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Efficient Preparation of Terminal Conjugated Dienes by Coupling of Dienol Phosphates with Grignard Reagents under Iron Catalysis

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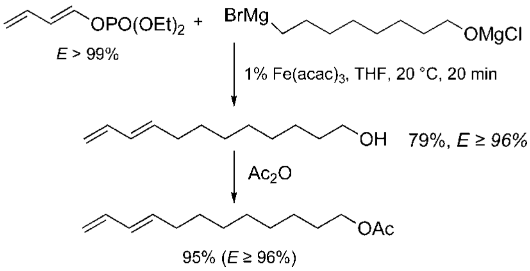
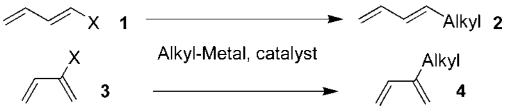
ABSTRACT



An efficient new route to prepare stereoselectively terminal conjugated dienes by coupling Grignard reagents and dienol phosphates in the presence of Fe(acac)$_3$ is described. The synthetic utility of this new iron-catalyzed procedure is illustrated by the synthesis of the pheromone of *Diparopsis castanea* according to a very expeditious strategy.

The stereoselective construction of olefins is a very important step for the preparation of various natural products such as terpenes[1] or insect pheromones.[2] Transition-metal-catalyzed cross-coupling reactions are frequently used because of their high efficiency in this field. Several compounds mentioned above have a terminal conjugated dienyl unit like **2** or **4** in their structure. One of the most straightforward strategies for introducing such units would be to couple an alkylmetal derivative with the dienyl halides **1** or **3** (Scheme 1).

Scheme 1. Straighthforward Strategy for the Synthesis of Terminal Conjugated Dienes



Unfortunately, despite its apparent simplicity, this strategy was very difficult to apply[3] because the starting dienyl halides **1** or **3** have a strong tendency to polymerize. A case in point would be chloroprene, which is the well-known precursor of a family of synthetic rubbers (e.g., neoprene). It is stored and transported under inert atmosphere below −10 °C, and an inhibitor must be added to prevent polymerization.[4] As a rule, butadienyl halides are not easy to store, and their reactions often lead to large amounts of polymers. As a consequence, the examples of coupling of **1** or **3** with

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(1) (a) Thomas, A. F.; Heathcock, C. H.; ApSimon, J. W.; Hooper, J. W. *The Total Synthesis of Natural Products*; ApSimon, J. W., Ed.; Wiley & Sons: New York, 1973; Vol. 2, pp 1−640. (b) Thomas, A. F.; Bessière, Y. *The Total Synthesis of Natural Products*; ApSimon, J. W., Ed.; Wiley & Sons: New York, 1981; Vol. 4, p 451.

(2) Mori, K. *The Total Synthesis of Natural Products*; ApSimon, J. W., Ed.; Wiley & Sons: New York, 1992; Vol. 9, p. 1.

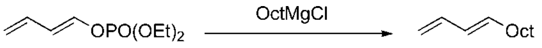
10.1021/ol800816f CCC: $40.75

Grignard reagents, which are one of the most interesting organometallics for preparative large-scale procedure, are very rare.[3c,d]

To overcome this difficulty, we would now like to report a general and very efficient method for preparing terminal dienes: the iron-catalyzed cross-coupling reaction between Grignard reagents and terminal dienol phosphates.[5]

In the past years, iron-catalyzed cross-coupling reactions have been extensively studied by us[6] and others.[7] In 1998, we showed that Grignard reagents readily couple with alkenyl halides in the presence of both iron salts and NMP.[6d] The reaction compares very favorably to the similar palladium or nickel procedures since it is highly stereo- and chemoselective and leads to excellent yields of olefins. Under iron catalysis, the oxidative addition step is clearly easier than with palladium or nickel. Thus, even the less reactive alkenyl chlorides or enol phosphates easily react. In light of these results, we thought that it would probably be possible to couple dienol phosphates, which are much more stable than the corresponding dienyl halides. Thus, they can be stored at room temperature without any special precaution and are easily purified by distillation or by chromatography on a silica gel column. According to our experience with enol phosphates, the first experiment was performed in THF, at −20 °C, in the presence of 1% $Fe(acac)_3$ and 9 equivalents of NMP (Table 1, entry 1). Under these conditions, butadienyl-diethylphosphate **5** coupled with octylmagnesium chloride to give 1,3-dodecadiene **6** in only 54% yield.

Table 1. Iron-Catalyzed Cross-Coupling Reaction of OctMgCl with 1-Butadienyl Phosphate **5**[a]



5 (*E*/*Z* = 99/1)

6 (*E*/*Z* = 98/2)

entry	solvent	$Fe(acac)_3$ (%)	temp (°C)	yield (%)
1	THF/NMP[b]	1	−20	54
2	THF	1	−20	82
3	ether	1	−20	75
4	DME	1	−20	79
5	THF	5	−20	78
6	THF	0.5	−20	40
7	THF	1	0	86
8	THF	1	20	92
9	THF	1	40	91

[a] OctMgCl (13 mmol) was added dropwise for 10 min to a solution of dienol phosphate **5** (10 mmol) and iron acetylacetonate (0.5−5 mol %, see table) in the solvent mentioned above (30 mL) under stirring. [b] Nine equivalents of NMP based on dienol phosphate.

In fact, we found that in the case of dienol phosphates, the presence of NMP is detrimental. Thus, in THF alone the yield is clearly better (82%, Table 1, entry 2). The reaction can also be performed in ether or in DME, but the yields are slightly lower (Table 1, entries 3 and 4). There is no advantage to using more than 1% $Fe(acac)_3$ (Table 1, entry 5). On the other hand, the yield significantly decreases when using only 0.5% (Table 1, entry 6). Finally, we found that, contrary to enol phosphates, dienol phosphates react more efficiently at room temperature since the coupling product is then obtained in excellent yields (Table 1, entry 8).

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(3) Only very few examples of cross-coupling reactions with halo-1,3-butadienes have been reported. (a) The coupling of 1-octyne with the (*Z*)- and (*E*)-1-chloro-1,3-butadienes under the Sonogashira conditions: Huynh, C.; Alami, M.; Linstrumelle, G. *Synth. Commun.* **1994**, *24*, 2273. (b) The Ni-catalyzed coupling reaction of (*Z*)-1-heptenylcyanocuprate with 1-bromo-1,3-butadiene, which leads to 65% yield of (*E*,*Z*)-1,3,5-undecatriene: Alexakis, A.; Barthel, A. M.; Normant, J. F.; Fugier, C.; Leroux, M. *Synth. Commun.* **1992**, *22*, 1839. (c) The Ni-catalyzed coupling of chloroprene with PhMgBr (yield 65%): Tamao, K.; Sumitani, K.; Zembayashi, M.; Fujioka, A.; Kodama, S.-i.; Nakajima, I.; Minato, A.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1958. (d) Me_3SiCH_2MgCl: Sakurai, H.; Hosomi, A.; Saito, M.; Sasaki, K.; Iguchi, H.; Sasaki, J.-i.; Araki, Y. *Tetrahedron* **1983**, *39*, 883.

(4) *Ullmann's Encyclopedia of Industrial Chemistry*, 6th ed.; Wiley-VCH: Weinheim, 2003; Vol. 8, p 89.

(5) To the best of our knowledge, no example of cross-coupling reaction from terminal dienyl phosphates has been reported. For a nickel-catalyzed coupling of nonterminal dienyl phosphate with Grignard reagents, see: Sofia, A.; Karlström, E.; Itami, K.; Bäckvall, J.-E. *J. Org. Chem.* **1999**, *64*, 1745.

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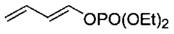
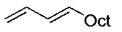
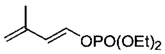
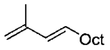
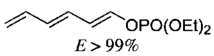
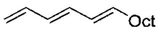
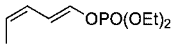
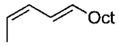
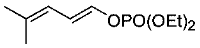
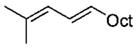
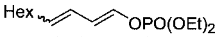
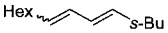
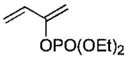
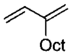
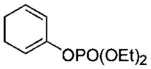
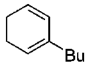
(7) (a) Fürstner, A.; Leitner, A.; Méndez, M.; Krause, H. *J. Am. Chem. Soc.* **2002**, *124*, 13856. (b) Fürstner, A.; Leitner, A. *Angew. Chem., Int. Ed.* **2002**, *41*, 609. (c) Quintin, J.; Frank, X.; Hocquemiller, R.; Figadère, B. *Tettrahedron Lett.* **2002**, *43*, 3547. (d) Martin, R.; Fürstner, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 3955. (e) Scheiper, B.; Bonnekessel, M.; Krause, H.; Fürstner, A. *J. Org. Chem.* **2004**, *69*, 3943. (f) Nakamura, M.; Matsuo, K.; Ito, S.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 3686. (g) Dos Santos, M.; Franck, X.; Hocquemiller, R.; Figadère, B.; Peyrat, J.-F.; Provot, O.; Brion, J.-D.; Alami, M. *Synlett* **2004**, 2697. (h) Nagano, T.; Hayashi, T. *Org. Lett.* **2004**, *6*, 1297. (i) Bedford, R. B.; Bruce, D. W.; Frost, R. M.; Goodby, J. W.; Hird, M. *Chem. Commun.* **2004**, 2822. (j) Martin, R.; Fürstner, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 3955. (k) Nakamura, M.; Matsuo, K.; Ito, S.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 3686. (l) Nagano, T.; Hayashi, T. *Org. Lett.* **2005**, *7*, 491. (m) Bedford, R. B.; Bruce, D. W.; Frost, R. M.; Hird, M. *Chem. Commun.* **2005**, 4161. (n) Bedford, R. B.; Betham, M.; Bruce, D. W.; Danopoulos, A. A.; Frost, R. M.; Hird, M. *J. Org. Chem.* **2006**, *71*, 1104. (o) Zhang, D.; Ready, J. *J. Am. Chem. Soc.* **2006**, *128*, 15050. (p) Xu, X.; Cheng, D.; Pei, W. *J. Org. Chem.* **2006**, *71*, 6637. (q) Durandetti, M.; Perichon, J. *Tetrahedron Lett.* **2006**, *47*, 6255. Durandetti, M.; Perichon, J. *Synthesis* **2006**, 1542. (r) Ottesen, L. K.; Ek, F.; Olsson, R. *Org. Lett.* **2006**, *8*, 1771. (s) Plietker, B. *Angew. Chem., Int. Ed.* **2006**, *45*, 1469. (t) Dunet, G.; Knochel, P. *Synlett* **2006**, 407. (u) Aakermark, B.; Sjoegren, M. P. T. *Adv. Synth. Catal.* **2007**, *349*, 2641. (v) Correa, A.; Bolm, C. *Angew. Chem., Int. Ed.* **2007**, *46*, 8862. (w) Lu, Z.; Chai, G.; Ma, S. *J. Am. Chem. Soc.* **2007**, *129*, 14546. (x) Song, R.-J.; Deng, C.-L.; Xie, Y.-X.; Li, J.-H. *Tetrahedron Lett.* **2007**, *48*, 7845. (y) Guerinot, A.; Reymond, S.; Cossy, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 6521. (z) Taillefer, M.; Xia, N.; Ouali, A. *Angew Chem., Int Ed* **2007**, *46*, 934. (aa) Hatakeyama, T.; Nakamura, M. *J. Am. Chem. Soc.* **2007**, *129*, 9844. (bb) Kofink, C. C.; Blank, B.; Pagano, S.; Goetz, N.; Knochel, P. *Chem. Commun.* **2007**, 1954. (cc) Dongol, K. G.; Koh, H.; Sau, M.; Chai, C. L. L. *Adv. Synth. Catal.* **2007**, *349*, 1015. Yamagami, T.; Shintani, R.; Shirakawa, E.; Hayashi, T. *Org. Lett.* **2007**, *9*, 1045. (dd) Fürstner, A.; De Souza, D.; Turet, L.; Fenster, M. D. B.; Parra-Rapado, L.; Wirtz, C.; Mynott, R.; Lehmann, C. W. *Chem. Eur. J.* **2007**, *13*, 115.

(8) **Fe-Catalyzed Coupling Reaction of Dienol Phosphates with Grignard Reagents. General Procedure.** An oven-dried and nitrogen-flushed 250 mL four-necked flask, equipped with a mechanical stirrer and a thermometer, was charged with a solution of $Fe(acac)_3$ (1 mol%, 0.25 mmol) in THF (50 mL). The dienol phosphate (25 mmol) was added at once under stirring, and then the Grignard reagent (30 mmol) was added dropwise for 20 min. After 15 min, the reaction mixture was quenched with a 1 M aqueous HCl solution (50 mL). The aqueous phase was extracted with cyclohexane (3 × 30 mL), dried with $MgSO_4$, and concentrated under reduced pressure. The product was purified by distillation or by column chromatography (see Supporting Information).

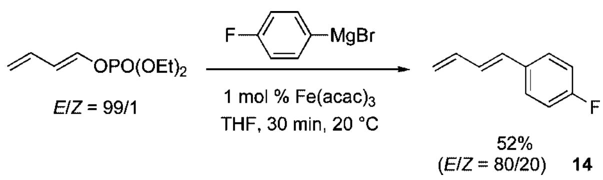
Several terminal dienol phosphates were coupled in excellent yields with octylmagnesium chloride (Table 2, entries 1, 2, and 7). A terminal conjugated trienol phosphate was also used successfully (entry 3). The reaction can be extended to cyclic or acyclic nonterminal dienol phosphates (entries 4−6 and 8). Secondary aliphatic Grignard reagents (entry 6) led to the expected coupling product in satisfactory yields.

Table 2. Iron-Catalyzed Cross-Coupling Reaction of Dienol and Trienol Phosphates with Grignard Reagents[a]

entry	phosphate	coupling product	yield (%)[b]
1	 $E/Z = 99/1$	 **6** $E/Z = 98/2$	92
2	 $E/Z = 96/4$	 **7** $E/Z = 90/10$	85
3	 $E > 99\%$	 **8** 99/1	88
4	 C_1-C_2: $E > 99\%$ C_3-C_4: $Z/E = 93/7$	 **9** C_1-C_2: $E > 99\%$ C_3-C_4: $Z/E = 93/7$	90
5	 $E > 99\%$	 **10** $E/Z = 99/1$	93
6	 C_1-C_2: $E > 99\%$ C_3-C_4: $Z/E = 57/43$	 **11** C_1-C_2: $E > 99\%$ C_3-C_4: $Z/E = 60/40$	78
7		 **12**	61
8		 **13**	78

[a] All reactions were performed on a 25 mmol scale. For a general procedure see ref . [b] Yield of isolated product.

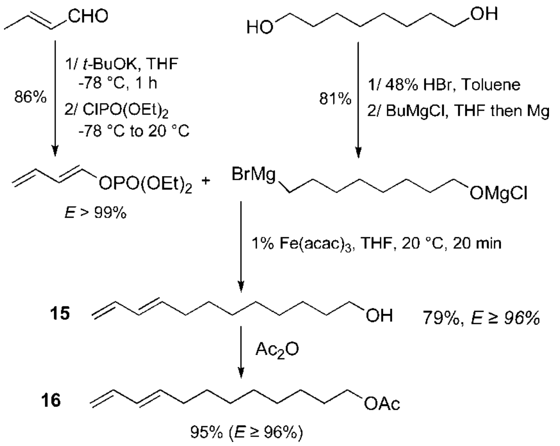
Scheme 2. Iron-Catalyzed Cross-Coupling Reaction of Dienol Phosphate **5** with Aryl Grignard Reagents



Aryl Grignard reagents can also be used; however, a partial isomerization occurs during the coupling (Scheme 2).

This procedure makes it possible to prepare various compounds of biological interest having a terminal dienic system, such as insect pheromones, according to a very efficient strategy. This is well-illustrated by the synthesis of the pheromone of *Diparopsis castanea*[9] described in Scheme 3. It is, to the best of our knowledge, the most expeditious and efficient preparative route reported until now.[10]

Scheme 3. Synthesis of the Insect Pheromone of *Diparopsis castanea* (Red Bollworm Moth) **16**



In conclusion, we have shown that the coupling of Grignard reagents with terminal dienol and trienol phosphates is efficiently catalyzed by 1 mol % Fe(acac)$_3$. The reaction is stereoselective and gives excellent yields of terminal conjugated dienes or trienes. It is the first general transition-metal-catalyzed reaction to achieve such a coupling. The synthetic interest of this new method of preparation of terminal dienes and trienes is well-illustrated by the expeditious preparation of an insect pheromone depicted in Scheme 3. The extension of the scope of iron catalysis in preparative

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organic chemistry is a very important target for sustainable development.

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Supporting Information Available: Detailed experimental procedures and complete compounds characterization data. This material is available free or charge via the Internet at http://pubs.acs.org.

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