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OPTICALLY ACTIVE QUATERNARY AMMONIUM SALTS FROM d- AND l-2-OCTYL p-BROMOBENZENESULFONATE AND TERTIARY AMINES

R. C. CARY, J. F. VITCHA AND R. L. SHRINER

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Numerous reactions of optically active compounds which involve the replacement of a group attached to the asymmetric carbon atom are known. If, in a reaction of the following type, an exchange of anions is involved (*i.e.*, the group A takes with it the shared pair of electrons),

would be a carbonium ion
$$\begin{bmatrix} \mathbf{R}' \\ \mathbf{R}: \mathbf{C}: \mathbf{A} + \mathbf{X}: \mathbf{Y} \to \mathbf{R}: \mathbf{C}: \mathbf{Y} + \mathbf{X}: \mathbf{A} \\ \mathbf{R}'' \\ \mathbf{R}'' \\ \mathbf{R}'' \\ \mathbf{R}'' \\ \mathbf{R}'' \\ \mathbf{R}'' \end{bmatrix}^+ \text{which would immediately}$$

combine with the anion (:Y) to form the reaction product. Such a replacement may result in racemization or in the formation of an optically active product with or without a Walden inversion. The optically active esters of sulfonic acids constitute one class of compounds which are especially suited to the study of such reactions. Phillips, Kenyon and their co-workers,¹ by treatment of an optically active ester of a sulfonic acid of the type R"

the residue

 $R'SO_2OCH$ with ionic reagents, such as potassium acetate, have shown

the sulfonate radical may be replaced by another anion without racemization. Ammonia and primary and secondary amines were also found to react with such esters to produce optically active amines.

In the present communication it is shown that the sulfonate radical of an optically active ester may be supplanted by a tertiary amino group

¹ PHILLIPS, J. Chem. Soc., **123**, 44 (1923); *ibid.*, **125**, 399 (1925); *ibid.*, **127**, 2552 (1927); KENYON AND PHILLIPS, *ibid.*, **1930**, 1676; Trans. Faraday Soc., **26**, 451 (1930); KENYON, PHILLIPS AND PITTMAN, J. Chem. Soc., **1935**, 1072; KENYON, PHILLIPS AND SHUTT, *ibid.*, **1935**, 1663.

TABLE I	$\left[\left\langle \sum_{\substack{\mathbf{O},\mathbf{H},\mathbf{a}\\\mathbf{O},\mathbf{H}\\\mathbf{O},\mathbf{H}\\\mathbf{O},\mathbf{H}\\\mathbf{O},\mathbf{H} \right\rangle^{-} \left(\cos \left\langle \sum_{\substack{\mathbf{O},\mathbf{A}\\\mathbf{O},\mathbf{H}\\\mathbf{O},\mathbf{H}} \right\rangle^{-} \right)^{-} \right]$	$\begin{bmatrix} \alpha \end{bmatrix}_{\mathbf{D}}^{25}$ (Ethanol)	
		M. P.	111–112° 88–96 94–96
	$\left[\begin{array}{c} C_{6}H_{4}\\ (CH_{4})_{1}N_{C}^{C}H\\ CH_{4} \end{array} \right]^{\uparrow} \left(OSO_{4} \swarrow Br \right)^{-}$	[α] ²⁵ (Ethanol)	+14.72 -14.95
		М. Р.	204-205° 208-209 208-210
	C4UaCHOSO2	[α] ²⁵ (Ethanol)	
		M. P.	40-41° 30 30
			dl- d- l-

leading to the formation of quaternary ammonium salts without destruction of optical activity.



The particular esters used were those obtained by treatment of dand l-2-octanol with p-bromobenzenesulfonyl chloride in the presence of a limited amount of pyridine. The d- and l-2-octyl p-bromobenzenesulfonates were solids which could be purified by recrystallization, and it was for this reason that the p-bromo derivative was used. The two tertiary amines used, trimethyl amine and pyridine, combined readily with the optically active sulfonates to form quaternary ammonium salts, which were found to be optically active. The racemic forms were also prepared for comparison; the formulas, melting points and rotations of the compounds are summarized in Table I.

Considerable experimental difficulties were encountered in the preparation of these compounds. The 2-octyl *p*-bromobenzenesulfonates were very sensitive to moisture and were easily hydrolyzed. The quaternary ammonium salts readily decomposed to give the amine salts of *p*-bromobenzenesulfonic acid and the unsaturated hydrocarbon. The analytical data indicate that the salt from trimethylamine is pure, whereas the active pyridine salt always contained some of the pyridinium *p*-bromobenzenesulfonate and some of the racemic salt. All attempts to purify the pyridinium salt caused further racemization or decomposition.

From the data in Table I, it will be noted that the *dextro* ester produced a *dextro* quaternary salt with trimethylamine, but a *levo* pyridinium salt. Also, the *levo* ester produced a *levo* trimethyl-2-octyl ammonium *p*-bromobenzenesulfonate, but a *dextro* pyridinium salt. Whether or not a Walden inversion occurred cannot be stated, since there is no direct means of determining the configurations of the two quaternary salts.

The most interesting point to be noted is that these salts were optically active and not racemic forms. If the reaction is written electronically,

:Ö: R':S:Ö: :Ö:	C6H13 C:H CH3	$+ \underset{\vec{R}}{\overset{R}{\overset{.}{\overset{.}{N}:}}} \rightarrow$	$\begin{bmatrix} \mathbf{R} & \mathbf{C}_{6}\mathbf{H}_{13} \\ \mathbf{R} : \mathbf{N} : \mathbf{C} : \mathbf{H} \\ \mathbf{R} & \mathbf{C}\mathbf{H}_{3} \end{bmatrix}^{T}$	$\begin{bmatrix} : \ddot{\mathbf{O}}: \\ \mathbf{R}': \mathbf{S}: \mathbf{O}: \\ : \ddot{\mathbf{O}}: \end{bmatrix}^{-}$
Ι	II	III	IV	V

it is evident that the sulfonic ester (I + II) in forming the sulfonate ion (V) leaves the octyl radical (II) with the asymmetric carbon atom carry-

ing only a sextet of electrons (the cleavage is indicated by the dashes). The latter combines with the tertiary amine (III), which has an unshared pair of electrons, to form the quaternary ammonium ion (IV). During these transformations the 2-octyl carbonium ion (II) retains its configuration and does not undergo racemization. This equation, however, only represents the completed process and does not prove that the carbonium ion (II) existed for any finite interval of time actually detached from the electron donor groups (I) or (III). Thus the reaction probably involves simultaneous addition of (III) and dissociation of (I), since immediate racemization appears to occur if the carbonium ion is formed in reactions² or conditions where it is not stabilized by an electron donor.

One of the best pictures indicating how such a substitution process can occur without racemization has been suggested by Lewis³ and elaborated by Olson.⁴ According to this mechanism, the entering group approaches the face of the tetrahedron opposite the group which is being displaced.



By a slight shift of the kernel, the asymmetric carbon atom then becomes the center of a new tetrahedron. A one-step reaction thus leads to an inversion of the configuration. Applied to the present compounds this means that the tertiary amine approaches the ester in an oriented position, such that the unshared pair of electrons at one apex is opposite that face of the asymmetric carbon atom which, in turn, is opposite the sulfonate group (Fig. 1).

The kernel of the carbon atom shifts its position and a new tetrahedron is formed, attached to the tetrahedron of the nitrogen atom, thus constituting the quaternary ammonium ion and simultaneously the sulfonate anion (Fig. 2). If the amine approaches the face indicated, then an inversion

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² For example, reaction of magnesium with *d*-2-bromoöctane produces an optically inactive Grignard reagent; PORTER, J. Am. Chem. Soc., **57**, 1436 (1935).

³ LEWIS, "Valence and the Structure of Atoms and Molecules," Chemical Catalog Co., New York, **1923**, p. 113.

⁴ Olson, J. Chem. Phys., 1, 418 (1933).

in configuration takes place. This appears to be the preferred line of approach.⁵ If, however, the amine approached any of the other three faces, the sulfonate ion might be displaced without inversion. This picture, admittedly speculative, does offer a working hypothesis for replacement reactions.

EXPERIMENTAL

dl-2-Octyl p-bromobenzenesulfonate.-Thirteen grams (0.1 mole) of dl-2-octanol was placed in a dry 200-cc., three-necked, round-bottomed flask equipped with a dropping funnel, a mercury-sealed stirrer and a calcium chloride drving tube. Thirty-one and two-tenths grams (0.125 mole) of p-bromobenzenesulfonyl chloride was then added. An ice-salt bath was applied, the stirrer started and, after the temperature had fallen to 0°, 31.6 g. (0.4 mole) of dry pyridine was added dropwise over a period of three hours. Stirring was continued for four hours more, the temperature being kept below 0°. The reaction mixture, while stirred vigorously, was made acid to litmus by the addition of about 100 cc. of cold, 4 N hydrochloric acid. The ester was extracted with ether, and the ether extract washed twice with cold water and dried with sodium sulfate. The ether was removed by vacuum distillation at room temperature, the ester recrystallized by dissolving it in three times its volume of methanol and then cooling in a mixture of solid carbon dioxide and acetone. The yield of colorless crystals melting at 40-41° was 29 g. (83 per cent. theoretical). The ester is rather unstable and decomposes slowly on standing. Moisture causes hydrolysis and must be excluded during all manipulations involving the preparation and use of the ester.

Anal. Calc'd for C14H21BrO3S: Br, 22.90. Found: Br, 22.76.

1-2-Octyl p-bromobenzenesulfonate.—The procedure described above was followed, using *l*-2-octanol ($[\alpha]_{b}^{25}$ in ethanol, -10.00°). The yield of product was 27 g. (77 per cent. theoretical). It melted at 30°, and had a specific rotation in ethanol at 25° of -6.70° (c = 4.62). It was less stable and more difficult to crystallize than the inactive product. It turned tan in four weeks, and its melting point dropped to 26°, while its specific rotation increased to -7.67° , due to the formation of *l*-2-octanol by hydrolysis.

Anal. Calc'd for C14H21BrO3S: Br, 22.9. Found: Br, 22.8.

d-2-Octyl p-bromobenzenesulfonate.—This ester was prepared from d-2-octanol $([\alpha]_{2}^{\text{D}}$ in ethanol, $\pm 10.00^{\circ}$) by the same procedure. Yield, 24 g. (70 per cent. theoretical), m.p., 30°. Specific rotation in absolute ethanol at 25°, ± 7.06 (c = 1.84). Anal. Calc'd for C₁₄H₂₁BrO₃S: Br, 22.9. Found: Br, 22.79.

l-Trimethyl-2-octylammonium p-bromobenzenesulfonate.—One gram of l-2-octyl p-bromobenzenesulfonate was placed in a bomb tube and cooled to -10° . Three cubic centimeters of dry, liquid trimethylamine was then added, the tube sealed, and allowed to stand at room temperature for two days. It was again cooled, opened, and the excess amine removed by a water pump. The salt was washed with dry ether, then dissolved in 7 cc. of absolute ethanol and, while the alcohol solution was warm (35°), dry ether was added until the solution became slightly cloudy. Upon cooling to -10° , 1 g. of plates precipitated; m.p., 206-208°. Upon recrystallization from alcohol-ether mixture, a constant melting point of 208-210° was obtained.

⁵ PAULING, J. Am. Chem. Soc., 53, 1367 (1931); SLATER, Phys. Rev., 37, 481 (1931).

Specific rotation in absolute ethanol at $25^{\circ} = -14.95^{\circ}$ (c = 1.54).

Anal. Calc'd for C₁₇H₃₀BrNO₈S: S, 7.83; N, 3.42; Br, 19.60.

Found: S, 7.71; N, 3.41; Br, 19.36.

d-Trimethyl-2-octylammonium p-bromobenzenesulfonate.—The above procedure was followed, using d-2-octyl p-bromobenzenesulfonate and trimethylamine; m.p., 208-209°. Rotation in absolute ethanol at $25^\circ = +14.72^\circ$ (c = 1.29).

Anal. Calc'd for C₁₇H₃₀BrNO₃S: N, 3.42. Found: N, 3.39.

dl-Trimethyl-2-octylammonium p-bromobenzenesulfonate.—The above procedure was followed, using dl-2-octyl p-bromobenzenesulfonate. This racemic form melted at 204°.

Anal. Calc'd for C17H30BrNO3S: N, 3.42. Found: N, 3.60.

Trimethylammonium p-bromobenzenesulfonate.—This salt was prepared for comparison with the above-discussed compounds. Dry trimethylamine gas was passed slowly into an absolute ether solution of one gram of d-2-octyl p-bromobenzenesulfonate. By refluxing this mixture for three hours the quaternary salt was decomposed into octene and the salt of trimethylamine. The crystals which separated were removed and recrystallized from absolute ethanol-ether mixture. Yield, 0.5 g.; m.p., 112-114°.

Anal. Calc'd for C₉H₁₄BrNO₃S: N, 4.73. Found: N, 4.96.

dl-2-Octylpyridinium p-bromobenzenesulfonate.—Two grams of dl-2-octyl p-bromobenzenesulfonate, 2 cc. of dry pyridine and 5 cc. of absolute ether were refluxed under anhydrous conditions for thirty-five minutes, cooled and 25 cc. of absolute ether added. The salt was filtered, washed with absolute ether and recrystallized from dry acetone until the melting point was constant; m. p., 111-112°; yield, 2 g.

Anal. Calc'd for C19H25BrNO3S: Br, 18.7. Found: Br, 18.65.

1-2-Octylpyridinium p-bromobenzenesulfonate.—The above-described procedure was followed, using d-2-octyl p-bromobenzenesulfonate. The product was recrystallized seven times from dry acetone at the end of which time it melted at 88-96°. Two series of fractional crystallizations were made from this product and from the product recovered from the combined filtrates. Each series was recrystallized four times from dry ethyl acetate, then six times from absolute ethanol-dry ether mixture. This yielded four fractions.

- (a) A white crystalline solid, melting at 133-134° which was shown to be pyridinium p-bromobenzenesulfonate by melting point of a mixture with a sample of this compound prepared as described below.
- (b) A solid melting at 112°, which was optically inactive, and which was the dl-pyridinium salt described above.
- (c) A fraction which melted at 110-112°; $[\alpha]_D^{20}$ in ethanol of -2.37° (c = 1.69). *Anal.* Calc'd for C₁₉H₂₆BrNO₃S: N, 3.27. Found: N, 3.30. This was evidently a mixture of the *l* quaternary salt with some of the *dl* salt.
- (d) A fraction melting at 78-96°. This was a mixture of the *dl* quaternary salt with the pyridinium *p*-bromobenzenesulfonate. It was optically inactive.

The preparation was repeated except that the reaction time was shortened to 15 minutes, and the precipitate which resulted upon addition of the dry ether was filtered, washed with dry ether and dried *in vacuo* for five minutes. The rotation was taken immediately and found to be -6.95° . The product was not homogeneous; it melted over a range of 74-105°, and the analyses indicate that it contained some of the pyridinium *p*-bromobenzenesulfonate.

Anal. Calc'd for $C_{19}H_{28}BrNO_3S$: Br, 18.70; N, 3.27; S, 7.46. Found: Br, 19.08; N, 3.39; S, 7.81. d-2-Octylpyridinium p-bromobenzenesulfonate.—Two grams of l-2-octyl p-bromobenzenesulfonate was placed in 10 cc. of dry pyridine. The flask was stoppered and allowed to stand at room temperature for twenty-seven hours. Then 100 cc. of dry ether was added, and the precipitate was filtered and washed with dry ether. The product, which melted at 74-98°, was then fractionally crystallized from absolute alcohol-ether mixture (1:1) and two samples, melting at 88-94° and 90-94°, were obtained. They were combined and dissolved in 50 cc. of the same mixed solvent, an additional 50 cc. of dry ether added and the solution placed in the refrigerator. After two weeks, another 100 cc. of dry ether was added. After standing a total of eight weeks, the fine needles were filtered and recrystallized once from dry alcoholether mixture. The product consisted of colorless plates which had a melting point of 94-96°, and had a specific rotation at 25° in absolute ethanol of +6.95° (c = 0.65). Anal. Calc'd for C₁₉H₂₆BrNO₃S: N, 3.34. Found: N, 3.40.



F1G. 3

The reaction with pyridine was followed polarimetrically. A sample of 0.45 g. of d-2-octyl p-bromobenzenesulfonate was treated with 0.4 g. of dry pyridine, and the mixture was diluted to 15 cc. in a volumetric flask. The rotation was taken immediately and at intervals for twenty-seven days. The change in specific rotation is shown in Fig. 3.

Pyridinium p-bromobenzenesulfonate.—In 10 cc. of dry ethanol 2.59 g. (0.01 mole) of dry sodium p-bromobenzenesulfonate was added to 1.155 g. (0.01 mole) of dry pyridine hydrochloride prepared from dry hydrogen chloride and dry pyridine. After standing overnight, the sodium chloride was filter0d off, and the pyridine p-bromobenzenesulfonate precipitated by adding about 5e cc. of dry ether. The melting point was constant after five recrystallizations from a mixture of absolute ethanol and dry ether; yield, 1.2 g.; m. p., 134–135°.

Anal. Cale'd for C11H10BrNO3S: N, 4.4. Found: N, 4.3.

SUMMARY

The reaction between d- and l-2-octyl p-bromobenzenesulfonate and trimethylamine and pyridine produced optically active quaternary ammonium salts. The salts obtained from trimethylamine had the same direction of rotation as the original esters whereas those prepared from pyridine had rotations in the opposite directions.

It is pointed out that the reaction probably involves simultaneous addition of the tertiary amine and expulsion of the sulfonate anion.