2-BENZOPYRYLIUM SALTS.

25.* REACTION OF 2-BENZOPYRYLIUM SALTS WITH SOME NUCLEOPHILES

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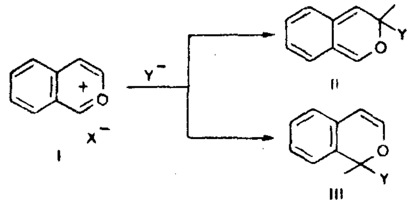
UDC 547.814.07

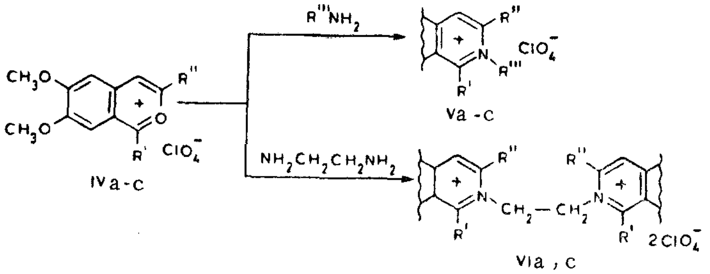
The reaction of 2-benzopyrylium salts with various amines was studied, and it was established that the structure of the reaction product is determined not only by the structure of the starting salt but also by the nature of the nucleophilic reagent.

Nucleophilic addition to the 2-benzopyrylium cation can take place at both α positions. However, since disruption of the aromatic character of the annelated benzene ring should certainly occur in the intermediate product of addition to C_3 (II), whereas, according to the results of quantum-mechanical calculations [2], the positive charge on C_1 is considerably higher than on C_3, it is customary to assume [2, 3] that attack by any nucleophile (Y^-) always takes place at C_1, i.e., through intermediate III. Nevertheless, concrete evidence in favor of this assertion has not yet been obtained.



A similar situation has also been encountered with respect to the reactivities of isoquinolinium salts [4], which are the closest structural isologs of 2-benzopyrylium salts.

The possibility of alternative addition in the 3 position of the 2-benzopyrylium cation can be checked in the reactions of some nucleophiles with salts of the IV type, which do not have substituents in the 1 position [5, 6].



IV a $R'=H$, $R''=CH_3$; b $R'=H$, $R''=4\text{-}OCH_3C_6H_4$; c $R'=H$, $R''=3,4\text{-}(OCH_3)_2C_6H_3$; V a $R'=H$, $R''=CH_3$, $R'''=C_6H_5$; b $R'=H$, $R''=4\text{-}OCH_3C_6H_4$, $R'''=CH_3$; c $R'=H$, $R''=3,4\text{-}(OCH_3)_2C_6H_3$, $R'''=C_6H_5$; VI a $R'=H$, $R''=CH_3$; c $R'=H$, $R''=3,4\text{-}(OCH_3)_2C_6H_3$

Like 1,3-disubstituted 2-benzopyrylium salts [2, 3], salts IVa-c (R' = H) react with aniline or methylamine to give isoquinolinium salts Va-c in high yields, whereas they react with ethylenediamine to give the corresponding biscations VIa, c.

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*See [1] for Communication 24.
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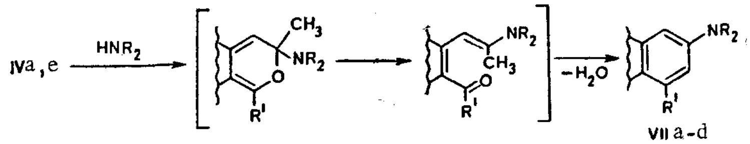
Rostov State University. Scientific-Research Institute of Physical and Organic Chemistry, Rostov-on-Don 344006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1608-1611, December, 1981. Original article submitted October 30, 1980; revision submitted January 27, 1981.

0009-3122/81/1712-1171$07.50

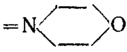
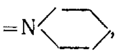
In this case the structure of the final product does not make it possible to determine the position of initial addition of the nucleophile.

A different pattern is observed when addition of the nucleophile to the cation subsequently leads to the formation of a new carbocycle constructed by the incorporation of an α-methylene group in this ring; this occurs in the reaction of α-alkylpyrylium salts with alkalis [7] or secondary amines [8]. The absence of an alkyl group in the 1 position of the salt should mean that the product of addition at C_1 will be incapable of further recyclizations. One therefore might have expected the formation of a compound of the III type or the product of its subsequent hydrolysis, viz., a dicarbonyl compound.

However, when we treated salt IVa with dimethylamine, we isolated a reaction product, in the PMR spectrum of a solution of which in CCl_4 we recorded a singlet at 2.8 ppm [protons of the $N(CH_3)_2$ group], singlets at 3.75 and 3.80 ppm (two OCH_3 groups), and a group of signals at 6.60-7.40 ppm (aromatic protons) with an intensity ratio of 6:3:3:5. In conjunction with the data from the IR spectra and the results of elementary analysis we assigned β-dialkylaminonaphthalene structure VIIa, the formation of which is possible only as a result of initial addition of the nucleophile at C_3, to the compound obtained.



VII a-d

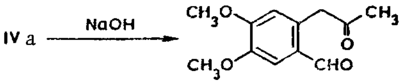
IV e $R'=C_2H_5$, $R''=CH_3$; VII a $NR_2=N(CH_3)_2$, $R'=H$; b $NR_2=$, $R'=H$;
c $NR_2=$, $R'=H$; d $NR_2=N(CH_3)_2$, $R'=C_2H_5$

Similar results were also obtained in the reaction of salt IVa with morpholine and piperidine.

We found that 1-ethyl-3-methyl-2-benzopyrylium perchlorate IVe (the ethyl substituent was introduced for simpler identification of the reaction product) also gives the corresponding β-dialkylaminonaphthalene VIId when it is treated with gaseous dimethylamine in alcohol.

In addition, dimethylamine hydrochloride in alcohol [9] or aqueous alkali [10] brings about the recyclization of 1,3-dialkyl-substituted 2-benzopyrylium salts to give α-naphthols. In these cases the reaction undoubtedly begins with the addition of the nucleophile at the 1 position of the heteroring.

In conformity with this, salt IVa reacts with alkali to give only open form VIII.



VIII

Similar results were obtained [11] in a study of the reaction of thieno[2,3-c]- and selenopheno[2,3-c]pyrylium salts with secondary amines and alkalis.

Thus the site of initial addition of the nucleophile to the 2-benzopyrylium cation and, consequently, the structure of the final recyclization product are determined not only by the structure of the starting pyrylium salt and the magnitude of the positive charge on the C_1 and C_3 atoms of the heteroring but also by the nature of the nucleophilic reagent.

EXPERIMENTAL

The IR spectra of mineral oil suspensions (with an NaCl prism) and KBr pellets of the compounds were recorded with Specord 71-IR and UR-20 spectrometers. The PMR spectra of solutions of the compounds in CCl_4 or CF_3COOH were recorded with Tesla BS spectrometers with operating frequencies of 60 and 80 MHz with hexamethyldisiloxane as the internal standard.

2-Phenyl-3-methyl-6,7-dimethoxyisoquinolinium Perchlorate (Va). A mixture of 0.3 g (1 mmole) of salt IVa and 0.1 ml (1 mmole) of aniline in 5 ml of ethanol was refluxed for 15 min, and the resulting solution was cooled and worked up to give 0.25 g (67%) of a product with mp 285°C (from acetic acid). IR spectrum: 1635, 1620, 1575, 1520, 1270, and 1090 cm^{-1}. Found: C 57.2; H 4.6; Cl 9.4%. $C_{18}H_{18}ClNO_6$. Calculated: C 56.9; H 4.8; Cl 9.6%.

2-Phenyl-3-(3,4-dimethoxyphenyl)-6,7-dimethoxyisoquinolinium Perchlorate (Vc). This compound, with mp 293°C (from acetic acid), was similarly synthesized in 60% yield. IR spectrum: 1635, 1620, 1610, 1590, 1570, 1270, and 1095 cm^{-1}. Found: C 59.9; H 5.0; Cl 7.5%. $C_{25}H_{24}ClNO_6$. Calculated: C 59.8; H 4.8; Cl 7.0%.

2-Methy-3-(4-methoxyphenyl)-6,7-dimethoxyisoquinolinium Perchlorate (Vb). A 0.5-ml sample of a 25% aqueous solution of methylamine and 3 ml of ethanol were added to 0.3 g (1 mmole) of salt IVb. After 30 min, the mixture was diluted with ether until precipitation ceased, and the precipitated product was removed by filtration to give 0.14 g (46%) of colorless crystals with mp 195°C (from ethanol). IR spectrum: 1620, 1602, 1566, 1496, 1250, and 1080 cm^{-1}. Found: C 55.3; H 4.7; Cl 8.5; N 3.5%. $C_{19}H_{20}ClNO_7$. Calculated: C 55.6; H 4.9; Cl 8.7; N 3.4%.

2,2'-(N,N'-Ethylene)bis(3-methyl-6,7-dimethoxy-2-benzopyrylium) Diperchlorate (VIa). A mixture of 0.3 g (1 mmole) of salt IVa and 0.1 ml of a 70% aqueous solution of ethylenediamine in 10 ml of ethanol was refluxed on a water bath for 30 min, after which it was cooled, and the crystalline precipitate was removed by filtration to give 0.42 g (67%) of a product with mp 304°C (from acetic acid). IR spectrum: 1640, 1620, 1580, 1270, and 1090 cm^{-1}. Found: C 49.4; H 4.8; Cl 11.0; N 4.2%. $C_{26}H_{30}Cl_2N_2O_{12}$. Calculated: C 49.4; H 4.8; Cl 11.0; N 4.4%.

2,2'-(N,N'-Ethylene)bis-3-(3,4-dimethoxyphenyl)-6,7-dimethoxyisoquinolinium Diperchlorate (VIc). This compound, with mp 315°C (from acetic acid), was similarly obtained in 50% yield. IR spectrum: 1640, 1620, 1585, 1470, 1280, and 1100 cm^{-1}. Found: C 55.2; H 4.5; Cl 8.4; N 3.5%. $C_{40}H_{42}Cl_2N_2O_{16}$. Calculated: C 54.8; H 4.8; Cl 8.0; N 3.2%.

2-Dimethylamino-6,7-dimethoxynaphthalene (VIIa). A 0.8-ml sample of a 33% aqueous solution of dimethylamine was added to 0.2 g (1 mmole) of salt IVa in 3 ml of ethanol, and the mixture was refluxed for 30 min. It was then cooled, and the resulting crystalline precipitate was removed by filtration and dried to give 0.14 g (93%) of a product with mp 123°C (from ethanol). IR spectrum (KBr pellet): 1630, 1610, 1520, 1250, and 1230 cm^{-1}. Found: C 72.6; H 7.6; N 5.8%. $C_{14}H_{17}NO_2$. Calculated: C 72.7; H 7.4; N 6.0%.

2-(N-Piperidino)-6,7-dimethoxynaphthalene (VIIc). A mixture of 0.61 g (2 mmole) of salt IVa and 0.43 ml (4 mmole) of piperidine in 3 ml of ethanol was refluxed for 1 h, after which it was cooled and diluted with water until precipitation ceased. The crystalline precipitate was removed by filtration and dried to give 0.43 g (80%) of a product with mp 130-131°C (from ethanol). IR spectrum (KBr pellet): 1635, 1610, 1520, 1470, 1380, 1250, and 1225 cm^{-1}. Found: C 75.5; H 8.1; N 5.2%. $C_{17}H_{21}NO_2$. Calculated: C 75.2; H 7.8; N 5.2%.

2-(N-Morpholino)-6,7-dimethoxynaphthalene (VIIb). This compound, with mp 190°C (from ethanol), was similarly obtained in 50% yield. IR spectrum (KBr pellet): 1630, 1610, 1515, 1470, 1250, and 1220 cm^{-1}. Found: C 70.3; H 6.9; N 5.4%. $C_{16}H_{19}NO_3$. Calculated: C 70.3; H 7.0; N 5.1%.

1-Ethyl-3-dimethylamino-6,7-dimethoxynaphthalene (VIId). Dimethylamine was passed through a refluxing suspension of 1 g (2 mmole) of salt IVe in 15 ml of ethanol for 1 h, during which the salt dissolved, and the color of the solution became lighter. The bulk of the alcohol (13 ml) was removed by distillation, and the residual solution was cooled. The precipitated substance was removed by filtration, washed with water, and dried to give 0.23 g (52%) of colorless crystals with mp 152°C (from ethanol). IR spectrum: 1605, 1580, and 1510 cm^{-1}. PMR spectrum (CF_3COOH, 60 MHz, 20°C): 0.98 (t, CH_3); 2.72 (q, CH_2); 3.03, 3.12 (d, two CH_3); 3.68 (s, two OCH_3); 7.13 (m, 4H); 8.80 ppm (s, $\geq\overset{+}{N}H$) . Found: C 74.3; H 8.1; N 5.3%. $C_{16}H_{21}NO_2$. Calculated: C 74.1; H 8.1; N 5.4%.

2-Formyl-4,5-dimethoxyphenylacetone (VIII). A mixture of 3.05 g (10 mmole) of salt IVa and 7.5 g of a 33% aqueous solution of sodium hydroxide in 15 ml of ethanol was refluxed for 1 h, after which the bulk of the alcohol was removed by distillation, and the residue was diluted to 10 times its original volume with water. The aqueous mixture was extracted twice with ether, and the ether layer was separated and dried. The solvent was removed by distillation to give 1.5 g (79%) of colorless crystals with mp 182°C (from ethanol). IR spectrum: 1715, 1690, 1610, 1580, 1530, and 1275 cm^{-1}. Found: C 64.6; H 6.3%. $C_{12}H_{14}O_4$. Calculated: C 64.8; H 6.4%. Starting salt IVa was regenerated in quantitative yield when a solution of VIII in glacial acetic acid was acidified with 70% $HClO_4$.

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^{13}C NMR SPECTRA AND THREE-DIMENSIONAL STRUCTURES OF ISOMERIC 3,4-SUBSTITUTED THIOPHANS

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UDC 547.732:543.422.25:541.621

The chemical shifts and the direct carbon–proton spin–spin coupling constants for a number of cis and trans isomers of 4-amino-substituted 3-hydroxy(acyloxy)-thiophans, the configurations of the substituents in which and the conformational states were previously established by an independent method, were studied. It was found that in the spectra of the cis isomers the signals of the vicinal ^{13}C atoms, which bear the substituents, are shifted to strong field as compared with the trans isomers ($\Delta\delta^{\text{trans-cis}}$ 1.7-4.3 ppm). Conformational γ effects of the substituents on the chemical shifts of the ring ^{13}C atoms were noted. It is shown that a relationship exists between the direct carbon–proton spin–spin coupling constants and the spatial orientations of the acyloxy and acylamino substituents for five-membered saturated rings.

The problem of the study of the three-dimensional structures of five-membered saturated rings has not been dealt with as thoroughly as the analogous problem in the case of six-membered saturated rings. It is known that, in contrast to six-membered rings, characteristic ranges of cis- and trans-vicinal proton–proton spin–spin coupling constants do not exist for five-membered rings. In a number of cases an examination of the vicinal proton–proton constants for all possible conformations of the five-membered ring within the framework of the angular dependence of these constants is useful in the study of the configuration of five-membered rings [1]. A method for the determination of the orientation of the substituents in five-membered saturated rings by means of temperature dependences

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All-Union Scientific-Research Vitamin Institute, Moscow 117246. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1612-1616, December, 1981. Original article submitted January 22, 1981.

0009-3122/81/1712-1174$07.50