QUININDINES

VI.* BROMINATION IN THE β-QUININDANE SERIES. SYNTHESIS OF THE 3H-β-QUININDINE SYSTEM

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Bromination of β-quinindane and β-quinindane-9-carboxylic acid leads to tribromo- and tetrabromo-substituted 1H- and 3H-β-quinindines. Hydrolysis of the tribromide of β-quinindine under the influence of silver nitrate gives 1-bromo-3H-β-quinindin-3-one, while hydrolysis under the influence of concentrated H_2SO_4 gives rearrangement to form 1,2-dibromo-3H-β-quinindin-3-one. The possible paths for the formation of the compounds obtained are discussed, and the IR, PMR, and UV spectral data are presented.

We have previously studied the chlorination of β-quinindane and several of its derivatives under the influence of phosphorus pentachloride [1]. In the process, the hydrogen atoms in the 3 position are primarily replaced by chlorine, while β-quinindane itself gives 1,1,2,3,3-pentachloro-β-quinindane. Los and Stafford [2] unsuccessfully attempted to brominate β-quinindane with N-bromosuccinimide. This paper is devoted to a study of the action of bromine on β-quinindane (Ia) and β-quinindane-9- carboxylic acid (Ib).

Only β-quinindane perbromide was isolated from the bromination of β-quinindane (Ia) in acetic acid at 50-55°C. This was confirmed by the conversion of the perbromide to β-quinindane hydrobromide by treatment with sodium bisulfite.

Bromination of Ia with 2 mole of bromine under the conditions proposed for quinaldine [3] (heating at 100° in acetic acid in the presence of sodium acetate) leads to resinification of the reaction mass. Lowering the reaction temperature to 55-57° makes it possible to avoid resinification, and a compound with empirical formula $C_{12}H_6Br_3N$ is isolated in good yield along with unchanged starting material, i.e., four bromine molecules react with one molecule of Ia ($C_{12}H_{11}N + 4Br_2 \rightarrow C_{12}H_6Br_3N + 5HBr$). When 3.3 mole of bromine was taken for the bromination of 1 mole of Ia, a significant amount of a tetrabromide ($C_{12}H_5Br_4N$) was isolated along with the same tribromide. Only signals from five aromatic protons are observed in the PMR spectrum of the tetrabromide: δ_5 8.30 ppm, doublet; 7.96 ppm, singlet; the $C_{(5)}$, $C_{(6)}$, and $C_{(7)}$ protons give a multiplet at 7.5-7.9 ppm. Consequently, all four bromine atoms are situated in the five-membered ring, and the absence of other protons attests to the formation of a new double bond in this ring. In fact, as compared with the UV spectrum of β-quinindane or 1,1,2,3,3-pentachloro-β-quinindane [1], the UV spectrum of the tetrabromide has a considerable (~ 20 nm) bathochromic shift as a consequence of lengthening of the conjugation chain. On the basis of the fact that the singlet from the $C_{(9)}$ proton, as in the spectrum of β-quinindane, is directly adjacent to the multiplet from the $C_{(6)}$, $C_{(7)}$, and $C_{(8)}$ protons and is not shifted to weak field, as in the spectrum of the pentachloride mentioned above [1], it can be assumed that only one bromine atom is attached to $C_{(1)}$. From the spectral data obtained, the structure of the tetrabromide was determined to be 1,2,3,3-tetrabromo-3H-β-quinindine (IIa).

Despite the fact that only one spot was observed on the chromatograms of the tribromide in various systems on a thin layer of aluminum oxide, the PMR spectrum of the tribromide contains signals of both 1,1,3-tribromo-1H-β-quinindine (IIIa) and 1,3,3-tribromo-3H-β-quinindine (IVa) (Fig. 1). The assignment was made on the basis of the position of the singlets from the $C_{(2)}$ and $C_{(9)}$ protons (the signals of the ben-

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*See [1] for communication V.

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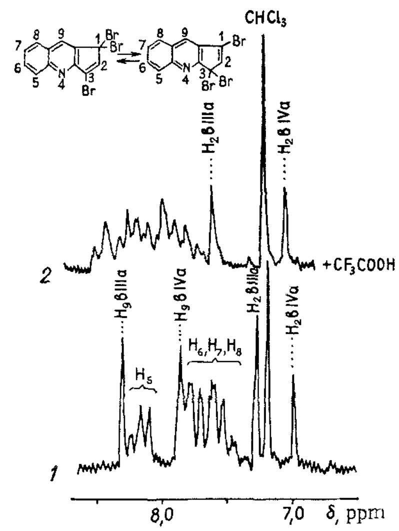


Fig. 1. PMR spectra of β-quinindine tribromide (IIIa + IVa) in deuterochloroform with added trifluoroacetic acid (2) and without acid (1).

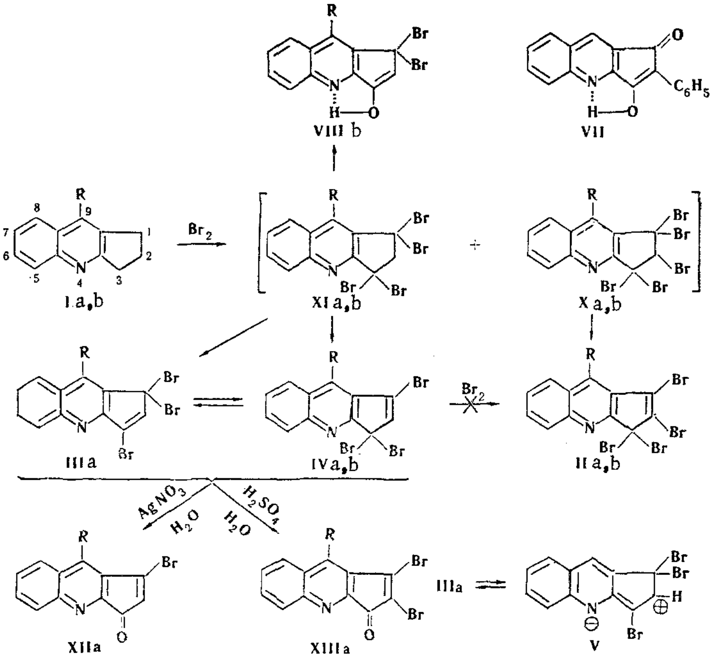
zene protons of IIIa and IVa are superimposed): the $C_{(9)}$ proton in IIIa, which is deshielded by two bromine atoms in the 1 position, absorbs at 8.41 ppm, compared with 7.97 ppm in IVa; in turn, the $C_{(2)}$ proton signal in IIIa is shifted to weaker field (7.36 ppm) because of conjugation with nitrogen and the contribution of saturated structure V, while there is no such conjugation in IVa, and the corresponding singlet from $H_{(2)}$ is found at 7.02 ppm. For the same reason, the addition of trifluoroacetic acid to a solution of the tribromide results in a strong shift to weak field of the $C_{(2)}$ proton signal in IIIa, while the corresponding singlet in IVa is virtually unshifted (Fig. 1).

Similar bromination of β-quinindane-9-carboxylic acid (Ib) also results in a tribromide and tetrabromide in approximately equal yields [5]. Judging from the PMR spectra, only one tribromide isomer – 1,3,3-tribromo-3H-β-quinindine-9-carboxylic acid (IVb) – is formed in the process; the lone singlet from the proton on the double bond (7.41 ppm) is virtually unshifted on acidification, as in the case of the analogous tribromide without a carboxyl group (IVa).

In analogy with IIa, the 1,2,3,3-tetrabromo-3H-β-quinindinecarboxylic acid structure (IIb) was assigned to the tetrabromide. Only a multiplet at 7.7-8.1 ppm from the four aromatic protons is observed in the PMR spectrum of IIb (dissolved in trifluoroacetic acid). The UV spectra of IIb and IVb also attest to lengthening of the conjugation chain: pronounced bathochromic shifts are observed, as compared with the absorption of starting acid Ib (see [4] for the spectrum of Ib).

Bands characteristic for the COOH group (ν_{CO} 1736 cm^{-1}, valence vibrations and composite frequencies for the acid hydroxyl group at 2400-2900 cm^{-1}) are noted in the IR spectra of IIb and IVb.

If the bromination of acid Ib is carried out for shorter times, the initially light-colored ether extract of the reaction products darkens rapidly, and a dark-blue precipitate is formed; solutions of this precipitate in alcohol are bright blue, it has the empirical formula $C_{13}H_7Br_2NO_3$, and its IR spectrum contains bands characteristic for the COOH group (ν_{CO} 1740 cm^{-1} and several bands at 2400-2800 cm^{-1}) and bands for the



a R = H; b R = COOH

$>C{=}C{-}OH\cdots N<$ fragment: C = C at 1652 cm^{-1}, and the absorption of the OH group bonded with an intramolecular hydrogen bond, manifested as a broad, weak band at 3130 cm^{-1}. On the basis of these data, the 1,1-dibromo-3-hydroxy-1H-β-quinindine structure (VIIIb) can be proposed (although not definitively) for the compound obtained. A compound (VII) with a similar structure is also intensely colored [11].

A tribromide is also formed when the benzene analog of quinindane – indane – is brominated in carbon tetrachloride. Meyer and Meyer, who first obtained this tribromide in 1918 [6], assigned the 1,2,3-tribromoindane structure to it only on the basis of the fact that phthalic acid is formed when it is oxidized. This tribromide was subsequently synthesized repeatedly, for example in [7, 8], but its structure was not investigated. Nevertheless, the structure proposed in [6] turned out to be correct. Our PMR spectrum of the product of bromination of indane confirmed that it is 1,2,3-tribromoindane: the four benzene protons, equalized owing to symmetry, give a broad singlet (δ 7.41 ppm), the identical $C_{(1)}$ and $C_{(3)}$ protons give an overall doublet (δ 5.58 ppm, J = 3 Hz), and the $C_{(2)}$ proton gives a triplet at 4.96 ppm (in CCl_4).

Thus a new double bond is not formed during the action of bromine on indane. However, bromination of indene in the presence of alkali gives 1,1,3-tribromoindene (IX) [9]. The bromination of indane with N-bromosuccinimide was studied recently [10]; in this case, as in the reaction of bromine with quinindane, a new double bond is formed, and 1,2,3- and 1,1,3-tribromoindene (IX) are isolated. As would be expected, the chemical shift of the $C_{(2)}$ proton in tribromide IX (6.88 ppm) is close to that of the analogous proton in IVa (7.02 ppm) but not to that in IIIa (7.36 ppm).

The formation of tri- and tetrabromoquinindines apparently proceeds as a result of splitting out of hydrogen bromide from the initially formed bromination products. In analogy with the formation of 1,1,2,-3,3-pentachloro-β-quinindane [1], it can be assumed that one such product is the corresponding pentabromide (X). It is also logical to assume the intermediate formation of 1,1,3,3-tetrabromo-β-quinindane (XI).

The fact that tetrabromide IIa is not formed as a result of bromination of tribromide IVa was confirmed by a special experiment: the tribromide is not altered by the action of bromine under the experimental conditions.

Judging from the products (IIa,b), the dehydrobromination of intermediate pentabromides Xa and Xb does not proceed unambiguously: a bromine atom is split out from the 1 position, which is more natural for a monomolecular cleavage mechanism (E 1) since the electron density is greater on $C_{(1)}$ in VII than on $C_{(3)}$, which is situated on the α-carbon atom of quinoline.

A bromine atom is also cleaved from the 1 position during the dehydrobromination of tetrabromide XIb, while cleavage probably occurs to about an equal extent from $C_{(1)}$ and $C_{(3)}$ in the case of XIa. We cannot, however, exclude the possibility that we are dealing here with an equilibrium between IIIa and IVa of the frequently encountered allylic type [12]. This assumption is confirmed by the fact that not only is it impossible to separate isomers IIIa and IVa by repeated recrystallizations and reprecipitations, one cannot even substantially change the isomer ratio: in all cases, judging from the $C_{(2)}$ and $C_{(9)}$ singlet intensities, the PMR spectrum indicates 40-45% IIIa and 55-60% IVa.

Polybromides II, III, and IV are very sensitive to alkali: solutions of them darken rapidly even under the influence of sodium carbonate. The hydrolysis of tribromides IIIa + IVa was therefore carried out by the action of silver nitrate in aqueous acetone; this yielded only one compound with the empirical formula $C_{12}H_6BrNO$. The IR spectrum of this product contained a carbonyl band (ν_{CO} 1720 cm^{-1}), while the PMR spectrum contained all of the aromatic protons of β-quinindine; δ_5 8.20 ppm, doublet; $H_{(6)}$, $H_{(7)}$, and $H_{(8)}$ 7.4-7.9 ppm, multiplet; δ_9 8.10 ppm, singlet; and a singlet from the proton attached to the double bond (δ_2 6.83 ppm). The magnitude of δ_2 changes slightly when acid is added. On the basis of this set of data the hydrolysis product was assigned the 1-bromo-3H-β-quinindin-3-one structure (XIIa).

On the other hand, the polybromides are very stable to the action of acids. In dilute acids they practically do not form salts, while polybromoquinindines IIa and IIIa + IVa do dissolve in concentrated H_2SO_4 but are precipitated unchanged on dilution with water. Tetrabromide IIa remains virtually unchanged even when it is heated at 90° for 2 h in concentrated sulfuric acid. Under these conditions, tribromide IIIa + IVa is converted to a ketone (ν_{CO} 1726 cm^{-1}) in 3 h with the empirical formula $C_{12}H_5Br_2NO$; only the "aromatic" protons of β-quinindine are observed in its PMR spectrum. These facts, together with the similarity in the UV spectra of this compound and ketone XIIa, make it possible to propose the 1,2-dibromo-3H-β-quinindin-

3-one structure (XIIIa) for the compound.* The formation of a similar compound, 2,3-dibromoinden-1-one (XIV), from 1,1,3-tribromoindene (IX) was observed in [10], during which hydrolysis with rearrangement to 2,2,3-tribromoindan-1-one occurred by the action of concentrated sulfuric acid; dibromoketone XIV was obtained from the latter by splitting out of hydrogen bromide. The reaction apparently proceeds similarly in the case of the formation of XIIIa. The course of several reactions and the purity of IIa, XIIa, and XIIIa were monitored by means of thin-layer chromatography on aluminum oxide.

Thus the first representatives of the previously unknown 3H-β-quinindine heterocyclic system have been synthesized. The presence of reactive bromine atoms in the compounds obtained makes it possible to make the transition from bromine-substituted compounds to 3H-β-quinindines with other substituents. For the first time it has been possible to introduce doublebonds into the five-membered ring of β-quinindane; β-quinindines were previously obtained from substituted cyclopentenones [2].

EXPERIMENTAL

Action of Bromine on β-Quinindane (Ia). A) A solution of 16 g (0.1 mole) of bromine in 10 ml of acetic acid was added with stirring in the course of 20 min to a suspension of 5.07 g (0.03 mole) of β-quinindane [4-13] in 50 ml of glacial acetic acid at 50-55°. After 2.5 h, the solution was decanted from the resulting heavy, dark oil, and the oil was triturated with a small amount of ether to give 10 g of residue. This was recrystallized from methanol and acetic acid to give the yellow perbromide of β-quinindane with mp 108-109°. Found %: C 35.1; H 2.9; Br 58.8. $C_{12}H_{11}N \cdot HBr_3$. Calc. %: C 35.1; H 2.9; Br 58.5.

Treatment of the perbromide with a minimal amount of sodium bisulfate solution precipitated a hydrobromide of β-quinindane with mp 265-267° (dec., from ethanol-butanol). Found %: C 57.4; H 4.8; Br 31.8. $C_{12}H_{11}N \cdot HBr$. Calc. %: C 57.8; H 4.9; Br 32.1.

B) A solution of 16 g (0.1 mole) of bromine in 5 ml of acetic acid was added dropwise with stirring to a mixture of 5.07 g (0.03 mole) of β-quinindane, 10.5 g (0.13 mole) of anhydrous sodium acetate, and 45 ml of glacial acetic acid at 55-57°. The mixture was stirred at this temperature for 4 h and cooled. The resulting precipitate was filtered and washed with water to give 4.0 g (42% based on bromine) of 1,2,3,3-tetrabromo-3H-β-quinindine (IIa) with mp 186-188° (dec., from alcohol). Found %: C 30.0; H 1.2; Br 66.9; N 3.0. $C_{12}H_5Br_4N$. Calc. %: C 30.3; H 1.1; Br 67.2; N 2.9. UV spectrum (alcohol), λ_{max}, nm (log ε): 278 (4.52), 310 (4.08, shoulder), 346 (2.20, shoulder).

A total of 5.6 g (55% based on bromine) of tribromo-β-quinindine (IIIa + IVa) was precipitated from the acetic acid mother liquor with 150 ml of water and decomposed without melting at 170-180°. A sample was crystallized from alcohol for analysis. Found %: C 35.4; H 1.4; Br 59.1. $C_{12}H_6Br_3N$. Calc. %: C 35.7; H 1.5; Br 59.4.

Bromination of β-Quinindane-9-carboxylic Acid (Ib). A) Bromine [16 g (0.1 mole)] was added during 30 min with stirring to a suspension of 5.0 g (0.023 mole) of β-quinindane-9-carboxylic acid (Ib) [4] and 10 g (0.12 mole) of anhydrous sodium acetate in 40 ml of glacial acetic acid at 67-68°. The mixture was stirred at this temperature for another 4.5 h and cooled. The resulting precipitate was filtered and washed with water to give 0.8 g of unchanged acid. Addition of 100 ml of water to the acetic acid mother liquor gave 7.5 g of a precipitate from which 2.5 g (28% based on converted acid) of 1,3,3-tribromo-3H-β-quinindine-9-carboxylic acid (IVb) was extracted with benzene. The product decomposed at ~125° (darkened without melting and did not melt up to 300°) and was purified by reprecipitation from benzene with hexane. Found %: C 34.4; H 1.8; Br 53.4; N 2.8. $C_{12}H_6Br_3NO_2$. Calc. %: C 34.3; H 1.3; Br 53.5; N 3.1. UV spectrum (alcohol), λ_{max}, nm (log ε): 254 (4.27); 276 (4.33), 317 (3.86, shoulder).

A total of 4.0 g (38% based on converted acid) of 1,2,3,3-tetrabromo-3H-β-quinindine-9-carboxylic acid (IIb), which decomposed at ~ 130° (darkened without melting and did not melt up to 300°), remained after extraction with benzene. It was purified by crystallization from alcohol. Found %: C 29.4; H 1.2; Br 59.9. $C_{13}H_5Br_4NO_2$. Calc. %: C 29.5; H 1.0; Br 60.5.

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*It is interesting that the carbonyl band in this compound and in ketone XIIa is found in the region characteristic for saturated ketones. Conjugation of the C = O and C = C bonds in XIIa and XIIIa is apparently very low because of distortion of the valence angles in the cyclopentadiene ring and also because of the energetic unsuitability of this conjugation for such systems (see for example, [14]); in addition, the effect of the bromine atoms should be taken into account.

B) Acid Ib was similarly brominated (for 2 h), and the precipitate that formed on cooling was filtered and washed with water to give 2 g of starting acid. The acetic acid mother liquor was evaporated in vacuo, and the residue was extracted with 100 ml of ether. On standing, the extract rapidly changed color from light yellow to dark blue, and a black precipitate formed and was filtered to give 1.0 g of 1,1-dibromo-3-hydroxy-1H-β-quinindine-9-carboxylic acid (VIIIb). It was purified by reprecipitation from acetone with ether and melted above 300°. Found %: C 40.8; H 2.1; N 3.6. $C_{13}H_7Br_2NO_3$. Calc. %: C 40.5; H 1.8; N 3.6.

1-Bromo-3H-β-quinindin-3-one (XIIa). A solution of 0.45 g of silver nitrate in 3 ml of water was added to a solution of 0.55 g of tribromo-β-quinindine in 10 ml of acetone. The mixture was held at 20° for 15 h, after which 10 ml of water was added. The mixture was neutralized with sodium bicarbonate and extracted with ether. The extract was dried, and the ether was removed by vacuum distillation to give 0.15 g of yellow 1-bromo-3H-β-quinindin-3-one (XIIa) with mp 126-127° (dec., from alcohol). Found %: C 55.1; H 2.3; Br 30.4. $C_{12}H_6BrNO$. Calc. %: C 55.4; H 2.3; Br 30.7. UV spectrum (alcohol), λ_{max}, nm (log ε): 214 (4.32), 239 (3.12, shoulder), 279 (4.58).

1,2-Dibromo-3H-β-quinindin-3-one (XIIIa). A solution of 0.2 g of tribromo-β-quinindine in 1 ml of concentrated H_2SO_4 was heated at 90° until hydrogen bromide evolution ceased (3 h). It was then cooled, poured over 10 g of ice, and the resulting yellow-orange precipitate was filtered and recrystallized from alcohol to give XIIIa with mp 209-210° (dec., darkened at 200°). Found %: C 42.4; H 1.9; Br 47.1. $C_{12}H_5Br_2NO$. Calc. %: C 42.5; H 1.5; Br 47.1. UV spectrum (alcohol), λ_{max}, nm (log ε): 214 (4.38), 242 (4.24, shoulder), 254 (4.26, shoulder), 289 (4.50).

Chromatography was carried out in a thin layer of aluminum oxide treated with acetic acid (2.5 wt. %) in benzene, hexane–benzene, benzene–chloroform, and chloroform systems with development by iodine vapors.

The IR, UV, and NMR spectra were obtained with the same spectrometers and under the same conditions as in [1]. The PMR spectra were obtained in deuterochloroform.

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