the base as well as to that of chlorimine (second order reaction), and the decomposition of an ald-chlorimine with a series of bases[4] (amines) in benzene solution is more rapid the stronger the base used. Second, it can be seen from Table IV that, with the exceptions of the ortho compounds (Nos. 1, 9, 13, 15), the rates of reactions of the ald-chlorimines (RCH=NCl) with sodium hydroxide are, in general, in the same relative order as the ionization constants of the corresponding carboxylic acids (RCOOH). Because of the proximity of the ortho substituents to the aldehydic hydrogen atom of the ald-chlorimines the abnormally low constants obtained for the ortho compounds might be attributed to a so-called "steric hindrance" factor.

It would seem unlikely that chloride ion is removed first from the ald-chlorimines in the presence of cold alkali, since keto-chlorimines (RCR=NCl) as well as most other nitrogen–chlorine compounds which possess no active hydrogen, show practically no tendency to release chloride ion under similar conditions. On the contrary, these compounds[14] undergo hydrolysis to form hypochlorous acid, in which the halogen is removed presumably with only a sextet of electrons.[15] It has been shown that the rate of hydrolysis of a keto-chlorimine is very much slower than the rate of removal of hydrogen chloride from an ald-chlorimine.[4] In fact, the latter reaction probably takes place only because it is so much faster than the hydrolysis of the (N–Cl) bond. This seems best explained by the mechanism suggested, for the removal of chlorine from nitrogen with a complete octet of electrons should be considerably facilitated by the presence of a negative charge on the molecule to which the chlorine is attached. It is well known that halide ion is removed more readily from the sodium salt of a halogen amide, (RCONHal)Na, or from its negative ion, $(RCONHal)^-$, than from the corresponding halogen amide itself.

(14) Slosson [*Am. Chem. J.*, **29**, 289 (1903)] showed that certain N-substituted halogen amides (RCONR–Hal) were hydrolyzed by alkali to form RCONRH.

(15) See Sidgwick, "Electronic Conception of Valence," 1927, p. 158.

The writers wish to express their indebtedness to Dr. Douglas G. Hill for the valuable suggestions concerning the kinetics of the reactions studied.

Summary

1. Second order velocity constants have been determined for the reaction of sodium hydroxide with seventeen ald-chlorimines in 92.5% alcohol. The constants for four chlorimines have been determined also using as solvent a 50% mixture of dioxane and water.

2. The temperature coefficients and heats of activation of five ald-chlorimines with alcoholic sodium hydroxide have been determined.

3. A general mechanism has been discussed for the removal of HX from organic compounds in the presence of bases with special reference to the removal of hydrogen chloride from ald-chlorimines.

DURHAM, N. C. RECEIVED DECEMBER 31, 1934

[CONTRIBUTION FROM THE LABORATORIES OF THE UPJOHN COMPANY]

Some Organic Mercurials

BY MERRILL C. HART AND HANS P. ANDERSEN

Previous work on alkyl mercury derivatives[1] in which mercury is attached to oxygen has shown that variations in structure have a very limiting influence on the bacteriostatic properties of the resulting compounds. In the present investigation the study was extended to include compounds in which mercury is linked to the carbon of the benzene ring.

Variations in properties with different structures have been reported. Some authors[2] have tried to explain this on the basis of mercury percentage in the particular compounds. Others[3] have attributed the properties to substituents in the molecules and the positions in which they occur. For example, nitro, halogen and alkyl groups have been said to enhance the bacteriological properties. In this research these groups were not found to be particularly effective. A number of different types of compounds were prepared and our studies indicate that the euthera-

(1) Hart and Andersen, THIS JOURNAL, **56**, 2752 (1934).

(2) Caius, Kamat and Naidu, *Indian J. Med. Res.*, **15**, 327 (1927).

(3) Schoeller and Schrauth, *Z. Hyg. Infektionskrankh.*, **70**, 24 (1911); Henry, Sharp and Brown, *Biochem. J.*, **19**, 513 (1925); Raiziss and Severac, *J. Lab. Clin. Med.*, **9**, 71 (1923),

TABLE I

	Compound	Yield, %	M. p., °C.		Mercury (and halogen) analyses, % Calcd.	Found	Inhibiting dilution to *Staph. Aureus* in 5 minutes
1	Anhydro-2-hydroxymercuri-3-nitrobenzoic acid[a]	86	.....		54.8	54.7	Not over 1-500[b]
2	Anhydro-3-hydroxymercuri-4-nitrobenzoic acid[c]	85	.....		54.8	53.2	Not over 1-500
3	Mercuric mandelate	..	183–184		39.8	40.2	[d]
4	4-Acetoxymercuri-2-nitroanisole	50	187–188		48.6	48.8	1-16,000
5	4-Nitratemercuri-2-nitroanisole	..	219–220		48.3	49.1	Not over 1-2000
6	Acetoxymercuri-*m*-cresol	62	177		54.6	54.6	1-18,000
7	3,5-Diacetoxymercuri-4-hydroxybenzoic acid	..	.....		61.1	61.2	1-2000
8	*p*-Aminophenylmercuric acetate[e]	..	168–169		..	..	1-5000
9	Diacetoxymercuri-amyl-*m*-cresol[f]	..	190		57.6	57.3	1-5000
10	Diacetoxymercuri-*p*-chlorophenol	99	.....		62	61.7	[d]
11	Diacetoxymercuri-2-chloro-5-hydroxytoluene	66	.....	Cl	5.4	5.0	[d]
12	Acetoxymercuri-*p*-chlorophenol	74	.....	Cl	9.1	8.9	1-10,000
13	Acetoxymercuri-2-chloro-5-hydroxytoluene	92	.....	Cl	8.8	8.6	1-10,000
14	Acetoxymercuri-*p*-bromo-*o*-butylphenol[g]	48	159–160	Br	16.4	16.4	1-1000
15	Phenylmercuric acetate[h]	50–80	149		59.5	59.7	1-30,000
16	Phenylmercuric nitrate (basic)[i]	50	179–183		63.2	62.8	1-40,000
17	Phenylmercuric lactate	20	155–157		53.0	53.3	1-20,000
18	*p*-Tolylmercuric acetate	61	138–140		57.3	57.1	1-10,000
19	*p*-Tolylmercuric nitrate[j]	47	179–180		56.9	57.0	1-10,000
20	*p*-Tolylmercuric lactate	53	.....		52.6	52.8	1-5000
21	*o*-Hydroxyphenylmercuric chloride[k]	64	150–151	Cl	10.8	10.7	1-75,000[l]

[a] "Organic Syntheses," 1927, Vol. VII, p. 1. [b] Phenol control, 1–80. [c] German Patent 249,725, December 4, 1910. [d] Not soluble. [e] Whitmore, "Organic Compounds of Mercury," Chemical Catalog Co., New York, 1921. [f] Amyl-*m*-cresol made by the method of Coulthard, Pyman and Marshall, *J. Chem. Soc.*, 280 (1930). [g] *p*-Bromo-*o*-butylphenol made by the method of Klarmann, Gates, Shternov and Cox, THIS JOURNAL, **55**, 4657 (1933). [h] Maynard, *ibid.*, **46**, 1510 (1924). [i] This analysis for basic phenylmercuric nitrate is also reported by Pyman and Stevenson, *Pharm. J.*, **133**, 269 (1934). [j] This is *p*-substituted. It can be converted to *p*-iodotoluene, m. p. 35°. [k] "Organic Syntheses," 1925, Vol. IV, p. 13. [l] This compound was bactericidal 1–1000.

peutic mercury compounds are not to be found among the more complex mercury derivatives, but consist rather of simple mercury derivatives of hydrocarbons or phenols with limited substituents. Weed and Ecker[4] have also shown that phenylmercuric nitrate, a compound of simple structure, possesses valuable bacteriological properties.

Table I gives the analytical data and bacteriostatic values.[5] These were obtained by the same methods as mentioned in an earlier paper.[1] Where necessary acids and phenols were tested in one equivalent of alkali. Compounds previously described are indicated by references in the table.

Experimental

General Procedure.—Mercuric acetate in dilute acetic acid solution was used as the mercurating agent. It was refluxed for one to five hours with the compound to be mercurated in acetic acid or alcoholic solution. On cooling, the precipitate was filtered, washed and recrystallized from alcohol or dilute acetic acid when possible. Equimolecular quantities of the reacting compounds were used except where di-mercury compounds could be formed. For that type an excess of mercuric acetate was used. For mono-mercury compounds a large excess of the compound to be mercurated was found to be advantageous in getting the best yields. A few special cases will be described. 2-Nitroanisole and amyl-*m*-cresol were heated with mercuric acetate using no solvent.

In the acetoxymercuri compounds other anions could be substituted by treating with an excess of a salt of the anion desired, or by reaction of the chloromercuri derivative with a silver salt. Anions of weak acids could be introduced by reaction of the acid with the hydroxymercuri compounds.

4-Acetoxymercuri-2-nitroanisole.—Seven grams of 2-nitroanisole was refluxed with 3 g. of mercuric acetate for four hours at 130°. No solvent was used so as to favor mono-substitution as suggested by Hodgson.[6] On cooling, the product was filtered, washed with alcohol, and recrystallized from dilute acetic acid as brownish needles. It was slightly soluble in water.

Mercury substituted in the 4-position as it did in anisole[7] itself. This was shown by making the iodine derivative using Hodgson's[6] method. It melted at 97–98°, corresponding to the melting point of 98° given by Robinson[8] for 4-iodo-2-nitroanisole.

4-Nitratemercuri-2-nitroanisole.—An excess of a potassium nitrate solution was added to one gram of 4-acetoxy-

(4) Weed and Ecker, *J. Infect. Dis.*, **49**, 440 (1931).

(5) We are indebted to Dr. J. F. Norton, Mr. F. Mantel and Mr. E. A. Gibson, Bacteriological Laboratory, The Upjohn Company, for these results.

(6) Hodgson, THIS JOURNAL, **49**, 2840 (1927).

(7) Dimroth, *Ber.*, **54**, 1504 (1921).

(8) Robinson, *J. Chem. Soc.*, **109**, 1084 (1916).

mercuri-2-nitroanisole and heated for a few minutes. On cooling, some of the slightly soluble nitrate derivative was obtained.

Acetoxymercuri-*m*-cresol.—Five grams of *m*-cresol in 5 cc. of acetic acid was heated for one hour with 5 g. of mercuric acetate in 5 cc. of acetic acid, adding enough water to just maintain a clear solution (about 9 or 10 cc.). After standing for twenty-four hours, crystals precipitated, and on recrystallizing from alcohol with a trace of acetic acid, they melted at 177°. On standing for an additional twenty-four hours, the mother liquor precipitated more crystals which, after recrystallization, melted at 155°. This corresponded to 4-acetoxymercuri-*m*-cresol described by Mameli and Piaggesi.[9] A mixed melting point with the 177° compound was depressed. None of the 6-acetoxymercuri derivative melting at 130° was obtained.

To determine the position of the mercury in the compound melting at 177°, a small amount of it was treated with more mercuric acetate in acetic acid solution. On purifying the product obtained, it melted with decomposition at 235°. This was the decomposition temperature reported by Mameli and Piaggesi[9] for the 2,4-diacetoxymercuri-*m*-cresol derivative of 4-acetoxymercuri-*m*-cresol melting at 155°. Since both gave the same diacetoxymercuri derivative, it follows that the compound melting at 177° is 2-acetoxymercuri-*m*-cresol.

Tolylmercuric Lactate.—Tolylmercuric chloride, made from the acetate and sodium chloride, was refluxed in alcoholic solution for one hour with an excess of moist silver oxide. After filtering from the insoluble material and concentrating to a small volume, a slight excess of lactic acid was added to the warm solution. On setting aside to cool, tolylmercuric lactate crystallized. It was recrystallized from alcohol and dissolved in water for bacteriological examination.

(9) Mameli and Piaggesi, *Gazz., chim. ital.*, **62**, 158 (1932).

Summary

A number of different types of aromatic mercury derivatives in which mercury is attached to carbon have been prepared and studied.

The mercury derivatives of more complex structure were not as effective as bacteriostatic agents as the mercury derivatives of hydrocarbons or phenols with limited substituents.

Orthohydroxyphenylmercuric chloride was found to be the most powerful bacteriostatic agent of the mercury derivatives studied.

KALAMAZOO, MICHIGAN RECEIVED JANUARY 7, 1935

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF IOWA STATE COLLEGE]

Relative Rates of Formation of Some Organomagnesium and Organolithium Compounds

BY HENRY GILMAN, E. A. ZOELLNER, J. B. DICKEY AND W. M. SELBY

It has been demonstrated that *n*-butylmagnesium bromide forms more rapidly than phenylmagnesium bromide;[1] and that the order of decreasing activity of *n*-butyl halides with lithium is C_4H_9I, C_4H_9Br, C_4H_9Cl.[2] The rate studies with lithium were carried out by Ziegler and Colonius[2] incidental to their classical investigation on the preparation of organolithium compounds. Inasmuch as the yields of some organolithium compounds have been improved and also because it has been shown that many organolithium compounds can be prepard as conveniently as the related Grignard reagents it seemed advisable to compare the relative rates of formation of some of these two organometallic types under corresponding conditions. A discussion of the results follows the Experimental Part.

(1) Gilman and Zoellner, THIS JOURNAL, **50**, 2520 (1928). See also, Rudd and Turner, *J. Chem. Soc.*, 686 (1928), for a study of the competitive reactions of RX compounds for magnesium.

(2) Ziegler and Colonius, *Ann.*, **479**, 135 (1930).

Experimental Part

The procedure was essentially that used in the earlier study with *n*-butyl- and phenylmagnesium bromides.[1] One refinement was in the reduction of time (from seventeen to one or two seconds) to arrest reaction after the designated periods during which the halides reacted with the magnesium in ether. In the shortened interval of one or two seconds the reaction mixture was cooled internally by the addition of cold, dry ether, and cooled externally by the application of an ice–salt bath; and the rate of stirring increased from 380–390 to 2000–2200 r.p.m. After detaching the special flask, aliquots were removed immediately for analysis by the acid titration method. The values given in the tables are averages of numerous experiments each of which, in turn, is an average of two or more aliquots. There was the usual agreement in results for work of this kind, details for which have been supplied in earlier papers. All values given in the tables have been corrected for "drop conditions" or the rapid addition of RX compound.

In some preliminary experiments the rates of formation of *n*-butylmagnesium chloride and phenylmagnesium bromide were determined, with stirring at 1000 and 380–390 r. p. m., respectively. These results are given in Table I.