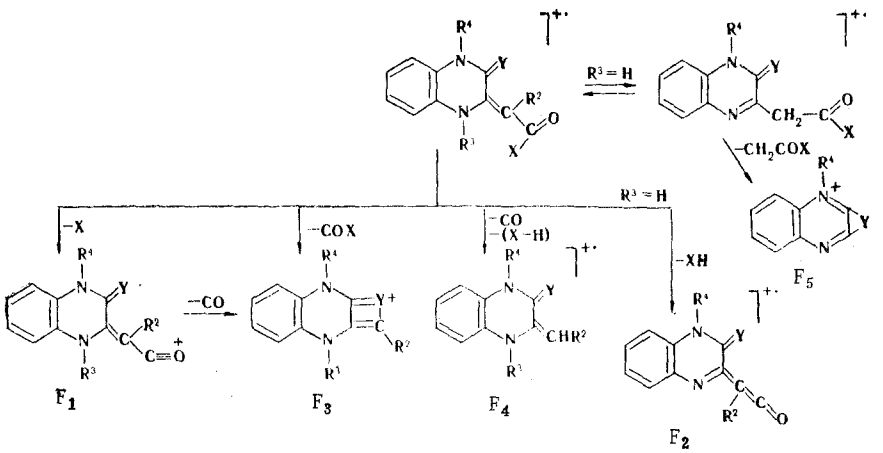
The mass spectra of 20 derivatives of 2-methyl-3-oxo(thioxo)-3,4-dihydroquinoxaline, as well as 2-nitromethylquinoxaline and 2-ethoxycarbonyl-3-oxopiperazine, were recorded in order to study the possibility of detection of a ketimine-enamine equilibrium in the gas phase. It was established that the mass-spectrometric criteria for the identification of the tautomeric forms that were previously proposed for analogous structures are inapplicable in the case of the investigated compounds. The mass spectra of all of the compounds are presented, and correlated schemes for their fragmentation are given.

We recently investigated the ketimine-enamine equilibrium of derivatives of 2-ethoxycarbonylmethylene- (I) and 2-cyanomethylene-3-oxo-1,2,3,4-tetrahydroquinoxalines (II) in solution in dimethyl sulfoxide (DMSO) by means of PMR spectroscopy [1]. However, under these conditions the solvation effect of the solvent may have had an appreciable effect on the shift of the tautomeric equilibrium. We therefore became intereseted in the research of Inagaki and Iwanami [2], who investigated the same equilibrium by means of mass spectrometry. They assert that intense F_2 peaks are characteristic for the fragmentation of the enamine form of ester I (Scheme 1), while the fragmentation of the molecular ions of ketimines takes place with detachment of the substituent from the 2 position as a whole (the F_5 ion).

Scheme 1



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