Pergamon

Tetrahedron Letters, Vol. 37, No. 49, pp. 8865-8868, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)02126-0

Highly Efficient Synthesis of Alka-1,3-dien-2-yltitanium Compounds from Alka-2,3-dienyl Carbonates. A New, Practical Synthesis of 1,3-Dienes and 2-Iodo-1,3-dienes

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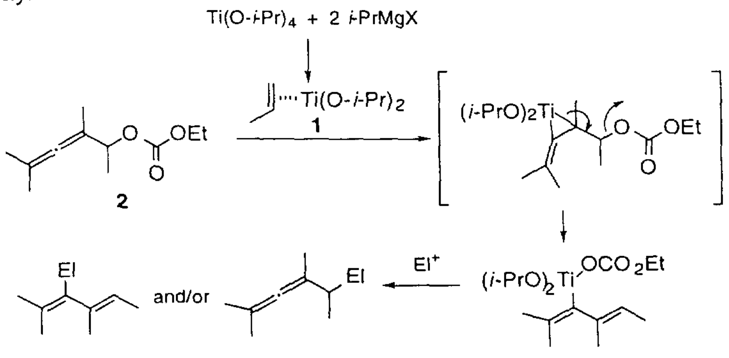
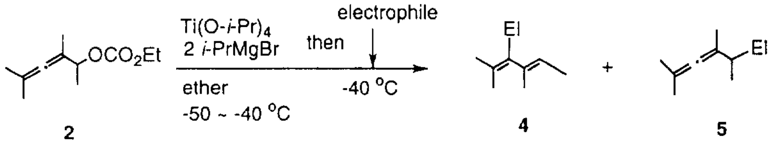
Abstract: *Treatment of carbonates of alka-2,3-dien-1-ols 2 with (η^2-propene)Ti(O-i-Pr)$_2$ (1) resulted in oxidative addition to afford 1,3-dien-2-yltitanium compounds 3, which react readily with electrophiles such as H^+, I_2 and aldehydes. The reaction with H^+ and I_2 proceeds highly regioselectively, thus providing an efficient and practical method for synthesis of 1,3-dienes and 2-iodo-1,3-dienes.* Copyright © 1996 Elsevier Science Ltd

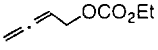
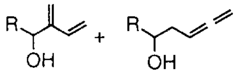
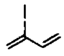
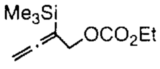
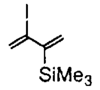
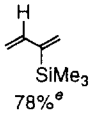
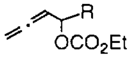
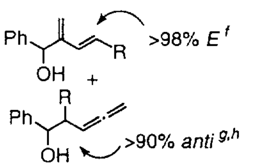
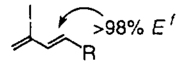
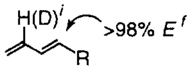
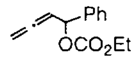
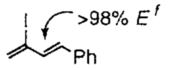
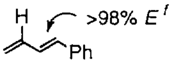
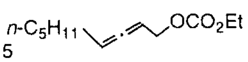
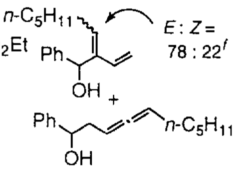
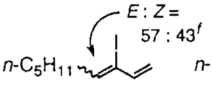
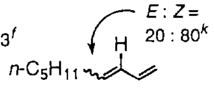
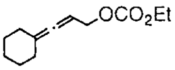
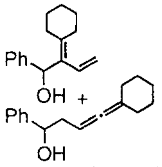
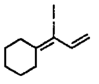
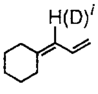
Recently we have found that the reaction of Ti(O-*i*-Pr)$_4$ with 2 equiv of *i*-PrMgX (X = Cl or Br) provides (η^2-propene)Ti(O-*i*-Pr)$_2$ (**1**) in an essentially quantitative yield and this compound acts as a versatile titanium(II) equivalent.[1] In the course of our studies to develop a synthetic methodology based on **1**, we have revealed that the reaction with allyl or propargyl compounds such as halides, carbonates and acetates proceeds *via* the replacement of the propene coordinated in **1** by the unsaturated carbon-carbon bond of the substrate and the successive β-elimination reaction to provide allylic[1a] or allenylic titanium compounds,[1b] respectively, in excellent yields. These results suggested to us that α-allenyl carbonates (alka-2,3-dienyl carbonates) **2** might afford the titanium compounds (alka-1,3-dien-2-yltitanium compounds) **3** by the reaction with **1** as shown in Scheme 1. Since a variety of **2** can be readily prepared by a conventional method,[2] it was expected that the reaction would provide an efficient synthetic methodology when the resulting **3** reacts with electrophiles with high regioselectivity.



Scheme 1

Table 1.[a] Synthesis of Alka-1,3-dien-2-yltitanium Compounds **3** from Alka-2,3-dienyl Carbonates **2** by Treatment with Ti(O-*i*-Pr)$_4$ / *i*-PrMgX and Their Reaction with Electrophiles



Entry	Substrate **2**	Product(s), Total Yield[b] (Ratio of **4** : **5**)[c]		
		electrophile : aldehyde	I_2	H_3O^+
1		 R = Ph; 74% (39 : 61) R = *n*-C_5H_{11}; 61% (21 : 79)	 76%[e]	———[d]
2		———[d]	 58%	 78%[e]
3		 R = Et : 69% (85 : 15) R = *n*-C_9H_{19} : 80% (83 : 17)	 R = *n*-C_5H_{11} : 77% R = *n*-C_9H_{19} : 98%	 R = *n*-C_5H_{11} : 74% R = *n*-C_9H_{19} : 92%
4[j]		———[d]	 79%	 90%
5		 62% (51 : 49)	 74%	 73%
6		 80% (74 : 26)	 82%	 85%

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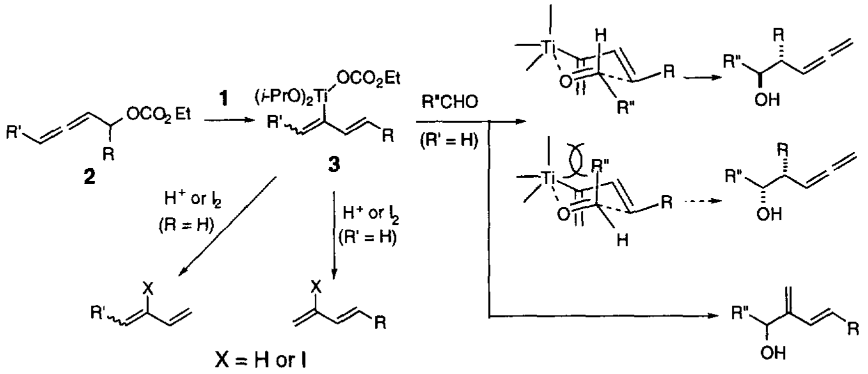
[a] Reaction procedure: see, footnote 7. [b] Isolated yield unless otherwise indicated. [c] Ratio of **4** and **5** was determined by 300MHz ^{1}H NMR and/or GC analysis. In the case of iodolysis and hydrolysis the corresponding **5** was not detected. [d] Reaction has not been carried out. [e] GC yields. [f] Olefin geometry was confirmed by NOE-difference experiments. Ratio of *E* and *Z* was determined by 300 MHz ^{1}H NMR and/or GC analysis. [g] Stereochemistry of major diastereomer was assigned to be *anti* based on ^{1}H NMR chemical sifts in analogy with 2-alkyl-1-phenyl-3-buten-1-ol.[1a] [h] Ratio of diastereomers was determined by 300 MHz ^{1}H NMR analysis. [i] Treatment with D_2O instead of aqueous 1N HCl gave the product containing >98% D which was confirmed by ^{1}H NMR analysis. [j] *i*-PrMgCl was used instead of *i*-PrMgBr. [k] Olefin geometry was assigned based on ^{1}H-coupling constants.

To a solution of **2** and Ti(O-*i*-Pr)$_4$ in ether was added 2 equiv of *i*-PrMgX (X = Br or Cl) at -78 °C. After stirring for 1.5 h at -50 °C ~ -40 °C, the reaction mixture was treated with electrophiles such as H^+, I_2 or an aldehyde. As can be seen from Table 1 which summarizes the results of the reaction, the expected oxidative addition reaction of **2** to **1** proceeded readily to provide titanium compound **3**, and which, in turn, reacted with the electrophiles in excellent yields.[3] The regiochemistry of the reaction was dependent on the electrophiles applied: the reaction with aldehydes provided two regioisomers, the ratio of which was dependent on the nature of **2** as well as the aldehydes. On the other hand, to our delight, the reaction with H^+ and I_2 resulted in nearly exclusive production (at least >95 : 5 by ^{1}H NMR and/or GC) of one regioisomer, *i.e.*, the corresponding conjugated diene derivatives.[4]

The stereochemistry of the reaction products shown in Table 1 deserves several comments. Firstly, the internal olefin moiety of the conjugated diene products derived from terminal allene derivatives has (*E*)-geometry (entries 3 and 4). This result strongly indicated that the internal olefin moiety present in the titanium compound **3** has (*E*)-geometry (Scheme 2). However, the geometry of the internal olefin part of the products derived from the carbonates having an internal allenyl moiety was a mixture, suggesting the presence of both (*E*)- and (*Z*)-**3** (entry 5). Secondly, the diastereochemistry of the homoallenyl alcohols shown in entry 3 is highly controlled to be *anti*-configuration. This stereochemical outcome can be explained by assuming that the reaction of **3** with an aldehyde proceeds *via* a 6-membered chair-like transition state as shown in Scheme 2.[5]



Scheme 2

The present one-pot procedure for synthesizing stereo-defined 1,3-diene compounds starting from readily preparable **2** is very useful and practical, since the reaction uses nontoxic, commercially available inexpensive starting materials [Ti(O-*i*-Pr)$_4$ and 2*i*-PrMgX], and the reaction procedure is operationally simple. Especially noteworthy is the easy synthesis of a variety of 2-iodo-1,3-dienes, because few efficient and general methods for preparing of these compounds are available.[6]

Acknowledgment. This work was partially supported by Grants-in-Aid from the Ministry of Education, Science, Culture and Sports, Japan (No. 07455359 and 07216223).

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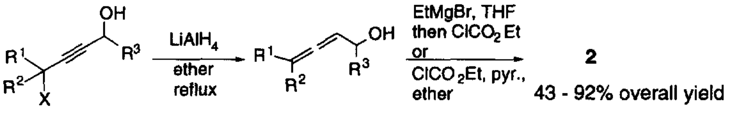
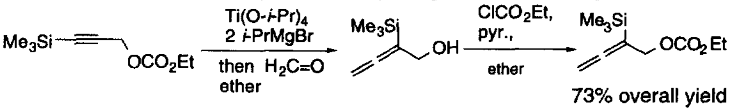
Commun. **1996**, 197-198. (e) Gao, Y.; Harada, K.; Sato, F. *ibid.* **1996**, 533-534. (f) Urabe, H.; Takeda, T.; Sato, F. *Tetrahedron Lett.* **1996**, *37*, 1253-1256. (g) Yamazaki, T.; Kasatkin, A.; Kawanaka, Y.; Sato, F. *J. Org. Chem.* **1996**, *61*, 2266-2267. (h) Okamoto, S.; Kasatkin, A.; Zubaidha, P. K.; Sato, F. *J. Am. Chem. Soc.* **1996**, *118*, 2208-2216 and references cited therein.

2. The compounds **2** except that shown in entry 2 in Table 1 were prepared according to the procedure reported in the literature ("*Synthesis of Acetylenes, Allenes and Cumulenes*," Brandsma, L.; Verkruijsse, H. D.; Elsevier: New York, 1981.) as shown below:



X = Cl, OMOM, OEE, OTBS

The compound shown in entry 2 was synthesized by the procedure developed by us[1b] as shown below:



3. Preparation of 2-metallo-1,3-diene compounds and their reactions with electrophiles, see: Mg: (a) Kondo, K.; Dobashi, S.; Matsumoto, M. *Chem. Lett.* **1976**, 1077-1080. (b) Nunomoto, S.; Yamashita, Y. *J. Org. Chem.* **1979**, *44*, 4788-4791. (c) Shea, K. J.; Pham, P. Q. *Tetrahedron Lett.* **1983**, *24*, 1003-1006 and ref. 3d. Zn, Al: (d) Pornet, J.; Randrianoelina, B.; Miginiac, L. *J. Organomet. Chem.* **1979**, *174*, 15-26 and ref. 3b. Li: (e) Wada, E.; Kanemasa, S.; Fujiwara, I.; Tsuge, O. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1942-1945. (f) Brown, P. A.; Jenkins, P. R.; *J. Chem. Soc. Perkin Trans. 1*, **1986**, 1129-1131. (g) Bloch, R.; Chaptal-Gradoz, N. *J. Org. Chem.* **1994**, *59*, 4162-4169. Syntheses of α-allenyl boron compounds have been reported: (h) Soumdararajan, R.; Li, G.; Brown, H. C. *Tetrahedron Lett.* **1995**, *36*, 2441-2444. (i) Zheng, B.; Srebnik, M. *J. Org. Chem.* **1995**, *60*, 486-487.
4. The formation of the regioisomer **4** in the reaction with aldehydes can also be explained by assuming the presence of 2,3-dien-1-yltitanium compounds at equilibrium through metallotropic rearrangement from **3** and their reaction *via* a 6-membered transition state.
5. The compounds **3** prepared here did not react with ketones such as acetophenone and 2-nonanone presumably due to steric reasons.
6. Ratovelomanana, V.; Hammoud, A.; Linstrumelle, G. *Tetrahedron Lett.* **1987**, *28*, 1649-1650. Mitani, M.; Kobayashi, Y.; Koyama, K. *J. Chem. Soc. Perkin Trans. 1*, **1995**, 653-655.
7. General procedure: to a solution of **2** (1.0 mmol) and Ti(O-*i*-Pr)4 (1.3 mmol) in ether (5 mL) was added dropwise *i*-PrMgBr or *i*-PrMgCl (2.6 mmol, 0.9-1.8 M, in ether) at -78 °C and the resulting mixture was allowed to warm up to -50 °C over 0.5 h and then stirred for 1.5 h at -50 °C ~ -40 °C to afford a solution of the titanium compound **3**. To this was added dropwise aldehyde (1.3 mmol), a solution of I_2 (1.3 mmol) in ether (4 mL), aqueous 1N HCl (2 mL) or D_2O (0.5 mL) at -40 °C, and then the mixture was warmed up to ambient temperature over 0.5 ~ 1 h. After addition of 1N HCl (3 mL), an usual extractive work-up afforded the crude mixture which was purified by column chromatography on silica gel. In the case of iodolysis, before chromatography, the crude residue was treated with THF (5 mL) and ~30% aqueous Me_2NH (1 mL) at room temperature for 2 ~ 6 h to remove a by-product, 1,4-diiodo-2,3-dimethylbutane, which was produced by iodolysis of a titanacyclopentane compound derived from **1** and propene generated *in situ.*

(*Received in Japan* 1 *July* 1996; *accepted* 28 *October* 1996)