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LETTERS

1,1-Bis(benzotriazolyl) Derivatives as Gem-dianion Synthons

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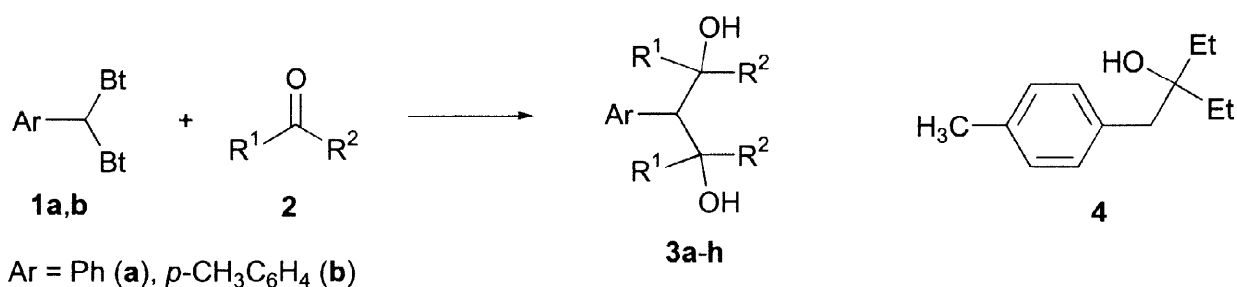
Abstract: Bis(benzotriazolyl)methylbenzenes **1a,b** were converted by excess lithium metal in the presence of ketones into the 1,3-diols **3a-g** in moderate to good yields. However, similar treatment of **5** gave only the mono reduction products **6, 7**. Compounds **1a,b** reacted with 1 equivalent of diketone **8** to form olefins **10a,b**. © 1998 Elsevier Science Ltd. All rights reserved.

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Carbon-carbon bond forming reactions of organolithium reagents to yield polyfunctionalized compounds have received much attention.¹⁻³ The chemistry of alkyllithium compounds is well studied but few geminal dilithium compounds have been reported, in part due to their instability.⁴ Methods of generating gem-dianions include (i) double deprotonation of an acidic CH₂ by *n*-butyllithium,^{1,5,6} (ii) reaction of bis(iodomercurio)alkanes with lithium powder,⁷ and (iii) cleavage of C-Se bonds by lithium 4,4'-di-*tert*-butylbiphenyl (LiDBB).⁸ The direct lithium halogen exchange of gem-dihalogenes has been successful in some instances, including the use of very low temperatures and a high concentration of *t*-butyllithium,⁹ or LiDBB,⁴ but it is not generally applicable to the synthesis of gem-dilithiated molecules due to the mono lithiated intermediates undergoing lithium halide elimination, producing carbenes.^{2,4}

We anticipated that the use of benzotriazole methodology for generating gem-dianions could be advantageous due to the higher stability of an α -lithiated *N*-alkylbenzotriazole compared to an α -lithiated alkyl halide. As an extension of our previous work on carbanion generation using lithium,¹⁰ we now report the generation of gem-dianion equivalents from geminal-bis(benzotriazolyl) derivatives and their reactions with electrophiles.

1,1-Bis(benzotriazolyl) derivatives **1a,b** and **5** were readily prepared from the reaction of benzotriazole, the appropriate aldehyde and thionyl chloride.¹¹ Under Barbier-type reaction conditions, treatment of **1a** in the presence of cyclopentanone, at -78 °C in THF, with excess lithium and lithium bromide (generated *in situ* from lithium and 1,2-dibromoethane), gave **3a** as the only product isolated after flash column chromatography (Scheme 1).¹² Similar treatment of **1a** with cyclohexanone, 4-heptanone or 2-pentanone gave **3b-d**, respectively, in good yields. The reactions were quenched with water at -78 °C after 4-6 hours to avoid the decomposition of the benzotriazole moiety which would have occurred if the reaction mixture had come to room temperature.¹⁰



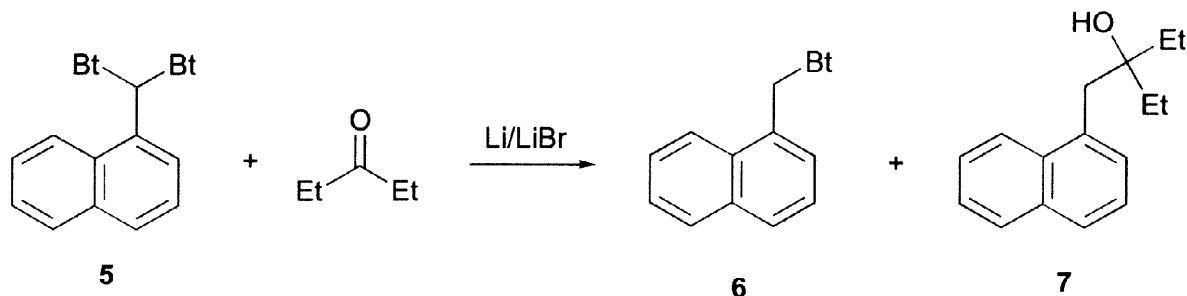
| 3 | R ¹ | R ² | Ar | Yield (%) |
|----------|--|--|---|-----------|
| a | -(CH ₂) ₄ - | | Ph | 58 |
| b | -(CH ₂) ₅ - | | Ph | 78 |
| c | -(CH ₂) ₂ CH ₃ | -(CH ₂) ₂ CH ₃ | Ph | 76 |
| d | -(CH ₂) ₂ CH ₃ | CH ₃ | Ph | 68 |
| e | -CH ₂ CH ₃ | -CH ₂ CH ₃ | <i>p</i> -CH ₃ C ₆ H ₄ | 70 |
| f | -(CH ₂) ₅ - | | <i>p</i> -CH ₃ C ₆ H ₄ | 52 |
| g | -CH(CH ₃) ₂ | CH ₃ | <i>p</i> -CH ₃ C ₆ H ₄ | 61 |
| h | -CH(CH ₃) ₂ | H | Ph | 25 |

Scheme 1

The reaction of **1b** with 3-pentanone gave, in addition to the 1,3-diol **3e**, 15% of **4** (Scheme 1). Compound **4** was separated by flash column chromatography and identified by NMR. Similar treatment of **1b** with cyclohexanone and 3-methyl-2-butanone gave the 1,3-diols **3f,g** in moderate yields. Reaction of **1a** with isobutyraldehyde gave only 25% of **3h** after 10 hours at -78 °C.

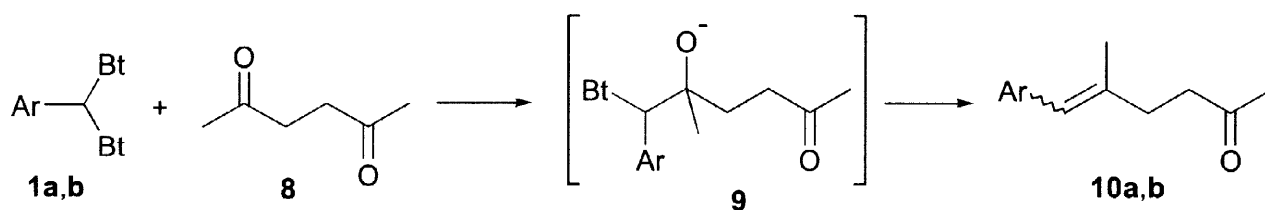
Treatment of **5** with 3-pentanone gave **6** and **7** as main products (Scheme 2) which were characterized by NMR. Compound **6** resulted from reductive cleavage of one C-Bt bond, while compound **7** is either the

reductive product of the first reductive coupling of **5** or the reductive coupling of **6**. Steric effects probably prevent the formation of the 1,3-diols in this case.



Scheme 2

Reaction of **1b** with 1 equivalent of 2,5-hexandione gave 56% of the alkene **10b** as the only product isolated (Scheme 3). Similarly, **1a** reacted with 2,5-hexandione to give **10a**. These results suggest that a monocarbanion intermediate reacted with 2,5-hexanedione at one carbonyl, generating the intermediate **9**. Lithium assisted elimination of the benzotriazolyl group then gave **10**. This is similar to the low-valent titanium (LVT) assisted olefination of carbonyl compounds recently reported by our group.¹³



1, 9, 10 Ar = Ph (**a**), *p*-CH₃C₆H₄ (**b**)

Scheme 3

In conclusion, a facile generation of 1,1-gem-dicarbanion equivalents and their application in the synthesis of 1,3-diols has been described. These results demonstrate that the rare umpolung of aromatic aldehydes to dianions can be achieved in two steps by initial conversion of aromatic aldehydes to 1,1-bis(benzotriazolyl) derivatives **1a,b** as previously reported,¹¹ followed by treatment of **1a,b** with lithium in THF. This method works well with ketones as electrophiles, but poorly with aldehydes.

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12. **General procedure for the preparation of 1,3-diols (3):** Lithium (25 mmol, 30% dispersion in mineral oil) was washed twice with dry THF under argon, then 1,2-dibromoethane (1.5 mmol) was added followed by THF (5 mL), and the suspension was cooled to -78 °C. A solution of the appropriate bis(benzotriazolyl)methylbenzene (2.5 mmol) and electrophile (6 mmol) in THF (25 mL) were added to the lithium suspension over 1 h and kept another 3-4 h before being quenched with water (15 mL) at the same temperature. After ether extraction, the crude product was purified by flash column chromatography on silica gel. All of the 1,3-diols prepared gave satisfactory ¹H and ¹³C NMR spectra, and novel products gave satisfactory microanalyses or HRMS.
1,1'-Benzylenebis(cyclohexanol) (3b): white solid; mp 153-154 °C; ¹H NMR (300 MHz/CDCl₃) δ 7.63 (d, *J* = 7.6 Hz, 1H), 7.33-7.24 (m, 3H), 7.04-7.03 (m, 1H), 3.35 (s, 2H), 2.79 (s, 1H), 1.86 (d, *J* = 12 Hz, 2H), 1.67-1.31 (m, 16H), 1.14-1.08 (m, 2H); ¹³C NMR (75 MHz/CDCl₃) δ 140.4, 133.0, 129.2, 127.7, 127.6, 126.3, 76.5, 40.0, 37.3, 25.4, 22.2, 22.0. Anal. Calcd for C₁₉H₂₈O₂: C, 79.12; H, 9.78. Found: C, 79.00; H, 10.09.
5-Phenyl-4,6-dipropyl-4,6-nonan-di-ol (3c): white solid; mp 114-115 °C; ¹H NMR δ 7.72 (d, *J* = 7.6 Hz, 1H), 7.30-7.20 (m, 3H), 6.98-6.97 (m, 1H), 3.41 (s, 2H), 2.91 (s, 1H), 1.78 (t, *J* = 8.5 Hz, 4H), 1.43-1.03 (m, 12H), 0.93 (t, *J* = 7.3 Hz, 6H), 0.67 (t, *J* = 7.0 Hz, 6H); ¹³C NMR δ 140.5, 131.9, 130.1, 127.4, 126.1, 79.5, 56.7, 42.1, 41.8, 17.3, 16.6, 14.6, 14.4. Anal. Calcd for C₂₁H₃₆O₂: C, 78.70; H, 11.32. Found: C, 78.55; H, 11.65.
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