How to cite: *Angew. Chem. Int. Ed.* **2024**, *63*, e202408154
doi.org/10.1002/anie.202408154

Photocatalysis

Photocatalytic Asymmetric Acyl Radical Truce–Smiles Rearrangement for the Synthesis of Enantioenriched α-Aryl Amides

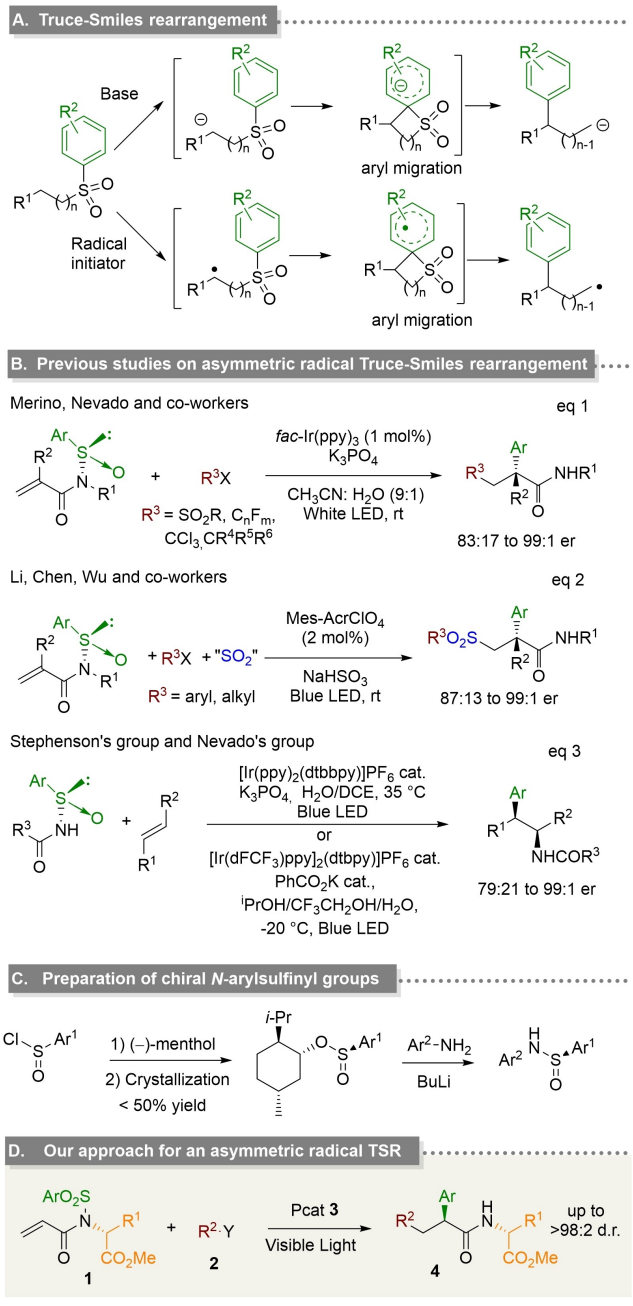
*Wei-Yang Ma, Matteo Leone, Etienne Derat, Pascal Retailleau, Chada Raji Reddy, Luc Neuville, and Géraldine Masson**

Abstract: The radical Truce–Smiles rearrangement is a straightforward strategy for incorporating aryl groups into organic molecules for which asymmetric processes remains rare. By employing a readily available and non-expensive chiral auxiliary, we developed a highly efficient asymmetric photocatalytic acyl and alkyl radical Truce–Smiles rearrangement of α-substituted acrylamides using tetrabutylammonium decatungstate (TBADT) as a hydrogen atom–transfer photocatalyst, along with aldehydes or C–H containing precursors. The rearranged products exhibited excellent diastereoselectivities (7:1 to >98:2 d.r.) and chiral auxiliary was easily removed. Mechanistic studies allowed understanding the transformation in which density functional theory (DFT) calculations provided insights into the stereochemistry-determining step.

Introduction

The Truce–Smiles rearrangement (TSR) is an aryl migration process that is conventionally an intramolecular nucleophilic aromatic substitution reaction of a nucleophilic carbanion with an electron-deficient aryl sulfone with the extrusion of sulfur dioxide (Scheme 1A).[1] Several variants of this

[*] W.-Y. Ma, M. Leone, P. Retailleau, Dr. L. Neuville, Dr. G. Masson
Institut de Chimie des Substances Naturelles CNRS, Univ. Paris-Saclay, 1 Avenue de la Terrasse, 91198 Gif-sur-Yvette Cedex, France
E-mail: geraldine.masson@cnrs.fr
Homepage: https://eq51power.wixsite.com/power
Dr. E. Derat
Sorbonne Université, Faculté des Sciences et Ingénierie, CNRS, Institut Parisien de Chimie Moléculaire, IPCM, 4 place Jussieu, 75005 Paris, France
Prof. C. R. Reddy
Department of Organic Synthesis & Process Chemistry CSIR—Indian Institute of Chemical Technology, Hyderabad 500007, India
Dr. L. Neuville, Dr. G. Masson
HitCat, Seqens-CNRS joint laboratory, Seqens'lab
8 rue de Rouen, 78440 Porcheville, France



Scheme 1. Truce–Smiles rearrangement.

anionic rearrangement have been described since the initial reported process,[2] providing a straightforward and robust method for installing aryl groups on various organic compounds. However, the requirement of an electron-deficient aryl group is a critical limitation of this polar migration.[3] This limitation was solved by the pioneering work of Speckamp on the radical TSR,[4] allowing the migration of electron-neutral and electron-rich aromatic rings from carbon-to-carbon radical through the formation of a spiro radical intermediate (Scheme 1A).[1,5] TSRs have been substantially improved while performing the rearrangement reaction under environmentally friendly radical conditions.[6,7]

The visible light–mediated photoredox catalysis[8] has made a significant contribution to the photocatalytic desulfonylative radical 1,4-aryl migrations, as reported by Stephenson,[9] Greaney,[10] Nevado,[11] Clayden,[12] Studer[13] and others.[14] Nevertheless, controlling the stereochemistry in these radical rearrangements remains a considerable challenge in part owing to the difficulty of establishing an appropriate chiral environment in the radical spirocyclization process. To date, only few examples of enantioselective radical TSRs have been reported based on the chirality transfer. Merino and Nevado et al. (Scheme 1B, eq 1).[15] were the first to report a photoredox catalytic protocol for converting enantiomerically pure *N*-arylsulfinylacrylamides into optically active 3-(arylsulfonyl)-2-arylpropanamides via a sequence involving the (i) addition of sulfonyl radicals, (ii) radical 1,4-aryl migration, and (iii) sulfur monoxide (SO) extrusion (eq 1). Further, they successfully used other radicals generated from haloalkanes or *N*-phthalimidoyl-oxalates. Following the same strategy, Li, Chen, and Wu et al. developed a photoinduced enantioselective synthesis of chiral sulfones bearing quaternary stereogenic carbon centers by the addition of in situ generated sulfonyl aryl radicals to chiral *N*-arylsulfinylacrylamides with a high degree of enantioselectivity and generality (Scheme 1B, eq 2).[16] Recent studies conducted by both the Stephenson[17] and Nevado[18] groups have independently found that enantioenriched arylsulfinylamides can effectively facilitate the asymmetric aminoarylation of alkenes under mild photoredox conditions through diastereoselective TSRs (Scheme 1B, eq 3). This method involves the generation of nitrogen radicals from arylsulfinylamides, which then react with alkene radical cations formed via photocatalytic oxidation. The resulting intermediates undergo diastereoselective Smiles-Truce rearrangement, ultimately leading to the formation of enantioenriched aminoarylation adducts. In each approach, the traceless sulfoxyle auxiliary was used to transfer both chiral information and the aryl group into the final rearranged product. Regardless of the significant progress,[19] both processes required the preparation of various individual enantioenriched *N*-arylsulfinyl groups to incorporate diverse aryl groups in the final structure, thereby requiring multistep syntheses with a chiral auxiliary *L*- or *D*-menthol (Scheme 1C).[20] In addition, while traceless chirality transfer occurs (loss of sulfoxyle), cleavage of the non-participating N-substituent also needs to be realized to access valuable acids or amides. Furthermore, the preparation of enantioenriched tertiary α-aryl amides have been less explored in comparison to their quaternary derivatives, probably because they are highly sensitive to racemization. Therefore, the development of new strategies to accomplish an asymmetric radical TSR would be desirable.

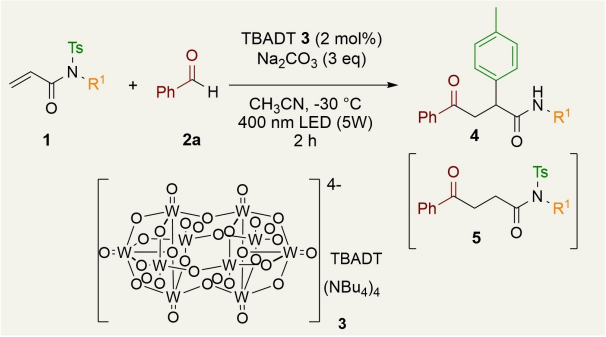
In that regard and inspired by these precedents, and on an early report of Intramolecular diastereospecific aryl radical migration,[21] we envisioned that the use of a non-transferable aryl-containing chiral auxiliary[22] attached to the nitrogen of *N*-arylsulfonylacrylamides might provide a practical strategy for the asymmetric synthesis of α-aryl amides. The chiral source had to be low-cost, readily available, and effectively cleavable in the final product with no apparent racemization; it had to be capable of promoting high diastereoselectivity during the 5-*ipso* cyclization step to make this transformation useful for synthetic chemists. In addition, a sustainable procedure had to be preferentially chosen to produce radicals and promote the radical 1,4-aryl migration. Herein, we report such approach involving the direct asymmetric desulfonylative radical 1,4-aryl migration of *N*-sulfonyl acrylamide derivatives via photoirradiation (Scheme 1D). A chiral amino acid auxiliary that is easy to incorporate and remove can transmit its chirality to the product with high to excellent diastereoselectivity. This novel radical-mediated aryl migration provides a new synthetic tool for the efficient preparation of enantioenriched α-aryl amides found in a range of pharmaceutical frameworks. Furthermore, these compounds can serve as key intermediates in drug synthesis.[23]

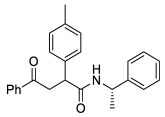
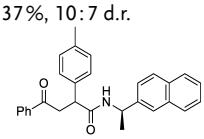
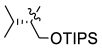
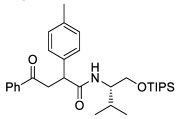
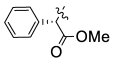
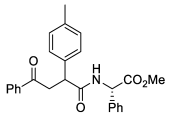
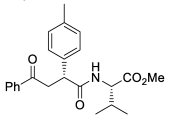
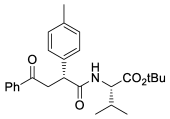
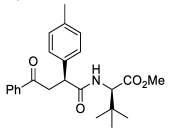
Results and Discussion

In recent years, significant efforts have been dedicated to advancing atom-economical radical formation under mild conditions. In this context, the direct photocatalyzed hydrogen atom transfer (HAT), involving the abstraction of a proton from a non-functionalized substrate, has proven to be effective. Specifically, tetrabutylammonium decatungstate (TBADT, $[W_{10}O_{32}]^{4-}$)[24,25] has demonstrated its high catalytic efficiency in performing HAT reactions and found extensive utility in the radical acylation of electron-deficient alkenes (Giese-type reactions).[26] Based on these previous studies and our recent work on the TBADT-catalyzed dearomative hydroacylation of indoles.[27] we reasoned that acyl radicals generated under these mild conditions would be suitable for our projected asymmetric radical 1,4-aryl migration. Although acyl radical–based TSRs have been relatively less developed[1,5] recent reports demonstrated the ability of acyl radicals to trigger the rearrangements effectively.[28] In addition, this photocatalyzed process would give access to optically enriched 2-aryl-4-oxobutanamide products, which are key intermediates for the synthesis of bioactive compounds.[1e,23,29] We initially verified the feasibility of acyl radical rearrangements of *N*-arylsulfonylacrylamides before developing the diastereoselective version.

Since the non-transferable group on nitrogen could affect the 1,4-aryl migration, a series of *N*-substituted *N*-tosylacrylamides was prepared and evaluated (Table 1, see

Table 1: Optimized Reaction Conditions and Effects upon Deviation.[a]

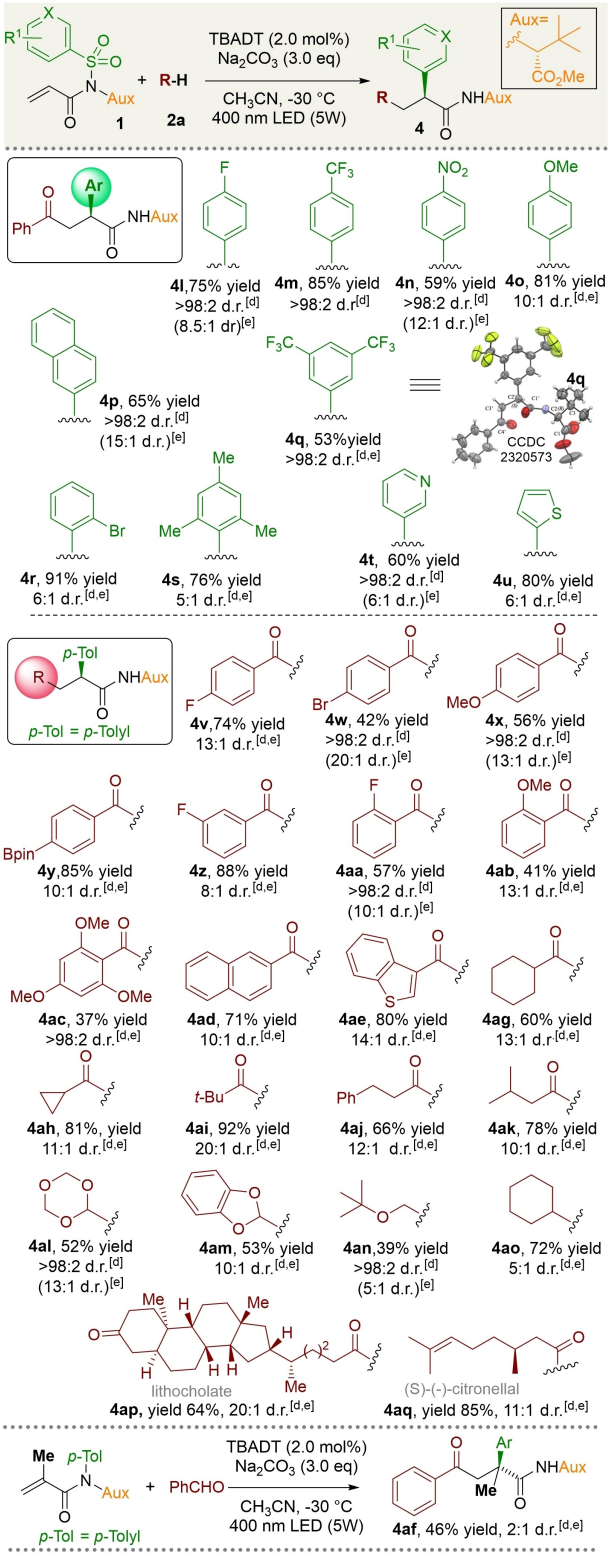


Entry	1, R^1	4 yield (%),[b] d.r.[c]
1	**1b**, t-Bu	**4b**, 84%
2	**1c**, i-Pr	**4c**, 86%
3	**1e**, 	 **4e**, 37%, 10:7 d.r.
4	**1f**, 	 **4f**, 20%, 5:2 d.r.
5	**1g**, 	 **4h**, 33%, 1.7:1 d.r.
6	**1h**, 	 **4h**, 33%, 1.7:1 d.r.
7	**1i**, 	 **4l**, 77%, 3:1 d.r.
8	**1j**, 	 **4j**, 70%, 3:1 d.r.
9	**1k**, 	 **4k**, 79%,[d] 13:1 d.r.
10[e]	**1k**	**4k**, 84%,[d] 11:1 d.r.
11[f]	**1k**	**4k**, –
12[g]	**1k**	**4k**, traces

[a] Reaction conditions: **1a** (0.1 mmol), **2** (0.2 mmol), **3** (0.02 mmol, 2 mol%) and Na_2CO_3 (0.3 mmol, 3 eq) in 1.0 mL of CH_3CN at −30 °C under argon, 18 h. [b] Yields refer to chromatographically pure compound. [c] d.r. values were determined by NMR analysis of crude products. [d] Yields refer to chromatographically pure major diastereomer (98:2 d.r.). [e] 1.0 mmol scale. [f] Without light. [g] Without TBADT **3** catalyst.

also table S1 and S2 in the Supporting Information).[30] Following our previous work,[27] we initially investigated the reaction of various acrylamides (**1a–d**) with benzaldehyde **2a** under conditions involving in the presence of 2 mol % of TBADT photocatalyst **3** and Na_2CO_3 in CH_3CN under visible-light irradiation. By adjusting solvents, bases, temperatures, concentrations, and the nature of the *N*-substituent of **1**, we found that reactions with *N-tert*-butyl or *N-iso*-propyl protected acrylamides **1b** and **1c** performed well at −30 °C with a substrate concentration of 0.025 M, yielding products **4b** and **4c** in 84 % and 86 % yield respectively (table 1, entries 1–2). Lowering the temperature was crucial in preventing the formation of non-rearranged product **5**, likely due to a competitive back-HAT reaction between reduced **3** ($[W_{10}O_{32}]^{4-}(H^+)$) and the alkyl radical generated after acyl radical addition to **1** prior to rearrangement. Based on these results, we further proceeded to investigate the asymmetric aryl migration using commercially-available and optically pure chiral auxiliaries. We first evaluated the acrylamide substrate bearing (*S*)-1-phenylethanamine, which has been extensively used in asymmetric synthesis.[22] The yield of the product using this substrate was lower than that of **4c** (entry 3, Table 1) with poor diastereoselectivity (10:7). Next, a series of chiral amines were evaluated such as (*R*)-1-(2-naphthyl)ethylamine and (*R*)-1-[(triisopropylsilyl)oxy]propan-2-amine (Entries 4–5, Table 1).[31] However, no improvement was observed. After these unsuccessful attempts, we turn our attention to other chiral amines. Recent work by Clayden et al. showed that imidazolidinones derived from chiral amino acids induced high diastereoselectivity in anionic 1,4-aryl migrations to form enantioenriched quaternary amino acids.[32] Inspired by this work, we decided to evaluate three amino acids as chiral auxiliaries.[33] Although low diastereoselectivity was observed with **1h** derived from (*S*)-methyl 2-amino-2-phenylacetate (entry 6, Table 1), an encouraging result was achieved with **1i** having (*S*)-valine methyl ester as the chiral auxiliary (entry 7). The replacement of methyl ester by *tert*-butyl ester did not affect the diastereoselectivity (entry 8). By contrast, the reaction with the chiral glycine derivative bearing a bulky group produced outstanding diastereoselectivity (13:1, entry 9).

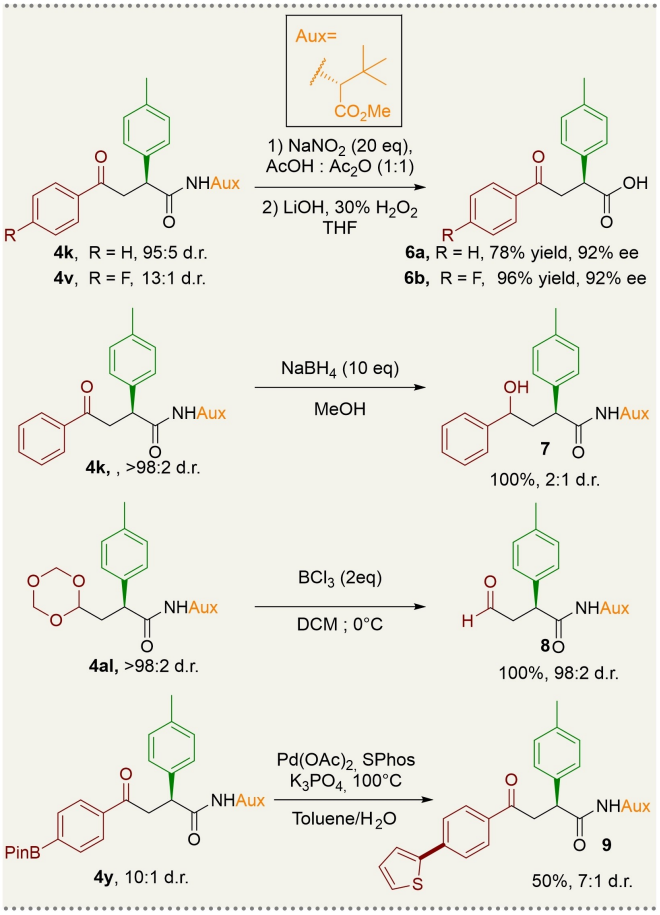
With conditions in hand, several *N*-(arylsulfonyl)acrylamides **1** bearing the chiral *D*-tert-butylglycine auxiliary were reacted with **2a** under the optimal reaction conditions, as summarized in Scheme 2. In general, the reaction did not seem to be sensitive to the electronic properties of the aromatic ring. The electron-withdrawing (F, CF_3, and NO_2) and electron-donating (OMe) groups at the para position of the aromatic ring were tolerated well, providing the desired rearranged products (**4l–o**) in high yields with up to 13:1 diastereomeric ratio (dr). Moreover, the reactions proceeded with electron-poor and -rich substituents at meta and ortho positions of the aromatic ring of **1** forming the corresponding products with high diastereoselectivity (**4p–r**). The challenging substrate bearing a di-ortho-substituted aromatic ring formed **4s** in high yield albeit with slightly lower diastereoselectivity. To our satisfaction, the acrylamides containing naphthyl or hetero-



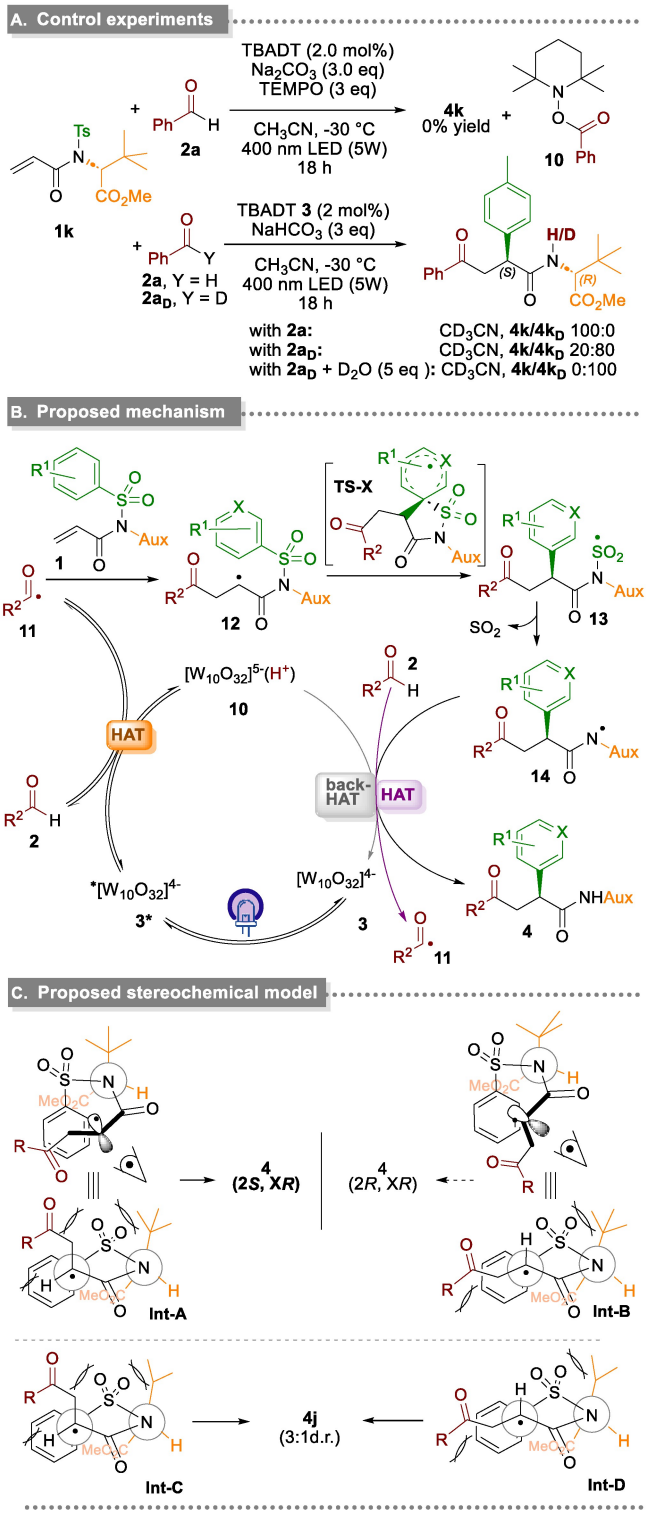
Scheme 2. Scope of HAT precursors in the asymmetric acyl and alkyl radical Truce–Smiles rearrangement [a] Reaction conditions: **1** (0.10 mmol), **2** (0.20 mmol), **3** (0.02 mmol, 2 mol %) and Na_2CO_3 (0.3 mmol, 3 eq) in 4.0 mL of CH_3CN under argon, 2 to 6 h. [b] Yields refer to chromatographically pure product **4**. [c] The absolute configuration of the entries was assigned by analogy to **4q**. [d] d.r. values of isolated product [e] d.r. values were determined by NMR analysis of crude products and on isolated **4**.

cycles such as pyridine and thiophene were able to undergo the TSR with moderate to high diastereoselectivity (**4p**, **4t** and **4u**).

Several aldehydes **2** were also examined in the presence of *N*-arylacrylamides **1k** (Scheme 2). Aromatic aldehydes having *para* or *meta* substituents on the phenyl ring were well tolerated affording the corresponding products (**4v–z**) with good to excellent diastereoselectivity. Interestingly, the pinacol boronic ester was tolerated allowing further functionalization of **4y** through cross-coupling reactions. Sterically hindered aromatic aldehydes *o*-anisaldehyde, *o*-fluorobenzaldehyde, and 2,4,6-trimethoxybenzaldehyde underwent the 1,4-aryl migration reaction to form **4aa**, **4ab**, and **4ac**, respectively, with high diastereomeric ratios (10:1 to >98:2) albeit with moderate yields. 2-Naphthaldehyde and a heteroaromatic aldehyde benzo[b]thiophene-3-carbaldehyde were compatible and yielded the corresponding TSR products **4ad** and **4ae**, respectively, in good yields and high diastereoselectivity. In addition, **4af** bearing a quaternary carbon showed a moderate yield and low diastereoselectivity. The predominant formation of the reduced product **5af** indicates that the reduction process proceeds faster than the spirocyclizative rearrangement.[34] Moreover, no diastereoselectivity was observed with *N*-arylsulfinylacrylamide bearing a methyl group at the β position, resulting in a complex mixture of diastereomers that could not be separated (see Supporting Information). It is noteworthy that aliphatic aldehydes also participated in the TSR and no decarbonylation was observed under these conditions.[35] Good to excellent diastereoselectivity was obtained with linear and branched aldehydes (**4ag–ak**). The TSR was extended to alkyl radicals generated by the HAT of alkanes. In particular, 1,4-aryl migrations with1,3,5-trioxane, 1,3-benzodioxole, tert-butylmethylether and cyclohexane were effectively achieved to form **4ak–4an**, in satisfactory yields with moderate to excellent diastereomeric ratios. We envisioned the possibility of performing the TSR on natural products (**4ap** and **4aq**) and for our delight obtained good yields and high diastereomeric ratios (11:1 and 20:1). This outcome has the potential to expand the applicability of this method for the late-stage functionalization of more complex molecules. We next conducted a reaction on a 1 mmol scale to illustrate the potential synthetic utility of the acyl-based TSR. The reaction afforded 2-aryl-4-oxobutanamide **4k** in similar yield and diastereoselectivity (entry 10, Table 1). Next, the removal of the chiral auxiliary from **4k** and **4v** was performed through a one-pot sequential two-step process involving selective nitration of the amide nitrogen atom followed by a saponification step, affording the desired 2-aryl-4-oxobutanoic acids **6a** and **6b** in high yields and with 92 % ee (after two steps) (Scheme 3).[36] The reduction of 2-aryl-4-oxobutanamide **4k** by $NaBH_4$ also provided alcohol **7** in quantitative yield as a mixture of diastereomers in the ratio of 2:1. Trioxane derivative **4al** was easily deprotected in quantitative yields to form the aldehyde **9** without erosion of diastereoselectivity (98:2);[37] additionally, a Suzuki–Miyaura cross coupling of **4y** with 2-iodo thiophene afforded the desired product **9** with moderate yields. The reaction was performed following reported conditions[14b] that re-



Scheme 3. Cleavage of chiral auxiliary and post-transformations.



Scheme 4. (A) Mechanistic study experiments. (B) Possible reaction mechanism (C) Stereochemical model.

sulted in a good diastereomeric ratio (7:1) even in presence of base and heating for a long period of time.

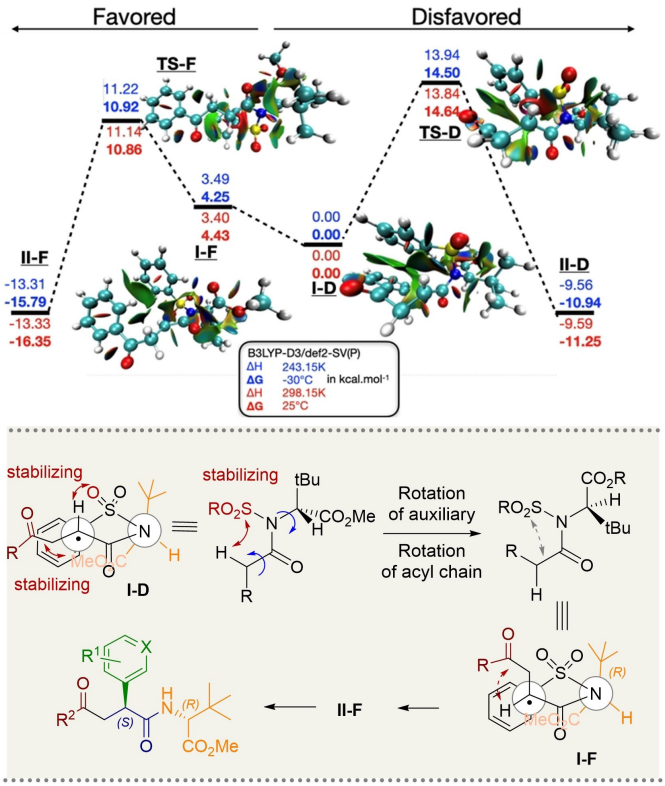
The mechanism of the current radical acyl TSR was investigated (Scheme 4). The addition of tetramethylpiperidine N-oxyl (TEMPO) as a radical quencher in the reaction medium completely inhibited the reaction, and the acyl-captured TEMPO **10** was identified via HRMS/MS (High-Resolution Mass Spectrometry/Mass Spectrometry). This experiment confirmed that acyl radicals were involved in the process. These acyl radicals were produced in the presence of both TBADT and the light source as indicated in Table 1 (Entries 9–10). Light on/off experiment (see Supporting Information, Figure S4) tended to indicate that that a radical chain reaction was quite unlikely. Nevertheless, based on Yoon's publication,[38] we performed quantum yield measurements to ascertain the pathway. As such, we calculate a quantum yield value of $\Phi = 17$ (see Supporting Information), indicating that the process occurred mainly through a radical chain propagation.

The presence of molecular oxygen was detrimental to the radical reaction, owing to the formation of an acid as the side product as observed in previous contribution.[27] Although degassing of CH_3CN mainly reduced its formation, the presence of a base was necessary to neutralize any trace of acid. Subsequently, when we performed the reaction of **1k** with benzaldehyde **2a** in deuterated acetonitrile, no deuteriation of **4k** was observed (Scheme 4A). Use of deuterated benzaldehyde **2aD** gave only 20 % D incorporation This result can be attributed to the rapid proton exchange occurring between the amino group of **4k** and

traces of water present under the reaction conditions (for more details, please see Supporting Information and Figure S6). Indeed, complete deuterium incorporation was observed when the reaction was performed in the presence of deuterated benzaldehyde **d-2a** and deuterium oxide (D_2O, near 100 %, Scheme 4A). This observation suggested that the hydrogen on nitrogen in the final product might originate from reduced TBADT. Finally, we conducted a competition experiment between two α,β-unsaturated amides. No cross-products were detected, which tends to indicate that intramolecular aryl migration is operative (for more details, please see Supporting Information and Figure S5) Based on these control experiments, we proposed a mechanism (Scheme 4B) initiated via the visible-light irradiation of TBADT generating a long-lived excited state [TBADT]* ($[W_{10}O_{32}]^{4-}$*, **3***). This exited species abstracted a hydrogen atom from aldehyde to form an acyl radical **11**. Consequently, the addition of **11** to α,β-unsaturated amide **1** formed the intermediate radical **12** that underwent a 1,5-ipso addition and a 1,4-aryl group migration through the spirocyclic dearomatized radical transition state **TS-X**, to lead to intermediate **13**. A subsequent desulfonylation step occurred to form the N-centered radical species **14**. Finally, TSR product **4** can be generated either after a back-HAT between **14** and $[W_{10}O_{32}]^{5-}(H^+)$,[39] or more likely via HAT directly from the aldehyde **2**. This chain-propagating pathway is mainly occurring based on the measured quantum yield.

The observed absolute stereochemistry as determined by X-ray crystallography (for more details, please see Supporting Information and Table S3, Figures S8, and S9) was tentatively explained from the mechanistic model proposed by Merino and Nevado[15] and others (Scheme 4C).[33] Based on prior DFT calculations performed for TSR, a 5-membered spirocyclic radical transition state, such as the one depicted as **TS-X**, can be assumed and could originate from two conformational intermediate **Int-A** and **Int-B**. The rearrangement involving **Int-A** would yield the observed (*S*)-product, aligning with Nevado's stereochemical proposal that steric minimization between the side chain and the transferable aryl group favors conformer **Int-A** over conformer **Int-B**. However, upon global inspection of conformational intermediate **A**, this favorable situation might not be as evident. Two additional steric interactions: (i) between the sulfone moiety and the bulky tert-butyl group and (ii) between the alkyl chain and the sulfone moiety needs to be considered. Accounting for these factors, intermediate **Int-B**, which will afford 2-aryl-4-oxobutanamide product 4 with the R configuration (through not experimentally observed), appears favorable as it reduces one of the steric interactions. Support for **Int-B** is strengthened by the fact that a significant loss of diastereoselectivity (1:3) was noted when L-valine was used as a chiral auxiliary. In this case, the corresponding intermediate **Int-C**, benefiting from reduced unfavorable steric interactions, exhibits less pronounced differences between the two intermediates **Int-C** and **Int-D**. Overall, steric analysis using a model did not perfectly align with the experimental results.

In order to clear these chemical intuitions, we decided to perform DFT calculations to elucidate the rationales behind the stereochemical determining step. The DFT calculations were performed with Turbomole V6.5 and were conducted at the UB3LYP/def2-SV(P) level, with the D3 dispersion correction. Before starting the DFT calculations, a conformational search was done with the crest software,[40] using the GFN2 semiempirical method.[41] Surprisingly, the most stable conformation found (**I-D**) is not the one leading to the major stereoisomer but to the minor one (Scheme 5). It can be observed, through the plotting of dispersion interactions by NCIplot, that this most stable conformer is establishing more π–π stacking and a specific interaction between the CH group bearing the radical and the SO_2 moiety of the tosyl group. From conformer **I-D**, the 1,5-ipso addition is characterized by the transition state **TS-D**. The calculated barrier at −30 °C is found to be 14.50 kcal/mol and the whole process is exothermic by −10.94 kcal/mol. On the other hand, the favored product (**II-F**) cannot be obtained from **I-D** but from a less stable conformer (**I-F**), which was found to be 4.25 kcal/mol above **I-D**. The main difference between **I-D** and **I-F** is the reduced amount of dispersion interactions especially between the aromatic groups (side chain and transferable aryl group). What can be seen as a penalty is in fact an advantage since it is not necessary to break down all the stabilizing interactions for



Scheme 5. Calculated Potential Energy Surface (UB3LYP-D3/def2-SV(P)) for the stereochemical determining step. NCIplot analyses are given for 1D, 1F, TS12D and TS12F. An insert containing a schematic representation of the proposed stereochemical pathway-based calculation is included.

reaching the corresponding 1,5-ipso addition transition state. The barrier for going to the favored product is found to be 10.92 kcal/mol (**TS-F**).

Conclusion

In summary, an efficient stereoselective photocatalytic radical TSR has been developed allowing building 2-aryl-4-oxo- or 2-aryl-4-substituted butanamides through an asymmetric 1,4-intramolecular aryl migration. The photocatalytic process uses aldehydes or C–H containing derivatives, simple low loading HAT-catalyst and *N*-arylsulfonylacrylamides to induce the tandem addition/migration sequence. We successfully thwarted the asymmetric problem by introducing a cheap, readily available and cleavable chiral auxiliary on the acrylamide partner. The relevance of this strategy was demonstrated by the asymmetric synthesis of various 2-aryl-(4-oxo)butanamide products in moderate to excellent yields. These highly functionalized α-arylamides can be used as valuable building blocks for accessing chemically diverse useful functionalized compounds. In addition, mechanistic insights, combining experimental studies and DFT calculations, unravel the intricate details of the stereochemistry-determining step.

Supporting Information

See the Supporting Information for synthetic procedures of starting materials and products, experimental details on the mechanistic study, as well as characterization data (NMR spectra). Additional references have been cited within the Supporting Information.[27a,42–53]

Acknowledgements

Financial support is provided by the Indo-French Centre for the Promotion of Advanced Research (IFCPAR/CEFIPRA 6505-N). W.-Y.M thanks CEFIPRA 6505-N for the postdoctoral fellowships. M.L. thanks the European Union Horizon 2020 innovation program for the Marie Skłodowska-Curie grant agreement no 956324 (PhotoReAct).

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: Truce–Smiles rearrangement · asymmetric photocatalysis · hydrogen atom transfer (HAT) · Chiral auxiliaries · aryl migration

[1] a) D. M. Whalley, M. F. Greaney, *Synthesis* **2022**, *54*, 1908; b) C. Holden, M. F. Greaney, *Chem. Eur. J.* **2017**, *23*, 8992; c) A. R. P. Henderson, J. R. Kosowan, T. E. Wood, *Can. J. Chem.* **2017**, *95*, 483; d) T. J. Snape, *Chem. Soc. Rev.* **2008**, *37*, 24528; e) N. G. Simonian, A. Guérinot, J. Cossy, *Synthesis* **2023**, *55*, 1616.

[2] Selected examples: a) R. Henriques, *Ber. Dtsch. Chem. Ges.* **1894**, *27*, 2993; b) O. Hinsberg, *J. Prakt. Chem.* **1914**, *90*, 345; c) L. A. Warren, S. Smiles, *J. Chem. Soc.* **1930**, 1327; d) A. A. Levy, H. C. Rains, S. Smiles, *J. Chem. Soc.* **1931**, 3264; e) W. H. Urry, M. S. Kharasch, *J. Am. Chem. Soc.* **1944**, *66*, 1438; f) W. E. Truce, E. M. Kreider, W. W. Brand, *Org. React.* **1970**, 99.

[3] Neutral aromatic ring can undergo aryl migration when strong bases are used, see: W. E. Truce, W. J. Ray, O. L. Norman, D. B. Eickemeyer, *J. Am. Chem. Soc.* **1958**, *80*, 3625.

[4] a) R. Loven, W. N. Speckamp, *Tetrahedron Lett.* **1972**, *13*, 1567; b) W. B. Motherwell, A. M. K. Pennell, *J. Chem. Soc. Chem. Commun.* **1991**, *13*, 877; c) M. Tada, H. Shijima, M. Nakamura, *Org. Biomol. Chem.* **2003**, *14*, 2499; d) H. Wieland, *Ber. Dtsch. Chem. Ges.* **1911**, *44*, 2550.

[5] a) A. R. P. Henderson, J. R. Kosowan, T. E. Wood, *Can. J. Chem.* **2017**, *95*, 483; b) A. R. Allen, E. A. Noten, C. R. J. Stephenson, *Chem. Rev.* **2022**, *122*, 2695; c) X. Wu, C. Zhu, *Acc. Chem. Res.* **2020**, *53*, 1620; d) W. Li, W. Xu, J. Xie, S. You, C. Zhu, *Chem. Soc. Rev.* **2018**, *47*, 654; e) Z.-M. Chen, X.-M. Zhang, Y.-Q. Tu, *Chem. Soc. Rev.* **2015**, *44*, 5220; f) M. Huynh, M. De Abreu, P. Belmont, E. Brachet, *Chem. Eur. J.* **2021**, *27*, 3581.

[6] a) M. Pudlo, I. Allart-Simon, B. Tinant, S. Gerard, J. Sapi, *Chem. Commun.* **2012**, *48*, 2442; b) W. Kong, M. Casimiro, E. Merino, C. Nevado, *J. Am. Chem. Soc.* **2013**, *135*, 14480; c) W. Kong, M. Casimiro, N. Fuentes, E. Merino C Nevado, *Angew. Chem. Int. Ed.* **2013**, *52*, 13086; *Angew. Chem.* **2013**, *125*, 13328; d) W. Kong, E. Merino, C. Nevado, *Angew. Chem. Int. Ed.* **2014**, *53*, 5078; *Angew. Chem.* **2014**, *126*, 5178; e) W. Kong, M. Casimiro, N. Fuentes, E. Merino C Nevado, *Angew. Chem. Int. Ed.* **2015**, *54*, 2487; *Angew. Chem.* **2015**, *127*, 2517; f) N. Fuentes, W. Kong, L. Fernández-Sánchez, E. Merino, C. Nevado, *J. Am. Chem. Soc.* **2015**, *137*, 964.

[7] a) M. Pudlo, I. Allart-Simon, B. Tinant, S. Gerard, J. Sapi, *Chem. Commun.* **2012**, *48*, 2442; b) Z. He, P. Tan, C. Ni, J. Hu, *Org. Lett.* **2015**, *17*, 1838; c) K. Liu, L.-C. Sui, Q. Jin, D.-Y. Li, P.-N. Liu, *Org. Chem. Front.* **2017**, *4*, 1606; d) N. Gillaizeau-Simonian, E. Barde, A. Guérinot, J. Cossy, *Chem. Eur. J.* **2021**, *27*, 4004; e) E. Bacqué, M. El Qacemi, S. Z. Zard, *Org. Lett.* **2005**, *7*, 3817.

[8] Selected reviews on photoredox catalysts: a) C. K. Prier, D. A. Rankic, D. W. MacMillan, *Chem. Rev.* **2013**, *113*, 5322; b) D. P. Hari, B. König, *Chem. Commun.* **2014**, *50*, 6688; c) M. D. Kärkäs, B. S. Matsuura, C. R. J. Stephenson, *Science* **2015**, *349*, 1285; d) A. Angnes, Z. Li, C. R. D. Correia, G. B. Hammond, *Org. Biomol. Chem.* **2015**, *13*, 9152; e) T. Courant, G. Masson, *J. Org. Chem.* **2016**, *81*, 6945; f) M. H. Shaw, J. Twilton, D. W. C. MacMillan, *J. Org. Chem.* **2016**, *81*, 6898; g) N. A. Romero, D. A. Nicewicz, *Chem. Rev.* **2016**, *116*, 10075; h) D. M. Arias-Rotondo, J. K. McCusker, *Chem. Soc. Rev.* **2016**, *45*, 5803; i) D. Ravelli, S. Protti, M. Fagnoni, *Chem. Rev.* **2016**, *116*, 9850; j) K. L. Skubi, T. R. Blum, T. P. Yoon, *Chem. Rev.* **2016**, *116*, 10035; k) L. Marzo, S. K. Pagire, O. Reiser, B. Konig, *Angew. Chem. Int. Ed.* **2018**, *57*, 10034; *Angew. Chem.* **2018**, *130*, 10188; l) I. K. Sideri, E. Voutyritsa, C. G. Kokotos,

Org. Biomol. Chem. **2018**, *16*, 4596; m) S. Fukuzumi, Y.-M. Lee, W. Nam, *ChemSusChem* **2019**, *12*, 3931; n) G. E. M. Crisenza, P. Melchiorre, *Nat. Commun.* **2020**, *11*, 803; o) J. D. Bell, J. A. Murphy, *Chem. Soc. Rev.* **2021**, *50*, 9540.

[9] a) J. J. Douglas, H. Albright, M. J. Sevrin, K. P. Cole, C. R. J. Stephenson, *Angew. Chem. Int. Ed.* **2015**, *54*, 14898; *Angew. Chem.* **2015**, *127*, 15111; b) D. Alpers, K. P. Cole, C. R. J. Stephenson, *Angew. Chem. Int. Ed.* **2018**, *57*, 12167; *Angew. Chem.* **2018**, *130*, 12344; c) T. M. Monos, R. C. McAtee, C. R. J. Stephenson, *Science* **2018**, *361*, 1369; d) A. R. Allen, J.-F. Poon, R. C. McAtee, N. B. Watson, D. A. Pratt, C. R. J. Stephenson, *ACS Catal.* **2022**, *12*, 8511.

[10] a) D. M. Whalley, H. A. Duong, M. F. Greaney, *Chem. Eur. J.* **2018**, *25*, 1927; b) D. M. Whalley, J. Seayad, M. F. Greaney, *Angew. Chem. Int. Ed.* **2021**, *60*, 22219; *Angew. Chem.* **2021**, *133*, 22393; c) J. Yan, H. W. Cheo, W. K. Teo, X. Shi, H. Wu, S. B. Idres, L.-W. Deng, J. Wu, *J. Am. Chem. Soc.* **2020**, *142*, 11357.

[11] W. Shu, A. Genoux, Z. Li, C. Nevado, *Angew. Chem. Int. Ed.* **2017**, *56*, 10521; *Angew. Chem.* **2017**, *129*, 10660.

[12] R. Abrams, J. Clayden, *Angew. Chem. Int. Ed.* **2020**, *59*, 11600; *Angew. Chem.* **2020**, *132*, 11697.

[13] a) F. W. Friese, C. Mück-Lichtenfeld, A. Studer, *Nat. Commun.* **2018**, *9*, 2808; b) N. Radhoff, A. Studer, *Angew. Chem. Int. Ed.* **2021**, *60*, 3561; *Angew. Chem.* **2021**, *133*, 3608.

[14] a) R. Ruzi, J. Ma, X. A. Yuan, W. Wang, S. Wang, M. Zhang, J. Dai, J. Xie, C. Zhu, *Chem. Eur. J.* **2019**, *25*, 1272; b) X. Gao, C. Li, Y. Yuan, X. Xie, Z. Zhang, *Org. Biomol. Chem.* **2020**, *18*, 263; c) Y. Li, B. Hu, W. Dong, X. Xie, J. Wan, Z. Zhang, *J. Org. Chem.* **2018**, *81*, 7036; d) C.-P. Chuang, Y.-Y. Chen, T.-H. Chuang, C.-H. Yang, *Synthesis* **2018**, *49*, 1273; e) J. Lan, K. Lin, X. Zhanga, T. Zhu, *Green Chem.* **2022**, *24*, 6138; f) C. He, K. Zhang, D.-N. Wang, M. Wang, Y. Niu, X.-H. Duan, L. Liu, *Org. Lett.* **2022**, *24*, 2767; g) M. De Abreu, P. Belmont, E. Brachet, *J. Org. Chem.* **2021**, *86*, 3758; h) S. Wei, S. Le, Z. Lei, L. Zhou, Z. Zhang, W. R. Dolbier Jr, *Org. Biomol. Chem.* **2022**, *20*, 2064; i) C. Faderl, S. Budde, G. Kachkovskyi, D. Rackl, O. Reiser, *J. Org. Chem.* **2018**, *83*, 12192; j) J. Li, Z. Liu, S. Wu, Y. Chen, *Org. Lett.* **2019**, *21*, 2077; k) S.-F. Wang, X.-P. Cao, Y. Li, *Angew. Chem. Int. Ed.* **2017**, *56*, 13809; *Angew. Chem.* **2017**, *129*, 13997; l) R. Ruzi, J. Ma, X. Yuan, W. Wang, S. Wang, M. Zhang, J. Dai, J. Xie, C. Zhu, *Chem. Eur. J.* **2019**, *25*, 12724; m) Z.-H. Xia, L. Dai, Z.-H. Gao, S. Ye, *Chem. Commun.* **2020**, *56*, 1525.

[15] C. Hervieu, M. S. Kirillova, T. Suárez, M. Müller, E. Merino, C. Nevado, *Nat. Chem.* **2021**, *13*, 327.

[16] J. Huang, F. Liu, L.-H. Zeng, S. Li, Z. Chen, J. Wu, *Nat. Commun.* **2022**, *13*, 7081.

[17] E. A. Noten, C. H. Ng, R. M. Wolesensky, C. R. J. Stephenson, *Nat. Chem.* **2024**, *16*, 599.

[18] C. Hervieu, M. S. Kirillova, Y. Hu, S. Cuesta-Galisteo, E. Merino, C. Nevado, *Nat. Chem.* **2024**, *16*, 607.

[19] a) Z. Wu, X. Zhang, N. Xu, X. Liu, X. Feng, *ACS Catal.* **2023**, *13*, 815; b) R.-Q. Jiao, Y.-N. Ding, M. Li, W.-Y. Shi, X. Chen, Z. Zhang, W.-X. Wei, X.-S. Li, X.-P. Gong, Y.-Y. Luan, X.-Y. Liu, Y.-M. Liang, *Org. Lett.* **2023**, *25*, 33; c) K. Guo, C. Han, X. Xie, B. Chen, S. Cao, W. Yuan, K. Chen, F. Liu, Y. Zhu, *Chem. Commun.* **2022**, *58*, 13353; d) J. Aubé, X. Peng, Y. Wang, F. Takusagawa, *J. Am. Chem. Soc.* **1992**, *114*, 5466.

[20] a) X. Zhang, F. Wang, C.-H. Tan, *JACS Au* **2023**, *3*, 700; b) E. Wojaczyńska, J. Wojaczyński, *Chem. Rev.* **2020**, *120*, 4578; c) H. B. Kagan, F. Rebiere, *Synlett* **1990**, 643.

[21] H. J. Köhler, W. N. Speckamp, *J. Chem. Soc. Chem. Commun.* **1980**, 142.

[22] a) G. Diaz-Muñoz, I. L. Miranda, S. K. Sartori, D. C. De Rezende, M. Alves Nogueira Diaz, *Chirality* **2019**, *31*, 776; b) Y. Gnas, F. Glorius, *Synthesis* **2006**, *12*, 1899.

[23] a) J. W. Dalley, B. J. Everitt, *Semin. Cell Dev. Biol.* **2009**, *20*, 403; b) A. Zhang, J. L. Neumeyer, R. J. Baldessarini, *Chem. Rev.* **2007**, *107*, 274; c) P. Jones, K. Wilcoxen, M. Rowley, C. Toniatti, *J. Med. Chem.* **2015**, *58*, 3302; d) A. Beccari, A. Aramini, G. Bianchini, A. Moriconi, *Preparation of 2-aryl-propionamide derivatives useful as bradykinin receptor antagonists.* WO2011051375 A1 **2011**.

[24] a) C. Raviol, S. Protti, D. Ravelli, M. Fagnoni, *Green Chem.* **2019**, *21*, 748; b) Y.-L. Liu, Y.-J. Ouyang, H. Zheng, H. Liu, W.-T. Wei, *Chem. Commun.* **2021**, *57*, 6111; c) D. Ravelli, S. Protti, M. Fagnoni, *Acc. Chem. Res.* **2016**, *49*, 2232; d) V. D. Waele, O. Poizat, M. Fagnoni, A. Bagno, D. Ravelli, *ACS Catal.* **2016**, *6*, 7174; e) D. Ravelli, M. Fagnoni, T. Fukuyama, T. Nishikawa, I. Ryu, *ACS Catal.* **2018**, *8*, 701; f) K. Suzuki, N. Mizuno, K. Yamaguchi, *ACS Catal.* **2018**, *8*, 10809; g) G. Laudadio, S. Govaerts, Y. Wang, D. Ravelli, H. F. Koolman, M. Fagnoni, S. W. Djuric, T. Noël, *Angew. Chem. Int. Ed.* **2018**, *57*, 4078; *Angew. Chem.* **2018**, *125*(130), 4142; h) I. B. Perry, T. F. Brewer, P. J. Sarver, D. M. Schultz, D. A. DiRocco, D. W. C. MacMillan, *Nature* **2018**, *560*, 70; i) Y. Xiaoya, Y. Guoping, Y. Bing, *Chin. J. Org. Chem.* **2020**, *40*, 3620; j) Z.-Y. Dai, Z.-S. Nong, S. Song, P.-S. Wang, *Org. Lett.* **2021**, *23*, 3157; k) V. Murugesan, A. Ganguly, A. Karthika, R. Rasappan, *Org. Lett.* **2021**, *23*, 5389; l) F. Raymenants, T. M. Masson, J. Sanjosé-Orduna, T. Noël, *Angew. Chem. Int. Ed.* **2023**, *62*, e202308563; *Angew. Chem.* **2023**, *135*, e20230856; m) M. Leone, J. P. Milton, D. Gryko, L. Neuville, G. Masson, *Chem. Eur. J.* **2024**, *30*, e202400363.

[25] a) L. Capaldo, D. Ravelli, M. Fagnoni, *Chem. Rev.* **2022**, *122*, 1875; b) H. Cao, X. Tang, H. Tang, Y. Yuan, J. Wu, *Chem. Catal.* **2021**, *1*, 523; c) J. M. Mayer, *Acc. Chem. Res.* **2011**, *44*, 36; d) L. Capaldo, D. Ravelli, *Eur. J. Org. Chem.* **2017**, *15*, 2056.

[26] a) S. Esposti, D. Dondi, M. Fagnoni, A. Albini, *Angew. Chem. Int. Ed.* **2007**, *46*, 2531; *Angew. Chem.* **2007**, *119*, 2583; b) S. Protti, D. Ravelli, M. Fagnoni, A. Albini, *Chem. Commun.* **2009**, 7351; c) D. Ravelli, M. Zema, M. Mella, M. Fagnoni, A. Albini, *Org. Biomol. Chem.* **2010**, *8*, 4158; d) I. Ryu, A. Tani, T. Fukuyama, D. Ravelli, S. Montanaro, M. Fagnoni, *Org. Lett.* **2013**, *15*, 2554; e) F. Bonassi, D. Ravelli, S. Protti, M. Fagnoni, *Adv. Synth. Catal.* **2015**, *357*, 3687.

[27] a) T. Varlet, D. Bouchet, E. Van Elslande, G. Masson, *Chem. Eur. J.* **2022**, *28*, e202201707; b) E. Montinho-Inacio, D. Bouchet, D. W.-Y. Ma, L. Neuville, G. Masson, *Eur. J. Org. Chem.* **2024**, e202400248.

[28] a) J. Yan, H. W. Cheo, W. K. Teo, X. Shi, H. Wu, S. B. Idres, L.-W. Deng, J. Wu, *J. Am. Chem. Soc.* **2020**, *142*, 11357; b) Q. Dou, C.-J. Li, H. Zeng, *Chem. Sci.* **2011**, *11*, 5740.

[29] J. L. Zigterman, J. C. S. Woo, S. D. Walker, J. S. Tedrow, C. J. Borths, E. E. Bunel, M. M. Faul, *J. Org. Chem.* **2007**, *72*, 8870.

[30] S. Tang, L. Yuan, Y.-L. Deng, Z.-Z. Li, L.-N. Wang, G.-X. Huang, R.-L. Sheng, *Tetrahedron Lett.* **2017**, *58*, 329.

[31] K. Osaka, M. Sugie, M. Yamawaki, T. Morita, Y. Yoshimi, *J. Photochem. Photobiol. A* **2016**, *317*, 50.

[32] a) R. C. Atkinson, F. Fernández-Nieto, J. Mas Rosellõ, J. Clayden, *Angew. Chem. Int. Ed.* **2015**, *54*, 8961; b) S. M. Wales, R. K. Saunthwal, J. Clayden, *Acc. Chem. Res.* **2022**, *55*, 1731.

[33] E. P. Carreiro, A. J. Burke, *Amino Acids as Chiral Building Blocks. In Chiral Building Blocks in Asymmetric Synthesis* (eds E. Wojaczyńska and J. Wojaczyński) **2022**.

[34] To account for the observed decrease in diastereoselectivity for **4af**, see the Supporting Information.

[35] To prevent the decarbonylation of pivaldehyde, the reaction should be conducted at −30 °C, see also references 27.

[36] Enrichment during the transformation is possible, but difference between observed selectivity in starting material and product most likely arrive from the precision of the method

used: ee of product is measured by HPLC while d.r. of precursor arose from NMR integration of crude which is less precise.
[37] a) E. Azzi, G. Ghigo, S. Parisotto, F. Pellegrino, E. Priola, P. Renzi, A. Deagostino, *J. Org. Chem.* **2021**, *86*, 3300; b) H. Khartabil, L. Doudet, I. Allart-Simon, M. Ponce-Vargas, S. Gérard, E. Hénon, *Org. Biomol. Chem.* **2020**, *18*, 6840; c) J. M. Ganley, M. Christensen, Y.-h. Lam, Z. i. Peng, A. R. Angeles, C. S. Yeung, *Org. Lett.* **2018**, *20*, 5752.
[38] M. A. Cismesia, T. P. Yoon, *Chem. Sci.* **2015**, *6*, 5426.
[39] In this final step, we can also propose a formal HAT involving disproportionation of 10 that undergoes a single-electron reduction of amidyl radical **14** followed by protonation of the resulting anion: D. Ravelli, M. Fagnoni, T. Fukuyama, T. Nishikawa, I. Ryu, *ACS Catal.* **2018**, *8*, 701 and references therein.
[40] P. Pracht, F. Bohle, S. Grimme, *Phys. Chem. Chem. Phys.* **2020**, *22*, 7169.
[41] C. Bannwarth, S. Ehlert, S. Grimme, *J. Chem. Theory Comput.* **2019**, *15*, 1652.
[42] N. Zhang, C. Zhang, X. Hu, X. Xie, Y. Liu, *Org. Lett.* **2021**, *23*, 6004.
[43] M. Lemmerer, H. Zhang, A. J. Fernandes, T. Fischer, M. Miesskes, Y. Xiao, N. Maulide, *Angew. Chem. Int. Ed.* **2022**, *61*, e202207475; *Angew. Chem.* **2022**, *134*, e202207475.
[44] J. Harnedy, M. D. Hareram, G. J. Tizzard, S. J. Coles, L. C. Morrill, *Chem. Commun.* **2021**, *57*, 12643.
[45] S. Protti, D. Ravelli, M. Fagnoni, A. Albini, *Chem. Commun.* **2009**, *47*, 7351.
[46] a) C. G. Hatchard, C. A. Parker, *Proc. Roy. Soc. (London)* **1956**, *A235*, 518; b) J. Rabani, H. Mamane, D. Pousty, J. R. Bolton, *Photochem. Photobiol.* **2021**, *97*, 873.
[47] M. A. Cismesia, T. P. Yoon, *Chem. Sci.* **2015**, *6*, 5426.
[48] D. A. Evans, P. H. Carter, C. J. Dinsmore, J. C. Barrow, J. L. Katz, D. W. Kung, *Tetrahedron Lett.* **1997**, *38*, 4535.
[49] D. Uraguchi, Y. Ueki, T. Ooi, *Chem. Sci.* **2012**, *3*, 842–845. https://doi.org/10.1039/C1SC00678A.
[50] H. R. Lee, S. Y. Kim, M. J. Park, Y. S. Park, *Org. Biomol. Chem.* **2021**, *19*, 7655.
[51] J. M. Ganley, M. Christensen, Y.-h. Lam, Z. Peng, A. R. Angeles, C. S. Yeung, *Org. Lett.* **2018**, *20*, 5752.
[52] M. Prieto, S. Mayor, P. Lloyd-Williams, E. Giralt, *J. Org. Chem.* **2009**, *74*, 9202.
[53] A. M. Davies, S. S. Londhe, E. E. Smith, J. A. Tunge, *Org. Lett.* **2023**, *25*, 863.

Manuscript received: April 30, 2024
Accepted manuscript online: June 18, 2024
Version of record online: August 6, 2024