

# Concise synthesis of stereodefined dienols and cyclopentadienes via direct addition of 1-bromomagnesiobutadienes and 1-lithiobutadienes to carbonyl compounds

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**Abstract**—Stereodefined all-*cis* substituted dienols could be readily prepared in excellent yields by the direct addition of 1-bromomagnesiobutadiene or 1-lithiobutadiene derivatives with aldehydes and ketones. Depending on the nature of substituents and workup procedures, multi-substituted cyclopentadienes could be also formed in high yields from these dienols. It is interesting to note that, unlike normal alkenyl magnesiumbromides, these conjugated butadienyl magnesiumbromide reagents do not react with ketones.

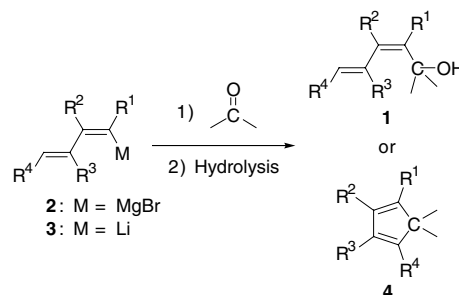
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Allylic alcohols are very important building blocks in synthetic chemistry. Limited reports have demonstrated that conjugated dienols are of rich and interesting reaction chemistry and can be used as versatile building blocks to synthesize functionalized compounds.<sup>1,2</sup> However, because of the lack of preparative methods for conjugated dienols **1**, especially for those stereodefined multiple substituted ones,<sup>1</sup> study on their reaction chemistry and applications in synthetic chemistry have been impeded.<sup>2</sup> Therefore, synthetically useful preparative methods for conjugated dienols **1** especially for those stereodefined ones bearing a wide variety of substituents, are in great demand.

Regio- and stereo-defined, multi-substituted 1-bromomagnesiobutadienes **2** or 1-lithiobutadienes **3** have become readily available from their corresponding butadienyl halides.<sup>3,4</sup> Thus, we applied these readily available 1-lithiobutadienes and 1-bromomagnesiobuta-

dienes in reactions with carbonyl compounds such as ketones and aldehydes, which has been a fundamental protocol for preparation of alcohols.

In this paper, we report a concise preparation of conjugated dienols **1** (Scheme 1). We also report an alternative preparation for multi-substituted cyclopentadienes **4** by a simple change of hydrolysis conditions (Scheme 1).<sup>5,6</sup>



**Scheme 1.** Formation of conjugated dienols or cyclopentadiene derivatives via direct addition of 1-bromomagnesiobutadienes and 1-lithiobutadienes to aldehydes and ketones.

**Keywords:** Aldehydes; 1-Bromomagnesiobutadienes; Conjugated dienols; Cyclopentadienes; Ketones; 1-Lithiobutadienes.

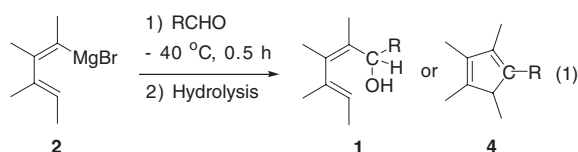
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The addition reactions of organolithium reagents and Grignard reagents to aldehydes or ketones are simple and fundamental for rapid synthesis of alcohols upon hydrolysis. However, we found that, either conjugated dienols **1** or multi-substituted cyclopentadienes **4** were obtained selectively in excellent yields from reactions of 1-bromomagnesiobutadienes **2** with aldehydes after hydrolysis (Table 1),<sup>7,8</sup> depending on the nature of

substituents on the butadienyl skeletons and the work-up procedures.

The formation of cyclopentadienes can be rationalized by acid-promoted cyclization of their corresponding conjugated dienols.<sup>6</sup> Results shown in Run 1 and 6 indicate that *p*-methoxyphenyl substituted dienol undergoes the cyclization more easily than the phenyl

**Table 1.** Reactions of 1-magnesiumbromobutadienes **2** with aldehydes<sup>a</sup>



Run	Reagent <b>2</b>	Aldehyde	Hydrolysis condition	Product <b>1</b> or <b>4</b>	Yield/% <sup>b</sup>
1		PhCHO	Satd aq NaHCO <sub>3</sub>		85
2	<b>2a</b>	PhCHO	Satd aq NH <sub>4</sub> Cl		87 (75)
3	<b>2a</b>	PhCHO	3 N HCl	<b>4a<sup>c</sup></b>	88 (80)
4	<b>2a</b>	PrCHO	Satd aq NaHCO <sub>3</sub>		73 (66)
5	<b>2a</b>	PrCHO	Satd aq NH <sub>4</sub> Cl		72 (67)
6	<b>2a</b>		Satd aq NaHCO <sub>3</sub>		90 (86)
7		PhCHO	Satd aq NaHCO <sub>3</sub>		92 (88)
8	<b>2b</b>	PhCHO	Satd aq NH <sub>4</sub> Cl		88 (82)
9	<b>2b</b>	PrCHO	Satd aq NH <sub>4</sub> Cl		78 (71)

<sup>a</sup> Reaction conditions: shown in Eq. 1.

<sup>b</sup> GC yields. Isolated yields are given in parentheses.

<sup>c</sup> Three isomers in 5:2:1.

<sup>d</sup> Two isomers in 1:1.

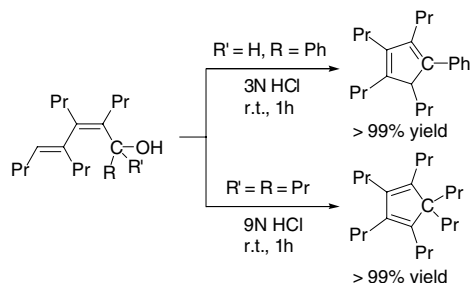
<sup>e</sup> Three isomers in 3:2:1.

<sup>f</sup> Two isomers in 9:1.

<sup>g</sup> A mixture of two isomers in 1:1.

substituted dienol **1a**. Results shown in Run 4 and 7 indicate that **1c** is not so easily cyclized as **1b**, probably due to structural differences. These isolated dienols **1a–c**

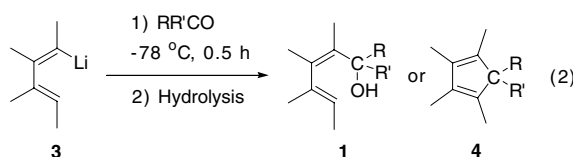
and **1d** could be quantitatively transformed to their corresponding cyclopentadiene derivatives when treated with a stronger acid, such as 3 N HCl (Scheme 2).



**Scheme 2.** Acid-promoted cyclization of conjugated dienols to cyclopentadiene derivatives.

It is noteworthy that 1-bromomagnesiobutadienes **2** did not react with ketones such as  $\text{Pr}_2\text{CO}$ ,  $\text{Ph}_2\text{CO}$ , or

**Table 2.** Reactions of 1-lithiobutadienes **3** with aldehydes and ketones<sup>a</sup>



Run	Reagent <b>3</b>	Aldehyde or ketone	Hydrolysis condition	Product <b>1</b> or <b>4</b>	Yield/% <sup>b</sup>
1		PhCHO	Satd aq $\text{NaHCO}_3$	<b>1a</b>	99 (95)
2	<b>3a</b>	PhCHO	3 N HCl	<b>4a</b> <sup>c</sup>	99
3	<b>3a</b>	PrCHO	Satd aq $\text{NaHCO}_3$	<b>1b</b>	82
4	<b>3a</b>	PrCHO	3 N HCl	<b>4b</b> <sup>d</sup>	85
5	<b>3a</b>	$\text{Pr}_2\text{CO}$	3 N HCl		81 (71)
6	<b>3a</b>	TolylMeCO	Satd aq $\text{NaHCO}_3$		(40)
7	<b>3a</b>	TolylMeCO	3 N HCl		71 (57)
8		$\text{Pr}_2\text{CO}$	3 N HCl		(81)
9		TolylCHO	3 N HCl		(76)

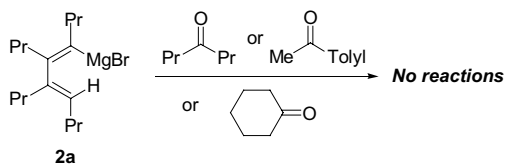
<sup>a</sup> Reaction conditions: shown in Eq. 2.

<sup>b</sup> GC yields. Isolated yields are given in parentheses.

<sup>c</sup> Two isomers in 5:2.

<sup>d</sup> Two isomers in 4:3.

<sup>e</sup> Compound **1f** was isolated as a mixture of two isomers in 3:2. Cyclized product **4e** was also obtained in 16% isolated yield.



**Scheme 3.** Conjugated bromomagnesiobutadienes do not react with ketones.

cyclohexanone under reaction conditions used (Scheme 3). These results indicate that the reactivity of butadienyl magnesiumbromides is remarkably different from that of normal Grignard reagents.

As a conclusion, we have reported a concise method for the preparation of otherwise unavailable all-*cis* substituted dienols. The results further demonstrate that these dienols can be easily transformed to cyclopentadiene derivatives.

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- Typical procedure for the preparation of dienols and cyclopentadiene derivatives from reactions of 1-magnesiobromo-1,3-butadienes with aldehydes. To a 25 mL Schlenk tube containing Mg powder (400 mg) and THF (5 mL) at 40 °C was added 1,2-dibromoethane (0.3 mL). 10 min later, a THF solution of 1-bromo-1,3-butadienes (1.0 mmol in 15 mL THF) was added dropwise with a syringe while stirring. After 2 h, the Grignard reagent **2a** was filtered under an atmosphere of nitrogen to remove the excess of magnesium. To a THF solution of benzaldehyde (1.1 mmol) at –40 °C, **2a** was added and the mixture was stirred at this temperature. After half an hour, the reaction mixture was quenched with satd aq NaHCO<sub>3</sub> and extracted with ether. Normal work-up afforded **1a** as a colorless liquid in 85% GC yield. When the reaction was quenched with satd aq NH<sub>4</sub>Cl instead of satd aq NaHCO<sub>3</sub>, the same work-up process afforded **4a** as a mixture of three double bond positional isomers (5:2:1) in 75% combined isolated yield (combined GC yield 87%).
- Typical procedure for the preparation of dienols and cyclopentadiene derivatives from reactions of 1-lithio-1,3-butadienes with aldehydes and ketones. 1-Lithio-1,3-butadiene derivative **3a** was generated in situ by lithiation of its corresponding 1-iodo-1,3-butadiene. Benzaldehyde (1.1 mmol) was then added to **3a** at –78 °C and the reaction mixture was stirred at the same temperature for 0.5 h. The reaction mixture was then quenched with satd aq NaHCO<sub>3</sub> and extracted with ether. Normal work-up afforded **1a** as a colorless liquid in 95% isolated yield (GC yield 99%). When the reaction was quenched with aqueous 3 N HCl instead of satd aq NaHCO<sub>3</sub>, the same work-up process afforded **4a** as a mixture of two double bond positional isomers (5:2) in 99% combined GC yield.