JOC Article

Triflic Anhydride Mediated Cyclization of 5-Hydroxy-Substituted Pyrrolidinones for the Preparation of α-Trifluoromethylsulfonamido Furans

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The reaction of α-angelica lactone with alkylamines under aqueous conditions afforded 5-hydroxy-5-methylpyrrolidinones in high yield. When the reaction was carried out under anhydrous conditions, the only products obtained were the corresponding 4-oxopentanoic acid amides. Treatment of either class of compound with triflic anhydride (Tf_2O) in pyridine resulted in the formation of various substituted sulfonamidofurans. The suggested mechanism involves initial formation of an iminium ion which is subsequently transformed into a transient imino triflate. Cyclization of the highly electrophilic imine onto the oxygen atom of the adjacent carbonyl group generates an imino dihydrofuran intermediate. This species reacts further with another equivalent of Tf_2O to give the observed product. The nature of the Lewis acid used was found to affect the outcome of the cyclization reaction. In certain cases, the sulfonamide furan was utilized as a cycloaddition substrate for the synthesis of indolines and related heterocyclic systems.

Introduction

Nitrogen-containing heterocycles are abundant in nature and exhibit diverse and important biological properties.[1] Accordingly, novel strategies for the stereoselective synthesis of azapolycyclic ring systems continue to receive considerable attention in the field of synthetic organic chemistry.[2−8] The utility of *N*-acyliminium ions in heterocyclic chemistry is now well documented.[9] Cyclic *N*-acyliminium ions with exo-cyclic *N*-acyl groups can adopt the *s-cis*-conformation and react as a 4π-electron system with olefins and acetylenes in a Diels−Alder cycloaddition reaction with inverse electron demand.[10] Alternatively, they may behave as dienophiles in reactions with conjugated dienes.[11] The α-amidoalkylation/cyclization sequence of *N*-acyliminium ions is widely regarded as a powerful method for the synthesis of many nitrogenated heterocyclic compounds.[12,13] In particular, the intramolecular reaction of cyclic iminium ions bearing endocyclic *N*-acyl groups and tethered nucleophiles has been successfully employed in the preparation of many nitrogen-containing natural products.[14−18] The presence of the electron-withdrawing acyl functionality on the nitrogen atom results in a more reactive iminium ion, and consequently, this species reacts with a wider range of intramolecular nucleophiles.[12] A variety of useful functionalities for terminating cyclization reactions have also been developed.[19,20] The most powerful of these are ones which both "control" the cyclization process so that a single product is produced and leave the cyclization product with useful functionality for further synthetic manipulation.[21]

Cyclic α-alkoxy amides (**2**) are among the most popular precursors for *N*-acyliminium ions.[22] Typically, these versatile systems are prepared by electrochemical oxidation of amides[23] or by treating cyclic imides with various organometallic reagents.[24] Subsequent *N*-acyliminium

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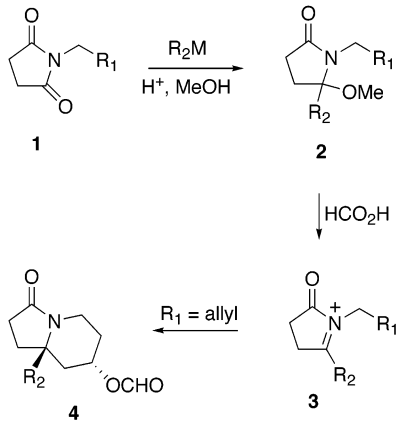
SCHEME 1

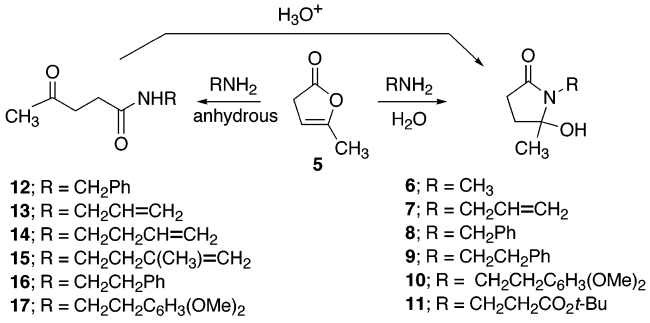


ion formation (**3**) by Lewis or protic acids followed by trapping with various tethered π-bonds returns the amido-alkylation products (**4**) in good to excellent yields (Scheme 1).[25] Often, the judicious choice of a Lewis acid can greatly influence the outcome of the cyclization reaction.[26] Our own interest in this area stems from an earlier observation made in our laboratory wherein cyclic carbinol amines were readily converted into α-trifluoromethylsulfonamido furans when treated with triflic anhydride.[27] Because initial studies into the cycloaddition chemistry of these aza-substituted furans were promising,[28] a more detailed investigation has been conducted. The results of these inquiries are reported herein.

Results and Discussion

Cyclic carbinol amides such as **6**−**11** were readily prepared by either exposing the corresponding *N*-alkyl-substituted succinimide to an organometallic reagent such as methylmagnesium iodide or by treating α-angelica lactone (**5**) with various alkylamines under aqueous conditions.[29] Interestingly, when lactone **5** was allowed to react with several primary amines under anhydrous conditions (i.e., THF), only the corresponding 4-oxopentanoic acid amides (**12**−**17**) were obtained (Scheme 2). Subjection of a typical γ-keto amide such as **12** to the aqueous acidic conditions resulted in the complete formation of cyclic carbinol amide **8** in 84% isolated yield. From these observations, it would seem as though the specific experimental conditions used control the equilibrium distribution of products. When

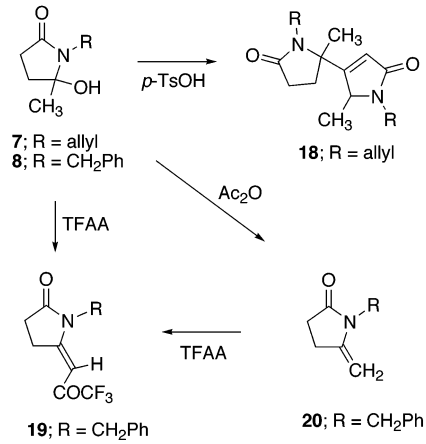
SCHEME 2



12; R = CH_2Ph
13; R = $CH_2CH{=}CH_2$
14; R = $CH_2CH_2CH{=}CH_2$
15; R = $CH_2CH_2C(CH_3){=}CH_2$
16; R = CH_2CH_2Ph
17; R = $CH_2CH_2C_6H_3(OMe)_2$

6; R = CH_3
7; R = $CH_2CH{=}CH_2$
8; R = CH_2Ph
9; R = CH_2CH_2Ph
10; R = $CH_2CH_2C_6H_3(OMe)_2$
11; R = $CH_2CH_2CO_2t$-Bu

SCHEME 3



the *N*-allyl-substituted pyrrolidinone **7** was treated with *p*-TsOH in benzene at 80 °C, dimer **18** was formed as the major product. On the other hand, reaction of the *N*-benzyl cyclic carbinol amide **8** with trifluoroacetic anhydride (TFAA) furnished enamide **19** in 79% yield, presumably by an elimination/acylation process. The structure of **19** was unequivocally established by a single-crystal X-ray analysis. The pathway suggested for the formation of **19** was supported by the finding that the reaction of **8** with acetic anhydride gave enamide **20** which, in turn, was converted to **19** upon treatment with TFAA (Scheme 3).

It is particularly interesting to note that when the γ-keto *N*-(3,4-dimethoxyphenethyl)amide **17** was treated with 10% HCl in THF, isoquinoline **23** was formed as the major product in 70% yield (Scheme 4). Under these conditions, *N*-acyliminium ion **22**, derived from the initially formed cyclic carbinol amide **21**, undergoes a well-established electrophilic aromatic substitution reaction with the tethered benzenoid ring. Since it is known that the nature of the Lewis acid can often influence the cyclization outcome,[26] we opted to study the conversion of **17** to **23** in greater detail using a variety of Lewis acids. It was during the course of these studies that we happened to discover that reaction of either the γ-keto amido system (i.e., **12**−**17**) or the isomeric cyclic carbinol amides (i.e., **6**−**11**) with triflic anhydride resulted in the clean formation of α-trifluoromethylsulfonamido furans (**28**−**35**). Sulfonamidofuran **35** was hydrolyzed to give the crystalline carboxylic acid **36** whose structure was unequivocally established by an X-ray crystal structure analysis. All of the other related sulfonamidofurans (i.e., **28**−**34**) showed comparable NMR signals (see Experi-

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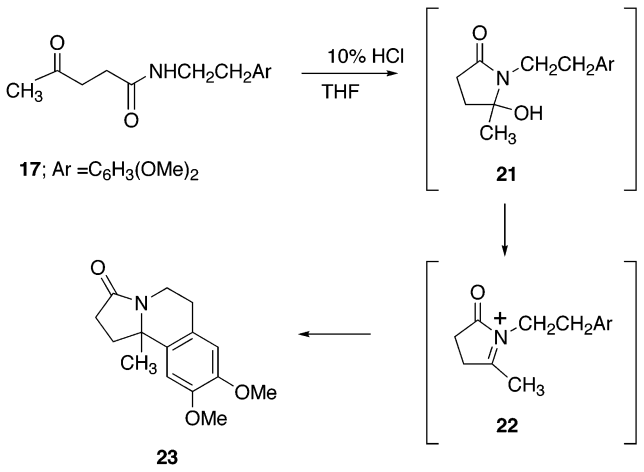
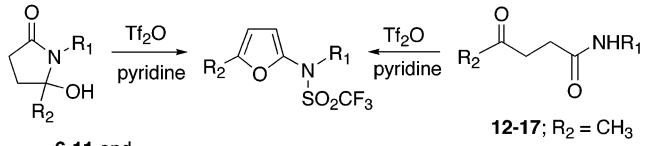
SCHEME 4



SCHEME 5



6-11 and

24; $R_1 = CH_3$; $R_2 = n\text{-}C_4H_9$
25; $R_1 = CH_3$; $R_2 = CH_2CH_2CH{=}CH_2$
26; $R_1 = CH_3$; $R_2 = (CH_2)_3CH{=}CH_2$
27; $R_1 = CH_3$; $R_2 = Ph$

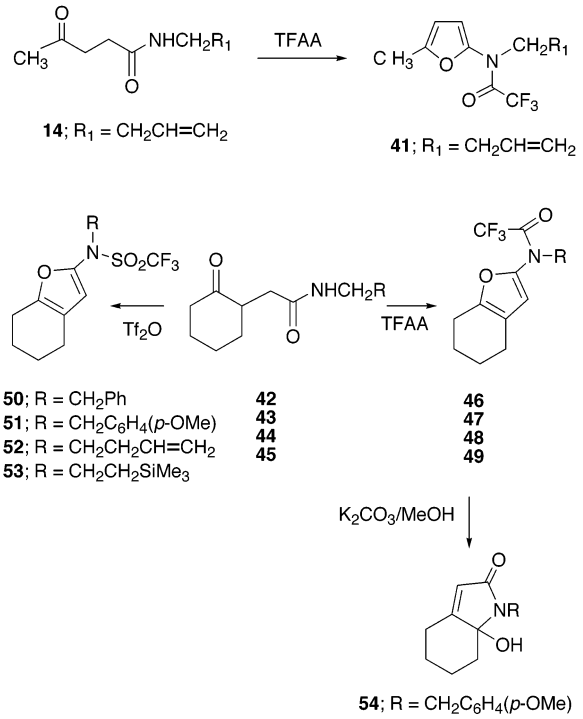
28; $R_1 = R_2 = CH_3$
29; $R_1 = CH_2CH{=}CH_2$; $R_2 = CH_3$
30; $R_1 = CH_2Ph$; $R_2 = CH_3$
31; $R_1 = CH_2CH_2CH{=}CH_2$; $R_2 = CH_3$
32; $R_1 = CH_2CH_2C(CH_3){=}CH_2$; $R_2 = CH_3$
33; $R_1 = CH_2CH_2Ph$; $R_2 = CH_3$
34; $R_1 = CH_2CH_2C_6H_3(OMe)_2$; $R_2 = CH_3$
35; $R_1 = CH_2CH_2CO_2t\text{-}Bu$; $R_2 = CH_3$
36; $R_1 = CH_2CH_2CO_2H$, $R_2 = CH_3$
37; $R_1 = CH_3$; $R_2 = n\text{-}C_4H_9$
38; $R_1 = CH_3$; $R_2 = CH_2CH_2CH{=}CH_2$
39; $R_1 = CH_3$; $R_2 = CH_2CH_2CH_2CH{=}CH_2$
40; $R_1 = CH_3$; $R_2 = Ph$

mental Section) to those exhibited by **35**. Cyclization to the furanyl sulfonamide systems also occurred with hydroxy pyrrolidinones **24**−**27** and Tf_2O. These cyclic carbinol amides afforded furans **37**−**40** wherein different substituent groups were incorporated into the 5-position of the heteroaromatic ring (Scheme 5).

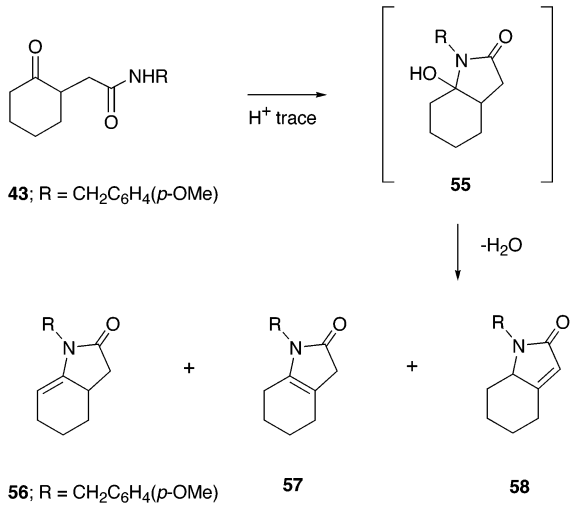
Cyclization of γ-keto amide **14**[30] to the furanyl system also took place when trifluoroacetic anhydride was used as the acylating agent. Both **14** and the related cyclic keto amides **42**−**45** underwent smooth cyclization with TFAA (or TF_2O) to furnish furans **41** and **46**−**53** in high yield (Scheme 6). Attempts to remove the trifluoroacetyl group of **47** under basic conditions with K_2CO_3/MeOH resulted in an oxidative rearrangement giving rise to carbinol amide **54** in modest yield.

We also attempted to prepare the trifluoroacetyl (**47**) or sulfonamido-substituted furan **51** starting from the isomeric cyclic carbinol amide **55** as was done with the previously described γ-keto amide system. However, all of our efforts to synthesize **55** from **43** only afforded a 2:1:4 mixture of hexahydroindolones **56**−**58** (Scheme 7), presumably derived by facile dehydration of **55**, and consequently we abandoned further studies with this system.

SCHEME 6



SCHEME 7



Trifluoromethanesulfonic (triflic) anhydride has been extensively used in synthetic organic chemistry as a reagent for the conversion of various compounds to the triflate functionality.[31] The reaction of secondary or tertiary amides with triflic anhydride is known to give rise to iminium and imino triflates, respectively. These salts are versatile reagents that can react with various N-, O-, and S-nucleophiles thereby transforming the amide group into other functionalities.[32] Iminium triflates

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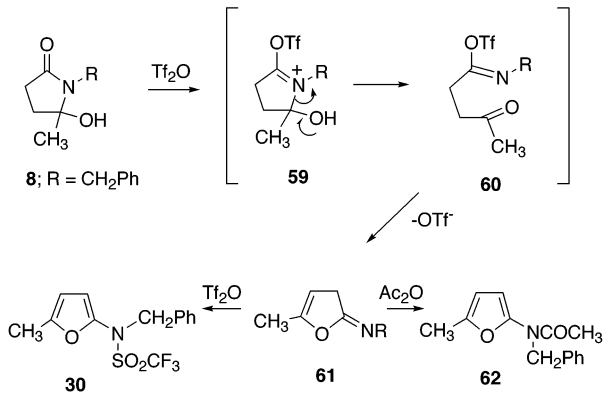
SCHEME 8

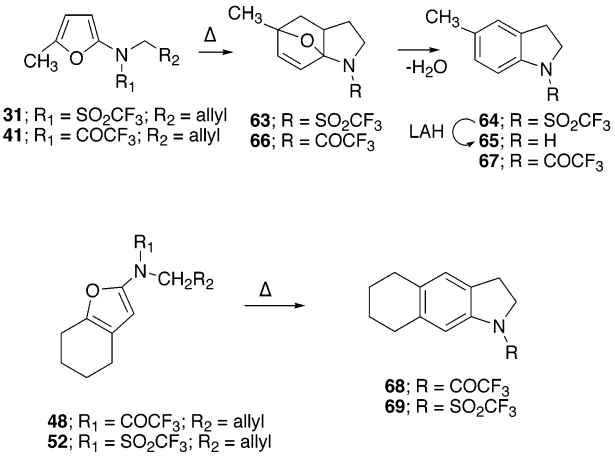


were originally used by Ghosez as precursors of ketiminium cations which can function as electrophilic substrates in [2 + 2]-cycloadditions.[33] It would seem that when a hydroxypyrrolidinone such as **8** is used as the tertiary amide, the resulting iminium ion (i.e., **59**) derived from the reaction of **8** with triflic anhydride undergoes a facile ring opening as a consequence of the adjacent hydroxyl group to produce imino triflate **60** (Scheme 8). Subsequent cyclization of this highly electrophilic imine[34] with the oxygen atom of the adjacent carbonyl group would result in the formation of imino dihydrofuran **61**. This transient species could react further with another equivalent of triflic anhydride to give the observed furan **30**. By using only 1 equiv of triflic anhydride and then adding a second equivalent of acetic anhydride, acetylation of **61** occurred in modest yield leading to the related *N*-acetyl furan **62**, thereby providing support for the proposed mechanism..

The indoline nucleus is a key structural feature found in a large number of alkaloids and related compounds, many of which exhibit potent pharmacological activity.[35] It is not surprising that numerous routes have been devised over the years to construct this important heterocyclic system.[36] New procedures that can selectively generate indolines with substituent groups in the aromatic ring would be of use to the medicinal community. During the course of our studies with these novel 2-sulfonamido furans, we found that rapid access to 5-substituted indolines could easily be achieved from thermolysis of the *N*-but-3-enyl furan **31** (or **41**).

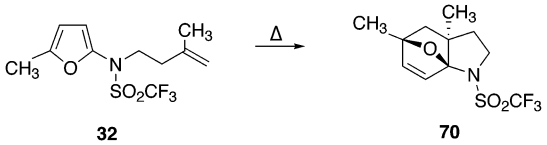
Previously, we had prepared 2-amido furans from either the *N*-alkylation of carbamates or the copper-catalyzed amidations of 2-bromo furans[37] and have shown that these heteroaromatic systems are useful substrates for [4 + 2]-cycloaddition chemistry.[38] We decided to

SCHEME 9



extend our earlier studies to include the IMDAF (intramolecular Diels–Alder of furans)[39] reaction of furans **31** and **41**. Thermolysis of furan **31** in toluene at 130 °C for 4 h furnished indoline **64** in 96% yield. More than likely, the reaction proceeds through the [4 + 2]-cycloadduct **63**, which readily loses water to produce **64** (Scheme 9). Reduction of **64** with $LiAlH_4$ furnished indoline **65** in 90% yield. A related set of reactions also occurred with the *N*-trifluoroacetyl furan **41** leading to indoline **67** via cycloadduct **66**. In a similar fashion, heating a sample of either **48** or **52** led to benzo[*f*]indoles **68** or **69** in 89% and 98% yield, respectively. The cycloaddition of sulfonamidofurans **31** and **52** proceeded three times faster than the corresponding trifluoroacetyl furans **41** and **48**. This is probably related to HOMO–LUMO considerations. It would seem as though the π-electron-withdrawing trifluoroacetyl group diminishes the ability of the electron pair on nitrogen to interact with the adjacent π-array of the heteroaromatic ring, thereby decreasing the overall rate of the HOMO-controlled reaction.

The [4 + 2]-cycloaddition was also carried out with a tethered alkene that possesses a substituent on the π-bond, and in this case, cycloadduct **70** could be isolated in 85% yield. The formation of a single diastereomer where the oxygen bridge and methyl groups are anti to each other is perfectly consistent with other reports in the literature for related furanyl systems possessing short tethers.[40] The Diels–Alder reaction prefers to occur where the sidearm of the tethered alkenyl group is oriented syn (exo) with respect to the oxygen bridge. This result is not so surprising since, in these mobile cycloaddition equilibria, the exo adducts are expected to be thermodynamically more favored.



In summary, an efficient method for the conversion of cyclic carbinol amides into α-trifluoromethylsulfonamido

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furans has been uncovered. The reaction takes place under very mild conditions with a wide set of representative hydroxy lactams. In certain cases, the resulting sulfonamidofurans have been utilized as substrates for the synthesis of indolines and related heterocyclic systems.

Experimental Section

General Procedure for the Preparation of Hydroxy Lactams. A solution of the appropriate amine (5.6 mmol) in water (0.5 mL) was added to α-angelica lactone (**5**) (0.5 g, 5.1 mmol), and the mixture was stirred at room temperature for 1 h. The mixture was concentrated under reduced pressure, and the resulting residue was purified by flash chromatography on silica gel using 20% acetone/$CHCl_3$ as the eluent.[41]

5-Hydroxy-1,5-dimethylpyrrolidin-2-one (6) was prepared in 92% yield from lactone **5** and a 30% aqueous solution of methylamine: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (s, 3H), 1.94−2.52 (m, 4H), 2.72 (s, 3H), and 4.60 (s, 1H). The spectral data of this compound is identical to that reported in the literature.[42]

1-Allyl-5-hydroxy-5-methylpyrrolidin-2-one (7) was prepared in 81% yield from lactone **5** and allylamine: IR (neat) 1673, 1454, 1409, and 1102 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 3H), 2.07−2.12 (m, 2H), 2.25−2.36 (m, 1H), 2.46−2.56 (m, 1H), 3.80−3.92 (m, 2H), 4.31 (s, 1H), 5.09 (dd, 1H, J = 10.0, 1.6 Hz), 5.16 (dd, 1H, J = 17.2, 1.6 Hz), and 5.80 (qt, 1H, J = 10.0, 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.0, 29.2, 35.0, 41.4, 90.5, 116.9, 134.6, and 174.9; HRMS calcd for $C_8H_{13}NO_2$ 155.0946, found 155.0950.

General Procedure for the Preparation of 4-Oxopentanoic Acid Amides. To a solution of lactone **5** (0.5 g, 5.1 mmol) in 10 mL of THF at 0 °C was added the appropriate amine (5.6 mmol) dropwise. The reaction was allowed to warm to room temperature and was stirred for 2 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel using 20% acetone/$CHCl_3$ as the eluent.

4-Oxopentanoic acid benzyl amide (12) was prepared in 74% yield from lactone **5** and benzylamine: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.10 (s, 3H), 2.45 (t, 2H, J = 5.5 Hz), 2.82 (t, 2H, J = 5.5 Hz), 4.40 (d, 2H, J = 6.0 Hz), 6.10 (brs, 1H), and 7.20−7.35 (m, 5H). The spectral data of this compound is identical to that reported in the literature.[43]

4-Oxopentanoic acid allyl amide (13) was prepared in 89% yield from lactone **5** and allylamine: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.19 (s, 3H), 2.45 (t, 2H, J = 6.4 Hz), 2.82 (t, 2H, J = 6.4 Hz), 3.84−3.88 (m, 2H), 5.12 (dd, 1H, J = 10.2, 1.4 Hz), 5.18 (dd, 1H, J = 17.2, 1.4 Hz), 5.82 (ddt, 1H, J = 17.2, 10.2, ,5.5 Hz), and 5.93 (brs, 1H). The spectral data of this compound is identical to that reported in the literature.[44]

1,1′-Diallyl-2,2′-dimethyl-1,2,3,4,1′,2′-hexahydro[2,3′]-bipyrrolyl-5,5′-dione (18). To a solution of *N*-allyl pyrrolidinone **7** (0.05 g, 0.3 mmol) in benzene (2 mL) was added 0.006 g (0.03 mmol) of *p*-TsOH. The mixture was heated at reflux for 5 h, allowed to cool, and concentrated under reduced pressure. After purification by flash chromatography on silica gel using 25% acetone/$CHCl_3$ as the eluent, 0.014 g of **18** (33% yield) was obtained as a yellow oil which consisted of a mixture of diastereomers: IR (neat) 1684, 1675, 1431, 1401, 1329 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 and 1.22 (d, 3H, J = 7.0 Hz), 1.60 (s, 3H), 1.84−1.97 (m, 1H), 2.29−2.44 (m, 3H), 3.44−3.67 (m, 2H), 3.87−4.17 (m, 2H), 4.34−4.42 (m, 1H), 5.03−5.18 (m, 4H), 5.67−5.84 (m, 2H), and 6.58 and 6.55 (t, 1H, J = 2.0 Hz); ^{13}C NMR (100 MHz $CDCl_3$) δ 16.8, 24.6, 24.7, 29.6, 29.7, 32.3, 32.4, 42.7, 43.2, 55.2, 62.9, 63.1, 116.6, 117.9, 133.6, 134.5, 140.6, 142.37, 142.41, 168.3, 168.4, 175.48, and 175.52; HRMS calcd for $C_{16}H_{22}N_2O_2$ 274.1681, found 274.1670.

1-Benzyl-5-(3,3,3-trifluoro-2-oxopropylidene)pyrrolidin-2-one (19). To a solution of cyclic carbinol amide **8** (0.1 g, 0.5 mmol) in CH_2Cl_2 (5 mL) at −78 °C was added pyridine (0.4 mL, 4.9 mmol) followed by TFAA (0.15 mL, 1.1 mmol). The mixture was allowed to warm to room temperature and was stirred for 10 min. The reaction was quenched with water (10 mL), and the organic layer was separated. The aqueous was extracted twice with $CHCl_3$, and the combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to give **19** (0.11 g, 79%) as a white solid: mp 81−82 °C; IR (KBr) 1754, 1692, 1569, 1417, and 1290 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68−2.71 (m, 2H), 3.30−3.36 (m, 2H), 4.77 (s, 2H), 5.89 (s, 1H), 7.20−7.25 (m, 2H), and 7.29−7.36 (m, 3H); ^{13}C NMR (100 MHz $CDCl_3$) δ 26.9, 27.5, 44.8, 92.3, 116.5 (q, J = 289.8 Hz), 127.6, 128.5, 129.2, 134.1, 168.1, 177.5, and 178.9 (q, J = 33.3 Hz). Anal. Calcd for $C_{14}H_{12}F_3NO_2$: C, 59.34; H, 4.27; N, 4.95. Found: C, 59.55; H, 4.26; N, 4.97.

***N*-Benzyl-5-methylenepyrrolidin-2-one (20).** To a solution of hydroxy pyrrolidinone **8** (0.1 g, 0.5 mmol) in CH_2Cl_2 (5 mL) was added pyridine (0.4 mL, 4.9 mmol) followed by Ac_2O (0.1 mL, 1.1 mmol). The mixture was heated at reflux for 16 h, cooled to room temperature, diluted with $CHCl_3$, and washed with water. The organic layer was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue showed the following spectral properties which are identical to those reported in the literature:[45] ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52−2.65 (m, 2H), 2.67−2.80 (m, 2H), 4.12 (d, 1H, J = 1.8 Hz), 4.19 (d, 1H, J = 1.8 Hz), 4.68 (s, 2H), and 7.20−7.39 (m, 5H). Treating a sample of **20** with TFAA as described above produced **19** in 85% yield.

General Procedure for the Preparation of *N*-Alkenyl-Substituted Sulfonamido Furans. To a solution of either the cyclic carbinol amide or the 4-oxopentanoic acid amide (5 mmol) in 5 mL of CH_2Cl_2 at −78 °C was added pyridine (25 mmol) followed by triflic anhydride (Tf_2O) (10 mmol). The reaction was allowed to warm to room temperature over 30 min and was stirred for 10 min. Water was added and the organic layer was separated. The aqueous layer was extracted with chloroform and the combined organic phase was washed with water and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel using 20% ether/hexane as the eluent.

***C,C,C*-Trifluoro-*N*-methyl-*N*-(5-methyl-furan-2-yl)methanesulfonamide (28)** was prepared in 60% yield from cyclic carbinol amide **6**: IR (neat) 1619, 1593, 1400, 1231, 1196, and 1128 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 3.40 (s, 3H), 5.97 (dd, 1H, J = 3.2 and 1.0 Hz), and 6.18 (d, 1H, J = 3.2 Hz); ^{13}C NMR (100 MHz $CDCl_3$) δ 13.9, 40.1, 107.4, 107.6, 120.2 (q, J = 322.4 Hz), 142.0, and 151.5; HRMS calcd for $C_7H_8F_3NO_3S$ 243.0177, found 243.0179.

***N*-Allyl-*C,C,C*-trifluoro-*N*-(5-methylfuran-2-yl)methanesulfonamide (29)** was prepared in 83% yield from **7** (or in 81% yield from **13**): IR (neat) 1616, 1559, 1400, 1228, 1199, 1133, and 1055 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 4.27 (d, 2H, J = 6.7), 5.19−5.23 (m, 1H), 5.24−5.26 (m, 1H), 5.83 (qt, 1H, J = 10.2, 6.7 Hz), 5.97 (dd, 1H, J = 3.2, 1.0 Hz), and 6.17 (d, 1H, J = 3.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$)

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δ 13.9, 55.5, 107.4, 109.7, 120.1 (q, J = 321.7 Hz), 120.9, 131.2, 140.1, and 151.9; HRMS calcd for $C_9H_{10}F_3NO_3S$ 269.0333, found 269.0338.

***N*-Benzyl-*C,C,C*-trifluoro-*N*-(5-methylfuran-2-yl)methanesulfonamide (30)** was prepared in 60% yield from **8** (or in 79% yield from **12**): IR (neat) 1619, 1497, 1404, 1209, 1141, and 1027 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3H), 4.82 (s, 2H), 5.85 (dd, 1H, J = 3.2, 1.0 Hz), 5.91 (d, 1H, J = 3.2 Hz), 7.20−7.27 (m, 2H), and 7.29−7.33 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 56.5, 107.4, 110.2, 120.2 (q, J = 321.1 Hz), 128.8, 129.1, 134.3, 139.7, and 151.8. Anal. Calcd for $C_{13}H_{12}F_3NO_3S$: C, 48.90; H, 3.79; N, 4.39. Found: C, 49.12; H, 3.85; N, 4.42.

***N*-But-3-enyl-*C,C,C*-trifluoro-*N*-(5-methylfuran-2-yl)-methanesulfonamide (31)** was prepared in 75% yield from **14**: IR (neat) 1619, 1558, 1402, 1230, 1196, 1131, and 1071 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 2.32 (q, 2H, J = 7.0 Hz), 3.74 (t, 2H, J = 7.0 Hz), 5.07−5.09 (m, 1H), 5.10−5.12 (m, 1H), 5.65−5.76 (m, 1H), 5.98 (dd, 1H, J = 2.8, 0.8 Hz), and 6.19 (d, 1H, J = 2.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 32.9, 52.1, 107.5, 109.9, 118.3, 120.1 (q, J = 321.7), 133.3, 139.9, and 152.0. Anal. Calcd for $C_{10}H_{12}F_3NO_3S$: C, 42.40; H, 4.27; N, 4.94. Found: C, 42.41; H, 4.33; N, 4.89.

***N*-(3-Methylbut-3-enyl)-*C,C,C*-trifluoro-*N*-(5-methylfuran-2-yl)methanesulfonamide (32)** was prepared in 62% yield from **15**: IR (neat) 1619, 1559, 1401, 1232, 1196, 1144, and 1023 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72 (s, 3H), 2.27 (d, 3H, J = 1.0 Hz), 2.28 (t, 2H, J = 7.4 Hz), 3.80 (dd, 2H, J = 7.4, 7.4 Hz), 4.71 (s, 1H), 4.83 (s, 1H), 5.99 (dd, 1H, J = 3.1, 1.0 Hz), and 6.21 (d, 1H, J = 3.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.4, 36.8, 51.1, 107.5, 109.9, 113.2, 120.2 (q, J = 322.2 Hz), 140.0, 141.0, and 151.9. Anal. Calcd for $C_{11}H_{14}F_3NO_3S$: C, 44.44; H, 4.75; N, 4.71. Found: C, 44.16; H, 4.69; N, 4.76.

***N*-But-3-enyl-2,2,2-trifluoro-*N*-(5-methylfuran-2-yl)acetamide (41).** To a cooled solution of **14** (0.1 g, 0.6 mmol) at −78 °C in freshly distilled CH_2Cl_2 (5 mL) was added pyridine (0.5 mL, 5.9 mmol) followed by TFAA (0.18 mL, 1.3 mmol). The mixture was allowed to warm to room temperature over 30 min and was stirred for an additional 10 min. Water was added, and the organic layer was separated. The aqueous layer was extracted with chloroform, and the combined organic phase was washed with water and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel using 20% ether/hexane as the eluent. Furan **41** was obtained in 76% yield (0.11 g) as a colorless oil: IR (neat) 1722, 1622, 1415, 1212, 1158, and 1023 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 3H), 2.29−2.38 (m, 2H), 3.72 (dd, 2H, J = 7.6, 7.6 Hz), 5.02−5.12 (m, 2H), 5.66−5.79 (m, 1H), 5.96 (dd, 1H, J = 3.2, 1.2 Hz), and 6.08 (d, 1H, J = 3.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 31.8, 49.3, 107.1, 108.1, 116.2 (q, J = 286.8 Hz), 117.7, 134.2, 142.0, 151.2, and 158.0 (q, J = 35.1). Anal. Calcd for $C_{11}H_{12}F_3NO_2$: C, 53.44; H, 4.89; N, 5.67. Found: C, 53.16; H, 4.84; N, 5.62.

General Procedure for the Preparation of *N*-Alkyl-2-(2-oxocyclohexyl)acetamides. To a solution of 2-(2-oxocyclohexyl)acetic acid[46] (1.0 g, 6.4 mmol) and the appropriate amine (7.0 mmol) in CH_2Cl_2 (15 mL) was added EDCI (1.4 g, 7.0 mmol) in one portion, followed by DMAP (0.05 g). The mixture was stirred at room temperature for 2 h and was diluted with water. The organic phase was separated, and the aqueous phase was extracted with $CHCl_3$. The combined organic phase was washed with 1 N HCl and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (10% acetone/$CHCl_3$).

***N*-Benzyl-2-(2-oxocyclohexyl)acetamide (42)** was obtained as a white solid in 80% yield: mp 110−112 °C; IR (KBr) 1694, 1637, 1547, 1453, and 1413 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (qd, 1H, J = 9.7, 3.8 Hz), 1.60−1.46 (m, 1H), 1.65 (qt, 1H, J = 13.0, 9.7 Hz). 1.75−1.84 (m, 1H), 2.01 (dd, 1H, J = 14.6, 5.4 Hz), 2.14−2.05 (m, 2H), 2.31 (d, 1H, J = 5.7 Hz), 2.21−2.34 (m, 1H), 2.58 (dd, 1H, J = 14.6, 7.3 Hz), 2.82−2.92 (m 1H), 4.27−4.39 (m, 2H), 6.53 (brs, 1H), and 7.16−7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.3, 28.0, 34.4, 36.6, 42.0, 43.4, 47.7, 127.3, 127.6, 128.6, 138.5, 171.9, and 212.6. Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.41; H, 7.85; N, 5.71.

***N*-(4-Methoxybenzyl)-2-(2-oxocyclohexyl)acetamide (43)** was obtained as a pale yellow solid in 86% yield: mp 114−116 °C; IR (KBr) 1708, 1693, 1637, 1512, 1248, 1175, and 1036 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (dq, 1H, J = 12.7 and 3.8 Hz), 1.55−1.92 (m, 3H), 2.07 (dd, 1H, J = 14.4, 4.8 Hz), 2.09−2.23 (m, 2H), 2.30−2.45 (m, 2H), 2.62 (dd, 1H, J = 14.4, 7.7 Hz), 2.89−3.01 (m, 1H), 3.79 (s, 3H), 4.35 (qd, 2H, J = 10.6, 5.3 Hz), 6.03 (brs, 1H), 6.82−6.90 (m, 2H), and 7.17−7.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.4, 28.2, 34.7, 36.9, 42.2, 43.2, 47.9, 55.4, 114.2, 129.2, 130.6, 159.1, 171.8, and 212.7. Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.74; H, 7.67; N, 5.07.

***N*-But-3-enyl-2-(2-oxocyclohexyl)acetamide (44)** was obtained as a colorless oil in 45% yield: IR (neat) 1705, 1697, 1627, 1510, and 1036 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (qd, 1H, J = 12.7, 3.8 Hz), 1.51−1.90 (m, 4H), 2.01 (dd, 1H, J = 14.4, 5.0 Hz), 2.06−2.40 (m, 5H), 2.58 (dd, 1H, J = 14.4, 7.7 Hz), 2.82−2.94 (m, 1H), 3.28 (q, 2H, J = 6.5 Hz), 5.03−5.12 (m, 2H), 5.67−5.81 (m, 1H), and 5.90 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.5, 28.2, 33.9, 34.7, 37.0, 38.6, 42.3, 48.1, 117.3, 135.5, 171.9, and 212.8; HRMS calcd for $C_{12}H_{19}NO_2$ [M + H]$^+$ 210.1494, found 210.1497.

General Procedure for the Preparation of *N*-Alkyltetrahydrobenzofuranyltrifluoroacetamides. To a solution of the appropriate ketoamide (1.2 mmol) in freshly distilled CH_2Cl_2 (12.0 mL) was added pyridine (12.0 mmol) followed by TFAA (2.5 mmol). The reaction mixture was stirred at room temperature for 6 h. The solution was quenched by the addition of water, and the organic layer was separated. The aqueous layer was extracted with chloroform, and the combined organic phase was washed with water and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel using 20% ether/hexane as the eluent.

2,2,2-Trifluoro-*N*-benzyl-*N*-(4,5,6,7-tetrahydrobenzofuran-2-yl)acetamide (46) was obtained in 77% yield as a colorless oil: IR (neat) 1716, 1577, 1210, and 1161 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.66−1.90 (m, 4H), 2.30−2.39 (m, 2H), 2.49−2.58 (m, 2H), 4.83 (s, 2H), 5.81 (s, 1H), and 7.24−7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 22.9, 23.0, 54.0, 108.2, 116.3 (q, J = 286.8 Hz), 118.2, 128.2, 128.7, 128.9, 135.4, 141.4, 149.8, and 157.9 (q, J = 35.5 Hz); HRMS calcd for $C_{17}H_{16}F_3NO_2$ 323.1133, found 323.1138.

2,2,2-Trifluoro-*N*-(4-methoxybenzyl)-*N*-(4,5,6,7-tetrahydrobenzofuran-2-yl)acetamide (47) was obtained in 79% yield as a colorless oil: IR (neat) 1716, 1513, 1251, 1209, and 1166 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.66−1.75 (m, 2H), 1.78−1.87 (m, 2H), 2.30−2.37 (m, 2H), 2.48−2.55 (m, 2H), 3.78 (s, 3H), 4.73 (s, 2H), 5.76 (s, 1H), 6.80−6.86 (m, 2H), and 7.15−7.22 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 22.9, 23.0, 53.5, 55.4, 108.2, 114.0, 116.2 (q, J = 288.4 Hz), 118.1, 127.6, 130.5, 141.4, 149.7, 157.8 (q, J = 35.1 Hz), and 159.6. Anal. Calcd. for $C_{18}H_{18}F_3NO_3$: C, 61.19; H, 5.13; N, 3.96. Found: C, 61.35; H, 5.28; N, 4.04.

2,2,2-Trifluoro-*N*-(but-3-enyl)-*N*-(4,5,6,7-tetrahydrobenzofuran-2-yl)acetamide (48) was obtained in 75% yield as a colorless oil: IR (neat) 1713, 1577, 1205, and 1158 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.68−1.88 (m, 4H), 2.31−2.42 (m, 4H), 2.53 (t, 2H, J = 6.0 Hz), 3.71 (t, 2H, J = 7.3 Hz), 5.03−5.13 (m, 2H), 5.50−5.68 (m, 1H), and 5.99 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 22.9, 23.0, 23.1, 31.8, 49.3, 108.0, 116.2 (q, J = 288.4 Hz), 117.6, 118.2, 134.2, 141.5, 149.8, and

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157.8 (q, J = 35.9 Hz). Anal. Calcd for $C_{14}H_{16}F_3NO_2$: C, 58.53; H, 5.61; N, 4.88. Found: C, 58.42; H, 5.63; N, 4.93.

General Procedure for the Preparation of *N*-Alkyltetrahydrobenzofuranyltrifluoromethanesulfonamides. To a solution of the appropriate keto amide (0.8 mmol) in freshly distilled CH_2Cl_2 (10 mL) was added pyridine (8.2 mmol) followed by Tf_2O (1.7 mmol). The reaction mixture was stirred at room temperature for 6 h and was then quenched by the addition of water. The organic layer was separated, and the aqueous layer was extracted with chloroform. The organic phase was washed with water and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel using 20% ether/hexane as the eluent.

***N*-Benzyl-*C,C,C*-trifluoro-*N*-(4,5,6,7-tetrahydrobenzofuran-2-yl)methanesulfonamide (50)** was obtained in 93% yield as a colorless oil: IR (neat) 1570, 1406, 1221, 1145, and 1029 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58−1.65 (m, 2H), 1.70−1.77 (m, 2H), 2.21−2.26 (m, 2H), 2.41−2.46 (m, 2H), 4.77 (s, 2H), 5.79 (s, 1H), and 7.18−7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 22.8, 23.0, 56.4, 109.9, 118.5, 120.2 (q, J = 323.6 Hz), 128.7, 128.8, 129.0, 134.5, 139.3, and 150.5; HRMS calcd for $C_{16}H_{16}F_3NO_3S$ 359.0803, found 359.0793.

***N*-(4-Methoxybenzyl)-*C,C,C*-trifluoro-*N*-(4,5,6,7-tetrahydrobenzofuran-2-yl)methanesulfonamide (51)** was obtained in 81% yield as a colorless oil: IR (neat) 1614, 1398, 1224, 1139, and 1030 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.60−1.70 (m, 2H), 1.76−1.84 (m, 2H), 2.26−2.34 (m, 2H), 2.46−2.55 (m, 2H), 3.78 (s, 3H), 4.77 (s, 2H), 5.84 (s, 1H), 6.81−6.87 (m, 2H), and 7.13−7.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 22.8, 23.0, 55.3, 56.1, 110.0, 114.1, 118.4, 120.2 (q, J = 323.5 Hz), 126.5, 130.5, 139.2, 150.4, and 159.9; HRMS calcd for $C_{17}H_{18}F_3NO_4S$: 389.0909, found 389.0913.

***N*-But-3-enyl-*C,C,C*-trifluoro-*N*-(4,5,6,7-tetrahydrobenzofuran-2-yl)methanesulfonamide (52)** was obtained in 80% yield as a colorless oil: IR (neat) 1570, 1403, 1224, 1196, and 1133 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.69−1.77 (m, 2H), 1.80−1.87 (m, 2H), 2.31−2.43 (m, 4H), 2.54 (t, 2H, J = 6.0 Hz), 3.74 (t, 2H, J = 7.3 Hz), 5.08−5.16 (m, 2H), 5.66−5.79 (m, 1H), and 6.11 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 22.8, 22.9, 23.1, 33.0, 52.1, 109.8, 118.2, 118.6, 120.2 (q, J = 323.5 Hz), 133.4, 139.4, and 150.6. Anal. Calcd for $C_{13}H_{16}F_3NO_3S$: C, 48.29; H, 4.99; N, 4.33. Found: C, 48.51; H, 4.96; N, 4.30.

7a-Hydroxy-1-(4-methoxybenzyl)-1,4,5,6,7,7a-hexahydroindol-2-one (54). To a solution of furan **47** (0.28 g, 0.8 mmol) in MeOH (5 mL) was added a solution of K_2CO_3 (0.55 g, 3.96 mmol) in 5 mL of water. The mixture was heated at reflux for 2 h, cooled to room temperature, diluted with water, and extracted with $CHCl_3$. The combined organic phase was washed with brine, dried over MgSO4, filtered, and concentrated under reduced pressure. The crude product was purified by recrystallization from ether/hexane to give **54** (0.04 g, 19%) as a white solid: mp 156−157 °C; IR (KBr) 1670, 1512, and 1245 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91−1.06 (m, 1H), 1.12−1.30 (m, 1H), 1.50−1.75 (m, 2H), 1.87−2.00 (m, 1H), 2.01−2.12 (m, 1H), 2.41 (tdd, 1H, J = 13.4, 5.5, 2.2 Hz), 2.55−2.65 (m, 1H), 3.76 (s, 3H), 3.79 (brs, 1H), 4.24 (d, 1H, J = 15.1 Hz), 4.64 (d, 1H, J = 15.1 Hz), 5.61 (d, 1H, J = 1.9 Hz), 6.76−6.83 (m, 2H), and 7.20−7.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 26.6, 27.7, 38.5, 41.2, 55.4, 89.3, 113.9, 117.4, 129.6, 131.4, 158.9, 163.9, and 170.4. Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 69.96; H, 7.31; N, 4.95.

1-(4-Methoxybenzyl)-1,3,3a,4,5,6-hexahydroindol-2-one (56). A solution of γ-keto amide **43** (1.0 g, 3.9 mmol) in xylene (2.0 mL) with a trace of *p*-TsOH was heated at 180 °C for 2 h in a sealed tube. The reaction was allowed to cool to room temperature and the mixture was subjected to a flash chromatography on silica gel using 50% ether/hexane as the eluent. The first fraction obtained from the column contained 0.25 g (25%) of **56** as a yellow oil: IR (neat) 1719, 1680, 1513, 1401, 1322, 1245, and 1176 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26−1.38 (m, 1H), 1.44−1.58 (m, 1H) 1.80−1.90 (m, 1H), 1.99−2.14 (m, 3H), 2.17 (dd, 1H, J = 15.9, 9.8 Hz), 2.60 (dd, 1H, J = 15.9, 8.9 Hz), 2.62−2.74 (m, 1H), 3.77 (s, 3H), 4.40 (d, 1H, J = 15.2 Hz), 4.69 (d, 1H, J = 15.2 Hz), 4.78 (q, 1H, J = 3.2 Hz), 6.80−6.85 (m, 2H), and 7.14−7.19 (m, 2H);^{13}C NMR (100 MHz, $CDCl_3$) δ 22.5, 23.3, 28.1, 34.9, 37.0, 42.9, 55.4, 98.0, 114.0, 128.9, 129.0, 142.0, 159.0, and 174.8.

The second fraction (0.12 g, 12%) obtained from the column was a pale yellow oil whose structure was assigned as 1-(4-methoxybenzyl)-1,3,4,5,6,7-hexahydroindol-2-one (**57**): IR (neat) 1700, 1673, 1512, 1398, and 1248 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.56−1.70 (m, 4H), 1.98−2.10 (m, 4H), 2.92−3.00 (m, 2H), 3.76 (s, 3H), 4.54 (s, 2H), 6.79−6.85 (m, 2H), and 7.12−7.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 22.5, 22.7, 23.5, 39.8, 42.8, 55.4, 111.1, 114.1, 128.7, 130.3, 137.5, 158.9, and 177.2.

The third fraction (0.4 g, 40%) isolated from the column was a colorless oil whose structure was assigned as 1-(4-methoxybenzyl)-1,4,5,6-tetrahydroindol-2-one (**58**): IR (neat) 1685, 1611, 1512, 1444, and 1247 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88−0.98 (m, 1H), 1.14−1.31 (m, 2H) 1.66−1.78 (m, 1H), 1.84−1.94 (m, 1H), 2.01−2.12 (m, 1H), 2.20−2.30 (m, 1H), 2.60−2.68 (m, 1H), 3.49 (dd, 1H, J = 11.4 and 6.0 Hz), 3.71 (s, 3H), 4.05 (d, 1H, J = 15.2 Hz), 4.85 (d, 1H, J = 15.2 Hz), 5.70 (s, 1H), 6.74−6.80 (m, 2H), and 7.07−7.13 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.0, 27.5, 28.4, 33.3, 42.9, 55.2, 61.2, 113.9, 118.0, 129.1, 130.0, 158.9, 162.4, and 171.4.

***N*-Benzyl-*N*-(5-methylfuran-2-yl)acetamide (62).** A mixture of cyclic carbinol **8** (0.1 g, 0.5 mmol) and pyridine (0.4 mL, 5.0 mmol) in CH_2Cl_2 (5.0 mL) was cooled at −78 °C. To this solution was added Tf_2O (0.07 mL, 0.53 mmol), the mixture was allowed to stir for 30 min, and then Ac_2O (0.07 mL, 0.75 mmol) was added. The reaction mixture was stirred at room temperature overnight. The mixture was partitioned between water and $CHCl_3$. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel using 25% ether/hexane as the eluent. Furan **62** (0.027 g, 25%) was obtained as a colorless oil: IR (neat) 1681, 1618 1571, 1380, 1289, 1208, and 1195 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.22 (d, 3H, J = 1.0 Hz), 4.75 (s, 2H), 5.70 (d, 1H, J = 1.0 Hz), 5.87 (dd, 1H, J = 3.2 and 1.0 Hz), and 7.20−7.29 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 22.1, 51.6, 105.8, 106.9, 127.5, 128.5, 128.6, 137.5, 146.9, 149.8, and 171.9.

5-Methyl-1-trifluoromethanesulfonyl-2,3-dihydro-1*H*-indole (64). A solution of furan **31** (0.27 g, 0.95 mmol) in toluene (5 mL) was heated in a sealed tube at 130 °C for 4 h. The mixture was allowed to cool to room temperature and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel to give **64** (0.26 g, 96%) as a colorless oil: IR (neat) 1487, 1402, 1228, 1189, 1148, and 1059 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H), 3.17 (t, 2H, J = 8.3 Hz), 4.20 (t, 2H, J = 8.3 Hz), 7.01 (dd, 1H, J = 8.3 and 1.0 Hz), 7.05 (d, 1H, J = 0.6 Hz), and 7.30 (d, 1H, J = 8.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 28.2, 51.6, 114.4, 120.5 (q, J = 323.2 Hz), 126.3, 128.7, 131.5, 135.1, and 137.5. Anal. Calcd for $C_{10}H_{10}F_3NO_2S$: C, 45.28; H, 3.80; N, 5.28. Found: C, 45.52; H, 3.90; N, 5.32.

5-Methyl-2,3-dihydro-1*H*-indole (65). To a solution of the above dihydroindole **64** (0.2 g, 0.75 mmol) in ether (7.0 mL) was added $LiAlH_4$ (0.09 g, 2.26 mmol) in one portion. The reaction was heated at reflux for 6 h, allowed to cool to 25 °C, and slowly quenched by the addition of $Na_2SO_4 \cdot 10H_2O$ until a white precipitate appeared. The mixture was filtered, and the precipitate was washed with ether. The combined filtrate was concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel to give indoline **64** as a pale yellow oil in 90% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.23 (s, 3H), 3.01 (t, 2H, J = 8.3 Hz), 3.56 (t, 2H, J = 8.3 Hz), 4.34 (s, 1H), 6.65 (d, 1H, J = 7.8 Hz), 6.86 (d, 1H,

J = 7.8 Hz), and 6.97 (s, 1H). The spectral data of this compound is identical to that reported in the literature.[47]

2,2,2-Trifluoro-1-(5-methyl-2,3-dihydroindol-1-yl)ethanone (67). A solution of furan **41** (0.12 g, 0.95 mmol) in toluene (2 mL) was heated in a sealed tube at 130 °C for 20 h. The mixture was allowed to cool to room temperature, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel to give **67** (0.11 g, 91%) as a white solid: mp 85−86 °C; IR (KBr) 1686, 1487, 1442, 1252, 1203, 1141, and 1071 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 2H), 3.21 (t, 2H, J = 8.3 Hz), 4.22−4.29 (m, 2H), 7.04−7.09 (m, 2H), and 8.07 (d, 1H, J = 8.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 28.5, 48.1, 116.0 (q, J = 288.1 Hz), 117.8, 125.7, 128.5, 131.9, 136.0, 139.5, and 154.0 (q, J = 35.4 Hz). Anal. Calcd for $C_{11}H_{10}F_3NO$: C, 57.64; H, 4.40; N, 6.11. Found: C, 57.61; H, 4.29; N, 5.99.

2,2,2-Trifluoro-1-(2,3,5,6,7,8-hexahydrobenzo[*f*]indol-1-yl)ethanone (68). A solution of furan **48** (0.2 g, 0.7 mmol) in toluene (7.0 mL) was heated in a sealed tube at 130 °C for 12 h. The mixture was allowed to cool to room temperature, and the solvent was removed under reduced pressure. The crude residue was purified by flash chromatography on silica gel to give 0.17 g (89%) of **68** as a white solid: mp 117−118 °C; IR (KBr) 1684, 1487, 1441, 1251, 1192, and 1137 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.75−1.84 (m, 4H), 2.76 (brd, 4H, J = 16.2 Hz), 3.17 (t, 2H, J = 8.3 Hz), 4.22 (dt, 2H, J = 8.3, 1.0 Hz), 6.96 (s, 1H), and 7.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.3, 28.1, 29.5, 29.9, 48.1, 116.3 (q, J = 287.6 Hz), 118.3, 125.3, 129.1, 135.0, 136.8, 139.4, and 153.9 (q, J = 37.4 Hz). Anal. Calcd for $C_{14}H_{14}F_3NO$: C, 62.45; H, 5.24; N, 5.20. Found: C, 62.46; H, 5.36; N, 5.27.

1-Trifluoromethanesulfonyl-2,3,5,6,7,8-hexahydro-1*H*-benzo[*f*]indole (69). A solution of furan **52** (0.2 g, 0.6 mmol) in toluene (6.0 mL) was heated in a sealed tube at 130 °C for 12 h. The mixture was allowed to cool to room temperature, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel to give **69** (0.19 g, 98% yield) as a white solid: mp 82−83 °C; IR (KBr) 1495, 1390, 1253, 1195, 1148, and 1062 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.77−1.82 (m, 4H), 2.74 (brd, 4H, J = 17.6 Hz), 3.15 (t, 2H, J = 8.1 Hz), 4.18 (t, 2H, J = 8.1 Hz), 6.96 (s, 1H), and 7.15 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2, 23.3, 27.9, 29.3, 29.9, 51.7, 114.8, 120.5 (q, J = 324.0 Hz), 126.1, 128.7, 134.3, 137.2, and 137.5. Anal. Calcd for $C_{13}H_{14}F_3NO_2S$: C, 51.14; H, 4.62; N, 4.59. Found: C, 51.20; H, 4.61; N, 4.63.

5,7-Dimethyl-2-trifluoromethanesulfonyl-10-oxa-2-aza-tricyclo[5.2.1.0^{1,5}]dec-8-ene (70). A solution of furan **32** (0.13 g, 0.44 mmol) in toluene (4 mL) was heated in a sealed tube at 130 °C for 36 h. The mixture was allowed to cool to room temperature, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel to give **70** (0.06 g, 46%) as a white solid: mp 100−102 °C; IR (KBr) 1398, 1248, 1183, 1146, and 1107 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (s, 3H), 1.31 (d, 1 H, J = 11.4 Hz), 1.54 (s, 3H), 1.83 (d, 1H, J = 11.4 Hz), 1.94 (ddd, 1H, J = 12.4, 7.0, 1.2 Hz), 2.21 (q, 1H, J = 11.4 Hz), 3.86−4.00 (m, 2H), 6.24 (d, 1H, J = 5.7 Hz), and 6.48 (d, 1H, J = 5.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 21.7, 36.3, 47.8, 52.0, 52.6, 85.4, 105.7, 120.0 (q J = 322.7 Hz), 132.3, and 139.0. Anal. Calcd for $C_{11}H_{14}F_3NO_3S$: C, 44.44; H, 4.75; N, 4.71. Found: C, 44.32; H, 4.76; N, 4.67.

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Supporting Information Available: ^1H and ^{13}C NMR spectra for new compounds lacking elemental analyses together with an ORTEP drawing for compounds **19** and **36**. Preparation and characterization of compounds **9**−**11**, **14**−**16**, **33**, **35**−**40**, **45**, **49**, and **53**. This material is available free of charge via the Internet at http://pubs.acs.org.

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