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DIRECT, STEREOSELECTIVE SYNTHESIS OF EITHER E- OR Z-1,3-DIENES

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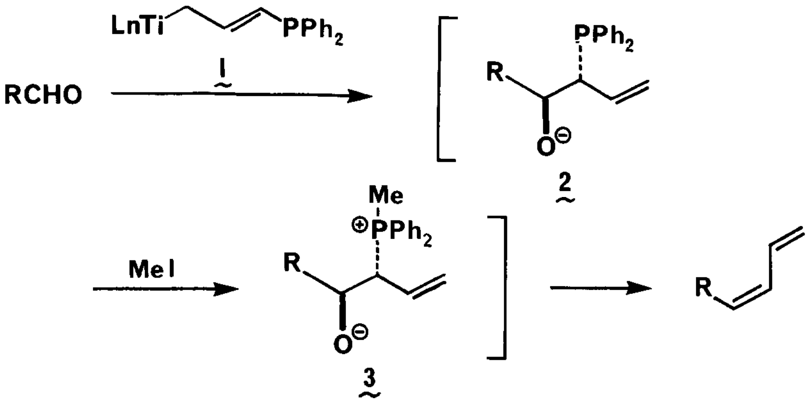
Summary: New synthetic methods for the preparation of Z- or E-1,3-dienes are described.

Despite the availability of many reagents for the carbonyl olefination reactions, there still exists a need for new method, especially for the stereoselective route to conjugated polyenes under mild conditions.[1] Herein we disclose the results of our new procedure involving (diphenylphosphino)allyltitanium reagent[2,3] which was prompted by our earlier success with (alkylthio)allyltitanium reagent.[4] The sequence of new process is as follows:



Reaction of (diphenylphosphino)allyltitanium reagent of type **1**, generated by the addition of titanium tetraisopropoxide to the lithiated allyldiphenylphosphine,[5] with aldehydes gave α-erythro-adduct **2** exclusively which may be converted directly to the β-oxido phosphonium salt of type **3** on treatment with methyl iodide.[6] The betaines so produced were smoothly transformed into the Z-1,3-dienes via the cycloelimination of the sort already established for the Wittig reaction.[6] Since the consecutive addition-elimination reactions were usually both satisfactory and convenient, it is advisable not to isolate and purify the intermediate β-hydroxyphosphines. The major results of our findings are illustrated in Table 1.

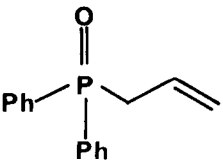
Table 1. Conversion R-CHO → $RCH=CHCH=CH_2$ using $Ph_2PCH_2CH=CH_2$[a]

Entry	Carbonyl compound	Yield[b]	E/Z[c]
1	Cyclohexanecarbaldehyde	86	4:96
2	n-Decanal	84	5:95[d]
3	Perillaldehyde	76	7:93
4	Benzaldehyde	89	4:96
5	trans-Cinnamaldehyde	82	6:94
6	4-tert-Butylcyclohexanone	32[e]	—

[a] All reactions were carried out on a 2-3 mmol scale as described in the text. [b] Yields of isolated product. The products were identified by PMR and IR spectra, and/or comparison with authentic materials. [c] Unless otherwise specified, E/Z ratio was determined by GC analysis with authentic materials. [d] E/Z ratio was estimated by the PMR assay. [e] Low reactivity of the titanium reagents, see ref. 2.

A typical procedure is as follows: To a solution of allyldiphenylphosphine[5] (0.54 g, 2.4 mmol) in dry THF (8 mL) was added tert-butyllithium (1.0 mL of a pentane solution, 2.4 mmol)[7] dropwise at -78°C, and the mixture was stirred at 0°C for 30 min. Titanium tetraisopropoxide (0.71 mL, 2.4 mmol) was added dropwise at -78°C, and the resulting redish solution was stirred for 10 min. Cyclohexanecarbaldehyde (0.24 mL, 2.0 mmol) was added over a period of 5 min at -78°C, and the mixture was stirred at -78°C for 10 min and then at 0°C for 1 h. Methyl iodide (0.15 mL, 2.4 mmol) was added at 0°C and the mixture was stirred at room temperature for 2 h. After the usual workup, the product was purified by column chromatography on silica gel to give 1-cyclohexyl-1,3-butadiene (0.23 g, 86%).[8]

In order to prove further the generality and limitations of our new process, we turned our attention to the possibility of synthesizing 1,3-dienes by means of readily available allyldiphenylphosphine oxide (**4**).[9] Unfortunately, however, the titanium derivative from **4** was found to be a totally unsatisfactory reagent for such transformations and no or very small amount of 1,3-diene was produced under the same reaction conditions.[10] In contrast, when the same reaction using the lithio derivative from **4** was conducted in dry THF with 2 equiv of hexamethylphosphorictriamide (HMPA) at -78°C for 10 min (followed by stirring at 20°C and isolation) the E-1,3-diene was formed with E/Z ratios in the range 90:10 to 95:5.[11] The results are illustrated in Table 2 and 3.



4

A typical experimental procedure for the E-1,3-diene synthesis is as follows: To a stirred solution of allyldiphenylphosphine oxide (0.27 g, 1.2 mmol) in dry THF (4 ml) and HMPA (0.43 g, 2.4 mmol) was added n-butyllithium (0.68 mL of a hexane solution, 1.2 mmol) dropwise at -78°C, and the mixture was stirred at -78°C for 10 min. Cyclohexanecarbaldehyde (0.13 mL, 1.0 mmol) was added over a period of 15 min at -78°C, and the resulting mixture was stirred at -78°C for 10 min, 0°C for 30 min, and finally 20°C for 2 h. After the usual workup, the product was purified by column chromatography on silica gel to afford 1-cyclohexyl-1,3-butadiene (0.11 g, 82%).[12]

Table 2. Conversion R-CHO $\longrightarrow$ $RCH{=}CHCH{=}CH_2$ using $Ph_2\overset{\overset{\displaystyle O}{\|}}{P}CH_2CH{=}CH_2$[a]

Entry	Carbonyl compound	Yield[b]	E/Z[c]
1	Cyclohexanecarbaldehyde	82	90:10
2	n-Decanal	88	95:5[d]
3	Perillaldehyde	42	94:6
4	Benzaldehyde	79	95:5
5	4-tert-Butylcyclohexanone	83	—

Table 3. Conversion R-CHO $\longrightarrow$ $RCH{=}\overset{\overset{\displaystyle Me}{|}}{C}{-}CH{=}CH_2$ using $Ph_2\overset{\overset{\displaystyle O}{\|}}{P}\underset{\underset{\displaystyle Me}{|}}{C}H{-}CH{=}CH_2$[a]

Entry	Carbonyl compound	Yield[b]	E/Z[c]
1	Cyclohexanecarbaldehyde	64	91:9
2	n-Decanal	78	—
3	Benzaldehyde	63	93:7
4	4-tert-Butylcyclohexanone	41	—

[a] All reactions were carried out on a 1-2 mmol scale as described in the text. The product were identified by PMR and IR spectra, and/or comparison with authentic materials.

[b] Yields of isolated product. [c] Unless otherwise specified, E/Z ratio was determined by GC analysis with authentic materials. [d] E/Z ratio was estimated by the PMR assay.

In conclusion, with a variety of carbonyl compounds, a simple, one-pot procedure is now available for the synthesis of E- or Z-1,3-diene with high stereoselectivity in good yield. These results may be rationalized as follows. The titanium reagent from allyldiphenylphosphine probably exists at least partially as the vinyl phosphine isomer **1**.[4] Reaction of **1** with aldehyde through a six-membered cyclic transition state with minimal steric repulsion is expected to lead to the Z-1,3-diene.[4] In THF-HMPA solution the condensation of the lithio conjugated base **4** with aldehyde may be reversible and the product ratio is thermodynamically controlled.[13]

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References and Notes

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2. For recent syntheses of 1,3-diene using trimethylsilylallyltitanium reagents, see (a) F. Sato, Y. Suzuki, and M. Sato, *Tetrahedron Lett.*, *23*, 4589 (1982); (b) M. T. Reetz and B. Wenderoth, *ibid.*, *23*, 5259 (1982); see also, (c) Y. Yamamoto, Y. Saito, and K. Maruyama, *ibid.*, *23*, 4597 (1982); (d) *idem*, *J. Chem. Soc., Chem. Commun.*, *1982*, 1327.
3. For recent reviews, (a) M. T. Reetz In "Topics in Current Chemistry, Vol. 106"; Springer-Verlag, Berling, 1982; (b) B. Weidmann and D. Seebach, *Angew. Chem. Int. Ed. Engl.*, *22*, 31 (1983).
4. Y. Ikeda, K. Furuta, N. Meguriya, N. Ikeda, and H. Yamamoto, *J. Am. Chem. Soc.*, *104*, 7663 (1982).
5. F. G. Mann and M. J. Pragnell, *J. Chem. Soc.*, *1965*, 4120.
6. E. Vedejs and P. L. Fuchs, *J. Am. Chem. Soc.*, *95*, 822 (1973).
7. The generation of the lithio derivative was also accomplished with *n*-butyllithium but in slightly lower yield.
8. *Z*-Isomer: ^{1}H NMR ($CDCl_3$) 2.41 (br, 1H), 5.12 (d, 17 Hz, 1H), 5.20 (d, 10 Hz, 1H), 5.29 (dd, 10 and 7 Hz, 1H), 5.87 (dd, 10 and 10 Hz, 1H), 6.64 (ddd, 10, 10, and 17 Hz, 1H); IR (film) 3074, 2990, 1645, 1600, 1002, 967, 910 cm^{-1}.
9. Prepared by the modified procedure of M. P. Savage and S. Trippett [*J. Chem. Soc.*, *1966*, 1842]: A mixture of allyl alcohol (6.8 mL), chlorodiphenylphosphine (18 mL) and pyridine (18 mL) in dry ether (200 mL) was stirred at 0°C for 1 h. Powdered $NaHSO_4 \cdot H_2O$ (30 g) was added and stirred for 5 min. The suspension was filtered and the filtrate was concentrated *in vacuo*. The residue was dissolved in xylene (100 mL) and the mixture was heated at reflux for 2-3 h. Concentration followed by recrystallization (ether-hexane) gave allyldiphenylphosphine oxide in 65-73% yield.
10. The similar low reactivity of the titanium reagent was observed for the conjugate anion of phenyl allyl sulfoxide (unpublished results by Y. I.).
11. The carbanion formed by treating an allylphosphonodiamide with *n*-butyllithium, see E. J. Corey and D. E. Cane, *J. Org. Chem.*, 38, 2921 (1969).
12. *E*-Isomer: ^{1}H NMR (CCl_4) 2.0 (1H), 4.80 (d, 9 Hz, 1H), 4.93 (d, 18 Hz, 1H), 5.45 (dd, 6 and 15 Hz, 1H), 5.89 (dd, 9 and 15 Hz, 1H), 6.10 (ddd, 9,9 and 18 Hz, 1H); IR (CCl_4) 3100, 3040, 1660, 1620, 1002, 975, 955 cm^{-1}.
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