Organic & Biomolecular Chemistry

PAPER

Cite this: *Org. Biomol. Chem.*, 2025, **23**, 5352

Triflic acid catalyzed intermolecular hydroamination of alkenes with Fmoc-NH_2 as the amine source†

Aswathi C. S., Chinraj Sivarajan and Raja Mitra *

Received 28th March 2025,
Accepted 6th May 2025

DOI: 10.1039/d5ob00519a

rsc.li/obc

Intermolecular hydroamination of alkenes is recognized as one of the most challenging synthetic pathways for directly obtaining primary amine derivatives from alkenes. While metal-catalyzed hydroamination is well established, metal-free hydroamination for synthesizing primary amines remains an attractive yet infrequent approach. In this study, we report the hydroamination of vinyl arenes using triflic acid as the catalyst and Fmoc-NH_2 as the amine source. The optimized conditions proved effective for a range of vinyl arenes and some endocyclic alkenes, yielding moderate to excellent results (40–91%). Mechanistic investigations conducted through NMR, variable temperature NMR, kinetic studies, and control reactions indicated that the transient interaction between triflic acid and Fmoc-NH_2 inhibited styrene polymerization. Primary amines were obtained by deprotecting the Fmoc group using KOH/MeOH.

Introduction

Primary amines are particularly interesting in the pharmaceutical and other industries.[1–4] Synthesizing primary amines from feedstock materials is a challenging task. Hydroamination is a primal, atom-economical, and by-product-free synthetic route for the synthesis of alkyl amines from olefins and amines;[2,3,5–8] however, additional efforts are required to acquire selectivity.[5,9–13] Metal-catalyzed intra- and intermolecular hydroamination of various alkynes[3,5,8,14–17] and alkenes[2,12,18–28] with N-protected amines is an established synthetic strategy to obtain primary amines. In many metal-catalyzed hydroamination reactions, Brønsted acids are used as additives or co-catalysts.[2,29–33] The emergence of organocatalysis[34–37] has prompted many scientists to search for metal-free alternatives for hydroamination.[30,38–41] However, an inherent problem of hydroamination using Brønsted acids is quenching of the catalyst by a basic nitrogen source. In 2002, Hartwig and co-workers addressed this problem using protected amines for intramolecular hydroamination (Fig. 1).[42] Since then, intramolecular hydroamination has been reported using various Brønsted acids[30,34,42,43] and enzymes[44] using N-protected amine sources.

Bergman and co-workers reported Brønsted acid-assisted intermolecular addition of anilines to alkenes (Fig. 1), highlighting the potential of Brønsted acids in assisting in hydroamination reactions, albeit with the concomitant alkylation reaction.[45] Among the potential hydroaminations, reactions

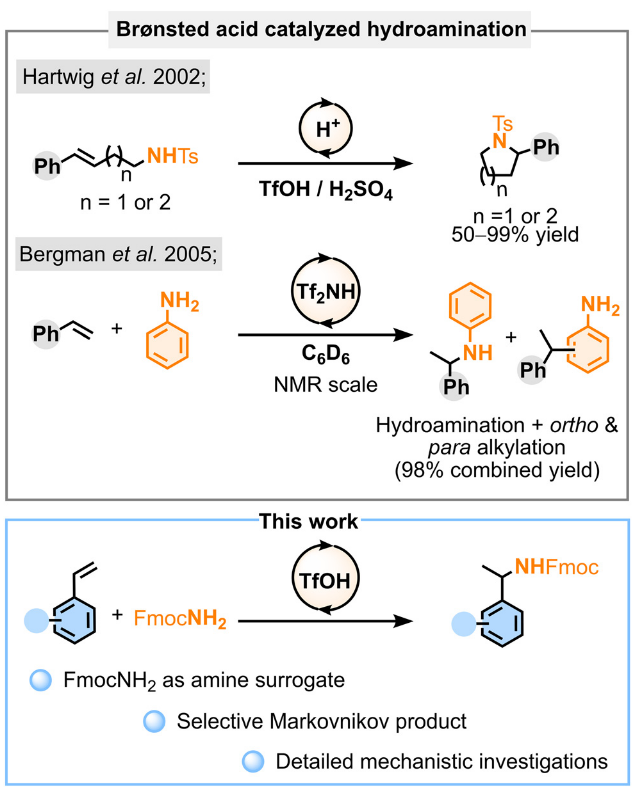


Fig. 1 Brønsted acid catalyzed hydroamination reactions.

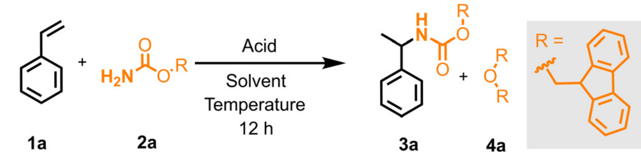
School of Chemical and Materials Sciences, Indian Institute of Technology Goa, Ponda, Goa–403401, India. E-mail: rajamitra@iitgoa.ac.in

† Electronic supplementary information (ESI) available. See DOI: https://doi.org/10.1039/d5ob00519a

involving ammonia are especially valuable because they provide direct access to primary amines.[46–49] Nevertheless, the challenging nature of this simplest amine has compelled researchers to look for ammonia surrogates; recently, Morandi and co-workers utilized ammonium carbamate as the "N" source for the oxidative amination of C=C bonds.[50] It is important to note that NH_3[51–53] and various NH_3 surrogates[54–59] have been utilized mainly in C–N cross-coupling reactions. The main criterion for choosing these surrogates, along with their compatibility with hydroamination reactions, is their facile deprotection. To develop a Brønsted acid-catalyzed hydroamination, the nitrogen source must be acid-tolerant and sufficiently nucleophilic under acidic conditions. List and co-workers reported an organocatalyzed asymmetric three-component homoallylic amine synthesis with Fmoc-NH_2 as the amine source, and facile single-step deprotection was performed to assign the configuration.[60] Hydroamination of an alkene with Fmoc-NH_2 as an ammonia surrogate is rare.[49,61]

Herein, we report a simple and efficient regioselective intermolecular hydroamination of primarily vinyl arenes with Fmoc-NH_2 (**2a**), using triflic acid as a catalyst. Amine transfer from **2a** in alkene hydroamination offers significant advantages over conventional hydroamination methods: (i) the product formed is an Fmoc-protected amine, (ii) Fmoc-NH_2 is acid tolerant, and (iii) Fmoc groups can be readily removed under mild conditions (base-catalyzed) to access primary amines.[62,63]

Table 1 Reaction method development[a]



Entry	Acid	Solvent	Temperature	^{1}H NMR yield **3a**[e] (%)
1	TfOH	Toluene	40 °C	0
2	TfOH	Toluene	60 °C	35[d]
3	TfOH	Toluene	80 °C	47[d]
4	TfOH	1,4-Dioxane	60 °C	0
5	TfOH	1,2-DCE	60 °C	35
6[b]	TfOH	CH_2Cl_2	RT	25
7	TfOH	$CHCl_3$	60 °C	47
8	CH_3SO_3H	$CHCl_3$	60 °C	15
9	H_2SO_4	$CHCl_3$	60 °C	31
10	*p*-TSA	$CHCl_3$	60 °C	Trace
11	CF_3COOH	$CHCl_3$	60 °C	0
12	$(CF_3SO_2)_2NH$	$CHCl_3$	60 °C	29[d]
13[c]	TfOH	$CHCl_3$	60 °C	63
14[c]	TfOH (10 mol%)	$CHCl_3$	60 °C	81
15[c]	TfOH (10 mol%)	$CHCl_3$	60 °C; 4 h	82
16[c]	TfOH (10 mol%)	$CHCl_3$	60 °C; 5 h	91

[a] Reaction conditions: styrene (**1a**, 0.344 mmol, 1 equiv.), Fmoc-NH_2 (**2a**, 0.344 mmol, 1 equiv.), TfOH (0.01 mmol, 5 mol%), solvent (0.5 M), temperature (°C), time 12 h. [b] Reaction carried out at RT. [c] Styrene : Fmoc-NH_2 (3 : 1 ratio). [d] Ether (**4a**) formation observed from Fmoc-NH_2. [e] ^{1}H NMR yield was calculated using 1,3,5-trimethoxybenzene as an internal standard. TfOH = CF_3SO_3H (see the ESI for complete optimization details†).

Results and discussion

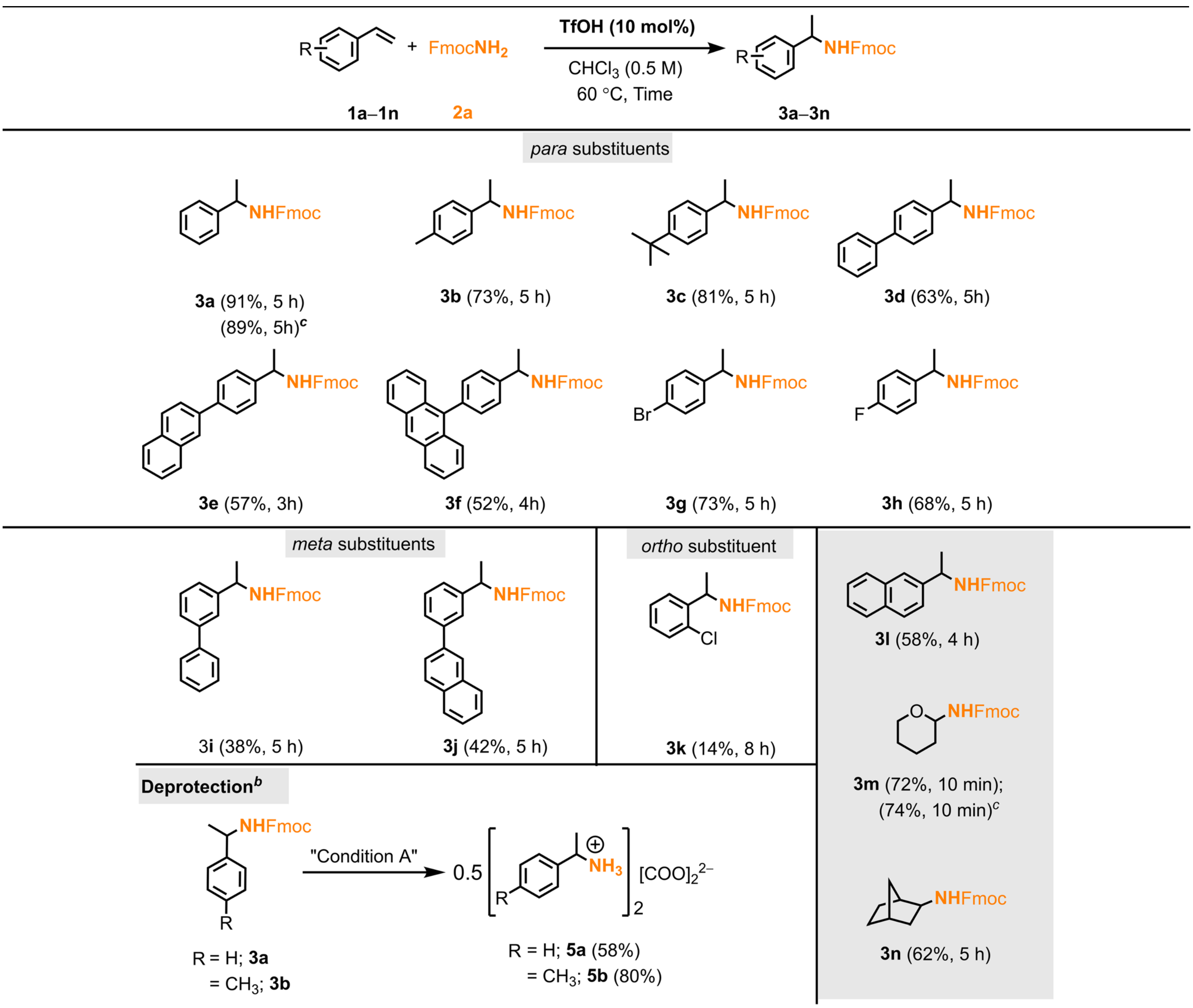
To determine the feasibility of the Brønsted acid-catalyzed intermolecular hydroamination reaction, we began our investigation using styrene (**1a**) and Fmoc-NH_2 (**2a**) as the model substrates in the presence of triflic acid (5 mol%) in toluene at 60 °C (Table 1, entry 2). The expected hydroamination product **3a** was detected in 35% yield[64,65] along with ether **4a** as a side product[66] (4%), generated by the hydrolysis[67] of Fmoc-NH_2 (Table S1, ESI†). Despite the low yield in this initial run, we were encouraged by the exclusive formation of the desired Markovnikov selectivity. Increasing the temperature from 60 °C to 80 °C gave 47% yield of **3a** within 4 h, and continuing the reaction for a longer time resulted in the formation of **4a** (isolated yield 6%) (Table 1, entry 3). Furthermore, increasing the temperature to 100 °C accelerated the reaction, and in 30 min, 37% yield of **3a** was formed along with 8% yield of **4a**. However, continuing the reaction for 12 h led to simultaneous decomposition (**3a**), increasing the polymerization of styrene (Table S1, ESI†). Thus, the reaction temperature was identified as a key factor for controlling the yield of the desired product. The ether solvent suppressed **3a** formation (Table 1, entry 4, and Table S2, ESI†). Halogenated solvents such as 1,2-dichloroethane (1,2-DCE) and DCM resulted in a lower yield compared to toluene (Table 1, entries 5 and 6), and chloroform gave the best yield of **3a** (47%, Table 1, entry 7) at 60 °C. Other screened solvents did not improve the yield (Table S2, ESI†). Screening other Brønsted acids as catalysts revealed that triflic acid was the most efficient (Table 1, entries 7–12 and Table S3, ESI†). The well-explored triflimide gave **3a** and **4a** in isolated yields of 29% and 6%, respectively. As mentioned earlier, the competing formation of ether **4a** and the tendency of styrene to undergo polymerization interfered with the hydroamination product yield. Increasing the equivalents of styrene with respect to Fmoc-NH_2 is a viable solution to overcome both challenges; therefore, the styrene to **2a** ratio was adjusted to 3 : 1, which resulted in a dramatic acceleration of the reaction with an improved product yield (63%) (Table 1, entry 13). However, a further increase in the styrene concentration decreased the yield from 63% to 56%. Increasing the equivalents of Fmoc-NH_2 (**2a**) did not improve the yield (Table S4, ESI†). Because adventitious water is responsible for the competing side reaction leading to ether **4a**,[67] we performed the reaction in the presence of molecular sieves under argon. Nevertheless, similar yields were obtained, proving that the reaction was unaffected by the presence of water (Table S4, entry 5, ESI†). When the catalyst loading was changed from 5 mol% to 10 mol%, the product yield increased to 81% after 12 h (Table 1, entry 14 and Table S5, ESI†). At this point, we believe that continuing the reaction for a longer time may lead to the decomposition of the product as well as Fmoc-NH_2. The reaction was carried out for 4 h and 5 h, resulting in 82% and 91% yield of **3a**, respectively

(Table 1, entries 15 and 16). Prolonging the reaction beyond 5 h led to a decrease in the yield (Table S6, ESI†). Thus, the optimized reaction conditions were: a 3 : 1 ratio of styrene (**1a**) to Fmoc-NH_2 (**2a**) and 10 mol% triflic acid at 60 °C for 5 h in chloroform as the solvent (Table 1, entry 16). Control reactions showed that no **3a** was formed in the absence any one of these reactants (Table S7, ESI†).

Under the optimized reaction conditions, we investigated the substrate scope of different vinylarenes and Fmoc-NH_2 (Table 2). A scaled-up reaction (4.1 mmol of **2a**) resulted in 89% (1.26 g of **3a**) yield. Hydroamination proceeded successfully with several *para*-substituted styrenes with various electronic and steric demands. Alkyl substitutions such as *p*-Me and *p*-*tert*-Bu resulted in good yields of **3b** (73%) and **3c** (81%), respectively. With respect to the aryl substituents at the *para* position, phenyl (**3d**), 2-naphthyl (**3e**), and 9-anthracenyl (**3f**) showed moderate yields of 63%, 57%, and 52%, respectively. The halogen substituents also performed well under the optimized conditions, affording **3g** (73%) and **3h** (68%). *m*-Phenyl and *m*-(2-naphthyl) substituents gave moderate yields of **3i** (38%) and **3j** (42%). However, *o*-chloro substitution resulted in a poor yield (**3k**, 14%), which might have been caused by steric hindrance near the reactive site, and decomposition of the product was also observed during purification. 1-Vinyl naphthalene exhibited moderate reactivity and afforded the desired product **3l** in 58%yield.

We also examined the hydroamination of endocyclic olefins, namely, 3,4-dihydro-2*H*-pyran and bicyclo[2.2.1]hept-2-

Table 2 Substrate scope[a] and deprotection[b]



[a] Reaction conditions: vinylarenes (1.5 mmol, 3 equiv.), Fmoc-NH_2 (0.5 mmol, 1 equiv.), TfOH (0.05 mmol, 10 mol%), $CHCl_3$ (0.5 M), 60 °C, stipulated time (h). [b] Condition A: hydroamination product (0.524 mmol, 1 equiv.), KOH (1.05 mmol, 2 equiv.), MeOH (0.25 M), RT, 5 min, oxalic acid (0.786 mmol, 1.5 equiv.). [c] Large scale (4.1 mmol of Fmoc-NH_2).

ene. Both compounds underwent hydroamination, affording **3m** in 72% yield (74% yield in a large-scale reaction)[68] and **3n** in 62% yield. Interestingly, while cyclohexene remained inert, 3,4-dihydro-2*H*-pyran reacted within minutes, indicating that the reaction proceeds through a carbocation intermediate that is stabilized in the case of pyran through the oxocarbenium ion.[69] To further expand the substrate scope, we examined the reactivity of styrene with EWGs, unactivated alkenes, alkynes, conjugated systems, and sterically demanding α and β-substituted vinyl arenes (section 2.6, ESI†). None of these substrates underwent hydroamination even under forced conditions; the by-product, ether **4a**, was the only isolable product in most cases. This suggests that the initial protonation of alkenes to give a sterically unhindered yet stable carbocation intermediate is the primary requirement for successful hydroamination. Deprotection of the Fmoc group over the benzylic group was achieved under mild conditions using 2 equivalents of KOH to release free amine in an excellent yield. However, the amine was moderately sensitive; it was isolated as the corresponding oxalate salt (Table 2, **5a** & **5b**) in 58% and 80% yields from **3a** and **3b**, respectively.[70]

To understand the mechanism of the hydroamination reaction, we performed detailed ^{1}H, ^{19}F{^{1}H} NMR studies. C_6F_6 (0.1 M in $CDCl_3$) in a closed capillary was used as the reference (δ = −165 ppm) for ^{19}F{^{1}H} NMR. Independent ^{19}F{^{1}H} and ^{1}H NMR analysis with triflic acid and reaction monitoring experiments indicated the interaction between **2a** and **3a** with triflic acid. In ^{19}F{^{1}H} NMR, triflic acid showed a peak at −79.1 ppm (−81.2 ppm due to moisture absorption)[31,71] (Fig. 2a). The 1 : 1 ratio of triflic acid to Fmoc-NH_2 (**2a**) showed a peak at −81.7 ppm (Fig. 2b and Fig. S2, ESI†), and triflic acid to product **3a** showed a peak at −81.6 ppm (Fig. 2c and Fig. S3, ESI†). The reaction monitored by ^{19}F{^{1}H} NMR also shows an overlapping peak at −81.2 ppm, and no free triflic acid peak was observed at −79.1 ppm, which affirms the interaction (Fig. S4, ESI†).[31,72,73]

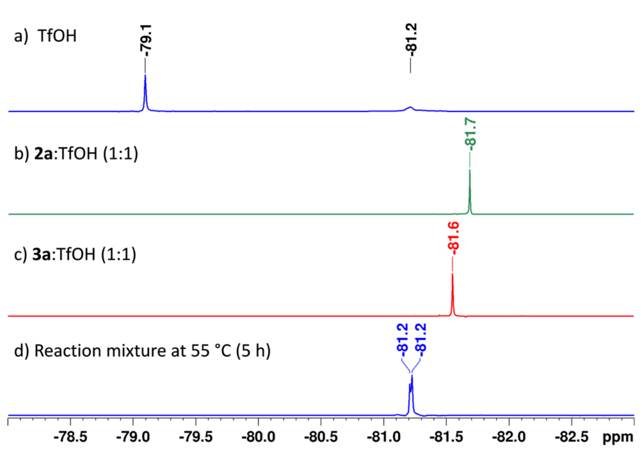


Fig. 2 ^{19}F{^{1}H} NMR analysis (the −78 to −83 ppm region was zoomed for clarity; C_6F_6 was used as a reference at −165 ppm) of TfOH along with Fmoc-NH_2 (**2a**), the hydroamination product (**3a**) and the reaction mixture after 5 h. For detailed reaction conditions and analysis, see the ESI.†

The ^{1}H NMR study of styrene with 10 mol% triflic acid showed immediate decomposition, probably due to polymerization (Fig. S5, ESI†).[74–76] The ^{1}H NMR experiment of triflic acid and Fmoc-NH_2 shows the disappearance of the NH peak at 4.71 ppm and a broad peak was observed with continuous drift (Fig. S6, ESI†). However, ^{1}H NMR analysis of **3a** with triflic acid showed substantial product decomposition in the presence of excess acid *via* benzyl group cleavage (Fig. S7, ESI†).[77–79] This experimental evidence corroborates the interaction between triflic acid with Fmoc-NH_2 and the product (**3a**). We believe that the interaction between triflic acid and **2a**/**3a** is the major factor preventing styrene polymerization.

We envisioned that variable time normalisation analysis (VTNA) kinetic studies developed by Burés and co-workers and product inhibition studies[80–84] could further confirm the interaction between triflic acid and **2a**/**3a**. The experiments for VTNA analysis were conducted using HPLC (see section 2.4, ESI†). The different excess experiments resulted in a reaction order value of 1 for styrene, 0.5 for Fmoc-NH_2, and 0.5 for triflic acid (Fig. 3A–C and Fig. S15–S17, ESI†). The fractional order for Fmoc-NH_2 and triflic acid pointed toward either catalyst deactivation or product inhibition.[82] To understand it further, a "same excess" kinetic experiment was conducted. A significant deviation from the standard reaction profile indicates product inhibition or catalyst deactivation (Fig. S14, ESI†). The deviation observed in the same excess experiments might be due to the interaction of the catalyst with Fmoc-NH_2 (**2a**) or with the product (**3a**).

To understand the reason for the selectivity of **3a** for over-alkylation, styrene (**1a**) was treated independently with **3a** and **3x** in the presence of triflic acid under optimized conditions as well as under forcing conditions, wherein **3a** and **3x** were recovered in near quantitative amounts (92% and 95%, respectively) (Fig. 3D1). We believe that the steric bulk of the Fmoc group may suppress over-alkylation. Next, we attempted to identify the nature of the intermediates involved in the hydroamination reaction. The potential of strong Brønsted acids to generate carbocations from styrene was previously reported by List and co-workers.[85,86] In addition, the exclusive formation of the Markovnikov product provides reliable evidence for the involvement of benzylic carbocation intermediates. To rule out the participation of radical intermediates, we repeated the experiment in the presence of TEMPO. Only a slight decline in the yield (<10% decrease) was observed, which ruled out radical pathways. Adding a base, triethylamine, inhibited the hydroamination reaction completely, suggesting that the Brønsted acid acted as the catalyst (Fig. 3D2). The optimized reaction was carried out in $CDCl_3$ instead of $CHCl_3$, and no H/D exchange between triflic acid and the solvent was observed (section 2.5 in the ESI†). Based on these NMR studies, VTNA kinetic studies, and control reactions, a plausible mechanism for the hydroamination reaction is proposed, as shown in Fig. 3E. The triflic acid dimer releases the monomer triflic acid in $CHCl_3$, as reported earlier.[71,72,87] It

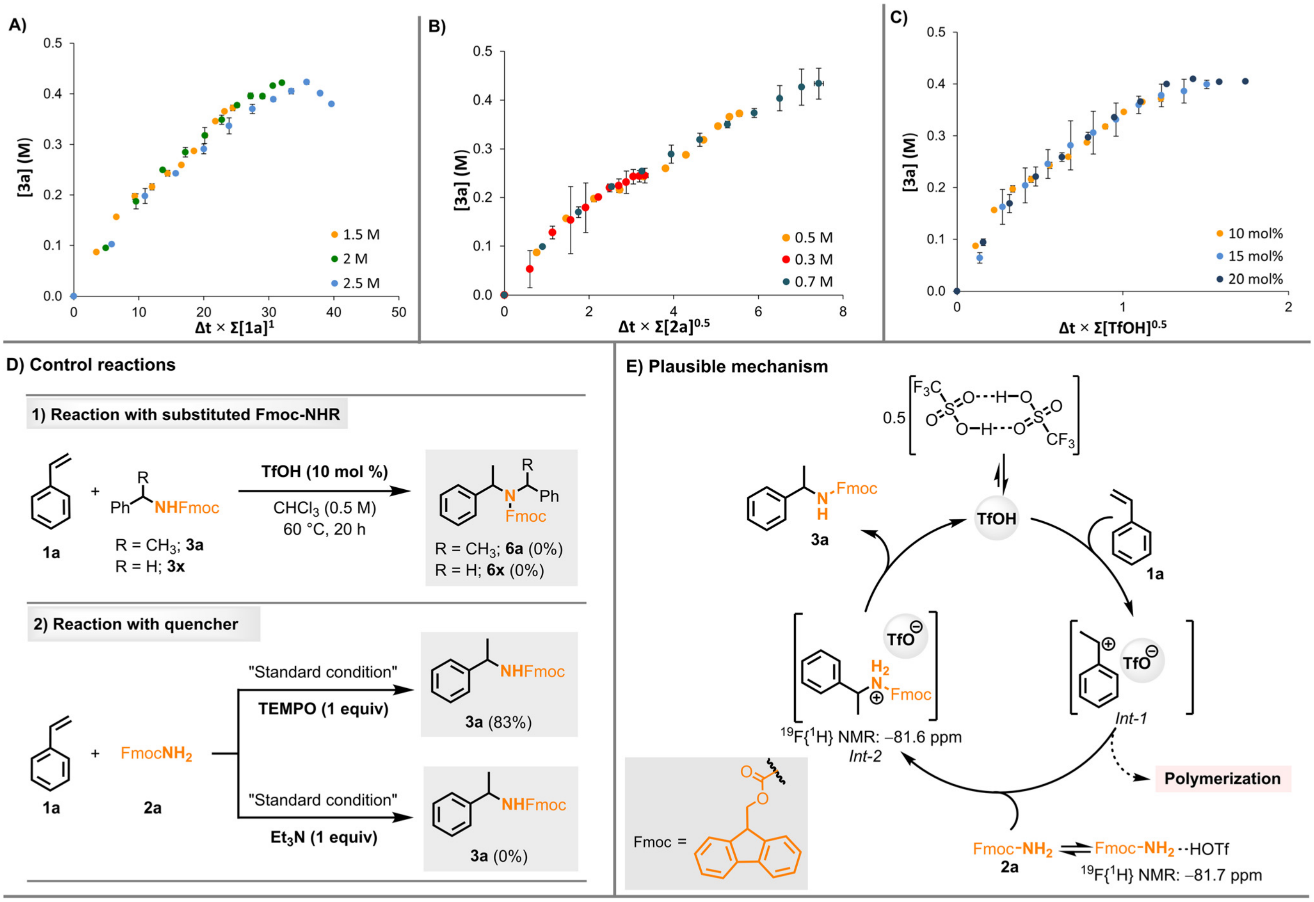


Fig. 3 VTNA plot of (A) styrene; (B) Fmoc-NH_2; and (C) TfOH (standard deviations are for two independent experiments). (D) Control reaction; standard conditions: styrene (3 equiv.), Fmoc-NH_2 (1 equiv.), TfOH (10 mol%), $CHCl_3$ (0.5 M), 60 °C, 5 h. (E) Plausible mechanism.

protonates styrene to form a benzylic carbocation intermediate that is stabilized by the triflate counter anion (**Int-1**, Fig. 3E). **Int-1** (styrene in the presence of triflic acid) may undergo cationic polymerization as observed in the control reaction without Fmoc-NH_2 (Fig. S5, ESI†). The intermediate (**Int-1**) undergoes a nucleophilic attack by Fmoc-NH_2, which results in the selective Markovnikov hydroamination product in the protonated form (**Int-2**, Fig. 3E), followed by deprotonation to yield the product and regenerate triflic acid. The free triflic acid and the protonated amines (**Int-2** or Fmoc-NH_2·TfOH) are likely in equilibrium. However, the equilibrium is largely shifted towards protonated amines, as we did not observe free TfOH in the $^{19}F\{^1H\}$ NMR of the reaction mixture. Hence, we speculate that a significantly low concentration of free TfOH prevents styrene polymerization.

Conclusions

In conclusion, we have demonstrated a scalable, metal-free intermolecular hydroamination reaction for the synthesis of Fmoc-protected 1-arylethylamines using triflic acid as the catalyst and Fmoc-NH_2 as the amine source. Various vinylarene substrates afforded good yields (up to 91%). Activated endocyclic alkenes also exhibited good reactivity. Subsequently, deprotection allowed access to the primary amine oxalate salt in excellent yield. Mechanistic investigations were performed using ^1H and $^{19}F\{^1H\}$ NMR techniques and showed the interaction between triflic acid and **2a**/**3a**. VTNA kinetic studies and product inhibition experiments further supported the transient hydrogen bonding interactions. This interaction prevented styrene polymerization; however, it was sufficient for hydroamination. The control reactions further supported the proposed mechanistic cycle along with the selective mono-alkylation. We believe that mechanistic investigation and the developed methodology will allow a comprehensive understanding of the hydroamination reaction of alkenes.

Author contributions

RM acquired the funding and supervised the project. ACS designed the project and performed the experiments. CS carried out mechanistic studies and reperformed a few substrate reactions. ACS prepared the first draft and wrote the

manuscript with contributions from CS and RM. All the authors approved the final version of the manuscript.

Data availability

The data supporting this article have been included as part of the ESI.† Materials and methods, detailed optimization table, experimental procedure, characterization data, NMR and VTNA analysis, and all NMR and HRMS spectra.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

The authors thank the Indian Institute of Technology Goa (IIT Goa) for the infrastructure and Santu Sinha for assisting in recording the VT NMR spectra. The authors thank the Max Planck Society (MPG) and Max-Planck-Institut für Kohlenforschung (MPI Kofo) for generous funding through the "Max Planck India partner group" project. The authors are grateful to Prof. Benjamin List for his support throughout this project. The authors thank the CAIF of IISER Berhampur for HRMS sample analysis.

References

1 R. Y. Liu and S. L. Buchwald, *Acc. Chem. Res.*, 2020, **53**, 1229–1243.
2 S. Ma and J. F. Hartwig, *Acc. Chem. Res.*, 2023, **56**, 1565–1577.
3 T. E. Müller, K. C. Hultzsch, M. Yus, F. Foubelo and M. Tada, *Chem. Rev.*, 2008, **108**, 3795–3892.
4 I. P. Beletskaya, C. Naájera and M. Yus, *Russ. Chem. Rev.*, 2020, **89**, 1074.
5 J. Huo, G. He, W. Chen, X. Hu, Q. Deng and D. Chen, *BMC Chem.*, 2019, **13**, 89.
6 K. C. Hultzsch, *Org. Biomol. Chem.*, 2005, **3**, 1819–1824.
7 F. Pohlki and S. Doye, *Chem. Soc. Rev.*, 2003, **32**, 104–114.
8 R. Severin and S. Doye, *Chem. Soc. Rev.*, 2007, **36**, 1407–1420.
9 J. Escorihuela, A. Lledós and G. Ujaque, *Chem. Rev.*, 2023, **123**, 9139–9203.
10 J. F. Hartwig, *Pure Appl. Chem.*, 2004, **76**, 507–516.
11 A. M. Johns, M. Utsunomiya, C. D. Incarvito and J. F. Hartwig, *J. Am. Chem. Soc.*, 2006, **128**, 1828–1839.
12 M. Nobis and B. Driessen-Hölscher, *Angew. Chem., Int. Ed.*, 2001, **40**, 3983–3985.
13 I. Bytschkov and S. Doye, *Eur. J. Org. Chem.*, 2003, 935–946.
14 A. Reyes-Sánchez, I. García-Ventura and J. J. García, *Dalton Trans.*, 2013, **43**, 1762–1768.
15 C. Lee, H.-J. Kang and S. Hong, *Chem. Sci.*, 2024, **15**, 442–457.
16 Y. Li and T. J. Marks, *J. Am. Chem. Soc.*, 1996, **118**, 9295–9306.
17 M. Patel, R. K. Saunthwal and A. K. Verma, *Acc. Chem. Res.*, 2017, **50**, 240–254.
18 A. N. Selikhov, A. V. Cherkasov, Y. V. Nelyubina and A. A. Trifonov, *ACS Catal.*, 2023, **13**, 12582–12590.
19 C. Lee, H.-J. Kang and S. Hong, *Chem. Sci.*, 2024, **15**, 442–457.
20 P. Colonna, S. Bezzenine, R. Gil and J. Hannedouche, *Adv. Synth. Catal.*, 2020, **362**, 1550–1563.
21 J. S. Bandar, M. T. Pirnot and S. L. Buchwald, *J. Am. Chem. Soc.*, 2015, **137**, 14812–14818.
22 Y. Yang, S.-L. Shi, D. Niu, P. Liu and S. L. Buchwald, *Science*, 2015, **349**, 62–66.
23 K. C. Hultzsch, *Adv. Synth. Catal.*, 2005, **347**, 367–391.
24 Y. Yang, N. I. Wong and P. Teo, *Eur. J. Org. Chem.*, 2015, 1207–1210.
25 D. A. Patton and M. E. Cremeens, *Rev. J. Chem.*, 2014, **4**, 1–20.
26 L. D. Julian and J. F. Hartwig, *J. Am. Chem. Soc.*, 2010, **132**, 13813–13822.
27 C. Lepori and J. Hannedouche, *Synthesis*, 2017, 1158–1167.
28 S. Bestgen and P. W. Roesky, in *Early Main Group Metal Catalysis*, John Wiley & Sons, Ltd, 2020, pp. 59–91.
29 J. G. Taylor, L. A. Adrio and K. K. (Mimi) Hii, *Dalton Trans.*, 2010, **39**, 1171–1175.
30 J. Chen, S. K. Goforth, B. A. McKeown and T. B. Gunnoe, *Dalton Trans.*, 2017, **46**, 2884–2891.
31 T. T. Dang, F. Boeck and L. Hintermann, *J. Org. Chem.*, 2011, **76**, 9353–9361.
32 S. Qin, Y. Liao, Q. Ni, R. Cao, A. S. C. Chan and L. Qiu, *J. Org. Chem.*, 2025, **90**, 1016–1023.
33 J. Penzien, R. Q. Su and T. E. Müller, *J. Mol. Catal. A: Chem.*, 2002, **182–183**, 489–498.
34 Y.-M. Wang, T.-T. Li, G.-Q. Liu, L. Zhang, L. Duan, L. Li and Y.-M. Li, *RSC Adv.*, 2014, **4**, 9517–9521.
35 B. List, *Chem. Rev.*, 2007, **107**, 5413–5415.
36 T. Akiyama and K. Mori, *Chem. Rev.*, 2015, **115**, 9277–9306.
37 N. Frank, M. Leutzsch and B. List, *J. Am. Chem. Soc.*, 2025, **147**, 7932–7938.
38 E. Bernoud, C. Lepori, M. Mellah, E. Schulz and J. Hannedouche, *Catal. Sci. Technol.*, 2015, **5**, 2017–2037.
39 Y.-D. Du, B.-H. Chen and W. Shu, *Angew. Chem., Int. Ed.*, 2021, **60**, 9875–9880.
40 P. Meena, A. M. Patel and A. K. Verma, *Chem. Commun.*, 2022, **58**, 8424–8427.
41 X. Cheng, Y. Xia, H. Wei, B. Xu, C. Zhang, Y. Li, G. Qian, X. Zhang, K. Li and W. Li, *Eur. J. Org. Chem.*, 2008, 1929–1936.
42 B. Schlummer and J. F. Hartwig, *Org. Lett.*, 2002, **4**, 1471–1474.
43 S. Guria, A. N. Volkov, R. Khudaverdyan, R. Van Lommel, R. Pan, C. G. Daniliuc, F. De Proft and U. Hennecke, *J. Am. Chem. Soc.*, 2024, **146**, 17180–17188.

44 F. C. Raps, A. Rivas-Souchet, C. M. Jones and T. K. Hyster, *Nature*, 2025, **637**, 362–368.
45 L. L. Anderson, J. Arnold and R. G. Bergman, *J. Am. Chem. Soc.*, 2005, **127**, 14542–14543.
46 S. Streiff and F. Jérôme, *Chem. Soc. Rev.*, 2021, **50**, 1512–1521.
47 J. I. van der Vlugt, *Chem. Soc. Rev.*, 2010, **39**, 2302–2322.
48 S. Park, J. Jeong, K. Fujita, A. Yamamoto and H. Yoshida, *J. Am. Chem. Soc.*, 2020, **142**, 12708–12714.
49 J. Urbiña-Alvarez, S. Rincón-Carvajal and D. Gamba-Sánchez, *Org. Biomol. Chem.*, 2023, **21**, 7036–7051.
50 Y. Brägger, A.-S. K. Paschke, N. Nasiri, B. B. Botlik, F. Felician and B. Morandi, *Science*, 2025, **387**, 1108–1114.
51 D. S. Surry and S. L. Buchwald, *J. Am. Chem. Soc.*, 2007, **129**, 10354–10355.
52 P. G. Alsabeh, R. J. Lundgren, R. McDonald, C. C. C. Johansson Seechurn, T. J. Colacot and M. Stradiotto, *Chem. – Eur. J.*, 2013, **19**, 2131–2141.
53 A. Borzenko, N. L. Rotta-Loria, P. M. MacQueen, C. M. Lavoie, R. McDonald and M. Stradiotto, *Angew. Chem.*, 2015, **127**, 3844–3848.
54 O. I. Afanasyev, E. A. Kuchuk, K. M. Muratov, G. L. Denisov and D. Chusov, *Eur. J. Org. Chem.*, 2021, 543–586.
55 X. Huang and S. L. Buchwald, *Org. Lett.*, 2001, **3**, 3417–3419.
56 D.-Y. Lee and J. F. Hartwig, *Org. Lett.*, 2005, **7**, 1169–1172.
57 S. Lee, M. Jørgensen and J. F. Hartwig, *Org. Lett.*, 2001, **3**, 2729–2732.
58 C. Sivarajan, S. Saha, S. Mulla and R. Mitra, *J. Org. Chem.*, 2024, **89**, 17021–17030.
59 S. Ma, C. K. Hill, C. L. Olen and J. F. Hartwig, *J. Am. Chem. Soc.*, 2021, **143**, 359–368.
60 S. Gandhi and B. List, *Angew. Chem., Int. Ed.*, 2013, **52**, 2573–2576.
61 S. K. Alamsetti, A.KÅ. Persson and J.-E. Bäckvall, *Org. Lett.*, 2014, **16**, 1434–1437.
62 R. Mansouri, Z. Aouf, S. Lakrout, M. Berredjem and N.-E. Aouf, *J. Braz. Chem. Soc.*, 2016, **27**, 546–550.
63 G. B. Fields, in *Peptide Synthesis Protocols*, ed. M. W. Pennington and B. M. Dunn, Humana Press, Totowa, NJ, 1995, pp. 17–27.
64 K. D. Collins, A. Rühling, F. Lied and F. Glorius, *Chem. – Eur. J.*, 2014, **20**, 3800–3805.
65 A. Chakraborty, R. Purkait, U. C. De, D. K. Maiti and S. Majumdar, *ChemistrySelect*, 2016, **1**, 2668–2672.
66 M. P. Doyle, A. B. Dyatkin and C. L. Autry, *J. Chem. Soc., Perkin Trans. 1*, 1995, 619–621.
67 A. F. Hegarty and L. N. Frost, *J. Chem. Soc., Perkin Trans. 2*, 1973, 1719–1728.
68 M. Sugiura, H. Hagio, R. Hirabayashi and S. Kobayashi, *J. Am. Chem. Soc.*, 2001, **123**, 12510–12517.
69 S. Lee, P. S. J. Kaib and B. List, *J. Am. Chem. Soc.*, 2017, **139**, 2156–2159.
70 H. R. Rajegowda, B. S. Chethan, R. U. R. Khan, N. K. Lokanath, P. A. Suchetan and P. R. Kumar, *J. Mol. Struct.*, 2023, **1272**, 134097.
71 M. P. Muñoz and G. C. Lloyd-Jones, *Eur. J. Org. Chem.*, 2009, 516–524.
72 E. S. Stoyanov, K.-C. Kim and C. A. Reed, *J. Phys. Chem. A*, 2004, **108**, 9310–9315.
73 G. A. Olah, T. Heiner, G. Rasul and G. K. S. Prakash, *J. Org. Chem.*, 1998, **63**, 7993–7998.
74 A. D. Allen, M. Rosenbaum, N. O. L. Seto and T. T. Tidwell, *J. Org. Chem.*, 1982, **47**, 4234–4239.
75 M. Chmelir, N. Cardona and G. V. Schulz, *Die Makromol. Chem.*, 1977, **178**, 169–185.
76 T. Kunitake and K. Takarabe, *Polym. J.*, 1978, **10**, 105–110.
77 G. A. Olah and M. Calin, *J. Am. Chem. Soc.*, 1968, **90**, 401–404.
78 H. Kurouchi, K. Kawamoto, H. Sugimoto, S. Nakamura, Y. Otani and T. Ohwada, *J. Org. Chem.*, 2012, **77**, 9313–9328.
79 F. Rombouts, D. Franken, C. Martínez-Lamenca, M. Braeken, C. Zavattaro, J. Chen and A. A. Trabanco, *Tetrahedron Lett.*, 2010, **51**, 4815–4818.
80 C. D.-T. Nielsen and J. Burés, *Chem. Sci.*, 2019, **10**, 348–353.
81 J. Burés, *Angew. Chem., Int. Ed.*, 2016, **55**, 16084–16087.
82 J. Burés, *Angew. Chem., Int. Ed.*, 2016, **55**, 2028–2031.
83 D. G. Blackmond, *Angew. Chem., Int. Ed.*, 2005, **44**, 4302–4320.
84 D. G. Blackmond, *J. Am. Chem. Soc.*, 2015, **137**, 10852–10866.
85 N. Tsuji, J. L. Kennemur, T. Buyck, S. Lee, S. Prévost, P. S. J. Kaib, D. Bykov, C. Farès and B. List, *Science*, 2018, **359**, 1501–1505.
86 V. K. Singh, C. Zhu, C. K. De, M. Leutzsch, L. Baldinelli, R. Mitra, G. Bistoni and B. List, *Science*, 2023, **382**, 325–329.
87 E. L. Varetti, *Spectrochim. Acta, Part A*, 1988, **44**, 733–738.