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A Route to Benzo-Annelated δ-Sultams through Michael Cyclization

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Keywords: Heterocycles / Sultams / Fused-ring systems / Michael addition / Cyclization

A new approach to benzo-annelated δ-sultams containing an aryl–nitrogen bond is described. The method, which involves the intramolecular Michael cyclization of *tert*-butyl *ortho*-[*N*-(methoxycarbonylmethyl)sulfonylamino]cinnamates, allows the synthesis of secondary sultams as well as their tertiary analogues and bridged tricyclic derivatives efficiently and diastereoselectively.

Introduction

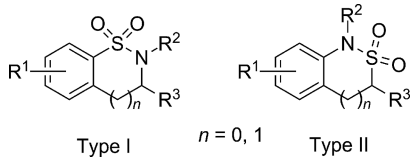
Sultams have shown a wide spectrum of biological activities, such as anti-inflammatory,[1] antiviral (HIV-1 in vitro),[2] antileukemic,[3] and antimicrobial[4] activities to name just a few. Therefore, a simple and convenient method for their synthesis has been required in order to access all that sultams have to offer. Currently, methods[5] that have been used to prepare sultams include Diels–Alder reactions,[6] radical cyclizations,[7] ring-closing metathesis reactions,[8] nucleophilic aromatic substitutions,[9] cyclizations of aminosulfonyl chlorides,[10] and intramolecular Heck reactions.[11]

The narrower class of benzo-annelated sultams is also very important; 1,2,4-benzothiadiazin-3-one 1,1-dioxide derivatives, for example, have demonstrated anti-HIV activity.[12] Approaches to benzosultams are more limited, but they are currently being designed.[13]

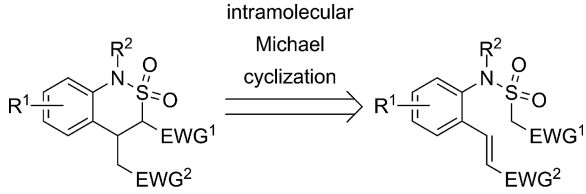
The vast majority of methods for the synthesis of benzosultams reported to date relate to compounds with an Ar–S bond (Scheme 1, type I). The development of approaches to structures of type II is still in its infancy. Actually, synthetic routes to sultams of type II with $n = 1$ are limited to an intramolecular oxidative cyclization of sulfonamides in the presence of hypervalent iodine compounds.[14] Thus the search for approaches to benzo-fused δ-sultams containing an Ar–N bond is highly warranted.

We decided to fill this gap, and we developed a synthetic strategy using as a key step an intramolecular Michael cyclization of sulfonamides bearing an additional *C*-nucleophilic centre and an activated C=C bond (Scheme 2).

We have also been interested in studying of the influence of a substituent on the nitrogen atom. Thus, we planned to involve in the reaction secondary sulfonamides ($R^2 = H$) as well as their tertiary analogues containing a *p*-methoxybenzyl (PMB) group. The PMB group could easily be removed later by acidic hydrolysis[15] or oxidatively by using ceric ammonium nitrate.[16]



Scheme 1. Benzo-annelated sultams.



Scheme 2. Proposed approach to benzo-fused δ-sultams; EWG = electron-withdrawing group.

Results and Discussion

The required sulfonamides were synthesized from the corresponding *ortho*-iodoanilines in two steps (Scheme 3, Table 1). Firstly, iodides **1** and **2**[17] were coupled with *tert*-butyl acrylate (**3**) in a Heck reaction to give *ortho*-aminocinnamates **4** and **5**. It is noteworthy that the $Pd(OAc)_2/P(o\text{-}Tol)_3/Et_3N/MeCN$ system has previously been used for the synthesis of **4a**.[18] Gratifyingly, the replacement of $P(o\text{-}Tol)_3$ with the cheaper and more readily available Ph_3P still allowed us to obtain **4a** as well as substituted analogues **4b**, **4c**, and **5b** in good yields. However, compound **5c** was isolated together with the unexpected product of chlorine substitution (i.e., **5c′**). The reason for this unusual lack of selectivity is definitely steric hindrance from the side of the bulky *ortho*-substituent adjacent to the iodine atom. The

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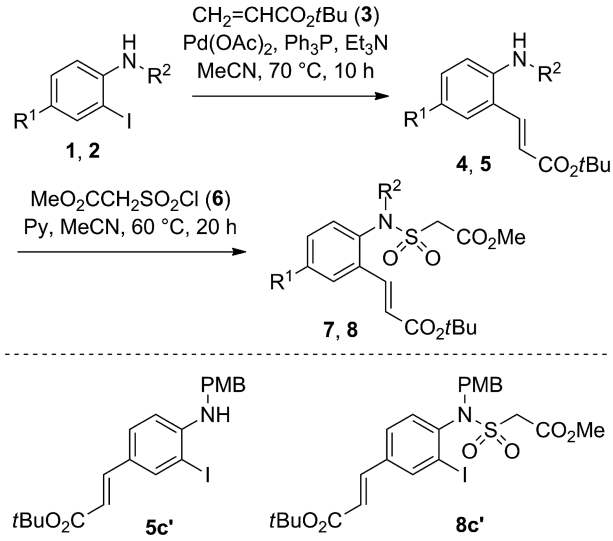
mixture of **5c** and **5c′** was inseparable, and was used in the next step directly. The *E* configurations of the C=C bonds in cinnamates **4** and **5** were established based on the values of the spin–spin coupling constants ($J \approx 16$ Hz).



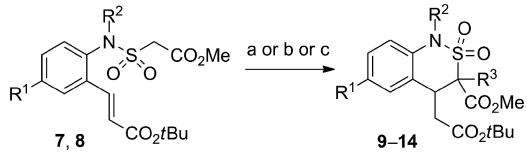
Scheme 3. Preparation of sulfonamides **7** and **8**.

Table 1. Preparation of sulfonamides **7** and **8**.

Starting material	R^1	R^2	Cinnamate (yield [%])	Sulfonamide (yield [%])
1a	H	H	**4a** (64)	**7a** (84)
1b	Me	H	**4b** (86)	**7b** (61)
1c	Cl	H	**4c** (70)	**7c** (56)
2b	Me	PMB	**5b** (85)	**8b** (63)
2c	Cl	PMB	**5c** (59) + **5c′**	**8c** (52) + **8c′**

Aminocinnamates **4** and **5** were sulfonylated using methyl (chlorosulfonyl)acetate (**6**) in MeCN at 60 °C. Unprotected anilines **4a**–**4c** were treated with an equimolar amount of sulfonyl chloride **6** to avoid double *N*-sulfonylation, and target sulfonamides **7a**–**7c** were isolated in 56–84% yields. With PMB-substituted anilines **5**, which are noticeably less reactive, at least a 2 equiv. of **6** was required to achieve full conversion of the starting material. Compound **8c** was isolated together with by-product **8c′**, as expected. Therefore, we obtained structures with two orthogonal ester groups that could be modified independently.

Initially, we planned to perform the Michael reaction on PMB-substituted sulfonamides **8b** and **8c**, and we were delighted to find that they did indeed cyclize in the presence of K_2CO_3 in DMF[19] to give the corresponding sultams (i.e., **9b** and **9c**) in acceptable yields (see Scheme 4, Table 2, entries 1 and 2). As by-product **8c′** could not react in a Michael fashion, compound **9c** was isolated in pure form. It is noteworthy that sultams **9b** and **9c** were formed as *cis*/*trans* mixtures of diastereomers with a strong prevalence of the latter. In some cases, the *trans* diastereomers could be isolated pure by recrystallization (for details, see below).

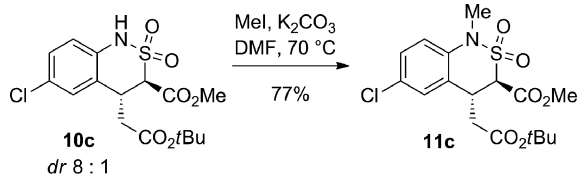


Scheme 4. Michael cyclization of sulfonamides **7** and **8**. (a) K_2CO_3, DMF, 70 °C; (b) MeI (1.0 equiv.) or BnCl (1.0 equiv.), K_2CO_3, DMF, 70 °C; (c) MeI (2.0 equiv.) or BnCl (2.0 equiv.), K_2CO_3, DMF, 70 °C.

The reactions of secondary sulfonamides **7** proved to be more complex and interesting. We managed to obtain secondary sultams **10**, but the reaction times increased dramatically, and only the chloro-substituted analogue (i.e., **10c**) formed relatively quickly (see Table 2, entries 3–5). We suppose that the presence of chlorine in aromatic ring can make the C=C bond more electron deficient, and thus accelerate the key cyclization step.

We believed that secondary sulfonamides would react more slowly than their tertiary analogues, but the synthesis of the latter is more complex, and involves one additional step. Therefore we decided to add an alkylating agent (MeI or BnCl) to the reaction mixture to obtain tertiary sulfonamides in situ, and thus accelerate the intramolecular cyclization. Gratifyingly, this approach proved to be successful, and allowed us to achieve the desired sultams (i.e., **11**, by using MeI, see Table 2, entries 6 and 7; and **12** by using BnCl, see Table 2, entries 8 and 9) in good yields as *cis*/*trans* mixtures of isomers as before, but much more quickly.

Interestingly, in the case of chloro-substituted sulfonamide **7c**, the desired sultam (i.e., **11c**) could not be isolated. The reaction of sulfonamide **7c** with 1.0 equiv. of MeI in the presence of K_2CO_3 in DMF gave the starting material and a product **13c** containing an additional *C*-methyl group in modest yield (see Table 2, entry 12). Nevertheless, sultam **11c** was obtained through *N*-methylation of compound **10c** under standard K_2CO_3/DMF conditions, and was isolated as a single *trans* diastereomer (Scheme 5).

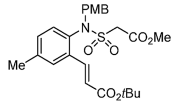
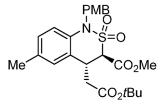
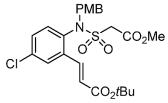
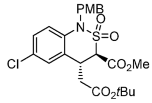
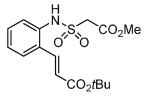
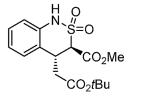
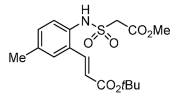
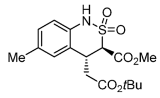
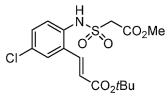
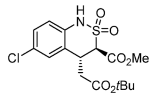
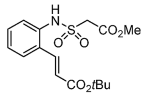
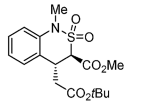
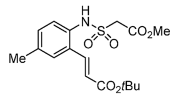
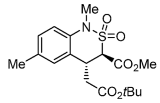
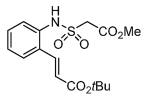
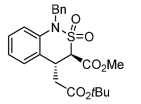
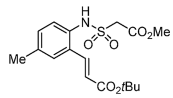
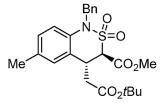
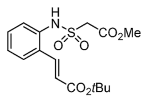
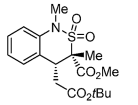
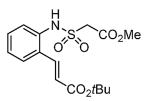
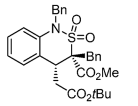
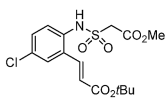
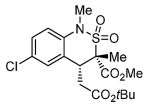


Scheme 5. Synthesis of sultam **11c**.

Thus, the possibility of an additional *C*-alkylation had been demonstrated. Inspired by this result, we proved the efficiency of the alkylation strategy, and performed one-pot double alkylation to obtain sultam derivatives **13a** and **14a**. Encouragingly, the desired products were formed in reasonable yields as single diastereomers (see Table 2, entries 10 and 11).

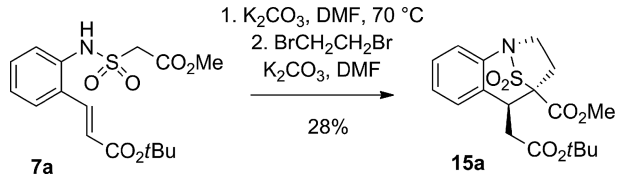
An attempt to cycloalkylate secondary sultams such as **10a** with a dihaloalkane was a logical continuation of our

Table 2. Michael cyclization of sulfonamides **7** and **8**.

Entry	Starting material		Product		Conditions	Time	Yield	*dr* *trans/cis*
1		**8b**		**9b**	a	10 h	68%	5 : 1
2		**8c**		**9c**	a	10 h	87%	– [a]
3		**7a**		**10a**	a	36 h	65%	– [a]
4		**7b**		**10b**	a	36 h	66%	7 : 1
5		**7c**		**10c**	a	10 h	52%	8 : 1
6		**7a**		**11a**	b	2 h	77%	– [a]
7		**7b**		**11b**	b	2 h	58%	6 : 1
8		**7a**		**12a**	b	4 h	40%	5 : 1
9		**7b**		**12b**	b	4 h	48%	– [a]
10		**7a**		**13a**	c	10 h	85%	– [a]
11		**7a**		**14a**	c	10 h	66%	– [a]
12		**7c**		**13c**	b	10 h	35%	– [a]

[a] Only the *trans* diastereomer was isolated.

studies of the intermolecular cycloalkylation of sultams,[20a] and became the ultimate zest. This idea was even more attractive given that examples of bicyclic sultams with sulfur at the apex position and nitrogen at the bridgehead are scarce.[7a,7e,11b,20] To the best of our knowledge, benzo-annelated bridgehead sultams of the type mentioned above have not been reported yet at all. Having added 1,2-dibromoethane to sultam **10a** generated in situ from the corresponding sulfonamide (i.e., **7a**) in the K_2CO_3/DMF system, we were excited to obtain the bridged sultam (i.e., **15a**) as a single diastereomer in an acceptable yield (Scheme 6). Thus, we managed to perform a three-step one-pot process, and the method has even more synthetic potential than we had initially expected.



Scheme 6. Preparation of tricyclic sultam **15a**.

The relative configuration of the substituents in products **10**–**14** was solved using 1D NOE NMR spectroscopy (for details see Supporting Information). In the case of sultams **10**–**12**, the *trans* isomer was always the major one in the reaction mixture. For sultams **13** and **14**, the compounds with a 3*R**,4*S** configuration were the only stereoisomers formed in the reactions. These results for **11a**, **13a**, and **14a** were proved using X-ray diffraction experiments (Figure 1).

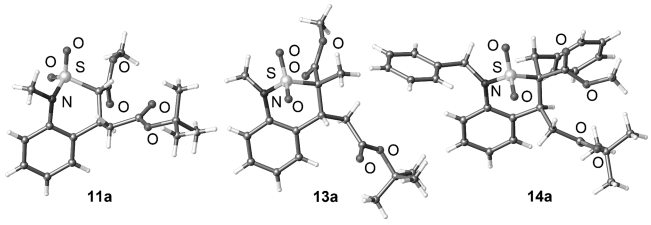


Figure 1. X-ray diffraction molecular views of sultams **11a**, **13a**, and **14a** in the crystal state.[21]

Moreover, we also managed to obtain a crystal structure of tricyclic sultam **15a**, and we found that it has an *exo* configuration (Figure 2). Several features of its molecular geometry should be noted. The S–C_{quat} and C=O bonds of the CO_2Me group are eclipsed with a torsional angle S–C–C–O of 0.2°. The extent of nitrogen pyramidality could be derived from a comparison of the sums of the bond angles at the nitrogen atoms (325.5°). This result resembles previous data obtained for methyl 1-aza-8-thiabicyclo[3.2.1]-octane-5-carboxylate 8,8-dioxide (325.3°).[20a] It is also interesting that the nitrogen and C-8 atoms are a little out of the plane of the benzene ring (the torsion angle N–C-2–C-7–C-8 is 3.0°).

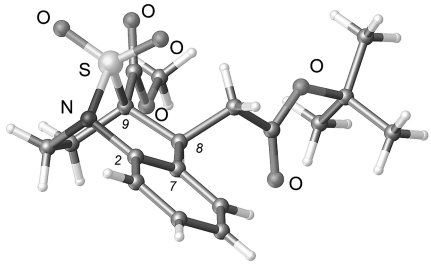


Figure 2. X-ray diffraction molecular view of sultam **15a** in the crystal state.[21]

The results concerning the stereochemistry can be generalized as follows. Bicyclic sultams with the *tert*-butoxycarbonylmethyl group and the biggest vicinal substituent in a *trans* orientation are formed preferentially. While for compounds **10**–**12** this is clear enough, for analogues **13**–**14** this conclusion is based on the fact that the methoxycarbonyl group is smaller than any alkyl group [the values of the conformational free energies (Δ*G*°) of the Me and CO_2Et groups are 1.8 and 1.1 kcal/mol, respectively].[22]

Conclusions

We have developed a new efficient approach to benzo-fused δ-sultams through intramolecular Michael cyclization. This method gives access to compounds functionalized at several centres and bearing two orthogonal ester groups simply and efficiently. Obviously, the synthetic potential of this approach has not been exhausted yet, so it unquestionably deserves further attention. We have also disclosed the stereochemical features of these transformations, having proved the structures of key products by the results of X-ray diffraction experiments.

Experimental Section

General Remarks: NMR spectra were recorded in $CDCl_3$ at ambient temperature with a Bruker DPX 300 instrument at 300.13 MHz (^{1}H NMR) and 75.47 MHz (^{13}C NMR, DEPT-135), a Bruker Avance 400 instrument at 400.13 MHz (^{1}H NMR, 1D-NOESY) and 100.61 MHz (^{13}C NMR, DEPT-135), and a Varian Inova 600 instrument at 599.74 MHz (^{1}H, 1D-NOESY). Chemical shifts (δ) are given in ppm, and spectra were calibrated using the resonances of the solvent signal (^{1}H NMR: δ = 7.28 ppm for $CHCl_3$; ^{13}C NMR: δ = 77.0 ppm for $CDCl_3$). Spin–spin coupling constants (J) are given in Hz. Multiplicities are described as s = singlet, d = doublet, t = triplet, q = quadruplet, and m = multiplet. The multiplicities of signals in the ^{13}C NMR spectra were determined by DEPT-135. The mass spectra were recorded with BrukerMicroTOF (ESI) and Bruker maXis HRMS-ESI-QTOF instruments. Reagents were used as purchased without further purification. Solvents were purified and dried before use according to standard methods. Chromatographic separations were carried out with Macherey–Nagel silica gel 60M (230–400 mesh). Analytical TLC was carried out with Macherey–Nagel ready-to-use AluGram® Sil G/UV_{254} plates. Detection was achieved using a UV lamp. Melting points were determined using capillary tubes with a Stuart SMP30 apparatus. Elemental analysis was carried out at the Analytical Laboratory of the Department of Organic Chemistry, Institute of Chemistry, St. Petersburg State University with a Euro EA 2000 automatic CHN analyser. Analytical separations of diastereomeric mixtures were carried out by LC–MS (if mentioned) on an Agilent 1200 instrument with a Zorbax SB-C18 column and with a Bruker maXis HRMS-ESI-QTOF mass spectrometer as a detector. Single-crystal X-ray diffraction experiments for compounds **11a** and **14a** were carried out with an Agilent Technologies Supernova diffractometer at 100 K using microfocussed monochromated Cu-K_α (λ = 0.154184 nm) radiation. Single-crystal X-ray diffraction experiments for compounds **13a** and **15a** were carried out with an Agilent Technologies Excalibur Eos diffractometer at 100 K using microfocussed monochromated Mo-K_α (λ = 0.071073 nm) radiation. The structures were solved by direct methods using the SHELXL program[23] incorporated in the OLEX2 program package.[24] The carbon-bound hydrogen atoms were placed in calculated positions, and were included in the refinement in the "riding" model approximation. An empirical absorption correction was applied in the CrysAlisPro[25] program complex using spherical harmonics, implemented in the SCALE3 ABSPACK scaling algorithm.

Typical Procedure for the Preparation of Sulfonamides 7 (TP 1): A solution of methyl (chlorosulfonyl)acetate **6** (2.44 g, 14.1 mmol) in MeCN (20 mL) was added dropwise to a solution of aniline **4a** (3.10 g, 14.1 mmol) and pyridine (1.68 g, 21.2 mmol) in MeCN (40 mL) at 60 °C, and the resulting mixture was stirred at this temperature for 20 h. The reaction mixture was then concentrated under reduced pressure on a rotary evaporator. The residue was dissolved in CH_2Cl_2 (50 mL), and this solution was successively washed with HCl (5% aq.; 2× 20 mL), water (3× 30 mL), and brine (30 mL), and then dried with Na_2SO_4. The solvents were removed under reduced pressure on a rotary evaporator, and the residue was subjected to flash column chromatography (EtOAc/hexane, 1:3) followed by recrystallization from a mixture of EtOAc/hexane (in the case of solid products).

(*E*)-*tert*-Butyl 3-[2-(Methoxycarbonylmethyl)sulfonylaminophenyl]-acrylate (7a): From methyl (chlorosulfonyl)acetate **6** (2.44 g, 14.1 mmol), aniline **4a** (3.10 g, 14.1 mmol), and pyridine (1.68 g, 21.2 mmol), TP 1 gave compound **7a** (4.20 g, 84%) as a brownish solid, m.p. 134–135 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.54 (s, 9 H, CMe_3), 3.84 (s, 3 H, OMe), 4.09 (s, 2 H, CH_2), 6.37 (d, J = 15.8 Hz, 1 H, HC=C*H*-CO_2tBu), 7.25 (s, 1 H, NH), 7.28 (td, J = 1.0, 7.9 Hz, 1 H, H-Ar), 7.41 (td, J = 1.6, 7.9 Hz, 1 H, H-Ar), 7.60 (dd, J = 1.0, 7.9 Hz, 1 H, H-Ar), 7.63 (dd, J = 1.6, 7.9 Hz, 1 H, H-Ar), 8.01 (d, J = 15.8 Hz, 1 H, *H*C=CH-CO_2tBu) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.1 (3 C, C*Me*$_3$), 53.4 (OMe), 54.5 (CH_2), 80.9 (*C*Me$_3$), 123.6, 125.2, 127.2 (C-Ar), 127.6, 130.2 (C-Ar), 130.8, 134.2 (C-Ar), 137.9, 164.1 (CO), 165.7 (CO) ppm. HRMS (ESI): calcd. for $C_{16}H_{25}N_2O_6S$ [M + NH_4]$^+$ 373.1428; found 373.1414. $C_{16}H_{21}NO_6S$ (355.4): calcd. C 54.1, H 6.0, N 3.9; found C 54.0, H 5.8, N 3.6.

(*E*)-*tert*-Butyl 3-[2-(Methoxycarbonylmethyl)sulfonylamino-5-methylphenyl]acrylate (7b): From methyl (chlorosulfonyl)acetate **6** (2.22 g, 12.9 mmol), aniline **4b** (3.00 g, 12.9 mmol), and pyridine (1.53 g, 19.3 mmol), TP 1 gave compound **7b** (2.90 g, 61%) as a yellow solid, m.p. 102–103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (s, 9 H, CMe_3), 2.39 (s, 3 H, Me), 3.86 (s, 3 H, OMe), 4.09 (s, 2 H, CH_2), 6.38 (d, J = 15.8 Hz, 1 H, HC=C*H*-CO_2tBu), 7.24 (s, 1 H, NH), 7.23 (d, J = 8.0 Hz, 1 H, H-Ar), 7.45–7.50 (m, 2 H, H-Ar), 8.02 (d, J = 15.8 Hz, 1 H, *H*C=CH-CO_2tBu) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 20.9 (Me), 28.1 (3 C, C*Me*$_3$), 53.3 (OMe), 54.3 (CH_2), 80.8 (*C*Me$_3$), 122.9, 125.9, 127.9, 130.5 (C-Ar), 131.6 (2 C, CH-Ar, C-Ar), 137.4 (C-Ar), 138.2, 164.1 (CO), 165.8 (CO) ppm. HRMS (ESI): calcd. for $C_{17}H_{23}NNaO_6S$ [M + Na]$^+$ 392.1138; found 392.1130. $C_{17}H_{23}NO_6S$ (369.4): calcd. C 55.3, H 6.3, N 3.8; found C 55.2, H 6.3, N 4.1.

(*E*)-*tert*-Butyl 3-{5-Chloro-2-[(methoxycarbonylmethyl)sulfonylamino]phenyl}acrylate (7c): From methyl (chlorosulfonyl)acetate **6** (2.04 g, 11.8 mmol), aniline **4c** (3.00 g, 11.8 mmol), and pyridine (1.40 g, 17.7 mmol), TP 1 gave compound **7c** (2.60 g, 56%) as a brownish solid, m.p. 113–114 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.52 (s, 9 H, CMe_3), 3.84 (s, 3 H, OMe), 4.09 (s, 2 H, CH_2), 6.36 (d, J = 15.8 Hz, 1 H, HC=C*H*CO_2tBu), 7.36 (dd, J = 2.2, 8.7 Hz, 1 H, H-Ar), 7.40 (br. s, 1 H, NH), 7.55 (d, J = 8.7 Hz, 1 H, H-Ar), 7.60 (d, J = 2.2 Hz, 1 H, H-Ar), 7.99 (d, J = 15.8 Hz, 1 H, *H*C=CH-CO_2tBu) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.1 (3 C, C*Me*$_3$), 53.4 (CO_2*Me*), 54.7 (CH_2), 81.2 (*C*Me$_3$), 124.5, 126.9, 127.3, 130.6, 131.8 (C-Ar), 132.8 (C-Ar), 133.0 (C-Ar), 136.7, 164.0 (CO), 165.4 (CO) ppm. HRMS (ESI): calcd. for $C_{16}H_{20}ClNNaO_6S$ [M(^{35}Cl) + Na]$^+$ 412.0592; found 412.0587. $C_{16}H_{20}ClNO_6S$ (389.8): calcd. C 49.3, H 5.2, N 3.6; found C 49.0, H 5.2, N 3.5.

Typical Procedure for the Preparation of Sulfonamides 8 (TP 2): A solution of methyl (chlorosulfonyl)acetate **6** (2.93 g, 17.0 mmol) in MeCN (20 mL) was added dropwise to a solution of aniline **5b** (3.00 g, 8.49 mmol) and pyridine (1.34 g, 17.0 mmol) in MeCN (40 mL) at 60 °C, and the resulting mixture was stirred at this temperature for 20 h. The reaction mixture was then concentrated under reduced pressure on a rotary evaporator, and the residue was dissolved in CH_2Cl_2 (50 mL). This solution was successively washed with HCl (5% aq.; 2× 20 mL), water (3× 30 mL), and brine (30 mL), and then dried with Na_2SO_4. The solvents were removed under reduced pressure on a rotary evaporator, and the residue was subjected to flash column chromatography (EtOAc/hexane, 1:3).

(*E*)-*tert*-Butyl 3-{2-[*N*-(4-Methoxybenzyl)-*N*-(methoxycarbonylmethyl)sulfonylamino]-5-methyl-phenyl}acrylate (8b): From methyl (chlorosulfonyl)acetate **6** (2.93 g, 17.0 mmol), aniline **5b** (3.00 g, 8.49 mmol), and pyridine (1.34 g, 17.0 mmol), TP 2 gave compound **8b** (2.60 g, 63%) as a brown oil. R_f = 0.2 (EtOAc/petroleum ether, 1:3). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.53 (s, 9 H, CMe_3), 2.35 (s, 3 H, Me), 3.75 (s, 3 H, OMe), 3.90 (s, 3 H, OMe), 4.06, 4.12 (ABq, J = 13.7 Hz, 2 H, NSO_2CH_2), 4.60, 4.89 (ABq, J = 13.8 Hz, 2 H, NCH_2), 6.08 (d, J = 16.0 Hz, 1 H, HC=C*H*-CO_2tBu), 6.71–6.76 (m, 2 H, H-Ar), 7.02–7.08 (m, 2 H, H-Ar), 7.20 (dd, J = 1.5, 8.0 Hz, 1 H, H-Ar), 7.34 (d, J = 8.0 Hz, 1 H, H-Ar), 7.38 (d, J = 1.5 Hz, 1 H, H-Ar), 7.60 (d, J = 16.0 Hz, 1 H, *H*C=CH-CO_2tBu) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 21.1 (Me), 28.1 (3 C, C*Me*$_3$), 53.2 (OMe), 55.1 (OMe), 55.4 (CH_2), 57.4 (CH_2), 80.2 (*C*Me$_3$), 113.7 (2 C, CH-Ar), 121.8, 127.2 (C-Ar), 127.7, 129.9, 130.9 (2 C, CH-Ar), 131.5, 134.6 (C-Ar), 135.7 (C-Ar), 138.9, 139.2 (C-Ar), 159.4 (C-Ar), 164.0 (CO), 165.5 (CO) ppm. HRMS (ESI): calcd. for $C_{25}H_{31}NNaO_7S$ [M + Na]$^+$ 512.1713; found 512.1715.

(*E*)-*tert*-Butyl 3-{5-Chloro-2-[*N*-(4-methoxybenzyl)-*N*-(methoxycarbonylmethyl)sulfonylamino]phenyl}acrylate (8c): From methyl (chlorosulfonyl)acetate **6** (1.57 g, 9.09 mmol), mixture of anilines **5c** and **5c′** (1.70 g, 4.32 mmol), and pyridine (719 mg, 9.09 mmol), TP 2 gave a mixture of **8c** and **8c′** (1.10 g, 5:1) as a colourless oil. R_f = 0.2 (EtOAc/petroleum ether, 1:3). The yield of **8c** (890 mg, 52%) was estimated by ^{1}H NMR spectroscopy. Characteristic data for major product **8c** are described below. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53 (s, 9 H, CMe_3), 3.75 (s, 3 H, OMe), 3.90 (s, 3 H, OMe), 4.09 (ABq, $\Delta\delta_{AB}$ and J could not be calculated correctly, 2 H, NSO_2CH_2), 4.57 (d, J = 13.7 Hz, 1 H, NC*H*H′), 4.89 (d, J = 13.7 Hz, 1 H, NCH*H*′), 6.07 (d, J = 16.0 Hz, 1 H, HC=C*H*-CO_2tBu), 6.72–6.76 (m, 1 H, H-Ar), 7.02–7.06 (m, 1 H, H-Ar), 7.35 (dd, J = 2.0, 8.5 Hz, 1 H, H-Ar), 7.44 (d, J = 8.5 Hz, 1 H, H-Ar), 7.53 (d, J = 2.0 Hz, *H*C=CH-CO_2tBu), 7.54 (d, J = 16.0 Hz, *H*C=CH-CO_2tBu) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.1 (3 C, C*Me*$_3$), 53.3 (OMe), 55.1 (OMe), 55.5 (CH_2), 57.5 (CH_2), 80.6 (*C*Me$_3$), 113.8 (2 CH-Ar), 123.3, 126.6 (C-Ar), 127.1, 130.5, 130.9 (2 CH-Ar), 131.7, 135.2 (C-Ar), 135.6 (C-Ar), 137.5, 137.9 (C-Ar), 159.6 (C-Ar), 163.9 (CO), 165.0 (CO) ppm. HRMS (ESI): calcd. for $C_{24}H_{32}ClN_2O_7S$ [M(^{35}Cl) + NH_4]$^+$ 527.1613; found 527.1608.

Typical Procedure for the Synthesis of Sultams 9 and 10 (TP 3): A mixture of sulfonamide **8b** (500 mg, 1.05 mmol) and K_2CO_3 (363 mg, 2.63 mmol) in DMF (10 mL) was stirred at 60–70 °C for 10–36 h, and the mixture was then concentrated on a rotary evaporator. The residue was dissolved in CH_2Cl_2 (20 mL), and the resulting solution was washed with HCl (5% aq.; 2× 10 mL), water (5× 10 mL), and brine (10 mL), and then dried with Na_2SO_4. The solvents were removed under reduced pressure on a rotary evaporator, and the crude product was subjected to flash column chromatography (EtOAc/hexane, 1:3) followed by recrystallization from a mixture of EtOAc/hexane (in the case of solid products).

Methyl 4-(*tert*-Butoxycarbonylmethyl)-1-(4-methoxybenzyl)-6-methyl-3,4-dihydro-1*H*-benzo[*c*][1,2]thiazine-3-carboxylate 2,2-Di-

oxide (9b): From sulfonamide **8b** (500 mg, 1.05 mmol) and K_2CO_3 (363 mg, 2.63 mmol), TP 3 (reaction time 10 h) gave compound **9b** (340 mg, 68%) as a mixture of *trans* and *cis* isomers (5:1), a colourless oil. R_f = 0.3 (EtOAc/petroleum ether, 1:3). HRMS (ESI): calcd. for $C_{25}H_{35}N_2O_7S$ $[M + NH_4]^+$ 507.2159; found 507.2152. LC–MS: t_R = 12.1 min (*trans* isomer; found *m*/*z* = 507 $[M + NH_4]^+$), t_R = 12.4 min (*cis* isomer; found *m*/*z* = 507 $[M + NH_4]^+$).

Data for the *trans* diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40 (s, 9 H, CMe_3), 2.30 (s, 3 H, Me), 2.57 (dd, *J* = 4.1, 16.8 Hz, 1 H, C*H*H′), 2.89 (dd, *J* = 8.4, 16.8 Hz, 1 H, CH*H*′), 3.80 (s, 3 H, OMe), 3.88 (s, 3 H, OMe), 4.14 (ddd, *J* = 4.1, 6.5, 8.4 Hz, 1 H, 4-H), 4.49 (d, *J* = 6.5 Hz, 1 H, 3-H), 4.79, 4.94 (ABq, *J* = 16.0 Hz, 2 H, NCH_2), 6.82 (d, *J* = 8.1 Hz, 1 H, H-Ar), 6.88–6.92 (m, 2 H, H-Ar), 6.97 (dd, *J* = 1.8, 8.1 Hz, 1 H, H-Ar), 7.07 (d, *J* = 1.8 Hz, 1 H, H-Ar), 7.30–7.32 (m, 2 H, H-Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.78 (Me), 27.88 (3 C, C*Me*$_3$), 38.3 (C-4), 40.0 (*C*H_2CO_2tBu), 53.4 (OMe), 54.2 (NCH_2), 55.2 (OMe), 64.3 (C-3), 81.4 (*C*Me_3), 114.1 (2 C, CH-Ar), 121.7 (CH-Ar), 127.7 (C-Ar), 128.2 (CH-Ar), 128.8 (2 C, CH-Ar), 128.97 (C-Ar), 129.00 (CH-Ar), 135.0 (C-Ar), 137.3 (C-Ar), 159.2 (C-Ar), 165.6 (CO), 170.3 (CO) ppm.

Data for the *cis* diastereomer, characteristic signals: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (s, 9 H, CMe_3), 2.79 (dd, *J* = 9.0, 16.8 Hz, 1 H, C*H*H′), 3.04 (dd, *J* = 5.6, 16.8 Hz, 1 H, CH*H*′), 3.80 (s, 3 H, OMe), 4.54 (d, *J* = 6.3 Hz, 1 H, 3-H), 4.68 (d, *J* = 16.5 Hz, 1 H, NC*H*H′), 5.04 (d, *J* = 16.5 Hz, 1 H, NCH*H*′) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.83 (Me), 27.94 (3 C, C*Me*$_3$), 37.1 (*C*H_2CO_2tBu), 37.3 (C-4), 52.9 (OMe), 54.1 (NCH_2), 60.3 (OMe), 62.7 (C-3), 81.6 (CMe_3), 120.6 (CH-Ar), 126.7 (C-Ar), 127.6 (CH-Ar), 128.9 (CH-Ar), 129.5 (C-Ar), 134.4 (C-Ar), 137.6 (C-Ar), 159.0 (C-Ar), 164.9 (CO) ppm.

Methyl *trans*-4-(*tert*-Butoxycarbonylmethyl)-6-chloro-1-(4-methoxybenzyl)-3,4-dihydro-1*H*-benzo[*c*][1,2]thiazine-3-carboxylate 2,2-Dioxide (9c): From the mixture of sulfonamides **8c** and **8c′** (500 mg, 952 μmol) and K_2CO_3 (348 mg, 2.52 mmol), TP 3 (reaction time 10 h) gave compound **9c** (350 mg, 87%) as a single *trans* diastereomer, a colourless solid, m.p. 68–69 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 9 H, CMe_3), 2.59 (dd, *J* = 4.0, 17.0 Hz, 1 H, C*H*H′), 2.97 (dd, *J* = 8.2, 17.0 Hz, 1 H, CH*H*′), 3.83 (s, 3 H, OMe), 3.90 (s, 3 H, OMe), 4.12 (ddd, *J* = 4.0, 6.5, 8.2 Hz, 1 H, 4-H), 4.55 (d, *J* = 6.5 Hz, 1 H, 3-H), 4.79, 4.95 (ABq, *J* = 16.1 Hz, 1 H, NCH_2), 6.85 (d, *J* = 8.7 Hz, 1 H, H-Ar), 6.90–6.94 (m, 2 H, H-Ar), 7.13 (dd, *J* = 2.2, 8.7 Hz, 1 H, H-Ar), 7.27 (d, *J* = 2.2 Hz, 1 H, H-Ar), 7.28–7.32 (m, 2 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 27.9 (3 C, C*Me*$_3$), 38.3 (C-4), 39.6 (*C*H_2CO_2tBu), 53.6 (OMe), 54.2 (NCH_2), 55.3 (OMe), 63.7 (C-3), 81.9 (*C*Me_3), 114.3 (2 C, CH-Ar), 122.9 (CH-Ar), 128.2 (CH-Ar), 128.5 (2 C, CH-Ar, C-Ar), 128.7 (2 C, CH-Ar), 129.6 (C-Ar), 130.7 (C-Ar), 138.7 (C-Ar), 159.4 (C-Ar), 165.4 (CO), 170.1 (CO) ppm. HRMS (ESI): calcd. for $C_{24}H_{32}ClN_2O_7S$ $[M(^{35}Cl) + NH_4]^+$ 527.1613; found 527.1619. $C_{24}H_{28}ClNO_7S$ (510.0): calcd. C 56.5, H 5.5, N 2.8; found C 56.7, H 5.7, N 2.8.

Methyl *trans*-4-(*tert*-Butoxycarbonylmethyl)-3,4-dihydro-1*H*-benzo[*c*][1,2]thiazine-3-carboxylate 2,2-Dioxide (10a): From sulfonamide **7a** (1.00 g, 2.81 mmol) and K_2CO_3 (972 mg, 7.03 mmol), TP 3 (reaction time 36 h) gave compound **10a** (650 mg, 65%) as a single *trans* diastereomer, a colourless solid, m.p. 118.5–119.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (s, 9 H, CMe_3), 2.70 (dd, *J* = 3.6, 17.5 Hz, 1 H, C*H*H′), 3.31 (dd, *J* = 9.4, 17.5 Hz, 1 H, CH*H*′), 3.86 (s, 3 H, OMe), 4.13 (ddd, *J* = 3.6, 4.2, 9.4 Hz, 1 H, 4-H), 4.62 (d, *J* = 4.2 Hz, 1 H, 3-H), 6.56 (br. s, 1 H, NH), 6.89 (d, *J* = 7.8 Hz, 1 H, H-Ar), 7.11–7.33 (m, 3 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.0 (3 C, C*Me*$_3$), 39.4 (C-4), 40.0 (CH_2), 53.5 (OMe), 62.2 (C-3), 81.8 (*C*Me_3), 121.5 (CH-Ar), 125.45 (CH-Ar), 125.54 (C-Ar), 128.3 (CH-Ar), 129.1 (CH-Ar), 135.6 (C-Ar), 166.1 (CO), 170.6 (CO) ppm. HRMS (ESI): calcd. for $C_{16}H_{21}NNaO_6S$ $[M + Na]^+$ 378.0982; found 378.0983. $C_{16}H_{21}NO_6S$ (355.4): calcd. C 54.1, H 6.0, N 3.9; found C 53.8, H 6.0, N 3.7.

Methyl 4-(*tert*-Butoxycarbonylmethyl)-3,4-dihydro-6-methyl-1*H*-benzo[*c*][1,2]thiazine-3-carboxylate 2,2-Dioxide (10b): From sulfonamide **7b** (500 mg, 1.41 mmol) and K_2CO_3 (486 mg, 3.52 mmol), TP 3 (reaction time 36 h) gave compound **10b** (330 mg, 66%) as a mixture of *trans* and *cis* isomers (7:1), a colourless solid, m.p. 141–142 °C. HRMS (ESI): calcd. for $C_{17}H_{27}N_2O_6S$ $[M + NH_4]^+$ 387.1584; found 387.1586. $C_{17}H_{23}NO_6S$ (369.4): calcd. C 55.3, H 6.3, N 3.8; found C 55.3, H 6.0, N 3.6.

Data for the *trans* diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (s, 9 H, CMe_3), 2.32 (s, 3 H, Me), 2.69 (dd, *J* = 3.8, 17.4 Hz, 1 H, C*H*H′), 3.29 (dd, *J* = 9.5, 17.4 Hz, 1 H, CH*H*′), 3.84 (s, 3 H, OMe), 4.09 (ddd, *J* = 3.8, 3.9, 9.5 Hz, 1 H, 4-H), 4.56 (d, *J* = 3.9 Hz, 1 H, 3-H), 6.59 (br. s, 1 H, NH), 6.79 (d, *J* = 8.0 Hz, 1 H, H-Ar), 6.99–7.14 (m, 2 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 20.8 (Me), 28.0 (3 C, C*Me*$_3$), 39.3 (C-4), 40.1 (CH_2), 53.5 (OMe), 62.1 (C-3), 81.7 (*C*Me_3), 121.7 (CH-Ar), 125.4 (C-Ar), 129.0 (CH-Ar), 129.5 (CH-Ar), 133.1 (C-Ar), 135.2 (C-Ar), 166.3 (CO), 170.7 (CO) ppm.

Data for the *cis* diastereomer, characteristic signals: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.15 (m, 1 H, 4-H), 4.61 (d, *J* = 4.3 Hz, 1 H, 3-H) ppm.

Methyl 4-(*tert*-Butoxycarbonylmethyl)-6-chloro-3,4-dihydro-1*H*-benzo[*c*][1,2]thiazine-3-carboxylate 2,2-Dioxide (10c): From sulfonamide **7c** (500 mg, 1.33 mmol) and K_2CO_3 (466 mg, 3.33 mmol), TP 3 (reaction time 10 h) gave compound **10c** (260 mg, 52%) as a mixture of *trans* and *cis* isomers (8:1), a brownish solid, m.p. 138–139 °C. HRMS (ESI): calcd. for $C_{16}H_{24}ClN_2O_6S$ $[M(^{35}Cl) + NH_4]^+$ 407.1038; found 407.1037. $C_{16}H_{20}ClNO_6S$ (389.8): calcd. C 49.3, H 5.2, N 3.6; found C 49.5, H 5.0, N 3.4.

Data for the *trans* diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (s, 9 H, CMe_3), 2.69 (dd, *J* = 4.0, 17.5 Hz, 1 H, C*H*H′), 3.27 (dd, *J* = 9.1, 17.5 Hz, 1 H, CH*H*′), 3.85 (s, 3 H, OMe), 4.09 (ddd, *J* = 4.0, 4.2, 9.1 Hz, 4-H), 4.57 (d, *J* = 4.2 Hz, 1 H, 3-H), 6.79 (d, *J* = 8.5 Hz, 1 H, H-Ar), 6.91 (br. s, 1 H, NH), 7.19 (dd, *J* = 2.1, 8.5 Hz, 1 H, H-Ar), 7.29 (d, *J* = 2.1 Hz, 1 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.0 (3 C, C*Me*$_3$), 39.2 (C-4), 39.8 (CH_2), 53.7 (OMe), 61.9 (C-3), 82.1 (*C*Me_3), 122.6 (CH-Ar), 127.1 (C-Ar), 128.4 (CH-Ar), 129.0 (CH-Ar), 130.6 (C-Ar), 134.4 (C-Ar), 166.0 (CO), 170.4 (CO) ppm.

Data for the *cis* diastereomer, characteristic signals: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52 (s, 9 H, CMe_3), 2.63 (dd, *J* = 8.6, 16.7 Hz, 1 H, C*H*H′), 3.07 (dd, *J* = 5.9, 16.7 Hz, 1 H, CH*H*′), 3.79 (s, 3 H, OMe), 4.24 (m, 1 H, 4-H), 4.52 (d, *J* = 5.9 Hz, 1 H, 3-H), 6.91 (br. s, 1 H, NH), 7.21–7.26 (m, 2 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 37.3 (CH_2), 37.6 (C-4), 53.3 (OMe), 60.3 (C-3), 82.2 (*C*Me_3), 122.5 (CH-Ar), 127.2 (CH-Ar), 128.5 (CH-Ar), 130.5 (C-Ar), 134.7 (C-Ar), 169.8 (CO) ppm.

Typical Procedure for the Synthesis of Sultams 11–14 (TP 4): A solution of MeI (397 mg, 2.80 mmol) in DMF (10 mL) was slowly added over 30 min to a mixture of sulfonamide **7a** (1.00 g, 2.80 mmol) and K_2CO_3 (967 mg, 7.00 mmol) in DMF (30 mL) at 60–70 °C. The resulting mixture was stirred for 2–10 h at this temperature, and was then concentrated on a rotary evaporator. The residue was dissolved in CH_2Cl_2 (30 mL), and this solution was washed with HCl (5% aq.; 2× 10 mL), water (5× 10 mL), and

brine (10 mL), and then dried with Na_2SO_4. The solvents were removed under reduced pressure on a rotary evaporator, and the crude product was purified by flash chromatography (EtOAc/hexane, 1:3) and recrystallized from a mixture of EtOAc/hexane.

Methyl *trans*-4-(*tert*-Butoxycarbonylmethyl)-3,4-dihydro-1-methyl-1*H*-benzo[*c*][1,2]thiazine-3-carboxylate 2,2-Dioxide (11a): From sulfonamide **7a** (1.00 g, 2.80 mmol), K_2CO_3 (967 mg, 7.00 mmol) and MeI (397 mg, 2.80 mmol), TP 4 (reaction time 2 h) gave compound **11a** (800 mg, 77%) as a single *trans* diastereomer, a colourless solid, m.p. 94–95 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 9 H, CMe_3), 2.66 (br. s, J = 17.0 Hz, 1 H, C*H*H′), 3.21 (dd, J = 7.9, 17.0 Hz, 1 H, CH*H*′), 3.42 (s, 3 H, NMe), 3.92 (s, 3 H, OMe), 4.18 (m, 1 H, 4-H), 4.71 (d, J = 6.4 Hz, 1 H, 3-H), 7.11 (d, J = 8.0 Hz, 1 H, H-Ar), 7.18–7.21 (m, 1 H, H-Ar), 7.29–7.36 (m, 2 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 27.9 (3 C, C*Me*$_3$), 36.0 (Me or C-4), 38.4 (Me or C-4), 39.2 (CH_2), 53.5 (OMe), 63.0 (C-3), 81.6 (*C*Me$_3$), 120.6 (CH-Ar), 124.9 (CH-Ar), 127.2 (C-Ar), 128.2 (CH-Ar), 128.5 (CH-Ar), 140.5 (C-Ar), 165.5 (CO), 170.3 (CO) ppm. HRMS (ESI): calcd. for $C_{17}H_{27}N_2O_6S$ [M + NH_4]$^+$ 387.1584; found 387.1589. $C_{17}H_{23}NO_6S$ (369.4): calcd. C 55.3, H 6.3, N 3.8; found C 55.4, H 6.2, N 3.5.

Methyl 4-(*tert*-Butoxycarbonylmethyl)-3,4-dihydro-1,6-dimethyl-1*H*-benzo[*c*][1,2]thiazine-3-carboxylate 2,2-Dioxide (11b): From sulfonamide **7b** (500 mg, 1.35 mmol), K_2CO_3 (468 mg, 3.38 mmol), and MeI (192 mg, 1.35 mmol) TP 4 (reaction time 2 h) gave compound **11b** (300 mg, 58%) as a mixture of *trans* and *cis* isomers (6:1), a yellowish oil. R_f = 0.3 (EtOAc/petroleum ether, 1:3). HRMS (ESI): calcd. for $C_{18}H_{25}NNaO_6S$ [M + Na]$^+$ 406.1295; found 406.1289. $C_{18}H_{25}NO_6S$ (383.5): calcd. C 56.4, H 6.6, N 3.7; found C 56.3, H 6.5, N 3.9.

Data for the *trans* diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 9 H, CMe_3), 2.61 (dd, J = 3.7, 16.9 Hz, 1 H, C*H*H′), 3.15 (dd, J = 8.1, 16.9 Hz, 1 H, CH*H*′), 3.35 (s, 3 H, NMe), 3.87 (s, 3 H, OMe), 4.10 (ddd, J = 3.7, 6.6, 8.1 Hz, 1 H, 4-H), 4.63 (d, J = 6.6 Hz, 1 H, 3-H), 6.97 (d, J = 8.5 Hz, 1 H, H-Ar), 7.06–7.12 (m, 2 H, H-Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8 (C*Me*), 27.9 (3 C, C*Me*$_3$), 36.4 (NMe or C-4), 38.3 (NMe or C-4), 39.2 (CH_2), 53.5 (OMe), 62.9 (C-3), 81.5 (*C*Me$_3$), 120.8 (CH-Ar), 127.0 (C-Ar), 128.9 (2 CH-Ar), 134.6 (C-Ar), 138.0 (C-Ar), 165.6 (CO), 170.4 (CO) ppm.

Data for the *cis* diastereomer, characteristic signals: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (s, 9 H, CMe_3), 2.32 (s, 3 H, Me), 2.77 (m, 1 H, C*H*H′), 3.05 (dd, J = 5.9, 16.7 Hz, 1 H, CH*H*′), 3.78 (s, 3 H, OMe), 4.19 (m, 1 H, 4-H), 4.54 (d, J = 6.1 Hz, 1 H, 3-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.0 (3 C, C*Me*$_3$), 34.8 (CH_2, NMe or C-4), 37.0 (CH_2, NMe or C-4), 37.1 (CH_2, NMe or C-4), 53.0 (OMe), 62.5 (C-3), 119.3 (CH-Ar), 127.6 (CH-Ar) ppm.

Methyl 1-Benzyl-4-(*tert*-butoxycarbonylmethyl)-3,4-dihydro-1*H*-benzo[*c*][1,2]thiazine-3-carboxylate 2,2-Dioxide (12a): From sulfonamide **7a** (500 mg, 1.41 mmol), K_2CO_3 (486 mg, 3.52 mmol), and BnCl (178 mg, 1.41 mmol), TP 4 (reaction time 4 h) gave compound **12a** (250 mg, 40%) as a mixture of *trans* and *cis* isomers (5:1), a yellow oil. R_f = 0.35 (EtOAc/petroleum ether, 1:3). HRMS (ESI): calcd. for $C_{27}H_{27}N_2O_6S$ [M + NH_4]$^+$ 463.1897; found 463.1909. LC–MS t_R = 11.5 min (*trans* isomer; found *m*/*z* = 463 [M + NH_4]$^+$), t_R = 11.8 min (*cis* isomer; found *m*/*z* = 463 [M + NH_4]$^+$).

Data for the *trans* diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 9 H, CMe_3), 2.63 (dd, J = 3.8, 17.0 Hz, 1 H, C*H*H′), 3.07 (dd, J = 8.6, 17.0 Hz, 1 H, CH*H*′), 3.90 (s, 3 H, OMe), 4.18 (ddd, J = 3.8, 6.1, 8.6 Hz, 1 H, 4-H), 4.62 (d, J = 6.1 Hz, 1 H, 3-H), 4.89 (d, J = 16.6 Hz, 1 H, NC*H*H′), 5.05 (d, J = 16.6 Hz, 1 H, NCH*H*′), 6.88–6.95 (m, 1 H, H-Ar), 7.07–7.21 (m, 2 H, H-Ar), 7.22–7.35 (m, 2 H, H-Ar), 7.35–7.51 (m, 4 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 27.95 (3 C, C*Me*$_3$), 38.6 (C-4), 39.9 (CH_2), 53.5 (OMe), 54.6 (NCH_2), 63.7 (C-3), 81.6 (*C*Me$_3$), 121.1 (CH-Ar), 125.1 (CH-Ar), 126.6 (C-Ar), 127.1 (2 C, CH-Ar), 127.3 (C-Ar), 127.7 (CH-Ar), 128.1 (CH-Ar), 128.7 (CH-Ar), 128.9 (2 C, CH-Ar), 140.2 (C-Ar), 165.7 (CO), 170.4 (CO) ppm.

Data for the *cis* diastereomer, characteristic signals: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52 (s, 9 H, CMe_3), 2.76 (dd, J = 9.3, 16.7 Hz, 1 H, C*H*H′), 3.81 (s, 3 H, OMe), 4.27 (m, 1 H, 4-H), 4.76 (d, J = 17.1 Hz, 1 H, NC*H*H′), 5.17 (d, J = 17.1 Hz, 1 H, NCH*H*′) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.0 (3 C, C*Me*$_3$), 37.3 (C-4), 37.5 (CH_2), 53.0 (OMe), 62.1 (C-3), 120.2 (CH-Ar), 124.6 (CH-Ar), 127.5 (CH-Ar), 128.3 (CH-Ar), 137.7 (C-Ar), 164.9 (CO), 170.2 (CO) ppm.

Methyl *trans*-1-Benzyl-4-(*tert*-butoxycarbonylmethyl)-3,4-dihydro-6-methyl-1*H*-benzo[*c*][1,2]-thiazine-3-carboxylate 2,2-Dioxide (12b): From sulfonamide **7b** (500 mg, 1.35 mmol), K_2CO_3 (468 mg, 3.38 mmol), and BnCl (171 mg, 1.35 mmol), TP 4 (reaction time 4 h) gave compound **12b** (300 mg, 48%) as a single *trans* diastereomer, a colourless solid, m.p. 82–83 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (s, 9 H, CMe_3), 2.30 (s, 3 H, Me), 2.61 (dd, J = 3.9, 16.9 Hz, 1 H, C*H*H′), 3.01 (dd, J = 8.6, 16.9 Hz, 1 H, CH*H*′), 3.89 (s, 3 H, OMe), 4.13 (ddd, J = 3.9, 6.0, 8.6 Hz, 1 H, 4-H), 4.55 (d, J = 6.0 Hz, 1 H, 3-H), 4.84, 5.02 (ABq, J = 16.4 Hz, 1 H, NCH_2), 6.78 (d, J = 8.1 Hz, 1 H, H-Ar), 6.96 (d, J = 8.1 Hz, 1 H, H-Ar), 7.08 (s, 1 H, H-Ar), 7.18–7.48 (m, 5 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 20.8 (Me), 28.0 (3 C, C*Me*$_3$), 38.5 (C-4), 40.0 (CH_2), 53.5 (*OMe*), 54.7 (NCH_2), 64.0 (C-3), 81.5 (*C*Me$_3$), 121.3 (CH-Ar), 127.2 (3 C, 2 CH-Ar, C-Ar), 127.7 (CH-Ar), 128.8 (2 C, CH-Ar), 128.9 (CH-Ar), 129.1 (CH-Ar), 134.9 (C-Ar), 137.3 (C-Ar), 137.6 (C-Ar), 165.7 (CO), 170.4 (CO) ppm. HRMS (ESI): calcd. for $C_{24}H_{29}NO_6S$ [M]$^{+\cdot}$ 459.1710; found 459.1701.

Methyl (3*R,4*S**)-4-(*tert*-Butoxycarbonylmethyl)-3,4-dihydro-1,3-dimethyl-1*H*-benzo[*c*][1,2]-thiazine-3-carboxylate 2,2-Dioxide (13a):** From sulfonamide **7a** (500 mg, 1.41 mmol), K_2CO_3 (486 mg, 3.52 mmol), and MeI (399 mg, 2.81 mmol), TP 4 (reaction time 10 h) gave compound **13a** (460 mg, 85%) as a single 3*R**,4*S** diastereomer, a colourless solid, m.p. 118.5–119.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40 (s, 9 H, CMe_3), 1.68 (s, 3 H, CMe), 2.71 (br. d, J = 5.2 Hz, 2 H, CH_2), 3.28 (s, 3 H, NMe), 3.72 (s, 3 H, OMe), 3.95 (t, J = 5.2 Hz, 1 H, 4-H), 6.91 (d, J = 8.2 Hz, 1 H, H-Ar), 7.02 (td, J = 0.9, 8.0 Hz, 1 H, H-Ar), 7.11–7.29 (m, 2 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 19.9 (C*Me*), 28.0 (3 C, C*Me*$_3$), 34.1 (C-4), 39.4 (CH_2), 44.3 (NMe), 53.2 (OMe), 67.4 (C-3), 81.4 (*C*Me$_3$), 118.0 (CH-Ar), 124.0 (CH-Ar), 127.95 (CH-Ar), 128.04 (C-Ar), 128.6 (CH-Ar), 139.4 (C-Ar), 167.5 (CO), 171.4 (CO) ppm. HRMS (ESI): calcd. for $C_{18}H_{25}NNaO_6S$ [M + Na]$^+$ 406.1295; found 406.1298. $C_{18}H_{25}NO_6S$ (383.5): calcd. C 56.4, H 6.6, N 3.7; found C 56.9, H 7.0, N 3.6.

Methyl (3*R,4*S**)-4-(*tert*-Butoxycarbonylmethyl)-6-chloro-3,4-dihydro-1,3-dimethyl-1*H*-benzo[*c*]-[1,2]thiazine-3-carboxylate 2,2-Dioxide (13c):** From sulfonamide **7c** (500 mg, 1.28 mmol), K_2CO_3 (443 mg, 3.21 mmol), and MeI (182 mg, 1.28 mmol), TP 4 (reaction time 10 h) gave compound **13c** (190 mg, 35%) as a single 3*R**,4*S** diastereomer, a yellowish solid, m.p. 108–109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52 (s, 9 H, CMe_3), 1.72 (s, 3 H, CMe), 2.72, 2.78 (AB part of ABX system, d, J_{AB} = 17.0 Hz, 2 H, CH_2), 3.35 (s, 3 H, NMe), 3.80 (s, 3 H, OMe), 3.99 (X part of ABX system, J_{AX} = 3.3, J_{BX} = 7.3 Hz, 1 H, 4-H), 6.94 (d, J = 8.5 Hz, 1

H, H-Ar), 7.20–7.32 (m, 2 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 19.4 (C*Me*), 28.0 (3 C, CMe_3), 34.5 (C-4), 39.0 (CH_2), 44.2 (NMe), 53.4 (OMe), 67.0 (C-3), 81.8 (*C*Me$_3$), 119.4 (CH-Ar), 128.0 (CH-Ar), 128.4 (CH-Ar), 129.3 (C-Ar), 129.8 (C-Ar), 138.2 (C-Ar), 167.2 (CO), 171.1 (CO) ppm. HRMS (ESI): calcd. for $C_{18}H_{28}ClN_2O_6S$ $[M + NH_4]^+$ 435.1351; found 435.1355.

Methyl (3*R,4*S**)-4-[2-(*tert*-Butoxycarbonyl)methyl]-1,3-dibenzyl-3,4-dihydro-1*H*-benzo[*c*][1,2]-thiazine-3-carboxylate 2,2-Dioxide (14a):** From sulfonamide **7a** (500 mg, 1.41 mmol), K_2CO_3 (486 mg, 3.52 mmol), and BnCl (356 mg, 2.81 mmol), TP 4 (reaction time 10 h) gave compound **14a** (500 g, 66%) as a single 3*R**,4*S** diastereomer, a colourless solid, m.p. 170–171 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (s, 9 H, CMe_3), 2.65 (dd, *J* = 8.4, 17.4 Hz, 1 H, C*H*H′CO_2tBu), 2.93 (dd, *J* = 1.9, 17.4 Hz, 1 H, C*H*H′CO_2tBu), 2.98 (d, *J* = 13.8 Hz, 1 H, CCH*H*′), 3.63 (d, *J* = 13.8 Hz, 1 H, CCH*H*′), 3.72 (s, 3 H, OMe), 4.17 (dd, *J* = 1.9, 8.4 Hz, 1 H, 4-H), 4.80 (d, *J* = 16.9 Hz, 1 H, NC*H*H′), 5.16 (d, *J* = 16.9 Hz, 1 H, NCH*H*′), 6.79 (d, *J* = 8.1 Hz, 1 H, H-Ar), 6.94–7.03 (m, 3 H, H-Ar), 7.09 (t, *J* = 7.4 Hz, 1 H, H-Ar), 7.16–7.25 (m, 4 H, H-Ar), 7.24–7.34 (m, 3 H, H-Ar), 7.38 (d, *J* = 7.4 Hz, 2 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.0 (3 C, C*Me*$_3$), 39.5 (C*C*H$_2$), 39.9 (C*C*H$_2$), 40.5 (C-4), 50.5 (NCH$_2$), 53.0 (OMe), 72.7 (C-3), 80.7 (*C*Me$_3$), 117.7 (CH-Ar), 123.8 (CH-Ar), 126.8 (2 C, CH-Ar), 127.6 (CH-Ar), 127.7 (C-Ar), 127.9 (CH-Ar), 128.2 (CH-Ar), 128.6 (2 C, CH-Ar), 128.9 (2 C, CH-Ar), 130.1 (CH-Ar), 130.2 (2 C, CH-Ar), 133.3 (C-Ar), 136.8 (C-Ar), 138.6 (C-Ar), 165.9 (CO), 171.2 (CO) ppm. HRMS (ESI): calcd. for $C_{30}H_{33}NNaO_6S$ $[M + Na]^+$ 558.1921; found 558.1917. $C_{30}H_{33}NO_6S$ (535.7): calcd. C 67.3, H 6.2, N 2.6; found C 67.6, H 6.2, N 2.7.

Methyl *trans*-4-(*tert*-Butoxycarbonylmethyl)-6-chloro-3,4-dihydro-1-methyl-1*H*-benzo[*c*][1,2]thiazine-3-carboxylate 2,2-Dioxide (11c): A solution of MeI (54.6 mg, 385 μmol) in DMF (5.0 mL) was slowly added over 30 min to a mixture of sultam **10c** (150 mg, 385 μmol) and K_2CO_3 (132 mg, 962 μmol) in DMF (5.0 mL) at 60–70 °C. The resulting mixture was stirred at this temperature for 20 h, and was then concentrated on a rotary evaporator. The residue was dissolved in CH_2Cl_2 (10 mL), and this solution was washed with HCl (5% aq.; 2× 5.0 mL), water (5× 8.0 mL), and brine (8.0 mL), and then dried with Na_2SO_4. The solvents were removed under reduced pressure on a rotary evaporator, and the crude product was subjected to flash column chromatography (EtOAc/hexane, 1:3) followed by recrystallization from EtOAc/hexane to give compound *trans*-**11c** (120 mg, 77%) as a colourless solid, m.p. 91–92 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 9 H, CMe_3), 2.63 (dd, *J* = 3.8, 17.0 Hz, 1 H, C*H*H′), 3.16 (dd, *J* = 8.0, 17.0 Hz, 1 H, CH*H*′), 3.37 (s, 3 H, NMe), 3.89 (s, 3 H, OMe), 4.11 (ddd, *J* = 3.8, 6.6, 8.0 Hz, 1 H, 4-H), 4.64 (d, *J* = 6.6 Hz, 1 H, 3-H), 7.02 (d, *J* = 8.6 Hz, 1 H, H-Ar), 7.26–7.30 (m, 2 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 27.9 (3 C, C*Me*$_3$), 36.1 (Me or C-4), 38.3 (Me or C-4), 39.1 (CH_2), 53.7 (OMe), 62.6 (C-3), 81.9 (*C*Me$_3$), 121.9 (CH-Ar), 128.4 (CH-Ar), 128.5 (CH-Ar), 129.1 (C-Ar), 130.3 (C-Ar), 139.3 (C-Ar), 165.3 (CO), 170.1 (CO) ppm. HRMS (ESI): calcd. for $C_{17}H_{26}ClN_2O_6S$ $[M (^{35}Cl) + NH_4]^+$ 421.1195; found 421.1198. $C_{17}H_{22}ClNO_6S$ (403.9): calcd. C 50.6, H 5.5, N 3.5; found C 50.6, H 5.8, N 3.4.

Methyl *exo*-8-(*tert*-Butoxycarbonylmethyl)-12-thia-1-azatricyclo-[7.2.1.0^{2,7}]dodeca-2,4,6-triene-9-carboxylate 12,12-Dioxide (15a): A mixture of sulfonamide **7a** (200 mg, 563 μmol), K_2CO_3 (194 mg, 1.41 mmol), and DMF (5.0 mL) was stirred for 36 h at 60–70 °C. Further K_2CO_3 (233 mg, 1.69 mmol) was then added, followed by the slow addition over 2 h using a syringe pump of a solution of 1,2-dibromoethane (127 mg, 675 μmol) in DMF (5.0 mL) at 60–70 °C. The resulting mixture was stirred at this temperature for 30 h, and was then concentrated under reduced pressure on a rotary evaporator. The residue was dissolved in CH_2Cl_2 (8.0 mL), and this solution was washed with HCl (5% aq.; 2× 5.0 mL), and water (5× 8.0 mL), and dried with Na_2SO_4. The volatiles were removed under reduced pressure, and the crude product was recrystallized from a mixture of EtOAc/hexane to give **15a** (60.0 mg, 28%) as a colourless solid, m.p. 165–166 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (s, 9 H, CMe_3), 2.59 (ddd, *J* = 6.9, 10.7, 13.8 Hz, 1 H, NCH$_2$C*H*H′), 2.67 (dd, *J* = 3.5, 18.7 Hz, 1 H, C*H*H′CO_2tBu), 3.03 (ddd, *J* = 2.8, 9.4, 13.8 Hz, 1 H, NCH$_2$CH*H*′), 3.24 (ddd, *J* = 2.8, 10.7, 12.6 Hz, 1 H, NC*H*H′), 3.59 (dd, *J* = 7.2, 18.7 Hz, 1 H, CH*H*′CO_2tBu), 3.80 (ddd, *J* = 6.9, 9.4, 12.6 Hz, 1 H, NCH*H*′), 3.88 (s, 3 H, OMe), 4.20 (dd, *J* = 3.5, 7.2 Hz, 1 H, 4-H), 7.17 (d, *J* = 7.5 Hz, 1 H, H-Ar), 7.25–7.38 (m, 3 H, H-Ar) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.1 (3 C, C*Me*$_3$), 33.9 (C-10), 40.5 (*C*H$_2$CO$_2t$Bu), 48.9 (C-8), 52.5 (C-11), 53.5 (OMe), 66.3 (C-9), 81.3 (*C*Me$_3$), 127.5 (CH-Ar), 128.7 (CH-Ar), 128.9 (CH-Ar), 129.8 (CH-Ar), 133.1 (C-Ar), 144.9 (C-Ar), 167.0 (CO), 171.8 (CO) ppm. HRMS (ESI): calcd. for $C_{18}H_{23}KNO_6S$ $[M + K]^+$ 420.0878; found 420.0876.

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[1] M. Inagaki, T. Tsuri, H. Jyoyama, T. Ono, K. Yamada, M. Kobayashi, Y. Hori, A. Arimura, K. Yasui, K. Ohno, S. Kakudo, K. Koizumi, R. Suzuki, M. Kato, S. Kawai, S. Matsumoto, *J. Med. Chem.* **2000**, *43*, 2040–2048.

[2] L. Zhuang, J. S. Wai, M. W. Embrey, T. E. Fisher, M. S. Egbertson, L. S. Payne, J. Guare, J. P. Vacca Jr., D. J. Hazuda, P. J. Felock, A. L. Wolfe, K. A. Stillmock, M. V. Witmer, G. Moyer, W. A. Schleif, L. J. Gabryelski, Y. M. Leonard, J. J. Lynch, S. R. Michelson Jr., S. D. Young, *J. Med. Chem.* **2003**, *46*, 453–456.

[3] a) R. Silvestri, G. Marfè, M. Artico, G. La Regina, A. Lavecchia, E. Novellino, M. Morgante, C. Di Stefano, G. Catalano, G. Filomeni, E. Abruzzese, M. R. Ciriolo, M. A. Russo, S. Amadori, R. Cirilli, F. La Torre, P. S. Salimei, *J. Med. Chem.* **2006**, *49*, 5840–5844; b) N. Lebegue, S. Gallet, N. Flouquet, P. Carato, B. Pfeiffer, P. Renard, S. Léonce, A. Pierré, P. Chavatte, P. Berthelot, *J. Med. Chem.* **2005**, *48*, 7363–7373.

[4] M. Zia-ur-Rehman, A. J. Choudary, S. Ahmad, H. L. Siddiqui, *Chem. Pharm. Bull.* **2006**, *54*, 1175–1178.

[5] For recent reviews on the synthesis of sultams, see: a) M. Szostak, J. Aube, *Chem. Rev.* **2013**, *113*, 5701–5765; b) V. A. Rassadin, D. S. Grosheva, A. A. Tomashevskiy, V. V. Sokolov, *Khim. Geterosikl. Soedin.* **2013**, 47–74; English translation: *Chem. Heterocycl. Compd.* **2013**, *49*, 39–65; c) K. C. Majumdar, S. Mondal, *Chem. Rev.* **2011**, *111*, 7749–7773.

[6] a) V. O. Rogachev, P. Metz, *Nat. Protoc.* **2006**, *1*, 3076–3087; b) V. O. Rogatchov, H. Bernsmann, P. Schwab, R. Fröhlich, B. Wibbeling, P. Metz, *Tetrahedron Lett.* **2002**, *43*, 4753–4756; c) I. R. Greig, M. J. Tozer, P. T. Wright, *Org. Lett.* **2001**, *3*, 369–371; d) B. Plietker, D. Seng, R. Fröhlich, P. Metz, *Tetrahedron* **2000**, *56*, 873–879; e) P. Metz, D. Seng, R. Fröhlich, B. Wibbeling, *Synlett* **1996**, 741–742; f) V. O. Rogachev, V. D. Filimonov,

R. Fröhlich, O. Kataeva, P. Metz, *Heterocycles* **2006**, *67*, 589–595.

[7] a) L. A. Paquette, W. R. S. Barton, J. C. Gallucci, *Org. Lett.* **2004**, *6*, 1313–1315; b) M. Ueda, H. Miyabe, A. Nishimura, O. Miyata, Y. Takemoto, T. Naito, *Org. Lett.* **2003**, *5*, 3835–3838; c) L. A. Paquette, C. S. Ra, J. D. Schloss, S. M. Leit, J. C. Gallucci, *J. Org. Chem.* **2001**, *66*, 3564–3573; d) S. M. Leit, L. A. Paquette, *J. Org. Chem.* **1999**, *64*, 9225–9229; e) L. A. Paquette, S. M. Leit, *J. Am. Chem. Soc.* **1999**, *121*, 8126–8127.

[8] a) M. Jiménez-Hopkins, P. R. Hanson, *Org. Lett.* **2008**, *10*, 2223–2226; b) S. Karsch, D. Freitag, P. Schwab, P. Metz, *Synthesis* **2004**, 1696–1712; c) D. Freitag, P. Schwab, P. Metz, *Tetrahedron Lett.* **2004**, *45*, 3589–3592; d) S. Hanessian, H. Sailes, E. Therrien, *Tetrahedron* **2003**, *59*, 7047–7056; e) D. D. Long, A. P. Termin, *Tetrahedron Lett.* **2000**, *41*, 6743–6747; f) C. Lane, V. Snieckus, *Synlett* **2000**, 1294–1296; g) M. D. McReynolds, J. M. Dougherty, P. R. Hanson, *Chem. Rev.* **2004**, *104*, 2239–2258.

[9] a) K. Wojciechowski, S. Kosinski, *Tetrahedron* **2001**, *57*, 5009–5014; b) S. Kosinski, K. Wojciechowski, *Eur. J. Org. Chem.* **2000**, 1263–1270; c) K. Wojciechowski, M. Makosza, *Synthesis* **1992**, 571–576.

[10] D. Enders, A. Moll, J. W. Bats, *Eur. J. Org. Chem.* **2006**, 1271–1284.

[11] a) S. Merten, R. Fröhlich, O. Kataeva, P. Metz, *Adv. Synth. Catal.* **2005**, *347*, 754–758; b) P. Evans, T. McCabe, B. S. Morgan, S. Reau, *Org. Lett.* **2005**, *7*, 43–46; c) R. Grigg, M. York, *Tetrahedron Lett.* **2000**, *41*, 7255–7258; d) R. Grigg, V. Sridharan, M. York, *Tetrahedron Lett.* **1998**, *39*, 4139–4142.

[12] a) E. M. Arranz, J. A. Diaz, S. T. Ingate, M. Witvrouw, C. Pannecouque, J. Balzarini, E. D. Clercq, S. Vega, *Bioorg. Med. Chem.* **1999**, *7*, 2811–2822; b) W. R. Buckheit, V. Fliaka-Boltz, D. W. Decker, L. J. Roberson, C. A. Pyle, L. E. White, B. J. Bowden, J. B. McMahon, M. R. Boyd, J. P. Bader, D. G. Nickell, H. Barth, T. K. Antonucci, *Antiviral Res.* **1994**, *25*, 43–56.

[13] For selected examples of the synthesis of benzosultams, see: a) Z. Yang, J. Xu, *Chem. Commun.* **2014**, *50*, 3616–3618; b) M. V. Pham, B. Ye, N. Cramer, *Angew. Chem. Int. Ed.* **2012**, *51*, 10610–10614; *Angew. Chem.* **2012**, *124*, 10762–10766; c) T. Miura, M. Yamauchi, A. Kosaka, M. Murakami, *Angew. Chem. Int. Ed.* **2010**, *49*, 4955–4957; *Angew. Chem.* **2010**, *122*, 5075–5077; d) N. G. Nørager, K. Juhl, *Synthesis* **2010**, 4273–4281; e) S. Rousseaux, S. I. Gorelsky, B. K. W. Chung, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 10692–10705; f) W. Zeng, S. R. Chemler, *J. Am. Chem. Soc.* **2007**, *129*, 12948–12949; g) A. Rolfe, K. Young, P. R. Hanson, *Eur. J. Org. Chem.* **2008**, 5254–5262; h) J. Blanchet, T. Macklin, P. Ang, C. Metallinos, V. Snieckus, *J. Org. Chem.* **2007**, *72*, 3199–3206; i) J. V. Ruppel, R. M. Kamble, X. P. Zhang, *Org. Lett.* **2007**, *9*, 4889–4892; j) X. Y. Liu, C. H. Li, C. M. Che, *Org. Lett.* **2006**, *8*, 2707–2710; k) C. Moutrille, S. Z. Zard, *Tetrahedron Lett.* **2004**, *45*, 4631–4634.

[14] a) Y. Ishimata, H. Togo, *Tetrahedron Lett.* **2009**, *50*, 5354–5357; b) H. Togo, Y. Harada, M. Yokoyama, *J. Org. Chem.* **2000**, *65*, 926–929.

[15] a) J. E. Semple, P. C. Wang, Z. Lusenko, M. M. Joullie, G. Zhou, P. Ting, R. Aslanian, J. Piwinski, *Org. Lett.* **2008**, *10*, 2517–2520; b) V. O. Rogachev, P. Metz, *ARKIVOC* **2007**, *5*, 167–190.

[16] J. Morris, D. Wishka, *J. Org. Chem.* **1991**, *56*, 3549–3556.

[17] PMB-substituted *ortho*-iodoanilines were obtained in our group previously. For details, see the Supporting Information.

[18] S. G. Davies, N. Mujtaba, P. M. Roberts, A. D. Smith, J. E. Thomson, *Org. Lett.* **2009**, *11*, 1959–1962.

[19] For a full account of our studies of the alkylation of sulfonamides under different conditions, see: a) V. A. Rassadin, D. S. Grosheva, I. A. Arefeva, A. A. Tomashevskiy, V. V. Sokolov, A. de Meijere, *Eur. J. Org. Chem.* **2012**, 5028–5037; b) V. A. Rassadin, A. A. Tomashevskiy, V. V. Sokolov, A. Ringe, J. Magull, A. de Meijere, *Eur. J. Org. Chem.* **2009**, 2635–2641; c) V. A. Rassadin, A. A. Tomashevskiy, V. V. Sokolov, A. A. Potekhin, *Khim. Geterotsikl. Soedin.* **2008**, 605–617; English translation: *Chem. Heterocycl. Compd.* **2008**, *44*, 474–485.

[20] a) V. A. Rassadin, D. S. Grosheva, A. A. Tomashevskiy, D. S. Yufit, S. I. Kozhushkov, V. V. Sokolov, A. de Meijere, *Eur. J. Org. Chem.* **2010**, 3481–3486; b) A. J. Preston, J. C. Gallucci, L. A. Paquette, *J. Org. Chem.* **2006**, *71*, 6573–6578.

[21] CCDC-963153 (for **11a**), -1006245 (for **13a**), -1006246 (for **14a**), and -1018004 (for **15a**) contain the crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[22] F. A. Carey, R. J. Sundberg, *Stereochemistry, Conformation, and Stereoselectivity*, in: *Advanced Organic Chemistry*, part A, 5th ed., Springer, New York, **2007** p. 158.

[23] G. M. Sheldrick, *Acta Crystallogr., Sect. A* **2008**, *64*, 112–122.

[24] OLEX2: A complete structure solution, refinement and analysis program: O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, *J. Appl. Crystallogr.* **2009**, *42*, 339–341.

[25] *CrysAlisPro*, version 1.171.36.20, Agilent Technologies, **2012**.

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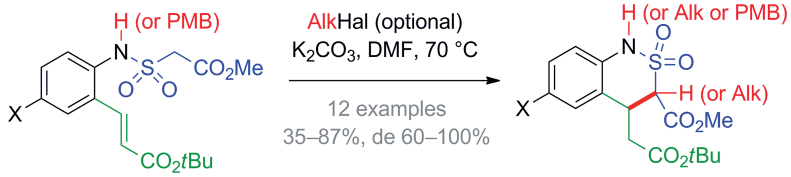
Sultams



The method described involves Michael cyclization of sulfonamides, and gives access to a wide range of benzo-annelated six-membered sultams.

Keywords: Heterocycles / Sultams / Fused-ring systems / Michael addition / Cyclization

