New Homo-coupling Reaction of Alkyl, Aryl, Vinyl, and Allyl Grignard Reagents Using Trifluoromethanesulfonic Anhydride

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(Received March 27, 1996)

Homo-coupling reaction of various alkyl, aryl, vinyl, and allyl Grignard reagents with trifluoromethanesulfonic anhydride provides a simple and straightforward method for the syntheses of symmetrical carbon-carbon coupling products under mild conditions and in moderate to good yields.

The transition metal promoted coupling reactions of organic halides are one of the most attractive and useful synthetic methods for formation of the carbon-carbon bond, because the reaction proceeds under mild conditions as compared with the classical Ullmann conditions.[1] Aryl halides dimerize (homo-coupling) readily in the presence of nickel species. Synthetically useful yields of homo-coupling products have been obtained using nickel species in situ generated from nickel(II) bromide and zinc,[2] nickel(II) complex and zinc,[3] nickel-phosphine complex[4] and a solvated nickel(0) reagent.[5] The homo-coupling reactions of benzyl, allyl and vinyl halides have also been reported using Te(II) generated in situ,[6] $CoCl(Ph_3P)_3$[7,8] and a solvated nickel(0) reagent.[5]

Reactions of organometallic reagents, such as organolithium and Grignard reagents, with transition metal salts also provide synthetic methods to the formation of the carbon-carbon bond; Ni,[9-11] Cu,[12,13] Ag[14] and various metals[15-17] have been used successfully.

We wish to report a new simple and general procedure for the homo-coupling reaction of alkyl, aryl, vinyl, and allyl magnesium halides using trifluoromethanesulfonic anhydride (Tf_2O) (Scheme 1). To the best of our knowledge, Tf_2O has never been utilized as a homo-coupling agent of Grignard reagents.

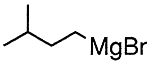
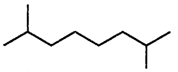
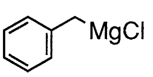
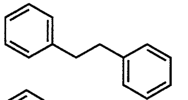
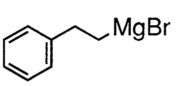
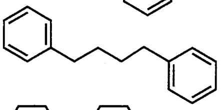
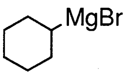
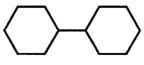
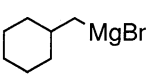
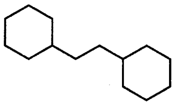
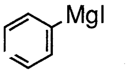
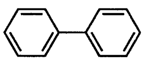
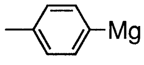
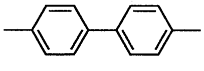
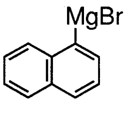
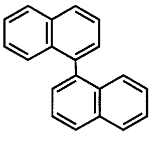
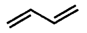
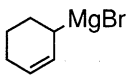
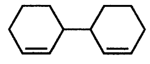
$$\text{RMgX} \xrightarrow[\text{5~30 °C, 20~30min}]{Tf_2O} \text{R}-\text{R}$$

R= alkyl, aryl, vinyl, allyl

Scheme 1.

Table 1 summarizes the results of the homo-coupling reaction of alkyl, aryl, vinyl, and allyl Grignard reagents with an equimolar amount of trifluoromethanesulfonic anhydride in refluxing dry diethyl ether. The ^1H NMR and mass spectra were fully in agreement with the structures shown.[18,19] This reaction sequence seems to be applicable to the coupling of primary and secondary alkyl Grignard reagents in moderate yields (entries 1 - 5). In this reaction, a stoichiometric amount of Tf_2O was necessary for the homo-coupling reaction. After treatment of phenethylmagnesium bromide with 0.5 and 0.2 equivalent of Tf_2O, the yield of 1,4-diphenylbutane decreased to 48 and 14%, respectively (entry 3). The effect of using a low temperature was examined in the case of cyclohexylmethylmagnesium bromide, and, when the homo-coupling reaction was carried out at 5 °C for 30 min, 1,1'-(1,2-ethanediyl)biscyclohexane was obtained in a yield of 75% (entry 5).

Table 1. Homo-Coupling Reaction of Grignard Reagents using Trifluoromethanesulfonic Anhydride[a]

Entry	Grignard reagent	Product	Yield / %[b]
1			80
2			95
3			81 48[c] 14[d]
4			95
5			75[e]
6			66
7			48
8			82
9			56[f,g]
10			85[g,h]

[a] Unless otherwise mentioned, all reactions proceeded in refluxing diethyl ether for 20 min. [b] Isolated yields. [c] The amount of Tf_2O was 0.5 equivalents. [d] The amount of Tf_2O was 0.2 equivalent. [e] Reaction runs at 5 °C for 30 min. [f] Product was trapped with excess bromine in carbon tetrachloride to give 1,2,3,4-tetrabromobutane. [g] In THF. [h] Meso and *dl*.

Phenylmagnesium iodide gave biphenyl in 66% yield (entry 6). Similarly, *para*-substituted aryl Grignard reagent gave coupled product in 48% yield under the same reaction conditions (entry 7). On the other hand, *ortho*-substituted aryl Grignard reagents gave poor yields of coupled biphenyls. Treatment of α-naphthylmagnesium bromide gave 1,1'-binaphthyl in 82% yield (entry 8). When vinylic magnesium bromide was used, conjugated 1,3-diene was obtained (entry 9): vinyl magnesium bromide gave 1,3-butadiene in 56% yield (entry 9). Furthermore, the allylic Grignard reagent gave a coupled product. Reaction of 2-cyclohexen-1-yl magnesium bromide with Tf_2O gave bi-2-cyclohexen-1-yl in 85% yield as a mixture of meso and *dl* (entry 10).[6]

As can be seen from Table 1, the reaction appears to be successful for alkyl, aryl, vinyl, and allyl magnesium halides and thus it has somewhat wider applicability than the comparable method for the homo-coupling reaction with Grignard reagents using Tl(I).[20]

In a typical experiment, benzylmagnesium chloride was prepared by the reaction of benzyl chloride (940 mg, 7.4 mmol) in dry diethyl ether (10 ml) with magnesium (187 mg, 7.7 mmol) at a refluxed temperature under nitrogen. After 0.5 h the resulting Grignard reagent was cooled to room temperature and a solution of trifluoromethanesulfonic anhydride (2.08 g, 7.4 mmol) in dry diethyl ether (5 ml) was gradually added over 10 min. The exothermic reaction took place and the reaction mixture turned from gray to reddish brown. After refluxing was allowed to continue for 20 min, the reaction mixture was cooled to room temperature, quenched with water, and extracted with diethyl ether. The extracts were chromatographed on silica gel to give 1,2-diphenylethane in 95% yield.

In summary, we developed a new homo-coupling reaction for the construction of a synthetically important carbon-carbon bond. The mild reaction conditions together with the simple experimental procedure may be widely applicable to a variety of Grignard reagents. Study on the reaction mechanism of the present homo-coupling reaction is currently under investigation.

References and Notes

1 P. E. Fanta, *Synthesis*, **1974**, 9.

2 K. Takagi, N. Hayama, and S. Inokawa, *Chem. Lett.*, **1979**, 917.

3 M. Iyoda, H. Otsuka, K. Sato, and M. Oda, *Bull. Chem. Soc. Jpn.*, **63**, 80 (1990).

4 M. Zenbayashi, K. Tamao, J. Yoshida, and M. Kumada, *Tetrahedron Lett.*, **1977**, 4089.

5 A. S. Kende, L. S. Liebeskid, and D. M. Braitsch, *Tetrahedron Lett.*, **1975**, 3375.

6 D. L. J. Clive, P. C. Anderson, N. Moss, and A. Singh, *J. Org. Chem.*, **47**, 1641 (1982).

7 Y. Yamada and D. Momose, *Chem. Lett.*, **1981**, 1277.

8 D. Momose, K. Iguchi, T. Sugiyama, and Y. Yamada, *Tetrahedron Lett.*, **1983**, 921.

9 E. Ibuki, S. Ozasa, Y. Fujioka, M. Okada, and K. Terada, *Bull. Chem. Soc. Jpn.*, **53**, 821 (1980).

10 T. Yamamato, Y. Hayashi, and A. Yamamoto, *Bull. Chem. Soc. Jpn.*, **51**, 2091 (1978).

11 T. Yamamoto, K. Sanechika, and A. Yamamoto, *Bull. Chem. Soc. Jpn.*, **56**, 1497 (1983).

12 G. M. Whitesides, J. SanFilippo, Jr., C. P. Casey, and E. J. Panek, *J. Am. Chem. Soc.*, **89**, 5302 (1967).

13 H. Felkin and G. Swierczewski, *Tetrahedron*, **31**, 2735 (1975).

14 M. Tamura and J. Kochi, *Synthesis*, **1971**, 303.

15 G. Cahiez, D. Bernard, and J. F. Normant, *Synthesis*, **1976**, 245.

16 M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Non-Metallic Substances," Constable and Co., Ltd., London (1954).

17 S. W. Breuer and F. A. Broster, *Tetrahedron Lett.*, **1972**, 219.

18 The following coupling products were identified by comparison of its ^{1}H NMR spectrum with established spectral data;[19] 1,2-diphenylethane, 1,4-diphenylbutane, bicyclohexyl, biphenyl, 4,4'-dimethylbiphenyl, 1,2,3,4-tetrabromo-butane, and bi-2-cyclohexen-1-yl.[6] Other compounds reported in this paper gave satisfactory spectral data consistent with the assigned structures. 2,7-dimethyloctane: ^{1}H NMR ($CDCl_3$, 270 MHz): δ 0.89 (d, *J*=6.0 Hz, 12H), 1.16-1.37(m, 10H); MS *m/z* (rel. int., %): 99(15), 71(11), 57(35), 43(100), 42(30), 41(69), 38(23), 29(54), 27(54). 1,1'-(1,2-ethanediyl)bis-cyclohexane: ^{1}H NMR ($CDCl_3$, 270 MHz): δ 0.84-0.89 (m, 4H), 1.12-1.26(m, 12H), 1.62-1.70(m, 10H); ^{13}C NMR ($CDCl_3$, 68 MHz): δ 26.5, 26.9, 33.6, 34.8, 38.1. MS *m/z* (rel. int., %): 194(M^+, 29), 96(12), 83(100), 82(74), 79(21), 67(12), 55(31). 1,1'-binaphtyl: MS *m/z* (rel. int., %): 254(M^+, 100), 253(81), 252(53).

19 C. J. Poucher and J. Behnke, "The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra" Aldrich Chemical Company, Inc. "Handbook of Proton-NMR Spectra and Data" Asahi Research Center Co., Ltd, Ed., Academic Press Inc., 1985.

20 A. McKillop, L. F. Elsom, and E. C. Taylor, *J. Am. Chem. Soc.*, **90**, 2423 (1968).