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Facile Synthesis of Trisubstituted Allenynes by Phosphane-Mediated Deoxygenation of 2,4-Pentadiyn-1-ol

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Keywords: Allenes / Phosphanes / Deoxygenation / Alkynes / Synthetic methods

A facile method for the synthesis of trisubstituted allenynes has been developed. The process involves phosphane-mediated deoxygenation of 2,4-pentadiyn-1-ol derivatives. A variety of propargyl alcohols can be transformed into allenynes in moderate to good yields under mild reaction conditions.

Introduction

Allenynes as a class of highly unsaturated compounds can serve as precursors in the synthesis of a diverse range of complex organic molecules of industrial importance,[1] and they are also important intermediates in organic synthesis.[2] For example, treatment of allenyne-1,6-diols with gold and silver catalysts selectively produces 2,5-dihydrofuran and furan derivatives, respectively.[3] In addition, quite an impressive number of naturally occurring allenynes with interesting biological activities[4] have been recently isolated and characterized (Figure 1). It is thus not surprising that these kinds of compounds have attracted the attention of both biologists and synthetic chemists. During the past 10 years, a variety of preparatively useful methodologies has emerged to access allenes,[5] but there are few reliable methods concerning the construction of allenynes, despite their increasing importance in organic synthesis.[6] Moreover, most of the procedures for preparing allenynes suffer from some drawbacks, including multiple-step procedures, harsh reaction conditions, leading to functional group intolerance, or the requirement of a transition-metal catalyst.[6b,6d–6f] To the best of our knowledge, no reports concerning the preparation of allenynes directly from propargyl alcohols have been disclosed. Therefore, the development of a direct, mild, conditional, and metal-free method for the preparation of functionalized allenynes is highly desirable.

Phosphanes are much weaker bases but stronger nucleophiles than amines, and most reactions of phosphanes for synthesis depends on their nucleophilicity.[7] The reactivity of organophosphanes is wide, as they react as nucleophiles at saturated and unsaturated carbon atoms or they attack a heteroatom, especially an oxygen atom, to give intermediates that either break down in situ to the desired products or react as a synthon in their own right. Recently, considerable attention has been paid to phosphane-promoted or phosphane-catalyzed reactions due to the ready availability, low cost, moisture tolerance, and air stability of phosphanes.[8] As a continuation of our studies on the synthesis of highly unsaturated allenes from propargyl alcohol derivatives,[9] our present research target is aimed at the synthesis of trisubstituted allenynes from 2,4-pentadiyn-1-ol, where phosphane could be employed as a deoxidizing agent. Herein we would like to detail the results.

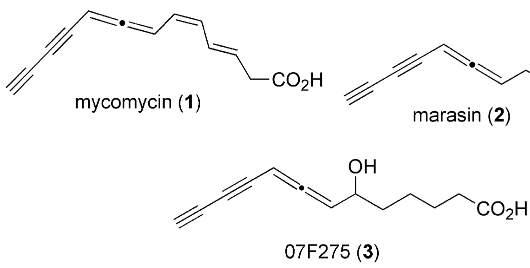

Figure 1. Naturally occurring allenynes with high antibiotic activity.

Results and Discussions

Initially, 1,1,6,6-tetramethyl-2,4-hexadiyne-1,6-diol (**4a**), easily prepared by dimerization of 3-methyl-butynyl-3-ol,[10] was chosen as the substrate. After treatment of **4a** with PPh_3 (1 equiv.) in 1,4-dioxane in air at 80 °C for 18 h, a new compound with a lower polarity than that of **4a** according to TLC was formed in 45% yield (Table 1, Entry 1). Spectroscopic data showed that the newly obtained compound was an alcohol and that the molecular weight of this new compound was 16 mass units lighter than **4a**. In its ^{13}C

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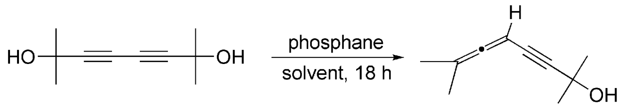
NMR spectrum, there were six quaternary carbon signals whose chemical shifts were δ = 210.1, 97.6, 93.0, 76.4, 72.7, 65.7 ppm. All these data clearly suggested that the product could be allenyne derivative **5a**. To the best of our knowledge, this is the first preparation of an allenyne derivative directly from propargyl alcohol with the use of an organocatalyst. Encouraged by this result, we made further efforts to adjust the reaction variants such as solvent, temperature, and phosphane to optimize the reaction conditions. More polar solvents such as DMF and CH_3CN led to **5a** in lower yields (Table 1, Entries 2 and 3) and the protic solvent ethanol gave no desired product[11] (Table 1, Entry 4). To our delight, when the toluene was used as solvent, the yield increased to 70% (Table 1, Entry 5). Lower and higher reaction temperatures gave rise to lower yields (Table 1, Entries 6 and 7). Moreover, other phosphanes such as tris(4-anisyl)phosphane, tricyclohexylphosphane, and tributylphosphane were also examined and **5a** was not produced in higher yields (Table 1, Entries 8–10). It is worth noting that when the reaction was performed under a nitrogen atmosphere in the presence of tributylphosphane as a deoxidizing agent, the reaction system was very complicated and desired **5a** was not isolated (Table 1, Entry 11). Finally, the influence of the amount of PPh_3 on the reaction was also examined. Increasing the amount of PPh_3 to 1.2 equiv. led to a higher yield of **5a**, but a further increase in the amount of PPh_3 (1.5 equiv.) had a minimal effect (Table 1, Entries 12 and 13).

Table 1. Optimization of the reaction conditions.[a]



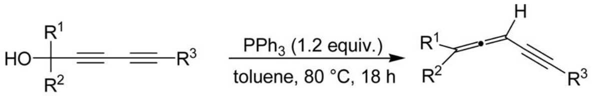
4a **5a**

Entry	Phosphane (equiv.)	Solvent	T [°C]	Yield[b] [%]
1	PPh_3 (1)	1,4-dioxane	80	45
2	PPh_3 (1)	DMF	80	13
3	PPh_3 (1)	CH_3CN	80	41
4	PPh_3 (1)	C_2H_5OH	80	n.r.
5	PPh_3 (1)	toluene	80	70
6	PPh_3 (1)	toluene	60	43
7	PPh_3 (1)	toluene	reflux	65
8	tris(4-anisyl)phosphane (1)	toluene	80	70
9	tricyclohexylphosphane (1)	toluene	80	60
10	$(n\mathrm{Bu})_3P$	toluene	80	36
11[c]	$(n\mathrm{Bu})_3P$	toluene	80	n.r.
12	PPh_3 (1.2)	toluene	80	78
13	PPh_3 (1.5)	toluene	80	79

[a] Unless otherwise specified, all reactions were carried out on a 0.50-mmol scale in 2.0 mL of solvent for 18 h in air with 1 equiv. of **4a** and phosphane. [b] GC yield. [c] This reaction was performed under a nitrogen atmosphere.

On the basis of the above results, we concluded that PPh_3 (1.2 equiv.)/80 °C in toluene were suitable conditions for this conversion. The scope of this reaction was next examined with different 2,4-pentadiyn-1-ols,[12] and the results were summarized in Table 2. When R^1, R^2 = alkyl and (or) phenyl, all the substrates can be converted into the corresponding allenynes in moderate to good yields. When R^3 = aryl, the yields are good. Moreover, those substrates carrying an electron-donating group on the benzene ring give better yields (**4m** < **4j** < **4k** < **4l**). It is noteworthy that under these reaction conditions, functional groups such as hydroxy and cyanide are tolerated. Interestingly, for substrates **4a**–**f** bearing two hydroxy groups, no diallene derivatives were observed under these conditions. The real reason is not clear presently, but the presence of a conjugated alkynyl group could be necessary for the conversion of a propargyl alcohol into an allenyne.[13] To further verify this point, propargyl alcohols **6** and **7**, lacking a conjugated alkynyl group in comparison to **4**, were also tested under the same reaction conditions (Scheme 1). Nevertheless, no reactions occurred and almost all the starting materials were recovered.

Table 2. Scope of the substrates.[a]



4 **5**

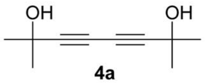
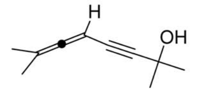
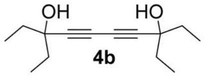
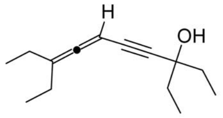
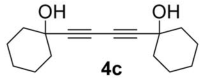
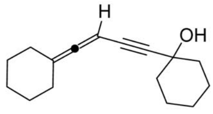
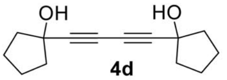
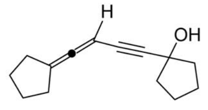
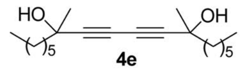
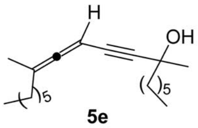
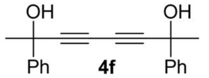
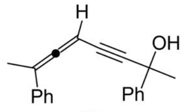
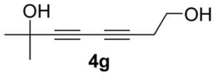
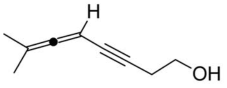
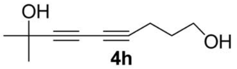
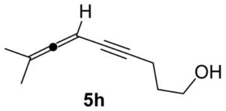
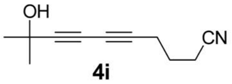
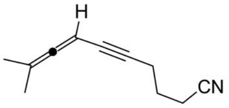
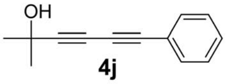
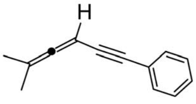
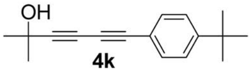
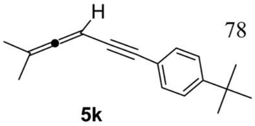
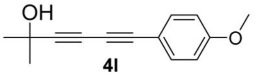
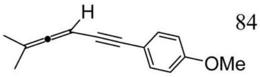
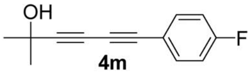
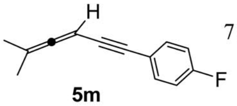
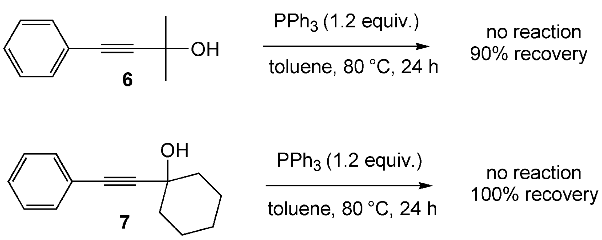
Entry	Substrate	Product	Yield[b] [%]
1	 **4a**	 **5a**	73
2	 **4b**	 **5b**	75
3	 **4c**	 **5c**	86
4[c]	 **4d**	 **5d**	53
5	 **4e**	 **5e**	65
6	 **4f**	 **5f**	51

Table 2. *(Continued)*

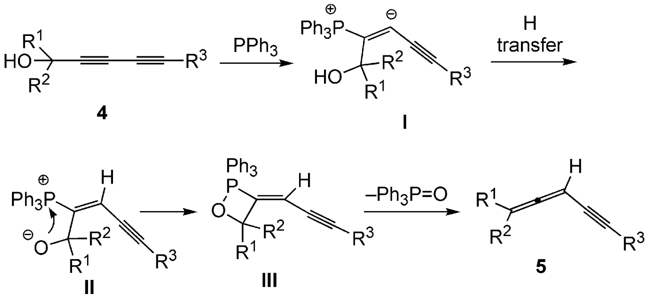
Entry	Substrate	Product	Yield[b] [%]
7	 **4g**	 **5g**	58
8	 **4h**	 **5h**	56
9	 **4i**	 **5i**	67
10	 **4j**	 **5j**	72
11	 **4k**	 **5k**	78
12	 **4l**	 **5l**	84
13	 **4m**	 **5m**	71

[a] Unless otherwise specified, all reactions were carried out using 0.20 mmol of **4** and 0.24 mmol of PPh_3 in 2.0 mL of toluene at 80 °C for 18 h. [b] Isolated yield. [c] Reactions were carried out at 50 °C for 12 h.



Scheme 1. Phosphane-mediated allenylation of propargyl alcohol derivatives without a conjugated triple bond.

On the basis of the above results, we propose a possible mechanism for this conversion (Scheme 2).[14] Initially, PPh_3 attacks the triple bond of **4** to form zwitterion **I**, which swiftly transforms into **II** through intramolecular hydrogen transfer. Intermediate **II** can then undergo intramolecular four-membered cyclization, leading to **III**. Subsequently, **III** is transformed into **5** followed by elimination of $Ph_3P{=}O$.



Scheme 2. Proposed route to trisubstituted allenynes **5**.

Conclusions

In summary, a facile method for the synthesis of trisubstituted allenynes has been developed, involving the PPh_3-mediated deoxygenation of propargyl alcohols. This method presents the first example of the preparation of allenynes directly from propargyl alcohol. Moreover, mild reaction conditions provide access to functionalized allenynes through a simple procedure. Further studies on the enantioselective synthesis of allenynes by using chiral phosphanes and the synthesis of allenyne-containing natural products are underway in our group, and the results will be reported in due course.

Experimental Section

General: All the reactions were carried out in round-bottomed flasks equipped with a magnetic stirring bar and monitored by thin-layer chromatography to detect completion of the reaction. Solvents and all reagents were used as received. NMR spectra were recorded with a Bruker Avance 400 or 600 MHz NMR spectrometer and referenced to 7.27 and 77.0 ppm, respectively, for $CDCl_3$ solvent with TMS as an internal standard. Infrared spectra were obtained as potassium bromide pellets or as liquid films between two potassium bromide discs with a Bruker Vector 22 spectrometer. Mass spectra were recorded with a Shimadzu GC–MS-QP5050 A at an ionization voltage of 70 eV equipped with a DB-WAX capillary column. Elemental analyses were carried out with an Elementar Vario EL instruments. TLC was performed by using commercially prepared 100–400 mesh silica gel plates (GF_{254}), and visualization was effected at 254 nm. All other chemicals were purchased from Aldrich Chemicals.

Typical Procedure for the Synthesis of 2,7-Dimethylocta-5,6-dien-3-yn-2-ol (5a): A round-bottomed flask containing PPh_3 (62.9 mg, 0.24 mmol) and a stirring bar was sequentially charged with 1,1,6,6-tetramethyl-2,4-hexadiyne-1,6-diol (**4a**, 33.2 mg, 0.20 mmol) and toluene (2 mL) under ambient conditions and air. The resulting solution was then stirring at 80 °C for 18 h. After cooling, the mixture was stirred at ambient temperature until completion of the reaction, as monitored by GC–MS and TLC. The crude product was purified by flash chromatography (petroleum ether/ethyl acetate = 10:1→10:2) to afford **5a** (22 mg, 73%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 5.21 (hept., $J_{H,H}$ = 2.8 Hz, 1 H, 1-C=C=C*H*), 1.71 [d, $J_{H,H}$ = 4.0 Hz, 6 H, 6-C-$(C\mathit{H}_3)_2$], 1.51 [s, 6 H, 6-C$(C\mathit{H}_3)_2$OH] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 210.1, 97.6, 93.0, 76.4, 72.7, 65.7, 31.5 (2 C) 20.0 (2 C) ppm. IR (KBr): $\tilde{\nu}$ = 3410 (br.), 3079, 2938, 2860, 2243, 1667, 1609, 1446, 985 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 150 $[M]^+$, 135 (100), 107, 91. $C_{10}H_{14}O$ (150.22): calcd. C 79.96, H 9.39; found C 79.73, H 9.36.

Supporting Information (see footnote on the first page of this article): Full experimental details and copies of the NMR spectra.

Acknowledgments

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[1] Selected examples of the cycloisomerization of 1-allen-*n*-ynes: a) Q. Shen, G. B. Hammond, *J. Am. Chem. Soc.* **2002**, *124*, 6534–6535; b) M. Petit, C. Aubert, M. Malacria, *Org. Lett.* **2004**, *6*, 3937–3940; c) G. Lemière, V. Gandon, N. Agenet, J. P. Goddard, A. de Kozak, C. Aubert, L. Fensterbank, M. Malacria, *Angew. Chem. Int. Ed.* **2006**, *45*, 7596–7599; d) M. Petit, C. Aubert, M. Malacria, *Tetrahedron* **2006**, *62*, 10582–10593; e) A. S. Bayden, K. M. Brummond, K. D. Jordan, *Organometallics* **2006**, *25*, 5204–5206; f) K. M. Brummond, T. O. Painter, D. A. Probst, B. Mitasev, *Org. Lett.* **2007**, *9*, 347–349; g) G. Y. Lin, C. Y. Yang, R. S. Liu, *J. Org. Chem.* **2007**, *72*, 6753–6757; h) R. Zriba, V. Gandon, C. Aubert, L. Fensterbank, M. Malacria, *Chem. Eur. J.* **2008**, *14*, 1482–1491.

[2] a) Y. Wang, D. J. Burton, *Org. Lett.* **2006**, *8*, 5295–5298; b) R. W. Shen, X. Huang, *Org. Lett.* **2008**, *10*, 3283–3286; c) S. Ma, *Acc. Chem. Res.* **2003**, *36*, 701–712; d) S. Ma, *Chem. Rev.* **2005**, *105*, 2829–2871.

[3] S. Kim, P. H. Lee, *Adv. Synth. Catal.* **2008**, *350*, 547–551.

[4] a) A. Hoffman-Röder, N. Krause, *Angew. Chem. Int. Ed.* **2004**, *43*, 1196–1216; b) F. Bohlmann, H. Bornowski, C. Arndt, *Chem. Ber.* **1965**, *98*, 2236–2242; c) F. Bohlmann, C. Zdero, *Tetrahedron Lett.* **1970**, *11*, 2465–2466; d) F. Bohlmann, C. Zdero, *Chem. Ber.* **1971**, *104*, 1329–1331; e) W. D. Celmer, I. A. Solomons, *J. Am. Chem. Soc.* **1952**, *74*, 2245–2248; f) W. D. Celmer, I. A. Solomons, *J. Am. Chem. Soc.* **1952**, *74*, 3838–3842; g) S. R. Landor, B. J. Miller, J. P. Regan, A. R. Tatchell, *J. Chem. Soc. Perkin Trans. 1* **1974**, 557–561; h) W. de Graaf, A. Smits, J. Boersma, G. van Koten, W. P. M. Hoekstra, *Tetrahedron* **1988**, *44*, 6699–6704; i) R. E. Bew, J. R. Chapman, E. R. H. Jones, B. E. Lowe, G. Lowe, *J. Chem. Soc. C* **1966**, 129–135.

[5] a) S. Kim, K. Lee, D. Seomoon, P. H. Lee, *Adv. Synth. Catal.* **2007**, *349*, 2449–2453; b) M. Shimizu, T. Kurahashi, H. Kitagawa, T. Hiyama, *Org. Lett.* **2003**, *5*, 225–227; c) M. Yokota, K. Fuchibe, M. Ueda, Y. Mayumi, J. Ichikawa, *Org. Lett.* **2009**, *11*, 3994–3997; d) K. Kobayashi, H. Naka, A. E. H. Wheatley, Y. Kondo, *Org. Lett.* **2008**, *10*, 3375–3377; e) H. J. Liu, D. S. Leow, K. W. Huang, C. H. Tan, *J. Am. Chem. Soc.* **2009**, *131*, 7212–7213; f) N. N. B. Kumar, M. Chakravarty, N. S. Kumar, K. V. Sajna, *J. Chem. Sci.* **2009**, *121*, 23–36; g) J. Li, W. Q. Kong, C. L. Fu, S. M. Ma, *J. Org. Chem.* **2009**, *74*, 5104–5106.

[6] There are only a few reports on the synthesis of allenynes, see: a) C. C. Leznoff, F. Sondheimer, *J. Am. Chem. Soc.* **1968**, *90*, 731–733; b) K. S. Feldman, C. K. Weinreb, *J. Org. Chem.* **1994**, *59*, 1213–1215; c) M. Brossat, M. P. Heck, C. Mioskowski, *J. Org. Chem.* **2007**, *72*, 5938–5941; d) Y. Takahashi, K. Tsutsumi, Y. Nakagai, T. Morimoto, *Organometallics* **2008**, *27*, 276–280; e) H. Maurer, H. Hopf, *Eur. J. Org. Chem.* **2005**, *13*, 2702–2707; f) R. W. Saalfrank, M. Haubner, C. Deutscher, W. Bauer, T. Clark, *J. Org. Chem.* **1999**, *64*, 6166–6168; g) M. Poonoth, N. Krause, *Adv. Synth. Catal.* **2009**, *351*, 117–122.

[7] a) S. L. Xu, L. L. Zhou, S. Zeng, R. Q. Ma, Z. H. Wang, Z. J. He, *Org. Lett.* **2009**, *11*, 3498–3501; b) J. McNulty, P. Das, *Tetrahedron Lett.* **2009**, *50*, 5737–5740; c) Y. S. Du, X. Y. Lu, C. M. Zhang, *Angew. Chem. Int. Ed.* **2003**, *42*, 1035–1037.

[8] a) K. C. K. Swamy, G. Gangadhararao, R. R. Suresh, N. N. B. Kumar, M. Chakravarty, *J. Organomet. Chem.* **2010**, *695*, 1042–1051; b) C. J. O. Brien, J. L. Tellez, Z. S. Nixon, L. J. Kang, *Angew. Chem. Int. Ed.* **2009**, *48*, 6836–6839.

[9] H. F. Jiang, X. H. Liu, L. Zhou, *Chem. Eur. J.* **2008**, *14*, 11305–11309.

[10] W. Y. Yin, C. He, M. Chen, H. Zhang, A. W. Lei, *Org. Lett.* **2009**, *11*, 709–712.

[11] The solvent polarity (E_T) see: C. Reichardt, *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 98–110.

[12] All the substrates were obtained, isolated, and purified by the Glaser method, see: a) R. Laurent, P. Dominique, R. Marie, Y. Frantz, *Tetrahedron* **2008**, *64*, 9430–9436; b) H. F. Jiang, A. Z. Wang, *Synthesis* **2007**, *11*, 1649–1654; c) A. S. Hay, *J. Org. Chem.* **1962**, *27*, 3320–3321.

[13] This can be explained by the fact that intermediate **I** (Scheme 2) could exist in more than one resonance form as a conjugated zwitterionic enyne, which makes the intermediate more stable: a) L. W. Ye, X. L. Sun, Q. G. Wang, Y. Tang, *Angew. Chem. Int. Ed.* **2007**, *46*, 5951–5954; b) J. C. Wang, S. S. Ng, M. J. Krische, *J. Am. Chem. Soc.* **2003**, *125*, 3682–3683; c) N. T. McDougal, S. E. Schaus, *Angew. Chem. Int. Ed.* **2006**, *45*, 3117–3119.

[14] a) K. C. K. Swamy, N. S. Kumar, *Acc. Chem. Res.* **2006**, *39*, 324–333; b) N. N. B. Kumar, M. Chakravarty, K. C. K. Swamy, *New J. Chem.* **2006**, *30*, 1614–1620; c) X. Y. Lu, C. M. Zhang, Z. R. Xu, *Acc. Chem. Res.* **2001**, *34*, 535–544.

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