2-BENZOPYRYLIUM SALTS.

24.* SYNTHESIS AND REACTIONS OF 3-(2-METHYLENECARBOXYARYL)-2-BENZOPYRYLIUM SALTS WITH AMINES

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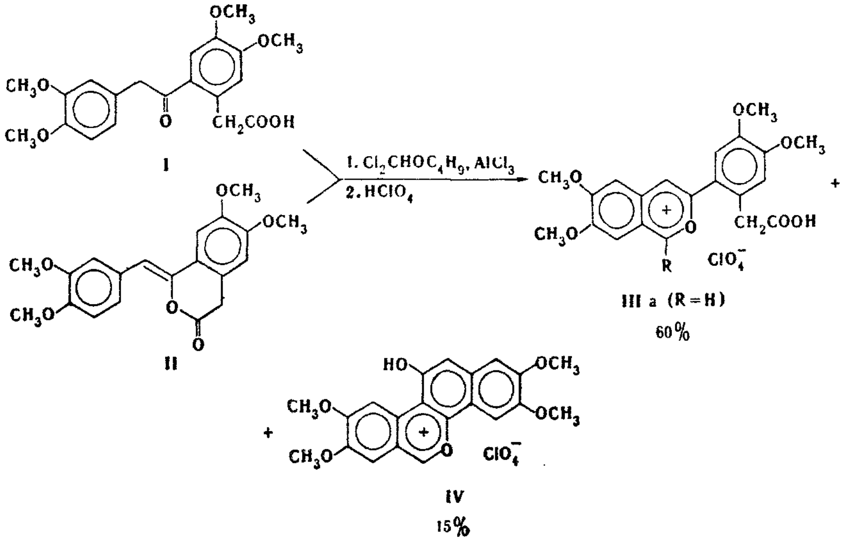
UDC 547.814.07

5-Oxoniachrysene and N-methylisoquinolinium perchlorates and substituted 1-naphthylamines were synthesized on the basis of 1-R-3-(2-methylenecarboxyaryl)-2-benzopyrylium salts.

Continuing our research on the synthesis and study of the properties of 3-(2-methylenecarboxyaryl)-2-benzopyrylium salts, we synthesized 1-unsubstituted salt IIIa in 60% yield by Riehe formylation [2] of keto acid I [3] or isochromenone II [4].



The IR spectrum of salt IIIa is similar to the spectra of the alkyl-substituted salts [1]; its PMR spectrum corresponds to the proposed structure.

Workup of the reaction mixture gave, in addition to salt IIIa, a slightly soluble high-melting salt product in low yield, the IR spectrum of which did not contain carboxy group absorption at 1700 cm^{-1} but did contain a band at 3500 cm^{-1}. Signals of four methoxy groups and six aromatic protons were observed in the PMR spectrum. The structure of a 5-oxoniachrysene salt (IV) with a fixed OH group was assigned to this compound on the basis of the data enumerated above and the results of elementary analysis.

The reaction probably proceeds through the intermediate formation of cyclic vinyl ether Va, the linear representatives of which readily undergo intermolecular electrophilic reaction [5]. The alternative synthesis of the same salt by treatment of a suspension of salt IIIa in refluxing absolute benzene with a 1.5-fold excess of PCl$_5$ (with the formation of the

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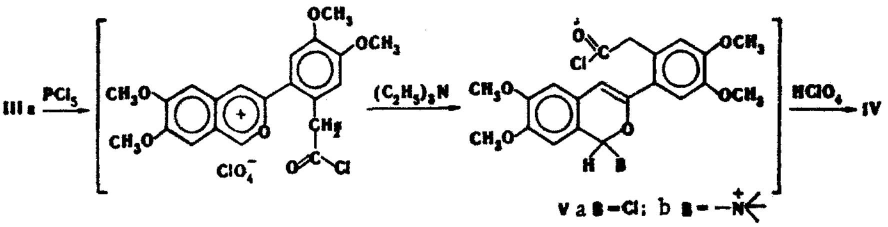
*See [1] for Communication 23.

†Deceased.

Rostov State University. Scientific-Research Institute of Physical and Organic Chemistry, Rostov-on-Don 344006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 313-316, March, 1981. Original article submitted June 17, 1980.

0009-3122/81/1703-0221$07.50 © 1981 Plenum Publishing Corporation

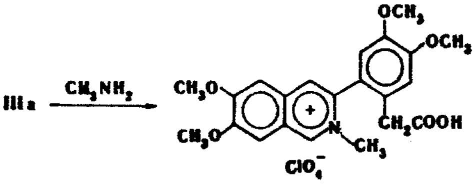
acid chloride) with the subsequent addition of excess Et_3N (with the formation of cyclic vinyl ether Vb) and acidification of the reaction mixture with perchloric acid served as a confirmation of this assumption and simultaneously as additional evidence for the formation of precisely IV.



Thus we demonstrated the possibility of intramolecular electrophilic attack, *in situ* on the vinyl ether obtained from heterocyclic cation IIIa.

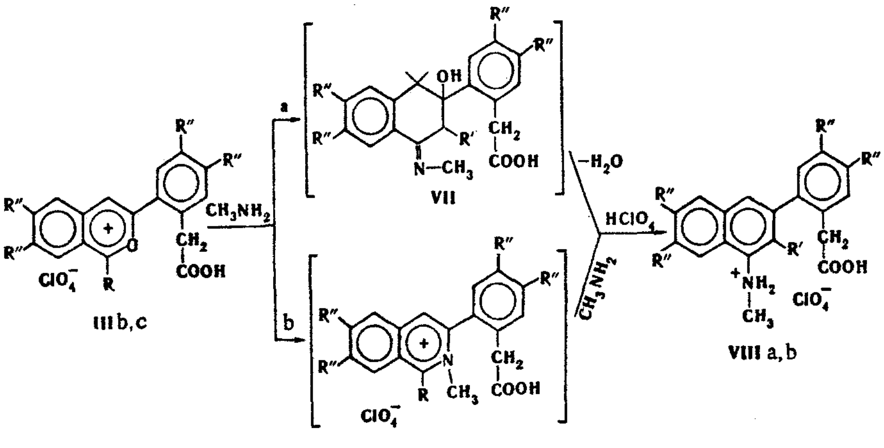
Salt IV has all of the properties of the previously described 5-oxoniachrysene salts [6] — it readily forms products of addition to the C_6 atom with various nucleophiles, which, however, do not undergo conversion to phenanthridine bases of the alkaloid sanguinarine series.

As expected on the basis of [7, 8], 1-unsubstituted 3-(2-methylenecarboxyaryl)-2-benzopyrylium salt IIIa on reaction with both dry methylamine in ethanol and with a solution of methylamine in aqueous alcohol forms the corresponding N-methylisoquinolinium perchlorate VI.



VI

However, when alkyl-substituted salts IIIb,c [1] are subjected to this reaction, naphthylamines VIIIa,b are formed instead of the expected isoquinolinium salts and are isolated from the reaction mixtures in the form of the perchlorates after acidification with perchloric acid. The reaction probably proceeds through the intermediate formation of VII, i.e., the alkyl substituent in the starting molecule participates in the formation of a new ring in the first step (pathway a), although the possibility of the realization of a Kost–Sagitullin rearrangement [9] (pathway b) is not excluded in this case.



IIIb $R=CH_3$; c $R=C_2H_5$; III, VII, VIII $R''=OCH_3$; VIII a $R'=H$; b $R'=CH_3$

An intense band at 1685 cm^{-1} is present in the IR spectrum of naphthylamine perchlorate VIIIa; signals of a methylene group and six aromatic protons and a two-proton signal of a protonated amino group are recorded distinctly in the PMR spectrum. The number of aromatic protons in the PMR spectrum of VIIIa in trifluoroacetic acid and the presence of the signal of a methylene group in the PMR spectrum of the potassium salt of VIIIa in D_2O exclude the possibility of the formation of tetraphene structures of the benzo[c]phenanthrene or benz[a]anthracene type as a consequence of intramolecular cyclization in the free positions of the naphthalene ring. The formation of an alternative eight-membered amide is impossible because of pronounced strain of the bond angles. The certain decrease in the ν_{COOH} stretching vibrations in VIIIa is ascribed to the formation of an intramolecular hydrogen bond between the carboxy and protonated amino groups [10]. This is confirmed by retention of the normal frequency of carboxy group C=O vibrations at 1710 cm^{-1} in the spectrum of the 2-methyl analog of VIIIa, viz., naphthylamine VIIIb, in which the methyl group hinders the formation of hydrogen bonds.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a Specord 71IR spectrometer. The PMR spectra of solutions of the compounds in CF_3COOH were recorded with Tesla spectrometers with operating frequencies of 60 and 80 MHz at 20 and 60°C, respectively, with hexamethyldisiloxane as the internal standard.

3-(2-Methylenecarboxy-3,4-dimethoxyphenyl)-6,7-dimethoxy-2-benzopyrylium Perchlorate (IIIa). A 1.3-g (0.01 mole) sample of anhydrous aluminum chloride and 1.5 g (0.01 mole) of dichloromethyl butyl ether were added with stirring to a cooled (to 10°C) solution of 1.87 g (5 mmole) of o-homoveratroylhomoveratric acid [3] [or 1.8 g (5 mmole) of isochromenone [4]] in dry methylene chloride. After 2 days, the markedly darkened mixture was poured over a mixture of ice and hydrochloric acid, and 57% $HClO_4$ was added. The precipitated salt was removed by filtration, dried, and refluxed for 5-10 min in 100 ml of glacial acetic acid in the presence of a few drops of 70% $HClO_4$. The hot suspension was filtered, and ether was added to the cooled filtrate until crystallization commenced. After a certain time, the precipitate was separated to give 1.4 g (60%) [1.5 g (65%) from isochromenone] of yellow crystals with mp 238°C (from acetic acid). IR spectrum: 3520, 1700, 1600, 1543, 1510, 1080 cm^{-1}. PMR spectrum* (60 MHz, 20°C): 3.60 (s, two CH_3O and CH_2); 3.73, 3.85 (two CH_3O); 6.82-9.45 ppm (m, 6H). Found: C 52.1; H 4.5; Cl 7.5%. $C_{21}H_{21}ClO_{11}$. Calculated: C 52.0; H 4.3; Cl 7.3%.

The reaction product that was insoluble during hot filtration was washed with ether and dried to give 0.37 g (15%) of red crystals of 2,3,8,9-tetramethoxy-11-hydroxy-5-oxoniachrysene perchlorate (IV) with mp 298°C (from nitromethane). IR spectrum: 3500, 1610, 1605, 1480, 1100 cm^{-1}. PMR spectrum* (80 MHz, 60°C): 3.75, 3.58, 3.80, 3.95 (four CH_3O); 6.98-9.38 ppm (m, 6H). Found: C 53.8; H 4.3; Cl 7.9%.. $C_{21}H_{19}ClO_{10}$. Calculated: C 53.9; H 4.1; Cl 6.7%.

Compound IV was also synthesized by the following method. A 0.5-g (2 mmole) sample of PCl_5 was added with stirring to a suspension of 0.5 g (1 mmole) of 3-(2-methylenecarboxy-3,4-dimethoxyphenyl)-6,7-dimethoxy-2-benzopyrylium perchlorate (IIIa) in 10 ml of dry benzene, and the mixture was heated at 50°C for 1 h. It was then cooled and treated with 1.5 ml of triethylamine. After 24 h, the darkened reaction product was removed by filtration, washed thoroughly with water, and dried. The red-brown salt was refluxed in a large volume of acetic acid with several drops of 70% $HClO_4$, after which the boiling suspension was filtered. The salt remaining on the filter was washed with hot acetic acid and ether to give 0.22 g (53%) of a substance that was identical to the substance described above with respect to its IR and PMR spectra and melting point.

N-Methyl-3-(2-methylenecarboxy-3,4-dimethoxyphenyl)-6,7-dimethoxyisoquinolinium Perchlorate (VI) A) A 1-ml sample of a 25% aqueous solution of methylamine was added to a suspension of 0.5 g (1 mmole) of 3-(2-methylenecarboxy-3,4-dimethoxyphenyl)-6,7-dimethoxy-2-benzopyrylium perchlorate in 2 ml of ethanol. After 3 days, the markedly darkened solution was diluted with 10 ml of water and acidified with excess perchloric acid. The precipitate was removed by filtration and dried to give 0.4 g (80%) of colorless crystals with mp 165°C (from ethanol). IR spectrum: 3500, 1720, 1610, 1510, 1080 cm^{-1}. PMR spectrum (60 MHz, 20°C): 3.23 (s, CH_2); 3.54 (s, $N-CH_3$); 3.65, 3.80 (four CH_3O); 6.68-8.95 ppm (m, 6H). Found: C 53.2; H 4.8; Cl 7.3; N 2.9%. $C_{22}H_{24}ClNO_{10}$. Calculated: C 53.1; H 4.8; Cl 7.1; N 2.8%.

B) Methylamine was passed through a suspension of salt IIIa in refluxing ethanol for 30 min, after which the solution was cooled, diluted with water, and acidified with 70%

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*For the chloride, which was obtained by passing HCl through a solution in $CHCl_3$ of the product of treatment of the perchlorate with 5% sodium carbonate solution.

$HClO_4$. Workup gave a product (70%) that was identical to the substance described in method A with respect to its IR spectrum and melting point.

N-Methyl-3-(2-methylenecarboxy-3,4-dimethoxyphenyl)-6,7-dimethoxylnaphthylamine Perchlorate (VIIIa). A) Methylamine was passed through a suspension of 0.5 g (1 mmole) of 1-methyl-3-(2-methylenecarboxy-3,4-dimethoxyphenyl)-6,7-dimethoxy-2-benzopyrylium perchlorate (IIIb) [1] in 5 ml of refluxing ethanol for 30 min, after which the markedly darkened solution was cooled and diluted with water and treated with excess 70% $HClO_4$. The precipitate was removed by filtration to give 0.42 g (90%) of colorless crystals with mp 163°C (from ethanol). IR spectrum: 3500, 1685, 1635, 1610, 1510, 1085 cm^{-} . PMR spectrum (60 MHz, 20°C): 3.10 (s, CH_3); 3.40 (s, CH_2); 3.63, 3.75 (four CH_3O); 6.65-7.55 (m, 6H); 8.60 ppm (broad s, $>\overset{+}{N}H_2$). PMR spectrum (60 MHz, 20°C, in a solution of K_2CO_3 in D_2O*): 2.5 (s, $N{-}CH_3$); 3.16 (two CH_3O and CH_2); 3.56, 3.60 (two CH_3O); 6.9-7.3 ppm (m, 6H). Found: C 55.1; H 5.0; Cl 7.0; N 2.5%. $C_{24}H_{26}ClNO_{10}$. Calculated: C 55.0; H 5.0; Cl 6.8; N 2.7%.

B) A 0.5-ml sample of a 25% aqueous solution of methylamine was added to a suspension of 0.5 g (1 mmole) of 1-methyl-3-(2-methylenecarboxy-3,4-dimethoxyphenyl)6,7-dimethoxy-2-benzopyrylium perchlorate (IIIb) [1] in 3 ml of ethanol. After 24 h, the markedly darkened solution was diluted with water and acidified with excess perchloric acid. Workup gave a product (in quantitative yield) that was completely identical to the product described in method A with respect to its IR spectrum and melting point.

N-Methyl-2-methyl-3-(2-methylenecarboxy-3,4-dimethoxyphenyl)-6,7-dimethoxylnaphthylamine Perchlorate (VIIIb). This compound was in 80% yield obtained as in methods A and B from 1-ethyl-3-(2-methylenecarboxy-3,4-dimethoxyphenyl)-6,7-dimethoxy-2-benzopyrylium perchlorate [1] and had mp 158°C (from ethanol). IR spectrum: 3520, 1720, 1630, 1600, 1520, 1080 cm^{-1}. PMR spectrum (60 MHz, 20°C): 3.12 (s, NCH_3); 3.70 (s, CH_2); 3.65, 3.60 (two CH_3O); 5.52-7.00 ppm (m, 7H). Found: C 54.8; H 5.1; Cl 6.5; N 2.7%. $C_{24}H_{28}ClNO_{10}$. Calculated: C 55.0; H 5.3; Cl 6.7; N 2.7%.

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*The chemical shift of the residual protons of the heavy water (5.2 ppm) was taken as the reference point.