

SYNTHESIS OF 3-ACYLAMINO- AND 3-CARBETHOXY- 2-BENZOPYRYLIUM SALTS

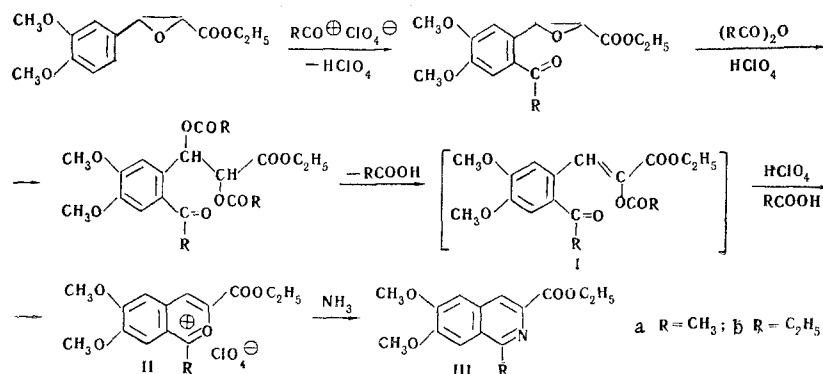
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High yields of 3-acylamino-2-benzopyrylium salts are formed in the acylation of 3,4-dimethoxy- and 3,4-methylenedioxyphenylacetonitrile. The salts are converted to 4-isoquinolones on treatment with ammonia. The acylation of ethyl 3,4-dimethoxyphenylglycidate ester also results in heterocyclization to 3-carbethoxy-2-benzopyrylium salts, which are converted to high yields of the corresponding 3-carbethoxyisoquinolines by treatment with ammonium hydroxide. The mechanisms of these transformations are discussed.

Until now, methods for the preparation of 2-benzopyrylium salts that contain active functional groups (amino, carboxyl, carbonyl, and others) have not been known in the chemistry of pyrylium compounds. 2-Benzopyrylium salts with alkyl and aryl substituents were obtained by the acylation of m-alkoxy-substituted phenylacetones [1], deoxybenzoins [2], arylacetic acid esters [3], or via other previously proposed and more cumbersome schemes [4,5].

In order to synthesize 2-benzopyrylium salts containing 3-carbethoxy and 3-acylamino groups, we acylated m-alkoxyphenylglycidic esters and the corresponding acetonitriles. As was expected, the reaction of ethyl 3,4-dimethoxyphenylglycidate with acetic and propionic anhydrides in the presence of equimolecular amounts of 70% HClO_4 results in acylation of the aromatic ring with simultaneous opening of the oxirane ring and subsequent heterocyclization of the enol acetate (I) formed during the reaction:



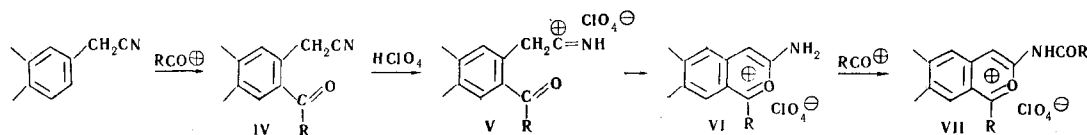
The formation of II occurs at ambient temperature in 10 min, but the yields of 2-benzopyrylium salts are low (17-25%). Increasing the reaction time or heating results in complete resinification of the reaction mixture. The glycidic ester is probably converted to homoveratraldehyde, which polymerizes in acid media [6].

The acylation of 3,4-dimethoxy- and 3,4-methylenedioxyphenylacetonitriles proceeds more readily under similar conditions with the formation of 1-alkyl-3-acylamino-2-benzopyrylium salts in high yields (54-94%). Thus, when equimolecular amounts of 70% HClO_4 are added to a mixture of the nitrile and excess anhydride, the reaction product begins to crystallize in copious amounts after only 15 min. In this

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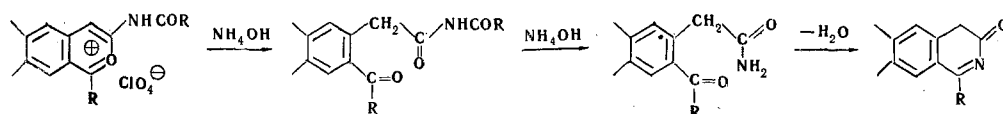
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case, the first step in the reaction also apparently involves acylation of the nitrile in the ortho position relative to the acetonitrile group to form ketones (IV), which add a molecule of HClO_4 and are converted to immonium salts (V) that cyclize to 3-amino-2-benzopyrylium salts (VI). The latter are acylated at the amino group under the reaction conditions to give 3-acylamino-2-benzopyrylium salts (VII) [7].



In the reaction of 1-methyl-3-carbethoxy-6,7-dimethoxy-2-benzopyrylium perchlorate (IIa) with ammonium hydroxide the heterocyclic oxygen atom is very readily and quantitatively replaced by nitrogen to form 1-methyl-3-carbethoxyisoquinoline (IIIa), and hydrolysis of the ester group is not observed. The method described here for the synthesis of isoquinoline bases may be of definite interest for the preparation of several alkaloids (salsolidine, for example).

The reaction of ammonium hydroxide with 1-methyl-3-acetamido-6,7-dimethoxy-2-benzopyrylium perchlorate proceeds anomalously with the formation of 1-methyl-6,7-dimethoxy-3-isoquinolone, previously synthesized from 1-methyl-3,6,7-trimethoxy-2-benzopyrylium perchlorate [8].



EXPERIMENTAL

Ethyl 3,4-Dimethoxyphenylglycidate was obtained by the Darzens condensation of veratraldehyde with ethyl monochloroacetate [9].

1-Methyl-3-carbethoxy-6,7-dimethoxy-2-benzopyrylium Perchlorate (IIa). A total of 0.6 ml (0.005 mole) of 70% HClO_4 was added dropwise to a mixture of 1.26 g (0.005 mole) of ethyl 3,4-dimethoxyphenylglycidate and 3 ml (0.03 mole) of acetic anhydride. After 30 min, the mixture was diluted with 10 ml of ether, and the precipitated resinous product was filtered and washed thoroughly with acetone to give 0.47 g (25%) of red crystals with mp 260°C (from acetic anhydride). IR spectrum: 1731, 1630, 1580, 1560, 1520, and 1100 cm^{-1} . Found %: C 47.5; H 4.6; Cl 9.3. $\text{C}_{15}\text{H}_{17}\text{O}_9\text{Cl}$. Calculated %: C 47.8; H 4.5; Cl 9.4.

1-Ethyl-3-carbethoxy-6,7-dimethoxy-2-benzopyrylium Perchlorate (IIb). This compound [0.33 g (17%)] was obtained as above from a mixture of 1.26 g of ethyl 3,4-dimethoxyphenylglycidate, 3.9 ml (0.03 mole) of propionic anhydride, and 0.6 ml of 70% HClO_4 . The orange-red crystals melted at 263° (from acetic anhydride). IR spectrum: 1728, 1642, 1600, 1580, 1548, 1500, and 1100 cm^{-1} . Found %: C 49.7; H 4.9; Cl 9.9. $\text{C}_{16}\text{H}_{19}\text{O}_9\text{Cl}$. Calculated %: C 49.2; H 4.9; Cl 9.1.

1-Methyl-3-carbethoxy-6,7-dimethoxyisoquinoline (IIIa). A total of 5 ml of 25% ammonium hydroxide was added to 0.38 g (0.001 mole) of IIa. After 30 min, 0.26 g (96%) of yellow crystals of IIIa with mp 185° (from benzene) was separated by filtration. IR spectrum: 1642, 1600, 1546, and 1510 cm^{-1} . Found %: C 65.3; H 6.3. $\text{C}_{15}\text{H}_{17}\text{NO}_4$. Calculated %: C 65.4; H 6.2.

1-Methyl-3-acetamido-6,7-dimethoxy-2-benzopyrylium Perchlorate. A total of 1.5 ml of 70% HClO_4 was added dropwise with stirring to a solution of 1.77 g (0.01 mole) of 3,4-dimethoxyphenylacetonitrile in 10 ml of acetic anhydride in such a way that the temperature did not rise above $50\text{--}60^\circ$. After 15–20 ml, all of the HClO_4 had been added, and copious crystallization of the product commenced. After 24 h, the product was filtered, washed with acetic anhydride and ether, and dried to give 3.4 g (94%) of a substance with mp 210° (from nitromethane). IR spectrum: 1648, 1620, 1550, 1500, and 1100 cm^{-1} . Found %: C 46.7; H 4.6; Cl 9.7. $\text{C}_{14}\text{H}_{16}\text{ClNO}_8$. Calculated %: C 46.5; H 4.4; Cl 9.8.

1-Ethyl-3-propionylamino-6,7-dimethoxy-2-benzopyrylium Perchlorate. This compound [0.42 g (54%)] was obtained in the same way from 0.35 g (0.002 mole) of 3,4-dimethoxyphenylacetonitrile, 2 ml of propionic anhydride, and 0.3 ml of 70% HClO_4 . After 30 min, 0.42 g (54%) of the perchlorate with mp $187\text{--}189^\circ$ (from nitromethane) was filtered. IR spectrum: 1630, 1608, 1540, and 1500 cm^{-1} . Found %: C 48.7; H 5.2; Cl 9.2. $\text{C}_{16}\text{H}_{20}\text{ClNO}_8$. Calculated %: C 49.3; H 5.1; Cl 9.1.

1-Methyl-3-acetamido-6,7-methylenedioxy-2-benzopyrylium Perchlorate. This compound [0.74 g (53%)] was obtained via the above method from 0.64 g (0.004 mole) of 3,4-methylenedioxyphenylacetonitrile, 2 ml of acetic anhydride, and 0.4 ml of 70% HClO_4 . The product was reprecipitated from nitromethane by the addition of ether and recrystallized from glacial acetic acid to give yellow crystals with mp 209°. IR spectrum: 1650, 1610, 1600, 1540, 1500, and 1100 cm^{-1} . Found %: C 45.0; H 3.6; Cl 10.2. $\text{C}_{13}\text{H}_{12}\text{ClNO}_8$. Calculated %: C 45.2; H 3.5; Cl 10.3.

1-Ethyl-3-propionylamino-6,7-methylenedioxy-2-benzopyrylium Perchlorate. This compound [0.5 g (34%)] was obtained from 0.64 g (0.004 mole) of 3,4-methylenedioxyphenylacetonitrile, 2.6 ml of propionic anhydride, and 0.4 ml of 70% HClO_4 by heating the mixture at 80° for 12 min. The yellow crystals melted at 183° (from acetic anhydride). IR spectrum: 1660, 1640, 1614, 1580, 1540, and 1490 cm^{-1} . Found %: C 47.6; H 4.0; Cl 9.8. $\text{C}_{15}\text{H}_{16}\text{ClNO}_8$. Calculated %: C 48.2; H 4.3; Cl 9.5.

1-Methyl-6,7-dimethoxy-3-isoquinolone. A total of 3-5 ml of 25% ammonium hydroxide was added gradually to 0.36 g (0.001 mole) of 1-methyl-3-acetamido-6,7-dimethoxy-2-benzopyrylium perchlorate. Warming of the reaction mixture was observed. After 30 min, 0.17 g (75%) of the isoquinolone was filtered to give white crystals with mp 185° (from ethanol). This product did not depress the melting point of the sample obtained in [3], and their IR spectra were identical. IR spectrum: 1634, 1598, 1560, and 1490 cm^{-1} . Found %: C 65.4; H 6.2; N 6.0. $\text{C}_{12}\text{H}_{13}\text{NO}_3$. Calculated %: C 65.8; H 5.9; N 6.4.

1-Methyl-6,7-dimethoxy-3-isoquinolone Hydrochloride. A total of 3 ml of 10% HCl was added to 0.44 g (0.002 mole) of 1-methyl-6,7-dimethoxy-3-isoquinolone. After 10 min, the precipitate was filtered and recrystallized from water to give 0.52 g (96%) of hydrochloride with mp 235° (from water). Found %: C 51.9; H 6.1; Cl 12.3. $\text{C}_{12}\text{H}_{13}\text{NO}_3 \cdot \text{HCl} \cdot \text{H}_2\text{O}$. Calculated %: C 52.6; H 6.0; Cl 13.0.

LITERATURE CITED

1. G. N. Dorofeenko, L. V. Dulenko, V. I. Dulenko, and S. V. Krivun, *Zh. Organ. Khim.*, **1**, 1171 (1965).
2. G. N. Dorofeenko, E. V. Kuznetsov, and S. V. Krivun, *Zh. Organ. Khim.*, **2**, 1499 (1966).
3. G. N. Dorofeenko, V. G. Korobkova, and S. V. Krivun, USSR Author's Certificate No. 207,921 (1967); *Byull. Izobr.*, No. 3 (1967).
4. A. Muller and A. Horvath, *Ber.*, **75**, 891 (1942).
5. M. Vajda, *Acta Chim. Hung.*, **40**, 295 (1964).
6. West German Patent No. 937,589 (1956); *Chem. Abstr.*, **53**, 3250g (1959).
7. G. N. Dorofeenko, E. I. Sadekova, S. V. Krivun, S. N. Baranov, and V. I. Dulenko, USSR Author's Certificate No. 269,436 (1968); *Byull. Izobr.*, No. 14 (1970).
8. G. N. Dorofeenko, V. G. Korobkova, and S. V. Krivun, *Khim. Geterotsikl. Soedin.*, No. 2, 200 (1970).
9. M. S. Newman and B.G. Majorlein, *Organic Reactions*, Vol. 5 [Russian translation], IL, Moscow (1951), p. 319.