SIGMA COMPLEXES IN THE PYRIMIDINE SERIES.

8.* RECYCLIZATION OF ACETONYL ANIONIC σ-COMPLEXES OF 5-NITROPYRIMIDINE AND ITS DERIVATIVES

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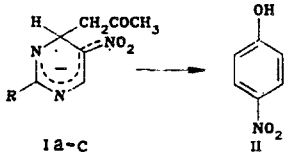
The transformation of the pyrimidine ring in the reaction of acetonyl anionic σ-complexes of 5-nitropyrimidine and its derivatives with strong base was studied. It is shown that when there is a geminal node at the 4 position, recyclization of the pyrimidine ring to a benzene ring takes place.

On reaction with C-nucleophiles, 5-nitropyrimidine and its methoxy derivatives are recyclized into compounds of the benzene and pyridine series [1-3]. It is known that anionic σ-complexes are intermediates in the recyclization of nitropyrimidines under the action of acetylacetone carbanion. Consequently, in the present work, we have studied the transformation of stable, acetonyl σ-complexes of the pyrimidine series when acted on by strong bases. As starting materials we chose σ-complexes in which all possible arrangements of the geminal node and the substituents in the pyrimidine ring are provided. This allows the attack of the nucleophile to be directed to a fixed position in the pyrimidine ring.

Only one product, p-nitrophenol II, was formed as the result of recyclization when strong bases acted on σ-complexes Ia-c (see Experimental section).



Ia-c II

Ia R=H; b R=OCH_3; c R=$N(C_2H_5)_2$

On the basis of the data in [1-3], a scheme for the recyclization of σ-complexes Ia-c can be proposed in which the reaction takes place along two paths.

Under these same conditions, anionic, σ-complex Id, in which position 6 of the pyrimidine ring is occupied by a methoxyl group , is not recyclized. According to the scheme, recyclization of complex Id is only possible aong path A. This allows one to assume that the recyclization of σ-complexes Ia-c takes place via bicyclic adduct III, but it has not been possible to obtain direct evidence of the formation of this compound.

Anionic, σ-complex Ie, in which the geminal node is located at the 2 position of the ring also does not recyclize in basic solution, because all of the ring positions are substituted and nucleophilic attack is, obviously, sterically hindered.

The formation of bicyclic adducts from the reaction of derivatives of trinitrobenzene and dinitropyridine with ketones in the presence of diethylamine is described in [4-6]. 5-Nitro-2-diethylaminopyrimidine (IV) was obtained from the reaction of σ-complex Ib with diethylamine in acetone (or methanol) solution. Apparently, σ-complex Ib decomposes to the initial 5-nitro-2-methoxypyrimidine (V) which then is converted into diethylaminopyrimidine IV, confirming the synthesis of IV from V.

*For Communication 7, see [1].

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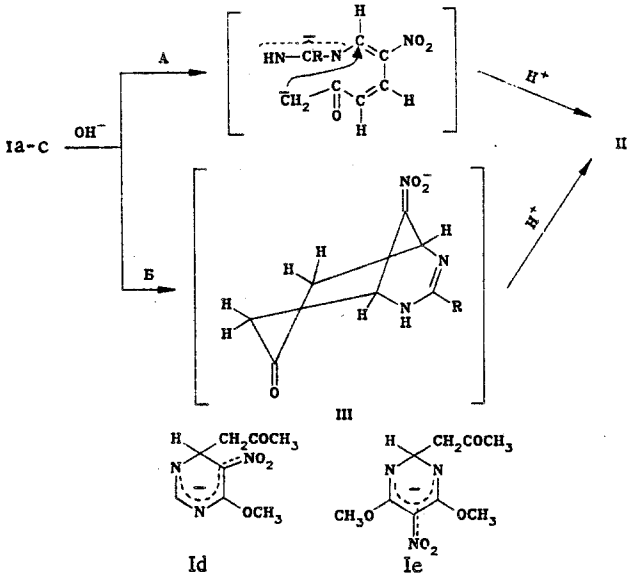
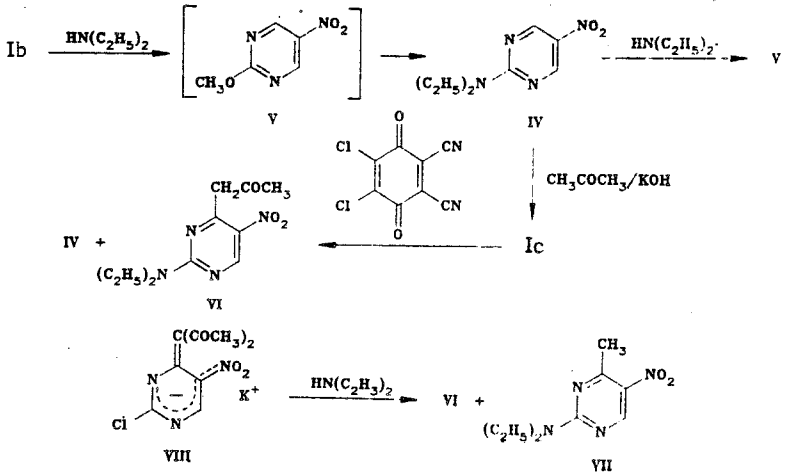


The σ-complex of the pyrimidine series (Ic) with a strong, electron-donor substituent was first obtained and isolated by the reaction of pyrimidine IV with acetone in the presence of potassium hydroxide. Complex Ic does not undergo any change in the presence of diethylamine. The structure of σ-complex Ic was shown by spectroscopic data (see Experimental section) and chemical transformations. It is oxidized by dichlorodicyanobenzoquinone in acetone solution to the initial pyrimidine IV and 5-nitro-4-acetonyl-2-diethylaminopyrimidine (VI), which was also obtained along with 5-nitro-4-methyl-2-diethylaminopyrimidine (VII) as a result of the deacylation of the potassium salt of anion VIII, described in [7]. The assignment of the signals in the PMR spectrum of acetonylpyrimidine VI (see Experimental section) gives evidence that the compound exists in two, tautomeric forms, ketonic and enolic (55:45).



EXPERIMENTAL

The PMR spectra were taken on a Tesla BS-467 (60 MHz) spectrometer in $CDCl_3$ with HMDS as an external standard. The electronic spectra were measured on a Specord UV-Vis instrument with a solution concentration of 10^{-4} M. The individuality of the substances synthesized was established by means of TLC on Silufol UV-254 plates; the eluent, chloroform.

The σ-complexes Ia and b were synthesized by the procedures in [8]; the potassium salt of VIII, by those in [7]; and pyrimidine V, by those in [9].

Recyclization of σ-Complexes Ia-c. Add 4.0 mmole of base with stirring to a solution of 2.0 mmole of σ-complex Ia-c (see Table 1) at 20°C. After 6-10 h, evaporate the solvent under reduced pressure. Add 3 ml of water to the residue and neutralize the resultant solution with 0.2 N H_2SO_4. Extract the oil that separates with sulfuric ether (3 × 30 ml), dry it over $MgSO_4$, distill off the solvent, and chromatograph the residue on silica gel (10 g; eluent,

TABLE 1. Reaction Conditions for σ-Complexes Ia-c

Compound	Base	Solvent	Yield of II, %	Compound	Base	Solvent	Yield of II, %
Ia	$\overset{+}{N}(C_2H_5)_4\overset{-}{O}H$	Methanol	19	Ib	KOH	Water	35
Ib	$\overset{+}{N}(C_2H_5)_4\overset{-}{O}H$	Methanol	68	Ib	NaH	DMFA	40
Ib	$\overset{+}{N}(C_2H_5)_4\overset{-}{O}H$	Water	75	Ic	$\overset{+}{N}(C_2H_5)_4\overset{-}{O}H$	Acetone	43

chloroform). Evaporate the chloroform solution under reduced pressure. Recrystallize the residue, p-nitrophenol II, from hexane and identify it by comparison with a known sample.

5-Nitro-2-diethylaminopyrimidine (IV). Add a solution of 0.7 ml (6.7 mmole) of diethylamine in 2 ml of methanol to a solution of 0.5 g (3.2 mmole) of pyrimidine V in 3 ml of methanol with stirring. Boil the reaction mixture for 3 h, evaporate the solution under reduced pressure, and filter off the precipitate that forms. Recrystallize it from hexane. Yield, 0.62 g (98%). T_{mp} 104-105°C; according to [10], T_{mp} is 104.5-105.5°C. PMR spectrum: 9.37 (s, 4,6-H); 4.07 (q, CH_2); 1.54 ppm (t, CH_3).

Potassium Salt of the Anion of 4H-5-Nitro-4-acetonyl-2-diethylaminopyrimidine (Ic). Add with vigorous stirring 0.3 g (5.3 mmole) of finely pulverized KOH to a solution of 1.0 g (5.1 mmole) of pyrimidine IV in 40 ml of absolute acetone. The solution takes on a yellow color that deepens with time. After 60 and 120 minutes, add two more 0.15 g (2.7 mmole) portions of KOH. Fifteen minutes after the last addition, filter the reaction mixture, concentrate the mother liquor to a volume of 3-4 ml, and precipitate dark violet compound Ic with absolute ethyl ether (150 ml). Yield, 1.03 g (68.5%). UV spectrum, λ_{max}: 422 nm (in acetone). PMR spectrum (DMSO-d_6): 8.63 (s, 6-H); 5.24 (q, CH); 3.67 (m, CH_2); 2.40 (s, CH_3); 1.25 ppm (t, CH_3).

Oxidation of σ-Complex Ic. Pour with stirring a solution of 0.50 g (2.2 mmole) of dichlorodicyanobenzoquinone in 10 ml of acetone into a solution of 0.65 g (2.2 mmole) of σ-complex Ic in 10 ml of acetone. After 2 h, evaporate the reaction mixture to dryness and chromatograph the residue on a silica gel column (20 g; eluent, chloroform). From the bottom zone, elute pyrimidine IV. Yield 0.12 g (28%). From the middle zone, elute acetonylpyrimidine VI. Yield, 0.24 g (43%). On being heated, compound VI decomposes instead of melting. UV spectrum of compound VI (methanol), λ_{max} 362 nm. PMR spectrum of ketonic form: 9.30 (1H, s, 6-H), 4.48 (2H, s, CH_2), 2.60 (3H, s, CH_3); enolic form: 16.36 (1H, s, OH), 9.28 (1H, s, 6-H), 6.86 (1H, s, CH), 2.46 (3H, s, CH_3); common signals: 4.00 (q, CH_2), 1.50 ppm (t, CH_3). Found: C 52.5, H 6.5, N 22.2%. $C_{11}H_{16}N_4O_3$. Calculated: C 52.4, H 6.4, N 22.2%.

Deacylation of the Potassium Salt of Anion VIII. Add with stirring a solution of 0.82 g (7.9 mmole) of diethylamine in 3 ml of methanol to a solution of 2.35 g (7.9 mmole) of potassium salt VIII in 5 ml of absolute methanol. After 24 h, filter off the precipitate, evaporate the mother liquor to dryness, and chromatograph the residue on a silica gel column (30 g; eluent, chloroform). From the botton zone, elute methylpyrimidine VII. Yield 0.08 g (5%). T_{mp} 54-56°C (from hexane). UV spectrum (methanol), 257 nm. PMR spectrum: 9.30 (s, 6-H), 4.03 (q, CH_2), 3.00 (s, CH_3), 1.57 ppm (t, CH_3). Found: C 51.4, H 6.8, N 26.6%. $C_9H_{14}N_4O_2$. Calculated: C 51.4, H 6.7, N 26.6%.

From the middle zone, elute acetonylpyrimidine VI. Yield 1.49 g (74.5%).

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