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Iodoarene-Catalyzed Oxyamination of Unactivated Alkenes to Synthesize 5-Imino-2-Tetrahydrofuranyl Methanamine Derivatives

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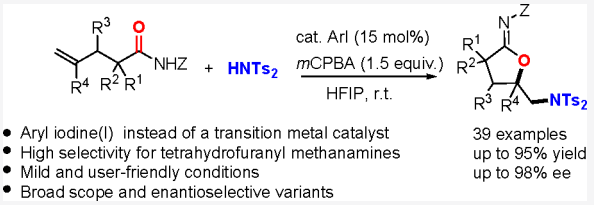
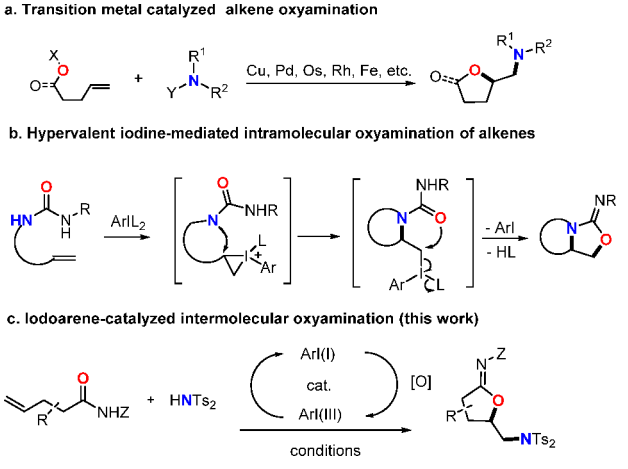
ABSTRACT: Reported here is the room-temperature metal-free iodoarene-catalyzed oxyamination of unactivated alkenes. In this process, the alkenes are difunctionalized by the oxygen atom of the amide group and the nitrogen in an exogenous $HNTs_2$ molecule. This mild and open-air reaction provided an efficient synthesis to *N*-bistosyl-substituted 5-imino-2-tetrahydrofuranyl methanamine derivatives, which are important motifs in drug development and biological studies. Mechanistic study based on experiments and density functional theory calculations showed that this transformation proceeds via activation of the substrate alkene by an *in situ* generated cationic iodonium(III) intermediate, which is subsequently attacked by an oxygen atom (instead of nitrogen) of amides to form a five-membered ring intermediate. Finally, this intermediate undergoes an S_N2 reaction by NTs_2 as the nucleophile to give the oxygen and nitrogen difunctionalized 5-imino-2-tetrahydrofuranyl methanamine product. An asymmetric variant of the present alkene oxyamination using chiral iodoarenes as catalysts also gave promising results for some of the substrates.



INTRODUCTION

The oxyamination of alkenes can be used to synthesize useful 1,2-amino alcohol derivatives.[1] A number of useful strategies for alkene oxyamination have been developed, and the majority of which are based on catalysis by transition metals such as copper,[2] palladium,[3] osmium,[4] rhodium,[5] iron,[6] and others[7] (Scheme 1a). However, some limitations of these reactions, including prior synthesis of the coupling components, the use of electron-rich nitrogen sources, and high reaction temperature, have been encountered.

Scheme 1. Related Works Regarding the Oxyamination of Alkenes



Recently, hypervalent iodine(III) reagents generated *in situ* through the oxidation of iodoarenes have been used as green alternatives to transition metals in the oxidative difunctionalization reaction- of alkenes.[8] Based on this strategy, various iodoarene-catalyzed reactions have been developed, including aminofluorination,[9] dioxygenation,[10] diamination,[11] difluorination,[12] and others.[13] Surprisingly, iodoarene-catalyzed oxyamination cyclizations that simultaneously generate both C−O and C−N bonds have rarely been reported. Although there are several reports about hypervalent iodine-mediated intramolecular oxyamination cyclization of alkenes (Scheme 1b), these reactions required stoichiometric amounts of hypervalent iodine compounds, and the oxygen and nitrogen functional groups need to be tethered in the substrate.[14] Inspired by recent advances of iodoarene catalysis, we envisioned that the traditional oxyamination cyclization reactions catalyzed by transition metals could be replaced by iodoarenes. However, there are two main challenges including the control of chemoselectivity and the compatibility of nitrogen nucleophiles in an oxidizing environment. We speculated that this transformation could be achieved by choosing an appropriate iodoarene and oxidant in a suitable catalytic system.

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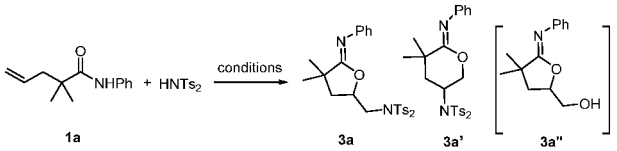
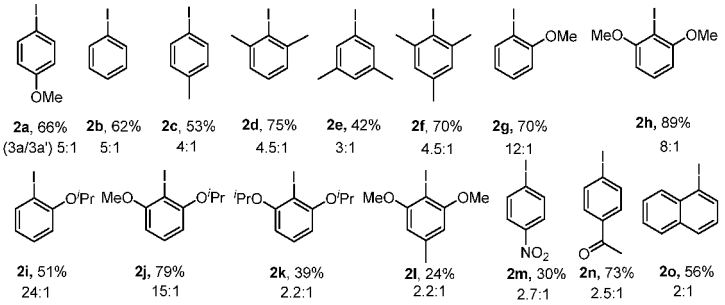
Table 1. Optimization of Reaction Conditions[a]



Entry	[Catalyst]	Oxidant (equiv.)	Solvent	3a+3a′yield[b]	[3a/3a"][c]
1	**2a** (10 mol%)	*m*CPBA (1.2)	CH_2Cl_2	13%	2:1
2	**2a** (10 mol%)	*m*CPBA (1.2)	HFIP	47%	3:1
3	**2a** (15 mol%)	*m*CPBA (1.2)	HFIP	55%	5:1
4	**2a** (15 mol%)	*m*CPBA (1.5)	HFIP	66%	5:1
5	**2a** (15 mol%)	*m*CPBA (2.0)	HFIP	52%	5:1
6	**2h** (15 mol%)	*m*CPBA (1.5)	HFIP	89%	8:1
7	**2j** (15 mol%)	*m*CPBA (1.5)	HFIP	79%	15:1
8	**2i** (15 mol%)	*m*CPBA (1.5)	HFIP	51%	24:1
9[d]	**2j** (15 mol%)	*m*CPBA (1.5)	HFIP/^{t}BuOMe	54%	2:1
10[d,e]	**2j** (15 mol%)	*m*CPBA (1.5)	HFIP	31%	3:1



[a]The reactions were conducted on **1a** (0.2 mmol, 1.0 equiv) with $HNTs_2$ (1.5 equiv) at room temperature for 7 h unless noted otherwise. [b]Isolated yield [c]The ratio of **3a**/**3a′** was determined by the ^{1}H NMR spectrum [d]The reaction time was extended to 15 h [e]The reaction was conducted at 0 °C.

Herein, we report the practical iodoarene-catalyzed oxyamination reaction of unactivated alkenes (Scheme 1c). This process uses $HNTs_2$ as an exogenous nitrogen source to access diverse 5-imino-2-tetrahydrofuranyl methanamine derivatives. In addition, the reaction mechanism and regiochemistry have also been investigated. Besides, an asymmetric version of this reaction has been tested, finding that several substrates can provide high enantioselectivity in the present alkene difunctionalization. Furthermore, the products from the present reaction are important motifs in drug development and biological studies. For example, the structure analogues were found to be studied as muscarinic receptors,[15] cardiac arrhythmias inhibitors,[16] and inhibitors for the binding of HIV GP120 to the CD4 receptor.[17] The present methodology could become an efficient approach to synthesize useful compounds for future pharmaceutical investigation.

RESULTS AND DISCUSSION

As an initial investigation, *N*-phenyl-2,2-dimethyl-4-pentenamide **1a** was chosen as a model substrate and reacted with various nitrogen-based nucleophiles. Products **3a** (5-*exo*) and **3a′** (6-*endo*) were obtained when $HNTs_2$ was used together with 1-iodo-4-methoxybenzene (**2a**, 10 mol %) as a catalyst and *m*CPBA (1.2 equiv) as an oxidant in dichloromethane (CH_2Cl_2) at room temperature. The **3a**/**3a′** molar ratio was 2:1 with a 13% total yield (Table 1, entry 1). In addition, the hydroxylation product **3a″** was isolated in 34% yield. This compound originated from a side reaction of the unsaturated amide **1a** with *m*CPBA.[18] No diamination product was detected, even though this is the major product resulting from copper-catalyzed cyclization reactions.[2f] An extensive solvent screening determined that hexafluoroisopropanol (HFIP) remarkably promoted the transformation. (Table S1) The oxyamination reaction became dominant when HFIP was used,[19] and gave **3a** and **3a′** in 47% yield with slightly increased regioselectivity (**3a**/**3a′** 3:1, entry 2). The yield and regioselectivity of the target compound were further improved by increasing the catalyst loading to 15 mol % and the amount of *m*CPBA to 1.5 equiv (entries 3 and 4), while further increasing the amount of oxidant obtained a slightly lower yield (entry 5). Among the different oxidants tested, *m*CPBA gave the best result for this reaction. (Table S3) To further screen the reaction conditions, a variety of iodoarene catalysts (**2b**−**o**) were investigated. (Table S4) Among these, 2,6-dimethoxy iodobenzene **2h** displayed the best catalytic activity, affording the target molecule in 89% yield with good regioselectivity (**3a**/**3a′** 8:1, entry 6). Satisfactory regioselectivity (**3a**/**3a′** 15:1) was obtained when **2j** was used as the

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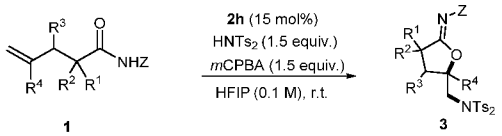
J. Org. Chem. 2021, 86, 235−253

Table 2. Substrate Scope of the Oxyamination[a]



Entry	Substrate	Product	Yield[b]
1	Z = Ph, **1a** Z = *p*-$CH_3C_6H_4$, **1b** Z = *o*-ClC_6H_4, **1c** Z = *m*-ClC_6H_4, **1d** Z = *p*-ClC_6H_4, **1e** Z = *p*-$NO_2C_6H_4$, **1f** Z = *p*-$CF_3C_6H_4$, **1g**	**3a** **3b** **3c** **3d** **3e** **3f** **3g**	79%, 15:1[c,e] 90%, 7:1[c] 84% 79%, 12:1[c,e] 62%, 5:1[c,e] 91% 65%
2	R = Bn, **1h** R = OMe, **1i**	**3h** **3i**	55%[d] 80%[d]
3	Z = Ph, **1j** Z = *p*-MeC_6H_4, **1k** Z = *p*-$OMeC_6H_4$, **1l** Z = *p*-FC_6H_4, **1m** Z = *o*-ClC_6H_4, **1n** Z = *m*-ClC_6H_4, **1o** Z = *p*-ClC_6H_4, **1p** Z = *p*-BrC_6H_4, **1q**	**3j** **3k** **3l** **3m** **3n** **3o** **3p** **3q**	95%, 12:1[c] 99% 98% 88% 85% 86% 90% 91%
4	R = Bn, **1r** R = OMe, **1s**	**3r** **3s**	93% 85%
5	R = Et, **1t** R = ^{i}Pr, **1u**	**3t** **3u**	92% 94%
6	R = Ph, **1v** R = *p*-FC_6H_4, **1w**	**3v** **3w**	67%[e], > 20:1 d.r.[f] 61%[e], > 20:1 d.r.[f]
7	**1x**	**3x**	73%[e], > 20:1 d.r.[f]
8	**1y**	**3y**	64%[d,e], > 20:1 d.r.[f]
9	**1z**	**3z**	73%,10:1[c], > 20:1 d.r.[f]
10	n = 1, **1aa** n = 3, **1ab** n = 4, **1ac**	**3aa** **3ab** **3ac**	79% 83% 91%
11	X = O, **1ad** X = N-Boc, **1ae**	**3ad** **3ae**	78%, 16:1[c] 67%[e]
12	R = Ph, **1af** R = Et, **1ag**	**3af** **3ag**	72%[d,g] 55%[d,g]
13	**1ah**	**3ah**	52%[e,g]
14	R = Me, **1ai** R = Et, **1aj**	**3ai** **3aj**	77%, 1:1 d.r.[f] 73%, 3:2 d.r.[f]
15	R = Me, **1ak** R = ^{i}Pr, **1al**	**3ak** **3al**	77%, 1:1 d.r.[f] 62%, 4:1 d.r.[f]
16	**1am**	**3am**	63% (4.1 g scale)[d]
17	R = H, **1an** R = Me, **1ao**	**3an**, not observed **3ao**, not observed	
18	**1ap**	**3ap**	45%[g]

[a]The reactions were conducted on a 0.2 mmol scale with **2h** (15 mol %), $HNTs_2$ (1.5 equiv), and *m*CPBA (1.5 equiv) at room temperature for 7 h unless noted otherwise. [b]Isolated yield. [c]The ratio of 5-*exo*/6-*endo* as determined by the ^{1}H NMR spectrum. [d]The reaction time was extended to 15 h. [e]Using **2j** (15 mol %) as the catalyst. [f]dr = diastereoselectivity as determined by the ^{1}H NMR spectrum. [g]With an HFIP/*tert*-BuOMe mixture (1:1, v/v) as the solvent.

catalyst, albeit with slightly lower yield (79%, entry 7). Meanwhile, excellent regioselectivity (**3a**/**3a′** 24:1) was obtained when **2i** was used as the catalyst, but the catalytic activity was reduced (entry 8). These results indicated that the ortho alkoxy substitution is beneficial to the transformation,[20] and it was also apparent that catalysts with different alkoxyl substituents between their 2- and 6-positions produced higher regioselectivity compared to more symmetric catalysts. Using an HFIP/*tert*-BuOMe mixture as the solvent in an attempt to inhibit the hydroxylation reaction resulted in both a reduced yield (54%) and poor regioselectivity (entry 9).[11g] The reaction temperature was found to be crucial, such that the yield of the oxyamination products was only 31% at 0 °C (entry 10).

With the optimized conditions in hand, various substituted pentenamides were examined (Table 2). The effects of substituents on the *N*-phenyl group of the 2,2-dimethyl pentenamide were initially assessed. The results showed that both electron-rich and electron-deficient substrates were tolerated in the reaction, affording the desired oxyamination products (**3a**−**g**) in good yields (62%−91%) and with good regioselectivities. The structures of products **3c** and **3f** were established by X-ray crystallographic analysis.[21] *N*-benzyl and *N*-methoxyl substituted substrates were compatible with the reaction, giving **3h** in 55% yield and **3i** in 80% yield, respectively. The 2,2-diphenyl pentenamides with more highly sterically hindered were also found to undergo the transformation smoothly and give **3j** in 95% yield with good regioselectivity. Interestingly, single 5-*exo* oxyamination products (**3k**−**q**) were obtained with excellent yields (85−99%), and these good results can be understood by the Thorpe−Ingold effect. The 2,2-diphenyl pentenamide with *N*-benzyl and *N*-methoxyl protecting groups were determined to function as suitable substrates for the reaction, giving **3r** and **3s** in 93% and 85% yields, respectively. In addition, substrates with different alkyl group substituents were compatible with the reaction, affording the corresponding tetrahydrofuranyl methanamine products **3t** and **3u** in 92% and 94% yields,

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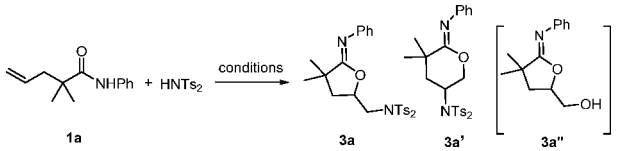
J. Org. Chem. 2021, 86, 235−253

respectively. To further investigate the substrate scope, various unsaturated amides with more complex substitutions were examined, giving corresponding products **3v**−**z** in good yields with *trans* configuration predominant, which demonstrated by the X-ray crystallographic analysis of **3w**. Furthermore, substrates with different alkyl ring sizes could also be applied to the reaction under the standard conditions, giving the corresponding *spiro*-tetrahydrofuranyl methanamine products (**3aa**−**ac**) in 79−91% yields. It is noteworthy that substrates bearing heterocycles were also suitable, affording the corresponding azabicyclo **3ad** and oxybicyclo **3ae** in good yields with high regioselectivities. Moreover, using a HFIP/*tert*-BuOMe mixed solvent, the products **3af**−**ah** with quaternary carbon centers can be obtained in 52−72% yields. Furthermore, substrates bearing a quaternary carbon center also worked well under the standard conditions, giving the oxyamination products **3ai**−**al** in good yields (62−77%), and these products have been found to function as cardiac arrhythmia inhibitor candidates.[16] Further upscaling of the oxyamination was facile and allowed us to prepare **3am** on a 4.1 g scale in 63% yield. Notably, this product could potentially serve as a precursor for the synthesis of tricyclic antidepressants.[22] Unfortunately, **1an** and **1am** were unsuitable for this oxyamination, which may indicate that the Thorpe−Ingold effect was an essential factor for the transformation. Surprisingly, the aromatic skeleton structure substrate was incompatible with the oxyamination but gave **3ap** as the major product, which originated from the elimination reaction of benzylic hydrogen and hypervalent iodine(III),[23] and the detailed discussion of this process was present in our latest study.[23d]

Control experiments were performed to obtain more information regarding this transformation. The results showed that the oxyamination did not proceed without the iodoarene catalyst, such that only the hydroxylation product was obtained (entry 1, Table 3). Then, replacing both 15 mol % **2h** and 1.5

Table 3. Control Experiments[a]



entry	conditions	3a+3a′ yield (%)	3a/3a′[b]	3a″ (%)
1	*m*CPBA (1.5 equiv), $HNTs_2$ (1.5 equiv), 3 h			78
2	$PhI(NTs_2)_2$ (1.2 equiv), 0.5 h	83	1:1	
3	**2h** (15 mol %), *m*CPBA (1.5 equiv), $NaNTs_2$ (1.5 equiv), 15 h			19

[a]The reactions were conducted in 1 mL of HFIP with 0.1 mmol **1a** as the substrate. [b]Determined by the ^1H NMR spectrum.

equiv of *m*CPBA directly with 1.2 equiv of $PhI(NTs_2)_2$ resulted in a shorter reaction time and considerably high yield (entry 2). Finally, using $NaNTs_2$ instead of $HNTs_2$ to prevent the formation of the bisimido iodine(III) and rendered the reaction ineffective (entry 3). These results indicate that the bisimido iodine(III) species generated *in situ* via the oxidation of the iodoarene(I) and *m*CPBA catalyzed the reaction.

On the basis of these data, a possible reaction mechanism was proposed (Scheme 2). In this process, bisimido iodine(III) compound **I** (generated *in situ* from Ar−I, $HNTs_2$ and *m*CPBA) exists in equilibrium with the electrophilic cationic iodine(III) species in solution,[8f,11g] which binds to and activates the olefin in the substrate for the nucleophilic attack, giving the iodonium ion intermediate (**Int1A**). The oxygen atom of the amide group subsequently attacks the activated alkene in an intramolecular fashion, giving alkyl-iodine(III) intermediate (**Int2A**) through **Ts1A**. Then, the iodine(III) group of **Int2A** acts as a leaving group, enabling the intermolecular S_N2 attack of $^-NTs_2$ to regenerate the iodoarene(Ar−I) and release the oxyamination product through **Ts2A**.[24] The dioxygenation byproduct generation proceeds via oxidation of the substrate alkene by an *in situ* generated epoxide intermediate (**Int1E**), which is subsequently attacked by the carbonyl oxygen through **Ts1E** under the acidic conditions.

To better understand the reaction mechanism and rationalize the preference for 5-*exo* products over 6-*endo* products, DFT calculations were performed for a model reaction using iodobenzene as catalyst and $HNMs_2$ as the nitrogen source. The results are shown in Figures 1 and 2. Initially, the dissociation of the bisimido iodine(III) compound gives the reactive (and high energy) cationic iodine fragment $[PhINMs_2]^+$, which is subsequently converted to **Int1** upon coordinating to the substrate. This intermediate then undergoes the intramolecular cyclization reaction, which is also the rate-determining step of the overall reaction, to give one of the four possible products. Several other transition states for different nucleophile attacks by *O* and *N* to give 5- and 6-membered rings have been computed, and their relative energies are given, suggesting that the *O*-5-*exo* **Ts1A** is the most favorable, while the *O*-6-*endo* **Ts1B** is slightly higher in energy. These results suggest that the tetrahydrofuran would be the major product, consistent with the experimental results. It is known that the nitrogen in an amide moiety is usually less nucleophilic than carbonyl oxygen,[25] both transition states **Ts1C** and **Ts1D**, which correspond to the intramolecular nucleophilic attack by a nitrogen atom, are much higher in energy. The resulting alkyl-iodine(III) intermediate **Int2A** subsequently undergoes a direct S_N2 attack by an Ms_2N^- anion, resulting in the formation of the protonated **ProdA** and the release of the iodobenzene catalyst. It is also possible for the deprotonation to proceed first, followed by S_N2 reaction via **Ts2A′** for this process (see note).[26] Finally, a proton can be abstracted from the protonated product by Ms_2N^- to give the neutral product, although this is an endergonic process. This may indicate that in the presence of an excess of the acidic Ms_2NH, the relatively basic product would remain protonated until workup.

To demonstrate the practicability of this oxyamination, further transformations of **3j** was conducted (Scheme 3). The useful 1-amino-5-anilinopentan-2-ol derivatives **4c** and **4f** were obtained by simple reduction and deprotection.[27] Additionally, hydrolysis and deprotection of **3j** gave the important intermediate **4h**. Subsequently, the 5-aminomethyldihydrofuran-2-one skeletons **4i** and **4k** were obtained from **4h** by the process of reductive amination and acetylation reactions, respectively. These compounds could serve as potential precursors for the preparation of antimuscarinics. Furthermore, tetrahydrofurfurylamine molecular **4j** with similar a structure

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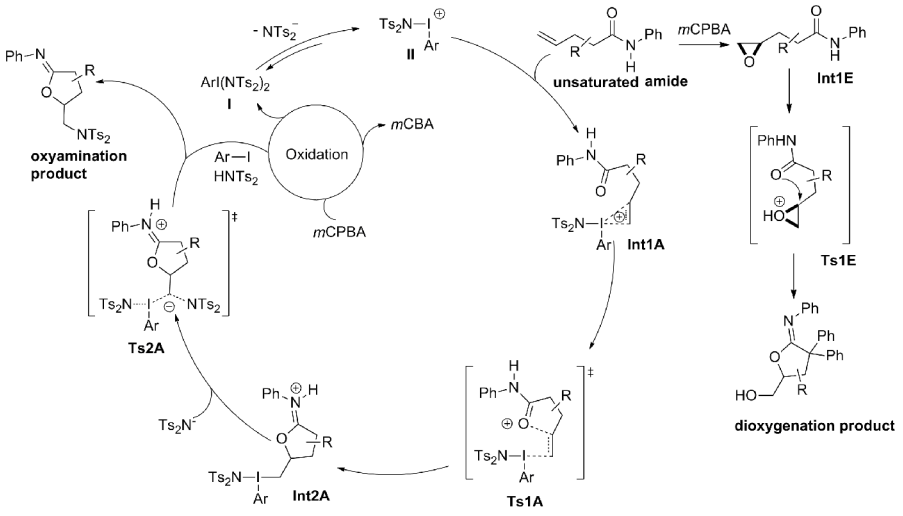
J. Org. Chem. 2021, 86, 235−253

Scheme 2. Proposed Reaction Mechanism



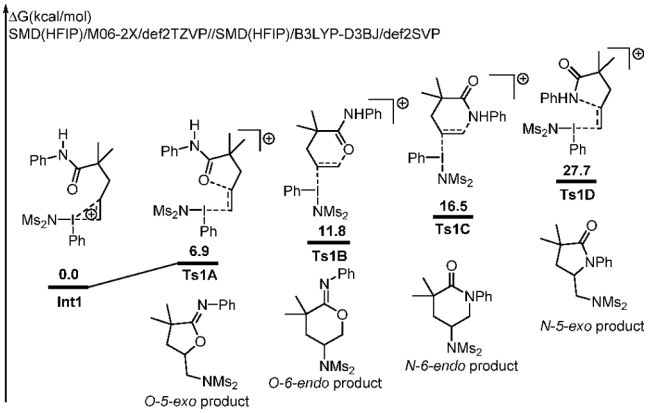


Figure 1. A comparison of the transition states that lead to all four possible products.

to serotonin reuptake inhibitors was obtained by simple transformations.[28]

An asymmetric variant of the present alkene oxyamination using chiral iodoarenes as catalysts was preliminarily investigated (Table 4). Solvents screening results show that trifluorotoluene was most suitable for the asymmetric oxyamination, while HFIP could only obtain the racemic product (entries 1 and 2). Then, a series of chiral iodoarene compounds were synthesized and examined (entries 3−8), and the results show that the chiral iodoarene with tertiary amide side chain was conducive to chiral induction, while secondary amine and ester structures were less effective. Finally, 94% ee of **3j*** was obtained when **5g** was used as a catalyst. Under optimized conditions, optically enriched products (**3m***, **3n***, **3o***, **3q***, **3s***) were synthesized in good yields (entries 9−13). Although the asymmetric reaction is only suitable for 2,2-diphenyl substituent pentenamides under current conditions, it provides evidence that chiral iodoarene compounds could be used as green alternatives to transition metals in the catalytic asymmetric cyclizations of alkenes.

CONCLUSION

In conclusion, we demonstrated a simple, effective iodoarene-catalyzed intermolecular oxyamination of unactivated alkenes

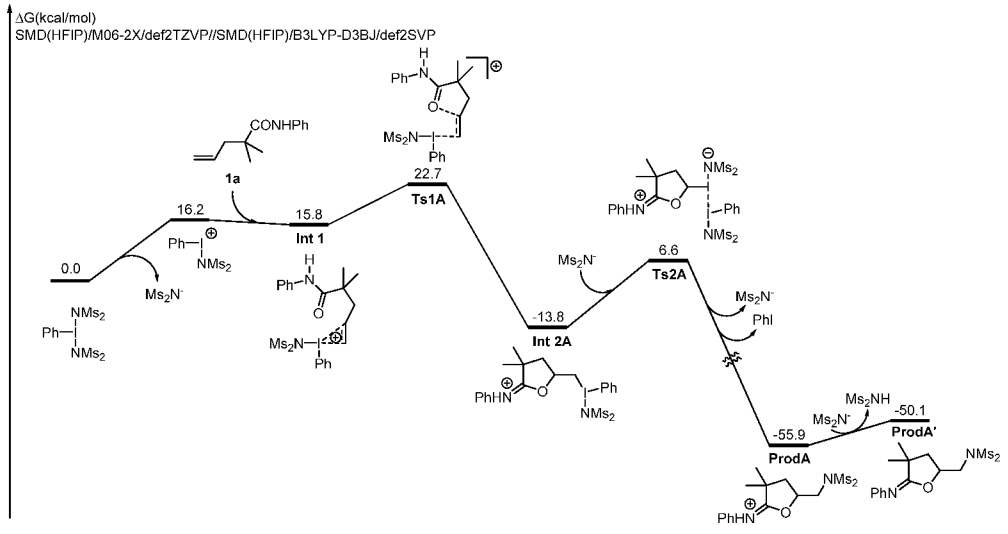


Figure 2. Gibbs energy profile for the oxyamination reaction.

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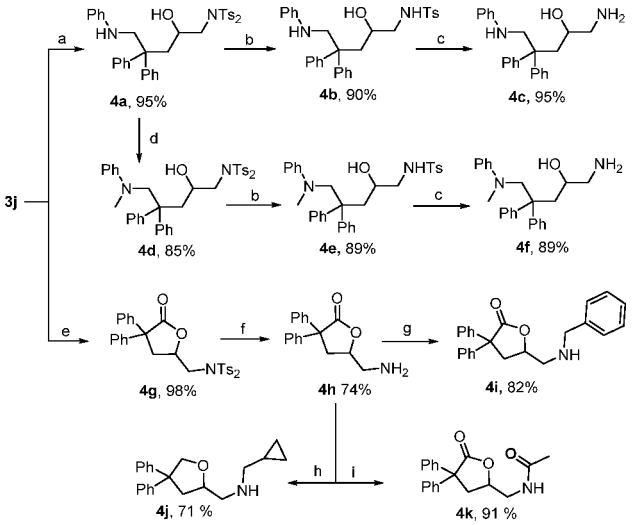
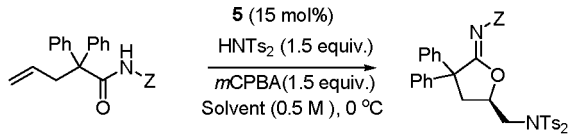
J. Org. Chem. 2021, 86, 235−253

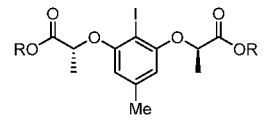
Scheme 3. Further Transformations[a]



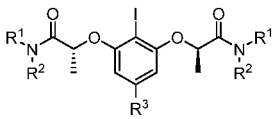
[a]Reaction conditions: (a) $LiAlH_4$, CH_2Cl_2, rt; (b) KOH, MeOH, reflux; (c) Na-naphthalenide, THF, rt; (d) Me_2SO_4, K_2CO_3, acetone, 60 °C; (e) HCl (aq), CH_2Cl_2, rt; (f) HBr/HOAc, phenol 80 °C; (g) C_6H_5CHO, $NaBH_3CN$, MeOH, rt; (h) C_3H_5CHO, $NaBH_4$, MeOH, rt; (i) acetyl chloride, NEt_3, CH_2Cl_2, rt.

Table 4. Asymmetric Oxyamination Investigations[a]





5a, R = Et
5b, R = H



5c, R^1 = Mes, R_2 = R_3 = H
5d, R^1 = 2,6-diisopropylphenyl, R^2 = R^3 = H
5e, R^1 = R^2 = ^{i}Pr, R^3 = Me
5f, R^1 = Ph, R^2 = ^{i}Pr, R^3 = Me
5g, R^1 = Cyclohexyl, R^2 = Et, R^3 = Me

entry	substrate	catalyst	solvent	product	yield (%)[b]	ee (%)[c]
1[b]	**1j**	**5e**	HFIP	**3j***	89	3
2	**1j**	**5e**	$PhCF_3$	**3j***	90	53
3	**1j**	**5a**	$PhCF_3$	**3j***	80	0
4	**1j**	**5b**	$PhCF_3$	**3j***	80	0
5	**1j**	**5c**	$PhCF_3$	**3j***	70	27
6	**1j**	**5d**	$PhCF_3$	**3j***	50	7
7	**1j**	**5f**	$PhCF_3$	**3j***	60	20
8	**1j**	**5g**	$PhCF_3$	**3j***	95	94
9	**1m**	**5g**	$PhCF_3$	**3m***	89	64
10	**1n**	**5g**	$PhCF_3$	**3n***	84	93
11	**1o**	**5g**	$PhCF_3$	**3o***	91	95
12	**1q**	**5g**	$PhCF_3$	**3q***	89	59
13	**1s**	**5g**	$PhCF_3$	**3s***	87	98

[a]The reactions were conducted on the 0.1 mmol scale with 15 mol % chiral iodoarenes as catalysts, $HNTs_2$ (1.5 equiv), and *m*CPBA (1.5 equiv) at 0 °C for 15 h. [b]Isolated yield. [c]The ee was determined by HPLC on a chiral stationary phase.

to afford various 5-imino-2-tetrahydrofuranyl methanamine derivatives. Notably, the present methodology tolerates a broad range of substrates, utilizing unadorned $HNTs_2$ as an exogenous nitrogen nucleophile and *m*CPBA as an oxidant in HFIP at room temperature. The products from the present reaction can be converted to 1,2-amino alcohol, methanamine-lactone, and methanamine-tetrahydrofuran derivatives, which could serve as useful molecules in medicinal research and other fields. More importantly, a mechanistic study based on experiments and density functional theory calculations has provided insights regarding the overall catalytic cycle of the reaction and the origin of the observed chemoselectivity and regioselectivity. This information will be helpful in terms of understanding the present reaction and will assist in the future design of new catalytic oxyaminations and other iodoarene-catalyzed alkene difunctionalization reactions. Finally, an enantioselective catalytic oxyamination process was developed, offering a simple and practical methodology for the preparation of optically enriched tetrahydrofuranyl methanamine derivatives.

EXPERIMENTAL SECTION

General. Unless noted, reactions were carried out in a 10 mL glass reaction tube, which were sealed with a rubber stopper in air. Tetrahydrofuran (THF) and dichloromethane (CH_2Cl_2) were obtained by distillation from sodium metal. Trifluorotoluene ($PhCF_3$) and hexafluoroisopropanol (HFIP) were purchased from Energy Chemical and used without further purification. All other commercially available compounds were purchased at the highest commercial quality. Flash column chromatography was performed on a glass column filled with (200−300 Mesh) silica gel, eluting with petroleum ether/EtOAc or dichloromethane/methanol/Et_3N. Reactions were monitored by analytical thin-layer chromatography (TLC, 0.2 mm) with visualization by exposure to a 254 nm UV lamp and a phosphomolybdic acid ethanol solution. NMR spectra were recorded at an ambient temperature on Agilent 400 or 600 MHz spectrometers. The chemical shifts are reported in parts per million (ppm) and are referenced to TMS (δ = 0 ppm for ^{1}H), $CDCl_3$ (δ = 77.0 ppm for ^{13}C). High-performance liquid chromatography was performed on Agilent 1260 interfaced to an HP 71 series computer workstation. High-Resolution mass spectral data were obtained on a Vion Ims Qtof spectrometer in ESI mode.

General Procedure A for the Synthesis of Pentenamides. Following a literature procedure.[29] To a solution of 2,2-disubstituted acid (1.0 equiv, 1 M) in MeOH was added $SOCl_2$ (10 mol %) slowly, and then the resulting mixture was allowed to stir at 80 °C oil bath temperature. The reaction was monitored by TLC. After completion, the mixture was quenched with H_2O, extracted with EtOAc, washed with brine, dried over Na_2SO_4, filtered, and concentrated under a vacuum. The ester productwas directly used for the next step without other purification.

A solution of *n*-butyllithium (^{n}BuLi, 2.5 M in hexane, 2.5 equiv) in THF was cooled to −78 °C in a low-temperature reactor under argon, and esters (1.0 equiv, 0.5 M) dissolved in THF were added dropwise. The resulting mixture was stired for 1 h, and then a solution of allyl bromide (1.1 equiv) was added; the mixture was allowed to stir for another 1 h. Then, the reaction was allowed to stir at room temperature for 24 h. After completion, the mixture was quenched with a saturated aqueous solution of NH_4Cl. The mixture was extracted with EtOAc. The combined organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated under a vacuum. Then, the residue was purified by flash column chromatography on silica gel to give pentenoate.

Pentenoate (1.0 equiv, 0.5 M) was dissolved by a mixture of MeOH/H_2O (3:1, v/v), and then NaOH (5.0 equiv) was added to the residue. The mixture was heated to reflux overnight. After completion, the solvent was removed under reduced pressure. The residue was dissolved in H_2O, acidified with HCl (1 M, aq), and then extracted with EtOAc. The organic phase was washed with brine,

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J. Org. Chem. 2021, 86, 235−253

dried over Na_2SO_4, filtered, and concentrated under a vacuum. The crude pentenoic acid was used directly for the next step without further purification.

To a solution of pentenoic acid (1.0 equiv, 0.5 M) in dichloromethane was added oxalyl chloride (3.0 equiv) under argon at 0 °C, and then DMF (1 drop) was added carefully. After stirring for 1 h at 0 °C, the mixture was allowed to stir at room temperature for another 5 h. Then, the resulting mixture was concentrated under a vacuum to remove the solvent and the excessive oxalyl chloride. Then, the residue was dissolved in CH_2Cl_2 (0.5 M) under argon at 0 °C, and then amine (1.2 equiv, dissolved in 2 mL of CH_2Cl_2) was slowly added. After stirring for 30 min, Et_3N (2.0 equiv) was added. The resulting mixture was stirred at room temperature overnight. Then, the reaction mixture was quenched by HCl (1 M, aq) and extracted with CH_2Cl_2. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated under a vacuum. The crude residue was purified by flash column chromatography on silica gel to give the pentenamide products.

General Procedure B for the Synthesis of Pentenamides. Following a literature procedure,[30] to a solution of the 2,2-disubstituted acid (1.2 equiv) in CH_2Cl_2 were added allylic alcohol (1.0 equiv, 0.5 M), DMAP (0.2 equiv), and Et_3N (2.0 equiv). After the mixture was stirred for 15 min at 0 °C, *N,N*-diisopropylcarbodiimide (DIC, 1.2 equiv) was added, and stirring was continued for 1 h. Then, the resulting mixture was allowed to stir at room temperature for 15 h. After completion, the mixture was concentrated under a vacuum. The residue was purified by flash column chromatography on silica gel to give the allylic ester product.

To a solution of allylic ester (1.0 equiv, 0.5 M) in THF was stirred in a −78 °C low temperature reactor for 30 min under argon, and then lithium diisopropylamide (LDA, 2.5 M in THF, 2.0 equiv) was added dropwise, and the stirring was continued for 1 h. Then, trimethylchlorosilane (TMSCl, 2.0 equiv) was added. After an additional 1 h of stirring at −78 °C, the resulting mixture was allowed to warmed to room temperature. After completion (monitored by TLC), the reaction was quenched by HCl (1 M, aq) and extracted with CH_2Cl_2. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated under a vacuum. The residue was purified by flash column chromatography on silica gel to give the carboxylic acid product.

To a solution of carboxylic acid (0.5 M in CH_2Cl_2, 1.0 equiv) was added oxalyl chloride (3.0 equiv) under argon at 0 °C, and then 1 drop of DMF was added to carefully. After stirring for 1h, the mixture was allowed to stir at room temperature for another 5 h. Then, the resulting mixture was concentrated under a vacuum, and the residue was dissolved in CH_2Cl_2 (0.2 M) at 0 °C under argon, and then amine (1.2 equiv, dissolved in 2 mL CH_2Cl_2.) was slowly added. The resulting mixture was allowed stir for 0.5 h at 0 °C, and then Et_3N (2.0 equiv) was added. Then, the reaction was warmed to room temperature. After completion (monitored by TLC), the reaction mixture was quenched by HCl (1 M, aq) and extracted with CH_2Cl_2. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel to give the desired products.

The spectrum of known reactants can be found in reported literatures: **1a**−**g**,[29] **1h**,[31] **1i**,[32] **1j**,[33] **1k**,[29] **1m**−**r**,[29] **1s**,[32] **1v**,[29] **1z**,[34] **1aa**−**ad**,[29] **1af**−**ag**,[29] **1an**,[35] **1ao**,[36] **1ap**.[37] The characterization of the new compounds as follows:

*N-(4-Methoxyphenyl)-2,2-diphenyl-4-pentenamide (**1l**).* Compound **1l** was prepared according to the general procedure A and purified by column chromatography (15:1 petroleum ether/EtOAc): white solid; mp 103.0−103.7 °C; ^{1}H NMR(400 MHz, $CDCl_3$) δ 7.48−7.21 (m, 12H), 7.15 (s, 1H), 6.81 (d, J = 8.6 Hz, 2H), 5.89−5.71 (m, 1H), 5.14−4.90 (m, 2H), 3.77 (s, 3H), 3.30 (d, J = 6.6 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.1, 156.5, 142.8, 135.2, 130.9, 129.0, 128.5, 127.2, 121.6, 118.1, 114.1, 61.3, 55.5, 43.5; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{24}H_{24}NO_2$358.1802, found 358.1802.

*N-Phenyl-2,2-diethyl-4-pentenamide (**1t**).* Compound **1t** was prepared according to general procedure A and purified by column chromatography (15:1 petroleum ether/EtOAc): white solid; mp 91.0−92.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 8.0 Hz, 2H), 7.33 (q, J = 8.0, 6.8 Hz, 3H), 7.10 (t, J = 7.6 Hz, 1H), 5.85−5.70 (m, 1H), 5.24−5.02 (m, 2H), 2.41 (d, J = 7.6 Hz, 2H), 1.76−1.54 (m, 4H), 0.90 (t, J = 7.6 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 174.6, 137.9, 134.0, 129.0, 124.3, 120.2, 118.3, 50.0, 37.8, 27.6, 8.4; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{22}NO$ 232.1696, found 232.1698.

*N-Phenyl-2,2-dipropyl-4-pentenamide (**1u**).* Compound **1u** was prepared according to general procedure A and purified by column chromatography (20:1 petroleum ether/EtOAc): white solid; mp 107.3−109.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.0 Hz, 2H), 7.40−7.27 (m, 3H), 7.10 (t, J = 7.6 Hz, 1H), 5.85−5.70 (m, 1H), 5.13 (dd, J = 14.0, 8.4 Hz, 2H), 2.42 (d, J = 7.6 Hz, 2H), 1.66−1.45 (m, 4H), 1.38−1.20 (m, 4H), 0.92 (t, J = 7.2 Hz, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 174.8, 137.9, 134.0, 129.0, 124.2, 120.2, 118.3, 49.5, 38.8, 38.0, 17.2, 14.7; IR ν_{max} (cm^{-1}) 3310, 2957, 1661, 1599, 1526, 1439, 1315, 1248, 916, 750, 694; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{17}H_{26}NO$ 260.2009, found 260.2009.

*N-(4-Fluorophenyl)-3-methyl-2,2-diphenyl-4-pentenamide (**1w**).* Compound **1w** was prepared according to the general procedure B and purified by column chromatography (30:1 petroleum ether/EtOAc): white solid; mp 126.4−127.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, J = 7.6, 2.0 Hz, 4H), 7.42−7.26 (m, 8H), 7.22 (s, 1H), 6.96 (t, J = 8.8 Hz, 2H), 5.89−5.74 (m, 1H), 5.07−4.95 (m, 2H), 4.15−4.00 (m, 1H), 0.99 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.8, 159.4 (d, J = 242.0 Hz), 140.5, 140.2, 140.0, 133.8, 133.8, 130.1, 128.2, 128.1, 127.3, 121.7 (d, J = 8.0 Hz), 121.6, 116.2, 115.5 (d, J = 22.0 Hz), 65.8, 41.1, 16.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{24}H_{23}FNO$ 360.1758, found 360.1751.

*N-Phenyl-2,2-diphenyl-3-ethyl-4-pentenamide (**1x**).* Compound **1x** was prepared according to the general procedure B and purified by column chromatography (30:1 petroleum ether/EtOAc): white solid; mp 101.7−102.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 7.6 Hz, 4H), 7.44−7.27 (m, 11H), 7.09 (t, J = 7.2 Hz, 1H), 5.55−5.42 (m, 1H), 5.23−5.12 (m, 2H), 3.62 (t, J = 9.6 Hz, 1H), 1.86−1.71 (m, 1H), 0.99 (t, J = 7.2 Hz, 3H), 0.80−0.67 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.7, 141.0, 140.8, 138.0, 137.9, 130.2, 130.0, 128.9, 128.1,128.1, 127.2,127.2, 124.3, 119.8 (2C), 118.6, 66.1, 50.2, 24.0, 12.4; IR ν_{max} (cm^{-1}) 3412, 2964, 1684, 1597, 1520, 1497, 1437, 1310, 1238, 918, 752, 719, 690, 561; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{25}H_{26}NO$, 356.2009, found 356.2004.

*N-Benzyl-2,2-diphenyl-3-methyl-4-pentenamide (**1y**).* Compound **1y** was prepared according to the general procedure B and purified by column chromatography (30:1 petroleum ether/EtOAc): white solid; mp 125.0−126.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.4 Hz, 4H), 7.33−7.22 (m, 6H), 7.20−7.13 (m, 3H), 6.86 (dd, J = 6.4, 3.2 Hz, 2H), 5.84−5.70 (m, 2H), 4.95 (d, J = 14.0 Hz, 2H), 4.37 (t, J = 6.0 Hz, 2H), 4.05−3.91 (m, 1H), 0.92 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.5, 140.9, 140.5, 140.3, 138.2, 130.3, 128.5, 127.8, 127.8, 127.3, 127.2, 126.9, 126.9, 115.9 65.4, 43.8, 40.8, 16.5; IR ν_{max} (cm^{-1}) 3331, 3109, 1645, 1531, 1496, 1452, 1279, 1028, 916, 714, 696; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{25}H_{26}NO$ 356.2009, found 356.2000.

*N-Phenyl-(4-(N-tert-Butyloxycarbonyl-4-allyl)piperidino)-carboxamide (**1ae**).* Compound **1ae** was prepared according to the general procedure A and purified by column chromatography (20:1 petroleum ether/EtOAc): white solid; mp 106.6−107.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.0 Hz, 2H), 7.33 (t, J = 8.0 Hz, 2H), 7.28−7.22 (m, 1H), 7.13 (t, J = 7.6 Hz, 1H), 5.85−5.70 (m, 1H), 5.19−5.08 (m, 2H), 3.77 (s, 2H), 3.20 (s, 2H), 2.37 (d, J = 7.6 Hz, 2H), 2.08 (d, J = 14.0 Hz, 2H), 1.61 (s, 2H), 1.46 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 172.8, 154.9, 137.4, 132.5, 129.0, 124.6, 120.5, 119.4, 79.7, 45.8, 43.8, 33.2, 28.4, 26.9; IR ν_{max} (cm^{-1}) 3303, 2976, 1695, 1668, 1525, 1501, 1437, 1420, 1366, 1246, 1175, 1155, 918, 750, 692; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{20}H_{29}N_2O_3$ 345.2173, found 345.2165.

*N-Phenyl-(1-(1-(2-methylallyl))cyclocyclohexyl)carboxamide (**1ah**).* Compound **1ah** was prepared according to the general procedure A and purified by column chromatography (20:1

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J. Org. Chem. 2021, 86, 235−253

petroleum ether/EtOAc): white solid; mp 150.9−152.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 8.3, 2H), 7.37−7.28 (m, 3H), 7.11 (t, J = 7.6 Hz, 1H), 4.89 (s, 1H), 4.72 (s, 1H), 2.32 (s, 2H), 1.73−1.63 (m, 5H), 1.58 (s, 3H), 1.54−1.39 (m, 4H), 1.37−1.29 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 174.3, 141.9, 137.9, 129.0, 124.2, 120.0, 114.9, 48.3, 47.2, 34.9, 25.9, 24.4, 23.0; IR ν_{max} (cm^{-1}) 3344, 3315, 2939, 1661, 1601, 1531, 1437, 1304, 891, 750, 694; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{17}H_{24}NO$ 258.1852, found 258.1854.

*N-Phenyl-2-methyl-2-phenyl-4-pentenamide (**1ai**).* Compound **1ai** was prepared according to the general procedure A and purified by column chromatography (20:1 petroleum ether/EtOAc): white solid; mp 91.1−92.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.29 (m, 7H), 7.27 (s, 2H), 7.06 (t, J = 7.6 Hz, 1H), 6.83 (s, 1H), 5.65−5.50 (m, 1H), 5.14−5.00 (m, 2H), 2.93−2.77 (m, 2H), 1.63 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 174.7, 142.9, 137.8, 133.9, 128.9, 128.9, 127.4, 127.0 124.2, 119.7, 118.6, 51.2, 43.6, 23.8; IR ν_{max} (cm^{-1}) 3337, 2978, 1668, 1599, 1520, 1499, 1437, 1311, 1242, 916, 770, 754, 692; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{18}H_{20}NO$ 266.1539, found 266.1541.

*N-Phenyl-2-ethyl-2-phenyl-4-pentenamide (**1aj**).* Compound **1aj** was prepared according to the general procedure A and purified by column chromatography (30:1 petroleum ether/EtOAc): white solid; mp 93.1−95.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.36 (m, 6H), 7.36−7.25 (m, 3H), 7.09 (t, J = 6.8 Hz, 1H), 6.92 (s, 1H), 5.66−5.47 (m, 1H), 5.20−4.98 (m, 2H), 2.95−2.75 (m, 2H), 2.23−2.05 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 174.0, 142.4, 137.9, 133.7, 128.9, 128.8, 127.4, 127.3, 124.2, 119.9, 118.4, 55.2, 39.5, 28.0, 8.5; IR ν_{max} (cm^{-1}) 3331, 2937, 1668, 1599, 1520, 1499, 1437, 1309, 1242, 914, 752, 700; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{19}H_{22}NO$ 280.1696, found 280.1690.

*N-Phenyl-2-methyl-2-(3-chlorophenyl)-4-pentenamide (**1ak**).* Compound **1ak** was prepared according to the general procedure A and purified by column chromatography (30:1 petroleum ether/EtOAc): white solid; mp 97.5−98.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.8 Hz, 3H), 7.29 (q, J = 8.8, 7.2 Hz, 5H), 7.08 (t, J = 7.6 Hz, 1H), 6.86 (s, 1H), 5.65−5.50 (m, 1H), 5.14−4.99 (m, 2H), 2.88−2.74 (m, 2H), 1.61 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.7, 145.2, 137.6, 134.9, 133.4, 130.2, 128.9, 127.6, 127.0, 125.3, 124.4, 119.9, 119.1, 51.1 43.6, 23.6; IR ν_{max} (cm^{-1}) 3325, 2978, 1663, 1597, 1522, 1439, 1313, 1242, 918, 752, 692; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{18}H_{19}ClNO$ 300.1150, found 300.1150.

*N-Phenyl-2-isopropyl-2-(3-chlorophenyl)-4-pentenamide (**1al**).* Compound **1al** was prepared according to the general procedure A and purified by column chromatography (30:1 petroleum ether/EtOAc): white solid; mp 105.2−106.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.33 (m, 4H), 7.32−7.20 (m, 4H), 7.09 (t, J = 7.3 Hz, 1H), 6.98 (s, 1H), 5.76−5.61 (m, 1H), 5.17−4.98 (m, 2H), 2.95−2.69 (m, 2H), 2.65−2.53 (m, 1H), 0.96 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.3, 137.9, 137.6, 133.6, 133.2, 130.7, 129.0, 128.3, 124.4, 120.0, 118.9, 59.4, 40.9, 32.0, 18.9, 18.0; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{20}H_{23}ClNO$ 328.1463, found 328.1456.

*N-Phenyl-(9-(9-Allyl-9H-fluorene)carboxamide (**1am**).* Compound **1am** was prepared according to the general procedure A and purified by column chromatography (30:1 petroleum ether/EtOAc): pale yellow solid; mp 122.0−123.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.2 Hz, 2H), 7.73 (d, J = 7.6 Hz, 2H), 7.53−7.47 (m, 2H), 7.46−7.40 (m, 2H), 7.33−7.27 (m, 2H), 7.27−7.20 (m, 2H), 7.08−7.01 (m, 1H), 6.89 (s, 1H), 5.43−5.27 (m, 1H), 4.99−4.79 (m, 2H), 3.25 (d, J = 7.2 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.5, 145.1, 141.0, 137.5, 133.1, 128.8, 128.7, 128.1, 124.8, 124.3, 120.5, 119.9, 118.6, 62.9, 40.9; IR ν_{max} (cm^{-1}) 3406, 3063, 1682, 1597, 1518, 1501, 1475, 1439, 1312, 1238, 916, 739, 690, 561, 505; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{23}H_{20}NO$ 326.1539, found 326.1534.

General Procedure for the Oxyamination Reaction. Aryl iodine catalyst (**2h**, 15% mol), $HNTs_2$ (1.5 equiv), and mCPBA (1.5 equiv) were dissolved in 2.0 mL of HFIP (0.1 M). The mixture was stirred at room temperature for 10 min, and then pentenamides **1** (0.20 mmol, 1.0 equiv) was added. The resulting mixture was stirred for 7 h at room temperature. After completion (monitored by TLC), the solvent was removed under a vacuum, and the residue was diluted with NaOH (1.0 M, 10 mL, aq) and stirred for 10 min. Then, the resulting mixture was extracted with CH_2Cl_2. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated under a vacuum. The residue was purified by flash column chromatography on silica gel to give the oxyamination product **3**.

*(Z)-N-((4,4-Dimethyl-5-(phenylimino)tetrahydrofuran-2-yl)-methyl)-4-methyl-N-tosylbenzenesulfonamide (**3a**).* The general procedure was followed with **2j** as the catalyst. The product was purified by column chromatography (10:3 petroleum ether/EtOAc) and obtained as a mixture of two inseparable isomers with 5-*exo*/6-*endo* = 15:1: white solid, 93.6 mg, 79% yield; mp 90.0−91 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, J = 8.4 Hz, 4H), 7.29−7.24 (m, 2H), 7.19 (d, J = 8.4 Hz, 4H), 7.06 (d, J = 7.8 Hz, 2H), 7.02 (t, J = 7.2 Hz, 1H), 4.88−4.63 (m, 1H), 4.13 (dd, J = 15.6, 7.2 Hz, 1H), 3.57 (dd, J = 15.6, 3.6 Hz, 1H), 2.41 (s, 6H), 2.07 (dd, J = 12.6, 6.0 Hz, 1H), 1.75 (dd, J = 12.6, 10.2 Hz, 1H), 1.37 (s, 3H), 1.30 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 167.0, 147.2, 145.0, 136.1, 129.5, 128.6, 128.5, 123.3, 122.4, 77.7, 51.6, 41.8, 40.8, 26.3, 26.3, 21.6; IR ν_{max} (cm^{-1}) 2968, 1701, 1595, 1492, 1373, 1352, 1167, 1164, 1045, 912, 815, 729, 663, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{27}H_{31}N_2O_5S_2$ 527.1669, found 527.1672.

*(Z)-N-((4,4-Dimethyl-5-(4-methylphenylimino)tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3b**).* The general procedure was followed, and the product was purified by column chromatography (5:1 petroleum ether/EtOAc). The product was given as a mixture of two inseparable isomers with 5-*exo*/6-*endo* = 7:1: white solid, 97.2 mg, 90% yield; mp 41−42 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 4H), 7.20 (d, J = 8.4 Hz, 4H), 7.06 (d, J = 8.4 Hz, 2H), 6.97 (d, J = 8.4 Hz, 2H), 4.75−4.68 (m, 1H), 4.13 (dd, J = 15.6, 7.2 Hz, 1H), 3.57 (dd, J = 15.6, 4.2 Hz, 1H), 2.42 (s, 6H), 2.26 (s, 3H), 2.05 (dd, J = 12.6, 6.0 Hz, 1H), 1.74 (dd, J = 12.6, 10.2 Hz, 1H), 1.36 (s, 3H), 1.29 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 166.9, 145.0, 144.6, 136.2, 132.6, 129.6, 129.2, 128.6, 122.3, 77.5, 51.6, 41.9, 40.9, 26.4, 26.4, 21.7, 20.9; IR ν_{max} (cm^{-1}) 2968, 1701, 1596, 1503, 1373, 1352, 1167, 1083, 1045, 914, 814, 663, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{28}H_{33}N_2O_5S_2$ 541.1825, found 541.1825.

*(Z)-N-((4,4-Dimethyl-5-(2-chlorophenylimino)tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3c**).* The general procedure was followed, and the product was purified by column chromatography (10:3 petroleum ether/EtOAc): white solid, 90.4 mg, 84% yield, mp 90−92 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, J = 8.4 Hz, 4H), 7.37 (d, J = 7.8 Hz, 1H), 7.19 (d, J = 8.4 Hz, 4H), 7.15 (t, J = 7.8 Hz, 1H), 7.01 (d, J = 7.8 Hz, 1H), 6.93 (t, J = 7.8 Hz, 1H), 4.81−4.68 (m, 1H), 4.11 (dd, J = 15.6, 7.2 Hz, 1H), 3.58−3.45 (m, 1H), 2.39 (s, 6H), 2.10 (dd, J = 12.6, 6.0 Hz, 1H), 1.77 (dd, J = 12.6, 10.2 Hz, 1H), 1.40 (s, 3H), 1.35 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.5, 145.1, 144.9, 136.0, 129.5, 129.2, 128.3, 127.0, 125.6, 123.9, 122.9, 78.3, 51.6, 41.7, 40.9, 26.1, 26.0, 21.5; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{27}H_{30}ClN_2O_5S_2$ 561.1279, found 561.1284.

*(Z)-N-((4,4-Dimethyl-5-(3-chlorophenylimino)tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3d**).* The general procedure was followed with **2j** as the catalyst, and the product was purified by column chromatography (10:3 petroleum ether/EtOAc). The product was given as a mixture of two inseparable isomers with 5-*exo*/6-*endo* = 12:1: white solid, 88.5 mg, 79% yield; mp 94−95 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, J = 8.4 Hz, 4H), 7.22 (d, J = 8.4 Hz, 4H), 7.16 (t, J = 7.8 Hz, 1H), 7.05 (t, J = 1.8 Hz, 1H), 6.99−6.96 (m, 1H), 6.95−6.92 (m, 1H), 4.78−4.71 (m, 1H), 4.12 (dd, J = 15.6, 7.8 Hz, 1H), 3.56 (dd, J = 15.6, 3.6 Hz, 1H), 2.42 (s, 6H), 2.09 (dd, J = 12.6, 6.0 Hz, 1H), 1.75 (dd, J = 12.6, 10.2 Hz, 1H), 1.36 (s, 3H), 1.30 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.0, 148.8, 145.1, 136.2, 134.1, 129.7, 129.6, 128.5, 123.4, 122.5, 120.9, 78.1, 51.6, 41.8, 41.1, 26.4, 26.3, 21.70; IR ν_{max} (cm^{-1}) 2970, 1754, 1703, 1589, 1467, 1373, 1352, 1167, 1050, 912,

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J. Org. Chem. 2021, 86, 235−253

815, 729, 663, 551; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{30}ClN_2O_5S_2$ 561.1279, found 561.1285.

*(Z)-N-((4,4-Dimethyl-5-(4-chlorophenylimino)tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3e**).* The general procedure was followed with **2j** as the catalyst, and the product was purified by column chromatography (10:3 petroleum ether/EtOAc). The product was given as a mixture of two inseparable isomers with 5-*exo*/6-*endo* = 5:1: white solid, 69.4 mg, 62% yield; mp 66−67 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, J = 8.4 Hz, 4H), 7.19 (dd, J = 18.0, 8.4 Hz, 6H), 6.99 (d, J = 8.4 Hz, 2H), 4.83−4.74 (m, 1H), 4.12 (dd, J = 15.6, 7.8 Hz, 1H), 3.54 (dd, J = 15.6, 3.6 Hz, 1H), 2.43 (s, 6H), 2.10 (dd, J = 12.6, 6.0 Hz, 1H), 1.74 (dd, J = 12.6, 10.2 Hz, 1H), 1.36 (s, 3H), 1.31 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 167.8, 145.9, 145.2, 136.1, 129.6, 128.8, 128.6, 128.5, 124.0, 77.8, 51.5, 41.8, 41.1, 26.5, 26.5, 21.7; IR ν_{max} (cm^{-1}) 2970, 1776, 1701, 1596, 1487, 1373, 1352, 1167, 1086, 925, 816, 729, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{30}ClN_2O_5S_2$ 561.1279, found 561.1282.

*(Z)-N-((4,4-Dimethyl-5-(4-nitrophenylimino)tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3f**).* The general procedure was followed, and the product was purified by column chromatography (10:3 petroleum ether/EtOAc): pale yellow solid, 104.0 mg, 91% yield; mp 115−116 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (d, J = 9.0 Hz, 2H), 7.75 (d, J = 8.4 Hz, 4H), 7.19 (d, J = 8.4 Hz, 4H), 7.10 (d, J = 9.0 Hz, 2H), 4.91−4.77 (m, 1H), 4.10 (dd, J = 15.6, 8.4 Hz, 1H), 3.55 (dd, J = 15.6, 3.6 Hz, 1H), 2.40 (s, 6H), 2.17 (dd, J = 12.6, 6.0 Hz, 1H), 1.79 (dd, J = 12.6, 9.6 Hz, 1H), 1.38 (d, J = 21.0 Hz, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 169.0, 154.2, 145.3, 143.7, 136.0, 129.6, 128.4, 124.5, 122.9, 78.3, 51.3, 41.6, 41.3, 26.6, 26.3, 21.6; IR ν_{max} (cm^{-1} 3361, 2962, 1716, 1589, 1497, 1375, 1333, 1167, 933, 862, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{30}N_3O_7S_2$ 572.1520, found 572.1536.

*(Z)-N-((4,4-Dimethyl-5-((4-(trifluoromethyl)phenyl)imino)-tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3g**).* The general procedure was followed, and the product was purified by column chromatography (10:3 petroleum ether/EtOAc): white solid, 77.2 mg, 65% yield; mp 43−44 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, J = 8.4 Hz, 4H), 7.49 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 8.4 Hz, 4H), 7.12 (d, J = 8.4 Hz, 2H), 4.86−4.79 (m, 1H), 4.12 (dd, J = 7.8, 3.6 Hz, 1H), 3.52 (dd, J = 15.6, 3.6 Hz, 1H), 2.40 (s, 6H), 2.14 (dd, J = 12.6, 6.0 Hz, 1H), 1.77 (dd, J = 12.6, 9.6 Hz, 1H), 1.40 (s, 3H), 1.35 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.7, 150.6, 145.2, 136.0, 129.6, 128.5, 125.9 (q, J = 3.5 Hz), 125.4 (q, J = 274.2 Hz), 122.6, 78.3, 51.4, 41.7, 41.2, 26.5, 26.3, 21.6; IR ν_{max} (cm^{-1}) 2970, 1776, 1703, 1610, 1373, 1325, 1167, 1118, 1065, 914, 816, 741, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{28}H_{30}F_3N_2O_5S_2$ 595.1543, found 595.1560.

*(Z)-N-((4,4-Dimethyl-5-benzyliminotetrahydrofuran-2-yl)-methyl)-4-methyl-N-tosylbenzenesulfonamide (**3h**).* The general procedure was followed, and the reaction time was extended to 15 h. The product was purified by column chromatography (10:3 petroleum ether/EtOAc), giving as a mixture of two inseparable isomers with 5-*exo*/6-*endo* = >20:1: white solid, 94.2 mg, 55% yield; mp 104−105.0 °C. Major isomer shown: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, J = 8.3 Hz, 4H), 7.76 (d, J = 8.3 Hz, 1H), 7.29 (d, J = 7.4 Hz, 1H), 7.24 (s, 6H), 7.21 (t, J = 7.2 Hz, 1H), 4.76−4.66 (m, 1H), 4.48−4.36 (m, 2H), 4.09 (dd, J = 15.7, 7.4 Hz, 1H), 3.66 (dd, J = 15.6, 3.6 Hz, 1H), 2.40 (s, 6H), 2.04 (dd, J = 12.6, 5.4 Hz, 1H), 1.67 (dd, J = 12.6, 10.2 Hz, 1H), 1.23 (s, 3H), 1.23 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.1, 145.2, 143.4, 140.8, 139.3, 136.6, 129.7, 129.7, 128.4, 128.2, 127.4, 126.4, 126.3, 76.9, 52.2, 50.8, 42.4, 40.4, 26.4, 26.3, 21.7, 21.5; IR ν_{max} (cm^{-1}) 2962, 1717, 1589, 1497, 1375, 1333, 1300, 1167, 1109, 1041, 933, 862, 820, 729, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{28}H_{33}N_2O_5S_2$ 541.1825, found 541.1842.

*(Z)-N-((4,4-Dimethyl-5-methoxyimino-tetrahydrofuran-2-yl)-methyl)-4-methyl-N-tosylbenzenesulfonamide (**3i**).* The general procedure was followed, and the reaction time was extended to 15 h. The product was purified by column chromatography (10:3 petroleum ether/EtOAc): white solid, 72.0 mg, 80% yield; mp 43−44 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.0 Hz, 4H), 7.34 (d, J = 8.0 Hz, 4H), 4.79−4.70 (m, 1H), 4.17 (dd, J = 15.6, 6.8 Hz, 1H), 3.85 (s, 3H), 3.74 (dd, J = 15.6, 5.2 Hz, 1H), 2.45 (s, 6H), 1.94 (dd, J = 12.4, 5.6 Hz, 1H), 1.79−1.69 (m, 1H), 1.24 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.7, 145.2, 136.3, 129.6, 128.9, 79.1, 62.1, 51.2, 42.7, 40.3, 26.9, 26.0, 21.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{29}N_2O_6S_2$ 481.1462, found 481.1461.

*(Z)-N-((4,4-Dimethyl-5-phenylimino-tetrahydrofuran-2-yl)-methyl)-4-methyl-N-tosylbenzenesulfonamide (**3j**).* The general procedure was followed with **2j** as the catalyst, and purified by column chromatography (20:3 petroleum ether/EtOAc). The product was given as a mixture of two inseparable isomers with 5-*exo*/6-*endo* = 12:1: white solid, 123.5 mg, 95% yield; mp 133−134 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 4H), 7.41 (d, J = 7.8 Hz, 2H), 7.36 (t, J = 7.8 Hz, 4H), 7.34−7.26 (m, 5H), 7.26−7.21 (m, 1H), 7.20−7.13 (m, 6H), 7.05 (t, J = 7.8 Hz, 1H), 4.68−4.52 (m, 1H), 4.14 (dd, J = 15.6, 6.6 Hz, 1H), 3.69 (dd, J = 15.6, 5.4 Hz, 1H), 2.92 (dd, J = 13.2, 5.4 Hz, 1H), 2.69 (dd, J = 13.2, 10.2 Hz, 1H), 2.40 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.7, 146.8, 145.1, 143.1, 141.7, 136.3, 129.7, 128.6, 128.6, 128.4, 128.4, 128.1, 127.8, 127.4, 127.0, 123.8, 122.6, 77.1, 57.9, 51.2, 42.6, 21.7; IR ν_{max} (cm^{-1}) 2924, 2550, 1693, 1596, 1575, 1490, 1417, 1375, 1303, 1275, 1163, 1083, 810, 750, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{37}H_{35}N_2O_5S_2$651.1982, found 651.1982.

*(Z)-N-((4,4-Diphenyl-5-(4-methylphenylimino)tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3k**).* The general procedure was followed, and the product was purified by column chromatography (20:3 petroleum ether/EtOAc): white solid, 131.5 mg, 99% yield; mp 94−95 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, J = 8.4 Hz, 4H), 7.40 (d, J = 7.8 Hz, 2H), 7.38−7.32 (m, 4H), 7.31−7.26 (m, 3H), 7.24−7.20 (m, 1H), 7.18 (d, J = 8.4 Hz, 4H), 7.09 (s, 4H), 4.62−4.52 (m, 1H), 4.13 (dd, J = 15.6, 6.6 Hz, 1H), 3.70 (dd, J = 15.4, 5.4 Hz, 1H), 2.90 (dd, J = 13.2, 5.4 Hz, 1H), 2.67 (dd, J = 13.2, 10.2 Hz, 1H), 2.40 (s, 6H), 2.29 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 162.3, 145.0, 144.0, 143.2, 141.8, 136.3, 133.1, 129.6, 129.1, 128.6, 128.4, 128.3, 128.1, 127.7, 127.3, 126.9, 122.6, 76.8, 57.8, 51.1, 42.6, 21.7, 20.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{38}H_{37}N_2O_5S_2$ 665.2138, found 665.2139.

*(Z)-N-((4,4-Diphenyl-5-(4-methoxyphenylimino)-tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3l**).* The general procedure was followed, and the product was purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 133.3 mg, 98% yield; mp 81−82 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, J = 8.4 Hz, 4H), 7.36 (dd, J = 15.6, 7.2 Hz, 6H), 7.31−7.27 (m, 3H), 7.20 (dd, J = 8.4, 3.0 Hz, 7H), 6.82 (d, J = 9.0 Hz, 2H), 4.62−4.52 (m, 1H), 4.13 (dd, J = 15.6, 6.6 Hz, 1H), 3.76−3.72 (m, 4H), 2.89 (dd, J = 13.2 4.8 Hz, 1H), 2.67 (dd, J = 13.2, 10.2 Hz, 1H), 2.40 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 161.7, 156.2, 145.1, 143.2, 141.9, 139.5, 136.3, 129.7, 128.6, 128.3, 128.0, 127.7, 127.3, 126.8, 124.4, 113.7, 76.7, 57.9, 55.4, 51.1, 42.5, 21.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{38}H_{37}N_2O_6S_2$ 681.2088, found 681.2088.

*(Z)-N-((4,4-Diphenyl-5-(4-fluorophenylimino)tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3m**).* The general procedure was followed, and the product was purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 117.6 mg, 88% yield; mp 86−87 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79−7.73 (m, 4H), 7.41−7.35 (m, 6H), 7.33−7.26 (m, 3H), 7.24 (t, J = 7.2 Hz, 1H), 7.21−7.12 (m, 6H), 6.95 (t, J = 9.0 Hz, 2H), 4.66−4.58 (m, 1H), 4.12 (dd, J = 15.6, 6.6 Hz, 1H), 3.70 (dd, J = 15.6, 4.8 Hz, 1H), 2.93 (dd, J = 13.2, 5.4 Hz, 1H), 2.69 (dd, J = 13.2, 10.2 Hz, 1H), 2.40 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 162.9, 160.3, 158.7, 159.5(d, J = 240.0 Hz), 145.1, 142.9, 142.6, 142.5, 141.7, 136.3, 129.6, 128.6, 128.3, 128.1, 127.7, 127.4, 127.0, 124.3(d, J = 6.0 Hz), 115.1(d, J = 23.0 Hz), 77.0, 58.0, 51.1, 42.4, 21.7; IR ν_{max} (cm^{-1}) 3029, 2359, 2341, 1695, 1596, 1502, 1373, 1352, 1167, 1083, 816, 698, 662, 550; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{37}H_{34}FN_2O_5S_2$ 669.1888, found 669.1888.

*(Z)-N-((4,4-Diphenyl-5-(2-chlorophenylimino)tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3n**).* The general

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J. Org. Chem. 2021, 86, 235−253

procedure was followed, and the product was purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 116.3 mg, 85% yield; mp 138−139 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72 (d, J = 8.4 Hz, 4H), 7.52 (d, J = 7.8 Hz, 2H), 7.43−7.36 (m, 5H), 7.34−7.29 (m, 3H), 7.25−7.21 (m, 1H), 7.18 (d, J = 8.4 Hz, 5H), 7.09 (d, J = 7.8 Hz, 1H), 6.97 (t, J = 7.2 Hz, 1H), 4.64−4.56 (m, 1H), 4.16 (dd, J = 15.6, 6.6 Hz, 1H), 3.67 (dd, J = 15.6, 4.8 Hz, 1H), 3.02 (dd, J = 13.2, 4.8 Hz, 1H), 2.68 (dd, J = 13.2, 10.2 Hz, 1H), 2.41 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 164.6, 145.1, 144.9, 142.9, 140.5, 136.2, 129.6, 129.5, 128.6, 128.4, 128.2, 127.9, 127.6, 127.0, 127.0, 126.1, 124.3, 123.1, 77.7, 58.0, 51.34, 42.9, 21.7; IR ν_{max} (cm^{-1}) 3061, 1701, 1587, 1492, 1472, 1447, 1375, 1352, 1167, 1084, 910, 816, 729, 663, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{37}H_{34}ClN_2O_5S_2$ 685.1592, found 685.1591.

*(Z)-N-((4,4-Diphenyl-5-(3-chlorophenylimino)tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3o**).* The general procedure was followed, and the product was purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 117.7 mg, 86% yield; mp 127−128 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 4H), 7.39−7.27 (m, 9H), 7.26−7.23 (m, 1H), 7.19 (d, J = 8.4 Hz, 5H), 7.14 (s, 1H), 7.02 (dd, J = 13.6, 8.4 Hz, 2H), 4.64−4.56 (m, 1H), 4.13 (dd, J = 15.6, 6.6 Hz, 1H), 3.68 (dd, J = 15.6, 4.8 Hz, 1H), 2.94 (dd, J = 13.2, 4.8 Hz, 1H), 2.69 (dd, J = 13.2, 10.2 Hz, 1H), 2.40 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 163.8, 148.3, 145.2, 142.9, 141.5, 136.2, 134.1, 129.7, 128.8, 128.3, 128.3, 128.2, 127.7, 127.6, 127.1, 123.8, 122.6, 121.0, 77.4, 58.0, 51.1, 42.5, 21.7; IR ν_{max} (cm^{-1}) 2970, 1703, 1589, 1373, 1475, 1373, 1352, 1167, 1083, 816, 741, 663, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{37}H_{34}ClN_2O_5S_2$685.1592, found 685.1591.

*(Z)-N-((4,4-Diphenyl-5-(4-chlorophenylimino)tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3p**).* The general procedure was followed, and the product was purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 123.2 mg, 90% yield; mp 126−127 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, J = 8.4 Hz, 4H), 7.40−7.34 (m, 6H), 7.31 (t, J = 7.8 Hz, 3H), 7.26−7.16 (m, 7H), 7.10 (d, J = 8.4 Hz, 2H), 4.68−4.59 (m, 1H), 4.10 (dd, J = 15.6, 7.2 Hz, 1H), 3.66 (dd, J = 15.6, 4.8 Hz, 1H), 2.95 (dd, J = 13.2, 5.4 Hz, 1H), 2.69 (dd, J = 13.2, 9.6 Hz, 1H), 2.41 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 163.4, 145.3, 145.1, 142.8, 141.6, 136.2, 129.6, 128.9, 128.7, 128.5, 128.4, 128.3, 128.2, 127.6, 127.4, 127.0, 124.1, 77.1, 57.9, 51.0, 42.5, 21.7; IR ν_{max} (cm^{-1}) 2961, 2359, 2341, 1697, 1585, 1485, 1375, 1306, 1263, 1167, 1083, 730, 663, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{37}H_{34}ClN_2O_5S_2$685.1592, found 685.1594.

*(Z)-N-((4,4-Diphenyl-5-(4-bromophenylimino)tetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3q**).* The general procedure was followed, and the product was purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 132.6 mg, 91% yield; mp 109−110 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, J = 8.4 Hz, 4H), 7.40−7.33 (m, 8H), 7.31 (t, J = 7.8 Hz, 3H), 7.24 (d, J = 5.4 Hz, 1H), 7.19 (d, J = 8.4 Hz, 4H), 7.04 (d, J = 8.4 Hz, 2H), 4.69−4.60 (m, 1H), 4.10 (dd, J = 15.6, 7.2 Hz, 1H), 3.64 (dd, J = 15.6, 4.8 Hz, 1H), 2.96 (dd, J = 13.2, 5.4 Hz, 1H), 2.69 (dd, J = 13.2, 9.6 Hz, 1H), 2.42 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 163.4, 145.9, 145.2, 142.8, 141.6, 136.2, 131.5, 129.7, 128.7, 128.3, 128.3, 128.2, 127.7, 127.5, 127.1, 124.5, 116.7, 77.2, 57.9, 51.0, 42.5, 21.7; IR ν_{max} (cm^{-1}) 3059, 2361, 1693, 1596, 1492, 1483, 1446, 1373, 1167, 1083, 1068, 814, 732, 662, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{37}H_{34}BrN_2O_5S_2$ 729.1087, found 729.1088.

*(Z)-N-((4,4-Diphenyl-5-benzyliminotetrahydrofuran-2-yl)-methyl)-4-methyl-N-tosylbenzenesulfonamide (**3r**).* The general procedure was followed, and the product was purified by column chromatography (10:3 petroleum ether/EtOAc), white solid, 123.6 mg, 93% yield; mp 60−61 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (d, J = 8.4 Hz, 4H), 7.34−7.25 (m, 12H), 7.24−7.16 (m, 7H), 4.68−4.57 (m, 2H), 4.56−4.46 (m, 1H), 4.12 (dd, J = 15.4, 6.5 Hz, 1H), 3.78 (dd, J = 15.6, 4.8 Hz, 1H), 2.88 (dd, J = 13.2, 4.8 Hz, 1H), 2.59 (dd, J = 12.6, 10.2 Hz, 1H), 2.38 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 163.6, 145.1, 143.1, 141.7, 140.7, 136.5, 129.7, 128.4, 128.3, 128.2, 128.1, 127.9, 127.6, 127.6, 127.1, 126.7, 126.2, 76.1, 57.4, 51.5, 51.0, 42.7, 21.6; IR ν_{max} (cm^{-1}) 3028, 1701, 1594, 1495, 1446, 1375, 1354, 1167, 1084, 910, 815, 733, 698, 663, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{38}H_{37}N_2O_5S_2$ 665.2138, found 665.2137.

*(Z)-N-((4,4-Diphenyl-5-methoxyiminotetrahydrofuran-2-yl)-methyl)-4-methyl-N-tosylbenzenesulfonamide (**3s**).* The general procedure was followed, and the product was purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 102.7 mg, 85% yield; mp 53−54 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.2 Hz, 4H), 7.37−7.18 (m, 14H), 4.54−4.45 (m, 1H), 4.19 (dd, J = 15.5, 5.4 Hz, 1H), 3.94−3.85 (m, 4H), 2.79−2.63 (m, 2H), 2.43 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.3, 145.2, 142.2, 141.7, 136.4, 129.7, 128.6, 128.2, 128.0, 127.6, 127.3, 126.9, 78.2, 62.7, 57.4, 50.6, 43.1, 21.7; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{32}H_{33}N_2O_6S_2$605.1775, found 605.1773.

*(Z)-N-((4,4-Diethyl-5-phenyliminotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3t**).* The general Procedure was followed, and purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 102.0 mg, 92% yield; mp 97−98 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, J = 8.4 Hz, 4H), 7.28−7.24 (m, 2H), 7.19 (d, J = 8.4 Hz, 4H), 7.01 (dd, J = 15.5, 7.8 Hz, 3H), 4.69−4.60 (m, 1H), 4.09 (dd, J = 15.5, 7.3 Hz, 1H), 3.54 (dd, J = 15.6, 4.2 Hz, 1H), 2.41 (s, 6H), 1.99 (dd, J = 13.2, 6.6 Hz, 1H), 1.82 (dd, J = 13.2, 9.6 Hz, 1H), 1.73−1.64 (m, 4H), 0.97 (td, J = 7.2, 3.0 Hz, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 165.5, 147.6, 145.0, 136.3, 129.6, 128.6, 128.6, 123.2, 122.3, 77.9, 52.1, 48.6, 36.0, 31.0, 29.7, 21.7, 8.8; IR ν_{max} (cm^{-1}) 2959, 1701, 1596, 1495, 1373, 1354, 1184, 1167, 1086, 852, 732, 663, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{29}H_{35}N_2O_5S_2$555.1982, found 555.1985.

*(Z)-N-((4,4-Dipropyl-5-phenyliminotetrahydrofuran-2-yl)-methyl)-4-methyl-N-tosylbenzenesulfonamide (**3u**).* The general Procedure was followed, and purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 109.5 mg, 94% yield; mp 125−126 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, J = 8.4 Hz, 4H), 7.29−7.23 (m, 2H), 7.19 (d, J = 8.4 Hz, 4H), 7.05−6.96 (m, 3H), 4.67−4.58 (m, 1H), 4.09 (dd, J = 15.6, 7.4 Hz, 1H), 3.54 (dd, J = 15.6, 4.2 Hz, 1H), 2.40 (s, 6H), 2.04−1.97 (m, 1H), 1.82 (dd, J = 13.2, 9.6 Hz, 1H), 1.73−1.63 (m, 1H), 1.61−1.54 (m, 3H), 1.48−1.28 (m, 4H), 0.94 (q, J = 7.2 Hz, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 165.8, 147.5, 144.9, 136.1, 129.5, 128.5, 128.4, 123.1, 122.2, 77.8, 51.9, 47.8, 40.9, 39.8, 36.9, 21.6, 17.6, 17.6, 14.5, 14.5; IR ν_{max} (cm^{-1}) 2968, 2932, 1701, 1595, 1495, 1373, 1354, 1188, 1167, 1086, 816, 723, 663, 551; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{31}H_{39}N_2O_5S_2$ 583.2295, found 583.2298.

*(2R,3R,Z)-N-((3-Methyl-4,4-diphenyl-5-phenyliminotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3v**).* The general procedure was followed, and the product was purified by column chromatography (10:1 petroleum ether/EtOAc). The product was given as a mixture of two inseparable isomers with dr > 20:1, white solid, 89.0 mg, 67% yield; mp 156−157 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, J = 8.4 Hz, 4H), 7.52 (d, J = 7.8 Hz, 2H), 7.34 (t, J = 7.8 Hz, 2H), 7.31−7.24 (m, 6H), 7.17 (d, J = 8.4 Hz, 4H), 7.10 (d, J = 7.8 Hz, 2H), 7.02 (t, J = 7.2 Hz, 1H), 6.86 (dd, J = 6.6, 3.0 Hz, 2H), 4.26 (dd, J = 15.6, 7.8 Hz, 1H), 4.19−4.17 (m, 1H), 3.74 (dd, J = 15.6, 1.8 Hz, 1H), 3.12−3.00 (m, 1H), 2.41 (s, 6H), 0.88 (d, J = 6.6 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 163.1, 147.1, 145.0, 141.2, 141.1, 136.4, 129.6, 129.2, 129.1, 128.7, 128.6, 128.0, 127.8, 127.3, 127.1, 123.6, 122.4, 82.3, 60.6, 50.8, 42.3, 21.8, 12.3; IR ν_{max} (cm^{-1}) 3043,1693, 1593, 1493, 1446, 1379, 1373, 1348, 1167, 1086, 1056, 843, 719, 698, 662, 550; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{38}H_{37}N_2O_5S_2$ 665.2138, found 665.2140.

*(2R,3R,Z)-N-((3-Methyl-4,4-diphenyl-5-(4-fluorophenylimino)otetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3w**).* The general procedure was followed, and the product was purified by column chromatography (20:3 petroleum ether/EtOAc). The product was given as a mixture of two inseparable isomers with dr > 20:1, white solid, 83.2 mg, 61% yield; mp 89−90 °C. Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 4H), 7.50 (d, J = 7.2 Hz, 2H), 7.37−7.30 (m, 4H), 7.27 (d, J = 2.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 4H), 7.12 (dd, J = 10.4, 3.6 Hz, 2H), 6.95 (t, J =

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J. Org. Chem. 2021, 86, 235−253

8.8 Hz, 2H), 6.83 (dd, J = 6.4, 2.8 Hz, 2H), 4.33−4.12 (m, 2H), 3.77 (d, J = 14.0 Hz, 1H), 3.02−3.03 (m, 1H), 2.42 (s, 6H), 0.88 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.3,159.5 (d, J = 240.0 Hz), 145.1, 142.8, 142.7, 141.1, 141.0, 136.4, 129.6, 129.5, 129.1, 129.0, 128.5, 128.0, 127.8, 127.3, 127.2, 124.3 (d, J = 8.0 Hz), 115.1 (d, J = 21.8 Hz), 82.0, 60.8, 50.8, 42.3, 21.7, 12.3; IR ν_{max} (cm^{-1}) 2924, 2358, 1697, 1596, 1502, 1373, 1354, 1167, 1084, 843, 814, 720, 662, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{38}H_{36}FN_2O_5S_2$ 683.2044, found 683.2051.

*(2R,3R,Z)-N-((3-ethyl-4,4-diphenyl-5-phenyliminotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3x**).* The general procedure was followed, and the product was purified by column chromatography (20:3 petroleum ether/EtOAc): white solid, dr > 20:1, 99.2 mg, 73% yield; mp 171−172 °C. Major isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.4 Hz, 4H), 7.58 (d, J = 7.2 Hz, 2H), 7.39−7.30 (m, 4H), 7.27−7.24 (m, 4H), 7.17 (d, J = 8.4 Hz, 4H), 7.09 (d, J = 7.2 Hz, 2H), 7.00 (t, J = 7.6 Hz, 1H), 6.93 (dd, J = 6.8, 3.2 Hz, 2H), 4.41−4.32 (m, 1H), 4.20 (dd, J = 15.6, 9.2 Hz, 1H), 3.76 (dd, J = 15.6, 1.2 Hz, 1H), 2.95−2.82 (m, 1H), 2.41 (s, 6H), 1.54−1.43 (m, 1H), 1.04 (dd, J = 14.8, 6.8 Hz, 1H), 1.00−0.94 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.1, 147.1, 144.8, 141.6, 141.3, 136.5, 129.6, 129.2, 128.6, 128.5, 128.0, 127.9, 127.4, 127.1, 123.5, 122.4, 82.1, 61.2, 51.8, 49.1, 21.8, 21.7, 13.1; IR ν_{max} (cm^{-1}) 2922, 2851, 1697, 1595, 1489, 1373, 1354, 1167, 1083, 815, 702, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{39}H_{39}N_2O_5S_2$ 679.2295, found 679.2296.

*(2R,3R,Z)-N-((3-methyl-4,4-diphenyl-5-benzyliminotetrahydrofuran-2-yl)methyl)-4-methyl -N-tosylbenzenesulfonamide (**3y**).* The general procedure was followed, and the reaction time was extended to 15 h. The product was purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, dr > 20:1, 86.8 mg, 64% yield; mp 142−143 °C. Major isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.2 Hz, 4H), 7.48 (d, J = 7.2 Hz, 2H), 7.36−7.22 (m, 11H), 7.19 (d, J = 6.8 Hz, 4H), 6.75 (d, J = 6.8 Hz, 2H), 4.66 (d, J = 16.0 Hz, 1H), 4.52 (d, J = 16.0 Hz, 1H), 4.22−4.11 (m, 2H), 3.88 (d, J = 13.6 Hz, 1H), 2.97 (d, J = 13.6 Hz, 1H), 2.42 (s, 6H), 0.86 (d, J = 5.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.56, 145.02 (2C), 141.6, 141.3, 141.2, 137.0, 129.7, 129.2, 129.1, 128.3, 128.0, 127.8, 127.6, 127.4, 127.1, 126.9, 126.0, 81.0, 60.3, 51.4, 50.7, 42.4, 21.7, 12.3. IR ν_{max} (cm^{-1}) 3125, 2931, 1772, 1699, 1596, 1508, 1446, 1373, 1354, 1167, 1086, 816, 700, 663, 551. HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{39}H_{39}N_2O_5S_2$679.2295, found 679.2260.

*(2R,3R,Z)-N-((3,4,4-trimethyl-5-phenyliminotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3z**).* The general procedure was followed with **2j** as the catalyst, and purified by column chromatography (5:1 petroleum ether/EtOAc). The product was obtained as inseparable isomers with 5-*exo*/6-*endo* = 10:1, dr >20:1, white solid, 78.8 mg, 73% yield; mp 133−134 °C. Major isomer: ^1H NMR (600 MHz, $CDCl_3$) δ 7.77 (d, J = 8.2 Hz, 4H), 7.28 (t, J = 7.8 Hz, 2H), 7.16 (d, J = 8.1 Hz, 4H), 7.08 (d, J = 7.5 Hz, 2H), 7.01 (t, J = 7.4 Hz, 1H), 4.34−4.29 (m, 1H), 4.15 (dd, J = 16.1, 8.0 Hz, 1H), 3.55−3.49 (m, 1H), 2.40 (s, 6H), 1.84−1.77 (m, 1H), 1.29 (s, 3H), 1.13 (s, 3H), 1.05 (d, J = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.4, 147.4, 144.9, 136.1, 129.6, 128.7, 128.7, 123.4, 122.4, 84.0, 50.9, 45.2, 43.2, 24.5, 21.7, 20.7, 10.1; IR ν_{max} (cm^{-1}) 2970, 1703, 1596, 1508, 1373, 1354, 1292, 1167, 1086, 1043, 945, 816, 733, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{28}H_{33}N_2O_5S_2$ 541.1825, found 541.1828.

*(Z)-N-((4-phenylimino-5-oxaspiro[2.4]heptan-6-yl) methyl)-4-methyl-N-tosylbenzenesulfon amide (**3aa**).* The general procedure was followed, and the product was purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 82.8 mg, 79% yield; mp 63−64 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 7.81 (d, J = 8.3 Hz, 4H), 7.27−7.20 (m, 6H), 7.07−6.99 (m, 3H), 4.96−4.84 (m, 1H), 4.16 (dd, J = 15.4, 7.3 Hz, 1H), 3.64 (dd, J = 15.4, 4.6 Hz, 1H), 2.42 (s, 6H), 2.24 (dd, J = 12.7, 7.3 Hz, 1H), 2.07 (dd, J = 12.7, 6.7 Hz, 1H), 1.39−1.31 (m, 1H), 1.30−1.25 (m, 1H), 0.98−0.83 (m, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 164.1, 146.0, 145.0, 136.2, 129.6, 128.6, 128.5, 123.2, 122.8, 78.2, 51.29, 34.5, 21.7, 21.4, 15.4, 14.9; IR ν_{max} (cm^{-1}) 2926, 1701, 1595, 1504, 1369, 1352, 1165, 1083, 814, 696, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{29}N_2O_5S_2$ 525.1512, found 525.1513.

*(Z)-N-((1-phenylimino-2-oxaspiro[4.4]nonan-3-yl)methyl)- −4-methyl-N-tosylbenzenesulfonamide (**3ab**).* The general procedure was followed, and the product was purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 91.7 mg, 83% yield; mp 62−63 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 4H), 7.28−7.25 (m, 2H), 7.20 (d, J = 8.4 Hz, 4H), 7.06 (d, J = 7.8 Hz, 2H), 7.01 (t, J = 7.2 Hz, 1H), 4.70−4.61 (m, 1H), 4.14 (dd, J = 15.6, 7.4 Hz, 1H), 3.58 (dd, J = 15.6, 4.2 Hz, 1H), 2.41 (s, 6H), 2.31 (dd, J = 14.4, 5.4 Hz, 1H), 2.09 (dd, J = 12.6, 6.0 Hz, 1H), 1.98−1.88 (m, 3H), 1.75−1.63 (m, 5H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.1, 147.4, 145.0, 136.2, 129.6, 128.6, 128.5, 123.3, 122.5, 78.2, 51.5, 51.2, 41.3, 38.8, 37.9, 25.2, 25.1, 21.7; IR ν_{max} (cm^{-1}) 2955, 1701, 1595, 1502, 1373, 1354, 1167, 1084, 912, 816, 742, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{29}H_{33}N_2O_5S_2$ 553.1825, found 553.1828.

*(Z)-N-((1-Phenylimino-2-oxaspiro[4.5]decan-3-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3ac**).* The general procedure was followed, and the product was purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 103.0 mg, 91% yield; mp 82−83 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 4H), 7.27−7.24 (m, 2H), 7.20 (d, J = 8.4 Hz, 4H), 7.08−6.99 (m, 3H), 4.70−4.63 (m, 1H), 4.12 (dd, J = 15.6, 7.2 Hz, 1H), 3.58 (dd, J = 15.6, 4.2 Hz, 1H), 2.42 (s, 6H), 2.28 (dd, J = 12.6, 6.0 Hz, 1H), 2.00−1.93 (m, 1H), 1.81−1.55 (m, 7H), 1.41−1.16 (m, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.6, 147.2, 145.0, 136.2, 129.6, 128.6, 128.5, 123.4, 122.4, 78.2, 51.8, 45.4, 37.2, 35.6, 33.4, 25.3, 22.8, 22.6, 21.7; IR ν_{max} (cm^{-1}) 2932, 1697, 1595, 1502, 1493, 1373, 1352, 1167, 1083, 912, 815, 732, 662, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{30}H_{35}N_2O_5S_2$567.1982, found 567.1985.

*(Z)-N-((1-Phenylimino-2,8-oxaspiro[4.5]decan-3-yl) methyl)-4-methyl-N-tosylbenzenesulfonamide (**3ad**).* The general procedure was followed with **2j** as the catalyst, and the product was purified by column chromatography (5:2 petroleum ether/EtOAc). The product was obtained as a mixture of two inseparable isomers with 5-*exo*/6-*endo* = 16:1: white solid, 88.6 mg, 78% yield; mp 92−92 °C. Major isomer: ^1H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 4H), 7.29−7.25 (m, 2H), 7.21 (d, J = 8.4 Hz, 4H), 7.08 (d, J = 7.2 Hz, 2H), 7.03 (t, J = 7.2 Hz, 1H), 4.75−4.66 (m, 1H), 4.14 (dd, J = 15.6, 7.2 Hz, 1H), 4.10−3.98 (m, 2H), 3.61 (dd, J = 15.6, 4.2 Hz, 1H), 3.56−3.50 (m, 1H), 3.50−3.43 (m, 1H), 2.42 (s, 6H), 2.33 (dd, J = 12.6, 6.0 Hz, 1H), 2.30−2.22 (m, 1H), 2.21−1.96 (m, 1H), 1.73 (dd, J = 12.6, 10.2 Hz, 1H), 1.53 (dd, J = 25.2, 13.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 165.0, 146.9, 145.2, 136.2, 129.7, 128.7, 128.6, 123.6, 122.6, 77.8, 64.6, 64.1, 51.6, 42.7, 37.8, 35.2, 33.9, 21.7; IR ν_{max} (cm^{-1}) 2953, 2852, 1699, 1595, 1207,1188, 1373, 1352, 1167, 1107, 1083, 912, 816, 735, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{29}H_{33}N_2O_6S_2$569.1775, found 569.1778.

*(Z)-N-((8-tert-Butyloxycarbonyl-1-phenylimino-2-oxa-8-azaspiro[4.5]decan-3-yl) methyl)-4-methyl-N-tosylbenzenesulfonamide (**3ae**).* The general procedure was followed, and the product was purified by column chromatography (5:1 petroleum ether/EtOAc). The product was obtained as a mixture of two inseparable isomers with 5-*exo*/6-*endo* = 20:1: white solid, 89.4 mg, 67% yield; mp 95−96 °C. Major isomer: ^1H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 4H), 7.28 (dd, J = 7.8, 6.0 Hz, 2H), 7.21 (d, J = 8.4 Hz, 4H), 7.08−7.00 (m, 3H), 4.76−4.67 (m, 1H), 4.18−3.87 (m, 3H), 3.61 (dd, J = 15.6, 4.2 Hz, 1H), 3.09−2.90 (m, 2H), 2.41 (s, 6H), 2.25 (dd, J = 12.6, 6.0 Hz, 1H), 2.13−2.05 (m, 1H), 1.88−1.81 (m, 1H), 1.71 (dd, J = 12.6, 10.2 Hz, 1H), 1.62−1.50 (m, 2H), 1.46 (s, 9H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 165.0, 154.5, 146.7, 145.1, 143.4, 139.2, 136.0, 129.6, 128.6, 128.5, 126.3, 123.6, 122.4, 79.6, 77.8, 51.5, 43.4, 37.2, 34.7, 28.4, 21.6, 21.4. IR ν_{max} (cm^{-1}) 2976, 1693, 1595, 1487, 1427, 1371, 1280, 1167, 1084, 1043, 912, 816, 733, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{34}H_{42}N_3O_7S_2$ 668.2459, found 668.2455.

*(Z)-N-((2-Methyl-4,4-diphenyl-5-phenyliminotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3af**).* The general

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J. Org. Chem. 2021, 86, 235−253

procedure was followed with mixture solvents (HFIP/*tert*-BuOMe= 1:1), and the reaction time was extended to 15 h. The product was purified by column chromatography (10:1 petroleum ether/EtOAc): white solid, 95.6 mg, 72% yield; mp 93−94 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, J = 8.4 Hz, 4H), 7.58 (d, J = 7.8 Hz, 2H), 7.39 (d, J = 7.8 Hz, 2H), 7.37−7.29 (m, 5H), 7.28 (d, J = 7.2 Hz, 2H), 7.23 (d, J = 7.8 Hz, 3H), 7.11 (d, J = 8.4 Hz, 4H), 7.06 (t, J = 7.2 Hz, 1H), 4.00 (d, J = 16.2 Hz, 1H), 3.86 (d, J = 16.2 Hz, 1H), 3.05 (s, 2H), 2.35 (s, 6H), 1.08 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 163.0, 147.3, 144.8, 144.5, 143.6, 136.4, 129.4, 128.6, 128.6, 128.4, 128.2, 128.0, 127.9, 127.9, 126.9, 126.7, 123.5, 122.5, 85.0, 58.0, 56.6, 48.4, 24.4, 21.6. IR ν_{max} (cm^{-1}) 3059, 1693, 1595, 1491, 1446, 1373, 1356, 1226, 1167, 1084, 910, 814, 766, 732, 662, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{38}H_{37}N_2O_5S_2$ 665.2138, found 665.2139.

*(Z)-N-((2-Methyl-4,4-diethyl-5-phenyliminotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3ag**).* The general procedure was followed with mixture solvents (HFIP/*tert*-BuOMe= 1:1), and the reaction time was extended to 15 h. The product was purified by column chromatography (10:1 petroleum ether/EtOAc): white solid, 62.5 mg, 55% yield; mp 81.0−82 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72 (d, J = 8.4 Hz, 4H), 7.30−7.22 (m, 2H), 7.15 (d, J = 8.4 Hz, 4H), 7.02 (d, J = 7.2 Hz, 2H), 6.98 (t, J = 7.2 Hz, 1H), 4.20 (d, J = 15.6 Hz, 1H), 3.74 (d, J = 15.6 Hz, 1H), 2.39 (s, 6H), 1.99 (d, J = 1.2 Hz, 2H), 1.79−1.65 (m, 4H), 1.24 (s, 3H), 1.04−0.96 (m, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 166.1, 148.3, 144.8, 136.7, 129.4, 128.8, 128.7, 123.0, 122.0, 84.5, 57.4, 48.8, 42.1, 31.9, 31.8, 25.6, 21.7, 9.1, 9.0; IR ν_{max} (cm^{-1}) 2966, 1699, 1595, 1489, 1373, 1356, 1232, 1167, 1086, 1061, 964, 914, 733, 665, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{30}H_{37}N_2O_5S_2$ 569.2138, found 569.2142.

*(Z)-N-((3-Methyl-1-phenylimino-2-oxaspiro[4.5]decan-3-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3ah**).* The general procedure was followed, and with mixture solvents (HFIP/*tert*-BuOMe = 1:1) and **2j** as the catalyst, the reaction time extend to 15 h. The product was purified by column chromatography (5:1 petroleum ether/EtOAc): white solid, 60.4 mg, 52% yield; mp 150−151 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, J = 8.4 Hz, 4H), 7.30−7.24 (m, 2H), 7.17 (d, J = 8.4 Hz, 4H), 7.07 (d, J = 7.8 Hz, 2H), 7.00 (t, J = 7.2 Hz, 1H), 4.12 (d, J = 16.2 Hz, 1H), 3.82 (d, J = 16.2 Hz, 1H), 2.40 (s, 6H), 2.07−1.99 (m, 2H), 1.90−1.82 (m, 1H), 1.82−1.70 (m, 4H), 1.66 (s, 1H), 1.49 (d, J = 13.2 Hz, 1H), 1.38−1.27 (m, 3H), 1.25 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 167.7, 148.0, 144.8, 136.6, 129.4, 128.8, 128.6, 123.1, 122.4, 85.1, 57.2, 45.8, 43.6, 37.5, 36.8, 25.9, 25.2, 22.8, 22.8, 21.7; IR ν_{max} (cm^{-1}) 2935, 2854, 1682, 1593, 1487, 1362, 1348, 1240, 1191, 1173, 1163, 1083, 1034, 973, 815, 775, 555; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{31}H_{37}N_2O_5S_2$ 581.2138, found 581.2135.

*(Z)-N-((4-Methyl-4-phenyl-5-phenyliminotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3ai**).* The general procedure was followed, and the product was purified by column chromatography (10:1 petroleum ether/EtOAc). The product was obtained as inseparable isomers with dr = 1:1, white solid, 90.6 mg, 77% yield; mp 67−68 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 4H), 7.71 (d, J = 8.4 Hz, 4H), 7.59 (d, J = 7.2 Hz, 2H), 7.42−7.35 (m, 6H), 7.33−7.27 (m, 6H), 7.19 (t, J = 8.4 Hz, 8H), 7.14 (d, J = 8.4 Hz, 4H), 7.07 (t, J = 7.2 Hz, 2H), 4.90−4.83 (m, 1H), 4.43−4.37 (m, 1H), 4.14 (dd, J = 15.6, 6.6 Hz, 1H), 3.85 (dd, J = 15.6, 8.4 Hz, 1H), 3.66 (dd, J = 15.6, 5.4 Hz, 1H), 3.33 (dd, J = 15.6, 3.6 Hz, 1H), 2.55 (dd, J = 12.6, 4.8 Hz, 1H), 2.48−2.43 (m, 1H), 2.42−2.39 (m, 7H), 2.38 (s, 6H), 2.04 (dd, J = 12.6, 11.4 Hz, 1H), 1.72 (s, 3H), 1.66 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 165.0, 164.4, 147.1, 146.8, 145.0, 144.9, 144.4, 142.9, 136.3, 136.2, 129.6, 129.5, 128.7, 128.7, 128.6, 128.6, 128.4, 128.4, 127.1, 126.9, 126.5, 125.8, 123.8, 123.5, 122.7, 122.5, 77.8, 76.9, 51.3, 51.10, 49.8, 48.5, 42.9, 42.8, 27.5, 27.2, 21.7, 21.6; IR ν_{max} (cm^{-1}) 2976, 1705, 1595, 1493, 1446, 1373, 1352, 1167, 1086, 912, 816, 768, 733, 700, 663, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{32}H_{33}N_2O_5S_2$ 589.1825, found 589.1821.

*(Z)-N-((4-Ethyl-4-phenyl-5-phenyliminotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3aj**).* The general procedure was followed, and the product was purified by column chromatography (10:1 petroleum ether/EtOAc). The product were inseparable isomers with d.r.= 3:2, white solid, 87.9 mg, 73% yield; mp 83−84 °C; ^{1}H NMR (400 MHz, $CDCl_3$), distinguishable signals for the minor diastereoisomer are reported in *italics*: δ 7.81 (d, J = 8.4 Hz, 4H), 7.77−7.68 (m, 4H), 7.52 (d, J = 9.0 Hz, 4H), 7.48−7.29 (m, 5H), 7.24 (d, J = 8.2 Hz, 4H), 7.20 (d, J = 7.3 Hz, 4H), 7.10 (q, J = 7.1 Hz, 1H), *4.94−4.84* (m, 1H), 4.55−4.41 (m, 1H), 4.18 (dd, J = 15.5, 6.4 Hz, 1H), *3.85−3.75* (m, 1H), 3.74−3.68 (m, 1H), *3.40−3.33* (m, 1H), 2.71−2.56 (m, 1H), 2.48 (s, 6H), 2.43 (s, 6H), 2.20−2.00 (m, 2H), 1.01 (t, J = 7.3 Hz, 3H), 0.92 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, distinguishable signals for the minor diastereoisomer are reported in *italics*) δ 163.5, 163.4, 147.3, 147.0, 145.1, 144.8, 143.2, 140.8, 136.4, 136.3, 129.7, 129.6, 128.7, 128.6, 128.5, 128.5, 128.4, 127.2, 127.0, 126.9, 126.5, 123.7, 123.4, 122.6, 122.5, 77.5, 77.1, 53.5, 5.19, 51.7, 51.4, 38.4, 37.8, 34.0, 33.2, 21.7, 21.7, 9.4. IR ν_{max} (cm^{-1}) 2926, 1697, 1595, 1493, 1373, 1353, 1166, 1085, 816, 764, 731, 700, 663, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{33}H_{35}N_2O_5S_2$ 603.1982, found 603.1993.

*(Z)-N-((4-Methyl-4-(3-chlorophenyl)-5-phenyliminotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3ak**).* The general procedure was followed, and the product was purified by column chromatography (20:3 petroleum ether/EtOAc). The product were inseparable isomers with d.r.= 1:1, white solid, 95.7 mg, 77% yield; mp 79−81 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.7−7.71 (m, 8.2 Hz, 8H), 7.56 (s, 1H), 7.51 (d, J = 7.8 Hz, 1H), 7.38 (s, 1H), 7.36−7.25 (m, 9H), 7.22−7.15 (m, 12H), 7.08 (q, J = 7.6 Hz, 2H), 4.90−4.82 (m, 1H), 4.46−4.28 (m, 1H), 4.14 (dd, J = 15.3, 6.3 Hz, 1H), 3.89 (dd, J = 15.6, 8.0 Hz, 1H), 3.67 (dd, J = 15.3, 5.5 Hz, 1H), 3.40 (dd, J = 15.6, 3.5 Hz, 1H), 2.52 (dd, J = 12.9, 4.8 Hz, 1H), 2.45 (dd, J = 13.1, 7.1 Hz, 1H), 2.41 (s, 6H), 2.40 (s, 7H), 2.33 (dd, J = 13.1, 6.8 Hz, 1H), 2.13−2.01 (m, 1H), 1.70 (s, 3H), 1.65 (s, 3H); ^{3}C NMR{^{1}H}(150 MHz, $CDCl_3$) δ 1164.4, 163.6, 146.7, 146.5, 145.1, 145.0, 136.2, 136.1, 134.6, 134.4, 130.0, 129.9, 129.6, 129.6, 129.6, 128.7, 128.6, 128.4, 128.3, 127.4, 127.1, 126.8, 126.3, 124.9, 124.1, 124.0, 123.7, 122.7, 122.5, 77.7, 76.7, 51.2, 51.0, 49.7, 48.4, 42.8, 42.7, 27.3, 27.2, 21.6, 21.6; IR ν_{max} (cm^{-1}) 2978, 1697, 1595, 1496, 1373, 1352, 1165, 1188, 1086, 912, 815, 734, 696, 663, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{32}H_{32}ClN_2O_5S_2$ 623.1436, found 623.1435.

*(Z)-N-((4-Isopropyl-4-(3-chlorophenyl)-5-phenyliminotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3al**).* The general procedure was followed with **2j** as the catalyst, and purified by column chromatography (20:3 petroleum ether/EtOAc). The products were inseparable isomers with dr = 4:1, white solid, 80.7 mg, 62% yield; mp 112−113 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, J = 8.4 Hz, 4H), 7.67 (d, J = 8.3 Hz, 1H), 7.54 (d, J = 8.7 Hz, 2H), 7.33 (s, 1H), 7.28 (d, J = 7.5 Hz, 2H), 7.19 (d, J = 8.2 Hz, 4H), 7.08 (d, J = 7.3 Hz, 2H), 7.04 (t, J = 7.4 Hz, 1H), 4.47−4.42 (m, 1H), 4.14 (dd, J = 15.6, 6.3 Hz, 1H), 3.69 (dd, J = 15.6, 5.1 Hz, 1H), 2.53 (dd, J = 13.3, 4.8 Hz, 1H), 2.44 (dd, J = 13.5, 6.7 Hz, 1H), 2.40 (s, 6H), 2.11−2.04 (m, 1H), 1.10 (d, J = 6.6 Hz, 3H), 0.68 (d, J = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 162.8, 146.9, 145.2, 138.4, 136.3, 133.2, 129.7,129.7, 128.7, 128.6, 128.5, 128.3, 128.3, 123.7, 122.4, 77.3, 56.3, 51.5, 35.9, 31.6, 21.7, 18.5, 18.0. IR ν_{max} (cm^{-1}) 2958, 1697, 1595, 1492, 1373, 1352, 1165, 1086, 934, 843, 815, 737, 700, 663, 552; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{34}H_{36}ClN_2O_5S_2$651.1749, found 651.1753.

*(Z)-N-((2′-(Phenylimino)-4′,5′-dihydro-2′H-spiro[fluorene-9,3′-furan]-5′-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**3am**).* The general procedure was followed and used **1am** (10 mmol) as a substrate; the reaction time was extended to 15 h. The product was purified by column chromatography (7:1 petroleum ether/EtOAc): pale yellow solid, 4.1 g, 63% yield; mp 67−68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.4 Hz, 4H), 7.82−7.74 (m, 2H), 7.48−7.33 (m, 6H), 7.29−7.22 (m, 6H), 7.06−6.93 (m, 3H), 5.31−5.25 (m, 1H), 4.46 (dd, J = 15.2, 6.0 Hz, 1H), 3.82 (dd, J = 15.7, 4.4 Hz, 1H), 2.70−2.63 (m, 1H), 2.52−2.47 (m, 1H), 2.44 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.4, 148.2, 147.0, 146.6, 145.2, 141.0, 140.1, 136.2, 129.7, 128.6, 128.5, 128.4, 128.3, 127.9, 124.0, 123.6, 122.7, 122.2, 120.7, 120.3, 78.9, 59.4, 51.8, 41.1, 21.7; IR ν_{max} (cm^{-1})

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J. Org. Chem. 2021, 86, 235−253

3065, 1697, 1595, 1493, 1448, 1373, 1354, 1167, 1084, 910, 815, 733, 663,552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{37}H_{33}N_2O_5S_2$649.1825, found 649.1824.

*N-(2-Hydroxy-4,4-diphenyl-5-(phenylamino)pentyl)-4-methyl-N-tosylbenzenesulfonamide (**4a**).* A solution **3j** (325 mg, 0.50 mmol, 1.0 equiv, dissolved in 5 mLCH_2Cl_2) cooled to 0 °C under argon, and H_4LiAl (2.5 M in THF, 1.0 mL) was added dropwise. Then, the mixture was allowed to stir at room temperature for 5 h. Then, the reaction was quenched with NaOH (1.0 M). The mixture was extracted with EtOAc. The combined organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel (10:1 petroleum ether/EtOAc) to give **4a** as a white solid (309.4 mg, 95% yield). mp 138−139 °C. ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.85−7.74 (m, 4H), 7.47−7.40 (m, 2H), 7.39−7.29 (m, 6H), 7.29−7.24 (m, 6H), 7.23−7.15 (m, 2H), 7.00−6.76 (m, 1H), 6.67−6.59 (m, 2H), 4.05 (d, J = 11.5 Hz, 1H), 4.01−3.86 (m, 2H), 3.78 (dd, J = 15.3, 9.2 Hz, 1H), 3.58 (dd, J = 15.3, 2.9 Hz, 1H), 3.43 (s, 1H), 2.58 (dd, J = 14.3, 7.7 Hz, 2H), 2.46 (s, 6H), 2.39 (dd, J = 14.3, 2.5 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 148.3, 146.7, 145.1, 144.9, 136.5, 129.6, 129.2, 128.6, 128.5, 128.5, 128.2, 127.8, 126.7, 126.7, 118.1, 113.9, 67.5, 54.9, 51.4, 42.8, 21.7. IR ν_{max} (cm^{-1}) 3053, 2359, 1601, 1504, 1495, 1371, 1165, 1084, 814, 700, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{37}H_{39}N_2O_5S_2$ 655.2295, found 655.2288.

*N-(2-Hydroxy-4,4-diphenyl-5-(phenylamino)pentyl)-4-methylbenzenesulfonamide (**4b**).* A solution of KOH (1 M in MeOH, 5 mL) was added **4a** (273.4 mg, 0.42 mol, 1.0 equiv), and the reaction mixture was heated to reflux. After completion, the mixture was quenched with HCl (1.0 M, aq) and extracted with CH_2Cl_2. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel (5:1, petroleum ether/EtOAc) to give **4b** as a white solid (189.1 mg, 90% yield). mp 75−76 °C. ^{1}H NMR (400 MHz,$CDCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$: δ 7.70 (d, J = 8.0 Hz, 2H), 7.42−7.18 (m, 15H), 6.82 (t, J = 7.3 Hz, 1H), 6.66 (d, J = 8.0 Hz, 2H), 5.43−5.32 (m, 1H), 4.03 (d, J = 11.3 Hz, 1H), 3.83 (d, J = 11.3 Hz, 1H), 3.67 (q, J = 6.0, 4.8 Hz, 1H), 3.40 (s, 1H), 2.95−2.85 (m, 1H), 2.82−2.68 (m, 1H), 2.53 (dd, J = 14.7, 8.0 Hz, 1H), 2.45 (s, 3H), 2.36 (d, J = 14.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 147.9, 146.4, 144.9, 143.3, 136.8, 129.8, 129.3, 128.8, 128.7, 127.9, 127.6, 127.1, 126.8, 119.0, 114.4, 67.1, 51.6, 49.6, 49.6, 42.7, 21.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{30}H_{33}N_2O_3S$, 501.2206, found 501.2204.

*1-Amino-4,4-diphenyl-5-(phenylamino)pentan-2-ol (**4c**).* Following a literature procedure.[38] To a solution of sodium naphthalenide [prepared by stirring a mixture of sodium (5.2 equiv, 1.0 mmol, 23.0 mg) and naphthalene (5.5 equiv, 1.0 mmol, 130.8 mg) in THF (4.5 mL) under argon at room temperature until the metal sodium is completely consumed]. After that, a solution of **4b** (95.0 mg, 0.19 mmol, 1.0 equiv) in 2 mL THF was added. The resulting reaction mixture was allowed to stir at room temperature for 3 h, and the reaction was quenched by the addition of ice−water, extracted with dichloromethane, and the combined organic layers were dried over Na_2SO_4. The filtered was concentrated and the residue was purified by flash column chromatography on silica gel (20:1:0.01 dichloromethane/Methanol/NEt_3) to give **4c** as a colorless oil (62.2 mg, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.18 (m, 11H), 7.04 (t, J = 7.6 Hz, 2H), 6.63 (t, J = 7.3 Hz, 1H), 6.52 (d, J = 7.8 Hz, 2H), 4.07 (d, J = 11.3 Hz, 1H), 3.69 (d, J = 10.9 Hz, 1H), 3.61 (s, 1H), 2.63 (dd, J = 14.0, 7.6 Hz, 1H), 2.51 (t, J = 10.7 Hz, 1H), 2.25 (d, J = 12.6 Hz, 1H), 1.98 (d, J = 14.2 Hz, 1H), 1.23−1.10 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 148.3, 146.9, 145.6, 129.2, 128.5, 128.5, 128.1, 127.8, 126.6, 126.6, 118.1, 113.8, 68.87, 51.61, 49.8, 48.4, 42.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{27}N_2O$ 347.2118, found 347.2113.

*N-(2-Hydroxy-5-(methyl(phenyl)amino)-4,4-diphenylpentyl)-4-methylbenzenesulfonamide (**4d**).* To a solution of **4a** (170.0 mg, 0.26 mmol) in 2 mL anhydrous acetone was added K_2CO_3 (72.8 mg, 0.52 mmol) and dimethyl sulfate (29.4 μL, 0.32 mmol), and then heated to reflux for 48 h. Subsequently the mixture was concentrated under vacuum and diluted with water. The mixture was extracted with EtOAc. The combined organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel (10:1 petroleum ether/EtOAc) to give **4d** as a white solid, 147.3 mg, 85% yield; mp 167.6−168.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86−7.76 (m, 4H), 7.41−7.18 (m, 16H), 6.84 (d, J = 8.2 Hz, 2H), 6.73 (t, J = 7.2 Hz, 1H), 4.59 (d, J = 14.4 Hz, 1H), 3.96 (d, J = 14.4 Hz, 1H), 3.85 (m, 1H), 3.71 (dd, J = 15.1, 9.7 Hz, 1H), 3.54 (dd, J = 15.0, 2.7 Hz, 1H), 2.59−2.51 (m, 1H), 2.48 (s, 6H), 2.30 (s, 3H), 2.28−2.22 (m, 1H), 1.78(s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.3, 147.5, 146.3, 144.8, 136.8, 129.6, 129.0, 128.9, 128.6, 128.4, 128.2, 128.0, 126.4, 116.6, 113.3, 67.3, 61.7, 54.6, 51.8, 41.3, 41.1, 21.7; IR ν_{max} (cm^{-1}) 3055, 2924, 1597, 1506, 1495, 1445, 1371, 1352, 1165, 1084, 814, 750, 733, 700, 663, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{38}H_{41}N_2O_5S_2$669.2451, found 669.2442.

*N-(2-Hydroxy-5-(methyl(phenyl)amino)-4,4-diphenylpentyl)-4-methyl-N-tosylbenzenesulfonamide (**4e**).* A solution of KOH (4 mL, 1M) was added **4d** (233.2 mg, 0.34 mmol, 1.0 equiv), and the reaction mixture was heated to reflux. After completion, the mixture was quenched with HCl (1 M, aq) and extracted with CH_2Cl_2. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The filtrate was concentrated under a vacuum, and the residue was purified by flash column chromatography on silica gel (7:1 petroleum ether/EtOAc) to give **4e** as a white solid (157.0 mg, 89% yield): mp 100.3−101.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.8 Hz, 2H), 7.37−7.00 (m, 15H), 6.76−6.57 (m, 3H), 4.14 (s, 2H), 3.65 (d, J = 7.9 Hz, 1H), 2.86−2.66 (m, 1H), 2.61−2.47 (m, 1H), 2.45 (s, 3H), 2.34−2.12 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.9, 146.5, 146.4, 143.0, 137.3, 129.6, 129.0, 128.5, 128.5, 128.3, 127.1, 126.7, 126.6, 117. 2, 113.5, 67.6, 61.1, 51.4, 49.1, 41.9, 41.2, 21.5; IR ν_{max} (cm^{-1}) 3057, 2922, 2359, 1597, 1506, 1497, 1447, 1329, 1159, 1092, 814, 750, 700, 552; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{31}H_{35}N_2O_3S$ 515.2363, found 515.2364.

*1-Amino-5-(methyl(phenyl)amino)-4,4-diphenylpentan-2-ol (**4f**).* Following literature procedure,[38] to a solution of sodium naphthalenide [prepared by stirring a mixture of sodium (32.0 mg, 1.4 mmol, 5.2 equiv) and naphthalene (189.8 mg, 1.5 mmol, 5.5 equiv) in THF (4.5 mL) at room temperature until the metal sodium is completely consumed]. After that, a solution of **4e** (90.0 mg, 0.18 mmol, 1.0 equiv) in THF (2 mL) was added. The resulting reaction mixture was allowed stirring at room temperature for 1 h, and the reaction was quenched by the addition of ice−water, extracted with dichloromethane, and the combined organic layers were dried over Na_2SO_4. The filtered was concentrated and the residue was purified by flash column chromatography on silica gel (30:1:0.01 dichloromethane/Methanol/NEt_3) to give **4f** as a colorless oil (57.6 mg, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.31 (m, 4H), 7.30−7.23 (m, 6H), 7.19−7.14 (t, J = 8.4 Hz, 2H), 6.73 (d, J = 8.4 Hz, 2H), 6.68 (t, J = 8.4 Hz, 1H), 4.29 (d, J = 14.4 Hz, 1H), 4.17 (d, J = 14.4 Hz, 1H), 3.53−3.46 (m, 1H), 2.46−2.20 (m, 8H), 2.17−2.08 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.1, 147.1, 146.7, 128.8, 128.8, 128.7, 128.2, 128.1, 126.5, 126.4, 116.8, 113.3, 69.6, 61.4, 51.7, 48.0, 42.0, 41.1. IR ν_{max} (cm^{-1}) 3057, 2924, 2881, 1599, 1558, 1506, 1497, 1445, 1373, 1267, 1034, 910, 748, 732, 700; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{29}N_2O$ 361.2274, found 361.2276.

*N-((5-Oxo-4,4-diphenyltetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**4g**).* A solution **3j** (325.4 mg, 0.50 mmol, 0.1 M in CH_2Cl_2) was add two drops concentrated hydrochloric acid, the solution was allowed stir 2 h at room temperature. Subsequently the reaction solution was diluted with water, extracted with CH_2Cl_2. The combined organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel (8:1 petroleum ether/EtOAc) to give **4g** as a white solid (284.3 mg, 98% yield). mp 186−187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.1 Hz, 4H), 7.43−7.08 (m, 14H), 4.66−4.60 (m, 1H), 4.19 (dd, J = 15.7, 6.2 Hz, 1H), 3.90 (dd, J = 15.8, 4.8 Hz, 1H), 2.98 (dd, J = 13.1, 5.0 Hz, 1H), 2.71 (dd, J = 12.8, 10.7 Hz, 1H), 2.46 (s, 6H);

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J. Org. Chem. 2021, 86, 235−253

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$):δ 176.0, 145.4, 141.4, 139.4, 136.3, 129.8, 129.0, 128.6, 128.4, 127.8, 127.7, 127.3, 127.2, 75.2, 57.8, 51.2, 41.0, 21.7; IR ν_{max} (cm^{-1}) 3061, 1776, 1597, 1493, 1448, 1375, 1354, 1167, 1084, 816, 698, 663, 552; HRMS (ESI) m/z $[M+NH_4]^+$ calcd for $C_{31}H_{33}N_2O_6S_2$593.1775, found 593.1773.

*5-(Aminomethyl)-3,3-diphenyldihydrofuran-2(3H)-one (**4h**).* In a thick-walled reaction tube was added phenol (66.5 mg, 0.7 mmol), **4g** (150 mg, 0.36 mmol) and a solution of hydrogen bromide in acetic acid (2 mL, 35 wt %). The reaction tube was sealed with a Teflon stopper, and the mixture was allowed to stir at 80 °C oil bath temperature for 5 h. Then, the acetic acid was removed under vacuum, and the brown residue was dissolved in water (30 mL), and washed with ether. The aqueous phase was added excess saturated sodium carbonate until PH > 7, then the mixture was extracted with dichloromethane, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel (20:1:0.01 dichloromethane/Methanol/NEt_3) to give **4h** as a colorless oil, 71.1 mg, 74% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55−7.25 (m, 10H), 4.49−4.35 (m, 1H), 3.09 (dd, J = 13.8, 3.6 Hz, 1H), 3.02−2.88 (m, 2H), 2.80 (dd, J = 12.9, 10.5 Hz, 1H), 1.62 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 177.1, 141.9, 139.9, 129.0, 128.4, 127.8, 127.7, 127.3, 127.23, 78.6, 58.2, 45.4, 40.2; IR ν_{max} (cm^{-1}) 3462, 2928, 1758, 1596, 1495, 1447, 1173, 966, 757, 698; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{18}NO_2$ 268.1332, found 268.1328.

*5-((Benzylamino)methyl)-3,3-diphenyldihydrofuran-2(3H)-one (**4i**).* To a solution of **4h** (80.6 mg, 0.30 mmol, 1.0 equiv, in 2 mL MeOH) was added benzaldehyde 46 μL (0.45 mmol, 1.5 equiv). The reaction mixture was stirred for 2 h at room temperature, and then sodium cyanoborohydride (38 mg, 0.6 mmol, 2.0 equiv) was added. The resulting mixture was stirred for 24 h at room temperature. After completion, the reaction solution was diluted with saturated sodium bicarbonate, extracted with ethyl acetate, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel (10:1 petroleum ether/EtOAc) to give **4i** as a colorless oil, 87.8 mg, 82% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.53−7.20 (m, 15H), 4.59−4.53 (m, 1H), 3.88 (d, J = 2.9 Hz, 2H), 3.12−2.95 (m, 2H), 2.94−2.86 (m, 2H), 1.77(s, 1H); ^{13}C NMR$\{^1H\}$(100 MHz, $CDCl_3$) δ 177.1, 142.0, 139.8, 129.0 128.5, 128.4, 128.2, 127.8, 127.4, 127.3, 127.2, 77.0, 58.1, 53.9, 52.2, 40.8. IR ν_{max} (cm^{-1}) 3026, 2932, 1765, 1495, 1447, 1176, 966, 750, 698; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{24}H_{24}NO_2$ 358.1802, found 358.1794.

*1-Cyclopropyl-N-((5,5-diphenyltetrahydrofuran-3-yl)methyl)-methanamine (**4j**).* To a solution of **4h** (250 mg, 0.94 mmol, 1.0 equiv, in 3 mL MeOH) was added cyclopropanecarboxaldehyde (60 μL, 1.1 equiv). The reaction mixture was stirred for 2 h at room temperature, and then sodium borohydride (113.4 mg, 3.0 equiv) was added. The resulting mixture was stirred for 24 h at room temperature. After completion, the reaction solution was diluted with saturated sodium bicarbonate, extracted with ethyl acetate (3× 15 mL), dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel (2:1:0.01 petroleum ether/EtOAc/NEt_3) to give **4j** as a colorless oil, 203.6 mg, 71% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 2H), 7.27−7.19 (m, 6H), 7.14−7.08 (m, 2H), 3.74−3.64 (m, 1H), 3.50−3.30 (m, 1H), 2.99−2.86 (m, 1H), 2.66−2.44 (m, 2H), 2.39 (dd, J = 12.8, 6.5 Hz, 1H), 2.30 (dd, J = 12.8, 6.8 Hz, 1H), 2.25−2.03 (m, 3H), 1.03−0.88 (m, 1H), 0.61−0.48 (m, 2H), 0.15 (d, J = 5.1 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.0, 146.9, 128.3, 128.1, 128.0, 127.0, 126.1, 125.8, 65.8, 63.3, 62.3, 61.1, 46.4, 43.6, 8.4, 4.4, 3.9; IR ν_{max} (cm^{-1}) 3334, 2942, 2772, 1496, 1447, 1208, 1067, 1050, 911, 755, 730, 699; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{26}NO$ 308.2009, found 308.2005.

*N-((5-Oxo-4,4-diphenyltetrahydrofuran-2-yl)methyl)acetamide (**4k**).* To a solution of **4h** (80.2 mg, 0.30 mmol, 1.0 equiv, in 2.0 mL CH_2Cl_2) was added acetyl chloride (22 μL, 1.0 equiv). The resulting mixture was allowed stir for 0.5 h at room tenperature, and then NEt_3 (100 μL, 2.5 equiv) was added. The reaction mixture was stirred for 2 h, and then diluted with saturated sodium bicarbonate, extracted with ethyl acetate, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel (1.5:1:0.01 petroleum ether/EtOAc/NEt_3) to give **4k** as a colorless oil, 84.3 mg, 91% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41−7.18 (m, 10H), 6.63−6.53 (m, 1H), 4.53−4.39 (m, 1H), 3.79−3.72 (m, 1H), 4.40−3.34 (m, 1H), 3.02 (dd, J = 13.1, 5.0 Hz, 1H), 2.67 (dd, J = 13.1, 10.6 Hz, 1H), 1.96 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 177.1, 170.9, 141.7, 139.5, 129.0, 128.5, 127.9, 127.7, 127.4, 127.2, 76.4, 58.1, 42.2, 40.0, 23.0. IR ν_{max} (cm^{-1}) 3058, 2931, 1764, 1598, 1494 1558, 1446, 1495, 1348, 1176, 1130, 1174, 1027, 966, 750, 698, 650; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{19}H_{20}NO_3$310.1438, found 310.1438.

*(2R,2′R)-Diethyl 2,2′-((2-Iodo-5-methyl-1,3-phenylene)bis(oxy))-dipropanoate (**5a**).* Following a procedure by Du,[39] to a solution of 2-iodo-5-methylbenzene-1,3-diol (2.50 g, 10.0 mmol), PPh_3 (6.56 g, 25.0 mmol), and ethyl L(−)-lactate (2.81 mL, 25.0 mmol) in THF (50 mL) was added slowly diisopropyl azodicarboxylate (DIAD, 1.9 M in toluene, 25.0 mmol, 13.2 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature. After stirring for 6 h, the resulting mixture was concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (20:1 petroleum ether/EtOAc) to give **5a** as a colorless oil: 3.69 g, 82% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 6.21 (s, 2H), 4.73 (q, J = 6.9 Hz, 2H), 4.22 (q, J = 7.1 Hz, 4H), 2.24 (s, 3H), 1.68 (d, J = 6.7 Hz, 6H), 1.31−1.22 (m, 6H).

*(2R,2′R)-2,2′-((2-Iodo-5-methyl-1,3-phenylene)bis(oxy))-dipropanoic Acid (**5b**).* To a solution of **5a** (3.15 g, 7.0 mmol) in 50 mL of the mixed solvent THF/MeOH (1:1, v:v) was added 25 mL of NaOH (2.0 M, aq) and stirred overnight at room temperature. The reaction mixture was cooled to 0 °C, quenched with HCl (2 M, aq), and extracted with EtOAc. The organic layers were dried over anhydrous Na_2SO_4, and the solvents were removed *in vacuo* to give pure **5b** as a white solid: 2.65 g, 96% yield; spectroscopic data in accordance with literature;[10f] ^1H NMR (400 MHz; DMSO-d_6) δ 6.29 (s, 2H), 4.84 (q, J = 6.9 Hz, 2H), 2.22 (s, 3H), 1.55 (dd, J = 6.8, 2.3 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 173.1, 157.9, 139.9, 107.4, 76.3, 73.2, 21.9, 18.8.

General Procedure for the Synthesis of 5c−5g. To a solution of corresponding (2*R*,2′*R*)-2,2′-((2-iodo-1,3-phenylene)bis(oxy))-dipropanoic acid (2.0 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added oxalyl chloride (0.63 mL,4.0 equiv) under argon at 0 °C, and then DMF (1 drop) was added carefully. After stirring for 1 h at 0 °C, the mixture was allowed to stir at room temperature for another 5 h. Then, the resulting mixture was concentrated under vacuum to remove the solvent and the excessive oxalyl chloride. Then, the residue was dissolved in 10 mL CH_2Cl_2 under argon at 0 °C, and then corresponding amine (2.4 mmol, 1.2 equiv) was slowly added. After stirring for 30 min, Et_3N (0.55 mL, 2.0 equiv) was added. The resulting mixture was stirred at room temperature for 5 h. Then, the reaction mixture was quenched by HCl (1 M, aq) and extracted with CH_2Cl_2. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated under a vacuum. The crude residue was purified by flash column chromatography on silica gel to give the desire products.

*(2R,2′R)-2,2′-((2-Iodo-1,3-phenylene)bis(oxy))bis(N-mesitylpropanamide) (**5c**).* The compound was purified by flash column chromatography on silica gel (3:1 petroleum ether/EtOAc) to give **5c** as a white solid: 503 mg, 41% yield; spectroscopic data in accordance with literature;[10f] ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 6.4 Hz, 2H), 7.39−7.31 (m, 1H), 6.90 (s, 4H), 6.65 (dd, J = 8.3, 2.2 Hz, 2H), 5.09−4.93 (m, 2H), 2.27 (s, 6H), 2.15 (s, 12H), 1.87−1.72 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.6, 157.0, 137.3, 135.1, 130.7, 130.1, 129.0, 107.1, 80.5, 76.2, 20.9, 18.8, 18.3.

*(2R,2′R)-2,2′-((2-Iodo-5-methyl-1,3-phenylene)bis(oxy))bis(N-(2,6-diisopropylphenyl)propanamide) (**5d**).* The compound was purified by flash column chromatography on silica gel (3:1 petroleum ether/EtOAc) to give **5d** as a white solid: 949 mg, 68% yield; spectroscopic data in accordance with literature;[10f] ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 38.4 Hz, 2H), 7.41 (t, J = 8.3 Hz, 1H), 7.32 (d, J = 15.6 Hz, 2H), 7.20 (d, J = 7.7 Hz, 4H), 6.72 (d, J = 8.4

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J. Org. Chem. 2021, 86, 235−253

Hz, 2H), 5.08 (q, J = 6.7 Hz, 2H), 3.09−2.80 (m, 4H), 1.81 (d, J = 6.6 Hz, 6H), 1.33−0.98 (m, 24H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.5, 157.0, 146.2, 130.6, 130.1, 128.6, 123.6, 107.2, 80.6, 76.1, 28.7, 23.6, 18.7.

*(2R,2′R)-((2-Iodo-5-methyl-1,3-phenylene)bis(oxy))bis(N,N-diisopropylpropanamide) (**5e**).* The compound was purified by flash column chromatography on silica gel (10:1 petroleum ether/EtOAc) to give **5e** as a white solid: 997 mg, 89% yield; spectroscopic data in accordance with literature;[11g] ^1H NMR (400 MHz, $CDCl_3$) δ 6.36 (d, J = 2.7 Hz, 2H), 4.87−4.74 (m, 2H), 4.50 (hept, J = 5.9, 5.3 Hz, 2H), 3.31 (hept, J = 6.9 Hz, 2H), 2.22 (s, 3H), 1.66 (dd, J = 6.7, 2.8 Hz, 6H), 1.42 (d, J = 6.7 Hz, 6H), 1.30 (dd, J = 6.9, 2.7 Hz, 6H), 1.18 (dd, J = 6.5, 3.6 Hz, 6H), 0.91 (d, J = 6.6 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.6, 157.4, 140.5, 107.1, 77.6, 74.6, 47.6, 21.7, 20.9, 20.9, 20.6, 20.6, 20.4, 19.8, 19.7, 17.9.

*(2R,2′R)-2,2′-((2-Iodo-5-methyl-1,3-phenylene)bis(oxy))bis(N-isopropyl-N-phenylpropanamide) (**5f**).* The compound was purified by flash column chromatography on silica gel (4:1 petroleum ether/EtOAc) to give **5e** as a white solid: 427 mg, 34% yield; mp 72.2−73.0 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48−7.30 (m, 6H), 7.06 (d, J = 7.5 Hz, 2H), 6.89 (dd, J = 23.0, 7.5 Hz, 2H), 6.14 (s, 2H), 5.09−4.99 (m, 2H), 4.42−4.33 (m, 2H), 2.23 (s, 3H), 1.47 (d, J = 6.5 Hz, 6H), 1.06 (d, J = 6.8 Hz, 6H), 1.02 (d, J = 6.8 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.8, 157.7, 139.0, 137.0, 130.2, 129.2, 128.6, 110.4, 109.7, 79.5, 73.6, 46.6, 21.4, 20.7, 18.2. IR ν_{max} (cm^{-1}) 2976, 1668, 1580, 1493, 1450, 1398, 1277, 1244, 1138, 1101, 706; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{31}H_{38}IN_2O_4$ 629.1871, found 629.1875.

*(2R,2′R)-2,2′-((2-Iodo-5-methyl-1,3-phenylene)bis(oxy))bis(N-cyclohexyl-N-isopropylpropanamide) (**5g**).* The compound was purified by flash column chromatography on silica gel (5:1 petroleum ether/EtOAc) to give **5g** as a white solid: 591 mg, 47% yield; mp 63.4−64.0 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 6.29 (s, 2H), 4.85 (dp, J = 14.3, 7.0 Hz, 2H), 4.04 (d, J = 11.8 Hz, 2H), 3.40−3.24 (m, 2H), 3.26−3.05 (m, 2H), 2.19 (s, 3H), 1.71−0.89 (m, 32H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.0, 157.6, 140.3, 107.1,77.3, 77.2, 75.2, 55.8, 37.1, 32.0, 31.5, 26.0, 25.3, 21.8, 18.2, 14.2; IR ν_{max} (cm^{-1}) 2931, 2856, 1647, 1635, 1578, 1452, 1429, 1375, 1242, 1132, 1101, 735; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{29}H_{46}IN_2O_4$613.2497, found 613.2495.

General Procedure for the Asymmetric Amino-Tetrahydrofuran Reaction. A solution of $PhCF_3$ (1.0 mL) was charged with **5g** (8.8 mg, 15% mol), $HNTs_2$ (30.5 mg, 1.5 equiv), and mCPBA (40.5 mg, 2.0 equiv, 85 wt %), and the resulting mixture was stirred for 15 min at 0 °C in a low-temperature reactor. Then, the 2,2-diphenylpent-4-enamide (0.1 mmol, 1.0 equiv) was added. The mixture was stirred for 15 h at 0 °C. After completion, the resulting mixture was diluted with aqueous NaOH (2.0 M, 5 mL) and extracted with dichloromethane. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated under a vacuum. The residue was purified by flash column chromatography on silica gel to give chiral 5-imino-2-tetrahydrofuranyl methanamine derivatives.

*(R,Z)-N-((4,4-Dimethyl-5-phenylimino-tetrahydrofuran-2-yl)-methyl)-N-tosyl-(4-methylbenzenesulfon)amide (**3j***):* $[\alpha]_D^{20}$ −27.68 (c 0.1, MeOH, 94% ee). HPLC analysis: Chiracel-IA3, n-hexane/isopropanol = 90:10, flow rate 0.8 mL/min, λ = 210 nm. Retention time: t_{major} = 8.54 min, t_{minor} = 13.05 min. The absolute configuration was tentatively assigned by analogy with **3n***.

*(R,Z)-N-((4,4-Diphenyl-5-(4-fluorophenylimino)tetrahydrofuran-2-yl)methyl)-N-tosyl-(4-methylbenzenesulfon)amide (**3m***):* $[\alpha]_D^{20}$ −28.45 (c = 0.10, MeOH, 64% ee). HPLC analysis: Chiracel-IA3, n-hexane/isopropanol = 90:10, flow rate 0.8 mL/min, λ = 254 nm. Retention time: t_{major} = 9.33 min, t_{minor} = 14.70 min. The absolute configuration was tentatively assigned by analogy with **3n***.

*(R,Z)-N-((4,4-Diphenyl-5-(2-chlorophenylimino)tetrahydrofuran-2-yl)methyl)-N-tosyl-(4-meth ylbenzenesulfon)amide (**3n***):* $[\alpha]_D^{20}$ −28.63 (c 0.10, MeOH, 93% ee). HPLC analysis: Chiracel-IA3, n-hexane/isopropanol = 90:10, flow rate 0.8 mL/min, λ = 210 nm. Retention time: t_{major} = 9.16 min, t_{minor} = 14.39 min. The absolute configuration was established by X-ray crystallography analysis.

*(R,Z)-N-((4,4-Diphenyl-5-(3-chlorophenylimino)tetrahydrofuran-2-yl)methyl)-N-tosyl-(4-me thylbenzenesulfon)amide (**3o***):* $[\alpha]_D^{20}$ −27.40 (c 0.10, MeOH, 95% ee). HPLC analysis: Chiracel-IA3, n-hexane/isopropanol = 90:10, flow rate 0.8 mL/min, λ = 210 nm. Retention time: t_{major} = 8.70 min, t_{minor} = 12.09 min. The absolute configuration was tentatively assigned by analogy with **3n***.

*(R,Z)-N-((4,4-Diphenyl-5-(4-bromophenylimino)-tetrahydrofuran-2-yl)methyl)-N-tosyl-(4-meth ylbenzenesulfon)-amide (**3q***):* $[\alpha]_D^{20}$ −16.46 (c 0.10, MeOH, 59% ee). HPLC analysis: Chiracel-IA3, n-hexane/isopropanol = 90:10, flow rate 0.8 mL/min, λ = 254 nm. Retention time: t_{major} = 10.34 min, t_{minor} = 14.09 min. The absolute configuration was tentatively assigned by analogy with **3n***.

*(R,Z)-N-((4,4-Diphenyl-5-methoxyiminotetrahydrofuran-2-yl)-methyl)-N-tosyl-(4-methylbenze nesulfon)amide (**3s***):* $[\alpha]_D^{20}$ +32.81 (c 0.10, MeOH, 98% ee). HPLC analysis: Chiracel-IA3, n-hexane/isopropanol = 90:10, flow rate 0.8 mL/min, λ = 210 nm. Retention time: t_{major} = 7.68 min, t_{minor} = 10.39 min. The absolute configuration was tentatively assigned by analogy with **3n***.

Procedure for Control Experiments. There are three reaction tubes numbered 1, 2, and 3. No. 1 reaction tube contains mCPBA (30.5 mg, 85 wt %, 0.15 mmol, 1.5 equiv), $HNTs_2$ (48.8 mg, 0.15 mmol, 1.5 equiv), and HFIP (1.0 mL). The reaction tube was capped, and the resulting mixture was stirred 10 min at room temperature. Then, **1a** (20.3 mg, 0.1 mmol, 1.0 equiv) was added. The mixture was stirred at room temperature, and **1a** was complete consumption in 3 h (monitored by TLC). It needs to mention that we did not detect the formation of **3a**. Then the solvent was removed under a vacuum, and the residue was diluted with aqueous NaOH (1.0 M, 10 mL) and stirred for 10 min. Then, the resulting mixture was extracted with dichloromethane. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated under a vacuum. The residue was purified by flash column chromatography on silica gel to give **3a″** as a colorless oil: 17.1 mg, 78% yield.[29]

No. 2 reaction tube contained $PhI(NTs_2)_2$ (102.2 mg, 0.12 mmol, 1.2 equiv), HFIP (1.0 mL), and **1a** (20.3 mg, 0.1 mmol, 1.0 equiv). The reaction tube was capped, and the resulting mixture was stirred at room temperature. We have found that **1a** was consumed completely in 30 min (monitored by TLC), and the mixture of **3a** and **3a′** was the only product. Then, the solvent was removed under vacuum, diluted with aqueous NaOH (1.0 M, 10 mL), extracted with CH_2Cl_2. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated under a vacuum. The residue was purified by flash column chromatography on silica gel to give the oxyamination products **3a** and **3a′**: 43.7 mg, 83% yield.

No. 3 reaction tube contained iodoarene **2h** (4.0 mg, 0.015 mmol, 15 mol %), mCPBA (30.5 mg, 85 wt %, 0.15 mmol, 1.5 equiv), $NaNTs_2$ (52.0 mg, 0.15 mmol, 1.5 equiv), and HFIP (1.0 mL). The reaction tube was capped, and the resulting mixture was stirred 10 min at room temperature. Then, **1a** (20.3 mg, 0.1 mmol, 1.0 equiv) was added. The mixture was stirred at room temperature for 15 h. It should be mentioned that we did not detect the formation of **3a**. Then the solvent was removed under a vacuum, and the residue was diluted with aqueous NaOH (1.0 M, 10 mL) and stirred for 10 min. Then, the resulting mixture was extracted with CH_2Cl_2. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated under a vacuum. The residue was purified by flash column chromatography on silica gel to give **1a** recovered (10.6 mg, 47% conversion) and **3a″**: 4.1 mg, 19% yield.

Computational Methods. DFT calculations were performed with the Gaussian 09 software package, E.01 version.[40] Geometric optimizations of intermediates and transition states were calculated at the B3LYP/def2-SVP level,[41a,b] with the default ECP applied to iodine atoms. The D3 version of Grimme's dispersion with Becke−Johnson damping were also applied.[42] Vibrational frequency calculations were also performed at the same level to confirm that the stationary points identified were either without imaginary frequencies or with one imaginary frequency. Thermal corrections to Gibbs free energy values at 298.15 K and 1 atm, including zero-point energy corrections, were calculated at the same level. Standard state concentrations of 1.0 mol/L were used for all species. Quasi-

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J. Org. Chem. 2021, 86, 235−253

harmonic corrections considering the contributions to the entropy of low-frequency vibrations were also applied to each structure by increasing all non-negative frequencies below 100 cm^{-1} to 100 cm^{-1}. Single-point energies were calculated at the M062X/def2-TZVP level[41b,c] and were added to the thermal corrections calculated previously to obtain the final Gibbs free energy values. All calculations were performed in HFIP implied using the SMD[43] model defined as a generic solvent with the following properties: Eps = 16.7; EpsInf = 1.631; HbondAcidity = 0.77; HbondBasicity = 0.03; SurfaceTensionAtInterface = 17.6; CarbonAromaticity = 0; ElectronegativeHalogenicity = 0.60. For more details, please see the Supporting Information.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02047.

Copies of ^{1}H and $^{13}C\{^{1}H\}$ NMR, IRν_{max}, HRMS (ESI) spectra for all new compounds, tables of detailed reaction condition screening, crystal data, and DFT computational data (PDF)

Accession Codes

CCDC 1906232−1906234 and 1906236 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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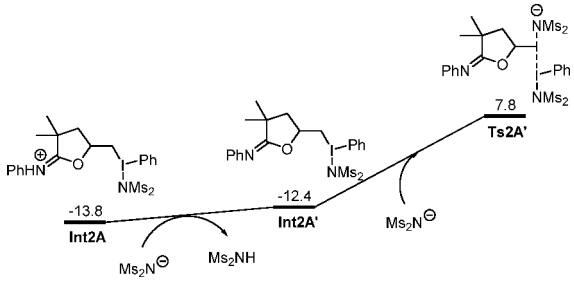

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