

Organometallic Reactions in Aqueous Media. Indium-Mediated 1,3-Butadien-2-ylation of Carbonyl Compounds

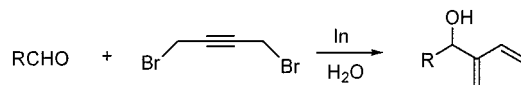
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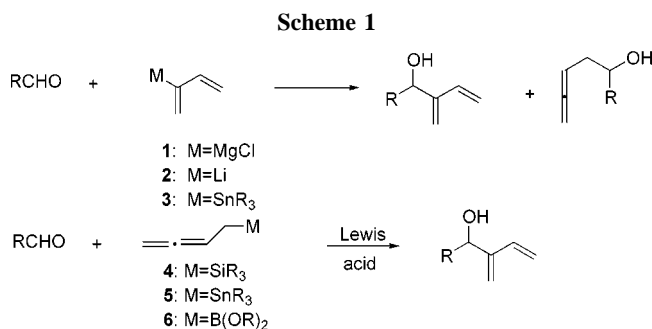
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ABSTRACT



Indium-mediated coupling of 1,4-dibromo-2-butyne with carbonyl compounds in aqueous media gave good yields of the 1,3-butadien-2-ylmethanols.

In view of the usefulness of functionalized dienes in organic synthesis, a number of reagents have been developed for the 1,3-butadien-2-ylation of carbonyl compounds (Scheme 1).



Of these, 2-(1,3-butadienyl)magnesium chloride (**1**) suffers from poor regioselectivity.¹ The corresponding lithium compound **2** has to be prepared indirectly from the 2-stannyl compound **3**.² Homoallylic silane **4**,³ stannane **5**,⁴ and boronate **6**,⁵ though quite effective in reacting with carbonyl

compounds to give regioselective 1,3-butadien-2-ylmethanols, are not convenient to prepare. From the viewpoint of atom economy,⁶ reagents **3–6**, requiring the use of a silyl, stannyl, or boron appendage, cannot be considered as atom economical.⁷ Finally, all these reactions must be carried out in anhydrous organic solvents.

The discovery⁸ in the past decade that the allylation of carbonyl compounds could be achieved in aqueous media through a Barbier-type reaction⁹ has drawn much interest. Metals such as Zn,¹⁰ In,¹¹ Bi,¹² Sn,¹³ Pb,¹⁴ Mn,¹⁵ Mg,¹⁶ or

(2) Wada, E.; Kanemasa, S.; Fujiwara, I.; Tsuge, O. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1942.

(3) (a) Nishiyama, T.; Esumi, T.; Iwabuchi, Y.; Irie, H.; Hatakeyama, S. *Tetrahedron Lett.* **1998**, *39*, 43. (b) Hatakeyama, S.; Yoshida, M.; Esumi, T.; Iwabuchi, Y.; Irie, H.; Kawamoto, T.; Yamada, H.; Nishizawa, M. *Tetrahedron Lett.* **1997**, *38*, 7887.

(4) (a) Luo, M.; Iwabuchi, Y.; Hatakeyama, S. *J. Chem. Soc., Chem. Commun.* **1999**, 267. (b) Yu, C.-M.; Lee, S.-J.; Jeon, M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3557.

(5) (a) Zheng, B.; Srebnik, M. *J. Org. Chem.* **1995**, *60*, 486. (b) Soundararajan, R.; Li, G.; Brown, H. C. *J. Org. Chem.* **1996**, *61*, 100.

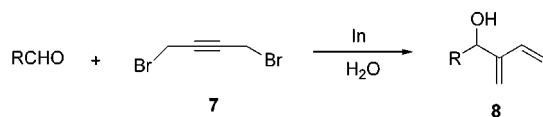
(6) Trost, B. M. *Science* **1991**, *254*, 1471.

(7) In the case of **4** or **5**, a stoichiometric amount of Lewis acid is further required to promote the reaction.

(8) For reviews, see: (a) Li, C. J.; Chan, T. H. *Organic Reactions in Aqueous Media*; John Wiley & Sons Inc.: New York, 1993. (b) Li, C. J. *Chem. Rev.* **1993**, *93*, 2023. (c) Chan, T. H.; Li, C. J.; Lee, M. C.; Wei, Z. Y. *Can. J. Chem.* **1994**, *72*, 1181. (d) Lubineau, A.; Auge, J.; Queneau, Y. *Synthesis* **1994**, 741. (e) Li, C. J. *Tetrahedron* **1996**, *52*, 5643.

(1) Nunomoto, S.; Yamashita, Y. *J. Org. Chem.* **1979**, *44*, 4788.

Scheme 2



Sb¹⁷ have been reported to be effective in mediating the coupling between allyl halides and carbonyl compounds to give the corresponding homoallylic alcohols in aqueous media. Among these reported metals, indium appears to be the metal of choice because it requires no activation, causes few side reactions, and is quite regio- and stereoselective.¹⁸ The indium-mediated coupling reaction has been extended to propargyl bromides.¹⁹ We report here that indium can effectively mediate the coupling between 1,4-dibromobut-2-yne (**7**) and carbonyl compounds in aqueous media to give regioselective 1,3-butadien-2-ylmethanols **8** in good yields (Scheme 2).²⁰

The results are summarized in Table 1. The reaction works

Table 1. Indium-Mediated 1,3-Butadien-2-ylation of Carbonyl Compounds in Water

entry	aldehyde	product	yield % ^a
1	9	10	53
2	11	12	55
3	13	14	60
4	15	16	64
5	17	18	67
6	19	20	68
7	21	22	65

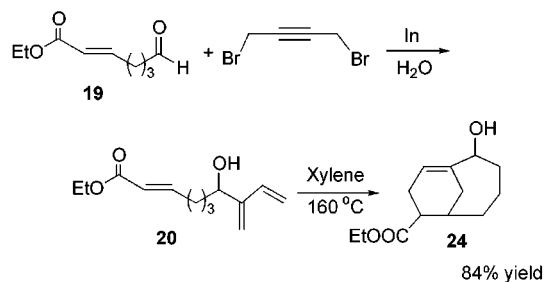
^a Isolated yield.

equally well for aryl and aliphatic aldehydes. With cinnamaldehyde (entry 3), the coupling occurred selectively in the 1,2-addition fashion. The ester function is not affected (entries 6 and 7). The incorporation of an α,β -unsaturated ester function into the structure as in compounds **20** or **22** is interesting since these compounds may serve as pre-

(9) Barbier, P. *Comp. Rend.* **1899**, 128, 110. For a recent monograph, see Blomberg, C. The Barbier Reaction and Related One-Step Processes. In *Reactivity and Structure: Concepts in Organic Chemistry*; Hafner, K., Lehn, J. M., Rees, C. W., von Rague Schleyer, P., Trost, B. M., Zahradnik, R., Eds.; Springer-Verlag: 1993.

cursors for an intramolecular Diels–Alder (IMDA) reaction.²¹ Indeed, when compound **20** was heated in xylene at 160° for 8 h, adduct **24** was obtained in 84% yield (Scheme 3). The possibility of such an IMDA approach to the

Scheme 3



construction of the taxoid skeleton has been noted previously.^{20,22,23}

The reaction is likely to proceed via an organoindium intermediate²⁴ which reacts with the aldehyde to give adduct **26** (Scheme 4). Further reaction of the bromide with indium can lead to another organoindium intermediate, **27**, which is quenched by water to give 1,3-butadienyl-2-methanol **8**. Reaction of **27** with another molecule of aldehyde to give di-adduct **28** was not observed, presumably because of steric hindrance. However, we were able to show that with glutaric dialdehyde **29** intramolecular trapping of intermediate **27** was possible and the cyclic di-adduct **30** was obtained in 40% isolated yield.

(10) (a) Nokami, J.; Otera, J.; Sudo, T.; Okawara, R. *Organometallics* **1983**, 2, 191. (b) Petrier, C.; Luche, J. L. *J. Org. Chem.* **1983**, 50, 910.

(11) (a) Li, C. J.; Chan, T. H. *Tetrahedron Lett.* **1991**, 32, 7017. (b) Paquette, L. A.; Bennett, G. D.; Isaac, M. B.; Chhatrwalla, A. *J. Org. Chem.* **1998**, 63, 1836. (c) Li, C. J.; Chan, T. H. *Tetrahedron* **1999**, 55, 11149 and references therein.

(12) Wada, M.; Ohki, H.; Akiba, K. Y. *Bull. Chem. Soc. Jpn.* **1990**, 63, 2751; *J. Chem. Soc., Chem. Commun.* **1987**, 708.

(13) (a) Nokami, J.; Otera, J.; Sudo, T.; Okawara, R. *Organometallics* **1983**, 2, 191. (b) Nokami, J.; Wakabayashi, S.; Okawara, R. *Chem. Lett.* **1984**, 869. (c) Uneyama, K.; Kamaki, N.; Moriya, A.; Torii, S. *J. Org. Chem.* **1985**, 50, 5396. (d) Wu, S. H.; Huang, B. Z.; Zhu, T. M.; Yao, D. Z.; Chu, Y. L. *Acta Chim. Sin.* **1990**, 48, 372. (e) Einhorn, C.; Luche, J. L. *J. Organomet. Chem.* **1987**, 322, 177.

(14) Zhou, J. Y.; Jia, Y.; Sun, G. F.; Wu, S. H. *Synth. Commun.* **1997**, 27, 1899.

(15) Li, C. J.; Meng, Y.; Yi, X. H.; Ma, J. H.; Chan, T. H. *J. Org. Chem.* **1998**, 63, 7498; *J. Org. Chem.* **1997**, 62, 8632.

(16) Zhang, W. C.; Li, C. J. *J. Org. Chem.* **1999**, 64, 3230. (17) (a) Wang, W.; Shi, L.; Huang, Y. *Tetrahedron* **1990**, 46, 3315. (b) Ren, P. D.; Jin, Q. H.; Yao, Z. P. *Synth. Commun.* **1997**, 27, 2761.

(18) Isaac, M. B.; Chan, T. H. *Tetrahedron Lett.* **1995**, 36, 8957. (19) Isaac, M.; Chan, T. H. *J. Chem. Soc., Chem. Commun.* **1995**, 1003.

(20) For recent reports of indium-mediated synthesis of 1,4-butadien-3-ylation of carbonyl compounds, see: (a) Melekhov, A.; Fallis, A. G. *Tetrahedron Lett.* **1999**, 40, 7867. (b) Woo, S.; Squires, N.; Fallis, A. G. *Org. Lett.* **1999**, 1, 573.

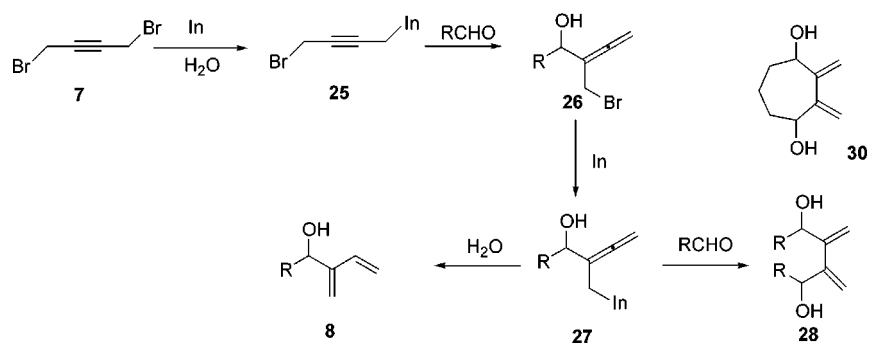
(21) For recent review, see: (a) Fallis, A. G. *Acc. Chem. Res.* **1999**, 32, 464. (b) Fallis, A. G. *Can. J. Chem.* **1999**, 77, 159.

(22) For recent reports, see: (a) Phillips, A. J.; Morris, J. C.; Abell, A. D. *Tetrahedron Lett.* **2000**, 41, 2723 (b) Forgione, P.; Wilson, P. D.; Yap, G. P. A.; Fallis, A. G. *Synthesis* **2000**, 921.

(23) IMDA reaction of **22** under the same reaction condition did not give the bicyclic adduct. See, however, ref 22.

(24) Chan, T. H.; Yang, Y. *J. Am. Chem. Soc.* **1999**, 121, 3228.

Scheme 4



In view of the simplicity of the present process for the synthesis of 2-substituted 1,3-butadienes, the reaction is likely to find considerable applications.²⁵

(25) Standard procedures for the reaction of aldehydes with **7** are as follows: To a mixture of aldehyde (1 mmol) in water (5 mL) and the bromide **7** (1.5 mmol),²⁶ was added indium powder (3 mmol) in one portion, and the mixture was vigorously stirred for 6 h. Ethyl ether was added to the reaction mixture, and the organic layer was separated. The aqueous phase was extracted with ethyl ether. The organic extracts were combined, dried over Na₂SO₄, filtered, and evaporated. The residue, for most of the aldehydes, afforded the corresponding 1,3-butadien-2-ylmethanols **8** as the major product according to ¹H NMR. If necessary, purification was performed by flash chromatography over silica gel using hexane and ethyl acetate as eluent.

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Supporting Information Available: Experimental details and spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL000239K

(26) Compound **7** was synthesized according to the literature: Johnson, A. W. *J. Chem. Soc.* **1946**, 1009.