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ENOLSTANNANES AS ELECTROFUGAL GROUPS IN ALLYLIC ALKYLATION

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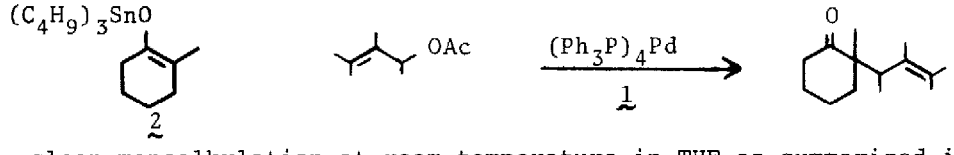
ABSTRACT: Enolstannanes serve as nucleophiles towards allylic acetates under the influence of palladium(0) catalyst.

Nucleophilic substitution of allylic acetates catalyzed by palladium generally requires stabilized carbanions such as malonates, anions of β-ketosulfides, etc.[1] Simple enolates such as that from acetophenone alkylate allyl acetate in the presence of tetrakis (triphenylphosphine)palladium (1) but gave the dialkylated product in 65% yield and the monoalkylated product in 34% yield. Attempts to improve the selectivity for monoalkylation by variation of catalyst, solvent, or other reaction conditions failed. Use of the enol silyl ether of acetophenone gave only the monoalkylated product with allyl acetate (59%), but the reaction could not be extended to substituted allyl acetates.

Switching to enol stannanes such as 2[2,3] led to a remarkably rapid and



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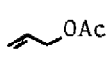
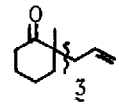
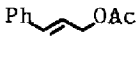
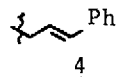
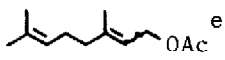
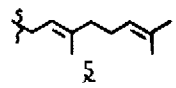
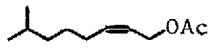
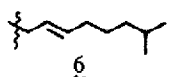
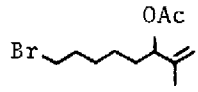
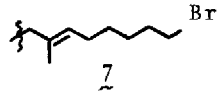
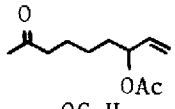
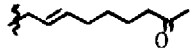
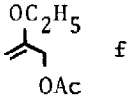
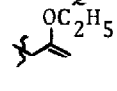
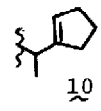
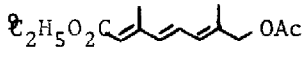
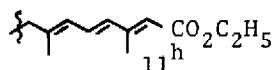
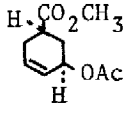
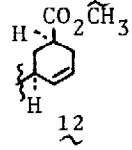
clean monoalkylation at room temperature in THF as summarized in the Table. Several aspects are quite noteworthy. First, a high regioselectivity is seen for alkylation at the less substituted end of the allyl moiety[4] with formation of the E isomer. The latter differs from the reactions with stabilized anions where the stereochemistry of the trisubstituted double bond was retained.[4,5] In the case of the disubstituted olefins such as 4, 6, and 8, the stereochemistry is assigned based upon the coupling constants of the vinyl protons (4, δ 6.14 and 6.40, J = 16 Hz; 6, δ 5.27 and 5.43, J = 15.3 Hz; 8, δ 5.32 and 5.44, J = 14.8 Hz). The stereochemistry of the trisubstituted olefins is

Table. Alkylation of Enol Stannane 2

Entry	Allyl Acetate[a]	Time (hr)[b]	Ratio 2:Acetate	Product[c]	% Yield[d]
1		1	1.1:1	 3	90-95
2		24	1.2:1	 4	82
			2.3:1		89
3	 e	42	1.8:1	 5	78
4		0.5	1.4:1	 6	96
5		19	1.5:1	 7	89
6		3	2.2:1	 8	91
7	 f	41	1.3:1	 9	72
8		42	1.1:1	 10	24
9	 g	22	3.8:1	 h 11	77
10		24	2.2:1	 12	85

a) All reactions were carried out at room temperature in dry THF using approximately 5 mol % of catalyst 1. For example, 287 gm (1.46 mmol) of a mixture of geranyl and neryl acetate and 1.08 g (2.69 mmol) of 2 in 6 mL of dry THF were stirred for 42 hr at room temperature in the presence of 73 mg (4.3 mol %) of 1. After preparative tlc (1:9 ether:hexane), the colorless oil was distilled on a Kugelrohr apparatus at 110-130° (pot temperature) @0.2 mm to give 238 mg (78%) of 5.

b) In most cases, monitoring the reaction by tlc showed disappearance of the allyl acetate in less time than the time allotted.

c) All new products have been fully characterized by spectral means and for elemental composition.

d) Yield after distillation unless otherwise noted.

e) Mixture of neryl and geranyl acetate.

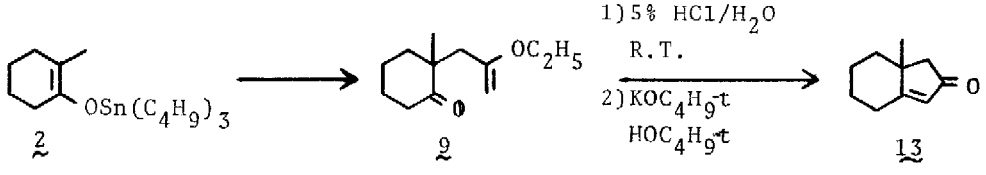
f) Prepared by Dr. Dennis Curran and will be reported separately.

g) Prepared by Dr. Michael Miller from the aldehyde kindly provided by Dr. Michael Rosenberger of the Hoffman-LaRoche Co.

h) In this case, the product was purified only by preparative tlc.

assigned mainly on the observation that only a single isomer is produced (even from stereoisomeric mixtures of starting materials) which should therefore reflect thermodynamic stability. For 5, the chemical shifts of the vinylic methyl groups (δ 1.59, 6H and 1.66, 3H) supported this assignment.[6]

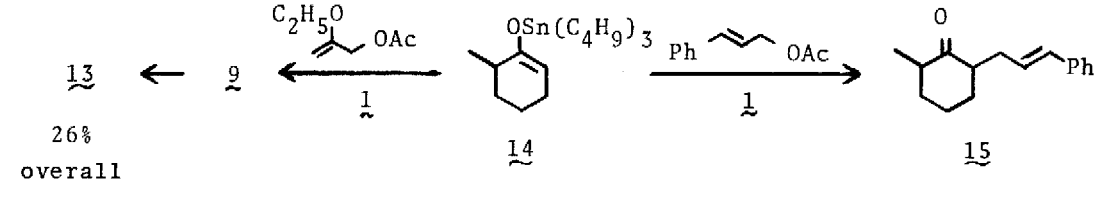
The chemoselectivity is high as evidenced by the compatibility of an ester (entries 9 and 10), a ketone (entry 6), an alkyl bromide (entry 5), and an enol ether (entry 7). The utility of the sequence is illustrated by the cyclopentanone annulation sequence as shown by the facile conversion of 9 to 13[7]



2 9 13

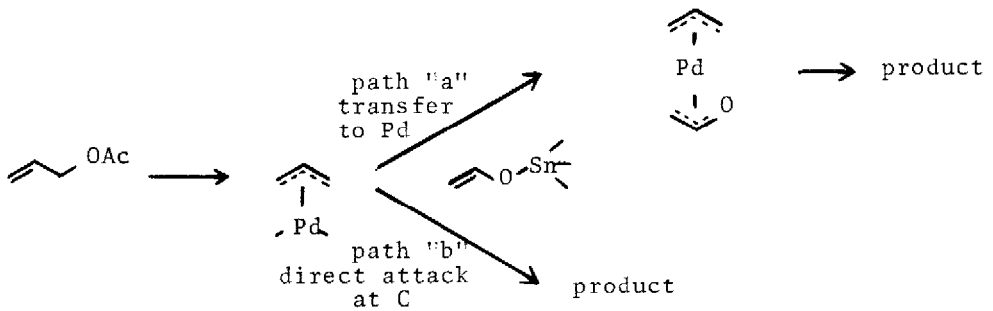
which can be obtained in 84% overall yield from the enol stannane without isolating any intermediates.

The regioselectivity appears to depend on the reactants. For example, generation of the enol stannane 14 *in situ* (by treatment of the lithium enolate with tri-n-butylstannylchoride[3]) and cinnamyl acetate led only to the desired



2,6-disubstituted product 15 as a E,Z mixture in a 1:1.2 ratio, separable by tlc (15E, δ 1.04, d, J = 7 Hz, 3H; 15Z, δ 1.10, d, J = 7 Hz). On the other hand, reaction with the much more sluggish[8] 2-ethoxyallyl acetate led only to 9, the product from the more stable enol stannane. Thus, with sluggish allyl acetates equilibration of the enol stannane appears to occur faster than alkylation.

Two mechanisms may be envisioned. The fact that organostannanes appear to transfer the alkyl group to palladium very well[9] and that oxa-π-allyl complexes have been formed from enol silyl ethers[10] makes path "a" quite



quite reasonable. Path "b" represents the type of reaction that has been defined for other nucleophiles such as malonates[4,11]. The fact that substitution occurs with net retention of configuration (entry 10) as also found for stabilized anions[4,11] strongly supports the latter pathway.

The expansion of the scope of the allylic alkylation to the less stabilized nucleophiles suggests a much broader applicability of this reaction in organic synthesis and also suggests that enol stannanes might be more useful enolate equivalents than presently accorded them.

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