# COPPER-CATALYZED COUPLING OF GRIGNARD REAGENTS AND ALKYL HALIDES IN TETRAHYDROFURAN SOLUTIONS*

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SUMMARY

The stoichiometry and the kinetics of the reaction between various Grignard reagents and alkyl halides with a copper catalyst have been examined in tetrahydrofuran solutions. The catalytically active species is an organocopper(I) complex produced by the rapid metathesis between copper(I) and -(II) halides and Grignard reagents. Primary alkyl bromides react with various Grignard reagents under these conditions to produce cross-coupled dimers exclusively. A mechanism is proposed in which coupling occurs between the alkyl halide and the alkylcopper(I) intermediate by displacement of the halide. On the other hand, only disproportionation products are produced from secondary and tertiary alkyl halides due to the unfavorable displacement process. The rate and the mechanism of the thermal decomposition of alkylcopper(I) species under the reaction conditions as well as side reactions involved in the coupling reaction are described.

INTRODUCTION

The reaction of organomagnesium and organolithium reagents with transition metal halides in ethereal solvent has been widely used as a synthetic method for obtaining coupled dimers[3-6]. This reaction, however, requires stoichiometric amounts of transition metal halides and is generally limited only to aryl, aralkyl and vinylic derivatives[6]. The Wurtz reaction[7] which also affords coupled dimers is only applicable to alkyl iodides and allylic as well as benzylic halides which are all more reactive than the corresponding chlorides or bromides. An undesirable mixture of three coupled products is generally obtained.

The reactions between arylcopper(I) complexes and organic halides [eqn. (1)] also yield the coupled products in high yields[8] and have been extensively investigated in connection with the Ullman synthesis[9]. Moreover, the coupling reaction between

$$RCu + R'X \rightarrow R-R' + CuX \tag{1}$$

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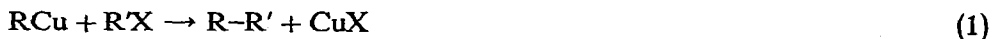
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diorganocuprates, usually designated as "ate" complexes[10], and organic halides [eqn. (2)] has recently been described and its broad applications have been shown independently by a number of investigators[11]. However, the stoichiometric amounts of copper

$$R_2CuLi + R'X \rightarrow R-R' + RCu + LiX \qquad (2)$$
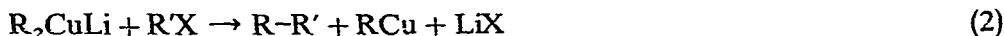
compounds required are not always convenient and organolithium compounds are not as readily available as the corresponding Grignard reagents.

The coupled dimers have been reported among the products of the reaction between Grignard reagents and organic halides with catalytic amounts of transition metal complexes, and the process is generally referred to as the Kharasch reaction[2,12].

$$RMgX + R'Y \xrightarrow{MY_n} R-R' + MgXY \qquad (3)$$

Unfortunately, both the yield and the selectivity of the coupled dimer are usually low, and the synthetic application of this reaction is limited only to special combinations, mainly those consisting of aryl or aralkyl derivatives. Those combinations which have employed alkyl derivatives with $\beta$-hydrogens usually afforded the corresponding alkane and alkene as the predominant products. This facile catalytic process has been widely investigated primarily to answer mechanistic questions[12,15a].

$$RMgX + R'Y \xrightarrow{MY_n} \begin{cases} \rightarrow RH + R'(-H) + MgXY \\ \rightarrow R'H + R(-H) + MgXY \end{cases} \qquad (4)$$
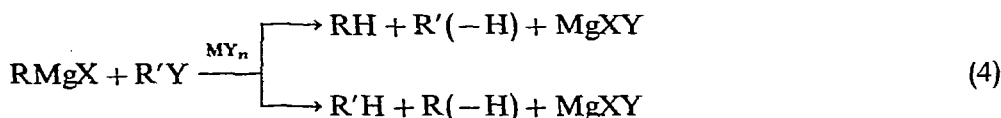
Catalytic amounts of copper species also induce the Kharasch reaction in ethereal media, but the low yield of the coupled product precludes its synthetic application. Furthermore, the mechanism of the catalysis has been obscured by the occurrence of several simultaneous homolytic and heterolytic processes[13].

We have reinvestigated the reaction of various transition metal halides with Grignard reagents[14] and the mechanism of the Kharasch reaction catalyzed by various transition metal halides in tetrahydrofuran (THF) solutions[15]. The latter is advantageous since most of the studies reported heretofore have been examined in diethyl ether solutions[2-6,12], in which the organometallic intermediates are less stable. In this paper we show a convenient method of obtaining the cross coupled product from a Grignard reagent and a primary alkyl halide in THF with a copper catalyst. The lower alkyl derivatives have been utilized both for the Grignard component and the alkyl halide in order to follow the reaction directly by analysis of the gaseous hydrocarbon products without recourse to prior hydrolysis.

RESULTS

In order to clarify the presentation of the results, the effect of copper salts on the reactions of Grignard reagents is presented in the following four categories:
I. The *stoichiometric* reactions between Grignard reagents and copper(I) or copper-(II) halides, including the decomposition of organocopper species.
II. The copper-*catalyzed* coupling and disproportionation of Grignard reagents with alkyl halides.

*A*. Stoichiometry of the catalytic reaction of ethylmagnesium bromide and ethyl bromide; coupling and disproportionation processes catalyzed by $Cu^I$ and $Cu^0$, respectively.

*B*. Kinetics of the catalytic coupling of ethylmagnesium bromide and ethyl bromide with copper(I).

*C*. Stoichiometry of the catalytic coupling of other alkylmagnesium halides with alkyl halides.

*D*. Effect of styrene as a free radical scavenger in the coupling and disproportionation reactions with various copper species.
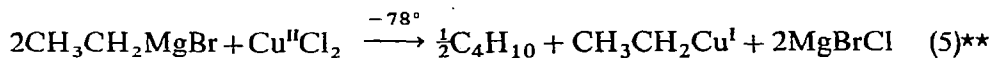
*III*. The *stoichiometric* reaction of alkylcopper(I) with alkyl halides.

*IV*. The autoxidation of alkylcopper(I) species.

Each of these interrelated topics will be discussed separately, and they will be treated as a whole in the discussion of the mechanism of the coupling and disproportionation processes involved in the catalytic reactions of Grignard reagents and alkyl halides.

*I. Reactions of cupric and cuprous halides with Grignard reagents in tetrahydrofuran: the formation and decomposition of alkylcopper(I) species**

When a solution of ethylmagnesium bromide and a suspension of cupric chloride were mixed (in a 2/1 molar ratio) in THF at $-78°$, a transitory pale orange color was observed and 0.5 mole of n-butane was generated spontaneously. An homogeneous and colorless solution was also obtained when ethylmagnesium bromide and a suspension of cuprous chloride were mixed in stoichiometric amounts in THF at $-78°$. The resulting colorless solutions were stable for prolonged periods at these temperatures. From the negative Gilman color test[16], we deduced that the ethylcopper(I) species was formed according to the following equations (see also Table 1).

$$2CH_3CH_2MgBr + Cu^{II}Cl_2 \xrightarrow{-78°} \tfrac{1}{2}C_4H_{10} + CH_3CH_2Cu^I + 2MgBrCl \quad (5)**$$

$$CH_3CH_2MgBr + Cu^ICl \xrightarrow{-78°} CH_3CH_2Cu^I + MgBrCl \quad (6)[17]$$

When the solutions of ethylcopper(I) resulting from the reactions of cupric or cuprous chloride with ethylmagnesium bromide in THF were held at $-10°$ for 10 to 30 min, they gradually turned purple and remained homogeneous, but no decomposition was apparent. Neither the color of the ethylcopper(I) solution nor the rate of decomposition was affected by the presence of excess ethylmagnesium bromide or styrene as shown in Fig. 1. The ethylcopper(I) species obtained from cuprous chloride was less stable than that formed from cupric chloride under comparable conditions. This difference may be ascribed to the presence of excess inorganic halide, since the ethylcopper(I) species showed enhanced stability when it was prepared in the same manner from the *soluble* lithium dichlorocuprate (made separately by mixing lithium chloride and cuprous chloride in equimolar amounts in THF at room temperature).

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* Formal oxidation states of copper are used only for convenience in order to keep an account of the equivalency changes and are not meant to convey structural connotations. The alkyl ligands are considered anionic in this context.

** Coordination by THF and/or magnesium halide is assumed (*vide infra*) but not specifically included.

A deep purple color was also observed with ethylcopper(I) made by the latter procedure.

Previous studies showed that the rates of decomposition of ethylcopper(I) and n-butylcopper(I) species in diethyl ether are greatly influenced by excess ethyllithium and n-butyllithium, respectively. The effect has been ascribed to the formation of the more stable dialkylcuprate complexes[10,11].

$$CH_3CH_2Cu + CH_3CH_2Li \rightarrow LiCu(CH_2CH_3)_2 \tag{7}$$

$$BuCu + BuLi \rightarrow LiCu(Bu)_2 \tag{8}$$

We deduce from these observations that diethylcuprate was not formed from the Grignard reagent either in THF or diethyl ether in the presence of excess ethylmagnesium bromide. House *et al.*, have also shown that dialkylcuprate is not produced in the reaction of cuprous iodide and an alkyl Grignard reagent in diethyl ether[17].

Alkylcopper(I) species which have $\beta$-hydrogens decomposed as shown in Table 1 to afford a mixture of the corresponding alkane and alkene in approximately equimolar amounts [eqn. (9)]. On the other hand, alkylcopper(I) species such as methyl, neopentyl and benzylcopper(I) species which have no readily available $\beta$-hydrogen decomposed mainly to dialkyl in THF solutions [eqn. (10)]. In both instances, reaction was accompanied by the formation of the corresponding amount of a black copper precipitate[1,14].
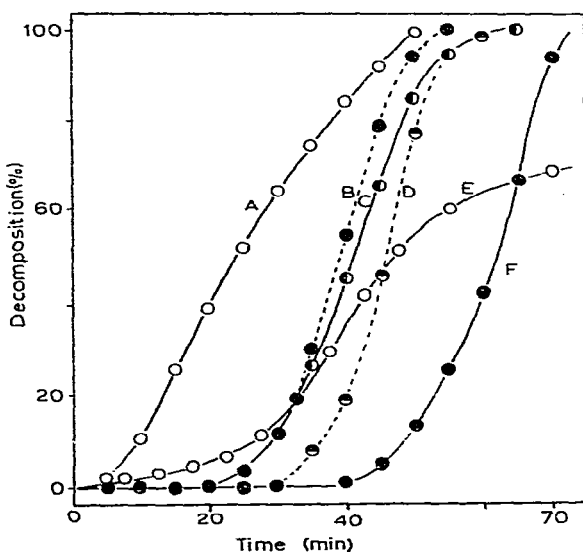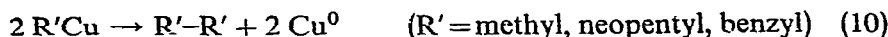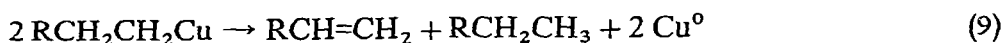
$$2 RCH_2CH_2Cu \rightarrow RCH=CH_2 + RCH_2CH_3 + 2 Cu^o \tag{9}$$

$$2 R'Cu \rightarrow R'-R' + 2 Cu^o \qquad (R' = methyl, neopentyl, benzyl) \tag{10}$$



Fig. 1. Rate of decomposition of ethylcopper species in THF solution at $2.0°$; *A*, EtMgBr/CuCl 7.0; *B*, EtMgBr/CuBr$_2$ 15.0, styrene/CuBr$_2$ 8.7; *C*, EtMgBr/CuBr$_2$ 15.0; *D*, EtMgBr/CuBr$_2$ 2.0; *E*, EtMgBr/LiCuCl$_2$ 5.0; *F*, EtMgBr/CuCl$_2$ 2.0.
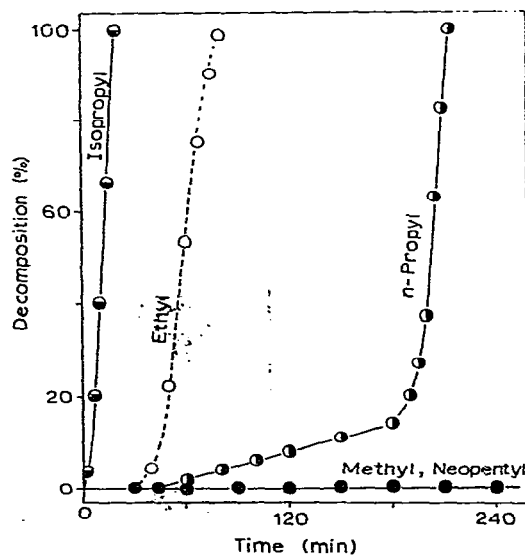
Fig. 2. Rate of decomposition of alkylcopper(I) species resulting from the reaction of cupric bromide (1.0 mmol) with the corresponding alkyl Grignard reagent (7.0 mmol) in THF (21 ml) at $2.0°$. ◓ Isopropylcopper; ◑ n-propylcopper; ○ ethylcopper; ● methyl and neopentylcoppers.

TABLE 1

THE REACTIONS OF CUPROUS AND CUPRIC HALIDES WITH GRIGNARD REAGENTS IN TETRAHYDROFURAN[a]

| Copper salt $CuX_n$ | Grignard reagent RMgBr | $RMgBr/CuX_n$[b] | Temp. (°C) | Period (min) | Products (mol %) | | | $\Sigma R/CuX_n$[d] |
|---|---|---|---|---|---|---|---|---|
| | | | | | $R(-H)$ | RH | $R-R$[c] | |
| CuCl | Methyl | 1.0 | 25 | 900 | | 7 | 93 | 0.9 |
| CuCl | Neopentyl | 2.0 | 25 | 5760 | | 47 | 53 | 1.0 |
| CuCl | Benzyl | 1.3 | 25 | 30 | | N.d.[e] | 88 | |
| CuCl | Phenyl | 3.0 | 60 | 1440 | | N.d. | 90 | |
| CuCl | Phenyl | 3.0 | 25 | 4200 | | N.dec.[f] | | |
| CuCl | Ethyl | 7.0 | 25 | 60 | 51 | 49 | 0 | 1.0 |
| CuCl[g] | Ethyl | 7.0 | 25 | 60 | 52 | 48 | 0 | 1.0 |
| CuBr | Ethyl | 5.0 | 25 | 60 | 51 | 49 | 0 | 1.0 |
| $CuCl_2$[i] | Ethyl | 7.0 | −78 | 5 | 0 | 0 | 100 | 1.0[j] |
| $CuCl_2$[i] | Ethyl | 2.5 | 2 | 2 | 3 | 3 | 94 | 1.0[j] |
| $CuCl_2$[g,h] | Ethyl | 5.7 | 2 | 180 | 42 | 36 | 5 | 2.0 |
| $CuCl_2$ | Ethyl | 7.0 | 25 | 60 | 26 | 28 | 46 | 2.1 |
| $CuBr_2$ | Ethyl | 2.25 | 2 | 90 | 26 | 24 | 50 | 2.0 |
| $CuBr_2$[i] | n-Propyl | 2.25 | 2 | 60 | 1 | 1 | 98 | 1.0[j] |
| $CuBr_2$ | n-Propyl | 2.25 | 2 | 180 | 51 | 49 | 50 | 2.0 |
| $CuBr_2$ | Isopropyl | 7.0 | 2 | 30 | 38 | 35 | 27 | 2.0 |

[a] In 21 ml THF solution containing 1.0 mmol copper salt. [b] Molar ratio. [c] Percentage of R–R was doubled. [d] $\Sigma R = R(-H) + RH + 2R-R$. [e] Not determined. [f] No decomposition (N.dec.) within a period cited (white precipitate suspension). [g] In diethyl ether. [h] In the presence of 26.1 mmol styrene, 15.6 % ethyl chloride was also formed. Yield of ethylbenzene was less than 0.01 mmol. [i] No copper precipitate (black) appeared within a period cited. [j] Partial decomposition within the cited period; alkylcopper(I) species are stable under these conditions.

The rate of decomposition of a typical alkylcopper(I) species formed *in situ* from the reaction of cupric bromide and excess Grignard reagent in THF solution is shown in Fig. 2. An induction period was apparent in the decomposition of each alkylcopper(I) species*. The thermal stability of the alkylcopper(I) species decreased in the sequence: neopentyl > methyl ≫ n-propyl > ethyl > isopropyl, which is the same as that previously observed in the decomposition of alkylmanganese complexes in THF solutions[18]. Autocatalysis and the presence of novel mixed valence copper(0) species during the decomposition of these alkylcopper(I) species in THF solutions was reported earlier[19].

Solutions of n-propylcopper(I) prepared from cupric chloride and excess n-propylmagnesium bromide showed a broad absorption band centered at 575 nm (log $\varepsilon \approx 2$). Quantitative measurements were not possible since the apparent absorptivity (based on the copper charged) changed with time and were difficult to reproduce. Furthermore, in this instance the addition of equimolar amounts of lithium chloride deepened the purple color. The change in color could also be induced by temperature (*vide supra*) and is probably due to changes in the degree of association of alkylcopper(I)

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* The induction period varied somewhat with different batches of copper salts and Grignard reagents probably due to metallic impurities which are also exceedingly efficient catalysts for the decomposition of alkylcopper species[19].

species and/or the formation of new complexes involving metallic halides. Examples of organocopper(I) clusters have recently been reported in analogous situations[20]. Furthermore, the lower thermal stability of ethylcopper(I) species in diethyl ether compared to THF may be attributed to THF as a better ligand for coordination to the alkylcopper(I) species[19,21].

It is noteworthy that ethyl chloride was formed together with ethane, ethylene and n-butane when the reaction of cupric chloride and ethylmagnesium bromide was carried out in diethyl ether at 2°. The mechanism of the formation of ethyl chloride and n-butane in this reaction has been discussed[14].

## II. Copper-catalyzed reaction of Grignard reagents with alkyl halides

A. Catalytic coupling and disproportionation of ethylmagnesium bromide with ethyl bromide. The copper-catalyzed reaction between a Grignard reagent and an alkyl halide was originally examined in di-n-butyl ether solutions by Parker and Noller[13], who showed that alkane and alkene were formed as the principal products.

$$RMgBr + R'X \xrightarrow[\cdot \ Bu_2O]{CuX} [RH, R(-H), R'H, R'(-H)] + MgBrX \qquad (11)$$
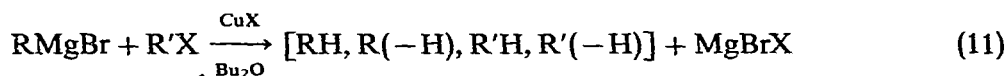
The reaction in THF solution between ethylmagnesium bromide and ethyl bromide with cuprous or cupric halide was initially examined under a standard set of reaction conditions given in Table 2. Two procedures were employed in which either: (A) the Grignard reagent was first exposed to the copper salt and the addition was followed later by reaction with ethyl bromide (after 60 min at 2°), or: (B) the ethylmagnesium bromide was the last component added. n-Butane was produced in very high yields by procedure (B) except when cuprous chloride was used (and in which case appreciable amounts of ethane and ethylene were also formed). On the other hand, ethylene and ethane, but no n-butane, were produced by procedure (A). The dramatic difference between these procedures is illustrated in Fig. 3. The stoichiometry of the

TABLE 2

THE REACTION OF ETHYLMAGNESIUM BROMIDE WITH ETHYL BROMIDE IN THE PRESENCE OF CUPRIC OR CUPROUS CHLORIDE IN TETRAHYDROFURAN[a]

| Cu salt | Method[b] | Period (min) | Distribution of product[c] (mol %) | | | $\Sigma Et/EtBr$[d] |
|---|---|---|---|---|---|---|
| | | | $C_2H_4$ | $C_2H_6$ | $n\text{-}C_4H_{10}$ | |
| CuCl$_2$ | A | 60 | 51.3 | 48.7 | 0.0 | 2.0 |
| CuCl$_2$ | B | 120 | 0.3 | 2.2 | 97.5 | 2.1 |
| CuBr$_2$ | B | 120 | 0.3 | 2.0 | 97.7 | 2.0 |
| CuCl | B | 60 | 17.6 | 18.4 | 64.0 | 1.9 |
| LiCuCl$_2$[e] | B | 120 | 2.0 | 4.4 | 93.6 | 2.0 |

[a] In 21 ml THF solution containing 7.0 mmol EtMgBr, 1.35 mmol EtBr and 1.0 mmol copper salt at 2.0°. [b] Method A: EtBr added after reaction of CuCl$_2$ and EtMgBr completed (60 min black suspension) B: EtBr added before EtMgBr. [c] All products produced from reaction of copper salt and EtMgBr were subtracted as a blank. Percentage of n-butane was doubled. [d] $\Sigma Et = C_2H_4 + C_2H_6 + 2n\text{-}C_4H_{10}$. [e] Lithium dichlorocuprate was prepared from an equimolar mixture of lithium chloride and cuprous chloride in THF at room temperature for 60 min. (A colorless uniform solution was obtained.)
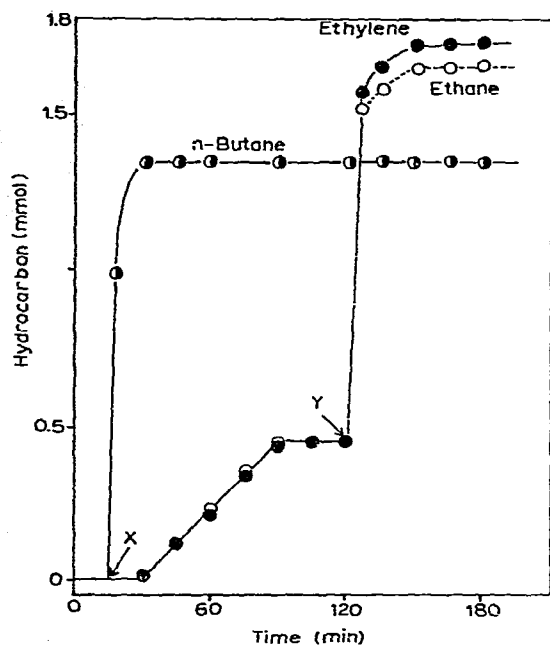
Fig. 3. The $Cu^I$ and Cu catalyzed reaction of ethylmagnesium bromide and ethyl bromide in THF at 2.0° ; X, addition of 1.35 mmol of ethyl bromide to a solution of 6.0 mmol of ethylmagnesium bromide and 1.0 mmol of $Cu^I$; Y, addition of 1.35 mmol of ethyl bromide to a suspension of 1.0 mmol of Cu and 4.65 mmol of ethylmagnesium bromide. ⬕ n-Butane, ○ ethane, ● ethylene.
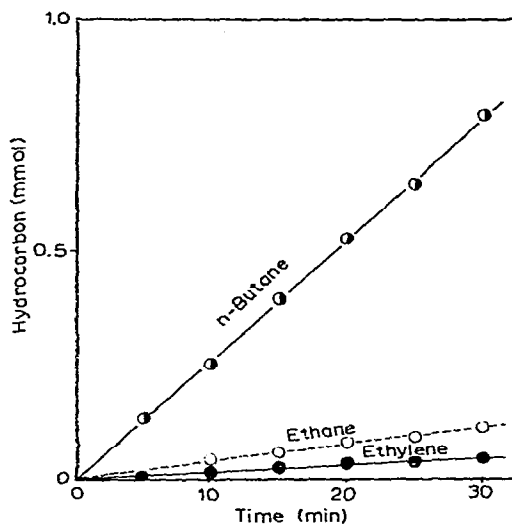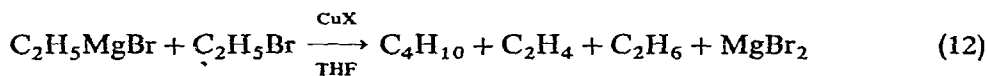
Fig. 4. Kinetics (initial rate) or the copper-catalyzed reaction of 0.27 $M$ ethylmagnesium bromide and 0.51 $M$ ethyl bromide at 2.0° in THF using $2.8 \times 10^{-4}$ $M$ cupric bromide. ⬕ n-Butane ($2.08 \times 10^{-5}$ $M \cdot sec^{-1}$), ○ ethane ($2.78 \times 10^{-6}$ $M \cdot sec^{-1}$), ● ethylene ($1.14 \times 10^{-6}$ $M \cdot sec^{-1}$).

reaction was represented in both procedures by eqn. (13), independently of the copper salt charged. Eqn. (13) was established previously in the Kharasch reaction catalyzed by various other transition metal salts[15,22].

$$C_2H_5MgBr + C_2H_5Br \xrightarrow[\text{THF}]{\text{CuX}} C_4H_{10} + C_2H_4 + C_2H_6 + MgBr_2 \qquad (12)$$

$$\frac{2C_4H_{10} + C_2H_4 + C_2H_6}{C_2H_5Br \text{ (or } C_2H_5MgBr)} = 2.0 \qquad (13)$$

The formation of ethylene and ethane using procedure (B) with cuprous chloride is related to the thermal instability of ethylcopper(I) species formed *in situ,* since the more thermally stable ethylcopper(I) species derived from lithium dichlorocuprate afforded n-butane exclusively (Fig. 1).

Copper halide in concentrations as low as $10^{-4}$ $M$ was also an effective catalyst for the reaction between ethylmagnesium bromide and ethyl bromide in THF solutions as shown in Fig. 4. n-Butane was the main product and the solution was apparently homogeneous since the pale yellow color of the solution was maintained throughout the reaction. There was no evidence of the black precipitation of metallic copper which otherwise accompanies the decomposition of alkylcopper(I) species. Catalytic

amounts $(10^{-3}-10^{-4} M)$ of cupric chloride, cuprous chloride, lithium dichlorocuprate and dilithium tetrachlorocuprate also catalyzed the reaction of ethylmagnesium bromide with ethyl bromide in THF solution at $2°$.

A reduced form of a soluble copper complex[23] was obtained when the reaction of cuprous chloride and excess ethylmagnesium bromide was carried out in the presence of lithium nitrate at $25°$ in THF* (Table 7). It exhibited essentially the same catalytic activity as those obtained with cuprous and cupric halides. In this case, n-butane (52 mol %) was obtained together with significantly larger amounts of ethane (34 mol %) and ethylene (14 mol %) when $6.0 \times 10^{-4}$ $M$ reduced soluble copper complex was used at $2°$.

*B. Kinetics of the copper-catalyzed reaction between ethylmagnesium bromide and ethyl bromide.* The reaction between ethylmagnesium bromide and ethyl bromide in the presence of the catalytic amounts of copper bromide was monitored by direct sampling and quantitative analysis of the gaseous products. The latter was carried out by the internal standard method after careful calibration of the system. An empirical rate expression was obtained by systematically varying the concentration of each component and was applied to roughly the first 10% of the reaction (Table 3). An extensive kinetic study was not performed because we felt that kinetics could not be rigorously established for this system consisting of a number of side reactions of varying importance (for example, see Fig. 5). The rate of formation of n-butane could be represented approximately by eqn. (14).

$$\frac{dC_4H_{10}}{dt} = k \cdot [CuBr]^{1.0} \cdot [EtMgBr]^{0.8} \cdot [EtBr]^{0.7} \qquad (14)$$

Several features of these results are noteworthy. Thus, the rate of formation of n-butane followed a roughly first order dependence on the concentrations of copper bromide, ethylmagnesium bromide and ethyl bromide. The dependence of the rate on the concentration of ethylmagnesium bromide was in sharp contrast to that previously observed in a similar reaction catalyzed by iron[15] and silver[22]. As side products, the rates of formation of both ethylene and ethane were rather insensitive to the concentrations of copper bromide and ethylmagnesium bromide, but they were affected by the concentration of ethyl bromide. The formation of ethylene and ethane was also more important at higher temperatures. The relative rate of formation of ethane was generally between *two* and *four* times greater than ethylene and was unaffected by variations in the concentrations of each component as well as the reaction temperature. The decrease in the rate of formation of n-butane at higher temperatures may be due to the thermal decomposition of ethylcopper(I) species prior to the attack of ethyl bromide and/or the change in the degree of association of the ethylcopper(I) species with temperature.

*C. Copper-catalyzed coupling between Grignard reagents and alkyl halides.* The products of the copper-catalyzed reactions of various Grignard reagents and alkyl halides in THF solutions are given in Table 4. It clearly shows that the cross-

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* The reduced form of soluble copper is tentatively identified as a copper(0) species. Compare, for example, refs. 22 and 23.

TABLE 3

THE RATES OF REACTION OF ETHYLMAGNESIUM BROMIDE AND ETHYL BROMIDE IN THE PRESENCE OF CUPRIC BROMIDE[a]

| $CuBr_2$ $(10^4 M)$ | $EtMgBr$ $(M)$ | $EtBr$ $(M)$ | Temp. $(°C)$ | Rates of product formation $(10^5 M \cdot sec^{-1})$ [b] | | | $C_2H_6/C_2H_4$ |
|---|---|---|---|---|---|---|---|
| | | | | $C_2H_4$ | $C_2H_6$ | $n\text{-}C_4H_{10}$ | |
| 1.4 | 0.180 | 0.160 | 2.0 | 0.008 | 0.022 | 0.34 | 2.7 |
| 2.8 | 0.180 | 0.160 | 2.0 | 0.014 | 0.050 | 0.70 | 3.6 |
| 4.8 | 0.180 | 0.160 | 2.0 | 0.017 | 0.058 | 1.15 | 3.5 |
| 2.8 | 0.090 | 0.512 | 2.0 | 0.186 | 0.350 | 0.89 | 1.9 |
| 2.8 | 0.270 | 0.512 | 2.0 | 0.114 | 0.278 | 2.08 | 2.4 |
| 2.8 | 0.360 | 0.512 | 2.0 | 0.097 | 0.292 | 2.57 | 3.0 |
| 2.8 | 0.180 | 0.064 | 2.0 | 0.011 | 0.036 | 0.39 | 3.3 |
| 2.8 | 0.180 | 0.256 | 2.0 | 0.108 | 0.203 | 0.91 | 1.9 |
| 2.8 | 0.360 | 0.320 | 2.0 | 0.103 | 0.250 | 1.89 | 2.4 |
| 2.8 | 0.360 | 0.320 | 11.0 | 0.117 | 0.359 | 2.78 | 3.1 |
| 2.8 | 0.360 | 0.320 | 22.8 | 0.545 | 1.551 | 2.44 | 2.8 |

[a] In THF solutions. [b] Initial rates.

TABLE 4

THE COPPER-CATALYZED REACTIONS OF GRIGNARD REAGENTS WITH ALKYL HALIDES IN TETRAHYDROFURAN[a]

| $RMgBr$ | $R'X$ | $CuBr_2$ $(10^4 M)$ | Period $(min)$ | Products $(mmol)$[b] | | Relative rate of $R-R'$ formation[c] |
|---|---|---|---|---|---|---|
| | | | | $R'H$ | $R-R'$ | |
| EtMgBr | EtBr | 4.8 | 30 | | 0.465 | 1.0 |
| EtMgBr | n-PrCl | 9.5 | 60 | 0.00 | 0.000[d] | 0.0 |
| EtMgBr | n-PrBr | 9.5 | 30 | 0.02 | 0.390 | 0.4 |
| EtMgBr | n-PrI | 0.95 | 5.0 | 0.01 | 0.126 | 4.1 |
| EtMgBr | i-PrBr | 4.8 | 15 | 0.00 | 0.000[d] | 0.0 |
| EtMgBr | t-BuBr | 4.8 | 15 | 0.00 | 0.000[d] | 0.0 |
| n-PrMgBr | EtBr | 9.5 | 30 | 0.02 | 1.167 | 1.3 |
| n-PrMgBr | n-PrBr | 9.5 | 30 | | 0.466 | 0.5 |
| i-PrMgBr | EtBr | 0.95 | 5.0 | 0.02 | 0.352 | 22.7 |
| i-PrMgBr | i-PrBr | 9.5 | 30 | | 0.000[d] | 0.0 |
| t-BuMgBr | EtBr | 0.95 | 10 | 0.00 | 0.127 | 4.1 |

[a] In 21 ml THF solution containing 0.18 $M$ RMgBr and 0.16 $M$ R'X at 2°. No homodimer (R–R) and R'–R') was detected in all runs. The yield of disproportionation products (RH, R'H, R(−H) and R'(−H)) was also negligibly small (less than 10% based on total yield) in all runs. [b] Analyzed after hydrolysis with dilute sulfuric acid at the period cited. [c] Yield of R–R' divided by time and CuBr$_2$ concentration (arbitrary units). [d] The yield of disproportionation products was also negligibly small (< 0.02 mmol).

coupled product (R–R') was formed in high yields from primary alkyl bromides and a variety of Grignard reagents.

$$RMgBr + R'Br \xrightarrow[\text{THF}]{\text{CuBr}} R-R' + MgBr_2 \tag{15}$$
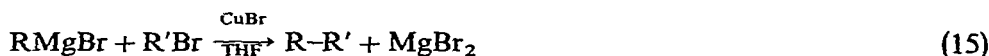
The relative reactivities of n-propyl halides were in the order: iodide > bromide $\gg$ chloride. The same sequence was observed in the reaction of dialkylcuprates with alkyl halides [eqn. (2)][11a]. The reactivities of various alkyl Grignard reagents toward ethyl bromide can be placed qualitatively in the following sequence.

$$\text{Isopropyl} > \text{tert-Butyl} > \text{Ethyl} \sim \text{n-Propyl} \tag{16}$$

Interestingly, appreciable amounts of the cross-coupled product were not produced from isopropyl and tert-butyl bromides under these conditions despite the lower dissociation energy of the C–Br bond in these compounds compared to primary alkyl bromides. The yield of the coupled dimer was also very low (12 mol %) in the reaction between isopropylmagnesium bromide and isopropyl bromide despite the higher concentration of copper bromide ($1.2 \times 10^{-3} M$), the higher temperature ($25°$) and the longer period (16 h) of reaction. Propane and propylene were the main products.

$$\text{i-PrMgBr} + \text{i-PrBr} \xrightarrow[25°C]{\text{CuBr}} C_3H_6 + C_3H_8 + MgBr_2 \tag{17}$$
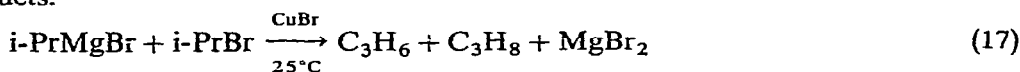
Homocoupled dimers (R–R and R'–R') were also not detected under these conditions. It is in sharp contrast with the results obtained in the silver-catalyzed coupling of Grignard reagents with alkyl halides in THF solution[22].

$$\text{RMgBr} + \text{R'Br} \xrightarrow[\text{THF}]{\text{AgX}} [R–R + R–R' + R'–R'] + MgBr_2 \tag{18}$$
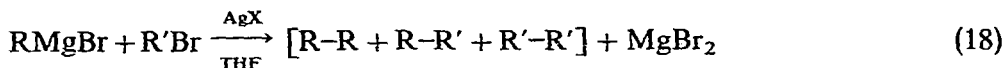
Alkyl exchange between the Grignard reagent and the alkyl halide was not apparent. Except for alkyl iodides, only negligibly small amounts or none of that alkane derivable from the alkyl halide was found after acidic hydrolysis of the reaction mixture. This behavior contrasts with the ready exchange observed when the same reaction was studied in the presence of silver[22], iron[15], manganese[18] and other transition metals[2,12,23].

$$\text{RMgBr} + \text{RX} \underset{\text{CuX}}{\rightleftharpoons} \text{R'MgBr} + \text{RX} \tag{19}$$

The exclusive formation of cross coupled product from the Grignard reagent and a primary alkyl bromide (or iodide) by catalytic amounts of copper can be used in synthetic procedures[24].

*D. Effect of styrene.* The copper-catalyzed reaction between an alkyl Grignard reagent and a primary alkyl halide was repeated in the presence of styrene to act as a scavenger for alkyl radicals. The rate of formation and the yield of cross coupled product were almost independent of the styrene in all the combinations shown in Table 5. This behavior differs from the pronounced inhibiting effect shown by styrene on other reactions catalyzed by transition metal salts[15,22]. We conclude that alkyl radicals are not involved in any significant way in the copper-catalyzed process for the cross coupled product.

On the other hand, styrene preferentially scavenged the tert-butyl group in the reaction between ethylmagnesium bromide and tert-butyl bromide when the soluble reduced copper complex* described earlier was used. Thus, the results in Table 6

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* See footnote after eqn. (13).

TABLE 5

EFFECT OF STYRENE ON THE COUPLING OF GRIGNARD REAGENT WITH ALKYL HALIDE[a]

| RMgBr | R'X | CuBr$_2$ (10$^4$ M) | Styrene (M) | Period (min) | R-R'[b] (mmole) |
|---|---|---|---|---|---|
| EtMgBr | n-PrBr | 9.5 | | 30 | 0.39 |
| EtMgBr | n-PrBr | 9.5 | 0.415 | 30 | 0.41 |
| EtMgBr | n-PrI | 0.95 | | 5.0 | 0.13 |
| EtMgBr | n-PrI | 0.95 | 0.415 | 5.0 | 0.60 |
| i-PrMgBr | EtBr | 0.95 | | 5.0 | 0.35 |
| i-PrMgBr | EtBr | 0.95 | 0.415 | 5.0 | 0.61 |
| t-BuMgBr | EtBr | 0.95 | | 10 | 0.13 |
| t-BuMgBr | EtBr | 0.95 | 0.415 | 10 | 0.12 |

[a] In 21 ml THF solution containing 0.18 $M$ RMgBr and 0.16 $M$ R'X at 2°. The yield of homodimers and disproportionation products as well as ethylbenzene was negligibly small in all runs. [b] Analyzed after acidic hydrolysis.
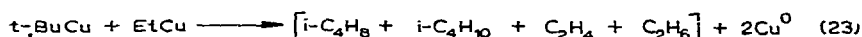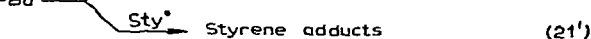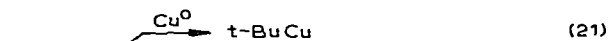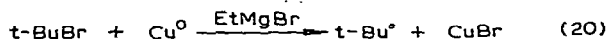
TABLE 6

EFFECT OF STYRENE ON THE REACTION BETWEEN ETHYLMAGNESIUM BROMIDE AND TERT-BUTYL BROMIDE CATALYZED BY REDUCED COPPER[a]

| Styrene (M) | Period (min) | Products (mmol) | | | |
|---|---|---|---|---|---|
| | | $C_2H_4$ | $C_2H_6$ | i-$C_4H_8$ | i-$C_4H_{10}$ |
| 0 | 60 | 0.27 | 0.32 | 0.30 | 0.33 |
| 0.415 | 90 | 0.20 | 0.21 | 0.00 | 0.00 |

[a] In 21 ml THF solution containing 0.18 $M$ EtMgBr, 0.30 $M$ t-BuBr and $1.9 \times 10^{-3}$ $M$ reduced form of soluble copper at 2°. Neither coupled dimer nor ethylbenzene was detected after acidic hydrolysis.

show that the products (isobutane and isobutylene) derived from tert-butyl moiety were not detected when the reaction was carried out in the presence of styrene. The tert-butyl adducts to styrene showed characteristic bands at 1357 and 1385 cm$^{-1}$ in the infrared spectrum but were not analyzed quantitatively. These results suggest that the reduced copper catalyst is involved in a series of redox reactions which differ distinctly from the copper(I) catalyzed process described in eqn. (12). The presence of alkyl radicals suggests its kinship to the redox process described previously for reduced iron[15].

$$\text{t-BuBr} + \text{Cu}^0 \xrightarrow{\text{EtMgBr}} \text{t-Bu}^\bullet + \text{CuBr} \qquad (20)$$

$$\text{t-Bu}^\bullet \begin{cases} \xrightarrow{\text{Cu}^0} \text{t-BuCu} & (21) \\ \xrightarrow{\text{Sty}^\bullet} \text{Styrene adducts} & (21') \end{cases}$$

$$\text{CuBr} + \text{EtMgBr} \longrightarrow \text{EtCu} + \text{MgBr}_2 \qquad (22)$$

$$\text{t-BuCu} + \text{EtCu} \longrightarrow \left[ \text{i-C}_4\text{H}_8 + \text{i-C}_4\text{H}_{10} + \text{C}_2\text{H}_4 + \text{C}_2\text{H}_6 \right] + 2\text{Cu}^0 \qquad (23)$$

Similar redox reactions appear to be responsible for some of the disproportionation products [RH and R(−H)] derived from side reactions of the $Cu^I$-catalyzed coupling process. Thus, the effect of styrene can be demonstrated when the copper-catalyzed reaction between ethylmagnesium bromide and ethyl bromide is studied under conditions to promote disproportionation. The latter, for example, is more important at 23° and the addition of styrene influenced the relative rates of formation of ethane and ethylene as shown in Fig. 5. The diminution of ethane (to the extent that it became equal to ethylene) suggests that it was derived from an ethyl radical. Homolytic cleavage of the ethylcopper(I) bond at the higher temperature is possible. It is not essential to the coupling reaction, however, since ethane was only a minor

$$EtCu \longrightarrow Et \cdot + Cu^0, \text{ etc.}$$
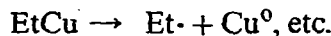
product when coupling was carried out under optimum conditions.

Styrene also increased the initial rate of formation of the coupled dimer somewhat as shown in Fig. 5 and Table 5. The effect of styrene is no doubt complex, but it may be partly ascribed to inhibiting the aggregation of alkylcopper(I) species. Autocatalysis (enhancing catalytic activity with time) was also observed in the absence of styrene (Fig. 5).

*III. Reaction of organocopper(I) species with alkyl bromide in tetrahydrofuran solution*

Some of organocopper(I) species are rather stable thermally in THF solutions as mentioned above (Fig. 1 and Fig. 2), and enabled the coupling between organocopper(I) species and alkyl bromides to be examined directly. When ethyl bromide was added to the purple solution resulting from the reaction of cupric chloride with excess ethylmagnesium bromide at 2° [prior to the apparent decomposition of ethylcopper(I) species], n-butane was formed instantaneously and quantitatively based on the ethyl bromide charged as shown in Fig. 3.

$$EtCu + EtBr \xrightarrow{\text{(EtMgBr)}} Et-Et + CuBr \qquad (24)$$

A similar result was also obtained in the reaction of ethylcopper(I) species with ethyl bromide in the absence of free ethylmagnesium bromide although the yield of n-butane was somewhat lower and the formation of ethane and ethylene higher.

n-Pentane was obtained quantitatively by treatment of the purple solution resulting from the reaction of cupric chloride and excess n-propylmagnesium bromide at 2°, with ethyl bromide.

$$n\text{-PrCu} + EtBr \xrightarrow{\text{(n-PrMgBr)}} n\text{-}C_5H_{12} + CuBr \qquad (25)$$
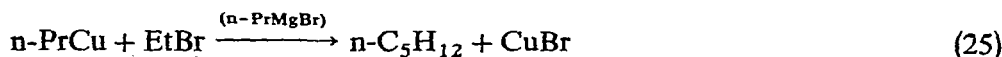
The equivalent result was obtained when the inverse combination was examined in the absence of free Grignard reagent.

$$EtCu + n\text{-PrBr} \longrightarrow n\text{-}C_5H_{12} + CuBr \qquad (26)$$

Analogously, only ethylbenzene was produced when ethyl bromide was added at 25° to the pale yellow suspension of phenylcopper(I) species* prepared from the reaction

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* Not isolated. However, the phenylsilver complex possessing $PhAg(THF)_3$ as the empirical formula has been isolated as pale yellow precipitate under similar reaction conditions (M. Tamura, unpublished study). See also ref. 6.
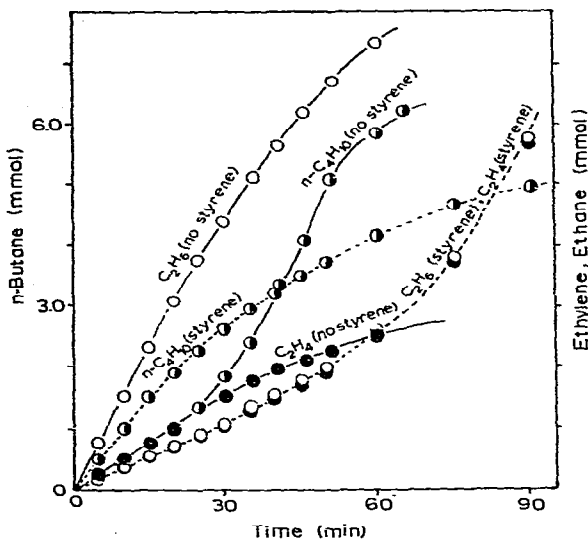
Fig. 5. Effect of styrene (8.7 mmol) on the rates of product formation in the reaction of EtMgBr (7.5 mmol) and EtBr (6.7 mmol) in THF (21 ml) at 23° in the presence of $4.5 \times 10^{-4}$ $M$ CuBr$_2$; ◑ n-Butane (dotted line; in the presence of styrene), ○ ethane (dotted line; in the presence of styrene), ● ethylene (dotted line; in the presence of styrene).
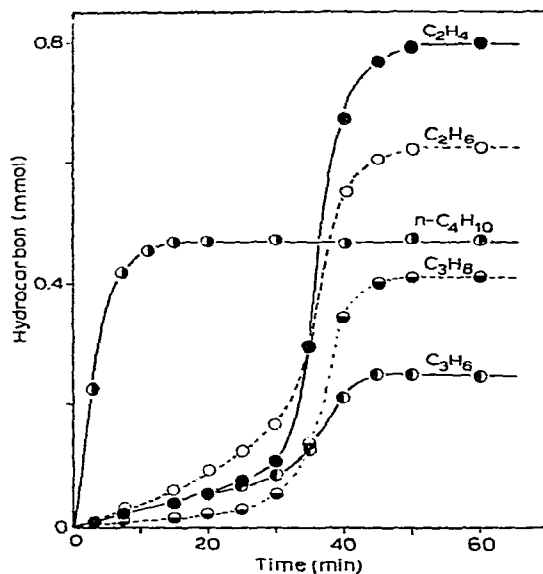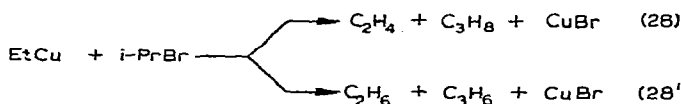
Fig. 6. Rates of product formation in the reaction of EtMgBr (2.5 mmol) with i-PrBr (10.0 mmol) in the presence of CuBr$_2$ (1.0 mmol) in THF (21 ml) at 2°; ◑ n-Butane, ○ ethane, ● ethylene, ◐ propane, ◑-propylene. Additional propane, ethane and 2,3 dimethylbutane were not formed even on acidic hydrolysis (at 60 min) and a trace of isopentane ( < 0.02 mmol) was detected.

of cuprous bromide and phenylmagnesium bromide in stoichiometric amounts at 25° for 30 min in THF solution.

$$PhCu + EtBr \longrightarrow PhEt + CuBr \qquad (27)$$

An equivalent amount of cuprous bromide was formed and no appreciable amount of metallic copper appeared in these reactions*.

The formation of n-butane and ethylcopper(I) from the reaction of cupric bromide and ethylmagnesium bromide is shown in Fig. 6. The addition of isopropyl bromide was followed by an induction period (30 min) after which ethylene, ethane, propylene and propane were formed rapidly. No additional coupled dimer (n-butane, isopentane and 2,3-dimethylbutane) was formed, and the corresponding amount of cuprous bromide was produced after completion of the reaction. The results in Fig. 6 suggest that alkane was derived mainly from the isopropyl moiety and alkene mainly from the ethyl group.

$$EtCu + i\text{-}PrBr \left\{ \begin{array}{l} \longrightarrow C_2H_4 + C_3H_8 + CuBr \qquad (28) \\ \longrightarrow C_2H_6 + C_3H_6 + CuBr \qquad (28') \end{array} \right.$$

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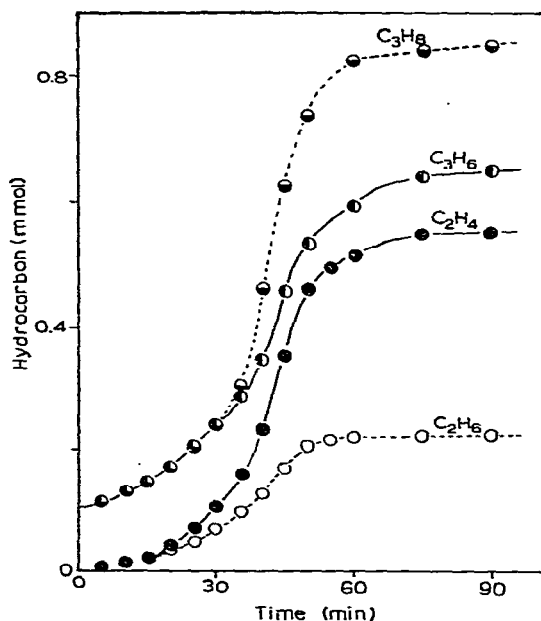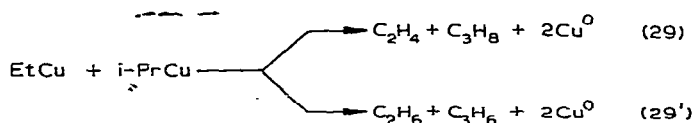* Metallic copper can be separated from cuprous halide by extraction with concentrated ammonia.

Fig. 7. Rates of product formation in the reaction of $CuBr_2$ (2.0 mmol) with an equimolar mixture of EtMgBr-(4.5 mmol) and i-PrMgBr (4.5 mmol) in THF (21 ml) at 2°. n-Butane (0.09 mmol), isopentane (0.39 mmol) and 2,3-dimethylbutane (0.37 mmol) were also formed.

The same tendency for alkane to be formed from the isopropyl group, and alkene from the ethyl group was obtained in the thermal decomposition of a mixture of isopropylcopper(I) and ethylcopper(I) resulting from the reaction of cupric bromide and an equimolar mixture of ethylmagnesium bromide and isopropylmagnesium bromide (Fig. 7). An equivalent amount of copper metal precipitated in the latter reaction.

$$EtCu + i\text{-}PrCu \begin{cases} \longrightarrow C_2H_4 + C_3H_8 + 2Cu^0 \quad (29) \\ \\ \longrightarrow C_2H_6 + C_3H_6 + 2Cu^0 \quad (29') \end{cases}$$

The lower reactivity of isopropyl bromide compared to ethyl bromide was shown clearly in the reaction of ethylmagnesium bromide and isopropyl bromide in the presence of catalytic amounts of cupric bromide (Fig. 8). The rates of formation of all the products were increased markedly by the addition of ethyl bromide (after 60 min).

*IV. Oxidation of alkylcopper(I) species with nitrogen-containing oxidants in tetrahydrofuran*

It has been reported recently that the coupled dimer is produced in a high yield during the oxidation of dialkylcuprate with molecular oxygen or nitrobenzene in ethereal solvents at low temperature[11a]. In the oxidation of the methylmanganese complex in THF solution with molecular oxygen or nitrogen dioxide, we also found that ethane was produced as a main product[18]. On the other hand, with ethyl-
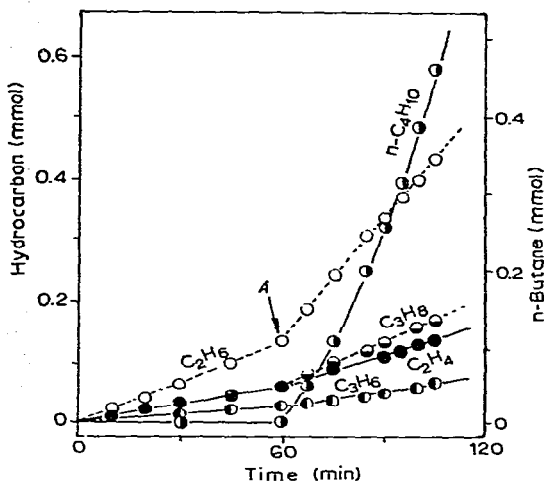
Fig. 8. Rates of product formation in the reaction of EtMgBr (7.0 mmol) with i-PrBr (6.75 mmol) in THF (21 ml) at 23° in the presence of $2.85 \times 10^{-4}$ M CuBr$_2$. A, EtBr (6.75 mmol) was added at this point. ◐ n-Butane, ○ ethane, ● ethylene, ◓ propane, ◑ propene. Isopentane and 2,3-dimethylbutane were not obtained even after 120 min.
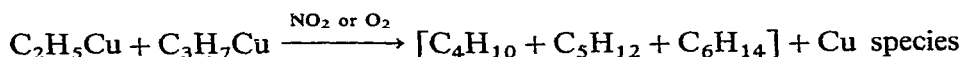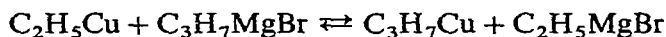
manganese and n-propylmanganese complexes which have $\beta$-hydrogens disproportionation products were the main products under similar conditions[18]. The oxidation of alkylcopper(I) species containing $\beta$-hydrogens with molecular oxygen or nitrogen dioxide selectively afforded coupled dimer as shown in Table 7. In the oxidation of a mixture of ethylcopper(I) and n-propylcopper(I) with nitrogen dioxide or molecular oxygen, a mixture of three coupled dimers was obtained in the same ratio as that observed in the reaction of cupric bromide with an equimolar mixture of ethylmagnesium and n-propylmagnesium bromides in THF[14].

TABLE 7

OXIDATION OF ALKYLCOPPER SPECIES WITH NITROGEN-CONTAINING OXIDANT IN TETRAHYDROFURAN SOLUTION[a]

| Alkyl-copper RCu | Additive R'MgBr | Oxidant | Temp. (°C) | Period (min) | Dimer distribution (mol %) | | | Dimer yield (%)[b] |
|---|---|---|---|---|---|---|---|---|
| | | | | | R–R | R–R' | R'–R' | |
| EtCu | | NO$_2$ | 2 | 15 | 100 | | | 80 |
| n-PrCu | | O$_2$ | −50 | 30 | 100 | | | 95 |
| EtCu | n-PrMgBr | NO$_2$ | 2 | 15 | 25.9 | 50.0 | 24.1 | 116 |
| n-PrCu | EtMgBr | NO$_2$ | 2 | 15 | 37.6 | 49.4 | 13.0 | 154 |
| n-PrCu | EtMgBr | O$_2$ | −78 | 30 | 31.8 | 51.7 | 16.5 | 100 |
| EtCu | (EtMgBr)[c] | LiNO$_3$ | 25 | 60 | 100 | | | 145 |

[a] In 21 ml THF solution containing 1.0 mmol alkylcopper(I) species in the presence or in the absence of 1.0 mmol Grignard reagent (R'MgBr) with 2.0 mmol oxidant. Alkylcopper(I) species was prepared from the reaction of cupric chloride (1.0 mmol) and the corresponding Grignard reagent (RMgBr, 2.0 mmol) at −10° for 15 min. R'MgBr was added before the addition of oxidant (5.0 min before). [b] R–R from the reaction of cupric chloride with RMgBr was subtracted as a blank. Dimer yield (2R–R+2R–R'+2R'–R') was based on alkylcopper (1.0 mmol). [c] In the presence of 7.0 mmol EtMgBr and 1.0 mmol lithium nitrate.

$$C_2H_5Cu + C_3H_7MgBr \rightleftharpoons C_3H_7Cu + C_2H_5MgBr$$

$$C_2H_5Cu + C_3H_7Cu \xrightarrow{\text{NO}_2 \text{ or } \text{O}_2} [C_4H_{10} + C_5H_{12} + C_6H_{14}] + Cu \text{ species}$$

The reaction mixture after these oxidations were complete was generally colorless. The structure of the copper species formed *in situ* has as yet not been identified.

Lithium nitrate was also capable of oxidizing ethylcopper(I) species. The formation of more than stoichiometric amounts of coupled dimer in the presence of excess ethylmagnesium bromide indicates substantial recycling of the copper species through several oxidation states similar to those observed earlier for silver and other transition metals[23]. The reaction mixture consisted of a partially homogeneous brown solution in which the copper species may be zerovalent, although no firm evidence is available yet concerning the structure or extent of aggregation of the species. An aliquot of this solution was used as a soluble reduced copper catalyst in some of this work (Table 6). The copper which remained in solution as a metastable species, however, was quantitatively precipitated as copper metal on standing or on treatment with dilute sulfuric acid.

DISCUSSION

*The catalytically active species in the coupling reaction*

A few organocopper(I) species, especially arylcopper(I) derivatives, have been prepared by metathesis of cuprous halide with the corresponding Grignard reagent or organolithium compound and then isolated from an ethereal solution[6].

$$ArM + CuX' \rightarrow ArCu + MX'$$
$$(M = MgX \text{ or } Li) \tag{30}$$

It has also been recently reported that arylcopper(I) species exist as polynuclear clusters in diethyl ether. Biphenyl derivatives appear to be produced stepwise on thermal decomposition[20a].

$$Ar_8Cu_8 \rightarrow Ar-Ar + Ar_6Cu_8 \text{ etc.} \tag{31}$$

A methylcopper(I) complex was obtained as a yellow precipitate in the reaction between stoichiometric amounts of cuprous iodide and methyllithium in diethyl ether at low temperature[25a]. Methylcopper(I) complexes have also been isolated from the alkylation of copper halides with tetramethyllead[25b] and dimethylzinc[25c] compounds. In the latter study, ethylcopper(I) and n-propylcopper(I) compounds were also isolated but reported to decompose explosively. Lithium dialkylcuprate can be formed from cuprous halide with two equivalents of alkyllithium compound. The thermal stability of these organocopper species is improved remarkably in diethyl ether solution, although their structure in solution has not been fully established[11a].

$$2RLi + CuX \rightarrow R_2CuLi + LiX \tag{32}$$

Most of reactions in this study were carried out with alkyl Grignard reagents and alkyl bromides which possess $\beta$-hydrogens and we did not attempt to isolate

the alkylcopper(I) species formed *in situ*. The negative Gilman color test, the afore-mentioned alkylation of copper halides and the stoichiometry of the reactions, however, strongly indicated that alkylcopper(I) species were produced when cuprous or cupric halide was treated with an equivalent amount of Grignard reagent in THF solution. The homogeneous purple solution resulting from the reaction of cupric chloride and ethylmagnesium or n-propylmagnesium bromide was fairly stable thermally at 2°, and the rate of its decomposition could be followed directly (Fig. 1 and 2).

We propose alkylcopper(I) species as the active intermediates in the coupling process. The kinetic results show that the rate of formation of dimer is roughly first order in the Grignard reagent even when catalytic amounts of copper halides were used (Table 2). The anation of $Cu^I$ under these conditions must be rapid and not rate-determining.

$$RMgX + Cu^IX \rightarrow RCu + MgX_2$$
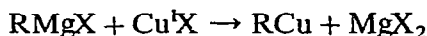
Lithium chloride and THF enhance the thermal stability of alkylcopper(I) species probably due to complex formation*, otherwise the thermal instability of the alkyl-copper(I) species leads to disproportionation of the alkyl group. For this reason optimum conditions for the cross-coupling process favor low temperatures and THF in preference to diethyl or dibutyl ether.

A metallic state of copper cannot be an essential active species for the coupling process, since only ethane and ethylene were produced quantitatively in the reaction of ethylmagnesium bromide and ethyl bromide with a copper metal catalyst (Table 2 and Fig. 3). Alternatively, an alkylcopper(II) species is not plausible as an active species since it is highly metastable and readily reduced to $Cu^I$ under the reaction conditions and even at the much lower temperatures given in Table 1. Furthermore, cuprous halides exhibited essentially the same catalytic activity in the coupling reaction as that shown by cupric halide. Further speculation on the details of the structure of the catalytically active species for coupling is unprofitable until more information concerning the state of aggregation of the alkylcopper(I) species in solution and the role of each component in the reaction is available.

*Mechanism of the coupling reaction*

Catalytic amounts of cuprous halide induce the cross coupling reaction between Grignard reagent and primary alkyl halides under mild reaction conditions. The rate of coupling between ethylmagnesium bromide and ethyl bromide is roughly first order in ethylmagnesium bromide, ethyl bromide and cuprous halide. The formation of only the cross-coupled product and the studies with styrene can be used to eliminate a process involving the bimolecular coupling of two alkylcopper(I) species similar to that proposed in the coupling reaction catalyzed by silver[22].

$$RAg + R'Ag \rightarrow R-R' + 2Ag^0 \tag{33}$$

$$RCu + R'Cu \nrightarrow R-R' + 2Cu^0 \tag{34}$$

In fact no homocoupled dimer is produced from alkylcopper(I) species generated from the reaction of cuprous halide and an alkyl Grignard reagent containing $\beta$-

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* The catalytically active species for the Kharasch reaction are also assumed to be the lower-valent transition metals complexed with Grignard reagents[12a,12z,15,22].

hydrogens (Table 1). We suggest that the cross-coupled dimer (n-butane) is formed by a displacement reaction between the alkylcopper(I) species and alkyl bromide, *e.g.*,

$$EtCu + EtBr \rightarrow Et-Et + CuBr \tag{24'}$$

The effect on the rate of the coupling reaction by structural variations in the alkyl halide as well as the reaction kinetics suggest a rate-determining step involving nucleophilic displacement of the halide. An $S_N2$ type of displacement at carbon was also indicated by the stereochemistry of the coupling between lithium diphenylcuprate and 2-bromobutane[11a]. The coupling between the more thermally stable arylcopper(I) complex with organic halides has been shown to proceed by a similar displacement[8].

$$ArCu + RX \rightarrow ArR + CuX \tag{1'}$$

The following catalytic process is suggested for the cross-coupling reaction.

$$RMgBr + Cu^IBr \rightarrow RCu^I + MgBr_2 \tag{35}$$

$$RCu^I + R'Br \rightarrow R-R' + Cu^IBr, \text{ etc.} \tag{36}$$

The coupling process is catalyzed by copper(I) compounds, and long kinetic chains due to the facility of reaction (36) are only observed with primary alkyl bromides.

An alternative mechanism involving oxidative addition[26] of alkyl halide to alkylcopper(I) is also a possibility, although oxidation of the lower-valent copper(I)

$$RCu^I + R'Br \rightarrow RR'Cu^{III}Br \rightarrow R-R' + Cu^IBr \tag{37}$$
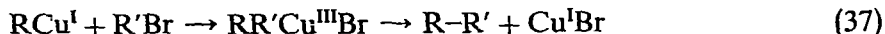
species with an alkyl halide usually proceeds by one-electron transfer oxidation[15,22,27]. There is recent evidence, however, for some substitution reactions catalyzed by copper(I) and gold(I) to proceed via oxidative addition[28]. However, the mechanistic distinction between displacement [eqn. (36)] and oxidative displacement [eqn. (37)] is not important for our purposes here. It should be reemphasized that alkyl radicals are not viable intermediates in the coupling process.
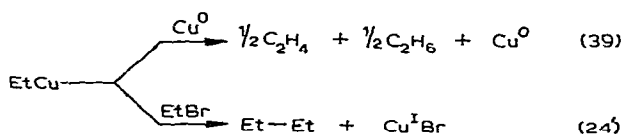
*The mechanism of the disproportionation process*

The catalytic reaction between Grignard reagents and secondary or tertiary alkyl bromides is very slow (Table 4 and Fig. 8) and affords only disproportionation products, despite the lower dissociation energy of the C–Br bonds in these alkyl bromides. The predominant formation of disproportionation products also observed in the reaction of the stoichiometric amounts of ethylcopper(I) species with isopropyl bromide (Fig. 6) can be attributed to the unfavorable displacement step compared to that of primary alkyl halides*. The similarity of the pattern of reactivity and the distribution of products in the reaction between ethylcopper(I) species and isopropyl bromide (Fig. 6) and that in the thermal decomposition of a mixture of ethylcopper(I) and isopropylcopper(I) (Fig. 7), suggest that isopropylcopper(I) plays an important role in disproportionation. The formation of isopropylcopper(I) from isopropyl bromide is possible by the reoxidation shown in eqn. (38) of the active copper resulting from the decomposition of ethylcopper(I) species previously given in eqn. (9) or (29).

$$i\text{-PrBr} + Cu^0 \rightarrow i\text{-Pr}\cdot + Cu^IBr \tag{38}$$

$$i\text{-Pr}\cdot + Cu^0 \rightarrow i\text{-PrCu, etc.} \tag{38'}$$

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* This behavior of secondary and tertiary alkyl halides has also been observed in the reactions of alkylcuprates with alkyl halides[11a].
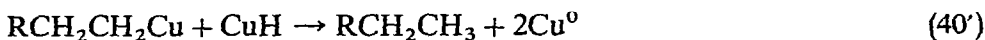
Catalytic disproportionation is also observed in the reaction of ethylmagnesium bromide and tert-butyl bromide with a reduced form of copper. The reaction sequence represented by eqn. (20)–(23) is consistent with this disproportionation since styrene selectively scavenged only the tert-butyl moiety (Table 6). A similar process may play a role in the reaction of ethylmagnesium bromide and ethyl bromide with catalytic amounts of the reduced form of copper, since ethane and ethylene are formed in addition to n-butane (52 mol %). The higher yield of coupled dimer in this case is, no doubt, attributable to the more facile displacement reaction shown by ethyl bromide compared to tert-butyl bromide (Table 4). In contrast, the coupled dimer is not obtained in the reaction between ethylmagnesium bromide and ethyl bromide in the presence of large amounts of the reduced form of copper (Fig. 3). This difference is readily ascribable to the catalysis of the decomposition of ethylcopper(I) by the reduced form of copper prior to the attack of ethyl bromide[19].

$$
\begin{array}{l}
\text{EtCu} \left\{
\begin{array}{ll}
\xrightarrow{\ \text{Cu}^0\ } \tfrac{1}{2}\,C_2H_4 \ + \ \tfrac{1}{2}\,C_2H_6 \ + \ Cu^0 & (39) \\[2ex]
\xrightarrow{\ \text{EtBr}\ } Et\!-\!Et \ + \ Cu^I Br & (24)
\end{array}
\right.
\end{array}
$$

Finally we wish to comment briefly on the mechanism of the decomposition of alkylcopper(I) species in solutions. A homolytic decomposition of the alkylcopper(I) species is not an important process under the reaction conditions employed in this work, since a large excess of styrene (as a radical trap) does not influence either the rate of decomposition or the relative rates of formation of ethane and ethylene. This point has also been emphasized in the thermal decomposition of alkenylcopper, alkenylsilver and alkylcopper complexes in ethereal solvent[29]. We have also shown earlier that alkyl radicals are not involved in the thermal decomposition of the alkyl-manganese species[18] and the disproportionation of the alkyliron complex[15] formed as an intermediate in the Kharasch reaction. However, ethane can be produced by the slow homolysis of ethylcopper(I) species in THF, especially at higher temperatures. Homolysis has also been recently shown in the decomposition of neophylcopper(I) derivatives which have no $\beta$-hydrogens[30].

The following two mechanisms have been presented for the non-radical decomposition of alkylcopper(I) species in solution.

*(i). Hydride mechanism[31]:*

$$RCH_2CH_2Cu \rightarrow RCH=CH_2 + CuH \tag{40}$$

$$RCH_2CH_2Cu + CuH \rightarrow RCH_2CH_3 + 2Cu^0 \tag{40'}$$

*(ii). Direct dismutation[1]:*

$$RCH_2CH_2Cu + RCH_2CH_2Cu \rightarrow RCH=CH_2 + RCH_2CH_3 + 2Cu^0 \tag{41}$$

The choice between either or both mechanisms cannot yet be made on the basis of the evidence at hand. The following results obtained in this study, however, are noteworthy. First, the relative rate of formation of ethane and ethylene is one in the presence of styrene even at low concentration ($\sim 10^{-4}$ M) of the alkylcopper(I)

species (Fig. 5). Ethylbenzene is not formed in the decomposition of alkylcopper(I) species in the presence of styrene. Second, ethylene and propane are favored products in the co-decomposition of ethylcopper(I) and isopropylcopper(I) (Fig. 7) despite the more facile $\alpha,\beta$-elimination expected of an hydrido-copper species from isopropylcopper*. Conversely, ethane and propylene are produced preferentially in the co-decomposition of ethylcopper(I) and n-propylcopper(I) species. In addition, n-butane (the cross coupled product) is the predominant product in the co-decomposition of methylcopper(I) and n-propylcopper(I) species[14].

$$\text{MeCu} + \text{n-PrCu} \rightarrow \text{C}_4\text{H}_{10} + 2\text{Cu}^0 \tag{42}$$

Third, the sterically more hindered neopentylcopper(I) species is more stable thermally than methylcopper(I)[14]. Fourth, no appreciable amounts of hydrogen are detected during the decomposition of n-propylcopper(I). Fifth, no dimer is formed in the decomposition of alkylcopper(I), despite the expected similarity in the transition states for dismutation and coupling. Sixth, the decomposition of the analogous alkylsilver(I) and alkylgold(I)[33] species affords dimers.

The mechanisms (i) and (ii) have also been discussed for the decomposition of alkylmanganese[18], alkyliron[15] and other alkyl transition metal complexes[14]. However, the solvent[21], the Grignard reagent[34], the magnesium halide[34] and the alkyl halide may all have a profound influence on the degree of association and the rate of decomposition of alkylcopper(I) species in solution. Any complete mechanism must take into account the extent of aggregation of the alkylcopper(I) species as well as the coordination by various ligands. For example, the difference between the hydride mechanism and the direct dismutation is essentially one of timing in the making and breaking of bonds and could well be vitiated by reactions occurring within a polynuclear aggregate. At this juncture further discussion of the mechanism of the decomposition of alkylcopper(I) species in solution must be deferred, especially in view of the unusual autocatalysis by the reduced form of copper generated during the decomposition of alkylcopper(I) species[19].

EXPERIMENTAL

*Materials*

A billet of triply sublimed magnesium was supplied from Dow Chemical Co., (Spectrographic analysis: Cu, $< 0.001$; Fe, $< 0.0003$; Mn, $< 0.001$; Ni, $< 0.0005$; Pb, $< 0.003$; Co, $< 0.005$; Cr, $< 0.005$; Ag, $< 0.001$; Rh, $< 0.005$; Pd, $< 0.001$; Mo, $< 0.005$; Ti, $< 0.005\%$). Anhydrous cuprous chloride, cuprous bromide, cupric chloride, cupric bromide, lithium chloride, and lithium nitrate were commercial grade substances and were dried *in vacuo* at $110°$ for 50 h and stored in a desiccator. Ethyllithium (benzene solution) and n-butyllithium (n-hexane solution) were also commercial grade substances and were used without further purification. Neopentyl bromide was prepared from the reaction of neopentyl alcohol and tri-n-butylphos-

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* The $\alpha,\beta$-elimination of metal hydrides from various main group and transition metal alkyls generally follows the trend, tert > sec ≫ prim (refs. 1 and 32). These results, however, must be interpreted with caution since the rates of protonolysis of the alkylcoppers in eqn. (40') must also be taken into account (private communication, Dr. G. M. Whitesides).

phine dibromide[35]. Triphenylphosphine and nitrogen dioxide were commercial grade substances and were used without further purification. Styrene and all organic halides were purified by distillation before use.

*Solvents*

Tetrahydrofuran was obtained in small sealed containers from E.I. DuPont Co., and purified further by refluxing over lithium aluminium hydride for 2 days, fractionated under nitrogen and stored under helium. Diethyl ether was purified similarly.

*Preparation of Grignard reagent*

Grignard reagents were prepared as usual except for the use of 1.5–2.0 times excess metallic magnesium and low temperatures (5–25°). After filtration under nitrogen, all solutions of Grignard reagents (0.5–2.0 $M$) were almost colorless. Determination of the concentration of each Grignard reagent was carried out both by back titration with base and by the measurement of the amount of hydrocarbon liberated after acidic hydrolysis.

*Analysis of product*

Organic products were analyzed by gas chromatography using the internal standard method after careful calibration under reaction conditions as previously reported[14,15a]. The low molecular hydrocarbons were analyzed directly by extracting a small sample of the gas from the reaction vessel. Internal standards were usually added prior to the reaction. Separation of metallic copper from cuprous bromide in the reaction mixture was effected by extraction with concentrated ammonia and filtration after dilution with distilled water. The amounts of each were determined separately by titration with a standard solution of 0.1 $N$ potassium thiocyanate after oxidation with nitric acid.

*The reaction of ethylmagnesium bromide and ethyl bromide induced by cupric bromide (a representative kinetic run)*

A 250 ml round bottomed flask was equipped with a magnetic stirrer bar, and a rubber serum cap was placed at the top of the flask. The atmosphere was replaced with helium for 30 min and 17 ml of THF, 3.0 ml of ethylmagnesium bromide (corresponding to 0.27 $M$ in reaction solution) and 0.80 ml of ethyl bromide (0.51 $M$ in reaction solution) were added by means of hypodermic syringes. After the flask was immersed in a dry ice/acetone bath, 25 ml of methane and 25 ml of isobutane (both markers) were added with gas-tight syringes. The flask was then transferred to an ice-water bath (2°). After 15 min agitation 0.30 ml of a solution of cupric bromide in THF (corresponding to $2.8 \times 10^{-4}$ $M$ after dilution in the reaction solution) was added to the solution with stirring. The color of the solution was colorless to pale yellow. At 5 min intervals, a small sample of the gas phase was removed with a hypodermic syringe and analyzed by gas chromatography. The amounts of n-butane, ethane and ethylene taken at 5 min intervals were plotted against time (Fig. 4). From the slope of the resulting line, the rate of formation of each product was calculated (initial rate, Table 3). In the cases of liquid products (*e.g.*, Table 4), the reaction was quenched by the addition of dilute aqueous sulfuric acid at the appropriate time and each product

(except gases) was analyzed by gas chromatography. The apparent rate of formation of each product was calculated by assuming that the rate of formation of each product was linear, at least in the initial stages of the reaction. All subsequent reactions were carried out in a similar manner.

### The rate of decomposition of ethylcopper(I) species in tetrahydrofuran solution

To the same glass apparatus, 1.0 mmol cupric chloride was added under nitrogen atmosphere. The atmosphere in the flask was then replaced with helium and 19.8 ml of THF was added with a hypodermic syringe. After the flask was immersed in a dry ice/acetone bath, 25 ml of methane and 25 ml of isobutane (both markers) were added with syringes. The flask was then transferred to an ice-water bath (2°). After 15 min agitation (cupric chloride was almost insoluble in THF), 1.20 ml of ethylmagnesium bromide (THF solution, 2.0 mmol) was added by means of a hypodermic syringe with rapid stirring. The reaction mixture became homogeneous immediately and turned purple, accompanied by the instantaneous formation of 0.46 mmol n-butane. The purple color persisted for about 30 min and no additional ethylene or ethane was evolved within this period. Evolution of ethylene and ethane commenced at 40 min and the color of the solution gradually changed to black. The amounts of ethylene and ethane were followed by continual sampling and analysis of the gas phase at 5 min intervals (Fig. 1). The induction period in the decomposition of various alkylcopper(I) species in solution, however, varied somewhat with different batches. After 75 min no additional ethylene or ethane was formed and the reaction mixture was composed of a black precipitate and a colorless supernatant solution. All subsequent decompositions of alkylcopper(I) species in solution were carried out in a similar manner. The products produced in the reactions of cuprous and cupric halides with Grignard reagents in THF are given in Table 1. All reactions in Table 1 were completed within the periods cited and the reaction mixture in each case consisted of a black precipitate and a colorless solution after completion.

### Preparation of n-decane from n-butylmagnesium bromide and n-hexyl bromide

n-Hexyl bromide (45 mmole), n-butylmagnesium bromide (50 ml of a 1.0 $M$ solution) and 100 ml of THF were added to a 500 ml round bottomed flask which was previously flushed with nitrogen and sealed with a rubber serum cap. A solution (1.5 ml) of dilithium tetrachlorocuprate which was prepared separately by reacting 0.2 $M$ lithium chloride and 0.1 $M$ cupric chloride in a 2/1 molar ratio in THF, was added and the mixture was stirred for 3 h at 0°. The reaction mixture was worked up in the usual manner after addition of dilute sulfuric acid and extraction with petroleum ether. Distillation afforded 4.97 g (78% based on n-hexyl bromide) n-decane (b.p. 105°/80 mmHg) which contained only negligibly small amounts of n-octane and n-dodecane.

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