CHEMISTRY OF HETEROCYCLIC QUINONIMINES.

10.* TRANSFORMATION OF BENZO[c]PHENOXAZINE RING INTO BENZO[c]PHENAZONE BY AROMATIC AMINES

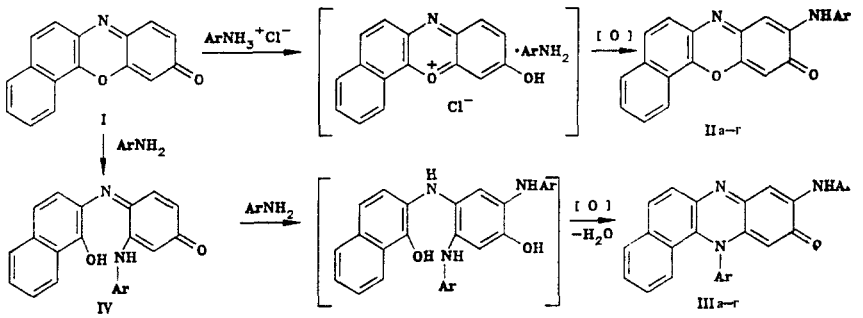
V. I. Vysokov, G. B. Afanas'eva
O. N. Chupakhin, and Ya. V. Dobrygina

UDC 547.867.7'865'551.1.07

Transformation of benzo[c]phenoxazin-3-one by free arylamines into 2-arylamino-5-arylbenzo[c]phenazin-3-ones is observed. The same reaction with protonation of substrate leads to selective formation of 2-arylaminobenzo[c]phenoxazin-3-ones.

It was shown [2-5] that several concurrent processes can occur during reaction of phenoxazinones with nucleophiles. Under mild conditions 1,4-addition to the quinonimine fragment dominates and the activated aromatic nucleophilic substitution of hydrogen in the position para to the bridging nitrogen atom is also reported and especially characteristic for benzo[a]phenoxazin-9-one [2]. With strong anionic nucleophiles (alcoholates, bases) the subsequent destruction of the oxazine ring occurs so that in a number of cases it is used for structure determination of phenoxazinone derivatives [3]. Under drastic conditions 1,2-addition of aromatic amines to the exocyclic carbonyl group with formation of the corresponding phenoxazimes [4] capable of transformation into the corresponding phenazimes is reported [5]. The ratio of the indicated reaction paths with nucleophiles can be specified as a feature of the nucleophile (position in the HSAB scale, basicity, steric factors) or the substrate (position of benzoannelation). The method of activation of the reagents, polarity of the solvent, etc., can also have a significant effect. The correct choice of conditions allows a high selectivity to be reached for the reaction.

In this work the reactions of benzo[c]phenoxazin-3-one with aromatic amines are examined.



II, IIIa Ar = C_6H_5; б Ar = C_6H_4—Cl-*p*; в Ar = C_6H_4—OCH_3-*p*; г Ar = C_6H_4—CH_3-*p*

Reaction with aniline, p-toluidine, p-anisidine, and p-chloroaniline proceed in polar solvents and the reaction path changes with activation of the substrate. Proton activation is achieved by introduction into the reaction mixture of mineral acid or running the reaction in the presence of the hydrochloride of the corresponding amine. Refluxing the substrate with hydrochlorides of amines in ethanol gives 2-arylaminobenzo[c]phenoxazin-3-ones IIa-d as the single reaction products. The reaction proceeds at a small rate which surely is explained by the low concentration of reacting particles, the protonated form of the substrate, and the free amine in solution.

The free amines cause complete conversion of the benzo[c]phenoxazin-3-one under these conditions during 20-30 min. The formation of 2-arylamino-5-arylbenzo[c]phenazine-3-ones IIIa-d and an insignificant impurity of compound II indicate the inversion of regioorientation

Ural Polytechnic Institute, Sverdlovsk 620002. Translated from Khimiya Geterotsiklicheskikh Soedinenií, No. 12, pp. 1679-1681, December, 1988. Original article submitted April 3, 1987.

 0009-3122/88/2412-1388$12.50

TABLE 1. Characteristics of Compounds II and III

Compound	Ar	T_{mp}, °C	λ_{max}, nm (lg ε)	Found, %			Empirical formula	Calculated, %			Yield %
				C	H	N		C	H	N	
IIa	C_6H_5	244...246	498 (4,51)	78,2	4,2	7,9	$C_{22}H_{14}N_2O_2$	78,1	4,2	8,3	18
IIb	C_6H_4—Cl-*p*	292...294	504 (4,48)	67,3	3,6	7,7	$C_{22}H_{13}N_2O_2Cl \cdot H_2O$	67,6	3,8	7,2	20
IIc	C_6H_4—OCH_3-*p*	271...272	500 (4,50)	74,8	4,4	7,9	$C_{23}H_{16}N_2O_3$	75,0	4,4	7,6	15
IId	C_6H_4—CH_3-*p*	290...292	503 (4,46)	78,0	4,5	8,0	$C_{23}H_{16}N_2O_2$	78,4	4,6	7,9	22
IIIa	C_6H_5	348...350	500 (4,46)	81,2	4,3	10,4	$C_{28}H_{19}N_3O$	81,4	4,6	10,2	66
IIIb	C_6H_4—Cl-*p*	335...337	507 (4,46)	69,3	3,5	8,7	$C_{28}H_{17}N_3OCl_2$	69,7	3,5	8,7	58
IIIc	C_6H_4—OCH_3-*p*	278...280	505 (4,46)	76,1	5,1	9,0	$C_{30}H_{23}N_3O_3$	76,1	4,9	8,9	68
IIId	C_6H_4—CH_3-*p*	300...302	506 (4,47)	81,6	5,2	9,5	$C_{30}H_{23}N_3O$	81,6	5,2	9,5	72

by the nucleophilic attack in the absence of substrate activation. It was confirmed experimentally that compound III is not formed under the reaction conditions from 2-arylaminobenzo[c]phenoxazin-3-ones II.

The attack of phenoxazinone I by free arylamine occurs primarily as a process of opening the oxazine ring forming a reactive noncyclic monoarylaminoquinonimine IV [5, 6], undergoing a secondary monoarylamination with subsequent condensation into 2-arylamino-5-arylbenzo[c]phenazin-3-ones. The alternative addition of arylamines to the exocyclic carbonyl group does not occur since it usually requires more drastic conditions [4].

The IR spectra of compounds II and III have characteristic absorption bands for the qunionimine fragment at 1640 and 1620 cm^{-1} and bands for the NH group at 3290 and 3260 cm^{-1}, respectively.

The NMR spectra of compounds II in the characteristic region are slightly subjected to the effect of the arylamine substituent and contain a singlet for the proton of the NH group at 1.52 ± 0.02 ppm and two singlets for protons 4-H and 1-H at 6.72 ± 0.02 and 7.20 ± 0.02 ppm, respectively. Besides this, signals for the protons of the substituent and multiplets for the aromatic protons of the substrate at 7.0-8.6 ppm are present. The absence of a signal for proton 2-H unambiguously indicates the introduction of the arylamine group at the 2-position of the molecule.

In the NMR spectra of the 2-arylamino-5-arylbenzo[c]phenazin-3-ones III, signals for the NH proton at 1.60 ± 0.02 ppm, a singlet from two (integrated intensity 2H) protons 1-H and 4-H at 5.95 ± 0.05 ppm, signals for aryl protons of two nonequivalent substituents, and a multiplet for protons of the aromatic fragment of the substrate at 6.9-8.0 ppm confirm the proposed structure. Besides this, compound IIIa is identical to 2-anilino-5-phenylbenzo[c]-phenazin-3-one obtained by an independent route [6].

Thus, in this work, the transformation of phenoxazinones into the corresponding substituted phenazinone not accompanied by 1,2-addition of arylamine to the C=O group is first noted. Activation of the substrate has great significance during reaction of benzo[c]phenoxazin-3-one with arylamines. The selective formation of 2-arylamino derivatives II in reactions with hydrochlorides of amines indicates the strong electrophilic activation of the 2-position in protonated benzo[c]phenoxazin-3-one.

EXPERIMENTAL

IR spectra were recorded on a UR-20 instrument in mineral oil. Electronic spectra (in ethanol) were obtained on a Specord UV-Vis instrument. NMR spectra were recorded on a Bruker WP-80 (80.13 MHz) instrument in deuterochloroform with TMS internal standard.

Benzo[c]phenoxazin-3-one was obtained from α-naphthol and p-nitrosophenol according to [2].

2-Arylaminobenzo[c]phenoxazin-3-ones (IIa-d). To a boiling solution of 0.5 g (~2 mmole) of benzo[c]phenoxazin-3-one in 50 ml of ethanol were added a 5-6-fold excess of the hydrochloride of the corresponding arylamine. The reaction was monitored by TLC in which the formation of the red compound was fixed with an R_f value larger than the starting compound. Even two days were not sufficient for complete consumption of the substrate. A 16 h reaction was optimal for the process, after which the ethanol was evaporated, the residue was dissolved in 50 ml chloroform and chromatographed on a silica gel (40-100 μm) column using chloroform as eluent. The first, red fraction containing compound II was collected; the second, dark red fraction contains unreacted benzo[c]phenoxazin-3-one which is used again. Yields and data on the physicochemical properties of the compounds are given in Table 1.

2-Arylamino-5-arylbenzo[c]phenoxin-3-ones (IIIa-d). Into a boiling solution of 0.5 g (~2 mmole) of compound is added a 2-3-fold excess of the corresponding arylamine. Complete consumption of the substrate is achieved after 30 min, after which the excess amine is steam distilled. The dried residue is dissolved in 50 ml chloroform and chromatographed on silica gel (40-100 μm) using chloroform as eluent. The first, red fraction contains an insignificant quantity of compound II; compound III, dark crystals with a metallic luster, is obtained from the second, bright crimson fraction after evaporation of eluent. Characteristics of the products III are given in Table 1. Compounds II and III are crystallized from a 1:1 mixture of acetone–chloroform.

LITERATURE CITED

1. V. I. Vysokov, G. B. Afanas'eva, and O. N. Chupakhin, Khim. Geterotsikl. Soed., No. 4, 538 (1988).
2. G. B. Afanas'eva, K. I. Pashkevich, I. Ya. Postovskiĭ, V. G. Vykhristyuk, N. P. Shimanskaya, and V. D. Bezuglyĭ, Khim. Geterotsikl. Soed., No. 10, 1345 (1972).
3. K. M. Kotoucek, I. Tomasova, and S. Durchacova, Coll. Chem. Commun., 34, 212 (1969).
4. G. B. Afanas'eva and I. Ya. Postovskii, Khim. Geterotsikl. Soed., No. 2, 167 (1969).
5. U. Fiedeldei and H. Baumgartel, Chem. Ber., 118, 397 (1984).
6. I. Tsoĭ, Dissertation, Sverdlovsk (1985).

HEXAHYDROBENZOTHIAZOLO[3,2-a]PYRIDINIUM SALTS

A. M. Shestopalov, V. N. Nesterov, Yu. A. Sharanin, V. P. Litvinov, V. E. Shklover, Yu. T. Struchkov, and V. K. Promonenkov

UDC 547.821.3'789.6.04:548.737:543.422.25:541.634

Salts of hexahydrobenzothiazolo[3,2-a]pyridine are obtained by exchange reactions. Anions are placed in the order $[(NC)_2CCHC(CN)_2]^-$ > ClO_4^- > I_3^- > Br^- according to the ability to displace each other. X-ray structural and spectroscopic studies establish the cis-attachment of the thiazolidine and cyclohexane rings in the hexahydrobenzothiazolo[3,2-a]pyridinium salts studied.

Electrophilic quaternization of 2-N-, O-, S-, and Se-allylpyridines is a convenient method for synthesis of annelated heterocycles which are useful in practice [1-3]. Quaternization of 2-[2-cyclohexen-1-ylthio(seleno)]pyridines by reaction with halogens occurs as an electrophilic intramolecular trans-quaternization with formation of 4a,10a-cis-4,4a-trans-1,2,3,4,4a,10a-hexahydrobenzothiazolo(selenazolo)[3,2-a]pyridinium salts [1]. In this work, the reaction of hexahydrobenzothiazolo[3,2-a]pyridinium salts with electrophilic and nucleophilic reagents is studied and some stereochemical aspects of this reaction are given.

The tribromide I in the absence of benzothiazolo[3,2-a]pyridinium triiodide II is shown to react with acetone. During this the tribromide I is converted into bromide III and the acetone into bromoacetone IV. The bromination of acetone proceeds with 72% yield of the final product IV even with heterogeneous phases at room temperature. Addition of an equivalent quantity of bromine to a suspension of benzothiazolo[3,2-a]pyridinium bromide III in chloroform again leads to the tribromide I. The bromide III plays a catalytic role.

The reaction of salts I-III with perchloric acid, iodine, potassium 1,1,3,3-tetracyanopropenide (VII) was also studied. Treatment of salts I-III with perchloric acid with heating in acetic acid leads to benzothiazolo[3,2-a]pyridinium perchlorates V and VI.

Heating bromide III in acetic acid with an excess of potassium iodide and iodine together with exchange of bromide for triiodide substitutes the bromine by iodine in the cation of the starting salt. However, the 1,1,3,3-tetracyanopropenide anion is more active in the exchange reactions.

The ability to displace the anions from the hexahydrobenzothiazolo[3,2-a]pyridinium salts depends on the nature of the conjugate base and is related to the strength of the corresponding acid. Thus, the tetracyanopropenide VIII and the perchlorate V are obtained from the tribromide I with yields of 86 and 78%, respectively. The bromide III is converted into the perchlorate V with an 85% yield. Besides this, the bromide III and perchlorate V upon

---

T. G. Shevchenko Voroshilovgrad State Pedagogical Institute, Voroshilovgrad 348011. N. D. Zelinskiĭ Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow 117913. A. N. Nesmeyanov Institute of Organometallic Compounds, Academy of Sciences of the USSR, Moscow 117813. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1682-1688, December, 1988. Original article submitted May 19, 1987; revision submitted November 20, 1987.

0009-3122/88/2412-1391$12.50