BROMOHYDRINS OF REISSERT COMPOUNDS

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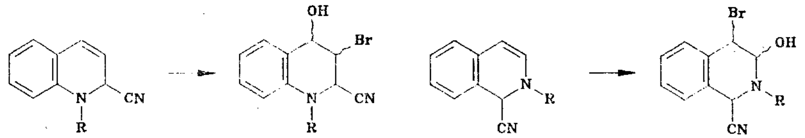
Reissert compounds that are derivatives of quinoline and isoquinoline are converted in high yields to the corresponding bromohydrins under the influence of N-bromosuccinimide in aqueous dimethyl sulfoxide. The reactions proceed regio- and stereospecifically.

The chemistry of Reissert compounds, which have found wide application in organic synthesis, has been studied in detail (see reviews [1, 2]). However, little is known about reactions at the double bond contained in compounds of this type. There are only individual publications devoted to the addition of bromine [3] and hypochlorous or hypobromous acid [4, 5] to Reissert compounds obtained from isoquinoline, as well as to oxidation with thallium nitrate [6]. Hypochlorous acid, N-chlorosuccinimide, and 1,3-dibromo-5,5-dimethylhydantoin have been used as sources of halide cations for the synthesis of halohydrins. The use of these reagents makes it possible to obtain halohydrins in 38-55% yields [4, 5].

Halohydrins of Reissert compounds obtained from quinolines have not been described in the literature.

We have shown that the corresponding bromohydrins (IIIa,b and IVa-c) are formed in high yields by the action of N-bromosuccinimide (NBS) in aqueous dimethyl sulfoxide (DMSO) on Reissert compounds of the quinoline (Ia,b) and isoquinoline (IIa-c) series. Compounds Ia,b and IIa-c, which contain a benzoyl, carbalkoxy, or tosyl residue attached to the nitrogen atom, give bromohydrins IIIa,b and IVa-c at room temperature under the conditions described for the preparation of bromohydrins of olefins [7]. The structures of the compounds were established by means of IR and PMR spectroscopy and were confirmed by the results of elementary analysis.



Ia,b IIIa,b IIa-c IVa-c

I–IV a R=COC_6H_5; I, III b R=$COOCH_3$; II, IV b R=$COOC_2H_5$, c R=$SO_2C_6H_4CH_3$-p

The PMR spectra of IIIa,b and IVa-c in solution in d_6-DMSO were recorded immediately after preparation of the samples (IIIb and IVb), after 4-6 days (IIIa,b and IVa-c), and with the addition of D_2O (IIIb and IVb) (Table 1). The latter method leads to simplification of the spectra due to deuterium exchange with the hydroxy group [5]. The spectra recorded 4-6 days after preparation of the samples have the same form as those obtained after the addition of D_2O. Thus the hydroxy proton shows up only in freshly prepared solutions that do not contain D_2O.

In addition to signals of aromatic protons and methyl protons, the PMR spectrum of quinoline derivative IIIb recorded immediately after preparation of the sample contains two doublets and two triplets, which correspond to three methylidyne protons and one hydroxy proton (Table 1). Since the doublet at 6.54 ppm vanishes after deuteration, the triplet is converted to a doublet, and the remaining signals remain unchanged, the position of the hydroxy group at $C_{(4)}$ is determined unequivocally. It should be noted that, in the case of IIIa,b, the compon-

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TABLE 1. Spectral Characteristics of the Bromohydrins (IIIa,b and IVa-c) of the Reissert Compounds

Compound	Recording conditions[a]	PMR spectrum in d_6-DMSO										IR spectrum, ν, cm^{-1}		
		chemical shift, δ, ppm							SSCC, $^3J(H, H)$, Hz			OH	CO	CN
		1-H	2-H	3-H	4-H	OH	Ar—H	other[b]	23	34	H, OH			
IIIa	C	—	5,81	4,58	5,01	—	6,68; 7,0—7,7	—	5,0	5,0	—	3445	1630	—
IIIb	A	—	5,79	4,54	4,79	6,54	7,2—7,8	3,80 (CH_3)	5,0	5,0	5,0	3200	1737	—
IIIb	B	—	5,78	4,53	4,76	—	7,2—7,8	3,79 (CH_3)	5,0	5,0	—	3285		
IIIb	C	—	5,76	4,54	4,78	—	7,2—7,8	3,76 (CH_3)	5,0	5,0	—			
IVa	C	6,27	—	5,66	5,46	—	7,4—7,8	—	—	3,0	—	3413	1650	2260
IVb	A	6,08	—	5,93	5,45	6,78	7,3—7,8	1,31 (CH_3); 4,28 (CH_2)	—	3,0	4,0	3420	1693	2255
IVb	B	6,04	—	5,92	5,41	—	7,3—7,8	1,29 (CH_3); 4,26 (CH_2)	—	3,0	—			
IVb	C	6,09	—	5,93	5,45	—	7,3—7,8	1,31 (CH_3); 4,28 (CH_2)	—	3,0	—			
IVc	C	6,08	—	5,86	5,42	—	7,3—7,7; 7,9—8,1	2,37 (CH_3)	—	3,0	—	3440	—	2260

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a) Symbols: A) recording immediately after preparation of the sample; B) the same conditions as A, but with the addition of one drop of D_2O; C) recording 4-6 days after preparation of the sample.

b) In the ethyl fragment $^3J(CH_3CH_2)$ ~ 7 Hz.

TABLE 2. Characteristics of the Bromohydrins (IIIa,b and IVa-c) of the Reissert Compounds

Compound	mp, °C (dec., 50% aqueous alcohol)	Found, %				Empirical formula	Calc., %				Yield, %
		C	H	Br	N		C	H	Br	N	
IIIa	137—138	56,8	3,7	22,6	8,0	$C_{17}H_{13}BrN_2O_2$	57,2	3,7	22,4	7,8	86
IIIb	119—120	46,6	3,8	26,2	9,0	$C_{12}H_{11}BrN_2O_3$	46,3	3,6	25,7	9,0	78
IVa	147—148[a]	56,8	3,4	22,2	7,9	$C_{17}H_{13}BrN_2O_2$	57,2	3,7	22,4	7,8	90
IVb	155—157	48,3	3,8	25,1	8,4	$C_{13}H_{13}BrN_2O_3$	48,0	4,0	24,6	8,6	87
IVc	148—151	50,4	3,8	19,4	6,6	$C_{17}H_{15}BrN_2O_3S$	50,1	3,7	19,6	6,9	82

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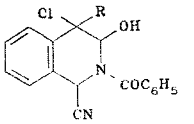
a) Recrystallized from dioxane—water (2:1).

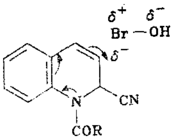
ents of the 4-H signal are broadened in all cases, and the width of the lines for 4-H (2.2 Hz) is approximately twice that for 2-H and 3-H (about 1 Hz). In experiments with double resonance and suppression of the aromatic protons we observed compression of the components to 1.3 Hz, which makes it possible to conclude that the observed broadening of the signal is due to allylic coupling (^4J) of 4-H with 5-H.

The assignment of the signals in the PMR spectra of isoquinoline derivatives IVa-c, which is presented in Table 1, was made with allowance for the data in [4]. In [4] the positions of the substituents were established by comparison of the PMR spectra of chlorohydrin Va and its deuterated analog Vb. Since the chemical shifts of the geminal proton relative to OH in IVa (5.66 ppm) and 3-H in Va (5.65 ppm), as well as the 1-H protons (6.27 and 6.23 ppm, respectively), are identical, and the 4-H chemical shifts in these compounds do not differ markedly (5.46 and 5.35 ppm, respectively) in view of the small difference in the effect of the Br and Cl atoms on the chemical shifts of the methylidyne protons [8], we made the assignments shown in Table 1.

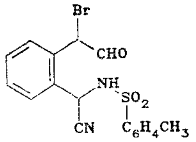
The IR spectra of all of the bromohydrins obtained (Table 1) contain strong broad bands corresponding to the OH stretching vibrations and strong bands corresponding to the carbonyl group (except for IVc, the spectrum of which contains absorption corresponding to S—O vibrations). In the region of C≡N stretching vibrations there is very weak absorption only for isoquinoline derivatives IVa-c; as in the case of the starting Reissert compounds [1], this absorption is absent in the spectra of bromohydrins IIIa,b.



Va R=H; b R=D



VI



VII

From general concepts regarding the electronic effects of substituents on the direction of addition of hypobromous acid to Ia,b, one should expect the formation of precisely these structures, as evidenced by the PMR spectra: Ia,b should be attacked by electrophilic halogen at $C_{(3)}$ (formula VI). Thus, the addition of hypohalous acids to quinoline derivatives Ia,b, as well as to isoquinoline derivatives IIa-c, takes place regiospecifically. We did not examine the problem of the stereochemistry of bromohydrins IIIa,b and IVa-c but, judging from the PMR spectra and the results of thin-layer chromatography (TLC), these substances are individual isomers; this provides a basis for the assumption that the addition of hypobromous acid to Reissert compounds is a stereospecific reaction (see [4]).

In conclusion, let us note that IVc, which was obtained in low yield by another method, was previously described as a substance with mp 184°C [see IVc in Table 2, in which it is reported as having mp 148-151°C (dec.)]; its IR, UV, and PMR spectra presented in [3] differ from the spectra that we obtained. According to the data of George and coworkers [3], the IR spectrum recorded in the solid state contains a carbonyl maximum at 1700 cm^{-1}, and they assume that IVc in the solid state exists in open form VII. Since we obtained results that contradict this, it may be assumed that in [3] George and coworkers described another geometrical isomer of bromohydrin IVc, which exists in the cyclic form in solution and in the open form in the solid state.

EXPERIMENTAL

The PMR spectra were recorded with a Tesla BS-567 spectrometer (100 MHz) under pulse conditions without accumulation with the use of a 90° pulse. The volume of the memory used for recording the free induction signal was 16K, the observation range was 1900 Hz, and the resolution in the memory cell was 0.23 Hz. Stabilization of the resonance conditions was accomplished from the signal of deuterium in the solvent. The investigated samples were solutions of the compounds in d_6-DMSO with a concentration of 0.33 mole/liter. The internal standard was DMSO, the chemical shift of which on the δ scale was assumed to be 2.5 ppm. The IR spectra of KBr pellets of the compounds were obtained with a UR-20 spectrometer. The UV spectra of solutions in 96% alcohol were recorded with a Specord UV-vis spectrophotometer. Monitoring of the course of the reaction and the purity of the compounds obtained was realized by TLC on Silufol plates in a chloroform—methanol system (10:1).

The starting Reissert compounds were obtained by the method in [9].

Bromohydrins (IIIa,b, IVa-c) of the Reissert Compounds. A 2.1-g (12 mmole) sample of N-bromosuccinimide, which dissolved rapidly, was added with stirring to a solution of 10 mmole of the Reissert compound (Ia,b, IIa-c) in a mixture of 15 ml of DMSO and 1.5 ml of water; the temperature of the mixture rose slightly. After 1 h, the reaction mass was diluted with 100 ml of water, and the precipitate was removed by filtration and recrystallized. Compound IIIb was isolated by extraction with ethyl acetate after dilution of the reaction mass with water. The ethyl acetate solution was washed with water, dried with $MgSO_4$, and evaporated *in vacuo*. The residue was recrystallized. The characteristics of the synthesized compounds are presented in Tables 1 and 2.

IR spectrum of IVc: 3440 (OH), 2260 (C≡N), 1600 (arom.), 1497, 1350 (S—O), 1165 (S—O), 1060, 1045, 743, 713, and 692 cm^{-1}. UV spectrum, λ_{max} (log ε): 231 (4.24), 275 (3.00), and 337 nm (1.76).

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BROMINATION OF QUINOLINE IN THE PRESENCE OF SOME LEWIS ACIDS

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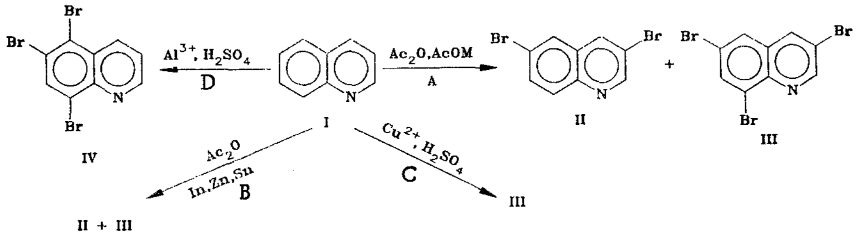
Data on the bromination of quinoline in acetic anhydride and in the presence of salts of p and d elements are presented. High catalytic activity of the investigated salts, particularly the salts of p elements, was demonstrated. An unexpected orientation of the bromination of quinoline in 94% sulfuric acid in the presence of copper sulfate was discovered.

Halogenation is considered to be one of the most thoroughly investigated reactions in the monoazine series [1]. However, some aspects of the catalysis of this reaction by salts of p and d elements of the Mendeleev periodic system have not been adequately studied. In particular, in [2] one of us demonstrated the high activation of pyridine to bromination in complexes for elements with p orbitals (Zn, Sn, Sb, Te, etc.), although such activation of a ligand is not obvious from the generally accepted concept [3-5]. Because of the possible d_π–p_π interaction (π back bonding), one might have expected, from the same concept, a somewhat different orientation of the bromination of quinoline with salts of d elements than in the case of its catalysis with silver sulfate [6].

In order to shed some light on the problems enumerated above, it was necessary to conduct additional investigations in the case of the bromination of quinoline in complexes with salts of p and d elements. It is known that the yields of bromoquinolines by known methods are rather low [6-8], although they are of practical interest as potential inhibitors of the nitrification of nitrogen fertilizers [9].

In the present communication we present data on the bromination of quinoline in acetic anhydride and in the presence of Al, In, Sn (p elements), Cu, Zn (d elements), and Na, Co, Ni, Cu, Ag, Zn, Ba, Pb, and other acetates. The role of acetic anhydride and acetates is evidently determined in the generation and facilitation of the addition of the AcO^-Br^+ bromo cation in the intermediate 1,4-dihydroquinoline [10] as a function of the degree of valence of the metal, the positive charge, the ability to coordinate at the ring nitrogen atom of quinoline, and other factors. The general method is similar to that described in [11] for the bromination of quinoline N-oxide. Exclusively 3,6-dibromo-substitution products are formed under the conditions in [11].



M=Na, Co, Ni, Cu, Zn, Ag, Ba, Pb

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