Tetrahedron Letters, Vol.22, No.17, pp 1609 - 1612, 1981
Printed in Great Britain

0040-4039/81/171609-04$02.00/0

Pd(0) PROMOTED ALKYLATION OF ENOL PHOSPHATES WITH ORGANOALUMINIUM COMPOUNDS AND ITS SYNTHETIC APPLICATIONS

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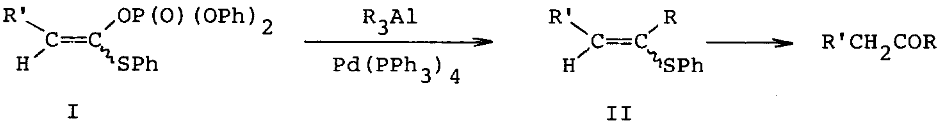
Abstract: Keto carbonyl 1,2- and 1,3-transpositions with and without alkylation of the substrate are described together with ketone synthesis from thiocarboxylic S-ester.

Organoaluminium compounds react with enol phosphates to give alkylative coupling products in the presence of a catalytic amount of $Pd(PPh_3)_4$.[1] The process provides a method of converting ketones into alkyl-substituted olefins regioselectively. Further synthetic applications have provided a novel ketone synthesis as well as a means of transposing a keto carbonyl group.

A hexane solution of trimethylaluminium (1.0 *M*, 4.0 ml, 4.0 mmol) was added to a solution of an enol phosphate I (2.0 mmol) derived from the thiocarboxylic S-ester and a catalytic amount of $Pd(PPh_3)_4$ (0.23 g, 0.2 mmol) in benzene under argon atmosphere. After being stirred at 25°C for an appropriate time described in Table 1, work up (ether, 1*N* HCl) and purification by silica gel column chromatography provided the expected alkenyl sulfide II in good yield.[2] Hydrolysis with $TiCl_4$[3] or $HgCl_2$[4] gave the corresponding ketone.[5]

The use of Et_3Al in the key step resulted in formation of a mixture of the ethylated product as well as hydrogenated one. It is worth noting that the ratios of these two have been effected by the solvent. The solvent and the ratio of hydrogenated and ethylated product in the reaction between Et_3Al and enol phosphate I (R' = ^{n}Pr) are given below: hexane, 71:29; 1,2-dichloroethane, 52:48; benzene, 38:62; ether, 29:71; tetrahydrofuran, 40:60; THF-HMPA (9:1), 29:71. The hydrogenated product increased in nonpolar solvents and ethylated one was favoured in polar solvents. The triisobutylaluminium-hexane system also provided a mixture of hydrogenated product and isobutylated one (73:27) in the reaction with I. The attempted reaction of diisobutylaluminium hydride with I in hexane did not give any detectable products within 5 h at 25°C.[6]

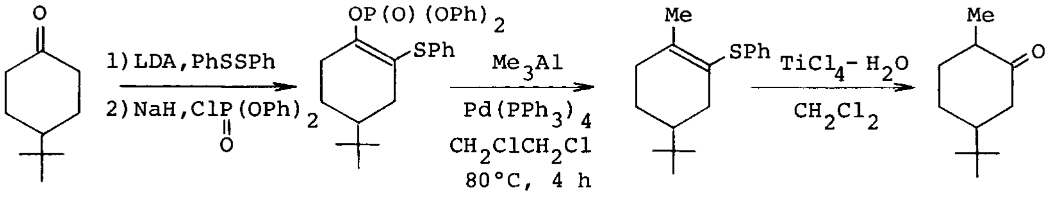
Table 1. Coupling reaction between enol phosphates derived from thiocarboxylic S-esters and organoaluminium reagents catalyzed by $Pd(PPh_3)_4$[a]



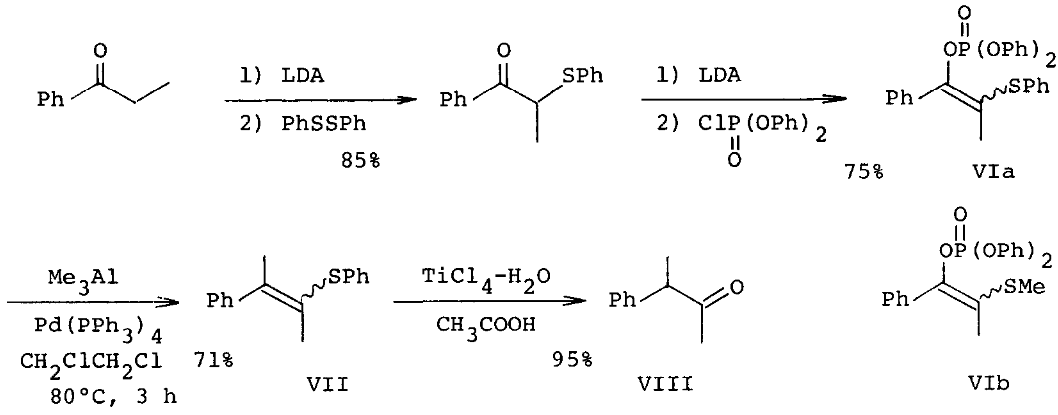
Enol Phosphate[b] R'	Aluminium Reagent	Reaction Time (h)	Yield of II(%)	Yield of Ketone(%)
$CH_3CH_2CH_2$	Me_3Al	1	83	70[c]
	Et_3Al	2	82[d]	—
	$PhC{\equiv}C\text{-}AlEt_2$	2	83[e]	—
	$CH_3(CH_2)_4CH{=}CH\text{-}AlBu^i_2$	3	62[e]	65[f]
Ph	Me_3Al	1	64	89[c]
	Et_3Al	2	55[d]	—

[a] Reactions were performed on 2.0 mmol scale at 25°C in benzene. Four mmol of aluminium reagent and 0.2 mmol of $Pd(PPh_3)_4$ were employed. [b] Prepared by phosphorylation of the corresponding lithium enolates with diphenyl chlorophosphate. [c] Hydrolysis with $TiCl_4$. See ref. 3. [d] Mixture of hydrogenated and ethylated product in 2:3 ratio. [e] Ethynylation or ethenylation product was obtained exclusively. [f] Hydrolysis with $HgCl_2$. See ref. 4.

Treatment of an enol phosphate III derived from 4-*tert*-butyl-2-phenylthiocyclohexanone[7] with Me_3Al and a catalytic amount of $Pd(PPh_3)_4$ gave the methylated alkenyl sulfide IV in 80% yield.[8] Hydrolysis with $TiCl_4$ provided the ketone V[9,10] (78% yield). The alkenyl sulfide VIb has been converted into phenylacetone in nearly 60% overall yield upon treatment with Et_3Al-$Pd(PPh_3)_4$ system and hydrolysis of the simple reduction product, PhCH=C(SMe)-Me, isolated in 72% yield.[11] The ethylated sulfide, PhC(Et)=C(SMe)Me, was isolated in less than 4% yield.

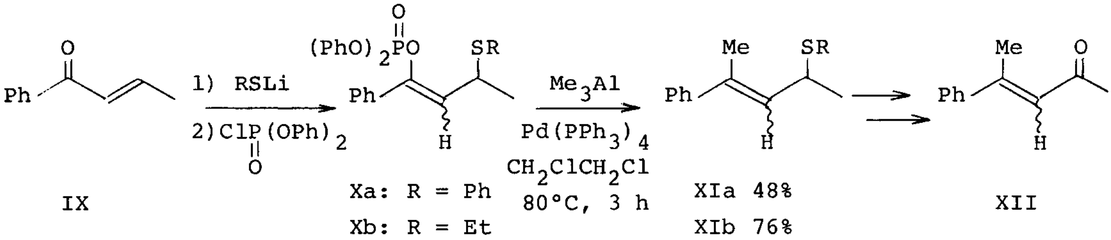


III IV V



VIa VII VIII VIb

Alkylative 1,3-transposition[12] of carbonyl groups could be achieved equally well. Exposure of phosphate X to a solution of Me_3Al[13] and a catalytic amount of $Pd(PPh_3)_4$ in 1,2-dichloroethane gave an ethenyl sulfide XI which was easily converted to the enone compound XII by Trost's method.[14] The enol phosphates Xa and Xb were prepared by 1,4-addition of lithium benzenethiolate (or ethanethiolate) to α,β-unsaturated carbonyl compound and successive trapping of the resulting enolates with diphenyl chlorophosphate in 74% and 76% yields, respectively.[15,16]



IX

Xa: R = Ph
Xb: R = Et

XIa 48%
XIb 76%

XII

References and Notes

1. K. Takai, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, 21, 2531 (1980).
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6. Heating the reaction mixture to reflux for 3 h provided $C_3H_7CH=C(SPh)-C(SPh)=CHC_3H_7$ (10%) and $CH_3CH_2CH_2C\equiv C-SPh$ (25%).
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9. Bp 80°C (bath temp, 2 Torr), IR (neat) 2970, 1708, 1448, 1364 cm^{-1}, NMR (CCl_4) δ0.95 (s, 9H), 1.00-2.55 (m, 11H). H. O. House and M. J. Umen, *J. Org. Chem.*, 38, 1000 (1973).
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13. The reaction of Xb with Et_3Al in 1,2-dichloroethane gave a mixture of the corresponding ethylated allylic sulfide and hydrogenated one in 1:2 ratio. The ratio could not be improved by changing the solvents. Another approach to 1,3-carbonyl transposition without alkylation is as follows: (1) reduction of conjugated enals or enones to allylic alcohols, (2) 1,3-migration of the hydroxyl group (A. Yasuda, H. Yamamoto, and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 52, 1757 (1979)), and (3) oxidation of the resulting isomers to the transposed carbonyls.
14. The sulfide XIa was converted into XII in 59% overall yield *via* sulfoxide according to the reported procedure. B. M. Trost and J. L. Stanton, *J. Am. Chem. Soc.*, 97, 4018 (1975).
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16. Financial support by the Ministry of Education, Science, and Culture, Japanese Government (Grant-in-Aid #530706), is acknowledged.

(Received in Japan 16 January 1981)