# SIGMA COMPLEXES IN THE PYRIMIDINE SERIES.

# 3.* SOME TRANSFORMATIONS OF ANIONIC SIGMA COMPLEXES OF 5-NITROPYRIMIDINES

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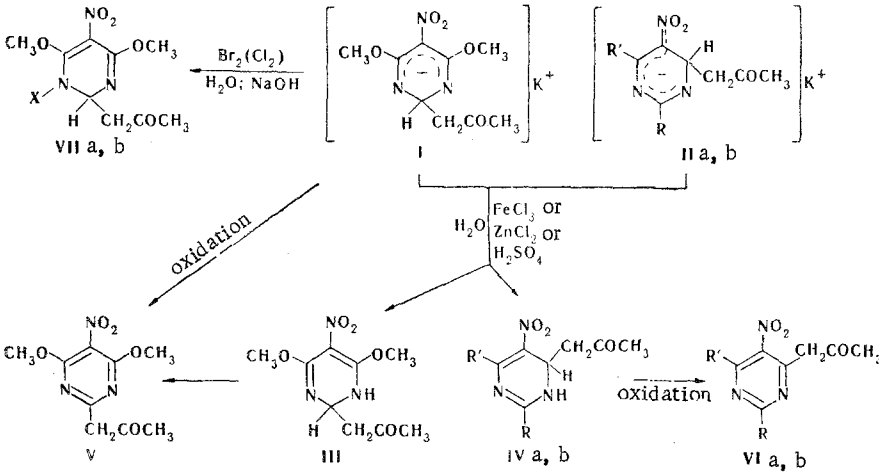
It is shown that sigma complexes of 5-nitropyrimidines with acetonide are protonated at the ring nitrogen atom in acidic media to give 5-nitroacetonyldihydropyrimidines. The latter are oxidized by dichlorodicyanobenzoquinone to 5-nitroacetonylpyrimidines.

We have previously [1, 2] described stable anionic sigma complexes obtained from 5-nitropyrimidines with acetone in the presence of potassium hydroxide. In the present research we studied some transformations of complexes I and IIa, b. Attempts to oxidize sigma complexes I and IIa with ferric chloride in aqueous solution led to the production of acetonyldihydropyrimidines III and IVa instead of the expected oxidation products V and VIa.

This is explained by the fact that the σ complexes undergo protonation at the ring nitrogen atom to give 1,2- and 1,6-dihydropyrimidines in aqueous solutions of ferric chloride under the influence of hydrochloric acid.

This reaction pathway was confirmed by the fact that in aqueous solutions of zinc chloride and in sulfuric acid solutions I and IIa, b are also converted to dihydropyrimidines III and IVa, b. The structure of IVa, b depends on which nitrogen atom is protonated and is proved by comparison of their UR spectra with the spectrum of III.

Relatively little study has been devoted to dehydrogenated pyrimidines; this is evidently due to the difficulty involved in their preparation. The formation of dihydropyrimidines (hydrogenated pyrimidines) from signa complexes in good yields may therefore serve as a preparative method.




II IV VI a R=OCH$_3$, R'=H; b R=R'=OCH$_3$; VII a X=Br; b X=Cl

In contrast to the σ complex obtained from trinitrobenzene and acetonide, which is oxidized by halogens in alkaline solutions [3], an attempt to oxidize complex I with bromine

*See [1] for Communication 2.

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and chlorine in potassium hydroxide solution did not give positive results; we isolated 1-N-halo-substituted 1,2-dihydropyrimidines VIIa, b. The mechanism of this reaction is unclear. The presence of positively charged halogen atoms was proved by the usual test, viz., by the liberation of iodine from an acidified solution of potassium iodide.

We were able to oxidize σ complex I and dihydropyrimidines III and IVa, b to acetonylpyrimidines V and VIa, b with dichlorodicyanobenzoquinone. The structures of the compounds obtained were proved by their PMR, IR, and UV spectra, as well as by their chemical transformations.

In connection with superimposition of the signals from the CH and NH protons, a multiplet at 6.06 ppm (with an intensity of two H) is observed in the PMR spectrum of III in $CDCl_3$, in addition to signals of protons of methoxy, methylene, and methyl groups with integral intensities of, respectively, six, two, and three H. The absence of a similar multiplet and the presence of a clearly expressed triplet at 5.71 ppm (with an intensity of one H) in the spectrum of a solution in trifluoroacetic acid are due to the production of the protonated form. This is also confirmed by the significant shift of the signals from the protons of the acetonyl group (∿0.3-0.4 ppm).

A triplet (with an intensity of one H), which characterizes the splitting of the 2-H proton by the protons of the methylene group of the acetonyl residue, is observed in the PMR spectra of VIIa, b. The low-field shift (∿0.2 ppm) of this signal relative to the corresponding signal in the spectrum of III is due to the inductive effect of the halogen atom. In connection with the fact that the protons of the methylene group in IVa, b are nonequivalent, as evidenced by their splitting by one another with a geminal constant of ∿16 Hz, splitting of the central component of the triplet into two symmetrical parts is characteristic for the absorption of the geminal proton of the ring (∿5 ppm). The magnitude of this splitting is ∿3 Hz. The spectra of IVa, b are similar to the spectrum of 2-oxo-3-acetonyl-6-nitro-1,2,3,4-tetrahydroquinoxaline, which is described in [4].

A singlet of a proton of a pyrimidine ring at 8.42 ppm that is similar to the signal of the proton in complex IIa (8.52 ppm) is observed in the PMR spectrum of IVa, and this also proves the nonaromatic structure of this compound. Compounds V and VIa, b can exist in several tautomeric forms, viz., keto, enol, and pyrimidylidene. The assignment of the signals shows that the keto structure predominates for V, and a low-field (∿1.0 ppm) shift of the signal of the methylene protons of the acetonyl group relative to the spectrum of III is observed; this constitutes evidence for aromatization of the dihydropyrimidine ring. The low-field (∿1.0 ppm) shift of the signal from the ring proton for VIa confirms the formation of a pyrimidine ring.

The presence in the spectra of VIa and VIb of signals from CH protons attached to a double bond and of signals of OH protons and the absence of a C=O band in the IR spectra confirm their enol structure. The chemical shifts of the signals of the OH protons in VIa, b are in good agreement with the data in [5] for other ketones. The shift of the signals to weak field in the spectra of VIa as compared with VIb can be explained by the electron-donor effect of the methoxy group [6].

## EXPERIMENTAL

The PMR spectra were recorded with a Tesla BS-467 spectrometer (60 MHz) with hexamethyldisiloxane as the external standard. The IR spectra of KBr pellets of the compounds were recorded with a Specord IR-71 spectrometer. The electronic spectra of solutions of the compounds in methanol ($\cong 10^{-4}$ mole/liter) were recorded with a Specord UV-vis spectrophotometer. Sigma complexes Ia-c were obtained by the methods in [1, 2].

5-Nitro-4,6-dimethoxy-2-acetonyl-1,2-dihydropyrimidine (III). A solution of 1.8 g (11.0 mmole) of ferric chloride in 15 ml of water was added dropwise with stirring to a solution of 1.6 g (5.7 mmole) of I in 40 ml of water, and the liberated oily substance was extracted with ether (three 75-ml portions). The ether extracts were dried with $MgSO_4$, the ether was removed by distillation, and the residue was crystallized from hexane to give 0.92 g (66%) of a product with mp 99-100°C. IR spectrum: 3400 (NH); 1730 (C=O); 1350, 1570 $cm^{-1}$ ($NO_2$). UV spectrum: $\lambda_{max}$ 269 nm. Found: C 44.5; H 5.5; N 17.3%. $C_9H_{13}N_3O_5$. Calculated: C 44.4; H 5.4; N 17.3%.

TABLE 1. PMR Spectra of III-VII

| Compound | Solvent | δ, ppm | | | | J, Hz H(CH)–H(CH₂) |
|---|---|---|---|---|---|---|
| | | CH | $CH_2$ | $CH_3$ | $OCH_3$ | |
| III | $CDCl_3$ | 6,06 m | 3,19 d | 2,62 s | 4,17 s | 7 |
| | $CF_3COOH$ | 5,71 t | 3,50 d | 2,25 s | 4,17 s | 7 |
| IVa* | $CDCl_3$ | 5,62 t | 3,30 m | 2,50 s | 4,21 s | 7 |
| | $CF_3COOH$ | 5,42 t | 3,33 d | 2,26 s | 4,22 s | 5 |
| IVa | $d_6$-DMSO | 5,33 t | 2,88 m | 2,31 s | 4,16 s<br>4,13 s | 6 |
| VIIa | $CDCl_3$ | 6,26 t | 3,11 d | 2,66 s | 4,20 s | 7 |
| VIIb | $CDCl_3$ | 6,25 t | 3,13 d | 2,60 s | 4,10 s | 6 |
| V | $CDCl_3$ | — | 4,25 s | 2,63 s | 4,38 s | — |
| VIa† | $CDCl_3$ | 6,83 s‡ | — | 2,50 s | 4,43 s | — |
| VIb** | $CDCl_3$ | 5,90 s‡ | — | 2,46 s | 4,46 s<br>4,41 s | — |

*The ring-proton signal is found at 8.42 ppm ($CDCl_3$) or at 7.88 ppm ($CF_3COOH$). †The signal of the ring proton is found at 9.46 ppm, while the signal of the OH proton is found at 15.33 ppm. ‡This is from the proton of the enol form. **The signal of the OH proton is found at 14.41 ppm.

5-Nitro-2-methoxy-6-acetonyl-1,6-dihydropyrimidine (IVa). A solution of 0.9 g (5.5 mmole) of ferric chloride in 15 ml of water was added dropwise with stirring to a solution of 0.7 g (2.7 mmole) of Ib in 30 ml of water. The residue (yellow crystals) obtained after extraction of the reaction mixture with ether (three 50-ml portions), drying, and removal of the solvent by distillation was purified by chromatography with a column filled with LSL-254 silica-gel [elution with chloroform–methanol (50:1)] to give 0.23 g (38%) of a product with mp 126-127°C (decomp.). IR spectrum: 3420 (NH); 1690 (C=O); 1320, 1550 $cm^{-1}$ ($NO_2$). UV spectrum: $\lambda_{max}$ 333 and 389 nm (sh). Found: C 45.0; H 5.2; N 19.5%. $C_8H_{11}N_2O_4$. Calculated: C 45.1; H 5.2; N 19.7%.

5-Nitro-2,4-dimethoxy-6-acetonyl-1,6-dihydropyrimidine (IVb). A 10-ml sample of a 0.57 N solution of sulfuric acid was added with stirring to a solution of 1.5 g (5.4 mmole) of IIb in 10 ml of water, and the resulting yellow crystalline precipitate was purified by chromatography with a column filled with LSL-254 silica gel [elution with chloroform–methanol (25:1)] to give 0.52 g (40%) of a product with mp 181-182°C (decomp.). IR spectrum: 3430 (NH); 1730 (C=O); 1370, 1540 $cm^{-1}$ ($NO_2$). UV spectrum: $\lambda_{max}$ 259 and 385 nm. Found: C 44.5; H 5.4; N 17.2%. $C_9H_{13}N_3O_5$. Calculated: C 44.4; H 5.4; N 17.3%.

Compounds III and IVa were obtained by a similar method in 60 and 66% yields, respectively. With respect to mixed-melting-point determinations, the results of elementary analysis, and the IR, UV, and PMR spectra they were identical to III and IVa obtained from I and IIa with ferric chloride.

5-Nitro-1-bromo-4,6-dimethoxy-2-acetonyl-1,2-dihydropyrimidine (VIIa). A mixture of 0.77 g (4.8 mmole) of bromine and 0.25 g (4.4 mmole) of potassium hydroxide in 10 ml of water were added with vigorous stirring to a solution of 1 g (3.5 mmole) of I in 20 ml of water. The yellow oil that precipitated from the reaction mixture was separated and dissolved in ether. The ether solution was dried, the ether was removed, and the residue was crystallized from hexane to give 0.72 g (47%) of a product with mp 109-111°C. Found: C 33.7; H 3.5; Br 24.5; N 12.8%. $C_9H_{12}BrN_3O_5$. Calculated: C 33.5; H 3.7; Br 24.8; N 13.0%.

5-Nitro-1-chloro-4,6-dimethoxy-2-acetonyl-1,2-dihydropyrimidine (VIIb). Chlorine gas was passed with stirring through a solution of 1.5 g (5.3 mmole) of I in 20 ml of water until the reaction mixture was neutral, and the precipitated light-colored oil was purified in the same way as IVa to give 0.4 g (27%) of a product with mp 95-96°C. Found: C 39.0; Cl 12.5; N 15.0%. $C_9H_{12}ClN_3O_5$. Calculated: C 38.9; Cl 12.8; N 15.1%.

5-Nitro-4,6-dimethoxy-2-acetonylpyrimidine (V). A) A solution of 0.8 g (3.5 mmole) of dichlorodicyanobenzoquinone in 15 ml of dioxane was added dropwise with stirring to a suspension of 1 g (3.5 mmole) of I in 10 ml of dioxane, after which the reaction mixture was refluxed for 3 h. The hydroquinone was separated, the solvent was removed, and the residue was chromatographed with a column filled with LSL-254 silica gel [elution with chloroform–methanol (50:1)] to give 0.27 g (31%) of a product with mp 84-86°C (from hexane). IR spectrum: 1720 (C=O); 1360, 1530 $cm^{-1}$ ($NO_2$). UV spectrum: $\lambda_{max}$ 253 and 300 nm. Found: C 45.0; H 4.5; N 17.6%. $C_9H_{11}N_3O_5$. Calculated: C 44.8; H 4.6; N 17.4%.

B) A mixture of 1 g (4.1 mmole) of III and 0.95 g (4.2 mmole) of dichloridicyanobenzoquinone was refluxed in 20 ml of benzene for 3 h. Workup and purification by method A gave 0.33 g (33%) of IIIa.

5-Nitro-2-methoxy-4-acetonylpyrimidine (VIa). This compound, with mp 118-120°C (from hexane), was obtained in the same way as V by method B. IR spectrum: 1330 and 1540 $cm^{-1}$ ($NO_2$). UV spectrum: $\lambda_{max}$ 269 and 340 nm. Found: C 45.3; H 4.3; N 19.7%. $C_8H_9N_3O_4$. Calculated: C 45.5; H 4.3; N 19.9%.

5-Nitro-2,6-dimethoxy-4-acetonylpyrimidine (VIb). This compound, with mp 122-124°C (from hexane), was obtained in the same way as V by method B. IR spectrum: 1340, 1550 $cm^{-1}$ ($NO_2$). UV spectrum: $\lambda_{max}$ 270 and 320 nm. Found: C 44.6; H 4.7; N 17.3%. $C_9H_{11}N_3O_5$. Calculated: C 44.8; H 4.6; N 17.4%.

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