acetylene and 1-bromo-1-hexyne was recovered as *n*-butylacetylene.

Since substituted silver acetylides are stable it was believed that the action of silver bromide on an acetylenic Grignard reagent would give a stable silver derivative. When butylacetylene magnesium bromide was treated with the calculated amount of silver bromide the reaction product was found to contain no dibutyldiacetylene whatsoever. Silver butylacetylide was obtained in 60% yield. This offers corroborative evidence that the first stage of reaction between a Grignard reagent and a metal halide in the type of reaction under consideration is the formation of an organometallic compound and, if the organometallic compound is sufficiently unstable, decomposition ensues.

Experimental

Materials.—The substituted acetylenes used in this work were prepared in liquid ammonia by the usual method. The metal halides used were of analytical reagent grade.

Preparation of Diphenyldiacetylene.—In a three-necked, one-liter flask equipped with a motor-driven, mercury-sealed stirrer, a reflux condenser and a dropping funnel, 0.4 mole of ethylmagnesium bromide was prepared. To this was added dropwise and with stirring 40 g. (0.4 mole) of phenylacetylene diluted with an equal volume of ether. The contents of the flask were refluxed on a water-bath for two hours to expel all ethane. In eight small portions 90 g. (0.4 mole) of cupric bromide was added with rapid stirring. Vigorous reaction occurred after each addition. When almost all the cupric bromide had been added the precipitation of a large amount of flocculated material occurred. It was found that the reaction was quite complete within fifteen minutes after the addition of all the cupric bromide; refluxing did not increase yields. Water was added slowly through the top of the reflux condenser until no further action occurred. The ether layer was separated from the sludge of cuprous bromide, dried over calcium chloride and the ether was evaporated under diminished pressure. The non-volatile residue consisted of 29 g. of diphenyldiacetylene and 3 g. of phenylacetylene. The diphenyldiacetylene was recrystallized from the minimum amount of boiling ethanol; m. p. 87°; 72% yield.

The technique was essentially the same for all experiments except that the dibutyldiacetylene (b. p. 104° at 8 mm.) and 1-bromo-1-hexyne (b. p. 46° at 26 mm.) were isolated by fractional distillation.

Preparation of Silver Butylacetylide.—The addition of 75 g. (0.4 mole) of silver bromide to the Grignard reagent made from 33 g. (0.4 mole) of *n*-butylacetylene resulted in the formation of 46 g. of crystalline silver butylacetylide (62% yield). The *n*-butylacetylene was regenerated from the silver butylacetylide by refluxing with twice the theoretical amount of aqueous potassium cyanide.

Summary

1. Acetylenic Grignard reagents react with cupric bromide, cupric chloride and ferric chloride to yield diacetylenes predominantly and some 1-bromo-1-alkyne.

2. Confirmatory evidence is given for the intermediate formation of organometallic compounds in all reactions of this type.

NOTRE DAME, INDIANA RECEIVED MAY 23, 1936

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

Urethans as Local Anesthetics. III. Alkyl N-(8-Quinolyl) Carbamates

BY R. E. DAMSCHROEDER AND R. L. SHRINER

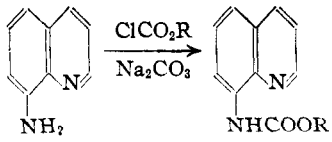
A study of *p*-aminophenyl urethans[1] showed that these compounds possessed high local anesthetic power, but were very irritating to the tissues. The irritation appeared to be associated with the *p*-phenylenediamine grouping and not with the urethan structure.[2] Since many different types of substituted quinolines exhibit local anesthetic action,[3] and are not especially irritating, it was thought that a combination of the quinoline nucleus with the urethan grouping would produce compounds with interesting pharmacological properties. Accordingly, a series of urethans derived from 8-aminoquinoline was prepared. These particular quinoline derivatives were chosen because the derivatives of 8-aminoquinoline, such as plasmoquin, are of value in treating malaria. Hence, these alkyl N-(8-quinolyl) carbamates would be of interest not only from a study of their local anesthetic action, but also because of the possibility of their antimalarial action.

8-Nitroquinoline was prepared by the Skraup reaction and reduced to 8-aminoquinoline. Treatment of the latter with alkyl chloroformates in the presence of saturated sodium carbonate solution produced the urethans.

(1) Horne, Cox and Shriner, THIS JOURNAL, **55**, 3435 (1933).

(2) Ma and Shriner, *ibid.*, **56**, 1630 (1934).

(3) Hirschfelder and Bieter, *Physiol. Rev.*, **12**, 190 (1932); Miescher, *Helv. Chim. Acta* **15**, 163 (1932).



Since the bases were insoluble, they were converted to the hydrochlorides which were used for the pharmacological tests.

Experimental

8-Nitroquinoline and 8-Aminoquinoline.—The procedures described by Smith and Getz[4] were followed. The average yield on six runs was 37% of 8-aminoquinoline, (based on the *o*-nitroaniline used) melting at 64–65° and boiling at 159–161° at 16 mm.

Alkyl Chloroformates.—The series of alkyl chloroformates was prepared from phosgene and the anhydrous alcohols according to the method of Adams, Kamm and Marvel.[5]

Alkyl N-(8-Quinolyl) Carbamates.—Two methods were used in order to obtain the urethans. The first method consisted in adding a slight excess of alkyl chloroformate to an ether solution of 8-aminoquinoline. The mixture was vigorously stirred and the precipitate of 8-aminoquinoline hydrochloride was removed by filtration. The ether was distilled, and the residue recrystallized from absolute alcohol. By this method only half of the 8-aminoquinoline was used to form the urethan, and difficulty was experienced in obtaining complete reactions, even though the mixture was stirred for several days. Better yields were obtained when the reaction was carried out in the presence of sodium carbonate.

A solution of 10 g. of 8-aminoquinoline in 75 cc. of ether and 75 cc. of saturated sodium carbonate solution was placed in a flask and stirred vigorously. A very slight excess of the alkyl chloroformate was added slowly. The mixture was stirred until a test portion of the ether layer failed to give a precipitate of 8-aminoquinoline hydrochloride upon addition of hydrochloric acid. The ether layer was then separated, dried with sodium sulfate and the ether distilled. After recrystallization from absolute alcohol the pure bases were obtained. The lower alkyl chlorocarbonates gave 80–90% yields, but the yields dropped as the alkyl group increased in size, so that the yield of the *n*-hexyl derivative was only about 10%. The properties and analyses are given in Table I. The *n*-amyl, *i*-amyl and *n*-hexyl derivatives were oils which could not be crystallized. They were converted to the hydrochlorides for analysis.

TABLE I

ALKYL N-(8-QUINOLYL) CARBAMATES

Alkyl group	M. p., °C.	Mol. formula	Nitrogen analyses, % Calcd.	Found
Methyl	61.5–62.5	$C_{11}H_{10}O_2N_2$	13.84	14.05
Ethyl	66–67	$C_{12}H_{12}O_2N_2$	12.95	12.84
n-Propyl	58–59	$C_{13}H_{14}O_2N_2$	12.16	12.07
n-Butyl	40	$C_{14}H_{16}O_2N_2$	11.46	11.83
i-Butyl	69–70	$C_{14}H_{16}O_2N_2$	11.46	11.67
n-Amyl	Oil	$C_{15}H_{18}O_2N_2$	...	...
i-Amyl	Oil	$C_{15}H_{18}O_2N_2$	...	...
n-Hexyl	Oil	$C_{16}H_{20}O_2N_2$	...	...

(4) Smith and Getz, *Chem. Rev.*, **16**, 114 (1935).

(5) Adams, Kamm and Marvel, "Organic Chem. Reagents I," *Univ. of Ill. Bull.*, **43**, 42 (1919).

Hydrochlorides.—The urethans were dissolved in anhydrous ether and the solution saturated with dry hydrogen chloride. The hydrochlorides precipitated at once as amorphous solids or viscous oils which solidified on stirring or standing. Recrystallization from absolute alcohol yielded the pure hydrochlorides as white or light yellow crystals. The salts hydrolyzed when dissolved in water and the free base precipitated. In order to obtain solutions for the pharmacological tests, it was necessary to add sufficient hydrochloric acid in order to prevent hydrolysis. The minimum normality of hydrochloric acid necessary to prevent separation of the free base is shown in Table II along with the analyses.

TABLE II

HYDROCHLORIDES OF ALKYL N-(8-QUINOLYL) CARBAMATES

Alkyl group	Minimum *N* of HCl for solution	M. p., °C. (dec.)	Chlorine analyses, % Calcd.	Found
Methyl	0.05	199–201	14.86	14.83
Ethyl	.09	165–166	14.04	14.02
n-Propyl	.19	156–157	13.30	12.83
n-Butyl	.35	146–149	12.63	11.98
i-Butyl	.7	155–165	12.63	12.33
n-Amyl	1.0	147–149	12.03	11.80
i-Amyl	1.0	149–152	12.03	11.72
n-Hexyl	1.0	145–147	11.50	12.21

Pharmacological Data

Through the courtesy of the Lilly Research Laboratories, the toxicity and local anesthetic action of the compounds shown in Table II were determined. The hydrochlorides were dissolved in the proper strength of hydrochloric acid, so as to obtain 1% solutions which were used for the tests. A brief summary of the essential data is given in Table III.

TABLE III

PHARMACOLOGICAL ACTION OF HYDROCHLORIDES OF ALKYL N-(8-QUINOLYL) CARBAMATES

Alkyl group	Toxicity Mice—intravenous, mg. per kg.	Anesthesia duration Rabbit eyes, min.	Guinea pig skin min.	Irritation rabbit eyes and rabbit skin
Methyl	65	None	56	
Ethyl	200	24	46	Severe
n-Propyl	100	None	None	Severe
n Butyl	70	None	None	Severe
i-Butyl	50	None	None	Severe
n-Amyl	70	None	None	Severe
i-Amyl	60	None	None	Severe
n-Hexyl	250	None	None	Severe

Examination of the data in Table III shows that these quinoline derivatives are not especially toxic as compared to other anesthetics, but that their local anesthetic effect is very low or absent. The severe irritation is undoubtedly due to the fact that the solutions tested were strongly acid,

the *p*H being between 1 and 2. The tests against the malarial parasite are not completed.

Summary

The hydrochlorides of a series of alkyl N-(8-quinolyl) carbamates in which the alkyl group was varied from methyl to *n*-hexyl were prepared and tested for their local anesthetic activity. The methyl and ethyl derivatives produced local anesthesia for a short time. All the compounds were irritating.

URBANA, ILLINOIS RECEIVED JUNE 15, 1936

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE CITY COLLEGE OF THE COLLEGE OF THE CITY OF NEW YORK]

The Binary System Potassium Dichromate–Sodium Dichromate

BY ALEXANDER LEHRMAN, HARRY SELDITCH AND PHILIP SKELL

The literature lists no determination of the liquidus curve of the system potassium dichromate–sodium dichromate. These are two fairly stable compounds having low melting points as compared with most salts and there existed the possibility of a low temperature eutectic mixture which could be used as a bath liquid. Furthermore as potassium dichromate has a transition point at about 240° the system offered the possibility of detecting the formation of solid solution by a change in the transition point due to solid solution. Still further the melting point of sodium dichromate is recorded in the literature on the basis of a determination made in 1886.[1] The report of this early work does not state the method of purification of the salt, nor the method of determining the melting temperature. It was thought advisable to measure it with more modern instruments.

In the work being reported the points on the liquidus curve were determined by two methods. The first was that of thermal analysis using copper–constantan couples and a potentiometer. The second was that of observing the temperature on a thermometer when crystallization of a homogeneous melt started or when the last crystal of a previously melted and solidified mix disappeared. The melting point of sodium dichromate and the transition point of potassium dichromate were determined by thermal analysis using time–temperature and time–differential temperature curves.

Experimental

Materials.—The potassium dichromate was twice recrystallized from a filtered solution of the C. P. salt and then fused in an electric furnace which was kept just above the melting point of potassium dichromate. As potassium dichromate expands on passing through its transition point the tube containing the molten salt was tilted before solidification to an almost horizontal position to prevent cracking of the tube when the expansion took place. On changing crystal form and expanding, the solid mass disintegrates and was poured from the tube as a coarse powder. In separating the crystals from the mother liquid and in subsequent handling care was taken to avoid contact with organic material.

Sodium dichromate was prepared from C. P. hydrated salt by recrystallizing twice after rejecting the first crop of crystals.[2] The recrystallized hydrate was kept in a porcelain dish at 170° for eight hours in which time it was converted to the anhydrous salt. It was then fused in Pyrex tubes set in a furnace which was maintained at a temperature just above the melting point. The molten salt was poured into a porcelain dish and the resulting solid ground to a powder and kept over phosphorus pentoxide.

The mixtures were made by weighing by difference, the weights being taken to the nearest centigram. The salts were poured from the weighing tubes directly into the Pyrex test-tubes used for the determinations.

Apparatus.—The apparatus for thermal analysis consisted of a cylinder of electrolytic copper 7.6 cm. in diameter and 12.7 cm. high, having three drilled wells. Two of the wells held Pyrex test-tubes 2.5 × 20 cm., one of which contained the dichromates and the other shredded asbestos. A thin layer of asbestos paper surrounded the test-tubes and ensured a small temperature difference between the salt and the copper block when the temperature of the block was changing. The third well, much smaller in diameter, held a chromel–alumel couple which was connected with a millivoltmeter graduated to read in degrees centigrade. This was used for the convenience of knowing the temperature of the copper block. The cylinder fitted snugly into a resistance furnace which was only slightly lagged. A rheostat and ammeter in series permitted control of the rate of heating and cooling.

The temperature measuring system consisted of two copper–constantan couples (24 gage wire) combined in the well-known way to allow a reading of the temperature of the sample, and of the difference in temperature between the sample and the shredded asbestos hereafter referred to as ΔT. Leeds and Northrup potentiometer indicators

1) A. Stanley, *Chem. News*, **54**, 195 (1886).

(2) In connection with this see Nikitina, *Trans. Inst. Pure Reagents*, **9**, 161 (1930), and Richards and Kelley, THIS JOURNAL, **33** 847 (1911).