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$Zn(OTf)_2$-Catalyzed Reactions of Ethenetricarboxylates with 2-Aminobenzaldehydes Leading to Tetrahydroquinoline Derivatives

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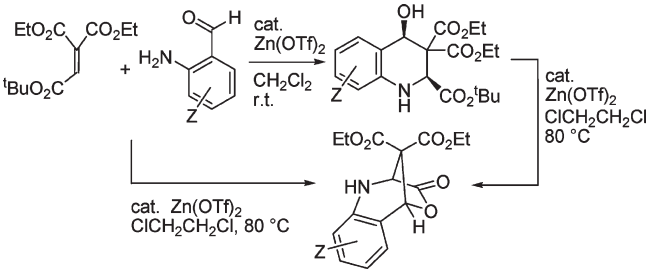
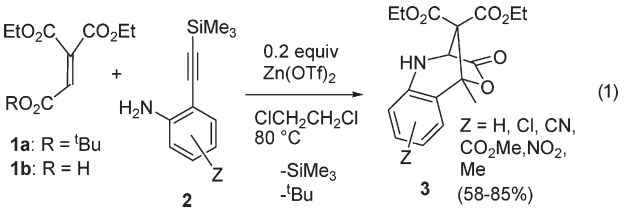


Quinolines are an important class of compounds, and the development of new efficient synthetic strategies for the construction of quinolines is of considerable interest. Zinc triflate catalyzed cyclization of ethenetricarboxylate derivatives with 2-aminobenzaldehydes has been examined. The reaction of ethenetricarboxylate with 2-aminobenzaldehydes in the presence of zinc triflate (0.2 equiv) at 80 °C in $ClCH_2CH_2Cl$ gave bridged tetrahydroquinoline derivatives in 15−95% yield. On the other hand, the reaction at room temperature in CH_2Cl_2 gave hydroxy tetrahydroquinoline derivatives in 38−90% yield. Heating the hydroxy tetrahydroquinolines with zinc triflate (0.2 equiv) at 80 °C in $ClCH_2CH_2Cl$ led to the bridged tetrahydroquinoline derivatives in 75−96% yield. Thermal reaction of the bridged tetrahydroquinolines (180 °C) gave indole derivatives regioselectively.

Introduction

Quinolines are an important class of compounds found in many naturally occurring and synthetic molecules possessing a variety of biological activities.[1] The development of new efficient synthetic strategies for the construction of quinolines is of considerable importance from the viewpoint of the medicinal and organic chemistry.[2] We have reported zinc-catalyzed cyclization of ethenetricarboxylate derivative **1** with 2-(trimethylsilylethynyl)anilines to afford bridged tetrahydroquinoline derivatives (eq 1).[3] The reaction of **1a** with 2′-aminoacetophenone **4** also gave the bridged tetrahydroquinoline derivative **3** (eq 2). It is supposed that the initially formed Michael-aldol-type product **X** undergoes further ring closure, giving the bridged tetrahydroquinoline **3**.



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(1) (a) Balasubramanian, M.; Keay, J. G. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 5, p 245. (b) Michael, J. P. *Nat. Prod. Rep.* **2008**, *25*, 166. (c) Michael, J. P. *Nat. Prod. Rep.* **2007**, *24*, 223. (d) Michael, J. P. *Nat. Prod. Rep.* **2005**, *22*, 627. (e) Michael, J. P. *Nat. Prod. Rep.* **2004**, *21*, 650.

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(3) Yamazaki, S.; Morikawa, S.; Miyazaki, K.; Takebayashi, M.; Yamamoto, Y.; Morimoto, T.; Kakiuchi, K.; Mikata, Y. *Org. Lett.* **2009**, *11*, 2796.

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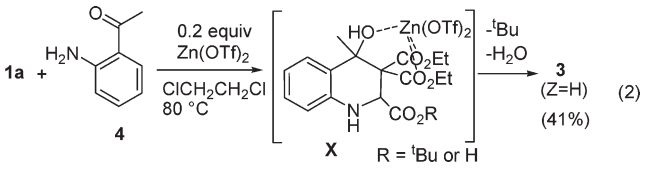


Recently, tandem thio-, oxa-, and aza-Michael-aldol and related ring-forming reactions have been studied as efficient processes.[4−6] Aza-Michael-aldol-type reactions of 2-aminobenzaldehydes and 2-aminophenyl ketones with α,β-unsaturated aldehydes lead to quinoline derivatives. However, only a few Michael acceptors other than reactive α,β-unsaturated aldehydes have been used.[4e,f] In order to investigate the intermediates in eq 2 and construct the synthetically useful quinoline skeletons with functional diversity, zinc triflate catalyzed cyclization of a highly reactive Michael acceptor **1** with various 2-aminobenzaldehydes **5** has been examined in this work.

Results and Discussion

Zn(OTf)$_2$-Catalyzed Reactions of Ethenetricarboxylates with 2-Aminobenzaldehydes. 2-Aminobenzaldehydes are expected to be more reactive than 2′-aminoacetophenones for the aldol ring-closing step. The first ring-closing step may occur at lower temperature (for example, room temperature), and the ^{t}Bu ester group may be retained at the temperature. Therefore isolation of the corresponding hydroxy tetrahydroquinoline products from intermediate **X** proposed in eq 2 may be possible. Various 2-aminobenzaldehydes **5** are also easily accessible and obtained according to the literature procedures.[7]

First, zinc triflate catalyzed reaction of **1a** with **5a**−**g** at 80 °C in ClCH$_2$CH$_2$Cl was examined. The reaction condition gave bridged tetrahydroquinoline derivatives **7** in 15−95% yield (Scheme 1, Table 1), similar to the reaction of **1a** and 2′-aminoacetophenone **4**.[3] The lower yield in the reaction of **1a** and unsubstituted 2-aminobenzaldehyde at 80 °C compared to the electron-withdrawing group-substituted 2-aminobenzaldehydes **5b**−**g** is in accord with that of **1a** and 2-(trimethylsilylethynyl)aniline,[3] probably because the electron-withdrawing groups on the aromatic ring suppress side reactions such as aromatic substitutions.[8] The reaction between free CO$_2$H **1b** and **5a** in the presence of Zn(OTf)$_2$ (0.2 equiv) at room temperature in CH$_2$Cl$_2$ also gave **7a** in 23% yield.

SCHEME 1

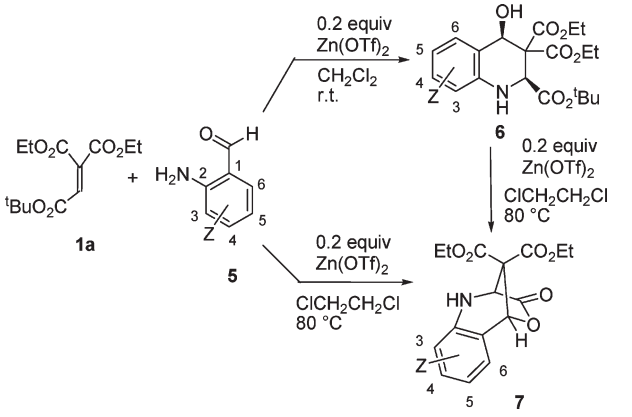


TABLE 1. Reaction of 1a with 5 at 80 °C

entry		Z	time (h)	product	yield (%)
1	**5a**	H	17	**7a**	15
2	**5b**	5-Cl	19	**7b**	90
3	**5c**	4-Cl	18	**7c**	45
4	**5d**	5-CO$_2$Me	18	**7d**	95
5	**5e**	4-CO$_2$Me	18	**7e**	72
6	**5f**	5-Br	18	**7f**	81
7	**5g**	3,5-Br$_2$	18	**7g**	63

On the other hand, the reaction of **1a** and **5a**−**f** with Zn(OTf)$_2$ (0.2 equiv) at room temperature in CH$_2$Cl$_2$ gave hydroxy tetrahydroquinoline derivatives **6a**−**f** in 35−90% yield (Scheme 1, Table 2).[9] The major isolated diastereoisomers obtained for the hydroxy tetrahydroquinoline derivatives **6** have 1,3-*cis* stereochemistry, which was determined by the presence of NOE peaks between 1,3-*cis* protons (C*H*N and C*H*OH) in the NOESY spectra.[10] 1,3-*Cis* stereoselectivity may arise from the stable diequatorial (OH and CO$_2$^{t}Bu) conformation of the six-membered ring in products **6**. The reaction of **1a** and **5g** with Zn(OTf)$_2$ did not proceed, probably because the amine addition step is slow due to both steric factors by the *o*-Br substituent and electronic effects by the two electronegative halogen substituents. The reaction of **1a** and 2′-aminoacetophenone **4** with Zn(OTf)$_2$ at room temperature gave only a noncyclized amine adduct and did not give a hydroxy tetrahydroquinoline derivative.

Heating **6a**−**e** with zinc triflate (0.2 equiv) at 80 °C in ClCH$_2$CH$_2$Cl gave bridged tetrahydroquinoline derivatives **7** in 75−96% yield (Table 3).

The obtained result suggests that the reaction at room temperature does not require the existence of a ^{t}Bu ester group in ethenetricarboxylate **1**. The zinc triflate catalyzed

(4) For thio-Michael-aldol and related reactions, see: (a) Wang, W.; Li, H.; Wang, J.; Zu, L. *J. Am. Chem. Soc.* **2006**, *128*, 10354. (b) Li, H.; Zu, L.; Xie, H.; Wang, J.; Jiang, W.; Wang, W. *Org. Lett.* **2007**, *9*, 1833. (c) Zu, L.; Wang, J.; Li, H.; Xie, H.; Jiang, W.; Wang, W. *J. Am. Chem. Soc.* **2007**, *129*, 1036. (d) Rios, R.; Sundén, H.; Ibrahem, I.; Zhao, G.-L.; Eriksson, L.; Córdova, A. *Tetrahedron Lett.* **2006**, *47*, 8547. (e) Dodda, R.; Mandal, T.; Zhao, C.-G. *Tetrahedron Lett.* **2008**, *49*, 1899. (f) Luo, G.; Zhang, S.; Duan, W.; Wang, W. *Tetrahedron Lett.* **2009**, *50*, 2946. (g) Brandau, S.; Maerten, E.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2006**, *128*, 14986.

(5) For oxa-Michael-aldol reactions, see: (a) Li, H.; Wang, J.; E-Nunu, T.; Zu, L.; Jiang, W.; Wei, S.; Wang, W. *Chem. Commun.* **2007**, 507. (b) Sundén, H.; Ibrahem, I.; Zhao, G.-L.; Eriksson, L.; Córdova, A. *Chem.—Eur. J.* **2007**, *13*, 574.

(6) For aza-Michael-aldol and related reactions, see: (a) Li, H.; Wang, J.; Xie, H.; Zu, L.; Jiang, W.; Duesler, E. N.; Wang, W. *Org. Lett.* **2007**, *9*, 965. (b) Makino, K.; Hara, O.; Takiguchi, Y.; Katano, T.; Asakawa, Y.; Hatano, K.; Hamada, Y. *Tetrahedron Lett.* **2003**, *44*, 8925. (c) Liu, G.-S.; Dong, Q.-L.; Yao, Y.-S.; Yao, Z.-J. *Org. Lett.* **2008**, *10*, 5393. (d) Yan, M.-C.; Tu, Z.; Lin, C.; Ko, S.; Hsu, J.; Yao, C.-F. *J. Org. Chem.* **2004**, *69*, 1565. (e) Kobayashi, K.; Nakanishi, R.; Shimizu, A.; Kitamura, T.; Morikawa, O; Konishi, H. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1547. (f) Apple, I. A.; Meth-Cohn, O. *ARKIVOC* **2002**, (vi) 4.

(7) (a) Zhang, C.; De, C. K.; Mal, R.; Seidel, D. *J. Am. Chem. Soc.* **2008**, *130*, 416. (b) Cordi, A. A.; Desos, P.; Randle, J. C. R.; Lepagnol, J. *Bioorg. Med. Chem.* **1995**, *3*, 129. (c) Guo, W.; Jiang, Q.-J.; Lu, F.; Yang, D.-Q. *Chin. J. Synth. Chem.* **2004**, 12.

(8) The reactions of **1a** and the aminobenzaldehyde with electron-donating groups, 2-amino-4,5-dimethoxybenzaldehyde[7c] with Zn(OTf)$_2$ (0.2 equiv) at both 80 °C and room temperature gave complex mixtures.

(9) The reaction of **1a** nd **5a** with zinc halides, ZnBr$_2$ or ZnCl$_2$ gave **6a** in lower yields (< 32%).

(10) The atom numbering in compounds **6**−**9** in Scheme 1 and eqs 3 and 4 is inconsistent with those of the heterocyclic systems. The atom numbering of compounds **9** for NMR assignments in the Experimental Section is based on the indole system.

TABLE 2. Reaction of 1a with 5 at Room Temperature[a]

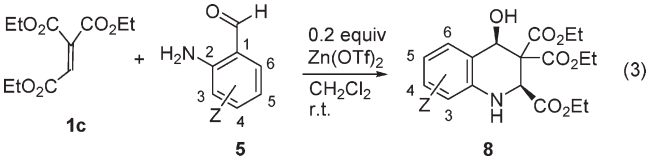
entry		Z	time (h)	product	yield (%)[b,c]
1	**5a**	H	24	**6a**	85[d]
2	**5b**	5-Cl	24	**6b**	90[d]
3	**5c**	4-Cl	18	**6c**	83
4	**5d**	5-CO_2Me	18	**6d**	38[e]
5	**5e**	4-CO_2Me	18	**6e**	69
6	**5f**	5-Br	18	**6f**	84
7	**5g**	3,5-Br_2	24	**6g**	0

[a]CH_2Cl_2 was used as solvent at room temperature. [b]Isolated yield of 1,3-*cis* diastereomers **6**. [c]Small amounts of possible *trans* diastereomers also formed; however, they could not be isolated. [d]The reaction of **5a** and **5b** in $ClCH_2CH_2Cl$ at room temperature gave **6a** in 84% and 86% yields, respectively. [e]A possible noncyclized amine adduct formed as a byproduct, which could not be isolated.

TABLE 3. Reaction of 6 to 7 at 80 °C

entry		Z	time (h)	product	yield (%)
1	**6a**	H	24	**7a**	75
2	**6b**	5-Cl	18	**7b**	80
3	**6c**	4-Cl	18	**7c**	80
4	**6d**	5-CO_2Me	18	**7d**	86
5	**6e**	4-CO_2Me	19	**7e**	96
6	**6f**	5-Br	18	**7f**	90

reaction of triethyl ester **1c** and 2-aminobenzaldehydes **5b**−**f** at room temperature in CH_2Cl_2 was examined (eq 3), and the reaction gave hydroxy tetrahydroquinoline derivatives **8b**−**f** in 60−76% yield stereoselectively (Table 4).[10] Only the major diastereoisomers **8** could be isolated and had 1,3-*cis* stereochemistry, which was determined by NOESY spectra. The reaction of diethyl benzylidene malonate ($PhCH{=}C(CO_2Et)_2$) with **5a** or **5b** gave a complex mixture including the starting benzylidene malonate.



(3)

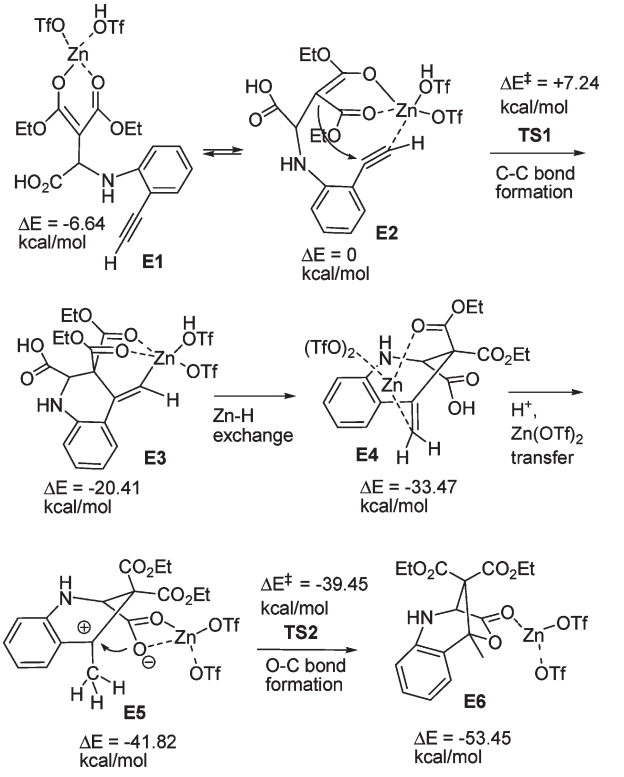
Reaction Mechanism. In order to explain the reaction mechanism to give the tetrahydroquinolines, first the similarity of the reactions to give the same bridged tetrahydroquinoline product **3** from 2-ethynylaniline (eq 1) and 2′-aminoacetophenone **4** (eq 2) was examined using density functional calculations. The proposed reaction mechanism for 2-ethynylaniline is shown in Scheme 2. The structures of the intermediates (Figure S1 in Supporting Information) and transition states (TS) of the ring-closing steps (Figure 1) were calculated. The zinc diester coordinated complex **E1** and zinc diester/alkyne coordinated complex **E2** were obtained. Since the difference in energy between **E1** and **E2** is small (6.64 kcal/mol), they are in equilibrium and the reaction may proceed from the precursor **E2**. The zinc coordination of both diester and alkyne was found in **E2**, transition state **TS1**, and the resulting intermediate **E3** for the first cyclization step. Then, a proton and zinc change places to give the intermediate **E4**. Protonation to the alkyne moiety of **E4** and zinc transfer may give the benzylic cation intermediate **E5**. This stable intermediate **E5** may be the same intermediate as that from 2′-aminoacetophenone **4** (vide post). The ring-closure transition state **TS2** with a zinc carboxylate

TABLE 4. Reaction of 1c with 5 at Room Temperature

entry		Z	time (h)	product	yield (%)[a,b]
1	**5b**	5-Cl	24	**8b**	68[c]
2	**5c**	4-Cl	18	**8c**	70[c]
3	**5d**	5-CO_2Me	20	**8d**	60[c]
4	**5e**	4-CO_2Me	20	**8e**	61
5	**5f**	5-Br	18	**8f**	76

[a]Isolated yield of 1,3-*cis* diastereomers **8**. [b]Small amounts of possible *trans* diastereomers also formed; however, they could not be isolated. [c]The reaction of **5b,c,d** and **1c** at 80 °C gave complex mixtures, and formation of the corresponding bridged tetrahydroquinolines **7b,c,d** was not detected.

SCHEME 2. Proposed Mechanism for the Reaction of 1 and 2-Ethynylaniline with $Zn(OTf)_2$ and B3LYP/6-31G* Calculated Energies[a]



[a]ΔE = sum of electronic and zero-point energies (kcal/mol).

moiety was obtained (Figure 1), and the second ring-closing step may be a facile process.

The proposed reaction mechanism for 2′-aminoacetophenone **4** is shown in Scheme 3. The structures of the intermediates **A1**−**6** are shown in Figure S2 in Supporting Information. The zinc coordination of both the diester and acetyl moiety was found in the precursor **A1**, transition state **TS1A** (Figure 2), and the resulting intermediate **A2** for the first cyclization step. Proton transfer from **A2** leads to the intermediate **A3**, which is shown as **X** in eq 2. Successive proton, zinc, and water transfers occur to give the same intermediate **A5** as that of ethynylaniline apart from the eliminated water, **E5** in Scheme 2. Then, the second ring closure takes place, similar to the reaction of ethynylaniline **2** to give the bridged tetrahydroquinoline derivative. Thus, reasonable reaction mechanisms for the reactions of ethynylaniline and 2′-aminoacetophenone have been provided.

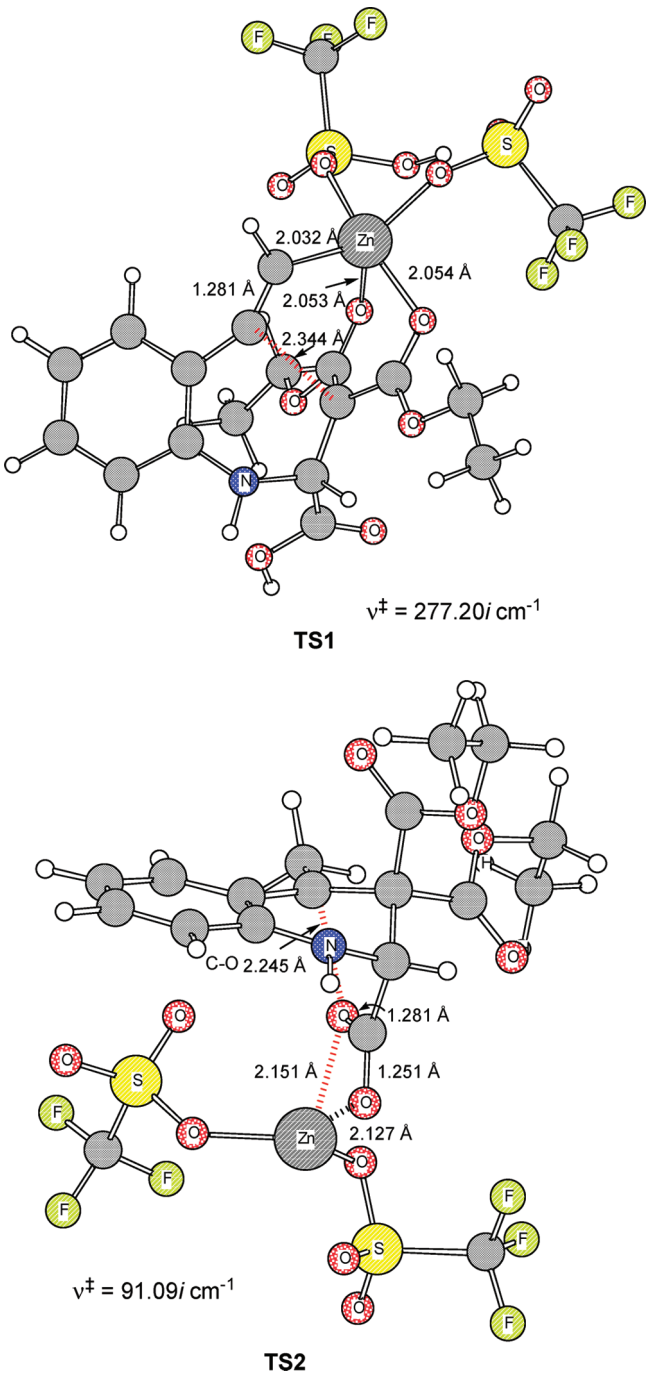
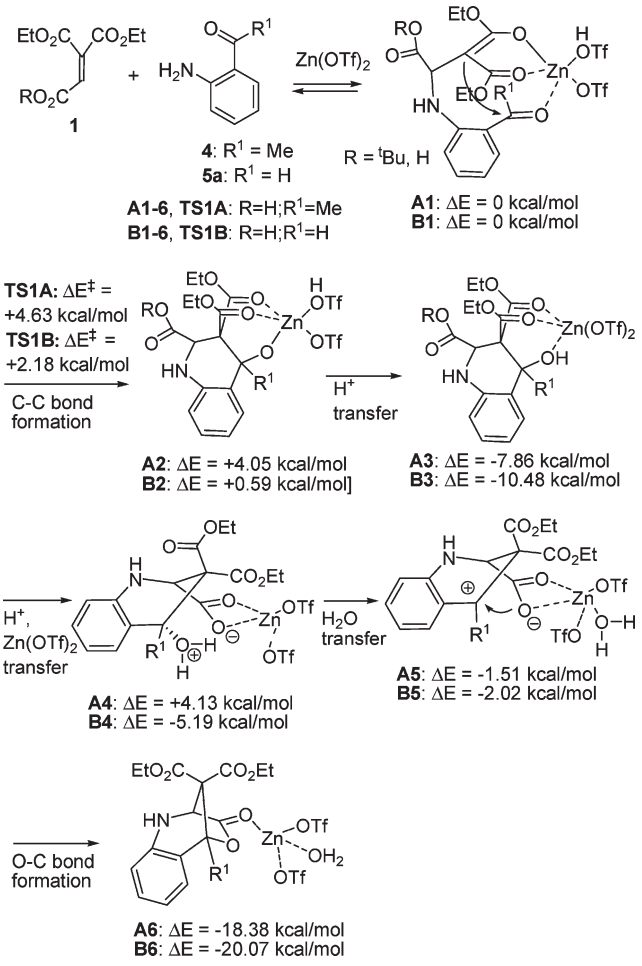


FIGURE 1. B3LYP/6-31G*-optimized structures of transition states **TS1** and **TS2** in Scheme 2.

Theoretical calculations suggest that both addition steps of ethynylaniline and aminoacetophenone involve a double-activation, where the zinc metal electrophilically activates the alkyne or acetyl groups to which the zinc enolate adds nucleophilically.

The proposed reaction mechanism for 2-aminobenzaldehyde **5a** is also shown in Scheme 3. The structures of the intermediates **B1**−**6** are shown in Figure S3 in Supporting Information. The ring-closing transition state **TSB1** was obtained (Figure 2), and the structure is similar to **TSA1** for 2′-aminoacetophenone **4**. The facile first ring closure

SCHEME 3. Proposed Mechanism for the Reaction of 1 and 2′-Aminoacetophenone (4)/2-Aminobenzaldehyde (5a) with Zn(OTf)$_2$ and B3LYP/6-31G* Calculated Energies



shown by the lower activation energy for **5a** (**TSB1**, $\Delta E^{\ddagger}$ = +2.18 kcal/mol) compared with that for **4** (**TSA1**, $\Delta E^{\ddagger}$ = +4.63 kcal/mol) and the stability shown by the lower energies of the formed hydroxy tetrahydroquinoline intermediates, **B2** and **B3**, compared with those of the corresponding 2′-aminoacetophenone intermediates **A2** and **A3** may explain the isolation of the hydroxy tetrahydroquinoline products **6**.[11]

Further mechanistic study including proton, zinc, and water transfer steps are under investigation.

Thermal Reaction of Bridged Tetrahydroquinolines. The thermal reaction of the bridged tetrahydroquinolines **7** was carried out. Heating **7** at 180 °C without solvent gave C-b substituted indoles **9** as major products (eq 4, Table 5).[10] The first formation of cyclopropane intermediates **Y** by loss of CO_2 is assumed. Then, the resulting cyclopropylindolines **Y** were transformed to C-b alkylated indoles **9**. The regiochemistry of **9** was determined by NOE and HMBC correlations. The observed regioselectivity can be explained, similar to

(11) In case of the reaction of aminoaldehydes **5**, the direct attack of the OH to the COO^{t}Bu instead of formation of a carbocation and the subsequent attack of the carboxylate (B4 → B5 → B6 (Scheme 3)) may not be excluded. However, the alternative mechanism is unlikely because of the failure of the reaction of aminoaldehydes **5b,c,d** and triethyl ester **1c** at 80 °C to give the bridged tetrahydroquinolines **7b,c,d** (footnote c in Table 4).

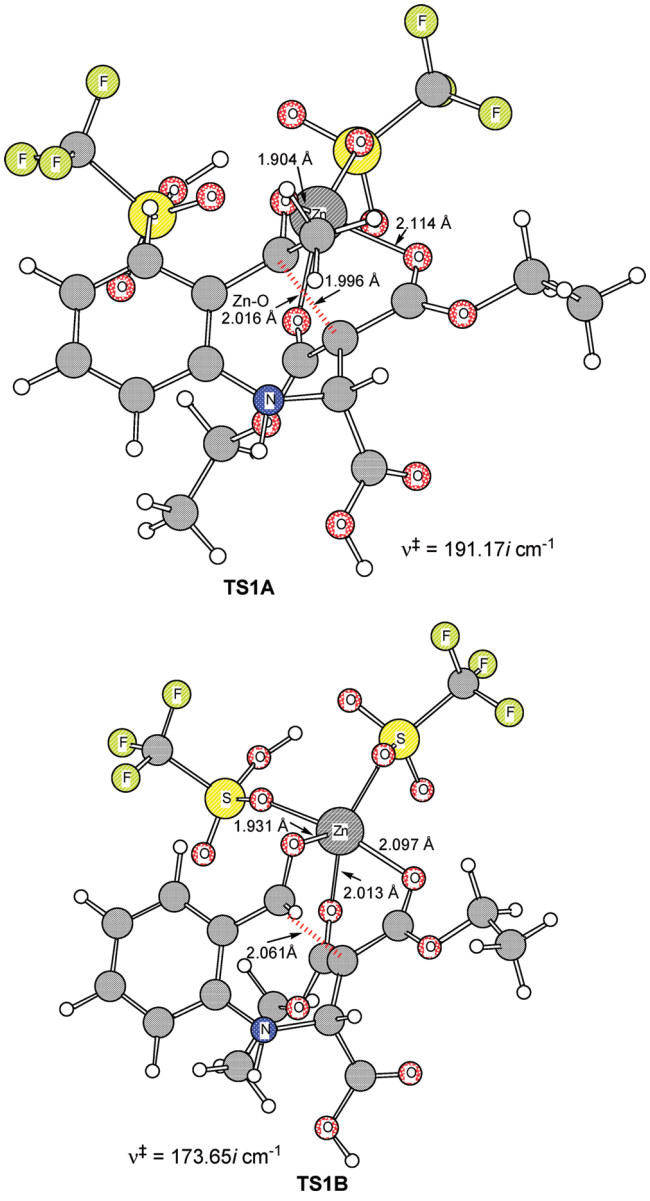
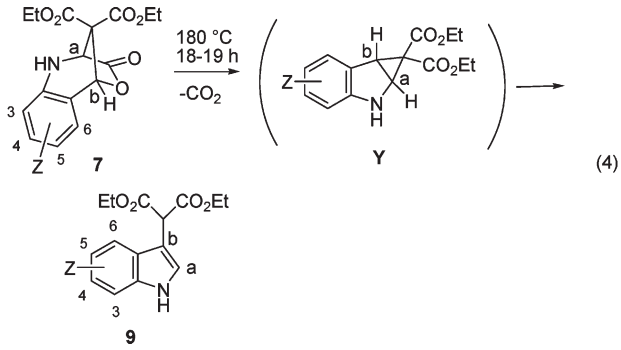


FIGURE 2. B3LYP/6-31G*-optimized structures of transition states **TS1A** and **TS1B** in Scheme 3.

TABLE 5. Thermal Reaction of 7

entry		Z	product	yield (%)
1	**7a**	H	**9a**	88
2	**7b**	5-Cl	**9b**	84
3	**7c**	4-Cl	**9c**	65
4	**7d**	5-CO_2Me	**9d**	93
5	**7e**	4-CO_2Me	**9e**	76
6	**7f**	5-Br	**9f**	69
7	**7g**	3,5-Br	**9g**	54

reported examples.[12] Cyclopropane intermediates were proposed for the reported metal-catalyzed carbenoid insertion. Existing substitution on the C-b in **Y** would force a malonate group on the C-a position of indole.[3] In C-a,b-unsubstituted substrates, a malonate group on the C-b position of the indole is favored since participation by the nitrogen lone pair would stabilize a developing positive charge in the cyclopropane ring cleavage.



(4)

In summary, zinc triflate catalyzed cyclization of **1** with 2-aminobenzaldehydes **5** gave bridged tetrahydroquinoline derivatives **7** at 80 °C. On the other hand, the reaction at room temperature gave hydroxy tetrahydroquinoline derivatives **6** stereoselectively. Thermal reaction of **7** gave indole derivatives **9** regioselectively. These reactions represent an efficient way to construct potentially useful heterocyclic compounds. The products are not readily obtainable by other methods. Further investigation of the scope of the cyclization reactions is underway.

Experimental Section

2-Amino-5-bromobenzaldehyde **5f** was prepared from methyl 2-amino-5-bromobenzoate through reduction ($LiAlH_4$) and oxidation (MnO_2), according to the literature procedures.[7b]

5f (56%): R_f = 0.5 (EtOAc/hexane = 1:1) including a small amount of impurity; brown crystals; mp 63−65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.16 (bs, 2H), 6.56 (dd, J = 8.8, 0.4 Hz, 1H), 7.36 (dd, J = 8.8, 2.4 Hz, 1H), 7.57 (d, J = 2.4 Hz, 1H), 9.78 (d, J = 0.5 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 107.2 (s), 118.0 (d), 119.9 (s), 137.5 (d), 137.9 (d), 148.7 (s), 192.9 (d); IR (KBr) 3433, 3327, 1670, 1654, 1617, 1546, 1473, 1188 cm^{-1}; MS (EI) m/z 201 (M^+, 79), 199 (M^+, 86), 173 (80), 171 (100%); HRMS M^+ 198.9633 (calcd for $C_7H_6{}^{79}BrNO$ 198.9633), 200.9612 (calcd for $C_7H_6{}^{81}BrNO$ 200.9612).

Typical Experimental Procedure (Table 2, entry 1). To a solution of **1** (276 mg, 1.0 mmol) in dichloromethane (1.8 mL) were added 2-aminobenzaldehyde (**5a**) (121 mg, 1.0 mmol) and $Zn(OTf)_2$ (74.5 mg, 0.2 mmol). The mixture was stirred at room temperature for 19 h. The reaction mixture was cooled to 0 °C and quenched with water. The mixture was diluted with dichloromethane, and then saturated aqueous $NaHCO_3$ was added. The organic phase was extracted with dichloromethane, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel with dichloromethane/ether as eluent to give **6a** (333 mg, 85%).

6a: R_f = 0.7 (CH_2Cl_2/ether = 5:1); pale yellow crystals; mp 114−115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.08 (t, J = 7.1 Hz, 3H), 1.33 (t, J = 7.1 Hz, 3H), 1.49 (s, 9H), 4.09 (bs, 1H), 4.13 (q, J = 7.1 Hz, 2H), 4.31 (q, J = 7.1 Hz, 2H), 4.42 (s, 1H), 4.68 (bs, 1H), 5.24 (bd, J = 4.4 Hz, 1H), 6.56 (dd, J = 8.1, 0.9 Hz, 1H), 6.74 (td, J = 8.0, 0.9 Hz, 1H), 7.05 (t-like, J = 7.7 Hz, 1H), 7.44 (d-like, J = 7.7 Hz, 1H). Selected NOEs are between δ 5.24 (C*H*OH) and δ 4.42 (C*H*N), 7.44 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.7 (q), 13.9 (q), 27.7 (q), 57.6 (d), 58.4 (s), 61.8 (t), 62.0 (t), 73.3 (d), 83.2 (s), 113.5 (d), 118.0 (d), 122.4 (s), 125.6 (d), 128.6 (d), 140.3 (s), 168.59 (s), 168.62 (s), 168.7 (s).

(12) (a) Gibe, R.; Kerr, M. A. *J. Org. Chem.* **2002**, *67*, 6247. (b) Salim, M.; Capretta, F. *Tetrahedron* **2000**, *56*, 8063. (c) Yadav, J. S.; Reddy, B. V. S.; Satheesh, G. *Tetrahedron Lett.* **2003**, *44*, 8331.

Selected HMBC correlations are between δ 4.42 (CHN) and δ 58.4 ($C(CO_2Et)_2$), 73.3 (CHOH) and between δ 7.44 (Ar) and δ 73.3 (CHOH). IR (neat) 3497, 3394, 2982, 1738, 1611, 1482, 1570, 1344, 1251, 1156, 1056 cm^{-1}; MS (EI) *m*/*z* 393 (M^+, 24), 320 (22), 292 (21), 246 (31), 202 (100%); HRMS M^+ 393.1786 (calcd for $C_{20}H_{27}NO_7$ 393.1788). Anal. Calcd for $C_{20}H_{27}NO_7$: C, 61.06; H, 6.92; N, 3.56. Found: C, 60.77; H, 6.75; N, 3.59.

6b: R_f = 0.8 (CH_2Cl_2/ether = 5:1); colorless crystals; mp 118−119 °C (hexane-EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.12 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.49 (s, 9H), 4.07−4.10 (broad, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.29−4.35 (m, 2H), 4.40 (s, 1H), 5.18 (bd, *J* = 8.1 Hz, 1H), 6.50 (d, *J* = 8.6 Hz, 1H), 7.01 (ddd, *J* = 8.6, 2.4, 0.7 Hz, 1H), 7.73 (dd, *J* = 2.4, 1.1 Hz, 1H). Selected NOEs are between δ 5.18 (CHOH) and δ 4.40 (CHN), 7.73 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.9 (q), 14.1 (q), 27.9 (q), 57.7 (d), 58.1 (s), 62.2 (t), 62.3 (t), 73.1 (d), 83.6 (s), 114.9 (d), 123.1 (s), 124.1 (s), 125.8 (d), 128.7 (d), 139.1 (s), 168.4 (s), 168.55 (s), 168.59 (s). Selected HMBC correlations are between δ 4.40 (CHN) and δ 58.1 ($C(CO_2Et)_2$), 73.1 (CHOH) and between δ 7.73 (Ar) and δ 73.1 (CHOH). IR (KBr) 3520, 3355, 2985, 1740, 1608, 1500, 1370, 1266, 1198, 1157 cm^{-1}; MS (EI) *m*/*z* 429 (M^+, 6.9), 427 (M^+, 18), 326 (18), 280 (26), 236 (100%); HRMS M^+ 427.1399 (calcd for $C_{20}H_{26}{}^{35}ClNO_7$ 427.1398), 429.1373 (calcd for $C_{20}H_{26}{}^{37}ClNO_7$ 429.1368). Anal. Calcd for $C_{20}H_{26}ClNO_7$: C, 56.14; H, 6.12; N, 3.27. Found: C, 56.14; H, 6.10; N, 3.48.

6c: R_f = 0.3 (CH_2Cl_2) including a small amount of impurity; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.13 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.49 (s, 9H), 4.08 (bs, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.29−4.34 (m, 2H), 4.41 (s, 1H), 5.18 (bs, 1H), 6.56 (d, *J* = 1.8 Hz, 1H), 6.71 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.36 (dd, *J* = 8.2, 1.1 Hz, 1H). Selected NOEs are between δ 5.18 (CHOH) and δ 4.41 (CHN), 7.36 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.9 (q), 14.0 (q), 27.8 (q), 57.6 (d), 58.2 (s), 62.15 (t), 62.24 (t), 73.1 (d), 83.6 (s), 113.1 (d), 118.2 (d), 121.1 (s), 127.2 (d), 134.3 (s), 141.5 (s), 168.3 (s), 168.5 (s), 168.6 (s). Selected HMBC correlations are between δ 4.41 (CHN) and δ 58.2 ($C(CO_2Et)_2$), 73.1 (CHOH) and between δ 7.36 (Ar) and δ 73.1 (CHOH). IR (neat) 3500, 3390, 2981, 1755−1716, 1606, 1579, 1488, 1368, 1159, 1093, 1050 cm^{-1}; MS (EI) *m*/*z* 429 (M^+, 5.6), 427 (M^+, 16), 326 (57), 280 (55), 236 (63), 57 (100%); HRMS M^+ 427.1393 (calcd for $C_{20}H_{26}{}^{35}ClNO_7$ 427.1398), 429.1361 (calcd for $C_{20}H_{26}{}^{37}ClNO_7$ 429.1368).

6d: R_f = 0.2 (CH_2Cl_2/ether = 19:1); colorless viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.08 (t, *J* = 7.1 Hz, 3H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.50 (s, 9H), 3.85 (s, 3H), 4.13 (q, *J* = 7.1 Hz, 2H), 4.30−4.36 (m, 2H), 4.47 (s, 1H), 5.22 (s, 1H), 6.56 (d, *J* = 8.4 Hz, 1H), 7.76 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.15 (dd, *J* = 1.8, 1.3 Hz, 1H). Selected NOEs are between δ 5.22 (CHOH) and δ 4.47 (CHN), 8.15 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.8 (q), 14.0 (q), 27.8 (q), 51.6 (q), 57.4 (d), 58.0 (s), 62.1 (t), 62.3 (t), 73.1 (d), 83.8 (s), 112.8 (d), 119.4 (s), 121.7 (s), 128.0 (d), 130.8 (d), 144.5 (s), 167.1 (s), 168.1 (s), 168.30 (s), 168.32 (s). Selected HMBC correlations are between δ 4.47 (CHN) and δ 58.0 ($C(CO_2Et)_2$), 73.1 (CHOH) and between δ 8.15 (Ar) and δ 73.1 (CHOH). IR (neat) 3390, 2982, 1738, 1716, 1614, 1514, 1437, 1370, 1241, 1157, 1108, 1056 cm^{-1}; MS (EI) *m*/*z* 451 (M^+, 18), 350 (73), 304 (60), 260 (100%); HRMS M^+ 451.1841 (calcd for $C_{22}H_{29}NO_9$ 451.1842).

6e: R_f = 0.4 (CH_2Cl_2/ether = 19:1); pale yellow crystals; mp 116−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.10 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.50 (s, 9H), 3.87 (s, 3H), 4.13 (q, *J* = 7.1 Hz, 2H), 4.25 (bs, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 4.45 (s, 1H), 5.24 (bs, 1H), 7.25 (d, *J* = 1.6 Hz, 1H), 7.40 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.52 (d-like, *J* = 8.1 Hz, 1H). Selected NOEs are between δ 5.24 (CHOH) and δ 4.45 (CHN), 7.52 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.8 (q), 14.0 (q), 27.8 (q), 52.0 (q), 57.6 (d), 58.1 (s), 62.1 (t), 62.2 (t), 73.2 (d), 83.5 (s), 114.5 (d), 119.0 (d), 126.0 (d), 127.2 (s), 130.5 (s), 140.4 (s), 167.0 (s), 168.2 (s), 168.4 (s), 168.5 (s). Selected HMBC correlations are between δ 4.45 (CHN) and δ 58.1 ($C(CO_2Et)_2$), 73.2 (CHOH) and between δ 7.52 (Ar) and δ 73.2 (CHOH). IR (KBr) 3505, 3367, 2978, 1744, 1706, 1577, 1473, 1370, 1249, 1153 cm^{-1}; MS (EI) *m*/*z* 451 (M^+, 18), 350 (70), 304 (66), 260 (100%); HRMS M^+ 451.1846 (calcd for $C_{22}H_{29}NO_9$ 451.1842).

6f: R_f = 0.3 (CH_2Cl_2); yellow oil; ^{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), 1.49 (s, 9H), 4.09 (bs, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 4.29−4.35 (m, 2H), 4.39 (s, 1H), 4.76 (bs, 1H), 5.18 (bd, *J* = 11.2 Hz, 1H), 6.45 (d, *J* = 8.6 Hz, 1H), 7.13 (dd, *J* = 8.6, 2.4, 0.7 Hz, 1H), 7.55 (dd, *J* = 2.4, 1.1 Hz, 1H). Selected NOEs are between δ 5.18 (CHOH) and δ 4.39 (CHN), 7.55 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.8 (q), 14.0 (q), 27.8 (q), 57.5 (d), 58.0 (s), 62.1 (t), 62.2 (t), 72.9 (d), 83.5 (s), 109.9 (s), 115.2 (d), 124.5 (s), 128.6 (d), 131.4 (d), 139.5 (s), 168.3 (s), 168.4 (s), 168.5 (s). Selected HMBC correlations are between δ 4.39 (CHN) and δ 58.0 ($C(CO_2Et)_2$), 72.9 (CHOH) and between δ 7.55 (Ar) and δ 72.9 (CHOH). IR (neat) 3491, 3393, 2981, 1738, 1602, 1489, 1370, 1343, 1247, 1156, 1092, 1055 cm^{-1}; MS (EI) *m*/*z* 473 (M^+, 28), 471 (M^+, 31), 372 (69), 370 (70), 326 (79), 324 (83), 282 (99), 280 (100%); HRMS M^+ 471.0883 (calcd for $C_{20}H_{26}{}^{79}BrNO_7$ 471.0893), 473.0906 (calcd for $C_{20}H_{26}{}^{81}BrNO_7$ 473.0872).

Typical Experimental Procedure (Table 1, entry 2). To a solution of **1** (278 mg, 1.02 mmol) in 1,2-dichloroethane (1.9 mL) were added 2-amino-5-chlorobenzaldehyde (**5b**) (156 mg, 1.0 mmol) and $Zn(OTf)_2$ (72 mg, 0.2 mmol). The mixture was heated at 80 °C and stirred for 19 h. The reaction mixture was cooled to 0 °C and quenched with water. The mixture was diluted with dichloromethane, and then saturated aqueous $NaHCO_3$ was added. The organic phase was extracted with dichloromethane, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel with dichloromethane as eluent to give **7b** (318 mg, 90%).

7b: R_f = 0.2 (CH_2Cl_2); colorless crystals; mp 125−128 °C (EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.03 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 3.99−4.11 (m, 1H), 4.12−4.19 (m, 1H), 4.27−4.39 (m, 2H), 4.58 (d, *J* = 3.3 Hz, 1H), 5.09 (bd, *J* = 4.2 Hz, 1H), 5.50 (d, *J* = 1.1 Hz, 1H), 6.56 (d, *J* = 8.5 Hz, 1H), 7.13 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.22 (d, *J* = 2.4 Hz, 1H). Selected NOEs are between δ 5.09 (NH) and δ 4.58 (CHN), 6.56 (Ar) and between δ 5.50 (CHO) and δ 7.22 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.6 (q), 13.9 (q), 56.1 (d), 57.5 (s), 62.3 (t), 63.5 (t), 79.0 (d), 116.1 (d), 121.5 (s), 123.7 (s), 128.2 (d), 130.8 (d), 138.9 (s), 164.0 (s), 166.5 (s), 170.1 (s). Selected HMBC correlations are between δ 4.58 (CHN) and δ 138.9 (Ar), 79.0 (CHO), between δ 5.50 (CHO) and δ 56.1 (CHN), 121.5 (Ar), 57.5 ($C(CO_2Et)_2$), and between δ 7.22 (Ar) and δ 79.0 (CHO). IR (KBr) 3402, 2991, 1792, 1726, 1488, 1305, 1254, 1234, 1144, 1047 cm^{-1}; MS (EI) *m*/*z* 355 (M^+, 5), 353 (M^+, 14), 236 (100%); HRMS M^+ 353.0670 (calcd for $C_{16}H_{16}{}^{35}ClNO_6$ 353.0666), M^+ 355.0635 (calcd for $C_{16}H_{16}{}^{37}ClNO_6$ 355.0637). Anal. Calcd for $C_{16}H_{16}ClNO_6$: C, 54.32; H, 4.56; N, 3.96. Found: C, 54.18; H, 4.56; N, 4.03.

7c: R_f = 0.2 (CH_2Cl_2); colorless crystals; mp 128−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.06 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 4.00−4.08 (m, 1H), 4.10−4.18 (m, 1H), 4.28−4.40 (m, 2H), 4.58 (d, *J* = 2.6 Hz, 1H), 4.91 (bs, 1H), 5.53 (d, *J* = 2.0 Hz, 1H), 6.64 (d, *J* = 2.0 Hz, 1H), 6.77 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 1H). Selected NOEs are between δ 4.91 (NH) and δ 4.58 (CHN), 6.64 (Ar) and between δ 5.53 (CHO) and δ 7.16 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.7 (q), 14.0 (q), 56.0 (d), 57.7 (s), 62.4 (t), 63.5 (t), 79.1 (d), 114.7 (d), 118.8 (s), 119.5 (d), 129.8 (d), 136.7 (s), 141.3 (s), 164.0 (s), 166.5 (s), 169.9 (s). Selected HMBC correlations are between δ 4.58 (CHN) and δ 141.3 (Ar), between δ 5.53 (CHO) and δ 56.0 (CHN), 129.8 (Ar), 57.7 ($C(CO_2Et)_2$), and between δ

7.16 (Ar) and δ 79.1 (*C*HO). IR (KBr) 3393, 2977, 1793, 1730, 1613, 1483, 1304, 1234 cm^{-1}; MS (EI) *m*/*z* 355 (M^+, 30), 353 (M^+, 42), 280 (41), 236 (94), 208 (100%); HRMS M^+ 353.0663 (calcd for $C_{16}H_{16}{}^{35}ClNO_6$ 353.0666), M^+ 355.0648 (calcd for $C_{16}H_{16}{}^{37}ClNO_6$ 355.0637). Anal. Calcd for $C_{16}H_{16}ClNO_6$: C, 54.32; H, 4.56; N, 3.96. Found: C, 54.16; H, 4.61; N, 3.98.

7d: R_f = 0.2 (CH_2Cl_2/ether = 19: 1); colorless crystals; mp 132−134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.992 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 3.87 (s, 3H), 3.98−4.06 (m, 1H), 4.07−4.16 (m, 1H), 4.30−4.40 (m, 2H), 4.65 (dd, *J* = 5.1, 1.3 Hz, 1H), 5.63 (d, *J* = 1.1 Hz, 1H), 5.83 (bd, *J* = 3.8 Hz, 1H), 6.64 (d, *J* = 8.6 Hz, 1H), 7.85 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.96 (d, *J* = 2.0 Hz, 1H). Selected NOEs are between δ 5.83 (N*H*) and δ 4.65 (C*H*N), 6.64 (Ar) and between δ 5.63 (C*H*O) and δ 7.96 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.5 (q), 13.8 (q), 51.8 (q), 55.8 (d), 57.2 (s), 62.3 (t), 63.5 (t), 79.3 (d), 113.9 (d), 119.2 (s), 120.2 (s), 130.5 (d), 132.7 (d), 144.5 (s), 163.8 (s), 166.47 (s), 166.54 (s), 169.7 (s). Selected HMBC correlations are between δ 4.65 (C*H*N) and δ 57.2 (*C*(CO_2Et)$_2$), 144.5 (Ar), 79.3 (*C*HO), between δ 5.63 (C*H*O) and δ 55.8 (*C*HN), 119.2 (Ar), 57.2 (*C*(CO_2Et)$_2$), and between δ 7.96 (Ar) and δ 79.3 (*C*HO). IR (KBr) 3370, 2978, 1793, 1732, 1720, 1622, 1509, 1288, 1102 cm^{-1}; MS (EI) *m*/*z* 377 (M^+, 10), 260 (100), 232 (44%); HRMS M^+ 377.1111 (calcd for $C_{18}H_{19}NO_8$ 377.1111). Anal. Calcd for $C_{18}H_{19}NO_8$: C, 57.29; H, 5.08; N, 3.71. Found: C, 57.17; H, 5.09; N, 3.79.

7e: R_f = 0.2 (CH_2Cl_2); colorless crystals; mp 175−177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.02 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 3.89 (s, 3H), 3.98−4.15 (m, 2H), 4.29−4.41 (m, 2H), 4.62 (bs, 1H), 4.99 (bs, 1H), 5.58 (d, *J* = 0.9 Hz, 1H), 7.31 (d, *J* = 7.7 Hz, 1H), 7.32 (s, 1H), 7.47 (dd, *J* = 7.7, 1.6 Hz, 1H). Selected NOEs are between δ 4.99 (N*H*) and δ 4.62 (C*H*N), 7.32 (Ar) and between δ 5.58 (C*H*O) and δ 7.31 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.7 (q), 14.0 (q), 52.4 (q), 56.1 (d), 57.6 (s), 62.4 (t), 63.6 (t), 79.0 (d), 115.9 (d), 120.3 (d), 124.6 (s), 128.8 (d), 132.6 (s), 140.4 (s), 164.0 (s), 166.47 (s), 166.51 (s), 169.8 (s). Selected HMBC correlations are between δ 4.62 (C*H*N) and δ 140.4 (Ar), 79.0 (*C*HO), between δ 5.58 (C*H*O) and δ 56.1 (*C*HN), 128.8 (Ar), 57.6 (*C*(CO_2Et)$_2$), and between δ 7.31 (Ar) and δ 79.0 (*C*HO). IR (KBr) 3366, 2990, 1813, 1749, 1734, 1707, 1482, 1237 cm^{-1}; MS (EI) *m*/*z* 377 (M^+, 64), 346 (36), 304 (29), 260 (100%); HRMS M^+ 377.1109 (calcd for $C_{18}H_{19}NO_8$ 377.1111). Anal. Calcd for $C_{18}H_{19}NO_8$: C, 57.29; H, 5.08; N, 3.71. Found: C, 56.83; H, 5.01; N, 3.57.

7f: R_f = 0.2 (CH_2Cl_2); colorless crystals; mp 143−145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.04 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 3.99−4.07 (m, 1H), 4.11−4.19 (m, 1H), 4.27−4.39 (m, 2H), 4.58 (dd, *J* = 4.8, 1.3 Hz, 1H), 5.03 (bd, *J* = 4.6 Hz, 1H), 5.49 (d, *J* = 1.3 Hz, 1H), 6.52 (d, *J* = 8.4 Hz, 1H), 7.27 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.36 (d, *J* = 2.3 Hz, 1H). Selected NOEs are between δ 5.03 (N*H*) and δ 4.58 (C*H*N), 6.52 (Ar) and between δ 5.49 (C*H*O) and δ 7.36 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.7 (q), 13.9 (q), 56.0 (d), 57.4 (s), 62.4 (t), 63.5 (t), 78.9 (d), 110.8 (s), 116.5 (d), 122.0 (s), 131.1 (d), 133.7 (d), 139.4 (s), 163.9 (s), 166.5 (s), 167.0 (s). Selected HMBC correlations are between δ 4.58 (C*H*N) and δ 139.4 (Ar), 78.9 (*C*HO), between δ 5.49 (C*H*O) and δ 56.0 (*C*HN), 122.0 (Ar), 57.4 (*C*(CO_2Et)$_2$), and between δ 7.36 (Ar) and δ 78.9 (*C*HO). IR (KBr) 3396, 1795, 1792, 1728, 1485, 1304, 1235, 1142, 1047 cm^{-1}; MS (EI) *m*/*z* 399 (M^+, 33), 397 (M^+, 33), 282 (99), 280 (100%); HRMS M^+ 397.0164 (calcd for $C_{16}H_{16}{}^{79}BrNO_6$ 397.0161), 399.0145 (calcd for $C_{16}H_{16}{}^{81}BrNO_6$ 399.0141).

7g: R_f = 0.5 (CH_2Cl_2/ether = 9: 1); pale yellow crystals; mp 135−136 °C (methanol); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.07 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 4.05−4.20 (m, 2H), 4.29−4.41 (m, 2H), 4.69 (dd, *J* = 4.9, 1.3 Hz, 1H), 5.15 (bd, *J* = 3.8 Hz, 1H), 5.49 (d, *J* = 1.1 Hz, 1H), 7.36 (d, *J* = 2.1 Hz, 1H), 7.58 (d, *J* = 2.1 Hz, 1H). Selected NOEs are between δ 5.15 (N*H*) and δ 4.69 (C*H*N) and between δ 5.49 (C*H*O) and δ 7.36 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.7 (q), 13.9 (q), 55.9 (d), 57.3 (s), 62.5 (t), 63.7 (t), 78.4 (d), 109.1 (s), 110.4 (s), 122.8 (s), 130.6 (d), 135.9 (d), 137.2 (s), 163.6 (s), 166.1 (s), 169.0 (s). Selected HMBC correlations are between δ 4.69 (C*H*N) and δ 137.2 (Ar), 78.4 (*C*HO), between δ 5.49 (C*H*O) and δ 55.9 (*C*HN), 130.6 (Ar), 57.3 (*C*(CO_2Et)$_2$), and between δ 7.36 (Ar) and δ 78.4 (*C*HO). IR (KBr) 3384, 3085, 2984, 1790, 1752, 1722, 1603, 1558, 1481, 1367, 1293, 1272, 1155, 1094 cm^{-1}; MS (EI) *m*/*z* 479 (M^+, 14), 477 (M^+, 28), 475 (M^+, 14), 362 (70), 360 (100), 358 (72), 334 (58), 332 (86), 330 (64%); HRMS M^+ 474.9270 (calcd for $C_{16}H_{15}{}^{79}Br_2NO_6$ 474.9266), 476.9264 (calcd for $C_{16}H_{15}{}^{79}Br^{81}BrNO_6$ 476.9246), 478.9251 (calcd for $C_{16}H_{15}{}^{81}Br_2NO_6$ 478.9225). Anal. Calcd for $C_{16}H_{15}Br_2NO_6$: C, 40.28; H, 3.17; N, 2.94. Found: C, 40.03; H, 3.16; N, 2.95.

Typical Experimental Procedure (Table 3, entry 1). To a solution of **6a** (102 mg, 0.26 mmol) in 1,2-dichloroethane (2.0 mL) was added $Zn(OTf)_2$ (18.7 mg, 0.05 mmol). The mixture was heated at 80 °C and stirred for 24 h. The reaction mixture was cooled to 0 °C and quenched with water. The mixture was diluted with dichloromethane, and then saturated aqueous $NaHCO_3$ was added. The organic phase was extracted with dichloromethane, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel with dichloromethane/hexane as eluent to give **7a** (62 mg, 75%).

7a: R_f = 0.5 (CH_2Cl_2/ether = 5:1); colorless crystals; mp 136−137 °C (methanol); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.995 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 3.96−4.04 (m, 1H), 4.09−4.17 (m, 1H), 4.28−4.40 (m, 2H), 4.58 (d, *J* = 1.3 Hz, 1H), 4.67 (bs, 1H), 5.54 (d, *J* = 0.9 Hz, 1H), 6.63 (d-like, *J* = 7.5 Hz, 1H), 6.80 (td, *J* = 7.5, 1.1 Hz, 1H), 7.18−7.22 (m, 1H), 7.23 (dd, *J* = 7.5, 1.3 Hz, 1H). Selected NOEs are between δ 4.67 (N*H*) and δ 6.63 (Ar) and between δ 5.54 (C*H*O) and δ 7.23 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.7 (q), 14.0 (q), 56.4 (d), 57.9 (s), 62.2 (t), 63.4 (t), 79.8 (d), 114.9 (d), 119.4 (d), 120.5 (s), 128.8 (d), 131.1 (d), 140.3 (s), 164.2 (s), 166.8 (s), 170.3 (s). Selected HMBC correlations are between δ 4.58 (C*H*N) and δ 57.9 (*C*(CO_2Et)$_2$), 140.3 (Ar), 79.8 (*C*HO), between δ 5.54 (C*H*O) and δ 56.4 (*C*HN), 128.8 (Ar), 57.9 (*C*(CO_2Et)$_2$), and between δ 7.23 (Ar) and δ 79.8 (*C*HO). IR (KBr) 3414, 2976, 1785, 1730, 1487, 1302, 1236, 1157, 1049 cm^{-1}; MS (EI) *m*/*z* 319 (M^+, 18), 202 (100), 174 (58%); HRMS M^+ 309.1054 (calcd for $C_{16}H_{17}NO_6$ 319.1056).

8b: R_f = 0.4 (CH_2Cl_2); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.14 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 4.07−4.36 (m, 8H), 4.52 (s, 1H), 5.21 (bs, 1H), 6.52 (d, *J* = 8.5 Hz, 1H), 7.02 (ddd, *J* = 8.5, 2.5, 0.7 Hz, 1H), 7.43 (dd, *J* = 2.5, 0.9 Hz, 1H). Selected NOEs are between δ 5.21 (C*H*OH) and δ 4.52 (C*H*N), 7.43 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.7 (q), 13.9 (q), 14.0 (q), 57.3 (d), 58.1 (s), 62.2 (t), 62.3 (t), 62.5 (t), 72.5 (d), 115.0 (d), 123.3 (s), 124.0 (s), 126.1 (d), 128.7 (d), 138.8 (s), 168.4 (s), 168.5 (s), 169.7 (s). Selected HMBC correlations are between δ 4.52 (C*H*N) and δ 58.1 (*C*(CO_2Et)$_2$), 72.5 (*C*HOH) and between δ 7.43 (Ar) and δ 72.5 (*C*HOH). IR (neat) 3479, 3347, 2983, 1739, 1608, 1489, 1264, 1094, 1055, 1023 cm^{-1}; MS (EI) *m*/*z* 401 (M^+, 30), 399 (M^+, 71), 326 (69), 308 (98), 236 (100%); HRMS M^+ 399.1088 (calcd for $C_{18}H_{22}{}^{35}ClNO_7$ 399.1085), 401.1078 (calcd for $C_{20}H_{26}{}^{37}ClNO_7$ 401.1055).

8c: R_f = 0.4 (CH_2Cl_2); colorless crystals, mp 118−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.15 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 4.08−4.38 (m, 7H), 4.53 (s, 1H), 4.78 (bs, 1H), 5.21 (dd, *J* = 11.9, 0.9 Hz, 1H), 6.59 (d, *J* = 2.0 Hz, 1H), 6.73 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.37 (dd, *J* = 8.2, 1.1 Hz, 1H). Selected NOEs are between δ 5.21 (C*H*OH) and δ 4.53 (C*H*N), 7.37 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.8 (q), 14.0 (q), 14.1 (q), 57.3 (d), 58.3 (s), 62.3 (t), 62.4

(t), 62.5 (t), 72.5 (d), 113.3 (d), 118.5 (d), 121.0 (s), 127.6 (d), 134.3 (s), 141.3 (s), 168.4 (s), 168.5 (s), 169.6 (s). Selected HMBC correlations are between δ 4.53 (C*H*N) and δ 58.3 ($C(CO_2Et)_2$), 72.5 (*C*HOH) and between δ 7.37 (Ar) and δ 72.5 (*C*HOH). IR (KBr) 3490, 3388, 2986, 1739, 1712, 1607, 1488, 1368, 1249, 1092 cm^{-1}; MS (EI) *m*/*z* 401 (M^+, 18), 399 (M^+, 51), 326 (95), 236 (96), 180 (100%); HRMS M^+ 399.1091 (calcd for $C_{18}H_{22}{}^{35}ClNO_7$ 399.1085), 401.1046 (calcd for $C_{20}H_{26}{}^{37}ClNO_7$ 401.1055). Anal. Calcd for $C_{18}H_{22}ClNO_7$: C, 54.07; H, 5.55; N, 3.50. Found: C, 53.86; H, 5.47; N, 3.52.

8d: R_f = 0.3 (CH_2Cl_2/ether = 19: 1); pale yellow crystals; mp 135−136 °C (EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.11 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 3.86 (s, 3H), 4.02 (bd, *J* = 11.9 Hz, 1H), 4.06−4.40 (m, 6H), 4.59 (s, 1H), 5.16 (bs, 1H), 5.25 (d, *J* = 11.9 Hz, 1H), 6.59 (d, *J* = 8.4 Hz, 1H), 7.78 (ddd, *J* = 8.4, 2.0, 0.7 Hz, 1H), 8.16 (dd, *J* = 2.0, 1.2 Hz, 1H). Selected NOEs are between δ 5.25 (C*H*OH) and δ 4.59 (C*H*N), 8.16 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.7 (q), 14.0 (q), 14.1 (q), 51.7 (q), 57.2 (d), 58.1 (s), 62.3 (t), 62.5 (t), 62.6 (t), 72.7 (d), 113.0 (d), 119.8 (s), 121.6 (s), 128.3 (d), 130.9 (d), 144.3 (s), 167.1 (s), 168.30 (s), 168.34 (s), 169.4 (s). Selected HMBC correlations are between δ 4.59 (C*H*N) and δ 58.1 ($C(CO_2Et)_2$), 72.7 (*C*HOH) and between δ 8.16 (Ar) and δ 72.7 (*C*HOH). IR (KBr) 3501, 3384, 2982, 1741, 1730, 1701, 1615, 1518, 1436, 1371, 1303, 1246, 1231, 1112 cm^{-1}; MS (EI) *m*/*z* 423 (M^+, 36), 350 (98), 260 (100%); HRMS M^+ 423.1530 (calcd for $C_{20}H_{25}NO_9$ 423.1529). Anal. Calcd for $C_{20}H_{25}NO_9$: C, 56.73; H, 5.95; N, 3.31. Found: C, 56.64; H, 5.91; N, 3.37.

8e: R_f = 0.2 (CH_2Cl_2); pale yellow crystals; mp 96−98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.13 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 3.87 (s, 3H), 4.06−4.39 (m, 7H), 4.57 (s, 1H), 4.88 (bs, 1H), 5.27 (bd, *J* = 4.9 Hz, 1H), 7.28 (d, *J* = 1.5 Hz, 1H), 7.43 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.54 (dd, *J* = 8.0, 0.9 Hz, 1H). Selected NOEs are between δ 5.27 (C*H*OH) and δ 4.57 (C*H*N), 7.54 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.7 (q), 13.9 (q), 14.0 (q), 52.1 (q), 57.3 (d), 58.2 (s), 62.2 (t), 62.3 (t), 62.5 (t), 72.7 (d), 114.7 (d), 119.3 (d), 126.3 (d), 127.1 (s), 130.6 (s), 140.3 (s), 167.0 (s), 168.4 (s), 168.5 (s), 169.6 (s). Selected HMBC correlations are between δ 4.57 (C*H*N) and δ 58.2 ($C(CO_2Et)_2$), 72.7 (*C*HOH) and between δ 7.54 (Ar) and δ 72.7 (*C*HOH). IR (KBr) 3483, 3389, 2989, 1735, 1718, 1486, 1251, 1099 cm^{-1}; MS (EI) *m*/*z* 423 (M^+, 6), 350 (24), 260 (57), 171 (79), 143 (100%); HRMS M^+ 423.1527 (calcd for $C_{20}H_{25}NO_9$ 423.1529). Anal. Calcd for $C_{20}H_{25}NO_9$: C, 56.73; H, 5.95; N, 3.31. Found: C, 56.65; H, 5.79; N, 3.41.

8f: R_f = 0.4 (CH_2Cl_2); colorless crystals (EtOAc); mp 80−82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.14 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 4.07−4.39 (m, 7H), 4.51 (s, 1H), 4.73 (bs, 1H), 5.21 (d, *J* = 11.9 Hz, 1H), 6.47 (d, *J* = 8.6 Hz, 1H), 7.16 (ddd, *J* = 8.6, 2.3, 0.7 Hz, 1H), 7.57 (dd, *J* = 2.3, 1.1 Hz, 1H). Selected NOEs are between δ 5.21 (C*H*OH) and δ 4.51 (C*H*N), 7.57 (Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.7 (q), 14.0 (q), 14.1 (q), 57.3 (d), 58.1 (s), 62.3 (t), 62.4 (t), 62.5 (t), 72.5 (d), 110.3 (s), 115.4 (d), 124.4 (s), 129.0 (d), 131.6 (d), 139.3 (s), 168.4 (s), 168.5 (s), 169.6 (s). Selected HMBC correlations are between δ 4.51 (C*H*N) and δ 58.1 ($C(CO_2Et)_2$), 72.5 (*C*HOH) and between δ 7.57 (Ar) and δ 72.5 (*C*HOH). IR (KBr) 3463, 3388, 2983, 1734, 1600, 1491, 1242, 1052 cm^{-1}; MS (EI) *m*/*z* 445 (M^+, 24), 443 (M^+, 25), 372 (33), 370 (34), 280 (45), 252 (46), 199 (50), 171 (84), 143 (100%); HRMS M^+ 443.0582 (calcd for $C_{18}H_{22}{}^{79}BrNO_7$ 443.0580), 445.0518 (calcd for $C_{18}H_{22}{}^{81}BrNO_7$ 445.0559). Anal. Calcd for $C_{18}H_{22}BrNO_7$: C, 48.66; H,4.99; N, 3.15. Found: C, 48.62; H, 4.86; N, 2.96.

Typical Experimental Procedure (Table 5, entry 2). Compound **7b** (100 mg, 0.283 mmol) was heated in a closed vessel (50 mL) at 180 °C for 18 h. After cooling, the residue was purified by column chromatography over silica gel with CH_2Cl_2 as eluent to give **9b** (74 mg, 84%).

9b: R_f = 0.2 (CH_2Cl_2); brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.28 (t, *J* = 7.1 Hz, 6H), 4.18−4.30 (m, 4H), 4.86 (d, *J* = 0.5 Hz, 1H), 7.11 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 1H), 7.29 (bs, 1H), 7.62 (d, *J* = 2.0 Hz, 1H), 8.45 (bs, 1H). Selected NOEs are between δ 8.45 (N*H*) and δ 7.29 (indole-2-*H*), 7.19 (indole-7-*H*) and between δ 4.86 (C*H*(CO_2Et)$_2$) and δ 7.29 (indole-2-*H*), 7.62 (indole-4-*H*).[10] ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.1 (q), 49.8 (d), 62.0 (t), 107.2 (s), 112.5 (d), 118.8 (d), 122.7 (d), 125.6 (d), 125.8 (s), 127.6 (s), 134.4 (s), 168.6 (s). Selected HMBC correlations are between δ 4.86 (C*H*(CO_2Et)$_2$) and δ 127.6 (indole-*C*-9), 107.2 (indole-*C*-3), 125.6 (indole-*C*-2). IR (neat) 3376, 2982, 1732, 1464, 1370, 1302, 1177, 1153, 1029 cm^{-1}; MS (EI) *m*/*z* 311 (M^+, 13), 309 (M^+, 38), 238 (34), 236 (100%); HRMS M^+ 309.0771 (calcd for $C_{15}H_{16}{}^{35}ClNO_4$ 309.0768), 311.0743 (calcd for $C_{15}H_{16}{}^{37}ClNO_4$ 311.0738).

9a: R_f = 0.2 (CH_2Cl_2); brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.27 (t, *J* = 7.1 Hz, 6H), 4.17−4.29 (m, 4H), 4.94 (d, *J* = 0.4 Hz, 1H), 7.12−7.16 (m, 1H), 7.18−7.22 (m, 1H), 7.35 (d-like, *J* = 8.1 Hz, 1H), 7.38 (d, *J* = 2.4 Hz, 1H), 7.66 (d-like, *J* = 7.9 Hz, 1H), 8.25 (bs, 1H). Selected NOEs are between δ 8.25 (N*H*) and δ 7.38 (indole-2-*H*), and between δ 4.94 (C*H*(CO_2Et)$_2$) and δ 7.38 (indole-2-*H*), 7.66 (indole-4-*H*). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.1 (q), 49.8 (d), 61.8 (t), 107.7 (s), 111.4 (d), 119.2 (d), 120.0 (d), 122.4 (d), 124.1 (d), 126.6 (s), 136.0 (s), 168.7 (s). Selected HMBC correlations are between δ 4.94 (C*H*(CO_2Et)$_2$) and δ 126.6 (indole-*C*-9), 107.7 (indole-*C*-3), 124.1 (indole-*C*-2). IR (neat) 3400, 2982, 1732, 1458, 1369, 1301, 1176, 1149, 1029 cm^{-1}; MS (EI) *m*/*z* 275 (M^+, 59), 202 (100), 130 (45%); HRMS M^+ 275.1158 (calcd for $C_{15}H_{17}NO_4$ 275.1158).

9c: R_f = 0.2 (CH_2Cl_2); brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.27 (t, *J* = 7.1 Hz, 6H), 4.18−4.29 (m, 4H), 4.88 (d, *J* = 0.5 Hz, 1H), 7.10 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.32 (d, *J* = 1.8 Hz, 1H), 7.34 (d, *J* = 2.6 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 8.30 (bs, 1H). Selected NOEs are between δ 8.30 (N*H*) and δ 7.34 (indole-2-*H*), 7.32 (indole-7-*H*) and between δ 4.88 (C*H*(CO_2Et)$_2$) and δ 7.34 (indole-2-*H*), 7.56 (indole-4-*H*). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.1 (q), 49.8 (d), 62.0 (t), 107.9 (s), 111.3 (d), 120.3 (d), 120.8 (d), 124.8 (d), 125.2 (s), 128.4 (s), 136.4 (s), 168.5 (s). Selected HMBC correlations are between δ 4.88 (C*H*(CO_2Et)$_2$) and δ 125.2 (indole-*C*-9), 107.9 (indole-*C*-3), 124.8 (indole-*C*-2). IR (neat) 3375, 2982, 1733, 1620, 1456, 1302, 1029 cm^{-1}; MS (EI) *m*/*z* 311 (M^+, 46), 309 (M^+, 99), 238 (80), 236 (100%); HRMS M^+ 309.0770 (calcd for $C_{15}H_{16}{}^{35}ClNO_4$ 309.0768), 311.0725 (calcd for $C_{15}H_{16}{}^{37}ClNO_4$ 311.0738).

9d: R_f = 0.2 (CH_2Cl_2/ether = 19:1) including a small amount of impurity (possibly the corresponding monoester[3]); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.28 (t, *J* = 7.1 Hz, 6H), 3.92 (s, 3H), 4.20−4.30 (m, 4H), 4.97 (d, *J* = 0.5 Hz, 1H), 7.29 (d, *J* = 8.6 Hz, 1H), 7.35 (d, *J* = 2.4 Hz, 1H), 7.87 (dd, *J* = 8.6, 1.6 Hz, 1H), 8.42−8.43 (m, 1H), 8.82 (bs, 1H). Selected NOEs are between δ 8.82 (N*H*) and δ 7.35 (indole-2-*H*), 7.29 (indole-7-*H*) and between δ 4.97 (C*H*(CO_2Et)$_2$) and δ 7.35 (indole-2-*H*), 8.42−8.43 (indole-4-*H*). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.1 (q), 49.6 (d), 51.9 (q), 62.0 (t), 108.8 (s), 111.2 (d), 122.0 (s), 122.1 (d), 123.7 (d), 125.7 (d), 126.2 (s), 138.7 (s), 168.2 (s), 168.6 (s). Selected HMBC correlations are between δ 4.97 (C*H*(CO_2Et)$_2$) and δ 126.2 (indole-*C*-9), 108.8 (indole-*C*-3), 125.7 (indole-*C*-2). IR (neat) 3357, 2983, 1705−1747, 1621, 1439, 1370, 1242, 1110, 1029 cm^{-1}; MS (EI) *m*/*z* 333 (M^+, 39), 302 (18), 260 (86), 188 (100%); HRMS M^+ 333.1211 (calcd for $C_{17}H_{19}NO_6$ 333.1212).

9e: R_f = 0.2 (CH_2Cl_2/ether = 19:1); brown crystals; mp = 86−88 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.27 (t, *J* = 7.1 Hz, 6H), 3.92 (s, 3H), 4.18−4.30 (m, 4H), 4.94 (d, *J* = 0.4 Hz,

1H), 7.48 (d, J = 2.6 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.81 (dd, J = 8.4, 1.5 Hz, 1H), 8.05 (dd, J = 1.5, 0.7 Hz, 1H), 8.88 (bs, 1H). Selected NOEs are between δ 8.88 (N*H*) and δ 7.48 (indole-2-*H*), 8.05 (indole-7-*H*) and between δ 4.94 (C*H*(CO_2Et)$_2$) and δ 7.48 (indole-2-*H*), 7.66 (indole-4-*H*). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.1 (q), 49.7 (d), 52.0 (q), 62.0 (t), 107.8 (s), 113.9 (d), 118.7 (d), 121.0 (d), 124.0 (s), 127.7 (d), 130.1 (s), 135.4 (s), 168.1 (s), 168.6 (s). Selected HMBC correlations are between δ 4.94 (C*H*(CO_2Et)$_2$) and δ 130.1 (indole-*C*-9), 107.8 (indole-*C*-3), 127.7 (indole-*C*-2). IR (KBr) 3374, 1744, 1707, 1458, 1437, 1319, 1210 cm^{-1}; MS (EI) m/z 333 (M$^+$, 36), 260 (100), 188 (98%); HRMS M$^+$ 333.1208 (calcd for $C_{17}H_{19}NO_6$ 333.1212).

9f: R_f = 0.2 (CH_2Cl_2); brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.28 (t, J = 7.1 Hz, 6H), 4.18−4.30 (m, 4H), 4.86 (s, 1H), 7.11 (d, J = 8.7 Hz, 1H), 7.220 (d, J = 3.1 Hz, 1H), 7.223 (dd, J = 8.7, 2.0 Hz, 1H), 7.77 (d, J = 2.0 Hz, 1H), 8.50 (bs, 1H). Selected NOEs are between δ 8.50 (N*H*) and δ 7.220 (indole-2-*H*), 7.11 (indole-7-*H*) and between δ 4.86 (C*H*(CO_2Et)$_2$) and δ 7.220 (indole-2-*H*), 7.77 (indole-4-*H*). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.1 (q), 49.7 (d), 62.0 (t), 107.0 (s), 112.9 (d), 113.3 (s), 121.8 (d), 125.2 (d), 125.5 (d), 128.2 (s), 134.7 (s), 168.6 (s). Selected HMBC correlations are between δ 4.86 (C*H*(CO_2Et)$_2$) and δ 128.2 (indole-*C*-9), 107.0 (indole-*C*-3). IR (neat) 3377, 2982, 1733, 1464, 1369, 1303, 1240, 1176, 1152, 1029 cm^{-1}; MS (EI) m/z 355 (M$^+$, 23), 353 (M$^+$, 23), 282 (57), 281 (60), 280 (58), 279 (53), 236 (59), 234 (59), 208 (60), 100 (62), 84 (100%); HRMS M$^+$ 353.0264 (calcd for $C_{15}H_{16}{}^{79}BrNO_4$ 353.0263), 355.0251 (calcd for $C_{15}H_{16}{}^{81}BrNO_4$ 355.0242).

9g: R_f = 0.3 (CH_2Cl_2); brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.28 (t, J = 7.1 Hz, 6H), 4.19−4.30 (m, 4H), 4.83 (s, 1H), 7.40 (d, J = 2.6 Hz, 1H), 7.44 (d, J = 1.6 Hz, 1H), 7.75 (dd, J = 1.6, 0.5 Hz, 1H), 8.59 (bs, 1H). Selected NOEs are between δ 8.59 (N*H*) and δ 7.40 (indole-2-*H*) and between δ 4.83 (C*H*(CO_2Et)$_2$) and δ 7.40 (indole-2-*H*), 7.75 (indole-4-*H*). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.1 (q), 49.9 (d), 62.1 (t), 105.3 (s), 108.5 (s), 113.1 (s), 121.5 (d), 126.1 (d), 127.0 (d), 128.7 (s), 133.6 (s), 168.2 (s). Selected HMBC correlations are between δ 4.83 (C*H*(CO_2Et)$_2$) and δ 126.1 (indole-*C*-2), 108.5 (indole-*C*-3). IR (neat) 3359, 2981, 1730, 1556, 1466, 1369, 1301, 1180, 1153, 1029 cm^{-1}; MS (EI) m/z 435 (M$^+$, 44), 433 (M$^+$, 66), 431 (M$^+$, 44), 362 (78), 360 (100), 358 (78), 288 (77%); HRMS M$^+$ 430.9359 (calcd for $C_{15}H_{15}{}^{79}Br_2NO_4$ 430.9368), 432.9348 (calcd for $C_{15}H_{16}{}^{79}Br^{81}BrNO_4$ 432.9347), 434.9346 (calcd for $C_{15}H_{16}{}^{81}Br_2NO_4$ 434.9327). Anal. Calcd for $C_{15}H_{15}Br_2NO_4$: C, 41.60; H,3.49; N, 3.23. Found: C, 41.33; H, 3.33; N, 3.22.

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Supporting Information Available: Figures S1−S3, Cartesian coordinates of the optimized geometries of Figures 1 and 2 and S1−S3, and ^{1}H and ^{13}C NMR data. This material is available free of charge via the Internet at http://pubs.acs.org.