Pergamon

Tetrahedron Letters 40 (1999) 3737–3740

TETRAHEDRON LETTERS

Electrophilic Amination of Racemic and Non-racemic Allenyltitaniums. One-pot Synthesis of α-Hydrazino-alkynes from Propargylic Alcohol Derivatives

Duk Keun An, Koichiro Hirakawa, Sentaro Okamoto and Fumie Sato*

Department of Biomolecular Engineering, Tokyo Institute of Technology, 4259 Nagatsuta-cho, Midori-ku, Yokohama, Kanagawa 226-8501, Japan

Received 19 February 1999; revised 11 March 1999; accepted 12 March 1999

Abstract

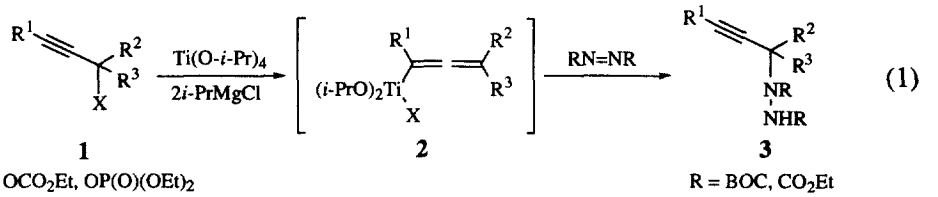
Successive treatment of propargylic carbonates or phosphates with a Ti(O-*i*-Pr)4/2*i*-PrMgCl reagent and dialkyl azodicarboxylates gave α-hydrazinoalkynes in good yields. The reaction, which proceeded with up to 86% chiral transfer, thus has opened up a new route to optically active α-hydrazinoalkynes from the optically active propargylic compounds.

Keywords: electrophilic amination; α-hydrazinoalkynes; titanium and compounds; asymmetric synthesis

We reported recently that the reaction of a Ti(O-*i*-Pr)4/2*i*-PrMgX (X = Cl or Br) reagent with propargylic alcohol derivatives **1** such as halide, carbonate or phosphate provides a convenient access to a variety of allenyltitaniums **2** [1]. We also reported that optically active **2** can be easily prepared by starting with optically active **1** [2]. With an efficient and practical access to **2** in hand, our research efforts have been focused on their synthetic utility as a nucleophilic reagent. In addition to the reaction with aldehydes [3] and imines [4] which have been reported to proceed with excellent regio- and stereoselectivity, we have found that they react smoothly with H_2O and Br_2 with excellent regio- and stereoselectivity [5]. The reaction with Bu_3SnCl also provides a highly practical method for synthesizing propargylstannanes [6]. We then focused our attention on the reaction with a source of electrophilic nitrogen.

Propargylic amines and their synthetic equivalents are useful intermediates in organic synthesis, and thus, their synthesis has attracted a considerable amount of interest [7]. Although electrophilic amination of carbanions has been a research subject of increasing attention as a result of the growing utility of diverse organometallic reagents [8], there has been no precedent for preparation of propargylic amines or their synthetic equivalents based on this method. We now report that electrophilic amination of allenyltitaniums by dialkyl azodicarboxylates (DAAD) proceeds readily, thus opening up a new entry to α-hydrazinoalkynes [9] (eq 1 and Table 1)

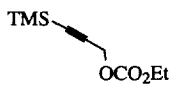
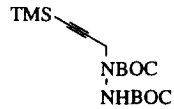
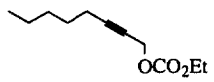
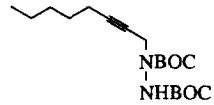
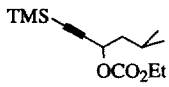
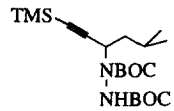
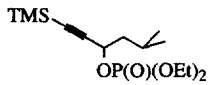
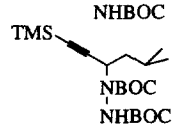
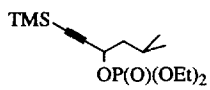
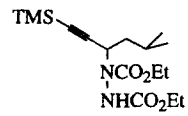
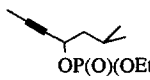
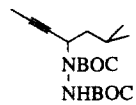
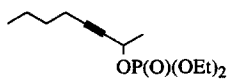
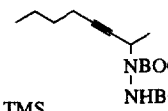
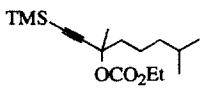
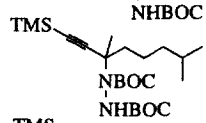
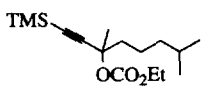
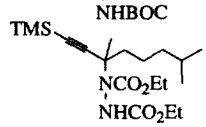
0040-4039/99/$ - see front matter
PII: S0040-4039(99)00584-5



1 (1)

X = OCO_2Et, $OP(O)(OEt)_2$ 2 R = BOC, CO_2Et

Table 1. One-pot Synthesis of α-Hydrazinoalkynes **3** from Propargylic Compounds **1** *via* Allenytitaniums[a]

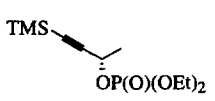
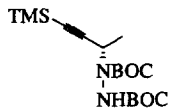
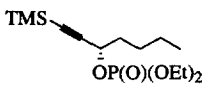
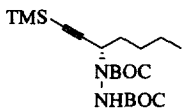
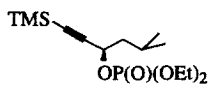
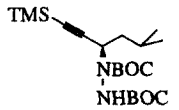
Entry	Propargylic Compound **1**	α-Hydrazinoalkyne **3**	Isolated Yield, %
1			49
2			51
3			80
4			75
5			52
6			62
7			61
8			61
9			50

[a]The reaction was carried out with a reactant ratio of the propargylic compound : $Ti(O\text{-}i\text{-}Pr)_4$: *i*-PrMgCl : DAAD = 1 : 1.5 : 3 : 1.5 for entries 1-7 and 1 : 3 : 6 : 3 for entries 8 and 9.

As can be seen from Table 1, primary, secondary and tertiary α-hydrazinoalkynes can be readily synthesized from the corresponding **1** in synthetically useful yields. It should be noted that, in all cases, other possible regioisomeric products (e.g., allenic hydrazines) were not detected. Noteworthy also is the fact that the yield of the reaction is somewhat dependent on the alkyl group of DAAD, and di-*tert*-butyl azodicarboxylate provides higher yield than diethyl azodicarboxylate (entries 4 *vs* 5 and 8 *vs* 9).

With the results shown in Table 1, our next concern was the degree of the chiral transfer in the reaction with optically active allenyltitaniums (Table 2) [10]. Starting from diethyl (*S*)-1-trimethylsilyl-1-butyn-3-yl phosphate with 94% ee, the secondary α-hydrazinoalkyne di-*tert*-butyl (*S*)-1-(1-trimethylsilyl-1-butyn-3-yl)-1,2-hydrazinedicarboxylate with 81% ee was obtained (entry 1 in Table 2). Thus, the calculated degree of chiral transfer *via* allenyltitanium is 86%, and, as the reaction of a secondary propargylic phosphate with a Ti(O-*i*-Pr)4/2*i*-PrMgCl reagent procceeded with 97% chiral transfer [2], the degree of chiral transfer for the reaction of allenyltitanium with DAAD was 89%. We found, however, that the degree of the chiral transfer is strongly affected by the structure of **1** and decreases accordingly as the steric bulk increases. Thus, by changing the methyl group in diethyl (*S*)-1-trimethylsilyl-1-butyn-3-yl phosphate to an *n*-butyl (entry 2) or *iso*-butyl group (entry 3) the degree of chiral transfer decreased from 86 to 55 and 27%, respectively. Although the degree of chiral transfer did not reach, in some cases, a synthetically useful level, as **1** can be accessed readily [11] with excellent optical purity, and the conversion of **1** to **3** can be carried out in a one-pot procedure, the reaction might find utility for synthesizing various kinds of optically active α-hydrazinoalkynes [12].

Table 2. Synthesis of Optically Active α-Hydrazinoalkynes from Optically Active Propargylic Compounds[a]

Entry	Propargylic Compound **1**	α-Hydrazinoalkyne **3**	Yield, %[b]	ee, %[c]
1	 (94% ee)	 **4**	77	81 (86)
2	 (96% ee)	 **5**	73	53 (55)
3	 (99% ee)	 **6**	74	27 (27)

[a]Propargylic compound : Ti(O-*i*-Pr)$_4$: *i*-PrMgCl : DAAD = 1 : 1.5 : 3 : 1.5. [b]Isolated yield. [c]For determination of ee value and configuration, see note 13. The calculated values expected by simple extrapolation if the substrate is of 100% are shown in parentheses.

Typical procedure for the preparation of 4 (entry 1 in Table 2). To a solution of diethyl (*S*)-1-trimethylsilyl-1-butyn-3-yl phosphate with 94% ee (303 mg, 1.0 mmol) and Ti(O-*i*-Pr)4 (444 μL, 1.5 mmol) in ether (10 mL) was added dropwise *i*-PrMgCl (2.7 mL, 1.11 M in ether, 3.0 mmol) at -50 °C. The resulting clear yellow solution was stirred for 2 h at -50 ~ -40 °C. During this period the color of the solution changed from orange to red-brown. After cooling to -78 °C, di-*tert*-butyl azodicarboxylate (345 mg, 1.5 mmol) was added to the reaction mixture and was gradually warmed to 0 °C over 1 h. The reaction mixture was quenched with aqueous saturated NaHCO3 and extracted with ether. The combined organic layers were dried over MgSO4 and concentrated *in vacuo*. The residue was chromatographed using silica gel to give a white solid that consisted of di-*tert*-butyl (*S*)-1-(1-trimethylsilyl-1-butyn-3-yl)-1,2-hydrazinedicarboxylate with 81% ee in 77% yield.

References and Notes

[1] Nakagawa T, Kasatkin A, Sato F. Tetrahedron Lett. 1995;36:3207-3210.

[2] Okamoto S, An DK, Sato F. Tetrahedron Lett. 1998;39:4551-4554.

[3] Furuta K, Ishiguro M, Haruta R, Ikeda N, Yamamoto H. Bull. Chem. Soc. Jpn. 1984;57:2768-2776.

[4] Yamamoto Y, Ito W, Maruyama K. J. Chem. Soc., Chem. Commun. 1984;1004-1005.

[5] An DK, Okamoto S, Sato F. Tetrahedron Lett. 1998;39:4555-4558.

[6] An DK, Okamoto S, Sato F. Tetrahedron Lett. 1998;39:4861-4864.

[7] Merino P, Anoro S, Castillo E, Merchan F, Tejero T. Tetrahedron:Asymmetry, 1996;7:1887-1890 and references cited therein.

[8] (a) Askani R, Taber DF. In: Trost BM. editor, Comprehensive Organic Synthesis, Oxford:Pergamon Press, 1991;Vol. 6:118-119. (b) Erdik E, Ay M. Chem. Rev. 1989;89:1947-1980. (c) Greck C, Genet JP. Synlett, 1997;741-748.

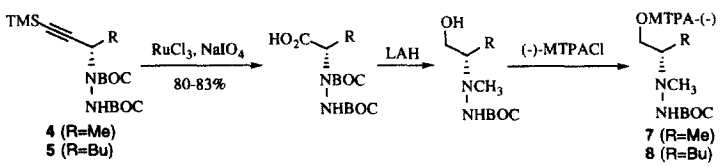
[9] For reaction of organometallic compounds with DAAD affording hydrazine derivatives, see references 8a and 8b(pp.1967-1968).

[10] Synthesis of optically active α-hydrazino carbonyl compounds through electrophilic amination of chiral enolates with DAAD has been reported, see references 8a and 8b.

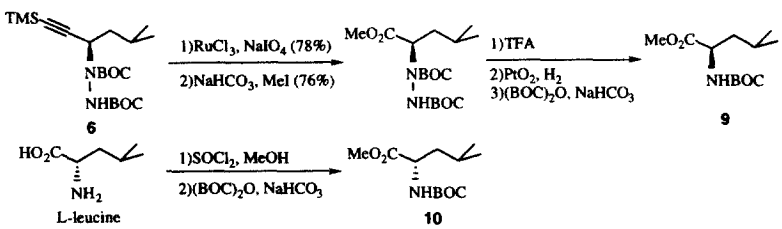
[11] Takano S, Samizu K, Sugihara T, Ogasawara K. J. Chem. Soc., Chem. Commun.1989;1344-1345. Yadav JS, Deshpande PK, Sharma GVM. Tetrahedron, 1990;46:7033-7046. Michelet V, Besnier I, Tanier S. Touzin AM, Genet JP, Demoute JP. Synthesis, 1995;165-167 and references cited therein.

[12] It should be noted that the stereochemical outcome of the reaction of the allenyltitanium with DAAD is different from that of the reaction with aldehydes [2]; the mechanistic rationale of the reaction is now in progress in our laboratory.

[13] The ee value of **4** and **5** was determined by ^{1}H NMR analysis after converting to MTPA esters **7** or **8** according to the procedure shown below, while the absolute configuration of **4** was confirmed by comparison of the ^{1}H NMR of **7** with the reported one [14].



The ee value of **6** was determined by GLC analysis (Chirasil-DEX CB, Chrompack) after derivatization to **9** according to the procedure shown below, while the absolute configuration was established by comparison of **9** with its antipode, **10**, derived from L-leucine.



[14] Gennari C, Colombo L, Bertolini G. J. Am. Chem. Soc. 1986;108:6394-6395.