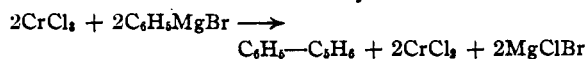


[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

**The Reaction of Metal Halides with Acetylenic Grignard Reagents**

BY JAMES P. DANEHY AND J. A. NIEUWLAND

That particular type of reaction between a Grignard reagent and a metal salt which involves the reduction of the salt and the coupling of the organic radicals was first observed by Bennet and Turner,<sup>1</sup> who treated phenylmagnesium bromide with chromic chloride in an attempt to prepare organochromium compounds of the type  $\text{RCrCl}_2$ . However, they obtained diphenyl and chromous chloride in almost theoretical yields.



This reaction was extended by the original investigators and others,<sup>2</sup> who showed that it is general for many types of Grignard reagents as well as for most metal salts which can be reduced to lower salts or, in the case of iron and silver, to the free metal. The intermediate formation of organometallic compounds is indicated by the work of Reich and of Krause and Wendt,<sup>3</sup> who obtained phenyl-silver from phenylmagnesium bromide and silver halides. The phenyl-silver so formed underwent decomposition to silver and diphenyl. The ephemeral nature of such intermediates is emphasized by Job and Champetier<sup>4</sup> who, working with ferric chloride and phenylmagnesium bromide, attempted unsuccessfully to isolate intermediate organoiron compounds but stated that their existence is probable, particularly at low temperatures.

We have investigated the reaction between certain metal halides and acetylenic Grignard reagents in order, first, to determine whether or not the general reaction as just described is applicable to acetylenic Grignard reagents and, second, to seek corroborative evidence for the intermediate formation of organometallic compounds in reactions of this type.

**Results**

It was found that the general reaction is applicable to acetylenic Grignard reagents and that the action of cupric bromide on acetylenic Grignard reagents produces diacetylenes and cuprous

(1) Bennet and Turner, *J. Chem. Soc.*, **105**, 1057 (1914).

(2) Krizewaky and Turner, *ibid.*, **115**, 559 (1919); Sakellarios and Kyrimis, *Ber.*, **57**, 322 (1924); Gilman and Kirby, *Rec. trav. chim.*, **48**, 155 (1929).

(3) Reich, *Compt. rend.*, **177**, 322 (1922); Krause and Wendt, *Ber.*, **56**, 2064 (1923).

(4) Job and Champetier, *Compt. rend.*, **189**, 1089 (1929).

bromide in good yields. In the case of phenylacetylenemagnesium bromide the addition of the stoichiometric amount of cupric bromide resulted in the formation of diphenyldiacetylene with a yield of 72%. A small amount of phenylacetylene was recovered from the hydrolyzed reaction mixture and the formation of no other products was observed.

When an equivalent amount of cupric bromide was added to *n*-butylacetylene magnesium bromide at 25° dibutyldiacetylene was obtained in 60% yield. In addition to the expected product a 7% yield of 1-bromo-1-hexyne was obtained. It was found that if the *n*-butylacetylene magnesium bromide was cooled to -5° by an ice-salt mixture and maintained at this temperature during the addition of the cupric bromide a 55% yield of dibutyldiacetylene was obtained and the yield of 1-bromo-1-hexyne was increased to 14%. Attempts to further increase the yield of 1-bromo-1-hexyne by maintaining the *n*-butylacetylene magnesium bromide at -33° (by immersing the reaction vessel in liquid ammonia) were unsuccessful since at this temperature no reaction takes place appreciably, even after four hours.

When cupric chloride was added to *n*-butylacetylene magnesium bromide at 25° dibutyldiacetylene was formed with a yield of 35%. No 1-chloro-1-hexyne was found but 5% of 1-bromo-1-hexyne was obtained in this case also. When cooling (-5°) was used the yield of 1-bromo-1-hexyne was increased by 2% and the yield of dibutyldiacetylene was found to be 30%. Cupric chloride, like cupric bromide, does not react appreciably with *n*-butylacetylene magnesium bromide at -33°. Cupric bromide reacts with *n*-butylacetylene magnesium chloride to yield dibutyldiacetylene (30%) and about 1% of 1-bromo-1-hexyne. Despite the variation of halogen in both Grignard reagent and salt no 1-chloro-1-hexyne was formed in any experiment. The behavior of ferric chloride toward the acetylenic Grignard reagent was similar to that of the copper halides, the yield of dibutyldiacetylene at 25° being 50%.

In no cases were higher boiling residues left; *n*-butylacetylene not accounted for as dibutyldi-

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 ad-

dition. 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<sup>1</sup> 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.<sup>2</sup> Since many different types of substituted quinolines exhibit local anesthetic action,<sup>3</sup> and are not especially irritating, it was thought that a combination of the quinoline nucleus with the urethan grouping would produce compounds with interesting pharmaco-

logical 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 plasmogin, 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 Shriver, *THIS JOURNAL*, **55**, 3435 (1933).

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

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