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TBADT-Mediated Photocatalytic Stereoselective Radical Alkylation of Chiral N-Sulfinyl Imines: Towards Efficient Synthesis of Diverse Chiral Amines

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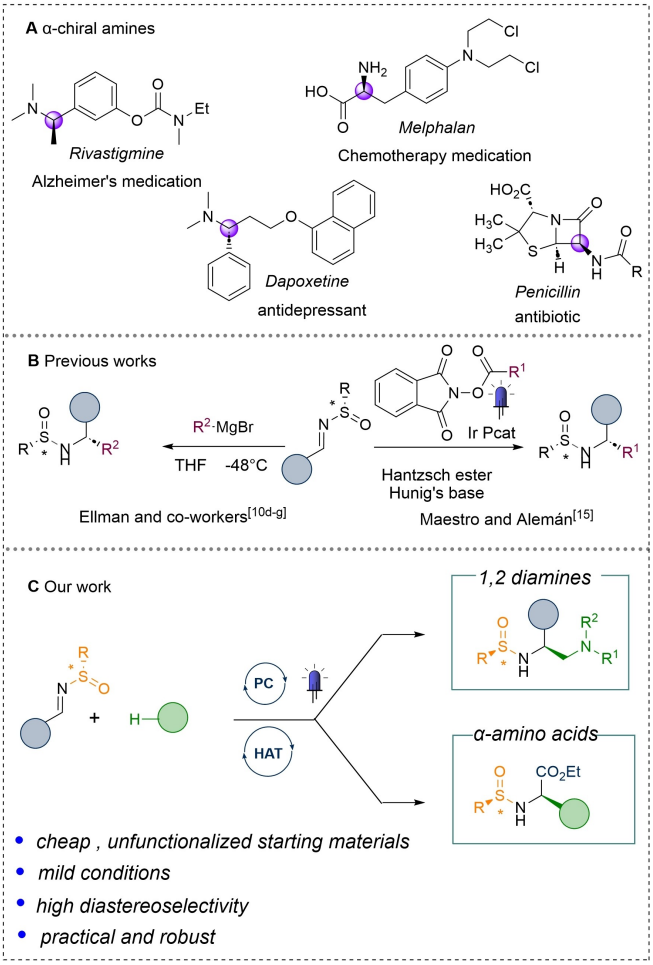
Herein we describe a sustainable and efficient photocatalytic method for the stereoselective radical alkylation of chiral sulfinyl imines. By employing readily available non-prefunctionalized radical precursors and the cost-effective TBADT as a direct HAT photocatalyst, we successfully obtain diverse chiral amines with high yields and excellent diastereoselectivity under mild conditions. This method provides an efficient approach for accessing a diverse array of medicinally relevant compounds, including both natural and synthetic α-amino acids, aryl ethyl amines, and other structural motifs commonly found in approved pharmaceuticals and natural product.

Chiral amines serve as essential building blocks in the development of pharmaceutical ingredients (Scheme 1A).[1] Illustrative data reveals that approximately 35% of the top 200 small molecule drugs marketed in 2018 feature at least one chiral amine center.[2] Furthermore, these compounds are prevalent in natural substances and can be utilized in organic synthesis as resolving agents or chiral auxiliaries.[3] Among the various strategies for the industrial synthesis of chiral amines, many of them still rely on traditional synthetic methods involving resolution[4] or costly precious metals-based catalytic approaches.[5] Furthermore, most of these metal-catalyzed methods require either harsh conditions or expensive chiral ligands.[6,7] Therefore, the high demand for the production of chiral amines, due to their varied applications, has pushed the scientific community to find alternative and sustainable ways towards their effective preparation.[3c,8] Chiral auxiliaries represent a valid alternative for the generation of chiral amines.[9] Among the various auxiliaries applied in asymmetric synthesis, chiral sulfoxides represent a powerful tool for the development



Scheme 1. (A) Examples of achiral amines of pharmaceutical interest (B) Previous examples of diastereoselective transformations: using metal-based reagents or photocatalyzed SET (C) Proposed asymmetric radical C(sp3)-C(sp3) coupling through a photocatalyzed HAT process.

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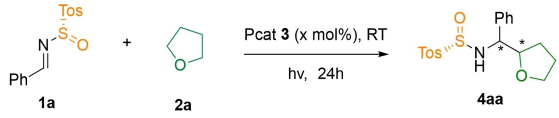
of a wide variety of enantioselective reactions.[10] The widespread use of chiral sulfoxides is mainly due to its significant asymmetric induction exhibited by the sulfinyl fragment, its high configurational stability and its easy and straightforward preparation. Several review articles have detailed the diverse applications of chiral sulfoxides in the field of organic synthesis,[9,11] such as for the preparation of α- and β-amino acids[12,13] and various substituted aziridines.[14] Nevertheless, most of these transformations require the use of expensive, highly reactive, and toxic metal-based compounds. Alemán and coworkers pioneered a potential substitute to circumvent these harsh conditions by introducing the first photocatalyzed asymmetric reaction utilizing chiral sulfinyl imines (Scheme 1B).[15] Following this example, several other reports have been developed exploiting the asymmetric induction and the electrophilic properties of sulfinyl imines in order to trap a wide variety of nucleophilic radicals generated under mild catalytic conditions.[16] However, in most cases the preparation of specific radical precursors such as redox active esters derived from *N*-hydroxyphthalimide (NHPI) as well as the use of stoichiometric amounts of reducing agent, need to be considered (Scheme 1B). To the best of our knowledge, only a limited number of procedures have documented the direct addition of alkyl radicals to chiral sulfinyl imines using non-pre-functionalized starting materials. In 2020, Martin and co-workers developed a photocatalytic, stereoselective alkylation of chiral *N*-sulfinyl imines with adamantane through Hydrogen Atom Transfer (HAT).[17] Although the resulting amines were generally isolated with high diastereoselectivity, the report was restricted to only adamantyl-containing substrates. One year later, Kärkäs and co-workers described a photodecarboxylative C–H alkylation of chiral glyoxylate-derived *N*-sulfinyl imines using carboxylic acids, providing access to various enantioenriched unnatural α-amino acids.[18] Very recently, Maruoka and coworkers disclosed an efficient asymmetric C–H aminoalkylation of chiral *N*-sulfinyl imines derived from glyoxylate employing an indirect HAT process with primary and secondary alcohol.[19] In spite of these notable achievements, it is noteworthy that the majority of these alkylations are primarily restricted to activated imines or to selected alkylating sources. Hence, the development of general photocatalytic asymmetric alkylations of chiral *N*-sulfinyl imines using non-prefunctionalized radical precursors is of significant interest. Pursuing our exploration in asymmetric photocatalyzed transformations,[20] we, herein, present an effective catalytic alkylation reaction of chiral imines with various non-activated alkylating substrates. This methodology yields a diverse array of chiral amines, encompassing both natural and unnatural amino acids,[21,22] α-amino alcohols,[23] amino aldehydes,[24] and 1,2-diamines.[25]

Based on our work involving photocatalyzed HAT processes[20e] and inspired by the methodologies developed by the groups of Alemàn[15] and Kärkäs,[18] we became interested in establishing a method for a diastereoselective radical addition to chiral *N*-sulfinyl imines. Our goal was to employ effective and readily available photocatalysts, utilizing common non-activated radical sources.[26] To develop this approach, we initiated our study by selecting THF (**2a**), serving both as a solvent and as a radical source, owing to the low C–H bond dissociation energy (BDE) in the α-position relative to the oxygen atom (92 kcal/mol).[27] We began by screening various photocatalysts for the alkylation of *N*-sulfinyl imines **1a** (Table 1). Several benzophenone (BP) derivatives were found to catalyze the desired transformation when exposed to the appropriate light source, offering good yields of adduct **4aa** in moderate diastereoselectivity (entry 1–3). Other organocatalysts known to perform direct HAT, such as thioxanthone, anthraquinone, and eosin Y,[26] did not afford the desired product (entry 4–6). In 2019, Dilman and coworkers reported TBADT as an efficient photocatalyst for promoting the radical alkylation of *N*-tosylimines.[28,29] Guided by their findings, the performance of such catalyst was subsequently evaluated. To our delight, TBADT exhibited superior results, achieving a higher yield and diastereoselectivity with a catalytic loading 10 times lower than that required by the aforementioned organo-photocatalysts (entry 7). It should be noted that the addition of a co-solvent was important for a successful transformation. Among the co-solvents dry acetonitrile played a key role in solubilizing the TBADT,[30] and was optimal compared to other tested solvents.

Optimization was pursued by examining the effect of various chiral *N*-sulfinyl auxiliaries. To address the diastereoselectivity issue, THF was replaced by 1,3,5-trioxane (**2b**) as the radical precursor. The reaction with **1a** resulted in the formation of product **4ab** with promising diastereoselectivity (Table 2, entry 1). The *tert*-butyl substituted *N*-sulfinyl imine **1b** showed poor performance (Table 2, entry 2), giving a low yield, moderate diastereoselectivity, and some side products. This unsatisfactory result may be attributed to partial cleavage of the *tert*-butyl-sulfur bond, initiated by radical migration or via fragmentation of a transient aminyl or alkylsulfinamide radical

Table 1. Survey of Reaction Conditions with THF **2a** as Alkyl Radical.[a]

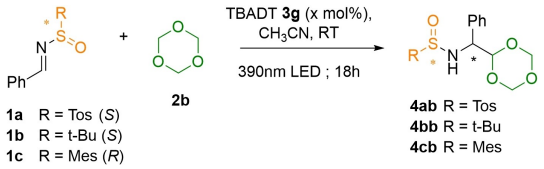


1a 2a 4aa

Entry	3 (x mol %)	hv (nm)	dr[b]	4aa Yield [%][c]
1	**3a**, BP (50 mol%)	390	6.4:3:3: 1	73
2	**3b**, DmBP (50 mol%)	390	6.4:3:3:1	50
3	**3c**, BcBP (50 mol%)	390	6.5:3:3:1	80
4	**3d**, AQ (50 mol%)	390	–	
5	**3e**, TX (50 mol%)	405	–	
6	**3f**, Eosin Y (50 mol%)	456	–	
7[d]	**3g**, TBADT (5 mol%)	390	6.9:3.1:3:1	80

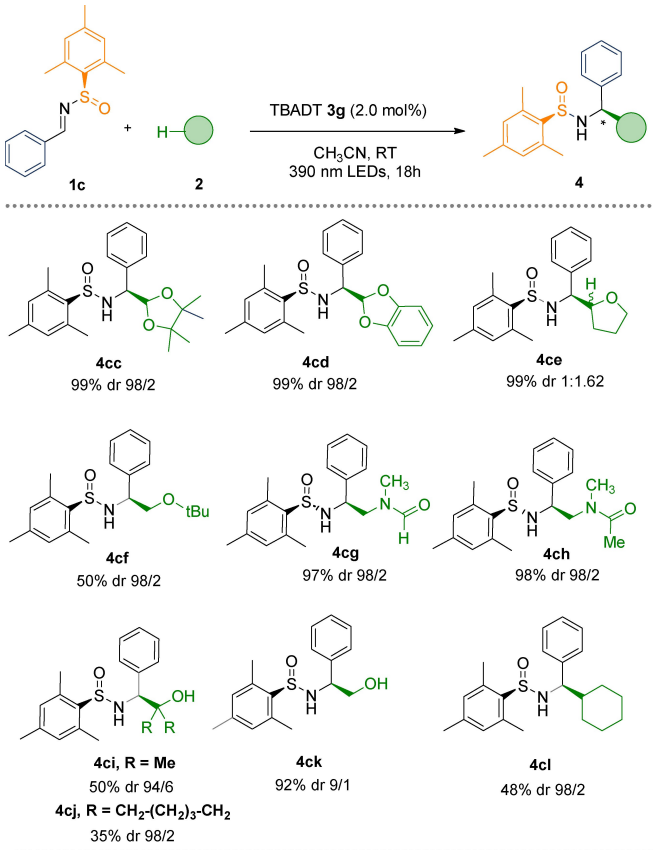
[a] Reaction conditions: **1a** (0.1 mmol), and **3** (5 to 50 mol%) in 1.0 mL of THF under argon, for 24 h. [b] dr Determined by 1H NMR analysis of the crude mixture. [c] ^{1}H NMR yield of **4** determined using 1,1,2-trichloroethene as internal standard. [d] Reaction was performed with an addition of CH_3CN 0.05 M. BP: Benzophenone; DmBP: 4,4′-Dimethoxybenzophenone DcBP: 4,4′-Dichlorobenzophenone AQ: Anthraquinone TX: Thioxanthone.

Table 2. Survey of Reaction Conditions of Photocatalyzed Alkylation of N-Sulfinyl Imines [a].[a]



Entry	1 (R*)	3g (x mol%)	hv (nm)	dr[b]	4 Yield [%][c]
1	**1a** (Tos)	5 mol%	390	6:1	**4ab**, 54
2	**1b** (*t*-Bu)	5 mol%	390	1.7:1	**4bb**, 38
3	**1c** (Mes)	5 mol%	390	>98:2	**4cb**, 70
4	**1c** (Mes)	2 mol%	390	>98:2	**4cb**, 75 (70)[d]
5	**1c** (Mes)	1 mol%	405	>98:2	**4cb**, 63
6[e]	**1c** (Mes)	2 mol%	390	>98:2	**4cb**, 50
7	**1c** (Mes)	–	390	–	–
8[f]	**1c** (Mes)	2 mol%	–	–	–
9[g]	**1c** (Mes)				

[a] Reaction conditions: **1** (0.1 mmol), and **3** (5 to 1 mol%) in CH_3CN 0.1 M, under argon, for 18 h. [b] dr Determined by ^1H NMR analysis of the crude mixture. [c] ^1H NMR yield of **4** determined using 1,1,2-trichloroethene as internal standard. [d] Yields refer to chromatographically pure product **4**. [e] in DCM. [f] No light irradiation. [g] Under air.

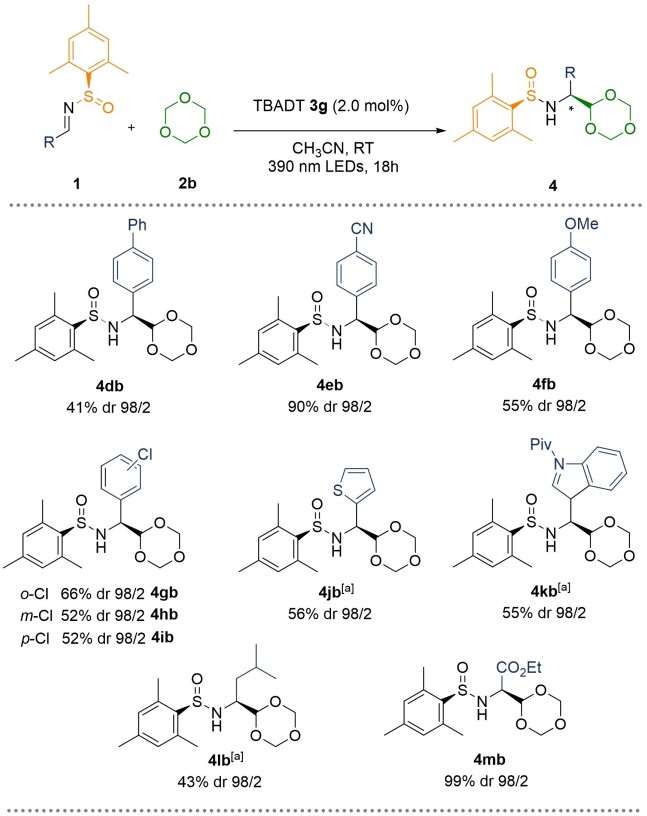


Scheme 2. Scope for the HAT radical addition to N-sulfinyl imine **1c**. Reaction conditions: **1** (0.1 mmol), **2** (1.0 mmol, 10 equiv.), and **3g** (2 mol%) in 1.0 mL of CH_3CN under argon and 390 nm irradiated with Kessil 40 W blue LED for 18 h. Yields are based on isolated pure product after column chromatography. dr Determined by ^1H NMR analysis of the crude mixture.

intermediate.[31,32] Pleasingly, optimal results were achieved with the mesityl-substituted *N*-sulfinyl imine **1c**,[15–19] providing **4cb** as a single diastereomer (entry 3). The catalyst loading was also investigated, affording comparable results with 1 mol% TBADT (entry 5). Acetonitrile was identified as the optimal solvent (entry 4 vs 6). Control experiments showed that the reaction is fully inhibited in the presence of air or in the absence of light or photocatalyst (entries 7–9).

With these results, we proceeded to investigate the asymmetric radical addition of diverse non-prefunctionalized radical precursors to imine **1c** (Scheme 2). We decided to focus our attention on the use of a cheap source of alkyl radicals, such as commonly used solvents or other easily accessible compounds to explore the scope. In analogy to 1,3,5-trioxane (**2b**), 4,4,5,5-tetramethyl-1,3-dioxolane (**2c**) and benzo[*d*][1,3]dioxole (**2d**) performed well in the reaction delivering corresponding adducts **4cc** and **4cd** in nearly quantitative yield and in near perfect diastereoselectivity (Scheme 2). The reaction involving THF and sulfonyl imine **1c** delivered product **4ce** with an enhanced yield (nearly quantitative) and improved diastereoselectivity compared to compound **4aa** obtained from imine **1a**. Indeed, among the four possible diastereoisomers, only two of them could be detected with a ratio of 1.6:1 highlighting the poor β-diastereoselectivity but a nearly perfect α-diastereoselectivity. Interestingly, acyclic methyl *tert*-butyl ether could also be used, albeit delivering the corresponding adduct **4cf** in a comparatively reduced but still valuable yield. We were pleased to find that DMF and DMA were suitable partners, providing direct access to 1,2-diamines **4cg** and **4ch** that are prevalent in numerous pharmaceutical compounds.[25] Most notably, the HAT process worked well with unprotected secondary alcohols such as isopropanol or cyclohexanol under optimized conditions, allowing the synthesis of 1,2-amino-alcohols **4ci** and **4cj** with excellent diastereoselectivity, albeit in moderate yields. Methanol could also be used in the reaction delivering corresponding adduct **4ck** in excellent yield (92%) albeit with slightly reduce dr (9:1). In addition, the fully aliphatic radical precursor cyclohexane participated successfully in the reaction to deliver **4cl** in a satisfactory yield and with again excellent diastereoselectivity.[33]

Subsequently, we evaluated a diverse range of substituted *N*-2,4,6-trimethylbenzene sulfinyl imines as radical acceptors using 1,3,5-trioxane (**2b**) as the radical donor (Scheme 3). The procedure tolerated various substituted aryl imines and consistently furnished the corresponding adduct with high diastereoselectivity. While slightly diminished yields (**4db** and **4fb**) were noted when using less reactive electron-rich imines, aryl imines bearing a strong electron-withdrawing group were particularly effective as seen with the synthesis of compound **4eb** isolated in 90% yield with 98:2 dr. The (*ortho, meta* and *para*)-substituted aromatic imines worked well leading to desired products **4gb**–**4ib** with similar yield and diastereoselectivity, thus indicating that the reaction is not sensitive to

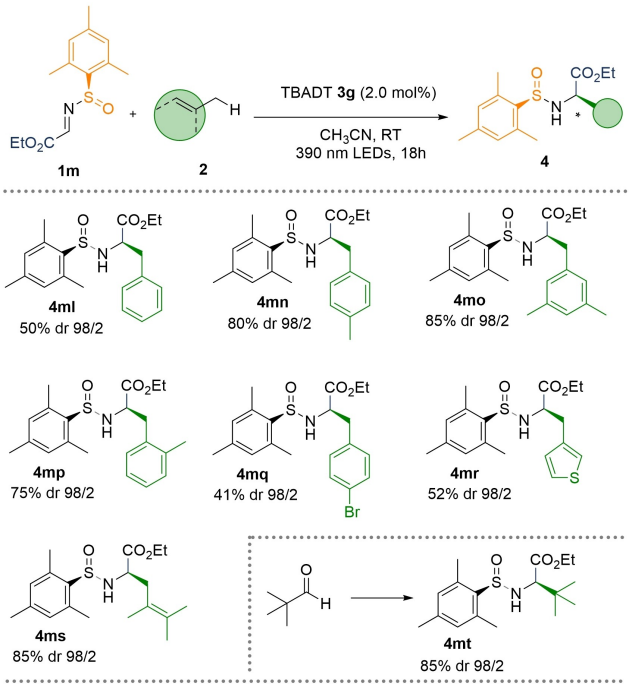


Scheme 3. Scope for the HAT radical addition of 1,3,5-trioxane (**2b**) to **1**. Reaction conditions: **1** (0.1 mmol), **2** (1.0 mmol, 10 equiv.), and **3g** (2 mol%) in 1.0 mL of CH_3CN under argon and 390 nm irradiated with Kessil 40 W blue LED for 18 h. Yields are based on isolated pure product after column chromatography. dr Determined by ^1H NMR analysis of the crude mixture. [a] Addition of Na_2CO_3 (0.1 mmol, 1 equiv.).

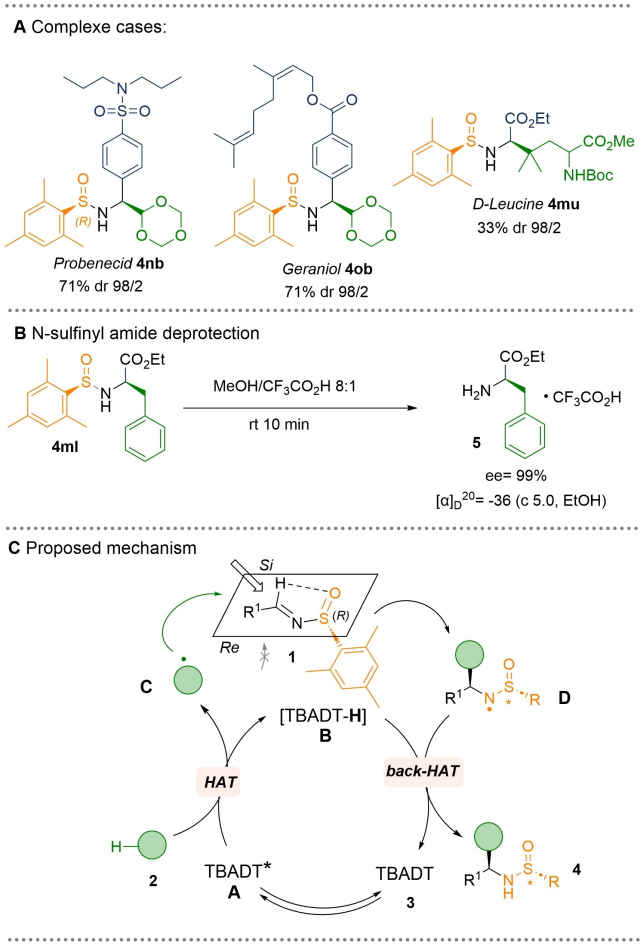
steric hindrance. The scope can be extended to different hetero-aromatic compounds, yielding the desired products in good yields (**4jb**; **4kb**). Ethyl glyoxylate-derived imine was also a suitable radical trap, leading to compound **4mb** in quantitative yield and with excellent diastereoselectivity. To our delight, reaction could be further extended to the use of challenging enolizable aliphatic imines like the one derived from isovaleraldehyde, resulting in the formation of enantioenriched desired product **4lb** in a satisfying yield of 43%.

In order to enlarge the scope, we next sought to explore more challenging alkyl radicals. Therefore, we explored the feasibility of conducting a diastereoselective addition of benzylic radicals generated by HAT of toluene.[27] However, reaction with *N*-sulfinyl imine **1c** and dry toluene under our standard conditions resulted in the recovery of the starting material. Lack of reactivity was probably not due to the absence of radical generation in the reaction given that the BDE of toluene (88 kcal/mol)[27] is lower than that of THF and that TBADT mediated benzylation of alkenes has precedent.[34] The unsuccessful result could however be attributed to the mild nucleophilicity of the benzyl radical. Consequently, we postulated that a more electrophilic imine might lead to a successful benzylation. Indeed, when the *N*-sulfinyl imine **1m** derived from ethyl glyoxylate was subjected to the standard conditions with toluene, it yielded product **4ml** in a 50% yield with high diastereoselectivity (Scheme 4). With this result we evaluated several other benzylic radical precursors. The use of *ortho* and *para*-xylene as well as mesitylene provided the desired enantioenriched products **4mp**, **4mn** and **4mo** in similar yields and dr. In contrast, electron-deficient toluene derivatives, such as *p*-bromotoluene, was less successful, affording only 41% yield of **4mq** albeit with no erosion of diastereoselectivity. To our delight, 3-methylthiophene was also competent, affording **4mr** in moderate yield and high dr (98:2). Tetramethylethylene turned out to be a good HAT substrate to afford the desired enantioenriched allylated product **4ms** in 88%. Finally, the tertiary alkyl radical, originating from the decarbonylation of the acyl radical produced from pivaldehyde, underwent an efficient reaction, leading to the formation of the enantioenriched protected *tert*-leucine compound **4mt**.

To further illustrate the practicality of this protocol, we conducted a series of late-stage functionalizations on imines derived from complex natural products and bioactive compounds (Scheme 5A). Pleasingly, the alkylation of imines derived from Probenecid[35] and geraniol[36] was successfully accomplished, yielding **4nb**, **4ob** in good yields. Moreover, we could selectively add the radical generated at the γ-position of *D*-leucine to **1m** resulting in the desired product **4mu** with a yield of 33%. Next, the reaction was scaled up on a 1 mmol scale under our optimized conditions and the product **4mb** was formed in 85% yield, validating the practicability of this protocol. Furthermore, the cleavage of the *N*-sulfinyl amide group of **4ml** under mild acidic conditions furnished *D*-phenyl-



Scheme 4. Scope for the HAT radical addition to N-sulfinyl imine **1m**. Reaction conditions: **1** (0.1 mmol), **2** (1.0 mmol, 10 equiv.), and **3g** (2 mol%) in 1.0 mL of CH_3CN under argon and 390 nm irradiated with Kessil 40 W blue LED for 18 h. Yields are based on isolated pure product after column chromatography. dr Determined by ^1H NMR analysis of the crude mixture.



Scheme 5. (**A**) Functionalization of complex molecules (**B**) Chiral auxiliary cleavage and determination of the absolute configuration of **5**. (**C**) Proposed mechanism for the photocatalyzed HAT transformation.

alanine amino ester **4** with 99% enantioselectivity in nearly quantitative yields (Scheme 5B). The absolute configuration was determined as (*R*) by comparing it with an independently synthesized authentic sample of compound **4**, thereby confirming the configuration. (For more details see Supporting Information).

Based on selected experiments and literature precedents,[20e,28,29] a mechanism for the developed transformation can be proposed (Scheme 5C). As shown in Table 2, light is mandatory, and an ON-OFF experiment was performed providing no evidence of a radical chain propagation mechanism in the reaction (see Supporting Information). As such, upon visible light irradiation of TBADT, a long-lived excited state, TBADT* (**A**), can form; this species subsequently abstracts a hydrogen atom from the respective alkyl compound (**2**) delivering an alkyl radical (**C**). Controlled by the chiral auxiliary, this radical undergoes a diastereoselective addition to N-sulfinyl imine leading to the N-centered radical (**D**). Previous studies, as well as, computational studies[18,30] has established that, because of the hydrogen bond between the sulfinyl-oxygen and the hydrogen of the imine, N-sulfinyl imine **1** adopts a well-defined *s-cis* conformation in which the mesityl group of (*S*)-2,4,6-trimethylbenzenesulfinamide shields the Re-face. Therefore, addition of the radical (**C**) is taking place from the less hindered face (Si-face) to form the enantioenriched N-centered radical (**D**). Finally, this radical species undergoes a back hydrogen atom transfer (BHAT) with the protonated TBADT–H (**B**) closing the catalytic cycle and generating the final product **4**.

In summary, we have established a practical and sustainable alkylative method for chiral *N*-sulfinyl imines, employing visible light and TBADT as the photocatalyst. The process exhibits excellent diastereoselectivity, delivering a range of chiral amine products, covering natural and unnatural amino acids, α-amino alcohols, amino aldehydes, and 1,2-diamines. Notably, its effectiveness with challenging substrates, including toluene-derived radicals, highlights its versatility. The late-stage functionalization of imines derived from complex compounds further emphasizes the practicality of this approach.

Experimental Section

General procedure for the HAT radical addition to N-sulfinyl imine: In a flame dried vial tube equipped with a stirring bar and a septum were placed **1** (0.1 mmol), the TBADT **3 g** (0.002 mmol, 2 mol%) and, if solid, the radical precursor **2** (1 mmol 10 equiv.). The solids were evacuated and back-filled with Argon three times, followed by addition of dry solvent and, if liquid, the radical precursor. Argon was bubbled for 1 min in the reaction tube through a long needle. Thereafter, the reaction mixture was placed ca. 5 cm from the light source (390 nm 40 W Kessil LED) and stirred with a fan cooling or air flow system. The reaction was monitored by TLC. Upon completion, the crude mixture is concentrated by rotary evaporator and dried under vacuo. Dr was determined by ^{1}H NMR from the crude mixture. The crude is concentrated and purified by column chromatography (silica gel PET/EtOAc).

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: Photocatalysis · HAT · Decatungstate · Sulfinyl imine · chiral auxiliary · diastereoselectivity

[1] S. Zhang, J. Del Pozo, F. Romiti, Y. Mu, S. Torker, A. H. Hoveyda, *Science* **2019**, *364*, 45–51.
[2] Q. Yin, Y. Shi, J. Wang, X. Zhang, *Chem. Soc. Rev.* **2020**, *49*, 6141–6153.
[3] a) C. Xie, Q. Guo, X. Wu, W. Ye, G. Hou, *J. Org. Chem.* **2023**, *88*, 15726–15738; b) A. Umanzor, N. A. Garcia, C. C. Roberts, *ACS Org. Inorg. Au* **2024**, *4* (1), 97–101; c) D. C. Blakemore, L. Castro, I. Churcher, D. C. Rees, A. W. Thomas, D. M. Wilson, A. Wood, *Nat. Chem.* **2018**, *10*, 383–394.
[4] R. Kuhn, F. Erni, T. Bereuter, J. Haeusler, *Anal. Chem.* **1992**, *64*, 2815–2820.

[5] A. Trowbridge, S. M. Walton, M. J. Gaunt, *Chem. Rev.* **2020**, *120*, 2613–2692.
[6] J. L. Tucker, *Org. Process Res. Dev.* **2006**, *10*, 315–319.
[7] G. Grogan, *Curr. Opin. Chem. Biol.* **2018**, *43*, 15–22.
[8] a) G. Bernadat, G. Masson, *Synlett* **2014**, *25*, 2842–2867; b) J. Merad, C. Lalli, G. Bernadat, J. Maury, G. Masson, *Chem. Eur. J.* **2018**, *24*, 3925–3943; c) D. Bouchet, T. Varlet, G. Masson, *Acc. Chem. Res.* **2022**, *55*, 3265–3283.
[9] G. Diaz-Muñoz, I. L. Miranda, S. K. Sartori, D. C. De Rezende, M. Alves Nogueira Diaz, *Chirality* **2019**, *31*, 776–812.
[10] Selected references a) J. Han, V. A. Soloshonok, K. D. Klika, J. Drabowicz, A. Wzorek, *Chem. Soc. Rev.* **2018**, *47*, 1307–1350; b) I. Fernández, N. Khiar, *Chem. Rev.* **2003**, *103*, 3651–3706; c) E. Wojaczyńska, J. Wojaczyński, *Chem. Rev.* **2020**, *120*, 4578–4611; d) D. A. Cogan, G. Liu, J. Ellman, *Tetrahedron* **1999**, *55*, 8883–8904; e) T. P. Tang, J. A. Ellman, *J. Org. Chem.* **1999**, *64*, 12–13; f) J. W. Evans, J. A. Ellman, *J. Org. Chem.* **2003**, *68*, 9948–9957; g) T. Kochi, T. P. Tang, J. A. Ellman, *J. Am. Chem. Soc.* **2003**, *125*, 11276–11282.
[11] a) E. Wojaczyńska, J. Wojaczyński, *Chem. Rev.* **2010**, *110*, 4303–4356; b) S. Otocka, M. Kwiatkowska, L. Madalińska, P. Kiełbasiński, *Chem. Rev.* **2017**, *117*, 4147–4181.
[12] a) T. Guo, R. Song, B.-H. Yuan, X.-Y. Chen, X.-W. Sun, G.-Q. Lin, *Chem. Commun.* **2013**, *49*, 5402; b) F. A. Davis, P. S. Portonovo, R. E. Reddy, Y. Chiu, *J. Org. Chem.* **1996**, *61*, 440–441.
[13] F. A. Davis, J. M. Szewczyk, R. E. Reddy, *J. Org. Chem.* **1996**, *61*, 2222–2225.
[14] a) F. A. Davis, H. Liu, P. Zhou, T. Fang, G. V. Reddy, Y. Zhang, *J. Org. Chem.* **1999**, *64*, 7559–7567; b) F. A. Davis, S. H. Lee, H. Xu, *J. Org. Chem.* **2004**, *69*, 3774–3781; c) F. A. Davis, W. McCoull, D. D. Titus, *Org. Lett.* **1999**, *1*, 1053–1055.
[15] A. F. Garrido-Castro, H. Choubane, M. Daaou, M. C. Maestro, J. Alemán, *Chem. Commun.* **2017**, *53*, 7764–7767.
[16] a) S. Ni, A. F. Garrido-Castro, R. R. Merchant, J. N. de Gruyter, D. C. Schmitt, J. J. Mousseau, G. M. Gallego, S. Yang, M. R. Collins, J. X. Qiao, K. Yeung, D. R. Langley, M. A. Poss, P. M. Scola, T. Qin, P. S. Baran, *Angew. Chem. Int. Ed.* **2018**, *57*, 14560–14565; b) K. M. Baker, A. Tallon, R. P. Loach, O. P. Bercher, M. A. Perry, M. P. Watson, *Org. Lett.* **2021**, *23*, 7735–7739; c) Z. Zhou, Z. S. Sales, D. J. Pippel, M. Qian, C. L. Martin, *J. Org. Chem.* **2022**, *87*, 14948–14952; d) G. Levitre, S. Keess, G. A. Molander, *Org. Lett.* **2023**, *25*, 3864–3869.
[17] W. K. Weigel III, H. T. Dang, H.-B. Yang, D. B. C. Martin, *Chem. Commun.* **2020**, *56*, 9699–9702.
[18] A. Shatskiy, A. Axelsson, E. V. Stepanova, J.-Q. Liu, A. Z. Temerdashev, B. P. Kore, B. Blomkvist, J. M. Gardner, P. Dinér, M. D. Kärkäs, *Chem. Sci.* **2021**, *12*, 5430–5437.
[19] J. Caner, A. Matsumoto, K. Maruoka, *Chem. Sci.* **2023**, *14*, 13879–13884.
[20] a) L. Jarrige, A. Carboni, G. Dagousset, G. Levitre, E. Magnier, G. Masson, *Org. Lett.* **2016**, *18*, 2906–2909; b) G. Levitre, C. Audubert, A. Dumoulin, N. Goual, P. Retailleau, X. Moreau, G. Masson, *ChemCatChem* **2019**, *11*, 5723–5727; c) J. Lyu, A. Claraz, M. R. Vitale, C. Allain, G. Masson, *J. Org. Chem.* **2020**, *85*, 12843–12855; d) J. Lyu, M. Leone, A. Claraz, C. Allain, L. Neuville, G. Masson, *RSC Adv.* **2021**, *11*, 36663–36669; e) T. Varlet, D. Bouchet, E. Van Elslande, G. Masson, *Chem. Eur. J.* **2022**, *28*, e202201707.
[21] *Biochemistry of the Amino Acids*, *Elsevier*, ***1965***.
[22] L. Pollegioni, S. Servi, Eds., *Unnatural Amino Acids: Methods – Protocols*, *Humana Press*, Totowa, NJ, **2012**.
[23] a) D. J. Ager, I. Prakash, D. R. Schaad, *Chem. Rev.* **1996**, *96*, 835–876; b) D. Ghislieri, N. J. Turner, *Top. Catal.* **2014**, *57*, 284–300; c) O. K. Karjalainen, A. M. P. Koskinen, *Org. Biomol. Chem.* **2012**, *10*, 4311; d) M. Breuer, K. Ditrich, T. Habicher, B. Hauer, M. Keßeler, R. Stürmer, T. Zelinski, *Angew. Chem. Int. Ed.* **2004**, *43*, 788–824; e) T. Sehl, Z. Maugeri, D. Rother, *J. Mol. Catal. B* **2015**, *114*, 65–71; f) S. C. Bergmeier, *Tetrahedron* **2000**, *56*, 2561–2576.
[24] a) J. F. Hooper, S. Seo, F. R. Truscott, J. D. Neuhaus, M. C. Willis, *J. Am. Chem. Soc.* **2016**, *138*, 1630–1634; b) D. Gryko, J. Chałko, J. Jurczak, *Chirality* **2003**, *15*, 514–541; c) M. T. Reetz, *Chem. Rev.* **1999**, *99*, 1121–1162; d) R. Hili, S. Baktharaman, A. K. Yudin, *Eur. J. Org. Chem.* **2008**, 5201–5213.
[25] a) G.-Q. Lin, M.-H. Xu, Y.-W. Zhong, X.-W. Sun, *Acc. Chem. Res.* **2008**, *41*, 831–840; b) D. Lucet, T. Le Gall, C. Mioskowski, *Angew. Chem. Int. Ed.* **1998**, *37*, 2580–2627; c) S. R. S. Saibabu Kotti, C. Timmons, G. Li, *Chem. Biol. Drug Des.* **2006**, *67*, 101–114.
[26] L. Capaldo, D. Ravelli, M. Fagnoni, *Chem. Rev.* **2022**, *122*, 1875–1924.
[27] a) G. W. Gribble, *Indole Ring Synthesis: From Natural Products to Drug* Y.-R. Luo, *Comprehensive Handbook of Chemical Bond Energies*, CRC Press, **2007**.
[28] V. I. Supranovich, V. V. Levin, A. D. Dilman, *Org. Lett.* **2019**, *21*, 4271–4274.
[29] For selected reviews on decatungstate anion-photocatalysis, see: a) C. L. Hill, *Synlett* **1995**, *1995*, 127–132; b) M. D. Tzirakis, I. N. Lykakis, M. Orfanopoulos, *Chem. Soc. Rev.* **2009**, *38*, 260–2621; c) D. Ravelli, S. Protti, M. Fagnoni, *Acc. Chem. Res.* **2016**, *49*, 2232–2242; d) D. Ravelli, M. Fagnoni, T. Fukuyama, T. Nishikawa, I. Ryu, *ACS Catal.* **2018**, *8*, 701–713; e) K. Suzuki, N. Mizuno, K. Yamaguchi, *ACS Catal.* **2018**, *8*, 10809–10825; f) Y. Xiaoya, Y. Guoping, Y. Bing, *Chin. J. Org. Chem.* **2020**, *40*, 3620–3632; See also: g) R. F. Renneke, C. L. Hill, *J. Am. Chem. Soc.* **1986**, *108*, 3528–3529; h) R. F. Renneke, C. L. Hill, *Angew. Chem. Int. Ed.* **1988**, *27*, 1526–1527; i) V. De Waele, O. Poizat, M. Fagnoni, A. Bagno, D. Ravelli, *ACS Catal.* **2016**, *6*, 7174–7182; For a selection of recent examples of decatungstate-photocatalyzed reactions, see: j) A. Jorea, C. Raviola, M. Giustiniano, D. Ravelli, *ChemCatChem* **2023**, *15*, e202300042. k) R. Canton-Vitoria, M. Quintana, N. G. Malliaros, N. Tagmatarchis, *Adv. Mater. Interfaces* **2023**, *10*, 2201575; l) K. El-Chami, R. Madsen, *ChemCatChem* **2023**, *15*, e202301143; m) D. Kolb, A. A. Almasalma, M. Morgenstern, L. Ganser, I. Weidacher, B. König, *ChemPhotoChem* **2023**, *7*, e202300167; n) W.-H. Lu, D. Yang, G.-Q. Wang, T. Wang, Y.-X. Zhou, L.-H. Jing, *Org. Biomol. Chem.* **2023**, *21*, 2822–2827; o) F. Raymenants, T. M. Masson, J. Sanjosé-Orduna, T. Noël, *Angew. Chem. Int. Ed.* **2023**, *62*, e202308563; p) R. Wang, C. Wang, *Chem. Sci.* **2023**, *14*, 6449–6456; q) A. Cruise, M. Baumann, *ChemCatChem* **2023**, *15*, e202201328; r) P. S. Gowda, D. S. Sharada, G. Satyanarayana, *Chem. Commun.* **2023**, *59*, 9094–9097; s) A. Pulcinella, S. Bonciolini, F. Lukas, A. Sorato, T. Noël, *Angew. Chem. Int. Ed.* **2023**, *62*, e202215374; t) S. Bonciolini, A. Pulcinella, M. Leone, D. Schiroli, A. L. Ruiz, A. Sorato, M. Dubois, R. Gopalakrishnan, G. Masson, N. Della Ca, S. Protti, M. Fagnoni, E. Zysman-Colman, M. Johansson, T. Noël, *Nat. Commun.* **2024**, *15*, 1509, doi: 10.1038/s41467-024-45804-.
[30] T. Yamase, N. Takabayashi, M. Kaji, *J. Chem. Soc. Dalton Trans.* **1984**, 793.
[31] J. A. Fernández-Salas, M. C. Maestro, M. M. Rodríguez-Fernández, J. L. García-Ruano, I. Alonso, *Org. Lett.* **2013**, *15*, 1658–1661.
[32] a) W. Huang, J.-L. Ye, W. Zheng, H.-Q. Dong, B.-G. Wei, *J. Org. Chem.* **2013**, *78*, 11229–11237; b) M. Oliva, G. A. Coppola, E. V. Van Der Eycken, U. K. Sharma, *Adv. Synth. Catal.* .**2021**, *363*, 1810–1834; c) F. Xue, F. Wang, J. Liu, J. Di, Q. Liao, H. Lu, M. Zhu, L. He, H. He, D. Zhang, H. Song, X. Liu, Y. Qin, *Angew. Chem. Int. Ed.* **2018**, *57*, 6667–6671.
[33] Unsuccessful reagents can be found in the SI.
[34] a) S. Montanaro, D. Ravelli, D. Merli, M. Fagnoni, A. Albini, *Org. Lett.* **2012**, *14*, 4218–4221; b) X. Fan, J. Rong, H. Wu, Q. Zhou, H. Deng, J. D. Tan, C. Xue, L. Wu, H. Tao, J. Wu, *Angew. Chem. Int. Ed.* **2018**, *57*, 8514–8518.
[35] R. M. Mason, *Ann. Rheum. Dis.* **1954**, *13*, 120–130.
[36] W. Chen, A. M. Viljoen, *S. Afr. J. Bot.* **2010**, *76*, 643–651.

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