Synthesis of Polycyclic Sultams by Palladium-Catalyzed Intramolecular Cyclization

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Abstract: A practical and high-yielding method for the synthesis of new sultams from readily available sulfonamides, 1-naphthylamine, and 2-halobenzyl bromides is reported. A variety of tricyclic, tetracyclic, and pentacyclic sultams have been prepared via palladium-catalyzed, ligand-free intramolecular cyclization. Detailed mechanistic studies of the reaction pathway are also described.

Keywords: cyclization, palladium acetate, sulfonamides, sultams

Compounds containing a sulfonamide group (SO_2NH_2), one of the most important pharmacophores,[1] are promising candidates in drug discovery.[2] Likewise, sultams (cyclic sulfonamides) are useful heterocycles in medicinal chemistry.[3] The most famous examples of biologically active sultams are brinzolamide (**1**)[4] for the treatment of glaucoma, the COX-2 inhibitors ampiroxicam (**2**)[5] and S-2474 (**3**),[6] benzoxathiazepine 1,1-dioxide **4**[7] as a glucokinase activator (type II diabetes), novel benzodithiazine dioxides such as **5**[8] with both antiviral and anticancer activities, selective inhibitors of calpain I such as **6**,[9] antiepileptic agent sulthiame (**7**),[10] and a number of benzodithiazine dioxides **8**[8] displaying anti-HIV-1 activity (Figure 1).

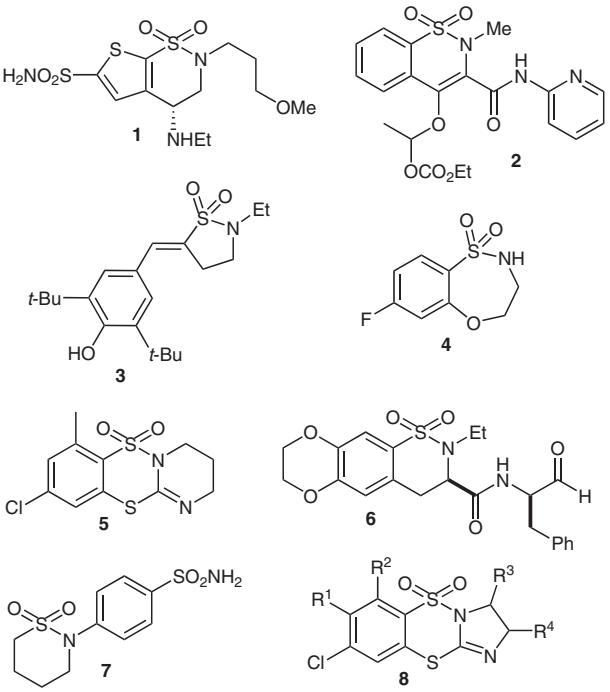

Figure 1 Biologically active sultams

Recently developed powerful methodologies for the generation of these sultams include Pictet–Spengler reactions,[11] Friedel–Crafts reactions,[12,13] sulfonamide dianion alkylation,[14] cyclization of aminosulfonyl chlorides,[15] [3+2] cycloadditions,[16] Diels–Alder reactions,[17] and Baylis–Hillman reactions.[18] Recently, however, a number of transition-metal-catalyzed approaches to sultams have come to light, including the use of silver-,[19] copper-,[20] rhodium-,[21] ruthenium-,[22] and a very few examples by palladium-catalyzed cyclization.[23] Our continued interest in the development of biologically important heterocycles based on palladium-catalyzed Sonogashira coupling[24] and intramolecular Heck cyclization[25] has prompted us to investigate a palladium-catalyzed, ligand-free intramolecular cyclization approach for the synthesis of polycyclic sultams. In our preliminary communication,[26] we have disclosed the efficient synthesis of pentacyclic sultams by palladium-catalyzed, ligand-free intramolecular cyclization. Here we report a full account of the same including a concise preparation of the tricyclic and tetracyclic sultams.

The required precursors **3a–d** for the synthesis of tricyclic sultams **9a–d** were synthesized in good to excellent yields by heating 2-bromo-5-methoxybenzylamines (**2a**) or 2-iodobenzylamine (**2b**) with 4-toluenesulfonyl chloride or benzenesulfonyl chloride in pyridine at 80 °C for four hours. The substituted benzylamines **2a**,**b** were in turn synthesized in 90% and 84% yields from their corresponding benzyl bromides **1a**,**b** by stirring with aqueous ammonia in ethanol at room temperature for four hours. The other precursor **3e** was prepared by refluxing benzenesulfonamide **4b** with 2-bromo-5-nitrobenzyl bromide (**1c**) in anhydrous methyl ethyl ketone (MEK) in the presence of anhydrous potassium carbonate and a small amount of sodium iodide. The precursor for tetracyclic sultam **3f** was prepared by sequential bromination and tosylation of 1-naphthylamine (**1e**) (Scheme 1).

The required starting materials **5a–f** for the synthesis of pentacyclic sultams **10a–f** were synthesized in 87–95% yields by refluxing sulfonamides **4a–c** with either 2-bromobenzyl bromide (**1d**) or 2-bromo-5-methoxybenzyl

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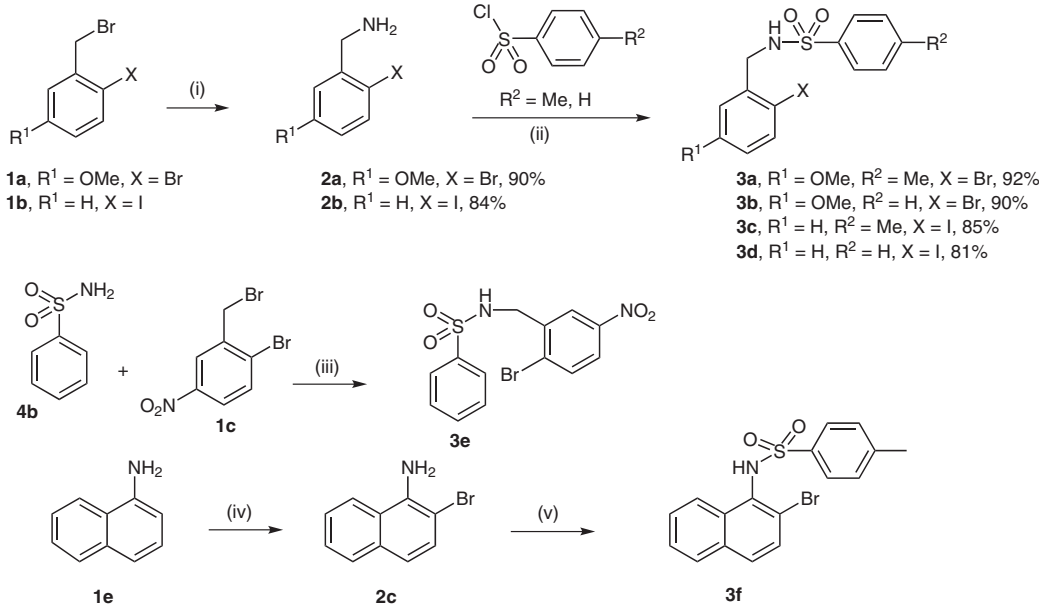
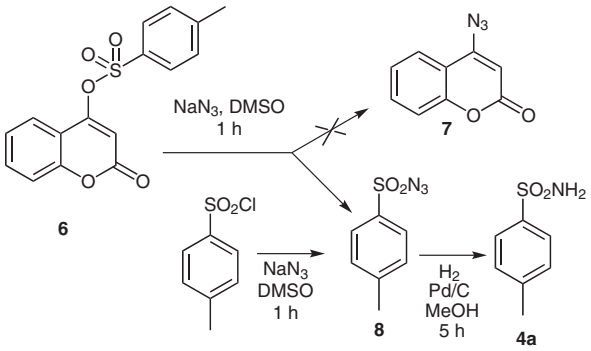


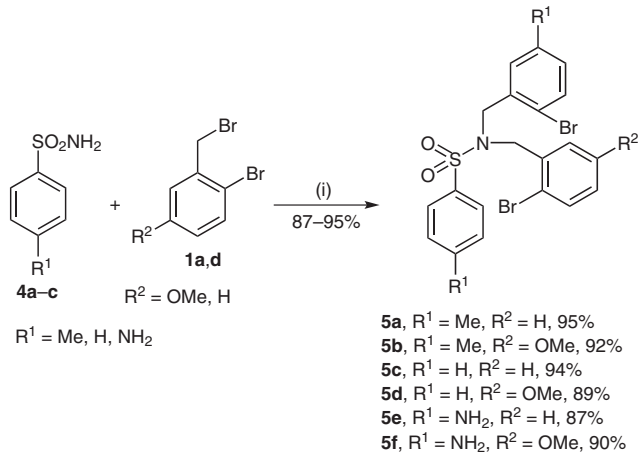
Scheme 1 Preparation of precursors for synthesizing tricyclic and tetracyclic sultams **3a–f**. *Reagents and conditions*: (i) aq NH_3, EtOH, r.t., 4 h; (ii) TsCl or $PhSO_2Cl$, pyridine, 80 °C, 4 h; (iii) K_2CO_3, NaI, MEK, reflux, 12 h, 65%; (iv) NBS, MeCN, r.t., 1 h, 75%; (v) TsCl, pyridine, 80 °C, 4 h, 90%.

bromide (**1a**) in anhydrous methyl ethyl ketone in the presence of anhydrous potassium carbonate and a small amount of sodium iodide (Scheme 2). The nitrogen of SO_2NH_2 group in the sulfanilamide **4c** is more nucleophilic than the aromatic amine moiety. This is why when **4c** was subjected to reaction with 2-bromobenzyl bromides **1a**,**d** in the presence of potassium carbonate, chemoselectively the compounds **5e**,**f** were obtained. This aromatic amine moiety is considered to be the trigger for serious drug reactions, due to the formation of reactive hydroxylamine intermediates and the subsequent haptenation product.[27]

Although the benzenesulfonamide (**4b**) and sulfanilamide (**4c**) were purchased, 4-toluenesulfonamide (**4a**) was obtained from a byproduct (O-tosylated coumarin **6**). Treatment of compound **6** with sodium azide in dimethyl sulfoxide, afforded 4-toluenesulfonyl azide (**8**) instead of 4-azidocoumarin (**7**). Hydrogenation of **8** with palladium on carbon in methanol provided 4-toluenesulfonamide (**4a**) (Scheme 3). The use of 4-toluenesulfonyl chloride instead of compound **6** also afforded compound **8** upon treatment with sodium azide.



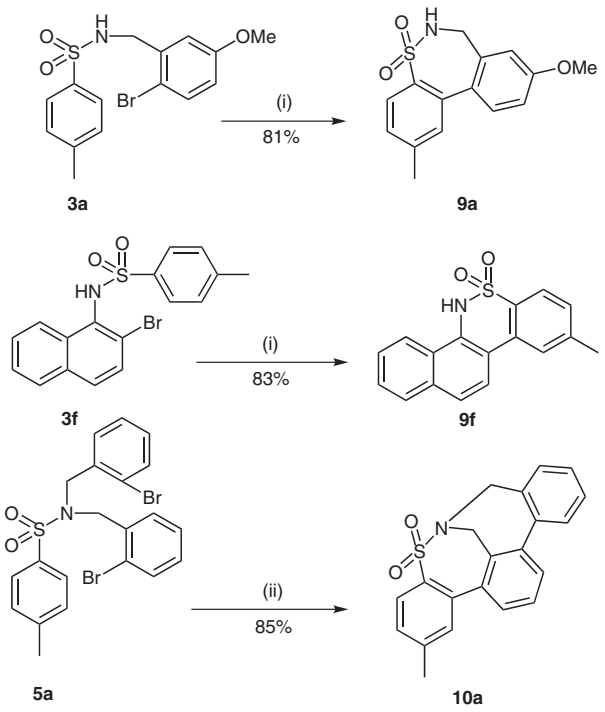
Scheme 3 Preparation of 4-toluenesulfonamide



Scheme 2 Preparation of the starting materials **5a–f**. *Reagent and conditions*: (i) K_2CO_3, NaI, MEK, reflux, 12 h.

When the intramolecular cyclization reaction was carried out with the substrates **3a**, **3f**, and **5a** using the concept of Jeffery's two-phase protocol in the presence of palladium catalyst [$Pd(PPh_3)_4$ for tricyclic and tetracyclic sultams and $Pd(OAc)_2$ for pentacyclic sultams] in anhydrous *N*,*N*-dimethylformamide and with tetrabutylammonium bromide as additive with an organic base at 120 °C for ten hours under a nitrogen atmosphere, corresponding sultams **9a**, **9f**, and **10a** were obtained in 81%, 83%, and 85% yields, respectively (Scheme 4).

It has been observed that for the synthesis of NH-sultams, e.g. **9a**, tetrakis(triphenylphosphine)palladium(0) and triethylamine is the appropriate catalyst and base whereas for the synthesis of **10a**, palladium(II) acetate and potas-



Scheme 4 Synthesis of sultams. *Reagents and conditions*: (i) $Pd(PPh_3)_4$ (10 mol%), Et_3N (3.0 equiv), TBAB (1.2 equiv), DMF, N_2, 120 °C, 10 h; (ii) $Pd(OAc)_2$ (10 mol%), KOAc (2.75 equiv), TBAB (1.2 equiv), DMF, N_2, 120 °C, 10 h.

sium acetate gave the best result. Relatively high temperatures were required for the formation of the sultams **9a** and **10a** by the intramolecular coupling reaction. When the reaction was carried out at 80 °C, no appreciable conversion was indicated on TLC. When the catalyst was changed to dichlorobis(triphenylphosphine)palladium or palladium(II) chloride the yield was reduced dramatically. Among several aprotic solvents examined, *N*,*N*-dimethylformamide gave the highest yields of the product, while dimethyl sulfoxide and acetonitrile were found to give lower yields of the product. The structure of **10a** was determined from spectral data and confirmed by single crystal X-ray diffraction (Figure 2).[28]

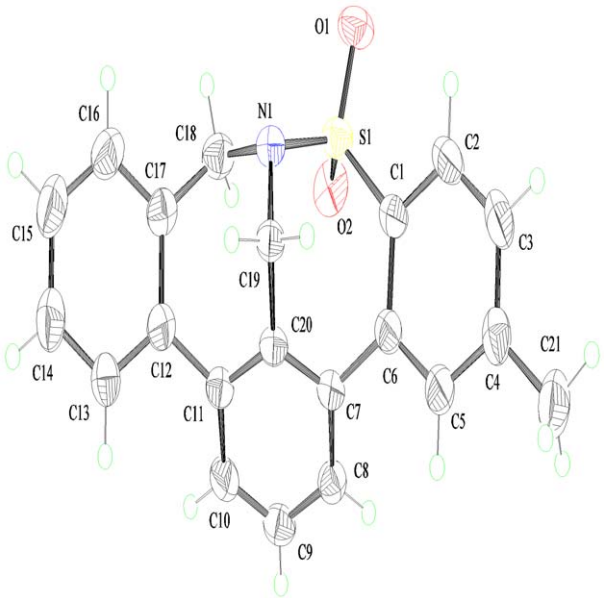


Figure 2 X-ray crystal structure of compound **10a**

The other precursors **3b–e** were treated similarly as in case of **3a** to afford tricyclic sultams **9b–e** in 62–85% yields and **5b–f** were treated similarly as in case of **5a** to afford pentacyclic sultams **10b–f** in 80–92% yields. The results of the synthesis of tricyclic sultams **9a–e**, tetracyclic sultam **9f**, and pentacyclic sultams **10a–f** are summarized in Table 1.

Table 1 Tricyclic, Tetracyclic, and Pentacyclic Sultams

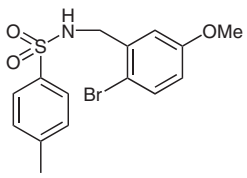
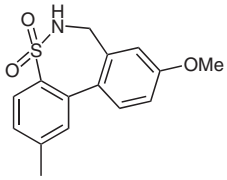
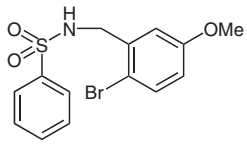
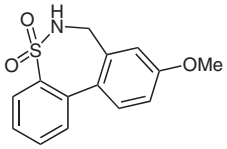
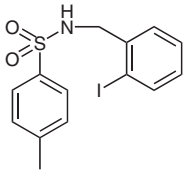
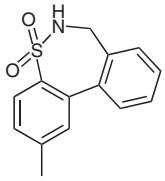
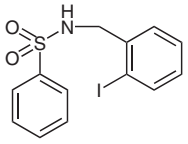
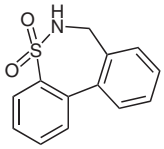
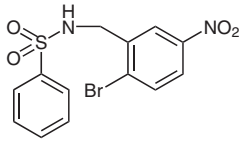
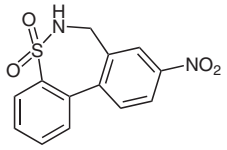
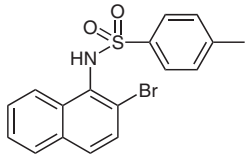
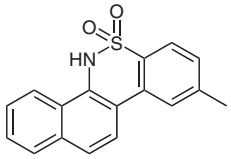
Entry	Starting material	Product	Yield (%)
1	 **3a**	 **9a**	81
2	 **3b**	 **9b**	80
3	 **3c**	 **9c**	85
4	 **3d**	 **9d**	83
5	 **3e**	 **9e**	62
6	 **3f**	 **9f**	83

Table 1 Tricyclic, Tetracyclic, and Pentacyclic Sultams (continued)

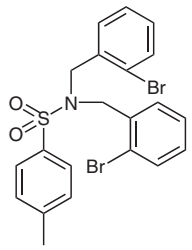
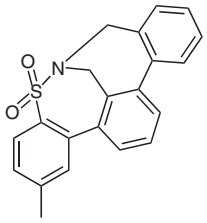
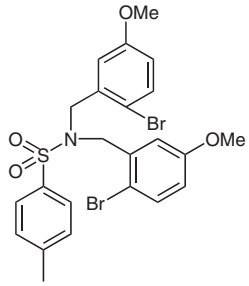
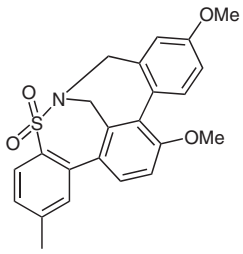
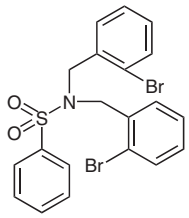
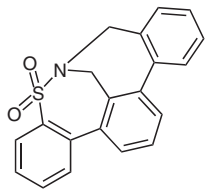
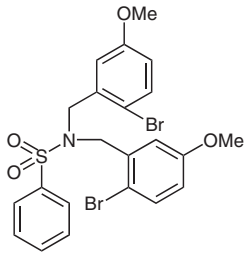
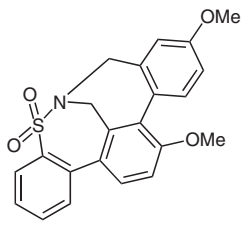
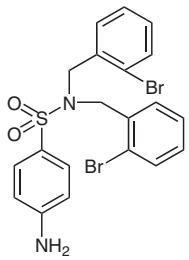
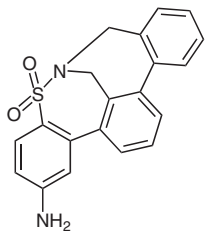
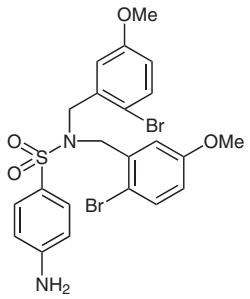
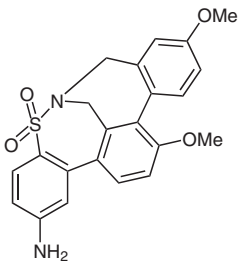
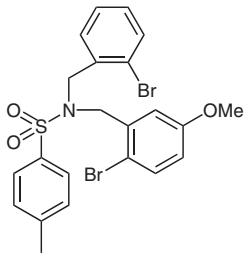
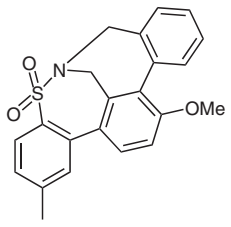
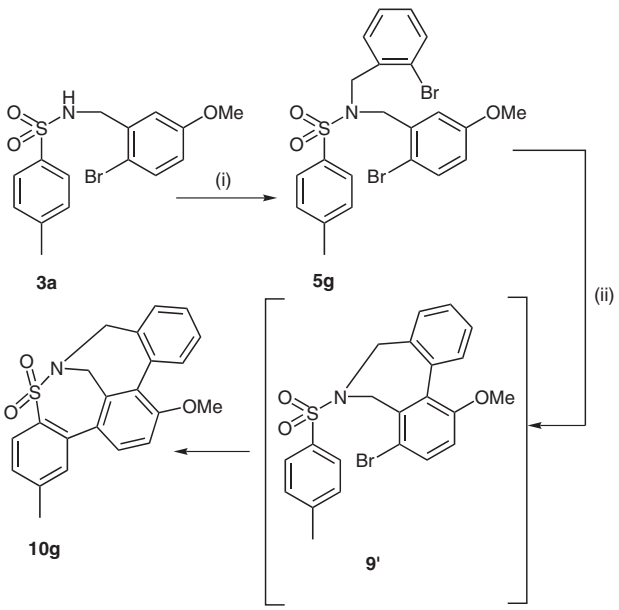
Entry	Starting material	Product	Yield (%)
7	 **5a**	 **10a**	85
8	 **5b**	 **10b**	80
9	 **5c**	 **10c**	92
10	 **5d**	 **10d**	87
11	 **5e**	 **10e**	84

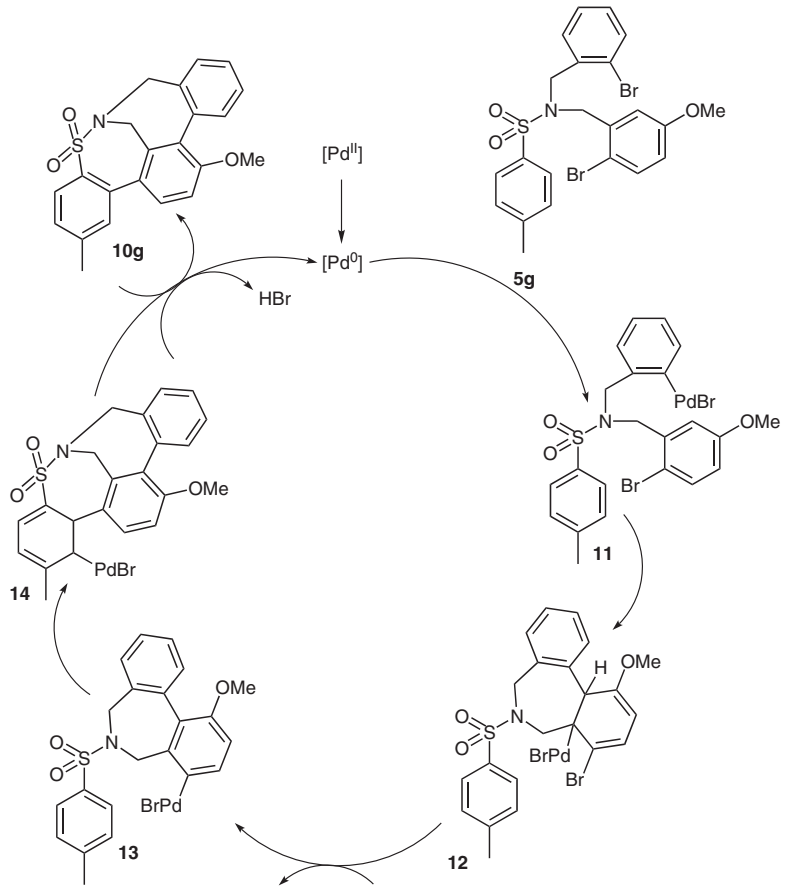
Table 1 Tricyclic, Tetracyclic, and Pentacyclic Sultams (continued)

Entry	Starting material	Product	Yield (%)
12	 **5f**	 **10f**	81
13	 **5g**	 **10g**	81

For the rationalization of the reaction pathway for the formation of pentacyclic sultams, we performed the reaction with dissymmetric benzyl bromides (Scheme 5) under the above conditions. The reaction was stopped after one hour well before completion in an attempt to isolate the tricyclic intermediate **9′**. Interestingly we have been lucky to be able to isolate the intermediate **9′**, which has been successfully converted into the final product **10g** under the aforesaid reaction conditions. Therefore, the mechanistic rationalization for the reaction may be depicted as in Scheme 6.



Scheme 5 *Reagents and conditions*: (i) 2-bromobenzyl bromide (**1d**), K_2CO_3, MEK, reflux, 12 h, 95%; (ii) $Pd(OAc)_2$, KOAc, TBAB, DMF, 120 °C, 10 h, 81%.



Scheme 6 Proposed mechanism

As illustrated in Scheme 6 for the formation of **10g**, it is proposed that initially, palladium(II) acetate may be reduced by the base[29] (KOAc) to give the active species palladium(0) and the reaction proceeds by the initial oxidation of compound **5g** to palladium(0) to form arylpalladium intermediate **11**. Complex **11** may then add to the double bond of the electron-rich 2-bromo-5-methoxybenzyl moiety to give a σ-alkyl–palladium intermediate **12**. β-Hydrogen elimination from **12** may give intermediate **13**. The intermediate **13** may again add to the double bond of the electron-poor aromatic ring of the sulfonamide moiety and to give finally the product sultam **10g**.

In summary, we have developed a practical and high yielding method for the efficient synthesis of tricyclic, tetracyclic, and pentacyclic sultams. Here it is important to note that, there are two reports on the synthesis of sultams by palladium-catalyzed intramolecular Heck reactions [Merten et al.[23a] synthesized sultams by intramolecular Heck cyclization using $Pd(OAc)_2$ (10 mol%), $(2\text{-Tol})_3P$ (11 mol%), silver or thallium salt (2 equiv), MeCN, reflux whereas Vasudevan et al.[23b] used $Pd(OAc)_2$ (5 mol%), $(2\text{-Tol})_3P$ (2 mol%), Et_3N, THF, microwave irradiation, 160 °C.] Our protocol is relatively simple [$Pd(PPh_3)_4$ or $Pd(OAc)_2$ (10 mol%), TBAB (1.2 equiv), Et_3N or KOAc, DMF, 120 °C]. In our case no ligand is necessary to effect the intramolecular cyclization reaction for the synthesis of the sultams.

Melting points were determined in open capillaries and are uncorrected. IR spectra were run for KBr discs on a Perkin-Elmer 120-000A apparatus and ^1H NMR spectra were determined for solns in $CDCl_3$ with TMS as internal standard on a Bruker DPX-400. ^{13}C NMR spectra were determined for solns in $CDCl_3$ on a Bruker DPX-125 and Bruker DPX-75. HRMS was recorded on a Qtof Micro YA263 instrument. Silica gel (60–120 mesh) was used for chromatographic separation. Silica gel-G [E-Mark (India)] was used for TLC. Petroleum ether (PE) refers to the fraction between bp 60–80 °C.

N-(2-Bromo-5-methoxybenzyl)-4-toluenesulfonamide (3a); Typical Procedure

A soln of **2a** (1.0 g, 4.63 mmol) and TsCl (1.06 g, 5.56 mmol) in pyridine (5 mL) was heated at 80 °C for 4 h. The mixture was cooled and then poured into ice-cooled H_2O (30 mL) and extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with 2 M HCl (20 mL), H_2O (20 mL), and brine (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure to afford compound **3a** as a white solid; yield: 92%; mp 108–110 °C.

Instead of TsCl, when **2a** was heated with $PhSO_2Cl$, compound **3b** was obtained. Similar treatment of compound **2b** with TsCl and $PhSO_2Cl$, afforded compounds **3c** and **3d** respectively.

IR (KBr): 3258 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 3 H), 3.67 (s, 3 H), 4.17 (d, *J* = 6.6 Hz, 2 H), 4.92 (t, *J* = 5.8 Hz, 1 H), 6.64 (dd, *J* = 8.5, 2.4 Hz, 1 H), 6.80 (d, *J* = 2.4 Hz, 1 H), 7.24 (d, *J* = 6.3 Hz, 2 H), 7.31 (d, *J* = 8.7 Hz, 1 H), 7.70 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.4, 47.3, 55.4, 113.3, 115.3, 115.4, 127.0, 129.5, 133.2, 136.3, 136.9, 143.4, 158.9.

MS: *m*/*z* = 369 [M$^+$], 371 [M + 2].

Anal. Calcd for $C_{15}H_{16}BrNO_3S$: C, 48.66; H, 4.36; N, 3.78. Found: C, 48.61; H, 4.29; N, 3.87.

***N*-(2-Bromo-5-methoxybenzyl)benzenesulfonamide (3b)**
White solid; yield: 90%; mp 84–86 °C.

IR (KBr): 3256 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.71 (s, 3 H), 4.20 (d, *J* = 6.6 Hz, 2 H), 4.96 (t, *J* = 5.9 Hz, 1 H), 6.64 (dd, *J* = 8.8, 2.9 Hz, 1 H), 6.80 (d, *J* = 2.8 Hz, 1 H), 7.30 (d, *J* = 8.8 Hz, 1 H), 7.45 (t, *J* = 7.7 Hz, 2 H), 7.53 (t, *J* = 7.2 Hz, 1 H), 7.81 (d, *J* = 7.4 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 47.4, 55.4, 113.4, 115.4, 115.6, 126.9, 127.2, 128.9, 132.5, 133.2, 136.2, 139.9, 159.0.

MS: *m*/*z* = 355 [M$^+$], 357 [M + 2].

Anal. Calcd for $C_{14}H_{14}BrNO_3S$: C, 47.20; H, 3.96; N, 3.93. Found: C, 47.31; H, 4.11; N, 3.91.

***N*-(2-Iodobenzyl)-4-toluenesulfonamide (3c)**
White solid; yield: 85%; mp 105–107 °C.

IR (KBr): 3260 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H), 4.12 (d, *J* = 6.0 Hz, 2 H), 4.62 (t, *J* = 5.8 Hz, 1 H), 7.18 (d, *J* = 6.6 Hz, 2 H), 7.25–7.31 (m, 4 H), 7.75 (d, *J* = 7.8 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.5, 51.6, 98.7, 127.1, 128.5, 129.4, 129.6, 129.8, 136.3, 138.6, 139.3, 143.4.

MS: *m*/*z* = 387 [M$^+$].

Anal. Calcd for $C_{14}H_{14}INO_2S$: C, 43.42; H, 3.64; N, 3.62. Found: C, 43.54; H, 3.70; N, 3.58.

***N*-(2-Iodobenzyl)benzenesulfonamide (3d)**
White solid; yield: 81%; mp 118–120 °C.

IR (KBr): 3258 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.20 (d, *J* = 6.2 Hz, 2 H), 4.95 (t, *J* = 5.8 Hz, 1 H), 6.92 (t, *J* = 7.7 Hz, 1 H), 7.26 (t, *J* = 7.3 Hz, 1 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 7.53 (t, *J* = 7.4 Hz, 1 H), 7.71 (d, *J* = 7.8 Hz, 1 H), 7.81 (t, *J* = 7.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 51.7, 98.7, 127.0, 128.5, 129.0, 129.6, 130.0, 132.6, 138.3, 139.4, 139.8.

MS: *m*/*z* = 373 [M$^+$].

Anal. Calcd for $C_{13}H_{12}INO_2S$: C, 41.84; H, 3.24; N, 3.75. Found: C, 41.71; H, 3.29; N, 3.69.

***N*-(2-Bromo-5-nitrobenzyl)benzenesulfonamide (3e)**
A mixture of **4b** (0.5 g, 3.19 mmol), 2-bromo-5-nitrobenzyl bromide (**1c**, 1.41 g, 4.78 mmol) and anhyd K_2CO_3 (1.32 g, 9.56 mmol) in anhyd MEK (20 mL) in the presence of NaI (cat.) was refluxed for 12 h. The mixture was cooled and filtered and the solvent was removed. The residual mass was extracted with CH_2Cl_2 (3 × 30 mL). The combined CH_2Cl_2 extracts were washed with H_2O (3 × 30 mL) followed by brine (1 × 10 mL) and dried (Na_2SO_4). Removal of CH_2Cl_2 gave the crude product, which was purified by chromatography (silica gel, EtOAc–PE, 1:9) to afford **3e** as a yellow viscous oil; yield: 65%.

IR (KBr): 3278, 1307, 1142.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.2 (d, *J* = 6.5 Hz, 2 H), 7.49–7.54 (m, 1 H), 7.60–7.66 (m, 1 H), 7.77–7.83 (m, 2 H), 8.22 (d, *J* = 7.5 Hz, 2 H), 8.64 (d, *J* = 2.1 Hz, 1 H), 8.75 (d, *J* = 1.5 Hz, 1 H).

MS: *m*/*z* = 370 [M$^+$], 372 [M + 2].

Anal. Calcd for $C_{13}H_{11}BrN_2O_4S$: C, 42.06; H, 2.99; N, 7.55. Found: C, 42.18; H, 3.21; N, 7.50.

***N*,*N*-Bis(2-bromobenzyl)arenesulfonamides 5a–f; General Procedure**
A mixture of sulfonamides **4a–c** (4.13 mmol), 2-bromobenzyl bromides **1a**,**d** (10.33 mmol) and anhyd K_2CO_3 (3 g) in anhyd MEK (20 mL) in the presence of NaI (cat.) was refluxed for 12 h. The mixture was cooled and filtered and the solvent was removed. The residual mass was extracted with CH_2Cl_2 (3 × 30 mL). The combined CH_2Cl_2 extracts were washed with H_2O (3 × 30 mL) followed by brine (1 × 10 mL) and dried (Na_2SO_4). Removal of CH_2Cl_2 gave the crude product, which was purified by chromatography (silica gel, EtOAc–PE, 1:9) to afford the bromo derivatives **5a–f**.

***N*,*N*-Bis(2-bromobenzyl)-4-toluenesulfonamide (5a)**
White solid; yield: 95%; mp 133–134 °C.

IR (KBr): 1342, 1160 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 3 H), 4.50 (s, 4 H,), 6.99 (t, *J* = 7.8 Hz, 2 H), 7.13 (t, *J* = 8.4 Hz, 2 H), 7.33 (t, *J* = 8.4 Hz, 6 H), 7.73 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.4, 52.2, 123.2, 127.1, 127.2, 128.8, 129.7, 130.0, 132.4, 134.7, 136.4, 143.5.

HRMS: *m*/*z* calcd for $C_{21}H_{19}Br_2NO_2S$: 529.9335 [M + Na], 531.9381 [M + 2 + Na], 533.9339 [M + 4 + Na]; found: 529.9401 [M + Na], 531.9401 [M + 2 + Na], 533.9401 [M + 4 + Na].

***N*,*N*-Bis(2-bromo-5-methoxybenzyl)-4-toluenesulfonamide (5b)**
White solid; yield: 92%; mp 110–111 °C.

IR (KBr): 1341, 1163 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 3 H), 3.67 (s, 6 H), 4.45 (s, 4 H,), 6.55 (dd, *J* = 8.8, 3.0 Hz, 2 H), 6.86 (d, *J* = 3 Hz, 2 H), 7.21 (d, *J* = 8.7 Hz, 2 H), 7.34 (d, *J* = 8.2 Hz, 2 H), 7.77 (d, *J* = 8.2 Hz, 2 H).

MS: *m*/*z* = 567 [M$^+$], 569 [M + 2], 571 [M + 4].

Anal. Calcd for $C_{23}H_{23}Br_2NO_4S$: C, 48.52; H, 4.07; N, 2.46. Found: C, 48.61; H, 4.12; N, 2.55.

***N*,*N*-Bis(2-bromobenzyl)benzenesulfonamide (5c)**
White solid; yield: 94%; mp 80–82 °C.

IR (KBr): 1327, 1157 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.54 (s, 4 H,), 6.99 (t, *J* = 7.6 Hz, 2 H), 7.13 (t, *J* = 7.4 Hz, 2 H), 7.30 (d, *J* = 7.6 Hz, 2 H), 7.35 (d, *J* = 7.8 Hz, 2 H), 7.51 (t, *J* = 7.5 Hz, 2 H), 7.59 (t, *J* = 7.1 Hz, 1 H), 7.84 (d, *J* = 7.5 Hz, 2 H).

MS: *m*/*z* = 493 [M$^+$], 495 [M + 2], 497 [M + 4].

Anal. Calcd for $C_{20}H_{17}Br_2NO_2S$: C, 48.51; H, 3.46; N, 2.83. Found: C, 48.65; H, 3.58; N, 2.73.

***N*,*N*-Bis(2-bromo-5-methoxybenzyl)benzenesulfonamide (5d)**
White solid; yield: 89%; mp 81–82 °C.

IR (KBr): 1343, 1168 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.67 (s, 6 H), 4.48 (s, 4 H,), 6.56 (dd, *J* = 8.7, 2.5 Hz, 2 H), 6.87 (d, *J* = 1.9 Hz, 2 H), 7.23 (t, *J* = 5.8 Hz, 2 H), 7.54 (t, *J* = 7.2 Hz, 2 H), 7.61 (t, *J* = 7.2 Hz, 1 H), 7.88 (d, *J* = 7.6 Hz, 2 H).

MS: *m*/*z* = 553 [M$^+$], 555 [M + 2], 557 [M + 4].

Anal. Calcd for $C_{22}H_{21}Br_2NO_4S$: C, 47.59; H, 3.81; N, 2.52. Found: C, 47.51; H, 3.89; N, 2.55.

***N*,*N*-Bis(2-bromobenzyl)-4-anilinesulfonamide (5e)**
White solid; yield: 87%; mp 161–162 °C.

IR (KBr): 3450, 3361, 1307, 1142 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.13 (br s, 2 H), 4.47 (s, 4 H,), 6.69 (d, *J* = 8.4 Hz, 2 H), 6.98 (t, *J* = 7.6 Hz, 2 H), 7.13 (t, *J* = 7.4 Hz, 2 H), 7.33 (d, *J* = 7.6 Hz, 4 H), 7.64 (d, *J* = 8.5 Hz, 2 H).

MS: *m*/*z* = 508 [M^+], 510 [M + 2], 512 [M + 4].

Anal. Calcd for $C_{20}H_{18}Br_2N_2O_2S$: C, 47.08; H, 3.56; N, 5.49. Found: C, 46.99; H, 3.60; N, 5.41.

***N*,*N*-Bis(2-bromo-5-methoxybenzyl)-4-anilinesulfonamide (5f)**
White solid; yield: 90%; mp 105–106 °C.

IR (KBr): 3479, 3374, 1594, 1324, 1154 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.68 (s, 6 H), 4.15 (br s, 2 H), 4.42 (s, 4 H,), 6.55 (dd, *J* = 8.7, 2.8 Hz, 2 H), 6.70 (d, *J* = 8.4 Hz, 2 H), 6.90 (d, *J* = 2.7 Hz, 2 H), 7.21 (d, *J* = 8.7 Hz, 2 H), 7.67 (d, *J* = 8.6 Hz, 2 H).

MS: *m*/*z* = 568 [M^+], 570 [M + 2], 572 [M + 4].

Anal. Calcd for $C_{22}H_{22}Br_2N_2O_4S$: C, 46.33; H, 3.89; N, 4.91. Found: C, 46.45; H, 4.07; N, 4.99.

***N*-(2-Bromobenzyl)-*N*-(2-bromo-5-methoxybenzyl)-4-toluenesulfonamide (5g)**
White gummy solid; yield: 95%.

IR (KBr): 1341, 1163 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 3 H), 3.83 (s, 3 H), 4.45 (s, 2 H), 4.49 (s, 2 H), 6.55 (dd, *J* = 8.7, 2.7 Hz, 1 H), 6.81 (d, *J* = 2.5 Hz, 1 H), 7.00 (t, *J* = 7.5 Hz, 1 H), 7.15 (t, *J* = 7.4 Hz, 1 H), 7.20 (d, *J* = 8.8 Hz, 1 H), 7.31–7.37 (m, 4 H), 7.75 (d, *J* = 8.0 Hz, 2 H).

MS: *m*/*z* = 537 [M^+], 539 [M + 2], 541 [M + 4].

Anal. Calcd for $C_{22}H_{21}Br_2NO_3S$: C, 49.00; H, 3.92; N, 2.60. Found: C, 49.12; H, 4.00; N, 2.52.

9-Methoxy-2-methyl-6,7-dihydrodibenzo[*d*,*f*][1,2]thiazepine 5,5-Dioxide (9a); Typical Procedure
A mixture of **3a** (250 mg, 0.675 mmol), TBAB (261.5 mg, 0.81 mmol), and anhyd Et_3N (0.28 mL, 2.03 mmol) was taken up in anhyd DMF (5 mL) under an N_2 atmosphere. $Pd(PPh_3)_4$ (78 mg, 0.067 mmol) was added and the mixture was stirred at 120 °C for 10 h. The mixture was cooled and H_2O (25 mL) was added. The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were washed with H_2O (2 × 40 mL) and brine (30 mL). The organic layer was dried (Na_2SO_4) and the solvent was removed in vacuo. The crude product was purified by column chromatography (silica gel, EtOAc–PE, 1:9) to afford the product **9a** as a viscous oil; yield: 81%.

The other substrates **3b–e** were treated similarly to give products **9b–e**.

IR (KBr): 3444 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.40 (s, 3 H), 3.86 (s, 3 H), 4.84 (s, 2 H), 6.89 (s, 1 H), 6.96 (d, *J* = 8.2 Hz, 1 H), 7.31 (d, *J* = 7.6 Hz, 2 H), 7.70 (d, *J* = 8.4 Hz, 1 H), 8.00 (d, *J* = 7.8 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.6, 47.2, 55.2, 113.1, 113.7, 120.1, 127.1, 127.2, 129.7, 129.8, 137, 138.0, 143.5, 159.8.

MS: *m*/*z* = 289 [M^+].

Anal. Calcd for $C_{15}H_{15}NO_3S$: C, 62.26; H, 5.23; N, 4.84. Found: C, 62.38; H, 5.19; N, 4.94.

9-Methoxy-6,7-dihydrodibenzo[*d*,*f*][1,2]thiazepine 5,5-Dioxide (9b)
Viscous oil; yield: 80%.

IR (KBr): 3440 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.86 (s, 3 H), 4.85 (s, 2 H), 6.94 (d, *J* = 8.1 Hz, 2 H), 7.06 (s, 1 H), 7.53–7.82 (m, 4 H), 8.13 (d, *J* = 2.8 Hz, 1 H).

MS: *m*/*z* = 275 [M^+].

Anal. Calcd for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76; N, 5.09. Found: C, 61.21; H, 4.72; N, 5.19.

2-Methyl-6,7-dihydrodibenzo[*d*,*f*][1,2]thiazepine 5,5-Dioxide (9c)
White solid; yield: 85%; mp 236–238 °C.

IR (KBr): 3450 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3 H), 4.91 (s, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 7.45 (t, *J* = 6.7 Hz, 2 H), 7.61 (t, *J* = 7.3 Hz, 1 H), 7.80 (d, *J* = 7.7 Hz, 1 H), 8.01 (d, *J* = 8.0 Hz, 2 H).

MS: *m*/*z* = 259 [M^+].

Anal. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40. Found: C, 64.87; H, 5.16; N, 5.32.

6,7-Dihydrodibenzo[*d*,*f*][1,2]thiazepine 5,5-Dioxide (9d)
White solid; yield: 83%; mp 218–220 °C.

IR (KBr): 3444 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.92 (s, 2 H), 7.47–7.62 (m, 5 H), 7.81–7.84 (m, 2 H), 8.11–8.14 (m, 2 H).

MS: *m*/*z* = 245 [M^+].

Anal. Calcd for $C_{13}H_{11}NO_2S$: C, 63.65; H, 4.52; N, 5.71. Found: C, 63.81; H, 4.66; N, 5.59.

9-Nitro-6,7-dihydrodibenzo[*d*,*f*][1,2]thiazepine 5,5-Dioxide (9e)
Yellow solid; yield: 62%; mp 152–154 °C.

IR (KBr): 3482, 1308, 1142 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.3 (s, 2 H), 7.44 (br s, 1 H), 7.51–7.54 (m, 2 H), 7.69–7.73 (m, 1 H), 7.87 (d, *J* = 9.0 Hz, 1 H), 8.07 (dd, *J* = 8.7, 2.8 Hz, 2 H), 8.90 (d, *J* = 2.8 Hz, 1 H).

MS: *m*/*z* = 290 [M^+].

Anal. Calcd for $C_{13}H_{10}N_2O_4S$: C, 53.79; H, 3.47; N, 9.65. Found: C, 53.68; H, 3.61; N, 9.53.

9-Methyl-5*H*-benzo[*e*]naphtho[1,2-*c*][1,2]thiazine 6,6-dioxide (9f)
White solid; yield: 83%; mp 208–210 °C.

IR (KBr): 3249, 1173 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.55 (s, 3 H), 7.15 (br s, 1 H), 7.40 (d, *J* = 7.9 Hz, 1 H), 7.58–7.66 (m, 2 H), 7.82 (d, *J* = 8.7 Hz, 1 H), 7.87 (s, 1 H), 7.92 (t, *J* = 8.5 Hz, 2 H), 8.05 (d, *J* = 8.8 Hz, 1 H), 8.15 (d, *J* = 8.0 Hz, 1 H).

MS: *m*/*z* = 295 [M^+].

Anal. Calcd for $C_{17}H_{13}NO_2S$: C, 69.13; H, 4.44; N, 4.74. Found: C, 69.33; H, 4.69; N, 4.61.

4-Bromo-1-methoxy-6-tosyl-6,7-dihydro-5*H*-dibenzo[*c*,*e*]azepine (9′)
Viscous oil.

IR (KBr): 1317, 1142 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H), 3.79 (s, 3 H), 4.53 (s, 4 H), 6.74–7.07 (m, 2 H), 7.39 (d, *J* = 12.5 Hz, 6 H), 7.74–8.12 (m, 2 H).

MS: *m*/*z* = 457 [M$^+$], 459 [M + 2].

Anal. Calcd for $C_{22}H_{20}BrNO_3S$: C, 57.65; H, 4.40; N, 3.06. Found: C, 57.78; H, 4.47; N, 3.00.

11-Methyl-5,9,15-[1,2]ethanediyl[1]ylidene-16*H*-dibenzo[*d*,*k*][1,2]thiaazacyclododecine 14,14-Dioxide (10a); Typical Procedure

A mixture of **5a** (200 mg, 0.39 mmol), TBAB (153 mg, 0.47 mmol), and anhyd KOAc (106 mg, 1.08 mmol) was taken up in anhyd DMF (5 mL) under an N_2 atmosphere. $Pd(OAc)_2$ (9 mg, 0.039 mmol) was added and the mixture was stirred at 120 °C for 10 h. The mixture was cooled and H_2O (25 mL) was added. The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were washed with H_2O (2 × 40 mL), followed by brine (30 mL). The organic layer was dried (Na_2SO_4), and the solvent was removed in vacuo. The crude product was purified by column chromatography (silica gel, EtOAc–PE, 1:9) to afford **10a** as a white solid; yield: 85%; mp 241–242 °C.

The other substrates **5b**–**g** were treated similarly to give products **10b**–**g**.

IR (KBr): 1462, 1317, 1149 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.52 (s, 3 H), 3.86 (d, *J* = 15.1 Hz, 1 H), 4.11–4.19 (q, *J* = 11.8 Hz, 2 H), 4.45 (d, *J* = 15.1 Hz, 1 H), 7.34–7.37 (m, 1 H), 7.39–7.44 (m, 2 H), 7.49–7.54 (m, 3 H), 7.57–7.62 (m, 3 H), 8.25 (d, *J* = 8.2 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 48.6, 49.2, 127.3, 127.4, 127.6, 128.5, 128.8, 129.0, 129.2, 129.7, 130.9, 133.7, 134.6, 136.2, 137.5, 139.5, 141.2, 144.9.

HRMS: *m*/*z* [M + Na] calcd for $C_{21}H_{17}NO_2S$: 370.0878; found: 370.0878 [M + Na].

2,6-Dimethoxy-11-methyl Derivative 10b

White solid; yield: 80%; mp 223–224 °C.

IR (KBr): 1303, 1148 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.50 (s, 3 H), 3.75 (d, *J* = 15 Hz, 1 H), 3.86 (s, 3 H), 3.89 (s, 3 H), 4.05 (d, *J* = 11.4 Hz, 1 H), 4.14 (d, *J* = 11.5 Hz, 1 H), 4.42 (d, *J* = 15 Hz, 1 H), 6.99 (d, *J* = 6.6 Hz, 2 H), 7.07 (d, *J* = 8.6 Hz, 1 H), 7.29 (d, *J* = 8.0 Hz, 1 H), 7.45 (s, 1 H), 7.51 (d, *J* = 8.5 Hz, 1 H), 7.70 (d, *J* = 9.2 Hz, 1 H), 8.21 (d, *J* = 8.1 Hz, 1 H).

HRMS: *m*/*z* [M + Na] calcd for $C_{23}H_{21}NO_4S$: 430.1086; found: 430.1089 [M + Na].

Unsubstituted Derivative 10c

White solid; yield: 92%; mp 173–174 °C.

IR (KBr): 1315, 1152 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.87 (d, *J* = 14.5 Hz, 1 H), 4.07 (d, *J* = 11.4 Hz, 1 H), 4.17 (d, *J* = 11.4 Hz, 1 H), 4.48 (d, *J* = 15.0 Hz, 1 H), 7.42 (d, *J* = 6.8 Hz, 2 H), 7.54–7.58 (m, 6 H), 7.73 (d, *J* = 9.0 Hz, 2 H) 8.38 (d, *J* = 8.2 Hz, 1 H).

HRMS: *m*/*z* [M + Na] calcd for $C_{20}H_{15}NO_2S$: 356.0722; found: 356.0721 [M + Na].

2,6-Dimethoxy Derivative 10d

White solid; yield: 87%; mp 199–200 °C.

IR (KBr): 1312, 1156 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.76 (d, *J* = 15.2 Hz, 1 H), 3.86 (s, 3 H), 3.89 (s, 3 H), 4.06 (d, *J* = 11.5 Hz, 1 H), 4.14 (d, *J* = 11.4 Hz, 1 H), 4.42 (d, *J* = 15.2 Hz, 1 H), 6.99 (d, *J* = 6.6 Hz, 2 H), 7.09 (d, *J* = 8.5 Hz, 1 H), 7.47–7.53 (m, 2 H), 7.65–7.72 (m, 3 H), 8.34 (d, *J* = 8.0 Hz, 1 H).

MS: *m*/*z* = 393 [M$^+$].

Anal. Calcd for $C_{22}H_{19}NO_4S$: C, 67.16; H, 4.87; N, 3.56. Found: C, 67.27; H, 4.83; N, 3.67.

11-Amino Derivative 10e

White solid; yield: 84%; mp 290–291 °C.

IR (KBr): 3478, 3382, 1288, 1139 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.83 (d, *J* = 15.1 Hz, 1 H), 4.09 (d, *J* = 11.9 Hz, 1 H), 4.20 (d, *J* = 11.8 Hz, 1 H), 4.27 (br s, 2 H), 4.48 (d, *J* = 14.9 Hz, 1 H), 6.69 (d, *J* = 8.7 Hz, 1 H), 6.89 (d, *J* = 1.7 Hz, 1 H), 7.34–7.40 (m, 4 H), 7.49 (t, *J* = 8.4 Hz, 2 H), 7.59 (d, *J* = 7.6 Hz, 1 H), 8.11 (d, *J* = 8.6 Hz, 1 H).

MS: *m*/*z* = 348 [M$^+$].

Anal. Calcd for $C_{20}H_{16}N_2O_2S$: C, 68.94; H, 4.63; N, 8.04. Found: C, 68.80; H, 4.74; N, 8.23.

11-Amino-2,6-dimethoxy Derivative 10f

White solid; yield: 81%; mp 206–207 °C.

IR (KBr): 3482, 3369, 1308, 1142 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.72 (d, *J* = 15.0 Hz, 1 H), 3.85 (s, 3 H), 3.87 (s, 3 H), 4.02 (d, *J* = 11.4 Hz, 1 H), 4.16 (d, *J* = 11.5 Hz, 1 H), 4.23 (br s, 2 H), 4.43 (d, *J* = 15.2 Hz, 1 H), 6.63 (d, *J* = 8.8 Hz, 1 H), 6.82 (d, *J* = 1.7 Hz, 1 H), 6.98 (d, *J* = 6.8 Hz, 2 H), 7.04 (d, *J* = 8.4 Hz, 1 H), 7.45 (d, *J* = 8.6 Hz, 1 H), 7.77 (d, *J* = 8.4 Hz, 1 H), 8.07 (d, *J* = 8.7 Hz, 1 H).

MS: *m*/*z* = 408 [M$^+$].

Anal. Calcd for $C_{22}H_{20}N_2O_4S$: C, 64.69; H, 4.94; N, 6.86. Found: C, 64.86; H, 4.90; N, 6.76.

6-Methoxy-11-methyl Derivative 10g

White solid; yield: 81%; mp 198–200 °C.

IR (KBr): 1303, 1148 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.50 (s, 3 H), 3.75 (d, *J* = 15 Hz, 1 H), 3.86 (s, 3 H), 4.06 (d, *J* = 6.8 Hz, 2 H), 4.40 (d, *J* = 15 Hz, 1 H), 7.08 (d, *J* = 8.6 Hz, 1 H), 7.29 (d, *J* = 8.3 Hz, 1 H), 7.35 (t, *J* = 7.5 Hz, 1 H), 7.43–7.48 (m, 2 H), 7.54 (d, *J* = 8.8 Hz, 2 H), 7.93 (d, *J* = 7.5 Hz, 1 H), 8.21 (d, *J* = 8.1 Hz, 1 H).

MS: *m*/*z* = 377 [M$^+$].

Anal. Calcd for $C_{22}H_{19}NO_3S$: C, 70.00; H, 5.07; N, 3.71. Found: C, 70.14; H, 5.17; N, 3.59.

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References and Notes

(1) Scozzafava, A.; Owa, T.; Mastrolorenzo, A.; Supuran, C. T. *Curr. Med. Chem.* **2003**, *10*, 925; and references cited therein.
(2) Drews, J. *Science* **2000**, *287*, 1960.
(3) (a) Hanessian, S.; Sailes, H.; Therrien, E. *Tetrahedron* **2003**, *59*, 7047. (b) Zhuang, L.; Wai, J. S.; Embrey, M. W.; Fisher, T. E.; Egbertson, M. S.; Payne, L. S.; Guare, J. P.; Vacca, J. P. Jr.; Hazuda, D. J.; Felock, P. J.; Wolfe, A. L.; Stillmock,

K. A.; Witmer, M. V.; Moyer, G.; Schleif, W. A.; Gabryelski, L. J.; Leonard, Y. M.; Lynch, J. J.; Michelson, S. R. Jr.; Young, S. D. *J. Med. Chem.* **2003**, *46*, 453. (c) Miller, R. A.; Humphrey, G. R.; Lieberman, D. R.; Ceglia, S. S.; Kennedy, D. J.; Grabowski, E. J. J.; Reider, P. J. *J. Org. Chem.* **2000**, *65*, 1399.
(4) Wroblewski, T.; Graul, A.; Castaner, J. *Drugs Future* **1998**, *23*, 365.
(5) Rabasseda, X.; Hopkins, S. J. *Drugs Today* **1994**, *30*, 557.
(6) Inagaki, M.; Tsuri, T.; Jyoyama, H.; Ono, T.; Yamada, K.; Kobayashi, M.; Hori, Y.; Arimura, A.; Yasui, K.; Ohno, K.; Kakudo, S.; Koizumi, K.; Suzuki, R.; Kato, M.; Kawai, S.; Matsumoto, S. *J. Med. Chem.* **2000**, *43*, 2040.
(7) McKerrecher, D.; Pike, K. G.; Waring, M. J. WO 2006,125,972, **2006**.
(8) Brzozowski, Z.; Saczewski, F.; Neamati, N. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5298.
(9) Wells, G. J.; Tao, M.; Josef, K. A.; Bihovsky, R. *J. Med. Chem.* **2001**, *44*, 3488.
(10) Tanimukai, H.; Inui, M.; Harigushi, S.; Kaneko, J. *Biochem. Pharmacol.* **1965**, *14*, 961.
(11) Silvestri, R.; Marfe, G.; Artico, M.; La Regina, G.; Lavecchia, A.; Novellino, E.; Morgante, M.; Di Stefano, C.; Catalano, G.; Filomeni, G.; Abruzzese, E.; Ciriolo, M. R.; Russo, M. A.; Amadori, S.; Cirilli, R.; La Torre, F.; Salimei, P. S. *J. Med. Chem.* **2006**, *49*, 5840.
(12) (a) Bravo, R. D.; Canepa, A. S. *Synth. Commun.* **2002**, *32*, 3675. (b) Orazi, O. O.; Corral, R. A.; Bravo, R. *J. Heterocycl. Chem.* **1986**, *23*, 1701.
(13) Katritzky, A. R.; Wu, J.; Rachwal, S.; Rachwal, B.; Macomber, D. W.; Smith, T. P. *Org. Prep. Proced. Int.* **1992**, *24*, 463.
(14) Lee, J.; Zhong, Y.-L.; Reamer, R. A.; Askin, D. *Org. Lett.* **2003**, *5*, 4175.
(15) Enders, D.; Moll, A.; Bats, J. W. *Eur. J. Org. Chem.* **2006**, 1271.
(16) Chiacchio, U.; Corsaro, A.; Rescifina, A.; Bkaithan, M.; Grassi, G.; Piperno, A. *Tetrahedron* **2001**, *57*, 3425.
(17) (a) Metz, P.; Seng, D.; Frohlich, R. *Synlett* **1996**, 741. (b) Plietker, B.; Seng, D.; Frohlich, R.; Metz, P. *Tetrahedron* **2000**, *56*, 873. (c) Greig, I. R.; Trozer, M. J.; Wright, P. T. *Org. Lett.* **2001**, *3*, 369.
(18) Zhou, A.; Hanson, P. R. *Org. Lett.* **2008**, *10*, 2951.
(19) Liu, X.-Y.; Li, C.-H.; Che, C.-M. *Org. Lett.* **2006**, *8*, 2707.
(20) (a) Dauban, P.; Dodd, R. H. *Org. Lett.* **2000**, *2*, 2327. (b) Dauban, P.; Saniere, L.; Aurelie, T.; Dodd, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 7707. (c) Sherman, E. S.; Chemler, S. R.; Tan, T. B.; Gerlits, O. *Org. Lett.* **2004**, *6*, 1573.
(21) (a) Liang, J.-L.; Yuan, S.-X.; Chan, P. W. H.; Che, C.-M. *Org. Lett.* **2002**, *4*, 4507. (b) Padwa, A.; Flick, A. C.; Leverett, C. A.; Stengel, T. *J. Org. Chem.* **2004**, *69*, 6377. (c) Hopkins, M. J.; Hanson, P. R. *Org. Lett.* **2008**, *10*, 2223.
(22) Hanson, P. R.; Probst, D. A.; Robinson, R. E.; Yau, M. *Tetrahedron Lett.* **1999**, *40*, 4761.
(23) (a) Merten, S.; Frohlich, R.; Kataeva, O. *Adv. Synth. Catal.* **2005**, *347*, 754. (b) Vasudevan, A.; Tseng, P.-S.; Djuric, S. W. *Tetrahedron Lett.* **2006**, *47*, 8591. (c) Rayabarapu, D. K.; Zhou, A.; Jeon, K. O.; Samarakoon, T.; Rolfe, A.; Siddiqui, H.; Hanson, P. R. *Tetrahedron* **2009**, *65*, 3180.
(24) (a) Majumdar, K. C.; Mondal, S. *Tetrahedron Lett.* **2007**, *48*, 6951. (b) Majumdar, K. C.; Mondal, S. *Tetrahedron Lett.* **2008**, *49*, 2418.
(25) (a) Majumdar, K. C.; Chakravorty, S.; De, N. *Tetrahedron Lett.* **2008**, *49*, 3419. (b) Majumdar, K. C.; Chattopadhaya, B.; Ray, K. *Tetrahedron Lett.* **2007**, *48*, 7633. (c) Majumdar, K. C.; Chattopadhaya, B.; Nath, S. *Tetrahedron Lett.* **2008**, *49*, 1609.
(26) Majumdar, K. C.; Mondal, S.; De, N. *Synlett* **2008**, 2851.
(27) Reilly, T. P.; Ju, C. *Curr. Opin. Allergy Clin. Immunol.* **2002**, *2*, 307.
(28) CCDC Ref. No. for the CIF file of **10a**: CCDC-693638.
(29) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009.