Chemistry of Heterocyclic Compounds, Vol. 31, No. 3, 1995

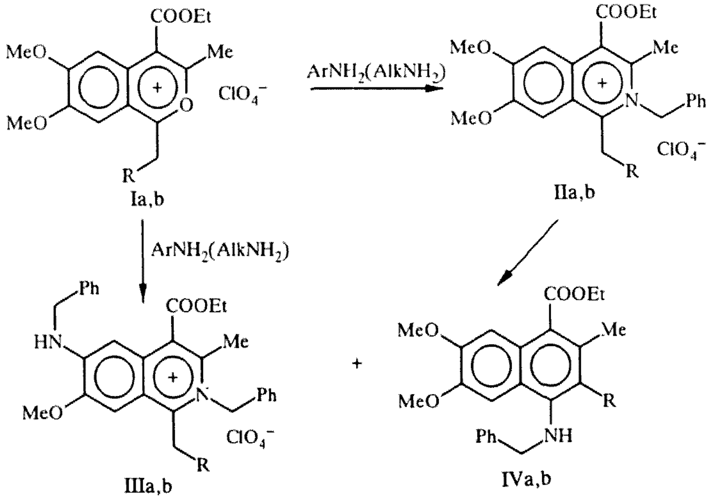
FUNCTIONALLY SUBSTITUTED BENZO[c]PYRILIUM SALTS. REACTIONS OF 4-CARBETHOXYBENZO[c]PYRILIUM SALTS WITH BENZYLAMINE

**S. L. Bogza, Yu. A. Nikolyukin, M. Yu. Zubritskii,
and V. I. Dulenko**

It was shown that benzo[c]pyrilium salts containing an acceptor group at position 4 react with benzylamine to form intermediate N-benzylisoquinolinium salts which then undergo conversion to 2-benzyl-6-benzylaminoisoquinolinium cations and napthylamines.

At this time the known types of interaction of benzo[c]pyrilium cations with primary amines and with compounds containing an NH group can result in three kinds of reaction, of which the most fully studied is the conversion of benzo[c]pyrilium salts to N-substituted isoquinolinium salts [1]. The recyclization of benzo[c]pyrilium cations to 1-naphthylamines is also known [2, 3] being more characteristic of secondary amines [1]. A third reaction type was shown by us [4] in the reaction of substituted benzo[c]pyrilium salts with hydrazine. It was shown that reaction of 1,3-dimethyl-4-cyano-6,7-dimethoxybenzo[c]pyrilium perchlorate with excess hydrazine occurs with recyclization of the oxonium cation according to the ANRORC scheme [5] accompanied by substitution of the 6-methoxy group by the remaining hydrazine to give a 1,3-dimethyl-2-amino-4-cyano-6-hydrazino-7-methoxyisoquinoline salt as the overall product.

Continuing our study of benzo[c]pyrilium cations substituted at position 4, we have shown [6] that the reaction of 4-carbethoxybenzo[c]pyrilium salts Ia, b with an excess of primary amine can occur to give both N-substituted isoquinolinium salts and 1-naphthylamines depending on the basicity of the amine. Both recyclization routes are characterized by their selectivity and by high yields.



I–IV a R = H, b R = Me

Institute for Physico-Organic Chemistry and Carbon Chemistry, National Academy of Sciences of Ukraine, Donetsk 340114. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 317-321, March, 1995. Original article submitted February 20, 1995.

TABLE 1. Parameters for Compounds II-IV, VII, VIII

Compound	Empirical formula	Mp, °C	Yield, %
IIa	$C_{23}H_{26}ClNO_8$	233...235 (decomp.)	77
IIb	$C_{24}H_{28}ClNO_8$	227...229 (decomp.)	69
IIIa	$C_{29}H_{31}ClN_2O_7$	254...256 (decomp.)	41
IIIb	$C_{30}H_{33}ClN_2O_7$	245...247 (decomp.)	43
IVa	$C_{23}H_{25}NO_4$	113...115	80
IVb	$C_{24}H_{27}NO_4$	106...108	77
VII	$C_{21}H_{21}ClN_2O_6$	220...222 (decomp.)	80
VIII	$C_{27}H_{26}ClN_3O_5$	237...238 (decomp.)	74

TABLE 2. Spectroscopic Data for II-IV, VII, VIII

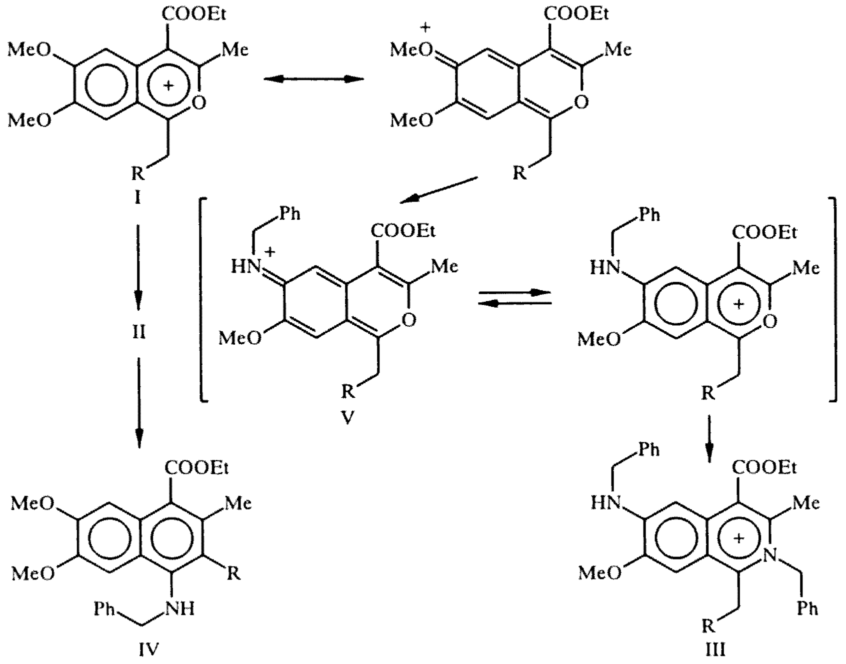
Compound	IR spectrum, ν, cm^{-1}	^1H NMR spectrum, δ, ppm
IIa	1745, 1620, 1100	1,50 (3H, t, CH_3), 2,80 (3H, s, CH_3), 3, 23 (3H, s, CH_3), 4,16 (6H, s, 2 OCH_3), 4,80 (2H, q, CH_2), 6,05 (2H, s, CH_2), 7,10 (1H, s, H arom), 7,13...7,50 (5H, m, H arom), 7,83 (1H, s, H arom)
IIb	1750, 1625, 1100	1,43 (3H, t, CH_3), 1,57 (3H, t, CH_3), 2,97 (3H, s, CH_3), 3,23 (2H, q, CH_2), 4,23 (6H, s, 2 OCH_3), 4,70 (2H, q, CH_2), 5,97 (2H, s, CH_2), 6,87...7,40 (6H, t, H arom), 7,73 (1H, s, H arom)
IIIa	3350, 1745, 1625, 1100	1,21 (3H, t, CH_3), 2,53 (3H, s, CH_3), 3,07 (3H, s, CH_3), 3,50 (2H, s, CH_2), 4,10 (3H, s, OCH_3), 4,39 (2H, q, CH_2), 5,97 (2H, s, CH_2), 7,20...7,43 (11H, m, H arom), 7,83 (1H, s, H arom)
IIIb	3300, 1740, 1625, 1090	1,37 (3H, t, CH_3), 1,50 (3H, t, CH_3), 2,70 (3H, s, CH_3), 3,53 (2H, s, CH_2), 4,17 (3H, s, OCH_3), 4,57 (2H, q, CH_2), 4,77 (2H, q, CH_2), 5,90 (2H, s, CH_2), 6,90...7,43 (11H, m, H arom), 7,70 (1H, s, H arom)
IVa	3415, 1700	1,37 (3H, t, CH_3), 2,30 (3H, s, CH_3), 3,82 (3H, s, OCH_3), 3,90 (3H, s, OCH_3), 4,35 (2H, q, CH_2), 4,52 (2H, s, CH_2), 6,25 (1H, s, NH), 7,12...7,37 (7H, m, H arom), 7,70 (1H, s, H arom)
IVb	3410, 1700	1,53 (3H, t, CH_3), 2,13 (3H, s, CH_3), 2,33 (3H, s, CH), 3,93 (3H, s, OCH_3), 4,00 (3H, s, OCH_3), 4,70 (2H, q, CH_2), 4,90 (2H, s, CH_2), 6,31 (1H, s, NH), 7,10...7,40 (7H, m, H arom)
VII	2225, 1620, 1100	3,10 (3H, s, CH_3), 3,27 (3H, s, CH_3), 4,20 (3H, s, OCH_3), 4,30 (3H, s, OCH_3), 6,03 (3H, s, CH_2), 7,10...7,56 (5H, m, H arom), 7,66 (1H, s, H arom), 7,83 (1H, s, H arom)
VIII	3320, 2230, 1605, 1100	2,83 (3H, s, CH_3), 2,95 (3H, s, CH_3), 3,97 (6H, s, 2 OCH_3), 4,55 (2H, s, CH_2), 5,63 (2H, s, CH_2), 6,60 (1H, s, H arom), 6,77...7,27 (11H, m, H arom)

In this publication we present an investigation of the reactions of 4-carbethoxybenzo[c]pyrilium salts Ia, b with benzylamine, the basicity of which lies between those of aromatic and aliphatic amines. We have found that the recyclization of benzo[c]pyrilium salts Ia, b can occur by all three routes according to the reaction conditions. Treatment of perchlorates Ia, b with an equimolar amount of benzylamine in the cold readily, and in high yields, gives the corresponding 2-benzylisoquinolinium salts IIa, b.

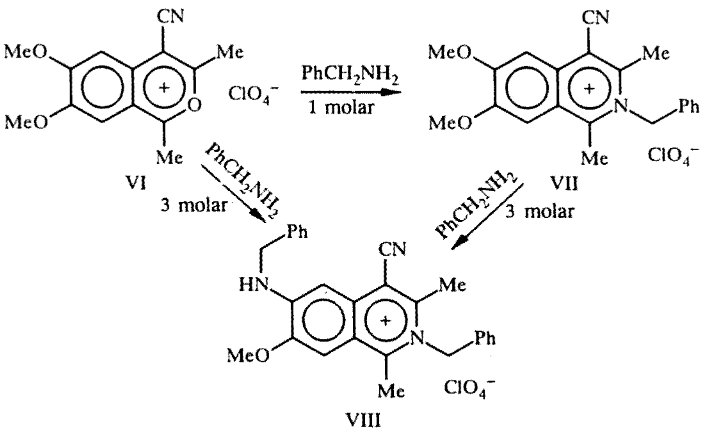
Heating salts Ia, b with an excess of benzylamine gives two compounds, the 2-benzylaminoisoquinolinium perchlorates IIIa, b and also the N-benzyl-1-(4-carbethoxy)-naphthylamines IVa, b. Compounds III and IV were formed in virtually the same amounts with an overall product yield of about 80%. The spectro-analytical data for perchlorates II and III and naphthylamines IV agree with the proposed structures and are given in Tables 1 and 2. The recyclization reaction to 1-naphthylamines [7, 8] and substitution of the 6-alkoxy group [9, 10] are well known for N-substituted isoquinolinium cations. Hence it was logical to propose that one reaction of salts Ia, b with excess benzylamine would involve the formation of an N-benzylisoquinolinium cation intermediate.

We found that heating salts IIa, b with benzylamine gives only the naphthylamines IVa, b in 77% and 80% yields respectively. Hence the isoquinolinium cations II are intermediates in the process of forming IV and the occurrence of 2-benzyl-6-benzylaminoisoquinolinium salts of type III is due to another mode of reaction of type I cations with benzylamine. It seems likely that the presence of the ester substituent at position 4 in the benzo[c]pyrilium cation evens out the reactivity of atoms

C_1 and C_6 and, with excess reagent, leads to an equal probability of addition of the amine molecule at positions 1 and 6 of the pyrilium cation in the first stage of the reaction. In this case the two intermediates formed in the reaction mixture are the isoquinolinium cation II and 6-benzylaminobenzo[c]pyran V. Cation II undergoes a Kost-Sagitullin type recyclization [7] and compound V an ANRORC transformation of the pyran ring.



The equal yields of the final reaction products also support this scheme. In our opinion it is significant that the occurrence of two routes for the reaction is found only in the recyclization of 4-carbethoxybenzo[c]pyrilium perchlorates which is a direct result of the specificity of the substrate and reagent. It should also be noted that the nature of the reaction depends on the type of acceptor at the 4 position of the pyrilium cation and this is well illustrated by the reaction of 1,3-dimethyl-4-cyano-benzo[c]pyrilium perchlorate VI with benzylamine. Here, the N-benzyl-4-cyanoisoquinolinium cation VII is an intermediate to the 2-benzyl-4-cyano-6-benzylaminoisoquinolinium salt VIII. Naphthylamine derivatives are not found in the reaction mixture.



The experimental data in this publication and the results of our previous investigations lead us to conclude that the reaction of benzo[c]pyrilium salts containing an acceptor substituent at position 4 with primary amines and with hydrazine generally occur via intermediate N-substituted isoquinolinium cations. The final reaction products arise through further reaction of the latter.

EXPERIMENTAL

IR spectra were recorded in vaseline oil on a UR-20 instrument and ^1H NMR spectra on a Tesla BS-467 instrument (60 MHz) with TMS internal standard. The spectra of naphthylamines IVa, b were taken in deuterochloroform and the remainder in trifluoroacetic acid. Parameters and spectral data for the synthesized compounds are given in Tables 1 and 2.

Elemental analytical data for C, H, Cl, and N agreed with those calculated.

2-Benzyl-7,8-dimethoxyisoquinolinium perchlorates II, VII. Perchlorates Ia, b or VI (5.5 mmole) were added to a solution of the primary (5 mmole) in 2-propanol (10 ml) and the product stirred for several hours at room temperature. The reaction mixture was diluted with ether, the isoquinolinium perchlorate filtered off, washed with ether, and dried.

1-Alkyl-2-benzyl-3-methyl-4-carbethoxy-6-benzylamino-7-methoxyisoquinolinium perchlorates (III) and **N-benzyl-2-R-3-methyl-4-carbethoxy-6,7-dimethoxy-1-naphthylamines (IV)**. Perchlorates Ia, b (5 mmoles) were added to a solution of benzylamine (25 mmole) in ethanol (50 ml) and refluxed for 6-7 h. The product was poured into ether (100 ml) and perchlorate III filtered off and washed with ether. The filtrate was washed with water (25 ml), dried with magnesium sulfate, and evaporated to give naphthylamine IV which was recrystallized from 2-propanol.

IV and 1,3-Dimethyl-2-benzyl-4-cyano-6-benzylamino-7-methoxyisoquinolinium perchlorate (VIII) were also obtained from the isoquinolinium perchlorates IIa, b and VII using the same method.

REFERENCES

1. E. V. Kuznetsov, I. V. Shcherbakova, and A. T. Balaban, Adv. Heterocyclic. Chem., **50**, 158 (1988).
2. E. V. Kuznetsov and G. N. Dorofeenko, Khim. Geterotsikl. Soedin., No. 10, 1437 (1971).
3. I. V. Shcherbakova, G. N. Dorofeenko, and E. V. Kuznetsov, Khim. Geterotsikl. Soedin., No. 3, 313 (1981).
4. S. L. Bogza and Yu. A. Nikolyukin, Khim. Geterotsikl. Soedin., No. 11, 1475 (1993).
5. H. C. van der Plas, Acc. Chem. Res., **11**, 462 (1978).
6. S. L. Bogza, M. Yu. Zubritskii, and V. I. Dulenko, Khim. Geterotsikl. Soedin., No. 9, 1222 (1994).
7. V. I. Terenin, L. G. Yudin, R. S. Sagitullin, V. N. Torocheshnikov, V. I. Dulenko, Yu. A. Nikolyukin, and A. N. Kost, Khim. Geterotsikl. Soedin., No. 1, 73 (1983).
8. R. S. Sagitullin, Tetrahedron, **39**, 1207 (1983).
9. D. Beaumont and R. Waigh, Chem. and Ind., No. 7, 291 (1980).
10. S. Naruto, H. Mizuta, J. Nakano, and H. Nichimura, Tetrahedron Lett., No. 19, 1595 (1976).