

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES, UNIVERSITY OF CALIFORNIA]

Investigation of Methods for Preparing Pure Secondary Alkyl Halides

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Received February 10, 1961

Investigation of various reagents has failed to reveal any method for one-step conversion of a secondary alcohol to the corresponding *sec*-alkyl bromide without some rearrangement to an isomeric secondary bromide. Conversion to a pure alkyl chloride in relatively low yield is possible by use of thionyl chloride and pyridine. Pure *sec*-alkyl bromides may be prepared in a two-step process involving preparation of the tosylate and displacement of tosylate by bromide. By carrying out the displacement in dimethyl sulfoxide, moderately good yields (50–66%, based on alcohol) may be realized, and this appears to be the best available method for converting a secondary alcohol to a pure secondary bromide. The process is not satisfactory for making optically active bromides, however, for multiple displacements result in almost complete racemization. Several reagents have been examined for isomerization of secondary bromides after their synthesis. Methods have been developed for convenient and effective analysis of mixtures of *sec*-amyl halides and alcohols by gas chromatography. These methods are more accurate and reliable than infrared analysis.

It has long been recognized that conversion of secondary alcohols to the corresponding alkyl halides is likely to be accompanied by rearrangement to isomeric secondary halides, and data presented about ten years ago¹ indicated that such preparations of bromides had always been accompanied by some rearrangement. In that work,¹ pure samples of 2- and 3-bromopentane were prepared by reaction of bromine with the silver salts of the appropriate carboxylic acids.² Mixtures were analyzed by use of the binary melting point diagram constructed with the pure anilides prepared by reaction of the *sec*-amylmagnesium bromides with phenyl isocyanate. In subsequent work, it was reported³ that pure *sec*-amyl bromides may be prepared in low yield from the alcohols *via* conversion to the tosylate and displacement by bromide ion in diethylene glycol at room temperature. In this work, analysis of mixtures was accomplished much more conveniently by use of infrared spectroscopy. In the present work, infrared analysis has been found useful; however, it is less accurate and less sensitive than is gas chromatography on polypropylene glycol.⁴ This analytical device has permitted an effective examination of the preparation and isomerization of secondary halides.

All efforts to convert a *sec*-amyl alcohol to the bromide in a one-step process have resulted in some rearrangement to give the isomeric secondary bro-

midide. The more pertinent results are summarized in Table I. It may be noted that the use of a basic solvent⁵ with phosphorus tribromide resulted in a drastic lowering of the yield of bromide, and significant rearrangement continued to occur, even when pyridine was also added (Runs 5, 6). Reduction of yield was probably due in part at least to decreased rate of reaction (Runs 5, 6); however, improvement in yield was not investigated since rearrangement occurred. Decrease in extent of rearrangement as well as rate of reaction may be ascribed to removal of acid which would be expected to form the more readily dissociated oxonium salt of the intermediate phosphite ester⁶; however, persistence of rearrangement in presence of base indicates that the phosphite ester of the secondary alcohol dissociates to some extent at room temperature without assistance from acid. This is in contrast with the results reported with a primary alcohol. The highly hindered neopentyl alcohol has been converted⁷ in moderately good yield to neopentyl bromide in a high temperature reaction with phosphorus tribromide in presence of quinoline. It is also of interest that *sec*-butyl alcohol has been converted⁸ to the bromide with phosphorus tribromide without rearrangement (secondary positions distinguished by use of carbon-14). This must be ascribed to the lesser hindrance in the *sec*-butyl structure, as compared with the *sec*-amyl or higher radical. Examination of models suggests that hindrance to back side attack is not as serious as hindrance in the transition state for an S_N2 reaction. This hindrance may be further

(1) J. Cason and R. H. Mills, *J. Am. Chem. Soc.*, **73**, 1354 (1951).

(2) Rearranged bromides have not been detected in the reaction product from the silver salt and bromine reaction, probably because the intermediate species is a free radical. Among numerous references concerned with this matter may be cited: S. J. Cristol, J. R. Douglass, W. C. Firth, Jr., and R. E. Krall, *J. Am. Chem. Soc.*, **82**, 1829 (1960); R. G. Johnson and R. K. Ingham, *Chem. Rev.*, **56**, 219 (1956); J. Cason, M. J. Kalm, and R. H. Mills, *J. Org. Chem.*, **18**, 1670 (1953).

(3) H. Pines, A. Ruden, and V. N. Ipatieff, *J. Am. Chem. Soc.*, **74**, 4063 (1952).

(4) The samples giving variable results by infrared analysis at different wave lengths contained an impurity not separable by fractional distillation but giving an extraneous band in the gas chromatographic analysis.

(5) It has been reported [A. M. Buswell, W. H. Rodebush, and M. F. Roy, *J. Am. Chem. Soc.*, **60**, 2528 (1938)] that anhydrous hydrogen chloride does not form ionic species in ether, but forms a strongly hydrogen-bonded complex with the ether.

(6) For a discussion of the mechanism of the reaction of alcohols with phosphorus tribromide, cf. W. Gerrard, *J. Chem. Soc.*, 848 (1945).

(7) L. H. Sommer, H. D. Blankman, and P. C. Miller, *J. Am. Chem. Soc.*, **76**, 803 (1954).

(8) A. T. Shulgin, *J. Am. Chem. Soc.*, **77**, 2338 (1955); P. S. Skell, R. G. Allen, and G. K. Helmkamp, *J. Am. Chem. Soc.*, **82**, 410 (1960).

TABLE I
 CONVERSION OF 3-PENTANOL TO THE BROMIDE

Run No.	Reagent	Solvent	Reaction Time, ^a Hr.	Yield, %	% 2-Isomer ^b	
					Infrared	VPC
1	PBr ₃	—	15	47	15	15
2		Ether	12	13	10	5
3		Ether	18 ^c	10	9	5
4		Dioxane	17	20	14	10
5		Ether ^d	42	10	10	5
6		Ether ^d	166	22	10	5
7	PBr ₅	Ether ^e	24	45	8	6
8		Ether ^e	36	47	7	7
9		Ether	22	40	10	6
10		Ether ^d	20	15	7	5
11		Benzene	22	40	10	8
12		Benzene ^d	26	22	9	7
13	SOBr ₂	f	3	60	—	1-3
14		f	6	55	—	1-3

^a As described in the Experimental, phosphorus halide was added dropwise to the alcohol at 0°, and the mixture allowed to stand for the indicated period of time, at room temperature unless otherwise specified. ^b The reported figures are per cent of 2-isomer in the product *sec*-amyl halides. ^c This run initially at -10°, then at 0°. ^d In these runs, one molar equivalent of pyridine was added to the reaction mixture prior to addition of the phosphorus halide. ^e In these runs, the alcohol was added to the phosphorus pentabromide solution. ^f The sulfite ester was prepared with thionyl chloride, isolated, and then allowed to react with thionyl bromide at 65° (Run 13) or 50° (Run 14) in presence of 0.005 molar equivalent of pyridine hydrobromide (*cf.* Experimental).

increased by formation of di- and trialkyl phosphites.⁹

Any interpretation of the results of the reactions with phosphorus pentabromide is handicapped by the meager knowledge of the mechanism of this reaction; however, it is apparent that rearrangement occurs. The much higher yields with phosphorus pentabromide in a basic solvent contraindicate the dependence of the reaction on phosphorus tribromide formed by dissociation of the pentabromide.¹⁰ It seems more probable that the ionic species,¹¹ PBr₄⁺ PBr₆⁻, are responsible for the conversion.

Formation of the dialkyl sulfite and its reaction with thionyl bromide (Runs 13, 14) were carried out essentially as described by Gerrard and co-workers.¹² The small but definite amount of rearranged product must be formed during the reaction, for heating of a *sec*-amyl bromide with thionyl chloride does not cause rearrangement (*cf.* Table III). The alkyl bromosulfite, which has been suggested¹³ as an intermediate in this process, may react *via* the S_N1 or S_N2 route to give unrearranged amyl bromide, or may dissociate to give the carbonium ion, hence, rearrangement. The S_N2 route must be important, as the conversion is catalyzed by traces of

pyridine hydrobromide; thus increase in bromide ion should help eliminate the undesirable S_N1 reaction path; however, reaction of thionyl bromide with pyridine hydrobromide¹⁴ interferes with this approach. Lack of reaction between thionyl chloride and pyridine hydrochloride allows the conversion to unrearranged alkyl chloride (see below).

The preparation of pure *sec*-amyl chlorides by use of thionyl chloride and pyridine was claimed by Whitmore and Karnatz,¹⁵ and application of the highly sensitive gas chromatographic analysis verifies this report (*cf.* Table II). Success of this conversion no doubt depends on favoring of the S_N2 reaction path for the chlorosulfite by the high concentration of chloride ion which is realized. Utility of the synthesis is limited by the disappointingly low yields obtained,¹⁶ especially for the 2-isomer.

It has been reported by Stevens and co-workers¹⁷ that thermal decomposition of optically active 2-

 TABLE II
 PREPARATION OF *sec*-AMYL CHLORIDES

Reactant	Reagent	Yield, %	% Isomer ^a (vpc)
3-Pentanol	SOCl ₂ , pyr.	42	0
2-Pentanol	SOCl ₂ , pyr.	25	0
3-Pentanol	CH ₃ CN, HCl	45	10

^a Per cent of rearranged chloride in product.

(14) M. J. Frazer and W. Gerrard, *J. Chem. Soc.*, 3624 (1955).

(15) F. C. Whitmore and F. A. Karnatz, *J. Am. Chem. Soc.*, 60, 2536 (1938).

(16) Similarly poor yields were reported by the earlier workers, and persistent efforts have failed to improve them. Large amounts of tarry nonvolatile material are formed, especially in preparation of the 2-isomer.

(17) C. L. Stevens, D. Morrow, and J. Lawson, *J. Am. Chem. Soc.*, 77, 2341 (1955).

(9) W. Gerrard, A. Nechvatal, and B. M. Wilson, *J. Chem. Soc.*, 2088 (1950), have isolated a 25% yield of di-neopentyl phosphonate after reaction of neopentyl alcohol with phosphorus tribromide and hydrolysis of the reaction product.

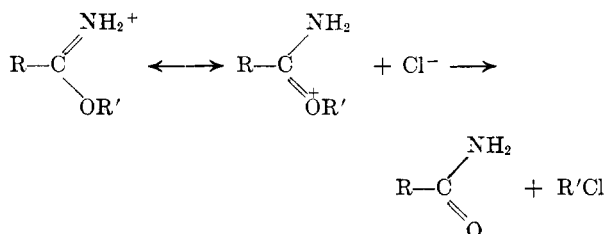
(10) A. I. Popov and N. E. Skelly, *J. Am. Chem. Soc.*, 76, 3916 (1954).

(11) G. S. Harris and D. S. Payne, *J. Chem. Soc.*, 4617 (1956).

(12) M. J. Frazer, W. Gerrard, G. Machell, and B. D. Shepherd, *Chem. & Ind.*, 931 (1954).

(13) W. Gerrard, *J. Chem. Soc.*, 99 (1939).

butyl iminoacetate hydrochloride yields a 2-chlorobutane with configuration opposite to that of the starting alcohol and regarded as optically pure. It may be assumed that these results depend on displacement of the amide from the imino ester cation:



As in reaction of an alcohol with phosphorus tribromide, however, utilization of the larger amyl group results in significant rearrangement, probably by way of dissociation of the imino ester cation to amide and amyl carbonium ion.

Pines and co-workers³ concluded, on the basis of infrared analysis, that pure *sec*-amyl bromides result from a displacement reaction on the tosylates, and application of gas chromatographic analysis has supported this claim. Furthermore, use of dimethylformamide or dimethyl sulfoxide (DMSO) as a solvent results in considerably higher yields than previously obtained. Use of dimethyl sulfoxide as solvent appears to be the preferred method¹⁸ for preparation of pure secondary bromides from the corresponding alcohols. Over-all yields of *sec*-amyl bromides were 57–66%, and yields of pure 2- and 3-octyl bromides were 50–52%.

Although the procedure described above completely avoids rearrangement of the *sec*-alkyl grouping and hence may be assumed to avoid the carbonium ion as an intermediate species, racemization occurred when the method was applied to (+)-2-butanol.¹⁹ This result indicates that, under the conditions employed, there occurs extensive displacement of bromide by either tosylate or bromide, or both, possibly some displacement of tosylate by tosylate.

The rearrangement of secondary bromides occurring under certain conditions was investigated, as summarized in Table III. It may be noted that the reaction conditions that were utilized for the syntheses do not promote significant rearrangement of pre-formed bromides, and a normal washing procedure with concentrated sulfuric acid is not objectionable. Prolonged exposure to sulfuric acid does cause rearrangement, presumably by way of ionization of the bromide, and reactions with phosphorus tribromide should not be continued for excessive lengths of time. The latter is significant in connection with the fact that a low temperature

(18) It is imperative that the dimethyl sulfoxide used as solvent be dried by fractional freezing or distillation, and subsequently protected from moisture; otherwise, some rearranged bromide results.

(19) We are indebted to Prof. F. R. Jensen, of this department, for the sample of active 2-butanol.

TABLE III
ISOMERIZATION OF *sec*-AMYL BROMIDES

Reagent	Time	Temp.	% 3-Bromopentane ^a
Concd. H ₂ SO ₄	1 min.	25	70
Concd. H ₂ SO ₄	2 hr.	25	59
PBr ₃	24 hr.	25	70
PBr ₃	120 hr.	25	66
PBr ₃	3 hr.	70–75	66
Concd. HCl	2.5 hr.	25	70
SOCl ₂	4 hr.	80–85	100 ^b

^a Except in the instance specified, the starting material contained 70% of 3-bromopentane. Experimental error is not more than $\pm 2\%$. ^b In this run, pure 3-bromopentane was used.

reaction with phosphorus tribromide may well represent the best conversion of an optically active alcohol.²⁰

When either of the *sec*-amyl bromides was equilibrated by shaking with concentrated sulfuric acid, the resultant mixture contained 66% $\pm 1\%$ of the 2-bromopentane. Similarly, when 3-bromopentane was treated with zinc chloride in concentrated hydrochloric acid, there was obtained a mixture of 66% of 2-chloropentane and 34% of 3-chloropentane. If the equilibration in both instances proceeds through the carbonium ion, as these data indicate, then the equilibrium concentrations must depend on the relative energies of the two isomers. As there are two 2-positions, the data indicate equal energy for the two secondary halides.

EXPERIMENTAL

Materials. *2-Pentanol*, prepared in the usual manner²¹ from methylmagnesium bromide and butyraldehyde (b.p. 74.2–75.0°), was obtained in 80% yield, b.p. 117–118°, n_D^{20} 1.4102.

A sample of this alcohol was also prepared by hydrogenation over Raney nickel catalyst at 1500 p.s.i. of commercial 2-pentanone, b.p. 101.1–101.8°. The product, b.p. 117.0–117.5°, contained 13% of 3-pentanol (gas chromatography), and hence was of no value for these studies.

3-Pentanol, prepared from ethylmagnesium bromide (ethyl bromide, b.p. 38.2–38.4°) and propionaldehyde (b.p. 47.8–48.2°), was obtained in yields of 75–90%, b.p. 114.4–115.0°, n_D^{20} 1.4060.

2-Bromopentane, b.p. 117.0–118.0°, n_D^{20} 1.4398, and *3-bromopentane*, b.p. 118.0–119.0°, n_D^{20} 1.4448, were prepared by the silver salt and bromine reaction as previously described.¹ These pure samples were used for reference in developing the analytical methods used for mixtures.

2-Octanol, prepared from *n*-hexylmagnesium bromide (*n*-hexyl bromide, b.p. 154.0–155.0°) and acetaldehyde (b.p. 20–25°), was obtained in 84% yield, b.p. 67.5–68.5°/6 mm., n_D^{20} 1.4275.

3-Octanol, prepared from *n*-amylmagnesium bromide (*n*-amyl bromide, b.p. 127.4–128.5°) and propionaldehyde

(20) For example, cf. F. S. Prout, J. Cason, and A. W. Ingersoll *J. Am. Chem. Soc.*, **70**, 298 (1948).

(21) J. Cason and H. Rapoport, *Laboratory Text in Organic Chemistry*, Prentice-Hall, Inc., Englewood Cliffs, 1950, p. 321.

(22) For all boiling points reported, the product was distilled through a 24-in. Podbielniak column of the simple design described in ref. 21, p. 237.

(b.p. 48.0–48.7°), was obtained in 78% yield, b.p. 69.5–70.4°/7 mm., n_D^{20} 1.4260.

Thionyl bromide was prepared from technical thionyl chloride and hydrogen bromide, as has been described,²³ in 95% yield, b.p. 67.0–69.0°/40 mm.

Phosphorus pentabromide. A solution of 160 g. of bromine in 300 ml. of chloroform was added dropwise, with vigorous stirring, to a solution of 270 g. of phosphorus tribromide in 300 ml. of chloroform. After the addition had been completed the supernatant liquid was decanted, and the crystals were transferred to a sintered glass filter where they were washed with chloroform and immediately transferred to a vacuum desiccator. The yield of bright yellow crystals was 420 g. (98%), m.p. 75–77° dec.; lit.²⁴ m.p. < 85°.

Dimethyl sulfoxide was purified by cooling a commercial sample in a refrigerator until about one-fourth of it had frozen. The white crystals remaining after decantation of the brown supernatant liquid had a m.p. of 19–20° and gave a pale yellow melt; lit.²⁵ m.p. 18.45°.

The infrared spectrum of the purified dimethyl sulfoxide was unchanged by heating at 60° (broad sulfoxide band at 9.45–9.82 μ); however, when a solution of sodium bromide in purified dimethyl sulfoxide was heated to 60°, then allowed to stand overnight, needle-like crystals separated (decomposed at 215–280°). After the crystals had been washed with acetone and dried in a vacuum at 80°, the analysis (C, 4.24; H, 1.54; S, 4.84) indicated presence of some organic material, and the elementary ratio was different from that in dimethyl sulfoxide. This product was not further examined, but it was concluded that dimethyl sulfoxide solutions of sodium bromide should not be heated.

Dimethylformamide was purified by shaking with potassium hydroxide, then with calcium oxide, and finally distilling, b.p. 151.0–151.3°.

Tosyl chloride was commercial material; "wet" samples were purified by crystallization from petroleum ether.

Other reagents and solvents were commercial materials which were purified by conventional methods.

Analytical. The infrared spectra recorded for the 2- and 3-bromopentanes were identical with those previously reported³; analytical bands were at 10.18, 13.23, and 13.39 μ in the 2-isomer and at 12.24 and 12.44 μ in the 3-isomer. Analytical bands for 2-chloropentane were at 10.17, 13.17, and 13.40 μ , while those for 3-chloropentane were at 12.18 and 12.38 μ . There was no band suitable for analysis of 2-bromooctane in mixtures of the 2- and 3-bromooctanes, but 3-bromooctane exhibits an analytical band at 12.55 μ . Limits of detection in the infrared analysis were 1% of 3-bromopentane in the isomer, and 3% of 2-bromopentane in the isomer. Analyses based on the different bands usually agreed to about 2%, but in Run 2, Table I, analysis based on the 13.23- and 13.39- μ bands indicated presence of 15% of 2-bromopentane, while analysis based on the 10.18- μ band indicated 5% of 2-bromopentane, in agreement with the analysis by gas chromatography, which revealed presence of an impurity. Analysis of known mixtures by infrared gave values within 3% of the true values, while gas chromatography gave values within 1% of the true values.

Gas chromatographic analysis was carried out on a 3-meter column containing polypropylene glycol as partitioning agent, and relative areas of the two bands were used as a measure of percentage composition. Numerous other partitioning agents were found to be relatively ineffective; tri-*o*-tolyl phosphite would be second choice. Retention times for the compounds analyzed are recorded in Table IV. It is of interest that the 3-isomers were always of shorter retention time, except for the bromopentanes, in which instance the 2-isomer has the shorter retention time.

(23) H. Hibbert and J. C. Pullman, *Inorg. Syntheses*, 1, 113 (1939).

(24) E. B. R. Prideaux, *J. Chem. Soc.*, 95, 445 (1909).

(25) T. Smedslund, *Nord Kemistmotet, Helsingfors*, 7, 199 (1950); *Chem. Abstr.*, 48, 6954 (1954).

TABLE IV

RETENTION TIMES IN GAS CHROMATOGRAPHY ON POLYPROPYLENE GLYCOL^a

Compound	Temp.	Retention Time, (Min.:Sec.)
2-Bromopentane	60	61:12
3-Bromopentane		65:24
2-Chloropentane	55	39:35
3-Chloropentane		36:58
2-Pentanol	50	130:52
3-Pentanol		120:16
2-Bromooctane	100	106:30
3-Bromooctane		101:56

^a Column was 1/4 in. by 3 m.; helium flow rate was 60 ml./min.

Limits of detection in gas chromatography analysis were 0.5% of 2-bromopentane in the isomer and 1% of 3-bromopentane in the isomer.

Reactions with phosphorus halides. In a typical procedure, a solution of 17.5 g. (0.20 mole) of 3-pentanol in 30 ml. of dry ether was stirred in a dry atmosphere and cooled to 0°. Then there was added dropwise 24.3 g. (0.09 mole) of phosphorus tribromide. Cooling was continued so as to maintain the temperature below 5° during the addition. After completion of addition the solution was allowed to warm to room temperature and stand for the specified period of time. After the reaction mixture had been poured onto crushed ice, the organic layer was separated, washed with water and with 10% sodium carbonate solution, then dried over anhydrous potassium carbonate and fractionally distilled. There was received a principal fraction of bromopentanes weighing 3.9 g. (13%), b.p. 115.2–115.8°. In most runs, there was only a small distillation residue. Results are summarized in Table I.

In runs utilizing phosphorus pentabromide, equimolar amounts of the pentabromide and the alcohol were used, and the pentabromide was dissolved in 100 ml. of benzene or 300 ml. of ether per 0.06 mole.

Reactions with thionyl bromide. A solution of 5.9 g. (0.05 mole) of thionyl chloride (distilled from quinoline and linseed oil) in 5 ml. of dry ether was added dropwise during 30 min. to a stirred solution of 8.8 g. (0.10 mole) of 3-pentanol and 7.9 g. (0.10) mole of dry pyridine in 10 ml. of dry ether. Reaction temperature was –10°. After addition had been completed, the precipitated pyridine hydrochloride was removed by filtration, and ether was distilled at reduced pressure. To the residue were added 10.40 g. (0.05 mole) of thionyl bromide and 0.08 g. (0.5 mmole) of pyridine hydrobromide. Then the mixture was heated at 65° for 3 hr. (vigorous gas evolution). At the end of the heating period, the reaction mixture was poured onto crushed ice and worked up as described for the phosphorus halide reactions. The yield of *sec*-amyl bromides was 9.0 g. (60%), b.p. 117.2–118.0°.

2-Chloropentane, prepared according to the described procedure,¹⁶ had a b.p. of 94.8–95.3°, n_D^{20} 1.4068.

3-Chloropentane, similarly prepared,¹⁶ had a b.p. of 95.4–96.3°, n_D^{20} 1.4102.

3-Amyl iminoacetate hydrochloride was prepared from 3-pentanol, acetonitrile (distilled from phosphorus pentoxide, b.p. 80.8–81.3°), and hydrogen chloride gas according to the described method.¹⁷ The yield of white crystals was 64%, m.p. 110.0–111.0° dec. Thermal decomposition of the salt gave 70% yield of chloropentanes, b.p. 95.3–96.7°.

Tosyl esters. These esters were prepared according to the method of Tipson,²⁶ with the following exceptions: ether

(26) R. S. Tipson, *J. Org. Chem.*, 9, 235 (1944).

was used as the extraction solvent; the ether and any residual alcohol were removed under reduced pressure at room temperature; the pyridine was distilled from barium oxide in a dry atmosphere, then stored over barium oxide in tightly stoppered bottles. When large runs were carried out, the alcohol-pyridine mixture was cooled to -20° , and the tosyl chloride was added in 20-g. portions at intervals of 2-3 min. so that the temperature did not rise above 0° .

The yield of 3-amyl tosylate, m.p. $43.2-44.0^{\circ}$, was 78%. Attempted distillation of the liquid 2-amyl tosylate at reduced pressure resulted in its decomposition to a tarry mass at a temperature of about 50° . The crude esters, without purification, were used in all experiments.

The octyl tosylates were prepared similarly except that a reaction period of about 3 hr. was used. Any unchanged alcohol could not be readily separated from the tosylates without heating, and there is no apparent objection to presence of some alcohol, so the crude products were used in the displacement reactions. From 10 g. of the octanol, there resulted 17.5-18 g. of the crude tosylate.

Pure sec-amyl bromides. A. *N,N*-Dimethylformamide as solvent. Sodium bromide (5.1 g., 0.05 mole) was dissolved by shaking in 100 ml. of purified *N,N*-dimethylformamide; then 12 g. (0.05 mole) of 3-amyl tosylate was added to the solution. The reaction mixture was allowed to stand in a dry atmosphere for 85 hr., and then the bromide was isolated by either of two procedures.

(a) After 500 ml. of water had been added to the reaction mixture, the product was extracted with two 100-ml. portions of ether. The extract was dried over anhydrous potassium carbonate, and then fractionally distilled to yield 4.8 g. (63%) of chromatographically pure 3-bromopentane, b.p. $117.8-118.8^{\circ}$, n_D^{20} 1.4448.

(b) The reaction mixture was rapidly distilled (b.p. $95-135^{\circ}$) through the 24-in. column until about 15 ml. of distillate had been collected. The lower layer of the two-phase distillate was separated, diluted with about 10 ml. of water, and then extracted with 20 ml. of ether. The ether layer was combined with the upper layer of the distillate, the combined fractions were dried over anhydrous potassium carbonate, and the product was obtained by fractional distillation; b.p. $118.2-119.0^{\circ}$, n_D^{20} 1.4448, 5.0 g. (67%).

B. *Dimethyl sulfoxide as solvent.* Sodium bromide (5.6 g., 0.05 mole) was added to 65 ml. of dimethyl sulfoxide (much salt undissolved). Then 9.2 g. (0.04 mole) of 3-amyl tosylate was added, and the mixture was shaken for 90 hr. The residual salt was removed by filtration, and the reaction mixture was extracted directly with three 40-ml. portions of ether. The ether extracts were washed with three 30-ml. portions of ice cold 10% sulfuric acid, dried over anhydrous potassium carbonate, and then fractionally distilled to yield 4.9 g. (85%) of pure 3-bromopentane, b.p. $117.8-118.5^{\circ}$, n_D^{20} 1.4449.

When the amount of sodium bromide was reduced to 0.04 mole, the yield was only slightly lower (80%). In a run in which most of the ether was distilled from a Claisen flask, rather than through the column, the yield was reduced to 72%.

2-Bromopentane, similarly prepared with an equimolar ratio of sodium bromide, was obtained in 73% yield, b.p. $117.3-117.8^{\circ}$, n_D^{20} 1.4399.

In a run on 3-amyl tosylate, in which there was used technical dimethyl sulfoxide, the product contained 10% of 2-bromopentane (gas chromatography). In a similar run in which there was used purified dimethyl sulfoxide to which had been added 10% of water, 14.0 g. (0.06 mole) of 3-pentyl tosylate yielded 6.6 g. of a mixture of bromopentanes and pentanols. Gas phase chromatography indicated that the bromides consisted of 8% of 2-bromopentane and 92% of 3-bromopentane, while the alcohols consisted of 50% of 2-pentanol and 50% of 3-pentanol.

sec-Butyl bromide was prepared in dimethyl sulfoxide by a similar procedure. From 3.5 g. (0.05 mole) of *D*(+)-2-butanol, $[\alpha]_D^{21} + 5.04^{\circ}$, there was obtained 6.4 g. (59%) of the tosylate, which was allowed to react with 2.9 g. (0.03 mole) of sodium bromide. The yield of 2-bromobutane, $[\alpha]_D^{20} - 0.73^{\circ}$, was 3.1 g. (82%), b.p. $89.3-90.5^{\circ}$, n_D^{20} 1.4340.

2-Bromooctane was prepared from 17.5 g. of crude 2-octyl tosylate and 6.4 g. (0.06 mole) of sodium bromide, according to the procedure described for amyl bromides, except that ether was removed from the extracts under reduced pressure in a Claisen flask, and the residue was washed with 5 ml. of concd. sulfuric acid. The yield of 2-octyl bromide was 7.7 g. (52%, over-all), b.p. $86.2-87.3^{\circ}/20$ mm., n_D^{20} 1.4506.

Infrared analysis of this product showed no detectable amount of 3-bromooctane (3% detectable), and gas phase chromatography also showed none of the isomer.

3-Bromooctane was prepared similarly to the 2-isomer, in an over-all yield of 50%; b.p. $84.4-85.1^{\circ}/20$ mm., n_D^{20} 1.4582. None of the 2-isomer could be detected in this product by gas phase chromatography, but separation of the peaks was sufficient to permit detection of no less than 5%.

Isomerizations of sec-amyl bromides. For obtaining the data recorded in Table III, the mixture containing 70% 3-bromopentane was shaken with reagents in which it was insoluble (sulfuric and hydrochloric acids), or allowed to stand with reagents in which solution occurred.

In a typical equilibration experiment, 3.0 g. of pure 3-bromopentane was shaken with 7.8 g. of concd. sulfuric acid. After 5 hr., an aliquot of bromide was withdrawn, washed with water, dried over anhydrous potassium carbonate, and subjected to analysis by gas chromatography. Content of 2-bromopentane was 54%. After 7 hr., 2-bromopentane content was 65%, and this value remained constant ($\pm 1\%$) on further shaking.

For *conversion to chlorides*, 8.0 g. of 3-bromopentane was added to a solution of 13.6 g. of zinc chloride in 10.5 g. of concd. hydrochloric acid (the Lucas reagent). After this mixture had been shaken for 72 hr., it was worked up in the manner described above. Gas chromatography showed the product to consist of 66% of 2-chloropentane and 34% of 3-chloropentane (no bromides detected).

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