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Synthesis of homoallylic amines and acylhydrazides by tin powder-promoted multicomponent one-pot allylation reactions

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An efficient process for the synthesis of homoallylic amines and N'-homoallylic hydrazides is developed from the one-pot reaction of carbonyl compounds, amines or N-acylhydrazines, allyllic bromide and tin powder using water as solvent. N-Acylhydrazines are found to be more reactive than amines in these processes. They can react not only with aldehydes but also with ketones to give the corresponding N'-homoallylic hydrazides. Copyright © 2016 John Wiley & Sons, Ltd.

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Keywords: tin powder; multicomponent reaction; homoallylic amines; homoallylic hydrazides; allylation

Introduction

Allylation of carbonyl and imino groups is one of the most convenient and efficient methods for synthesis of homoallylic compounds,^[1-8] which are versatile building blocks in the preparation of many biologically active molecules and natural products.^[9-21] As reported in the literature, allylic organometallics such as allylic Mg,^[22,23] Zn,^[24,25] In,^[26-29] Sn,^[30-38] Si,^[39,40] B^[25,41] and Sm^[42,43] have been intensively investigated in allylation reactions. Among these organometallics, allylic stannanes have been widely used because of their easy availability, air and moisture stability, tolerance to functional groups and high selectivity.^[44-46] However, most stannanes are toxic.^[47,48] Furthermore, only the allyl group in allylic stannanes is delivered into the product molecules and the other residues are usually discarded as waste after the reactions. In 1981, Mukaiyama and Harada^[49] reported that combination of tin and allylic bromide or iodide could replace allylic stannanes in allylation of aldehydes or ketones to give the corresponding allylic alcohols in organic solvents, but the yield was less than 50%. Subsequently, Nokami and co-workers reported that addition of water to the reaction system could accelerate the reaction and increase the product yields up to 75%.^[50] This is unique considering strictly anhydrous operations compared to other traditional organometallic reagents. Subsequently, allylations mediated by metallic tin were investigated in the presence of water or just using water as solvent, but most studies focused on allylation of aldehydes.^[31,51–55] Some other substrates such as nitroalkenes,^[11] enol ethers^[56] and aldoximes^[57] were also allylated using allylic bromide and metallic tin in water to give homoallylic alcohols.

In view of various advantages of tin-promoted reactions, we are interested in developing some new reactions mediated by metallic tin, especially reactions in water because water is considered to be the cleanest solvent available to synthetic chemists.^[58–60] In our previous investigation, we found tin powder could promote one-

pot allylation reactions of aldehydes, amines and allylic bromide in 1,4-dioxane to give homoallylic amines in good yields.^[61] In our on-going studies, we found that acylhydrazines could replace amines in a similar reaction using water as solvent. In particular, acylhydrazines could react not only with aldehydes but also with less reactive ketones to afford *N'*-homoallylic hydrazides, which are relatively new scaffolds found in a wide variety of biologically active molecules,^[62–64] and also show potential applications in material science (Scheme 1).^[65–69] Herein, we report our results concerning these one-pot allylation reactions in water.

Results and discussion

Initially, the one-pot allylation reaction of aldehydes and amines was investigated in water. Thus, aniline (**1a**; 1 equiv.), benzaldehyde (**2a**; 1 equiv.), allylic bromide (**3**; 1.5 equiv.) and tin (2.5 equiv.) were mixed in water, and stirred at room temperature for 24 h. After work-up, the desired product **4a** is obtained in 47% yield and by-product **5a**, which is formed from double allylation of aniline, is also obtained in 20% yield (Table 1, entry 6). In order to increase the yield of **4a** and improve chemoselectivity, the reaction conditions were examined next. The results are summarized in Table 1. It is found that the molar ratio of substrates has great influence on the yield and selectivity. When the ratio of aniline, benzaldehyde and allylic bromide is fixed at 1/1/1, the yield of **4a** increases with

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Scheme 1. One-pot allylation for the synthesis of homoallylic amines and hydrazides.

increasing amount of metal tin (Table 1, entries 1–5), but stops increasing when the amount of tin is above 2.5 equiv. (Table 1, entries 4 and 5). The amount of allylic bromide also affects the yield of **4a**, which increases with increasing allylic bromide. A reasonable amount of allylic bromide is found to be 2.0 equiv. (Table 1, entries 6–8). It is worth noticing that **5a** is always formed in a yield of around 20% in every experiment when the ratio of aniline and benzaldehyde is fixed at 1/1 (Table 1, entries 3–8). Thus, the ratio of aniline and benzaldehyde was checked again. With the proportion of benzaldehyde increasing, the yield of **4a** increases quickly, and **5a** cannot be detected (Table 1, entries 9–11). Finally, the best molar ratio of **1a/2a/3**/Sn was determined to be 1.0/1.5/2.0/ 2.5 (Table 1, entry 10).

Under the optimized reaction conditions, we investigated the generality of the allylation reaction with respect to a range of amines and aldehydes. The results are collected in Table 2. Firstly, different amines were reacted with benzaldehyde. It is found that all the aromatic amines can react with benzaldehyde smoothly to give the desired products **4** (Table 2, entries 1–7), but aliphatic amines such as *n*-BuNH₂ and *t*-BuNH₂ cannot produce products **4** (Table 2, entries 21 and 22). Aromatic amines with electron-withdrawing groups produce the products in slightly higher yields than with electron-donating groups. This can be

 $\label{eq:table_$

$\bigcup_{h=1}^{NH_2} + \bigcup_{a}^{CHO} \xrightarrow{a}_{Sn, H_2O, r.t.}^{Br} Ph \xrightarrow{NHPh} + \bigvee_{a}^{Ph}$

Entry	Mole ratio of 1a/2a/3 /Sn	Time (h)	Yield (%) ^b		
			4a	5a	
1	1.0/1.0/1.0/1.0	24	0	0	
2	1.0/1.0/1.0/1.5	24	Trace	Trace	
3	1.0/1.0/1.0/2.0	24	13	15	
4	1.0/1.0/1.0/2.5	24	42	12	
5	1.0/1.0/1.0/3.0	24	38	17	
6	1.0/1.0/1.5/2.5	24	47	20	
7	1.0/1.0/2.0/2.5	24	53	18	
8	1.0/1.0/2.5/2.5	24	52	21	
9	1.0/1.2/2.0/2.5	12	74	Trace	
10	1.0/1.5/2.0/2.5	12	83	Trace	
11	1.0/2.0/2.0/2.5	12	79	Trace	

^aReaction conditions: aniline (**1a**, 1.0 mmol), benzaldehyde (**2a**, 1.0–2.0 mmol), allylic bromide (**3**, 1.0–2.5 mmol), tin (1.0–3.0 mmol), H₂O (4.0 ml). ^bIsolated yield. **Table 2.** Reaction of various amines and various aldehydes for the onepot synthesis of homoallylic amines^a

$$R_2NH_2 + R_1CHO \xrightarrow{3} R_1 + R_1CHO \xrightarrow{3} R_1 + R_1 + R_2$$

Entry	R ₁	R ₂	Yield (%) ^b		
			4	5	
1	Ph	Ph	4a (83)	5a (trace)	
2	Ph	p-MeC ₆ H ₄	4b (54)	5b (16)	
3	Ph	o-MeC ₆ H ₄	4c (65)	5c (trace)	
4	Ph	Mes	4d (70)	5d (trace)	
5	Ph	p-MeOC ₆ H ₄	4e (45)	5e (18)	
6	Ph	p-BrC ₆ H ₄	4f (74)	5f (trace)	
7	Ph	p-ClC ₆ H ₄	4 g (79)	5 g (trace)	
8	p-MeOC ₆ H ₄	Ph	4 h 82)	5a (12)	
9	o-CIC ₆ H ₄	Ph	4i (79)	5a (trace)	
10	o-FC ₆ H ₄	Ph	4j (86)	5a (trace)	
11	2-Thienyl	Ph	4 k (78)	5a (trace)	
12	2-Furyl	Ph	4 I (75)	5a (trace)	
13	p-MeOC ₆ H ₄	o-MeC ₆ H ₄	4 m (72)	5c (trace)	
14	p-MeOC ₆ H ₄	p-MeC ₆ H ₄	4n (61)	5b (10)	
15	p-MeOC ₆ H ₄	p-CIC ₆ H ₄	4o (78)	5 g (trace)	
16	p-MeOC ₆ H ₄	p-BrC ₆ H ₄	4p (79)	5f (trace)	
17	o-FC ₆ H ₄	o-MeC ₆ H ₄	4q (82)	5c (trace)	
18	o-FC ₆ H ₄	p-MeC ₆ H ₄	4r (65)	5b (trace)	
19	o-FC ₆ H ₄	p-ClC ₆ H ₄	4 s (87)	5 g (trace)	
20	o-FC ₆ H ₄	p-BrC ₆ H ₄	4 t (90)	5f (trace)	
21	Ph	<i>n</i> -Bu	4u (0) ^c	5 h (trace)	
22	Ph	<i>t</i> -Bu	4v (0)	5i (trace)	
23	<i>n</i> -Pr	Ph	4w (0)	5a (68)	

^aReaction conditions: amines (**1**, 1.0 mmol), aldehydes (**2**, 1.5 mmol), allylic bromide (**3**, 2.0 mmol), tin (2.5 mmol), H₂O (4.0 ml). ^bIsolated yield.

^cHomoallylic alcohol (hept-1-en-4-ol) was obtained in 47% yield.

explained in terms of the inductive effect. We believe that the reaction starts with the formation of imines, which then react with allylic tin species formed in situ to give the products. As shown in Fig. 1, electron-withdrawing groups on aromatic amines can make the in situ generated imines more electrophilic, and thus accelerate the reaction to form the products in higher yields. However, when the inductive effect of the substituents on aromatic amines is the same, such as electron-donating groups, the amines with ortho-substituents afford products in slightly higher yield than with para-substituents (Table 2, entries 2 and 3). This may be due to the steric hindrance around the amine group. The ortho-substituents of aromatic amines give more steric hindrance around the amine group than the para-substituents. This steric hindrance slows down the direct allylation of amine groups, which leads to the formation of 5. For instance, 5b is obtained in 16% yield when p-methylaniline is used (Table 2, entry 2). However, when o-methylaniline or more hindered mesidine is used, 5c or 5d cannot be obtained (Table 2, entries 3 and 4).

Next, various aldehydes were reacted with aniline to test the scope of these substrates (Table 2, entries 8–12). The results show electron-donating or electron-withdrawing groups on phenyl rings



Figure 1. Effects of substituents of arylamines on electrophilicity of imines formed *in situ*.

of aromatic aldehydes have little influence on the yields of the products **4**. Investigation of synergistic effects of substituents on both aromatic amines and aromatic aldehydes reveals that yields of **4** are higher when the substituents on both amines and aldehydes are electron-withdrawing groups. In contrast, the yield is lower when the substituents on both amines and aldehydes are electron-donating groups (Table 2, entries 13–20). When an aliphatic aldehyde such as butyraldehyde is used, the desired product **4w** does not form, but **5a** is obtained in 68% yield (Table 2, entry 23).

In order to further investigate the generality of the substrate scope, aldehydes were replaced by ketones in the reaction. For instance, cyclohexanone (**6a**) was reacted with aniline, allylic bromide and tin powder under the reaction conditions mentioned above, but there is no desired product **7** formed at room temperature after 24 h. After raising the reaction temperature to 60 °C, only allylic alcohol **8** is obtained in 63% yield (Scheme 2). The reason is that the corresponding ketimine cannot be formed during the reaction because there is no ketimine detected even after aniline and cyclohexanone were allowed to react under the same reaction conditions for 12 h.

N-Acylhydrazones, which serve as storable and stable imine equivalents, have attracted increasing attention in organic synthesis in the last decade.^[70] Some of their reactions can even proceed smoothly in water.^[71,72] Thus, we aimed to determine if the amines in the above reaction could be replaced by N-acylhydrazines to afford the corresponding N'-homoallylic hydrazides. The investigation started by stirring benzaldehyde, benzoylhydrazine (9a), allylic bromide and tin powder in water at room temperature. After 56 hours, N'-homoallylic hydrazide **10a** is not detected and only the N-acylhydrazone 11 is obtained in 62% yield (Table 3, entry 1). Careful examination shows that addition of 10 mol% of benzoic acid can catalyze the formation of 10a in 12% yield (Table 3, entry 2). Encouraged by this result, other Brønsted acids were tested (Table 3, entries 1–7), and trifluoromethanesulfonic acid (TfOH) is found to be the best acid. For example, the yield of **10a** is improved to 33% with 11 formed in 35% yield at the same time if 10 mol% of TfOH is used (Table 3, entry 5). The influence of the loading of TfOH was then examined (Table 3, entries 8-11). It is found that 20 mol% of TfOH gives the best yield. If the loading of TfOH is above 20 mol%, the yield does not improve. Also, a study of the mole ratio of substrates



Scheme 2. One-pot allylation of cyclohexanone.

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Table 3. Optimization of reaction conditions for one-pot synthesis of N'-homoallylic hydrazides^a

$$\begin{array}{ccc} PhCHO & + & \overbrace{\bigcup}^{O_{i}} & \stackrel{NHNH_2}{\underbrace{3}} & \stackrel{Ph}{\underbrace{3}} & \stackrel{Ph}{\underbrace{N}_{i}} & \stackrel{O}{\underbrace{N}_{i}} & \stackrel{Ph}{\underbrace{N}_{i}} & \stackrel{Ph}{\underbrace{N}_{i}} \\ \hline 2a & ga & 10a & 11 \end{array}$$

Entry Mole ratio		Catalyst	Amount of	Т	Time	Yield (%) ^b	
	of 2a/9a/3 / Sn		catalyst (mol%)	(°C)	(h)	10a	11
1	1/1.5/2/2.5	_	—	r.t.	56	0	62
2	1/1.5/2/2.5	PhCOOH	10	r.t.	36	12	37
3	1/1.5/2/2.5	TsOH	10	r.t.	27	29	24
4	1/1.5/2/2.5	TFA	10	r.t.	32	11	33
5	1/1.5/2/2.5	TfOH	10	r.t.	27	33	35
6	1/1.5/2/2.5	HCI	10	r.t.	36	10	20
7	1/1.5/2/2.5	H_2SO_4	10	r.t.	36	16	23
8	1/1.5/2/2.5	TfOH	5	r.t.	52	26	30
9	1/1.5/2/2.5	TfOH	15	r.t.	35	51	24
10	1/1.5/2/2.5	TfOH	20	r.t.	27	59	20
11	1/1.5/2/2.5	TfOH	25	r.t.	27	58	19
12	1/1.5/2/2	TfOH	20	r.t.	27	51	25
13	1/1.5/2/3	TfOH	20	r.t.	27	60	22
14	1/1.5/2/3.5	TfOH	20	r.t.	27	58	21
15	1/1.5/3/2.5	TfOH	20	r.t.	27	63	17
16	1/1.5/4/2.5	TfOH	20	r.t.	27	70	10
17	1/1.5/4.5/2.5	TfOH	20	r.t.	27	68	12
18	1/1.5/5/2.5	TfOH	20	r.t.	27	68	13
19	1/1.5/4/2.5	TfOH	20	45	27	77	8
20	1/1.5/4/2.5	TfOH	20	65	27	83	Trace
21	1/1.5/4/2.5	TfOH	20	85	27	77	Trace
22	1/1.5/4/2.5	TfOH	20	Reflux	27	35	0
^a Reaction conditions: benzaldehyde (2a , 1.0 mmol), benzoylhydrazine (9a , 1.5 mmol), allylic bromide (3 , 2.0–5 mmol), tin (2.0–3.5 mmol), TfOH (5–25 mol%), H ₂ O (4.0 ml).							

^blsolated yield.

reveals that the amount of allylic bromide has a great influence on the product yield. When the ratio of **2a/9a**/Sn is fixed at 1/1.5/2.5, the yield of **10a** increases with increasing allylic bromide, but 4 equiv. is a reasonable amount (Table 3, entries 15–18). The reason for the use of excess allylic bromide is that part of it would be hydrolyzed during the reaction. Finally, optimal reaction temperature was also explored with the results showing that the yield of **10a** increases with increasing reaction temperature. The best temperature is found to be around 65 °C. If the temperature is above 65 °C, the yield of **10a** decreases; in particular, when the reaction is performed at reflux, the yield of **10a** decreases markedly to 35% (Table 3, entry 22). This might be explained by the acceleration of hydrolyzation of allylic bromide at high temperature during the reaction.

Table 4 summarizes the results of expanding the range of various aldehydes and *N*-acylhydrazines under the above optimized reaction conditions. Most of the tested aromatic and aliphatic aldehydes can react with various *N*-acylhydrazines in the presence of allylic bromide and tin to afford the corresponding *N'*-homoallylic hydrazides in good yields. As for *N*-acylhydrazines, all of the aromatic ones can react smoothly with various aldehydes

Table 4. Reaction of various aldehydes and various acylhydrazines for one-pot synthesis of N'-homoallylic hydrazides ^a						
$\begin{array}{c} 0\\ R_1CHO + R_4 & NHNH_2\\ 2 & 9 \\ \end{array} \begin{array}{c} 3\\ R_1OH & (20 \text{ moR6})\\ R_1OH & (20 \text{ moR6})\\ R_1 & R_1 \\ \end{array} \begin{array}{c} R_4 & O\\ HN, NH\\ R_1 & HN\\ R_1 & HN\\ \end{array}$						
Entry	R ₁	R ₄	Time (h)	Product	Yield (%) ^b	
1	Ph	Ph	27	10a	83	
2	Ph	p-MeOC ₆ H ₄	12	10b	82	
3	Ph	m-MeC ₆ H ₄	13	10c	81	
4	Ph	p-MeC ₆ H ₄	12	10d	89	
5	Ph	p-FC ₆ H ₄	12	10e	79	
6	Ph	p-CIC ₆ H ₄	12	10f	64	
7	Ph	2-Furyl	36	10 g	48	
8	Ph	Me	36	_	0	
9	p-MeOC ₆ H ₄	Ph	12	10 h	75	
10	p-MeC ₆ H ₄	Ph	9	10i	79	
11	p-ClC ₆ H ₄	Ph	9	10j	85	
12	o-CIC ₆ H ₄	Ph	12	10 k	71	
13	m-ClC ₆ H ₄	Ph	17	10 l	65	
14	3-Thienyl	Ph	24	10 m	60	
15	<i>n</i> -Pr	Ph	16	10n	72	
16	Bn	Ph	11	10o	79	
17	Cinnamyl	Ph	16	10p	83	
18	p-MeC ₆ H ₄	p-MeC ₆ H ₄	24	10q	53	
19	p-ClC ₆ H ₄	p-MeC ₆ H ₄	18	10r	75	
20	p-MeC ₆ H ₄	p-ClC ₆ H ₄	24	10s	65	
21	p-ClC ₆ H ₄	p-ClC ₆ H ₄	18	10 t	70	
22	3-Thienyl	2-Furyl	24	10u	51	
23	<i>n</i> -Pr	p-ClC ₆ H ₄	15	10v	78	
24	Cinnamyl	p-MeC ₆ H ₄	24	10w	69	
^a Reaction conditions: aldehydes (2 , 0.5 mmol), acvlhvdrizines (9 ,						

^aReaction conditions: aldehydes (**2**, 0.5 mmol), acylhydrizines (**9**, 0.75 mmol), allylic bromide (**3**, 2.0 mmol), tin (1.25 mmol), H₂O (4.0 ml). ^bIsolated yield.

to afford the products in good to excellent yields. However, aliphatic *N*-acylhydrazines such as acetohydrazide do not give the product (Table 4, entry 8).

Although cyclohexanone does not react with aniline in the presence of allylic bromide and tin in water (Scheme 2), we still wondered if N-acylhydrazines could replace amines to react with ketones to produce the corresponding N'-homoallylic hydrazides in water. With this idea in mind, cyclohexanone and benzoylhydrazine were tentatively stirred with allylic bromide and tin in water at 65 °C for 14 h. To our delight, the desired product 12a is readily obtained. Afterwards, different kinds of ketones were reacted with various aromatic N-acylhydrazines in the presence of allylic bromide and tin in water, and the results are summarized in Table 5. Cyclohexanone and cyclopentanone can react with various N-acylhydrazines to give the products 12 in good yields (Table 5, entries 1-4 and 11-13). However, when the α -position of cyclohexanone has a substituent, the yield of the corresponding product is lower (Table 5, entry 5). Cyclobutanone and cycloheptanone afford products in lower yields (Table 5, entries 8-10 and 14), but cyclooctanone

$$\begin{array}{c} 0\\ R_1 & R_3 & + \end{array} \begin{array}{c} 0\\ R_4 & R_4 \end{array} \begin{array}{c} 0\\ R_1 & R_1 R_1 & R_1 \end{array} \end{array}$$

Entry	R ₁ , R ₃	R ₄	Time (h)	Product	Yield (%) ^b
1	-(CH ₂) ₅ -	Ph	14	12a	72
2	-(CH ₂) ₅ -	p-OMeC ₆ H ₄	16	12b	68
3	-(CH ₂) ₅ -	p-ClC ₆ H ₄	13	12c	79
4	-(CH ₂) ₅ -	2-Furyl	16	12d	70
5	-CH(CH ₃)(CH ₂) ₄ -	p-ClC ₆ H ₄	24	12e	54
6	-CH ₂ CH(CH ₃)(CH ₂) ₃ -	p-ClC ₆ H ₄	24	12f	60
7	-(CH ₂) ₂ CH(CH ₃)(CH ₂) ₂ -	p-ClC ₆ H ₄	18	12 g	72
8	-(CH ₂) ₃ -	Ph	24	12 h	53
9	-(CH ₂) ₃ -	p-MeC ₆ H ₄	24	12i	46
10	-(CH ₂) ₃ -	p-ClC ₆ H ₄	24	12j	55
11	-(CH ₂) ₄ -	p-ClC ₆ H ₄	13	12 k	75
12	-(CH ₂) ₄ -	Ph	18	12 I	70
13	-(CH ₂) ₄ -	p-MeC ₆ H ₄	18	12 m	64
14	-(CH ₂) ₆ -	$p-CIC_6H_4$	20	12n	43
15	-(CH ₂) ₇ -	p-ClC ₆ H ₄	36	—	0
16	Me, Me	$p-CIC_6H_4$	18	12o	62
17	Me, Et	Ph	16	12p	73
18	Ph, Me	Ph	36	—	0
19	<i>p</i> -BrC ₆ H ₄ , Me	p-MeC ₆ H ₄	36	—	0
^a Reaction conditions: ketones (6 , 0.5 mmol), acylhydrizines (9 , 0.7 mmol) allydic bramide (3 , 20 mmol) tir (1.25 mmol) $\downarrow 0.040$ mm					

0.75 mmol), allylic bromide (**3**, 2.0 mmol), tin (1.25 mmol), H_2O (4.0 ml). ^bIsolated yield.

does not give the product at all (Table 5, entry 15). Some aliphatic acyclic ketones such as acetone and butanone react to give products in good yields (Table 5, entries 16 and 17), but aromatic ketones do not afford the products (Table 5, entries 18 and 19).

Finally, the activities of amines and *N*-acylhydrazines were investigated. As shown in Scheme 3, when equal amounts of aniline and benzoylhydrazine are reacted with benzaldehyde, allylic bromide and tin powder in water at room temperature for 12 h, products **10a** from benzoylhydrazine and **5a** from double allylation of aniline are obtained in 41 and 30% yields, respectively. Product **4a** from aniline does not form at all. This indicates that *N*-acylhydrazines are more reactive than amines in the reactions.

Based on the experimental results and the literature,^[31,51] a possible mechanism is tentatively proposed as shown in Scheme 4. Amines or *N*-acylhydrazines react with aldehydes or ketones firstly



Scheme 3. Comparison of reactivity of aniline and benzoylhydrazine in one-pot allylation.



Scheme 4. Proposed mechanism for formation of 4, 10 or 12.

to produce intermediate **13**. The reaction between allylic bromide and tin powder affords intermediate **14**, which undergoes nucleophilic addition reaction to intermediate **13** to give intermediate **16**. After hydrolysis of intermediate **16**, the products **4**, **10** or **12** are produced.

Conclusions

In summary, an efficient process for the synthesis of homoallylic amines or *N'*-homoallylic hydrazides is described. In these processes, water is used as solvent and a combination of allylic bromide and tin powder is used to replace toxic allylic stannane reagents. *N*-Acylhydrazines are more reactive than amines in these processes. They can react not only with aldehydes but also with ketones to give corresponding *N'*-homoallylic hydrazides. However, amines do not react with ketones to afford the corresponding products in water.

Experimental

General procedure for synthesis of homoallylic amines and N'homoallylic hydrazides

Synthesis of compounds 4

Aldehydes **2** (1.5 mmol) and amines **1** (1 mmol) were mixed in water (4 ml), and then tin powder (2.5 mmol) and allylic bromide **3** (2.0 mmol) were added into the mixture. After being stirred at room temperature (monitored using TLC), 2 ml of HCl (1 mol l⁻¹) was added to quench the reaction. The resulting mixture was extracted with EtOAc (3 × 10 ml). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether–ethyl acetate (10:1, v/v) as eluent to afford compounds **4**.

Synthesis of compounds 10 or 12

A solution of aldehydes **2** or ketones **6** (0.5 mmol) and acylhydrazine **9** (0.75 mmol) in water (4 ml) was stirred at room temperature for 15 min, and then tin powder (1.25 mmol), allylic bromide **3** (2 mmol) and TfOH (0.1 mmol) were added into the mixture. After being stirred at 65 °C (monitored using TLC), 2 ml of HCl (1 mol l⁻¹) was added to quench the reaction. The resulting mixture was extracted with EtOAc (3 × 10 ml). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether–ethyl acetate (4:1, v/v) as eluent to afford the corresponding products **10** or **12**.

4-Methoxy-N'-(1-phenylbut-3-en-1-yl)benzohydrazide (10b). White solid; 0.122 g (82%) yield; m.p. 95–96 °C. IR (KBr, v_{max} , cm⁻¹): 3367, 3274, 1640, 1482, 1283, 1183, 1023. ¹H NMR (400 MHz, CDCl₃, δ , ppm): 7.56–7.54 (m, protons of C13, C17 and NHa, 3H), 7.39–7.24 (m, 5H), 6.84 (d, *J* = 8.8 Hz, protons of C14 and C16, 2H), 5.88–5.76 (m, proton of C3, 1H), 5.24 (br, NHb, 1H), 5.18–5.09 (m, protons of C4, 2H), 4.14 (t, *J* = 8.0 Hz, proton of C1, 1H), 3.79 (s, protons of C18, 3H), 2.56–2.42 (m, protons of C2, 2H). ¹³C NMR (100 MHz, CDCl₃, δ , ppm): 166.8 (C11), 162.3 (C15), 141.7 (C5), 134.5 (C3), 128.6, 128.4, 127.7, 127.5, 125.0, 117.8 (C4), 113.7 (C14 and C16), 63.8 (C18), 55.3 (C1), 40.3 (C2). HRMS: calcd for C₁₈H₂₁N₂O₂ [M + H]⁺ 297.1598; found 297.1596. Anal. Calcd for C₁₈H₂₀N₂O₂ (%): C, 72.95; N, 9.45; H, 6.80. Found (%): C, 72.87; N, 9.34; H, 6.74. Structure:



N'-(1-allylcyclohexyl)-4-chlorobenzohydrazide (12c). White solid; 0.115 g (79%) yield; m.p. 111–112 °C. IR (KBr, v_{max} , cm⁻¹): 3225, 2924, 1624, 1436, 1330, 1086. ¹H NMR (400 MHz, CDCl₃, δ , ppm): 7.66 (d, *J* = 8.4 Hz, protons of C3 and C7, 2H), 7.50 (br, NHa, 1H), 7.39 (d, *J* = 8.4 Hz, protons of C4 and C6, 2H), 6.06–5.93 (m, proton of C10, 1H), 5.24–4.89 (m, NHb and protons of C11, 3H), 2.26 (d, *J* = 7.2 Hz, protons of C9, 2H), 1.71–1.59 (m, C₆H₁₀, 2H), 1.55–1.36 (m, C₆H₁₀, 8H). ¹³C NMR (100 MHz, CDCl₃, δ , ppm): 165.9 (C1), 137.8 (C5), 134.7 (C10), 131.3 (C2), 128.8 (C3 and C7), 128.2 (C4 and C6), 117.5 (C11), 58.9 (C8), 41.4 (C9), 33.6 (C12 and C16), 25.7 (C13 and C15), 21.9 (C14). HRMS: calcd for C₁₆H₂₂ClN₂O [M + H]⁺ 293.1415; found 293.1420. Anal. Calcd for C₁₆H₂₁ClN₂O (%): C, 65.63; N, 9.57; H, 7.23. Found (%): C, 65.60; N, 9.35; H, 7.12. Structure:

$$\begin{array}{c} 3 \\ 4 \\ -7 \\ -7 \\ -7 \\ -7 \\ -11 \\ -10 \\ -$$

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