Copper-Catalyzed Cyclization of *N*-Allylhalodifluoroacetamides: An Efficient Synthesis of α,α-Difluorinated γ-Lactams

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Introduction

Numerous investigations in the past 20 years have made radical cyclization an important synthetic protocol to produce carbo- or heterocyclic compounds.[1] Reductive and atom-transfer radical cyclization of ω-haloolefins are one of the well studied examples, and many reactions including facile access to synthetically useful cyclic skeletons have been reported.[1] As reported earlier, certain transition metal complexes efficiently catalyzed cyclization of *N*-allyltrichloroacetamides to α,α,γ-trichlorinated γ-lactams.[2−5] We found that important factors in facilitating the cyclization were appropriate choice of a transition metal catalyst such as CuCl(bipy) (bipy = bipyridine) and introduction of electron-withdrawing substituents to the nitrogen atom of the amide. These factors contribute to increasing the rate of homolytic cleavage of a carbon−chlorine bond in the substrate at the initiation of the cyclization.[3] There is another important role of electron-withdrawing groups on the amide nitrogen: substantial decrease of the energy barrier of amide rotation.[5b] As pointed out by Stork, Ikeda, Curran, and Newcomb,[6] there are two rotamers in the amide substrate; one is suitable for the cyclization and the other is not. When the exchange rate of two rotamers is low and there is a side reaction pathway from the radical intermediate, one rotamer successfully gives the product, whereas the other forms byproducts or does not react at all. Thus, we have achieved facile cyclization of *N*-alkoxycarbonyl or *N*-tosyl *N*-allyltrichloroacetamides at room temperature, using the CuCl(bipy) catalyst and introduction of Ts, Cbz, and other electron-withdrawing substituents to the amide nitrogen.[3b,d]

As an application of this system, we were interested in cyclization of *N*-allylhalodifluoroacetamide derivatives. Since the difluoromethylene group biologically resembles ether-oxygen, potential biological activity of α,α-difluorinated γ-lactams has received considerable attention.[7] However, activation of a carbon−halogen bond in fluorinated halocarbons such as CF_3C-X or $ROCOCF_2-X$ is difficult to achieve compared with that in chlorinated homologues. In fact, addition of CF_3C-X or $ROCOCF_2-X$ to olefins works well only when X = I, and reactions of the corresponding easily available fluorinated starting materials, CF_3C-X or $ROCOCF_2-X$ (X = F, Cl, Br), are difficult to accomplish.[8,9] Other examples showing that polyfluorinated halocarbons are difficult to activate are seen in atom transfer radical cyclizations of allyl iodoacetate, monofluoroiodoacetate, and difluoroiodoacetate; the former two compounds give the corresponding lactones in moderate yields,[10] whereas no reaction takes place with allyl difluoroiodoacetate.[10] Difficulty in achieving the cyclization of *N*-allylhalodifluoroacetamides is also expected because of the high rotational barrier of polyfluorinated amides. For example, the energy barrier required for amide rotation of CF_3CONR_2 is higher than the corresponding trichlorinated analogue by 4 kcal/mol.[11] The energy barrier of the amide rotation of the fluorinated amide XCF_2CONR_2 is expected to be higher than the corresponding chlorinated amides; this could be a factor in the lower yield of the product in the cyclization of *N*-alkyl-*N*-allylhalodifluoroacetamide derivatives.

In this paper, we report that cyclization of *N*-allylhalodifluoroacetamides was actually accomplished using the reactive catalyst, CuX(bipy), and by introduction of tosyl group to the amide nitrogen as shown in Scheme 1. Although the rate of the reaction is slower than the cyclization of *N*-allyl-*N*-tosyltrichloroacetamides, the reaction offers a novel and effective synthetic method for α,α-difluoro-γ-lactams in good yields.

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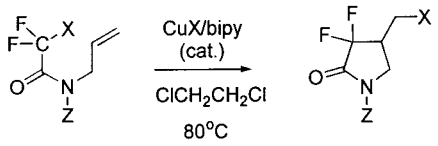
Scheme 1



X=Br, I; Z=allyl, benzyl, tosyl

Table 1. Cyclization of *N*-Substituted *N*-Allylhalodifluoroacetamides[a]

entry	amide	X	Z	cat. (%)	temp (°C)	time (h)	product	yield (%)
1	**2a**	Br	allyl	30	80	15	**4a**	81
2	**2b**	Br	Bn	30	80	15	**4b**	58
3	**2c**	Br	Ts	30	80	15	**4c**	84
4	**3a**	I	allyl	10	80	15	**5a**	92
5	**3b**	I	Bn	10	80	15	**5b**	34
6	**3c**	I	Ts	10	80	15	**5c**	69
7	**3c**	I	Ts	10	40	15	**5c**	69

[a] To avoid the halogen exchange of both the starting material and the product, CuX, of which X group (X = Cl, Br, I) was the same as that in the starting material, was used.

Results and Discussion

A series of *N*-allylhalodifluoroacetamide derivatives was synthesized and subjected to cyclization in the presence of a catalytic amount of CuX(bipyridine) in dichloroethane. The results are summarized in Table 1. The *N*-allylbromodifluoroacetamides, **2a**−**c**, were successfully cyclized to the corresponding γ-lactams, **4a**−**c**, with 30 mol % of CuBr(bipy) at 80 °C for 15 h. Cyclization of the difluoroiodoacetamides, **3a**−**c**, in the presence of CuI(bipy) proceeded smoothly even with lower concentration of the catalyst (~10 mol %) or at lower temperature (40 °C) as shown in entries 6−9. Attempts to cyclize *N*-allyl-*N*-benzylchlorodifluoroacetamide (**1b**) and *N*-allyl-*N*-tosylchlorodifluoroaceamide (**1c**) resulted in complete recovery of the starting materials under the same conditions. Thus, the reactivity of these halodifluoroacetamides decreased in the order, halogen = I > Br ≫ Cl.

The *N*-allyl and *N*-tosyl derivatives, **2a**, **3a**, **2c**, and **3c**, underwent the cyclization to give the product in good to high yields. In contrast, the *N*-benzyl analogues, **2b** and **3b**, gave the corresponding lactams in lower yields as shown in entries 2 and 5. This is attributed to the amide rotation effect reported earlier. Variable temperature ^{1}H NMR spectra of **2b** and **2c** in toluene-d_8 showed that the coalescence temperature of the peak due to the methylene protons adjacent to the olefinic bond was 70 °C for **2b**, whereas it was at −90 °C for **2c** as shown in Figure 1. We reported that the coalescence temperature of the peak due to the methylene protons adjacent to the olefinic bond was 20 °C for *N*-allyl-*N*-benzyltrichloroacetamide, whereas no coalescence occurred even at −105 °C for *N*-allyl-*N*-tosyltrichloroacetamides.[5b] Thus, it is apparent that the rotational barrier of the fluorinated amides, **2b** or **2c**, is higher than the corresponding trichlorinated amides. Introduction of *N*-tosyl group essentially helps to lower the rotational barriers of the fluorinated amides leading to facile access of the rotamer favorable for the cyclization. This results in high yield formation of the N-tosylated α,α-difluoro-γ-lactams.

For cyclization of *N*-allylbromodifluoroacetamides, addition of the copper catalyst is crucial. In fact, screening of the catalyst for cyclization of **2a**−**c** revealed that no reaction occurred with CuCl(*N*,*N*,*N*′,*N*′-tetramethylpropanediamine), $Pd(PPh_3)_4$, or $RuCl_2(PPh_3)_3$, whereas decrease of the product yields was observed with CuOTf(bipy). In sharp contrast, *N*-allyldifluoroiodoacetamide **3c** is photosensitive, and a small amount of the cyclization product **5c** was detectable when a THF solution of **3c** was stirred in fluorescent light at room temperature for 12 h.[12] The reaction was accelerated in the presence of a catalytic amount of either PPh_3 (20 − 40 mol %) or $Pd(PPh_3)_4$ (10 mol %) as shown in Scheme 2. For example, **3c** was cyclized to **5c** with the aid of PPh_3 (40 mol %) or $Pd(PPh_3)_4$ (5 mol %) in THF in the fluorescent light at room temperature; the product was obtained in moderate to good yields after 12 h. No reaction catalyzed by PPh_3 or $Pd(PPh_3)_4$ occurred in the dark. Some amounts (5−20%) of reduction product, *N*-allyl-*N*-tosyldifluoroacetamide, were formed as a byproduct. Cyclization reaction of **3a**, **3b**, or **3c** with 10 mol % of $Pd(PPh_3)_4$ in THF in fluorescent light at room temperature for15 h afforded the corresponding lactam in 98, 34, and 94% yield, respectively. The low yield formation of **5b** can be explained by the high amide rotational barrier as described above. Thus, facile cyclization of **3a**−**c** in fluorescent light with the aid of PPh_3 or $Pd(PPh_3)_4$ is an attractive method for preparation of fluorinated γ-lactams under mild conditions, though there are drawbacks in that access of *N*-allyl-*N*-tosyldifluoroiodoacetamides is not as easy as synthesis of **2a**−**c**, and high photosensitivity of **3a**−**c** leads to their decomposition to give a mixture of products even during storage in a refrigerator.

Table 2 summarizes the cyclization of various *N*-allyl-*N*-tosylbromodifluoroacetamides. The substrates derived from primary allylic amines generally gave the product in good yields. In contrast, a bromodifluoroacetamide from 2-cyclohexenylamine afforded a substantial amount of intractable products when 30 mol % of the catalyst was used. Using 100 mol % of CuCl(bipy), the corresponding cyclization products were available in moderate yields. As shown in entries 1 and 5, the reaction was sometimes accompanied by dehydrobromination reaction as a side reaction.

In summary, we found that efficient cyclization of *N*-allylhalodifluoroacetamides was achieved by catalysis of CuX(bipy). Introduction of *N*-tosyl group is effective to raise product yields. Radical cyclization to synthesize fluorinated carbo- and heterocyclic compounds has recently received considerable attention from organic chemists; however, only a few successful examples have been reported.[9,10,13−16] As the closest examples to the fluori-

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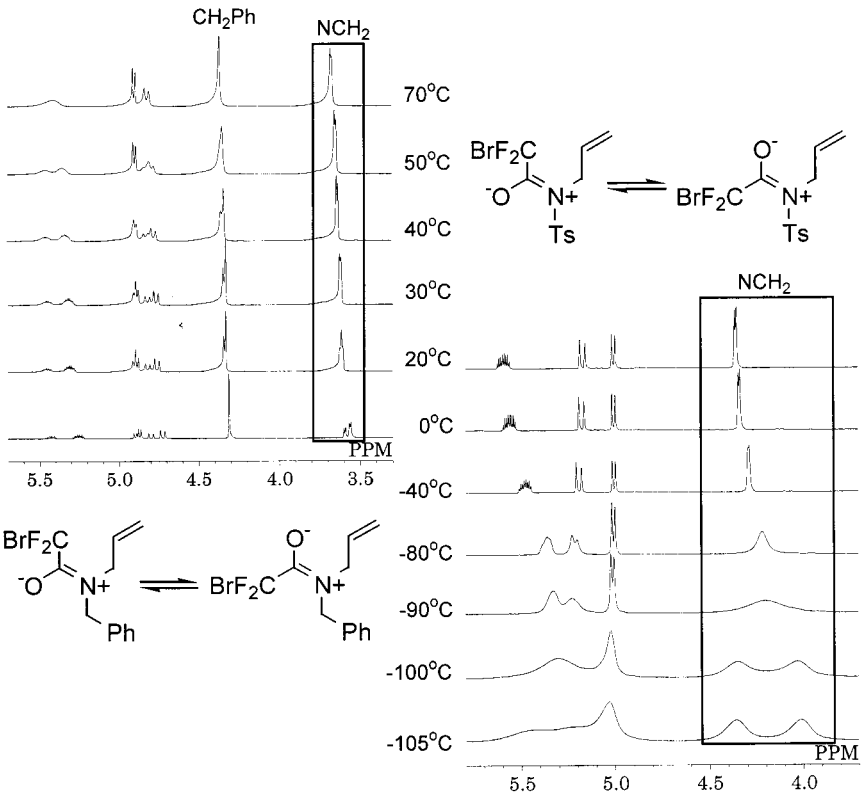
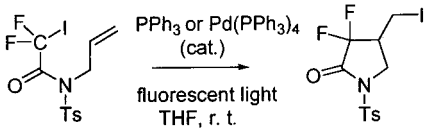


Figure 1. Variable temperature NMR spectra of **2b** (left) and **2c** (right).

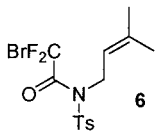
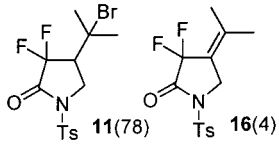
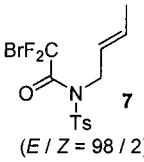
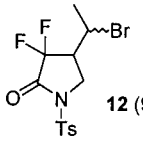
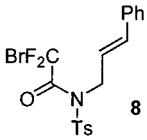
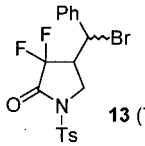
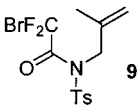
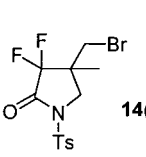
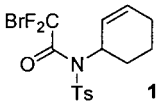
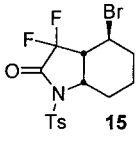
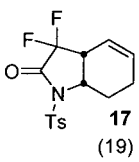
Scheme 2



PPh_3 (40mol%): 67%
$Pd(PPh_3)_4$ (5mol%): 87%
(10mol%): 94%

nated γ-lactam synthesis presented in this paper, preparation of α,α-difluorinated lactones or lactams was investigated by several groups.[10,13,14,15b] Atom transfer radical cyclization of allyl halodifluoroacetates or *N*-allylhalodifluoroacetamides did not work well;[10,14] the only exception is cyclization of certain bromodifluoroacetates having a carbon−carbon double bond in the molecule which reportedly afforded a macrocyclic α,α-difluorolactone.[13] Elegant cyclization of *N*-allylbromodifluoroacetamide promoted by phenylseleno radicals at room temperature was reported by Uneyama and coworkers;[15a] however, one drawback is that a stoichiometric amount of phenylseleno group is required, and yield of the product is not very high in the cyclization of *N*-allyl-*N*-benzylbromodifluoroacetamide compared with the corresponding *N*,*N*-diallyl homologue due to the high energy barrier of amide rotation. Thus, the reaction described in this paper is a rare synthetic method for α,α-difluorinated γ-lactams by cyclization of easily available *N*-allylbromodifluoroacetamides and is valuable as a novel successful example of direct radical cyclization of α,α,α-halodifluoro carbonyl compounds.

Table 2. Cyclization of Various *N*-Allyl-*N*-tosylbromodifluoroacetamides[a]

entry	substrate	cat.(%)	products (yield; %)
1	 **6**	30	 **11**(78) **16**(4)
2	 **7** (*E* / *Z* = 98 / 2)	30	 **12** (91, 69/31[b])
3	 **8** (*E* / *Z* = 100 / 0)	30	 **13** (78, 63/37[b])
4	 **9**	30	 **14**(79)
5	 **10**	30 100	 **15** (29) (52)  **17** (19) (8)

[a] All of the reactions were carried out in dichloroethane at 80 °C for 15 h. [b] Diastereomer ratio.

Experimental Section

General. All manipulations were performed under an argon atmosphere unless otherwise noted. Cuprous chloride (CuCl) was prepared from $CuCl_2$ hydrate[17] and stored under a dry argon atmosphere. Purification of 2,2′-bipyridine was made by sublimation. Solvents were distilled under an inert atmosphere in the presence of drying reagents. The solvent used for the cyclization was degassed by three freeze−pump−thaw cycles just prior to use. Difluoroiodoacetyl chloride was prepared by the procedure in the literature.[12] Column chromatography was carried out using silica gel (Merck No. 1.07734.9025 or Wakogel FC-40). Thin-layer chromatography was carried out with silica gel 60 F_{254} (Merck). Typical experimental procedures including analytical and spectroscopic data are described below. Other data are summarized in the Supporting Information in detail.

General Procedure for the Preparation of *N*-Alkyl-*N*-allylhalodifluoroacetamides (alkyl = allyl, benzyl). In a typical example, to a solution of *N*,*N*-diallylamine (0.5 mL, 394 mg, 4.1 mmol) containing triethylamine (0.68 mL, 493 mg, 4.9 mmol) in ether (10 mL) was added dropwise bromodifluoroacetyl chloride (970 mg, 5.0 mmol), and the mixture was stirred at room temperature for 5 h. The reaction was quenched by adding aqueous NH_4Cl and then extracted with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography by eluting with 15% ether in hexane to give *N*,*N*-diallylbromodifluoroacetamide (**2a**) as a colorless oil (840 mg, 83%).

***N*,*N*-Diallylbromodifluoroacetamide (2a):** 83% yield; colorless oil; ^{1}H NMR ($CDCl_3$) δ 5.83−5.72 (m, 2H), 5.31−5.19 (m, 4H), 4.09 (d, J = 6 Hz, 2H), 4.01 (d, J = 6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 159.09 (t, J = 27 Hz), 131.70, 130.78, 119.10, 118.44, 110.80 (t, J = 315 Hz), 50.08 (t, J = 4 Hz), 48.47; ^{19}F NMR ($CDCl_3$) δ 107.47; IR (CH_2Cl_2) 1685 cm^{-1}; EI-MS m/z 255 [M^+ + 2], 253 [M^+]; HRMS calcd for $C_8H_{10}NOBrF_2$ 252.9914, found 252.9913.

***N*,*N*-Diallyldifluoroiodoacetamide (3a):** 89% yield; colorless oil; ^{1}H NMR ($CDCl_3$) δ 5.85−5.73 (m, 2H), 5.31−5.19 (m, 4H), 4.07 (d, J = 6 Hz, 2H), 3.99 (d, J = 6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 159.96 (t, J = 24 Hz), 131.56, 130.79, 119.09, 118.41, 90.19 (t, J = 323 Hz), 50.66 (t, J = 4 Hz), 48.61; ^{19}F NMR ($CDCl_3$) δ 111.22; IR (CH_2Cl_2) 1680 cm^{-1}; FAB-MS m/z 302 [MH^+]; FAB−HRMS calcd for $C_8H_{10}NOF_2I$+H 301.9853, found 301.9862.

General Procedure for the Preparation of *N*-Allyl-*N*-tosylhalodifluoroacetamides. A solution of *N*-allyltosylamide (115 mg, 0.54 mmol) in THF (2 mL) was treated with n-BuLi (1.6 M in hexane, 0.35 mL) at −78 °C. After 10 min, bromodifluoroacetyl chloride (0.70 mL, 126 mg, 0.65 mmol) was added, and the mixture was kept at this temperature for 30 min with stirring. The mixture was quenched with aq NH_4Cl and then extracted with ether. The combined organic layers were washed with cold aq $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography at −78 °C (eluent; 15% ether in hexane) to give *N*-allyl-*N*-tosylbromodifluoroacetamide (**2c**) as a white solid (187 mg, 94%).

***N*-Allyl-*N*-tosylbromodifluoroacetamide (2c):** 94% yield; colorless solid; mp 47.5−48.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.92 (d, J = 8 Hz, 2H), 7.34 (d, J = 8 Hz, 2H), 5.90 (ddt, J = 17, 11, 5 Hz, 1H), 5.39 (d, J = 17 Hz, 1H), 5.35 (d, J = 11 Hz, 1H), 4.70−4.66 (m, 2H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 157.75 (t, J = 29 Hz), 145.90, 134.25, 131.94, 129.47, 129.41, 119.52, 109.80 (t, J = 317 Hz), 49.47 (t, J = 3 Hz), 21.72; ^{19}F NMR ($CDCl_3$) δ 105.33; IR (CH_2Cl_2) 1718 cm^{-1}; FAB-MS m/z 370 [MH^++2], 368 [MH^+]; FAB−HRMS calcd for $C_{12}H_{12}NO_3BrF_2S$+H 367.9768, found 367.9767.

***N*-Allyl-*N*-tosyldifluoroiodoacetamide (3c):** 62% yield; colorless solid; mp 56−58 °C; ^{1}H NMR ($CDCl_3$) δ 7.92 (d, J = 8 Hz, 2H), 7.34 (d, J = 8 Hz, 2H), 5.90 (ddt, J = 17, 11, 5 Hz, 1H), 5.41 (d, J = 17 Hz, 1H), 5.36 (d, J = 11 Hz, 1H), 4.66 (d, J = 5 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 158.40 (t, J = 26 Hz), 145.84, 134.25, 131.87, 129.47, 129.41, 119.50, 88.87 (t, J = 325 Hz), 49.98 (t, J = 3 Hz), 21.77; ^{19}F NMR ($CDCl_3$) δ 111.22; IR (CH_2Cl_2) 1713 cm^{-1}; FAB-MS m/z 416 [MH^+]; FAB−HRMS calcd for $C_{12}H_{12}NO_3IF_2S$+H 415.9629, found 415.9623.

General Procedure for the Copper-Catalyzed Cyclization. In a typical example, CuBr (12.8 mg, 0.09 mmol) and *N*-allyl-*N*-tosylbromodifluoroacetamide (**2c**) (110 mg, 0.3 mmol) were measured into a flask, and the atmosphere was replaced by argon. Degassed dichloroethane (1.2 mL) was added, and the mixture was allowed to warm at 80 °C. Then, a dichloroethane solution of bipyridine (0.3 M, 0.3 mL, 0.09 mmol) was added. After heating at this temperature for 15 h, the mixture was cooled to room temperature and transferred to the head of a short pad of a silica gel column and eluted with ether. The eluent was concentrated, and the residue was purified by column chromatography (eluent; 25% ether in hexane) to afford the lactam **5c** as a colorless solid (92 mg, 84%).

***N*-Benzyl-*β*-bromomethyl-α,α-difluoro-*γ*-lactam (4b):** 58% yield; colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.41−7.31 (m, 3H), 7.28−7.23 (m, 2H), 4.54 (s, 2H), 3.64 (dd, J = 10, 5 Hz, 1H), 3.51 (ddd, J = 10, 8, 2 Hz, 1H), 3.33 (t, J = 10 Hz, 1H), 3.10 (ddd, J = 10, 7, 3 Hz, 1H), 3.03−2.87 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 162.73 (t, J = 30 Hz), 134.16, 129.11, 128.42, 128.34, 116.68 (dd, J = 256, 251 Hz), 47.45, 46.74 (d, J = 6 Hz), 42.38 (dd, J = 22, 20 Hz), 25.79 (d, J = 11 Hz); ^{19}F NMR ($CDCl_3$) δ 65.50 (ddd; J = 271, 14, 2 Hz, 1F), 56.95 (dd, J = 271, 15 Hz, 1F); IR (CH_2Cl_2) 1734 cm^{-1}; EI-MS m/z 305 [M^+ + 2], 303 [M^+]; HRMS calcd for $C_{12}H_{12}BrF_2NO$ 303.0070, found 303.0070; Anal. Calcd for $C_{12}H_{12}BrF_2NO$: C, 47.39; H, 3.98; N, 4.61. Found: C,47.29; H, 4.05; N, 4.57.

***N*-Benzyl-α,α-difluoro-*β*-iodomethyl-*γ*-lactam (5b)**: 34% yield; colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.40−7.33 (m, 3H), 7.27−7.23 (m, 2H), 4.55 (d, J = 15 Hz, 1H), 4.52 (d, J = 15 Hz, 1H), 3.49 (t, J = 10 Hz, 1H, NCH_2), 3.40 (dd, J = 11, 5 Hz, 1H), 3.07 (t, J = 11 Hz, 1H), 3.02−2.98 (m, 1H), 2.95−2.83 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 162.97 (dd, J = 31, 30 Hz), 134.17, 129.07, 128.36, 128.27, 116.53 (dd, J = 257, 251 Hz), 48.57 (d, J = 6 Hz), 47.37, 43.01 (dd, J = 22, 21 Hz), −4.40 (d, J = 10 Hz); ^{19}F NMR ($CDCl_3$) δ 51.75 (dd, J = 269, 14 Hz, 1F), 44.15 (dd, J = 269, 16 Hz, 1F); IR (CH_2Cl_2) 1733 cm^{-1}; FAB-MS m/z 352 [MH^+]; FAB−HRMS calcd for $C_{12}H_{12}F_2INO$+H 352.0010, found 352.0014. Anal. Calcd for $C_{12}H_{12}F_2INO$: C, 41.05; H, 3.44; N, 3.99. Found: C, 40.77; H, 3.69; N, 4.09.

***N*-Tosyl-*β*-bromomethyl-α,α-difluoro-*γ*-lactam (4c):** 84% yield; colorless solid; mp. 168−169 °C; ^{1}H NMR ($CDCl_3$) δ 7.96 (d, J = 8 Hz, 2H), 7.39 (d, J = 8 Hz, 2H), 4.22 (dd, J = 11, 8 Hz, 1H), 3.64−3.56 (m, 2H), 3.34 (t, J = 11 Hz, 1H), 3.07−2.91 (m, 1H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 160.38 (t, J = 32 Hz), 146.62, 133.53, 130.14, 128.34, 115.15 (dd, J = 261, 255 Hz), 46.68 (d, J = 5 Hz), 42.32 (dd, J = 22, 20 Hz), 24.35 (d, J = 9 Hz), 21.80; ^{19}F NMR ($CDCl_3$) δ 52.21 (dd, J = 272, 13 Hz, 1F), 43.27 (dd, J = 272, 17 Hz, 1F); IR (CH_2Cl_2) 1771 cm^{-1}; FAB-MS m/z 370 [MH^+ + 2], 368 [MH^+]; FAB−HRMS calcd for $C_{12}H_{12}BrF_2NO_3S$+H 367.9768, found 367.9770. Anal. Calcd for $C_{12}H_{12}BrF_2NO_3S$: C, 39.14; H, 3.29; N, 3.80. Found: C, 39.36; H, 3.21; N, 3.73.

***N*-Tosyl-α,α-difluoro-*β*-iodomethyl-*γ*-lactam (5c):** 69% yield; colorless solid; mp 160−161 °C; ^{1}H NMR ($CDCl_3$) δ 7.95 (d, J = 8 Hz, 2H), 7.39 (d, J = 8 Hz, 2H), 4.22 (dd, J = 10, 8 Hz, 1H), 3.47 (dd, J = 10, 8 Hz, 1H), 3.36 (dd, J = 10, 5 Hz, 1H), 3.06 (t, J = 10 Hz, 1H), 2.96−2.85 (m, 1H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 160.64 (dd, J = 33, 32 Hz), 146.59, 133.50, 130.12, 128.28, 114.99 (dd, J = 254, 252 Hz), 48.52 (d, J = 6 Hz), 42.95 (dd, J = 22, 21 Hz), 21.77, −6.60 (d, J = 8 Hz); ^{19}F NMR ($CDCl_3$) δ 50.93 (dd, J = 271, 12 Hz, 1F), 43.23 (dd, J = 271, 17 Hz, 1F); IR (CH_2Cl_2) 1770 cm^{-1}; FAB-MS m/z 416 [MH^+]; FAB−HRMS calcd for $C_{12}H_{12}F_2INO_3S$+H 415.9629, found 415.9630; Anal. Calcd for $C_{12}H_{12}$ F_2INO_3S: C, 34.71; H, 2.91; N, 3.37. Found: C, 34.86; H, 2.91; N, 3.34.

Photochemical Cyclization of 3c with the Aid of Pd(PPh_3)$_4$. In a typical example, a THF solution of **3c** (0.05 mmol, 20.8 mg, in 1 mL of THF) was treated with a catalytic amount of $Pd(PPh_3)_4$, prepared from Pd_2(dibenzylideneacetone)$_3$·$CHCl_3$ (1.3 mg, 0.00125 mmol) and PPh_3 (2.6 mg, 0.01 mmol) in THF (1 mL) at room temperature, in fluorescent light for 16 h. Metallic components were removed by passing the resulting reaction mixture through a short column of silica gel by eluting with ether. After concentration of the eluents, purification of the residue by medium-pressure liquid chromatography (silica, by eluting with 40% ether in hexane) gave **5c** as a colorless solid

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in 87% yield (18 mg). As described in the text, no reaction took place without exposure to fluorescent light. Similar results were obtainable when PPh_3 was used as the catalyst, but yield of the product was lower.

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Supporting Information Available: List of other spectroscopic data except those described in the Experimental Section. Copies of ^1H and ^{13}C NMR spectra of all compounds lacking elemental analysis [**2a**−**c**, **3a**−**c**, **6**, **7**, **9**, **10**, **12**, **13** (the minor isomer), **14** (the minor isomer)]. This material is available free of charge via the Internet at http://pubs.acs.org.

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