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Construction of Linked Nitrogen Heterocycles by Palladium(0)-Catalyzed Intramolecular Domino Cyclization of 2-Alkynylaziridines Bearing a 2-Aminoethyl Group via Ring Expansion with Isocyanate

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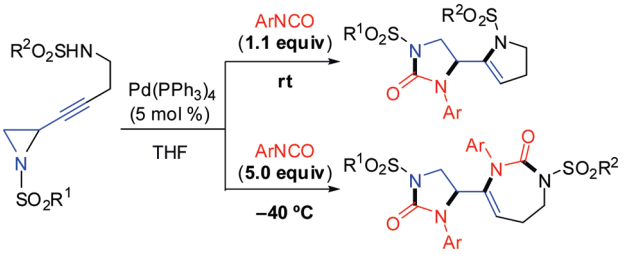
Received March 13, 2010

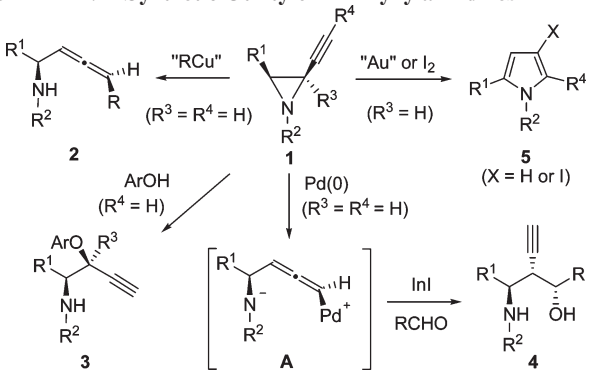


A novel palladium(0)-catalyzed domino cyclization of 2-alkynylaziridines with isocyanates through ring expansion is described. Treatment of *N*-protected 2-(4-aminobut-1-ynyl)aziridine derivatives with a catalytic amount of $Pd(PPh_3)_4$ and aryl isocyanates in THF at room temperature affords 4-(4,5-dihydropyrrol-2-yl)imidazolidin-2-one derivatives in good yields. Interestingly, bis-adducts were selectively obtained by use of excess isocyanate (5 equiv) at lower reaction temperature.

Introduction

2-Alkynylaziridines **1** are valuable intermediates for the synthesis of nitrogen-containing compounds due to the presence of a strained three-membered ring at the propargylic position (Scheme 1). Previously we reported a stereoselective synthesis of α-amino allenes **2** by an *anti*-S_N2' ring-opening reaction of 2-ethynylaziridines with an organocopper reagent.[1] S_N2-type ring-opening of 2-ethynylaziridines with phenol derivatives to give **3** is useful for stereoselective construction of a tertiary ether motif in ustiloxin D.[2] We have also demonstrated that 2-ethynylaziridines can function as a chiral carbon nucleophile by umpolung with InI in the presence of a palladium(0) catalyst and water, to produce 2-ethynyl-1,3-amino alcohols **4** stereoselectively by reaction with an aldehyde.[3] This reaction clearly shows that 2-ethynylaziridines can form allenylpalladium(II) intermediate **A** by a stereoselective ring-opening reaction with palladium(0). Quite recently, efficient syntheses of pyrroles **5** by reaction with a gold catalyst or iodine were also reported.[4] However, to the best of our knowledge, there have been no precedents for domino cyclization with 2-alkynylaziridines.

SCHEME 1. Synthetic Utility of 2-Alkynylaziridines



(1) (a) Ohno, H.; Toda, A.; Miwa, Y.; Taga, T.; Fujii, N.; Ibuka, T. *Tetrahedron Lett.* **1999**, *40*, 349–352. (b) Ohno, H.; Toda, A.; Fujii, N.; Takemoto, Y.; Tanaka, T.; Ibuka, T. *Tetrahedron* **2000**, *56*, 2811–2820. Quite recently, Yudin reported a highly related allene synthesis by S_N2' reduction of unprotected 2-ethynylaziridines with 9-BBN, see: (c) He, Z.; Yudin, A. K. *Angew. Chem., Int. Ed.* **2010**, *49*, 1607–1610.

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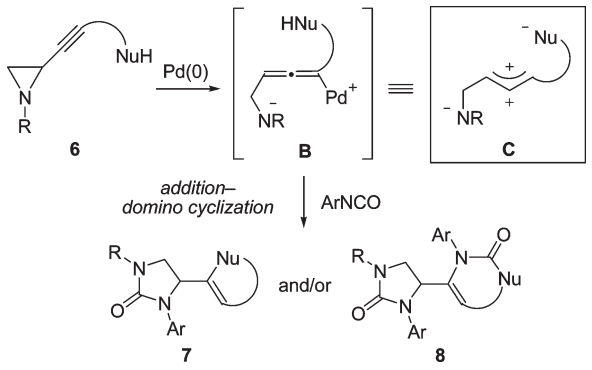
(4) (a) Davies, P. W.; Martin, N. *Org. Lett.* **2009**, *11*, 2293–2296. (b) Yoshida, M.; Al-Amin, M.; Shishido, K. *Tetrahedron Lett.* **2009**, *50*, 6268–6270. (c) Chen, D.-D.; Hou, X.-L.; Dai, L.-X. *Tetrahedron Lett.* **2009**, *50*, 6944–6946. (d) Du, X.; Xie, X.; Liu, Y. *J. Org. Chem.* **2010**, *75*, 510–513.

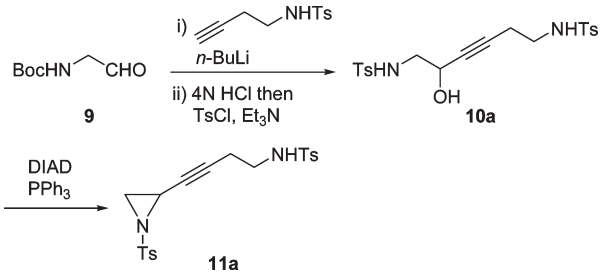
Published on Web 04/20/2010 DOI: 10.1021/jo100462w

SCHEME 2. Domino Cyclization of 2-Alkynylaziridines 6 with Aryl Isocyanates in the Presence of a Palladium(0) Catalyst



It is well-known that palladium(0)-catalyzed reactions of propargylic compounds developed by Tsuji and co-workers provide an efficient approach to not only introduce two nucleophiles into a substrate[5] but also construct various heterocyclic compounds.[6] Furthermore, our recent studies on bromoallenes and propargyl bromides have demonstrated that this type of reactivity is extremely useful for construction of medium-sized heterocycles,[7] bicyclic sulfamides,[8] and pyrrolo[3,2-*b*]pyridine derivatives.[9] Thus allenic/propargylic compounds can act as allylic dication equivalents in the presence of a palladium(0) catalyst. On the basis of these findings and sufficient reactivity of 2-alkynylaziridines with palladium(0), we envisioned that 2-alkynylaziridines **6**, bearing nucleophilic functional groups on the alkyne terminus, would facilitate palladium(0)-catalyzed ring-opening followed by domino cyclization through allenylpalladium(II) intermediate **B**, an equivalent of allyl dication **C** (Scheme 2). In this paper, we describe a novel synthesis of linked heterocycles **7**[10] by palladium(0)-catalyzed domino cyclization of **6**, via ring-expansion by addition with an aryl isocyanate.[11] A bis-addition cascade with an excess amount of isocyanate to form linked cyclic ureas **8** selectively is also presented.

SCHEME 3. Preparation of 2-Alkynylaziridine 11a[a]

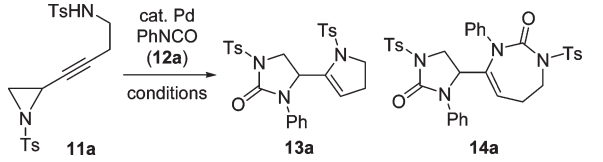


[a]Abbreviation: DIAD = diisopropyl azodicarboxylate.

Results and Discussion

2-Alkynylaziridine **11a**, a representative substrate for the domino cyclization, was readily prepared as follows (Scheme 3). Addition of lithium acetylide derived from *N*-tosylbut-3-yn-1-amine to commercially available *N*-Boc-glycinal **9** followed by removal of the Boc group and tosylation provided propargyl alcohol **10a**. Aziridination under the Mitsunobu conditions afforded the desired alkynylaziridine **11a** bearing a nucleophilic functional group. Other aziridines were prepared in a similar manner.

TABLE 1. Domino Reaction of Alkynylaziridine 11a with Phenyl Isocyanate 12a under Various Reaction Conditions



					yield (%)[b]	
entry[a]	catalyst system	solvent	temp (°C)	time (min)	**13a**	**14a**
1[c]	$Pd(OAc)_2$, PPh_3	THF	rt	20	4	0
2	$PdCl_2(dppf)\cdot CH_2Cl_2$	THF	rt	180	0	0
3[d]	$Pd_2(dba)_3\cdot CHCl_3$	THF	rt	240	trace	0
4	$Pd(PPh_3)_4$	THF	rt	1	82	0
5	$Pd(PPh_3)_4$	MeCN	rt	45	22	13
6	$Pd(PPh_3)_4$	DMF	rt	60	39	4
7	$Pd(PPh_3)_4$	dioxane	rt	20	80	0
8	$Pd(PPh_3)_4$	CH_2Cl_2	rt	40	37	6
9	$Pd(PPh_3)_4$	THF	0	15	59	24
10	$Pd(PPh_3)_4$	THF	−40	40	17	44
11	$Pd(PPh_3)_4$	THF	−78	40	No reaction	
12[e]	$Pd(PPh_3)_4$	THF	−40	40	18	82
13[f]	$Pd(PPh_3)_4$	THF	−40	40	7	93

[a]Unless otherwise stated, all reactions were carried out with palladium catalyst (5 mol %) and PhNCO (1.1 equiv). [b]Yields of isolated products. [c]PPh_3 (10 mol %) was used. [d]$Pd_2(dba)_3\cdot CHCl_3$ (2.5 mol %) was used. [e]PhNCO (2.0 equiv) was used. [f]PhNCO (5.0 equiv) was used.

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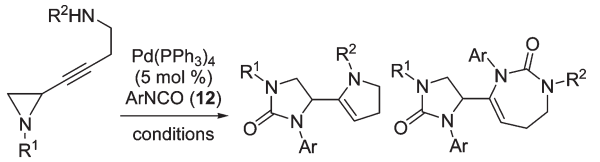
TABLE 2. Domino Cyclization of Various Alkynylaziridines and Aryl Isocyanates



11a ($R^1 = R^2$ = Ts)
11b (R^1 = Ms, R^2 = Ts)
11c (R^1 = Mts, R^2 = Ts)
11d ($R^1 = R^2$ = Mts)

					product (yield[b], %)	
entry	substrate	isocyanate (Ar)	condition[a]	time (min)	**13**	**14**
1	**11a**	**12a** (Ph)	A	1	**13a** (82)	**14a** (0)
2	**11b**	**12a** (Ph)	A	1	**13b** (0)	**14b** (73)[c]
3	**11c**	**12a** (Ph)	A	1	**13c** (75)	**14c** (0)
4	**11d**	**12a** (Ph)	A	1	**13d** (89)	**14d** (0)
5	**11a**	**12b** (4-MeC_6H_4)	A	1	**13e** (73)	**14e** (2)
6	**11a**	**12c** (4-^{i}PrC_6H_4)	A	1	**13f** (86)	**14f** (0)
7	**11a**	**12d** (4-FC_6H_4)	A	1	**13g** (71)	**14g** (11)
8	**11a**	**12e** (4-ClC_6H_4)	A	1	**13h** (84)	**14h** (8)
9	**11a**	**12f** [3-$(CF_3)C_6H_4$]	A	1	**13i** (80)	**14i** (13)
10	**11a**	**12g** [3-$(NO_2)C_6H_4$]	A	1	**13j** (93)	**14j** (0)
11	**11a**	**12h** (2-MeC_6H_4)	A	1	**13k** (83)	**14k** (0)
12	**11a**	**12a** (Ph)	B	40	**13a** (7)	**14a** (93)
13	**11b**	**12a** (Ph)	B	25	**13b** (0)	**14b** (99)
14	**11c**	**12a** (Ph)	B	30	**13c** (62)	**14c** (0)
15	**11d**	**12a** (Ph)	B	30	**13d** (67)	**14d** (0)
16	**11a**	**12b** (4-MeC_6H_4)	B	40	**13e** (8)	**14e** (89)
17	**11a**	**12c** (4-^{i}PrC_6H_4)	B	25	**13f** (0)	**14f** (99)
18	**11a**	**12d** (4-FC_6H_4)	B	35	**13g** (6)	**14g** (92)
19	**11a**	**12e** (4-ClC_6H_4)	B	40	**13h** (trace)	**14h** (74)
20	**11a**	**12f** [3-$(CF_3)C_6H_4$]	B	30	**13i** (45)	**14i** (54)
21	**11a**	**12g** [3-$(NO_2)C_6H_4$]	B	30	**13j** (76)	**14j** (0)
22	**11a**	**12h** (2-MeC_6H_4)	B	40	**13k** (14)	**14k** (80)

[a]Conditions A: $Pd(PPh_3)_4$ (5 mol %), ArNCO (1.1 equiv), THF, rt. Conditions B: $Pd(PPh_3)_4$ (5 mol %), ArNCO (5.0 equiv), THF, −40 °C. [b]Yields of isolated products based on **11** unless otherwise noted. [c]Based on isocyanate.

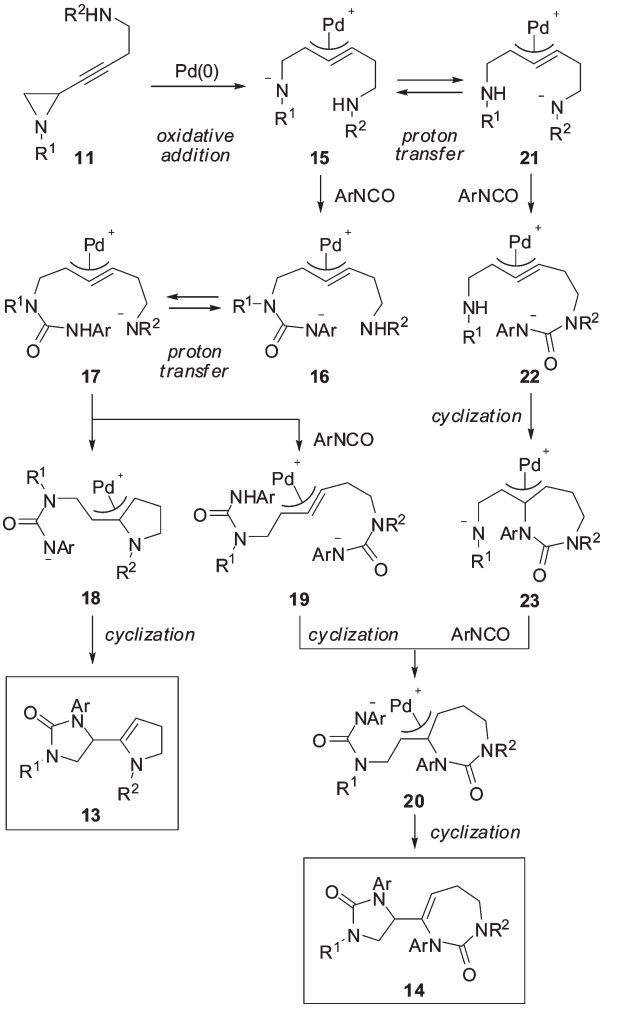
We started our investigation of the domino cyclization with 2-alkynylaziridine **11a** and phenyl isocyanate **12a** (1.1 equiv) under various reaction conditions (Table 1). The reaction in the presence of $Pd(OAc)_2$ and PPh_3 at room temperature, standard conditions for vinylaziridine cycloaddition,[11a] gave only 4% yield of the desired product **13a** (entry 1). Similarly, $PdCl_2$-(dppf)·CH_2Cl_2 was ineffective for the desired reaction (entry 2). After screening several palladium catalysts, we found that Pd-$(PPh_3)_4$ (5 mol %) was the most effective catalyst for the domino cyclization to provide the desired bicyclic product **13a** in 82% yield (entry 4). Next, we examined the influence of reaction solvent and temperature. MeCN, DMF, and CH_2Cl_2 were ineffective as the solvent (entries 5, 6, and 8). Interestingly, the reaction at 0 °C afforded bis-adduct **14a** in 24% yield along with the monoadduct **13a** (59%, entry 9).[12] The selectivity for bis-addition was improved by conducting the reaction at −40 °C (entry 10, **13a**:**14a** = 17:44), while the reaction did not proceed at −78 °C (entry 11). As we expected, the reaction with an increased amount of isocyanate **12a** (5.0 equiv) at −40 °C more efficiently promoted bis-addition to give **14a** selectively in 93% yield (entry 13).

Having established the optimal reaction conditions for selective formation of **13a** (entry 4) and **14a** (entry 13), we investigated the domino cyclization using various 2-alkynylaziridines and aryl isocyanates under two sets of reaction conditions [conditions A: $Pd(PPh_3)_4$ (5 mol %), aryl isocyanate (1.1 equiv), THF, rt; conditions B: $Pd(PPh_3)_4$ (5 mol %), aryl isocyanate (5.0 equiv), THF, −40 °C]. The results are summarized in Table 2. Interestingly, the reaction of *N*-mesylalkynylaziridine **11b** under conditions A, monoaddition conditions for the *N*-tosylaziridine **11a** (entry 1), selectively afforded the bis-adduct **14b** in 73% yield (based on isocyanate, entry 2). In sharp contrast, alkynylaziridines **11c** and **11d** bearing a 2,4,6-trimethylphenylsulfonyl (Mts) group on the aziridine nitrogen were efficiently converted into the corresponding monoadducts **13c** (75%) and **13d** (89%), respectively, under conditions A (entries 3 and 4). We next investigated the substitution effect of the aryl isocyanates using the aziridine **11a** (entries 5−11). The reaction with 4-methylphenyl or 4-isopropylphenyl isocyanates **12b** and **12c** under conditions A gave bicyclic products **13e** and **13f** in good yields (73% and 86%, entries 5 and 6). Similarly, exposure of **11a** to aryl isocyanates **12d** and **12e** containing a halogen atom (F or Cl) at the 4-position under conditions A afforded the desired bicyclic products **13g** (71%) and **13h** (84%), respectively (entries 7 and 8). The reaction with isocyanates **12f**−**h** containing an electron-withdrawing group (CF_3 or NO_2) at the 3-position or a methyl group at the 2-position also afforded monoadducts **13i**−**k** in 80−93% yields (entries 9−11).

Next, the reaction under conditions B was investigated. When the reaction of the *N*-mesylaziridine **11b** was carried

(12) Structures of bicyclic heterocycles **13a** and **14a** were characterized by COSY, HMQC and HMBC spectroscopic analysis and NOE experiment (see the Supporting Information).

SCHEME 4. Plausible Reaction Mechanism of Palladium(0)-Catalyzed Domino Cyclization of 2-Alkynylaziridines in the Presence of Aryl Isocyanates



out under conditions B, bis-adduct **14b** was obtained in 99% yield (entry 13), similar to the reaction of *N*-tosylaziridine **11a** (entry 12). On the other hand, treatment of the aziridines **11c** and **11d** bearing an *N*-Mts group under conditions B afforded the monoadducts **13c** (62%, entry 14) and **13d** (67%, entry 15), respectively, the same products produced by the reaction under conditions A (entries 3 and 4). Furthermore, the bis-adducts **14e**−**h** and **14k** were selectively obtained in 74−99% yields from **11a** when using 4-substituted aryl isocyanates **12b**−**e** or the 2-methyl one **12h** (entries 16−19 and 22). For a reason that is unclear, substitution with an electron-withdrawing group at the 3-position of phenyl isocyanate increased formation of monoadducts **13i** and **13j** (entries 20 and 21). These observations have revealed that *N*-arylsulfonylaziridines allow selective formation of the linked heterocycles **13** through monoaddition under conditions A, while the selectivity of the bis-adduct under conditions B depends on the substituent on the phenyl isocyanates as well as the aziridine nitrogen.[13]

(13) Unfortunately, the reaction with *N*-benzyl or *N*-tosyl isocyanates gave a mixture of unindentified products without producing the desired bis-cyclization products.

Plausible reaction mechanisms for the formation of the linked nitrogen heterocycles **13** and **14** are shown in Scheme 4. Oxidative addition of alkynylaziridine **11** to palladium(0) followed by nucleophilic addition of the resulting η^3-propargylpalladium complex **15**[14] to aryl isocyanates forms η^3-propargylpalladium complex **16**, which is in equilibrium with **17**. The first cyclization onto the central carbon atom of **17** and the second cyclization of the resulting η^3-allylpalladium complex **18** produces the monoadducts **13**. On the other hand, addition of **17** to a second molecule of aryl isocyanate before the successive cyclization will afford the bis-adducts **14** via **19** and **20**.[15] Excess isocyanate (5.0 equiv, conditions B) will apparently promote the second addition of **17** to form **19**, which will increase the ratio of the bis-adducts **14**. Another pathway to form the intermediate **20** would be conversion of **15** to **21** by proton transfer, addition of **21** to aryl isocyanate, cyclization to form **23**, and addition to the second molecule of aryl isocyanate. Selective formation of bis-adduct **14b** from *N*-mesylaziridine **11b** (R^1 = Ms, R^2 = Ts) can be rationalized as follows. The intermediate **15** bearing an *N*-mesyl group as R^1 will be rapidly converted to **21** because of the weaker electron-withdrawing effect of a mesyl group than that of a tosyl group (as R^2).[16] This can assist the reaction of **21** with isocyanate to produce **22**, a precursor of the bis-adduct **14**.[17,18]

Conclusion

In conclusion, we have developed a novel synthesis of linked nitrogen heterocycles by palladium(0)-catalyzed domino cyclization of 2-alkynylaziridines via addition with an aryl isocyanate. This reaction selectively provides mono- and bis-adducts by simply changing the reaction conditions. Further investigation for the construction of other heterocycles is in progress in our laboratory.

Experimental Section

General Procedure for Preparation of Propargyl Alcohols 10: Synthesis of *N*,*N*′-(2-Hydroxyhex-3-yne-1,6-diyl)bis(4-methylphenylsulfonamide) (10a). To a stirred mixture of *N*-(but-3-ynyl)-4-methylphenylsulfonamide (1.51 g, 6.78 mmol) in dry THF (20 mL) under nitrogen was added *n*-BuLi (1.65 mol/L; 8.03 mL, 13.2 mmol) at −78 °C, and the mixture was stirred at the same temperature for 20 min. *N*-Boc glycinal **9** (502 mg, 3.15 mmol) in THF (10 mL) was added to the above stirred reagent at −78 °C, and the mixture was stirred at 0 °C for 2 h, followed by quenching with saturated NH_4Cl (2 mL). The whole was extracted with EtOAc,

(14) (a) Ogoshi, S.; Tsutsumi, K.; Nishiguchi, S.; Kurosawa, H. *J. Organomet. Chem.* **1995**, *493*, C19–C21. (b) Tsutsumi, K.; Ogoshi, S.; Nishiguchi, S.; Kurosawa, H. *J. Am. Chem. Soc.* **1998**, *120*, 1938–1939. (c) Tsutsumi, K.; Kawase, T.; Kakiuchi, K.; Ogoshi, S.; Okada, Y.; Kurosawa, H. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2687–2692.

(15) We previously reported that medium-sized rings easily formed from η^3-propargylpalladium complexes; see ref 7.

(16) In other words, the higher basicity of the anionic mesylamide nitrogen in **15** (R^1 = Ms, R^2 = Ts) in comparison to the anionic tosylamide nitrogen in **21** would shift the equilibrium in the direction of **21** thus favoring the formation of **14b**. The following pK_a values were reported. $PhSO_2NH_2$: pK_a = 16.1 (DMSO); $MeSO_2NH_2$: pK_a = 17.5 (DMSO), see: Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463.

(17) Although the exact reason for the temperature effect on the selectivity (entry 4 vs 10) is unclear, a lower reaction temperature might decrease the impact of the entropy loss ($-T\Delta S$) in the intermolecular addition to a second molecule of isocyanate. This effect can promote formation of the bis-adduct **14a**. Because the entropy loss in the intramolecular cyclization reaction to form **13a** would be smaller than that in the intermolecular addition reaction, the cyclization reaction will receive less benefit of the effect of lower reaction temperature than the intermolecular addition reaction.

(18) At present, the effect of the electron-withdrawing group at the 3-position of the aryl isocyanate **12f** and **12g** on the selectivity is unclear.

and the extract was washed successively with water and brine, and dried over Na_2SO_4. The filtrate was concentrated and purified by flash chromatography over silica gel with *n*-hexane/EtOAc (1:1) to give a crude propargyl alcohol as an oil. This crude propargyl alcohol was dissolved in 4 N HCl/dioxane (1 mL) at room temperature, and the mixture was stirred at the same temperature for 30 min. TsCl (230 mg, 1.21 mmol) in $CHCl_3$ (2 mL) was added to the mixture. The mixture was cooled to 0 °C and Et_3N (1.5 mL) was added to the mixture, and the resulting mixture was stirred at room temperature for 30 min. The mixture was partitioned between EtOAc and water. The organic layer was separated, washed with water and brine, and dried over Na_2SO_4. The filtrate was concentrated under reduced pressure to give an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (1:1 to 1:2) to give **10a** (120 mg, 69% yield, 3 steps): colorless oil; IR (neat) (cm^{-1}) 3482 (OH), 3282 ($NHSO_2$), 2237 (C≡C), 1324 ($NHSO_2$), 1159 ($NHSO_2$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.36 (td, J = 6.0, 1.6 Hz, 2H), 2.42 (s, 6H), 3.05−3.11 (m, 4H), 3.67 (ddd, J = 9.2, 6.8, 4.0 Hz, 1H), 4.38−4.43 (m, 1H), 5.43−5.49 (m, 1H), 7.29−7.31 (m, 4H), 7.75−7.77 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.3, 21.5 (2C), 41.6, 48.7, 61.4, 80.5, 83.4, 127.0 (2C), 127.1 (2C), 129.8 (4C), 136.9, 137.1, 143.57, 143.61; MS (FAB) *m*/*z* (%) 437 (MH^+, 100); HRMS (FAB) calcd for $C_{20}H_{25}N_2O_5S_2$ (MH^+) 437.1205, found 437.1225.

General Procedure for Preparation of 2-Alkynylaziridines 11: *N*-{4-[1-(4-Methylphenylsulfonyl)aziridin-2-yl]but-3-ynyl}-4-methylphenylsulfonamide (11a). To a stirred mixture of the propargyl alcohol **10a** (323 mg, 0.488 mmol) and PPh_3 (233 mg, 0.888 mmol) in THF (5 mL) was added diisopropyl azodicarboxylate (386 μL, 1.15 mmol; 40% in toluene solution) at room temperature, and the resulting mixture was stirred at the same temperature for 1 min. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (5:4) to give **11a** (249 mg, 82% yield): colorless oil; IR (neat) (cm^{-1}) 3300 ($NHSO_2$), 2253 (C≡C), 1329 ($NHSO_2$), 1161 ($NHSO_2$); ^1H NMR (500 MHz, $CDCl_3$) δ: 2.32 (td, J = 6.5, 1.5 Hz, 2H), 2.34 (d, J = 4.5 Hz, 1H), 2.43 (s, 3H), 2.46 (s, 3H), 2.67−2.68 (m, 1H), 3.05 (td, J = 6.5, 6.5 Hz, 2H), 3.17−3.20 (m, 1H), 4.77−4.87 (m, 1H), 7.30 (d, J = 8.5 Hz, 2H), 7.36 (d, J = 8.5 Hz, 2H), 7.73 (d, J = 8.5 Hz, 2H), 7.83 (d, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.2, 21.5, 21.7, 28.1, 34.7, 41.4, 77.2, 79.8, 127.0 (2C), 128.0 (2C), 129.8 (2C), 129.9 (2C), 134.4, 136.9, 143.6, 145.1; MS (FAB) *m*/*z* (%) 419 (MH^+, 54), 154 (100); HRMS (FAB) calcd for $C_{20}H_{23}N_2O_4S_2$ (MH^+) 419.1099, found 419.1112.

General Procedure for Domino Cyclization of 2-Alkynylaziridines and Aryl Isocyanates (Conditions A): Synthesis of 1-(4-Methylphenylsulfonyl)-4-[1-(4-methylphenylsulfonyl)-4,5-dihydro-1*H*-pyrrol-2-yl]-3-phenylimidazolidin-2-one (13a) (Table 1, Entry 4). To a stirred mixture of 2-alkynylaziridine **11a** (25.2 mg, 0.0603 mmol) and PhNCO **12a** (7.2 μL, 0.0663 mmol) in THF (0.6 mL) was added $Pd(PPh_3)_4$ (3.5 mg, 0.00301 mmol) at room temperature, and the resulting mixture was stirred at the same temperature for 1 min. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (5:2 to 3:2) to give **13a** (26.5 mg, 82% yield): colorless oil; IR (neat) (cm^{-1}) 1736 (C=O), 1598 (C=C), 1364 (NSO_2), 1171 (NSO_2); ^1H NMR (500 MHz, $CDCl_3$) δ 1.96−2.04 (m, 1H), 2.10−2.17 (m, 1H), 2.42 (s, 3H), 2.44 (s, 3H), 3.76 (ddd, J = 11.5, 10.5, 6.5 Hz, 1H), 3.84−3.90 (m, 1H), 4.05 (dd, J = 9.5, 9.0 Hz, 1H), 4.20 (dd, J = 9.5, 2.5 Hz, 1H), 5.09−5.11 (m, 1H), 5.41−5.43 (m, 1H), 7.09−7.12 (m, 1H), 7.24−7.29 (m, 4H), 7.33 (d, J = 8.5 Hz, 2H), 7.37 (d, J = 8.5 Hz, 2H), 7.65 (d, J = 8.5 Hz, 2H), 7.96 (d, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6 (2C), 27.5, 47.5, 51.2, 52.4, 116.1, 120.2 (2C), 124.7, 127.5 (2C), 128.2 (2C), 129.0 (2C), 139.7 (2C), 130.0 (2C), 134.3, 134.7, 137.4, 140.7, 144.5, 145.0, 151.5; MS (FAB) *m*/*z* (%) 538 (MH^+, 100); HRMS (FAB) calcd for $C_{27}H_{28}N_3O_5S_2$ (MH^+) 538.1470, found 538.1470.

General Procedure for Domino Cyclization of 2-Alkynylaziridines and Aryl Isocyanates (Conditions B): Synthesis of 3-(4-Methylphenylsulfonyl)-7-[1-(4-methylphenylsulfonyl)-2-oxo-3-phenylimidazolidin-4-yl]-1-phenyl-4,5-dihydro-1*H*-1,3-diazepin-2(3*H*)-one (14a) (Table 1, Entry 13). To a stirred mixture of 2-alkynylaziridine **11a** (26.8 mg, 0.0641 mmol) and PhNCO **12a** (34.9 μL, 0.321 mmol) in THF (0.6 mL) was added $Pd(PPh_3)_4$ (3.7 mg, 0.00320 mmol) at −40 °C, and the resulting mixture was stirred at the same temperature for 40 min. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (5:2 to 3:2) to give **14a** (39.0 mg, 93% yield) and **13a** (2.4 mg, 7% yield).

Compound 14a: colorless oil; IR (neat) (cm^{-1}) 1736 (C=O), 1697 (C=O), 1597 (C=C), 1358 (NSO_2), 1170 (NSO_2); ^1H NMR (500 MHz, $CDCl_3$) δ 2.33−2.44 (m, 2H), 2.41 (s, 3H), 2.44 (s, 3H), 3.65−3.69 (m, 1H), 3.87−3.93 (m, 2H), 4.00 (dd, J = 10.0, 3.5 Hz, 1H), 4.40 (dd, J = 10.0, 3.5 Hz, 1H), 5.76 (dd, J = 6.5, 6.5 Hz, 1H), 7.06−7.09 (m, 1H), 7.15−7.17 (m, 1H), 7.20−7.26 (m, 5H), 7.30−7.40 (m, 7H), 7.96 (d, J = 8.5 Hz, 2H), 8.02 (d, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 21.7, 24.6, 47.2, 51.8, 54.2, 119.8 (2C), 120.1, 124.7, 127.6 (2C), 128.5 (2C), 128.6, 128.9 (2C), 129.0 (2C), 129.4 (2C), 129.5 (2C), 129.8 (2C), 134.9, 135.1, 136.8, 137.4, 138.3, 144.5, 145.0, 151.5, 154.8; MS (FAB) *m*/*z* (%) 657 (MH^+, 45), 154 (100); HRMS (FAB) calcd for $C_{34}H_{33}N_4O_6S_2$ (MH^+) 657.1842, found 657.1846.

Acknowledgment. This work was supported in part by Grants-in-Aid for Encouragement of Young Scientists (A) (H.O.) and for Scientific Research (B) (T.T.) from the Ministry of Education, Culture, Sports, Science and Technology of Japan, and Targeted Proteins Research Program. A.O. is grateful for Research Fellowships from the Japan Society for the Promotion of Science (JSPS) for Young Scientist. Appreciation is expressed to Fundamental Studies in Health Sciences of the National Institute of Biomedical Innovation (NIBIO).

Supporting Information Available: Experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.