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A LEWIS-ACID CATALYZED SYNTHESIS OF SUBSTITUTED OXINDOLE DERIVATIVES

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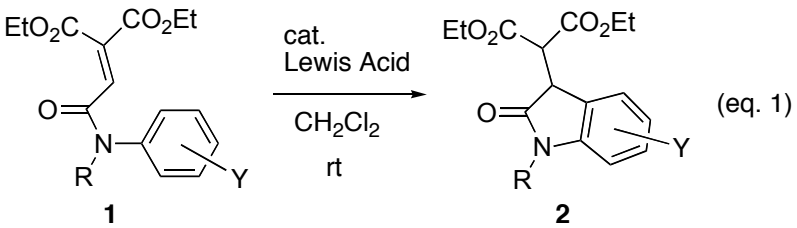
Abstract - Lewis acid-catalyzed cyclization of various 2-(*N*-arylcarbamoyl)-methylenemalonates to give nitrogen-containing benzo-annelated heterocycles was investigated in terms of selectivity. Reaction of substrates with various alkyl groups on nitrogen proceeded to give oxindole derivatives. Cyclization reaction of diester-amides of MeO and halogen-substituted anilines in the presence of catalytic Lewis acid ($ZnCl_2$, $SnCl_4$, $AlCl_3$, $Zn(OTf)_2$, $Sc(OTf)_3$, etc.) gave oxindoles in high yields. Interesting regioselectivity was observed for *meta*-halogen substrates. Dimethoxyisoquinoline analogs were also obtained by this reaction using a catalytic Lewis acid.

INTRODUCTION

Nitrogen-containing benzo-annelated heterocyclic systems such as indoles and related compounds are important structures in organic chemistry because of their presence in many biologically active compounds.[1] Although various methods for the synthesis of indoles and related compounds have been investigated,[1,2] general and mild procedures for formation of diversely substituted indoles are highly desirable. Recently, we have reported Lewis acid-promoted aromatic cyclizations to afford oxindoles and benzofuranones.[3] In the previous study, the cyclization in some cases required more than 1 equivalent of Lewis acids and poor regioselectivity for *meta*-Me substituted derivatives was observed. In this paper, we have investigated the reactivity and selectivity on the cyclization of diversely substituted substrates and the catalytic use of Lewis acids and report in full detail the catalytic Friedel-Crafts intramolecular Michael addition towards substituted nitrogen-containing benzo-annelated heterocycles and its scope and limitations (eq. 1).



1 2 (eq. 1)

RESULTS AND DISCUSSION

Preparation of Substrates. The precursors, diester-amides (**1**) were prepared by condensation of 1,1-diethyl 2-hydrogen ethenetricarboxylate (prepared from 1,1-diethyl 2-*tert*-butyl ethenetricarboxylate upon treatment with CF_3CO_2H) with 1-hydroxybenzotriazole (HOBT) and 1-[3-dimethylaminopropyl]-3-ethylcarbodiimide hydrochloride (EDCI), followed by reaction with the corresponding anilines[3] (eq. 2, Table 1). Formation of considerable amounts of amine adduct by-products (**3**) was suppressed by the stepwise addtion of HOBT/EDCI and anilines for *N*-alkylaniline derivatives.[3] However, the formation of by-products (**3a-b**) could not be suppressed by this procedure for *N*-unsubstituted anilines. Thus, the reaction with *N*-unsubstituted anilines gave **1a** and **1b** in low yields (Entries 1-2).

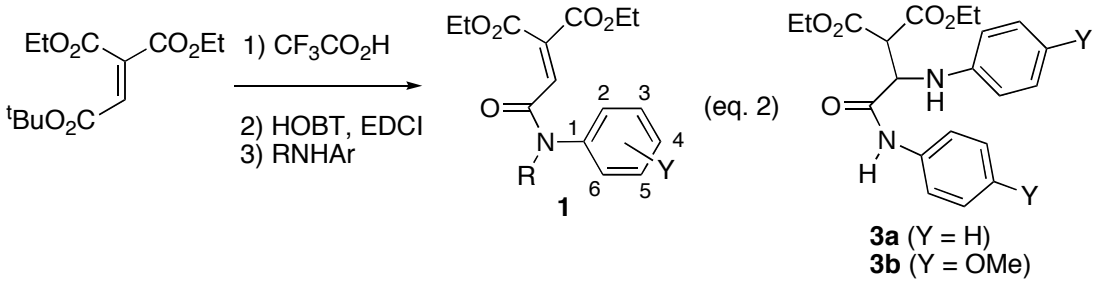
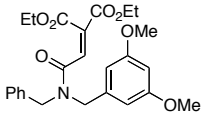
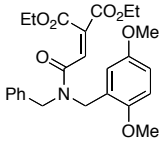


Table 1. Preparation of **1** and **7**

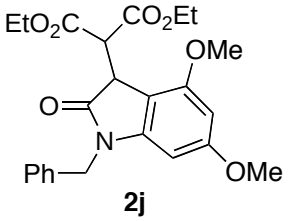
Entry	Product	R	Y	Yield (%)	Entry	Product	R	Y	Yield (%)
1	**1a**	H	H	25[a]	12	**1l**	CH_2Ph	4-Br	49
2	**1b**	H	4-OMe	22[b]	13	**1m**	CH_2Ph	4-I	40
3	**1c**	CH_2Ph	H	57	14	**1n**	CH_2Ph	3-OMe	*ca.* 22[f]
4	**1d**	allyl	H	45	15	**1o**	CH_2Ph	3-Cl	21[g]
5	**1e**	*i*-Pr	H	43	16	**1p**	CH_2Ph	3-Br	37[h]
6	**1f**	CHMePh	H	27[c]	17	**1q**	CH_2Ph	3-I	21[i]
7	**1g**	CH_2Ph	4-OMe	65	18	**1r**	CH_2Ph	3-F	42
8	**1h**	CH_2Ph	2-OMe	57	19	**1s**	CH_2Ph	3-CF_3	33
9	**1i**	CH_2Ph	2,3-OMe	60	20	**7a**			63
10	**1j**	CH_2Ph	3,5-di-OMe	0[d]	21	**7b**			72
11	**1k**	CH_2Ph	2-Cl	0[e]					

a. Amine adduct (**3a**) was also formed in 24% yield. b. Amine adduct (**3b**) was also formed in 20% yield. c. 50% Of amine was recovered. d. The cyclized product (**2j**) and compound (**4**) were also obtained in 11 and 7% yields, respectively. e. 82% of amine was recovered. f. Obtained as a mixture with **5n**, see reference 6. g. 69% Of amine was recovered. h. 46% Of amine was recovered. i. 76% Of amine was recovered.

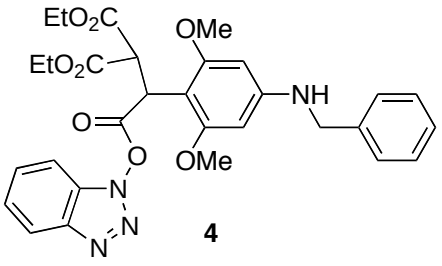
A number of *N*-benzylaniline derivatives were prepared by condensation of aniline derivatives and

benzaldehyde and subsequent reduction by $NaBH_4$[4] or Pd-catalyzed amination reactions of aryl bromides.[5] The benzyl-protected amides were also prepared according to eq. 2. The condensation of amine with 1,1-diethyl 2-hydrogen ethenetricarboxylate gave **1** in modest yields. However, *meta*-halogen substituted substrates were obtained in lower yields along with the starting amines (Entries 15-17). *N*-Benzyl-*o*-chloroaniline did not react with 1,1-diethyl 2-hydrogen ethenetricarboxylate and was recovered (Entry 11).

Attempted preparation of 3,5-dimethoxyaniline-derived precursor (**1j**) led directly to cyclized oxindole (**2j**) (11%) without the need for Lewis acid, along with the product of reaction of the intermediate HOBT ester with amine (**4**) (Entry 10). Cyclized products were also partially produced for *meta*-methoxy substitued precursor (**1n**) (Entry 14).[6]



2j



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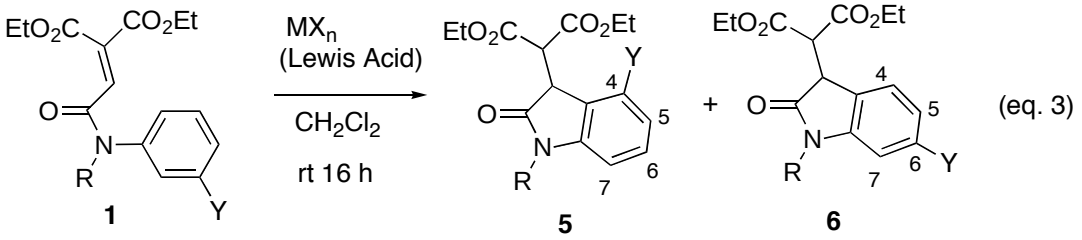
Cyclization of *N*-Substituted Derivatives. Reaction of various *N*-alkyl substituted substrates was examined in order to explore the electronic and steric effects and also further synthetic utility. The cyclization reaction (eq. 1, Table 2) of *N*-unsubstituted aniline derivatives (**1a-b**) in the presence of $ZnCl_2$ or $SnCl_4$ in CH_2Cl_2 at room temperature was first attempted. The reaction of **1a** and **1b** with strong Lewis acid $SnCl_4$ in catalytic amounts (0.2 equivalents) gave **2a** and **2b**, respectively. However, the reaction of **1b** with $ZnCl_2$ (1.2 equiv.) did not give **2b**. The cyclization reaction of *N*-methyl derivatives (**1**) (R = Me, Y = H,[3] OMe[7]) with $ZnCl_2$ (1.2 equiv.) proceeded smoothly. The lower reactivity of NH derivative (**1b**) with $ZnCl_2$ compared to *N*-methyl derivatives (**1**) (R = Me) probably arises from reduced activation of aromatic rings.

Next, the cyclization reaction of *N*-benzyl, *N*-allyl, and *N*-iso-propylaniline derivatives (**1c-e**) was examined. Reaction proceeded with catalytic amounts (0.2 equivalents) of Lewis acids such as $SnCl_4$, $ZnBr_2$, $Sc(OTf)_3$, and $Zn(OTf)_2$. *N*-Allylaniline derivative (**1c**) gave **2d** exclusively in spite of the existence of another double bond which could form a five-membered ring under these catalytic conditions. The reaction of secondary alkylamine derivative (**1f**) showed no diastereoselectivity.

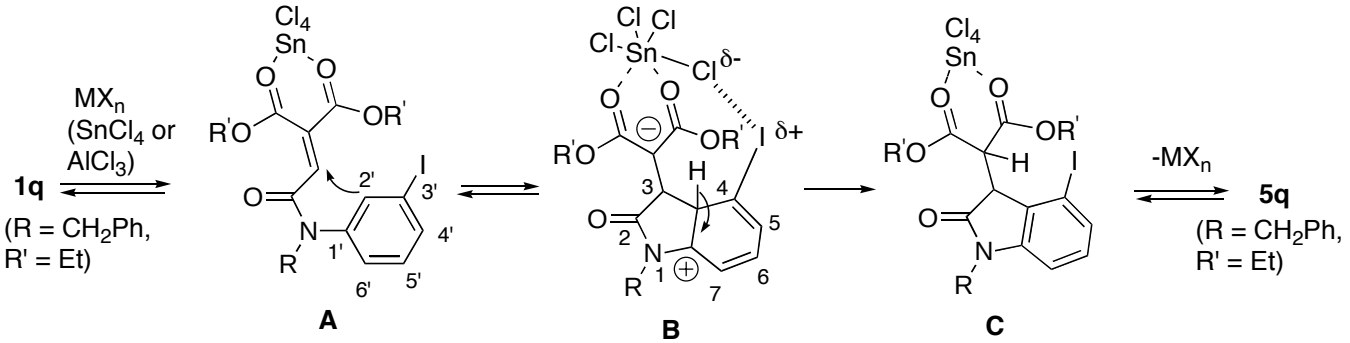
Aromatic Ring Substituent Effects. A variety of *N*-benzyl substituted aniline derivatives were examined. First, substrates with *o,p*-substituents which form a single regioisomer by cyclization are shown in Table 3. Various substrates underwent cyclization with catalytic amounts of Lewis acid to afford oxyindoles in high yields. Removal of the *N*-benzyl group of oxindoles is known.[8] Therefore, introduction of a *N*-benzyl group has merit for preparation of starting material and facile cyclization compared to NH amide substrates.

Meta-substituted substrates (**1**) were next investigated in order to examine 4- and 6-substitution regioselectivity in the products (eq. 3, Table 4). Although Me and MeO-substituted substrates showed

low regioselectivity (Entry 1 and reference 6), *meta*-Cl, Br, I-substituted substrates showed interesting regioselectivity which gave 4-isomers (**5**) preferentially against steric hindrance (Entries 2-4). The selectivity increases in the order I > Br > Cl. The selectivity also depends on Lewis acids. When stronger Lewis acids such as $SnCl_4$ and $AlCl_3$ were used, the 4-selectivity increased. On the other hand, F-substrate (**1r**) gave the sterically less hindered 6-isomer (**6r**) preferentially (Entry 5). The regiochemistries of **5** and **6** were confirmed by NMR spectrum, the coupling patterns of H7 and NOEs of H7---R or H4---C*H*-C*H*$(CO_2Et)_2$, and HMBC correlation of H4---*C*H-CH$(CO_2Et)_2$.



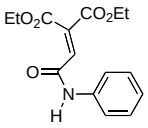
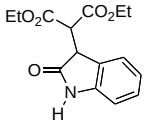
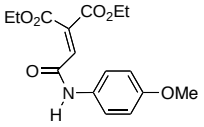
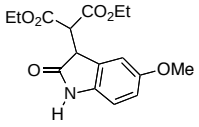
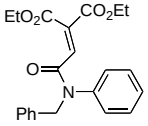
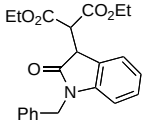
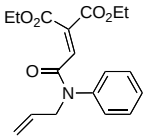
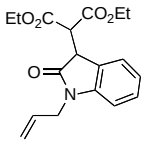
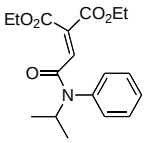
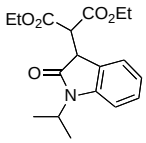
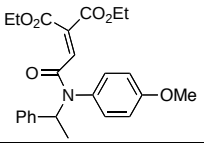
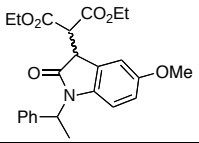
The probable aromatic substitution mechanism to explain regioselective 4-iodo ring formation is considered (Scheme 1). Nucleophilic attack of the *ortho* C2' aromatic carbon to sp^2 carbon of the electrophilic olefin in metal-coordinated intermediate (**A**) gives an intermediate (**B**), which yields the cyclized product (**5q**). Because of longer bond length, larger atomic size, and the relative electronegativity, iodine in benzene ring most flexibly and effectively interacts with a chloride ligand of stronger (metal-halogen polarized) Lewis acid such as $SnCl_4$ and $AlCl_3$ in **B**. The B3LYP/LANL2DZ[9,10] optimized structure of an intermediate model (**B**) (R, R' = CH_3) (Figure 1) shows the distance of I and Cl is 3.648 Å. The atomic charges by B3LYP/LANL2DZ SCRF=PCM[11]//B3LYP/LANL2DZ suggest a Coulombic attraction between I (+0.28) and Cl (-0.48). Thus, the electrostatic stability of intermediate (**B**) may cause the regioselectivity of cyclization for **1q**. Mechanistic considerations for regioselectivity in individual examples are under further investigation.



Scheme 1

Six-membered ring formation. Six-membered ring formation was examined next. Ring formation did not proceed for a simple benzyl amide derivative with a catalytic amount of Lewis acid, as studied previously.[3] Introduction of two OMe groups to one benzyl group leads to catalytic cyclization (eq. 4, Table 5). Thus, 5,7-dimethoxyisoquinoline derivative (**8a**) was obtained using catalytic Lewis acids such as $ZnCl_2$, $Zn(OTf)_2$, $Cu(OTf)_2$, and $Sc(OTf)_3$ and 5,8-dimethoxyisoquinoline derivative (**8b**) was obtained by catalytic $SnCl_4$ or $AlCl_3$.

Table 2. Lewis Acid-promoted Cyclization of **1**[a]

Entry		Substrate	Lewis Acid	equiv.	**2** (Yield)	
1	**1a**		$SnCl_4$	1.2	**2a** (83)	
			$SnCl_4$	0.2	**2a** (83)	
2	**1b**		$SnCl_4$	1.2	**2b** (87)	
			$SnCl_4$	0.2	**2b** (86)	
			$ZnCl_2$	1.2	**2b** (0)	
3	**1c**		$SnCl_4$	0.2	**2c** (94)	
			$Sc(OTf)_3$	0.2	**2c** (69)	
			$Zn(OTf)_2$	0.2	**2c** (61)	
4	**1d**		$SnCl_4$	0.2	**2d** (78)	
			$Sc(OTf)_3$	0.2	**2d** (60)	
			$ZnBr_2$	0.2	**2d** (72)	
5	**1e**		$SnCl_4$	0.2	**2e** (60)	
			$Sc(OTf)_3$	0.2	**2e** (59)	
6	**1f**		$ZnCl_2$	1.2	**2f** (81)[b]	
			$ZnCl_2$	0.2	**2f** (79)[b]	

a. The reactions were carried out at room temperature for 16 h. b. Total yield. Stereoisomer ratio 1:1.

Table 3. Lewis Acid-promoted Cyclization of *N*-Benzyl Aniline Derivatives (**1**)

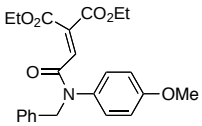
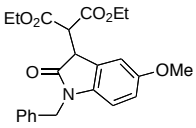
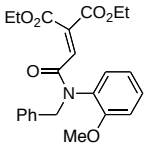
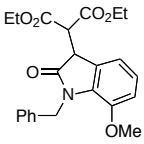
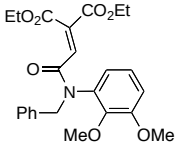
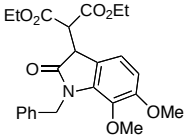
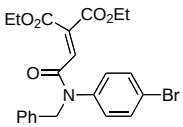
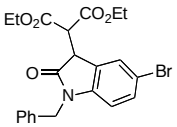
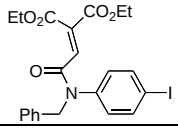
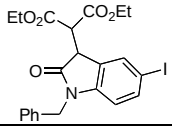
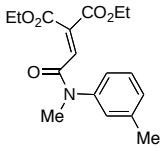
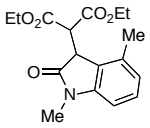
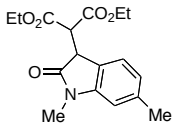
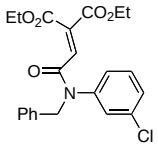
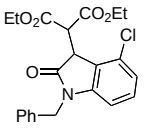
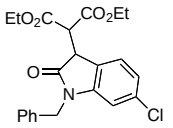
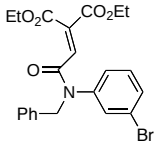
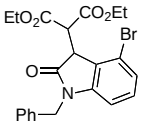
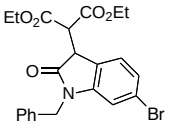
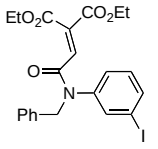
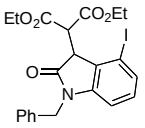
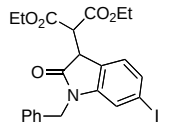
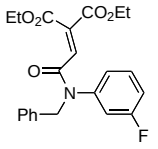
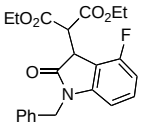
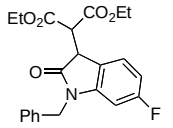
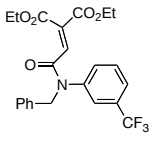
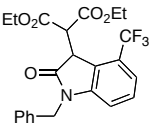
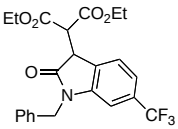
Entry		Substrate	Lewis Acid	equiv.	**2** (Yield)	
1	**1g**		$SnCl_4$	0.2	**2g** (86)	
			$ZnCl_2$	1.2	**2g** (87)	
			$ZnCl_2$	0.2	**2g** (88)	
2	**1h**		$SnCl_4$	0.2	**2h** (83)	
			$AlCl_3$	0.2	**2h** (82)	
3	**1i**		$SnCl_4$	0.2	**2i** (71)	
			$AlCl_3$	0.2	**2i** (74)	
			$Sc(OTf)_3$	0.2	**2i** (83)	
			$ZnCl_2$	0.2	**2i** (87)	
4	**1l**		$SnCl_4$	0.2	**2l** (78)	
			$ZnCl_2$	1.2	**2l** (79)	
			$ZnCl_2$	0.2	**2l** (18)	
			$Sc(OTf)_3$	0.2	**2l** (59)	
5	**1m**		$SnCl_4$	0.2	**2m** (81)	
			$AlCl_3$	0.2	**2m** (80)	
			$Sc(OTf)_3$	0.2	**2m** (8)	

Table 4. Lewis Acid-promoted Cyclization of *Meta*-substituted Aniline Derivatives (**1**)[a]

Entry		Substrate	Lewis Acid	**5** : **6** (ratio)[c]	**5** + **6** (Yield)		
1	**1t**[b]		$SnCl_4$	1.5 : 1	70		
			$ZnCl_2$	1 : 1	90	**5t**	**6t**
2	**1o**		$SnCl_4$	2.3 : 1	93		
			$AlCl_3$	2.5 : 1	86	**5o**	**6o**
3	**1p**		$SnCl_4$	4.3 : 1	76		
			$AlCl_3$	5.4 : 1	71		
			$InBr_3$	3.3 : 1	71		
			$ZnCl_2$	1.4 : 1	84		
			$ZnBr_2$	1.2 : 1	76	**5p**	**6p**
4	**1q**		$SnCl_4$	11 : 1	80		
			$AlCl_3$	7.2 : 1	92		
			$AlEtCl_2$	6.9 : 1	87		
			$ZnCl_2$	2.1 : 1	70		
			$Sc(OTf)_3$	2.1 : 1	77	**5q**	**6q**
5	**1r**		$SnCl_4$	1 : 8.5	80		
			$AlCl_3$	1 : 5.0	86		
			$ZnCl_2$	1 : 14	85		
			$Sc(OTf)_3$	1 : 30	85		
			$Zn(OTf)_2$	1 : 23	76	**5r**	**6r**
6	**1s**		$SnCl_4$	1.5 : 1	87		
			$AlCl_3$	3.6 : 1	86		
			$ZnCl_2$	-	0		
						5s	**6q**

a. 0.2 Equivalent of Lewis acid was used. b. Preparation of **1t**, see reference 3. c. **5** : **6** Ratios were determined by ^{1}H NMR.

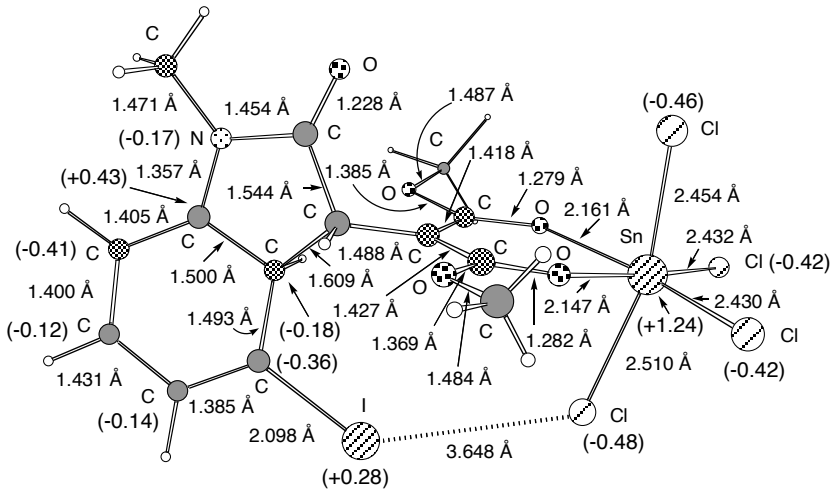


Figure 1. B3LYP/LANL2DZ-optimized structure of an intermediate model **B** (R, R' = CH_3). Numbers in parentheses denote atomic charges (positive, cationic) of B3LYP/LANL2DZ SCRF=PCM// B3LYP/LANL2DZ.

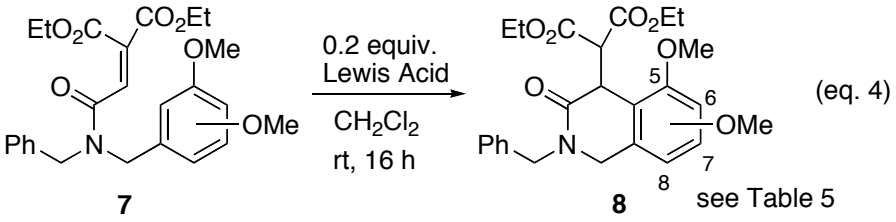
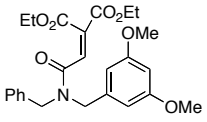
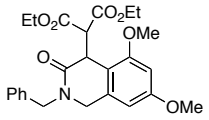
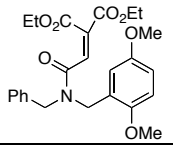
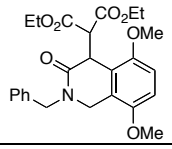
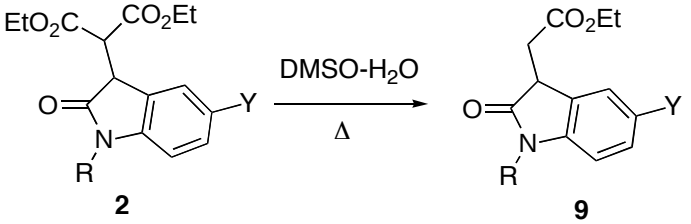


Table 5. Lewis Acid-promoted Cyclization towards Six-membered Ring Formation in eq. 4.

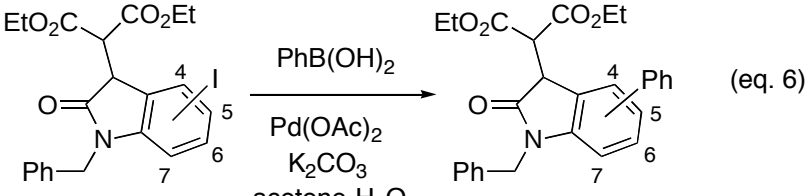
Entry	Substrate	Lewis Acid	**8** (Yield)
1	**7a** 	$ZnCl_2$	**8a** (71)
		$Zn(OTf)_2$	**8a** (77)
		$Cu(OTf)_2$	**8a** (80)
		$Sc(OTf)_3$	**8a** (75) 
2	**7b** 	$SnCl_4$	**8b** (84)
		$AlCl_3$	**8b** (88) 
		$ZnCl_2$	**8b** (0)

Application. Product elaboration was next investigated. The oxindole derivatives (**2**) underwent facile monodecarboxylation under Krapcho conditions[12] to afford monoester derivatives (**9**) (eq. 5). Optimal decarboxylation conditions involved heating the oxindoles in wet DMSO in the absence of salts such as LiCl.



9A: R = Me, Y = H, 140 °C, 5 h , 74%
9B: R = Allyl, Y = H, 160 °C, 4 h , 69%
9C: R = Benzyl, Y = H, 160 °C, 4 h , 75%
9D: R = Benzyl, Y = OMe, 160 °C, 4 h , 76%

In order to demonstrate the utilyty of halogen-substituted oxindoles, Suzuki-coupling reaction[13] with phenylboronic acid was performed. The reactions of 4- and 5-iodine substituted oxindoles proceeds smoothly to give phenyl-substituted oxindoles (**10**) (eq. 6).



2k: 5-I
5q: 4-I

10A: 5-Ph, 78%
10B: 4-Ph, 91%

In summary, we have shown an efficient and selective Lewis acid-promoted cyclization reaction yielding benzo-annulated nitrogen cyclic compounds. The reaction proceeds with catalytic amounts of Lewis acids. By use of stronger Lewis acids, $SnCl_4$ or $AlCl_3$, catalytic reaction was successfully achieved with less reactive substrates such as **1b**, **1s**, and **7b**. High regioselectivity has been achieved by choice of halogen atoms and Lewis acids. Further elaboration of the functionalized cyclized products has been also demonstrated.

ACKNOWLEDGMENT

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EXPERIMENTAL

General Methods. Melting points are uncorrected. IR spectra were recorded in the FT-mode. ^{1}H NMR spectra were recorded at 400 MHz. ^{13}C NMR spectra were recorded at 100.6 MHz. ^{1}H Chemical shifts are reported in ppm relative to Me_4Si. ^{13}C Chemical shifts are reported in ppm relative to $CDCl_3$ (77.1 ppm). ^{13}C mutiplicities were determined by DEPT and HSQC. ^{19}F Chemical shifts are reported in ppm relative to $CFCl_3$. Mass spectra were recorded at an ionizing voltage of 70 eV by EI. All reactions were carried out under a nitrogen atmosphere.

Prepation of 1, typical procedure for 1c (Table 1, Entry 3). To a solution of 1,1-diethyl 2-hydrogen ethenetricarboxylate (649 mg, 3 mmol) (prepared from 1,1-diethyl 2-*tert*-butyl ethenetricarboxylate upon treatment with CF_3CO_2H) in CH_2Cl_2 (4.1 mL) were added HOBt (1-hydroxybenzotriazole) (405 mg, 3 mmol) and EDCI (1-[3-dimethylaminopropyl]-3-ethylcarbodiimide hydrochloride) (575 mg, 3 mmol) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C. *N*-Benzylaniline (550 mg, 3 mmol) was added to the mixture and the reaction mixture was allowed to warm to rt and stirred for 16 h. The mixture was diluted with CH_2Cl_2 and the organic phase was washed with saturated aqueous $NaHCO_3$ solution, 2M aqueous citric acid, saturated aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel eluting with hexane-ether (2 : 1) to give **1c** (657 mg, 57%). **1c** (R_f = 0.7 (hexane-ether = 1 : 4)): Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.21 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.96 (s, 2H), 6.82 (s, 1H), 7.02-7.05 (m, 2H), 7.18-7.33 (m, 8H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.84 (q), 13.92 (q), 52.93 (t), 61.81 (t), 61.96 (t), 127.56 (d), 127.85 (d), 128.41 (d), 128.49 (d), 128.65 (d), 129.68 (d), 133.46 (d), 135.60 (s), 136.48 (s), 140.53 (s), 162.73 (s), 163.09 (s), 165.06 (s); IR (neat) 2982, 1730, 1657, 1592, 1250, 1068 cm^{-1}; MS (EI) *m/z* 381; exact mass M^+ 381.1562 (calcd for $C_{22}H_{23}NO_5$ 381.1576).

1a (R_f = 0.2 (hexane-ether = 1 : 1)): Yellow crystals; mp 96-97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.27-1.34 (m, 6H), 4.24-4.30 (m, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 7.02 (br s, 1H), 7.11 (t-like, *J* = 7.3 Hz, 1H), 7.28-7.31 (m, 2H), 7.54 (d, *J* = 7.7 Hz, 2H), 7.99 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.02 (q), 62.33 (t), 62.58 (t), 120.19 (d), 125.32 (d), 129.17 (d), 133.80 (d), 136.56 (s), 137.13 (s), 160.33 (s), 162.90 (s), 165.20 (s); IR (KBr) 3343, 1734, 1675, 1546, 1446, 1269, 1223, 1183 cm^{-1}; MS (EI) *m/z* 291; exact mass M^+ 291.1110 (calcd for $C_{15}H_{17}NO_5$ 291.1107).

3a (R_f = 0.5 (hexane-ether = 1 : 1)): Pale yellow crystals; mp 118-120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ

(ppm) 1.01 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 3.78-3.96 (m, 2H), 4.15-4.31 (m, 2H), 4.44 (d, *J* = 4.0 Hz, 1H), 4.71 (br d, *J* = 3.6 Hz, 1H), 5.13 (br s, 1H), 6.77 (d-like, *J* = 8.6 Hz, 2H), 6.85 (t-like, *J* = 7.3 Hz, 1H), 7.11 (t-like, *J* = 7.4 Hz, 1H), 7.20-7.25 (m, 2H), 7.29-7.34 (m, 2H), 7.52 (d-like, *J* = 7.5 Hz, 2H), 8.92 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.70 (q), 13.99 (q), 52.52 (d), 59.57 (d), 62.08 (t), 114.86 (d), 119.92 (d), 120.23 (d), 124.72 (d), 129.08 (d), 129.61 (d), 137.26 (s), 146.44 (s), 167.86 (s), 168.94 (s), 169.04 (s); IR (KBr) 3254, 1728, 1665, 1602, 1254, 1187, 1034 cm^{-1}; MS (EI) *m/z* 384; exact mass M$^+$ 384.1689 (calcd for $C_{21}H_{24}N_2O_5$ 384.1685); Anal. Calcd for $C_{21}H_{24}N_2O_5$: C, 65.01; H, 6.29; N, 7.29. Found: C, 65.19; H, 6.18; N, 7.26.

1b (R_f = 0.2 (hexane-ether = 1 : 2)): Yellow crystals; mp 117-118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.33 (t, *J* = 7.1 Hz, 3H), 1.35 (t, *J* = 7.1 Hz, 3H), 3.79 (s, 3H), 4.31 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 6.84-6.88 (m, 2H), 7.02 (s, 1H), 7.46-7.50 (m, 2H), 7.82 (br s, 1H).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.04 (q), 14.05 (q), 55.56 (q), 62.28 (t), 62.53 (t), 114.33 (d), 121.91 (d), 130.19 (s), 133.77 (d), 136.32 (s), 157.14 (s), 160.06 (s), 162.91 (s), 165.21 (s); IR (KBr) 3333, 2991, 1731, 1670, 1550, 1512, 1262, 1242, 1177, 1035 cm^{-1}; MS (EI) *m/z* 321; exact mass M$^+$ 321.1212 (calcd for $C_{16}H_{19}NO_6$ 321.1212) ; Anal. Calcd for $C_{16}H_{19}NO_6$: C, 59.81; H, 5.96; N, 4.36. Found: C, 59.71; H, 6.04; N, 4.26.

3b (R_f = 0.4 (hexane-ether = 1 : 2)): Colorless crystals; mp 95-96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.00 (t, *J* = 7.1 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H), 3.71 (s, 3H), 3.74 (s, 3H), 3.70-3.80 (m, 1H), 3.85-3.93 (m, 1H), 4.10-4.26 (m, 2H), 4.37 (d, *J* = 4.0 Hz, 1H), 4.54 (br s, 1H), 4.84-4.86 (br, 1H), 6.67-6.70 (m, 2H), 6.74-6.77 (m, 2H), 6.81 (d-like, *J* = 9.2 Hz, 2H), 7.40 (d-like, *J* = 9.2 Hz, 2H), 8.94 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.67 (q), 13.94 (q), 52.32 (d), 55.46 (q), 55.70 (q), 60.52 (d), 61.90 (t), 114.11 (d), 114.87 (d), 116.38 (d), 121.49 (d), 130.47 (s), 140.25 (s), 153.77 (s), 156.54 (s), 167.94 (s), 168.83 (s), 168.89 (s); IR (KBr) 3349, 3305, 2936, 1732, 1654, 1512, 1245, 1036 cm^{-1}; MS (EI) *m/z* 444; exact mass M$^+$ 444.1895 (calcd for $C_{23}H_{28}N_2O_7$ 444.1897).

1d (R_f = 0.6 (hexane-ether = 1 : 4)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.23 (t, *J* = 7.1 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.37 (dt, *J* = 6.2, 1.3 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 5.09-5.16 (m, 2H), 5.86 (ddt, *J* = 16.5, 10.3, 6.3 Hz, 1H), 6.81 (s, 1H), 7.18-7.20 (m, 2H), 7.34-7.43 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.95 (q), 14.04 (q), 52.32 (t), 61.91 (t), 62.09 (t), 118.52 (t), 127.77 (d), 128.54 (d), 129.84 (d), 132.27 (d), 133.40 (d), 135.72 (s), 140.91 (s), 162.82 (s), 162.88 (s), 165.22 (s); IR (neat) 2983, 1729, 1660, 1595, 1495, 1401, 1251, 1207, 1069 cm^{-1}; MS (EI) *m/z* 331; exact mass M$^+$ 331.1421 (calcd for $C_{18}H_{21}NO_5$ 331.1420); Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.15; H, 6.48; N, 4.40.

1e (R_f = 0.5 (hexane-ether = 1 : 4)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.11 (t, *J* = 6.8 Hz, 6H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 4.14 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.97 (septet, *J* = 6.8 Hz, 1H), 6.64 (s, 1H), 7.14-7.19 (m, 2H), 7.40-7.46 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.73 (q), 13.86 (q), 20.64 (q), 46.80 (d), 61.58 (t), 61.74 (t), 128.88 (d), 129.38 (d), 130.02 (d), 133.99 (d), 134.69 (s), 136.98 (s), 162.59 (s), 162.71 (s), 165.10 (s); IR (neat) 2980, 1731, 1657, 1593, 1495, 1401, 1313, 1253, 1209, 1067 cm^{-1}; MS (EI) *m/z* 333; exact mass M$^+$ 333.1570 (calcd for $C_{18}H_{23}NO_5$ 333.1576).

1f (R_f = 0.5 (hexane-ether = 1 : 2)): Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.21 (t, *J* = 7.1 Hz, 3H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.44 (d, *J* = 7.1 Hz, 3H), 3.79 (s, 3H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.41 (m, 2H), 6.22 (q, *J* = 7.1 Hz, 1H), 6.67 (s, 1H), 6.74 (br m, 4H), 7.18-7.22 (m, 2H), 7.25-7.28 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.93, 14.06, 16.92, 52.72, 55.42, 61.85, 61.97, 114.25, 127.80, 128.27, 129.24, 131.41, 134.46, 134.87, 140.24, 159.68, 162.96, 163.43, 165.31; IR (neat) 2981, 1732, 1656, 1511, 1251, 1208, 1068 cm^{-1}; MS (EI) *m/z* 425; exact mass M^+ 425.1838 (calcd for $C_{24}H_{27}NO_6$ 425.1838).

1g (R_f = 0.4 (hexane-ether = 1 : 2)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.23 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 3.79 (s, 3H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.91 (s, 2H), 6.79-6.83 (m, 2H), 6.84 (s, 1H), 6.91-6.95 (m, 2H), 7.17-7.28 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.95 (q), 14.02 (q), 53.15 (t), 55.47 (q), 61.89 (t), 62.05 (t), 114.85 (t), 127.63 (d), 128.49 (d), 128.90 (d), 129.20 (d), 133.18 (s), 133.83 (d), 135.41 (s), 136.64 (s), 159.43 (s), 162.93 (s), 163.45 (s), 165.24 (s); IR (neat) 2982, 1728, 1658, 1512, 1402, 1252, 1199, 1069 cm^{-1}; MS (EI) *m/z* 411; exact mass M^+ 411.1687 (calcd for $C_{23}H_{25}NO_6$ 411.1682).

1h (R_f = 0.4 (hexane-ether = 1 : 2)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.21 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 3.75 (s, 3H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.45 (d, *J* = 14.3 Hz, 1H), 5.30 (d, *J* = 14.3 Hz, 1H), 6.77 (s, 1H), 6.79-6.86 (m, 2H), 6.90-6.92 (m, 1H), 7.16-7.24 (m, 5H), 7.26-7.30 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.93 (q), 14.02 (q), 51.69 (t), 55.58 (q), 61.79 (t), 61.96 (t), 112.03 (d), 120.88 (d), 127.42 (d), 128.21 (d), 128.71 (s), 129.12 (d), 130.16 (d), 130.35 (d), 133.55 (d), 135.49 (s), 136.82 (s), 155.03 (s), 163.04 (s), 163.71 (s), 165.23 (s); IR (neat) 2982, 1729, 1661, 1597, 1500, 1404, 1252, 1196, 1068, 1025 cm^{-1}; MS (EI) *m/z* 411; exact mass M^+ 411.1691 (calcd for $C_{23}H_{25}NO_6$ 411.1682).

1i (R_f = 0.4 (hexane-ether = 1 : 2)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.23 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 3.65 (s, 3H), 3.87 (s, 3H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.54 (d, *J* = 14.3 Hz, 1H), 5.34 (d, *J* = 14.3 Hz, 1H), 6.49 (dd, *J* = 7.5, 2.0 Hz, 1H), 6.85 (s, 1H), 6.87-6.94 (m, 2H), 7.16-7.25 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.91 (q), 14.00 (q), 52.11 (t), 55.99 (q), 60.91 (q), 61.79 (t), 62.02 (t), 112.88 (d), 121.62 (d), 123.85 (d), 127.54 (d), 128.32 (d), 129.17 (d), 132.96 (d), 133.78 (s), 135.94 (s), 136.75 (s), 145.16 (s), 153.55 (s), 162.95 (s), 163.33 (s), 165.26 (s); IR (neat) 2982, 2940, 1732, 1660, 1586, 1477, 1404, 1252, 1202, 1117, 1029 cm^{-1}; MS (EI) *m/z* 441; exact mass M^+ 441.1799 (calcd for $C_{24}H_{27}NO_7$ 441.1788).

2j (R_f = 0.4 (hexane-ether = 1 : 2)): Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.08 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 3.69 (s, 3H), 3.79 (s, 3H), 3.96-4.04 (m, 1H), 4.08-4.16 (m, 1H), 4.20 (d, *J* = 4.4 Hz, 1H), 4.27-4.35 (m, 2H), 4.49 (d, *J* = 4.4 Hz, 1H), 4.80 (d, *J* = 15.7 Hz, 1H), 4.96 (d, *J* = 15.7 Hz, 1H), 5.95 (d, *J* = 1.9 Hz, 1H), 6.07 (d, *J* = 1.9 Hz, 1H), 7.22-7.37 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.98 (q), 14.09 (q), 43.42 (d), 44.20 (t), 50.95 (d), 55.49 (q), 55.51 (q), 61.23 (t), 61.92 (t), 89.73 (d), 91.91 (d), 103.80 (s), 127.54 (d), 128.71 (d), 136.14 (s), 145.88 (s), 156.54 (s), 161.82 (s), 167.23 (s), 168.11 (s), 176.01 (s); IR (neat) 2980, 1733, 1616, 1456, 1378, 1345, 1201, 1153, 1031 cm^{-1}; MS (EI) *m/z* 441; exact mass M^+ 441.1787 (calcd for $C_{25}H_{29}NO_7$ 441.1788).

4 (R_f = 0.3 (hexane-ether = 1 : 2)): Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.98 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 3.790 (s, 3H), 3.791 (s, 3H), 3.84-3.97 (m, 2H), 4.17-4.29 (m, 2H), 4.34 (s,

2H), 4.51 (d, *J* = 11.0 Hz, 1H), 5.49 (d, *J* = 11.0 Hz, 1H), 5.88 (s, 2H), 7.25-7.38 (m, 7H), 7.45-7.48 (m, 1H), 7.97 (dd, *J* = 8.4, 0.7 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.70 (q), 13.99 (q), 37.47 (d), 48.18 (t), 52.12 (d), 55.71 (q), 61.33 (t), 61.84 (t), 89.28 (d), 98.55 (s), 108.68 (d), 120.13 (d), 124.61 (d), 127.38 (d), 127.48 (d), 128.40 (d), 128.62 (d), 128.68 (s), 138.96 (s), 143.30 (s), 150.50 (s), 159.35 (s), 166.86 (s), 168.15 (s), 169.36 (s); IR (neat) 3418, 2981, 2939, 1815, 1733, 1750, 1615, 1455, 1232, 1123 cm^{-1}; MS (EI) *m/z* 576; exact mass M$^+$ 576.2240 (calcd for $C_{30}H_{32}N_4O_8$ 576.2220).

1l (R_f = 0.3 (hexane-ether = 1 : 1)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.24 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.93 (s, 2H), 6.80 (s, 1H), 6.89-6.93 (m, 2H), 7.16-7.18 (m, 2H), 7.24-7.29 (m, 3H), 7.43-7.47 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.96 (q), 14.02 (q), 52.95 (t), 62.01 (t), 62.22 (t), 122.58 (s), 127.86 (d), 128.65 (d), 128.77 (d), 129.60 (d), 133.02 (d), 133.33 (d), 136.05 (s), 136.20 (s), 139.62 (s), 162.73 (s), 163.10 (s), 164.99 (s); IR (neat) 2983, 1733, 1661, 1489, 1253, 1199, 1269, 1010 cm^{-1}; MS (EI) *m/z* 459, 461; exact mass M$^+$ 459.0690 (calcd for $C_{22}H_{22}NO_5{}^{79}Br$ 459.0681), 461.0653 (calcd for $C_{22}H_{22}NO_5{}^{81}Br$ 461.0661).

1m (R_f = 0.4 (hexane-ether = 1 : 1)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.25 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.93 (s, 2H), 6.76-6.80 (m, 2H), 7.16-7.18 (m, 2H), 7.23-7.29 (m, 3H), 7.63-7.67 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.96 (q), 14.01 (q), 52.91 (t), 62.00 (t), 62.22 (t), 94.10 (s), 127.84 (d), 128.64 (d), 128.72 (d), 129.75 (d), 133.29 (d), 136.08 (s), 136.20 (s), 138.99 (d), 140.31 (s), 162.73 (s), 163.02 (s), 165.00 (s); IR (neat) 2982, 1728, 1659, 1582, 1485, 1410, 1253, 1199, 1069, 1007 cm^{-1}; MS (EI) *m/z* 507; exact mass M$^+$ 507.0546 (calcd for $C_{22}H_{22}NO_5I$ 507.0543).

1n (R_f = 0.4 (hexane-ether = 1 : 2)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) measured as a mixture with **5n** and **6n**. Peaks for **1n** δ (ppm) 1.23 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 3.70 (s, 3H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.94 (s, 2H), 6.55 (t, *J* = 2.2 Hz, 1H), 6.63 (ddd, *J* = 7.9, 2.0, 0.9 Hz, 1H), 6.85 (ddd, *J* = 8.4, 2.3, 0.9 Hz, 1H), 6.86 (s, 1H), 7.19-7.38 (m, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.93 (q), 13.99 (q), 52.94 (t), 55.40 (q), 61.90 (t), 62.06 (t), 113.46 (d), 114.34 (d), 120.23 (d), 127.65 (d), 128.49 (d), 128.77 (d), 130.41 (d), 133.57 (d), 135.65 (s), 136.65 (s), 141.70 (s), 160.41 (s), 162.87 (s), 163.12 (s), 165.18 (s); IR (neat) 2982, 1733, 1659, 1602, 1253 cm^{-1}; MS (EI) *m/z* 411; exact mass M$^+$ 411.1688 (calcd for $C_{23}H_{25}NO_6$ 411.1682).

1o (R_f = 0.6 (hexane-ether = 1 : 2)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.24 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.94 (s, 2H), 6.80 (s, 1H), 6.91 (ddd, *J* = 7.7, 2.0, 1.2 Hz, 1H), 7.09 (t-like, *J* = 1.9 Hz, 1H), 7.16-7.20 (m, 2H), 7.23-7.32 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.95 (q), 14.02 (q), 53.00 (t), 62.03 (t), 62.22 (t), 126.55 (d), 127.88 (d), 127.96 (d), 128.65 (d), 128.71 (d), 128.94 (d), 130.70 (d), 133.02 (d), 135.28 (s), 136.10 (s), 136.21 (s), 141.76 (s), 162.70 (s), 163.01 (s), 164.99 (s); IR (neat) 2983, 1728, 1662, 1590, 1477, 1398, 1255, 1199, 1070 cm^{-1}; MS (EI) *m/z* 415, 417; exact mass M$^+$ 415.1181 (calcd for $C_{22}H_{22}NO_5{}^{35}Cl$ 415.1187), 417.1157 (calcd for $C_{22}H_{22}NO_5{}^{37}Cl$ 417.1157).

1p (R_f = 0.5 (hexane-ether = 1 : 2)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.24 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.94 (s, 2H), 6.80 (s, 1H), 6.95 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.17-7.20 (m, 3H), 7.25-7.30 (m, 4H), 7.46 (ddd, *J* = 7.1, 1.8,

1.0 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.95 (q), 14.00 (q), 53.03 (t), 62.02 (t), 62.21 (t), 123.09 (s), 127.04 (d), 127.87 (d), 128.64 (d), 128.71 (d), 130.82 (d), 130.92 (d), 131.83 (d), 133.02 (d), 136.07 (s), 136.18 (s), 141.88 (s), 162.69 (s), 163.01 (s), 164.96 (s); IR (neat) 2983, 1732, 1661, 1587, 1570, 1477, 1397, 1255, 1200, 1069 cm^{-1}; MS (EI) *m/z* 459, 461; exact mass M^+ 459.0679 (calcd for $C_{22}H_{22}NO_5{}^{79}Br$ 459.0681), 461.0660 (calcd for $C_{22}H_{22}NO_5{}^{81}Br$ 461.0661).

1q (R_f = 0.6 (hexane-ether = 1 : 2)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.24 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.93 (s, 2H), 6.79 (s, 1H), 6.97 (ddd, *J* = 7.9, 2.0, 1.1 Hz, 1H), 7.04 (t-like, *J* = 7.9 Hz, 1H), 7.17-7.19 (m, 2H), 7.25-7.29 (m, 3H), 7.45 (t-like, *J* = 1.8 Hz, 1H), 7.66 (dt-like, *J* = 7.9, 1.4 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.97 (q), 14.02 (q), 53.03 (t), 62.03 (t), 62.22 (t), 96.47 (s), 127.70 (d), 127.87 (d), 128.63 (d), 128.74 (d), 131.05 (d), 132.99 (d), 136.07 (s), 136.17 (s), 136.60 (d), 137.72 (d), 141.73 (s), 162.70 (s), 162.95 (s), 164.99 (s); IR (neat) 2982, 1732, 1661, 1582, 1566, 1474, 1393, 1254, 1198, 1070 cm^{-1}; MS (EI) *m/z* 507; exact mass M^+ 507.0547 (calcd for $C_{22}H_{22}NO_5I$ 507.0543).

1r (R_f = 0.5 (hexane-ether = 1 : 2)): Pale yellow crystals; mp 55-56 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.23 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 4.19 (q, *J* = 7.1 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.95 (s, 2H), 6.80 (dt, *J* = 9.3, 2.2 Hz, 1H), 6.83 (s, 1H), 6.85 (br d, *J* = 9.0 Hz, 1H), 7.03 (td, *J* = 8.3, 1.9 Hz, 1H), 7.18-7.20 (m, 2H), 7.24-7.32 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.86 (CH_3), 13.92 (CH_3), 52.85 (CH_2), 61.91 (CH_2), 62.10 (CH_2), 115.18 (d, J_{CF} = 22 Hz, CH), 115.74 (d, J_{CF} = 21 Hz, CH), 123.90 (d, J_{CF} = 3 Hz, CH), 127.77 (CH), 128.56 (CH), 128.60 (CH), 130.90 (d, J_{CF} = 9 Hz, CH), 133.18 (CH), 136.00 (C), 136.15 (C), 142.01 (d, J_{CF} = 9 Hz, C), 162.64 (C), 162.83 (d, J_{CF} = 249 Hz, C), 163.01 (C), 164.87 (C); ^{19}F NMR (376.3 MHz, $CDCl_3$) δ (ppm) –110.44; IR (KBr) 3066, 2985, 2930, 1743, 1712, 1661, 1605, 1492, 1397, 1210, 1069, 1016 cm^{-1}; MS (EI) *m/z* 399; exact mass M^+ 399.1497 (calcd for $C_{22}H_{22}NO_5F$ 399.1482).

1s (R_f = 0.5 (hexane-ether = 1 : 2)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.22 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 4.19 (q, *J* = 7.1 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.98 (s, 2H), 6.76 (s, 1H), 7.16-7.19 (m, 2H), 7.22 (d, *J* = 8.1 Hz, 1H), 7.34 (s, 1H), 7.26-7.27 (m, 3H), 7.46 (t, *J* = 7.9 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.91 (CH_3), 14.00 (CH_3), 52.99 (CH_2), 62.07 (CH_2), 62.23 (CH_2), 123.30 (q, J_{CF} = 273 Hz, C), 124.83 (q, J_{CF} = 3.8 Hz, CH), 125.36 (q, J_{CF} = 3.8 Hz, CH), 128.00 (CH), 128.72 (CH), 128.77 (CH), 130.44 (CH), 131.61 (CH), 132.32 (q, J_{CF} = 32 Hz, C), 133.16 (CH), 135.97 (C), 136.21 (C), 162.62 (C), 163.16 (C), 164.81 (C); ^{19}F NMR (376.3 MHz, $CDCl_3$) δ (ppm) –63.32; IR (neat) 2985, 1732, 1663, 1495, 1449, 1399, 1327, 1256, 1131, 1071 cm^{-1}; MS (EI) *m/z* 449; exact mass M^+ 449.1452 (calcd for $C_{23}H_{22}NO_5F_3$ 449.1450).

7a (R_f = 0.4 (hexane-ether = 1 : 2)): Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1:1) δ (ppm) 1.29 (t, *J* = 7.1 Hz, 3H), 1.326 (t, *J* = 7.1 Hz, 0.5×3H), 1.330 (t, *J* = 7.1 Hz, 0.5×3H), 3.77 (s, 0.5×6H), 3.78 (s, 0.5×6H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 4.39 (s, 0.5×2H), 4.46 (s, 0.5×2H), 4.52 (s, 0.5×2H), 4.61 (s, 0.5×2H), 6.32 (d, *J* = 2.2 Hz, 0.5×2H), 6.38-6.40 (m, 0.5×2H+1H), 7.18-7.39 (m, 5H), 7.38 (s, 0.5×1H), 7.40 (s, 0.5×1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.96 (q), 14.01 (q), 47.56 (t), 47.82 (t), 50.46 (t), 50.65 (t), 55.39 (q), 55.43 (q), 61.96 (t), 62.20 (t), 99.74 (d), 104.94 (d), 106.31 (d), 127.11 (d), 127.74 (d), 128.10 (d), 128.60 (d), 128.71 (d), 129.08 (d), 134.56 (d),

134.98 (d), 135.28 (s), 135.43 (s), 135.48 (s), 136.28 (s), 137.98 (s), 138.48 (s), 161.09 (s), 161.44 (s), 162.92 (s), 162.93 (s), 164.46 (s), 164.48 (s), 164.74 (s), 164.84 (s); IR (neat) 2981, 1728, 1652, 1611, 1598, 1463, 1429, 1256, 1205, 1158, 1068 cm^{-1}; MS (EI) *m/z* 455; exact mass M^+ 455.1938 (calcd for $C_{25}H_{29}NO_7$ 455.1944).

7b (R_f = 0.5 (hexane-ether = 1 : 3)): Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 7:3) δ (ppm) 1.26-1.34 (m, 6H), 3.69 (br s, 0.3×3H, minor rotamer), 3.74 (br s, 0.7×3H, major rotamer), 3.77 (br s, 0.3×3H+0.7×3H), 4.23-4.37 (m, 4H), 4.41 (s, 0.7×2H), 4.53 (s, 0.3×2H), 4.58 (s, 0.7×2H), 4.63 (s, 0.3×2H), 6.65 (d, *J* = 1.6 Hz, 0.7×1H), 6.76 (br s, 0.3×2H), 6.80 (br s, 0.7×2H), 6.905-6.913 (m, 0.3×1H), 7.19 (d, *J* = 7.3 Hz, 0.7×1H), 7.24-7.35 (m, 0.3×5H+0.7×4H), 7.37 (s, 0.3×1H), 7.58 (s, 0.7×1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.87 (q), 13.94 (q), 13.97 (q), 14.01 (q), 42.96 (t), 46.64 (t), 47.39 (t), 51.17 (t), 55.51 (q), 55.73 (q), 55.75 (q), 61.81 (t), 61.87 (t), 62.04 (t), 62.10 (t), 111.30 (d), 113.30 (d), 113.41 (d), 115.54 (d), 124.35 (s), 125.38 (s), 126.89 (d), 127.48 (d), 127.81 (d), 128.33 (d), 128.57 (d), 128.85 (d), 134.75 (s), 134.78 (d), 135.16 (d), 136.10 (s), 136.51 (s), 151.66 (s), 151.74 (s), 153.52 (s), 153.75 (s), 162.93 (s), 163.13 (s), 164.48 (s), 164.68 (s), 164.77 (s); IR (neat) 2983, 2836, 1728, 1652, 1501, 1464, 1450, 1255, 1222, 1068 cm^{-1}; MS (EI) *m/z* 455; exact mass M^+ 455.1942 (calcd for $C_{25}H_{29}NO_7$ 455.1944).

Typical cyclization procedure (Table 2, Entry 3). To a solution of **1c** (820 mg, 2.15 mmol) in dichloromethane (4.0 mL) was added $SnCl_4$ (0.05 mL, 112 mg, 0.43 mmol) at 0 °C. The mixture was allowed to warm to rt and stirred for 16 h. The reaction mixture was quenched by water at 0 °C. The mixture was extracted with dichloromethane and the organic phase was washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel eluting with CH_2Cl_2 to give to give **2c** (770 mg, 94%). **2c** (R_f = 0.6 (hexane-ether = 1 : 4)): Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.86 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 3.87-3.95 (m, 1H), 3.97-4.05 (m, 1H), 4.13 (d, *J* = 3.4 Hz, 1H), 4.22-4.35 (m, 2H), 4.29 (d, *J* = 3.4 Hz, 1H), 4.90 (d, *J* = 15.7 Hz, 1H), 4.95 (d, *J* = 15.7 Hz, 1H), 6.72 (d, *J* = 7.7 Hz, 1H), 6.98 (td, *J* = 7.6, 0.9 Hz, 1H), 7.16 (tt, *J* = 7.8, 1.0 Hz, 1H), 7.23-7.38 (m, 5H), 7.40 (d-like, *J* = 7.4 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.55 (q), 14.05 (q), 44.10 (t), 44.67 (d), 52.32 (d), 61.69 (t), 61.95 (t), 109.01 (d), 122.58 (d), 124.97 (d), 125.65 (s), 127.57 (d), 127.67 (d), 128.50 (d), 128.71 (d), 135.78 (s), 143.80 (s), 166.97 (s), 168.15 (s), 175.43 (s); IR (neat) 2981, 1720, 1613, 1489, 1467, 1368, 1181, 1031 cm^{-1}; MS (EI) *m/z* 381; exact mass M^+ 381.1570 (calcd for $C_{22}H_{23}NO_5$ 381.1576).

2a (R_f = 0.3 (hexane-ether = 1 : 2)): Pale yellow crystals; mp 89-91 °C; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.01 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 3.96-4.10 (m, 2H), 4.07 (d, *J* = 3.6 Hz, 1H), 4.22 (d, *J* = 3.6 Hz, 1H), 4.23-4.35 (m, 2H), 6.88 (d-like, *J* = 7.9 Hz, 1H), 7.00 (td, *J* = 7.5, 0.9 Hz, 1H), 7.22 (tt, *J* = 7.8, 1.1 Hz, 1H), 7.38 (d-like, *J* = 7.7 Hz, 1H), 8.59 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.71 (q), 14.09 (q), 45.20 (d), 52.25 (d), 61.84 (t), 62.04 (t), 109.79 (d), 122.61 (d), 125.30 (d), 126.25 (s), 128.71 (d), 141.92 (s), 167.03 (s), 168.11 (s), 177.65 (s); IR (KBr) 3186, 3083, 2989, 1744, 1707, 1618, 1472, 1340, 1289, 1231, 1212, 1189, 1179, 1021 cm^{-1}; MS (EI) *m/z* 291; exact mass M^+ 291.1102 (calcd for $C_{15}H_{17}NO_5$ 291.1107).

2b (R_f = 0.2 (hexane-ether = 1 : 5)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.03 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 3.76 (s, 1H), 3.97-4.10 (m, 2H), 4.04 (d, *J* = 3.7 Hz, 1H), 4.21 (d, *J* = 3.7 Hz, 1H), 4.23-4.36 (m, 2H), 6.76 (ddd, *J* = 8.5, 2.4, 0.6 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 1H), 7.03 (br s, 1H), 8.72 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.73 (q), 14.10 (q), 45.65 (d), 52.24 (d), 55.83 (q), 61.84 (t), 62.04 (t), 110.14 (d), 112.30 (d), 113.52 (d), 127.55 (s), 135.41 (s), 155.77 (s), 166.97 (s), 168.14 (s), 177.60 (s); IR (neat) 3542, 2983, 1733, 1603, 1489, 1372, 1304, 1210, 1032 cm^{-1}; MS (EI) *m/z* 321; exact mass M^+ 321.1217 (calcd for $C_{16}H_{19}NO_6$ 321.1212).

2d (R_f = 0.6 (hexane-ether = 1 : 4)): Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.99 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 3.94-4.07 (m, 2H), 4.07 (d, *J* = 3.6 Hz, 1H), 4.21-4.35 (m, 2H), 4.24 (d, *J* = 3.6 Hz, 1H), 4.36-4.38 (m, 2H), 5.23 (ddt, *J* = 10.4, 2.8, 1.5 Hz, 1H), 5.30 (ddt, *J* = 17.2, 2.8, 1.6 Hz, 1H), 5.85 (ddt, *J* = 17.2, 10.4, 5.3 Hz, 1H), 6.83 (d, *J* = 7.9 Hz, 1H), 7.02 (td, *J* = 7.7, 1.0 Hz, 1H), 7.25 (tt, *J* = 7.8, 1.1 Hz, 1H), 7.40 (d-like, *J* = 7.5 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.73 (q), 14.08 (q), 42.68 (t), 44.63 (d), 52.35 (d), 61.71 (t), 61.95 (t), 108.94 (d), 117.85 (t), 122.55 (d), 124.96 (d), 125.66 (s), 128.53 (d), 131.35 (d), 143.91 (s), 166.97 (s), 168.12 (s), 175.12 (s); IR (neat) 2982, 1732, 1613, 1489, 1467, 1366, 1182, 1033 cm^{-1}; MS (EI) *m/z* 331; exact mass M^+ 331.1421 (calcd for $C_{18}H_{21}NO_5$ 331.1420); Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 64.85; H, 6.39; N, 4.26.

2e (R_f = 0.6 (hexane-ether = 1 : 4)): Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.97 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.50 (d, *J* = 7.1 Hz, 6H), 3.92-4.08 (m, 2H), 3.99 (d, *J* = 3.5 Hz, 1H), 4.20-4.34 (m, 2H), 4.22 (d, *J* = 3.5 Hz, 1H), 4.65 (septet, *J* = 7.1 Hz, 1H), 6.97-7.01 (m, 2H), 7.25 (t-like, *J* = 7.8 Hz, 1H), 7.40 (d-like, *J* = 7.7 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.67 (q), 14.05 (q), 19.16 (q), 19.29 (q), 44.03 (d), 44.62 (d), 52.41 (d), 61.62 (t), 61.84 (t), 109.67 (d), 121.95 (d), 125.09 (d), 126.10 (s), 128.27 (d), 143.41 (s), 167.04 (s), 168.20 (s), 175.02 (s); IR (neat) 2980, 1734, 1712, 1610, 1486, 1466, 1360, 1319, 1225, 1178, 1157, 1098 cm^{-1}; MS (EI) *m/z* 333; exact mass M^+ 333.1579 (calcd for $C_{18}H_{23}NO_5$ 333.1576).

2f (R_f = 0.6 (hexane-ether = 1 : 2)): Red-brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 diastereomers, ratio 1:1) δ (ppm) 0.92 (t, *J* = 7.1 Hz, 0.5×3H), 1.00 (t, *J* = 7.1 Hz, 0.5×3H), 1.297 (t, *J* = 7.1 Hz, 0.5×3H), 1.301 (t, *J* = 7.1 Hz, 0.5×3H), 1.80 (d, *J* = 7.1 Hz, 0.5×3H), 1.81 (d, *J* = 7.1 Hz, 0.5×3H), 3.70 (s, 3H), 3.97-4.13 (m, 3H), 4.24-4.27 (m, 3H), 5.82-5.90 (m, 1H), 6.34 (d, *J* = 8.8 Hz, 0.5×1H), 6.36 (d, *J* = 9.2 Hz, 0.5×1H), 6.56 (dd, *J* = 8.6, 2.7 Hz, 1H), 7.02 (dd, *J* = 2.7, 1.2 Hz, 1H), 7.24-7.44 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.64 (q), 13.76 (q), 14.11 (q), 14.17 (q), 15.79 (q), 16.19 (q), 44.85 (d), 45.05 (d), 49.07 (d), 49.36 (d), 52.29 (d), 52.48 (d), 55.73 (q), 61.77 (t), 61.81 (t), 61.93 (t), 61.98 (t), 111.09 (d), 111.20 (d), 112.08 (d), 112.12 (d), 112.70 (d), 126.72 (d), 126.96 (d), 127.33 (s), 127.42 (d), 128.53 (d), 128.68 (d), 135.88 (s), 135.98 (s), 139.18 (s), 139.34 (s), 155.45 (s), 155.47 (s), 167.04 (s), 168.16 (s), 168.23 (s), 174.80 (s), 175.22 (s); IR (neat) 2982, 1737, 1709, 1489, 1341, 1217, 1032 cm^{-1}; MS (EI) *m/z* 425; exact mass M^+ 425.1845 (calcd for $C_{24}H_{27}NO_6$ 425.1838).

2g (R_f = 0.3 (hexane-ether = 1 : 2)): Red-brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.90 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 3.73 (s, 3H), 3.90-4.07 (m, 2H), 4.10 (d, *J* = 3.6 Hz, 1H), 4.23-4.36 (m, 2H), 4.28 (d, *J* = 3.6 Hz, 1H), 4.88 (d, *J* = 15.7 Hz, 1H), 4.93 (d, *J* = 15.7 Hz, 1H), 6.60 (d, *J* = 8.5 Hz,

1H), 6.69 (ddd, *J* = 8.5, 2.6, 0.7 Hz, 1H), 7.05 (dd, *J* = 2.6, 1.3 Hz, 1H), 7.23-7.36 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.68 (q), 14.14 (q), 44.23 (t), 45.11 (d), 52.37 (d), 55.83 (q), 61.75 (t), 62.03 (t), 109.39 (d), 112.39 (d), 113.09 (d), 127.00 (s), 127.59 (d), 127.70 (d), 128.76 (d), 135.91 (s), 137.34 (s), 155.92 (s), 166.97 (s), 168.23 (s), 175.12 (s); IR (neat) 2982, 1743, 1712, 1601, 1494, 1370, 1341, 1298, 1181, 1037 cm^{-1}; MS (EI) *m/z* 411; exact mass M^+ 411.1688 (calcd for $C_{23}H_{25}NO_6$ 411.1682).

2h (R_f = 0.6 (hexane-ether = 1 : 2)): Brown crystals; mp 87-89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.90 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 3.67 (s, 3H), 3.84-4.08 (m, 2H), 4.09 (dt, *J* = 3.5, 0.9 Hz, 1H), 4.19-4.33 (m, 2H), 4.25 (d, *J* = 3.5 Hz, 1H), 5.16 (d, *J* = 15.0 Hz, 1H), 5.22 (d, *J* = 15.0 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.94 (dd, *J* = 8.3 Hz, 1H), 7.02 (dt, *J* = 7.5, 1.1 Hz, 1H), 7.18-7.22 (m, 1H), 7.25-7.29 (m, 2H), 7.34-7.37 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.55 (q), 14.00 (q), 44.83 (d), 45.90 (t), 52.35 (d), 55.71 (q), 61.59 (t), 61.84 (t), 112.70 (d), 117.52 (d), 123.14 (d), 126.95 (d), 127.20 (s), 127.50 (d), 128.19 (d), 131.82 (s), 138.40 (s), 144.88 (s), 166.94 (s), 168.07 (s), 175.59 (s); IR (KBr) 2986, 2940, 2905, 1747-1708, 1613, 1595, 1497, 1464, 1358, 1335, 1279, 1202, 1181, 1031 cm^{-1}; MS (EI) *m/z* 411; exact mass M^+ 411.1678 (calcd for $C_{23}H_{25}NO_6$ 411.1682); Anal. Calcd for $C_{23}H_{25}NO_6$: C, 67.14; H, 6.12; N, 3.40. Found: C, 67.36; H, 6.03; N, 3.36.

2i (R_f = 0.5 (hexane-ether = 1 : 2)): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.93 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 3.46 (s, 3H), 3.81 (s, 3H), 3.87-3.95 (m, 1H), 3.97-4.06 (m, 1H), 4.08 (dd, *J* = 3.5, 1.3 Hz, 1H), 4.22-4.34 (m, 2H), 4.25 (d, *J* = 3.5 Hz, 1H), 5.15 (d, *J* = 15.4 Hz, 1H), 5.19 (d, *J* = 15.4 Hz, 1H), 6.52 (d, *J* = 8.3 Hz, 1H), 7.10 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.19-7.23 (m, 1H), 7.27-7.31 (m, 2H), 7.35-7.37 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.67 (q), 14.04 (q), 44.21 (d), 45.59 (t), 52.60 (d), 55.83 (q), 61.17 (q), 61.57 (t), 61.87 (t), 105.67 (d), 119.09 (s), 120.26 (d), 127.03 (d), 127.06 (d), 128.35 (d), 134.27 (s), 135.80 (s), 137.55 (s), 153.77 (s), 166.99 (s), 168.21 (s), 176.10 (s); IR (neat) 2980, 2938, 1734, 1622, 1498, 1464, 1380, 1344, 1266, 1178, 1115, 1031 cm^{-1}; MS (EI) *m/z* 441; exact mass M^+ 441.1786 (calcd for $C_{24}H_{27}NO_7$ 441.1788).

2l (R_f = 0.4 (hexane-ether = 1 : 4)): Colorless crystals; mp 125-126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.94 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 3.92-4.08 (m, 2H), 4.10 (d, *J* = 3.4 Hz, 1H), 4.24-4.38 (m, 2H), 4.28 (d, *J* = 3.4 Hz, 1H), 4.88 (d, *J* = 15.6 Hz, 1H), 4.95 (d, *J* = 15.6 Hz, 1H), 6.57 (d, *J* = 8.4 Hz, 1H), 7.26-7.33 (m, 6H), 7.55 (dd, *J* = 1.6, 1.2 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.72 (q), 14.13 (q), 44.25 (t), 44.70 (d), 52.25 (d), 61.95 (t), 62.22 (t), 110.49 (d), 115.37 (s), 127.52 (d), 127.80 (s), 127.89 (d), 128.33 (d), 128.88 (d), 131.44 (d), 135.32 (s), 142.95 (s), 166.69 (s), 168.04 (s), 174.85 (s); IR (KBr) 2978, 1750, 1735, 1711, 1608, 1482, 1334, 1160, 1152 cm^{-1}; MS (EI) *m/z* 459, 461; exact mass M^+ 459.0688 (calcd for $C_{22}H_{22}NO_5{}^{79}Br$ 459.0681), 461.0656 (calcd for $C_{22}H_{22}NO_5{}^{81}Br$ 461.0661); Anal. Calcd for $C_{22}H_{22}NO_5Br$: C, 57.40; H, 4.82; N, 3.04. Found: C, 57.51; H, 4.71; N, 3.04.

2m (R_f = 0.6 (hexane-ether = 1 : 2)): Colorless crystals; mp 122-123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.95 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 3.93-4.07 (m, 2H), 4.09 (bd, *J* = 2.5 Hz, 1H), 4.24-4.38 (m, 2H), 4.27 (d, *J* = 2.5 Hz, 1H), 4.87 (d, *J* = 15.7 Hz, 1H), 4.94 (d, *J* = 15.7 Hz, 1H), 6.48 (d, *J* = 8.2 Hz, 1H), 7.25-7.33 (m, 5H), 7.48 (ddd, *J* = 8.2, 1.6, 0.9 Hz, 1H), 7.71 (t, *J* = 1.4 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.74 (q), 14.14 (q), 44.18 (t), 44.50 (d), 52.25 (d), 61.96 (t), 62.21 (t), 85.23 (s), 111.10 (d), 127.50 (d), 127.89 (d), 128.12 (s), 128.87 (d), 133.77 (d), 135.30 (s), 137.44 (d),

143.63 (s), 166.69 (s), 168.01 (s), 174.68 (s); IR (KBr) 2976, 1752, 1735, 1710, 1604, 1480, 1336, 1152 cm^{-1}; MS (EI) *m/z* 507; exact mass M^+ 507.0546 (calcd for $C_{22}H_{22}NO_5I$ 507.0543); Anal. Calcd for $C_{22}H_{22}NO_5I$: C, 52.08; H, 4.37; N, 2.76. Found: C, 52.15; H, 4.38; N, 2.83.

5n+6n (1 : 1.9) (R_f = 0.4 (hexane-ether = 1 : 2)): Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.91 (t, *J* = 7.1 Hz, 3H for **6n**), 1.05 (t, *J* = 7.1 Hz, 3H for **5n**), 1.29 (t, *J* = 7.1 Hz, 3H for **6n**), 1.31 (t, *J* = 7.1 Hz, 3H for **5n**), 3.71 (s, 3H for **6n**), 3.81 (s, 3H for **5n**), 3.88-4.15 (m, 2H for **5n**+**6n**), 4.07 (dd, *J* = 3.5, 1.2 Hz, 1H for **6n**), 4.22-4.36 (m, 2H for **5n**+**6n**, 1H for **5n**), 4.24 (d, *J* = 3.5 Hz, 1H for **6n**), 4.57 (d, *J* = 4.4 Hz, 1H for **5n**), 4.83 (d, *J* = 15.7 Hz, 1H for **5n**), 4.88 (d, *J* = 15.9 Hz, 1H for **6n**), 4.91 (d, *J* = 15.9 Hz, 1H for **6n**), 4.98 (d, *J* = 15.7 Hz, 1H for **5n**), 6.31 (d, *J* = 2.2 Hz, 1H for **6n**), 6.36 (d, *J* = 7.9 Hz, 1H for **5n**), 6.48 (dd, *J* = 8.3, 2.3 Hz, 1H for **6n**), 6.54 (d, *J* = 8.2 Hz, 1H for **5n**), 7.14 (td, *J* = 8.2, 0.8 Hz, 1H for **5n**), 7.26-7.38 (m, 5H for **5n**+**6n**, 1H for **6n**); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.72 (q, **6n**), 13.93 (q, **5n**), 14.10 (q, **5n**), 14.13 (q, **6n**), 43.78 (d, **5n**), 44.20 (t, **5n**+**6n**), 44.25 (d, **6n**), 50.75 (d, **5n**), 52.59 (d, **6n**), 55.46 (q, **6n**), 55.55 (q, **5n**), 61.27 (t, **5n**), 61.71 (t, **6n**), 61.97 (t, **5n**), 62.00 (t, **6n**), 97.37 (d, **6n**), 102.71 (d, **5n**), 105.53 (d, **5n**), 106.04 (d, **6n**), 111.82 (s, **5n**), 117.54 (s, **6n**), 125.77 (d, **6n**), 127.55 (d, **5n**), 127.57 (d, **6n**), 127.64 (d, **6n**), 127.75 (d, **5n**), 128.71 (d, **5n**), 128.80 (d, **6n**), 129.89 (d, **5n**), 135.78 (s, **6n**), 136.15 (s, **5n**), 145.12 (s, **5n**), 145.28 (s, **6n**), 155.88 (s, **5n**), 160.34 (s, **6n**), 167.10 (s, **6n**), 167.17 (s, **5n**), 168.09 (s, **5n**), 168.30 (s, **6n**), 175.50 (s, **5n**), 176.11 (s, **6n**); IR (neat) 2981, 1732, 1626, 1502, 1472, 1381, 1344, 1264, 1164, 1031 cm^{-1}; MS (EI) *m/z* 411; exact mass M^+ 411.1689 (calcd for $C_{23}H_{25}NO_6$ 411.1682).

5o+6o (2.3 : 1) (R_f = 0.6 (hexane-ether = 1 : 2)): Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.91 (t, *J* = 7.1 Hz, 3H for **6o**), 1.08 (t, *J* = 7.1 Hz, 3H for **5o**), 1.30 (t, *J* = 7.1 Hz, 3H for **6o**), 1.35 (t, *J* = 7.1 Hz, 3H for **5o**), 3.91-4.18 (m, 2H for **5o**+**6o**, 1H for **6o**), 4.22-4.44 (m, 2H for **5o**+**6o**, 1H for **6o**), 4.31 (d, *J* = 4.4 Hz, 1H for **5o**), 4.78 (d, *J* = 4.4 Hz, 1H for **5o**), 4.86 (d, *J* = 15.7 Hz, 1H for **5o**+**6o**), 4.94 (d, *J* = 15.7 Hz, 1H for **6o**), 5.01 (d, *J* = 15.7 Hz, 1H for **5o**), 6.59 (d, *J* = 7.7 Hz, 1H for **5o**), 6.71 (d, *J* = 1.8 Hz, 1H for **6o**), 6.93 (dd, *J* = 8.2, 0.7 Hz, 1H for **5o**), 6.96 (dd, *J* = 7.9, 1.8 Hz, 1H for **6o**), 7.10 (td, *J* = 8.2, 0.7 Hz, 1H for **5o**), 7.24-7.38 (m, 5H for **5o**+**6o**, 1H for **6o**); ^{13}C NMR (100.6 MHz, $CDCl_3$) for **5o** δ (ppm) 13.87 (q), 14.08 (q), 44.29 (t), 44.86 (d), 50.30 (d), 61.54 (t), 62.30 (t), 107.77 (d), 122.98 (d), 123.01 (s), 127.50 (d), 127.70 (d), 128.77 (d), 129.97 (d), 130.33 (s), 135.47 (s), 145.73 (s), 166.67 (s), 167 63 (s), 174.36 (s); IR (neat) 2982, 1733, 1610, 1588, 1461, 1342, 1161, 1031 cm^{-1}; MS (EI) *m/z* 415; exact mass M^+ 415.1194 (calcd for $C_{22}H_{22}NO_5{}^{35}Cl$ 415.1187), 417.1185 (calcd for $C_{22}H_{22}NO_5{}^{37}Cl$ 417.1157).

5p+6p (4.3 : 1) (R_f = 0.6 (hexane-ether = 1 : 2)): Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (t, *J* = 7.1 Hz, 3H for **6p**), 1.08 (t, *J* = 7.1 Hz, 3H for **5p**), 1.30 (t, *J* = 7.1 Hz, 3H for **6p**), 1.37 (t, *J* = 7.1 Hz, 3H for **5p**), 3.90-4.17 (m, 2H for **5p**+**6p**, 1H for **6p**), 4.24-4.45 (m, 2H for **5p**+**6p**, 1H for **6p**), 4.25 (d, *J* = 4.5 Hz, 1H for **5p**), 4.84 (d, *J* = 15.7 Hz, 1H for **5p**), 4.86 (d, *J* = 15.7 Hz, 1H for **6p**), 4.93 (d, *J* = 15.7 Hz, 1H for **6p**), 4.93 (d, *J* = 4.5 Hz, 1H for **5p**), 5.01 (d, *J* = 15.7 Hz, 1H for **5p**), 6.63 (dd, *J* = 7.6, 0.8 Hz, 1H for **5p**), 6.86 (d, *J* = 1.8 Hz, 1H for **6p**), 7.03 (td, *J* = 8.0, 0.7 Hz, 1H for **5p**), 7.09 (dd, *J* = 8.2, 1.1 Hz, 1H for **5p**), 7.12 (dd, *J* = 8.0, 1.7 Hz, 1H for **6p**), 7.24-7.38 (m, 5H for **5p**+**6p**, 1H for **6p**); ^{13}C NMR (100.6 MHz, $CDCl_3$) for **5p** δ (ppm) 13.91 (q), 14.12 (q), 44.23 (t), 45.97 (d), 52.15 (d), 61.55

(t), 62.34 (t), 108.30 (d), 118.71 (s), 125.03 (s), 126.00 (d), 127.54 (d), 127.74 (d), 128.81 (d), 130.23 (d), 135.47 (s), 145.94 (s), 166.66 (s), 167.63 (s), 174.27 (s); IR (neat) 2982, 1733, 1607, 1581, 1455, 1342, 1160, 1030 cm^{-1}; MS (EI) *m/z* 459, 461; exact mass M^+ 459.0681 (calcd for $C_{22}H_{22}NO_5{}^{79}Br$ 459.0681), 461.0648 (calcd for $C_{22}H_{22}NO_5{}^{81}Br$ 461.0661).

5q+6q (11 : 1) (R_f = 0.6 (hexane-ether = 1 : 1)): Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) for **5q** δ (ppm) 1.08 (t, *J* = 7.1 Hz, 3H), 1.38 (t, *J* = 7.1 Hz, 3H), 3.93-4.01 (m, 1H), 4.08-4.16 (m, 1H), 4.16 (d, *J* = 4.4 Hz, 1H), 4.33-4.46 (m, 2H), 4.82 (d, *J* = 15.7 Hz, 1H), 5.02 (d, *J* = 15.7 Hz, 1H), 5.07 (d, *J* = 4.4 Hz, 1H), 6.55 (d, *J* = 7.8 Hz, 1H), 6.83 (td, *J* = 8.0, 0.9 Hz, 1H), 7.23-7.38 (m, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) for **5q** δ (ppm) 13.91 (q), 14.13 (q), 44.18 (t), 47.57 (d), 50.07 (d), 61.51 (t), 62.35 (t), 90.94 (s), 109.05 (d), 127.52 (d), 127.70 (d), 128.68 (s), 128.78 (d), 130.36 (d), 132.27 (d), 135.44 (s), 145.64 (s), 166.52 (s), 167.49 (s), 174.11 (s); IR (neat) 2982, 1732, 1601, 1575, 1452, 1342, 1159, 1030 cm^{-1}; MS (EI) *m/z* 507; exact mass M^+ 507.0537 (calcd for $C_{22}H_{22}NO_5I$ 507.0543).

5r+6r (1 : 5.0) (R_f = 0.5 (hexane-ether = 1 : 2)): Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.89 (t, *J* = 7.1 Hz, 3H for **6r**), 1.15 (t, *J* = 7.1 Hz, 3H for **5r**), 1.25 (t, *J* = 7.1 Hz, 3H for **5r**), 1.30 (t, *J* = 7.1 Hz, 3H for **6r**), 3.87-4.11 (m, 3H for **5r**+**6r**), 4.17-4.38 (m, 3H for **5r**+**6r**), 4.86 (d, *J* = 15.6 Hz, 1H for **6r**), 4.94 (d, *J* = 15.6 Hz, 1H for **6r**), 4.87-4.98 (m, 2H for **5r**), 6.46 (dd, J_{FH} = 9.0, J_{HH} = 2.4 Hz, 1H for **6r**), 6.51 (d, *J* = 7.9 Hz, 1H for **5r**), 6.66 (ddd, J_{FH} = 9.6, J_{HH} = 8.4, 2.4 Hz, 1H for **6r**), 6.64-6.70 (m, 1H for **5r**), 7.13-7.16 (m, 1H for **5r**), 7.25-7.39 (m, 5H for **5r**+**6r**, 1H for **6r**); ^{13}C NMR (100.6 MHz, $CDCl_3$) for **6r** δ (ppm) 13.66 (CH_3), 14.10 (CH_3), 44.25 (CH), 44.32 (CH_2), 52.37 (CH), 61.81 (CH_2), 62.08 (CH_2), 97.89 (d, J_{CF} = 28 Hz, CH), 108.67 (d, J_{CF} = 22 Hz, CH), 120.94 (d, J_{CF} = 3 Hz, C), 126.23 (d, J_{CF} = 10 Hz, CH), 127.61 (CH), 127.93 (CH), 128.88 (CH), 135.28 (C), 145.37 (d, J_{CF} = 12 Hz, C), 163.18 (d, J_{CF} = 245 Hz, C), 166.83 (C), 168.18 (C), 175.80 (C); ^{19}F NMR (376.3 MHz, $CDCl_3$) δ (ppm) –118.1 for **5r**, –111.9 for **6r**; IR (neat) 2983, 1732, 1620, 1611, 1498, 1382, 1342, 1162, 1031 cm^{-1}; MS (EI) *m/z* 399; exact mass M^+ 399.1493 (calcd for $C_{22}H_{22}NO_5F$ 399.1482).

5s+6s (3.6 : 1) (R_f = 0.6 (hexane-ether = 1 : 2)): Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.88 (t, *J* = 7.1 Hz, 3H for **6s**), 1.09 (t, *J* = 7.1 Hz, 3H for **5s**), 1.31 (t, *J* = 7.1 Hz, 3H for **5s**), 1.37 (t, *J* = 7.1 Hz, 3H for **6s**), 3.88-4.15 (m, 2H for **5s**+**6s**, 1H for **6s**), 4.25-4.46 (m, 2H for **5s**+**6s**, 2H for **5s**, 1H for **6s**), 4.91 (d, *J* = 15.6 Hz, 1H for **6s**), 4.92 (d, *J* = 15.7 Hz, 1H for **5s**), 5.00 (d, *J* = 15.6 Hz, 1H for **6s**), 5.04 (d, *J* = 15.7 Hz, 1H for **5s**), 6.87 (dd, *J* = 7.5 Hz, 1H for **5s**), 6.93 (s, 1H for **6s**), 7.21-7.40 (m, 5H for **5s**+**6s**, 2H for **5s**, 1H for **6s**), 7.54 (d, *J* = 7.7 Hz, 1H for **6s**); ^{13}C NMR (100.6 MHz, $CDCl_3$) for **5s** δ (ppm) 13.87 (CH_3), 14.05 (CH_3), 44.31 (CH_2), 44.56 (CH), 51.81 (q, J_{CF} = 3 Hz, CH), 61.49 (CH_2), 62.34 (CH_2), 112.68 (CH), 119.05 (q, J_{CF} = 5 Hz, CH), 123.48 (q, J_{CF} = 2 Hz, C), 123.85 (q, J_{CF} = 273 Hz, C), 126.43 (q, J_{CF} = 33 Hz, C), 127.45 (CH), 127.77 (CH), 128.84 (CH), 129.18 (CH), 136.25 (C), 145.66 (C), 166.63 (C), 167.50 (C), 174.49 (C); ^{19}F NMR (376.3 MHz, $CDCl_3$) δ (ppm) –60.64 for **5s**, –63.00 for **6s**; IR (neat) 2982, 1733, 1612, 1472, 1346, 1320, 1124, 1031 cm^{-1}; MS (EI) *m/z* 449; exact mass M^+ 449.1449 (calcd for $C_{23}H_{22}NO_5F_3$ 449.1450).

8a (R_f = 0.3 (hexane-ether = 1 : 2)): Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.14 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 3.73 (s, 3H), 3.84 (s, 3H), 3.91-3.99 (m, 1H), 4.05-4.13 (m, 1H), 4.11 (d,

J = 15.7 Hz, 1H), 4.28 (d, *J* = 4.2 Hz, 1H), 4.29-4.34 (m, 2H), 4.44 (d, *J* = 14.9 Hz, 1H), 4.49-4.50 (m, 1H), 4.64 (dd, *J* = 15.7, 2.4 Hz, 1H), 5.10 (d, *J* = 14.9 Hz, 1H), 6.13 (d, *J* = 2.2 Hz, 1H), 6.34 (d, *J* = 2.2 Hz, 1H), 7.23-7.33 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.90 (q), 14.10 (q), 40.60 (d), 49.91 (t), 50.30 (t), 53.52 (d), 55.29 (q), 55.55 (q), 61.05 (t), 61.54 (t), 97.24 (d), 100.95 (d), 113.32 (s), 127.35 (d), 128.29 (d), 128.49 (d), 133.89 (s), 136.73 (s), 157.36 (s), 159.88 (s), 168.28 (s), 168.76 (s), 168.97 (s); IR (neat) 2981, 1733, 1652, 1615, 1497, 1455, 1203, 1151 cm^{-1}; MS (EI) *m/z* 455; exact mass M^+ 455.1934 (calcd for $C_{25}H_{29}NO_7$ 455.1944); Anal. Calcd for $C_{25}H_{29}NO_7$: C, 65.92; H, 6.42; N, 3.08. Found: C, 65.67; H, 6.50; N, 3.13.

8b (R_f = 0.4 (hexane-ether = 1 : 3)): Colorless crystals; mp 127-129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.11 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 3.71 (s, 3H), 3.83 (s, 3H), 3.89-3.97 (m, 1H), 4.03-4.11 (m, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 4.29-4.36 (m, 2H), 4.36 (br s, 1H), 4.54 (d, *J* = 14.8 Hz, 1H), 4.55-4.56 (m, 1H), 5.04 (d, *J* = 14.8 Hz, 1H), 6.66 (d, *J* = 8.9 Hz, 1H), 6.70 (d, *J* = 8.9 Hz, 1H), 7.22-7.36 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.95 (q), 14.17 (q), 40.81 (d), 46.21 (t), 50.30 (t), 53.48 (d), 55.51 (q), 55.77 (q), 61.11 (t), 61.63 (t), 108.49 (d), 108.66 (d), 122.20 (s), 122.29 (s), 127.30 (d), 128.38 (d), 128.49 (d), 136.98 (s), 149.12 (s), 150.03 (s), 168.12 (s), 168.32 (s), 168.80 (s); IR (KBr) 2982, 1749, 1737, 1650, 1482, 1263, 1151, 1073 cm^{-1}; MS (EI) *m/z* 455; exact mass M^+ 455.1944 (calcd for $C_{25}H_{29}NO_7$ 455.1944); Anal. Calcd for $C_{25}H_{29}NO_7$: C, 65.92; H, 6.42; N, 3.08. Found: C, 65.76; H, 6.48; N, 3.23.

Preparation of 9C (eq. 5).[12] A solution of **2c** (R = benzyl, Y = H) (110 mg, 0.288 mmol) in DMSO (1,8 ml) and H_2O (0.09 mL) was stirred for 4 h at 160 °C. The reaction mixture was cooled to rt, diluted with a small amount of EtOAc and saturated aqueous NH_4Cl (30 mL) was added to the mixture. The mixture was extracted with EtOAc (30 mL×3). The combined extracts were washed with water (10 mL) and brine (10 mL), dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel eluting with hexane-ether (4 : 1) to give **9C** (66 mg, 74%). **9C** (R_f = 0.7 (hexane-ether = 1 : 9)): Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.17 (t, *J* = 7.1 Hz, 3H), 2.87 (dd, *J* = 16.8, 7.9 Hz, 1H), 3.13 (dd, *J* = 16.8, 4.6 Hz, 1H), 3.88 (dd, *J* = 7.9, 4.6 Hz, 1H), 4.06-4.20 (m, 2H), 4.92 (d, *J* = 15.7 Hz, 1H), 4.94 (d, *J* = 15.7 Hz, 1H), 6.72 (d, *J* = 7.7 Hz, 1H), 7.00 (td, *J* = 7.5, 0.9 Hz, 1H), 7.17 (tdd, *J* = 7.7, 1.3, 0.9 Hz, 1H), 7.23-7.35 (m, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.13 (q), 35.02 (t), 41.92 (d), 43.95 (t), 60.99 (t), 109.15 (d), 122.57 (d), 123.90 (d), 127.39 (d), 127.66 (d), 128.18 (s), 128.25 (d), 128.80 (d), 135.85 (s), 143.50 (s), 171.00 (s), 176.91 (s); IR (neat) 2980, 1737, 1716, 1614, 1489, 1467, 1364, 1209, 1167 cm^{-1}; MS (EI) *m/z* 309; exact mass M^+ 309.1358 (calcd for $C_{19}H_{19}NO_3$ 309.1365).

9A (R_f = 0.5 (hexane-ether = 1 : 4)): Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.20 (t, *J* = 7.1 Hz, 3H), 2.78 (dd, *J* = 16.8, 8.1 Hz, 1H), 3.07 (dd, *J* = 16.8, 4.6 Hz, 1H), 3.23 (s, 3H), 3.78 (dd, *J* = 8.1, 4.6 Hz, 1H), 4.09-4.17 (m, 2H), 6.84 (d, *J* = 7.9 Hz, 1H), 7.03 (td, *J* = 7.5, 1.0 Hz, 1H), 7.24-7.31 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.11 (q), 26.34 (q), 34.98 (t), 41.87 (d), 60.90 (t), 108.07 (d), 122.50 (d), 123.84 (d), 128.21 (s), 128.32 (d), 144.39 (s), 171.06 (s), 176.77 (s); IR (neat) 2981, 1714, 1614, 1495, 1471, 1376, 1349, 1205, 1090 cm^{-1}; MS (EI) *m/z* 233; exact mass M^+ 233.1050 (calcd for

$C_{13}H_{15}NO_3$ 233.1052).

9B (R_f = 0.5 (hexane-ether = 1 : 4)): Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.20 (t, *J* = 7.1 Hz, 3H), 2.83 (dd, *J* = 16.8, 7.9 Hz, 1H), 3.10 (dd, *J* = 16.8, 4.5 Hz, 1H), 3.82 (dd, *J* = 7.9, 4.5 Hz, 1H), 4.07-4.19 (m, 2H), 4.35-4.38 (m, 2H), 5.21-5.29 (m, 2H), 5.85 (ddt, *J* = 17.2, 10.4, 5.2 Hz, 1H), 6.83-6.85 (m, 1H), 7.03 (td, *J* = 7.5, 1.0 Hz, 1H), 7.23-7.27 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.12 (q), 34.94 (t), 41.81 (d), 42.47 (t), 60.93 (t), 108.98 (d), 117.61 (t), 122.45 (d), 123.85 (d), 128.15 (s), 128.20 (d), 131.38 (d), 143.54 (s), 170.97 (s), 176.50 (s); IR (neat) 2982, 1737, 1716, 1489, 1467, 1361, 1210 cm^{-1}; MS (EI) *m/z* 259; exact mass M^+ 259.1206 (calcd for $C_{15}H_{17}NO_3$ 259.1208).

9D (R_f = 0.5 (hexane-ether = 1 : 2)): Red-brown crystals; mp 73-74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.19 (t, *J* = 7.1 Hz, 3H), 2.86 (dd, *J* = 16.8, 8.1 Hz, 1H), 3.13 (dd, *J* = 16.8, 4.4 Hz, 1H), 3.73 (s, 3H), 3.87 (dd, *J* = 8.1, 4.4 Hz, 1H), 4.08-4.21 (m, 2H), 4.89 (d, *J* = 15.6 Hz, 1H), 4.92 (d, *J* = 15.6 Hz, 1H), 6.60 (d, *J* = 8.6 Hz, 1H), 6.68 (ddd, *J* = 8.6, 2.6, 0.7 Hz, 1H), 6.90 (ddd, *J* = 2.6, 1.1, 0.4 Hz, 1H), 7.23-7.32 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.17 (q), 35.06 (t), 42.28 (d), 44.01 (t), 55.77 (q), 61.02 (t), 109.44 (d), 111.58 (d), 112.34 (d), 127.36 (d), 127.63 (d), 128.80 (d), 129.58 (s), 135.91 (s), 136.94 (s), 155.92 (s), 171.03 (s), 176.55 (s); IR (KBr) 2984, 2935, 1735, 1709, 1499, 1257, 1195 cm^{-1}; MS (EI) *m/z* 339; exact mass M^+ 339.1469 (calcd for $C_{20}H_{21}NO_4$ 339.1471).

Preparation of 10A (eq. 6).[13] To a mixture of phenylboronic acid (40 mg, 0.331 mmol), **2k** (160 mg, 0.315 mmol), K_2CO_3 (109 mg, 0.789 mmol) were added acetone (0.63 ml), water (0.79 mL), and $Pd(OAc)_2$ (4.0 mmol/L acetone solution, 0.16 mL, 0.64 μmol), successively. The mixture was heated at 65 °C for 45 min. The reaction mixture was extracted with dichloromethane (4×10 mL) and the organic phase was washed with water (10 mL), dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel eluting with hexane-ether (1 : 2) to give **10A** (131 mg, 91%). **10A** (R_f = 0.6 (hexane-ether = 1 : 2)): Yellow crystals; mp 100-100.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.86 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 3.88-3.96 (m, 1H), 4.00-4.08 (m, 1H), 4.19 (d, *J* = 3.4 Hz, 1H), 4.23-4.36 (m, 2H), 4.34 (d, *J* = 3.4 Hz, 1H), 4.92 (d, *J* = 15.7 Hz, 1H), 5.00 (d, *J* = 15.7 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 7.24-7.41 (m, 9H), 7.46-7.49 (m, 2H), 7.65 (t, *J* = 1.5 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.58 (q), 14.10 (q), 44.21 (t), 44.79 (d), 52.34 (d), 61.78 (t), 62.02 (t), 109.22 (d), 123.90 (d), 126.29 (s), 126.85 (d), 126.98 (d), 127.37 (d), 127.58 (d), 127.74 (d), 128.77 (d), 128.79 (d), 135.72 (s), 136.00 (s), 140.82 (s), 143.17 (s), 166.95 (s), 168.16 (s), 175.46 (s); IR (KBr) 2980, 1743, 1735, 1716, 1619, 1483, 1368, 1338, 1184 cm^{-1}; MS (EI) *m/z* 457; exact mass M^+ 457.1867 (calcd for $C_{28}H_{27}NO_5$ 457.1889) ; Anal. Calcd for $C_{28}H_{27}NO_5$: C, 73.51; H, 5.95; N, 3.06. Found: C, 73.52; H, 5.98; N, 3.11.

10B (R_f = 0.4 (hexane-ether = 1 : 2)): Pale brown crystals; mp 44-45 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.95 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 3.49 (d, *J* = 4.4 Hz, 1H), 3.81-3.89 (m, 1H), 3.92-4.00 (m, 1H), 4.21-4.34 (m, 2H), 4.50 (d, *J* = 4.4 Hz, 1H), 4.84 (d, *J* = 15.7 Hz, 1H), 5.10 (d, *J* = 15.7 Hz, 1H), 6.70 (d, *J* = 7.3 Hz, 1H), 6.93 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.20-7.29 (m, 2H), 7.31-7.49 (m, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.83 (q), 14.02 (q), 44.15 (t), 44.51 (d), 50.15 (d), 61.08 (t), 62.11 (t), 108.25 (d), 122.86 (s), 123.52 (d), 127.61 (d), 127.90 (d), 128.20 (d), 128.74 (d), 128.86 (d), 128.94

(d), 135.93 (s), 138.46 (s), 138.98 (s), 144.62 (s), 166.45 (s), 167.87 (s), 175.29 (s); IR (KBr) 2981, 1734, 1717, 1594, 1464, 1343, 1158, 1030 cm^{-1}; MS (EI) *m/z* 457; exact mass M^+ 457.1902 (calcd for $C_{28}H_{27}NO_5$ 457.1889) ; Anal. Calcd for $C_{28}H_{27}NO_5$: C, 73.51; H, 5.95; N, 3.06. Found: C, 73.36; H, 5.98; N, 3.14.

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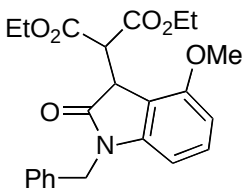
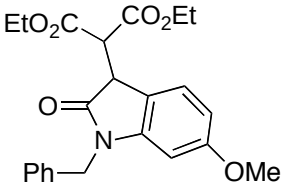
6. By the preparation of **1n**, **6n** (14%) and the mixture of **1n** and **5n** (total 27%, **1n**:**5n** = 5:1) were obtained by column chromatography separation. On standing the mixture of **1n** and **5n**, **6n** and **5n** gradually increased. Treatment of the mixture of **1n** containing small amounts of **5n** and **6n** with $SnCl_4$ or $ZnCl_2$ gave **5n** : **6n** (*ca.* 1 : 1.9) in 82-86% yield. Therefore, the effect of Lewis acid towards **5n** : **6n** selectivity is not accurate.



5n



6n

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