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# Aminolactonization of Unactivated Alkenes Catalyzed by Aryl Iodine

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Cite This: J. Org. Chem. 2021, 86, 5152−5165 Read Online

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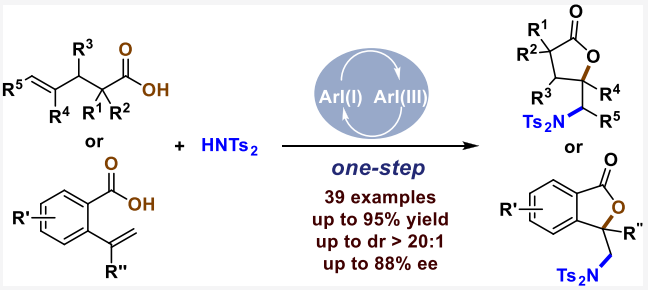
**ABSTRACT:** A one-step protocol of the aryl iodine-catalyzed aminolactonization of unactivated alkenes under oxidation conditions was first reported to efficiently construct diverse amino lactones in a short time using $HNTs_2$ as the compatible nitrogen source. In addition, we investigated the influence of the reaction rate based on the structure of the iodoarene precatalyst, which revealed the selective adjustment effect on aminolactonization and oxylactonization. Finally, preliminary experiments verified the feasibility of asymmetric aminolactonization catalyzed by a chiral iodoarene precatalyst.



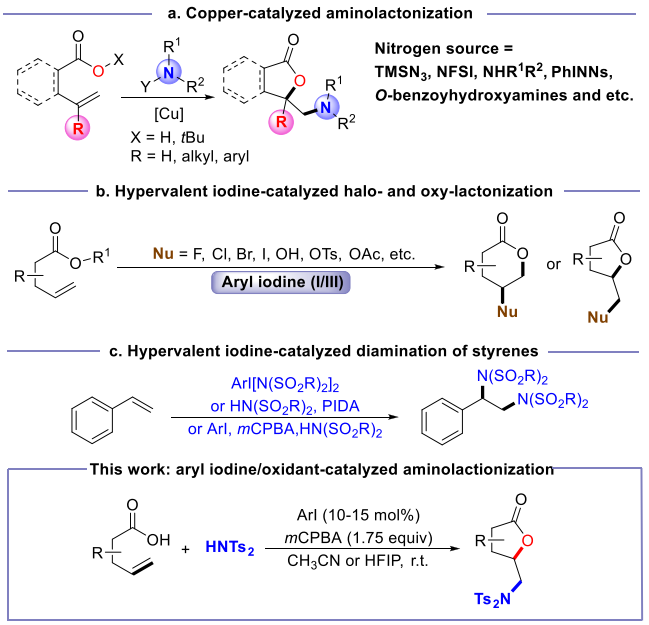



## INTRODUCTION

The oxyamination of alkenes[1] is a recently developed synthesis strategy used to simultaneously construct C−O bonds and C−N bonds, and transition metals, such as Cu,[2] Pd,[3] Fe,[4] Os,[5] Ir,[6] Rh,[7] Mn,[8] etc.,[9] are widely applied in these reactions. The direct aminoxygenation of alkenes can yield privileged amino lactones, which are prevalent motifs in diverse natural and synthetic biologically active compounds,[10] and they can be converted to other skeletons,[11] such as 1,2-amino alcohol and tetrahydrofuran derivatives. At present, the majority of reports on the aminolactonization of alkenes involve catalysis by the transition metal copper[12] (Scheme 1a). Usually, several strategies require olefin substrates containing backbones to favor cyclization via radical processes.[12c−e] Some copper-catalyzed methods need pre-synthesis of nitrogen reagents that are relatively unstable.[12a,b,d] In addition, due to the requirements of the backbone in the substrates, the product range is always inflexible.[12b,c] Therefore, there are still opportunities to develop novel and facile methods to realize the aminolactonization with mild conditions.

Iodine(I/III) has low toxicity and mild properties and is regarded as a "green substitute" for transition metals in organic synthesis.[13] Iodoarene is an efficient and atom-economic catalyst that can generate hypervalent iodine *in situ* under oxidative conditions and catalyze the difunctionalization[14] of alkenes for the construction of C−X bonds.[15−21] At present, general catalytic strategies based on aryl iodine(I/III) can realize the halolactonization,[22] oxylactonization,[23] and other transformations[24] of alkenes (Scheme 1b). However, up to now, to the best of our knowledge, the aminolactonization of unactivated alkenes catalyzed by aryl iodine (I/III) has seldom been reported. We think that there are two main challenges in realizing the aryl iodine(I)/oxidant-catalyzed amino lactonization of unactivated alkenes: (1) nitrogen reagents must be compatible with oxidants/substrates and can generate $ArI[N]_2$ species *in situ*,[15e] and (2) the background dioxidation reaction should be avoided to reduce the formation of byproducts.[25] Recently, some literature reports[15a−d] have used equivalents of $ArI[N(SO_2R)_2]_2$ or a catalytic amount of $ArI/HN(SO_2R)_2$ to

**Scheme 1. Related Works**




**Received:** January 11, 2021
**Published:** March 24, 2021



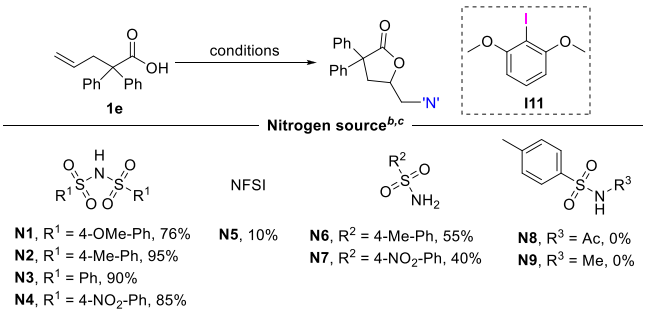

https://doi.org/10.1021/acs.joc.1c00074
J. Org. Chem. 2021, 86, 5152−5165

achieve the diamination of olefins and suggested[15c] that the $PhI(NTs_2)_2$ species tends to dissociate in solution, releasing $[PhINTs_2]^+$ with catalytic activity, and a large amount of excellent nitrogen nucleophile $[NTs_2]^-$, which can effectively construct C−N bonds (Scheme 1c). Therefore, using $HN(SO_2R)_2$ as a compatible nitrogen reagent may realize the aryl iodine-catalyzed aminolactonization of unactivated alkenes. In our previous work,[26] iodoarene-catalyzed oxyamination of alkenes was successfully performed to synthesize 5-imino-2-tetrahydrofuranyl methanamine derivatives using $HN(SO_2R)_2$, but the product needed to be further hydrolyzed to obtain amino lactones. On the above basis, herein, we used more easily available unactivated alkenyl acids as substrates and developed a one-step aryl iodine/oxidant catalyst system to construct diverse amino lactones.

## RESULTS AND DISCUSSION

In the initial investigation, $HNTs_2$ was used as the nitrogen reagent, and iodoarene **I11** was used as the precatalyst to catalyze the aminolactonization of 2,2-diphenylpent-4-enoic acid **1e** in HFIP to obtain 5-amino-γ-butyrolactone **2e** with a yield of 44% (Table 1, entry 1). Therefore, we used **1e** as the model substrate for condition screening. First, a series of solvents were screened to improve the reaction result (Table 1, entries 2−9), and the yield of **2e** was improved to 95% when the reaction proceeded in $CH_3CN$ (Table 1, entry 9). Next, we

**Table 1. Reaction Optimizations**



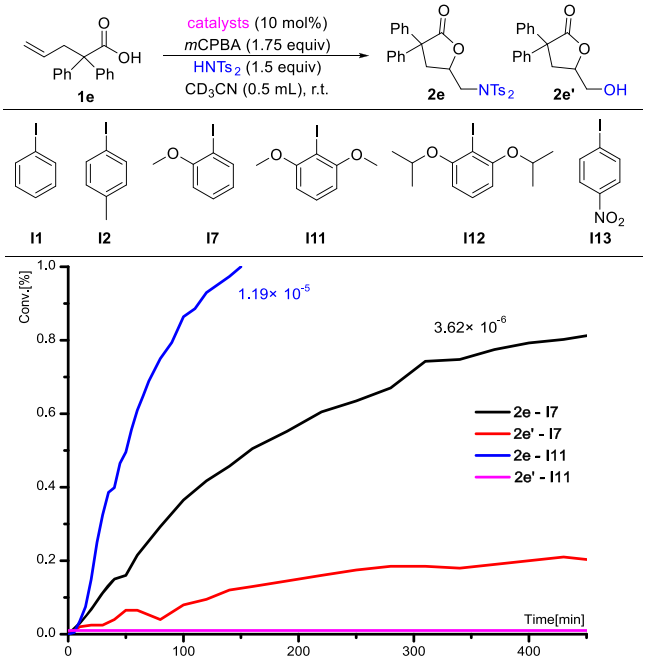

| entry[a] | cat. (Y mol %) | oxidant (X equiv) | solvent | yield (%)[b] |
|---|---|---|---|---|
| 1 | **I11** (15) | *m*CPBA (2.0) | HFIP | 44 |
| 2 | **I11** (15) | *m*CPBA (2.0) | THF | |
| 3 | **I11** (15) | *m*CPBA (2.0) | EtOH | 5 |
| 4 | **I11** (15) | *m*CPBA (2.0) | MeOH | 20 |
| 5 | **I11** (15) | *m*CPBA (2.0) | TFE | 74 |
| 6 | **I11** (15) | *m*CPBA (2.0) | DCM | 63 |
| 7 | **I11** (15) | *m*CPBA (2.0) | DCE | 85 |
| 8 | **I11** (15) | *m*CPBA (2.0) | $CF_3$-Ph | 82 |
| 9 | **I11** (15) | *m*CPBA (2.0) | $CH_3CN$ | 95 |
| 10[d] | **I11** (15) | *m*CPBA (1.75) | $CH_3CN$ | 98[e] |
| 11[d] | **I11** (10) | *m*CPBA (1.75) | $CH_3CN$ | 98[e] |
| 12[d] | **I11** (5) | *m*CPBA (1.75) | $CH_3CN$ | 50[e] |
| 13[f] | KI | *m*CPBA (1.75) | $CH_3CN$ | 10 |
| 14[g] | $I_2$ | *m*CPBA (1.75) | $CH_3CN$ | 56 |

[a]General conditions: **1e** (0.2 mmol), $HNTs_2$ (1.5 equiv), **I11** (15 mol %), *m*CPBA (*X* equiv), solvent (2 mL), r.t., 2−12 h, air atmosphere. [b]Isolated yield. [c]**1e** (0.2 mmol), nitrogen reagent (1.5 equiv), **I11** (15 mol %), *m*CPBA (2.0 equiv), $CH_3CN$ (2 mL), r.t., 2.5−5 h, air atmosphere. [d]**1e** (0.05 mmol), $HNTs_2$ (1.5 equiv), **I11** (*Y* mol %), *m*CPBA (1.75 equiv), $CD_3CN$ (0.5 mL), r.t. [e]Detected by NMR and 1,2-dibromomethane as the internal standard. [f]KI (1.0 equiv) instead of **I11**. [g]$I_2$ (1.0 equiv) instead of **I11**.

focused our attention on the screening of nitrogen reagents and found that, among all the tested nitrogen sources, **N1**−**N4** could be used as compatible nitrogen reagents with yields of 75−95% (Table 1, nitrogen source), and $HNTs_2$ was the best nitrogen reagent. Subsequently, a detailed screening of the type and amount of oxidant was carried out (see the Supporting Information (SI)), and ultimately, we chose 1.75 equiv of *m*CPBA as the matching oxidant (Table 1, entry 10). Then, the amount of catalyst was screened (Table 1, entries 10−12), showing that 0.1 equiv of **I11** had better performance. In addition, KI and $I_2$ were investigated under the same conditions (Table 1, entries 13 and 14). Compared with KI, $I_2$ has better solubility in $CH_3CN$ and better catalytic result, but both results were disappointing.

We also screened the type (see the SI) of catalysts, and the results indicated that the structure of the iodoarene precatalyst largely affected the catalytic activity. Therefore, $^1H$ NMR was used to monitor the conversion of **1e** to **2e** catalyzed by six precatalysts with different structures, and the initial reaction rates were calculated based on the change in substrate concentration−time (Table 2). Taking **I11** and **I7** as examples, the structure on the aryl iodophenyl group affected the target product conversion rate, and the reaction rate of **I11** was higher than that of **I7**, while **I11** effectively reduced the extent

**Table 2. Reaction Rates for the Conversion of 4-Pentenoic Acid, 1e, to 2e with Iodoarene Precatalysts I1−I2, I7, I11−I13, Detected by $^1H$ NMR Analysis**




| entry[a] | ArI | time | **2e** yield (%)[b] | **2e′** yield (%)[b] | *K*[c] |
|---|---|---|---|---|---|
| 1 | **I1** | 12.5 | 50 | 17 | $1.68 \times 10^{-6}$ |
| 2 | **I2** | 10.5 | 75 | 25 | $2.63 \times 10^{-6}$ |
| 3 | **I7** | 7.5 | 80 | 20 | $3.62 \times 10^{-6}$ |
| 4 | **I11** | 2.5 | 98 | ND[d] | $1.19 \times 10^{-5}$ |
| 5 | **I12** | 4.0 | 90 | 8 | $6.15 \times 10^{-6}$ |
| 6 | **I13** | 10.5 | 8 | 44 | $1.44 \times 10^{-6}$ |

[a]General conditions: **1e** (0.05 mmol), $HNTs_2$ (1.5 equiv), **ArI** (10 mol %), *m*CPBA (1.75 equiv), $CD_3CN$ (0.5 mL), r.t. [b]Detected by NMR and 1,2-dibromomethane as the internal standard. [c]K mol/L·$S^{-1}$. [d]Not detected.



https://doi.org/10.1021/acs.joc.1c00074
J. Org. Chem. 2021, 86, 5152−5165

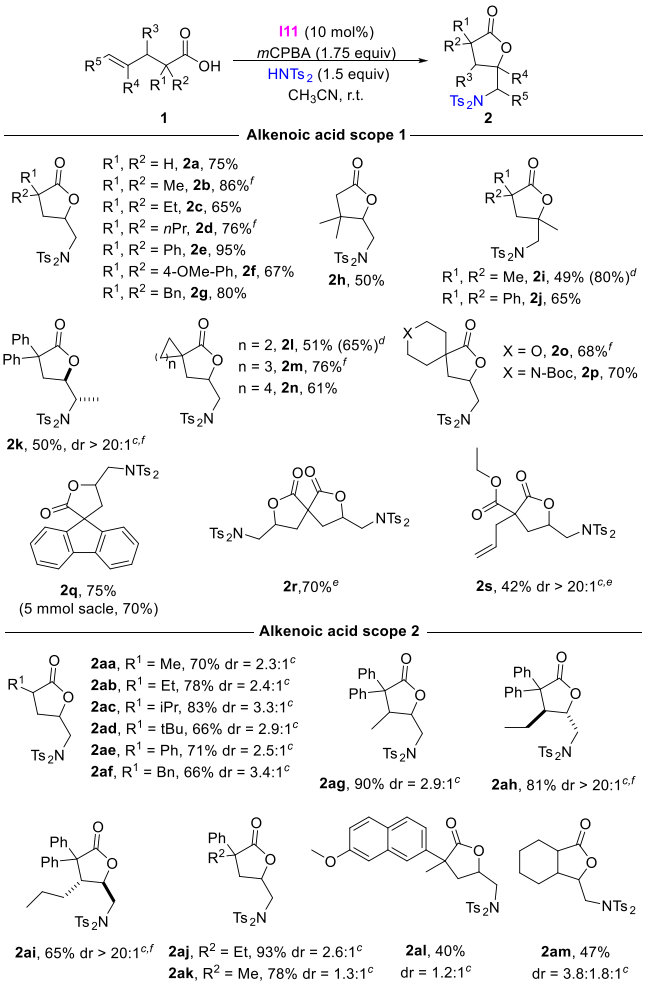
of dioxygenation, which differs from the results presented in the literature.[27] However, the presence of the more electron-donating *o*-isopropoxy groups in **I12** had a detrimental effect on this transformation. The precatalyst **I13** with a strong electron-withdrawing substitution group ($-NO_2$), which affected the transformation of amino lactone, led to the formation of byproduct **2e′** with a 44% yield. These results indicated that a catalyst with a higher initial reaction rate will affect the reaction time, which effectively reduced the extent of dioxygenation and increased the yield of the target product. Essentially, the electronics of the precatalyst can adjust the selectivity of this transformation due to the oxidation rate of iodoarenes by *m*CPBA and the dissociation rate of $ArI(NTs_2)_2$ to generate $[ArINTs_2]^+$ and $[NTs_2]^-$.

With the optimal conditions in hand, we then examined the scope of alkenyl acids substrates (Scheme 2). First, 4-pentenoic acid was submitted to catalytic conditions, and **2a** was obtained in a 75% yield. In general, 2,2-disubstituted 4-pentenoic acids containing different steric bulk groups (Me, Et, *n*Pr, Ph, Bn, and 4-OMe-Ph) worked well in all cases, furnishing the desired products in 65−95% yields (**2b**−**2g**). 3,3-Dimethyl 4-pentenoic acid, **1h**, showed slightly worse reactivity, obtaining **2h** with a 50% yield, which indicated that 3-substitution on the substrate had a weak effect on the reaction. Moreover, **2i** and **2j** were generated in moderate isolated yields and contained a sterically congested carbon center at C4. The yield of internal olefin substrate **1k** was 50% under standard conditions with a high diastereomer ratio. A diverse series of 2-cyclo-4-pentenoic acids containing carbon and heterocyclic motifs, **1l**−**1q**, were converted to spirocyclic lactone structures with good efficiencies. Interestingly, 2,2-diallylmalonic acid, **1r**, was converted to 2,7-dioxaspiro[4.4]-nonane-1,6-dione, **2r**, with double the equivalents of the reagents to prove the practicability of this method. In addition, the product of **2s** was generated with a 42% yield by the cyclization/amination of carbonyl acid (without the participation of carbonyl ester), showing that the activity of the carboxylic acid is higher than that of the ester in this reaction system.

Then, we explored the scope of *mono*- and *multiple*-substituted unactivated alkenes. First, a range of 3-substituted lactones were constructed, which furnished good yields (**2aa**−**2af**). The steric bulk of the 3-position substituent will dramatically affect the diastereomer ratios of the products. When substituted $-R^3$ was a methyl group, the diastereomer ratio was only 2.8:1 (**2ag**), whereas, when it was an ethyl group (**2ah**) or *n*-propyl group (**2ai**), excellent diastereoselectivities were observed. The substrates of **1aj** and **1ak** also produced good yields. Substrate **1al** had greater steric hindrance than **1ak**, but its diastereomeric ratio was not satisfactory. Finally, a product containing three chiral centers, **2am**, was obtained with a moderate yield. The structures of **2b**, **2d**, **2k**, **2m**, **2o**, **2ah**, and **2ai** were determined via X-ray crystallographic analysis (see the SI).

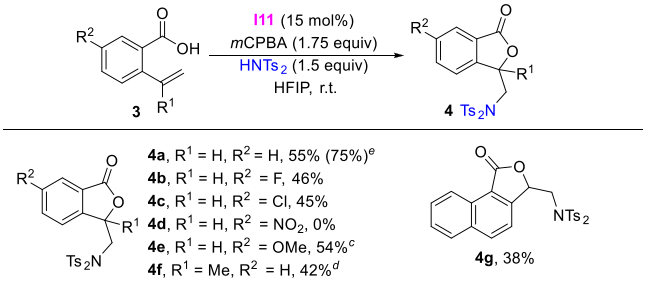
Under standard conditions, the aromatic substrate **3a** was converted to product **4a** with a low yield of 18% and poor selectivity. We further optimized the reaction conditions, and a series of aromatic substrates were smoothly converted to 5-*exo* products[12e] (Scheme 3), furnishing the amino lactones with moderate yields and excellent selectivities. In this transformation, the solvent effect was apparent, and when HFIP was used instead of $CH_3CN$ as the reaction solvent, **4a**−**4c** and **4g** were regioselectively obtained. **3f**, with a methyl group tethered with olefin, could be converted to 5-*exo* products in $CH_3CN$. Unfortunately, *para*-$NO_2$-substituted acid **3d** was not

**Scheme 2. Substrate Scope 1**[a,b]




[a]General conditions: **1** (0.2 mmol), $HNTs_2$ (1.5 equiv), **I11** (10 mol %), *m*CPBA (1.75 equiv), $CH_3CN$ (2 mL), r.t., 2.5−5 h, air atmosphere. [b]Isolated yield. [c]Diastereomeric ratio determined by NMR. [d]Detected by NMR and 1,2-dibromomethane as the internal standard. [e]**1** (0.2 mmol), $HNTs_2$ (3.0 equiv), **I11** (20 mol %), *m*CPBA (2.5 equiv), $CH_3CN$ (4 mL), r.t., 5 h, air atmosphere. [f]The structure determined via X-ray.

**Scheme 3. Substrate Scope 2**[a,b]




[a]General conditions: **3** (0.2 mmol), **I11** (15 mol %), *m*CPBA (1.75 equiv), $HNTs_2$ (1.5 equiv), HFIP(3 mL), r.t. 5−12 h, air atmosphere. [b]Isolated yield. [c]**I1** as catalyst. [d]$CH_3CN$ as solvent. [e]Detected by NMR and 1,2-dibromomethane as the internal standard.

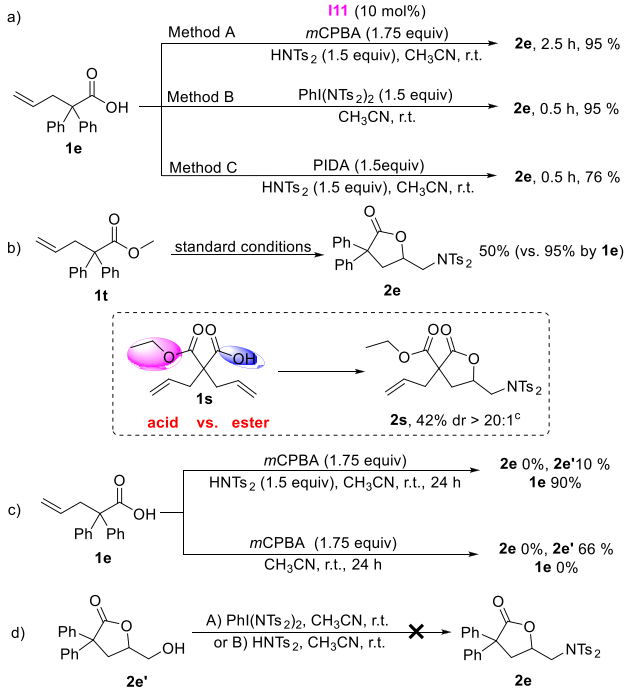


https://doi.org/10.1021/acs.joc.1c00074
J. Org. Chem. 2021, 86, 5152−5165

converted to a product in either HFIP or $CH_3CN$. The simple iodobenzene **I1** catalyst can convert **3e** to **4e** with high regioselectivity, but **I11** was very poor for this substrate.

Control experiments were conducted to investigate the reaction process. First, the catalyst was explored. Substrate **1e** was converted into **2e** within 2.5 h, resulting in a yield of 95% via method A, which was more atom economical and practical than methods B and C (Scheme 4a). The strategy of generated

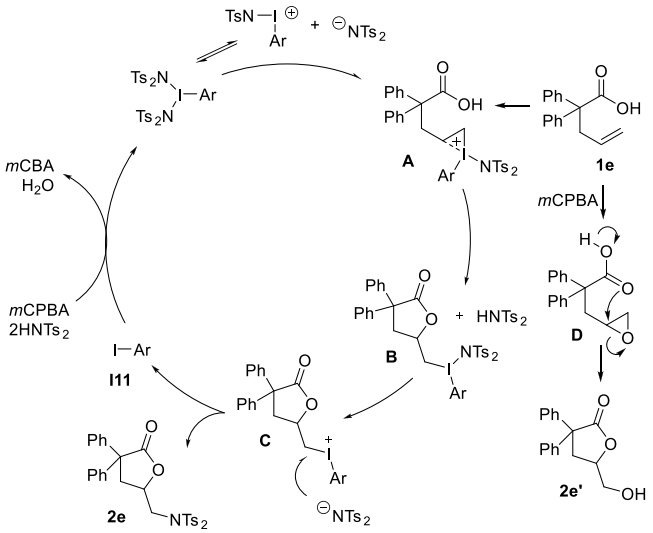
**Scheme 4. Control Experiments**




hypervalent iodine *in situ* is a more atom economical catalytic method and was also applicable in our reactions. The prepreparation[15c] process of $PhI(NTs_2)_2$ was complicated, and an excessive dose was needed. Second, the difference in the activities of carboxylic acid and the corresponding ester was further confirmed. When ester substrate **1t** was tested, the same product, **2e**, was observed but with a lower yield (50% vs 95%) under the same conditions (Scheme 4b). These results were consistent with those of the previous substrate **1s**, illustrating that unsaturated carboxylic acids were more compatible with these amino oxygenation conditions than ester substrates. Third, to investigate the mechanism of this process, several control experiments were conducted (Scheme 4c,d). The absence of an iodoarene precatalyst resulted in complete inhibition of aminolactonization, while, in the presence of *m*CPBA, dioxygenation product **2e′** was observed, which was formed by the main side reaction. However, with *m*CPBA and $HNTs_2$, a 10% yield of **2e′** was produced and **1e** still has 90% remaining, which was in sharp contrast with the result obtained for the condition where only *m*CPBA was used (Scheme 4c). Moreover, **2e** cannot be produced from byproduct **2e′** by directly using $PhI(NTs_2)_2$ or $HNTs_2$ (Scheme 4d). This result indicated that the mechanism of the byproduct is epoxidation/dioxidation mediated by *m*CPBA, which is different from that of the target product catalyzed by iodoarene.

On the basis of the current results,[14a,23d] a plausible reaction pathway of this iodoarene-catalyzed aminolactonization reaction is shown in Scheme 5. The reaction was initiated by

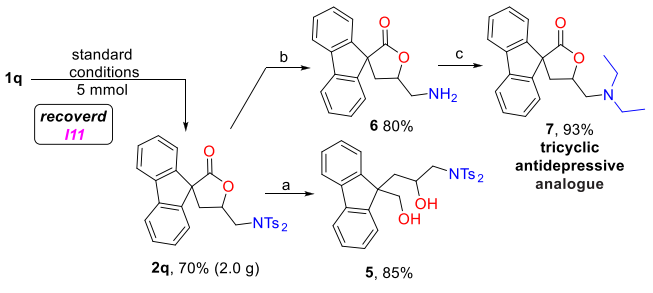
**Scheme 5. Plausible Reaction Mechanism**




the *m*CPBA oxidation of precatalyst **I11** in the presence of $HNTs_2$ to generate aryl-$\lambda^3$-iodane *in situ*. Next, aryl-$\lambda^3$-iodane can dissociate[15c] into $[ArINTs_2]^+$ and $[NTs_2]^-$, and then, substrate **1e** could undergo electrophilic addition with $[ArINTs_2]^+$, converting to iodonium intermediate **A**. Further, intermediate **B** was achieved by the intramolecular nucleophilic cyclization of intermediate **A**. $[NTs_2]^-$ was removed, and cationic intermediate **C** underwent nucleophilic addition to produce target product **2e**. Meanwhile, precatalyst **I11** was released, which finished the catalytic cycle. On the basis of previous studies,[25] oxylactonization byproduct generation proceeds via oxidation of substrate alkene **1e** by an *in situ* generation epoxide intermediate **D** when using *m*CPBA as the oxidant. Subsequently, epoxide intermediate **D** was attacked by carbonyl groups and cyclized to produce oxylactone byproducts.

To prove the synthetic utility and versatility of this reaction, a gram-scale reaction was achieved, and desired product **2q** was obtained in a 70% yield (Scheme 6). Notably, 48% of precatalyst **I11** was recovered and reused for the reaction, giving the same reaction result. Next, amino lactone **2q** was transformed into 1,5-dihydroxyamine **5** in a 85% yield using $BH_3$·THF for carbon reduction. Furthermore, **2q** can be

**Scheme 6. Further Transformations**[a]




[a]General conditions: a: $BH_3$·THF, 1 h, r.t. b: HBr (33 wt % in acetic acid), resorcinol, 85 °C, 24 h. c: $CH_3CH_2I$, $K_2CO_3$, THF, 69 °C, 24 h.



https://doi.org/10.1021/acs.joc.1c00074
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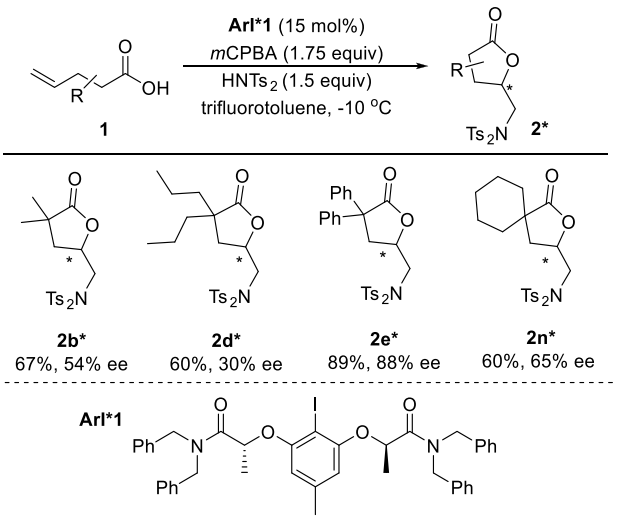
converted to tricyclic antidepressant analogue **7**[10b] by simple deprotection and alkylation processes. These derivatives showcased the synthetic value of this method and could provide numerous nitrogen-containing heterocyclic compounds, which may serve as potential pharmaceutical precursors.

Finally, to achieve the asymmetric aminolactonization of alkenyl acids, preliminary studies were conducted with chiral aryl iodine catalyst **1** (Scheme 7). Model substrate **1e** can

**Scheme 7. Asymmetric Transformation**[a,b,c]




[a]General conditions: **1** (0.1 mmol), $HNTs_2$ (1.5 equiv), **ArI*1** (15 mol %), *m*CPBA (1.75 equiv), benzotrifluoride (1 mL), −10 °C, 60 h. [b]Isolated yield. [c]Enantiomeric excess determined by chiral HPLC analysis.

obtain an 88% enantiomeric excess and an 89% yield. However, a series of substrates obtained less enantiomeric excess (**2b***, **2d***, **2n***) for initial substrate expansion. Through analysis, the catalytic system was highly dependent on the substrate structure of the 2,2-diphenyl substituent.[26] It is necessary to further adjust the structure of the catalyst and optimize the reaction conditions, and further research is still being carried out in our laboratory.

## CONCLUSION

In conclusion, the aryl iodine/oxidant system was first applied in the aminolactonization of unactivated alkenes. This protocol was compatible with *mono*-substituted, *multiple*-substituted, and *benzoyl*-alkenes to produce diverse amino lactones. Through control experiments and calculations of the reaction rate, a reasonable reaction mechanism was proposed. Moreover, a tricyclic antidepressant analogue was synthesized through this transformation, which confirmed the potential value for synthetic applications in pharmacophoric and medicinal research. In addition, this work also provided a basis for the exploration of rare asymmetric aminolactonizations by using a new chiral aryl iodine reagent, and further research is being carried out in our laboratory.

## EXPERIMENTAL SECTION

**General Information.** All of the reactions were carried out in oven-dried glassware with magnetic stirring. Unless otherwise indicated, all solvents, reagents, and all deuterated solvents were obtained from the commercial provider and used without further purification. Reaction progress was monitored by thin layer chromatography (0.15−0.2 mm thickness) with visualization by exposure to a 254 nm UV lamp or molecule iodine, and TLC purchased from Rushan Taiyang Company of China. Flash column chromatography was performed on the glass column filled in 200−300 mesh silica gel (silica gel purchased from Yantai Company of China) and eluted with petroleum ether/EtOAc or dichloromethane/methanol. All $^1$H NMR, $^{13}$C {$^1$H} NMR spectra were recorded on Bruker AV-400 or AV-600. Chemical shifts were reported relative to internal tetramethylsilane ($\delta$ 0.00 ppm), $CDCl_3$ ($\delta$ 7.26 ppm) for $^1$H and $CDCl_3$ ($\delta$ 77.16 ppm) for $^{13}$C {$^1$H}, $(CD_3)_2SO$ ($\delta$ 2.50 ppm) for $^1$H and $(CD_3)_2SO$ ($\delta$ 39.52 ppm) for $^{13}$C {$^1$H}, $CD_3OD$ ($\delta$ 3.31 ppm) for $^1$H and $CD_3OD$ ($\delta$ 49.00 ppm) for $^{13}$C {$^1$H}, $CD_3CN$ ($\delta$ = 1.94 ppm) for $^1$H. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), dt (doublet of triplets), dq (doublet of quartets), td (triplet of doublets), ddd (doublet of doublet of doublets). Coupling constants were reported in hertz (Hz). HRMS were performed on a Waters I-Class VION IMS Q-TOF Mass Spectrometer or a Bruker ESI-Q-TOF (maxis) Mass Spectrometer. Enantiomeric excess (ee) determination was carried out on an Agilent 1260 interfaced to a HP 71 series computer workstation with Chiralpak $IA_3$/OD-H column. Melting points were determined by a microscopic melting point tester (X-6). IR spectra were recorded as KBr disks (Shimadzu FTIR-8400S). X-ray single-crystal diffraction data were collected on a Bruker APEX-II CCD diffractometer

**General Procedures for Preparation of Substrates.** All the substrates **1** and **3** were synthesized according to reported procedures.[28] **1ah**−**1ai** and **1al** are new compounds characterized by NMR, HRMS (ESI), and IR.

*2,2-Diphenylhex-4-enoic Acid (**1k**).* Synthesized from 2,2-diphenylacetic acid according to the literature.[28e] Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 10:1) as a white solid (2.1 g, 80%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.34−7.29 (m, 10H), 5.28 (ddt, $J$ = 16.8, 12.0, 6.0 Hz, 2H), 3.10 (d, $J$ = 6.0 Hz, 2H), 1.51 (d, $J$ = 5.6 Hz, 3H).

*3-Ethyl-2,2-diphenylpent-4-enoic Acid (**1ah**).* Synthesized from 2,2-diphenylacetic acid according to the literature.[28e] Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 10:1) as a white solid (1.4 g, 41%). mp 186.3−187.0 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.35−7.22 (m, 10H), 5.34−5.08 (m, 3H), 3.42 (t, $J$ = 9.2 Hz, 1H), 1.72−1.60 (m, 1H), 0.87 (t, $J$ = 7.2 Hz, 3H), 0.65−0.48 (m, 1H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 179.6, 140.2, 139.6, 137.6, 131.0, 130.2, 127.7, 127.1, 127.1, 126.9, 119.0, 64.9, 48.8, 23.6, 12.1. IR$\nu_{max}$ ($cm^{-1}$): 3075, 2975, 2875, 2625, 1700, 1680, 1665, 1600, 1497, 1450, 1260, 922, 713, 663. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{19}H_{20}NaO_2$ 303.1356; found 303.1352.

*2,2-Diphenyl-3-vinylhexanoic Acid (**1ai**).* Synthesized from 2,2-diphenylacetic acid according to the literature.[28e] Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 10:1) as a white solid (2.4 g, 68%). mp 152.5−153.3 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.38−7.25 (m, 10H), 5.36−5.08 (m, 3H), 3.58 (t, $J$ = 9.6 Hz, 1H), 1.64−1.51 (m, 1H), 1.44−1.32 (m, 1H), 1.27 (dt, $J$ = 14.8, 8.0 Hz, 1H), 0.87 (t, $J$ = 7.2 Hz, 3H), 0.59 (q, $J$ = 9.6 Hz, 1H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 179.6, 140.2, 139.6, 138.1, 131.0, 130.2, 127.7, 127.1, 127.1, 126.9, 118.7, 64.9, 46.6, 32.6, 20.6, 14.0. IR $\nu_{max}$ ($cm^{-1}$): 3060, 2956, 2620, 1732, 1704, 1635, 1500, 1443, 1395, 1258, 922, 711. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{20}H_{22}NaO_2$ 317.1510; found 317.1512.

*2-(6-Methoxynaphthalen-2-yl)-2-methylpent-4-enoic Acid (**1al**).* Synthesized from pentylbenzene according to the literature.[28a] Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 10:1) as a white solid (1.5 g, 54% yield). mp 152.1−152.9 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.71 (dd, $J$ = 8.8, 1.6 Hz, 3H), 7.48 (dd, $J$ = 8.8, 2.0 Hz, 1H), 7.19−7.08 (m, 2H), 5.63 (ddt, $J$ = 17.2, 10.0, 7.2 Hz, 1H), 5.15−4.97 (m, 2H), 3.92 (s, 3H), 2.90 (dd, $J$ = 13.6, 7.2 Hz, 1H), 2.79 (dd, $J$ = 13.6, 7.2 Hz, 1H), 1.65 (s, 3H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 182.0, 157.9, 137.4, 133.8, 133.5, 129.6, 128.7, 127.0, 125.2, 124.7, 119.0, 118.7, 105.5, 55.3, 49.6, 43.4, 22.2. IR $\nu_{max}$ ($cm^{-1}$): 3070, 2980, 2940, 1700, 1635,


https://doi.org/10.1021/acs.joc.1c00074
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1605, 1460, 1395, 1267, 1220, 1165, 1027, 920, 850, 814, 475. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{17}H_{18}NaO_3$ 293.1148; found 293.1144.

*2-Vinylcyclohexane-1-carboxylic Acid (**1am**).* Synthesized from hexahydroisobenzofuran-1,3-dione according to the literature.[28g] Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a colorless oil (1.5 g, 40% yield). $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 11.81 (s, 1H), 5.98 (ddd, $J$ = 17.2, 10.4, 8.0 Hz, 1H), 5.13−5.00 (m, 2H), 2.72−2.65 (m, 1H), 2.61 (dt, $J$ = 8.8, 4.4 Hz, 1H), 1.86−1.69 (m, 4H), 1.64−1.56 (m, 2H), 1.48−1.30 (m, 2H).

**General Procedures for Nitrogen Reagents.** All nitrogen reagents are known compounds that are commercially available or prepared by the literature.[29]

**General Procedures for Amino Lactones.** *Procedure A.* A 10 mL Pyrex tube was charged with substrates **1** (0.2 mmol), *m*CPBA (0.35 mmol, 71 mg, 85 wt %), $HNTs_2$ (0.3 mmol, 98 mg), and **I11** (0.02 mmol, 5.3 mg) in $CH_3CN$ (2 mL), which was stirred at room temperature for 2.5−5 h. The reaction solution was detected by TLC until completely finished. After completion, the mixture was quenched with an aqueous solution of NaOH (2 mol/L). The mixture was extracted with EtOAc (20 mL × 3). The combined organic phase was washed with brine, dried over $Na_2SO_4$, filtered, and concentrated under vacuum. Then, the residue was purified by flash chromatography on silica gel (PE/EtOAc = 10:1−1:1) to afford the desired products **2**.

*Procedure B.* A 10 mL Pyrex tube was charged with substrates **3** (0.2 mmol), *m*CPBA (0.35 mmol, 71 mg, 85 wt %), $HNTs_2$ (0.3 mmol, 98 mg), and **I11** (0.03 mmol, 7.9 mg) in HFIP (3 mL), which was stirred at room temperature for 5−10 h. The reaction solution was detected by TLC until completely finished. After completion, the mixture was quenched with an aqueous solution of NaOH (2 mol/L). The mixture was extracted with EtOAc (20 mL × 3). The combined organic phase was washed with brine, dried over $Na_2SO_4$, filtered, and concentrated under vacuum. Then, the residue was purified by flash chromatography on silica gel (PE/EtOAc = 5:1−3:1) to afford the desired products **4**. Substrate **3e** used **I1** (0.03 mmol, 6.1 mg) instead of **I11**, and substrate **3f** used $CH_3CN$ (3 mL) as solvent.

*$^1H$ NMR Experiments.* An NMR tube was charged with substrates (0.05 mmol), *m*CPBA (1.75 equiv, 85 wt %), **I11** (10 mol % or 15 mol %), and $HNTs_2$ (1.5 equiv), in $CD_3CN$ (0.5 mL) with $CH_2Br_2$ (0.05 mmol) as an internal standard.

*4-Methyl-N-((5-oxotetrahydrofuran-2-yl)methyl)-N-tosylbenzenesulfonamide (**2a**).* Synthesized from **1a** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 1:1) as a white solid (63.5 mg, 75%). mp 59.8−60.6 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.94 (d, $J$ = 8.4 Hz, 4H), 7.35 (d, $J$ = 8.0 Hz, 4H), 4.86−4.79 (m, 1H), 4.07 (dd, $J$ = 15.6, 7.6 Hz, 1H), 3.65 (dd, $J$ = 15.6, 4.4 Hz, 1H), 2.56−2.47 (m, 2H), 2.45 (s, 6H), 2.34−2.21 (m, 1H), 1.95 (ddd, $J$ = 16.8, 13.2, 8.8 Hz, 1H). $^{13}C$ $\{^1H\}$ NMR (100 MHz, $CDCl_3$): $\delta$ 176.0, 145.4, 136.1, 129.7, 128.7, 78.5, 51.2, 28.0, 25.2, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 2925, 1780, 1683, 1653, 1558, 1373, 1165, 1083, 816, 664, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{19}H_{21}NNaO_6S_2$ 446.0702; found 446.0716.

*N-((4,4-Dimethyl-5-oxotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**2b**).* Synthesized from **1b** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (77.6 mg, 86%). mp 166.3−167.4 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.95 (d, $J$ = 7.6 Hz, 4H), 7.35 (d, $J$ = 8.0 Hz, 4H), 4.78−4.67 (m, 1H), 4.10 (dd, $J$ = 15.6, 7.2 Hz, 1H), 3.70 (dd, $J$ = 16.0, 3.6 Hz, 1H), 2.45 (s, 6H), 2.10 (dd, $J$ = 12.8, 6.0 Hz, 1H), 1.80−1.74 (m, 1H), 1.23 (s, 3H), 1.20 (s, 3H). $^{13}C$ $\{^1H\}$ NMR (100 MHz, $CDCl_3$): $\delta$ 180.6, 145.3, 136.2, 129.7, 128.7, 75.3, 51.9, 40.6, 40.1, 24.9, 24.4, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 2970, 2932, 2876, 2360, 2340, 1775, 1657, 1558, 1373, 1166, 815, 664, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{21}H_{25}NNaO_6S_2$ 474.1016; found 474.1016.

*N-((4,4-Diethyl-5-oxotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**2c**).* Synthesized from **1c** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 4:1) as a white solid (62.3 mg, 65%). mp 59.6−60.3 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.98 (d, $J$ = 8.4 Hz, 4H), 7.38 (d, $J$ = 8.0 Hz, 4H), 4.76−4.69 (m, 1H), 4.09 (dd, $J$ = 16.0, 7.6 Hz, 1H), 3.69 (dd, $J$ = 15.6, 4.8 Hz, 1H), 2.49 (s, 6H), 2.05 (dd, $J$ = 13.6, 6.8 Hz, 1H), 1.87 (dd, $J$ = 13.2, 9.2 Hz, 1H), 1.64−1.57 (m, 4H), 0.91 (td, $J$ = 7.6, 2.4 Hz, 6H). $^{13}C$ $\{^1H\}$ NMR (100 MHz, $CDCl_3$): $\delta$ 179.6, 145.3, 136.3, 129.7, 128.7, 75.1, 53.4, 52.3, 48.4, 34.9, 29.1, 28.3, 21.7, 8.6. IR $\nu_{max}$ ($cm^{-1}$): 2960, 2925, 2854, 1770, 1683, 1653, 1558, 1456, 1373, 1265, 1167, 948, 811, 727, 663, 551. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{23}H_{29}NNaO_6S_2$ 502.1329; found 502.1324.

*4-Methyl-N-((5-oxo-4,4-dipropyltetrahydrofuran-2-yl)methyl)-N-tosylbenzenesulfonamide (**2d**).* Synthesized from **1d** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 4:1) as a white solid (77.1 mg, 76%). mp 95.8−96.3 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.95 (d, $J$ = 8.0 Hz, 4H), 7.35 (d, $J$ = 8.0 Hz, 4H), 4.73−4.61 (m, 1H), 4.06 (dd, $J$ = 15.6, 7.2 Hz, 1H), 3.68 (dd, $J$ = 15.6, 4.4 Hz, 1H), 2.45 (s, 6H), 2.03 (dd, $J$ = 13.2, 6.8 Hz, 1H), 1.85 (dd, $J$ = 12.8, 9.2 Hz, 1H), 1.58−1.15 (m, 8H), 0.94−0.84 (m, 6H). $^{13}C$ $\{^1H\}$ NMR (100 MHz, $CDCl_3$): $\delta$ 179.9, 145.3, 136.2, 129.7, 128.7, 75.3, 52.2, 47.8, 39.0, 38.4, 35.7, 21.7, 17.6, 17.6, 14.4, 14.4. IR $\nu_{max}$ ($cm^{-1}$): 2961, 2933, 2873, 1772, 1685, 1652, 1558, 1376, 1167, 1084, 816, 663, 547. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{25}H_{33}NNaO_6S_2$ 530.1642; found 530.1645.

*4-Methyl-N-((5-oxo-4,4-diphenyltetrahydrofuran-2-yl)methyl)-N-tosylbenzenesulfonamide (**2e**).* Synthesized from **1e** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 5:1) as a white solid (109.3 mg, 95%). mp 171.3−171.8 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.92 (d, $J$ = 8.0 Hz, 4H), 7.36−7.21 (m, 14H), 4.64−4.58 (m, 1H), 4.16 (dd, $J$ = 15.6, 6.4 Hz, 1H), 3.88 (dd, $J$ = 15.6, 4.8 Hz, 1H), 2.95 (dd, $J$ = 13.2, 5.2 Hz, 1H), 2.69 (dd, $J$ = 12.8, 10.8 Hz, 1H), 2.43 (s, 6H). $^{13}C$ $\{^1H\}$ NMR (100 MHz, $CDCl_3$): $\delta$ 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 $\nu_{max}$ ($cm^{-1}$): 3060, 3030, 2962, 2925, 2855, 1771, 1683, 1652, 1558, 1373, 1165, 1083, 966, 945, 817, 700, 665, 551. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{31}H_{29}NNaO_6S_2$ 598.1329; found 598.1335.

*5-(Hydroxymethyl)-3,3-diphenyldihydrofuran-2(3H)-one (**2e′**).* Synthesized from **1e** via control experiment, sticky solid.[30] $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.40−7.27 (m, 9H), 7.26−7.21 (m, 1H), 4.51−4.40 (m, 1H), 3.95 (dd, $J$ = 12.8, 2.4 Hz, 1H), 3.68 (dd, $J$ = 12.8, 4.4 Hz, 1H), 3.02−2.84 (m, 2H), 2.64 (s, 1H). $^{13}C$ $\{^1H\}$ NMR (100 MHz, $CDCl_3$): $\delta$ 177.3, 141.8, 139.8, 129.0, 128.4, 127.8, 127.8, 127.3, 127.3, 63.0, 58.3, 38.3.

*N-((4,4-Bis(4-methoxyphenyl)-5-oxotetrahydrofuran-2-yl)-methyl)-4-methyl-N-tosylbenzenesulfonamide (**2f**).* Synthesized from **1f** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 2:1) as a white solid (85.1 mg, 67%). mp 92.9−93.9 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.92 (d, $J$ = 8.4 Hz, 4H), 7.31 (d, $J$ = 8.0 Hz, 4H), 7.13 (dd, $J$ = 18.8, 8.8 Hz, 4H), 6.83 (dd, $J$ = 15.2, 8.8 Hz, 4H), 4.63−4.56 (m, 1H), 4.14 (dd, $J$ = 16.0, 6.4 Hz, 1H), 3.85 (dd, $J$ = 15.6, 4.8 Hz, 1H), 3.80 (s, 3H), 3.77 (s, 3H), 2.89 (dd, $J$ = 12.8, 4.8 Hz, 1H), 2.61 (dd, $J$ = 13.2, 10.4 Hz, 1H), 2.43 (s, 6H). $^{13}C$ $\{^1H\}$ NMR (100 MHz, $CDCl_3$): $\delta$ 176.6, 159.0, 158.61, 145.4, 136.2, 133.9, 131.4, 129.8, 128.8, 128.6, 128.3, 114.2, 113.7, 75.2, 56.6, 55.3, 55.2, 51.2, 41.2, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 2955, 2935, 2835, 1772, 1684, 1653, 1558, 1506, 1375, 1254, 1165, 816, 664, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{33}H_{33}NNaO_8S_2$ 658.1540; found 658.1534.

*N-((4,4-Dibenzyl-5-oxotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**2g**).* Synthesized from **1g** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 5:1) as a white solid (96.5 mg, 80%). mp 197.2−197.5 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.73 (d, $J$ = 8.4 Hz, 4H), 7.36−7.27 (m, 10H), 7.21−7.16 (m, 4H), 3.71−3.64 (m, 1H), 3.37 (dd, $J$ = 15.6, 6.8 Hz, 1H), 3.20 (d, $J$ = 13.6 Hz, 1H), 3.16−3.10 (m, 2H), 2.74 (dd, $J$ = 17.6, 13.6 Hz, 2H), 2.46 (s, 6H), 2.16 (dd, $J$ = 13.6, 7.6 Hz, 1H), 1.93 (dd, $J$ = 13.6, 9.2 Hz, 1H). $^{13}C$


https://doi.org/10.1021/acs.joc.1c00074
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{$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 179.8, 145.1, 136.5, 136.1, 135.9, 130.4, 129.9, 129.6, 128.7, 128.6, 127.4, 127.1, 75.2, 51.7, 51.5, 44.4, 43.4, 32.6, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 3067, 3032, 2922, 1772, 1683, 1653, 1558, 1375, 1167, 1085, 816, 664, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{33}H_{33}NNaO_6S_2$ 626.1642; found 626.1640.

*N-((3,3-Dimethyl-5-oxotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**2h**).* Synthesized from **1h** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (45.1 mg, 50%). mp 204.9−205.6 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.02 (d, $J$ = 8.4 Hz, 4H), 7.37 (d, $J$ = 8.0 Hz, 4H), 4.47 (d, $J$ = 9.2 Hz, 1H), 4.15 (dd, $J$ = 16.0, 9.6 Hz, 1H), 3.55 (d, $J$ = 16.0 Hz, 1H), 2.46 (s, 6H), 2.38 (d, $J$ = 16.8 Hz, 1H), 2.31 (d, $J$ = 16.8 Hz, 1H), 1.24 (s, 3H), 1.06 (s, 3H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 174.7, 145.6, 136.2, 129.6, 128.9, 86.6, 48.1, 44.2, 38.9, 25.2, 21.7, 21.0. IR $\nu_{max}$ ($cm^{-1}$): 2963, 1792, 1772, 1734, 1683, 1653, 1520, 1506, 1372, 1165, 847, 664, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{21}H_{25}NNaO_6S_2$ 474.1016; found 474.1030.

*4-Methyl-N-tosyl-N-((2,4,4-trimethyl-5-oxotetrahydrofuran-2-yl)methyl)benzenesulfonamide (**2i**).* Synthesized from **1i** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (45.6 mg, 49%). mp 101.2−102.3 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.98 (d, $J$ = 8.4 Hz, 4H), 7.34 (d, $J$ = 8.4 Hz, 4H), 4.01 (d, $J$ = 1.6 Hz, 2H), 2.44 (s, 6H), 2.16 (d, $J$ = 13.6 Hz, 1H), 1.92 (d, $J$ = 13.6 Hz, 1H), 1.38 (s, 3H), 1.29 (s, 3H), 1.06 (s, 3H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 180.9, 145.1, 136.8, 129.6, 128.9, 81.8, 56.7, 45.4, 40.4, 27.4, 27.1, 26.3, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 2974, 2934, 2870, 1767, 1683, 1652, 1506, 1375, 1168, 1084, 937, 815, 766, 664, 552. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{22}H_{27}NNaO_6S_2$ 488.1172; found 488.1173.

*4-Methyl-N-((2-methyl-5-oxo-4,4-diphenyltetrahydrofuran-2-yl)-methyl)-N-tosylbenzenesulfonamide (**2j**).* Synthesized from **1j** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 4:1) as a white solid (76.6 mg, 65%). mp 271.9−272.7 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.95 (d, $J$ = 8.0 Hz, 4H), 7.37−7.31 (m, 4H), 7.25−7.20 (m, 8H), 7.10−7.07 (m, 2H), 4.24 (d, $J$ = 16.4 Hz, 1H), 3.94 (d, $J$ = 16.4 Hz, 1H), 3.21 (d, $J$ = 14.0 Hz, 1H), 2.92 (d, $J$ = 14.0 Hz, 1H), 2.37 (s, 6H), 1.14 (s, 3H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 175.7, 145.1, 142.6, 142.1, 136.7, 129.6, 128.9, 128.6, 128.4, 127.4, 127.3, 127.2, 127.0, 82.9, 57.8, 56.2, 44.8, 24.9, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 3060, 3030, 1766, 1666, 1597, 1492, 1447, 1370, 1168, 1085, 815, 775, 730, 700, 665, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{32}H_{31}NNaO_6S_2$ 612.1485; found 612.1498.

*(E)-4-Methyl-N-(1-(5-oxo-4,4-diphenyltetrahydrofuran-2-yl)-ethyl)-N-tosylbenzenesulfonamide (**2k**).* Synthesized from **1k** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 4:1) as a white solid (58.9 mg, 50%), dr > 20:1. mp 82.4−83.6 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.97−7.74 (m, 4H), 7.37−7.29 (m, 12H), 7.20 (d, $J$ = 7.2 Hz, 2H), 4.97 (td, $J$ = 9.6, 5.2 Hz, 1H), 4.26 (dq, $J$ = 15.2, 8.0, 7.2 Hz, 1H), 3.11 (dd, $J$ = 13.2, 5.2 Hz, 1H), 2.44 (s, 6H), 2.40 (d, $J$ = 4.0 Hz, 1H), 1.46−1.42 (m, 3H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 175.1, 141.7, 139.1, 129.3, 128.8, 128.7, 128.4, 128.3, 128.2, 127.7, 127.3, 127.1, 127.0, 76.2, 61.8, 57.7, 42.0, 21.4, 15.5. IR $\nu_{max}$ ($cm^{-1}$): 3075, 2925, 2854, 2360, 2260, 1777, 1597, 1495, 1450, 1372, 1165, 1084, 1052, 967, 915, 858, 740, 697, 667, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{32}H_{31}NNaO_6S_2$ 612.1485; found 612.1475.

*4-Methyl-N-((5-oxo-6-oxaspiro[3.4]octan-7-yl)methyl)-N-tosylbenzenesulfonamide (**2l**).* Synthesized from **1l** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 5:1) as a white solid (47.2 mg, 51%). mp 150.9−151.6 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.94 (d, $J$ = 7.6 Hz, 4H), 7.35 (d, $J$ = 7.6 Hz, 4H), 4.69−4.60 (m, 1H), 4.01 (dd, $J$ = 15.6, 7.6 Hz, 1H), 3.68−3.58 (m, 1H), 2.56−2.49 (m, 1H), 2.45 (s, 6H), 2.42−2.36 (m, 2H), 2.17−2.07 (m, 1H), 2.05−1.95 (m, 4H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 179.9, 145.3, 136.1, 129.7, 128.7, 75.5, 51.5, 43.8, 39.0, 31.3, 29.8, 21.7, 16.4. IR $\nu_{max}$ ($cm^{-1}$): 2990, 2937, 2865, 2360, 1773, 1684, 1654, 1599, 1373, 1295, 1272, 1165, 1084, 1040, 815, 664, 551. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{22}H_{25}NNaO_6S_2$ 486.1016; found 486.1021.

*4-Methyl-N-((1-oxo-2-oxaspiro[4.4]nonan-3-yl)methyl)-N-tosylbenzenesulfonamide (**2m**).* Synthesized from **1m** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (72.5 mg, 76%). mp 155.9−156.6 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.95 (d, $J$ = 8.4 Hz, 4H), 7.34 (d, $J$ = 8.0 Hz, 4H), 4.73−4.62 (m, 1H), 4.10 (dd, $J$ = 15.6, 7.2 Hz, 1H), 3.69 (dd, $J$ = 16.0, 4.4 Hz, 1H), 2.44 (s, 6H), 2.15−2.07 (m, 2H), 1.86−1.76 (m, 4H), 1.65−1.49 (m, 4H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 181.2, 145.3, 136.2, 129.7, 128.7, 75.9, 51.7, 49.8, 40.2, 37.4, 36.9, 25.4, 25.4, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 2925, 2855, 1771, 1683, 1653, 1558, 1508, 1455, 1373, 1164, 1084, 947, 920, 813, 750, 662, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{23}H_{27}NNaO_6S_2$ 500.1172; found 500.1176.

*4-Methyl-N-((1-oxo-2-oxaspiro[4.5]decan-3-yl)methyl)-N-tosylbenzenesulfonamide (**2n**).* Synthesized from **1n** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (60.0 mg, 61%). mp 151.4−152.2 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.96 (d, $J$ = 8.0 Hz, 4H), 7.35 (d, $J$ = 8.0 Hz, 4H), 4.74−4.67 (m, 1H), 4.09 (dd, $J$ = 15.6, 7.2 Hz, 1H), 3.69 (dd, $J$ = 16.0, 4.4 Hz, 1H), 2.45 (s, 6H), 2.25 (dd, $J$ = 12.8, 6.4 Hz, 1H), 1.81−1.55 (m, 6H), 1.43 (d, $J$ = 13.2 Hz, 1H), 1.36−1.18 (m, 4H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 180.3, 145.3, 136.2, 129.7, 128.7, 75.5, 52.1, 44.6, 36.6, 34.1, 31.7, 25.2, 22.1, 22.0, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 2925, 2852, 1770, 1683, 1653, 1597, 1558, 1456, 1373, 1310, 1295, 1265, 1162, 1087, 1027, 943, 930, 815, 737, 660, 547. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{24}H_{29}NNaO_6S_2$ 514.1329; found 514.1331.

*4-Methyl-N-((1-oxo-2,8-dioxaspiro[4.5]decan-3-yl)methyl)-N-tosylbenzenesulfonamide (**2o**).* Synthesized from **1o** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 1:1) as a white solid (67.0 mg, 68%). mp 183.5−184.4 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.95 (d, $J$ = 8.4 Hz, 4H), 7.36 (d, $J$ = 8.0 Hz, 4H), 4.80−4.73 (m, 1H), 4.11 (dd, $J$ = 15.6, 7.2 Hz, 1H), 4.02 (dt, $J$ = 11.6, 4.4 Hz, 1H), 3.89 (dt, $J$ = 12.4, 4.0 Hz, 1H), 3.71 (dd, $J$ = 15.6, 4.4 Hz, 1H), 3.57−3.41 (m, 2H), 2.46 (s, 6H), 2.33 (dd, $J$ = 12.8, 6.4 Hz, 1H), 2.04 (ddd, $J$ = 13.6, 10.0, 4.0 Hz, 1H), 1.92−1.74 (m, 2H), 1.53−1.39 (m, 2H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 178.6, 145.4, 136.1, 129.7, 128.7, 75.4, 63.9, 63.6, 51.8, 41.9, 37.2, 33.6, 32.0, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 2955, 2855, 1773, 1652, 1558, 1375, 1165, 1085, 816, 664, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{23}H_{27}NNaO_7S_2$ 516.1121; found 516.1125.

*tert-Butyl 3-(((4-Methyl-N-tosylphenyl)sulfonamido)methyl)-1-oxo-2-oxa-8-azaspiro[4.5]decane-8-carboxylate (**2p**).* Synthesized from **1p** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (82.9 mg, 70%). mp 72.5−73.6 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.94 (d, $J$ = 8.4 Hz, 4H), 7.35 (d, $J$ = 8.4 Hz, 4H), 4.79−4.72 (m, 1H), 4.10 (dd, $J$ = 15.6, 7.2 Hz, 1H), 3.92 (s, 1H), 3.80 (s, 1H), 3.71 (dd, $J$ = 15.6, 4.4 Hz, 1H), 3.04 (dt, $J$ = 23.4, 10.6 Hz, 2H), 2.45 (s, 6H), 2.24 (dd, $J$ = 13.2, 6.4 Hz, 1H), 1.88 (ddd, $J$ = 13.8, 10.0, 4.0 Hz, 1H), 1.79−1.69 (m, 2H), 1.51 (dd, $J$ = 15.6, 6.4 Hz, 2H), 1.45 (s, 9H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 178.7, 154.6, 145.5, 136.1, 129.7, 128.7, 79.9, 75.5, 51.8, 42.7, 36.6, 33.2, 31.5, 28.4, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 2977, 2930, 1771, 1690, 1682, 1653, 1596, 1425, 1370, 1282, 1265, 1252, 1165, 1085, 1045, 818, 790, 664, 552. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{28}H_{36}N_2NaO_8S_2$ 615.1805; found 615.1812.

*4-Methyl-N-((2′-oxo-4′,5′-dihydro-2′H-spiro[fluorene-9,3′-furan]-5′-yl)methyl)-N-tosylbenzenesulfonamide (**2q**).* Synthesized from **1q** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 5:1) as a white solid (86.0 mg, 75%). mp 231.3−231.8 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.03 (d, $J$ = 8.4 Hz, 4H), 7.74 (d, $J$ = 7.6 Hz, 2H), 7.47−7.40 (m, 2H), 7.39−7.28 (m, 8H), 5.34−5.27 (m, 1H), 4.39 (dd, $J$ = 15.8, 7.2 Hz, 1H), 3.98 (dd, $J$ = 15.8, 4.4 Hz, 1H), 2.72 (dd, $J$ = 13.6, 10.4 Hz, 1H), 2.61 (dd, $J$ = 13.6, 6.4 Hz, 1H), 2.44 (s, 6H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 175.7, 145.5, 145.4, 144.6,


https://doi.org/10.1021/acs.joc.1c00074
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141.4, 140.6, 136.2, 129.8, 129.0, 128.9, 128.8, 128.3, 128.1, 123.6, 122.8, 120.7, 120.4, 76.6, 58.5, 52.1, 38.9, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 3068, 2925, 1780, 1685, 1597, 1450, 1375, 1165, 817, 735, 667, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{31}H_{27}NNaO_6S_2$ 596.1172; found 596.1177.

*5′-(Hydroxymethyl)-4′,5′-dihydro-2′H-spiro[fluorene-9,3′-furan]-2′-one (**2q′**).* Byproduct of **2q**, yellow solid. mp 123.9−130.6 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.76 (d, $J$ = 6.4 Hz, 2H), 7.56 (d, $J$ = 7.2 Hz, 1H), 7.46−7.38 (m, 4H), 7.32 (dd, $J$ = 8.8, 5.2 Hz, 1H), 4.92 (dq, $J$ = 10.4, 6.4, 5.2 Hz, 1H), 3.63 (dt, $J$ = 10.0, 5.2 Hz, 2H), 2.79 (tt, $J$ = 9.6, 5.4 Hz, 2H). $^{13}C$ {$^1H$} NMR (100 MHz, $CDCl_3$): $\delta$ 175.9, 145.8, 144.8, 141.4, 140.6, 129.0, 129.0, 128.4, 128.1, 123.8, 122.6, 120.8, 120.4, 75.9, 59.3, 42.3, 8.3. IR $\nu_{max}$ ($cm^{-1}$): 3067, 3018, 2925, 2852, 1775, 1683, 1448, 1332, 1155, 1011, 971, 752, 734. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{17}H_{14}NaO_3$ 289.0835; found 289.0835.

*N,N′-((1,6-Dioxo-2,7-dioxaspiro[4.4]nonane-3,8-diyl)bis(methylene))bis(4-methyl-N-tosylbenzenesulfonamide) (**2r**).* Synthesized from **1r** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (116.3 mg, 70%). mp 134.5−135.6 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.94 (d, $J$ = 8.0 Hz, 8H), 7.36 (d, $J$ = 8.0 Hz, 8H), 5.14−5.07 (m, 2H), 4.08 (dd, $J$ = 15.6, 6.8 Hz, 2H), 3.73 (dd, $J$ = 15.6, 5.2 Hz, 2H), 2.66 (dd, $J$ = 13.6, 6.8 Hz, 2H), 2.45 (s, 12H), 2.04 (dd, $J$ = 13.2, 8.8 Hz, 2H). $^{13}C$ {$^1H$} NMR (100 MHz, $CDCl_3$): $\delta$ 172.0, 145.6, 136.0, 129.9, 128.6, 76.6, 52.2, 50.6, 35.7, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 3070, 2962, 2927, 1770, 1653, 1597, 1558, 1495, 1373, 1295, 1265, 1167, 1084, 921, 812, 738, 665, 580, 554. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{37}H_{38}N_2NaO_{12}S_4$ 853.1200; found 853.1205.

*Ethyl 3-allyl-5-(((4-methyl-N-tosylphenyl)sulfonamido)methyl)-2-oxotetrahydrofuran-3-carboxylate (**2s**).* Synthesized from **1s** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (45.0 mg, 42%), dr > 20:1. mp 56.7−58.3 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.95 (d, $J$ = 7.6 Hz, 4H), 7.36 (d, $J$ = 8.0 Hz, 4H), 5.62 (dq, $J$ = 16.8, 7.2 Hz, 1H), 5.21−5.11 (m, 2H), 4.91−4.82 (m, 1H), 4.29−4.14 (m, 2H), 4.09 (dd, $J$ = 15.6, 6.8 Hz, 1H), 3.75−3.67 (m, 1H), 2.73 (dd, $J$ = 14.0, 8.0 Hz, 1H), 2.63 (dd, $J$ = 13.6, 6.0 Hz, 1H), 2.52 (dd, $J$ = 14.4, 6.8 Hz, 1H), 2.46 (s, 6H), 1.99−1.88 (m, 1H), 1.27 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ {$^1H$} NMR (100 MHz, $CDCl_3$): $\delta$ 172.7, 168.8, 145.4, 136.1, 131.7, 129.7, 128.7, 120.5, 77.2, 62.5, 55.3, 51.4, 38.3, 34.7, 21.7, 14.0. IR $\nu_{max}$ ($cm^{-1}$): 2985, 2917, 2857, 1785, 1734, 1683, 1653, 1375, 1297, 1165, 1083, 920, 820, 664, 551. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{25}H_{29}NNaO_8S_2$ 558.1227; found 558.1222.

*4-Methyl-N-((4-methyl-5-oxotetrahydrofuran-2-yl)methyl)-N-tosylbenzenesulfonamide (**2aa**).* Synthesized from **1aa** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (61.2 mg, 70%). The product was obtained as a mixture of two inseparable isomers with dr = 2.3:1. mp 69.8−70.3 °C. For major isomer shown: $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.95 (d, $J$ = 8.4 Hz, 4H), 7.35 (d, $J$ = 8.4 Hz, 4H), 4.71−4.60 (m, 1H), 4.10 (dd, $J$ = 16.0, 7.2 Hz, 1H), 3.72 (dd, $J$ = 16.0, 4.0 Hz, 1H), 2.76−2.56 (m, 2H), 2.46 (s, 6H), 1.60−1.50 (m, 1H), 1.22 (d, $J$ = 7.2 Hz, 3H). $^{13}C$ {$^1H$} NMR (100 MHz, $CDCl_3$): $\delta$ 178.2, 145.4, 136.2, 129.7, 128.7, 77.3, 51.7, 35.5, 34.6, 21.7, 15.0. IR $\nu_{max}$ ($cm^{-1}$): 2973, 2945, 2877, 1777, 1684, 1653, 1596, 1506, 1375, 1165, 1085, 1032, 816, 663, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{20}H_{23}NNaO_6S_2$ 460.0859; found 460.0866.

*N-((4-Ethyl-5-oxotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**2ab**).* Synthesized from **1ab** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 2:1) as a white solid (70.4 mg, 78%). The product was obtained as a mixture of two inseparable isomers with dr = 2.4:1. mp 130.9−132.6 °C. For major isomer shown: $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.94 (d, $J$ = 8.8 Hz, 4H), 7.34 (d, $J$ = 8.2 Hz, 4H), 4.72−4.60 (m, 1H), 4.09 (dd, $J$ = 15.6, 6.8 Hz, 1H), 3.72 (dd, $J$ = 15.6, 4.4 Hz, 1H), 2.61−2.47 (m, 1H), 2.45 (s, 6H), 2.42−2.36 (m, 1H), 1.91−1.78 (m, 1H), 1.61−1.32 (m, 2H), 0.96 (d, $J$ = 8.0 Hz, 3H). $^{13}C$ {$^1H$} NMR (100 MHz, $CDCl_3$): $\delta$ 177.5, 145.4, 136.1, 129.7, 128.7, 76.9, 51.8, 42.0, 32.0, 23.3, 21.7, 11.6. IR $\nu_{max}$ ($cm^{-1}$): 2965, 2928, 1770, 1597, 1558, 1456, 1375, 1260, 1167, 1084, 945, 816, 664, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{21}H_{25}NNaO_6S_2$ 474.1016; found 474.1023.

*N-((4-Isopropyl-5-oxotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**2ac**).* Synthesized from **1ac** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (77.2 mg, 83%). The product was obtained as a mixture of two inseparable isomers with dr = 3.3:1. mp 142.7−143.6 °C. For major isomer shown: $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.94 (d, $J$ = 8.4 Hz, 4H), 7.34 (d, $J$ = 8.4 Hz, 4H), 4.67−4.60 (m, 1H), 4.08 (dd, $J$ = 15.6, 6.8 Hz, 1H), 3.72 (dd, $J$ = 16.0, 4.4 Hz, 1H), 2.61−2.46 (m, 1H), 2.44 (s, 6H), 2.26−1.97 (m, 2H), 1.69−1.60 (m, 1H), 1.00 (d, $J$ = 6.8 Hz, 3H), 0.87 (d, $J$ = 6.8 Hz, 3H). $^{13}C$ {$^1H$} NMR (100 MHz, $CDCl_3$): $\delta$ 176.7, 145.4, 136.2, 129.7, 128.7, 76.6, 51.8, 46.6, 28.1, 27.6, 21.7, 20.6, 18.3. IR $\nu_{max}$ ($cm^{-1}$): 2960, 2875, 2360, 1775, 1653, 1600, 1558, 1373, 1165, 1084, 817, 663, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{22}H_{27}NNaO_6S_2$ 488.1172; found 488.1172.

*N-((4-(tert-Butyl)-5-oxotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**2ad**).* Synthesized from **1ad** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (63.2 mg, 66%). The product was obtained as a mixture of two inseparable isomers with dr = 2.9:1. mp 197.5−198.3 °C. For major isomer shown: $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.95 (d, $J$ = 8.0 Hz, 4H), 7.35 (d, $J$ = 8.0 Hz, 4H), 4.57 (dd, $J$ = 10.4, 5.2 Hz, 1H), 4.08 (dd, $J$ = 16.0, 6.8 Hz, 1H), 3.72 (dd, $J$ = 15.6, 4.0 Hz, 1H), 2.45 (s, 6H), 2.42−2.38 (m, 1H), 2.26−2.20 (m, 1H), 1.68 (q, $J$ = 11.8 Hz, 1H), 1.01 (s, 9H). $^{13}C$ {$^1H$} NMR (100 MHz, $CDCl_3$): $\delta$ 175.5, 145.3, 136.2, 129.7, 128.7, 75.7, 51.8, 50.4, 31.7, 29.4, 27.1, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 2962, 2872, 1770, 1683, 1654, 1597, 1558, 1385, 1166, 1084, 815, 663, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{23}H_{29}NNaO_6S_2$ 502.1329; found 502.1336.

*4-Methyl-N-((5-oxo-4-phenyltetrahydrofuran-2-yl)methyl)-N-tosylbenzenesulfonamide (**2ae**).* Synthesized from **1ae** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (70.9 mg, 71%). The product was obtained as a mixture of two inseparable isomers with dr = 2.5:1. mp 81.9−82.5 °C. For major isomer shown: $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.97 (dd, $J$ = 8.0, 4.4 Hz, 4H), 7.39−7.18 (m, 9H), 4.85−4.79 (m, 1H), 4.19 (dd, $J$ = 16.0, 6.8 Hz, 1H), 3.88−3.78 (m, 2H), 2.73 (ddd, $J$ = 13.2, 8.4, 5.6 Hz, 1H), 2.45 (s, 6H), 2.16−2.02 (m, 1H). $^{13}C$ {$^1H$} NMR (100 MHz, $CDCl_3$): $\delta$ 175.5, 145.4, 136.1, 135.9, 129.7, 128.9, 128.8, 128.0, 127.8, 76.8, 51.5, 46.6, 35.2, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 3065, 3030, 2926, 1780, 1684, 1652, 1506, 1374, 1165, 1084, 945, 817, 663, 552. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{25}H_{25}NNaO_6S_2$ 522.1016; found 522.1021.

*N-((4-Benzyl-5-oxotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**2af**).* Synthesized from **1af** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (67.7 mg, 66%). The product was obtained as a mixture of two inseparable isomers with dr = 3.4:1. mp 190.4−190.7 °C. For major isomer shown: $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.94 (d, $J$ = 8.0 Hz, 4H), 7.37−7.14 (m, 9H), 4.68−4.59 (m, 1H), 4.04 (dd, $J$ = 16.0, 7.2 Hz, 1H), 3.64 (dd, $J$ = 16.0, 4.0 Hz, 1H), 3.26 (dd, $J$ = 14.0, 4.0 Hz, 1H), 2.91−2.83 (m, 1H), 2.64 (dd, $J$ = 14.0, 10.0 Hz, 1H), 2.45 (s, 6H), 2.26 (ddd, $J$ = 13.6, 8.4, 6.0 Hz, 1H), 1.59 (q, $J$ = 12.0 Hz, 1H). $^{13}C$ {$^1H$} NMR (100 MHz, $CDCl_3$): $\delta$ 176.8, 145.3, 138.3, 136.1, 129.7, 128.8, 128.7, 126.8, 77.2, 51.7, 42.4, 36.1, 32.3, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 3066, 3032, 2925, 1776, 1683, 1652, 1558, 1374, 1165, 1084, 817, 663, 550. HRMS (ESI) $m/z$: $[M + Na]^+$ Calcd for $C_{26}H_{27}NNaO_6S_2$ 536.1172; found 536.1178.

*4-Methyl-N-((3-methyl-5-oxo-4,4-diphenyltetrahydrofuran-2-yl)-methyl)-N-tosylbenzenesulfonamide (**2ag**).* Synthesized from **1ag** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 10:1) as a white solid (106.0 mg, 90%). The product was obtained as a mixture of two inseparable isomers with dr = 2.9:1. mp 118.2−119.0 °C. For


https://doi.org/10.1021/acs.joc.1c00074
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major isomer shown: $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.99 (d, $J$ = 8.0 Hz, 4H), 7.50−7.18 (m, 12H), 6.82−6.80 (m, 2H), 4.25 (ddd, $J$ = 22.8, 16.8, 7.6 Hz, 2H), 3.94−3.82 (m, 1H), 3.12−3.04 (m, 1H), 2.44 (d, $J$ = 11.6 Hz, 6H), 0.89 (d, $J$ = 6.8 Hz, 3H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 176.4, 145.3, 139.6, 138.5, 136.4, 129.7, 128.9, 128.7, 128.6, 128.5, 128.4, 128.2, 80.7, 60.8, 50.8, 41.3, 21.7, 12.6. IR $\nu_{max}$ ($cm^{-1}$): 3060, 2973, 1773, 1684, 1653, 1558, 1375, 1167, 1085, 816, 701, 664, 551. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{32}H_{31}NNaO_6S_2$ 612.1485; found 612.1487.

*(E)-N-((3-Ethyl-5-oxo-4,4-diphenyltetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**2ah**).* Synthesized from **1ah** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 2:1) as a white solid (97.7 mg, 81%), dr > 20:1. mp 116.3−116.9 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.02 (d, $J$ = 8.0 Hz, 4H), 7.46 (d, $J$ = 7.2 Hz, 2H), 7.37 (d, $J$ = 8.2 Hz, 6H), 7.29−7.21 (m, 4H), 6.90−6.79 (m, 2H), 4.50 (t, $J$ = 8.4 Hz, 1H), 4.18 (dd, $J$ = 15.6, 9.2 Hz, 1H), 3.85 (d, $J$ = 16.0 Hz, 1H), 2.88 (s, 1H), 2.47 (s, 6H), 1.25 (s, 2H), 1.02−0.97 (m, 3H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 176.4, 145.2, 139.6, 139.3, 136.3, 129.6, 128.9, 128.6, 128.5, 128.4, 128.2, 127.8, 127.5, 80.8, 61.2, 52.2, 47.7, 22.2, 21.8, 12.9. IR $\nu_{max}$ ($cm^{-1}$): 2963, 2925, 2853, 1773, 1734, 1684, 1652, 1559, 1506, 1458, 1260, 1166, 1087, 1020, 810, 662, 550, 418. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{33}H_{33}NNaO_6S_2$ 626.1642; found 626.1643.

*(E)-4-Methyl-N-((5-oxo-4,4-diphenyl-3-propyltetrahydrofuran-2-yl)methyl)-N-tosylbenzenesulfonamide (**2ai**).* Synthesized from **1ai** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (80.2 mg, 65%), dr > 20:1. mp 200.7−201.3 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.02 (d, $J$ = 7.6 Hz, 4H), 7.52−7.29 (m, 12H), 6.88 (s, 2H), 4.49 (t, $J$ = 8.8 Hz, 1H), 4.19 (dd, $J$ = 15.6, 9.2 Hz, 1H), 3.85 (d, $J$ = 15.6 Hz, 1H), 3.03−2.91 (m, 1H), 2.46 (s, 6H), 1.45−1.31 (m, 2H), 1.30−1.27 (m, 1H), 1.02 (dt, $J$ = 13.2, 7.2 Hz, 1H), 0.86 (t, $J$ = 6.8 Hz, 3H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 176.5, 145.3, 139.7, 139.2, 136.3, 129.7, 128.9, 128.7, 128.6, 128.4, 128.2, 127.8, 127.6, 80.7, 61.3, 52.1, 46.0, 31.2, 21.8, 21.5, 14.4. IR $\nu_{max}$ ($cm^{-1}$): 3062, 3032, 2960, 3932, 2873, 2257, 1775, 1653, 1495, 1445, 1375, 1352, 1307, 1292, 1167, 1085,1057, 912, 816, 735, 700, 663, 554. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{34}H_{35}NNaO_6S_2$ 640.1798; found 640.1806.

*N-((4-Ethyl-5-oxo-4-phenyltetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**2aj**).* Synthesized from **1aj** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 4:1) as a white solid (98.0 mg, 93%). The product was obtained as a mixture of two inseparable isomers with dr = 2.6:1. mp 72.8−73.9 °C. For major isomer shown: $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.92 (d, $J$ = 8.0 Hz, 4H), 7.50−7.27 (m, 9H), 4.52−4.45 (m, 1H), 4.14 (dd, $J$ = 15.6, 6.0 Hz, 1H), 3.81 (dd, $J$ = 15.6, 5.2 Hz, 1H), 2.67 (dd, $J$ = 13.2, 4.8 Hz, 1H), 2.45 (d, $J$ = 5.6 Hz, 6H), 2.06 (dd, $J$ = 13.2, 10.8 Hz, 1H), 2.01−1.88 (m, 2H), 0.83−0.75 (m, 3H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 177.5, 145.3, 137.8, 136.3, 129.7, 128.9, 128.6, 127.6, 126.2, 75.1, 53.5, 51.4, 37.2, 32.3, 21.7, 9.0. IR $\nu_{max}$ ($cm^{-1}$): 3060, 2970, 2934, 1775, 1654, 1597, 1492, 1447, 1375, 1352, 1166, 1084, 941, 913, 816, 664, 551. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{27}H_{29}NNaO_6S_2$ 550.1329; found 550.1336.

*4-Methyl-N-((4-methyl-5-oxo-4-phenyltetrahydrofuran-2-yl)-methyl)-N-tosylbenzenesulfonamide (**2ak**).* Synthesized from **1ak** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (80.0 mg, 78%). The product was obtained as a mixture of two inseparable isomers with dr = 1.3:1. mp 72.5−72.8 °C. For major isomer shown: $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.92 (dd, $J$ = 8.8, 4.4 Hz, 5H), 7.45−7.22 (m, 8H), 4.49−4.2 (m, 1H), 4.15 (dd, $J$ = 15.6, 6.4 Hz, 1H), 3.80 (dd, $J$ = 15.6, 5.2 Hz, 1H), 2.65 (dd, $J$ = 13.2, 5.2 Hz, 1H), 2.46 (s, 6H), 2.07 (dd, $J$ = 12.8, 11.2 Hz, 1H), 1.52 (s, 3H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 178.5, 145.3, 140.2, 136.3, 129.7, 129.0, 128.6, 127.6, 125.6, 75.0, 51.2, 49.6, 41.6, 26.3, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 2975, 2930, 1780, 1684, 1653, 1375, 1166, 1083, 815, 664, 550. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{26}H_{27}NNaO_6S_2$ 536.1172; found 536.1174.

*N-((4-(7-Methoxynaphthalen-2-yl)-4-methyl-5-oxotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**2al**).* Synthesized from **1al** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 5:1) as a white solid (47.4 mg, 40%). The product was obtained as a mixture of two inseparable isomers with dr = 1.2:1. mp 85.1−86.6 °C. For major isomer shown: $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.88 (t, $J$ = 7.6 Hz, 4H), 7.80−7.13 (m, 10H), 4.51−4.44 (m, 1H), 4.17 (dd, $J$ = 15.6, 6.4 Hz, 1H), 3.92 (s, 3H), 3.84 (dd, $J$ = 15.6, 5.2 Hz, 1H), 2.74 (dd, $J$ = 13.0, 4.8 Hz, 1H), 2.41 (s, 6H), 2.18−2.07 (m, 1H), 1.58 (s, 3H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 178.4, 158.1, 145.3, 136.3, 136.1, 133.7, 129.7, 129.6, 128.5, 127.9, 124.2, 124.1, 119.4, 105.5, 75.1, 55.4, 51.2, 49.7, 41.7, 26.2, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 2965, 2925, 2855, 1771, 1683, 1652, 1505, 1454, 1372, 1265, 1166, 1087, 1035, 810, 661, 549. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{31}H_{31}NNaO_7S_2$ 616.1434; found 616.1439.

*4-Methyl-N-((3-oxooctahydroisobenzofuran-1-yl)methyl)-N-tosylbenzenesulfonamide (**2am**).* Synthesized from **1am** according to the procedure A. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (44.8 mg, 47%). The product was obtained as a mixture of three inseparable isomers with dr = 3.8:1.8:1. mp 212.3−214.1 °C. For major isomer shown: $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.00 (d, $J$ = 8.0 Hz, 4H), 7.36 (d, $J$ = 8.4 Hz, 4H), 4.62−4.50 (m, 1H), 4.22 (dd, $J$ = 16.4, 8.4 Hz, 1H), 3.66 (dd, $J$ = 16.4, 2.0 Hz, 1H), 2.66 (t, $J$ = 6.0 Hz, 1H), 2.45 (s, 6H), 2.15 (d, $J$ = 13.6 Hz, 1H), 2.04−0.95 (m, 8H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 176.6, 145.3, 136.3, 129.6, 128.8, 80.7, 48.5, 41.6, 38.3, 23.4, 22.6, 22.3, 22.3, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 2934, 2858, 2360, 2345, 1777, 1653, 1558, 1375, 1165, 816, 664, 550. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{23}H_{27}NNaO_6S_2$ 500.1172; found 500.1174.

*4-Methyl-N-((3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl)-N-tosylbenzenesulfonamide (**4a**).* Synthesized from **3a** according to the procedure B. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (51.8 mg, 55%). mp 191.5−192.8 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.03 (d, $J$ = 8.4 Hz, 4H), 7.91 (d, $J$ = 7.6 Hz, 1H), 7.67 (t, $J$ = 7.4 Hz, 1H), 7.57 (t, $J$ = 7.4 Hz, 1H), 7.51 (d, $J$ = 7.6 Hz, 1H), 7.39 (d, $J$ = 8.0 Hz, 4H), 5.82 (dd, $J$ = 8.4, 2.8 Hz, 1H), 4.10 (dd, $J$ = 16.0, 8.8 Hz, 1H), 3.96 (dd, $J$ = 16.0, 3.2 Hz, 1H), 2.47 (s, 6H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 169.4, 146.2, 145.5, 136.1, 134.3, 130.0, 129.8, 128.8, 126.2, 126.1, 122.5, 80.0, 52.3, 21.8. IR $\nu_{max}$ ($cm^{-1}$): 3075, 2925, 2855, 1770, 1684, 1600, 1512, 1372, 1285, 1168, 1085, 1063, 1038, 930, 765, 724, 665, 552. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{23}H_{21}NNaO_6S_2$ 494.0702; found 494.0707.

*N-((5-Fluoro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**4b**).* Synthesized from **3b** according to the procedure B. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 5:1) as a white solid (45.0 mg, 46%). mp 173.4−174.7 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.99 (d, $J$ = 8.0 Hz, 4H), 7.55 (d, $J$ = 6.4 Hz, 1H), 7.49 (dd, $J$ = 8.0, 4.0 Hz, 1H), 7.38 (d, $J$ = 8.0 Hz, 4H), 7.37−7.33 (m, 1H), 5.80 (d, $J$ = 5.2 Hz, 1H), 4.11 (dd, $J$ = 16.0, 8.4 Hz, 1H), 3.94 (dd, $J$ = 16.0, 2.8 Hz, 1H), 2.48 (s, 6H). $^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 168.1 (168.1), 164.8 (162.3), 145.5, 141.8 (141.7), 136.1, 129.7, 128.8, 128.4 (128.3), 124.5 (124.4), 122.3 (122.1), 112.6 (112.3), 79.8, 52.2, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 3073, 2926, 2855, 1777, 1684, 1499, 1374, 1165, 1085, 1040, 923, 815, 720, 663, 549. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{23}H_{20}FNNaO_6S_2$ 512.0608; found 512.0599.

*N-((5-Chloro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**4c**).* Synthesized from **3c** according to the procedure B. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 5:1) as a white solid (45.5 mg, 45%). mp 191.3−192.6 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.98 (d, $J$ = 8.4 Hz, 4H), 7.86 (s, 1H), 7.58 (d, $J$ = 8.4 Hz, 1H), 7.44 (d, $J$ = 8.0 Hz, 1H), 7.38 (d, $J$ = 8.4 Hz, 4H), 5.80 (dd, $J$ = 8.0, 3.6 Hz, 1H), 4.11 (dd, $J$ = 16.0, 8.4 Hz, 1H), 3.93 (dd, $J$


https://doi.org/10.1021/acs.joc.1c00074
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= 16.0, 3.6 Hz, 1H), 2.47 (s, 6H). $^{13}$C {$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 167.9, 145.6, 144.4, 136.4, 136.0, 134.5, 129.8, 128.7, 127.9, 125.88, 124.1, 79.7, 52.0, 21.8. IR $\nu_{max}$ ($cm^{-1}$): 3075, 2925, 2852, 2362, 2256, 1775, 1683, 1597, 1373, 1290, 1165, 1085, 1058, 1040, 930, 819, 663, 552. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{23}H_{20}ClNNaO_6S_2$ 528.0313; found 528.0304.

*N-((5-Methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**4e**).* Synthesized from **3e** according to the procedure B. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 4:1) as a white solid (54.1 mg, 54%). mp 158.9−160.4 °C. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.93 (d, $J$ = 8.4 Hz, 4H), 7.54 (s, 1H), 7.35 (d, $J$ = 8.4 Hz, 4H), 7.11 (s, 2H), 6.39 (dd, $J$ = 12.8, 3.2 Hz, 1H), 4.20 (dd, $J$ = 15.6, 12.8 Hz, 1H), 3.84 (s, 3H), 2.83 (dd, $J$ = 15.6, 3.2 Hz, 1H), 2.46 (s, 6H). $^{13}$C {$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 163.3, 159.3, 145.5, 136.9, 129.8, 129.5, 128.7, 128.6, 125.2, 122.2, 113.1, 85.8, 55.7, 32.5, 21.8. IR $\nu_{max}$ ($cm^{-1}$): 2930, 2836, 1734, 1682, 1652, 1558, 1506, 1377, 1282, 1169, 1052, 885, 814, 771, 738, 665, 550. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{24}H_{23}NNaO_7S_2$ 524.0808; found 524.0805.

*4-Methyl-N-((1-methyl-3-oxo-1,3-dihydroisobenzofuran-1-yl)-methyl)-N-tosylbenzenesulfonamide (**4f**).* Synthesized from **3f** according to the procedure B. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 4:1) as a white solid (40.7 mg, 42%). mp 203.5−204.3 °C. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.99 (d, $J$ = 7.6 Hz, 4H), 7.85 (d, $J$ = 7.6 Hz, 1H), 7.70 (t, $J$ = 7.6 Hz, 1H), 7.58−7.51 (m, 2H), 7.35 (d, $J$ = 8.0 Hz, 4H), 4.28 (d, $J$ = 16.0 Hz, 1H), 4.13 (d, $J$ = 16.0 Hz, 1H), 2.45 (s, 6H), 1.53 (s, 3H). $^{13}$C {$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 168.7, 151.2, 145.1, 136.7, 134.3, 129.8, 129.5, 128.9, 126.2, 125.9, 121.9, 86.3, 56.3, 23.5, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 3070, 2936, 1770, 1684, 1598, 1395, 1381, 1295, 1160, 1070, 1058, 865, 772, 743, 660, 551. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{24}H_{23}NNaO_6S_2$ 508.0859; found 508.0866.

*4-Methyl-N-((1-oxo-1,3-dihydronaphtho[1,2-c]furan-3-yl)-methyl)-N-tosylbenzenesulfonamide (**4g**).* Synthesized from **3g** according to the procedure B. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 5:1) as a white solid (39.6 mg, 38%). mp 217.3−218.5 °C. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.21 (d, $J$ = 7.2 Hz, 1H), 8.16 (d, $J$ = 8.0 Hz, 4H), 8.05 (dd, $J$ = 14.8, 8.0 Hz, 2H), 7.88 (d, $J$ = 8.4 Hz, 1H), 7.82−7.75 (m, 2H), 7.44 (d, $J$ = 7.6 Hz, 4H), 6.25 (d, $J$ = 9.2 Hz, 1H), 4.39 (d, $J$ = 16.0 Hz, 1H), 4.01 (dd, $J$ = 16.0, 9.6 Hz, 1H), 2.50 (s, 6H). $^{13}$C {$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 169.8, 145.8, 145.4, 136.3, 131.3, 129.7, 129.6, 129.3, 129.1, 128.9, 128.4, 126.9, 124.2, 124.0, 120.7, 80.5, 53.1, 21.6. IR $\nu_{max}$ ($cm^{-1}$): 3070, 2926, 2853, 1770, 1597, 1375, 1292, 1165, 1084, 1035, 818, 762, 723, 663, 552. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{27}H_{23}NNaO_6S_2$ 544.0859; found 544.0848.

*4-Methoxy-N-((4-methoxyphenyl)sulfonyl)-N-((5-oxo-4,4-diphenyltetrahydrofuran-2-yl)methyl)benzenesulfonamide (**2e-N1**).* Synthesized from **1e**. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 3:1) as a white solid (92.3 mg, 76%). mp 217.9−218.5 °C. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.97 (d, $J$ = 8.8 Hz, 4H), 7.33 (ddd, $J$ = 17.2, 13.2, 6.2 Hz, 6H), 7.25−7.16 (m, 4H), 6.96 (d, $J$ = 8.8 Hz, 4H), 4.60 (dq, $J$ = 10.2, 5.2 Hz, 1H), 4.14 (dd, $J$ = 16.0, 6.4 Hz, 1H), 3.90−3.82 (s, 7H), 2.96 (dd, $J$ = 13.2, 5.2 Hz, 1H), 2.74−2.63 (m, 1H). $^{13}$C {$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 176.1, 164.0, 141.4, 139.5, 130.9, 130.6, 129.0, 128.4, 127.8, 127.7, 127.3, 127.2, 114.3, 75.3, 57.8, 55.8, 51.1, 41.0. IR $\nu_{max}$ ($cm^{-1}$): 3062, 2947, 2842, 2360, 1773, 1595, 1577, 1496, 1459, 1449, 1375, 1266, 1162, 1086, 1024, 835,806, 738, 697, 667, 556. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{31}H_{29}NNaO_8S_2$ 630.1227; found 630.1224.

*N-((5-Oxo-4,4-diphenyltetrahydrofuran-2-yl)methyl)-N-(phenylsulfonyl)benzenesulfonamide (**2e-N3**).* Synthesized from **1e**. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 4:1) as a white solid (106.0 mg, 90%). mp 87.7−88.4 °C. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.06 (d, $J$ = 7.6 Hz, 4H), 7.64 (t, $J$ = 7.6 Hz, 2H), 7.53 (t, $J$ = 7.6 Hz, 4H), 7.39−7.21 (m, 10H), 4.63 (dq, $J$ = 10.4, 5.2 Hz, 1H), 4.20 (dd, $J$ = 16.0, 6.4 Hz, 1H), 3.90 (dd, $J$ = 16.0, 4.8 Hz, 1H), 2.98 (dd, $J$ = 13.2, 5.2 Hz, 1H), 2.70 (dd, $J$ = 13.2, 10.2 Hz, 1H). $^{13}$C {$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 176.0, 141.4, 139.4, 139.1, 134.3, 129.2, 129.0, 128.6, 128.5, 127.9, 127.7, 127.4, 127.2, 75.2, 57.8, 51.5, 41.0. IR $\nu_{max}$ ($cm^{-1}$): 3067, 3030, 2947, 2260, 1780, 1600, 1585, 1496, 1448, 1378, 1291, 1170, 1085, 1064, 965, 945, 913, 800, 740, 699, 685, 853,550. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{29}H_{25}NNaO_6S_2$ 570.1016; found 570.1011.

*4-Nitro-N-((4-nitrophenyl)sulfonyl)-N-((5-oxo-4,4-diphenyltetrahydrofuran-2-yl)methyl)benzenesulfonamide (**2e-N4**).* Synthesized from **1e**. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 4:1) as a white solid (108.3 mg, 85%). mp 163.9−164.7 °C. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.38−8.24 (m, 8H), 7.33−7.26 (m, 4H), 7.26−7.17 (m, 6H), 4.63−4.53 (m, 1H), 4.22 (dd, $J$ = 16.2, 8.0 Hz, 1H), 3.98−3.89 (m, 1H), 3.01 (dd, $J$ = 13.2, 5.2 Hz, 1H), 2.61 (dd, $J$ = 13.2, 10.0 Hz, 1H). $^{13}$C {$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 175.5, 150.9, 144.0, 140.9, 139.3, 130.3, 129.1, 128.6, 128.1, 127.7, 127.5, 127.0, 124.4, 75.3, 57.5, 52.5, 40.4. IR $\nu_{max}$ ($cm^{-1}$): 3110, 3070, 3040, 2935, 2873, 2257, 1780, 1608, 1535, 1507, 1447, 1370, 1317, 1290, 965, 945, 912, 856, 800, 740, 613, 546, 470. HRMS (ESI) $m/z$: [M + H]$^+$ Calcd for $C_{29}H_{24}N_3O_{10}S_2$ 638.0898; found 638.0893.

*4-Methyl-N-((5-oxo-4,4-diphenyltetrahydrofuran-2-yl)methyl)-benzenesulfonamide (**2e-N6**).* Synthesized from **1e**. Purified by silica gel column chromatography (the eluent was EtOAc) as a white solid (46.3 mg, 55%). mp 106.2−107.0 °C. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.98 (d, $J$ = 8.4 Hz, 2H), 7.55 (d, $J$ = 4.0 Hz, 4H), 7.61−7.45 (m, 9H), 7.46 (d, $J$ = 4.8 Hz, 2H), 4.70−4.62 (m, 1H), 4.17 (dd, $J$ = 12.8, 2.4 Hz, 1H), 3.89 (dd, $J$ = 12.8, 4.4 Hz, 1H), 3.20−3.11 (m, 1H), 3.08 (dd, $J$ = 12.9, 5.3 Hz, 1H), 2.60 (s, 3H). $^{13}$C {$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 177.3, 143.5, 141.7, 139.7, 139.1, 129.7, 129.0, 128.4, 127.8, 127.8, 127.3, 127.3, 126.4, 63.0, 58.3, 38.3, 21.5. IR $\nu_{max}$ ($cm^{-1}$): 3368, 3262, 3070, 2928, 2365, 1762, 1683, 1522, 1507, 1450, 1302, 1162, 1102, 913, 816, 748, 697, 555, 532. HRMS (ESI) $m/z$: [M + H]$^+$ Calcd for $C_{24}H_{24}NO_4S$ 422.1421; found 422.1418.

*4-Nitro-N-((5-oxo-4,4-diphenyltetrahydrofuran-2-yl)methyl)-benzenesulfonamide (**2e-N7**).* Synthesized from **1e**. Purified by silica gel column chromatography (the eluent was petroleum ether/EtOAc 1:1) as a white solid (44.0 mg, 40%). mp 106.2−107.0 °C. $^{1}$H NMR (400 MHz, $CD_3OD$): $\delta$ 8.38 (d, $J$ = 8.8 Hz, 1H), 8.12 (d, $J$ = 8.8 Hz, 1H), 7.50−7.19 (m, 13H), 4.43 (ddd, $J$ = 10.0, 8.0, 4.8 Hz, 1H), 3.88 (dd, $J$ = 12.8, 2.8 Hz, 1H), 3.65 (dd, $J$ = 12.8, 4.8 Hz, 1H), 3.04 (dd, $J$ = 13.2, 5.2 Hz, 1H), 2.86 (dd, $J$ = 13.2, 10.8 Hz, 1H). $^{13}$C {$^{1}$H} NMR (100 MHz, $CD_3OD$): $\delta$ 177.8, 142.4, 139.7, 128.4, 128.3, 127.9, 127.8, 127.4, 127.3, 127.1, 127.1, 126.6, 123.7, 78.0, 61.8, 58.0, 38.0. IR $\nu_{max}$ ($cm^{-1}$): 3250, 2968, 2873, 2460, 1770, 1595, 1495, 1455, 1440, 1426, 1350, 1268, 1100, 1035, 826, 703, 680, 551. HRMS (ESI) $m/z$: [M + H]$^+$ Calcd for $C_{23}H_{21}N_2O_6S$ 453.1115; found 453.1107.

**Gram-Scale Synthesis of Compound 2q and Recovered Experiment of Catalyst.** To a 100 mL flask were added **1q** (1.26 g, 5 mmol), **I11** (132 mg, 0.5 mmol), $HNTs_2$ (2.44 g, 7.5 mmol), and *m*CPBA (1.78 g, 8.75 mmol, 85 wt %) in $CH_3CN$ (50 mL). The mixture was stirred at room temperature for 5 h. After completion, the mixture was quenched with an aqueous solution of NaOH (2 mol/L). The mixture was extracted with EtOAc (50 mL × 3). The combined organic phase was washed with brine, dried over $Na_2SO_4$, filtered, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel (PE/EtOAc = 6:1) to give the compound **2q** as a white solid (2.00 g, 70%), byproduct **2q′** as a yellow solid (120 mg, 9%), and catalyst **I11** (63 mg, 48%) was recovered as a yellow solid. The recovered catalyst also can catalyze the same reaction under standard conditions and gave the same result (**2q**, 65%).

*N-(2-Hydroxy-3-(9-(hydroxymethyl)-9H-fluoren-9-yl)propyl)-4-methyl-N-tosylbenzenesulfonamide (**5**).*[11a] To a 25 mL flask equipped with a stir bar were added **2q** (114 mg, 0.2 mmol) and $BH_3$·THF (10 mL, 1.0 M) under argon protected. The mixture was stirred at room temperature for 1 h. After completion, MeOH was added dropwise to quench the reaction. Then, the mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (DCM/MeOH = 15:1) to give the compound **5** as a white solid (95 mg, 85%). mp 87.6−88.3 °C. $^{1}$H


https://doi.org/10.1021/acs.joc.1c00074
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NMR (400 MHz, $CDCl_3$): $\delta$ 7.79 (dd, $J$ = 7.2, 4.2 Hz, 2H), 7.71 (d, $J$ = 8.0 Hz, 4H), 7.54 (d, $J$ = 7.6 Hz, 1H), 7.49 (d, $J$ = 7.6 Hz, 1H), 7.43 (t, $J$ = 7.6 Hz, 2H), 7.34 (dt, $J$ = 6.6, 3.2 Hz, 2H), 7.24 (d, $J$ = 8.4 Hz, 4H), 3.84 (s, 1H), 3.77 (d, $J$ = 11.2 Hz, 1H), 3.65 (d, $J$ = 11.2 Hz, 1H), 3.56 (dd, $J$ = 15.6, 9.1 Hz, 1H), 3.32 (dd, $J$ = 15.6, 3.0 Hz, 1H), 2.62−2.52 (m, 2H), 2.48−2.36(m, 7H),1.93 (dd, $J$ = 14.4, 3.2 Hz, 1H).$^{13}$C {$^1$H} NMR (100 MHz, $CDCl_3$): $\delta$ 148.3, 146.8, 145.0, 140.8, 140.3, 136.4, 129.6, 128.3, 128.0, 127.9, 127.5, 127.3, 124.7, 123.8, 120.4, 120.3, 69.3, 67.8, 55.0, 54.6, 40.1, 21.7. IR $\nu_{max}$ ($cm^{-1}$): 3560, 3425, 3075, 2926, 2863, 1597, 1494, 1477, 1448, 1371, 1166, 1085, 1053, 815, 738, 663, 552. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{31}H_{31}NNaO_6S_2$ 600.1485; found 600.1481.

*5′-(Aminomethyl)-4′,5′-dihydro-2′H-spiro[fluorene-9,3′-furan]-2′-one (**6**).*[31] To a 50 mL pressure flask were added **2q** (300 mg, 0.52 mmol) and resorcinol (250 mg, 5.0 equiv). A solution of hydrogen bromide in acetic acid (5 mL, 33 wt %) was dropwise added to the pressure flask, which was heated in an oil bath at 85 °C for 24 h. After completion, the acetic acid was removed under vacuum, and the brown residue was dissolved in water (30 mL) and washed with ether (30 mL × 3). To the aqueous phase was added excess saturated sodium carbonate until pH > 7; then the mixture was extracted with dichloromethane (30 mL × 3), washed with brine, dried over $Na_2SO_4$, filtered, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel (DCM/MeOH = 20:1−2:1) to give the compound **6** as a yellowish solid (106 mg, 80%). mp 143.9−144.5 °C. $^1$H NMR (400 MHz, $(CD_3)_2SO$): $\delta$ 7.81 (dd, $J$ = 17.6, 8.4 Hz, 3H), 7.59 (d, $J$ = 7.2 Hz, 2H), 7.42−7.33 (m, 2H), 7.31 (s, 1H), 5.24 (s, 1H), 4.47 (s, 1H), 3.58 (d, $J$ = 11.2 Hz, 1H), 3.31 (s, 2H), 2.354 (t, $J$ = 11.6 Hz, 1H), 1.88 (d, $J$ = 12.8 Hz, 1H). $^{13}$C {$^1$H} NMR (100 MHz, $(CD_3)_2SO$): $\delta$ 170.4, 150.9, 150.6, 141.0, 140.8, 128.2, 128.1, 127.9, 127.8, 124.8, 124.0, 120.6, 120.3, 62.1, 57.4, 49.0, 42.5. IR $\nu_{max}$ ($cm^{-1}$): 2925, 2858, 1761, 1684, 1449, 1167, 970, 731, 619. HRMS (ESI) $m/z$: [M + Na]$^+$ Calcd for $C_{17}H_{15}NNaO_2$ 288.0995; found 288.0996.

*5′-((Diethylamino)methyl)-4′,5′-dihydro-2′H-spiro[fluorene-9,3′-furan]-2′-one (**7**).*[10b] To a 50 mL flask were added **6** (106 mg, 0.4 mmol), potassium carbonate (500 mg, 3.6 mmol), and iodoethane (5 mL, excessive) in tetrahydrofuran (20 mL). The reaction mixture was heated in an oil bath under reflux at 69 °C for 24 h. After completion, the mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (DCM/MeOH = 30:1−15:1) to give the compound 7 as a yellow oil (120 mg, 93%). $^1$H NMR (400 MHz, $(CD_3)_2SO$): $\delta$ 7.94−7.87 (m, 2H), 7.68 (dd, $J$ = 19.6, 7.2 Hz, 2H), 7.46 (t, $J$ = 7.2 Hz, 2H), 7.38 (dt, $J$ = 14.4, 7.2 Hz, 2H), 5.30−5.16 (m, 1H), 2.89 (t, $J$ = 10.0 Hz, 2H), 2.84−2.76 (m, 1H), 2.70−2.56 (m, 5H), 1.03 (t, $J$ = 7.2 Hz, 6H). $^{13}$C {$^1$H} NMR (100 MHz, $(CD_3)_2SO$): $\delta$ 177.0, 146.7, 146.1, 141.4, 140.4, 129.1, 129.0, 128.6, 128.6, 124.4, 123.7, 121.0, 120.8, 78.1, 58.8, 57.2, 47.8, 38.5, 12.4. IR $\nu_{max}$ ($cm^{-1}$): 2970, 2930, 2816, 1762, 1557, 1522, 1448, 1170, 1057, 1035, 967, 753, 732. HRMS (ESI) $m/z$: [M + H]$^+$ Calcd for $C_{21}H_{24}NO_2$ 322.1802; found 322.1795.

*(2R,2′R)-2,2′-((2-Iodo-5-methyl-1,3-phenylene)bis(oxy))bis(N,N-dibenzylpropanamide) (**ArI*1**).*[17b] Step one: To a solution of (2R,2′R)-2,2′-((2-iodo-5-methyl-1,3-phenylene)bis(oxy))dipropionic acid (0.5 g, 1.27 mmol) in DCM (20 mL) was added oxalyl chloride (1.0 mL, 10 mmol) dropwise. Then, *N*,*N*-dimethylformamide (2 drops) was added. After stirring for 2 h, the mixture was concentrated under vacuum. Step two: To a flask were added dibenzylamine (1.0 mL, 5 mmol), $Et_3N$ (1 mL, 7 mmol), and DCM (20 mL). Then, the product of the step one (in 10 mL DCM) was dropwise added to the reaction mixture at 0 °C. After stirring for 4 h at room temperature, the mixture was acidified with an aqueous solution of HCl (2 mol/L). The mixture was extracted with dichloromethane (20 mL × 3). The combined organic phase was washed with brine, dried over $Na_2SO_4$, filtered, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel (PE/EtOAc = 5:1) to give the compound **ArI*1** as a white solid (694 mg, 73%). mp 173.5−174.8 °C. $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.18−7.10 (m, 8H), 7.08 (dd, $J$ = 7.2, 4.0 Hz, 4H), 7.00−6.88 (m, 8H), 6.23 (d, $J$ = 5.2 Hz, 2H), 4.95 (dq, $J$ = 9.6, 6.8 Hz, 2H), 4.67−4.33 (m, 8H), 2.11 (d, $J$ = 4.8 Hz, 3H), 1.55 (dd, $J$ = 8.8, 6.8 Hz, 6H). $^{13}$C {$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 171.2, 171.2, 157.4, 157.3, 140.6, 140.6, 136.8, 136.6, 136.3, 136.3, 128.9, 128.8, 128.6, 128.5, 128.1, 128.1, 127.6, 127.6, 127.4, 127.4, 126.9, 126.9, 108.4, 107.9, 76.4, 76.0, 75.8, 75.7, 49.5, 49.4, 48.3, 48.3, 21.9, 21.8, 18.2, 18.1. IR $\nu_{max}$ ($cm^{-1}$): 3080, 3065, 3027, 2983, 2925, 2355, 2335, 1665, 1575, 1495, 1453, 1425, 1380, 1361, 1240, 1215, 1135, 1102, 1028, 1022, 817, 735, 698, 570, 460. HRMS (ESI) $m/z$: [M + H]$^+$ Calcd for $C_{41}H_{42}IN_2O_4$ 753.2184; found 753.2183.

**General Procedures for Asymmetric Aminolactonization Reaction.** A 10 mL pyrex tube was charged with **ArI*1** (11.3 mg, 15 mol %), $HNTs_2$ (48.8 mg, 1.5 equiv), and *m*CPBA (35.5 mg, 1.75 equiv, 85 wt %) in $PhCF_3$ (1 mL). After stirring at −10 °C for 15 min, the substrate **1** (0.1 mmol, 1.0 equiv) was added. The mixture was stirred for 60 h at −10 °C. After completed, the resulting mixture was diluted with an aqueous NaOH (2 mol/L, 5 mL) and extracted with EtOAc (15 mL × 3). The organic phase was washed with brine, dried over $Na_2SO_4$, filtered, and concentrated under vacuum. The residue was purified by flash column chromatography on silica gel (PE/EtOAc = 10:1−1:1) to give the chiral aminolactonization products **2b***, **2d***, **2e***, and **2n***.

*N-((4,4-Dimethyl-5-oxotetrahydrofuran-2-yl)methyl)-4-methyl-N-tosylbenzenesulfonamide (**2b***).* White solid in 67% yield after 60 h. HPLC (Chiralpak $IA_3$ column, hexane/*i*-PrOH = 90/10), flow rate 0.8 mL/min, $\lambda$ = 214 nm, *t*R (minor) = 19.64 min, *t*R (major) = 27.79 min, 54% ee.

*4-Methyl-N-((5-oxo-4,4-dipropyltetrahydrofuran-2-yl)methyl)-N-tosylbenzenesulfonamide (**2d***).* White solid in 60% yield after 60 h. HPLC (Chiralpak OD-H column, hexane/*i*-PrOH = 95/5), flow rate 0.8 mL/min, $\lambda$ = 214 nm, *t*R (minor) = 19.67 min, *t*R (major) = 22.90 min, 30% ee.

*4-Methyl-N-((5-oxo-4,4-diphenyltetrahydrofuran-2-yl)methyl)-N-tosylbenzenesulfonamide (**2e***).* White solid in 89% yield after 60 h. HPLC (Chiralpak $IA_3$ column, hexane/*i*-PrOH = 90/10), flow rate 0.8 mL/min, $\lambda$ = 214 nm, *t*R (minor) = 31.86 min, *t*R (major) = 37.01 min, 88% ee.

*4-Methyl-N-((1-oxo-2-oxaspiro[4.5]decan-3-yl)methyl)-N-tosylbenzenesulfonamide (**2n***).* White solid in 60% yield after 60 h. HPLC (Chiralpak $IA_3$ column, hexane/*i*-PrOH = 90/10), flow rate 0.8 mL/min, $\lambda$ = 214 nm, *t*R (minor) = 26.80 min, *t*R (major) = 30.36 min, 65% ee.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00074.

Tables of detailed reaction condition screening, picture of kinetic experiments, crystal data, NMR spectra (PDF)

### Accession Codes

CCDC 2050572, 2050577, 2050580, 2050581, 2060874, 2063255, and 2063265 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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https://doi.org/10.1021/acs.joc.1c00074
J. Org. Chem. 2021, 86, 5152−5165

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

This work was supported by the Shaanxi Province Key Research and Development Program (grant no. 2019ZDLSF-03-03) and the National Science and Technology Major Project of China Key New Drug Creation and Development Program (project no. 2014ZX09J14104-06C). We also would like to give great thanks to professor Sheng-Yong Zhang and professor Zhi-Xiang Yu for valuable discussions.

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