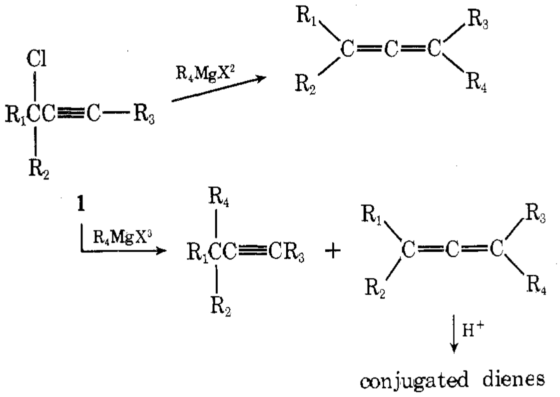
Reaction of Propargyl Halides with Grignard Reagents. Iron Trichloride Catalysis in Allene Formation[1]

Summary: Ferric chloride catalyzes the highly selective formation of allenes in the reaction of propargyl chlorides with Grignard reagents; this procedure possesses many advantages for the preparation of allenes compared to those involving the reactions of lithium dialkylcuprates with proparyl and allenyl halides and acetates.

Sir: Several reports on the reactions of propargylic halides of general structure 1 with Grignard reagents have appeared describing contrasting results. In particular, Zakharova[2] describe the formation allenes as the major products, whereas Jacobs and Meyers[3a] report the formation of alkynes and conjugated dienes as major products, the latter later being shown to arise by facile acid-catalyzed isomerization.[3b] In a comprehensive study of the reactions of terminal and nonterminal propargylic chlorides with organometallic reagents and transition metal catalysts, we have discovered a highly selective, iron catalyzed formation of allenes from the reactions of 1 with Grignard reagents.[4,5] The recent appearance of several articles describing the formation of allenes from propargylic and allenylic halides and acetates prompts us to report our preliminary results on the ferric chloride catalyzed formation of allenes from propargylic chlorides with Grignard reagents.



The reaction of both terminal (1, R_3 = H) and nonterminal (1, $R_3 = CH_3$) propargylic chlorides with primary and secondary Grignard reagents in the presence of 5×10^{-5} M ferric chloride results in the rapid formation of allenes in good yield[6] via proposed organoiron species similar to those proposed by Koichi[7] in the coupling of vinyl halides with Grignard reagents.[5] In contrast, the reactions of terminal propargylic chlorides (1, R_3 = H) with primary Grignard reagents occur very slowly (24 h at 25 °C) to produce mixtures of terminal and nonterminal alkynes and allene via an allene carbene[8] intermediate,[9] while nonterminal propargylic halides react as reported by Jacobs and Meyers.[3] It is concluded that the difference between the results reported by Zakharova[2] and Jacobs and Meyers[3] must be due to presence of iron, or possibly some other transition metal, capable of catalyzing the allene forming process.

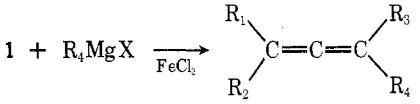


Table I. Yields of Allene Formation in Reactions of 1 with Grignard Reagents in the Presence of Iron

1	R_4MgX	% yield[a]
$R_1 = R_2 = CH_3, R_3 = H$	R_4 = *n*-Bu	80
$R_1 = CH_3, R_2 = R_3 = H$	R_4 = *n*-Bu	90
$R_1 = R_2 = R_3 = CH_3$	R_4 = *n*-Bu	87
$R_1 = R_2 = R_3 = CH_3$	$R_4 = CH_3$	40–43[b]
$R_1 = R_2 = R_3 = CH_3$	R_4 = *i*-Pr	88
$R_1, R_2 = -(CH_2)_5-, R_3 = H$	$R_4 = CH_3$	84
$R_1, R_2 = -(CH_2)_5-, R_3 = CH_3$	$R_4 = CH_3$	45[b]
$R_1, R_2 = -(CH_2)_5-, R_3 = CH_3$	R_4 = *n*-Bu	70–80

[a] GLC yields. [b] Alkyne and allene are formed in a 1:1 mixture. Alkynes are not formed in the reactions of these substrates with *n*-butylmagnesium bromide.

The presently reported synthesis of allenes possesses several advantages over the recently reported syntheses of allenes using lithium dialkylcuprates[10] with propargyl and allenylic halides and acetates. In the reactions with the dialkylcuprates only one of the alkyl groups attached to the Cu is utilized, and the preparation of the reagent requires reacting the alkyllithium with cuprous halide. In contrast, our procedure uses the more easily and directly prepared Grignard reagent in 25–50% excess.[6]

A typical experimental procedure follows. To a solution of 0.0625–0.075 mol of 0.3 M Grignard reagent, to which a sufficient amount of ferric chloride in tetrahydrofuran is added to make the reaction mixture 5×10^{-5} M in ferric chloride, at 0 °C under a nitrogen atmosphere is slowly added 0.05 mol of the propargyl chloride in 15 ml of ether. After stirring at 0° for 15 min, the reaction mixture is hydrolyzed with water and worked up as normal. Table I lists the yields of allene formation in the reactions thus far studied.

References and Notes

(1) The authors acknowledge partial financial support of this research by a grant in aid to G.F.H. from Eli Lilly and Co., Indianapolis, Ind.

(2) A. I. Zakharova, *Zh. Obshch. Khim.*, **17**, 1277 (1947) [*Chem. Abstr.*, **42**, 3722 (1948)]; *Zh. Obshch. Khim.*, **19**, 1297 (1949) [*Chem. Abstr.*, **44**, 1001 (1950)]; A. I. Zakharova and R. A. Sapozhnikova, *Zh. Obshch. Khim.*, **22**, 1804 (1952) [*Chem. Abstr.*, **47**, 6857 (1953)].

(3) (a) T. L. Jacobs and R. A. Meyers, *J. Am. Chem. Soc.*, **86**, 5244 (1964); (b) T. L. Jacobs and P. Prempree, *ibid.*, **89**; 6177 (1967).

(4) The magnesium used by Jacobs and Meyers[3] contained a stated impurity level of iron of ≤0.001% which corresponds to $\lesssim 4 \times 10^{-6}$ M iron in their experiments. The iron content of the magnesium used by Zakharova[2] was not indicated.

(5) A detailed description of this work and proposed mechanisms for product formation will be presented in subsequent full articles.

(6) Low yields (<5%) of dimeric products derived from the Grignard reagent and the propargylic chloride are also formed.[5]

(7) R. S. Smith and J. K. Koichi, *J. Org. Chem.*, **41**, 502 (1976).

(8) For examples of nucleophilic attack on allenecarbene, see G. F. Hennion and J. F. Motier, *J. Org. Chem.*, **34**, 1319 (1969), and references cited therein.

(9) D. J. Pasto, G. F. Hennion, R. Shults, and J. A. McGrath, unpublished results.

(10) P. Crabbé, E. Barreiro, J.-M. Dollat, and J.-L. Luche, *J. Chem. Soc., Chem. Commun.*, 183 (1976); J.-L. Luche, E. Barreiro, J.-M. Dollat, and P. Crabbé, *Tetrahedron Lett.*, 4615 (1975); M. Kalli, P. D. Landor, and S. R. Landor, *J. Chem. Soc., Perkin Trans. 1*, 1347 (1973); P. Crabbé and H. Carpino, *J. Chem. Soc., Chem. Commun.*, 904 (1972); P. Rona and P. Crabbé, *J. Am. Chem. Soc.*, **91**, 3289 (1969).

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