

TABLE III (Concluded)

Esters of 5-amino-1-naphthoic acid		M. p., °C.	Formula	Chlorine, %	
				Calcd.	Found
15	β -Diethylaminoethyl	169-170	C ₁₇ H ₂₃ O ₂ N ₂ Cl	10.99	10.95
16	β -Di- <i>n</i> -butylaminoethyl	178-179	C ₂₁ H ₃₁ O ₂ N ₂ Cl	9.36	9.53
17	β -Diethylaminopropyl	171-172	C ₁₈ H ₂₅ O ₂ N ₂ Cl	10.53	10.52
18	β -Di- <i>n</i> -butylaminopropyl	157-159	C ₂₂ H ₃₃ O ₂ N ₂ Cl	9.03	8.87
19	γ -Diethylaminopropyl	175-177	C ₁₈ H ₂₅ O ₂ N ₂ Cl	10.53	10.59
20	γ -Di- <i>n</i> -butylaminopropyl	159-160	C ₂₂ H ₃₃ O ₂ N ₂ Cl	9.03	8.98
Ester of 6-amino-1-naphthoic acid					
21	β -Diethylaminoethyl	169-170	C ₁₇ H ₂₃ O ₂ N ₂ Cl	10.99	11.08

^a Sergievskaya and Nesvad'ba [*J. Gen. Chem.* (U. S. S. R.), **8**, 931 (1938); *C. A.*, **33**, 1307 (1939)] found 212°. ^b Ref. a. The melting point is reported to be 187-188°.

oily base was extracted with ether, the solution dried with fused sodium sulfate, the solvent removed and the calcd. amount of concd. hydrochloric acid added to the base. The crystalline hydrochloride formed immediately.

Summary

Esters have been prepared which represent

combinations between eight different dialkyl-amino alcohols and 3-, 4-, 5- and 6-amino-1-naphthoic acid.

All of the esters showed decided local anesthetic activity.

ANN ARBOR, MICHIGAN

RECEIVED MARCH 14, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF ILLINOIS AND THE UNIVERSITY OF ROCHESTER]

The Action of Lithium on an Optically Active Aliphatic Chloride

BY D. S. TARBELL AND MARVIN WEISS¹

It is well known that a Grignard reagent, formed from an optically active halide in which the halogen is attached to the asymmetric carbon atom, is optically inactive.² The object of the present work was to determine whether racemization occurs likewise in the formation of a lithium compound from an optically active halide. This study of the optical stability of an alkyl lithium compound was suggested by the work of Ott,³ who showed that the action of sodium on optically active α -phenylethyl chloride yielded optically active 2,3-diphenylbutane,⁴ along with the *meso* form of the hydrocarbon, while the recovered chloride was found to be extensively racemized. Treatment of the active α -phenylethyl chloride with magnesium in moist ether gave only inactive diphenylbutane. These results indicated that, in this case, the action of sodium on the active halide was accompanied by less racemization than that of magnesium. Since sodium alkyls are too

reactive, we have studied the action of lithium on optically active 2-chlorooctane.

A few secondary aliphatic lithium compounds have been prepared by Gilman and co-workers⁵ directly from the halide and lithium metal, but the effect of varying conditions on the yield has not been studied as carefully as in the case of the primary lithium compounds or the Grignard reagent. Yields of lithium compound obtained from 2-chlorooctane in the present research under various conditions are given in Table I.

TABLE I^a

Solvent	Temp., °C.	Time, hrs.	Yield, %
Benzene	80	20	18
Dibutyl ether	140	3	0
Ethylene glycol dimethyl ether	80	2	10
Diethyl ether	35	7	22
Diethyl ether	0	5	35
Diethyl ether	0	5	52

^a Amounts of 2-chlorooctane (0.05 mole) and lithium wire (0.11 mole) were the same in all runs except the last when 0.05 mole of the chloride and 0.3 mole of lithium were used.

Low temperature and an excess of lithium increase the yield, the former probably by decreasing

(1) Part of the material in this paper is taken from the Master's Thesis of Marvin Weiss, University of Illinois, June, 1938.

(2) Pickard and Kenyon, *J. Chem. Soc.*, **99**, 65 (1911); Schwartz and Johnson, *THIS JOURNAL*, **53**, 1063 (1931); Porter, *ibid.*, **57**, 1436 (1935).

(3) Ott, *Ber.*, **61**, 2124 (1928).

(4) Wallis and Adams [*THIS JOURNAL*, **55**, 3838 (1933)] showed that in other cases the Wurtz reaction gave completely racemized products.

(5) (a) Gilman, Zoellner and Selby, *ibid.*, **55**, 1252 (1933); (b) Gilman, Zoellner, Selby and Boatner, *Rec. trav. chim.*, **54**, 584 (1935).

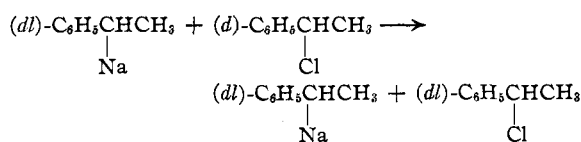
ing the amount of coupling of the lithium compound with unreacted chloride, and the latter by providing more surface of lithium metal for reaction. The lithium compound was carbonated with dry-ice to give 2-methyloctanoic acid, which was characterized by preparation of the amide. A yield of about 4% of the lithium compound was obtained from *s*-butyl bromide under the conditions used for 2-chlorooctane; Gilman^{5a} reported similar unsatisfactory results with cyclohexyl bromide.

When optically active 2-chlorooctane was treated with lithium, the acid formed by carbonation was completely inactive, and the unreacted chloride which was recovered had a lower specific rotation than the starting material. However, the boiling point and refractive index of this material showed that it contained some impurity which could not be separated completely by the fractionation of the small amount of material available. Therefore the amount of actual racemization must have been slight. The rotation of the solution of the lithium compound itself was not measured due to the difficulty of obtaining a clear solution for measurement and the high rotation of the unreacted chloride. It is possible that racemization occurred during the carbonation rather than during the formation of the lithium compound from the chloride, but the latter alternative seems more probable, especially in view of Porter's work.²

Discussion

These results support the view that free radicals, which are configurationally unstable,⁴ are an intermediate stage in the formation of the lithium compound.^{5a} The formation of active 2,3-diphenylbutane in Ott's experiments may be explained as the result of a reaction between an inactive organosodium compound and active α -phenylethyl chloride.

The racemization of the unchanged chloride which he observed⁶ may be due to an "exchange" reaction of the following type in which the sodium changes places with the chlorine of another molecule.



A similar reaction evidently does not take place

(6) Cf. Bergmann and Bondi, *THIS JOURNAL*, **58**, 1814 (1936).

between *s*-octyllithium and 2-chlorooctane under the conditions of our experiments since the recovered halide was optically active, but analogous "exchange" reactions involving lithium compounds have been reported recently.⁷

Experimental

2-Chlorooctane was prepared, following the method of Mackenzie and Tudhope,⁸ by the action of thionyl chloride in pyridine on 2-octanol. Thus, 35.3 g. of *d*-2-octanol, $\alpha^{25}_D +6.9^\circ$, without solvent, 1-dm. tube, yielded 44 g. (55%) of 2-chlorooctane, b. p. 59–63° at 12 mm., $\alpha^{25}_D -24.7^\circ$.

Preparation of *s*-Octyllithium.—All preparations were carried out in a three-necked flask with mercury-sealed stirrer, in an atmosphere of purified nitrogen. The following run is typical. Twelve g. (0.081 mole) of *l*-2-chlorooctane as above dissolved in 30 cc. of Grignard-dried ether was added over a half-hour period to 2.78 g. of lithium (0.4 mole) in 50 cc. of dry ether while cooling the flask in an ice-bath. The lithium was used as wire, and cut into the flask in small pieces, protected from oxidation by a nitrogen stream from the neck of the flask. Lithium chloride started to precipitate at once, and after six hours of stirring the mixture was allowed to settle for a half-hour and analyzed for lithium compound by titrating an aliquot portion with standard acid; yield 56%.

Preparation of 2-Methyloctanoic Acid.—The solution of lithium compound prepared above was forced through a plug of cotton in a Gooch funnel to remove unchanged lithium, and carbonated by spraying onto finely divided dry-ice. After the excess dry-ice had been removed, dilute sulfuric acid was added, the ether layer separated and the aqueous layer extracted with an additional portion of ether. The combined ether layers were extracted with 5% sodium carbonate solution, the carbonate solution washed with ether to remove any neutral material, and acidified with dilute sulfuric acid, which caused the 2-methyloctanoic acid to separate as an oil. The acid was obtained by ether extraction (weight, 1.45 g. or 20% yield based on the lithium compound present). The acid, dissolved in 15 cc. of methanol, had no optical activity whatever. Another sample of the acid made in a previous run was converted to the amide, which melted at 79–80°.⁹ An attempt to obtain a derivative of the lithium compound by treatment with phenyl isocyanate was unsuccessful, the products isolated being triphenyl isocyanurate¹⁰ and a small amount of an unidentified compound melting at 149–150°.

Isolation of 2-Chlorooctane.—The ether solution of the carbonation products of the lithium compound, from which the 2-methyloctanoic acid had been removed by sodium carbonate extraction, yielded 6.23 g. of neutral material. On fractional distillation 0.87 g. of slightly impure 2-chlorooctane was obtained, b. p. 160–170° at atmospheric

(7) Wittig, Pockels and Dröge, *Ber.*, **71**, 1903 (1938); Wittig and Pockels, *ibid.*, **72**, 89 (1939); Gilman, Langham and Jacoby, *THIS JOURNAL*, **61**, 106 (1939).

(8) Mackenzie and Tudhope, *J. Biol. Chem.*, **62**, 551 (1924).

(9) Kullhem, *Ann.*, **173**, 322 (1874), gives the melting point as 80–81°.

(10) Hofmann, *Ber.*, **18**, 765 (1885).

pressure, $n = 1.426$, while for the pure chloride, $n = 1.429$ and b. p. 168–170°. The specific rotations of the recovered chloride and of the pure chloride were determined in methanol as follows: $[\alpha]^{25}_D -26.4^\circ$ (c , 5.40) for the recovered chloride; $[\alpha]^{25}_D -31.6^\circ$ (c , 5.35) for the pure chloride. Similar results were obtained in another run; the recovered chloride had slightly less activity than the starting material.

Summary

1. *s*-Octyllithium has been prepared in 56% yield from 2-chlorooctane and lithium, and car-

bonated to give 2-methyloctanoic acid.

2. When optically active 2-chlorooctane is used, the 2-methyloctanoic acid obtained is optically inactive.

3. The 2-chlorooctane recovered from the reaction is only slightly racemized.

4. Phenyl isocyanate has been found to be unsatisfactory for characterization of *s*-octyllithium.

ROCHESTER, NEW YORK RECEIVED FEBRUARY 21, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

Kinetic Salt and Medium Effects in the Reaction between Ethylene Chlorohydrin and Hydroxyl Ion¹

BY LEON O. WINSTROM AND J. C. WARNER

In continuing our studies on the kinetic salt and medium effects and the temperature coefficients of reactions in solutions,² we have investigated the reaction between ethylene chlorohydrin and hydroxyl ion as an example of a reaction between an ion and an uncharged molecule. In this investigation, rate constants have been determined at 0, 15, 25 and 35° in water, in ethyl alcohol–water mixtures and in 1,4-dioxane–water mixtures of such composition that the dielectric constant of the mixed solvent at each temperature was equal to that of water at 35° ($D = 74.86$). The results of these experiments were used to calculate the energy of activation or critical increment of the reaction at constant solvent composition and at constant dielectric constant. The difference between these two critical increments was compared with that calculated from the relation advanced by Svrbely and Warner.^{2c} At 25°, experiments were made over a considerable range of initial concentrations and in the presence of added neutral salts. These results are compared with the predictions of the Brönsted–Christiansen theory of the salt effect.

The kinetics of this reaction was the subject of an early investigation by Evans.³ However, it is now generally recognized that he worked with impure ethylene chlorohydrin and that his hypothe-

sis that the back reaction was important was in error.^{4,5} Evans did recognize that complications were introduced by the presence of carbonate or bicarbonate ions. In later investigations, Smith⁶ studied the reaction of ethylene chlorohydrin with several hydroxides and found a drift toward higher values in his bimolecular constants, "dilution effect," with decreasing initial concentrations of reactants. Smith also made one experiment with added sodium chloride and found no appreciable effect on the velocity.

That the side reaction of ethylene chlorohydrin with water is unimportant is demonstrated by the investigation of Radulescu and Muresonu.⁷ When their pseudo-unimolecular constants for the reaction at temperatures of 56–99° are converted to bimolecular constants, a calculation of the temperature coefficient permits an estimation of the constant at 25°. The result is $k = 1.0 \times 10^{-9}$ min.⁻¹ and from this one may conclude that the side reaction of ethylene chlorohydrin with the solvent is negligible compared to the main reaction with hydroxyl ion.

Previous investigators^{3,8} have demonstrated that ethylene chlorohydrin reacting with hydroxyl ion yields ethylene oxide but the reaction with carbonate or bicarbonate ion leads to the formation of ethylene glycol.

(1) Abstracted from the thesis submitted by Leon O. Winstrom to the Committee on Graduate Instruction of Carnegie Institute of Technology in partial fulfillment of the requirements for the degree of Doctor of Science. Original manuscript received August 1, 1938.

(2) (a) Warner and Stitt, *THIS JOURNAL*, **55**, 4807 (1933); (b) Warner and Warrick, *ibid.*, **57**, 1491 (1935); (c) Svrbely and Warner, *ibid.*, **57**, 1883 (1935); (d) Eagle and Warner, *ibid.*, **58**, 2335 (1936).

(3) Evans, *Z. physik. Chem.*, **7**, 335 (1891).

(4) Brönsted, Kilpatrick and Kilpatrick, *THIS JOURNAL*, **51**, 428 (1929).

(5) Smith, *Z. physik. Chem.*, **130**, 162 (1927).

(6) Smith, *ibid.*, **51**, 339 (1912); **A152**, 153 (1931).

(7) Radulescu and Muresonu, *Bull. soc. sci. Cluj, Roumanie*, **7**, 128 (1932).

(8) Brooks, *Chem. Met. Eng.*, **22**, 629 (1920); Schrader, *Z. angew. Chem.*, **42**, 541 (1929).