

Stereoselective Olefination of Carbonyl Compounds with *N*-Benzyl- and *N*-Allylbenzotriazoles by Low-Valent Titanium-Promoted Dehydroxybenzotriazolylolation

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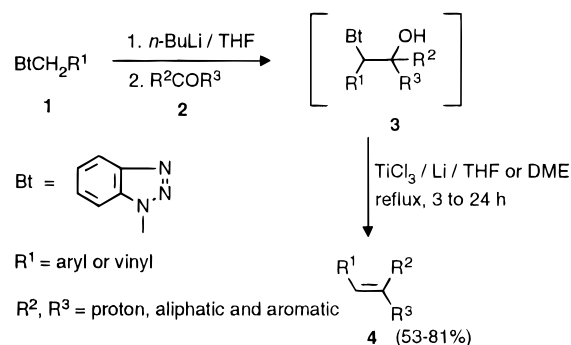
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Olefination of aldehydes and ketones is very important in organic synthesis. Wittig reactions represent a highly effective and general method of alkene formation from carbonyl derivatives,^{1,2} but their low stereoselectivity for allylic and benzylic ylides, the difficult removal of byproduct phosphine oxide, and poor reactivity with hindered ketones have all encouraged the development of alternative protocols. Among such complementary methods previously developed, the Peterson and Julia reactions have shown significant advantages and are the most frequently used.^{1–3} However, they are not without drawbacks. Peterson reactions require the separation of diastereomeric intermediates in order to control the stereoselectivity of the alkenes produced. Disadvantages of the original Julia protocol reaction are a rather lengthy procedure and difficulties in the preparation of trisubstituted alkenes. More recently, an improved Julia coupling reaction has employed benzothiazolyl sulfones;^{4–6} this gives excellent stereoselectivity for aliphatic sulfones, but in the cases of allylic and benzylic benzothiazolyl sulfones, the *trans:cis* outcome is less predictable.^{6,7}

During the last two decades, low-valent titanium has been found to be a useful reagent for the preparation of alkenes from aldehydes and ketones by reductive deoxygenation.^{8,9} Very recently, such McMurry reaction analogs have been extended to the intramolecular coupling of ketones with amides.¹⁰ Low-valent titanium can also be used in the deprotection of allyl and benzyl derivatives of alcohols and amines.^{11,12} However, olefin formation *via* the reductive elimination of two different hetero atoms α to each other using low-valent titanium has not previously been reported.

Scheme 1



We now show that lithiation of *N*-allyl- or *N*-benzylbenzotriazoles **1** followed by reaction with aldehydes or ketones to give *N*-(α -hydroxyallyl)- or *N*-(α -hydroxybenzyl)benzotriazole derivatives **3**, and subsequent treatment *in situ* with low-valent titanium generated from lithium and titanium(III) chloride in THF or DME, affords the corresponding alkenes **4** in good yields with the *trans*-isomers predominant (Scheme 1 and Table 1).

N-Allyl- and *N*-benzylbenzotriazoles **1** are easily prepared from allyl or benzyl halides or alcohols.^{13a–c} In the present work, compounds **1a**,¹⁴ **1b**,¹⁵ and **1d**¹⁶ were prepared by literature methods. Compound **1c** was obtained from the reaction of benzotriazole and the corresponding allyl halide in the presence of sodium hydroxide in ethanol according to a literature analogy.^{13a} In order to avoid complications in the monitoring of the intermediates **3** (TLC and ¹H NMR), benzotriazol-1-yl isomers **1** were used in the present study. However, a mixture of benzotriazol-1-yl and benzotriazol-2-yl derivative **1c** was also tested for the transformation (Scheme 1), and the result showed no difference from the use solely of the benzotriazol-1-yl derivative **1c**.

Compound **1** was reacted with 1 equiv of *n*-butyllithium in THF at -78 °C for 1 h to generate a dark blue solution that was treated with a solution of an aldehyde or a ketone **2** (1 equiv) in THF for 2 h to give a diastereomeric mixture **3** in high yield based on ¹H NMR data with a nearly 1:1 ratio. The alkylation occurred regioselectively at the carbon attached to the benzotriazolyl group; no γ -alkylated products were found in the cases of **1c–d** by ¹H NMR. After aqueous workup, the intermediate **3** was treated with low-valent titanium in THF or DME to give the alkene **4**. When THF was used in the case of allylbenzotriazoles **1c,d**, small amounts of reduced byproduct alkanes¹⁷ were detected by GCMS, which indicated that THF acted as a proton source. The use of DME instead of THF suppressed the formation of byproduct alkanes, with the ratio of *E:Z* alkenes unaffected. Since the low-valent titanium-promoted dehydroxybenzotriazolylolation gives a high proportion of *E*-alkenes and the reaction in THF gives reduced products as alkanes, the reaction pathway probably involves free-radical intermediates as proposed by McMurry.¹⁸

The low-valent titanium was prepared on the basis of literature procedure.^{12,18} To optimize the reaction yields,

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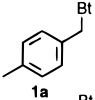
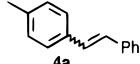
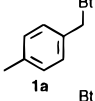

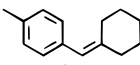
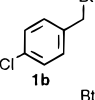

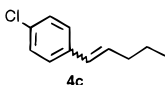
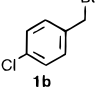

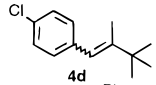


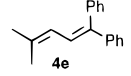
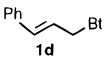
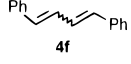
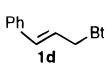

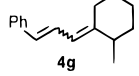
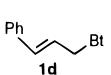

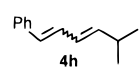
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Table 1. Preparation of Olefins 4a–h from Benzyl- and Allylbenzotriazoles 1 and Carbonyl Compounds 2

entry	Bt-deriv 1	carbonyl 2	solvent	time (h) ^a	olefin	yield (%) ^b	(E) : (Z) ratio ^c
1		PhCHO	THF	3		65	24.0 : 1
2			THF	6		73	-
3			DME	18		55	40.3 : 1
4			DME	6		72	100 : 0
5			DME	5		75	-
6		PhCHO	DME	8		81	12.7 : 1
7			DME	16		71	4.3 : 1
8			DME	24		53	12.0 : 1

^a For reduction; ^b Overall isolated yield based on Bt-derivatives 1; ^c Determined by GCMS.

a 10:1 ratio (by equivalent) of low-valent titanium vs substrates **3** was employed. However, the ratio of 5:1 worked equally well in several reactions.

As shown in Table 1, the reaction can be applied to aromatic and aliphatic aldehydes and ketones as well as cyclic ketones. However, when the adduct **3** ($R^1 = p\text{-MeC}_6\text{H}_4$; $R^2 = R^3 = \text{Ph}$; derived from benzophenone and **1a**) was treated with low-valent titanium in THF, the expected product **4** was detected by GCMS in relatively low yield and GCMS of the reaction mixture indicated the occurrence of retroreaction under these conditions. Fortunately, the treatment of **3** ($R^1 = 3,3\text{-dimethylallyl}$; $R^2 = R^3 = \text{Ph}$; derived from benzophenone and **1c**) with low-valent titanium in DME afforded the alkene **4e** in 75% yield. Presumably, the solvent THF led to the retroreaction of **3** in the above case. The stereoselectivity depended on the substituents as illustrated by the *E*:*Z* ratios of products **4c** and **4d** as well as **4g** and **4h**. Obviously, *N*-benzylbenzotriazole gave better stereoselectivity than *N*-allylbenzotriazole as shown by the *E*:*Z* ratios of alkenes **4a** and **4f**. All products were characterized by ^1H and ^{13}C NMR and microanalysis. The structures of the *E*-alkenes were confirmed by large *trans*-

proton coupling constants, and NOE spectra and the *Z*-isomers were detected by ^1H NMR and GCMS. The *E*:*Z* ratios were determined from the GCMS of the crude products.

In summary, a convenient and stereocontrolled olefination of aldehydes and ketones with *N*-allyl- and *N*-benzylbenzotriazoles is described. In terms of high stereoselectivity, easy separation, unnecessary isolation of diastereoisomers, and simple procedure for both di- and trisubstituted alkenes, this method complements the three most frequently used protocols for alkene formation from carbonyl compounds: the Wittig, Peterson, and Julia reactions. Further investigations of the scope and limitations of this dehydroxybenzotriazolylolation promoted by low-valent titanium are underway.

Acknowledgment. We thank Professor James W. Leahy (UC, Berkeley) for helpful discussion.

Supporting Information Available: Experimental procedure for the preparation of *trans*-1-(*N*-benzotriazolyl)-4-methyl-2-butene (**1c**) and alkenes **4a–h** and the characterization data of the compounds described above (4 pages).

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