

*Anal.* Calcd. for  $C_{11}H_{16}N_2O$ : C, 68.72; H, 8.39; N, 14.57. Found: C, 68.80; H, 8.45; N, 14.40.

**Oxidation** of 2.6 g. of IVa was effected with excess potassium permanganate in 1 *M* sodium hydroxide (refluxed 20 hr.) to give 1.0 g. (54%) of *o*-phthalic acid, identified by mixture m.p. and infrared spectrum.

**Hydrolysis** of 5.7 g. of IVa was effected with potassium hydroxide in refluxing water and diglyme. A test of the evolved gas with filter paper moistened with Nessler reagent<sup>18</sup> gave a dark red-brown precipitate identical with that obtained in a blank run with aqueous ammonia. A blank run with aqueous methylamine gave a pale yellow precipitate with this reagent.

**The methiodide** of IVa (*o*-(carbamoylmethyl)-benzyltrimethylammonium iodide) melted at 212–213° after recrystallization from ethanol.

*Anal.* Calcd. for  $C_{12}H_{19}IN_2O$ : C, 43.12; H, 5.73; N, 8.38. Found: C, 43.32; H, 5.81; N, 8.17.

The infrared spectrum of IVa showed only a single strong peak, at 3250  $cm^{-1}$ , along with a very weak, broad band, near 3050  $cm^{-1}$ , in the N–H region (3400–3000  $cm^{-1}$ ). Primary amides generally exhibit two peaks, near 3350 and 3180  $cm^{-1}$ , in this region.<sup>19</sup> Such peaks were observed in the spectra of quaternary amide IIIa and of the corresponding amino amide from which IIIa was prepared by quaternization. The methiodide of IVa did exhibit two normal peaks, at 3380 and 3160  $cm^{-1}$ .

**Rearrangement of IIIb to IVb.**—To a solution of 0.12 mole of potassium amide in 450 ml. of liquid ammonia was added 15.85 g. (0.04 mole) of  $\alpha$ -(phenylcarbamoyl)-benzyltrimethylammonium iodide (IIIb).<sup>14</sup> After 6 hr., the yellow-brown mixture was neutralized inversely with ammonium chloride in ammonia, and the ammonia replaced by ether. The mixture was worked up as described above for the rearrangement of IIIa, except that the mixture obtained on making the acidic extracts basic was extracted with ether rather than separated by filtration. The solvent was removed from the dried ether solution and the residue (10.4 g.) was recrystallized from hexane-ethanol to afford 6.6 g. (62%) of 2-(*o*-dimethylaminomethylphenyl)-acetanilide (IVb), m.p. 129–130.5°, and 129.5–130.5°, after a second recrystallization.

*Anal.* Calcd. for  $C_{17}H_{20}N_2O$ : C, 76.08; H, 7.51; N, 10.44. Found: C, 75.93; H, 7.65; N, 10.48.

**Hydrolysis** of 3.7 g. of IVb was effected with refluxing hydrochloric acid to give, after making basic, 1.2 g. (95%) of aniline, identified by v.p.c. (enhancement technique) and infrared spectrum.

**Oxidation** of IVb was effected by refluxing the basic aqueous extract from the above hydrolysis with excess potassium per-

manganate to give 0.9 g. (40%) of *o*-phthalic acid, m.p. 210–212°, identified by mixture m.p. and infrared spectrum.

The infrared spectrum of IVb failed to show the single secondary amide peak usually observed near 3270  $cm^{-1}$ .<sup>20</sup> Instead, it exhibited two weak peaks at 3240 and 3180  $cm^{-1}$ . Unusual absorption in the N–H region was similarly observed with IVa (see above). The amino amide from which quaternary amide IIIb was prepared showed the normal secondary amide peak at 3280  $cm^{-1}$ .<sup>14</sup>

**$\alpha$ -Carboxybenzyltrimethylammonium Iodide (V).**—A suspension of 17.9 g. (0.10 mole) of  $\alpha$ -dimethylaminophenylacetic acid<sup>15</sup> in 150 ml. of acetonitrile was treated with 0.20 mole of methyl iodide. After 10 hr. each at 65° and room temperature, ether was added. The tacky solid was rinsed with several portions of ether and recrystallized from ethanol-ether to give 15.6 g. (49%) of V, m.p. 139–141° dec., and 150.5–152.5° dec. after three recrystallizations from ethanol.

*Anal.* Calcd. for  $C_{11}H_{16}INO_2$ : C, 41.14; H, 5.02; N, 4.36. Found: C, 41.10; H, 5.25; N, 4.18.

**Treatment of V with Potassium Amide to Form VI and VII.**—To a solution of 0.21 mole of potassium amide in 450 ml. of liquid ammonia was added 22.5 g. (0.07 mole) of V. After 6 hr., the yellow-brown mixture was neutralized inversely with ammonium iodide and the ammonia replaced by ether. Water was added to dissolve all solid. The layers were separated and the ether layer was washed with water and dried over sodium sulfate. Distillation gave 4.1 g. (30%) of methyl  $\alpha$ -dimethylaminophenylacetate (VI), b.p. 69–74° at 0.5 mm. This product was soluble in dilute acid, but insoluble in dilute base or water. The infrared spectrum showed principal peaks at 1740, 1455, 1265, 1215, 1150, 1050, 735, and 695  $cm^{-1}$ . The hydrochloride melted at 177.5–178° dec., lit.<sup>9</sup> m.p. 177° dec. The methiodide melted at 167.5–168.5° (see below).

The aqueous layer (see above) was adjusted to pH 7 and evaporated under reduced pressure to a volume of about 60 ml. After cooling, the precipitate was collected and dried to give 11.8 g. of solid. The latter was recrystallized from ethanol (filtered from insoluble portion) to give 8.0 g. (34%) of  $\alpha$ -(methoxycarbonyl)-benzyltrimethylammonium iodide (VII), m.p. 166–167°, undepressed on admixture with the methiodide of VI (see above). The infrared spectra were identical. A second recrystallization from ethanol gave the analytical sample, m.p. 167.5–168.5°.

*Anal.* Calcd. for  $C_{12}H_{18}INO_2$ : C, 42.79; H, 5.37. Found: C, 43.00; H, 5.41.

**Oxidation** of 2.2 g. of VII was effected by refluxing with excess potassium permanganate in 1 *M* sodium hydroxide to give 0.4 g. (35%) of benzoic acid, m.p. 120–122°, undepressed on admixture with an authentic sample.

(18) M. L. Nichols and C. O. Willits, *J. Am. Chem. Soc.*, **56**, 759 (1934).

(19) Reference 4, p. 206.

(20) Reference 4, p. 207.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY, STANFORD, CALIF., AND VARIAN ASSOCIATES, PALO ALTO, CALIF.]

## The Catalyzed Reaction of Alkylmagnesium Halides with Alkyl Halides. II.<sup>1</sup> The Nature of the Catalyst

BY V. D. PARKER,<sup>2</sup> L. H. PIETTE, R. M. SALINGER, AND C. R. NOLLER

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An investigation of the colored solutions that result from the reaction of copper, nickel, cobalt, and iron halides with an excess of alkylmagnesium bromide and that markedly catalyze the reaction of alkylmagnesium bromides with alkyl bromides indicates that they are solvated complexes of organometallic compounds with alkylmagnesium bromides.

A reasonably detailed investigation of the catalyzed reaction of ethylmagnesium bromide with ethyl bromide to give ethylene and ethane was reported in 1936.<sup>1</sup> The material added to bring about the reaction was cuprous bromide or cuprous chloride, but it was concluded that the active catalyst was a sol of metallic copper, referred to as colloidal copper. Subsequently, largely because of the work of Kharasch and his associates, the attention of others shifted to the action of cobaltous chloride<sup>3</sup>

and this trend has continued to the present.<sup>4</sup> Much of this work has been concerned with whether the active catalyst is colloidal cobalt or a reduced form of cobaltous chloride usually represented as  $\cdot CoCl$ , and whether the reactions involve free radicals or take place *via* a transition state by either homolytic or heterolytic scission without ever yielding truly free groups.

A few years ago it was decided to repeat and extend the earlier work, making use of the newer techniques and methods of analysis. One phase of this work clearly involves the nature of the catalyst. Most of the present work has been carried out on the red solu-

(1) Paper I: C. B. Linn and C. R. Noller, *J. Am. Chem. Soc.*, **58**, 816 (1936).

(2) American Chemical Society Fellow, 1961–1963.

(3) See M. S. Kharasch and O. Reimuth, "Grignard Reactions of Non-metallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, Chapters V and XVI.

(4) (a) F. W. Frey, Jr., *J. Org. Chem.*, **26**, 5187 (1961); (b) L. H. Slaugh, *J. Am. Chem. Soc.*, **83**, 2734 (1961); (c) W. B. Smith, *J. Org. Chem.*, **26**, 4206 (1961).

tions obtained by the reaction of cuprous bromide with alkylmagnesium bromides in *n*-butyl ether, although some attention has been given also to the behavior of halides of iron, cobalt, nickel, and manganese. The reaction of cuprous bromide with ethyl- and propylmagnesium bromides leads to stable, deep red solutions only when an excess of Grignard reagent is present. Under these conditions, solutions containing as much as 0.022 g.-atom of copper per liter could be obtained. The concentrated solutions under nitrogen or helium have stood for as long as 1 year without any evidence of flocculation or deposition of solid and appear to be stable indefinitely at room temperature. When spun in a Spinco preparative centrifuge under  $G_{av}$  30,000 for 90 min., no sedimentation occurred. This behavior, especially the stability of the solutions, makes it unlikely that a metallic sol is present.

Concentrated solutions appear black, but when diluted sufficiently with 1 *N* Grignard solution, the color is ruby red. Dilution with ether, however, precipitates all of the colored material as an unstable solid. Thus a fairly high concentration of Grignard reagent is necessary to stabilize the red solution, indicating complexing between the Grignard reagent and the copper compound. *n*-Amylmagnesium bromide in 2,2,4-trimethylpentane<sup>5</sup> reduces cuprous bromide but does not give a red solution. The concentrated red solution prepared from *n*-amylmagnesium bromide in *n*-butyl ether, however, can be diluted with four volumes of *n*-amylmagnesium bromide in 2,2,4-trimethylpentane without causing flocculation of the red product. Hence the complex is not insoluble in 2,2,4-trimethylpentane but coordination with ether appears to be necessary for its formation.

Calvin<sup>6</sup> first reported that when hydrogen is shaken with a solution of cupric acetate in quinoline at 80°, sufficient hydrogen is absorbed to convert cupric to cuprous ion and that a ruby red solution is obtained. He noted also that noncoordinating solvents do not yield red solutions. The red solutions catalyze the conversion of para- to orthohydrogen. Calvin and Wilmarth<sup>7</sup> postulated an intermediate  $AcO^{-}+Cu-H$ , which is unstable thermodynamically with respect to acetic acid and elemental copper but is stabilized by coordination with pure quinoline. Since the early work<sup>1</sup> indicated that the copper powder prepared by the reduction of copper oxide with hydrogen, as well as the copper residue resulting from the reaction of ethylmagnesium bromide with cuprous chloride, had surface catalytic activity, the behavior of so-called copper hydride prepared by the reduction of copper sulfate solution with sodium dihydrogen hypophosphite<sup>8</sup> was investigated. When the addition of copper hydride to the solution of ethylmagnesium bromide was followed immediately by the addition of ethyl bromide, only a slow evolution of gas took place. If, however, the mixture of copper hydride and ethylmagnesium bromide was allowed to stand overnight, the supernatant liquid turned light red. Addition of ethyl bromide to the red solution led to a rapid evolution of gas. Clearly the slight activity of copper hydride and presumably also the previously investigated preparations of copper<sup>1</sup> result from reaction with the ethylmagnesium bromide to give the active catalyst.

From these results it seems likely that a highly-colored organocopper complex is the active catalyst. The infrared spectrum of the solution supports this

view. Ethylmagnesium bromide in *n*-butyl ether exhibits strong absorption at 500  $cm^{-1}$ . This band undoubtedly is due to the C-Mg stretching vibration, since the absorption maxima of gaseous methylzinc, methylcadmium, and methylmercury at 615, 538, and 550  $cm^{-1}$ , respectively, have been assigned to the antisymmetrical stretch of the C-M-C bonds.<sup>9</sup> The transmittancy of the red catalyst solutions in this region is the same as that of the colorless Grignard solutions indicating that the color is not due to the presence of colloidal copper. The spectrum shows the same band exhibited by the colorless Grignard solution shifted slightly to 495  $cm^{-1}$ , but a broad shoulder is present with the maximum between 525 and 550  $cm^{-1}$ . This additional absorption is attributed to the Cu-C bond. Solid methylcopper is reported<sup>10</sup> to absorb in this region at 615, 645, and 648  $cm^{-1}$ .

It was hoped that the nuclear magnetic resonance (n.m.r.) spectrum of the copper catalyst solution might give more conclusive evidence of an ethyl-copper bond, since ethylmagnesium bromide gives a quartet of signals corresponding to the methylene group at higher field strength ( $\tau$  10.55) than the signal from the methyl groups of tetramethylsilane. At the concentrations of copper attainable, it was uncertain whether the methylene signal of an ethyl-copper bond was observed. When a computer of average transients was used in conjunction with a Varian A-60 n.m.r. spectrometer, a quartet of signals appeared downfield ( $\tau$  10.07) from the methylene signals of the ethylmagnesium bromide. The centrifuged red copper-containing catalyst solution gives a weak electron paramagnetic resonance (e.p.r.) signal, in the neighborhood of  $g = 2$ , but it is about the same as that of the centrifuged Grignard reagent itself indicating that both signals probably are due to impurities.

Infrared evidence for a carbon-metal bond is even more definite in catalyst solutions prepared from other metal halides. Filtration of mixtures resulting from the reaction of an excess of ethylmagnesium bromide in *n*-butyl ether with nickel bromide, cobaltous bromide, or ferric chloride gives dark, stable solutions that in thin films are greenish brown for cobalt and brownish black for nickel and iron. These solutions are highly active catalysts for the reaction of alkylmagnesium bromides with alkyl bromides. The mid-infrared spectra of the nickel, cobalt, and iron solutions show the C-Mg absorption at 495, 495, and 500  $cm^{-1}$  and in addition strong absorption with maxima at 542, 545, and 550  $cm^{-1}$ , respectively. Ferric chloride in *n*-butyl ether absorbs at 411  $cm^{-1}$ . This band is entirely lacking in the iron-containing catalyst solution, thus eliminating intermediates of the composition  $C_2H_5FeCl_2$  or  $(C_2H_5)_2FeCl$ .

The iron, nickel, and cobalt catalyst solutions also give e.p.r. signals, but their great strength even at room temperature indicates that these metals are in a ferromagnetic state. Hence it is not possible to draw any conclusions regarding their valence states.

It may be noted that whereas Kharasch and his co-workers<sup>3</sup> added from 1 to 6 mole % of metallic halide in their investigations, these colored solutions are highly active at low metal content. The copper solutions cause rapid reaction when 0.07 mole % is present (concentration 0.0007 *M*), and reaction takes place at a measurable rate at one-fifth of this concentration.

(5) L. I. Zakharkin, O. Yu. Okhlobystin, and B. N. Strunin, *Tetrahedron Letters*, 631 (1962).

(6) M. Calvin, *Trans. Faraday Soc.*, **34**, 1181 (1938).

(7) M. Calvin and W. K. Wilmarth, *J. Am. Chem. Soc.*, **78**, 1301 (1956).

(8) A. Sieverts and A. Gotta, *Ann.* **453**, 289 (1927).

(9) (a) H. S. Gutowsky, *J. Am. Chem. Soc.*, **71**, 3194 (1949); *J. Chem. Phys.*, **17**, 128 (1949); (b) a detailed study of the infrared spectra of Grignard solutions will be published by R. M. Salinger and H. S. Mosher, *J. Org. Chem.*, in press.

(10) G. Costa and G. De Alti, *Gazz. chim. ital.*, **87**, 1273 (1957); *Chem. Abstr.*, **52**, 19452a (1958).

### Experimental

**Grignard Reagents.**—Throughout this work purified *n*-butyl ether and alkyl halides were used, and all Grignard solutions were prepared and handled under an atmosphere of pure nitrogen or helium. They were filtered into storage flasks through a 1-cm. layer of ignited Celite on sintered glass. The filtered solutions were entirely colorless and clear.

It frequently is stated that high-purity sublimed magnesium must be used in work of this type to avoid the catalytic effect of impurities. Using carefully filtered water-clear solutions, we have noted no difference in the behavior of solutions prepared from fresh turnings of sublimed magnesium and those prepared from 99.9% commercial magnesium rod purchased from the Dow Chemical Co. Spectrographic analyses<sup>11</sup> of the rod indicated the percentages of impurities: Al, —; Si, —; Ca, 0.0004; Fe, —; Cu, 0.0002; Sn, 0.006; Pb, 0.01. Spectrographic analysis of a 99.99% rod of sublimed magnesium, available from Aluminum Company of America before 1936, gave the results: Al, 0.015; Si, 0.003; Ca, 0.001; Fe, 0.004; Cu, 0.0002; Sn, —; Pb, —.

The storage flasks were fitted with a Teflon stopcock, the outer end of which was covered by a rubber septum. Solutions were transferred by means of syringes fitted with long needles that

(11) Analyses by American Spectrographic Laboratories, San Francisco 3, Calif.

could be passed through the septum and the bore of the stopcock into the solution. Grignard reagents were approximately 1 *N* and were standardized by titration with standard acid.

**Catalyst Solutions.**—To 3 equivalents of approximately 1 *N* Grignard reagent cooled in an ice bath was added 1 equivalent of metallic halide. The mixture darkened immediately. When allowed to warm to room temperature, gas was evolved and allowed to escape. After standing overnight, the mixture was filtered through Celite into the same type of reservoir used to store Grignard reagents. The copper, cobalt, and nickel solutions were standardized for metal content electrolytically. Iron was determined colorimetrically as the thiocyanate.

**Infrared Spectra.**—Infrared absorption was measured with a Perkin-Elmer 421 spectrograph fitted with the Perkin-Elmer mid-infrared interchange grating. Fixed thickness cesium bromide cells with Teflon spacers and plugs were used.

**Electron paramagnetic resonance spectra** were obtained with a Varian Model Y4501 spectrometer. Samples were observed at both room temperature and at the temperature of liquid nitrogen over a range of 500 gauss on either side of  $g = 2$ .

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY, STANFORD, CALIF.]

## The Catalyzed Reaction of Alkylmagnesium Halides with Alkyl Halides. III.<sup>1</sup> Course of the Reaction

BY V. D. PARKER<sup>2</sup> AND C. R. NOLLER

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A reinvestigation of the products of the copper-catalyzed reaction of ethylmagnesium bromide with ethyl bromide has shown that butane, as well as ethane and ethylene, is a product of the reaction. An attempt to determine whether the alkene arises from the Grignard reagent or from the alkyl bromide by using different alkyl groups in the two reagents was inconclusive because the catalyst causes rapid functional exchange between the reagents. A study of the reaction of 1-C<sup>14</sup>-isopropyl bromide with isopropylmagnesium bromide and of 1-C<sup>14</sup>-isopropylmagnesium bromide with isopropyl bromide indicates that the alkene arises from the Grignard reagent and the alkane from the alkyl bromide. The results of the work as a whole support the view that the reaction proceeds by two pathways, one involving the intermediate formation of free radicals and the other a homolytic or heterolytic process that takes place by way of a transition state without the formation of free radicals.

Earlier work<sup>3</sup> showed that the copper-containing red solution formed by the reaction of ethylmagnesium bromide with cuprous chloride or cuprous bromide markedly catalyzes the reaction of ethylmagnesium bromide and ethyl bromide. The gaseous products were found to be ethane and ethylene in a ratio of 1.2 or less. No butane was detected. With the development of analysis by gas chromatography, it seemed desirable to repeat and extend this work.

Four series of reactions have been carried out in which all but one variable was held constant for each series, the variables being the amount of catalyst, the amount of ethyl bromide, the amount of ethylmagnesium bromide, and the total volume of the solution. The data are summarized in Tables I–IV. The amount of

TABLE I  
EFFECT OF VARYING THE AMOUNT OF CATALYST  
C<sub>2</sub>H<sub>5</sub>MgBr, 5.90 mmoles; C<sub>2</sub>H<sub>5</sub>Br, 2.68 mmoles; volume, 5.5 ml.

Catalyst, milliatom	C <sub>2</sub> H <sub>6</sub> , mmoles	C <sub>2</sub> H <sub>4</sub> , mmoles	C <sub>4</sub> H <sub>10</sub> , mmoles	Yield, %	Abstrn. — combn. total
0.001	2.43	0.94	0.16	69	0.49
.002	2.74	1.36	.33	89	.43
.004	2.59	1.66	.39	94	.34
.008	2.68	1.82	.39	99	.31
.016	2.75	1.80	.33	97	.31
.024	2.39	1.71	.28	87	.27

(1) Paper II: V. D. Parker, L. H. Piette, R. M. Salinger, and C. R. Noller, *J. Am. Chem. Soc.*, **86**, 1110 (1964).

(2) American Chemical Society Fellow, 1961–1963.

(3) C. B. Linn and C. R. Noller, *J. Am. Chem. Soc.*, **58**, 816 (1936).

TABLE II

EFFECT OF VARYING THE AMOUNT OF ETHYL BROMIDE  
C<sub>2</sub>H<sub>5</sub>MgBr, 6.78 mmoles; catalyst, 0.004 milliatom; volume, 5.5 ml.

C <sub>2</sub> H <sub>5</sub> Br, mmoles	C <sub>2</sub> H <sub>6</sub> , mmoles	C <sub>2</sub> H <sub>4</sub> , mmoles	C <sub>4</sub> H <sub>10</sub> , mmoles	Yield, %	Abstrn. + combn. total
1.34	1.70	0.65	0.18	101	0.52
2.68	2.91	1.61	.40	99	.40
5.36	4.58	3.33	.87	90	.31
6.70	5.09	3.69	1.07	82	.32
8.03	5.28	3.47	1.11	81	.37

TABLE III

EFFECT OF VARYING THE AMOUNT OF GRIGNARD REAGENT  
C<sub>2</sub>H<sub>5</sub>Br, 6.70 mmoles; catalyst, 0.004 milliatom; volume, 5.5 ml.

C <sub>2</sub> H <sub>5</sub> MgBr, mmoles	C <sub>2</sub> H <sub>6</sub> , mmoles	C <sub>2</sub> H <sub>4</sub> , mmoles	C <sub>4</sub> H <sub>10</sub> , mmoles	Yield, %	Abstrn. + combn. total
2.04	1.39	1.14	0.22	73	0.23
3.16	2.45	1.88	.43	82	.28
4.28	3.27	2.66	.62	84	.26
5.40	4.07	3.34	.85	84	.27
6.52	4.95	3.77	1.05	83	.30

catalyst always is expressed in terms of milliatoms of metallic copper. All amounts of reagents and of products are given in millimoles. The yields are calculated from the sum of the amounts of ethane, ethylene, and twice the butane, and are based on the limiting reagent. The solvent in all of this work was *n*-butyl ether.