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Efficient Allylation of Aldehydes Promoted by Carboxylic Acids

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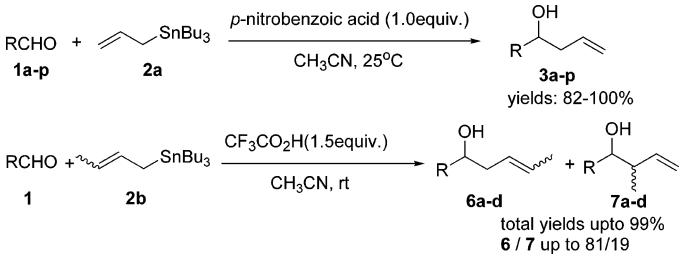

A variety of carboxylic acids have been screened for mediating the allylation of aldehydes with allytributyltin in different solvents. A novel, general, and practical method of allylation of aldehydes promoted by carboxylic acids under mild reaction conditions has been developed. Among them, *p*-nitrobenzoic acid afforded high to quantitative yields of the homoallylic alcohol products, and can be easily recovered after workup by aqueous HCl. Glyoxylic acid self-catalyzed the allylation without adding any other promoter or catalyst to give the corresponding allylation product in good yield. The regioselectivity of the crotylation of aldehydes is tunable by controlling the acidity of the carboxylic acids. The crotylation of aldehydes produced the α-adduct as major products in moderate to good yields with CF_3CO_2H as a promoter. A possible mechanism for the allylation is also discussed.

Introduction

The allylation of carbonyl compounds, especially aldehydes, using allylstannanes, is a very important synthetic method for forming synthetically useful homoallylic alcohols and has been extensively investigated.[1] Since the first example of thermally induced allylation of aldehydes with allylstannanes, [2] a large number of other methods have been reported.[3] Among them, Lewis acids (especially metal Lewis acids) or transition metal complexes have been utilized to promote the allylation of aldehydes or ketones with allyltributyltin.[1g] However, the traditional methods with these Lewis acids (e.g., $Et_2O{\cdot}BF_3$, $TiCl_4$, and $SnCl_4$) in organic synthesis must be carried out under strictly anhydrous conditions, which cause inconvenience in handling and manipulating. Recently, new types of water-tolerant Lewis acids, including lanthanide triflates, have been developed as catalysts for this reaction. These catalysts show some advantages including mild reaction conditions, high yields of products, and simple experimental procedures. [4] However, they are rather expensive. From the viewpoints above, the development of less expensive, environmentally benign, and easily handled promoters for allylation of aldehydes is still highly desirable.

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(1) For recent reviews, see: (a) Davies, A. G. *Organotin Chemistry*; Wiley-VCH: Weinheim, Germany, 2004. (b) Hisashi, Y.; Koichiro, O. *Main Group Metals in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2004; Vol. 2, pp 621−720. (c) Junzo, O. *Modern Carbonyl Chemistry*; Wiley-VCH: Weinheim, Germany, 2000. (d) Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163−3185. (e) Marshall, J. A. *Chem. Rev.* **1996**, *96*. 31−47. (f) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207−2293. (g) Nishigaichi, Y.; Takuwa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395−7426.

(2) König, K.; Neumann, W. P. *Tetrahedron Lett.* **1967**, *8*, 495−498.

(3) Brønsted acid and Lewis acids (reported in recent years), see: (a) Loh, T.-P.; Xu, J. *Tetrahedron Lett.* **1999**, *40*, 2431−2434. (b) Loh, T.-P.; Xu, J.; Hu, Q.-Y.; Vittal, J. J. *Tetrahedron*: *Asymmetry* **2000**, *11*, 1565. (c) Bartoli, G.; Bosco, M.; Giuliani, A.; Marcantoni, E.; Palmieri, A.; Petrini, M.; Sambri, L. *J. Org. Chem.* **2004**, *69*, 1290−1297. (d) Lu, J.; Ji, S.-J.; Qian, R.; Chen, J.-P.; Liu, Y.; Loh, T.-P. *Synlett* **2004**, 534−536. (e) Boyapati, M. C.; Karangula, J.; Sateesh, M.; Mannepalli, L. K. *Synlett* **2004**, 231−234. (f) Yadav, J. S.; Reddy, B. V. S.; Krishna, A. D.; Sadasiv, K.; Chary, Ch. J. *Chem. Lett.* **2003**, *32*, 248−249. (g) Kobayashi, S.; Aoyama, N.; Manabe, K. *Synlett* **2002**, 483−485. (h) Shibata, I.; Yoshimura, N.; Yabu, M.; Baba, A. *Eur. J. Org. Chem.* **2001**, 3207−3211.

(4) (a) Steel, P. G. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2727−2751. (b) Kobayashi, S. *Lanthanides*: *Chemistry and Use in Organic Synthesis*; Springer-Verlag: Heidelberg, Germany, 1999. (c) Kobayashi, S. *Eur. J. Org. Chem.* **1999**, 15−27. (d) Chen, J.; Sakamoto, K.; Orita, A.; Otera, J. *Synlett* **1996**, 877−879. (e) Cozz, P. G.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *Synlett* **1994**, 857−858.

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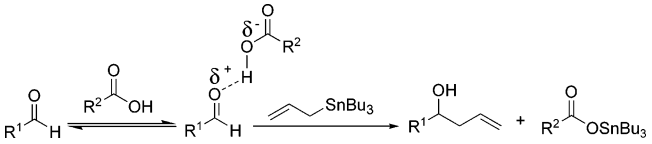
SCHEME 1. The Proposed Allylation of Aldehyde Promoted by Carboxylic Acid



In recent years, increasing attention has been paid to organocatalysts owing to their environmentally benign nature and other notable advantages (reactions catalyzed by organocatalysts often proceed under an aerobic atmosphere even in wet solvents; the organocatalysts are usually inexpensive and commercially available).[5] The proton of Brønsted acids, the smallest Lewis acid, is one of the best Lewis acids that is especially effective in carbonyl activation.[6] Yamamoto and co-workers reported the allylation of aldehydes with allytributyltin using Sn catalysts in acidic aqueous solution, but that reaction did not afford the allylation product in the presence of HCl.[7] Loh et al. developed a new method of addition of allyltributyltin to aldehydes using trifluoromethane sulfonic acid as a promoter in water.[3a,b] Very recently, an asymmetric allylation of aldehydes with tetraallyltin, using α-amino acids as a chiral Brønsted acid promoter, was reported to provide the corresponding homoallylic alcohols in high yields with moderate enantioselectivities. The same reaction did not proceed when tetraallyltin was replaced with allyltributyltin.[8] Herein, we would like to describe how carboxylic acids can be used to promote the allylation of aldehydes with allyltributyltin under mild reaction conditions.

Results and Discussion

Recently, Aspinall et al. reported the use of stoichiometric benzoic acid as an additive for accelerating the allylation of aldehydes with allyltributyltin in the presence of Yb(III) triflate. They proposed that the action of benzoic acid was to form an enhanced Brønsted acid with the Lewis acid to catalyze the reaction, and then destroy the ties between Lewis acid and alkoxide.[9] Thus the activity of the Lewis acid was regenerated. In our studies on the allylation of aldehydes, we consider that the use of carboxylic acids can form a hydrogen bond to activate the carbonyl group of aldehydes, and then produce the tin ester (Scheme 1), thus promote the reaction. With this idea in mind, we first chose benzoic acid as a promoter and acetonitrile as a solvent. Benzaldehyde reacted with allyltributyltin at room temperature (25 °C) in 3 days resulting in 30% isolated yield of the homoallylic alcohol **3a** (entry 6 in Table 1).

Encouraged by this result, we screened a variety of substituted benzoic acids, other carboxylic acids, and

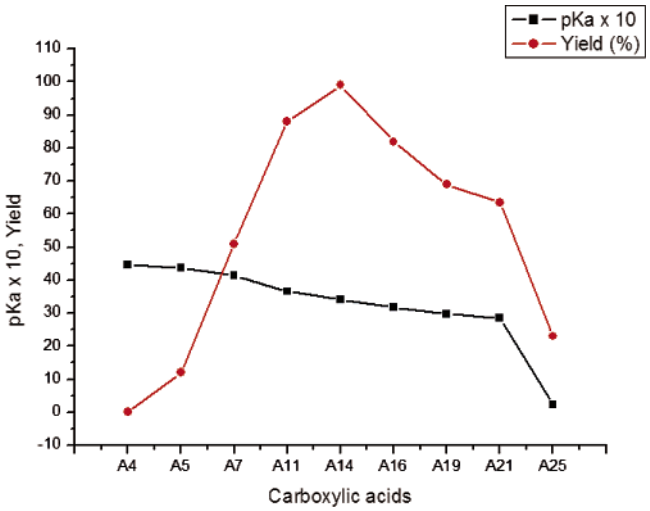


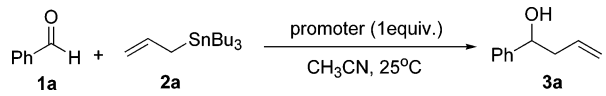
FIGURE 1. Plot of pK_a vs yields.

Brønsted acids. The results are summarized in Table 1 (in the order of pK_a value). When *p*-nitrobenzoic acid was used as a promoter, the allylation proceeded smoothly in quantitative yield, using acetonitrile as a solvent (entry 14); we observed that the reaction solution gradually turned from a heterogeneous mixture to a single homogeneous phase. We consider that the appropriate acidity of the promoter is the key factor to activate the carbonyl group of aldehydes. Therefore, according to the pK_a value, various weak and strong carboxylic acids were tested. As shown in Table 1, generally, but not always, the stronger acids (pK_a ≤ 3.66) gave the product in moderate to high yields. When acids that are stronger than *p*-nitrobenzoic acid were used (entries 15−26), the allylation product was obtained in lower yield. It was observed that the allylation did not proceed smoothly when pK_a ≥ 4.2 (entries 1, 2, 4, and 5) except for *p*-hydroxylbenzoic acid (entry 3). Dicarboxylic acids such as *o*-phthalic acid (entry 20), malonic acid (entry 22), and maleic acid (entry 24) could promote the allylation to give good yield of the desired product; in contrast, *m*-phthalic acid (entry 12), *p*-phthalic acid (entry 13), and fumaric acid (entry 18) provided only trace amounts of product. L-(+)-Tartaric acid provided a racemic product in 65% yield (entry 15). In addition, the yields of allylation decreased successively from *p*-fluorobenzoic acid (51%, entry 7), to *p*-chlorobenzoic acid (40.5%, entry 8), to *p*-bromobenzoic acid (14%, entry 9) though their pK_a values are similar (4.14, 4.0, and 3.97, respectively). When the carboxyl group of *p*-nitrobenzoic acid was protected as an ester, the allylation did not take place (entry 27), which supports that the carboxyl group is critical. Reducing the amount of *p*-nitrobenzoic acid to 0.5 equiv produced only a 50% yield of **3a** (entry 28).

To demonstrate the relation between the pK_a value of the promoter, its solubility in acetonitrile,[11] and the yield of allylation product, we selected some representative data from Table 1 and list them in Figures 1 and 2. As

(5) Peter, P. I. D.; Moisan, L. *Angew. Chem., Int. Ed.* **2001**, *40*, 3726−3748.
(6) (a) Stewart, R. *The Proton: Application in Organic Chemistry*; Academic Press: Orlando, FL, 1985. (b) Pinko, P. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2026−2064.
(7) Yanagisawa, A.; Morodome, M.; Nakashima, H.; Yamamoto, H. *Synlett* **1997**, 1309−1311.
(8) Yanagisawa, A.; Nakashima, H.; Takayoshi, A. *Tetrahedron: Asymmetry* **2004**, *15*, 1909−1913.
(9) (a) Aspinall, H. C.; Greeves, N.; McIver, E. G. *Tetrahedron Lett.* **1998**, *39*, 9283−9286. (b) Aspinall, H. C.; Bissett, J. S.; Greeves, N.; Levin, D. *Tetrahedron Lett.* **2002**, *43*, 319−321.
(10) The values are cited from: (a) David R. L. *CRC Handbook of Chemistry and Physics*, 78th ed.; CRC Press: Boca Raton, FL, 1997. (b) Hand, C. W.; Blewitt, H. L. *Acid−Base Chemistry*; Macmillan Publishing Co.: New York, 1986.
(11) Two reviewers suggested that an additional factor of the allylation might be the solubility of the acid in acetonitrile.

TABLE 1. Effect of Various Types of Brønsted Acids as the Promoter on the Allylation of Benzaldehyde with Allyltributyltin[a]



1a 2a 3a

entry	Brønsted acid	pK_a(acid)[10]	solubility, mmol/L[b]	time, h	yield, %[c]
1	*p*-$NH_2C_6H_4CO_2H$ (**A1**)	4.92		23	trace
2	*c*-$C_5H_{11}CO_2H$ (**A2**)	>4.78		23	trace
3	*p*-$OHC_6H_4CO_2H$ (**A3**)	4.57	239	23	23
4	*p*-$CH_3OC_6H_4CO_2H$ (**A4**)	4.47	43	23	trace
5	*p*-$CH_3C_6H_4CO_2H$ (**A5**)	4.38	99	23	12
6	$PhCO_2H$ (**A6**)	4.2		73	31
7	*p*-$FC_6H_4CO_2H$ (**A7**)	4.14	150	23	51
8	*p*-$ClC_6H_4CO_2H$ (**A8**)	4.0	22	23	40.5
9	*p*-$BrC_6H_4CO_2H$ (**A9**)	3.97	7	23	14
10	*o*-$CH_3C_6H_4CO_2H$ (**A10**)	3.91		23	26
11	*p*-$CF_3C_6H_4CO_2H$ (**A11**)	3.66		23	88
12	*m*-$C_6H_4(CO_2H)_2$ (**A12**)	3.54	3	23	trace
13	*p*-$C_6H_4(CO_2H)_2$ (**A13**)	3.51	3	23	trace
14	*p*-$NO_2C_6H_4CO_2H$ (**A14**)	3.42	36	23	99
15	L-(+) tartaric acid (**A15**)	3.22		23	65[d]
16	α-furancarboxylic acid (**A16**)	3.17		23	82
17	citric acid (**A17**)	3.17		12	62
18	fumaric acid (**A18**)	3.02	2	23	trace
19	*o*-$OHC_6H_4CO_2H$ (**A19**)	2.98		23	69
20	*o*-$C_6H_4(CO_2H)_2$ (**A20**)	2.89	21	23	88
21	$ClCH_2CO_2H$ (**A21**)	2.85		23	63.5
22	malonic acid (**A22**)	2.83		23	72
23	*o*-$NO_2C_6H_4CO_2H$ (**A23**)	2.21		23	73
24	maleic acid (**A24**)	1.92	332	1	81
25	CF_3CO_2H (**A25**)	0.23		23	23
26	TsOH (**A26**)	−2.7		23	15
27	*p*-$NO_2C_6H_4CO_2Et$ (**A27**)			96	NR
28	*p*-$NO_2C_6H_4CO_2H$ (**A14**)	3.42		48	50[e]

[a] **1a/2a** = 1 equiv (0.5 mmol)/1.2 equiv (0.6 mmol). [b] The concentration of saturated solution of corresponding carboxylic acids in acetonitrile at 20 °C (see the Supporting Information). [c] Isolated yields. [d] $[\alpha]^{20}_D$ 0. [e] 0.5 equiv (0.25 mmol) of *p*-$NO_2C_6H_4CO_2H$ was used as a promoter.

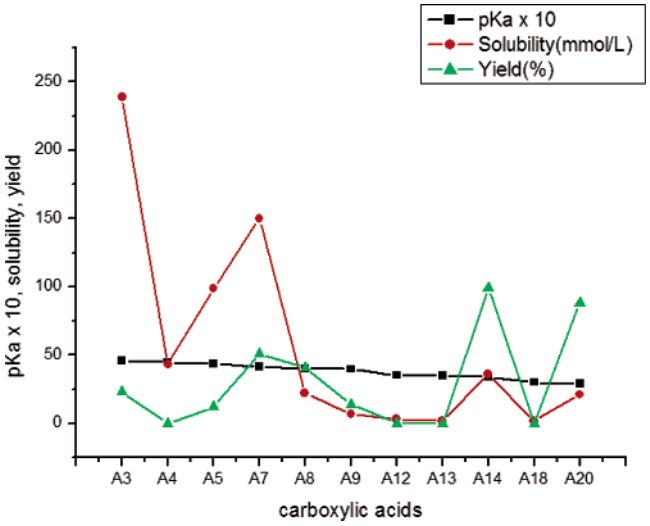


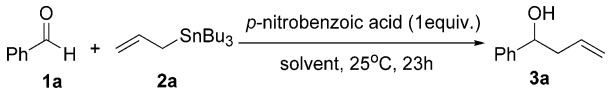
FIGURE 2. Plot of pK_a and solubility vs yields.

illustrated by Figure 1, the pK_a value plays a crucial role in this allylation. The allylation yields increased from trace to quantitative amount (**A14**), then decreased gradually to 23% (**A25**), along with the decrease of pK_a values from 4.92 to 0.23. These increased yields are rationalized on the basis of the stronger acid promoter being more inclined to forming a hydrogen bond with aldehyde. The decreased yield of allylation when pK_a < 3.42 is partly due to the fact that allyltributyltin decomposed under such strongly acidic conditions. In addition, as revealed in Figure 2, the concentration of the carboxylic acids in acetonitrile also affects the yields considerably. For example, carboxylic acids possessing similar pK_a values provide different allylation yields, which is in part due to the fact that they have differing solubilities in acetonitrile (**A7**, **A8**, and **A9**; **A12**, **A13**, and **A14**; **A18** and **A20**, Figure 2). Thus increased solubility of the acid generally leads to an increase in the yield of the allylation product.

Using *p*-nitrobenzoic acid as a promoter, we further examined the effect of solvents on this allylation. As shown in Table 2, the solvents exerted a great influence on this reaction. Only trace amounts of allylation product were produced in the nonpolar solvents and water. These results can be explained partly by the insolubility of *p*-nitrobenzoic acid in the nonpolar solvents and the insolubility of the reagents in H_2O. Low yields were obtained in DMF (40%, entry 9) and DMSO (19%, entry 10). In addition, both EtOH (entry 7) and mixed solvent[3g] ($EtOH/H_2O$ = 9/1, entry 8) provided good yields of product (88%), which indicates that this allylation can tolerate water. CH_3CN was found to be the best solvent (entry 1).

Under the optimized reaction conditions, the allylation of various aldehydes was investigated. The results are summarized in Table 3. Apparently, variation in the

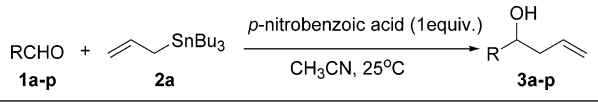
TABLE 2. Effect of Solvent on Allylation of Aldehydes Promoted by *p*-Nitrobenzoic Acid[a]



entry	solvent	isolated yield, %	entry	solvent	isolated yield, %
1	CH_3CN	99	7	EtOH	88
2	*n*-hexane	trace	8[b]	EtOH/ H_2O	88
3	toluene	trace	9	DMF	40
4	CH_2Cl_2	trace	10	DMSO	19
5	THF	trace	11	H_2O	trace
6	Et_2O	trace			

[a] **1a/2a** = 1 equiv (0.5 mmol)/1.2 equiv (0.6 mmol). [b] EtOH/ H_2O = 9/1 (v/v).

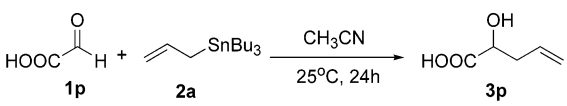
TABLE 3. The Allylation of Aldehydes Promoted by *p*-Nitrobenzoic Acid[a]



entry	RCHO[b]	time, h	product[c]	yield, %[d]
1	PhCHO	12	**3a**	92
2	*p*-$NO_2C_6H_4CHO$	5	**3b**	100
3	3-$MeOC_6H_4CHO$	10	**3c**	99
4	4- *n*-$BuOC_6H_4CHO$	23	**3d**	87
5	α-furaldehyde	22	**3e**	86
6	*p*-FC_6H_4CHO	12	**3f**	90
7	3,4,5-$F_3C_6H_2CHO$	10	**3g**	82
8	*p*-$CH_3CONHC_6H_4CHO$	23	**3h**	87
9	*p*-$MeOC_6H_4CHO$	40	**3i**	92
10	*p*-ClC_6H_4CHO	11	**3j**	99
11	2,4-$Cl_2C_6H_3CHO$	6	**3k**	98
12	*c*-$C_6H_{11}CHO$	10	***3l***	100
13	*n*-$C_8H_{17}CHO$	10	**3m**	99
14	*n*-$C_5H_{11}CHO$	12	**3n**	86
15	*trans*-PhCH=CHCHO	10	**3o**	87
16	$HO_2CCHO{\cdot}H_2O$	24	**3p**	74[e]
17	$PhCOCH_3$	71	NA	NR

[a] **1/2** = 1 equiv (0.5 mmol)/1.2 equiv (0.6 mmol). [b] All aldehydes had not been purified before use. [c] All new products were identified by ^1H NMR, IR, MS. [d] Isolated yield. [e] No *p*-nitrobenzoic acid was added.

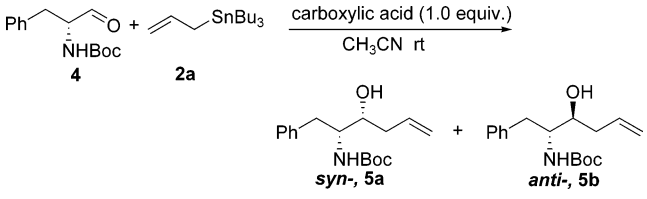
electronic nature of the substituents of aromatic aldehydes has little influence on the reaction. For example, the allylation of *p*-nitrobenzaldehyde (entry 2), *m*-anisaldehyde (entry 3), *p*-chlorobenzaldehyde (entry 10), and 2,4-dichlorobenzaldehyde (entry 11) gave almost quantitative yields. Other aromatic aldehydes afforded good to high yields. As for aliphatic aldehydes, the allylation promoted by *p*-nitrobenzoic acid also exhibited high efficiency (entries 12−14). This allylation method could not be extended to a ketone substrate (entry 17). It is noteworthy that glyoxylic acid could self-catalyze the allylation without adding any other promoter or catalyst in a yield of 74% (eq 1; Table 3, entry 16). The results



(1)

further display the generality of the allylation promoted by carboxylic acids. Finally, the promoter of *p*-nitrobenzoic acid can be recovered (more than 95%) simply by acidifying the reaction solution by HCl (2 M) (see the Experimental Section).

TABLE 4. Distereoselectivity of Allylation of Chiral α-Aminoaldehyde Promoted by Carboxylic Acids



entry	carboxylic acid	time, h	*syn*-**5a**/*anti*-**5b** (product)[a]	yield, %[b]
1	*p*-$NO_2C_6H_4CO_2H$	4.5	27/73	98
2	maleic acid	0.25	27/73	88
3	*o*-$C_6H_4(CO_2H)_2$	4	27/73	100
4	Salicylic acid	4	25/75	89

[a] Determined by ^1H NMR. [b] Combined isolated yield.

Next, the allylation of a chiral α-aminoaldehyde was tested. Boc-D-phenylalaninal[12] was chosen as a model substrate. As shown in Table 4, the allylation gave high to quantitative yields with moderate distereoselectivity (entry 1−4). The diastereoisomer of *anti*-**5b** was the major product. The results are similar to those allylations of chiral α-aminoaldehydes catalyzed by strong Lewis acids.[13]

Finally, the regioselectivity of the crotylation of aldehydes was also studied. As summarized in Table 5, when *p*-nitrobenzoic acid (pK_a = 3.42) was employed as a promoter, good regioselectivity was obtained (entry 1, α/γ = 13/87), which is the same with the result that γ-adduct is the major product provided by the traditional Lewis acids.[1] It is surprising that the α/γ ratio increases along with the increase of the promoter's acidity. *o*-Phthalic acid (pK_a = 2.89) provided no regioselectivity (entry 2, α/γ = 50/50), maleic acid (pK_a = 1.92) gave the α-adduct as the major product (entry 3, α/γ = 68/32), and further increased α-adduct selectivity was provided by trifluoroacetic acid (pK_a = 0.23) (entry 4, α/γ = 78/22). As far as we know, there are few examples of α-adduct selective crotylation of carbonyl compounds with allyltin reagents.[14] Such α-selective crotylation provides a synthetically useful route to linear homoallylic alcohols. Furthermore, quantitative yields were obtained in a short period of time with the excess of tributylallyltin and trifluoroacetic acid (1.5 equiv, respectively) (entries 5 and 6). Under the same reaction conditions, the crotylation of octanal provided a good selectivity of α-adduct (α/γ = 81/19, entry 7). So far, no better results have been obtained, although some attempts have been made to improve the regioselectivity.[15]

To verify the proposed allylation promoted by carboxylic acids (Scheme 1), the *p*-nitrobenzoic acid-mediated

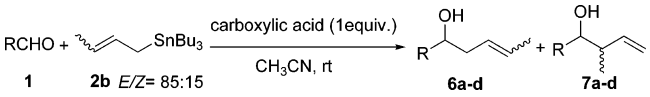
(12) Boc-D-phenylalaninal was used freshly after its preparation or it would racemize in a period of time.

(13) Vara Prasad, J. V. N.; Rich, D. H. *Tetrahedron Lett.* **1990**, *31*, 1803−1806.

(14) (a)Yamamoto, Y.; Yatagai, H.; Ishihara, Y.; Maeda, N.; Maruyama, K. *Tetrahedron* **1984**, *40*, 2239−2246. (b) Iqbal, J.; Joseph, S. P. *Tetrahedron Lett.* **1989**, *30*, 2421−2422.

(15) For example, inferior regioselectivities and lower yields are obtained when the protic solvent H_2O (48 h; α/γ = 61.5/38.5; yield 75%) and EtOH (8 h; α/γ = 69/31; yield 55%) are employed as solvents for the crotylation promoted by CF_3CO_2H.

TABLE 5. Regioselectivity of the Allylation of Aldehydes Promoted by Carboxylic Acid[a]



1 2b *E/Z*= 85:15 6a-d 7a-d

entry	aldehyde	carboxylic acid	time, h	products[b] **6** (*E*:*Z*)/ **7** (syn:anti)	yield,[c] %
1	PhCHO	*p*-$NO_2C_6H_4CO_2H$	96	**6a** (12:88)/**7a** (60:40) (13/87)	53
2	PhCHO	*o*-$C_6H_4(CO_2H)_2$	96	**6a** (1:99)/**7a** (60:40) (50/50)	79
3	PhCHO	maleic acid	1.5	**6a** (1:99)/**7a** (58:42) (68/32)	84
4	PhCHO	CF_3CO_2H	1.5	**6a** (1:99)/**7a** (43:57) (78/22)	72
5	*p*-$NO_2C_6H_4CHO$	CF_3CO_2H	0.5	**6b** (2:98)/**7b** (39:61) (76/24)	99[d]
6	*m*-$CH_3OC_6H_4CHO$	CF_3CO_2H	0.5	**6c** (1:99)/**7c** (50:50) (75/25)	99[d]
7	*n*-$C_7H_{15}CHO$	CF_3CO_2H	1.0	**6d** (−:−)/**7d** (56:44) (81/19)	99[d]

[a] **1/2** = 1 equiv (0.5 mmol)/1.2 equiv (0.6 mmol); **2b** was prepared from Bu_3SnLi and crotyl chloride according to the literature[16a] and *E*/*Z* of **2b** was determined by GC and ^{13}C NMR.[16b] [b] Determined by ^1H NMR.[17] [c] Isolated combined yield. [d] **1/2**/carboxylic acid = 1 equiv (0.2 mmol)/1.5 equiv (0.3 mmol)/1.5 equiv (0.3 mmol).

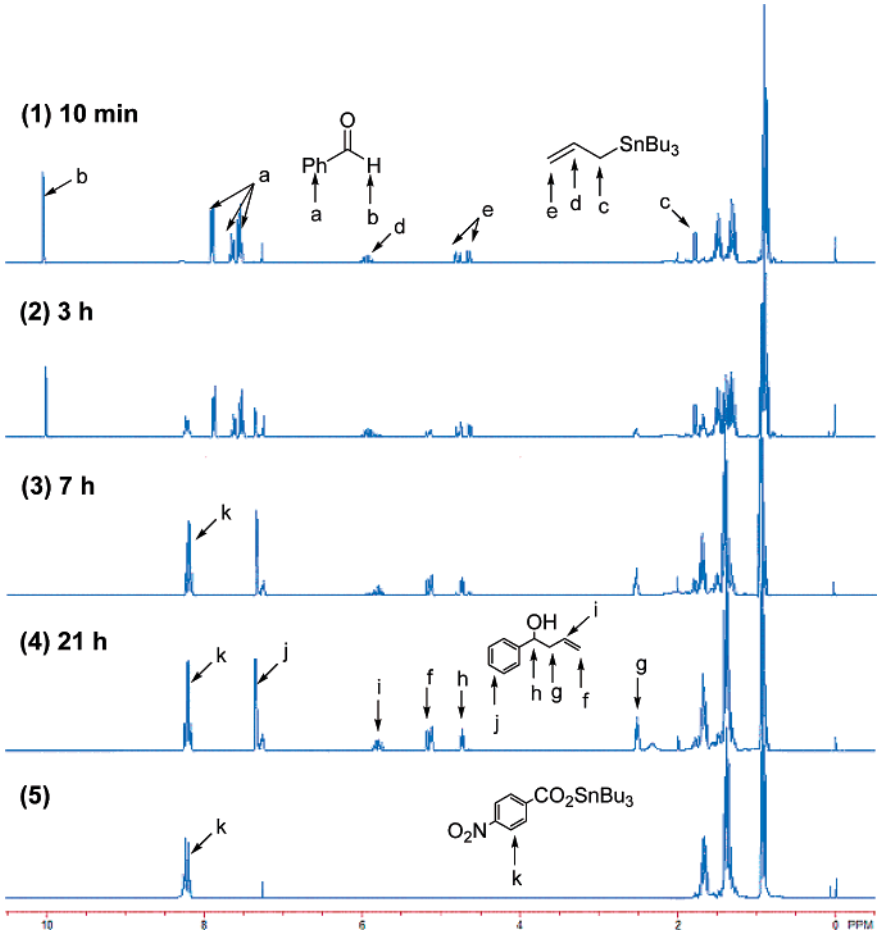
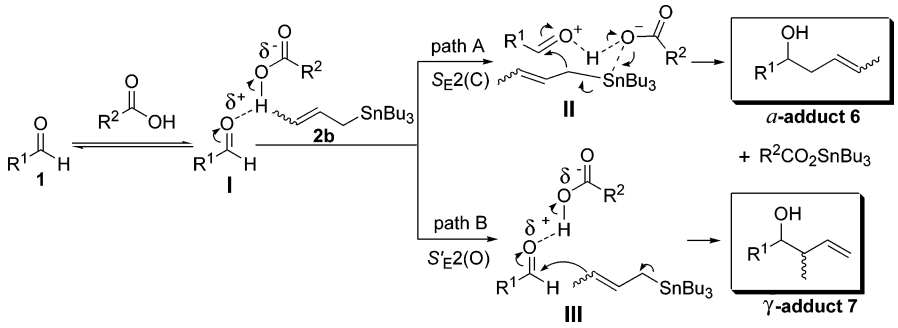


FIGURE 3. ^1H NMR study on the allylation of benzaldehyde promoted by *p*-nitrobenzoic acid (in $CDCl_3$ after removing acetonitrile under reduced pressure).

allylation of benzaldehyde was monitored by ^1H NMR after removing acetonitrile under reduced pressure at various intervals. The spectra were taken at 10 min and 3, 7, and 21 h intervals, respectively (see Figure 3). It was obvious that the allylation proceeded rapidly to produce the homoallylic alcohol within 3 h (as indicated by the appearance of the peaks at about δ 2.5, 5.1, and 7.3 ppm; g, f, and j in Figure 3, respectively), and the benzaldehyde completely consumed within 7 h (as indicated by the disappearance of the peak at about δ 10.0

SCHEME 2. Proposed Mechanism for the Regioselective Allylation Promoted by Carboxylic Acids



ppm; b in Figure 3). At the same time, allyltributyltin disappeared gradually (as indicated by the disappearance of the peaks at about δ 1.76, 4.6, and 4.7 ppm; c and e in Figure 3, respectively). During this reaction, it was observed that the heterogeneous reaction mixture (as revealed in Table 1, *p*-nitrobenzoic acid is only slightly soluble in CH_3CN) gradually became homogeneous. Correspondingly, as illustrated in Figure 3, new peaks at about 8.2 ppm appeared gradually indicating the formation of tributyltin ester of *p*-nitrobenzoic acid (*p*-nitrobenzoic acid is insoluble in $CDCl_3$, as shown in Figure 3, (1)), which is confirmed by comparison with the ^{1}H NMR spectrum of the tin ester prepared independently[18] (Figure 3, (5)).

At the same time, we performed another experiment in which the allyltributyltin was stirred in the presence of *p*-nitrobenzoic acid for about 21 h and monitored by ^{1}H NMR. Only trace decomposition of the allyltributyltin was observed. To further disclose the mechanism of the allylation, the mixture of *o*-phthalic acid and allyltributyltin in acetonitrile was stirred and monitored by ^{1}H NMR as above. It was found that allyltributyltin had decomposed completely within 230 min. In addition, in the allylation promoted by maleic acid, allyltributyltin disappeared within 1 h according to TLC. These facts support the observation that the acidity of the carboxylic acid plays an important role in weakening the C−Sn bond, and this action makes the allyltributyltin more nucleophilic and at the same time more susceptible to decomposition.

At this time, the exact process of the regioselective crotylation promoted by carboxylic acids is not very clear. Based on the results of experiments, a possible mechanism is proposed. First, the aldehyde (**1**) is activated by the carboxylic acid through hydrogen bonding. Then, in general, the resulting electrophile intermediate **I** could attack **2b** on C_1 (adjoining tin atom) or C_3 through two pathways, namely S_E2 and S'_E2, respectively.[19] It is known that strong Lewis acids mediating crotylation proceed by a S'_E2 (open) mechanism to afford the γ-adduct (**7**) exclusively.[1,20] Therefore, it may be understood that the carboxylic acids, as Lewis acids, could promote the crotylation through a S'_E2 mechanism predominantly (**III**, path B, Scheme 2). This is observed in the case of *p*-nitrobenzoic acid and the low distereoselectivity (syn/anti) can be ascribed to its weak action toward the aldehydes through hydrogen bonding (entry 1, Table 5). On the other hand, the increasing acidity of carboxylic acids was accompanied by an increase in the donor ability of the carboxylate anion. It might facilitate the coordination to the Sn (the C−Sn bond fission under the nucleophilic attack of various carboxylic acids may throw light on this).[21] Therefore, **2b** should be attacked by **I** on C_1 involving a six-centered cyclic transition state (S_E2, closed) other than on C_3 involving eight-centered ones (S'_E2, closed) (**II**, path A, Scheme 2). This is observed in the cases of maleic acid and trifluoroacetic acid, in which α-adducts are obtained as the major products (entries 3−7, Table 5). In addition, experiments[22] proved that it is impossible to produce the mixture of adducts by the rearrangement[23] between adducts **4** and **5** under these reaction conditions.

Conclusion

A novel, general, and practical method of allylation of aldehydes promoted by carboxylic acids under mild conditions has been developed. Under the promotion of *p*-nitrobenzoic acid, the allylation of various aldehydes with allytributyltin proceeded smoothly to provide high to quantitative yields of the homoallylic alcohols. *p*-Nitrobenzoic acid could be recovered by working up with HCl (2 M). The regioselectivity of the crotylation of aldehydes was also studied. The α-adduct could be

(16) (a) Hoffmann, R. W.; Feussner, G.; Zeiss, H.-J.; Schulz, S. *J. Organomet. Chem.* **1980**, *18*, 321−329. (b) Alessandro, G.; Daniele, M.; Valerio, P.; Giuseppe, T. *J. Organomet. Chem.* **1981**, *204*, 191−196.

(17) Nokami, J.; Yoshizane, K.; Matsuura, H.; Sumida, S. *J. Am. Chem. Soc.* **1998**, *120*, 6609−6610.

(18) Max, F.; David, G.; Daniel, W.; Albert, Z. *J. Organomet. Chem.* **1967**, *9*, 83−88 (tributyltin ester was prepared according to a similar procedure in this literature).

(19) (a) Roberts, R. M. G. *J. Organomet. Chem.* **1970**, *24*, 675−685. (b) Roberts, R. M. G. *J. Organomet. Chem.* **1969**, *18*, 307−319. (c) Kuivila, H. G.; Verdone, J. A. *Tetrahedron Lett.* **1964**, *2*, 119−123. (d) Verdone, J. A.; Mangravite, J. A.; Scarpa, N. M. *J. Am. Chem. Soc.* **1975**, *97*, 843−849.

(20) Denmark, S. E.; Shinzo, H. *J. Org. Chem.* **1994**, *59*, 5133−5135.

(21) (a) Rappoport, Z. *The Chemistry of Organic Germanium*, *Tin and Lead*; Wiley: New York, 2002; Vol. 2, Part 2, p 963. (b) If benzaldehyde was added after the mixture of crotyltributyltin and maleic acid in acetonitrile was stirred for 3 h, no desired product was obtained. TLC indicated that crotyltributyltin was decomposed.

(22) (a) The mixture of the pure compound **7a** (1.0 equiv), benzaldehyde (1.0 equiv), and trifluoroacetic acid (1.0 equiv) was stirred for 1.0 h in acetonitrile. And no **6a** was produced. (b) No **6a** was produced after the mixture of the pure compound **7a** (1.0 equiv), benzaldehyde (0.5 equiv), $CF_3CO_2SnBu_3$ (0.5 equiv), and trifluoroacetic acid (0.5 equiv) was stirred for 1.0 h in acetonitrile. (c) The ^{1}H NMR study of crotylation of benzaldehyde shows that adducts **6** and **7** are produced simultaneously.

(23) (a) Cheng, H.-S.; Loh, T.-P. *J. Am. Chem. Soc.* **2003**, *125*, 4990−4991. (b) Hussain, I.; Komasaka, T.; Ohga, M.; Nokami, J. *Synlett* **2002**, 640−642. (c) Nokami, J.; Anthony, L.; Sumida, S. *Chem. Eur. J.* **2000**, *6*, 2909−2913. (d) Nokami, J.; Nomiyama, K.; Matsuda, S.; Imai, N.; Kataoka, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 1273−1276.

obtained as the major product in moderate to good yields under the promotion of maleic acid or trifluoroacetic acid. A possible mechanism for this allylation was also discussed.

Experimental Section

Typical Procedure for the Allylation of Aldehydes. To a suspension of *p*-nitrobenzoic acid (84 mg, 0.5 mmol) in acetonitrile (1.5 mL) were added successively benzaldehyde (53 mg, 0.5 mmol) and allyltributyltin (198 mg, 0.6 mmol) at room temperature. After being stirred about 3 h, the solution turned clear. The reaction was quenched with HCl (2 M, 2 mL) after completion (23 h), then filtered and washed with CH_2Cl_2 (2×5 mL) to recover *p*-nitrobenzoic acid (80 mg, 95%). The filtrate (aqueous layer) was extracted with CH_2Cl_2 (3×5 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to furnish the crude product, which was purified by silica gel chromatography (typical eluent: petroleum ether/EtOAc 14:1 (v/v)) to afford **3a** (73 mg, 99%).

1-(4-*n*-Butoxyphenyl)-3-buten-1-ol (3d): R_f 0.81(petroleum ether/EtOAc 7:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, 2H, J = 8.3 Hz), 6.86 (d, 2H, J = 8.5 Hz), 5.84−5.75 (m, 1H), 5.18−5.11 (m, 2H), 4.66 (t, 1H, J = 6.4 Hz), 3.93 (t, 2H, J = 6.3 Hz), 2.47 (t, 2H, J = 6.2, 6.8 Hz), 1.97 (s, 1H), 1.81−1.72 (m, 2H), 1.53−1.45 (m, 2H), 0.95 (t, 3H, J = 7.8, 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.7, 135.9, 134.6, 127.0, 118.0, 114.4, 73.0, 67.8, 43.6, 31.3, 19.2, 13.7; IR (KBr, film) υ 3415, 3075, 2959, 2873, 1640, 1612, 1512, 1240 cm^{-1}; MS (70 eV, EI) 220 (M^+), 179, 123, 95, 77, 41. Anal. Calcd for $C_{14}H_{20}O_2$ (220.31): C 76.33; H 9.15. Found: C 75.94; H 9.31.

1-(3,4,5-Trifluorophenyl)-3-buten-1-ol (3g): R_f 0.38 (petroleum ether/EtOAc 7:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.02 (t, 2H, J = 7.5 Hz), 5.83−5.70 (m, 1H), 5.21−5.15 (m, 2H), 4.71−4.68 (m, 1H), 2.50−2.39 (m, 2H), 2.13 (s, 1H); IR (KBr, film) υ 3390, 3082, 2915, 1642, 1622, 1531, 1038 cm^{-1}; MS (70 eV, EI) 202 (M^+), 161, 133, 113, 81. Anal. Calcd for $C_{10}H_9F_3O$ (202.17): C 59.41, H 4.49. Found: C 59.91, H 4.88.

1-(4-Acetamidophenyl)-3-buten-1-ol (3h): R_f 0.25 (petroleum ether/EtOAc 1:2) mp 121.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (d, 2H, J = 8.8 Hz), 7.39 (s, 1H), 7.27 (d, 2H, J = 8.5 Hz), 5.83−5.74 (m, 1H), 5.11 (t, 2H, J = 9.2, 5.6 Hz), 4.68 (t, 1H, J = 4.3, 5.6 Hz), 2.51−2.46 (m, 2H), 2.16 (s, 3H); IR (KBr, film) υ 3292, 3125, 3069, 2900, 1662, 1610, 1557, 1324 cm^{-1}; MS (70 eV, EI) 205 (M^+), 164, 122, 94, 77, 43. Anal. Calcd for $C_{12}H_{15}NO_2$ (205.25): C 70.22, H 7.37, N 6.82. Found: C 69.86, H 7.40, N 6.68.

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Supporting Information Available: General methods, ^{1}H NMR, IR, MS data, and spectra of other compounds from **3a** to **7c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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