HFIP-mediated 2-aza-Cope rearrangement : metal-free synthesis of alpha-substituted homoallylamines at ambient temperature

HFIP-mediated 2-aza-Cope rearrangement: metal-free synthesis of α-substituted homoallylamines at ambient temperature

Karthik Gadde, Bert U. W. Maes and Kourosch Abbaspour Tehrani[a]*

Department of Chemistry, University of Antwerp, Groenenborgerlaan 171, B-2020 Antwerp, Belgium. E-mail: kourosch.abbaspourtehrani@uantwerpen.be

Abstract

An efficient metal-free strategy for the synthesis of α-substituted homoallylamine derivatives has been developed *via* a 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP)-promoted 2-aza-Cope rearrangement of aldimines, generated *in situ* by condensation of aldehydes with easily accessible 1,1-diphenylhomoallylamines. This reaction provides rapid access to α-substituted homoallylamines with excellent functional group tolerance and yields. The reaction takes place at room temperature and no chromatographic purification is required for product isolation. The synthetic utility of the current method is further demonstrated by the transformation of the obtained benzophenone ketimines into *N*-unprotected homoallylamines, an α-amino alcohol and an α-amino amide.

Introduction

Over the past decades, 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) has flourished as a popular solvent in promoting chemical reactions[1] including C–H activation reactions[2] and electrochemical transformations.[3] HFIP has been used to activate functional groups such as carbonyls,[4] epoxides,[5] alcohols,[6] halides,[7] sulfonates,[8] phenols,[3] nitrosoarenes,[9] alkynes[10] and alkenes.[11] The widespread application of HFIP is due to its extreme properties, including its strong hydrogen-bond donating ability ($\alpha = 1.96$), high ionizing power, high polarity ($\varepsilon = 15.7$), high oxidative stability, mild acidity ($pK_a = 9.3$), weak nucleophilicity, low viscosity, low boiling point (58 °C) and recyclability.[1,2] The current report discusses an HFIP promoted imine activation reaction to access scarcely available α-substituted homoallylamines under metal-free conditions.[1,12]

Substituted homoallylamines are privileged precursors for the preparation of nitrogen-containing natural products and heterocycles in synthetic organic chemistry and

pharmaceutical and agrochemical industries.[13] The most commonly used method to prepare α-substituted homoallylamines is the direct nucleophilic addition of allylic organometallic reagents to aldimines (Fig. 1A).[14] However, the addition of Grignard reagents to aldimines is limited to non-enolizable imines.[15] Aldimines containing α-hydrogens often undergo α-deprotonation by the basic Grignard reagents. For this reason, less basic allylating reagents such as allyl stannanes, allyl silanes, allyl boronates and allyl boranes have been used for the synthesis of α-substituted homoallylamines. However, these reagents are relatively expensive, exhibit major operational safety issues and generate stoichiometric amounts of metal-containing (toxic) waste, which restrict their widespread application. Furthermore, harsh deprotection conditions are often required for the removal of the nitrogen protecting group to obtain the more synthetically useful primary amines. During this latter process, by-products are generated which often cannot be recovered and are consequently not reused for reagent synthesis.

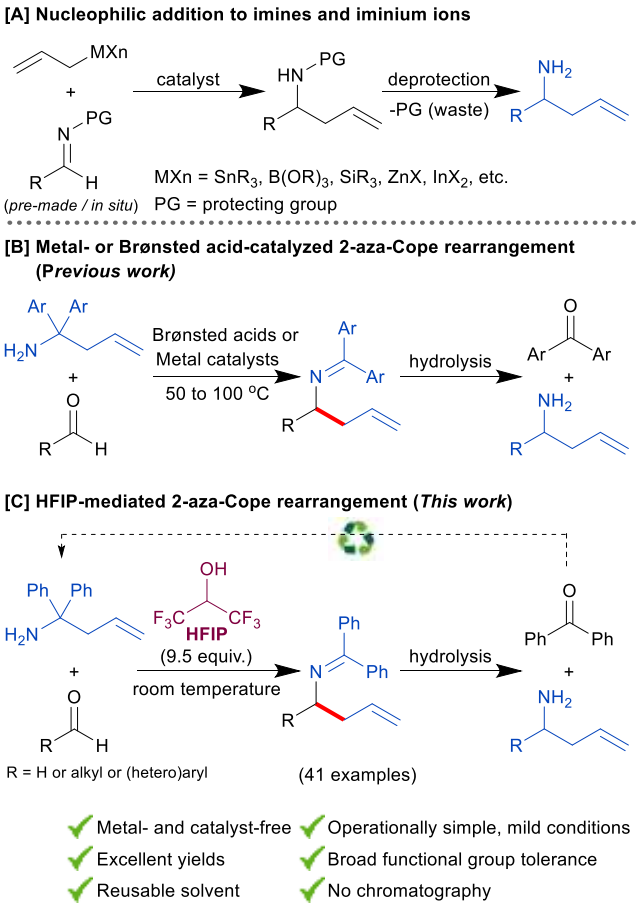
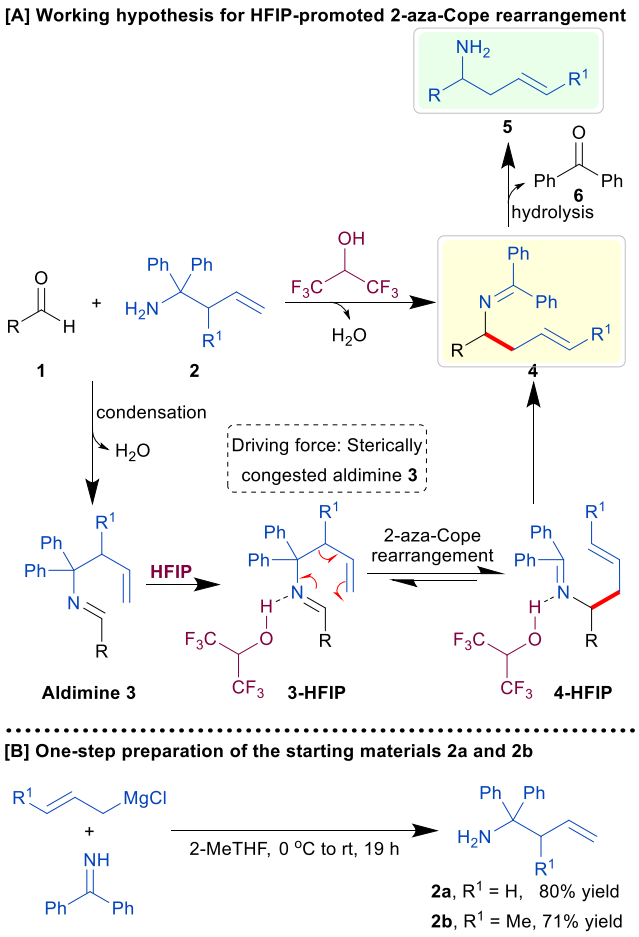


Fig.1 Synthesis of a-substituted homoallylamines.

In 1950, Horowitz and Geissman were the first to report a cationic 2-aza-Cope rearrangement of ene-imines.[16] Pioneering studies from Overman and co-workers showed extensive applications of cationic 2-aza-Cope rearrangement in combination with a Mannich reaction for alkaloid syntheses.[17] However, the 2-aza-Cope rearrangement strategy has rarely been used for the synthesis of α-substituted homoallylamines.[18-22] There are only a limited number of protocols in the literature using aldehydes for the synthesis of chiral α-substituted homoallylamine by means of a 2-aza-Cope rearrangement strategy involving either chiral amine precursors[18] or chiral catalysts[19](Fig 1B). We recently reported that iron(III) chloride can be used as a Lewis acid catalyst at 90 °C in dimethyl carbonate to trigger the 2-aza-Cope rearrangement for the synthesis of α-substituted homoallylamines.[20] Most recently, Yang and co-workers reported a bismuth(III)-catalyzed 2-aza-Cope rearrangement method for β-aminophosphonate synthesis from α-phosphoryl aldehydes and 1,1-diphenylhomoallylamines at 100 °C in 1,2-dichloroethane under an argon atmosphere.[21] Despite significant advantages of the 2-aza-Cope rearrangement method for the synthesis of α-substituted homoallylamines, unfortunately, all of these methods still show some limitations, including the use of a (metal) catalyst, elevated temperature, inert atmosphere and low yields. Therefore, further exploration of new mild and generally applicable methods to access α-substituted homoallylamines is still highly desirable. To overcome the abovementioned limitations and in continuation of our interest in imine activation reactions,[12,23] we hypothesized that HFIP could be effective to promote the 2-aza-Cope rearrangement of aldimines to access α-substituted homoallylamines starting from commercially available aldehydes and easily accessible 1,1-diphenylhomoallylamines at room temperature under metal-free conditions (Fig 1C). We envisioned that aldimine **3** would be formed first by condensation of aldehyde **1** and 1,1-diphenylhomoallylamine **2**. Subsequently, the strong hydrogen-bond donating ability and mild acidity of HFIP would promote the aldimine to undergo a 2-aza-Cope rearrangement to give the corresponding rearranged ketimine **4** (Scheme 1A). Further, the obtained rearranged imine **4** could be easily hydrolyzed under mild acidic conditions, and by means of simple acid-base workup the more synthetically useful *N*-unprotected α-substituted homoallylamines **5** could be obtained. Based on previous knowledge,[19-22] we noticed that the choice of 1,1-diphenylhomoallylamine **2** was crucial for generating the sterically congested aldimine **3**, which favours the 2-aza-Cope rearrangement of **3** to the more stable ketimine **4** through a cyclic transition state mediated by either a Lewis acid or a Brønsted acid. The required 1,1-diphenylhomoallylamines **2** can be easily prepared on a gram scale from benzophenone imines

and allylmagnesium chlorides and could be easily purified *via* acid-base extraction without using any chromatographic technique (Scheme 1B).[19]

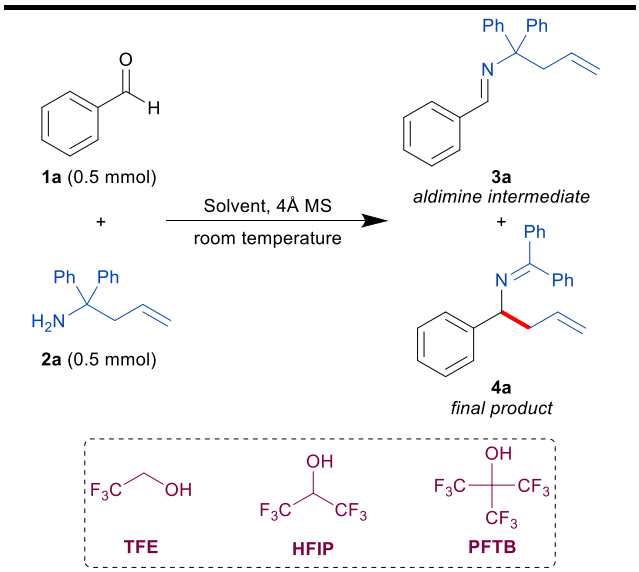


Scheme 1 (A) Working hypothesis. (B) Preparation of the starting materials.

Results and discussion

To verify our hypothesis, we commenced test reactions in HFIP by using benzaldehyde (**1a**) and 1,1-diphenylbut-3-en-1-amine (**2a**) as model substrates and the results are summarized in Table 1. We were delighted to observe the formation of the targeted product **4a** in 99% yield by using an equimolar mixture of **1a** and **2a** in HFIP in the presence of 4Å molecular sieves at room temperature (Table 1, entry 1). It is important to mention that no extra catalyst was used for this reaction. Next, HFIP was employed as an additive in combination with solvents such as tetrahydrofuran (THF), acetonitrile, toluene and dichloromethane (DCM) (entries 2-5). As expected, the use of hydrogen bond acceptor co-solvents, THF and acetonitrile, did not yield the desired product **4a**, but rather delivered aldimine **3a** exclusively (entries 2 and 3). On the

Table 1 Evaluation of various reaction parameters for the synthesis of **4a**.



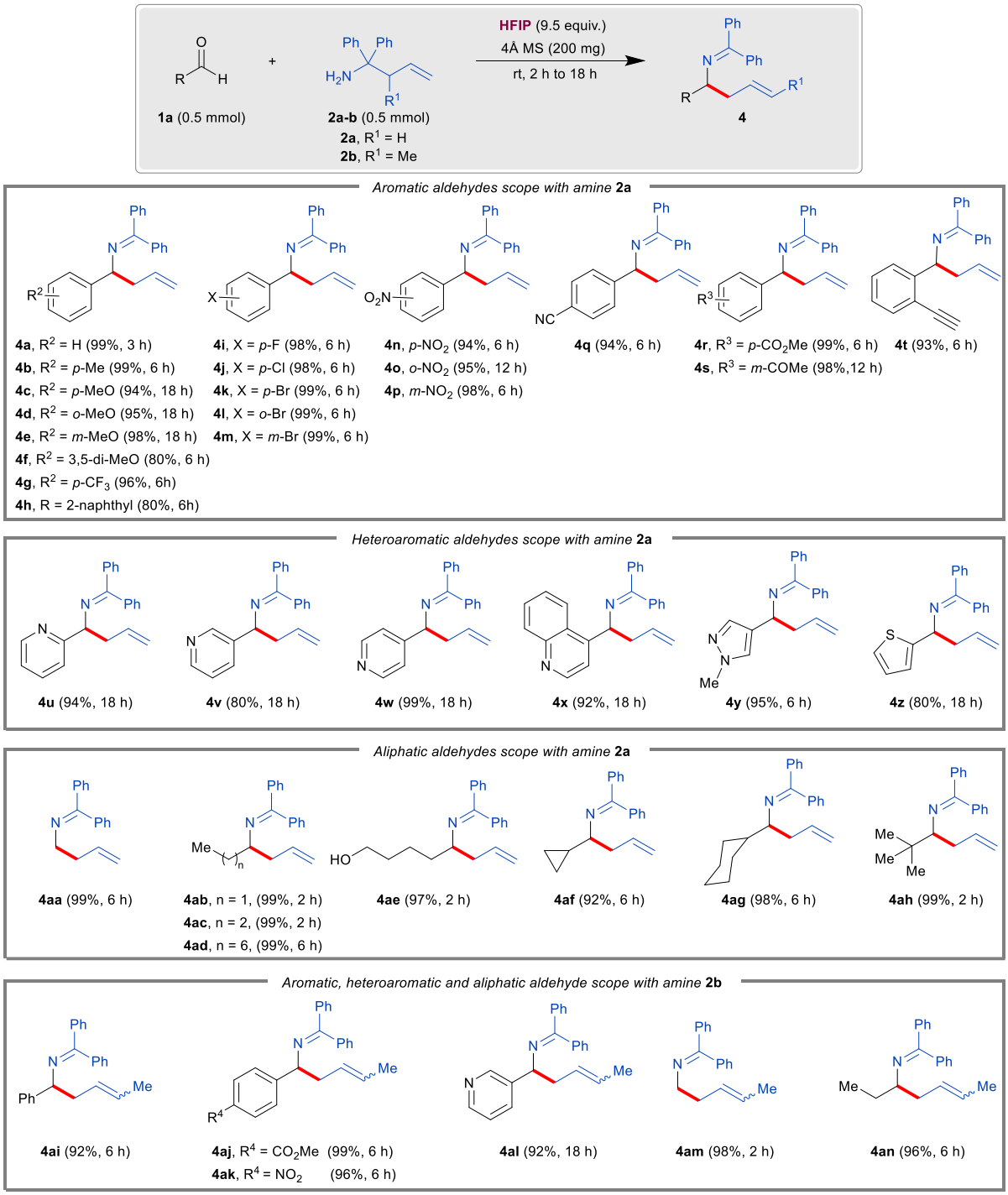
Entry	Solvent	HFIP (equiv.)	Time (h)	Yield (%) [a]	
				3a	**4a**
1	**HFIP**	**9.5**	**3**	**0**	**99**
2	HFIP/THF (1:1)	5.0	12	99	0
3	HFIP/MeCN (1:1)	5.0	12	99	0
4	HFIP/toluene (1:1)	5.0	12	0	99
5	HFIP/DCM (1:1)	5.0	12	0	99
6	Toluene		12	99	0
7	DCM		12	99	0
8	PFTB		12	5	95
9	TFE		12	99	0
10	*i*-PrOH		12	99	0
11	AcOH		12	9	68
12[b]	HFIP		12	0	38

Reaction conditions: **1a** (0.5 mmol, 1.0 equiv.), **2a** (0.5 mmol, 1.0 equiv.), 4 Å MS (200 mg), solvent (0.5 mL), air, room temperature. [a]^{1}H NMR yields were determined by means of 1,3,5-trimethoxybenzene as the internal standard. [b]The reaction was performed without 4 Å MS. MS = molecular sieves. HFIP = 1,1,1,3,3,3-hexafluoro-2-propanol. THF = tetrahydrofuran. DCM = dichloromethane. PFTB = perfluoro-*tert*-butyl alcohol. TFE = 2,2,2-trifluoroethanol.

other hand, the use of poor hydrogen bonding co-solvents, toluene and DCM, yielded the desired product **4a** exclusively (entries 4 and 5). When the reaction was performed in pure toluene or DCM, in the absence of HFIP, only the non-rearranged aldimine **3a** was isolated (entries 6 and 7). Other fluorinated solvents such as 2,2,2-trifluoroethanol (TFE) and perfluoro-*tert*-butanol (PFTB) were subsequently evaluated (entries 8 and 9). Among them, PFTB (pK_a = 5.2) gave the desired product **4a** (95%) in a comparable yield in HFIP (pK_a = 9.3). The comparatively less acidic fluorinated alcohol TFE (pK_a = 12.4) led to no detectable product **4a** and furnished **3a** in a quantitative yield (entry 9). Replacing HFIP with its non-fluorinated analogue isopropanol (pK_a = 16.5) did not yield the desired product **4a**, showing that the hydrogen bonding network and hydrogen bond donating ability of HFIP are crucial for the success of the 2-aza-Cope rearrangement step (entry 10). The use of an alternative acidic solvent, acetic acid (pK_a = 4.76), was found to be inferior and led to a significantly reduced yield of **4a**, probably due to the fact that acetic acid is an inferior hydrogen bond donor compared to HFIP (entry 11).[24] Omitting the 4 Å molecular sieves was not beneficial for the yield of **4a** and led to incomplete conversion of the starting material and hydrolysis of **4a** (entry 12). Solvent screening studies revealed that either HFIP or a combination of HFIP with toluene or DCM was the best choice of solvent in terms of delivering near-quantitative yields of **4a**. Eventually, HFIP was selected as the sole solvent for the substrate scope study.

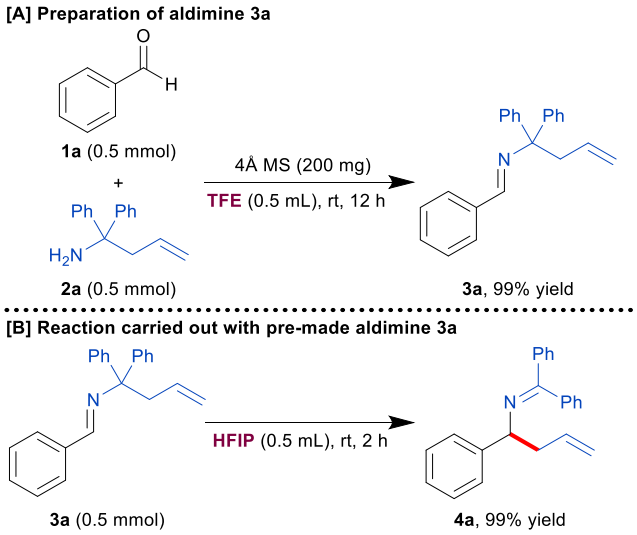
With the optimized reaction conditions in hand (Table 1, entry 1), we next investigated the generality of this methodology on a range of aldehydes **1** with 1,1-diphenylhomoallylamine **2**. As presented in Scheme 2, a broad range of aldehydes having various functional groups were well tolerated under the reaction conditions and furnished the desired products in excellent yields. The reaction of homoallylamine **2a** with *p*-tolualdehyde (**1b**), *p*-anisaldehyde (**1c**), *o*-anisaldehyde (**1d**), *m*-anisaldehyde (**1e**), 3,5-dimethoxybenzaldehyde (**1f**), *p*-(trifluoromethyl)benzaldehyde (**1g**) and 2-naphthaldehyde (**1h**) delivered the products **4b–h** in 99%, 94%, 95%, 98%, 80%, 96% and 80% yields, respectively. The reaction with halogenated benzaldehydes, *p*-fluorobenzaldehyde (**1i**), *p*-chlorobenzaldehyde (**1j**), *p*-bromobenzaldehyde (**1k**), *o*-bromobenzaldehyde (**1l**) and *m*-bromobenzaldehyde (**1m**), afforded the corresponding homoallylamines **4i–m** in near-quantitative yields. Gratifyingly, a broad range of functional groups, including nitro (**1n–p**), nitrile (**1q**), ester (**1r**), ketone (**1s**) and alkyne (**1t**), were well tolerated under the reaction conditions, furnishing the corresponding homoallylamines **4n–t** in excellent yields. It is important to note that the reaction of benzaldehydes bearing electron-donating groups (-Me, -OMe) at the *ortho*- and *para*-positions required longer reaction time

than that of benzaldehydes bearing electron-withdrawing groups (-F, -Cl, -Br, -NO_2, -CN, -CO_2Me, -CF_3). Importantly, the substrate scope with respect to heteroatom-containing aromatic aldehydes such as pyridinecarboxaldehydes (**1u–w**), 4-quinolinecarboxaldehyde (**1x**),



Scheme 2 Substrate scope of HFIP-promoted 2-aza-Cope rearrangement.

1-methyl-1*H*-pyrazole-4-carboxaldehyde (**1y**) and 2-thiophenecarboxaldehyde (**1z**) furnished the products **4t–z** in yields ranging from 80% to 99%, highlighting the expediency of this protocol. Moreover, aliphatic aldehydes also proved to be efficient substrates in this transformation and afforded the corresponding homoallylamines **4aa–ah** in good to excellent yields. We next extended the scope of the reaction with respect to the amine partner, using 2-methyl-1-1-diphenylbut-3-en-1-amine (**2b**). The selected aldehydes with **2b** furnished the corresponding homoallylamines **4ai–an** in good to excellent yields. It is noteworthy that none of the examples in Scheme 2 required column chromatographic purification.



Scheme 3 Control experiments.

Subsequently, in order to validate our hypothesis, we carried out a few control experiments (Scheme 3) and systematic ^{1}H NMR experiments as shown in Fig. 2. First, we prepared aldimine **3a** by using benzaldehyde (**1a**) and 1,1-diphenylbut-3-en-1-amine (**2a**) in 2,2,2-trifluoroethanol (Scheme 3A). Then, aldimine **3a** was used as the starting material applying standard reaction conditions in the absence of 4 Å molecular sieves to obtain **4a** in a quantitative yield (Scheme 3B). These experiments implied that aldimine **3a** was an intermediate and that the use of HFIP was necessary for 2-aza-Cope rearrangement step under standard reaction conditions.

To further showcase the role of HFIP, the ^{1}H NMR spectrum was recorded immediately after mixing aldimine **3a** and HFIP (1.3 equiv.) in deuterated chloroform at room temperature (Fig. 2C). Clear shifts of the aldimine proton peak (from 7.82 ppm to 7.88 ppm), the OH peak of

HFIP (from 2.94 ppm to 3.94 ppm) and CH peak of HFIP (from 4.40 ppm to 4.10 ppm) were observed. These observations clearly indicated the H-bond interaction between the aldimine **3a** and HFIP, showing that aldimine **3a** was activated by hydrogen bonding interactions with HFIP towards the product **4a**.[12c]

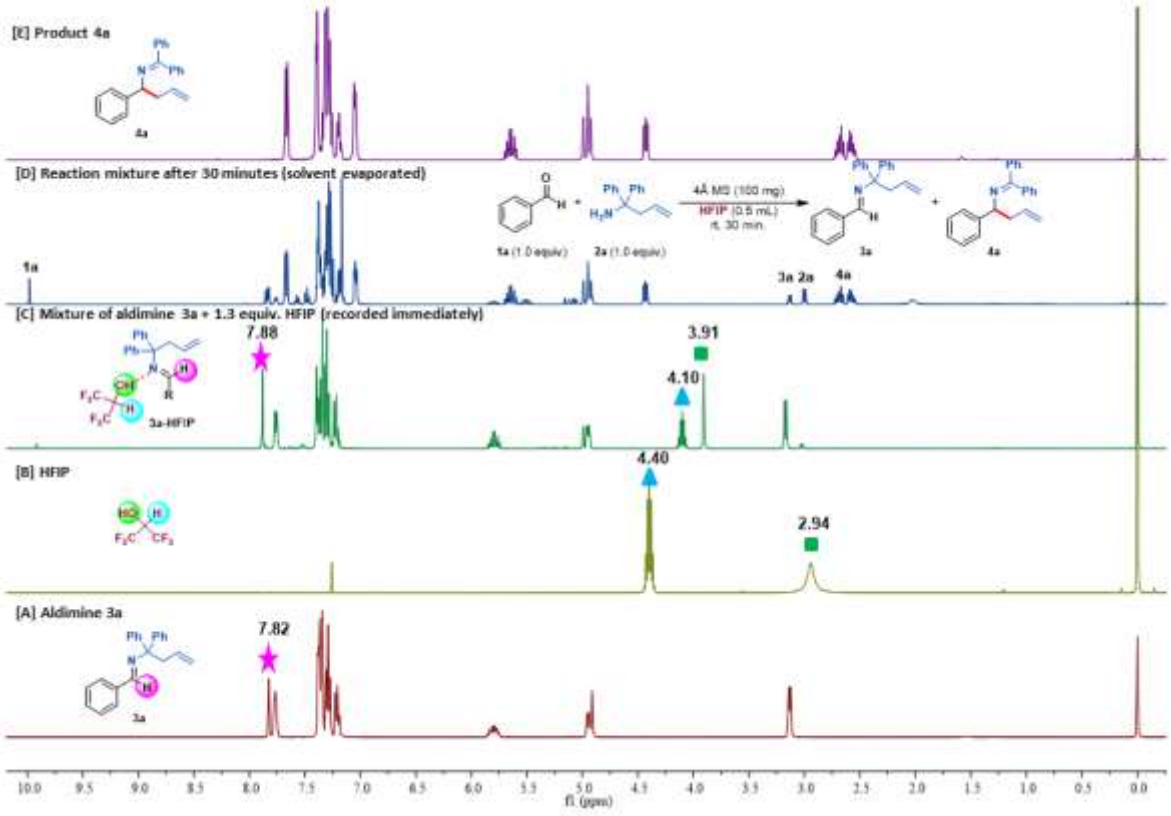
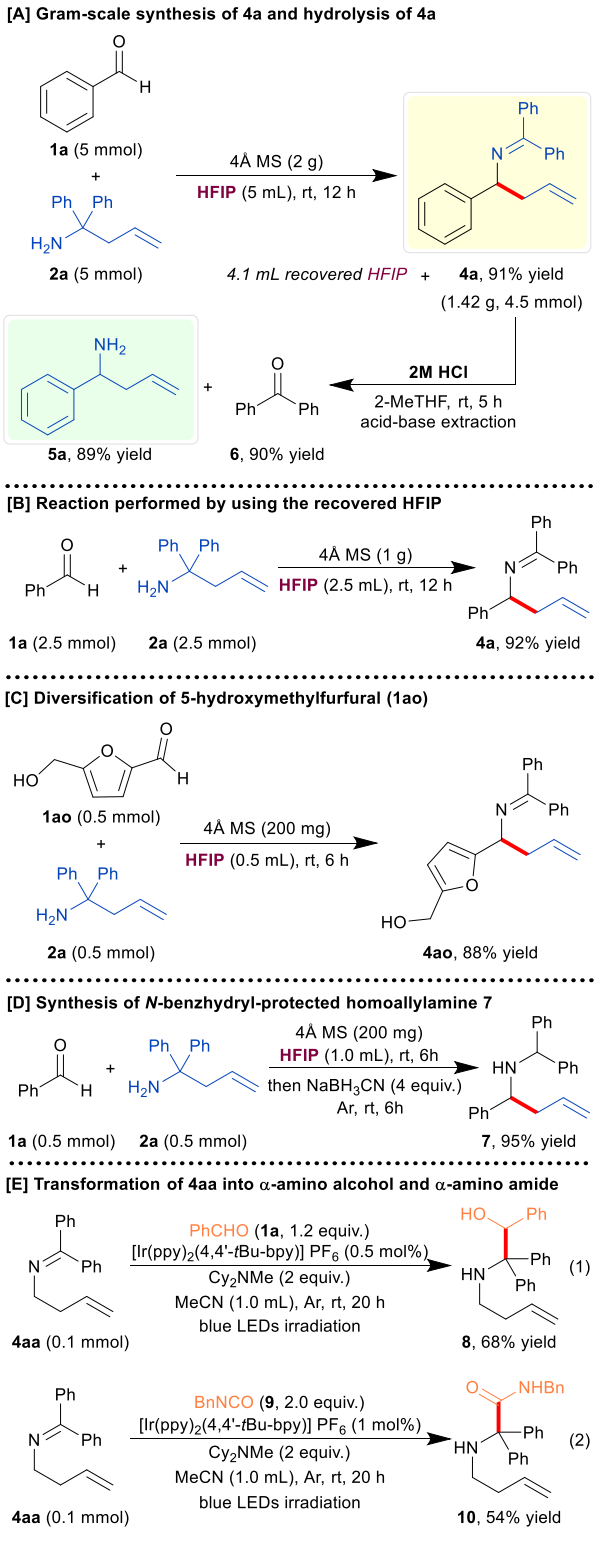


Fig. 2 Stacked ^{1}H NMR (400 MHz, $CDCl_3$) spectra of (A) aldimine **3a**, (B) HFIP, (C) a 1:1.3 mixture of aldimine **3a** and HFIP (0.25 mmol), (D) the reaction mixture (0.25 mmol, 30 min later), and (E) product **4a**. In spectrum (C), the pink star indicates the position of the deshielded aldimine proton peak and the green square indicates the position of the deshielded O-H peak of HFIP.

A gram-scale experiment was performed for showcasing the scalability of this method (Scheme 4A). A 5 mmol scale reaction between benzaldehyde (**1a**) and 1,1-diphenylbut-3-en-1-amine (**2a**) was carried out in HFIP (5 mL) at room temperature, furnishing the desired product **4a** in 91% yield and HFIP (4.1 mL) was recovered after distillation using a Kugelrohr apparatus. Furthermore, **4a** was easily hydrolyzed under mild acidic conditions which delivered primary α-substituted homoallylamine **5a** in 89% yield and benzophenone (**6**) in 90% yield after simple acid-base extraction. Importantly, the recovered benzophenone can be reused for the synthesis



Scheme 4 Scalability and synthetic utility of the developed method. (A) Gram-scale experiment and hydrolysis of ketimine **4a**. (B) Recycling study of HFIP. (C) Diversification of 5-hydroxymethylfurfural. (D) Synthesis of *N*-benzhydryl protected homoallylamine **7**. (E) The synthetic transformation of **4aa** into a-amino alcohol **8** and a-amino amide **10**.

of substrate **2a**.[25] Further, recovered HFIP was reused in a subsequent reaction between **1a** and **2a** to afford **4a** in 92% yield (Scheme 4B).

To further illustrate the utility of our methodology, a direct diversification to a renewable aldehyde was attempted. 5-Hydroxymethylfurfural (**1ao**) was selected as a model bio-platform molecule as it features the carbonyl group, the hydroxy group, and the furan ring. The reaction of **1ao** with **2a** under the optimal reaction conditions delivered the target product **4ao** in 88% yield (Scheme 4C). Next, a two-step, one-pot synthesis of *N*-benzhydryl-protected primary amine **7** was achieved from benzaldehyde (**1a**) and 1,1-diphenylbut-3-en-1-amine (**2a**). The HFIP-promoted 2-aza-Cope rearrangement of aldimine and the subsequent reduction (same pot) of ketimine with sodium cyanoborohydride led to **7** in 95% yield (Scheme 4D). The synthetic utility of the reaction was further highlighted by post-synthetic modification of a homoallylamine derivative **4aa** towards the synthesis of α-amino alcohol **8** and α-amino amide **10** *via* visible-light-mediated cross-coupling reactions using benzaldehyde (**1a**) and benzyl isocyanate (**9**) as electrophiles respectively (Scheme 4E).[26,27] One-step conversion of the homoallylamine derivative **4aa** into α-amino alcohol **8** was achieved in 68% yield (Scheme 4E, eqn (1)).[26] The synthesis of α-amino amide **10** was achieved in 54% yield from the reaction of homoallylamine derivative **4aa** with benzyl isocyanate (**9**) (Scheme 4E, equation 2).[27]

Conclusions

We herein developed an efficient and robust HFIP-promoted 2-aza-Cope rearrangement reaction leading to the formation of a broad range of α-substituted homoallylamines from commercially available aldehydes and easily synthesizable 1,1-diphenylhomoallylamines. This method allows rapid access to α-substituted homoallylamines under mild conditions in good to excellent yields with excellent functional group tolerance and water as the sole by-product. Notably, the method is metal-free and works for both aliphatic and (hetero)aromatic aldehyde substrates; the reactions operate at ambient temperature under an open-air atmosphere and without the requirement of chromatographic purification for product isolation. Furthermore, the obtained products (benzophenone ketimines) are easily hydrolyzed under mild acidic conditions to obtain more synthetically useful *N*-unprotected α-substituted homoallylamines. Post-synthetic modification of ketimines into an α-amino alcohol and an α-amino amide demonstrated the further synthetic utility of this method.

Experimental section

General information

All aldehydes used were purchased from commercial sources and used as received. Starting materials, 1,1-diphenylbut-3-en-1-amine (**2a**) and 2-methyl-1,1-diphenylbut-3-en-1-amine (**2b**), were prepared using known literature procedures.[19] 4 Å molecular sieves (powder) were purchased from Sigma-Aldrich and activated prior to use by drying in a vacuum oven at 200 °C for 24 h. HFIP was purchased from Fluorochem and used as received. All reactions were carried out in oven-dried vials. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Model Avance 400 Fourier transform NMR spectrometer in $CDCl_3$ at room temperature (unless stated otherwise). All spectra were referenced to the TMS peak (δ= 0.00 ppm for both ^1H NMR and ^{13}C NMR in $CDCl_3$). High-resolution mass spectrometry (HRMS) samples were prepared by dissolving 0.1–3.0 mg of compound in MeCN and further diluting to a concentration of 10^{-5} –10^{-6} M with 50% MeCN/50% H_2O. The samples were injected in the MS system using a CapLC system (Waters) and a nanoelectrospray source operated in the positive ion mode at a potential of 1.5 or 1.7 kV. The eluent used was 30% A (0.1% formic acid in H_2O) and 70% B (0.1% formic acid in MeCN/H_2O-95/5) at a flow rate of 6.0 mL min^{-1}. Samples were injected with an interval of 3 min. Before analysis, 2.0 mL of a 0.025% H_3PO_4 solution (MeOH/H_2O-50/50) or 10.0 mL of 10^{-6} M deoxyadenosine solution (MeOH/H_2O-50/50) was injected as a lock mass. Positive-ion mode accurate mass spectra were acquired using a Q-TOF instrument. Melting points were measured on a Buchi B-545 capillary melting point apparatus. Full characterization data and NMR spectra for all compounds are provided in the ESI.

General procedure for the synthesis of α–substituted homoallylamines 4

In an oven-dried 10 mL vial, 1,1-diphenylbut-3-en-1-amine (**2a** or **2b**) (0.5 mmol, 1.0 equiv.), aldehyde **1** (0.5 mmol, 1.0 equiv.), 4 Å molecular sieves (200 mg) and HFIP (0.5 mL, 9.5 equiv.) were added successively, and the vial was capped under air. The reaction mixture was then vigorously stirred for the indicated time (see Scheme 2) at room temperature. After the reaction time, the reaction mixture was filtered and the solvent was removed under reduced pressure to afford pure α-substituted homoallylamine derivatives **4** (see Scheme 2 for yields and the ESI for the detailed experimental procedure, characterization data and NMR spectra).

Procedure for the gram-scale synthesis of 4a

In an oven-dried 25 mL vial, 1,1-diphenylbut-3-en-1-amine (**2a**) (1.117 g, 5.0 mmol, 1.0 equiv.), benzaldehyde (**1a**) (0.531 g, 5.0 mmol, 1.0 equiv.), 4 Å molecular sieves (2 g) and HFIP (5 mL) were added successively, and the vial was capped under air. The reaction mixture was then vigorously stirred for 12 h at room temperature. After the reaction time, the reaction mixture was filtered and HFIP was distilled off under reduced pressure at room temperature with a Kugelrohr distillation apparatus to obtain pure 1,1-diphenyl-*N*-(1-phenylbut-3-en-1-yl) methanimine (**4a**) in 91% yield and HFIP (4.1 mL) was recovered.

Procedure for the hydrolysis of 4a and recovery of benzophenone

In a 100 mL round bottom flask, **4a** (1.417 g, 4.55 mmol) was dissolved in 2-MeTHF (20 mL), followed by the addition of 2 N aqueous HCl solution (10 mL). The reaction mixture was then stirred for 5 h at room temperature and monitored by TLC. Upon completion of the reaction, 2-MeTHF was removed under reduced pressure and 10 mL of H_2O was added. The mixture was washed with EtOAc (4 × 5 mL) and the combined organic phase was extracted with water (5 mL) and then washed with EtOAc (1 mL). The ethyl acetate fractions were combined and dried using $MgSO_4$, following which the solvent was removed under reduced pressure to afford pure benzophenone (**6**, 0.746 g, 90%). The previous combined aqueous phase was neutralized with 3 N aqueous NaOH solution and extracted with ethyl acetate; the organic fractions were combined and dried using $MgSO_4$, following which the solvent was removed under reduced pressure to afford pure 1-phenylbut-3-en-1-amine (**5a**, 0.596 g, 89%).

Procedure for the synthesis of 4ao from 5-hydroxymethylfurfural

In an oven-dried 10 mL vial, 1,1-diphenylbut-3-en-1-amine (**2a**) (112 mg, 0.5 mmol, 1.0 equiv.), 5-hydroxymethylfurfural (**1ao**) (63 mg, 0.5 mmol, 1.0 equiv.), 4 Å molecular sieves (200 mg) and HFIP (0.5 mL) were added successively, and the vial was capped under air. The reaction mixture was then vigorously stirred for 6 h at room temperature. After the reaction time, the reaction mixture was filtered and the solvent was removed under reduced pressure to afford the desired product **4ao** (0.146 g, 88%).

Procedure for the synthesis of *N*-benzhydryl-protected homoallylamine 7

In an oven-dried 10 mL vial, 1,1-diphenylbut-3-en-1-amine (**2a**) (0.5 mmol, 1.0 equiv.), benzaldehyde (**1a**) (0.5 mmol, 1.0 equiv.), 4 Å molecular sieves (200 mg) and HFIP (1.0 mL) were added successively, and the vial was capped under air. The reaction mixture was then

stirred for 6 hours at room temperature. After 6 hours, sodium cyanoborohydride (126 mg, 4.0 equiv.) was added to the reaction mixture. Then, the reaction vial was flushed with argon for 5 minutes and then the vial was sealed with a septum. The reaction vial was stirred at room temperature under argon for 6 hours. After the reaction time, the reaction mixture was filtered, and the solvent was removed under reduced pressure. Then the reaction mixture was diluted with DCM and washed with 1 N aqueous NaOH solution. The aqueous layer was extracted with DCM. The combined DCM layers were dried using $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified with an automated flash chromatography system on silica gel using an *n*-heptane/EtOAc gradient (from 100% n-heptane to 10% EtOAc in 25 minutes, 25 mL min^{-1}.). *N*-Benzhydryl-1-phenylbut-3-en-1-amine (**7**) was obtained in 95% (149 mg) yield.

Procedure for the synthesis of α-amino alcohol 8 from 4aa

This experimental procedure was adapted from a literature procedure.[26] In an oven-dried 4 mL Wheaton vial, *N*-(but-3-en-1-yl)-1,1-diphenylmethanimine (**4aa**) (24 mg, 0.1 mmol, 1.0 equiv.), $[Ir(ppy)_2(4,4'\text{-}t\text{Bu-bpy})]$ PF_6 (0.5 mg, 0.5 mol%), methyldicyclohexylamine (39 mg, 0.2 mmol, 2.0 equiv.), benzaldehyde (**1a**) (13 mg, 0.120 mmol, 1.2 equiv.) and anhydrous MeCN (1 mL) were added successively. The reaction vial was flushed with argon in 5 minutes, and then the vial was sealed with a septum. The reaction mixture was placed under a 19 W blue LED light source and stirred at ambient temperature (~30 °C) for 20 h. After 20 h, the vial was opened to air and the volatile materials were removed using a rotary evaporator under reduced pressure. The crude residue was purified with an automated flash chromatography system on silica gel using an *n*-heptane/EtOAc gradient (from 100% *n*-heptane to 10% EtOAc in 25 minutes, 25 mL min^{-1}.). 2-(But-3-en-1-ylamino)-1,2,2-triphenylethan-1-ol (**8**) was obtained in 68% (23 mg) yield.

Procedure for the synthesis of α-amino amide 10 from 4aa

This experimental procedure was adapted from a literature procedure.[27] In an oven-dried 4 mL Wheaton vial, *N*-(but-3-en-1-yl)-1,1-diphenylmethanimine (**4aa**) (24 mg, 0.1 mmol, 1.0 equiv.), $[Ir(ppy)_2(4,4'\text{-}t\text{Bu-bpy})]$ PF_6 (1 mg, 1.0 mol%), methyldicyclohexylamine (39 mg, 0.2 mmol, 2 equiv.), benzyl isocyanate (**9**) (27 mg, 0.2 mmol, 2 equiv.) and anhydrous MeCN (1 mL) were added successively. The reaction vial was flushed with argon for 5 minutes and then the vial was sealed with a septum. The reaction mixture was placed under a 19 W blue LED light source and stirred at ambient temperature (~30 °C) for 20 h. After 20 h, the vial was opened to air and the volatile materials were removed using a rotary evaporator under reduced

pressure. The crude residue was purified with an automated flash chromatography system on silica gel using an *n*-heptane/EtOAc gradient (from 100% *n*-heptane to 10% EtOAc in 25 minutes, 25 mL min^{-1}). *N*-Benzyl-2-(but-3-en-1-ylamino)-2,2-diphenylacetamide (**10**) was obtained in 54 % (20 mg) yield.

Conflicts of interest

There are no conflicts to declare.

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GRAPHICAL ABSTRACT