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Comprehensive Synthesis of Photoreactive (3-Trifluoromethyl)diazirinyl Indole Derivatives from 5- and 6-Trifluoroacetylindoles for Photoaffinity Labeling

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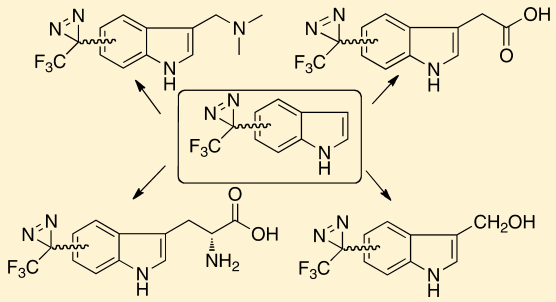
Supporting Information

ABSTRACT: 5- and 6-trifluoromethyldiazirinyl indoles were synthesized from corresponding bromoindole derivatives for the first time. They acted as mother skeletons for the comprehensive synthesis of various bioactive indole metabolites. These can be used in biological functional analysis as diazirine-based photoaffinity labels.



INTRODUCTION

Indoles are electron-rich aromatic compounds that owe their characteristic properties to the presence of a pyrrole moiety. The indole substructure is a basic element for a number of biologically active natural and synthetic products. The synthesis and chemical modification of indoles, therefore, has attracted enormous attention. Photolabeling is one of the methods used to study the interactions between low molecular weight biological substrate compounds with their biomolecular targets or receptors. Target molecule affinity for the low molecular weight substrate can provide selectivity in the photolabeling reactions.[1] Selection of a suitable photophore for photoaffinity labeling is critical to obtain meaningful results, but there are currently no "universal photoreactive spiecies".[2] The chemical properties of 3-(trifluoromethyl)phenyldiazirine—including the stability of the functional group before irradiation, higher reactivities of the generated species after irradiation, and suppression of side reactions—give this molecule many advantages over aryl azides and benzophenones as photophores for photoaffinity labeling.[1c] Although photoaffinity labeling reagents containing arylazide[3] or benzophenone[4] derivatives of the indole scaffold have been reported, to the best of our knowledge, there have been no reports of synthetic studies on 3-(trifluoromethyl)phenyldiazirine containing indole derivatives for use as the photoaffinity labeling reagents. A major advantage of easy derivatizations from the mother photoreactive indole skeleton into various indole-containing biologically active compounds avoids the need to construct the 3-(trifluoromethyl)diazirinyl moiety each time. In this study, we focused on synthesizing photoreactive indoles, containing 3-trifluoromethyldiazirine at the 5- or 6-position and outlining comprehensive derivatizations for their biologically active indole derivatives.

RESULTS AND DISCUSSION

Construction of a (trifluoromethyl)diazirinyl moiety on indole at the 5- or 6-position began by treating the corresponding bromide derivatives (**1a** and **1b**) with potassium hydride–*t*-BuLi followed by treatment with trifluoroacetylated reagents. Trifluoroactylations of 5- or 6-bromoindole with trifluoroacetic anhydride[5] with potassium hydride–*t*-BuLi were not effective (30–60%), and replacement of potassium hydride with sodium hydride did not influence the isolated yield. Replacement of trifluoroacetic anhydride with ethyl trifluoracetate or trifluoroacetyl piperidine improved the yield of the products (**2a** and **2b**; ∼80%), because the leaving groups did not decrease the reaction mixture basicity.

The trifluoroacetyl groups were converted to oximes with hydroxylamine hydrochloride in pyridine (**3a** and **3b**) followed by tosylation with tosyl chloride in triethylamine and acetone at 0 °C. Tosylation with tosyl chloride in pyridine under reflux was not acceptable because the product was broken down under these conditions. The isolated yield for **4a** and **4b** dramatically decreased (yield of purified tosyl oxime **4a**: 28%) due to the instability of the tosyl oxime of indole. To avoid the decrease in yield, the tosyl oximes **4a** and **4b** were not isolated and were directly subjected to conversion to diaziridine (**5a** and

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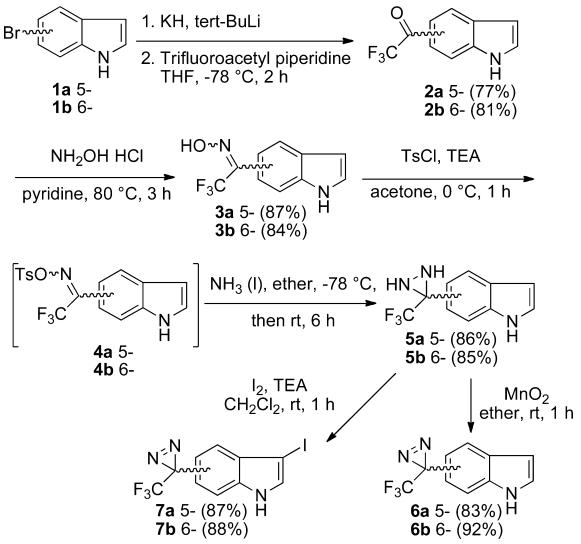
5b) with liquid ammonia. This modification drastically improved the yield (84−87% for two steps). Oxidation of diaziridine to diazirine (**6a** and **6b**) with activated MnO_2 can occur without any side reactions in good yield (80−92%). The use of iodine in triethylamine, which is an alternative oxidation method for diaziridine to diazirine, caused a side reaction of iodination at the 3-position of the indole skeleton (**7a** and **7b**; Scheme 1).

Scheme 1. Synthesis of (Trifluoromethyl)diazirinyl Indoles 6a and 6b

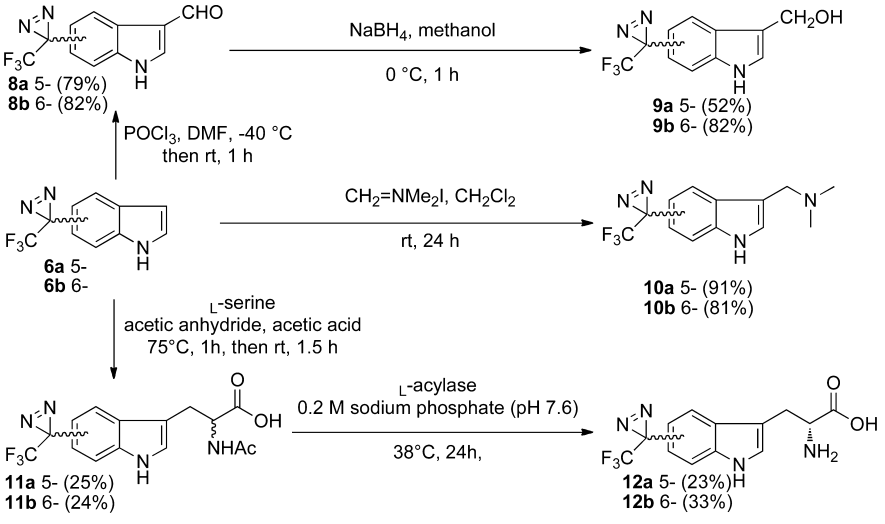


The derivatizations under mild conditions were preferable for 5- and 6-(trifluoromethyl)diazirinyl indoles (**6a** and **6b**) as these conditions avoided the decomposition of the diazirinyl ring. Diazirinyl indoles were converted with $POCl_3$ and DMF at rt to 3-formylindole derivatives (**8a** and **8b**) which were then reduced with sodium borohydride in methanol[6] to construct indole carbinols (**9a** and **9b**). These are reported to have anticarcinogenic, antioxidant, and antiatherogenic effects.[7] Gramine derivatives, which play a defensive role in plants,[8] were constructed from diazirinyl indoles with $CH_2{=}NMe_2I$ at rt for 24 h with moderate yields[9] (**10a** and **10b**; Scheme 2).

Tryptophan is one of the most biologically significant metabolites synthesized from indole. Although synthesis of tryptophan from various aromatics has been reported,[10] these methods are too difficult to apply to the diazirinyl derivatives because of the harsh conditions required for the constructions of tryptophan skeletons. For example, (1) Larock heteroannulation or Mori−Ban−Hegedus indole synthesis of an *o*-iodoaniline skeleton with Schöllkopf reagent,[11] (2) Heck-type synthesis of an *o*-iodoaniline skeleton with pyroglutamate derivatives,[12] and (3) Fisher indole synthesis of phenyl hydrazones[13] were ineffective when starting with diazirinyl derivatives, as the diazirinyl moiety is decomposed during the reactions. Tryptophan has been synthesized from indole with serine in acetic acid and acetic anhydride under reflux conditions.[14] In the original report, active species were generated at high temperature in the presence of indole derivatives. The diazirinyl moieties of **6a** and **6b** were also destroyed in acetic acid under the reflux conditions.. Active species were generated from L-serine, acetic anhydride, and acetic acid in reflux conditions without indole derivatives, followed by addition of diazirinyl indoles to the mixture at low temperature to prevent decomposition of the diazirinyl ring. The racemate of diazirinyl *N*-acetyltryptophans **11a** and **11b** was subjected to enzymatic resolution with L-acylase to afford optically pure diazirinyl L-tryptophan without decomposition of the diazirinyl moiety. The optical purities for **12a** and **12b** were also confirmed by chiral column chromatography.

Indole-3-acetic acid (IAA), commonly known as auxin, is essential throughout the life cycles of plants and controls diverse cellular processes.[15] The biology of IAA and the underlying mechanisms of its action are not completely understood because there are no biochemical tools with which to investigate them. No IAA skeletons were found when the diazirinyl indoles (**6a** and **6b**) in acetone were reacted with ethyl chloroacetate under reflux.[16] The diazirinyl indoles were reacted with oxalyl chloride,[17] followed by methanolysis to afford 3-(α-oxo, methyl ester) indole derivatives (**13a** and **13b**). The selective reduction of the α-keto moiety to methylene with triethylsilane and trifluoroacetic acid, which has already been reported to have no effect on the diazirinyl moiety,[18] was not successful, and reduction of both the α-keto and alkene moiety between the 2- and 3-positions afforded **14a** and **14b** under

Scheme 2. Post-Functional Synthesis of Diazirinyl Indole Derivatives from Diazirinyl Indoles



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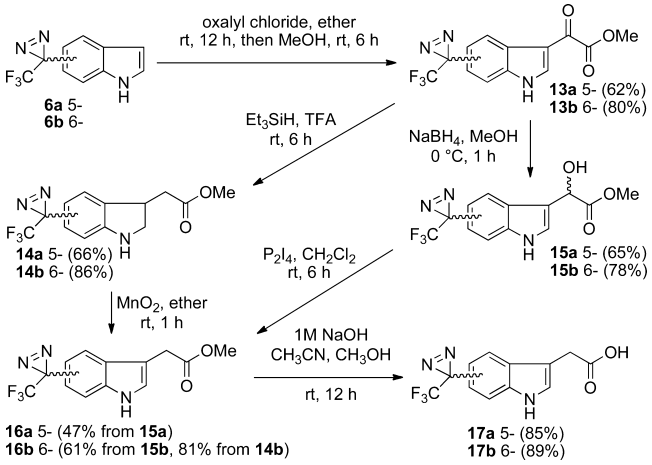
these conditions. Accordingly, the compound **14a** was very unstable, it was very difficult to obtain ^{13}C NMR spectra. Selective dehydrogenation at the 2,3-position of **14a** and **14b** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone or bis-(trifluoroacetoxy)iodobenzene afforded a complex mixture. Dehydrogenation with MnO_2 can be applied to construct indole skeleton **16b** from **14b**, but the condition promoted decomposition of the diazirinyl moiety of the 5-trifluoromethyldiazirinyl derivative **14a**. To construct 5-(trifluoromethyl)-diazirinyl IAA methyl ester, 3-α-oxo, methyl ester **13a** was reduced with sodium borohydride to afford α-hydroxy ester (**15a**), followed by dehydration with P_2I_4[19] to afford diazirinyl IAA methyl ester derivative **16a** with moderate yield. The conditions can also be applied to the 6- (trifluoromethyl)-diazirinyl isomer (**13b**). Finally, hydrolysis of the methyl ester under alkaline conditions afforded 5- and 6-diazirinyl IAA derivatives without decomposition of photophores (**17a** and **17b**; Scheme 3).

Scheme 3. Synthesis of Diazirinyl Indole-3-Acetic Acid Derivatives from Diazirinyl Indole Derivatives



The diazirinyl indole derivatives in methanol (1 mM, 1 mL) were subjected to irradiation with black light to confirm their photoreactive properties.[20] The characteristic broad adsorptions around 360 nm for diazirine indicated the presence of (trifluoromethyl)diazirinyl moieties on indole rings. Irradiation with black light (100 W) in methanol revealed that a decrease in absorbance at around 380 nm that was associated with the irradiation time. These results indicated that the irradiation promoted decomposition of the diazirinyl ring and that a highly reactive carbene intermediate was generated effectively. The irradiation afforded a complex mixture due to the high reactivity of carbenes. The half-lives ($t_{1/2}$) of the diazirinyl indole derivatives are listed in Table 1. All of the compounds have suitable characteristics for the photoaffinity labeling reagents.

Indole-3-acetic acid (IAA), the main auxin in higher plants, has profound effects on plant growth and development.[21] The synthetic diazirinyl IAA derivatives (**17a** and **17b**) were subjected to oat coleoptile segment growth bioassays.[22] The typical auxin responses, which were growth acceleration at optimum concentration and growth inhibition at higher and lower concentration than optimum concentration, were observed for the synthetic compounds. The optimum concentrations for elongation of coleoptile segments were observed at between 10^{-4} and 10^{-6} M for IAA (A) as well as 5-(B) and 6-diazirinyl (C) IAA. The results indicated that the chemical modifications of IAA with trifluoromethyldiazirinyl group at the 5- and 6-positions do not cause serious reduction of biological activities (Figure 1).

Table 1. Calculated Half-Lives of the Diazirinyl Moiety Decomposition for Indole Derivatives in Methanol with Black Light (100 W) at 1 cm Distance[a]

compd	$t_{1/2}$ (min)	compd	$t_{1/2}$ (min)
6a	9.6	**10a**	6.9
6b	9.8	**10b**	7.9
7a	5.3	**12a**	8.0
7b	5.7	**12b**	8.6
9a	8.6	**17a**	7.9
9b	9.2	**17b**	8.0

[a]Half-lives were calculated from decay of the A_{380} as a function of photolysis time in a semilog representation.

CONCLUSION

Diazirinyl indoles were prepared, for the first time, from the corresponding trifluoroacetyl indoles. These indole derivatives acted as mother skeletons for the synthesis of diazirinyl derivatives for many indole metabolites, including tryptophan. Comprehensive synthesis of the photoaffinity labeled indole derivatives described in this study would contribute to future elucidation of the role of these indole metabolites in target protein's biological functional analysis. The photoreactive tryptophan derivatives are now subjected to biological functional analysis for gustatory response.[23]

EXPERIMENTAL SECTION

General Methods. All reactions were performed in a test tube under air. Column chromatography was performed using silica gel (200−400 mesh). ^1H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded on 270, 400, or 500 MHz in $CDCl_3$ and CD_3OD. All new compounds (except **14a**) were further characterized by HRMS (ESI-TOF). Commercially available reagents and solvents were used without further purification. The reactions for diazirinyl compounds were carried out in the dark.

2,2,2-Trifluoro-1-(1*H*-indol-5-yl)ethanone (2a).[5] A solution of 5-bromoindole **1a** (1.57 g, 8.00 mmol) in THF (8 mL) was added dropwise to a suspension of potassium hydride (1.09 g, 30% suspension in mineral oil, 8.00 mmol) in THF (16.0 mL) at 0 °C under N_2. After being stirred for 1 h at 0 °C, the mixture was cooled to −78 °C and a solution of *t*-BuLi (10 mL of 1.7 M pentane solution, 17.0 mmol) was added dropwise over a period of 15 min. (Trifluoroacetyl)piperidine (2.40 mL, 17.0 mmol) was added at −78 °C, and the mixture was stirred for 2 h, quenched saturated ammonium chloride (7.00 mL), and then extracted with diethyl ether. The organic layer was washed with brine and dried over $MgSO_4$. The residue was purified by column chromatography (CH_2Cl_2/hexane 1/4 to 1/2) to yield 5-(trifluoroacetyl)indole **2a** (1.31 g, 77%) as yellow amorphous mass.

2,2,2-Trifluoro-1-(1*H*-indol-6-yl)ethanone (2b). The same treatment of **1b** (1.0 g, 5.12 mmol) as that just described gave **2b** (0.89 g, 81%) as a pale yellow amorphous mass: ^1H NMR ($CDCl_3$) δ 8.61 (brs, 1H), 8.20 (s, 1H), 7.85 (d, J = 8.6 Hz, 1H), 7.74 (d, J = 8.6 Hz, 1H), 7.51 (t, J = 2.9 Hz, 1H), 6.67 - 6.65 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 180.5 (q, $^2J_{CF}$ = 36.0 Hz), 135.0, 133.6, 129.9, 123.7, 121.2, 121.1, 117.2 (q, $^1J_{CF}$ = 291.9 Hz), 114.7, 103.7; ^{19}F NMR ($CDCl_3$) δ −70.05; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{10}H_6F_3NO$ 214.0480, found 214.0468.

2,2,2-Trifluoro-1-(1*H*-indol-5-yl)ethanone Oxime (3a). 5-(Trifluoroacetyl)indole **2a** (109 mg, 0.509 mmol) and hydroxylamine hydrochloride (60.0 mg, 0.645 mmol) were dissolved in pyridine (3

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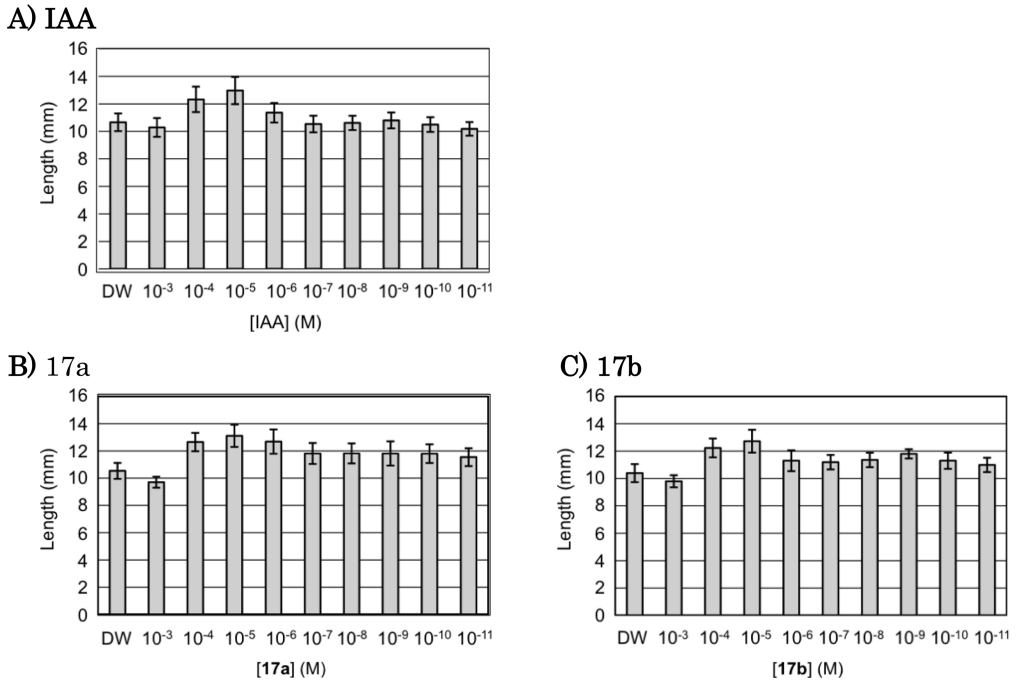

Figure 1. Typical experiments on elongation in oat coleoptile segments inoculated with IAA, **17a**, and **17b**. Coleoptile segments (10 mm, six segments) were immersed in a treatment solution (IAA, **17a**, and **17b**) at 25 °C for 24 h, followed by measurements of segment lengths. Control experiment, which was carried out without IAA derivatives, presented as DW (in distilled water).

mL). The reaction mixture was stirred at 80 °C for 3 h and concentrated. The residue was dissolved in diethyl ether (20 mL). The organic layer was washed with 1 M HCl and brine, dried over $MgSO_4$, filtrated, and concentrated. The residue was purified by column chromatography (CH_2Cl_2 to AcOEt/hexane 1/3) to yield 5-trifluorooxime indole **3a** (101 mg, 87%, mixture of *syn*- and *anti*-isomers) as a colorless amorphous mass: ^{1}H NMR (CD_3OD) δ 7.70 (s, 0.7H), 7.63 (s, 0.3H), 7.42 (d, J = 8.6 Hz, 0.7H), 7.39 (d, J = 8.6 Hz, 0.3H), 7.28 (d, J = 3.2 Hz, 0.7H), 7.27 (d, J = 3.2 Hz, 0.3H), 7.21 (d, J = 8.6 Hz, 0.7H), 7.17 (d, J = 8.6 Hz, 0.3H), 6.50−6.48 (m, 1H); ^{13}C NMR (CD_3OD) δ 148.4 (q, $^2J_{CF}$ = 30.8 Hz), 138.0, 129.0, 126.7, 123.0 (q, $^1J_{CF}$ = 273.5 Hz), 122.7 and 122.5, 122.3 and 122.0, 119.0, 112.0, 103.1; ^{19}F NMR (CD_3OD) δ −62.07, −66.37; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{10}H_8F_3N_2O$ 229.0589, found 229.0553.

2,2,2-Trifluoro-1-(1*H*-indol-6-yl)ethanone Oxime (3b). The same treatment of **2b** (782 mg, 3.66 mmol) as that just described gave **3b** (701 mg, 84%, mixture of *syn*- and *anti*- isomers) as a colorless amorphous mass: ^{1}H NMR (CD_3OD) δ 7.59 (d, J = 8.6 Hz, 0.7H), 7.57 (s, 0.7H), 7.55 (d, J = 8.6 Hz, 0.3H), 7.48 (s, 0.3H), 7.33 (t, J = 3.2 Hz, 0.7H), 7.31 (t, J = 3.2 Hz, 0.3H), 7.10 (d, J = 8.6 Hz, 0.7H), 7.08 (d, J = 8.6 Hz, 0.3H), 6.47−6.46 (m, 1H); ^{13}C NMR (CD_3OD) δ 148.1 (q, $^2J_{CF}$ = 30.8 Hz), 136.9, 130.5, 127.8 and 127.6, 123.0 (q, $^1J_{CF}$ = 273.5 Hz), 120.9, 120.7, 120.3, 113.2 and 112.7, 102.6 and 102.5; ^{19}F NMR (CD_3OD) δ −61.85, −66.00; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{10}H_8F_3N_2O$ 229.0589, found 229.0627.

5-(3-(Trifluoromethyl)diaziridin-3-yl)-1*H*-indole (5a). 5-Trifluorooxime indole **3a** (336 mg, 1.47 mmol) was dissolved in acetone (14 mL) and cooled to 0 °C. Triethylamine (0.710 mL) and *p*-toluenesulfonyl chloride (562 mg, 2.95 mmol) were added to the reaction, successively. The reaction mixture was stirred for 1 h at the same temperature and concentrated in vacuo, and the residue was dissolved in diethyl ether. In a shield tube, liquid ammonia (excess) was added at −78 °C and the ether solution of the crude tosyl oxime was added. The reaction mixture was warmed to rt and then stirred for 6 h at the same temperature. After excess ammonium gas was removed in a draft chamber, the residual solution was concentrated. The crude residue was purified by column chromatography (AcOEt/hexane 1/2) to afford **5a** (288 mg, 86%) as a colorless amorphous mass: ^{1}H NMR ($CDCl_3$) δ 8.32 (brs, 1H), 7.92 (s, 1H), 7.43 (s, 2H), 7.29 (t, J = 2.9 Hz, 1H), 6.60 (t, J = 2.9 Hz, 1H), 2.81 (d, J = 8.6 Hz), 2.28 (d, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ 136.4, 127.7, 125.5, 123.9 (q, $^1J_{CF}$ = 278.3 Hz), 123.1, 121.7, 121.2, 111.3, 103.1, 58.6 (q, $^2J_{CF}$ = 35.2 Hz); ^{19}F NMR ($CDCl_3$) δ −75.45; UV (MeOH) λ_{max} (ε) 380 (523); HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{10}H_9F_3N_3$ 228.0749, found 228.0713.

6-(3-(Trifluoromethyl)diaziridin-3-yl)-1*H*-indole (5b). The same treatment of **3b** (152 mg, 0.67 mmol) and *p*-toluenesulfonyl chloride (318 mg, 1.67 mmol), followed by treatment of liquid ammonia, as that just described gave **5b** (129 mg, 85%) as a colorless amorphous mass: ^{1}H NMR ($CDCl_3$) δ 8.31 (brs, 1H, 1-H), 7.68 (s, 1H), 7.67 (d, J = 8.6 Hz, 1H), 7.35 (d, J = 8.6 Hz, 1H), 7.30 (t, J = 2.9 Hz, 1H), 6.59−6.58 (m, 1H), 2.81 (d, J = 8.6 Hz), 2.27 (d, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ 135.2, 129.1, 126.0, 125.1, 123.8 (q, $^1J_{CF}$ = 278.9 Hz), 121.0, 119.4, 111.2, 102.7, 58.6 (q, $^2J_{CF}$ = 36.4 Hz); ^{19}F NMR ($CDCl_3$) δ −75.48; UV (MeOH) λ_{max} (ε) 390 (307); HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{10}H_9F_3N_3$ 228.0749, found 228.0743.

5-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indole (6a). 5-Diaziridine indole **5a** (73.5 mg, 0.32 mmol) and activated MnO_2 (150.0 mg) were suspended in diethyl ether (15 mL). The reaction mixture was stirred at rt for 1 h followed by filtration of the insoluble material. The filtrate was concentrated, and the residue was purified by column chromatography (CH_2Cl_2) to yield 5-diazirinyl indole **6a** (60.4 mg, 83%) as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 8.27 (s, 1H), 7.54 (s, 1H), 7.40 (d, J = 8.6 Hz, 1H), 7.27 (t, J = 2.9 Hz, 1H), 7.08 (d, J = 8.6 Hz, 1H), 6.58−6.57 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 136.1, 127.9, 125.7, 122.5 (q, $^1J_{CF}$ = 275.1 Hz), 120.3 (2C), 120.0, 111.6, 103.1, 29.0 (q, $^2J_{CF}$ = 40.0 Hz); ^{19}F NMR ($CDCl_3$) δ −65.41; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{10}H_7F_3N_3$ 226.0592, found 226.0589.

6-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indole (6b). The same treatment of **5b** (73.4 mg, 0.32 mmol) as that just described gave **6b** (66.8 mg, 92%) as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 8.22 (brs, 1H), 7.66 (d, J = 8.6 Hz, 1H), 7.28 (t, J = 2.9 Hz, 1H), 7.27 (s, 1H), 6.98 (d, J = 8.6 Hz, 1H), 6.59−6.58 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 135.3, 128.8, 126.1, 122.5 (q, $^1J_{CF}$ = 275.1 Hz), 122.4, 121.3, 117.9, 109.9, 102.8, 29.0 (q, $^2J_{CF}$ = 40.8 Hz); ^{19}F NMR ($CDCl_3$) δ −65.19; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{10}H_7F_3N_3$ 226.0592, found 226.0569.

3-Iodo-5-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indole (7a). Compound **5a** (69.9 mg, 0.31 mmol) was dissolved in CH_2Cl_2 (3

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mL) and triethylamine (0.200 mL, 1.44 mmol) at 0 °C. Iodine (86.2 mg, 0.34 mmol) was added in small portions until a brown color persisted. The solution was washed with 1 M NaOH and brine and dried over $MgSO_4$. The organic layer was removed, and the residue was purified by column chromatography (CH_2Cl_2/hexane 1/2) to yield **7a** (94.0 mg, 87%) as a brown oil: ^{1}H NMR ($CDCl_3$) δ 8.46 (brs, 1H), 7.38 (d, J = 8.6 Hz, 1H), 7.34 (d, J = 2.9 Hz, 1H), 7.28 (s, 1H), 7.18 (d, J = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 136.0, 129.9 (2C), 122.4 (q, $^2J_{CF}$ = 275.9 Hz), 121.5, 121.5, 120.3, 111.9, 57.9, 28.9 (q, $^1J_{CF}$ = 39.6 Hz); ^{19}F NMR ($CDCl_3$) δ −65.38; UV (MeOH) λ_{max} (ε) 375 (457); HRMS-ESI (m/z) [M + H]$^+$ calcd for $C_{10}H_6F_3IN_3$ 351.9559, found 351.9562.

3-Iodo-6-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indole (7b). The same treatment of **5b** (89.9 mg, 0.40 mmol) as that just described gave **7b** (122.0 mg, 88%) as a brown oil: ^{1}H NMR ($CDCl_3$) δ 8.39 (brs, 1H), 7.44 (d, J = 8.6 Hz, 1H), 7.31 (d, J = 2.3 Hz, 1H), 7.22 (s, 1H), 7.01 (d, J = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 135.2, 130.8, 130.3, 123.8, 122.3 (q, $^1J_{CF}$ = 275.9 Hz), 121.7, 118.8, 110.2, 57.5, 28.9 (q, $^2J_{CF}$ = 40.8 Hz); ^{19}F NMR ($CDCl_3$) δ −64.94; UV (MeOH) λ_{max} (ε) 386 (450); HRMS-ESI (m/z) [M + H]$^+$ calcd for $C_{10}H_6F_3IN_3$ 351.9559, found 351.9540.

5-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indole-3-carbaldehyde (8a). Phosphorus oxychloride (26.9 mL, 0.29 mmol) was added dropwise to DMF (630 mL) at −40 °C and stirred for 1 h. A solution of 5-diairinyl indole **6a** (44.1 mg, 0.20 mmol) in DMF (270 mL) was added dropwise to the above mixture at −40 °C. The reaction was stirred at rt for 1 h and poured into ice−water, basified with KOH, and stirred for 5 min. The resulting precipitate was purified by column chromatography (AcOEt/hexane 1/1) to yield **8a** (39.3 mg, 79%) as a yellow amorphous mass: ^{1}H NMR (CD_3OD) δ 9.89 (s, 1H), 8.18 (s, 1H), 8.07 (s, 1H), 7.54 (d, J = 8.6 Hz, 1H), 7.18 (d, J = 8.6 Hz, 1H); ^{13}C NMR (CD_3OD) δ 187.4, 140.9, 139.3, 125.9, 123.9 (q, $^1J_{CF}$ = 274.3 Hz), 123.9, 123.1, 121.4, 119.9, 114.1, 30.0 (q, $^2J_{CF}$ = 40.8 Hz); ^{19}F NMR (CD_3OD) δ −67.12; HRMS-ESI (m/z) [M + H]$^+$ calcd for $C_{11}H_7F_3N_3O$ 254.0541, found 254.0521.

6-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indole-3-carbaldehyde (8b). The same treatment of **6b** (28.8 mg, 0.13 mmol) as that just described gave **8b** (26.7 mg, 82%) as a yellow amorphous mass: ^{1}H NMR (CD_3OD) δ 9.90 (s, 1H), 8.21 (d, J = 8.0 Hz, 1H), 8.20 (s, 1H), 7.38 (s, 1H), 7.08 (d, J = 8.0 Hz, 1H); ^{13}C NMR (CD_3OD) δ 187.3, 141.1, 138.5, 126.9, 125.2, 123.8 (q, $^1J_{CF}$ = 273.9 Hz), 123.3, 121.4, 119.9, 112.0, 30.0 (q, $^2J_{CF}$ = 40.0 Hz); ^{19}F NMR (CD_3OD) δ −67.00; HRMS-ESI (m/z) [M + H]$^+$ calcd for $C_{11}H_7F_3N_3O$ 254.0541, found 254.0496.

(5-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)-methanol (9a). Compound **8a** (39.3 mg, 0.16 mmol) was dissolved in MeOH (3 mL) and cooled to 0 °C. $NaBH_4$ (12.0 mg, 0.31 mmol) was dissolved in CH_3OH (4 mL) and added dropwise to the above solution at 0 °C. The reaction was stirred at 0 °C for 1 h. After the solution was concentrated, the residue was purified by column chromatography (AcOEt) to yield **9a** (20.6 mg, 52%) as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 8.30 (brs, 1H), 7.56 (s, 1H), 7.36 (d, J = 8.6 Hz, 1H), 7.23 (d, J = 2.3 Hz, 1H), 7.15 (d, J = 8.6 Hz, 1H), 4.87 (s, 2H), 1.65 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 136.7, 126.6, 124.4, 122.5 (q, $^1J_{CF}$ = 274.3 Hz), 120.9, 120.4, 118.3, 116.6, 111.8, 57.0, 29.0 (q, $^2J_{CF}$ = 40.8 Hz); ^{19}F NMR ($CDCl_3$) δ −65.41; UV (MeOH) λ_{max} (ε) 375 (423); HRMS-ESI (m/z) [M + H − N_2]$^+$ calcd for $C_{11}H_9F_3NO$ 228.0636, found 228.0607.

(6-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)-methanol (9b). The same treatment of **8b** (28.8 mg, 0.13 mmol) as that just described gave **9b** (26.7 mg, 82%) as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 8.27 (brs, 1H), 7.75 (d, J = 8.6 Hz, 1H), 7.29 (d, J = 2.3 Hz, 1H), 7.27 (s, 1H), 6.99 (d, J = 8.6 Hz, 1H), 4.88 (s, 2H), 1.58 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 136.0, 127.5, 124.8, 123.0, 122.4 (q, $^1J_{CF}$ = 274.3 Hz), 119.8, 118.0, 116.4, 110.2, 57.1, 29.0 (q, $^2J_{CF}$ = 39.6 Hz); ^{19}F NMR ($CDCl_3$) δ −65.22; UV (MeOH) λ_{max} (ε) 387 (321); HRMS-ESI (m/z) [M + H −- N_2]$^+$ calcd for $C_{11}H_9F_3NO$ 228.0636, found 228.0636.

***N*,*N*-Dimethyl-1-(5-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)methanamine (10a).** 5-(Diazirinyl)indole **6a** (41.2 mg, 0.18 mmol) and *N*-methyl-*N*-methylenemethanaminium iodide (51.3 mg, 0.24 mmol) were dissolved in CH_2Cl_2 at rt. The reaction was stirred for 24 h. The solution was concentrated, and then the residue was purified by column chromatography (AcOEt to AcOEt/MeOH 9/1) to yield **10a** (46.9 mg, 91%) as a yellow amorphous mass: ^{1}H NMR ($CDCl_3$) δ 9.68 (brs, 1H), 8.00 (s, 1H), 7.55 (d, J = 8.6 Hz, 1H), 7.34 (s, 1H), 7.12 (d, J = 8.6 Hz, 1H), 4.42 (s, 2H), 2.77 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 136.2, 131.1, 127.2, 122.4 (q, $^1J_{CF}$ = 274.7 Hz), 121.7, 121.2, 116.4, 113.1, 102.7, 52.3, 42.2, 28.9 (q, $^2J_{CF}$ = 40.8 Hz); ^{19}F NMR (CD_3OD) δ −65.28; UV (MeOH) λ_{max}(ε) 375 (368); HRMS-ESI (m/z) [M + H]$^+$ calcd for $C_{13}H_{14}F_3N_4$ 283.1171, found 283.1149.

***N*,*N*-Dimethyl-1-(6-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)methanamine (10b).** The same treatment of **6b** (30.3 mg, 0.13 mmol) as that just described gave **10b** (30.7 mg, 81%) as a yellow amorphous mass: ^{1}H NMR ($CDCl_3$) δ 8.47 (brs, 1H), 7.70 (d, J = 9.2 Hz, 1H), 7.21 (s, 1H), 7.19 (d, J = 2.3 Hz, 1H), 6.93 (d, J = 9.2 Hz, 1H), 3.61 (s, 2H), 2.26 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 135.8, 128.8, 125.6, 122.5, 122.5 (q, $^1J_{CF}$ = 275.9 Hz), 119.9, 117.7, 113.6, 110.0, 54.3, 45.3, 29.0 (q, $^2J_{CF}$ = 39.6 Hz); ^{19}F NMR ($CDCl_3$) δ −65.34; UV (MeOH) λ_{max} (ε) 385 (300); HRMS-ESI (m/z) [M + H]$^+$ calcd for $C_{13}H_{14}F_3N_4$ 283.1171, found 283.1152.

2-Acetamido-3-(5-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)propanoic Acid (11a). L-Serine (93.7 mg, 0.89 mmol) was dissolved in AcOH (1.00 mL) and Ac_2O (0.340 mL). After the solution was stirred for 1 h at 75 °C, the solution was added to 5-diazirinylindole **6a** (100 mg, 0.45 mmol) at rt. The reaction mixture was stirred for 1.5 h and then concentrated. The residue was dissolved in diethyl ether, washed with 1 M HCl and brine, dried over $MgSO_4$, filtrated, and then concentrated. The residue was purified by column chromatography (CH_2Cl_2 to AcOEt/MeOH/H_2O 8/1/1) to yield **11a** (39.1 mg, 25%) as a yellow amorphous mass: ^{1}H NMR (CD_3OD) δ 7.41 (s, 1H), 7.39 (d, J = 8.6 Hz, 1H), 7.19 (s, 1H), 7.07 (d, J = 8.6 Hz, 1H), 4.61 (dd, J = 7.4, 5.2 Hz, 1H), 3.34 (dd, J = 14.6, 5.2 Hz, 1H), 3.13 (dd, J = 14.6, 7.4 Hz, 1H), 1.89 (s, 3H); ^{13}C NMR (CD_3OD) δ 177.3, 173.0, 138.4, 129.3, 126.3, 124.1 (q, $^1J_{CF}$ = 273.5 Hz), 120.5, 119.9, 118.6, 113.1, 112.4, 56.0, 30.3 (q, $^2J_{CF}$ = 40.0 Hz), 28.3, 22.6; ^{19}F NMR (CD_3OD) δ −67.12; HRMS-ESI (m/z) [M + H]$^+$ calcd for $C_{15}H_{14}F_3N_4O_3$ 355.1018, found 355.0993.

2-Acetamido-3-(6-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)propanoic Acid (11b). The same treatment of **6b** (53.6 mg, 0.24 mmol) as that just described gave **11b** (19.8 mg, 24%) as a yellow amorphous mass: ^{1}H NMR (CD_3OD) δ 7.62 (d, J = 8.6 Hz, 1H), 7.23 (s, 1H), 7.21 (s, 1H), 6.87 (d, J = 8.6 Hz, 1H), 4.70 (dd, J = 8.0, 5.2 Hz, 1H), 3.32 (dd, J = 14.9, 5.2 Hz, 1H), 3.13 (dd, J = 14.9, 8.0 Hz, 1H), 1.87 (s, 3H); ^{13}C NMR (CD_3OD) δ 175.0, 173.2, 137.5, 130.2, 127.0, 124.0 (q, J = 274.3 Hz), 122.5, 120.2, 117.7, 111.7, 111.2, 54.7, 30.2 (q, $^2J_{CF}$ = 39.6 Hz), 28.3, 22.4; ^{19}F NMR (CD_3OD) δ −67.03; HRMS-ESI (m/z) [M + H]$^+$ calcd for $C_{15}H_{14}F_3N_4O_3$ 355.1018, found 355.1013.

(*S*)-2-Aamino-3-(5-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)propanoic Acid (12a). *N*-Acetyl-5′-diazirinyl-DL-tryptophan **11a** (13.3 mg, 37.0 μmol) was dissolved in 0.2 M phosphate buffer (pH 7.6, 4 mL), and L-aminoacylase (1.0 mg) and 0.42 mM of $CoCl_2$ hexahydrate in the buffer (0.42 μmol) were added to the solution, successively. The solution was incubated at 37 °C for 24 h. The reaction mixture was subjected to chromatography (SEPABEADS SP207, 100 mL of H_2O, followed by 200 mL of MeOH). The MeOH fraction was concentrated, and the residue was purified by column chromatography (AcOEt/MeOH/H_2O 8/1/1 to 4/1/1) to afford 5′-diazirinyl-L-tryptophan **12a** as a pale yellow amorphous mass (2.7 mg, 23%): $[\alpha]_D$ = −17.9 (c 1 MeOH); ^{1}H NMR (CD_3OD) δ 7.57 (s, 1H), 7.44 (d, J = 8.6 Hz, 1H), 7.29 (s, 1H), 7.14 (d, J = 8.6 Hz, 1H), 3.80 (dd, J = 9.2, 4.0 Hz, 1H), 3.46 (dd, J = 15.2, 4.0 Hz, 1H), 3.13 (dd, J = 15.5, 9.2 Hz, 1H); ^{13}C NMR (CD_3OD) δ 174.3, 138.8, 128.7, 127.2, 124.1 (q, $^1J_{CF}$ = 273.9 Hz), 121.1, 120.3, 118.8, 113.3, 110.3, 56.5, 30.2 (q, $^2J_{CF}$ = 40.0 Hz), 28.1; ^{19}F NMR (CD_3OD) δ −67.15; UV (MeOH) λ_{max} (ε) 380 (354); HRMS-ESI (m/z) [M + H]$^+$ calcd for $C_{13}H_{12}F_3N_4O_2$ 313.0912, found 313.0901; Chiral HPLC (Astec Chirobiotic T, 10% MeOH) t_R = 10.59 min.

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(*S*)-2-Amino-3-(6-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)propanoic Acid (12b). The same treatment of **11b** (14.2 mg, 0.04 mmol) as that just described gave **12b** (3.5 mg, 33%) as a yellow amorphous mass: $[\alpha]_D$ = −25.3 (*c* 1 MeOH); ^{1}H NMR (CD_3OD) δ 7.78 (d, *J* = 8.6 Hz, 1H), 7.33 (s, 1H), 7.28 (s, 1H), 6.93 (d, *J* = 8.6 Hz, 1H), 3.84 (dd, *J* = 8.6, 4.0 Hz, 1H), 3.47 (dd, *J* = 15.2, 4.0 Hz, 1H), 3.19 (d, *J* = 15.2, 8.6 Hz, 1H); ^{13}C NMR (CD_3OD) δ 174.2, 137.9, 129.8, 127.8, 124.0 (q, $^1J_{CF}$ = 273.5 Hz), 122.9, 120.5, 118.0, 111.4, 110.1, 56.6, 30.2 (q, $^2J_{CF}$ = 40.0 Hz), 28.1; ^{19}F NMR (CD_3OD) δ −67.09; UV (MeOH) λ_{max} (ε) 388 (369); HRMS-ESI (*m*/*z*) [M + H]$^+$ calcd for $C_{13}H_{12}F_3N_4O_2$ 313.0912, found 313.0892; Chiral HPLC (Astec Chirobiotic T, 10% MeOH) t_R = 10.24 min.

Methyl 2-Oxo-2-(5-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)acetate (13a). Compound **6a** (120 mg, 0.53 mmol) was dissolved in ether (3 mL) and cooled to 0 °C. Oxalyl chloride (91 μL, 1.06 mmol) was added dropwise to the above solution, and the reaction was warmed to rt and stirred for 12 h. After being stirred, the reaction was cooled to 0 °C, and then MeOH was added to the solution. The reaction mixture was warmed to rt and stirred for 6 h. After the reaction mixture was concentrated, the residue was purified by column chromatography ($CHCl_3$ then $CHCl_3$/MeOH 95/5) to yield **13a** (103 mg, 62%) as a yellow amorphous mass: ^{1}H NMR (DMSO-d_6) δ 8.59 (s, 1H, 2′-H), 8.09 (s, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 178.6, 163.3, 140.2, 137.3, 125.8, 122.2 (q, $^1J_{CF}$ = 274.4 Hz), 121.9, 121.8, 119.7, 114.0, 112.4, 54.9, 28.6 (q, $^2J_{CF}$ = 39.5 Hz); ^{19}F NMR (DMSO-d_6) δ −64.53; HRMS-ESI (*m*/*z*) [M + H]$^+$ calcd for $C_{13}H_9F_3N_3O_3$ 312.0596, found 312.0574.

Methyl 2-Oxo-2-(6-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)acetate (13b). The same treatment of **6b** (72.7 mg, 0.32 mmol) as that just described gave **13b** (80.1 mg, 80%) as a yellow amorphous mass: ^{1}H NMR (DMSO-d_6) δ 8.60 (s, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 7.49 (s, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 178.6, 163.5, 140.3, 136.5, 126.9, 122.7, 122.2, 122.1 (q, $^1J_{CF}$ = 275.9 Hz).120.6, 112.3, 111.5, 52.7, 28.6 (q, $^2J_{CF}$ = 38.4 Hz); ^{19}F NMR (DMSO-d_6) δ −64.53; HRMS-ESI (*m*/*z*) [M + H]$^+$ calcd for $C_{13}H_9F_3N_3O_3$ 312.0596, found 312.0585.

Methyl 2-(5-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)indolin-3-yl)acetate (14a). Compound **13a** (60.2 mg, 0.19 mmol) was dissolved in TFA (300 μL), and Et_3SiH (186 μL, 1.16 mmol) was added at 0 °C. The reaction mixture was stirred at rt for 6 h and evaporated with toluene. The residue was purified by column chromatography (CH_2Cl_2, then CH_2Cl_2/MeOH 95/5) to yield **14a** (38.1 mg, 66%) as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 6.93 (s, 1H), 6.87 (d, *J* = 8.2 Hz, 1H), 6.65 (d, *J* = 8.2 Hz, 1H), 3.83 (t, *J* = 9.1 Hz, 1H), 3.72 (s, 3H), 3.70−3.68 (m, 1H), 3.32 (dd, *J* = 8.7, 6.1 Hz, 1H), 2.73 (dd, *J* = 15.8, 6.1 Hz, 1H), 2.56 (dd, *J* = 15.8, 8.7 Hz, 1H). It is difficult to measure ^{13}C NMR due to the compound **14a** was not stable in $CDCl_3$ solution. Although we checked the stability of **14a** carefully, the partial decomposition of **14a** was observed after ^{1}H NMR measurement, which took less than 5 min.

Methyl 2-(6-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)indolin-3-yl)acetate (14b). The same treatment of **13b** (76.3 mg, 0.25 mmol) as that just described gave **14b** (63.1 mg, 86%) as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.31 (d, *J* = 8.0 Hz, 1H), 7.06 (s, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 4.05 (t, *J* = 10.0 Hz, 1H), 3.94−3.88 (m, 1H), 3.71 (s, 3H), 3.57 (dd, *J* = 8.6, 6.0 Hz, 1H), 2.84 (dd, *J* = 16.9, 6.0 Hz, 1H), 2.68 (dd, *J* = 16.9, 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 171.6, 142.1, 137.0, 130.2, 125.2, 124.5, 121.9 (q, $^1J_{CF}$ = 280.7 Hz), 114.4, 52.0, 51.9, 51.8, 37.9, 28.3 (q, $^2J_{CF}$ = 40.4 Hz); ^{19}F NMR ($CDCl_3$) δ −65.22; HRMS-ESI (*m*/*z*) [M + H]$^+$ calcd for $C_{13}H_{13}F_3N_3O_2$ 300.0960, found 300.0930.

Methyl 2-Hydroxy-2-(5-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)acetate (15a). To a solution of compound **13a** (108 mg, 0.34 mmol) in MeOH (6 mL) was added $NaBH_4$ (13.0 mg, 0.36 mmol) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C, the solvent was concentrated, and the residue was dissolved in AcOEt (30 mL). The organic layer was washed with brine, dried over $MgSO_4$, filtered, and evaporated. The crude product was purified by column chromatography (AcOEt/hexane 1/2) to yield **15a** (70.8 mg, 65%) as a yellow amorphous mass: ^{1}H NMR ($CDCl_3$) δ 8.39 (brs, 1H), 7.58 (s, 1H), 7.35 (d, *J* = 8.6 Hz, 1H), 7.28 (d, *J* = 2.3 Hz, 1H), 7.10 (d, *J* = 8.6 Hz, 1H), 5.48 (d, *J* = 4.6 Hz, 1H), 3.78 (s, 3H), 3.38 (d, *J* = 4.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 174.1, 136.7, 125.4, 124.6, 122.4 (q, $^1J_{CF}$ = 275.9 Hz), 120.9, 120.7, 118.7, 114.1, 112.0, 66.9, 53.0, 28.9 (q, $^2J_{CF}$ = 40.8 Hz); ^{19}F NMR ($CDCl_3$) δ −65.44; HRMS-ESI (*m*/*z*) [M + H]$^+$ calcd for $C_{13}H_{11}F_3N_3O_3$ 314.0753, found 314.0753.

Methyl 2-Hydroxy-2-(6-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)acetate (15b). The same treatment of **13b** (104.0 mg, 0.33 mmol) as that just described gave **15b** (80.5 mg, 78%) as a yellow amorphous mass: ^{1}H NMR ($CDCl_3$) δ 8.36 (brs, 1H), 7.70 (d, *J* = 8.6 Hz, 1H), 7.31 (d, *J* = 3.4 Hz, 1H), 7.24 (s, 1H), 6.97 (d, *J* = 8.6 Hz, 1H), 5.46 (d, *J* = 5.2 Hz, 1H), 3.76 (s, 3H), 3.35 (d, *J* = 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 174.2, 136.0, 126.3, 125.1, 123.2, 122.4 (q, $^1J_{CF}$ = 273.5 Hz), 120.1, 118.3, 114.0, 110.3, 67.0, 53.0, 28.9 (q, $^2J_{CF}$ = 40.8 Hz); ^{19}F NMR ($CDCl_3$) δ −65.22; HRMS-ESI (*m*/*z*) [M + H]$^+$ calcd for $C_{13}H_{11}F_3N_3O_3$ 314.0753, found 314.0744.

Methyl 2-(5-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)acetate (16a). To a solution of **15a** (64.3 mg, 0.21 mmol) in CH_2Cl_2 (3 mL) was added P_2I_4 (228.0 mg, 0.41 mmol) at 0 °C. The reaction mixture was stirred at rt for 6 h. The mixture was poured into saturated $NaHSO_3$, and CH_2Cl_2 and saturated $NaHCO_3$ were added. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and evaporated. The crude product was purified by column chromatography (AcOEt/hexane 1/3) to yield **16a** (29.1 mg, 47%) as a yellow amorphous mass: ^{1}H NMR ($CDCl_3$) δ 8.26 (brs, 1H), 7.45 (s, 1H), 7.32 (d, *J* = 8.6 Hz, 1H), 7.18 (d, *J* = 2.3 Hz, 1H), 7.08 (d, *J* = 8.6 Hz, 1H), 3.76 (s, 2H), 3.73 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 172.2, 136.4, 127.2, 124.6, 122.5 (q, $^1J_{CF}$ = 279.5 Hz), 120.5, 120.2, 118.1, 111.7, 108.9, 52.1, 30.8, 29.0 (q, $^2J_{CF}$ = 42.0 Hz); ^{19}F NMR ($CDCl_3$) δ −65.41; HRMS-ESI (*m*/*z*) [M + H]$^+$ calcd for $C_{13}H_{11}F_3N_3O_2$ 298.0803, found 298.0779.

Methyl 2-(6-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)acetate (16b). (a) From **15b**. The same treatment of **15b** (45 mg, 0.143 mmol) as that just described gave **16b** (26 mg, 61%) as a yellow amorphous mass. (b) From **14b**. Compound **14b** (16.5 mg, 0.055 mmol) was dissolved in diethyl ether (3 mL). Activated MnO_2 was suspended into the solution. The reaction was stirred at rt for 1 h and filtrated. After concentration, the residue was purified by column chromatography ($CHCl_3$) to give **16b** (13.2 mg, 81%) as a yellow amorphous mass: ^{1}H NMR ($CDCl_3$) δ 8.24 (brs, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.23 (s, 1H), 7.21 (d, *J* = 2.2 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 3.77 (s, 2H), 3.71 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 172.2, 135.6, 128.2, 125.1, 122.8, 122.4 (q, $^1J_{CF}$ = 276.0 Hz), 119.5, 117.8, 110.1, 108.7, 52.1, 30.9, 29.0 (q, $^2J_{CF}$ = 40.7 Hz); ^{19}F NMR ($CDCl_3$) δ −65.15; HRMS-ESI (*m*/*z*) [M + H]$^+$ calcd for $C_{13}H_{11}F_3N_3O_2$ 298.0803, found 298.0789.

2-(5-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)-acetic Acid (17a). Compound **16a** (43.5 mg, 0.15 mmol) was dissolved in MeCN (3 mL) and MeOH (1.5 mL). NaOH (1 M, 1.5 mL) was added dropwise to the above solution at 0 °C. The reaction was warmed to rt, stirred for 12 h, and then concentrated. The residue was purified by column chromatography (AcOEt/MeOH 2/1) to yield **17a** (35.6 mg, 85%) as a yellow amorphous mass: ^{1}H NMR ($CDCl_3$) δ 8.20 (brs, 1H), 7.43 (s, 1H), 7.33 (d, *J* = 8.6 Hz, 1H), 7.20 (d, *J* = 2.3 Hz, 1H), 7.11 (d, *J* = 8.6 Hz, 1H), 3.79 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 177.6, 136.3, 127.1, 124.8, 122.5 (q, $^1J_{CF}$ = 274.7 Hz), 120.7, 120.4, 118.0, 111.8, 108.2, 30.7, 29.0 (q, $^2J_{CF}$ = 39.6 Hz); ^{19}F NMR ($CDCl_3$) δ −65.41; UV (MeOH) λ_{max} (ε) 380 (402); HRMS-ESI (*m*/*z*) [M + H]$^+$ calcd for $C_{12}H_9F_3N_3O_2$ 284.0647, found 284.0647.

2-(6-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)-1*H*-indol-3-yl)-acetic Acid (17b). The same treatment of **16b** (11.2 mg, 0.038 mmol) as that just described gave **17b** (9.50 mg, 89%) as a yellow amorphous mass: ^{1}H NMR ($CDCl_3$) δ 8.20 (brs, 1H), 7.60 (d, *J* = 8.6 Hz, 1H), 7.24 (s, 1H), 7.23 (d, *J* = 2.3 Hz, 1H), 6.96 (d, *J* = 8.6 Hz, 1H), 3.78 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 177.2, 135.6, 128.1, 125.2, 122.9, 122.4 (q, $^1J_{CF}$ = 273.5 Hz), 119.5, 118.0, 110.2, 108.1, 30.8, 29.0 (q, $^2J_{CF}$ = 40.8 Hz); ^{19}F NMR ($CDCl_3$) δ −65.22; UV (MeOH) λ_{max} (ε) 380 (364); HRMS-ESI (*m*/*z*) [M + H]$^+$ calcd for $C_{12}H_9F_3N_3O_2$ 284.0647, found 284.0623.

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Photolysis of Diazirinylindole Derivatives.[20] A 1 mM methanolic solution (1 mL) of the diazirinylindole derivatives was placed in a quartz cuvette. After the inner atmosphere was replaced with nitrogen, photolysis was carried out with 100 W black-light at a distance 1 cm from the surface of light source. Specrtra were measured after each minute, and then the half-life was calculated from the decrements of the absorbance around 380 nm.

Biological Assay for on Elongation of Oat Coleoptile Segments.[21] Coleoptiles were obtained from dark-grown oat seedlings. Coleoptile tips (5 mm in length) were removed, and the next 10 mm was excised. Coleoptile segments were immersed in a treatment solution (**17a**, **17b**, and IAA) at 25 °C for 24 h, followed by measurements of segments.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR charts of the new compounds, overlay charts of photolysis of diazirinyl indole derivatives, and photographs of biological assays for on elongation of oat coleoptile segments. All of these materials are available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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