Carbon–Carbon Bond Formation at the γ-Position of Dienolates *via* the Palladium Catalysed Coupling of the Tin Masked Dienolates

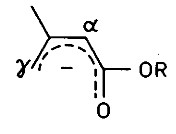
Yoshinori Yamamoto,* Satoshi Hatsuya, and Jun-ichi Yamada

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan

The palladium catalysed coupling reaction of the tin masked dienolate (**2**) with organic halides takes place at the position substituted by tin, thereby providing a new method for C–C bond formation at the γ-position of dienolates.

Carbon–carbon bond formation at the γ-position of dienolates has long been a problem in organic chemistry. It is generally accepted that dienolates (**1**) undergo selective alkylation at the α-position rather than the γ-position. Since carbon–carbon bond formation at the γ-position is important for the synthesis of terpenoid natural products, especially isoprenoid alkenes, a number of methods have been developed to produce γ-regioselectivity.[1] We report that the palladium catalysed coupling reaction of the tin masked dienolate (**2**) with acyl, aryl, and vinyl halides takes place at the position directly bonded to tin (Scheme 1), though coupling of γ-substituted allylic tin compounds, *e.g.* crotyltin, normally proceeds through allylic transposition to give the branched isomer (**5**) as the major product (Scheme 2).[2]

We recently reported that the tin masked dienolates (**2**) are easily obtainable from the corresponding dienolate (**1**).[3] The results of the palladium catalysed coupling reactions of (**2a**) are summarized in Table 1. The couplings of (**2b**) or more highly chlorine substituted derivatives (R^1_3 = Cl_3 or $BuCl_2$) were unsuccessful, presumably owing to formation of the Lewis acid Bu_xSnCl_{4-x} ($x = 0, 1, 2$). The coupling took place at the carbon directly bonded to tin and the allylic transposition[2] product was not detected. Aryl halides (Table 1, entries 1—4), acid halides (entries 5—7), and vinyl bromide (entry 8) produced (**4**); the aromatic acid halide and aryl halides substituted with an electron withdrawing group gave good yields. In some cases, the β,γ-unsaturated ester derivatives (**7**) were produced as by-products. The coupling of aliphatic acid halides and vinyl halide produced low yields.

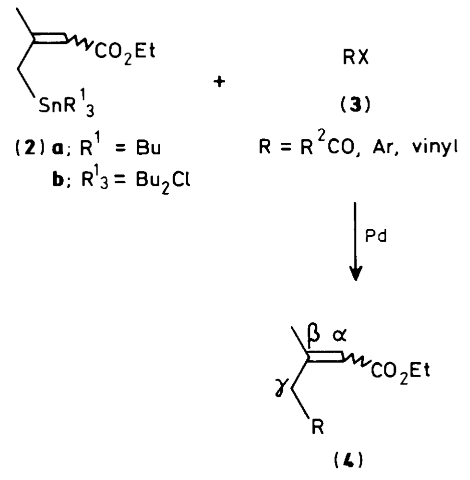


(**1**)

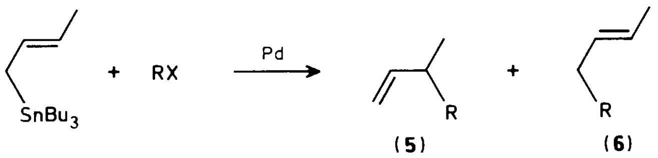
Table 1. γ-Regioselective coupling of (**2a**) with (**3**).[a]

Entry	Halide (**3**)	Procedure[b]	Isomer ratio[c] *E*:*Z*	Isolated total yield of (**4**)/%
1	PhBr	A	1:4	55[d]
2	$MeCOC_6H_4Br$-*p*	A	1:3	60
3	$MeOC_6H_4Br$-*p*	B	1:1.5	30
4	α-Naphthyl bromide	B	1:10	50
5	PhCOCl	C	1:8	70[e]
6	$Me(CH_2)_6COCl$	C	1:5	25
7	$Me(CH_2)_3CEtHCOCl$	C	1:2	25
8	Me_2C=CHBr	A	1:3	20

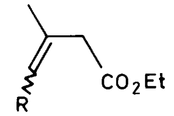
[a] All reactions were carried out on 1 mmol scale under N_2. Products were isolated by column chromatography (silica gel). [b] A: 5% $Pd(PPh_3)_4$, benzene, reflux, 21 h; B: 5% $Pd(OAc)_2$, 20% PPh_3, toluene (entry 3) or benzene (entry 4), reflux, 17—20 h; C: 1—1.5% $PhCH_2PdCl(Ph_3P)_2$, $CHCl_3$, reflux 20—24 h. [c] Isomer ratio was determined by ^1H n.m.r. analysis. [d] As a by-product, the β,γ-unsaturated ester derivatives of (**4**) were obtained in 5% yield. [e] The isomerized β,γ-unsaturated ester was obtained in 20% yield.



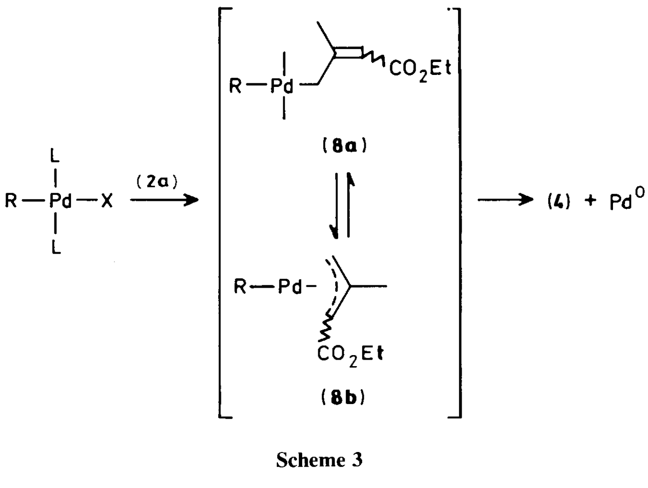
Scheme 1



Scheme 2



(**7**)



Scheme 3

The coupling of allylic tin reagents without allylic transposition has been reported previously.[4] It should be noted that there is a remarkable contrast between the very high extent of aldehydes at the α-position of (**2a**) in the presence of $BF_3 \cdot OEt_2$[2] and the exclusively γ reaction of halides with (**2a**) in the presence of the palladium containing catalysts. Although it may be premature to speculate on the mechanism of the present regioselective carbon–carbon bond formation, we propose a π-allyl mechanism (Scheme 3) instead of the direct attack mechanism[2b,c] of allylic tins. Transmetallation of the initially formed Pd^{II} species presumably gives the intermediate (**8**), which undergoes reductive elimination to produce (**4**) and Pd^0 species. The π-allyl mechanism is supported by the *E*:*Z* ratio of (**4**) (see Table 1); if the σ-allyl species (**8a**) is the only intermediate involved, the ratio should be the same as those of the starting material (**2a**) (*E*:*Z* 1:7). Experimental results indicate that the ratio is independent of the geometry of (**2a**), suggesting intermediacy of (**8b**). Irrespective of the precise mechanism, the dienolate masked by tin seems to be useful for chain elongation at the γ-position.

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