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Palladium-Catalyzed Allylidenation of Aldehyde. A Simple and Convenient Method for the Preparation of Conjugated Diene and Polyene Compounds

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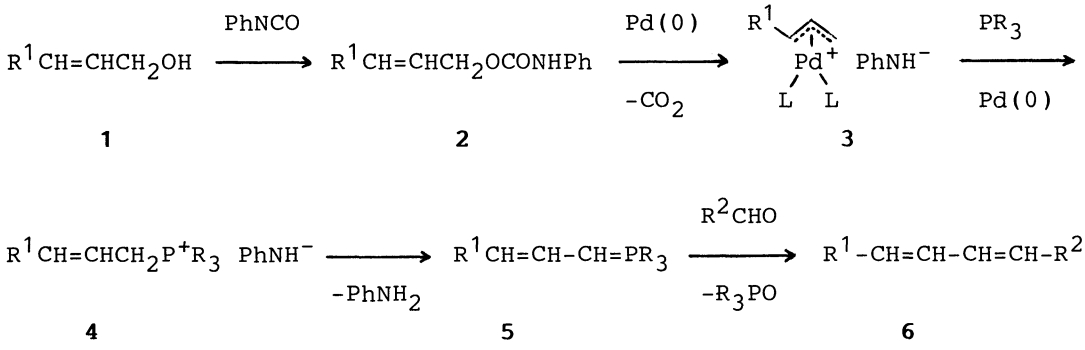
Allylic phenylcarbamates prepared from allylic alcohols and phenyl isocyanate in situ reacted with aldehydes to give conjugated dienes in good yields in the presence of tributylphosphine and a catalytic amount of $Pd(PPh_3)_4$. This method proved to be suitable for the preparation of polyene compounds such as carotenoids.

The reactions of π-allylpalladium complexes with nucleophiles such as stabilized carbanions, enamines, and amines have been well established and are of great synthetic utility.$^{1)}$ Phosphines are also good nucleophiles and can be expected to react with π-allylpalladium complexes. In fact, the reaction of excess triphenylphosphine with di-μ-chloro-bis(2-methylallyl)dipalladium is reported to give an allylic phosphonium salt and $Pd(PPh_3)_4$.$^{2)}$ Based on this observation, several Pd-catalyzed allylidenation reactions have been developed. For example, Moreno-Manas et al. obtained conjugated dienes simply by refluxing allylic alcohols with aldehydes and PPh_3 in the presence of $Pd(acac)_2$ in dioxane, however, the reactions were extremely slow.$^{3)}$ Inoue et al. reacted 2-allyl-1,3-dicyclohexylisoureas with aldehydes in the presence of PPh_3 and $Pd(PPh_3)_4$ to obtain conjugated dienes in good yields.$^{4)}$ Kinoshita et al. also reported a one-pot reaction utilizing allylic phosphonium bromides obtained by Pd-catalyzed reaction of allylic acetates with PPh_3 in the presence of NaBr.$^{5)}$ In this paper, we wish to report also a very simple and convenient method for the preparation of conjugated diene and polyene compounds by Pd(0)-catalyzed reaction of allylic carbamates with aldehydes in the presence of tributylphosphine.

We speculated that like well-established allylic carbonates,$^{6,7)}$ an allylic phenylcarbamate (**2**) would react with Pd(0) complex to afford a π-allylpalladium complex (**3**) with the concomitant elimination of carbon dioxide. If a phosphine such as PPh_3 reacts with **3**, an allylphosphonium salt (**4**) might be formed and the anilide anion formed simultaneously may be sufficiently basic to abstract a proton from the salt (**4**) to afford a phosphorane (**5**),$^{8)}$ which would react with an aldehyde to produce a conjugated diene (**6**) by the Wittig-type reaction$^{9)}$ as shown in Scheme 1.

According to this speculation, we tried some reactions of cinnamyl phenylcarbamate with heptanal in the presence of a phosphine and a catalytic amount of $Pd(PPh_3)_4$.$^{10)}$ It soon turned out that tributylphosphine gave better results than triphenylphosphine and that acetonitrile (CH_3CN) was the most effective among the



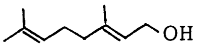
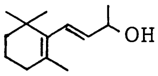
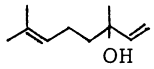
Scheme 1.

solvents tested. Thus, we could obtain the desired product consisting of two stereoisomers in a ratio of 4:1 in 83% yield by simply refluxing a mixture of cinnamyl phenylcarbamate, heptanal, tributylphosphine and a catalytic amount of $Pd(PPh_3)_4$ in CH_3CN (Method A). We found further that the preparation and isolation of the carbamate prior to the reaction was unnecessary and that the carbamate prepared from the alcohol and phenyl isocyanate in situ gave the same product in a comparative yield. Thus, more conveniently, the same product mixture with the same isomer ratio was obtained by only heating a mixture of cinnamyl alcohol, phenyl isocyanate, heptanal, tributylphosphine, and a catalytic amount of $Pd(PPh_3)_4$ in CH_3CN under reflux for 5 h (Method B). Though phenyl isocyanate is known to react with some phosphoranes,11) keteneimine compounds expected from such a reaction were not detected under these reaction conditions. The stereoisomers were not isolated, but structures of each isomer were determined by direct comparison with authentic samples prepared by methods known to give the stereo-defined products;12) (1E,3E)- and (1E,3Z)-1-phenyl-1,3-decadiene prepared by the palladium-catalyzed reaction of (E)-1-(2-phenylethenyl)-diisobutylalane with (E)- and (Z)-1-octenyl iodide, respectively, were identical with the major and minor products, respectively. Thus, stereoisomerism exists at the newly formed double bonds as in the normal Wittig reaction products. No other isomers were detected under these reaction conditions. These facts seem to indicate that the phosphine attacks the less-hindered carbon of the π-allylpalladium complex and that the (E)-geometry of the original allylic alcohol is retained.

The reactions of some allylic alcohols with aldehydes under these reaction conditions are summarized in Table 1. All products are mixtures of stereoisomers, but showed reasonable spectral data (^1H NMR and IR) and new compounds gave satisfactory elemental analysis. Though the reactions of aldehydes proceed smoothly and gave the products in satisfactory yields, those of ketones were very sluggish. In the case of primary and secondary allylic alcohols, in situ prepared carbamates reacted quite smoothly (Method B), however, tertiary allylic alcohol such as linalool, which does not react with phenyl isocyanate readily, required first the conversion of the alcohol to the corresponding carbamate.

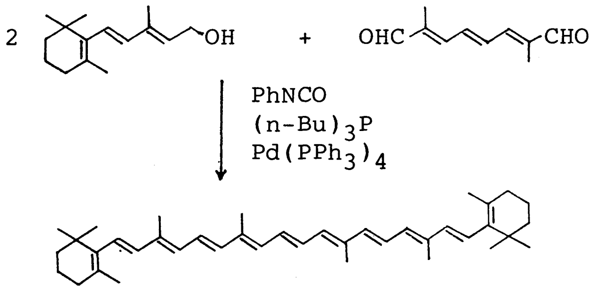
Though this reaction does not provide for the control of stereochemistry of the newly formed double bonds, the reaction seems to be synthetically useful, as the preparation of phosphonium salts and their base treatment are unnecessary and

Table 1. Allylidenation Reaction of Aldehydes[a]

Run	Allylic alcohol	Aldehyde	Conditions	Yield[b]/%	Isomer ratio[c]
1	$PhCH{=}CHCH_2OH$	$n\text{-}C_7H_{15}CHO$	A	83	4:1
2	"	"	B	82	4:1
3	"	PhCHO	A	84	1:1
4	"	"	B	79	1:1
5	$n\text{-}C_3H_7CH{=}CHCH_2OH$	$n\text{-}C_7H_{15}CHO$	B	52	3:1[d]
6	"	PhCHO	B	67	1:1
7		$n\text{-}C_7H_{15}CHO$	B	58[e]	3:1[d]
8	"	PhCHO	B	40[e]	5:2[d]
9		$n\text{-}C_7H_{15}CHO$	B	59	-[f]
10		"	A	56	-[g]
11	"	"	B	9	-[g]

a) Carbamate (1.3 mmol) (A) or a mixture of allylic alcohol (1.3 mmol) and phenyl isocyanate (1.3 mmol) (B) was refluxed with tributylphosphine (1.3 mmol), aldehyde (1 mmol) and $Pd(PPh_3)_4$ (5 mol%) in CH_3CN for 5 h, unless otherwise mentioned. b) Isolated yields. c) (E,E):(E,Z) ratio. The ratios were determined by GLC. d) The configuration was assigned tentatively by GLC behaviors. e) Two equiv. of the alcohol, phenyl isocyanate, and the phosphine were used. f) The ratio could not be determined by GLC. g) More than three peaks were observed in GLC.

the reaction proceeds under mild and neutral conditions. These reactions appear to be specially suitable for the preparation of polyene compounds such as carotenoids, for carotenoids are known to be able to undergo cis-trans isomerization readily under the diffused light, especially in the presence of a catalytic amount of iodine.[13] To test the utility of this methodology, we carried out the synthesis of β-carotene and obtained crystalline all-trans β-carotene in 65% yield



Scheme 2.

by simply refluxing a mixture of 2.6 equivalents of β-ionylideneethanol (C_{15}-alcohol)[14], phenyl isocyanate and tributylphosphine, 1 equivalent of 2,7-dimethyl-2,4,6-octatriene-1,8-dial (C_{10}-dialdehyde),[15] and 10 mol% of $Pd(PPh_3)_4$ in CH_3CN for 5 h as shown in Scheme 2. The product was identical in every respects with the authentic sample of β-carotene.

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7) Allylic carbonates seemed to react similarly. We tried some reactions using cinnamyl carbonate, however, good results were not obtained.
8) As long as the carbamate exists in the reaction system, the exact base which abstracts a proton from the phosphonium salt may be an anion formed by the following reaction.
$$RNH\text{-}COOR' + PhNH^- \longrightarrow RN^-\text{-}COOR' + PhNH_2$$
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