α-Regioselective Carbonyl Allylation by an Allylic Tin Compound Prepared from 1-Bromobut-2-ene and Tin(II) Bromide at a Nonpolar Organic–Aqueous Interface

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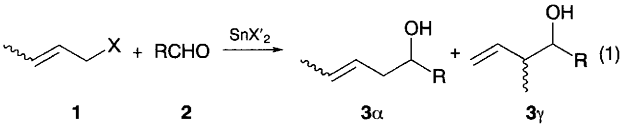
1-Bromobut-2-ene on a dichloromethane–water biphasic system at 25 °C causes α-regioselective addition to aldehydes with $SnBr_2$ to produce 1-substituted pent-3-en-1-ols, and causes γ-regioselective addition to aldehydes with $SnBr_2$–Bu_4NBr to produce 1-substituted 2-methylbut-3-en-1-ols.

The allylation of aldehydes (carbonyl allylation) with γ-substituted allylmetal reagents, derived from γ-substituted allylic halides with metals or metal halides, usually occurs diastereoselectively at the γ-position of the allylmetal reagents.[1] A few α-regioselective carbonyl allylations by γ-substituted allylic halides have been achieved using metals such as Mg/$AlCl_3$[2] and Ba.[3] We have been developing palladium-catalysed carbonyl allylation by allylic alcohols with tin(II) chloride.[4] The regioselectivities in the palladium-catalysed carbonyl allylation correlate with the dielectric constants of the solvents used: γ-regioselection in polar solvents such as 1,3-dimethylimidazolidin-2-one (DMI), DMF, Me_2SO, ethylene glycol and THF–H_2O, and α-regioselection in nonpolar solvents such as diethyl ether. However, the α-regioselective allylation in diethyl ether suffers from the defect that the reaction rate is hopelessly slow, because of the low solubility of tin(II) chloride in diethyl ether.† No carbonyl allylation by 1-bromobut-2-ene with tin(II) halides in nonpolar solvents such as dichloromethane and toluene occurs, similarly to the palladium-catalysed allylation by (*E*)-but-2-en-1-ol under the same conditions. Tin(II) bromide and tin(II) chloride are highly soluble in water. We thus hoped that we could prepare γ-substituted allylic tin intermediates from γ-substituted allylic halides and tin(II) halides at the interface of a nonpolar solvent and water, followed by α-regioselective carbonyl allylation in the nonpolar solvent.

The allylation of heptanal (**2**, R = n-C_6H_{13}) by 1-halobut-2-enes **1** with tin(II) halides to produce homoallylic alcohols **3**α and **3**γ was investigated at 25 °C in nonpolar solvent–water systems [eqn. (1)].‡ The results are summarized in Table 1. The carbonyl allylation by 1-bromobut-2-ene (**1**, X = Br)§ with tin(II) bromide in dichloromethane–water (two phases) system proceeded with high α-regioselectivity, in contrast with γ-regioselectivity in polar solvents such as DMF and DMI (entry 3).¶[5] The carbonyl allylation also occurred in water with α-regioselectivity (entry 10). Addition of tetra-butylammonium bromide (TBA) to any solvent system used promoted the carbonyl allylation by **1** (X = Br) with tin(II) bromide,[6] but lowered the α-regioselectivity (entries 6, 7, 11 and 12). The reaction with one equimolar amount of TBA to heptanal in either dichloromethane–water or water exhibited high γ-regioselectivity (entries 7 and 12). The use of tin(II) chloride instead of tin(II) bromide, or the use of 1-chlorobut-2-ene (**1**, X = Cl) instead of 1-bromobut-2-ene (**1**, X = Br) depressed the reactivity of the carbonyl allylation in dichloromethane–water (entries 4 and 5).



The regiocontrolled allylation of various aldehydes **2** by **1** (X = Br) with tin(II) bromide (X′ = Br) was carried out at 25 °C either by method A (without TBA in dichloromethane–water) or by method B (with TBA in water), as summarized in Table 2 [eqn. (1)]. Method A led to α-regioselection and method B led to γ-regioselection, similarly to the allylation of heptanal. The allylation of benzaldehydes containing electron-withdrawing groups such as chloro or cyano groups by method A did not exhibit α-regioselectivity but γ-regioselectivity (4-ClC_6H_4CHO, 68 h, 83%, α : γ = 11 : 89; 4-NCC_6H_4CHO, 46 h, 95%, α : γ = 1 : 99). The regioselectivities in the allylation of benzaldehyde by method A were therefore investigated at various reaction temperatures (10–35 °C), as shown in Fig. 1. As the reaction temperature rose, the α-regioselectivity improved (α : γ = 99 : 1 at 32 °C). The reaction temperature of method A affected the α-regioselection in the allylation of all the benzaldehydes used, bearing either an electron-withdrawing or an electron-donating group, similarly to that of benzaldehyde (4-ClC_6H_4CHO, 32 °C, 24 h, 38%, α : γ = 87 : 13; 4-$MeOOCC_6H_4CHO$, 32 °C, 24 h, 33%, α : γ = 52 : 48; 4-NCC_6H_4CHO, 32 °C, 24 h, 36%, α : γ = 25 : 75). The

Table 1 Allylation of heptanal by **1** with tin(II) halides[a]

Entry	X	X′	Solvent system	TBA/mol%	**3** (R = C_6H_{13}) Yield (%)[b]	α : γ[c]
1	Br	Br	CH_2Cl_2	0	N.R.[d]	—
2	Br	Br	CH_2Cl_2	10	trace	—
3	Br	Br	CH_2Cl_2–H_2O	0	48	91 : 9
4	Br	Cl	CH_2Cl_2–H_2O	0	25	81 : 19
5	Cl	Br	CH_2Cl_2–H_2O	0	28	65 : 35
6	Br	Br	CH_2Cl_2–H_2O	10	89	52 : 48
7	Br	Br	CH_2Cl_2–H_2O	100	83	9 : 91
8	Br	Br	$CHCl_3$–H_2O	0	78	56 : 44
9	Br	Br	Et_2O–H_2O	0	73	13 : 87
10	Br	Br	H_2O	0	36	77 : 23
11	Br	Br	H_2O	10	42	13 : 87
12	Br	Br	H_2O	100	48	1 : 99

[a] The allylation of heptanal (1 mmol) by **1** (2 mmol) was carried out with tin(II) halide (2 mmol) at 25 °C for 24 h in organic solvent (3 ml)–water (3 ml) or water (6 ml). [b] Isolated yields. [c] The ratio was determined by ^1H NMR (JEOL GX-270) and by GC (capillary column PEG 20M 0.25 mm × 30 m); α, *E* : *Z* = 85 : 15–62 : 38; γ, *syn* : *anti* = 65 : 35–51 : 49. [d] N.R. = no reaction.

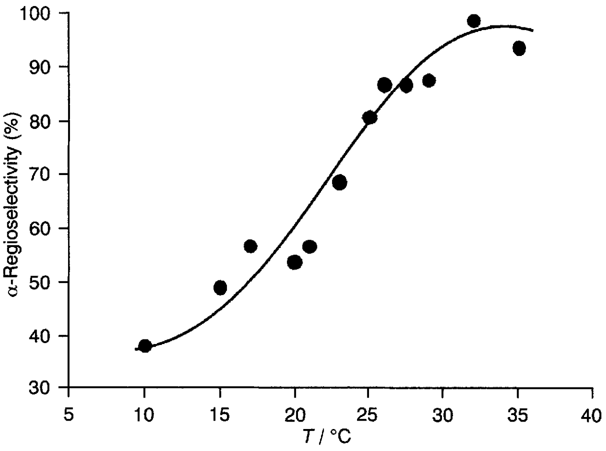


Fig. 1 Dependence of α-regioselectivity upon reaction temperature. The allylation of benzaldehyde (4 mmol) by 1-bromobut-2-ene (2 mmol) was carried out with $SnBr_2$ (2 mmol) for 24 h at 10–35 °C in CH_2Cl_2 (3 ml) and H_2O (3 ml) to produce a mixture of 1-phenylpent-3-en-1-ol and 2-methyl-1-phenylbut-3-en-1-ol in 30–45% yield.

Table 2 Carbonyl allylation by **1** (X = Br) with tin(II) bromide[a]

Entry	R	Method[b]	*t*/h	**3**, Yield[c] (%)	Ratio[d] α(*E*:*Z*):γ(*syn*:*anti*)
1	C_6H_5	A	24	60	94 (85:15): 6 (90:10)
2	C_6H_5	B[e]	24	83	5 (89:11):95 (33:67)
3	MeC_6H_4	A	24	66	86 (97:3) :14 (36:64)
4	MeC_6H_4	B[e]	24	70	10 (93:7) :90 (31:69)
5	$PhCH_2CH_2$	A	24	61	92 (58:42): 8 (79:21)
6	$PhCH_2CH_2$	B	24	99	7 (62:38):93 (57:43)
7	C_6H_{13}	A	75	98	87 (64:36):13 (62:38)
8	C_6H_{13}	B	24	83	9 (62:38):91 (51:49)
9	$H_2C{=}CH(CH_2)_8$	A	24	68	92 (66:34): 8 (79:21)
10	$H_2C{=}CH(CH_2)_8$	B[f]	25	75	1[g]:99 (53:47)
13	c-C_6H_{11}	A	50	76	92 (80:20): 8 (28:72)
14	c-C_6H_{11}	B[f]	26	79	2[g]:98 (30:70)
15	$(Me)_3C$	A	31	60	89 (18:82):11[g]
16	$(Me)_3C$	B[e]	24	38	31 (37:63):69 (76:24)

[a] The allylation of **2** (1 mmol) by **1** (X = Br, 2 mmol) was carried out with $SnBr_2$ (2 mmol) at 25 °C in CH_2Cl_2–H_2O (1:1, 6 ml). [b] A: Without TBA. B: After the solution of **1** and $SnBr_2$ was stirred with TBA (1 mmol) for 2 h, **2** was added. [c] Isolated yields. [d] The ratio was determined by ^1H NMR (JEOL GX-270) and by GC (capillary column PEG 20M, 0.25 mm × 30 m). [e] H_2O (6 ml) was used as a solvent. [f] CH_2Cl_2 (1 ml) and H_2O (5 ml) were used as solvents. [g] The ratio (*E*:*Z* or *syn*:*anti*) was not confirmed.

α-regioselection of aliphatic aldehydes was not much influenced by reaction temperature.

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Footnotes

† Ultrasonic irradiation improved the α-regioselective allylation: the reaction of (*E*)-but-2-en-1-ol and benzaldehyde in diethyl ether produced the allylated regioisomers in 76% yield. However, the α-regioselectivity (α:γ = 75:25) was lower than that (α:γ = 94:6) without ultrasonic irradiation.[7]

‡ A typical procedure for the α-regioselective carbonyl allylation by 1-bromobut-2-ene with tin(II) bromide is as follows. To a solution of tin(II) bromide (0.56 g, 2 mmol) in dichloromethane (3 ml) and water (3 ml) were added heptanal (0.11 g, 1 mmol) and 1-bromobut-2-ene (0.27 g, 2 mmol). The solution was vigorously stirred at 25 °C for 75 h under a nitrogen atmosphere, then poured into water (30 ml) and extracted with diethyl ether–dichloromethane (2:1, 100 ml). The extract was washed first with water and then with brine, and was dried over $MgSO_4$. Evaporation of solvents and purification by preparative TLC (Harrison centrifugal thin-layer chromatotron; Merck Kiesel-gel 60 PF_{254} Art. 7749; hexane:ethyl acetate = 10:1) and/or HPLC (Japan Analytical Industry Co., Ltd. LC-908; JAIGEL-2H; chloroform) afforded a mixture of undec-2-en-5-ol (α-adduct) and 3-methyldec-1-en-4-ol (γ-adduct) (0.17 g, 98%, α:γ = 87:13) as a colourless oil.

§ 1-Bromobut-2-ene (**1**, X = Br, *E*:*Z* = 85:15), purchased from Tokyo Chemical Industry Co., Ltd., contains 14% 3-bromobut-1-ene.

¶ The allylation of heptanal by 1-bromobut-2-ene (**1**, X = Br) with tin(II) bromide at 25 °C in 1,3-dimethylimidazolidin-2-one (DMI) for 22 h gave **3** (α:γ = 20:80) in 74% yield.[8]

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