SYNTHESIS OF SOME 4-CHLOROBENZOPYRYLIUM SALTS AND THEIR REACTIONS

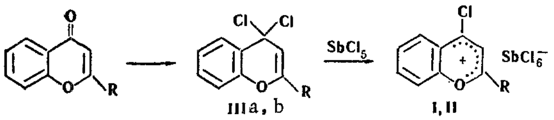
V. A. Zagorevskii, E. K. Orlova,
and I. D. Tsvetkova

UDC 547.814.1.07

4-Chlorobenzopyrylium and 4-chloroflavylium salts have been synthesized, and some reactions of benzopyrylium cations of this type have been studied.

4-Chlorobenzopyrylium salts are little-studied compounds. 2-Alkoxycarbonyl-4-chlorobenzopyrylium hexachloroantimonates have been obtained [1]. It is assumed that the nucleophilic replacement of the halogen in 4,4-dichlorochromenes takes place through the intermediate formation of a 4-chlorobenzopyrylium cation [2].

In the present work we have synthesized 4-chlorobenzopyrylium and 4-chloroflavylium salts in the form of the hexachloroantimonates (I,II) for the first time. The cation of I is the simplest 4-chlorobenzopyrylium cation. The salts I and II were obtained by the reaction of 4,4-dichlorochromene (IIIa) [3] or 4,4-dichloroflavene (IIIb) [4] with antimony pentachloride in neutral solvents. Compound IIIa is obtained more conveniently from chromone by the action not of thionyl chloride [3] but of dichloromethyl methyl ether, which is an effective halogen carrier [5].



I R=H; II R=C$_6$H$_5$

The reactions of I and II with p-nitroaniline lead to 4-p-nitrophenyliminochromene (IV) [3] and 4-p-nitrophenyliminoflavene (V). Similarly, the attack of p-nitroaniline on the cation of 4-chloro-2-methoxycarbonylbenzopyrylium antimonate (VI) is directed to position 4, with the formation of 2-methoxycarbonyl-4-p-nitrophenyliminochromene (VII). Compound VI [1] is decomposed by water to 2-methoxycarbonylchromone (yield 84%). A further similarity in reactivity between 4-chlorobenzopyrylium hexachloroantimonates and the corresponding 4,4-dichlorochromenes was demonstrated on the basis of the reactions of the salts (VI) and 4-chloro-2-ethoxycarbonylbenzopyrylium salts (VIII) [1] with cyanoacetic ester, as a result of which the known [6] 2-methoxycarbonyl- and 2-ethoxycarbonyl-4-(ethoxycarbonylcyanomethylene)-chromenes (IX,X) are formed. It is true that in contrast to the reaction of cyanoacetic ester with the corresponding 2-alkoxycarbonyl-4,4-dichlorochromenes, in the present cases it is impossible to isolate products of the attack of the nucleophilic reagent on position 2 of the chromene system, probably because of their instability, leading to their resinification under the reaction conditions. Compound VI also reacts more smoothly than the initial dichloride [1] with 1-piperidinocyclohexene, forming (after hydrolysis) the known 4-chloro-2-methoxycarbonyl-2-(2-oxocyclohexyl)chromene (XI) [1].

Thus the cations of the 4-chlorobenzopyrylium series may undergo the action of nucleophilic reagents at positions 4 and 2. In order to evaluate the distribution of the π-electron density in the 4-chlorobenzopyrylium cation, we have calculated its molecular diagram by Hückel's MO LCAO method. For comparison

---

Institute of Pharmacology, Academy of Medical Sciences of the USSR, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, Vol. 6, No. 8, pp. 1028-1030, August, 1970. Original article submitted March 25, 1969.

TABLE 1. Values of the π-Electron Densities on the Atoms Given*

Cation	$O_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(8)}$	Cl
Benzopyrylium	1,724	0,795	0,975	0,738	0,949	0,989	0,937	1,004	
4-Chlorobenzopyrylium	1,719	0,755	0,956	0,811	0,952	0,987	0,936	1,003	$Cl_{(4)}$ 1,971
3,4-Dichlorobenzopyrylium	1,718	0,733	1,021	0,792	0,949	0,987	0,933	1,003	$Cl_{(3)}$ 1,984; $Cl_{(4)}$ 1,971

*The parameters recommended by A. Streitwieser [7] were used in the calculation: $h_{\overset{+}{O}}$ 2.5; h_{Cl} 2; $k_{C=\overset{+}{O}}$ 1; k_{C-Cl} 0.4; auxiliary induction parameter 0.1 h_X.

we also give calculations* with the same parameters of the heteroatoms of the unsubstituted benzopyrylium and 3,4-dichlorobenzopyrylium cations (for the reactivity of 3,4,4-trichlorochromene, see [3]).

The calculations show that the carbon atoms with the greatest positive charge are C_2 and C_4, which must obviously also exhibit the greatest electrophilicity. This is in harmony with the experimental results. However, a quantitative evaluation of the relative electrophilicities of the C_2 and C_4 atoms during reaction is difficult, since the primary orientation of the nucleophile must be affected not only by the magnitude of the positive charges of the electrophilic centers but also by the nucleophilicity of the reactant, which (especially the polarizability component) will affect the energy of the transition state in the localization of the nucleophilic particle at the particular electrophilic center.

EXPERIMENTAL

4-Chlorobenzopyrylium Hexachloroantimonate (I). A mixture of 2 g (13.7 mmoles) of chromone and 7 ml of dichloromethyl methyl ether was boiled for 4 hr, the excess of the dichloro ether was driven off in vacuum, and the residue was distilled in vacuum to give 1.76 g (63.5%) of IIIa, bp 110°C (2 mm). To a solution of 0.8 g (4 mmoles) of IIIa in 30 ml of anhydrous benzene was added 1.16 g (3.9 mmoles) of $SbCl_5$, and the mixture was left for 3 hr. The precipitate that had deposited was separated off and washed with anhydrous benzene and absolute ether to give 1.9 g (95%) of the light yellow salt (I), decomp. temperature > 300°C. Found, %: Cl 49.5. Calculated for $C_9H_6Cl_7OSb$, %: Cl 49.6.

4-Chloroflavylium Hexachloroantimonate (II). A mixture of 1.1 g (5 mmoles) of flavone and 10 ml of $SOCl_2$ was boiled for 10 hr, the excess of $SOCl_2$ was driven off in vacuum, the residue of 4,4-dichroflavene was dissolved in 100 ml of anhydrous benzene at the boil, and the solution was filtered and treated with 1.86 g (6.2 mmoles) of $SbCl_5$. The reaction mixture was left for 2 hr and heated to the boil, and the precipitate was filtered off and washed with benzene and ether to give 2.7 g (93.6%) of the yellow-orange salt (II) decomp. temperature ~260°C. Found, %: Cl 42.7. Calculated for $C_{15}H_{10}Cl_7OSb$, %: Cl 43.1.

4-p-Nitrophenyliminochromene (IV). A solution of 0.57 g (4 mmoles) of p-nitroaniline in 15 ml of dichloroethane was added to a suspension of 1.9 g (3.8 mmoles) of I in 100 ml of dry dichloroethane, the mixture was boiled for 12 hr and cooled, a solution of sodium carbonate was added, and the resulting mixture was stirred and rapidly filtered. The organic layer was separated off, washed with water, and evaporated in vacuum, and the residue was triturated with 10 ml of ethanol, after which 0.6 g (59.4%) of IV was filtered off, mp 187-187.5°C (mixed melting point) [3].

4-p-Nitrophenyliminoflavene (V). A solution of 0.64 g (5 mmoles) of p-nitroaniline in 20 ml of dichloroethane was added to a suspension of 2.88 g (5 mmoles) of II in 100 ml of dry dichloroethane at ~40°C, and the mixture was boiled for 2 hr. In a similar manner to IV, 0.95 g (56%) of V was isolated, mp 189-189.5°C. Found, %: C 73.7; H 4.3; N 8.5. Calculated for $C_{21}H_{14}N_2O_3$, %: C 73.7; H 4.1; N 8.2.

2-Methoxycarbonyl-4-p-nitrophenyliminochromene (VII). A solution of 0.57 g (4 mmoles) of p-nitroaniline in 15 ml of dichloroethane was added to a solution of 2.3 g (4 mmoles) of VI in 150 ml of dry dichloroethane, the mixture was left for 16 hr and was then rapidly evaporated in vacuum at 40-50°C, and the

---

*We extend our deep gratitude to V. I. Minkin and V. G. Vinokurov for the quantum-chemical calculations which they performed.

residue was treated with sodium carbonate solution and extracted with benzene. The extract was evaporated in vacuum, the residue was triturated with 15 ml of methanol, and 0.8 g (60%) VII was filtered off, mp 202-203°C (from a mixture of ethanol and benzene). Found, %: C 63.1; H 3.8; N 8.9. Calculated for $C_{17}H_{12}N_2O_5$, %: C 63.0; H 3.7; N 8.6.

4-(Ethoxycarbonylcyanomethylene)-2-methoxycarbonylchromene (IX). 10 ml of cyanoacetic ester was added to 2.4 g (4.3 mmoles) of VI, and the mixture was left for 18 hr. The precipitate that deposited was separated off and washed with a mixture of benzene and petroleum ether (1 : 3) to give 0.5 g (38%) of IX [6] (mixed melting point).

2-Ethoxycarbonyl-4-(ethoxycarbonylcyanomethylene)chromene (X). Similarly, 5.72 g (10 mmoles) of VIII and 10 ml of cyanoacetic ester (the excess of ester was distilled off) gave 1.06 g (33%) of X [6] (mixed melting point).

4-Chloro-2-methoxycarbonyl-2-(2-oxocyclohexyl)chromene (XI). A solution of 16.5 g (200 mmoles) of 1-piperidinocyclohexene was added to a suspension of 11.16 g (20 mmoles) of VI in 100 ml of anhydrous benzene, the mixture was left for two days and filtered, the filtrate was treated with 150 ml of 2N HCl, and after about 18 hr the benzene layer was separated off and the benzene was distilled off in vacuum. The residue was triturated with a small amount of methanol, giving 0.5 g of a mixture of two racemates of XI (according to thin-layer chromatography the low-melting isomer [1] was present in insignificant amounts). The washing solutions yielded another 0.24 g of the mixture of isomers, the total yield being 0.74 g (11.5%). The high melting isomer, mp 168-169°C, identical with that obtained previously (mixed melting point), was isolated by fractional crystallization [1].

LITERATURE CITED

1. E. K. Orlova, I. D. Tsvetkova, V. S. Troitskaya, V. G. Vinokurov, and V. A. Zagorevskii, KhGS [Chemistry of Heterocyclic Compounds], 5, 429 (1969).
2. I. D. Tsvetkova, Investigations of the Reactions of γ, γ-Dichlorobenzopyrans with Some Nucleophilic Reagents [in Russian], Dissertation, Moscow (1967).
3. V. A. Zagorevskii, I. D. Tsvetkova, and E. K. Orlova, KhGS [Chemistry of Heterocyclic Compounds], 3, 786 (1967).
4. V. A. Zagorevskii, I. D. Tsvetkova, and E. K. Orlova, The Synthesis of Natural Compounds and Their Analogs and Fragments [in Russian], p. 142 (1965).
5. H. Gross, Z. Chem., 4, 411 (1964).
6. V. A. Zagorevskii, I. D. Tsvetkova, E. K. Orlova, and S. L. Portnova, KhGS [Chemistry of Heterocyclic Compounds], 5, 422 (1969).
7. A. Streitwieser, Molecular Orbital Theory for Organic Chemists, Wiley (1961).