2-BENZOPYRYLIUM SALTS

XXI.* SYNTHESIS AND PROPERTIES OF OXONIACHRYSENE SALTS

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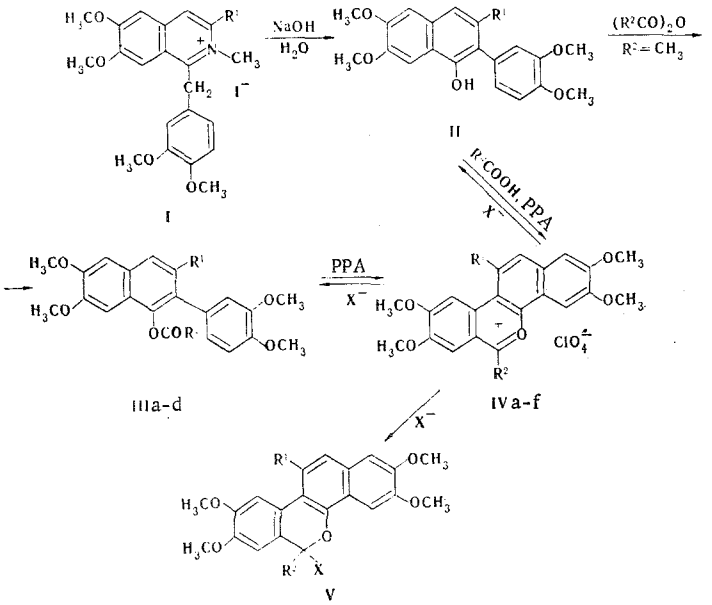
Oxoniachrysene salts, which on reaction with bases form either addition products or undergo anomalous cleavage of the heteroring bond, were obtained from papaverine methiodide.

We have previously reported the synthesis of oxoniachrysene salts from 1-benzyl-substituted 2-benzopyrylium salts [2].

In the present research we expanded the number of polycyclic 2-benzopyrylium salts by accomplishing the synthesis of 6-unsubstituted salts IVa-c,f from papaverine methiodide (I).



I R^1=H; II a R^1=H; b R^2=CH_3; IV a R^1=H, R^2=H; b R^1=H, R^2=CH_3; c R^1=H, R^2=C_6H_5; d R^1=CH_3, R^2=H; e R^1=CH_3, R^2=CH_3; f R^1=H, R^2=$CH_2C_6H_5$; V X=NH_2, $NHCH_3$, $NHNH_2$, OH

The preparation and isolation of salts IVa-c,f were carried out by the methods in [2].† The synthesized oxoniachrysene salts (IVa-f) are oxygen analogs of alkaloids of the sanguinarine group, and we therefore attempted conversion to them by replacement of the oxygen in IVa-f by nitrogen.

In contrast to 2-benzopyrylium salts [3, 4], salts IVa-e react with bases in two ways to give either addition products V or products of anomalous opening of the heteroring (IIIa-d and IIa) (Table 1). Whereas the first property of the oxoniachrysene salts is extremely characteristic for benzopyrylium salts, the second – cleavage of the C_1 – ring bond – has not been previously observed in either the 2-benzopyrylium salt series or the benzo-

* See [1] for communication XX.

† Acylation of naphthol IIa with acetic anhydride in the presence of perchloric acid leads to intensely colored unidentified products.

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TABLE 1. Reactions of Oxoniachrysene Salts with Bases

Compound	Base X	Reaction conditions	Reaction product
IVa, IVd	NH_3	28% aqueous solution, 48 h, 20°C	Va, X=NH_2
IVd			IIId
IVa	NH_4OAc	Refluxing in excess AcOH for 2 H, dilution with water	IIIa
IVd			IIId
IVb			IIa
IVd	NH_3	100°C, 6 h under pressure in ethanol, dilution with water	IIId
IVa	$CH_3NH_2 \cdot HCl$	Refluxing for 2 h in ethanol	IIIa
IVd			IIId
IVb			IIIb
IVe			Does not react
IVc			IIIc
IVa, IVd	CH_3NH_2	100°C, 6 h in ethanol under pressure	Va, X=$NHCH_3$; Vd, X=$NHCH_3$
IVa, IVd, IVe	$NH_2NH_2 \cdot H_2O$	Refluxing with a 1.5-fold excess in alcohol, dilution with water	Va, X=$NHNH_2$; Vd, X=$NHNH_2$; Ve, X=$NHNH_2$
IVb			IIa
IVc			IIa
IVa, IVb, IVc, IVd, IVe	KOH	24 h in excess 50% aqueous solution	Va, X=OH; Vb, X=OH; Vc, X=OH; Vd, X=OH; Ve, X=OH

TABLE 2. Oxoniachrysene Perchlorates (IV)*

Compound	Preparative conditions	Crystal color	Found, % C	Found, % H	Found, % Cl	Empirical formula	Calc., % C	Calc., % H	Calc., % Cl	Yield, %
IVa	20 min at 70°, 30 min at 100°	Light-orange	55,7	4,1	7,9	$C_{21}H_{19}O_9Cl$	55,9	4,2	8,0	72
IVb†	40 min at 80°	Orange	56,7	4,6	7,7	$C_{22}H_{21}O_9Cl$	56,8	4,5	7,7	50
IVc	1 h at 70°	Yellow	61,3	4,4	6,7	$C_{27}H_{23}O_9Cl$	61,5	4,4	6,8	68
IVf	1 h at 60—70°	Red	62,0	4,5	6,7	$C_{28}H_{25}O_9Cl$	62,1	4,6	6,7	53

* The IR spectra of salts IV contain a number of characteristic bands at 1605-1615, 1490-1495, 1260-1280, and 1080-1090 cm^{-1}. All of the compounds obtained (recrystallized from nitromethane) melted above 320°C.

† Salt IVb was also obtained by heating naphthol acetate IIIb in a fivefold excess of polyphosphoric acid at 60°C for 20 min.

pyrylium salt series. It seemed evident that this sort of bond cleavage should proceed through the intermediate formation of addition products V, but we were unable to accomplish this sort of transformation under the conditions of the formation of the latter.

The structures and compositions of the synthesized compounds were confirmed by IR spectroscopic data and the results of elementary analysis; previously described products (IIa) and IIIb) were obtained in some cases. The reaction conditions, the substituents in salts IVa-e, the bases used, and the compounds obtained are indicated in Table 1.

We note that substances that do not contain nigrogen and, according to the IR spectra, are identical to the compounds obtained by treatment of these salts with alkali (Vb,c,e, when X = OH) are formed in the reaction of salts IVb,e with a saturated alcohol solution of ammonia under pressure and in the reaction of salt IVc with excess ammonium hydroxide under standard conditions.

Mixtures of addition products Va,b,e (where X = OH and NH_2 and X = OH and $NHCH_3$, respectively) are evidently formed when salts IVa,b,e are treated with ammonium hydroxide or a saturated alcohol solution of methylamine under pressure.

Thus the methods that are acceptable for replacement of oxygen by nitrogen in 2-benzo- [5] and naphthopyrylium [6] salts are unsuitable for their polycyclic analogs – oxoniachrysene salts. This fact is apparently associated with the higher strength of the C_1-O-C bonds in the heteroring than one might have assumed.

TABLE 3. Dibenzo[c,h]chromenes (V)

Compound	X	mp, °C	IR spectrum, cm^{-1}	Found, %			Empirical formula	Calc., %			Yield, %
				C	H	N		C	H	N	
Va	NH_2	173—175	3450, 1610, 1505	66.6	5.9	3.9	$C_{21}H_{21}NO_5$	66.8	5.6	3.8	75
Vd	$NHCH_3$	162	1605, 1590, 1300	68.7	5.9	3.4	$C_{22}H_{23}NO_5$	69.0	6.0	3.5	55
Va	$NHNH_2$	250 (dec.)	3420 w, 1610, 1570, 1510	68.2	6.0	7.0	$C_{21}H_{22}N_2O_5$	68.4	6.0	7.3	50
Vd	$NHNH_2$	264—266 (dec.)	3250 w, 1610, 1580, 1508	66.5	6.0	6.9	$C_{22}H_{24}N_2O_5$	66.7	6.1	7.0	52
Ve	$NHNH_2$	135—137 (dec.)	3350 w, 1605, 1580, 1505	67.1	6.2	6.5	$C_{23}H_{26}N_2O_5$	67.3	6.3	6.8	54
Va	OH	>320	3450, 1605, 1490	68.2	5.2	—	$C_{21}H_{20}O_6$	68.4	5.4	—	89
Vb	OH	>320	3350, 1600, 1500	69.0	5.6	—	$C_{22}H_{22}O_6$	69.1	5.8	—	92
Vc	OH	170	3270, 1615, 1510	74.5	5.7	—	$C_{27}H_{24}O_6$	74.7	5.5	—	96
Vd	OH	210—213	3460, 1600, 1490	69.0	5.8	—	$C_{22}H_{22}O_6$	69.1	5.7	—	92
Ve	OH	>320	3500, 1605	70.0	5.9	—	$C_{23}H_{24}O_6$	69.7	6.0	—	92

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a Specord 71 IR spectrometer.

2-(3,4-Dimethoxyphenyl)-6,7-dimethoxy-1-naphthol (IIa). A suspension of 4.67 g (0.01 mole) of papaverine methiodide in 200 ml of 14% aqueous NaOH was refluxed for 6 h, after which the markedly darkened solution was cooled and filtered. The filtrate was acidified with hydrochloric acid, and the resulting precipitate was removed by filtration, and dried to give 1.70 g (50%) of colorless crystals with mp 181°C (from ethanol) (mp 180°C [7]). IR spectra: 3400, 1610, 1580, and 1515 cm^{-1}.

2-(3,4-Dimethoxyphenyl)-6,7-dimethoxy-1-naphthol Acetate (IIIb). A solution of 3.40 g (0.01 mole) of naphthol IIa in 30 ml of acetic anhydride was refluxed for 5 h, after which it was cooled and poured into water. The aqueous mixture was neutralized with sodium carbonate, and the resulting oil, which crystallized rapidly, was separated, washed with water, and dried to give 3.14 g (80%) of light-yellow crystals with mp 172°C (from ethanol). Found: C 69.5; H 5.5%. $C_{22}H_{22}O_6$. Calculated: C 69.6; H 5.6%. IR spectrum: 1755, 1605, and 1520 cm^{-1}.

2-(3,4-Dimethoxyphenyl)-6,7-dimethoxy-1-naphthol Benzoate (IIIc). A mixture of 5.37 g (0.01 mole) of 2,3,8,9-tetramethoxy-6-phenyl-5-oxoniachrysene perchlorate (IVc) and 1.36 g (0.02 mole) of $CH_3NH_2 \cdot HCl$ in 15 ml of ethanol was refluxed for 2 h, after which it was cooled, and the resulting precipitate was removed by filtration to give 3.6 g (80%) of colorless needles with mp 192°C (from alcohol). Found: C 70.9; H 5.2%. $C_{27}H_{24}O_9$. Calculated: C 71.1; H 5.3%. IR spectrum: 1735, 1600, and 1510 cm^{-1}.

The following ring-opening products were synthesized in accordance with the conditions indicated in Table 1. 2-(3,4-Dimethoxyphenyl)-6,7-dimethoxy-1-naphthol formate (IIIa), with mp 245°C (from nitromethane), was obtained in 75% yield from salt IVa. Found: C 68.3; H 5.4%. $C_{21}H_{20}O_6$. Calculated: C 68.5; H 5.4%. IR spectrum: 1730, 1595, and 1510 cm^{-1}. 2-(3,4-Dimethoxyphenyl)-3-methyl-6,7-dimethoxy-1-naphthol formate (IIId), with mp 226°C (from nitromethane), was obtained in 70% yield from salt IVd. Found: C 67.9; H 5.5%. $C_{20}H_{18}O_6$. Calculated: C 67.8; H 5.6%. IR spectrum: 1725, 1625, and 1610 cm^{-1}.

The above-described 2-(3,4-dimethoxyphenyl)-6,7-dimethoxy-1-naphthol acetate (IIIb) and 2-(3,4-dimethoxyphenyl)-6,7-dimethoxy-1-naphthol (IIa) were similarly obtained from salt IVb.

2-H-2-Methylamino-7-methyl-4,5,10,11-tetramethoxydibenzo[c,h]chromene (Vd, X= $NHCH_3$). A suspension of 0.5 g (0.001 mole) of 2,3,8,9-tetramethoxy-11-methyl-5-oxoniachrysene perchlorate (IVd) in 7 ml of ethanol in an ampul was cooled to −10°C and saturated with methylamine. The ampul was then sealed and heated at 100°C for 6 h, after which it was cooled, and the bulk of the solvent was removed by distillation at reduced pressure. The resulting precipitate was removed by filtration to give 0.19 g (52%) of light-red

crystals with mp 162°C (from alcohol). Found: C 70.2; H 6.5; N 3.4%. $C_{23}H_{25}NO_5$. Calculated: C 69.9; H 6.3; N 3.5%. IR spectrum: 1600, 1585, and 1260 cm^{-1}.

The remaining addition products, some of the constants of which are indicated in Table 3, were obtained in accordance with the conditions indicated in Table 1.

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CHEMISTRY OF HETEROANALOGS OF ISOFLAVONES

VI.* SYNTHESIS AND PROPERTIES OF PYRIDINE ANALOGS OF ISOFLAVONES

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Condensation of 2-pyridylacetonitrile with polyphenols gave the corresponding α-(2-pyridyl)-acetophenones, which were converted to the pyridine analogs of natural isoflavones and to 3-pyridylchromones with methyl, trifluoromethyl, and ethoxycarbonyl groups in the 2 position. The antimicrobial activity of 3-pyridylchromones and their reaction with alkylating and acylating agents and phosphorus pentasulfide were investigated.

The synthesis and study of the properties of heterocyclic analogs of isoflavones are of great interest in connection with the fact that compounds of this sort may display diverse biological properties [2]. Pyridine analogs of isoflavones that do not contain a hydroxyl group in the benzene ring of the chromone and compounds with a hydroxyl group in the 5 or 7 position have been described in a patent [3]. 3-(3-Pyridyl)chromones affect the adrenal glands and induce a reduction in the secretion of hydrocortisone, and 3-(4-pyridyl)chromones regulate the functions of the hypophysis. 3-(2-Pyridyl)chromones with hydroxyl groups in the 5 or 7 position have not been obtained. This compelled us to synthesize 3-pyridylchromones in which the pyridine ring is bonded to the chromone in the α position. 2-Pyridylacetonitrile, resorcinol, and orcinol served as the starting materials. In contrast to the method in [4], the synthesis of 2-pyridylacetonitrile was carried out in dimethylformamide (DMF) at room temperature. According to the data in [3], the condensation of 3- and 4-pyridylacetonitriles with resorcinol and phloroglucinol was realized in benzene solution in the presence of zinc chloride. This method is extremely laborious, and the yields of the compounds were not indicated. We carried out the condensation of 2-pyridylacetonitrile with the above-indicated phenols in boron trifluoride etherate; this made it

*See [1] for communication V.

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