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Synthesis of Unprotected 2-Arylglycines by Transamination of Arylglyoxylic Acids with 2-(2-Chlorophenyl)glycine

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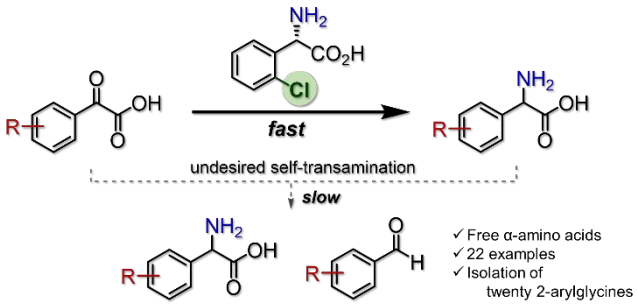


Abstract: The transamination of α-keto acids with 2-phenylglycine is an effective methodology for directly synthesizing unprotected α-amino acids. However, the synthesis of 2-arylglycines by transamination is problematic because the corresponding products 2-arylglycines transaminate the starting arylglyoxylic acids. Herein, we demonstrate the use of commercially available L-2-(2-chlorophenyl)glycine as the nitrogen source in the transamination of arylglyoxylic acids, producing the corresponding 2-arylglycines without interference from the undesired self-transamination process.

INTRODUCTION

2-Arylglycines comprise an important class of non-proteinogenic α-amino acids, which are found in peptide drugs, antibiotics such as amoxicillin, cefprozil and vancomycin, and other biologically active compounds (Figure 1).[1,2] Although the Strecker synthesis is their most reliable preparation method, it requires toxic cyanide reagents and harsh conditions for hydrolysis of the α-amino nitriles.[3] Harmless and effective alternative methods have also been developed, including the addition of arylboronic acids to α-imino acids (Petasis reaction),[4] reduction of α-iminoesters,[5] α-arylation of glycine derivatives,[6] and carboxylation using CO_2 as a C1 source for benzyl amine derivatives.[7,8] These methods afford protected 2-arylglycines, which require an additional step for deprotection to access unprotected 2-arylglycines. There are few methods to directly prepare unprotected 2-arylglycines.[9] Therefore, the development of a versatile preparation method would be desirable.

In biological systems, the transamination of α-keto acids is used to synthesize α-amino acids; the reaction is catalyzed by transaminases using pyridoxal/pyridoxamine 5'-phosphate as a coenzyme.[10] This process affords unprotected α-amino acids. In 1934, Herbst and Engel reported thermally promoted biomimetic transaminations between α-keto acids and 2-phenylglycine without any catalysts to form the corresponding unprotected α-amino acids (Scheme 1a).[11] Although related research has been reported, the methods have not been applied to organic synthesis.[12,13] Intrigued by the potential usefulness of transamination, we recently reported a modified protocol.[14] Combining transamination with the oxidation of 1,2-diols to α-keto acids, we established a direct method for the synthesis of unprotected α-amino acids. Owing to the method's high functional group compatibility, a variety of unnatural α-amino acids including fluorescent and photoactivatable species were prepared.[14b]

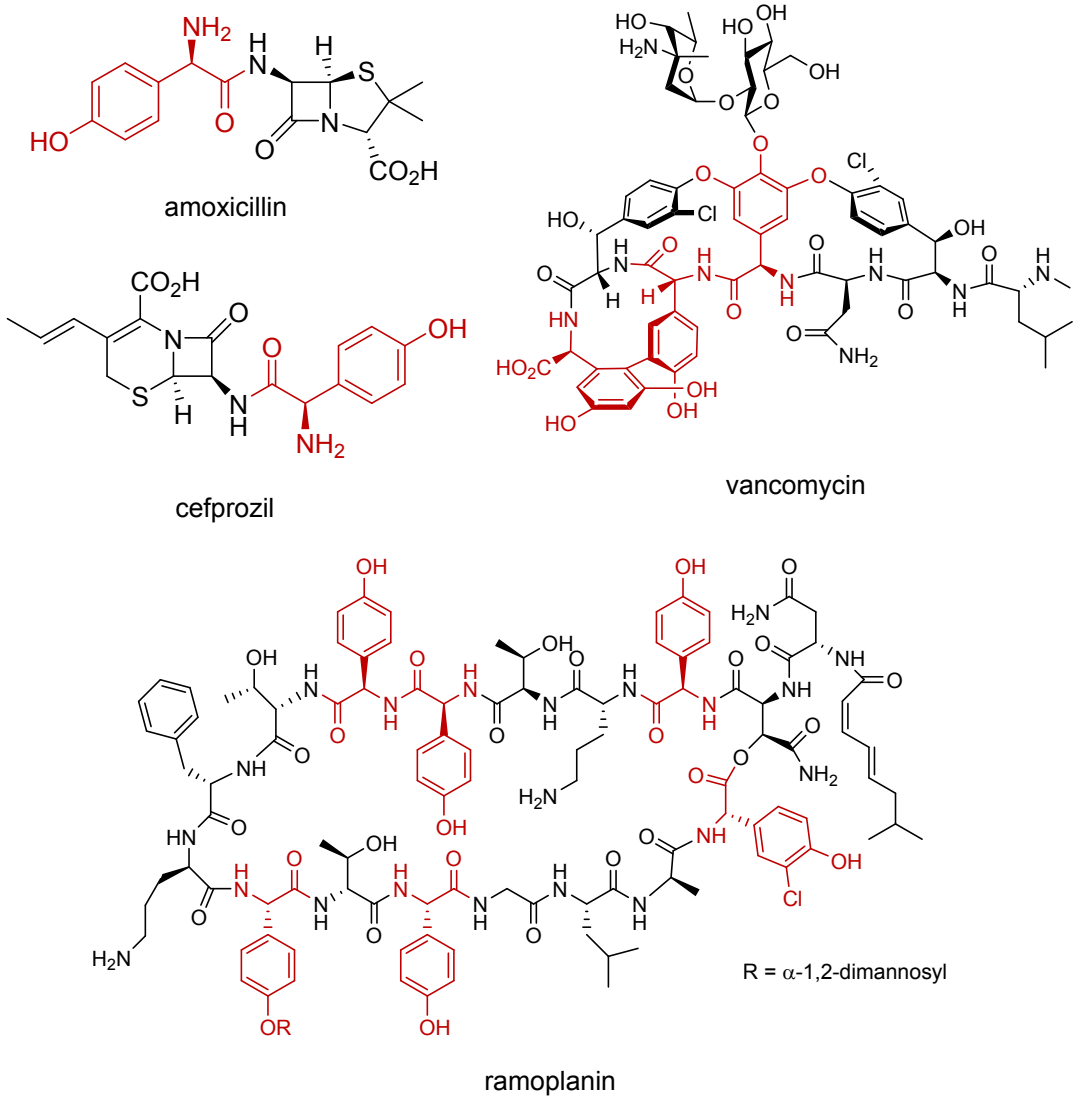


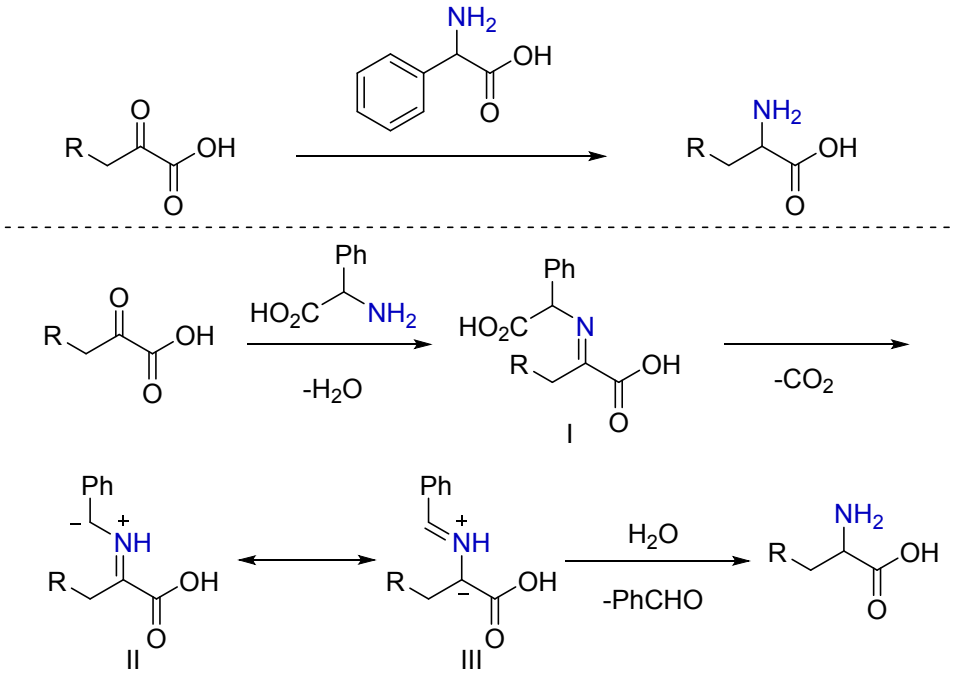
Figure 1. Arylglycine-containing drugs.

In the thermal transamination, 2-phenylglycine is used as a nitrogen source (Scheme 1a). The phenyl group at the 2-position stabilizes the benzylic anion to promote the decarboxylation of intermediate **I** under the reaction conditions. Thus, alkyl-substituted glyoxylic acids efficiently undergo transamination to produce the corresponding α-amino acids. On the other hand, in the transamination between 2-phenylglycine and arylglyoxylic acids, the formed 2-arylglycine can undergo transamination with the starting arylglyoxylic acid as the nitrogen source (Scheme 1b). This self-transamination is a potential problem for the preparation of 2-arylglycines by transamination. Herein, we report

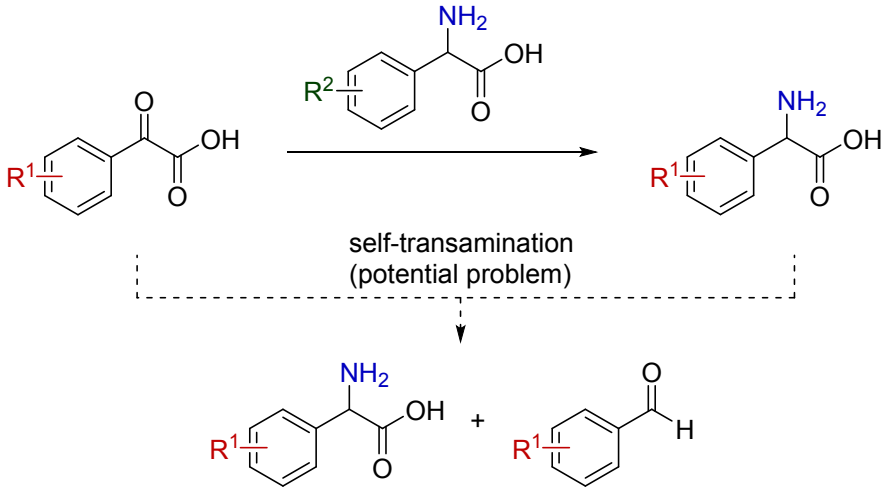
that L-2-(2-chlorophenyl)glycine efficiently transaminates arylglyoxylic acids as the nitrogen source to afford the corresponding 2-arylglycines.

Scheme 1. Transamination of α-Keto Acids with 2-Arylglycines: Prior and Current Work

a) Transamination of α-Keto Acids with 2-Phenylglycine[11]



b) This Work: Transamination of Arylglyoxylic Acid



RESULTS AND DISCUSSION

We initially investigated the transamination of 4-chlorophenylglyoxylic acid with 2-phenylglycine (Scheme 2).

Almost no reaction occurred at 50 °C. This suggests that a higher temperature is required for transamination with 2-phenylglycine. To identify a more effective nitrogen source, transaminations of phenylglyoxylic acid (**1a**) with various 2-arylglycines were examined at 50 °C (Table 1). Gratifyingly, the reaction of **1a** with L-2-(2-chlorophenyl)glycine(1 equiv) produced 2-phenylglycine (**2a**) in 29% yield after 5 h at 50 °C (entry 1). The reaction with DL-2-(2-chlorophenyl)glycine afforded **2a** in slightly lower yield, presumably because of the lower solubility of the racemic reagent over the L-isomer (entry 2). Several other 2-(2-substituted-phenyl)glycines exhibited high reactivities similar to that of L-2-(2-chlorophenyl)glycine (entries 3–7), whereas 2-(2-fluorophenyl)glycine and 2-(2-methylphenyl)glycine exhibited low reactivities (entries 8 and 9). Interestingly, 2-(3-chlorophenyl)glycine and 2-(4-chlorophenyl)glycine did not undergo the reaction at 50 °C (entries 10 and 11). According to these results, we selected L-2-(2-chlorophenyl)glycine as the optimal nitrogen source because of its advantageous commercial availability among the 2-arylglycines with the high reactivities. Although a nitrogen source is L-2-(2-chlorophenyl)glycine, the desired 2-arylglycines are obtained in racemic form. The reaction conditions were then optimized. Extending the reaction time to 24 h improved the yield of **2a** to 50% (entry 12). Increasing the quantity of L-2-(2-chlorophenyl)glycine to 1.5 equiv slightly improved the yield of **2a** to 59% (entry 13). Increasing the quantity of L-2-(2-chlorophenyl)glycine to 2.0 equiv further improved the yield to 71% (entry 14).

Scheme 2. Transamination of 4-Chlorophenylglyoxylic Acid with 2-Phenylglycine

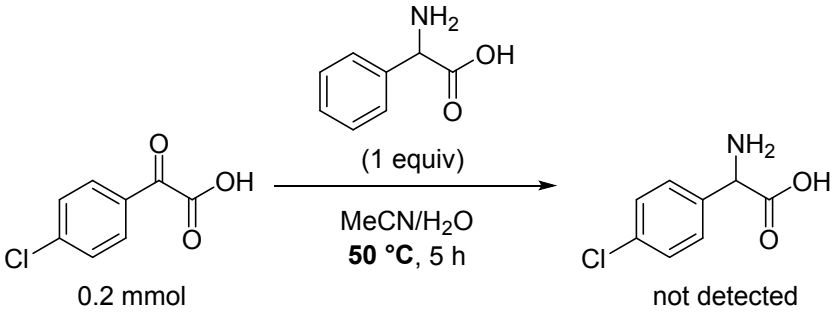
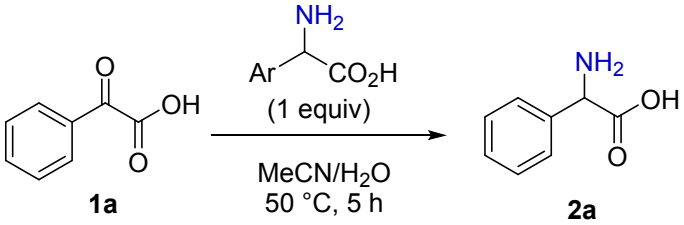


Table 1. Transamination Using 2-(Substituted-phenyl)glycines and Optimization of Reaction Conditions



1a **2a**

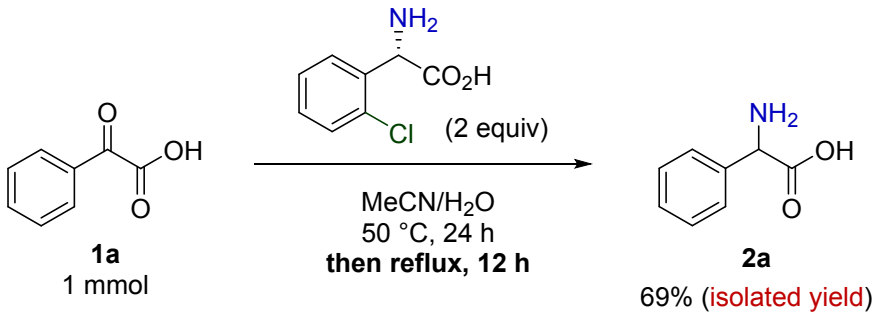
entry	nitrogen source	yield (%)[a]
1	Ar = 2-Cl-C_6H_4[b]	29
2	Ar = 2-Cl-C_6H_4[c]	23
3	Ar = 2-Br-C_6H_4[c]	29
4	Ar = 2-MeO-C_6H_4[c]	25
5	Ar = 2-HO-C_6H_4[c]	23
6	Ar = 2-CF_3-C_6H_4[c]	28
7	Ar = 2-Ph-C_6H_4[c]	30
8	Ar = 2-F-C_6H_4[c]	7
9	Ar = 2-CH_3-C_6H_4[c]	7
10	Ar = 3-Cl-C_6H_4[c]	0
11	Ar = 4-Cl-C_6H_4[c]	0
12[d]	Ar = 2-Cl-C_6H_4[b]	50
13[d,e]	Ar = 2-Cl-C_6H_4[b]	59
14[d,f]	Ar = 2-Cl-C_6H_4[b]	71

[a]Yields were determined by ^{1}H NMR using 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) as an internal standard. [b]L-Isomer. [c]Racemate. [d]Reaction time was 24 h. [e]1.5 equiv of nitrogen source was used. [f]2.0 equiv of nitrogen source was used

As the yields were determined by ^{1}H NMR analysis of the crude products in the foregoing examination, an isolation protocol was investigated (Scheme 3). The crude products contained unreacted L-2-(2-chlorophenyl)glycine and 2-chlorobenzaldehyde as the major impurities. Separation of the desired product **2a** and unreacted L-2-(2-chlorophenyl)glycine is a particularly formidable problem owing to their similar physical properties. Eventually, we found that simply refluxing the reaction mixture induced the degradation of L-2-(2-chlorophenyl)glycine. After 12 h,

the L-2-(2-chlorophenyl)glycine was almost completely consumed. After precipitation by the addition of diethyl ether to the reaction mixture, the precipitate was washed with acetonitrile and water to afford the desired racemic product **2a** in 69% isolated yield.

Scheme 3. Isolation of 2a



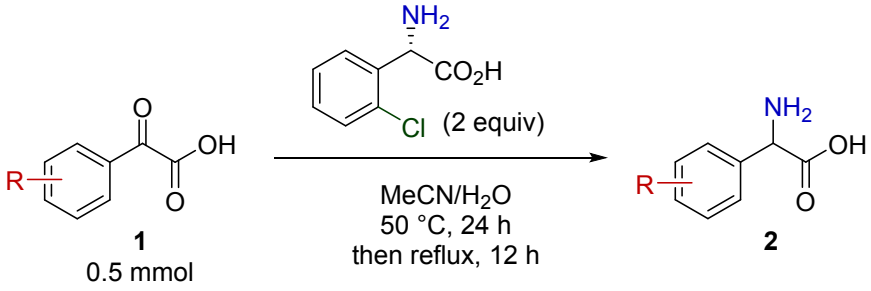
1a
1 mmol

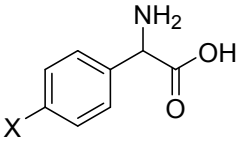
2a
69% (isolated yield)

With the optimal reaction conditions and isolation protocol in hand, the substrate scope was investigated (Scheme 4). First, the effects of the substituents at the 4-position of **1** were examined. The reactions of 4-halo-substituted phenylglyoxylic acids efficiently proceeded to produce arylglycines **2b**–**d** in 50–62% yields. The reaction of highly electron-withdrawing 4-trifluoromethyl-substituted phenylglyoxylic acid **1e** also efficiently proceeded to produce arylglycine **2e** in 67% NMR yield. However, heating to reflux led to the decomposition of **2e**. Thus, the reaction was stopped without heating to reflux and **2e** was isolated by reprecipitation in 38% yield (See the Experimental Section for details). Highly electron-withdrawing 4-benzyloxycarbonyl-substituted phenylglycine **2f** was not obtained because it readily decomposed under the reaction conditions. Moderately electron-donating methyl-, *tert*-butyl-, and phenylglycines **2g** and **2h**, and phenyl-substituted phenylglycine **2i** were obtained in good to high isolated yields (45–79%). The highly electron-donating 4-methoxy-substituted phenylglycine **2j** was obtained in 63% isolated yields. Although the reaction of 4-dimethylamino-substituted phenylglyoxylic acid **1k** was slow, the desired product **2k** was obtained in 40% isolated yield after 3 days. Interestingly, labile 4-chloromethyl-substituted phenylglycine **2l** was

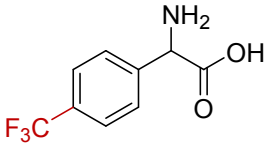
obtained in 44% isolated yield without notable decomposition, which suggests high functional group compatibility. Arylglycines **2m** and **2n** having moderately electron-withdrawing chloro- and electron-donating methoxy-substituents at the 3-positions were also efficiently formed in 55% (isolated) and 59% (NMR) yields, respectively. Because **2n** was partly decomposed by heating to reflux, the isolated yield was 38%. 2-Substituted phenylglyoxylic acids **1o−r** were transformed into the corresponding arylglycines **2o−r** in high NMR yields. Since 2-(2-bromophenyl)glycine (**2r**) exhibited good reactivity as the nitrogen source as shown in Table 1, its self-transamination was a concern. Nonetheless, **2r** was produced in 61% NMR yield. Hence, the transamination of 2-chlorophenylglyoxylic acid with **2r** was also examined (Scheme 5); the reaction afforded L-2-(2-chlorophenyl)glycine in lower NMR yield (26%). These results suggest that L-2-(2-chlorophenyl)glycine has higher reactivity as the nitrogen source than 2-(2-bromophenyl)glycine (**2r**). Because heating at reflux degraded **2o**–**r**, their isolations were difficult. Only arylglycines **2o** and **2p** could be isolated in moderate yields. 2-(2-Naphthyl)glycine (**2s**) was obtained in 72% isolated yield. Finally, we tried to prepare 2-(4-hydroxyphenyl)glycine and its derivatives, *O*-benzylated 2-(3-chloro-4-hydroxyphenyl)glycine and 2-(3,5-dihydroxyphenyl)glycine, which are important unnatural α-amino acids contained in biologically active peptides (Figure 1).[1] Although the reaction to prepare 2-(3,5-dibenzyloxyphenyl)glycine produced a complex mixture, arylglycines **2t−w** were obtained in 48−65% isolated yields. Phenolic hydroxy group, and allyl and benzyl ethers are compatible. These products are useful building blocks to synthesize the biologically active peptides. We also examined the reactions of alkylglyoxylic acids. α-Amino acids **3a-c** were obtained in high yields. It suggests that this method is effective to the synthesis of arylglycines as well as α-amino acids having alkyl side chains.

Scheme 4. Substrate Scope[a]

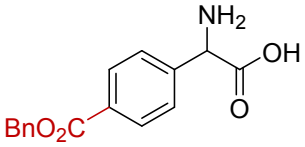




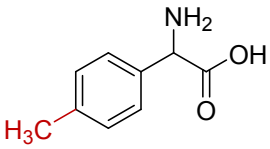
X = F **2b**, 50% (62%)[b]
X = Cl **2c**, 61%
X = Br **2d**, 62%



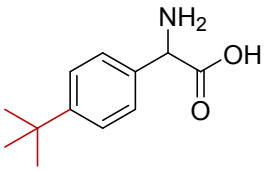
2e, 38%[c,d] (67%)[b]



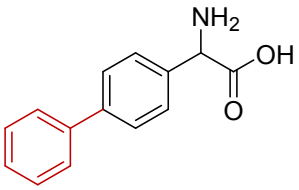
2f, 0%



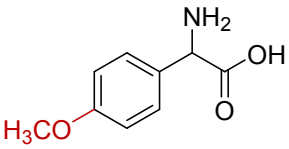
2g, 62%



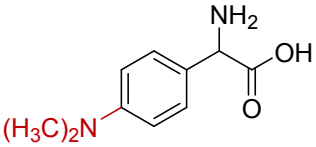
2h, 45% (61%)[b]



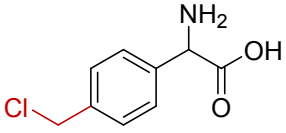
2i, 79%



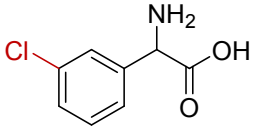
2j, 63%



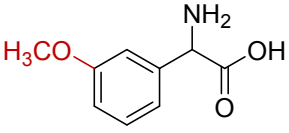
2k, 40%[e]



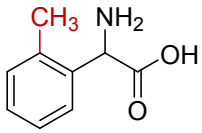
2l, 44%



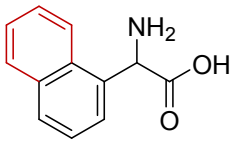
2m, 55%



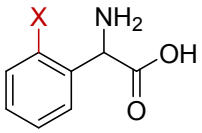
2n, 38% (59%)[b]



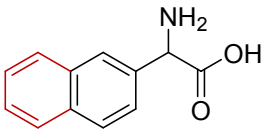
2o, 44% (80%)[b]



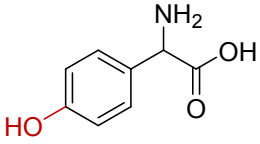
2p, 36%[c,d] (71%)[b]



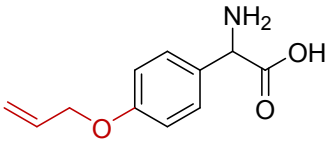
X = F **2q**, (82%)[b]
X = Br **2r**, (61%)[b]



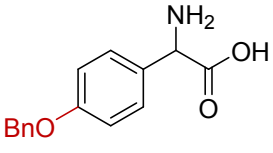
2s, 72%



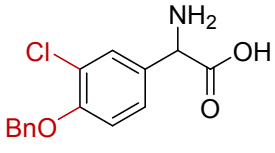
2t, 48%



2u, 65%

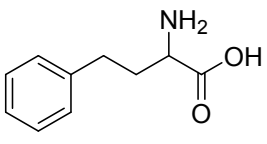


2v, 50%[c]

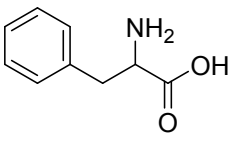


2w, 63%

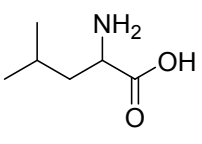
From Alkylglyoxylic Acid



3a, 82%



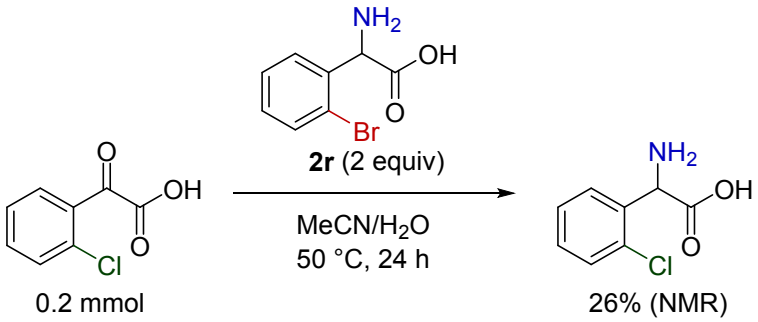
3b, 80%



3c, 68%

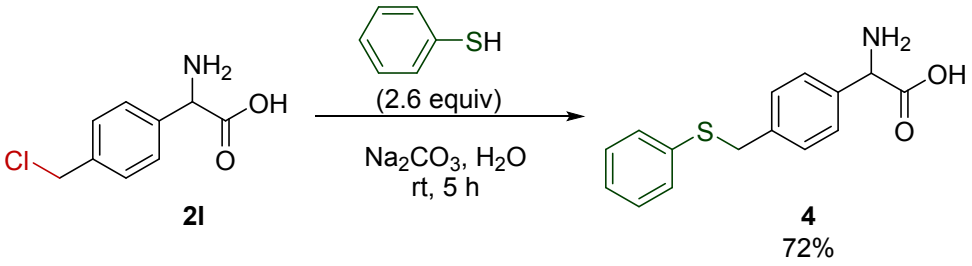
[a]Isolated yield. [b]Percentages in parentheses are the yields determined by ^{1}H NMR using DSS as an internal standard. These reactions were separately conducted on 0.2 mmol scale from the reactions to determine isolated yields, and worked up without heating to reflux. [c]Isolated as the HCl salt. [d]The reactions were worked up without heating to reflux. [e]Reaction time was 3 days.

Scheme 5. Transamination of 2-Chlorophenylglyoxylic Acid with 2-(2-Bromophenyl)glycine (2r)



Arylglycine **2l** has a chloromethylphenyl moiety as a handle for further modification. To demonstrate the utility of **2l**, its coupling with benzene thiolate anion was examined (Scheme 6). The reaction efficiently proceeded in the presence of the unprotected α-amino acid moiety to afford thioether **4** in 72% isolated yield.

Scheme 6. Derivatization of 2l



As above, L-2-(2-chlorophenyl)glycine enabled the synthesis of a variety of 2-arylglycines by the transamination of arylglyoxylic acids. The effect of the chloro substituent at the 2-position is unclear at this time.[15] An electron-withdrawing effect that stabilizes the formed anion intermediate may promote the decarboxylation step. However, as 2-methoxy- and 2-hydroxyphenylglycines also exhibited high reactivity similar to L-2-(2-chlorophenyl)glycine

(Table 1), there is not a good correlation between the electronic effect of the substituents and the reactivity as the nitrogen source.

CONCLUSIONS

In conclusion, we have developed a synthetic method of unprotected 2-arylglycines by the transamination of arylglyoxylic acids. Commercially available L-2-(2-chlorophenyl)glycine was found as an effective nitrogen source, although further investigation is required to clarify the effect of the chloro substituent. The optimized protocol enables the preparation of a variety of arylglycines having a free α-amino acid moiety, including labile 2-(4-chloromethylphenyl)glycine (**2l**) and medicinally important 2-(4-hydroxyphenyl)glycine and 2-(3-chloro-4-hydroxyphenyl)glycine derivatives (**2t−w**). This method would be a useful tool for preparing arylglycines in peptide drug development.

EXPERIMENTAL SECTION

All reactions were carried out under an argon atmosphere, stirred magnetically, unless otherwise noted. An oil bath was used as a heating source for all the reactions that required heating in this work. Reactions were monitored by thin-layer chromatography (TLC: Merck Silica Gel 60 F_{254}). Column chromatography was carried out using neutral silica gel (Cica silica gel 60N, particle size 0.040−0.050 mm, neutral, KANTO CHEMICAL CO., INC.) or SO_3H silica gel (CHROMATOREX®, FUJI SILYSIA CHEMICAL LTD.). NMR spectra were measured by JEOL ECS-400 (^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz)). ^{13}C{^{1}H} NMR spectra were fully decoupled. ^{1}H and ^{13}C{^{1}H} NMR chemical shifts are reported in parts per million (ppm, δ scale) relative to residual solvents or internal references

(^{1}H NMR: $CHCl_3$ at 7.26 ppm or tetramethylsilane at 0.00 ppm in $CDCl_3$, CD_2HOD at 3.31 ppm in CD_3OD, DMSO-d_5 at 2.50 ppm in DMSO-d_6, sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) at 0.00 ppm as an internal reference in D_2O; ^{13}C NMR: $CDCl_3$ at 77.0 ppm in $CDCl_3$, CD_3OD at 49.0 ppm in CD_3OD, DMSO-d_6 at 39.52 ppm in DMSO-d_6, DSS at 0.00 ppm as an internal reference in D_2O). Coupling constants (*J*) are reported in Hz. Multiplicities are reported using the following abbreviations; s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet; br, broad. Infrared (IR) spectra were recorded on a JASCO FT-IR-4200 at 4.0 cm^{-1} resolution and reported in wavenumbers. Mass spectra were measured by JEOL JMS-T100LP using Electrospray Ionization (ESI) and Direct Analysis in Real Time (DART).

L-2-(2-Chlorophenyl)glycine, phenylglyoxylic acid (**1a**), DL-2-(2-chlorophenyl)glycine, DL-4-(2-chlorophenyl)glycine, 2-oxo-4-phenylbutanoic acid, phenylpyruvic acid, and 4-methyl-2-oxovaleric acid were purchased from Tokyo Chemical Industry Co., Ltd. (TCI) and used as received.

Preparation of 2-(2-Bromophenyl)glycine as the Nitrogen Source

Methyl 2-(2-bromophenyl)glycinate. To a solution of 2-bromobenzaldehyde (5.56 g, 30.1 mmol) and NH_4Cl (3.39 g, 63.4 mmol) in MeOH (45 mL) and H_2O (15 mL) was added KCN (4.12 g, 63.3 mmol) at 0 °C. The reaction mixture was stirred for 24 h at room temperature. After CH_2Cl_2 and aq. HCl (6 M) were added, the resultant mixture was separated into the organic layer and the aqueous layer. After the aqueous layer was washed with CH_2Cl_2, the two organic layers were combined and extracted with aq. HCl (6 M). The two aqueous layers were combined and refluxed for 34 h. After it was cooled to room temperature, MeOH was added. The solvents were removed to afford the crude

material. After it was dissolved into MeOH (150 mL), $SOCl_2$ (7.58 mL, 105 mmol) was added at 0 °C. The reaction mixture was refluxed for 18 h. It was cooled to room temperature and concentrated in vacuo. After aq. $NaHCO_3$ was added to the residue, it was extracted with AcOEt. The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 2/1 to 3/2) to afford methyl 2-(2-bromophenyl)glycinate (2.41 g, 33%) as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60−7.56 (m, 1H), 7.36−7.29 (m, 2H), 7.17 (ddd, J = 8.4, 6.4, 2.8 Hz, 1H), 5.03 (s, 1H), 3.73 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.8, 139.8, 133.2, 129.4, 128.4, 128.0, 123.6, 58.2, 52.5; IR (neat, cm^{-1}) 1738; HRMS (DART, m/z) Calcd. for $C_9H_{10}BrNO_2$·H ([M+H]$^+$): 243.9973, found 243.9975.

2-(2-Bromophenyl)glycine. After methyl 2-(2-bromophenyl)glycinate (244.1 mg, 1.00 mmol) was dissolved in aq. KOH (10%, 5.3 mL), the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was neutralized with aq. HCl (20%) and charged on a cationic ion exchange chromatography (DOWEX 50W−8, 200−400 mesh). The product was eluted with aq.NH_3 (3%). The eluent was concentrated in vacuo to afford 2-(2-bromophenyl)glycine as a pale brown solid (198 mg, 86%). Mp 208 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 4 eq of KOH) δ 7.64 (d, J = 8.0 Hz, 1H), 7.42−7.31 (m, 2H), 7.22 (td, J = 8.0, 2.0 Hz, 1H), 4.69 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, D_2O with 4 eq of KOH) δ 183.0, 144.0, 135.7, 131.8, 131.7, 130.8, 125.9, 62.8; IR (KBr, cm^{-1}) 3300−1900, 1664, 1589, 1508; HRMS (DART, m/z) Calcd. for $C_8H_8BrNO_2$·H ([M+H]$^+$): 229.9817, found 229.9793.

Typical Procedure for the Preparation of 2-Arylglycine as a Nitrogen Source.

2-(2-Methoxyphenyl)glycine. To a solution of 2-methoxybenzaldehyde (2.07 g, 15.2 mmol) and NH_4Cl (1.72 g, 32.1 mmol) in MeOH (15 mL) and H_2O (7.6 mL) was added KCN (2.08 g, 32.0 mmol) at 0 °C. The reaction mixture was stirred for 5 h at room temperature. After CH_2Cl_2 and aq. HCl (6 M) were added, the resultant mixture was separated into the organic layer and the aqueous layer. After the aqueous layer was washed with CH_2Cl_2, the two organic layers were combined. The organic layer was extracted with aq. HCl (6 M), the two aqueous layers were combined. The resultant aqueous solution was refluxed for 13 h. After it was cooled to room temperature, MeOH was added. The solvents were removed to afford the crude material. After it was dissolved into MeOH (76 mL), $SOCl_2$ (3.84 mL, 53.3 mmol) was added at 0 °C. The reaction mixture was refluxed for 7 h. It was cooled to room temperature and concentrated in vacuo. After aq. $NaHCO_3$ was added to the residue, it was extracted with AcOEt. The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 1/1 to 1/2 to 0/1) to afford methyl 2-(2-methoxyphenyl)glycinate. After methyl 2-(2-methoxyphenyl)glycinate was dissolved in aq. KOH (10%, 14 mL), the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was neutralized with aq. HCl (20%) and charged on a cationic ion exchange chromatography (DOWEX 50W−8, 200−400 mesh). The product was eluted with aq. NH_3 (3%). The eluent was concentrated to afford 2-(2-methoxyphenyl)glycine as a white solid (504 mg, 18%). Mp 150.1−150.6 °C; ^{1}H NMR (400 MHz, D_2O) δ 7.47 (t, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.05 (t, *J* = 8.0 Hz, 1H), 4.81 (s, 1H), 3.85 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, D_2O) δ 176.2, 159.9, 134.0, 133.9, 124.7, 123.7, 114.3, 58.4, 58.0; IR (KBr, cm^{-1}) 3600−1900, 1633, 1603, 1498, 1458; HRMS (DART, m/z) Calcd. for $C_9H_{11}NO_3 \cdot H$ ($[M+H]^+$): 182.0817, found 182.0843.

2-(2-Hydroxyphenyl)glycine. Methyl 2-(2-hydroxyphenyl)glycinate was purified by flash column chromatography on silica gel ($CHCl_3$/MeOH = 20/1 to 10/1 to 8/1). Brown solid (332 mg, 20% yield), mp 161 °C (decomp.); ^{1}H NMR (400 MHz, D_2O) δ 7.37−7.26 (m, 2H), 7.02−6.90 (m, 2H), 4.87 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, D_2O) δ 176.2, 157.3, 133.7, 133.4, 123.4, 123.2, 118.5, 58.0; IR (KBr, cm^{-1}) 3700−2200, 1622, 1595, 1495, 1460; HRMS (DART, m/z) Calcd. for $C_8H_9NO_3 \cdot H$ ($[M+H]^+$): 168.0661, found 168.0649.

2-(2-Trifluoromethylphenyl)glycine. Methyl 2-(2-trifluoromethylphenyl)glycinate was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1 to 3/1). 2-(2-Trifluoromethylphenyl)glycine was isolated by precipitation; After Et_2O was added to the reaction mixture, 2-(2-trifluoromethylphenyl)glycine was appeared as a precipitate. It was corrected by filtration and washed with H_2O and Et_2O. White solid (128 mg, 4%), mp 260 ºC (decomp.); ^{1}H NMR (400 MHz, D_2O with 6 eq of KOH) δ 7.74 (d, J = 8.0 Hz, 1H), 7.63 (t, J = 8.0 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 8.0 Hz, 1H), 4.72 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, D_2O with 6 eq of KOH) δ 182.9, 143.7, 135.6, 130.8, 130.4, 130.2 (q, J = 29.6 Hz), 128.6 (q, J = 5.8 Hz), 127.2 (q, J = 271.8 Hz), 58.7; IR (KBr, cm^{-1}) 3300−1900, 1658, 1589, 1506, 1315; HRMS (DART, m/z) Calcd. for $C_9H_8F_3NO_2 \cdot H$ ($[M+H]^+$): 220.0585, found 220.0561.

2-(2-Fluorophenyl)glycine. Methyl 2-(2-fluorophenyl)glycinate was purified by flash column chromatography on silica gel (hexane/AcOEt = 2/1 to 1/1). Brown solid (522 mg, 21%), mp 246 °C (decomp.); ^{1}H NMR (400 MHz, D_2O

with 6 eq of KOH) δ 7.41−7.30 (m, 2H), 7.20 (t, *J* = 8.0 Hz, 1H), 7.14 (t, *J* = 8.0 Hz, 1H), 4.55 (s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O with 6 eq of KOH) δ 183.1, 163.0 (d, *J* = 242.2 Hz), 132.0 (d, *J* = 8.5 Hz), 131.8 (d, *J* = 14.3 Hz), 131.8 (d, *J* = 3.8 Hz), 127.3 (d, *J* = 2.9 Hz), 118.3 (d, *J* = 21.9 Hz), 57.5; IR (KBr, cm^{-1}) 3400−1800, 1662, 1624, 1587, 1537; HRMS (DART, m/z) Calcd. for $C_8H_8FNO_2 \cdot H$ ($[M+H]^+$): 170.0617, found 170.0601.

2-(2-Methylphenyl)glycine. Methyl 2-(2-methylphenyl)glycinate was purified by flash column chromatography on silica gel (hexane/AcOEt = 1/1). Brown solid (470 mg, 19%), mp 204 ºC (decomp.). ^{1}H NMR (400 MHz, D_2O with 4 eq of KOH) δ 7.30−7.19 (m, 4H), 4.56 (s, 1H), 2.38 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O with 4 eq of KOH) δ 184.2, 143.3, 139.0, 133.3, 130.1, 129.3, 129.1, 59.8, 21.3; IR (KBr, cm^{-1}) 3300−1800; 1628, 1568, 1520; HRMS (DART, m/z) Calcd. for $C_9H_{11}NO_2 \cdot H$ ($[M+H]^+$): 166.0868, found 166.0846.

2-(3-Chlorophenyl)glycine. Methyl 2-(3-chlorophenyl)glycinate was purified by flash column chromatography on silica gel. Pale brown solid (412 mg, 15%), mp 235 ºC (decomp.); ^{1}H NMR (400 MHz, D_2O with 4 eq of KOH) δ 7.42−7.26 (m, 4H), 4.34 (s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O with 4 eq of KOH) δ 183.0, 146.9, 136.4, 132.9, 130.1, 129.5, 127.9, 62.8; IR (KBr, cm^{-1}) 3300−1900, 1655, 1631, 1583, 1522; HRMS (DART, m/z) Calcd. for $C_8H_8ClNO_2 \cdot H$ ($[M+H]^+$): 186.0322, found 186.0347.

Methyl N-Boc-2-(2-bromophenyl)glycinate. To a solution of methyl 2-(2-bromophenyl)glycinate (689 mg, 2.82 mmol) prepared by the above procedure and Et_3N (831 μL, 5.99 mmol) in CH_2Cl_2 (15 mL) was added di-*tert*-butyl

dicarbonate (826 μL, 3.60 mmol) at 0 °C. After the reaction mixture was stirred for 4 h at room temperature, it was quenched with saturated aq. NH_4Cl and extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 15/1 to 10/1) to afford methyl *N*-Boc-2-(2-bromophenyl)glycinate (835 mg, 86%) as a white solid. Mp 95.6−96.1 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.36−7.27 (m, 2H), 7.18 (ddd, *J* = 8.4, 6.8, 2.4 Hz, 1H), 5.73−5.48 (m, 2H), 3.73 (s, 3H), 1.50−1.21 (m, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.1, 154.8, 136.9, 133.5, 129.8, 129.7, 127.8, 123.7, 80.3, 57.6, 52.9, 28.3; IR (neat, cm^{-1}) 1747, 1714; HRMS (DART, m/z) Calcd. for $C_{14}H_{18}BrNO_4 \cdot H$ ($[M+H]^+$): 344.0498, found 344.0517.

N-Boc-2-(2-phenylphenyl)glycinate. To a flask charged with methyl *N*-Boc-2-(2-bromophenyl)glycinate (377 mg, 1.64 mmol), phenylboronic acid (300 mg, 2.46 mmol), and [1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride dichloromethane adduct (67.6 mg, 82.8 μmol), were added THF (6.6 mL) and aq. Na_2CO_3 (1 M, 1.6 mL). The mixture was degassed by freeze–pump–thaw cycles. After it was refluxed for 2 h, it was diluted with AcOEt and H_2O and extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1) to afford methyl *N*-Boc-2-(2-phenylphenyl)glycinate with small amount of the starting material. Because it was difficult to separate the desired product and the starting material, the mixture was exposed to Suzuki-Miyaura coupling conditions again using phenylboronic acid (155 mg, 1.27 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride dichloromethane adduct (68.5 mg, 83.9 μmol), THF (6.6 mL), and aq. Na_2CO_3 (1 M, 1.6 mL). After the reaction

mixture was refluxed for 1 h, it was diluted with AcOEt and H_2O and extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1) to methyl *N*-Boc-2-(2-phenylphenyl)glycinate (356 mg, 64%) in pure form as a white amorphous. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.31 (m, 8H), 7.31−7.26 (m, 1H), 5.45−5.34 (m, 1H), 5.28 (br s, 1H), 3.63 (s, 3H), 1.50−1.19 (m, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.1, 154.4, 142.4, 140.2, 134.4, 130.9, 129.4, 128.3, 128.2, 128.0, 127.4, 126.7, 79.9, 54.5, 52.5, 28.3; IR (neat, cm^{-1}) 1745, 1714; HRMS (DART, m/z) Calcd. for $C_{20}H_{23}NO_4$·H ([M+H]$^+$): 342.1705, found 342.1732.

2-(2-Phenylphenyl)glycine. To a solution of methyl *N*-Boc-2-(2-phenylphenyl)glycinate (356 mg, 1.04 mmol) in CH_2Cl_2 (5.2 mL) was added trifluoroacetic acid (1.76 μL, 22.9 mmol) at room temperature. The reaction mixture was stirred for 1 h at room temperature and it was concentrated in vacuo. After the residue was dissolved in aq. KOH (10%, 5.2 mL), the reaction mixture was stirred for 1 h at room temperature. Then, 1,4-dioxane (5.2 mL) was added and the reaction mixture was stirred for 30 min at room temperature. After the reaction mixture was neutralized with aq. HCl (20%), Et_2O was added. The reaction mixture was separated into organic layer and aqueous layer. The aqueous layer was charged on a cationic ion exchange chromatography (DOWEX 50W−8, 200−400 mesh). The product was eluted with aq. NH_3 (3%). The eluent was concentrated in vacuo to afford 2-(2-phenylphenyl)glycine as a white solid (200 mg, 84%). Mp 182.2−182.8 ºC; ^{1}H NMR (400 MHz, D_2O with 5 eq of KOH) δ 7.54−7.34 (m, 8H), 7.27 (d, *J* = 8.0 Hz, 1H), 4.45 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, D_2O with 4 eq of KOH) δ 183.9, 144.0, 143.5, 142.7, 132.8, 132.1, 131.1, 130.9, 130.02, 129.99, 129.3, 59.3; IR (KBr, cm^{-1}) 3700−1800, 1626, 1481; HRMS

(DART, m/z) Calcd. for $C_{14}H_{13}NO_2 \cdot H$ ($[M+H]^+$): 228.1025, found 228.1010.

Preparation of Arylglyoxylic Acids.

Typical Procedure A: Preparation from the Corresponding Mandelic Acids.[16]

*4-Fluorophenylglyoxylic acid (**1b**)*. To a 200 mL flask charged with 4-fluoromandelic acid (541 mg, 3.18 mmol) and AZADOL (24.4 mg, 0.159 mmol) in MeCN (16 mL) was added $NaNO_2$ (44.1 mg, 0.639 mmol) at room temperature. The reaction mixture was stirred under air (balloon) for 2 h. Then, it was quenched with aq. HCl (1 M) and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude materials were purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 4/1) and azeotropic dried with hexane to afford arylglyoxylic acid **1b** (518 mg, 97%) as a white solid. Mp 89.7−92.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55−8.50 (m, 2H), 7.22 (t, *J* = 9.2 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 182.6, 167.3 (d, *J* = 259.3 Hz), 161.6, 134.4 (d, *J* = 9.5 Hz), 128.2 (d, *J* = 2.9 Hz), 116.4 (d, *J* = 21.9 Hz); IR (neat, cm^{-1}) 3800−2300, 1728, 1682, 1597; HRMS (DART, m/z) Calcd. for $C_8H_5FO_3 \cdot NH_4$ ($[M+NH_4]^+$): 186.0567, found 186.0569.

*4-Bromophenylglyoxylic acid (**1d**)*.[16] Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 2/1), White solid (681 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (dt, *J* = 8.8, 2.0 Hz, 2H), 7.70 (dt, *J* = 8.8, 2.0 Hz, 2H).

*4-(Trifluoromethyl)phenylglyoxylic acid (**1e**)*.[16] Purified by column chromatography on silica gel (SO_3H,

hexane/AcOEt = 2/1), White solid (556 mg, quant.).; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 8.0 Hz, 2H).

*3-Chlorophenylglyoxylic acid (**1m**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 2/1). Pale yellow solid (550 mg, 99%), mp 54.5−58.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (t, *J* = 1.8 Hz, 1H), 8.32 (dt, *J* = 8.0, 1.8 Hz, 1H), 7.69 (dq, *J* = 8.0, 1.8 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 183.3, 162.5, 135.5, 135.3, 133.1, 130.7, 130.3, 129.2; IR (neat, cm^{-1}) 3600−2800; 1711, 1682; HRMS (DART, m/z) Calcd. for $C_8H_5ClO_3 \cdot NH_4$ ($[M+NH_4]^+$): 202.0271, found 202.0242.

2-(4-Benzyloxyphenyl)-2-hydroxyacetic acid. To a 200 mL flask charged with 2-hydroxy-2-(4-hydroxyphenyl)acetic acid monohydrate (1.87 g, 10.1 mmol) and K_2CO_3 (9.79 g, 70.8 mmol) in DMF (14 mL) was added BnBr (3.58 mL, 30.2 mmol) at 0 °C. After the reaction mixture was stirred for 2 h at room temperature, it was quenched with H_2O and extracted with a solution of hexane and AcOEt (4/1). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. To a solution of the crude material in THF (11 mL) and EtOH (2.9 mL) was added aq. NaOH (5.2 M, 14.0 mL, 72.5 mmol) at room temperature. The reaction mixture was stirred for 3 h. Then, the reaction mixture was acidified with aq. HCl (10%) and extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The solid material was dissolved in hot AcOEt and reprecipitated by an addition of hexane. After filtration, the precipitate was washed with hexane and dried under reduced pressure. 2-(4-(Benzyloxy)phenyl)-2-hydroxyacetic acid (1.26 g) was obtained in 49% yield (2 steps) as a white solid. Mp 133.4−

136.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.32 (m, 7H), 6.99 (d, *J* = 8.8 Hz, 2H), 5.21 (s, 1H), 5.07 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 174.3, 157.9, 137.1, 132.6, 128.4, 127.9, 127.8, 127.6, 114.4, 71.9, 69.2; IR (KBr, cm^{-1}) 3546, 3489, 3500−2300, 1697; HRMS (DART, m/z) Calcd. for $C_{15}H_{14}O_4 \cdot NH_4$ ([M+NH_4]$^+$): 276.1236, found 276.1251.

*4-Benzyloxyphenylglyoxylic acid (**1v**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 6/1 to 4/1). Pale yellow solid (646 mg, 83%). Mp 90.8−91.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 8.8 Hz, 2H), 7.46−7.33 (m, 5H), 7.07 (d, *J* = 8.8 Hz, 2H), 5.19 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 181.7, 164.9, 161.0, 135.6, 134.5, 128.8, 128.5, 127.5, 124.8, 115.2, 70.4; IR (neat, cm^{-1}) 3800−2300, 1741, 1672; HRMS (DART, m/z) Calcd. for $C_{15}H_{12}O_4 \cdot H$ ([M+H]$^+$): 257.0814, found 257.0810.

2-Chlorophenylglyoxylic acid. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 4/1). White solid (539 mg, 97%), mp 112.6−114.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.7, 164.0, 134.6, 134.1, 132.3, 131.9, 130.8, 127.2; IR (neat, cm^{-1}) 3700−2300, 1684; HRMS (DART, m/z) Calcd. for $C_8H_5ClO_3 \cdot NH_4$ ([M+NH_4]$^+$): 202.0271, found 202.0266.

Typical Procedure B: Preparation from the Corresponding Styrenes.

1-(4-Chlorophenyl)ethane-1,2-diol. To a solution of 1-chloro-4-vinylbenzene (1.41 g, 10.2 mmol) and *N*-

methylmorpholine *N*-oxide (1.79 g, 15.3 mmol) in acetone (46 mL) and H_2O (5.1 mL) was added osmium tetroxide (4% in H_2O, 621 μL, 102 μmol) at 0 °C. After the reaction mixture was stirred for 18 h at room temperature, it was quenched with saturated aq. $Na_2S_2O_3$ and extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 1/1) to afford 1-(4-chlorophenyl)ethane-1,2-diol (1.57 g, 90%) as a white solid. Mp 79.9−80.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.29 (m, 4 H), 4.82 (dt, *J* = 8.0, 3.6 Hz, 1H), 3.76 (ddd, *J* = 10.8, 7.2, 3.6 Hz, 1H), 3.63 (ddd, *J* = 10.8, 8.0, 4.4 Hz, 1H), 2.53 (d, *J* = 3.6 Hz, 1H), 1.98 (dd, *J* = 7.2, 4.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 138.8, 133.7, 128.7, 127.4, 74.0, 67.8; IR (neat, cm^{-1}) 3800−3000, 1082; HRMS (DART, m/z) Calcd. for $C_8H_9ClNO_2 \cdot NH_4$ ($[M+NH_4]^+$): 190.0635, found 190.0662.

*4-Chlorophenylglyoxylic acid (**1c**)*. To a 100 mL flask charged with 1-(4-chlorophenyl)ethane-1,2-diol (345 mg, 2.00 mmol), nor-AZADO (27.7 mg, 0.200 mmol), and AcOH (229 μL, 4.00 mmol) in MeCN (5.0 mL) and H_2O (5.0 mL) was added $NaNO_2$ (55.2 mg, 0.800 mmol) at room temperature. After the reaction mixture was stirred under air (balloon) for 18 h, it was quenched with aq. HCl (1 M) and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude materials were purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 2/1) to afford arylglyoxylic acid **1c** (346 mg, 94%) as a white solid. Mp 84.9−87.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 183.4, 162.0, 142.6, 132.5, 130.1, 129.4; IR (neat, cm^{-1}) 3800−3000, 1718, 1670; HRMS (DART, m/z) Calcd. for $C_8H_6ClO_3 \cdot H$ ($[M+H]^+$): 185.0006, found 185.0020.

Benzyl 4-(1,2-dihydroxyethyl)benzoate. Benzyl 4-vinylbenzoate was prepared from 4-vinylbenzoic acid according to the previous report.[17] Benzyl 4-(1,2-dihydroxyethyl)benzoate was purified by flash column chromatography on silica gel (hexane/AcOEt = 1/1 to 1/2). White solid (2.46 g, 90% (3 steps from benzyl 4-vinylbenzoate)), mp 45.4−45.8 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 2H), 7.45−7.31 (m, 7H), 5.36 (s, 2H), 4.89 (dt, *J* = 7.6, 3.6 Hz, 1H), 3.80 (ddd, *J* = 11.2, 6.8, 3.6 Hz, 1H), 3.64 (ddd, *J* = 11.2, 7.6, 4.4 Hz, 1H), 2.66 (d, *J* = 3.6 Hz, 1H), 2.06 (dd, *J* = 6.8, 4.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.2, 145.7, 135.9, 129.9, 129.7, 128.6, 128.3, 128.1, 126.0, 74.2, 67.8, 66.7; IR (neat, cm^{-1}) 3800−2800, 1714; HRMS (DART, m/z) Calcd. for $C_{16}H_{16}O_4 \cdot NH_4$ ([M+NH_4]$^+$): 290.1392, found 290.1418.

*4-(Benzyloxycarbonyl)phenylglyoxylic acid (**1f**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 5/1 to 4/1). White solid (689 mg, 79%), mp 50.3−52.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (dt, *J* = 8.8, 2.0 Hz, 2H), 8.21 (dt, *J* = 8.8, 2.0 Hz, 2H), 7.48−7.34 (m, 5H), 5.41 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 184.0, 165.3, 161.1, 135.8, 135.3, 134.9, 131.1, 130.4, 128.7, 128.6, 128.4, 67.5; IR (neat, cm^{-1}) 3800−2300, 1722, 1695; HRMS (DART, m/z) Calcd. for $C_{16}H_{12}O_5 \cdot NH_4$ ([M+NH_4]$^+$): 302.1029, found 302.1042.

1-(p-Tolyl)ethane-1,2-diol. Purified by column chromatography on silica gel (hexane/AcOEt = 1/1 to 1/2). White solid (1.47 g, 96%), mp 75.4−75.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 4.81 (dt, *J* = 8.0, 4.0 Hz, 1H), 3.75 (ddd, *J* = 10.8, 7.2, 4.0 Hz, 1H), 3.67 (ddd, *J* = 10.8, 8.0, 5.2 Hz, 1H), 2.38 (d, *J* = 4.0 Hz, 1H), 2.35 (s, 3H), 1.98 (dd, *J* = 7.2, 5.2 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.7, 137.5,

129.2, 126.0, 74.5, 68.1, 21.1; IR (neat, cm^{-1}) 3700−2400; HRMS (DART, m/z) Calcd. for $C_9H_{11}O_2 \cdot NH_4$ ([M+ $NH_4]^+$): 1701181, found 170.1166.

*4-Methylphenylglyoxylic acid (**1g**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 6/1). White solid (417 mg, 84%), mp 92.9−94.3 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 2.46 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.6, 161.3, 147.4, 131.6, 129.7, 129.2, 22.0; IR (neat, cm^{-1}) 3300−2300, 1724, 1678; HRMS (DART, m/z) Calcd. for $C_9H_8O_3 \cdot NH_4$ ([M+ $NH_4]^+$): 182.0817, found 182.0816.

1-(4-tert-Butylphenyl)ethane-1,2-diol. Purified by column chromatography on silica gel (hexane/AcOEt = 2/1 to 1/1). White solid (1.77 g, 90%), mp 126.3−127.2 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.81 (dt, *J* = 8.0, 4.0 Hz, 1H), 3.77 (ddd, *J* = 11.6, 8.0, 4.0 Hz, 1H), 3.69 (ddd, *J* = 11.6, 8.0, 4.8 Hz, 1H), 2.36 (d, *J* = 4.0 Hz, 1H), 1.99 (dd, *J* = 8.0, 4.8 Hz, 1H), 1.32 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.9, 137.4, 125.8, 125.4, 74.5, 68.0, 34.5, 31.3; IR (neat, cm^{-1}) 3600−3100; HRMS (DART, m/z) Calcd. for $C_{12}H_{18}O_2 \cdot NH_4$ ([M+$NH_4]^+$): 212.1651, found 212.1647.

*4-tert-Butylphenylglyoxylic acid (**1h**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 6/1). White solid (562 mg, 91%), mp 58.9−61.8 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.8 Hz, 2H), 7.55 (d, *J* = 8.8 Hz, 2H), 1.36 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.9, 161.8, 160.0, 131.4, 129.1, 126.0, 35.5,

30.9; IR (neat, cm^{-1}) 3800−2300, 1734, 1682; HRMS (DART, m/z) Calcd. for $C_{12}H_{14}O_3 \cdot NH_4$ ($[M+NH_4]^+$): 224.1287, found 224.1263.

1-(4-phenylphenyl)ethane-1,2-diol. Purified by column chromatography on silica gel (hexane/AcOEt = 1/1 to 0/1). Pale brown solid (1.47 g, 99%), mp 144.0−146.0 °C; ^1H NMR (400 MHz, CD_3OD) δ 7.63−7.55 (m, 4H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 1H), 4.73 (dd, *J* = 7.6, 5.6 Hz, 1H), 3.67−3.62 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 142.4, 142.2, 141.7, 129.8, 128.3, 127.94, 127.92, 127.8, 75.7, 68.7; IR (KBr, cm^{-1}) 3600−3000; HRMS (DART, m/z) Calcd. for $C_{14}H_{14}O_2 \cdot NH_4$ ($[M+NH_4]^+$): 232.1338, found 232.1319.

*4-Phenylphenylglyoxylic acid (**1i**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 6/1). Pale yellow solid (638 mg, 79%), mp 100.0−101.9 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 8.4 Hz, 2H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 7.2 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 2H), 7.44 (t, *J* = 7.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.7, 161.7, 148.3, 139.2, 132.0, 130.3, 129.1, 128.9, 127.5, 127.4; IR (neat, cm^{-1}) 3600−2200, 1730, 1682; HRMS (DART, m/z) Calcd. for $C_{14}H_{10}O_3 \cdot NH_4$ ($[M+NH_4]^+$): 244.0974, found 244.0969.

1-(4-Methoxyphenyl)ethane-1,2-diol. Purified by column chromatography on silica gel (hexane/AcOEt = 1/1 to 2/3). White solid (1.59 g, 94%), mp 77.7−79.7 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 4.79 (dt, *J* = 8.0, 3.6 Hz, 1H), 3.81 (s, 3H), 3.74 (ddd, *J* = 11.2, 7.6, 3.6 Hz, 1H), 3.66 (ddd, *J* = 11.2, 8.0, 4.8 Hz, 1H), 2.39 (d, *J* = 3.6 Hz, 1H), 2.00 (dd, *J* = 7.6, 4.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.2,

132.6, 127.3, 113.8, 74.2, 67.9, 55.2; IR (neat, cm^{-1}) 3600−3000; HRMS (DART, m/z) Calcd. for $C_9H_{12}O_3 \cdot NH_4$ ($[M+NH_4]^+$): 186.1130, found 186.1144.

*4-Methoxyphenylglyoxylic acid (**1j**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 2/1). White solid (352 mg, 86%), mp 81.4−84.4 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.53−8.46 (m, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 3.92 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 182.2, 166.8, 161.7, 134.3, 124.7, 114.4, 55.7; IR (neat, cm^{-1}) 3800−2300, 1730, 1670: HRMS (DART, m/z) Calcd. for $C_9H_8O_4 \cdot H$ ($[M+H]^+$): 181.0501, found 181.0497.

1-(4-(Chloromethyl)phenyl)ethane-1,2-diol. Purified by column chromatography on silica gel (hexane/AcOEt = 1/1 to 2/3). White solid (824 mg, 44%), mp 102.2−103.6 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42−7.36 (m, 4H), 4.85 (dt, *J* = 8.0, 3.2 Hz, 1H), 4.59 (s, 2H), 3.78 (ddd, *J* = 10.8, 6.8, 3.2 Hz, 1H), 3.66 (ddd, *J* = 10.8, 8.0, 4.8 Hz, 1H), 2.48 (d, *J* = 3.2 Hz, 1H), 1.97 (dd, *J* = 6.8, 4.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 140.8, 137.2, 128.8, 126.5, 74.3, 68.0, 45.9; IR (neat, cm^{-1}) 3500−2800; HRMS (DART, m/z) Calcd. for $C_9H_{11}ClO_2 \cdot NH_4$ ($[M+NH_4]^+$): 204.0791, found 204.0771.

*4-(Chloromethyl)phenylglyoxylic acid (**1l**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 6/1 to 4/1). White solid (550 mg, 91%), mp 53.8−57.7 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 4.64 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.8, 162.0, 145.1, 131.7, 131.5, 129.0, 45.0; IR (neat, cm^{-1}) 3600−2300, 1718, 1684; HRMS (DART, m/z) Calcd. for $C_9H_7ClO_3 \cdot NH_4$ ($[M+NH_4]^+$): 216.0428,

found 216.0426.

1-(3-Methoxyphenyl)ethane-1,2-diol. Purified by column chromatography on silica gel (hexane/AcOEt = 1/1 to 0/1). White solid (1.34 g, 90%), mp 67.2−67.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (t, *J* = 8.0 Hz, 1H), 6.97−6.92 (m, 2H), 6.88−6.83 (m, 1H), 4.82 (dt, *J* = 7.6, 3.6 Hz, 1H), 3.82 (s, 3H), 3.78 (ddd, *J* = 11.2, 7.6, 3.6 Hz, 1H), 3.67 (ddd, *J* = 11.2, 7.6, 4.4 Hz, 1H), 2.46 (d, *J* = 3.6 Hz, 1H), 1.98 (dd, *J* = 7.6, 4.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.8, 142.2, 129.6, 118.3, 113.4, 111.6, 74.6, 68.0, 56.2; IR (neat, cm^{-1}) 3700−3000; HRMS (DART, m/z) Calcd. for $C_9H_{12}O_3 \cdot NH_4$ ($[M+NH_4]^+$): 186.1130, found 186.1139.

*3-Methoxyphenylglyoxylic acid (**1n**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 3/1). Yellow solid (531 mg, 96%), mp 66.1−66.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.6 Hz, 1H), 7.87−7.85 (m, 1H), 7.45 (t, *J* = 7.6 Hz, 1H). 7.28−7.24 (m, 1H), 3.89 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 184.2, 161.8, 159.8, 132.8, 130.0, 124.3, 122.7, 114.4, 55.6; IR (neat, cm^{-1}) 3800−2400, 1741, 1684; HRMS (DART, m/z) Calcd. for $C_9H_8O_4 \cdot NH_4$ ($[M+H]^+$): 181.0501, found 181.0506.

1-(o-Tolyl)ethane-1,2-diol. Purified by column chromatography on silica gel (hexane/AcOEt = 1/1). White solid (1.47 g, 94%), mp 107.2−109.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.4 Hz, 1H), 7.27−7.13 (m, 3H), 5.08 (dt, *J* = 8.0, 3.2 Hz, 1H), 3.74 (ddd, *J* = 11.2, 7.2, 3.2 Hz, 1H), 3.62 (ddd, *J* = 11.2, 8.0, 4.0 Hz, 1H), 2.36 (d, *J* = 3.2 Hz, 1H), 2.35 (s, 3H), 2.08 (dd, *J* = 7.2, 4.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 141.0, 136.0, 131.1, 128.3,

127.0, 126.9, 72.4, 67.8, 19.2; IR (KBr, cm^{-1}) 3600−2300; HRMS (DART, m/z) Calcd. for $C_9H_{12}O_2 \cdot NH_4$ ($[M+NH_4]^+$): 170.1166, found 170.1181.

*2-Methylphenylglyoxylic acid (**1o**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 6/1). White solid (487 mg, 98%), mp 34.3−35.9 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 7.6 Hz, 1H), 7.54 (td, *J* = 7.2, 1.2 Hz, 1H), 7.39−7.32 (m, 2H), 2.59 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 187.3, 165.3, 141.8, 134.2, 132.8, 132.3, 130.4, 126.0, 21.5; IR (neat, cm^{-1}) 3600−2400, 1739, 1685; HRMS (DART, m/z) Calcd. for $C_9H_8O_3 \cdot NH_4$ ($[M+NH_4]^+$): 182.0845, found 182.0817.

1-(1-Naphthalenyl)ethane-1,2-diol. Purified by column chromatography on silica gel (hexane/AcOEt = 1/1 to 0/1). Pale brown solid (1.83 g, 97%), mp 135.8−137.8 °C; ^1H NMR (400 MHz, CD_3OD) δ 8.14 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 6.8 Hz, 1H), 7.55−7.54 (m, 3H), 5.53 (dd, *J* = 8.4, 4.0 Hz, 1H), 3.85 (dd, *J* = 12.0 4.0 Hz, 1H), 3.69 (dd, *J* = 12.0, 8.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 138.7, 135.2, 132.1, 129.9, 128.9, 127.0, 126.5, 126.4, 124.7, 124.0, 72.8, 68.4; IR (neat, cm^{-1}) 3600−2900, 1676; HRMS (DART, m/z) Calcd. for $C_{12}H_{12}O_2 \cdot NH_4$ ($[M+NH_4]^+$): 206.1181, found 206.1157.

*1-Naphthylglyoxylic acid (**1p**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 4/1). Pale yellow solid (516 mg, 86%), mp 92.3−94.3 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 8.0 Hz, 1H), 8.56 (d, *J* = 6.4 Hz, 1H), 8.18 (d, *J* =8.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.71 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 7.64−7.58 (m,

2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 186.6, 163.5, 136.5, 135.1, 133.9, 131.1, 129.5, 129.0, 127.4, 127.1, 125.4, 124.4; IR (neat, cm^{-1}) 3800−2300, 1732, 1674; HRMS (DART, m/z) Calcd. for $C_{12}H_8O_3 \cdot NH_4$ ($[M+NH_4]^+$): 218.0817, found 218.0822.

Typical Procedure C: Preparation from the Corresponding Arylaldehydes.

1-(2-Fluorophenyl)ethane-1,2-diol. To a well-dried flask charged with CH_3PPh_3Br (5.18 g, 14.5 mmol) and dry THF (30 mL) was added ^{n}BuLi (15wt%, 8.53 mL, 14.5 mmol) dropwise at 0 °C. After the mixture was stirred for 20 min, a solution of 2-fluorobenzaldehyde (1.50 g, 12.1 mmol) in THF (24 mL) was added at -78 °C. The reaction mixture was stirred for 3 h at 0 °C. Then, it was quenched with saturated aq. NH_4Cl and extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/Et_2O = 20/1) to afford 1-fluoro-2-vinylbenzene containing impurities, which was used to the next reaction without further purification. To a solution of 1-fluoro-2-vinylbenzene and *N*-methylmorpholine *N*-oxide (2.19 g, 18.7 mmol) in acetone (55 mL) and H_2O (6.1 mL) was added osmium tetroxide (4% in H_2O, 739 μL, 121 μmol) at 0 °C. The reaction mixture stirred for 17 h at room temperature. It was quenched with saturated aq. $Na_2S_2O_3$ and extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 1/1) to afford 1-(2-fluorophenyl)ethane-1,2-diol (715 mg, 38% (2 steps)) as a white solid. Mp 80.4−81.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (td, *J* = 7.6, 2.0 Hz, 1H), 7.32−7.24 (m, 1H), 7.20−7.15 (m, 1H), 7.04 (dd, *J* = 10.0, 8.4 Hz, 1H), 5.16 (dt, *J* = 7.6, 3.6 Hz, 1H), 3.87 (ddd, *J* = 10.8, 7.2, 3.6 Hz, 1H), 3.67 (ddd, *J* = 10.8, 7.6, 5.2 Hz, 1H),

2.54 (d, *J* = 4.0 Hz, 1H), 1.99 (dd, *J* = 7.2, 5.2 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.7 (d, *J* = 244 Hz), 129.3 (d, *J* = 8.5 Hz), 127.6 (d, *J* = 4.8 Hz), 127.4 (d, *J* = 13.3 Hz), 124.3 (d, *J* = 2.9 Hz), 115.2 (d, *J* = 21.0 Hz), 68.9, 66.7; IR (neat, cm^{-1}) 3700−3000; HRMS (DART, m/z) Calcd. for $C_8H_9FO_2 \cdot NH_4$ ($[M+NH_4]^+$): 174.0930, found 174.0923.

*2-Fluorophenylglyoxylic Acid (**1q**)*. To a 200 mL flask charged with 1-(2-fluorophenyl)ethane-1,2-diol (469 mg, 3.00 mmol), nor-AZADO (41.7 mg, 0.302 mmol), and AcOH (229 μL, 4.00 mmol) in MeCN (7.5 mL) and H_2O (7.5 mL) was added $NaNO_2$ (82.9 mg, 1.20 mmol) at room temperature. After the reaction mixture was stirred under air (balloon) for 18 h, it was quenched with aq. HCl (1 M) and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude materials were purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 6/1) to afford arylglyoxylic acid **1q** (412 mg, 81%) as a white solid. Mp 72.6−73.4 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10−8.03 (m, 1H), 7.71−7.64 (m, 1H), 7.35−7.30 (m, 1H), 7.21 (ddd, *J* = 10.8, 8.4, 1.2 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 183.1, 166.2, 162.7 (d, *J* = 257.4 Hz), 137.1 (d, *J* = 9.6 Hz), 131.3, 124.9 (d, *J* = 3.8 Hz), 131.3 (d, *J* = 9.6 Hz), 116.7 (d, *J* = 20.9 Hz); IR (neat, cm^{-1}) 3800−2300, 1739, 1687, 1610; HRMS (DART, m/z) Calcd. for $C_8H_5FO_3 \cdot NH_4$ ($[M+NH_4]^+$): 186.0567, found 186.0573.

1-(2-Bromophenyl)ethane-1,2-diol. Purified by column chromatography on silica gel (hexane/AcOEt = 1.5/1). White solid (1.11 g, 96%), mp 118.9−119.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.52 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.35 (td, *J* = 7.6, 1.2 Hz, 1H), 7.16 (td, *J* = 7.6, 2.0 Hz, 1H), 5.19 (dt, *J* = 7.6, 3.6 Hz, 1H), 3.91

(ddd, J = 10.4, 7.2, 3.6 Hz, 1H), 3.56 (ddd, J = 10.4, 7.6, 4.8 Hz, 1H), 2.60 (d, J = 3.6 Hz, 1H), 1.98 (dd, J = 7.2, 4.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 141.9, 132.1, 128.9, 128.6, 127.6, 121.6, 73.0, 65.8; IR (neat, cm^{-1}) 3600−2500; HRMS (DART, m/z) Calcd. for $C_8H_9BrO_2 \cdot NH_4$ ($[M+NH_4]^+$): 236.0109, found 236.0089.

*2-Bromophenylglyoxylic acid (**1r**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 10/1 to 8/1). White solid (605 mg, 88%), mp 100.7−101.1 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82−7.77 (m, 1H), 7.72−7.68 (m, 1H), 7.50−7.44 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.5, 162.8, 134.3 (2C), 134.0, 132.0, 127.6, 121.8; IR (neat, cm^{-1}) 3500−2500, 1687; HRMS (DART, m/z) Calcd. for $C_8H_5BrO_3 \cdot NH_4$ ($[M+NH_4]^+$): 245.9766, found 245.9746.

1-(2-Naphthalenyl)ethane-1,2-diol. Purified by column chromatography on silica gel (hexane/AcOEt = 1/1 to 0/1). White solid (1.12 g, 59% (2 steps)), mp 135.1−135.4 °C, ^1H NMR (400 MHz, $CDCl_3$) δ 7.88−7.81 (m, 4H), 7.53−7.44 (m, 3H), 5.01 (dt, J = 8.0, 3.6 Hz, 1H), 3.87 (ddd, J = 11.2, 7.2, 3.6 Hz, 1H), 3.77 (ddd, J = 11.2, 8.0, 4.8 Hz, 1H), 2.58 (d, J = 3.6 Hz, 1H), 2.02 (dd, J = 7.2, 4.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 140.8, 134.8, 134.5, 128.9 (2C), 128.6, 127.0, 126.7, 126.2, 125.5, 76.0, 68.6; IR (KBr, cm^{-1}) 3600−2500; HRMS (ESI, m/z) Calcd. for $C_{24}H_{24}O_4 \cdot Na$ ($[2M+Na]^+$): 399.1572, found 399.1561.

*2-Naphthylglyoxylic acid (**1s**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 4/1). Yellow solid (593 mg, 98%), mp 87.8−89.2 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.23 (dd, J = 7.6, 1.6

Hz, 1H), 8.05 (d, *J* = 7.6 Hz, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.61 (t, *J* = 7.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 184.2, 162.5, 136.6, 135.4, 132.2, 130.4. 130.1, 129.0 (2C), 127.9, 127.3, 124.5; IR (neat, cm^{-1}) 3700−2300, 1734, 1676; HRMS (DART, m/z) Calcd. for $C_{12}H_8O_3 \cdot H$ ($[M+H]^+$): 218.0817, found 218.0800.

1-(4-Benzyloxy-3-chlorophenyl)ethane-1,2-diol. 4-(Benzyloxy)-3-chlorobenzaldehyde was prepared by the benzylation (BnBr, K_2CO_3, DMF) of 3-chloro-4-hydroxybenzaldehyde. 1-(4-(Benzyloxy)-3-chlorophenyl)ethane-1,2-diol was purified by flash column chromatography on silica gel (hexane/AcOEt = 1/1 to 2/3). White solid (1.93 g, 58% (3 steps from 3-chloro-4-hydroxybenzaldehyde)), mp 128.5−130.4 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 2.4 Hz, 1H), 8.46 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.48−7.33 (m, 5H), 7.06 (d, *J* = 8.8 Hz, 1H), 5.29 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 181.2, 160.6, 160.1, 135.1, 133.6, 132.8, 128.8, 128.5, 127.0, 125.2, 124.1, 113.0, 71.1; IR (neat, cm^{-1}) 3300−2300, 1712, 1676, 1591; HRMS (DART, m/z) Calcd. for $C_{15}H_{11}ClO_4 \cdot H$ ($[M+H]^+$): 291.0424, found 291.0430.

*4-Benzyloxy-3-chlorophenylglyoxylic acid (**1w**)*. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 6/1 to 4/1). White solid (745 mg, 84%), mp 128.5−130.4 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 2.4 Hz, 1H), 8.46 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.48−7.33 (m, 5H), 7.06 (d, *J* = 8.8 Hz, 1H), 5.29 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 181.2, 160.6, 160.1, 135.1, 133.6, 132.8, 128.8, 128.5, 127.0, 125.2, 124.1, 113.0, 71.1; IR (neat, cm^{-1}) 3300−2300, 1712, 1676, 1591; HRMS (DART, m/z) Calcd. for $C_{15}H_{11}ClO_4 \cdot H$ ($[M+H]^+$): 291.0424,

found 291.0430.

1-(3,5-Bis(benzyloxy)phenyl)ethane-1,2-diol. Purified by flash column chromatography on silica gel (hexane/AcOEt = 2/1 to 1/1 to 1/2). White solid (2.03 g, 58% (2 steps)), mp 102.9−103.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.30 (m, 10H), 6.63 (d, *J* = 2.4 Hz, 2H), 6.56 (t, *J* = 2.4 Hz, 1H), 5.04 (s, 4H), 4.76 (dt, *J* = 8.0, 3.6 Hz, 1H), 3.75 (ddd, *J* = 11.2, 7.6, 3.6 Hz, 1H), 3.65 (ddd, *J* = 11.2, 8.0, 4.8 Hz, 1H), 2.45 (d, *J* = 3.6 Hz, 1H), 1.96 (dd, *J* = 7.6, 4.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.1, 143.1, 136.7, 128.6, 128.0, 127.5, 105.1, 101.4, 74.6, 70.1, 67.9; IR (neat, cm^{-1}) 3800−2800, 1597; HRMS (DART, m/z) Calcd. for $C_{22}H_{22}O_4$·H ($[M+H]^+$): 351.1596, found 351.1600.

3,5-Bis(benzyloxy)phenylglyoxylic acid. Purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 6/1 to 4/1). Orange solid (771 mg, 67%), mp 104.6−105.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.63 (m, 2H), 7.46−7.31 (m, 10H), 6.94 (t, *J* = 2.4 Hz, 1H), 5.10 (s, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 184.1, 162.4, 160.0, 136.0, 133.2, 128.6, 128.2, 127.6, 110.0, 109.7, 70.4; IR (neat, cm^{-1}) 3600−3400, 1593; HRMS (DART, m/z) Calcd. for $C_{22}H_{18}O_5$·H ($[M+H]^+$): 363.1233, found 363.1255.

Preparation of 1k, 1t, and 1u.

*4-(Dimethylamino)phenylglyoxylic acid (**1k**)*. Ethyl 4-(*N*,*N*-dimethylamino)phenylglyoxylate was synthesized according to the previous report[18]; To a well-dried flask charged with 4-bromo-*N*,*N*-dimethylaniline (3.01 g, 15.0 mmol) and dry THF (25 mL) was added ^{n}BuLi (15wt%, 10.1 mL, 15.8 mmol) dropwise at -78 °C. After 15 min, the

solution was added dropwise to a solution of diethyl oxalate (3.52 g, 24.1 mmol) in dry THF (24 mL) at -78 °C. After the reaction mixture was stirred for 20 min, it was quenched with H_2O and extracted with Et_2O. The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 5/1 to 4/1) to afford ethyl 4-(*N*,*N*-dimethylamino)phenylglyoxylate (2.07 g, 62%) as a yellow solid.

To a flask charged with ethyl 4-(dimethylamino)phenylglyoxylate (665 mg, 3.01 mmol) were added aq. NaOH (1 M, 7.5 mL, 7.5 mmol), THF (5.0 mL), and ethanol (1.5 mL) at room temperature. After the reaction mixture was stirred for 1 h, the reaction mixture was acidified with aq. HCl (1 M) and extracted with AcOEt. The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo to afford arylglyoxylic acid **1k** (566 mg, 98%) as a yellow solid. Mp 177 °C (decomp.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 9.2 Hz, 2H), 6.68 (d, J = 9.2 Hz, 2H), 3.15 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 186.0, 167.3, 154.4, 131.7, 118.8, 111.1, 39.6; IR (KBr, cm^{-1}) 3600−1800, 1722, 1623, 1562, 1527; HRMS (DART, m/z) Calcd. for $C_{10}H_{11}NO_3$·H ([M+H]$^+$): 194.0817, found 194.0842.

*4-Hydroxyphenylglyoxylic acid (**1t**)*.[19] To a solution of 4'-hydroxyacetophenone (1.42 g, 10.4 mmol) in pyridine (42 mL) was added SeO_2 (1.40 g, 12.6 mmol) at room temperature. After the reaction mixture was stirred for 1 h at 110 °C, it was stirred for 3 h at 90 °C. Then, it was diluted with H_2O, acidified with aq. HCl (12 M) to pH 1, and filtered. The filtrate was extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/AcOEt = 2/1 to 0/1) to afford arylglyoxylic acid **1t** (212 mg, 12%) as a brown solid. Mp. 149 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.8 (s,

1H), 7.80 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 187.0, 166.8, 163.9, 132.3, 123.3, 116.1; IR (KBr, cm^{-1}) 3600−2800, 1732, 1666, 1653; HRMS (DART, m/z) Calcd. for $C_8H_6O_4 \cdot H$ ($[M+H]^+$): 167.0344, found 167.0324.

4-(1,2-Dihydroxyethyl)phenyl acetate. To a solution of 4-vinylphenyl acetate (1.62 g, 9.99 mmol) and *N*-methylmorpholine *N*-oxide (1.76 g, 15.0 mmol) in acetone (45 mL) and H_2O (5.0 mL) was added osmium tetroxide (4% in H_2O, 611 μL, 100 μmol) at 0 °C. After the reaction mixture was stirred for 4 h at room temperature, it was quenched with saturated aq. $Na_2S_2O_3$ and extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 1/1 to 1/2) to afford 4-(1,2-dihydroxyethy)phenyl acetate (1.90 g, 97%) as a white solid. Mp 46.6−50.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 4.78 (dt, *J* = 8.0, 3.2 Hz, 1H), 3.71 (ddd, *J* = 11.2, 7.2, 3.2 Hz, 1H), 3.60 (ddd, *J* = 11.2, 8.0, 4.0 Hz, 1H), 2.85 (br s, 1H), 2.39−2.33 (m, 1H), 2.30 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 169.6, 150.2, 138.2, 127.2, 121.6, 74.1, 67.9, 21.1; IR (neat, cm^{-1}) 3700−3000, 1751; HRMS (DART, m/z) Calcd. for $C_{10}H_{12}O_4 \cdot NH_4$ ($[M+NH_4]^+$): 214.1079, found 214.1096.

4-(2,2-Dimethyl-1,3-dioxolan-4-yl)phenol. To a solution of 4-(1,2-dihydroxyethy)phenyl acetate (1.26 g, 6.47 mmol) and 2,2-dimethoxypropane (3.96 mL, 32.4 mmol) in CH_2Cl_2 (32 mL) was added $TsOH \cdot H_2O$ (126 mg, 0.661 mmol) at 0 °C. The reaction mixture was stirred for 1 h at room temperature. Then, it was quenched with saturated aq. $NaHCO_3$ and extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo

to provide the corresponding acetonide, which was used to the next reaction without further purification. To a solution of the acetonide in acetone (29 mL) and H_2O (3.2 mL) was added K_2CO_3 (2.70 g, 19.5 mmol) at room temperature. After the reaction mixture was stirred for 30 min, it was quenched with saturated aq. $NaHCO_3$ and extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/AcOEt = 4/1) to afford 4-(2,2-dimethyl-1,3-dioxolan-4-yl)phenol (1.21 g, 98% (2 steps)) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 5.01 (dd, J = 8.4, 6.4 Hz, 1H), 4.77−4.73 (m, 1H), 4.25 (dd, J = 8.4, 6.4 Hz, 1H), 3.68 (t, J = 8.4 Hz, 1H), 1.54 (s, 3H), 1.47 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.8, 130.3, 127.9, 115.4, 109.7, 77.8, 71.5, 26.6, 25.9; IR (neat, cm^{-1}) 3700−3000; HRMS (DART, m/z) Calcd. for $C_{11}H_{14}O_3 \cdot H$ ([M+H]$^+$): 195.1021, found 195.1003.

4-(4-Allyloxyphenyl)-2,2-dimethyl-1,3-dioxolane, To a solution of 4-(2,2-dimethyl-1,3-dioxolan-4-yl)phenol and K_2CO_3 (1.70 g, 12.3 mmol) in acetone (8.8 mL) was added allyl bromide (623 μL, 7.37 mmol) at 0 °C. The reaction mixture was stirred for 10 h at room temperature. Then, it was quenched with H_2O and extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/AcOEt = 15/1) to afford 4-(4-(allyloxy)phenyl)-2,2-dimethyl-1,3-dioxolane (1.40 g, 97%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 6.05 (ddt, J = 17.2, 10.8, 5.2 Hz, 1H), 5.41 (ddd, J = 17.2, 2.4, 1.6 Hz, 1H), 5.25 (ddd, J = 10.8, 2.4, 1.6 Hz, 1H), 5.02 (dd, J = 8.0, 6.4 Hz, 1H), 4.55−4.52 (m, 2H), 4.25 (dd, J = 8.0, 6.4 Hz, 1H), 3.69 (t, J = 8.0 Hz, 1H), 1.54 (s, 3H), 1.47 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.6, 133.3, 131.1, 127.8, 1117.8, 114.9, 109.6, 77.8, 71.7,

68.9, 26.8, 26.1; IR (neat, cm^{-1}) 1612; HRMS (DART, m/z) Calcd. for $C_{14}H_{18}O_3 \cdot H$ ($[M+H]^+$): 235.1334, found 235.1324.

1-(4-Allyloxyphenyl)ethane-1,2-diol. To a solution of 4-(4-(allyloxy)phenyl)-2,2-dimethyl-1,3-dioxolane (1.38 g, 5.89 mmol) in MeOH (24 mL) and H_2O (5.9 mL) was added DOWEX 50W−8 (200−400 mesh, 599 mg) at room temperature. After the reaction mixture was stirred for 47 h, additional DOWEX 50W−8 (200−400 mesh, 183 mg) was added and the reaction mixture was stirred for 47 h. Then, it was filtered through a pad of Celite and the filtrate was concentrated in vacuo. The residue was purified with flash column chromatography on silica gel (hexane/AcOEt = 2/1 to 1/1) to afford styrene 1-(4-allyloxy)phenyl)ethane-1,2-diol (851 mg, 74%) as a white solid. Mp 68.3−68.8 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dt, *J* = 8.8, 2.8 Hz, 2H), 6.91 (dt, *J* = 8.8, 2.8 Hz, 2H), 6.05 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.41 (dq, *J* = 17.6, 2.0 Hz, 1H), 5.29 (dq, *J* = 10.4, 2.0 Hz, 1H), 4.78 (dt, *J* = 8.0, 3.2 Hz, 1H), 4.54 (dq, *J* = 5.6, 2.0 Hz, 2H), 3.74 (ddd, *J* = 11.2, 7.6, 3.2 Hz, 1H), 3.66 (ddd, *J* = 11.2, 8.0, 5.2 Hz, 1H), 2.40−2.36 (m, 1H), 2.01-1.95 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.4, 133.1, 132.7, 127.3, 117.7, 114.8, 74.3, 68.8, 68.0; IR (neat, cm^{-1}) 3700−3000, 1610; HRMS (DART, m/z) Calcd. for $C_{11}H_{14}O_3 \cdot NH_4$ ($[M+ NH_4]^+$): 212.1287, found 212.1286.

*4-Allyloxyphenylglyoxylic acid (**1u**)*, To a 200 mL flask charged with 1-(4-allyloxy)phenyl)ethane-1,2-diol (585 mg, 3.01 mmol), nor-AZADO (41.6 mg, 0.301 mmol), and AcOH (345 μL, 6.03 mmol) in MeCN (7.5 mL) and H_2O (7.5 mL) was added $NaNO_2$ (83.1 mg, 1.20 mmol) at room temperature. After the reaction mixture was stirred under air

(balloon) for 17 h, it was quenched with aq. HCl (1 M) and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude materials were purified by column chromatography on silica gel (SO_3H, hexane/AcOEt = 6/1 to 4/1) to afford arylglyoxylic acid **1u** (587 mg, 94%) as a pale yellow solid. Mp 51.4−52.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52−8.46 (m, 2H), 7.03−6.98 (m, 2H), 6.05 (ddt, *J* = 17.2, 10.4, 5.2 Hz, 1H), 5.44 (ddd, *J* = 17.2, 2.0, 1.2 Hz, 1H), 5.35 (dq, *J* = 10.4, 1.6, 1.2 Hz, 1H), 4.68−4.64 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 181.8, 164.8, 161.0, 134.4, 131.9, 124.7, 118.6, 115.0, 69.1; IR (neat, cm^{-1}) 3700−2300, 1736, 1672, 1597, 1570; HRMS (DART, m/z) Calcd. for $C_{11}H_{10}O_4$·H ([M+ H]$^+$): 207.0657, found 207.0653.

Transamination of Arylglyoxylic Acids.

*2-Phenylglycine (**2a**)*. To a flask charged with phenylglyoxylic acid (**1a**) (156 mg, 1.04 mmol) and L-2-(2-chlorophenyl)glycine (387 mg, 2.08 mmol), MeCN (7.3 mL) and H_2O (3.1 mL) were added at room temperature. After the reaction mixture was stirred for 24 h at 50 °C, it was refluxed for 12 h. Then, it was cooled to room temperature, and diethyl ether (10 mL) was added. The reaction mixture was stirred until the product was fully precipitated. After filtration, the precipitate was washed with Et_2O, and it was added to a solution of MeCN (6.2 mL) and H_2O (2.7 mL). The resultant suspension was refluxed for 2 h. The precipitate was collected by filtration and washed with Et_2O. After the residual solvents was removed under reduced pressure, arylglycine **2a** (109 mg, 69%) was obtained as a white solid. Mp 256 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 4 eq of KOH) δ 7.44−7.30 (m, 5H), 4.34 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, D_2O with 4 eq of KOH) δ 183.8, 144.8, 131.5, 130.2, 129.5, 63.2; IR (KBr, cm^{-1}) 3300−1800, 1658, 1630, 1612, 1585, 1522; HRMS (DART, m/z) Calcd. for $C_8H_9NO_2$·H ([M+H]$^+$):

152.0712, found 152.0734.

Typical Procedure A for Transamination of Arylglyoxylic Acids

*2-(4-Chlorophenyl)glycine (**2c**)*. To a flask charged with 4-chlorophenylglyoxylic acid (**1c**) (92.5 mg, 0.501 mmol) and L-2-(2-chlorophenyl)glycine (186 mg, 1.00 mmol), MeCN (3.5 mL) and H_2O (1.5 mL) were added at room temperature. After the reaction mixture was stirred for 24 h at 50 °C, it was refluxed for 12 h. Then, it was cooled to room temperature and diethyl ether (5.0 mL) was added. The solution was stirred until the product was fully precipitated. After filtration, the precipitate was washed with diethyl ether and the residual solvents was removed under reduced pressure to afford arylglycine **2c** (56.9 mg, 61%) as a white solid. Mp 266 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 6 eq of KOH) δ 7.39 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 4.34 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, D_2O with 6 eq of KOH) δ 183.4, 143.5, 135.2, 131.3, 131.0, 62.6; IR (KBr, cm^{-1}) 3300−1800, 1657, 1631, 1585, 1525; HRMS (DART, m/z) Calcd. for $C_8H_8ClNO_2 \cdot H$ ([M+H]$^+$): 186.0322, found 186.0339.

*2-(4-Fluorophenyl)glycine (**2b**)*. Isolated as a HCl salt; Purification of **2b** was carried out by the following procedure. After the completion of the reaction, Et_2O (5.0 mL) was added to the reaction mixture, which was stirred until the product was fully precipitated. After filtration, the precipitate was washed with Et_2O. After the precipitate was transferred to a flask, HCl in Et_2O (1 M) was added. The resultant suspension was sonicated. Then, the suspension was concentrated under reduced pressure and recrystallized from EtOH/H_2O to afford **2b•HCl** (43.7 mg) as a white solid. The filtrate was concentrated in vacuo and recrystallized from EtOH/H_2O again to afford **2b•HCl** (7.5 mg) The

combined yield of **2b•HCl** was 50% (51.2 mg). Mp 281 °C (decomp).; ^{1}H NMR (400 MHz, D_2O with 6 eq of KOH) δ 7.36 (dd, *J* = 8.4, 6.0 Hz, 2H), 7.12 (t, *J* = 8.4 Hz, 2H), 4.34 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, D_2O with 6 eq of KOH) δ 183.6, 164.5 (d, *J* = 241.2 Hz), 140.8 (d, *J* = 1.9 Hz), 131.2 (d, *J* = 8.5 Hz), 118.0 (d, *J* = 21.9 Hz), 62.5; IR (KBr, cm^{-1}) 3300−1800, 1657, 1622, 1585, 1522; HRMS (DART, m/z) Calcd. for $C_8H_8FNO_2$·H ([M+H]$^+$): 170.0598, found 170.0617.

*2-(4-Bromophenyl)glycine (**2d**)*. White solid (71.7 mg, 62%), mp 281 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 5 eq of KOH) δ 7.54 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 4.32 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, D_2O with 5 eq of KOH) δ 183.3, 144.0, 134.3, 131.4, 123.3, 62.6; IR (KBr, cm^{-1}) 3300−1800, 1658, 1633, 1585, 1523; HRMS (DART, m/z) Calcd. for $C_8H_8BrNO_2$·H ([M+H]$^+$): 229.9817, found 229.9800

*2-(4-Methylphenyl)glycine (**2g**)*. Precipitation was carried out using MeCN (10 mL) instead of Et_2O. White solid (51.3 mg, 62%), mp 239 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 4 eq of KOH) δ 7.27 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 4.30 (s, 1H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, D_2O with 4 eq of KOH) δ 183.9, 141.9, 140.3, 132.0, 129.4, 62.8, 22.8; IR (KBr, cm^{-1}) 3400−1800, 1658, 1628, 1585, 1523; HRMS (DART, m/z) Calcd. for $C_9H_{11}NO_2$·H ([M+H]$^+$): 166.0868, found 166.0844.

*2-(4-tert-Butylphenyl)glycine (**2h**)*. Precipitation was carried out using MeCN (10 mL) instead of Et_2O. White solid (47.0 mg, 45%), mp 186.3−187.2 °C; ^{1}H NMR (400 MHz, D_2O with 8 eq of KOH) δ 7.48 (d, *J* = 8.0 Hz, 2H), 7.33

(dt, J = 8.0 Hz, 2H), 4.32 (s, 1H), 1.29 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O with 8 eq of KOH) δ 183.7, 153.6, 142.0, 129.3, 128.4, 62.8, 36.5, 33.2; IR (KBr, cm^{-1}) 3600−1800, 1618, 1589, 1500; HRMS (DART, m/z) Calcd. for $C_{12}H_{17}NO_3 \cdot H$ ($[M+H]^+$): 208.1338, found 208.1309.

*2-(4-Phenylphenyl)glycine (**2i**)*. Purification was carried out as follows. After the completion of the reaction, Et_2O (5.0 mL) was added to the reaction mixture, which was stirred until the product was fully precipitated. The precipitate was collected by filtration and washed with Et_2O. After the precipitate was transfer to flask, MeCN (3.2 mL) and H_2O (1.4 mL) were added. The resultant suspension was refluxed for 2 h. The precipitate was collected by filtration and washed with Et_2O. This process was carried out once again using MeCN (6.4 mL) and H_2O (2.7 mL). After the residual solvents was removed under reduced pressure, arylglycine **2i** (90.4 mg, 79%) was obtained as a white solid. Mp 232 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 15 eq of KOH) δ 7.56−7.50 (m, 4H), 7.44 (d, J = 8.4 Hz, 2H), 7.32 (t, J = 7.2 Hz, 2H), 7.23 (t, J = 7.2 Hz, 1H), 4.39 (s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O with 15 eq of KOH) δ 183.1, 144.3, 142.6, 142.0, 131.6, 130.1, 129.9, 129.7, 129.4, 62.9; IR (KBr, cm^{-1}) 3600−2000, 1657, 1635, 1585, 1523; HRMS (DART, m/z) Calcd. for $C_{14}H_{13}NO_2 \cdot H$ ($[M+H]^+$): 228.1025, found 228.1003.

*2-(4-Methoxyphenyl)glycine (**2j**)*. White solid (56.7 mg, 63%), mp 258 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 5 eq of KOH) δ 7.32 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 4.30 (s, 1H), 3.82 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O with 5 eq of KOH) δ 184.0, 160.8, 137.7, 130.8, 116.9, 62.5, 58.1; IR (KBr, cm^{-1}) 3300−2000; 1649, 1633, 1622, 1585, 1520; HRMS (DART, m/z) Calcd. for $C_9H_{11}NO_3 \cdot H$ ($[M+H]^+$): 182.0817, found 182.0825.

*2-(4-(Dimethylamino)phenyl)glycine (**2k**)*. The reaction mixture was stirred for 72 h at 50 °C and then it was refluxed for 12 h. MeCN (10 mL) was added for the precipitation instead of Et_2O. White solid (38.4 mg, 40%), mp 205 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 5 eq of KOH) δ 7.29 (d, J = 8.4 Hz, 2H), 6.98 (d, J = 8.4 Hz, 2H), 4.27 (s, 1H), 2.82 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, D_2O with 5 eq of KOH) δ 184.0, 153.3, 135.9, 130.3, 118.5, 62.5, 43.9; IR (KBr, cm^{-1}) 3300−1800, 1618, 1591, 1502; HRMS (ESI, m/z) Calcd. for $C_{10}H_{14}N_2O_2$·Na ([M+Na]$^+$): 217.0953, found 217.0975.

*2-(4-(Chloromethyl)phenyl)glycine (**2l**)*. Purification was carried out as follows. After the completion of the reaction, Et_2O (5.0 mL) was added to the reaction mixture. It was stirred until the product was fully precipitated. The precipitate was collected by filtration and washed with Et_2O. After the precipitate was transferred into a flask, aq. NaOH (1 M) was added until the precipitate was almost completely dissolved. Then, this solution was neutralized with aq. HCl (10%). After the precipitate was collected by filtration and washed with H_2O and Et_2O. After the residual solvents were removed under reduced pressure, arylglycine **2l** (41.4 mg, 44%) was obtained as a pale brown solid. Mp 179 °C (decomp.); ^{1}H NMR (400 MHz, 5wt% deuterium chloride solution in D_2O) δ 7.61 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 8.0 Hz, 2H), 5.29 (s, 1H), 4.74 (s, 3H); IR (KBr, cm^{-1}) 3600−2000, 1657, 1630, 1587, 1523; HRMS (DART, m/z) Calcd. for $C_9H_{10}ClNO_2$·H ([M+H]$^+$): 200.0478, found 200.0471. ^{13}C{^{1}H} NMR spectrum of **2l** could not be collected because of their low solubility and stability.

*2-(3-Chlorophenyl)glycine (**2m**)*. White solid (51.1 mg, 55%), mp 264 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 4 eq of KOH) δ 7.42−7.26 (m, 4H), 4.33 (s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O with 4 eq of KOH) δ 183.0, 146.9, 136.4, 132.9, 130.1, 129.5, 127.9, 62.8; IR (KBr, cm^{-1}) 3300−1800, 1631, 1581, 1522; HRMS (DART, m/z) Calcd. for $C_8H_8ClNO_2 \cdot H$ ($[M+H]^+$): 186.0322, found 186.0339

*2-(3-Methoxyphenyl)glycine (**2n**)*. White solid (34.4 mg, 38%), mp 223 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 4 eq of KOH) δ 7.34 (t, J = 8.4 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 6.98 (t, J = 2.0 Hz, 1H), 6.93 (dd, J = 8.4, 2.0 Hz, 1H), 4.32 (s, 1H), 3.83 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O with 4 eq of KOH) δ 183.5, 161.7, 146.7, 132.7, 122.3, 115.8, 115.0, 63.1, 58.0; IR (KBr, cm^{-1}) 3700−1800, 1637, 1612, 1500; HRMS (DART, m/z) Calcd. for $C_9H_{11}NO_3 \cdot H$ ($[M+H]^+$): 182.0817, found 182.0791.

*2-(2-Methylphenyl)glycine (**2o**)*. White solid (36.4 mg, 44%), mp 225 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 7 eq of KOH) δ 7.25−7.23 (m, 4H), 4.56 (s, 1H), 2.38 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O with 4 eq of KOH) δ 184.3, 143.3, 139.0, 133.3, 130.2, 129.3, 129.2, 59.8, 21.3; IR (KBr, cm^{-1}) 3700−1800; 1676, 1628, 1570, 1523; HRMS (DART, m/z) Calcd. for $C_9H_{11}NO_2 \cdot H$ ($[M+H]^+$): 166.0868, found 166.0848.

*2-(2-Naphthyl)glycine (**2s**)*. Pale yellow solid (72.0 mg, 72%), mp 204 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 11 eq of KOH) δ 7.94−7.84 (m, 4H), 7.58−7.49 (m, 3H), 4.53 (s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, D_2O with 4 eq of KOH) δ 183.3, 142.5, 135.7, 134.9, 131.0, 130.4, 130.2, 129.1, 128.7, 128.1, 127.6, 63.2; IR (KBr, cm^{-1}) 3400−1900,

1595, 1506; HRMS (DART, m/z) Calcd. for $C_{12}H_{11}NO_2 \cdot H$ ($[M+H]^+$): 202.0868, found 202.0839

*2-(4-Hydroxyphenyl)glycine (**2t**)*. Et_2O (5.0 mL) and MeCN (10 mL) were added for precipitation. White solid (40.6 mg, 48%), mp 173 °C (decomp.); ^1H NMR (400 MHz, D_2O with 4 eq of KOH) δ 7.08 (d, J = 8.0 Hz, 2H), 6.58 (d, J = 8.0 Hz, 2H), 4.18 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, D_2O with 4 eq of KOH) δ 184.8, 168.1, 130.8, 130.8, 121.4, 62.7; IR (KBr, cm^{-1}) 3600−1900, 1653, 1631, 1620, 1587; HRMS (DART, m/z) Calcd. for $C_8H_9NO_3 \cdot H$ ($[M+H]^+$): 168.0661, found 168.0632

*2-(4-Allyloxyphenyl)glycine (**2u**)*. White solid (67.5 mg, 65%), mp 247 °C (decomp.); ^1H NMR (400 MHz, D_2O with 7 eq of KOH) δ 7.31 (d, J = 8.4 Hz, 2H), 6.98 (d, J = 8.4 Hz, 2H), 6.07 (ddt, J = 17.2, 10.8, 5.6 Hz, 1H), 5.42 (dq, J = 17.2, 2.0 Hz, 1H), 5.32 (dq, J = 10.8, 2.0 Hz, 1H), 4.59 (dt, J = 5.6, 2.0 Hz, 2H), 4.30 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, D_2O with 7 eq of KOH) δ 183.8, 159.5, 138.0, 135.6, 130.7, 121.1, 117.8, 71.8, 62.5; IR (KBr, cm^{-1}) 3300−2300, 1658, 1631, 1583, 1520; HRMS (DART, m/z) Calcd. for $C_{11}H_{13}NO_3 \cdot H$ ($[M+H]^+$): 208.0974, found 208.0982.

*2-(4-Benzyloxyphenyl)glycine (**2v**)*. Isolated as a HCl salt. 74.0 mg (50%); Purification was carried out as follows. After the completion of the reaction, Et_2O (5.0 mL) was added to the reaction mixture, which was stirred until the product was fully precipitated. The precipitate was collected by filtration and washed with Et_2O. After the precipitate was transferred to a flack, HCl in Et_2O (1 M) was added. The resultant suspension was sonicated. Then, it was

concentrated under reduced pressure. After EtOH and H_2O were added to the residue, the suspension was sonicated. After it was stirred at 60 °C, the precipitate was collected by filtration and washed with Et_2O. After the residual solvents were removed under reduced pressure, **2v•HCl** (68.2 mg) was obtained as a white solid. The filtrate was concentrated in vacuo and washed with EtOH and H_2O again as described above to afford **2v•HCl** (5.8 mg) as a white solid. The combined yield of **2v•HCl** is 50% (74.0 mg). Mp 240 °C (decomp).; ^{1}H NMR (400 MHz, D_2O with 8 eq of KOH) δ 7.30 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 6.8 Hz, 2H), 7.20 (t, *J* = 6.8 Hz, 2H), 7.14 (t, *J* = 6.8 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 2H), 4.77 (s, 2H), 4.31 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, D_2O with 8 eq of KOH) δ 182.9, 159.7, 139.1, 138.0, 130.9 (2C), 130.4 (3C), 130.2 (2C), 117.4 (2C), 72.2, 62.3; IR (KBr, cm^{-1}) 3400−2300, 1658, 1631, 1583, 1518; HRMS (ESI, m/z) Calcd. for $C_{15}H_{15}NO_3 \cdot Na$ ([M+Na]$^+$): 280.0950, found 280.0930.

*4-Benzyloxy-3-chlorophenylglycine (**2w**)*. White solid (92.3 mg, 63%), mp 232 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 8 eq of KOH) δ 7.40 (d, *J* = 2.0 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 2H), 7.14 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 2H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 4.69 (s, 2H), 4.24 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, D_2O with 8 eq of KOH) δ 182.1, 155.1, 139.2, 138.6, 130.8 (3C), 130.3, 129.7 (2C), 128.6, 124.7, 116.7, 72.9, 62.1; IR (KBr, cm^{-1}) 3400−2300, 1635, 1606, 1579, 1514; HRMS (DART, m/z) Calcd. for $C_{15}H_{14}ClNO_3 \cdot H$ ([M+H]$^+$): 292.0741, found 292.0724.

Typical Procedure B for Transamination of Arylglyoxylic Acids

*2-(4-Trifluoromethylphenyl)glycine (**2e**)*. To a flask charged with arylglyoxylic acid **1e** (109 mg, 0.501 mmol) and

L-2-(2-chlorophenyl)glycine (186 mg, 1.00 mmol) were added MeCN (3.5 mL) and H_2O (1.5 mL) at room temperature. After the reaction mixture was stirred for 24 h at 50 °C, it was cooled to room temperature. After Et_2O (5.0 mL) was added, the reaction mixture was stirred until the product was fully precipitated. After the precipitate was collected by filtration and washed with Et_2O, it was dissolved into a solution of H_2O and aq. NaOH (10%). Then, the solution was neutralized with aq. HCl (10%) and a precipitate appeared. It was collected by filtration and washed with H_2O and Et_2O, and dissolved into a solution of H_2O and aq. NaOH (10%) again. The solution was neutralized with aq. HCl (10%), and a precipitate appeared. It was collected by filtration and washed with H_2O and Et_2O. After the residual solvents were removed under reduced pressure, **2e•HCl** (41.2 mg, 38%) was obtained as a white solid. Mp 263 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 4 eq of KOH) δ 7.37 (t, J = 7.6 Hz, 2H), 7.31 (d, J = 7.6 Hz, 2H), 7.36 (t, J = 7.6 Hz, 1H), 4.43 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, D_2O with 7 eq of KOH) δ 182.9, 149.0, 131.3 (q, J = 63.9 Hz), 129.9, 128.3 (q, J = 3.8 Hz), 127.0 (q, J = 269.8 Hz), 62.9; IR (KBr, cm^{-1}) 3200−2200, 1658, 1630, 1585, 1522; HRMS (DART, m/z) Calcd. for $C_9H_8F_3NO_2 \cdot H$ ($[M+H]^+$): 220.0585, found 220.0557.

*2-(1-Naphthyl)glycine (**2p**)*. Isolated as a HCl salt. Purification was carried out as follows. After the completion of the reaction, Et_2O (5.0 mL) was added to the reaction mixture, which was stirred until the product was fully precipitated. The precipitate was collected by filtration and washed with Et_2O. After the precipitate was dissolved into a solution of H_2O and aq. NaOH (10%), the solution was neutralized with aq. HCl (10%). The resultant solution was concentrated in vacuo until a precipitate appeared. The precipitate was collected by filtration and washed with H_2O and Et_2O. After the residual solvents were removed under reduced pressure, **2p•HCl** (35.9 mg, 36%) was

obtained as a white solid. Mp 210 °C (decomp.); ^{1}H NMR (400 MHz, D_2O with 5 eq of KOH) δ 8.18 (d, *J* = 8.0 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.65−7.47 (m, 4H), 5.0 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, D_2O with 5 eq of KOH) δ 184.1, 140.9, 136.4, 133.4, 131.5, 130.7, 129.2, 128.7, 128.6, 127.9, 126.2, 60.3; IR (KBr, cm^{-1}) 3600−1800, 1668, 1641, 1574, 1510; HRMS (DART, m/z) Calcd. for $C_{12}H_{12}NO_2 \cdot H$ ($[M+H]^+$): 202.0868, found 202.0841.

Typical Procedure for Transamination of Alkylglyoxylic Acids

*DL-Homophenylalanine (**3a**)*.[14] To a flask charged with 2-oxo-4-phneylbutanoic acid (**1c**) (90.2 mg, 0.506 mmol) and L-2-(2-chlorophenyl)glycine (186.7 mg, 1.01 mmol), MeCN (3.5 mL) and H_2O (1.5 mL) were added at room temperature. After the reaction mixture was stirred for 24 h at 50 °C, it was refluxed for 12 h. Then, MeCN (3.5 ml) and H_2O (1.5 ml) were added, and the mixture was reflux for 2 h. After the mixture was cooled to room temperature, Et_2O (10 ml) was added. The solution was stirred until the product was fully precipitated. After filtration, the precipitate was washed with diethyl ether and the residual solvents was removed under reduced pressure to afford **3a** (74.0 mg, 82%) as a white solid; ^{1}H NMR (400 MHz, D_2O with 4 eq of KOH) δ 7.39 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 3.25 (t, *J* = 6.4 Hz, 1H), 2.64 (t, *J* = 8.0 Hz, 2H), 1.95-1.79 (m, 2H).

*DL-Phenylalanine (**3b**)*.[14] White solid (65.8 mg, 80%); ^{1}H NMR (400 MHz, D_2O with 4 eq of KOH) δ 7.38 (t, *J* = 7.2 Hz, 2H), 7.32-7.25 (m, 3H), 3.50 (dd, *J* = 7.2, 5.6 Hz, 1H), 2.98 (dd *J* = 13.2, 5.6 Hz, 1H), 2.85 (dd *J* = 13.2, 7.2 Hz, 1H).

*DL-Leucine (**3b**)*.[14] White solid (44.3 mg, 68%); ^{1}H NMR (400 MHz, D_2O with 4 eq of KOH) δ, 3.24 (dd, *J* = 8.4, 5.6 Hz, 1H), 1.70-1.58 (m, 1H), 1.49-1.32 (m, 2H), 0.90 (d, *J* = 7.2, 3H), 0.88 (d *J* = 6.8 Hz, 3H).

*Synthesis of 2-(4-((Phenylthio)methyl)phenyl)glycine (**4**)*. To a suspension of arylglycine **2l** (17.5 mg, 0.0877 mmol) and thiophenol (11.6 μL, 0.114 mmol) in H_2O was added Na_2CO_3 (23.4 mg, 0.221 mmol) at room temperature. After the reaction mixture was stirred for 3 h, additional thiophenol (11.6 μL, 0.114 mmol) and Na_2CO_3 (24.0 mg, 0.226 mmol) were added. The reaction mixture was stirred for 2 h. After the reaction mixture was acidified with aq. HCl (2 M), it was neutralized with aq. NaOH (1 M). After the addition of Et_2O (5.0 mL), the reaction mixture was stirred until the product was fully precipitated. After filtration, the precipitate was washed with H_2O and Et_2O. After the residual solvents were removed under reduced pressure, **4** (17.2 mg, 72%) was obtained as a white solid. ^{1}H NMR (400 MHz, D_2O with 37 eq of KOH) δ 7.33−7.15 (m, 9H), 4.27 (s, 1H), 4.09 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, D_2O with 37 eq of KOH) δ 183.4, 144.0, 139.5, 137.4, 132.5, 131.8, 131.7, 129.6, 129.4, 62.8, 40.1; IR (KBr, cm^{-1}) 3300−2200, 1658, 1631, 1585, 1522; HRMS (DART, m/z) Calcd. for $C_{15}H_{15}NO_2S{\cdot}H$ ($[M+H]^+$): 274.0902, found 274.0928.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Characterization of new compounds, and ^{1}H and $^{13}C\{^1H\}$ NMR spectra

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