Behavior of Ethylene Oxide in a Dimethylformamide Solution. Ethylene oxide (25 ml., measured at 0°) was cooled to −60° and added over a 12-min. period to a well stirred solution containing 1.384 g. of 8-quinolineboronic acid and 0.8 ml. of 1-butanol in 100 ml. of dimethylformamide at 88.8°. The reaction flask was equipped with a Dry Ice trap to collect volatile material. In the course of the addition and for about 5 min. afterward a gas (ethylene oxide) could be observed boiling out of the solution. Approximately 20 ml. of ethylene oxide condensed in the cold trap; after an hour it was added back to the reaction mixture. The solution was stirred for 2 hr., and then three 5-ml. aliquots were withdrawn over a period of 4.5 hr. for titrations with periodic acid. The results of the titrations were consistent in indicating the concentration of ethylene oxide to be 0.090 *M*. The pressure on the system was then reduced to where dimethylformamide began to distil, at which point the ethylene oxide concentration was 0.007 *M*. On repetition of the vacuum treatment 12 hr. later the concentration of oxidizable substance was only 0.004 *M*. These experiments show that some ethylene oxide is retained by a dimethylformamide solution containing 8-quinolineboronic acid at 88.8° and that, at most, only a very small amount (0.004 *M*) is converted to ethylene glycol. The oxidizable substance which remained after the pressure reductions corresponded to less than 5% of the 8-quinolineboronic acid present.

Evidence that the Product of Reaction of Chloroethanol and 8-Quinolineboronic Acid was not Ethylene Oxide.—8-Quinolineboronic acid (1.39 g.) and chloroethanol (0.648 g.) were heated together in 50 ml. of dimethylformamide at 88.8° for 4 hr. A titration with periodic acid indicated the concentration of reducing agent (ethylene glycol or its ester or ethylene oxide) to be 0.0388 *M*. After the reduced pressure treatment described in the previous experiment, a titration showed the concentration of reducing agent to be 0.0394 *M*. Since none of the reducing agent was lost under these conditions, it must have been the glycol (or a glycol ester of the boronic acid) and not ethylene oxide.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NORTHWESTERN UNIVERSITY, EVANSTON, ILL.]

Organoboron Compounds. XV.[1] Stereochemistry of the Reaction of 8-Quinolineboronic Acid with Chloroalcohols

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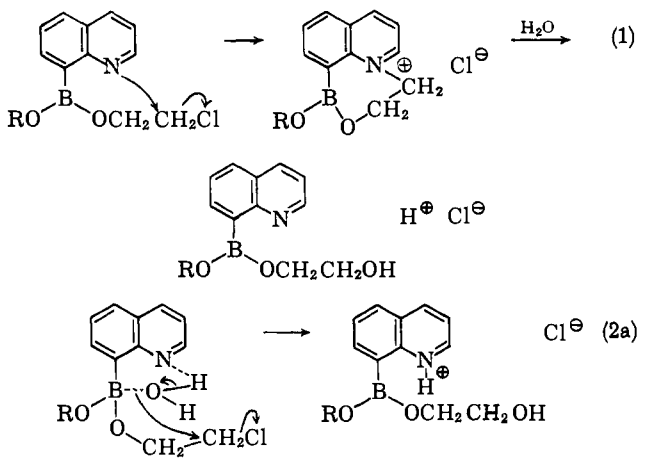
The reaction of 8-quinolineboronic acid with two pairs of stereoisomeric chlorohydrins was investigated. In two-step reactions, involving treatment of the chlorohydrin with 8-quinolineboronic acid and hydrolysis of the cyclic esters thereby produced, *trans*-2-chloro-1-indanol was converted to *cis*-1,2-indandiol and *erythro*-2-chloro-1,2-diphenylethanol was converted to *dl*-hydrobenzoin in good yield. *cis*-2-Chloro-1-indanol did not undergo carbon–chlorine fission when treated with 8-quinolineboronic acid under the conditions used for reaction of the *trans* isomer, and *threo*-2-chloro-1,2-diphenylethanol afforded in a very slow reaction a low yield of *meso*-hydrobenzoin. The mechanistic implications of the stereoselectivity of the reaction of 8-quinolineboronic acid are discussed.

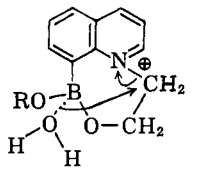
It was shown in the previous paper that 8-quinolineboronic acid is a polyfunctional catalyst for hydrolysis of chloroethanol and 3-chloro-1-propanol in dimethylformamide solutions containing water and collidine.[3] Several features relevant to the mechanism of the transformation were noted. The most interesting reaction in the proposed, generalized scheme is the one in which the carbon–halogen bond is broken, for it is in this step that the coöperative action of the neighboring boron and nitrogen should play a decisive role. The work described in the present paper was undertaken with the objective of learning more about this process.

The various mechanisms that may be envisaged for the substitution reaction may be classified into two categories: (1) those in which halogen is displaced by nitrogen and (2) those in which halogen is displaced by oxygen, the nucleophilicity of which has been increased by a neighboring nitrogen. In the former, the borono group would function as a binding site and nitrogen would act as a nucleophilic transforming site.[3] The carbon–oxygen bond would be formed by attack of water on an intermediate quaternary ammonium salt. Several pathways for the latter case (2) seem plausible. In each, boron would serve as a binding site and also participate in activation of oxygen. Sequence 2a illustrates a pathway of this type.

Since each displacement on carbon should occur with preponderate inversion of configuration, the stereochemical consequence at an asymmetric carbon would be net retention of configuration if the reaction followed sequence 1 and inversion of configuration if it went by sequence 2. The likelihood that displacement by water in sequence 1 proceeds with retention of configuration in an SNi type mechanism, *via* an intermediate



such as (a), is remote since the geometry of the groups about boron would be very unfavorable for such a process.



(a)

As a means of distinguishing between sequences 1 and 2 we therefore investigated the stereochemistry of the reaction of 8-quinolineboronic acid with two pairs of isomers: *trans*-2-chloro-1-indanol (I) and *cis*-2-chloro-1-indanol (II), and *erythro*-2-chloro-1,2-diphenylethanol (III) and *threo*-2-chloro-1,2-diphenylethanol (IV).

The stereoisomeric 2-chloroindanols were obtained by hydrolysis of 1,2-dichloroindane.[4] Based on the

(1) This work was supported by the National Science Foundation.

(2) National Science Foundation Cooperative Fellow, 1960–1961; Esso Educational Foundation Fellow, 1961–1962.

(3) R. L. Letsinger, S. Dandegaonker, W. J. Vullo and J. D. Morrison, *J. Am. Chem. Soc.*, **85**, 2223 (1963).

(4) C. M. Suter and G. A. Lutz, *ibid.*, **60**, 1360 (1938).

consistency of a number of independent structural assignments, which depend upon the relative ease of dehydrochlorination,[4,5] relative boiling points[4] and the shifts in the stretching frequencies of the O–H and C–O bonds,[6] the higher melting isomer may be assigned the *trans* configuration and the lower melting isomer the *cis* configuration with confidence. Additional support for these structures has been adduced by Stach from the stereoselective conversion of the chloroindanols to the 1,2-dichloroindanes.[7] The configuration of the indandiols has been established by infrared spectral data[8] and by the rates of cleavage of the diols with periodic acid[8] and lead tetraacetate.[9]

Compounds III and IV were prepared by the action of hydrogen chloride on *trans*-stilbene oxide and *cis*-stilbene oxide, respectively. The configuration of the chloroalcohols follows from the method of preparation and the fact that aqueous potassium hydroxide reconverted III to *trans*-stilbene oxide and IV to *cis*-stilbene oxide. The configuration of the related diols, *dl*- and *meso*-hydrobenzoin, is well established. In agreement with the assignment, the infrared spectrum of a dilute solution of the *dl*-isomer exhibited a doublet in the 2.8–2.9 μ region, indicative of intramolecular hydrogen bonding,[10] whereas a single sharp absorption band was found in this region of the spectrum of *meso*-hydrobenzoin.

Data for the reactions of the stereoisomeric chloroindanols with 8-quinolineboronic acid in dimethylformamide solution are presented in Table I. The most significant feature is the high degree of stereoselectivity in the displacement reaction. Titrations for chloride ion and for "glycol" revealed that the *cis* isomer did not react within a 14-hr. period whereas the *trans* isomer reacted to the extent of 24–25% (expt. A, B). On heating *trans*-2-chloro-1-indanol with excess 8-quinolineboronic acid for 60.5 hr., complete conversion to a product titratable with periodic acid was achieved (expt. C). Hydrolysis of this substance with an aqueous solution of mannitol afforded an 82% yield of pure *cis*-1,2-indandiol. None of the *trans*-diol was found. Since the intermediate (presumably the indanediol ester of 8-quinolineboronic acid) was hydrolyzed under conditions that do not cause isomerization of indandiol and since it is well established that hydrolysis of simple borate esters[11] involves O–B rather than O–C fission, it may be concluded that the C–Cl cleavage proceeded with predominant, if not exclusive, inversion of configuration. The low reactivity of *cis*-2-chloro-1-indanol in the displacement reaction with 8-quinolineboronic acid may be ascribed to the geometry of the intermediate boronate ester, which is unfavorable for a backside attack on carbon by the oxygen joined to boron. From a preparative point of view, lack of a direct reaction between *trans*-2-chloroindanol and dimethylformamide (expt. D) is noteworthy since, in the absence of competing solvolytic reactions, a clean, stereospecific hydrolysis of the chloroalcohol can be effected.

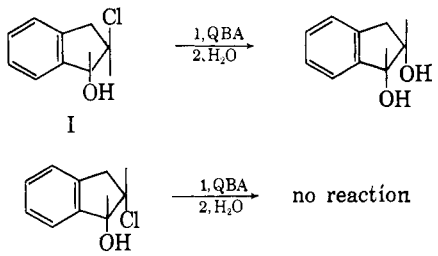


TABLE I

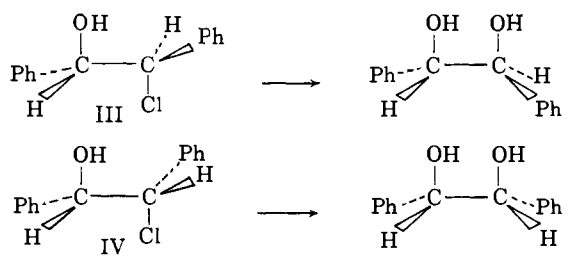
REACTION OF 8-QUINOLINEBORONIC ACID WITH *cis*- AND *trans*-2-CHLOROINDANOL IN DIMETHYLFORMAMIDE AT 88.8°[a]

Expt.	2-Chloroindanol isomer, mmoles	8-Quinoline-boronic acid, mmoles	Time, hours	Cl^-, %	"Glycol,"[b] %
A	*cis*, 1.4	1.4	14	0	0
B	*trans*, 1.4	1.4	14	25	24
C	*trans*, 2.0	5.35	52.5	90	
			60.5		100
D	*trans*, 2.0	0	51.5	0	
			59.5		0

[a] In each case the total volume at 88.8° was 10.0 ml. [b] % "glycol" refers to the product titratable with periodic acid; the glycol is present as an ester of the boronic acid.

Attempts to hydrolyze *trans*-2-chloro-1-indanol by use of collidine and catalytic amounts of 8-quinolineboronic acid were unsuccessful. The absence of *catalytic* activity of 8-quinolineboronic acid in this case correlates with the fact that *cis*-1,2-cyclopentanediol is a very effective inhibitor for the catalyzed hydrolysis of chloroethanol.[3] Both *cis*-1,2-cyclopentanediol and *cis*-1,2-indandiol, the product derived from *trans*-2-chloro-1-indanol, would tie up the boronic acid as a stable cyclic ester which would not exchange appreciably with chloroalcohol in the solution.

8-Quinolineboronic acid was found to displace chloride from *erythro*-2-chloro-1,2-diphenylethanol faster than from *threo*-2-chloro-1,2-diphenylethanol (Table II, expt. E, G). As in β-elimination reactions involving stereoisomers, it seems probable that the lower reactivity of the *threo* isomer results from eclipsing of the phenyl groups in the transition state for the transformation of this substance.[12] *dl*-Hydrobenzoin was isolated in 74% yield from a reaction of *erythro*-2-chloro-1,2-diphenylethanol which had run for 50 hr. (expt. I). No *meso*-hydrobenzoin was found among the products. This displacement reaction must have yielded directly a compound with the two oxygen atoms in the *dl*-configuration, for *meso*-hydrobenzoin did not isomerize in the presence of 8-quinolineboronic acid in dimethylformamide under the reaction conditions. It may be noted, from expt. E, I and K, that the displacement reactions proceeded satisfactorily in dimethylacetamide and sulfolane as well as in dimethylformamide. The reaction of the *threo* isomer with 8-quinolineboronic acid was less satisfactory in a preparative sense since the rate was very low; however, a low yield of *meso*-hydrobenzoin was isolated from a reaction that had run for 240 hr. (expt. J).



(5) H. D. Porter and C. M. Suter, *J. Am. Chem. Soc.*, **57**, 2024 (1935).
(6) A. Nickon, *ibid.*, **79**, 243 (1959).
(7) L. Stach, Ph.D. Dissertation, Northwestern University, 1963.
(8) J. S. Brimacombe, A. B. Foster, M. Stacey and D. H. Wiffen, *Tetrahedron*, **4**, 351 (1958).
(9) C. J. W. Brooks and L. Young, *Biochem. J.*, **63**, 264 (1956).
(10) J. Dale, *J. Chem. Soc.*, 910 (1961).
(11) A. Scattergood, W. H. Miller and J. J. Gammon, *J. Am. Chem. Soc.*, **67**, 2150 (1945).
(12) See E. S. Gould, "Mechanism and Structure in Organic Chemistry, Henry Holt and Co., New York, N. Y., 1959, pp. 492–496, for references pertaining to "eclipsing effects" in elimination reactions.

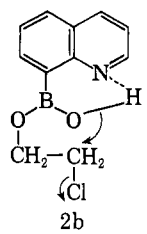
TABLE II

REACTION OF 8-QUINOLINEBORONIC ACID WITH *erythro*- AND *threo*-2-CHLORO-1,2-DIPHENYLETHANOL AT 88.8°

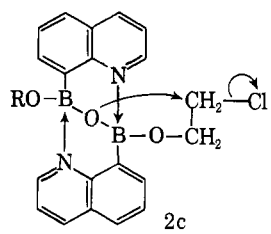
Expt.	2-Chloro-1,2-diphenylethanol Isomer,	mmoles	QBA, mmoles	Solvent[a]	Time, hours	Cl^-, %	"Glycol," %
E	*erythro*	0.884	2.54	DMAc	11.2	46.4	
F	*erythro*	.884	0	DMAc	11.0	5.1	
G	*threo*	.884	2.54	DMAc	13.0	12.9	
H	*threo*	.884	0	DMAc	13.2	1.2	
I	*erythro*	1.29	3.86	DMF	12	74	
					34	83	
					36[b]	89[b]	75
					50	..	..
J	*threo*	1.29	3.86	DMF	60	..	12
					85	52	..
					240	99	48
K	*erythro*	0.70	1.45	Sulfolane	25	75	
					46	82	79

[a] Total volume 10.0 ml. at 88.8°; DMAc = N,N-dimethylacetamide, DMF = N,N-dimethylformamide, QBA = 8-quinolineboronic acid. [b] This point was from a duplicate experiment, run for 36 hr.

These experiments show that the reaction of 8-quinolineboronic acid with the isomeric chloroindanols and chlorodiphenylethanols is stereoselective. Displacement occurs with inversion of configuration to give esters which afford 1,2-glycols on mild hydrolysis. Stereochemically the reaction is similar to the solvolysis of *trans*-2-acetoxycyclohexyl brosylate in wet acetic acid, which yields *cis*-2-acetoxycyclohexanol as a product.[13] The results are consistent with a mechanism for the reaction of 8-quinolineboronic acid in which halogen is displaced by oxygen (path 2) rather than by nitrogen (path 1). The nature of the activation and bonding of the nucleophilic oxygen cannot be ascertained from the data presently available. Attractive possibilities include: 2a, in which the oxygen is located in a water molecule held between boron and nitrogen; 2b, in which the oxygen is covalently bound to boron and one hydrogen; and 2c, in which the oxygen is covalently bound to two boron atoms.



2b



2c

Experimental

Reaction of 8-Quinolineboronic Acid with *trans*-2-Chloroindanol (Expt. C).—*trans*-2-Chloroindanol[4] (0.338 g.,2 mmoles, m.p. 123–124°) and 8-quinolineboronic acid (0.9257 g., 5.35 mmoles) were dissolved in sufficient dimethylformamide to make 10 ml. of solution at 88.8°. After 60.5 hr., titration of a 1-ml. aliquot for glycol indicated 100% reaction. Dimethylformamide was distilled from the remaining solution at 2.5 mm. and a temperature below 50° in a Roto-vac apparatus. The yellow-brown residue was treated with 40 ml. of an aqueous solution containing 1.3 g. of mannitol, and the tan solid which precipitated was collected and dissolved in hot water. After cooling and filtration to remove traces of quinolineboronic acid which had carried through, the solution was evaporated to dryness at reduced pressure. The resulting solid, 0.257 g., m.p. 96–99°, afforded on recrystallization from water short white needles of *cis*-1,2-indandiol, m.p. 105–106°, lit.[9] m.p. 107–108°, weight 0.2208 g. (82%).

(13) S. Winstein, H. V. Hess and R. E. Buckles, *J. Am. Chem. Soc.*, **64**, 2796 (1942). For a related reaction see S. L. Lapport and L. L. Fernstandig, *J. Org. Chem.*, **26**, 3681 (1961).

erythro-**2-Chloro-1,2-diphenylethanol.**—Desyl chloride (20 g.) was reduced by 1.0 g. of lithium aluminum hydride in 300 ml. of ether by the procedure employed by Lutz, Wayland and France[14] for reduction of bromohydrins. On hydrolysis and crystallization of the resulting oil from a hexane–pentane solution at 0°, 8.0 g. (40%) of *erythro*-2-chloro-1,2-diphenylethanol was obtained, m.p. 76–77°, lit.[15] m.p. 76°.

In an alternate and more convenient procedure this chlorohydrin was prepared by treating 2.0 g. of *trans*-stilbene oxide (m.p. 66–67°, prepared by the method of Curtin and Kellom[16]) with 50 ml. of a saturated, anhydrous ethereal hydrogen chloride solution. Anhydrous hydrogen chloride was bubbled through the solution for a few minutes and the mixture was set aside at room temperature for 15 hr. The ether solution was then washed with ice-water, dried over magnesium sulfate, and concentrated on a steam-bath. Crystallization of the resulting oil from hexane–pentane yielded 1.9 g. (80%) of the chlorohydrin, m.p. 76–77°. The infrared spectrum was identical with that of the chlorohydrin obtained by reduction of desyl chloride with lithium aluminum hydride.

Attempts to prepare the chlorohydrin by use of aqueous, concentrated hydrochloric acid were unsuccessful.

threo-**2-Chloro-1,2-diphenylethanol**, 1.9 g. (56%), m.p. 42–43°, lit.[15] m.p. 47°, was obtained from 3.0 g. of *cis*-stilbene oxide,[16] (m.p. 36–37°, lit. m.p. 37–37.5°) by the same method used to convert the *trans*-oxide to the *erythro*-chlorohydrin. The infrared spectrum of the *threo* compound was the same as that of the *erythro* isomer except for a small bathochromic shift in the position for the O–H stretching band.

Reaction of the Chlorodiphenylethanols with Base.—The stereochemical assignment of the isomeric chlorodiphenylethanols was confirmed by reconverting the alcohols to the corresponding stilbene oxides. For this purpose a solution of 0.46 g. of *erythro*-2-chloro-1,2-diphenylethanol in 20 ml. of ethanol was added to 10 ml. of 8 *M* aqueous potassium hydroxide. Sufficient ethanol was added to give a clear solution, and the mixture was heated on a steam-bath for 15 min. Cooling in an ice-bath, while scratching the sides of the flask with a glass rod, caused the separation of *trans*-stilbene oxide, 0.39 g. (83%), m.p. 66–67°. The infrared spectrum was identical with that of the *trans*-stilbene oxide used for the synthesis of the chlorohydrin.

In the same manner and with identical quantities of reagents, a 66% yield of *cis*-stilbene oxide, m.p. 35°, was obtained from *threo*-2-chloro-1,2-diphenylethanol.

Reaction of *erythro*-2-Chloro-1,2-diphenylethanol with 8-Quinolineboronic Acid (Expt. I).—To 0.670 g. (3.86 mmoles) of 8-quinolineboronic acid and 0.300 g. (1.29 mmoles) of *erythro*-2-chloro-1,2-diphenylethanol in a volumetric flask was added enough dimethylformamide to give 10 ml. of solution at 88.8°. The temperature was maintained at 88.8° for 50 hr. Aliquots (0.5 ml. each) taken at the end of 12 and 34 hr. indicated 74% and 83% conversion to chloride ion, respectively. At the end of 50 hr. the mixture was evaporated on a Roto-vac at 40°. The residue was heated with boiling water and the solution was cooled and filtered to remove 8-quinolineboronic acid (0.482 g.). After three extractions with 50-ml. portions of ether, the aqueous filtrate deposited, on standing, an additional 0.12 g. of 8-quinolineboronic acid. From the ether extracts was obtained 0.258 g. of a solid residue, which on recrystallization from alcohol–water afforded white needles melting at 101–103°. After recrystallization from benzene–hexane the *dl*-hydrobenzoin melted at 117–118°, lit.[10] m.p. 119–120°, yield 0.182 g. (73.5%).

Anal.[17] Calcd. for $C_{14}H_{14}O_2$: C, 78.5; H, 6.59. Found: C, 78.9; H, 6.53.

In order to test the possibility that *meso*-hydrobenzoin might have been produced and isomerized to the *dl*-hydrobenzoin, a mixture of 0.400 g. of 8-quinolineboronic acid, 0.272 g. of 8-quinolineboronic acid hydrochloride and 0.257 g. of *meso*-hydrobenzoin was heated in dimethylformamide (10 ml. of solution) at 88.8° for 60 hours. The mixture was worked up as in the above experiment. Only *meso*-hydrobenzoin, m.p. 137°, 88% yield, was recovered from the ether extracts.

Reaction of *threo*-2-Chloro-1,2-diphenylethanol with 8-Quinolineboronic Acid (Expt. J).—This reaction was carried out just as the experiment with the *erythro* isomer except that the time was extended to 240 hr. and four 0.5-ml. aliquots of solution were removed for titration for chloride ion and glycol. By the procedure employed in the *erythro* experiment, a 19% yield of glycol was obtained after crystallization from alcohol–water. The melting point, 131–134°, and infrared spectrum showed this substance to be primarily *meso*-hydrobenzoin.

(14) R. E. Lutz, R. L. Wayland and H. G. France, *J. Am. Chem. Soc.*, **72**, 5511 (1950).

(15) M. D. Reulos and M. S. Letellier, *Compt. rend.*, **217**, 698 (1943).

(16) D. Y. Curtin and D. B. Kellom, *J. Am. Chem. Soc.*, **75**, 6016 (1953).

(17) Carbon, hydrogen and nitrogen analyses were made by H. Beck.