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Insights into the β-Sultam Ring Formation in the Sulfa-Staudinger Cycloadditions

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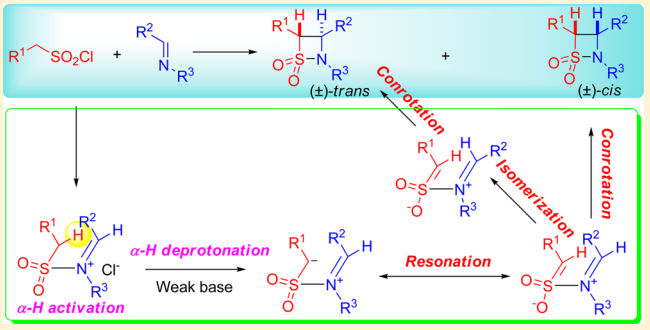
Supporting Information

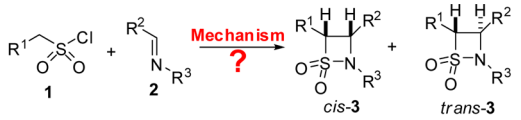
ABSTRACT: The reaction of imines with sulfonyl chlorides or even direct sulfenes to form β-sultams is herein named as sulfa-Staudinger cycloaddition. The β-sultam formation is proposed to follow a stepwise mechanism of sulfonylation, deprotonation, and conrotatory ring closure with 2,3-thiazabutadiene-type zwitterionic intermediates as key intermediates. Cyclic (*Z*)-imines give rise to *trans*-β-sultams exclusively, suggesting that the intermediates generated from linear (*E*)-imines undergo a conrotatory ring closure directly to afford *cis*-β-sultams. Meanwhile, their iminium isomers lead to *trans*-β-sultams via the conrotatory ring closure.



β-Sultams, the sulfur analogues of β-lactams, but with more distorted rings, display a wide spectrum of biological activities[1] and significant importance as synthetic building blocks.[2] Nevertheless, only limited methods for the synthesis of β-sultams have been reported,[2a,b] including the reactions of electron-rich alkenes with *N*-sulfonylimines,[3] and the intramolecular cyclizations of various sulfonic acid derivatives,[4] reactions of sulfonyl chlorides with electron-rich imines (sulfa-Staudinger cycloaddition).[5] Because of the rich diversities of sulfonyl chlorides and imines, their reactions represent one of the most promising methodologies. However, the mechanism still remains unclear. Since Tsuge and Iwanami first reported the synthesis of β-sultams through reactions of reactive sulfonyl chlorides with 2 equiv of imines in the absence of triethylamine,[5a] the reaction mechanism was popularly accepted as a concerted [π2s + π2a] cycloaddition of imines and sulfene intermediates (Scheme 1), even though without any convincing experimental or computational evidence. This mechanism was proposed on the basis of Staudinger and Pfenninger's report,[6] in which a β-sultam was synthesized from benzylideneaniline and diphenylsulfene, in situ generated from diphenyldiazomethane and sulfur dioxide. The preference of *cis*-β-sultams to the corresponding *trans*-β-sultams was attributed to "the secondary effect of the Hoffman–Woodward rule" previously (Scheme 1a).[5b] The unconvincing mechanism is the first and only one assumed for the formation of β-sultams through the direct reactions of alkanesulfonyl chlorides and electron-rich imines. Additionally, Peters and co-workers proposed the catalytic mechanism for the synthesis of β-sultams from sulfonyl chlorides and electron-deficient *N*-tosyl imines.[7]

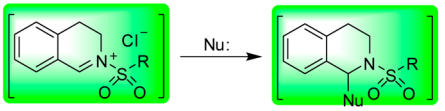
For quite a long time, our efforts have been directed to the mechanisms of the Staudinger reaction (ketene–imine cycloaddition)[8] and sulfa-Staudinger reactions;[9] the products of the former are β-lactams, whereas those of the latter are β-sultams.

Scheme 1. Proposed Mechanisms for the Sulfa-Staudinger cycloaddition



(a) *Hiraoka's mechanism: concerted sulfene-imine [π2s+π2a] cycloaddition with secondary effect of the Hoffman-Woodward rule*

(b) Our mechanism: stepwise mechanism with *N*-sulfonyl iminium chlorides as key intermediates.



N-Sulfonyl iminium chlorides, captured by various nucleophiles in our previous work using cyclic imine 2,4-dihydroisoquiniline. see ref. 9

Previously, we intensively studied the reactions of various sulfonyl chlorides and cyclic imines.[9] The presence of the divergent products from reactions of different sulfonyl chlorides with 3,4-dihydroisoquiniline was considered to generate via the capture of the highly reactive key intermediates *N*-sulfonyl iminium chlorides by various nucleophiles, such as water, chloride anion, oxirane, and even 1,4-dioxane (Scheme 1).[9] On the basis of these observations, we hypothesized that the formation of β-sultams in the sulfa-Staudinger cycloaddition should follow a stepwise mechanism rather than a concerted sulfene–imine [π2s + π2a] cycloaddition (Scheme 1). In this stepwise mechanism, the key intermediates are trapped and

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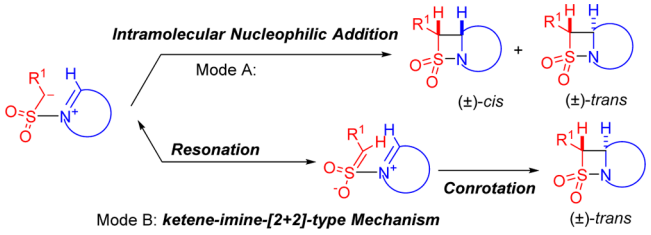
postulated to be *N*-sulfonyl iminium chlorides, whose α-protons, if R is an alkyl group, are activated by the electron-withdrawing iminium moiety and could be easily abstracted to form α-anionic *N*-sulfonyliminiums. However, a new problem emerges: What is the mode of the cyclization, intramolecular nucleophilic addition, or conrotatory ring closure as in the Staudinger ketene−imine cycloaddition?[8] Employing an appropriate cyclic imine as a probe to react with different sulfonyl chlorides, we successfully tackled the problem and finally propose the mechanism for β-sultam formation. Herein, we present our results and hope that the results provide an important guide to the synthesis of β-sultams via the sulfa-Staudinger cycloaddition.

The reactions of sulfonyl chlorides **1** and linear imines **2** generally produce a mixture of *cis*- and *trans*-β-sultams **3** in low diastereoselectivity. Thus, one possibly considers the cyclization as an intramolecular nucleophilic addition inside the α-anionic *N*-sulfonyliminiums (Mode A, Scheme 2). However, there also

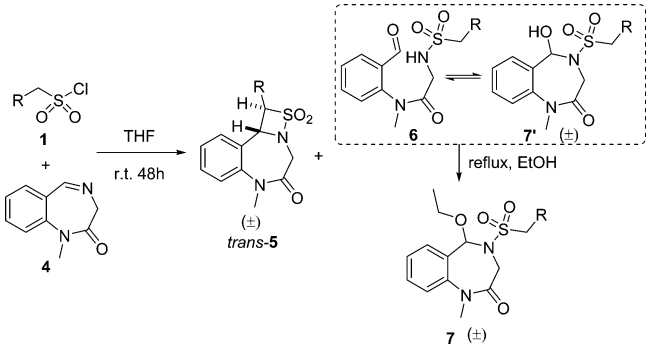
Scheme 2. Two Plausible Stepwise Mechanisms and How To Distinguish Them



exists another possibility following the ketene−imine-[2 + 2]-type mechanism,[8] involving the conrotatory ring closure of the 2,3-thiazabutadiene-type zwitterionic intermediates and their isomers around their C═N bonds to form *cis*- and *trans*-β-sultams **3** (Mode B, Scheme 2). To distinguish the two different possible mechanisms, we need to design an appropriate cyclic imine, which cannot isomerize around the C═N bond, as a probe to react with sulfonyl chlorides **1**. The mechanism of this reaction could be identified easily on the basis of products. As rationalized in reactions of sulfonyl chlorides **1** with cyclic (*Z*)-imines, *trans*-β-sultams would be formed exclusively if the cyclization step follows the ring closure in the Mode B, whereas a mixture of *cis*- and *trans*-β-sultams would be generated if the cyclization step follows the intramolecular nucleophilic addition in the Mode A.

After numerous failures,[9] we found that bicyclic imine **4** is the one of our best choices.[10] The cyclic imine **4** shows some specific structural features that the conjugated amide group is more stable than an ester and is an electron-donating group, increasing the nucleophicility of the imine nitrogen atom due to its vinylous imidamide character. Thus, we conducted a series of reactions of the imine **4** with different alkanesulfonyl chlorides **1**, and the results are summarized in Table 1. Gratifyingly, reactions of imine **4** with benzyl sulfonyl chloride (**1a**) and substituted benzyl sulfonyl chlorides (**1b−f**) provided the desired products, tricyclic β-sultams (*trans*-**5a−f**) with *trans*-configuration stereospecifically, accompanied by the byproducts, aldehydes **6a−f**, which were generated during workup and converted to *N*,*O*-acetals **7** for convenient purification and characterization (Table 1, entries 1−6). However, sulfonyl chlorides **1g−i** did not produce the corresponding β-sultams, possibly due to weak acidity of their

Table 1. Reactions of Bicyclic Imine 4 with Different Sulfonyl Chlorides 1



			isolated yield (%)	
entry	**1**	R	**5**	**7**
1	**1a**	Ph	16	20
2	**1b**	*p*-ClC_6H_4	15	22
3	**1c**	*o*-ClC_6H_4	20	15
4	**1d**	*m*-ClC_6H_4	18	10
5	**1e**	*p*-FC_6H_4	12	20[a]
6	**1f**	*p*-BrC_6H_4	12	28
7	**1g**	*p*-MeC_6H_4	[b]	44
8	**1h**	Me		19
9	**1i**	vinyl		11
10[c]	**1a**	Ph	40	42

[a]Isolated yield of 7′. [b]Product was not observed. [c]Reaction conducted on 5 mmol scale based on benzylsulfonyl chloride (**1a**).

α-protons (vide post) (Table 1, entries 7−9). The results provide convincing evidence to support the conrotatory ring closure (Mode B) rather than the intramolecular nucleophilic addition (Mode A). Now, we can propose the formation mechanism of tricyclic *trans*-β-sultams *trans*-**5** from sulfonyl chlorides **1** and the cyclic (*Z*)-imine **4** (Scheme 3). The cyclic (*Z*)-imine **4** first attacks sulfonyl chlorides **1** (sulfonylation) to afford sulfonyl iminium chlorides **A**, which are deprotonated by another molecule of the imine **4**, yielding anionic sulfonyl iminiums **B**, which can be (*R*)- and (*S*)-forms depending on abstraction of two different protons on the α-carbon atom of the sulfonyl moiety. The intermediates **B** further resonate into 2,3-thiazabutadiene-type zwitterionic intermediates **C**, which undergo a conrotatory ring closure to give rise to final tricyclic *trans*-β-sultams *trans*-**5** (Scheme 3).

With the success in understanding the nature of the formation of tricyclic β-sultams *trans*-**5**, we can give the reasonable mechanism for the formation of *cis*- and *trans*-β-sultams **3** from sulfonyl chlorides **1** and linear imines **2** in Scheme 4. The reaction commences with a nucleophilic attack of (*E*)-imines **2** to sulfonyl chlorides **1**, leading to sulfonyl iminium chlorides **D**, of which α-protons are activated and show stronger acidity than those of the corresponding sulfonyl chlorides **1** due to the existence of the strong electron-withdrawing iminium group. As a consequence, imines **2** or another weak base, such as pyridine, can abstract one of the α-protons to generate α-anionic *N*-sulfonyl iminiums **E**, which further resonate smoothly into 2,3-thiazabutadiene-type zwitterionic intermediates **F**, which undergo a conrotatory ring closure to produce *cis*-β-sultams *cis*-**3**. Alternatively, the intermediates **F** isomerize over their iminium moiety to form **G**,[11] which further undergo a conrotatory ring closure to produce the *trans*-β-sultams *trans*-**3**. Since the imines **2** exist in

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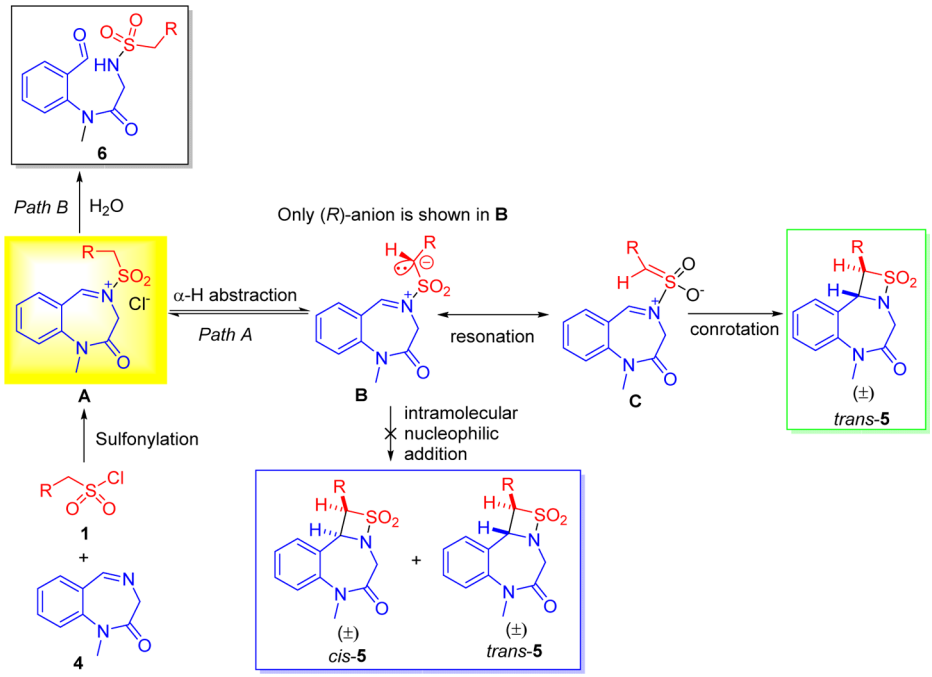
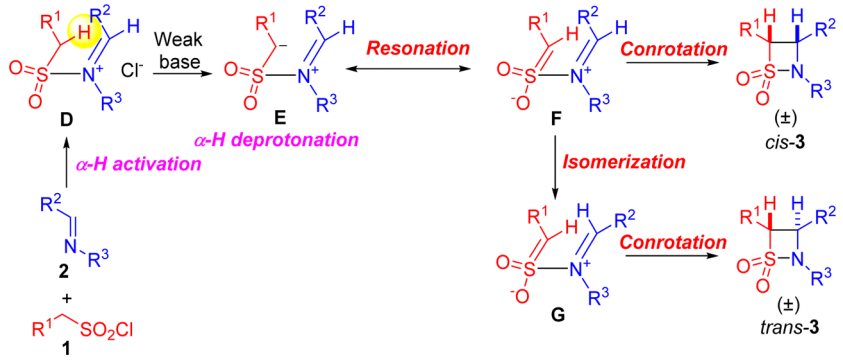
Scheme 3. Proposed Mechanism for the Formation of *β*-Sultams from Sulfonyl Chlorides 1 and Cyclic (*Z*)-Imine 4



Scheme 4. Proposed Mechanism for the Formation of *cis*- and *trans*-*β*-Sultams in the Sulfa-Staudinger reactions



exclusive (*E*)-configurations under thermal conditions,[11c] only after they are sulfonylated could their iminium moiety isomerize due to steric hindrance of vicinal alkanesulfonyl and R^2 groups. The C═S and N═C double bonds in the 2,3-thiazabutadiene-type zwitterionic intermediates **F** and **G** are probably not coplannar. However, similar to the zwitterionic intermediates in the Staudinger ketene−imine cycloaddition, the conrotatory ring closure inside **F** and **G** may occur. Direct adoption of the classical Woodward−Hoffmann [π4c] mechanism is not proper, since the frontier molecular orbitals of the intermediates **F** and **G** are different apparently from those of 1,3-butadiene.[12]

In this process depicted in Scheme 4, the nucleophilicity of the imines **2** must be strong enough to initiate a nucleophilic attack to the sulfonyl chlorides **1** and the basicity of the imines **2** should also be strong enough to abstract the α-proton of **D**. The α-proton abstraction step demands that the substituents in the imines **2** would better be electron-donating groups because only *N*-alkyl imines can react with various sulfonyl chlorides **1**,[5] while only one example of the reaction of *N*-aryl imines **2** (R^2 = R^3 = Ar) and a sulfonyl chloride **1** with a strong electron-withdrawing substituent (R^1 = PhCO) was reported until now, affording the corresponding *β*-sultam **3** in a low yield.[5a] In this case, the basicity of benzylideneaniline (*N*-aryl imine) is strong enough to abstract the more acidic α-proton of 2-oxo-2-phenylethanesulfonyliminium chloride because its α-carbon is attached with a strong electron-withdrawing benzoyl group. Considering the sulfonyl chlorides **1**, when their α-position is attached to an electron-withdrawing group, the α-protons of **D** will be easier to be abstracted by imines **2** to form intermediates **E**. If the nucleophilicity of the imines **2** is not strong enough, **D** cannot be generated, and as a result, no reaction will take place.[9] Additionally, if strong bases such as triethylamine are used in the reaction, the corresponding sulfenes would be generated, resulting in the formation of olefins as the predominant products.[9]

In conclusion, the formation mechanism of *β*-sultams in the sulfa-Staudinger cycloadditions was investigated. By reactions of sulfonyl chlorides with cyclic (*Z*)-imines, the presence of *trans*-*β*-sultams and the absence of the *cis*-*β*-sultams support that the conrotatory ring closure of the 2,3-thiazabutadiene-type zwitterionic intermediates, which are resulted from resonation of the anionic *N*-sulfonyl iminiums, is the reasonable cyclization mode. Therefore, the mechanism is explicated as a stepwise

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one. First, sulfonyl chlorides and imines react to generate *N*-sulfonyl iminium chlorides. Then, weak bases (excessive imines, pyridine, etc.) abstract their α-proton to give rise to α-anionic *N*-sulfonyl iminiums, which resonate into 2,3-thiazabutadiene-type zwitterionic intermediates. For cyclic imines, the intermediates undergo a conrotatory ring closure to afford the corresponding β-sultams stereospecifically. For linear (*E*)-imines, the zwitterionic intermediates subsequently undergo a conrotatory ring closure to afford *cis*-β-sultams. Meanwhile, their iminium moiety isomerizes to form more stable 2,3-thiazabutadiene-type zwitterionic intermediates, which undergo the conrotatory ring closure to afford *trans*-β-sultams. As for the Staudinger cycloaddition,[8b] it is the competition between the direct ring closure and the isomerization of the 2,3-thiazabutadiene-type zwitterionic intermediates that controls the diastereoselectivty in the reactions.

EXPERIMENTAL SECTION

General Information. Tetrahydrofuran was refluxed over sodium with diphenyl ketone as indicator and freshly distilled prior to use. Melting points were obtained on a melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer in $CDCl_3$ with TMS as an internal standard, and the chemical shifts (δ) are reported in parts per million (ppm). The IR spectra (KBr pellets, ν [cm^{-1}]) were taken on an FTIR spectrometer. HRMS measurements were carried out on an LC/MSD TOF mass spectrometer. TLC separations were performed on silica gel GF254 plates, and the plates were visualized with UV light.

Sulfonyl chlorides **1a**−**1h** were prepared according to the method in our previous reports,[13] while **1i** was prepared according to the method reported by Johary and Owen,[14] respectively. Cyclic imine **4** was prepared according to Bergman's procedure.[10]

Reaction of Alkanesulfonyl Chlorides 1 with Imines 4: General Procedure. To a solution of imine **4** (348 mg, 2 mmol) in anhydrous THF (2.5 mL) was added dropwise a solution of an alkanesulfonyl chloride **1** (1 mmol) in anhydrous THF (2.5 mL) in an ice−water bath. After addition, the resulting mixture was allowed to warm to room temperature and stirred for 48 h. Then, diethyl ether (10 mL) was added and a large amount of white solid precipitated. After the filtration of the salts and removal of the solvent, the residue was purified on silica gel column chromatography (PE/EA 2:1 to 1:1, v/v) to recover the unconsumed cyclic imine **4** and to afford the aldehydes **6** as a sticky oil and/or the tricyclic β-sultams **5** as colorless crystals. Refluxing the impure aldehydes **6** with 95% ethanol overnight and then purification by column chromatography on silica gel (PE:EA 2:1, v/v) afforded products **7a**−**7j** as a sticky oil or colorless crystals in almost complete conversion.

*trans-6-Methyl-1-phenyl-1,10b-dihydro-6H-benzo[f][1,2]-thiazeto[2,3-d][1,4]diazepin-5(4H)-one 2,2-Dioxide (**5a**).* Yield 53 mg (16%). TLC R_f = 0.5 (PE:EA = 2:1, v/v). Colorless crystals, mp 237−239 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64−7.26 (m, 9H, ArH), 5.82 (d, *J* = 3.2 Hz, 1H), 4.93 (d, *J* = 3.2 Hz, 1H), 3.83 (d, *J* = 12.0 Hz, 1H), 3.79 (d, *J* = 12.0 Hz, 1H), 3.40 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.1, 142.7, 130.6, 130.3, 130.0, 129.4, 128.9, 127.1, 126.8, 126.2, 123.6, 78.7, 55.3, 46.1, 36.1 ppm; IR (film) ν cm^{-1} 3007, 2919, 1663, 1599, 1495, 1456, 1420, 1381, 1324, 1210, 1192, 1165, 1120, 1069, 971, 793, 767, 698; ESI-HRMS [M + H]$^+$ calc for $C_{17}H_{17}N_2O_3S$ *m*/*z* 329.0960, found 329.0956.

*4-(Benzylsulfonyl)-5-ethoxy-1-methyl-4,5-dihydro-1H-benzo[f]-[1,4]diazepin-2(3H)-one (**7a**).* Yield 75 mg (20%). TLC R_f = 0.4 (PE:EA = 2:1, v/v). Yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.50−7.29 (m, 9H), 5.92 (s, 1H), 4.61 (d, *J* = 13.6 Hz, 1H), 4.53 (d, *J* = 13.6 Hz, 1H), 4.20 (d, *J* = 14.0 Hz, 1H), 3.57 (d, *J* = 14.0 Hz, 1H), 3.50 (dq, *J* = 14.6, 7.3 Hz, 1H), 3.36 (s, 3H), 3.19 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.14 ppm (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.6, 141.8, 131.0, 130.6, 130.0, 129.1, 128.7, 128.5, 128.3, 126.5, 123.9, 89.0, 62.8, 60.5, 48.1, 35.4, 14.9 ppm; IR (film) ν cm^{-1} 2974, 2928, 1667, 1602, 1495, 1456, 1423, 1385, 1350, 1286, 1203, 1152, 1064, 1008, 953, 770, 698; ESI-HRMS [M + H]$^+$ calc for $C_{19}H_{23}N_2O_4S$ *m*/*z* 375.1379, found 375.1379.

*trans-1-(4-Chlorophenyl)-6-methyl-1,10b-dihydro-6H-benzo[f]-[1,2]thiazeto[2,3-d][1,4]diazepin-5(4H)-one 2,2-Dioxide (**5b**).* Yield 54 mg (15%). TLC R_f = 0.5 (PE:EA = 2:1, v/v). Colorless crystals, mp 244−246 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.58−7.32 (m, 8H, ArH), 5.82 (d, *J* = 2.6 Hz, 1H), 4.93 (d, *J* = 2.6 Hz, 1H), 3.82 (d, *J* = 12.0 Hz, 1H), 3.78 ppm (d, *J* = 12.0 Hz, 1H), 3.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.0, 142.7, 130.6, 130.3, 130.0, 129.4, 128.9, 127.1, 126.8, 126.2, 123.6, 77.9, 55.4, 46.1, 36.1 ppm; IR (film) ν cm^{-1} 3002, 2926, 1659, 1601, 1491, 1454, 1417, 1384, 1333, 1289, 1191, 1176, 1163, 1073, 1047, 767, 665; ESI-HRMS [M + H]$^+$ calc for $C_{17}H_{16}ClN_2O_3S$ *m*/*z* 363.0570, found 363.0567.

*4-(4-Chlorobenzylsulfonyl)-5-ethoxy-1-methyl-4,5-dihydro-1H-benzo[f][1,4]diazepin-2(3H)-one (**7b**).* Yield 90 mg (22%). TLC R_f = 0.4 (PE:EA = 2:1, v/v). Yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.53−7.29 (m, 8H), 5.91 (s, 1H), 4.59 (d, *J* = 14.0 Hz, 1H), 4.51 (d, *J* = 14.0 Hz, 1H), 4.19 (d, *J* = 14.4 Hz, 1H), 3.61 (d, *J* = 14.4 Hz, 1H), 3.50 (dq, *J* = 14.6, 7.3 Hz, 1H), 3.37 (s, 3H), 3.19 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.14 ppm (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.6, 141.8, 134.8, 132.2, 131.0, 130.8, 130.1, 128.9, 127.0, 126.6, 123.9, 89.0, 62.8, 60.5, 48.1, 35.4, 14.9 ppm; IR (film) ν cm^{-1} 2975, 2930, 1672, 1603, 1492, 1462, 1386, 1351, 1205, 1153, 1065, 1086, 1008, 952, 840, 766; ESI-HRMS [M + H]$^+$ calc for $C_{19}H_{22}ClN_2O_4S$ *m*/*z* 409.0989, found 409.0987.

*trans-1-(2-Chlorophenyl)-6-methyl-1,10b-dihydro-6H-benzo[f]-[1,2]thiazeto[2,3-d][1,4]diazepin-5(4H)-one 2,2-Dioxide (**5c**).* Yield 72 mg (20%). TLC R_f = 0.5 (PE:EA = 2:1, v/v). Colorless crystals, mp 230−231 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.97−7.31 (m, 8H, ArH), 6.52 (d, *J* = 3.6 Hz, 1H), 4.92 (d, *J* = 3.6 Hz, 1H), 3.84 (d, *J* = 11.3 Hz, 1H), 3.79 (d, *J* = 11.3 Hz, 1H), 3.40 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.9, 142.7, 134.4, 133.1, 131.1, 130.7, 129.6, 128.6, 128.1, 127.4, 127.0, 126.0, 123.6, 74.3, 54.8, 46.1, 36.1 ppm; IR (film) ν cm^{-1} 2923, 1677, 1600, 1494, 1455, 1423, 1380, 1332, 1280, 1172, 1128, 1074, 1052, 978, 839, 754, 668; ESI-HRMS [M + H]$^+$ calc for $C_{17}H_{16}ClN_2O_3S$ *m*/*z* 363.0570, found 363.0567.

*4-(2-Chlorobenzylsulfonyl)-5-ethoxy-1-methyl-4,5-dihydro-1H-benzo[f][1,4]diazepin-2(3H)-one (**7c**).* Yield 61 mg (15%). TLC R_f = 0.4 (PE:EA = 2:1, v/v). Colorless crystals, mp 164−166 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60−7.27 (m, 8H), 5.94 (s, 1H), 4.87 (d, *J* = 13.8 Hz, 1H), 4.81 (d, *J* = 13.8 Hz, 1H), 4.26 (d, *J* = 14.2 Hz, 1H), 3.67 (d, *J* = 14.2 Hz, 1H), 3.50 (dq, *J* = 14.1, 7.0 Hz, 1H), 3.37 (s, 3H), 3.18 (dq, *J* = 14.1, 7.0 Hz, 1H), 1.16 ppm (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.7, 141.9, 135.6, 133.1, 130.7, 130.0, 129.1, 127.0, 126.8, 126.5, 124.0, 89.1, 63.0, 57.3, 48.1, 35.5, 15.0 ppm; IR (film) ν cm^{-1} 2975, 2927, 1673, 1603, 1494, 1463, 1385, 1353, 1154, 1064, 1084, 1008, 952, 772; ESI-HRMS [M + H$^+$] calc for $C_{19}H_{22}ClN_2O_4S$ *m*/*z* 409.0989, found 409.0992.

*trans-1-(3-Chlorophenyl)-6-methyl-1,10b-dihydro-6H-benzo[f]-[1,2]thiazeto[2,3-d][1,4]diazepin-5(4H)-one 2,2-Dioxide (**5d**).* Yield 65 mg (18%). TLC R_f = 0.5 (PE:EA = 2:1, v/v). Colorless crystals, mp 229−231 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.99−7.34 (m, 8H, ArH), 6.52 (d, *J* = 3.6 Hz, 1H), 4.92 (d, *J* = 3.6 Hz, 1H), 3.83 (d, *J* = 11.3 Hz, 1H), 3.79 (d, *J* = 11.3 Hz, 1H), 3.40 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.9, 142.6, 134.4, 131.1, 130.6, 129.8, 129.5, 128.5, 128.1, 127.3, 127.0, 125.9, 123.6, 77.3, 54.7, 46.0, 36.1 ppm; IR (film) ν cm^{-1} 2921, 1677, 1601, 1494, 1458, 1422, 1380, 1330, 1172, 1128, 1074, 1052, 978, 839, 754, 669; ESI-HRMS [M + H]$^+$ calc for $C_{17}H_{16}ClN_2O_3S$ *m*/*z* 363.0570, found 363.0574.

*4-(3-Chlorobenzylsulfonyl)-5-ethoxy-1-methyl-4,5-dihydro-1H-benzo[f][1,4]diazepin-2(3H)-one (**7d**).* Yield 48 mg (10%). TLC R_f = 0.4 (PE:EA = 2:1, v/v). Colorless crystals, mp 168−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.53−7.29 (m, 8H), 5.92 (s, 1H), 4.59 (d, *J* = 13.8 Hz, 1H), 4.51 (d, *J* = 13.8 Hz, 1H), 4.19 (d, *J* = 14.2 Hz, 1H), 3.61 (d, *J* = 14.2 Hz, 1H), 3.47 (dq, *J* = 9.2, 7.0 Hz, 1H), 3.37 (s, 3H), 3.16 (dq, *J* = 9.2, 7.0 Hz, 1H), 1.14 ppm (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.6, 141.8, 134.4, 131.0, 130.8, 130.3, 130.0, 129.9, 129.2, 128.9, 128.8, 126.6, 123.9, 89.0, 62.9, 60.0, 48.1, 35.4, 14.9 ppm; IR (film) ν cm^{-1} 2975, 2929, 1672, 1602, 1495, 1463, 1386,

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1351, 1154, 1084, 1064, 1008, 952, 765, 682; ESI-HRMS [M + H$^+$] calc for $C_{19}H_{22}ClN_2O_4S$ m/z 409.0989, found 409.0992.

*trans-1-(4-Fluorophenyl)-6-methyl-1,10b-dihydro-6H-benzo[f][1,2]thiazeto[2,3-d][1,4]diazepin-5(4H)-one 2,2-Dioxide (**5e**).* Yield 41 mg (12%). TLC R_f = 0.5 (PE:EA = 2:1). Colorless crystals, mp 248−249 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64−7.16 (m, 8H, ArH), 5.80 (d, J = 3.5 Hz, 1H), 4.88 (d, J = 3.5 Hz, 1H), 3.82 (d, J = 11.5 Hz, 1H), 3.79 (d, J = 11.5 Hz, 1H), 3.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.1, 163.6 (d, J_{C-F} = 250.3 Hz), 142.7, 130.9 (d, J_{C-F} = 8.6 Hz), 130.7, 127.1, 126.7, 126.3 (d, J_{C-F} = 3.2 Hz), 126.0, 123.7, 116.5 (d, J_{C-F} = 22.0 Hz), 77.9, 55.6, 46.1, 36.1 ppm; IR (film) ν cm^{-1} 2924, 1668, 1600, 1511, 1494, 1456, 1416, 1383, 1326, 1192, 1164, 1120, 1071, 1012, 974, 835, 765, 737, 664; ESI-HRMS [M + H]$^+$ calc for $C_{17}H_{16}FN_2O_3S$ m/z 347.0866, found 347.0871.

*4-(4-Fluorobenzylsulfonyl)-5-hydroxy-1-methyl-4,5-dihydro-1H-benzo[f][1,4]diazepin-2(3H)-one (**7e**).* Yield 73 mg (20%). TLC R_f = 0.4 (PE:EA = 2:1, v/v). Colorless crystals, mp 162−164 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.51−7.05 (m, 8H), 6.16 (d, J = 3.3 Hz, 1H), 4.51 (d, J = 14.1 Hz, 1H), 4.47 (d, J = 14.1 Hz, 1H), 4.13 (d, J = 14.0 Hz, 1H), 3.53 (d, J = 14.0 Hz, 1H), 3.39 (s, 3H), 2.57 ppm (d, J = 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.5, 161.2 (d, J_{C-F} = 254.5 Hz), 142.9, 132.9 (J_{C-F} = 8.2 Hz), 132.7, 130.8, 130.1, 129.2, 126.8 (J_{C-F} = 3.3 Hz), 123.9, 116.0 (d, J_{C-F} = 21.7 Hz), 83.0, 59.1, 47.9, 35.6 ppm; IR (film) ν cm^{-1} 2972, 2923, 1647, 1601, 1508, 1459, 1394, 1347, 1329, 1223, 1205, 1148, 1083, 1003, 948, 918, 842, 772; ESI-HRMS [M + H]$^+$ calc for $C_{17}H_{18}FN_2O_4S$ m/z 365.0971, found 365.0968.

*trans-1-(4-Bromophenyl)-6-methyl-1,10b-dihydro-6H-benzo[f][1,2]thiazeto[2,3-d][1,4]diazepin-5(4H)-one 2,2-Dioxide (**5f**).* Yield 49 mg (12%). TLC R_f = 0.5 (PE:EA = 2:1, v/v). Colorless crystals, mp 259−261 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64−7.32 (m, 8H, ArH), 5.76 (d, J = 3.5 Hz, 1H), 4.87 (d, J = 3.5 Hz, 1H), 3.82 (d, J = 11.5 Hz, 1H), 3.78 (d, J = 11.5 Hz, 1H), 3.40 ppm (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ = 165.0, 142.7, 132.6, 130.7, 130.5, 129.3, 127.2, 126.7, 125.9, 124.4, 123.7, 77.9, 55.3, 46.1, 36.1 ppm; IR (film) ν cm^{-1} 2919, 1677, 1601, 1489, 1456, 1416, 1384, 1328, 1189, 1165, 1125, 1072, 1012, 974, 836, 766, 664; ESI-HRMS [M + H]$^+$ calc for $C_{17}H_{16}BrN_2O_3S$ m/z 407.0065, found 407.0060.

*4-(4-Bromobenzylsulfonyl)-5-ethoxy-1-methyl-4,5-dihydro-1H-benzo[f][1,4]diazepin-2(3H)-one (**7f**).* Yield 126 mg (28%). TLC R_f = 0.4 (PE:EA = 2:1, v/v). Colorless crystals, mp 170−172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.52−7.28 (m, 8H), 5.90 (s, 1H), 4.57 (d, J = 13.8 Hz, 1H), 4.49 (d, J = 13.8 Hz, 1H), 4.18 (d, J = 14.2 Hz, 1H), 3.61 (d, J = 14.2 Hz, 1H), 3.46 (dq, J = 9.0, 7.0 Hz, 1H), 3.37 (s, 3H), 3.19 (dq, J = 9.0, 7.0 Hz, 1H), 1.13 ppm (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.7, 141.9, 132.6, 131.9, 130.8, 130.1, 129.0, 127.5, 126.6, 123.9, 123.0, 89.0, 62.9, 60.0, 48.1, 35.4, 14.9 ppm; IR (film) ν cm^{-1} 2974, 2928, 1672, 1603, 1489, 1460, 1386, 1350, 1207, 1153, 1085, 1070, 1008, 952, 838, 767; ESI-HRMS [M + H]$^+$ calc for $C_{19}BrH_{22}N_2O_4S$ m/z 453.0484, found 453.0482.

*5-Ethoxy-1-methyl-4-(4-methylbenzylsulfonyl)-4,5-dihydro-1H-benzo[f][1,4]diazepin-2(3H)-one (**7g**).* Yield 171 mg (44%). TLC R_f = 0.4 (PE:EA = 2:1, v/v). Colorless crystals, mp 146−148 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.51−7.16 (m, 8H), 5.91 (s, 1H), 4.56 (d, J = 14.0 Hz, 1H), 4.49 (d, J = 14.0 Hz, 1H), 4.19 (d, J = 14.0 Hz, 1H), 3.56 (d, J = 14.0 Hz, 1H), 3.49 (dq, J = 13.6, 6.8 Hz, 1H), 3.36 (s, 3H), 3.19 (dq, J = 13.6, 6.8 Hz, 1H), 2.36 (s, 3H), 1.14 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.7, 141.9, 138.5, 130.8, 130.6, 130.0, 129.4, 129.2, 126.5, 125.2, 123.9, 89.0, 62.9, 60.3, 48.1, 35.4, 21.2, 14.9 ppm; IR (film) ν cm^{-1} 2974, 2927, 1672, 1603, 1514, 1495, 1461, 1386, 1349, 1153, 1085, 1065, 1008, 952, 823, 767; ESI-HRMS [M + Na]$^+$ calc for $C_{20}H_{24}N_2NaO_4S$ m/z 411.1354, found 411.1355.

*5-Ethoxy-4-(ethylsulfonyl)-1-methyl-4,5-dihydro-1H-benzo[f][1,4]diazepin-2(3H)-one (**7h**).* Yield 59 mg (19%). TLC R_f = 0.4 (PE:EA = 2:1, v/v). Yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.51−7.29 (m, 4H), 5.90 (s, 1H), 4.11 (d, J = 14.0 Hz, 1H), 3.57 (d, J = 14.0 Hz, 1H), 3.45 (dq, J = 15.2, 7.6 Hz, 1H), 3.38 (d, J = 15.2, 7.6 Hz, 1H), 3.35 (s, 3H), 3.30 (dq, J = 14.4, 7.2 Hz, 1H), 3.12 ((dq, J = 14.4, 7.2 Hz, 1H), 1.46 (t, J = 7.6 Hz, 3H), 1.09 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.7, 141.8, 130.6, 130.0, 129.1, 126.5, 123.8, 88.7, 62.7, 49.1, 47.9, 35.3, 14.9, 7.5 ppm; IR (film) ν cm^{-1} 2974, 2929, 1671, 1603, 1495, 1463, 1423, 1386, 1349, 1150, 1085, 1065, 1008, 952, 768, 659; ESI-HRMS [M + H]$^+$ calc for $C_{14}H_{21}N_2O_4S$ m/z 313.1222, found 313.1221.

*4-(Allylsulfonyl)-5-ethoxy-1-methyl-4,5-dihydro-1H-benzo[f][1,4]diazepin-2(3H)-one (**7i**).* Yield 36 mg (11%). TLC R_f = 0.4 (PE:EA = 2:1, v/v). Yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.52−7.30 (m, 4H), 6.00 (dt, J = 17.2, 7.5 Hz, 1H), 5.91 (s, 1H), 5.47−5.43 (m, 2H), 4.14 (d, J = 14.1 Hz, 1H), 4.12 (dd, J = 7.2, 13.8 Hz, 1H), 4.00 (dd, J = 7.2, 13.8 Hz, 1H), 3.59 (d, J = 14.1 Hz, 1H), 3.52−3.44 (m, 1H), 3.35 (s, 3H), 3.20−3.11 (m, 1H), 1.13 ppm (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.6, 141.8, 130.7, 130.1, 129.0, 126.5, 124.7, 124.4, 123.9, 88.9, 62.8, 59.1, 48.1, 35.4, 14.9 ppm; IR (film) ν cm^{-1} 2974, 2929, 1671, 1603, 1495, 1463, 1423, 1386, 1349, 1151, 1085, 1065, 1008, 952, 920, 768, 659; ESI-HRMS [M + H]$^+$ calc for $C_{15}H_{21}N_2O_4S$ m/z 325.1222, found 325.1222.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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