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CARBON-CARBON BOND FORMATION BY CROSS-COUPLING OF ENOL PHOSPHATES WITH ORGANOALUMINIUM COMPOUNDS CATALYZED BY PALLADIUM(0) COMPLEX

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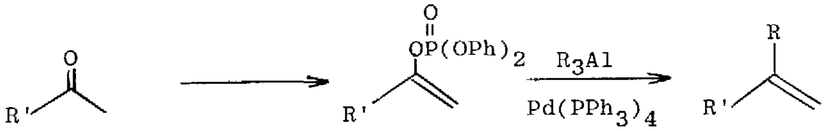
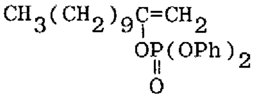
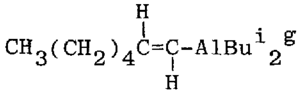
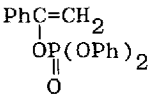
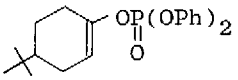
Abstract: Trialkylaluminium-mediated alkylation of enol phosphates under the C-O bond cleavage is performed stereospecifically in the presence of a catalytic amount of $Pd(PPh_3)_4$. Alkenylation and alkynylation are also described.

The Pd(0)-catalyzed reactions of organometallics with organic halides have been extensively studied to provide a new approach to selective cross-coupling.[1] However, this type of substitution at sp^2 carbon is limited to aryl halides and alkenyl halides.[2,3] We wish to report here that phosphates[4] derived from enolizable ketones can be used as substrates of palladium promoted C-C bond formation. Owing to the accessibility of a wide variety of such enolates,[5] the new method provides an effective tool for the specific transformation of ketones into alkyl-substituted olefins.[6]



To a solution of 1-decylethenyl diphenyl phosphate (0.83 g, 2.0 mmol) and a catalytic amount of $Pd(PPh_3)_4$ (0.23 g, 0.2 mmol) in 1,2-dichloroethane (10 ml) was added a hexane solution of trimethylaluminium (1.0 *M*, 4.0 ml, 4.0 mmol) at 25°C under argon atmosphere. The yellow colour of the solution turned to red immediately.[7] After being stirred for 2 h, the resulting mixture was diluted with ether (20 ml) and treated with *1N HCl (20 ml). The* organic layer was washed with brine, dried, and concentrated. Purification by thin layer chromatography on silica gel (hexane) gave 2-methyl-1-dodecene (0.33 g, 91% yield) as a colourless oil.

Table 1. Coupling reactions between enol diphenyl phosphates and organoaluminium reagents catalyzed by $Pd(PPh_3)_4$[a]

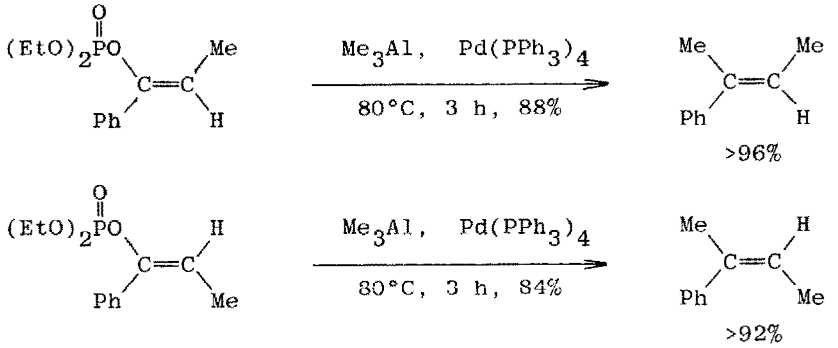
Run	Enol Phosphate[b]	Aluminium Reagent	Reaction Time (h)	Yield[c] of Coupling Product (%)
1	 $CH_3(CH_2)_9C(=CH_2)OP(=O)(OPh)_2$	Me_3Al	2	91
2		Et_3Al	3	71
3		$PhC{\equiv}C\text{-}AlEt_2$[d]	2	82[e]
4		$CH_3(CH_2)_4C{\equiv}C\text{-}AlEt_2$[f]	3	57[e]
5		 $CH_3(CH_2)_4CH{=}CH\text{-}AlBu^i_2$[g]	4	66
6	 $PhC(=CH_2)OP(=O)(OPh)_2$	Me_3Al	2	94[h]
7		Et_3Al	2	80
8		$PhC{\equiv}C\text{-}AlEt_2$[d]	3	67[e]
9		Me_3Al	5	72
10		$PhC{\equiv}C\text{-}AlEt_2$[d]	6	70[e]

a. Reactions were performed on 2.0 mmol scale at 25°C. Four mmol of aluminium reagent and 0.2 mmol of $Pd(PPh_3)_4$ were employed. b. Prepared by the phosphorylation of the corresponding lithium enolates with chloro diphenyl phosphate. c. Yields represent isolated, purified products. Spectral data were consistent with assigned structures. d. Prepared from $PhC{\equiv}CLi$ and Et_2AlCl in hexane. e. Ethylated product was not detected. The sole product was the respective 2-substituted ethynylation product. f. Prepared from $CH_3(CH_2)_4C{\equiv}CLi$ and Et_2AlCl. g. Prepared from 1-heptyne and $^iBu_2AlH$ *in situ* according to ref. 8. The sole product was 6(*E*)-$CH_3(CH_2)_9C(=CH_2)\text{-}CH{=}CH\text{-}(CH_2)_4\text{-}CH_3$. See ref. 9. h. Glpc yield.

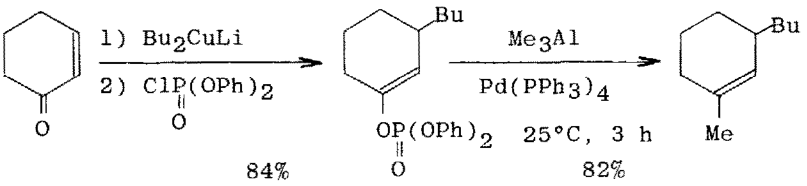
As shown in Table 1, not only alkyl group but also alkynyl (run 3, 4, 8, and 10) and alkenyl group (run 5) are introduced selectively in preference to the ubiquitous alkyl group. The success of the procedure heavily depends on the use of organoaluminium compounds[10] which are less reactive toward electrophilic centres than the corresponding lithium or magnesium derivatives. Indeed, MeLi or MeMgI attacked phosphorus atom of the ester to generate the metallic enolate which gave the original ketone upon workup.

In the absence of the metal phosphine catalyst the reaction did not proceed at all. Such potential catalysts as $PdCl_2(PhCN)_2$, $Pd(acac)_2$, $Ni(acac)_2$, and $Ni(PPh_3)_4$ gave less satisfactory results. Although the longer reaction period (10-15 h) was required, the amount of $Pd(PPh_3)_4$ could be reduced from 10 mol% to 3 mol% without significant decrease of the yields of olefins.

High stereospecificity of the reaction was demonstrated in the transformation of (*Z*) and (*E*)-1-phenyl-1-propenyl diethyl phosphates[11] to trisubstituted ethenes[12] with Me_3Al. All steps seem to proceed with retention of configuration similar to the case of alkenyl halides.



Simple synthetic application of the new method to 1,3-disubstituted cyclohexene is shown below.[13]



References and Notes

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2. A variety of organometallics are reported to couple with aryl halides and alkenyl halides in the presence of Pd(0) catalyst. (a) Mg and Li: S. Murahashi, M. Yamamura, K. Yanagisawa, N. Mita, and K. Kondo, *J. Org.*

Chem., 44, 2408 (1979). (b) Cu: H. P. Dang and G. Linstrumelle, *Tetrahedron Lett.*, 1978, 191. (c) B: N. Miyaura and A. Suzuki, *J. Chem. Soc. Chem. Comm.*, 1979, 866; H. Yatagai, Y. Yamamoto, and K. Maruyama, *ibid.*, 1977, 852. (d) Zn: E. Negishi, A. O. King, and N. Okukado, *J. Org. Chem.*, 42, 1821 (1977); A. O. King, E. Negishi, F. J. Villani, Jr, and A. Silveira, Jr, *ibid.*, 43, 358 (1978).

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7. The red colour remained throughout the reaction. Insufficient development of the colour with some lot of the catalyst resulted in failure of the coupling reaction.
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9. Bp 175°C (2 Torr, bath temp); IR (neat) 2925, 1608, 1468, 1460, 962, 880 cm^{-1}; NMR (CCl_4) δ0.73-1.07 (m, 6H), 1.07-1.73 (m, 22H), 1.73-2.27 (m, 4H), 4.77 (s, 2H), 5.57 (dt, 1H, J = 15, 6 Hz), 5.97 (d, 1H, J = 15 Hz); MS m/e (%) 264 (M^+, 8), 193 (14), 138 (82), 95 (91), 82 (72), 81 (100), 55 (58).
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11. Prepared from α-bromopropiophenone and triethyl phosphite according to the reported procedure.[4b] The (*Z*) and (*E*)-isomer were carefully separated by column chromatography on silica gel.
12. The (*E*)-isomer: NMR (CCl_4) δ1.79 (d, 3H, J = 7 Hz), 2.02 (s, 3H), 5.76 (q, 1H, J = 7 Hz), 7.03-7.37 (m, 5H). (*Z*)-Isomer: NMR (CCl_4) δ1.53 (d, 3H, J = 7 Hz), 2.00 (s, 3H), 5.49 (q, 1H, J = 7 Hz), 6.95-7.40 (m, 5H). S. A. Theine and J. G. Traynham, *J. Org. Chem.*, 39, 153 (1974).

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