SYNTHESIS OF 8-OXA-2-AZABICYCLO[3.2.1]OCTANE USING A 1,3-DIPOLAR CYCLOADDITION REACTION

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Abstract – Herein, we report the application of 1,3-dipolar cycloaddition reaction toward the synthesis of a variety of 8-oxa-2-azabicyclo[3.2.1]octane compounds, the core structure of atkamine. The target compounds were obtained using a combination of a vinyl ether and carbonylylide, which was generated from a diazo compound and rhodium catalyst, in the presence of a Lewis acid.

INTRODUCTION

A large number of unique molecules with novel skeletons and important biological activities have been discovered from marine organisms, and have great potential as novel lead compounds for drug discovery. Since the late 1980s, a number of pyrroloiminoquinone alkaloids have been isolated and characterized (Figure 1), which show inhibitory activity against DNA topoisomerase II.¹ For example, discorhabdin A (1) exhibits cytotoxicity against L5178Y and P388 mouse leukemia cells, and makaluvamine F (2) and tsitsikammamine A (3a) and B (3b) display cytotoxicity against human colon tumor cell line HCT116. Aleutianamine (4), the most recently isolated compound, has cytotoxic activity toward pancreatic cancer (PANC-1).² In 2013, a new pyrroloiminoquinone alkaloid, atkamine (5), was isolated from *Latrunculia* sp., an Alaska sponge, and its structure was elucidated.³ Since this compound has a pyrroloiminoquinone structure, its biological activity has attracted substantial interest, however, no data have been reported to date. Additionally, atkamine (5) has an 8-oxa-2-azabicyclo[3.2.1]octane skeleton (6) possessing four continuous asymmetric centers at the central structure, which is not found in common pyrroloiminoquinone alkaloids, and a linear 20-carbon side chain bearing *cis* alkene positioned at the junction of the benzo thiophene ring. Therefore, atkamine (5) is a biologically and synthetically attractive molecule.
The formation of 8-oxa-2-azabicyclo[3.2.1]octane (6) has been reported using a Heck reaction and subsequent cyclization, and via an intramolecular carbonyl-ene reaction. However, these methods are difficult to apply to the synthesis of 5 due to a substituent tolerance and a steric control. On the other hand, 1,3-dipolar cycloaddition reaction is one of the most valuable synthetic methods used for the construction of a variety of heterocyclic compounds corresponding to the combination of a wide range of dipoles and dipolarophiles. Among them, the cycloaddition of a cyclic carbonyl ylide generated from an \( \alpha \)-diazocarbonyl compound in the presence of a rhodium(II) catalyst can give oxabicyclic compounds. This type of reaction was first reported by Takebayashi and Ibata in 1972 and has led to its subsequent use toward the preparation of several polysubstituted oxabicyclic skeletons utilizing various dipolarophiles. Further investigations have been reported by Suga, Hashimoto and Padwa, including the asymmetric variant of the reaction and its application in natural product synthesis. Thus, 1,3-dipolar cycloaddition would be an efficient synthetic method for the highly stereoselective construction of polysubstituted 8-oxa-2-azabicyclo[3.2.1]octane ring systems 7. Here we report a 1,3-dipolar cycloaddition using \( \alpha \)-diazocarbonyl compounds 8 as a carbonyl ylide precursor to prepare 8-oxa-2-azabicyclo[3.2.1]octane skeleton of the core structure of atkamine (5).
RESULTS AND DISCUSSION

N-Arylcarbamate derivatives 11 bearing different substituents on the nitrogen atom were synthesized (Scheme 2). A methoxycarbonyl group was introduced into compounds 9 and 10 to give their corresponding N-phenyl and N-tosyl derivatives, 11b and 11f, respectively. Compound 11a was treated with a variety of acid anhydrides to give carbamates 11c-e.

Thereafter, the diazotizations of carbamate 11 were studied (Table 1). The diazo (azido) transfer reactions were examined for azidation reagents and bases referring to the guidelines of Evans. The reaction of 11a was carried out using tosyl azide and DBU to obtain diazo compound 12a in 67% yield (entry 1). However, the reaction of 11b with the same reagents afforded diazo compound 12b and azide 13b as an inseparable mixture (entry 2). In the case of p-acetylaminobenzenesulfonyl azide, the ratio of...
12b and 13b was reversed (entry 3). On the other hand, by the use of nonafluorobutanesulfonyl azide, which is known as a bench-stable electron-deficient diazo transfer reagent, a mixture of 12b and 13b was obtained with high selectivity in a moderate yield (entry 4). Furthermore, using diphenylphosphoryl azide and LDA at –78 °C, high selectivity toward the diazo form was observed, but the yield was low (entry 5). The diazotization of N-arylcarbamate derivatives 11c-f was investigated using the condition of entry 4. Reaction of Boc 11c and tosyl 11f derivatives gave the diazo compounds as the major products (entries 6 and 9). In the case of methoxycarbonyl compound 11d, diazo form 12d was obtained with excellent selectivity (entry 7). When an electron withdrawing group substituted on the nitrogen atom in the substrate 11, the ratio of azide 13 tended to be increased (entry 1 vs 2, 7 vs 8).

Table 1. Diazotization of N-arylcarbamate 11a-f

<table>
<thead>
<tr>
<th>entry</th>
<th>11 (X =)</th>
<th>R-N3 (equiv.)</th>
<th>base (equiv.)</th>
<th>solvent</th>
<th>temp.</th>
<th>time (h)</th>
<th>yield (%) and ratio of 12 : 13 a,b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11a (H)</td>
<td>p-Me-C6H4-SO2N3 (2.0)</td>
<td>DBU (3.0)</td>
<td>MeCN</td>
<td>rt</td>
<td>3.5</td>
<td>67 (12a only)</td>
</tr>
<tr>
<td>2</td>
<td>11b (Ph)</td>
<td>p-Me-C6H4-SO2N3 (1.5)</td>
<td>DBU (2.0)</td>
<td>MeCN</td>
<td>rt</td>
<td>5</td>
<td>66 (2 : 1)</td>
</tr>
<tr>
<td>3</td>
<td>11b (Ph)</td>
<td>p-AcNH-C6H4-SO2N3 (1.5)</td>
<td>DBU (1.5)</td>
<td>MeCN</td>
<td>rt</td>
<td>6</td>
<td>81 (1 : 2)</td>
</tr>
<tr>
<td>4</td>
<td>11b (Ph)</td>
<td>F9C5SO2N3 (1.5)</td>
<td>DBU (1.5)</td>
<td>MeCN</td>
<td>rt</td>
<td>3</td>
<td>43 (15 : 1)</td>
</tr>
<tr>
<td>5</td>
<td>11b (Ph)</td>
<td>(PhO)2P(O)N3 (1.2)</td>
<td>LDA (1.2)</td>
<td>THF</td>
<td>–78 ºC</td>
<td>1.5</td>
<td>33 (15 : 1)</td>
</tr>
<tr>
<td>6</td>
<td>11c (Boc)</td>
<td>F9C5SO2N3 (1.5)</td>
<td>DBU (1.5)</td>
<td>MeCN</td>
<td>rt</td>
<td>3</td>
<td>49 (6 : 1)</td>
</tr>
<tr>
<td>7</td>
<td>11d (CO2Me)</td>
<td>F9C5SO2N3 (1.5)</td>
<td>DBU (1.5)</td>
<td>MeCN</td>
<td>rt</td>
<td>16</td>
<td>22 (22 : 1)</td>
</tr>
<tr>
<td>8</td>
<td>11e (Ac)</td>
<td>F9C5SO2N3 (1.5)</td>
<td>DBU (1.5)</td>
<td>MeCN</td>
<td>rt</td>
<td>1.5</td>
<td>50 (2.5 : 1)</td>
</tr>
<tr>
<td>9</td>
<td>11f (Ts)</td>
<td>F9C5SO2N3 (1.5)</td>
<td>DBU (1.5)</td>
<td>MeCN</td>
<td>rt</td>
<td>23</td>
<td>41 (6 : 1)</td>
</tr>
</tbody>
</table>

a) combined yields for the inseparable mixtures of 12 and 13
b) Ratio of 12 and 13 was determined by 1H NMR.
The 1,3-dipolar cycloaddition reactions between diazo esters 12 and dimethyl acetylenedicarboxylate (DMAD) were studied in the presence of rhodium(II) acetate dimer (Scheme 3). When compound 12a (X = H) was used in the reaction, 6H-1,3-oxazine 15 was obtained as the sole product. In the case of N-phenyl compound 12b (X = Ph), oxirane 16 was obtained. Considering these results, we assumed that the carbonyl ylide intermediate 14 should be formed under the reaction condition. Although a mixture of compound 16 and DMAD in toluene was stirred at 50 ºC, the reaction did not proceed at all.

![Scheme 3. Reaction of carbonyl ylide 14 with DMAD](image)

Subsequently, the addition of lanthanum(III) triflate as a Lewis acid to the reaction was investigated (Table 2). A solution of 12b and DMAD in dichloromethane was added slowly to a solution of lanthanum(III) triflate in dichloromethane under the reflux condition, however, the desired product was not obtained (entries 1 and 2). The reaction of butyl vinyl ether and 12b without the addition of a Lewis acid, a trace amount of the desired product 8-oxa-2-azabicyclo[3.2.1]octane 17b was generated (entry 3). When a catalytic amount of lanthanum(III) triflate was added and the resulting mixture was stirred at room temperature, 17b was obtained in 6% yield (entry 4). The reaction was carried out at refluxing temperature of dichloromethane, the yield of 17b was improved to 35% yield (entry 5), however, at 80 ºC in 1,2-dichloromethane, the yield of 17b decreased to 18% (entry 6). In the reaction using Boc derivative 12c, the product 17c was not be detected (entry 7). The desired compounds were obtained in 5% yield for methoxycarbonyl compound 17d (entry 8), trace amounts for acetyl compound 17e (entry 9), and 10% yield for tosyl derivative 17f (entry 10). The reaction using other dipolarophiles such us vinyl acetate, 1-hexene, and 4-methoxystyrene did not form the corresponding cycloadducts.
The stereochemistry of compound 17b was determined as follows (Figure 2). HMBC correlations were observed between each hydrogen atom at C6 and C7 and both carbon atoms at C1 and C5. Moreover, the NOE of hydrogens between the phenyl group and C7 were observed. In addition, the coupling constant of 1H NMR spectrum between two hydrogens at C6 and C7 suggest the dihedral angle of H7β-C7-C6-H6. From the above results, it was determined that compound 17b includes 8-oxa-2-azabicyclo[3.2.1]octane as an endo adduct.
Finally, we examined the scope of the dipolarophiles in the reaction (Scheme 4). The reaction of 12b with cyclohexyl vinyl ether gave cycloadduct 17g in 19% yield. In the case of a silyl ether-type dipolarophiles such as trimethylsilyl vinyl ether and silylketene acetal, the desired products 17h and 17i were obtained in low yields, respectively. The cyclization reaction also proceeded using 2,3-dihydrofuran as a cyclic vinyl ether to obtain the desired product 17j in 12% yield.

Scheme 4. The 1,3-dipolar cycloaddition with various vinyl ethers
CONCLUSION

We have examined the construction of the 8-oxa-2-azabicyclo[3.2.1]octane skeleton contained in atkamine (5) using the 1,3-dipolar cycloaddition of a variety of carbonyl ylides and vinyl ethers in the presence of rhodium acetate dimer and lanthanum(III) triflate as catalysts. This method provides a new synthetic approach to the 8-oxa-2-azabicyclo[3.2.1]octane framework.

EXPERIMENTAL

General. All melting points were measured on a Yanagimoto micro melting point apparatus. IR spectra were recorded on a JASCO FT/IR-4100 spectrometer and absorbance bands are reported in wavenumber (cm⁻¹). ¹H NMR spectra were recorded on JEOL JNM-AL 300 (300 MHz) spectrometer or JEOL JNM-ECA 400 (400 MHz) spectrometer. Chemical shifts are reported relative to internal standard (tetramethylsilane at δH 0.00, CDCl₃ at δH 7.26, DMSO-d₆ at δH 2.50). Data are presented as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant and integration. ¹³C NMR spectra were recorded on JEOL JNM-ECA 400 (100 MHz) spectrometer. Chemical shifts are reported relative to internal standard (CDCl₃ at δ 77.00, DMSO-d₆ at δ 40.45). Mass spectra were recorded on a JEOL JMS 700 instrument with a direct inlet system. Column chromatography was carried out on Kanto silica gel 60 N (40–50 mesh). Analytical thin layer chromatography (TLC) was carried out on Merck Kieselgel 60 F₂₅₄ plates with visualization by ultraviolet, anisaldehyde stain solution or phosphomolybdic acid stain solution. All non-aqueous reactions were carried out in flame-dried glassware under Ar atmosphere unless otherwise noted. Reagents and solvents were used without purification. 4Å MS from nacalai tesque was used after drying. Nonfluorobutanesulfonfyl azide was prepared according to the literature.


To a solution of triphosgene (197 mg, 0.66 mmol) in CH₂Cl₂ (3.0 mL) was added pyridine (321 μL, 5.30 mmol) at 0 °C. After stirring at the same temperature for 5 min, a solution of 9 (480 mg, 1.99 mmol) in CH₂Cl₂ (7.0 mL) was added via cannula. After stirring at the room temperature for 3 h, the reaction was quenched with saturated aqueous NH₄Cl, and the mixture was extracted with CH₂Cl₂. The combined organic extracts were dried over anhydrous MgSO₄. Filtration and evaporation in vacuo furnished the crude product, which was purified by column chromatography (silica gel, 4:1 n-hexane/EtOAc) to give acid chloride (483 mg, 80%) as a colorless oil.

To a solution of obtained acid chloride (483 mg, 1.59 mmol) in MeOH (20 mL) was added pyridine (176 μL, 2.19 mmol), and the mixture was refluxed for 8 h. After the completion of the reaction, the whole
mixture was concentrated in vacuo to furnish the crude product, which was purified by column chromatography (silica gel, 3:1 n-hexane/EtOAc) to give 11b (419 mg, 88%) as a brown oil. The spectroscopic data of the product were fully consistent with those reported in the literature.\footnote{12}

2. Typical procedure for the acylation of methyl (2-methoxycarbonylaminophenyl)acetate (11a).

To a solution of 11a,\footnote{13} Et$_3$N, and acid anhydride (X$_2$O) in MeCN was added DMAP. After the completion of the reaction, the whole mixture was concentrated in vacuo to furnish the crude product, which was purified by column chromatography.

Methyl [2-[(tert-butoxycarbonyl)(methoxycarbonyl)amino]phenyl]acetate (11c)

Carbamate 11a (500 mg, 2.24 mmol), Et$_3$N (468 µL, 3.36 mmol), Boc$_2$O (772 µL, 3.36 mmol), DMAP (821 mg, 6.72 mmol), and MeCN (22 mL) were used (reaction time: 10 h). The crude product was purified by column chromatography (silica gel, 3:1 n-hexane/EtOAc) to give 11c (625 mg, 96%) as an orange oil: IR (CHCl$_3$) $\nu$ 3025, 2984, 2955, 1788, 1743 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ 1.39 (9H, s), 3.55 (2H, s), 3.66 (3H, s), 3.70 (3H, s), 7.13 (1H, dd, $J = 7.4, 1.6$ Hz), 7.25-7.44 (3H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 27.4, 36.3, 51.7, 53.4, 82.9, 127.8, 128.2, 128.4, 130.6, 131.8, 137.2, 150.6, 152.8, 170.5; MS (FAB) m/z (%) 324 ([M+H]$^+$, 44), 268 (98), 224 (47), 192 (94), 185 (78), 164 (20), 132 (28), 93 (100), 75 (24), 57 (29); HRMS (FAB) calcd for C$_{16}$H$_{22}$NO$_6$ [M+H]$^+$ 324.1447, found 324.1441.

Methyl {2-[bis(methoxycarbonyl)amino]phenyl}acetate (11d)

Carbamate 11a (500 mg, 2.24 mmol), Et$_3$N (468 µL, 3.36 mmol), (MeOCO)$_2$O (288 µL, 2.69 mmol), DMAP (82 mg, 0.67 mmol), and MeCN (22 mL) were used (reaction time: 21 h). The crude product was purified by column chromatography (silica gel, 1:1 n-hexane/EtOAc) to give 11d (350 mg, 56%) as a light yellow solid: mp 125–127 °C (EtOAc); IR (CHCl$_3$) $\nu$ 3031, 2956, 1793, 1740 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ 3.54 (2H, s), 3.64 (3H, s), 3.71 (6H, s), 7.16 (1H, d, $J = 7.3$ Hz), 7.26-7.48 (3H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 36.6, 51.8, 53.7 (CH$_3$×2), 128.0, 128.7 (CH×2), 131.0, 131.9, 136.7 (C×2), 152.6 (C×2), 170.4; MS (EI) m/z (%) 281 ([M]$^+$, 36), 250 (10), 249 (28), 206 (35), 205 (100), 190 (41), 178 (11), 162 (54), 147 (19), 146 (41), 132 (57), 118 (14), 91 (10), 77 (12), 59 (10); HRMS (EI) calcd for C$_{13}$H$_{15}$NO$_6$ [M]$^+$ 281.0899, found 281.0898.

Methyl [2-[(acetyl)(methoxycarbonyl)amino]phenyl]acetate (11e)

Carbamate 11a (500 mg, 2.24 mmol), Et$_3$N (937 µL, 6.72 mmol), Ac$_2$O (635 µL, 6.72 mmol), DMAP (821 mg, 6.72 mmol), and MeCN (22 mL) were used (reaction time: 1.5 h). The crude product was purified by column chromatography (silica gel, 1:1 n-hexane/EtOAc) to give 11e (590 mg, quant.) as a light yellow solid: mp 62–65 °C (EtOAc); IR (CHCl$_3$) $\nu$ 3027, 2956, 1745, 1711 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ 2.65 (3H, s), 3.46 (2H, d, $J = 1.2$ Hz), 3.64 (3H, s), 3.68 (3H, s), 7.08 (1H, dd, $J = 7.1, 1.6$ Hz), 7.31-7.43 (3H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 26.1, 37.5, 52.0, 53.8, 128.4, 128.9, 129.2,
131.4, 132.3, 137.3, 154.5, 170.7, 172.5; MS (EI) m/z (%) 265 ([M]+, 7), 223 (70), 192 (25), 191 (53), 163 (38), 159 (14), 133 (11), 132 (100), 118 (10); HRMS (EI) calcd for C_{13}H_{15}NO_5 [M]+ 265.0950, found 265.0947.


To a solution of 10^{19} (500 mg, 1.57 mmol), Et_3N (327 μL, 2.35 mmol), and (MeOCO)_2O (336 μL, 3.13 mmol) in MeCN (16 mL) was added DMAP (57 mg, 0.47 mmol). After stirring at room temperature for 11 h, the whole mixture was concentrated in vacuo to furnish the crude product, which was purified by column chromatography (silica gel, 1:1 n-hexane/ EtOAc) to give 11f (550 mg, 93%) as a colorless solid: mp 135–138 °C (EtOAc); IR (CHCl_3) ν 3036, 2956, 1739, 1598 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, 80 °C): δ 2.45 (3H, s), 3.55 (3H, s), 3.59 (3H, s), 3.64 (2H, d, J = 5.9 Hz), 7.15 (1H, dd, J = 7.8, 1.0 Hz), 7.37 (1H, dt, J = 7.8, 2.0 Hz), 7.44 (1H, dt, J = 7.3, 1.0 Hz), 7.48 (3H, d, J = 7.8 Hz), 7.87 (2H, d, J = 8.3 Hz); ^13C NMR (100 MHz, DMSO-d_6, 80 °C): δ 20.7, 35.8, 51.2, 53.5, 127.9, 128.3, 128.5, 129.2, 129.4, 131.1, 134.0, 134.4, 135.5, 144.8, 151.4, 169.6; MS (EI) m/z (%) 377 ([M]+, 2), 314 (19), 313 (100), 222 (28), 207 (11), 206 (91), 191 (73), 190 (15), 162 (56), 155 (23), 132 (51), 91 (39); HRMS (EI) calcd for C_{18}H_{19}NO_6S [M]+ 377.0933, found 377.0931.

4. Procedure for the diazotization of methyl (2-methoxycarbonylaminophenyl)acetate (11a).

To a solution of 11a (300 mg, 1.34 mmol) and TsN_3 (11-15% in toluene, 2.75 mL, ca. 2.69 mmol) in MeCN (7.0 mL), DBU (603 μL, 4.03 mmol) was slowly added at 0 °C. After stirring at room temperature for 3 h, the reaction was quenched with 10% aqueous citric acid, and the mixture was extracted with EtOAc. The combined organic extracts were successively washed with brine, and dried over anhydrous MgSO_4. Filtration and evaporation in vacuo furnished the crude product, which was purified by column chromatography (silica gel, 4:1 n-hexane/EtOAc) to give 12a (225 mg, 67%) as a yellow oil: IR (CHCl_3) ν 3029, 2956, 2100, 1732, 1681 cm^{-1}; ^1H NMR (400 MHz, CDCl_3): δ 3.77 (3H, s), 3.88 (3H, s), 7.16 (1H, dt, J = 7.3, 1.0 Hz), 7.23 (1H, dd, J = 7.8, 1.5 Hz), 7.36 (1H, dt, J = 8.0, 2.0 Hz), 7.60 (1H, brs), 7.86 (1H, brd, J = 6.8 Hz); ^13C NMR (100 MHz, CDCl_3): δ 52.4, 52.6, 60.0, 116.8, 124.0, 124.7, 128.8, 129.6, 136.8, 154.6, 167.1; MS (FAB) m/z (%) 249 ([M]+, 14), 223 (13), 222 (100), 221 (58), 190 (33), 162 (26), 155 (23), 154 (90), 146 (23), 138 (26), 137 (49), 136 (58), 107 (16), 89 (13), 77 (12); HRMS (FAB) calcd for C_{11}H_{11}N_3O_4 [M]+ 249.0750, found 249.0751.

5. Typical procedure for the diazotization of methyl (2-methoxycarbonylaminophenyl)acetates 11b-f.

To a solution of arylacetate 11 (1.0 equiv) and C_4F_9SO_2N_3 (1.2-1.5 equiv) in MeCN (0.1 M), DBU (1.4-1.5 equiv) was slowly added at 0 °C and the mixture was stirred at room temperature. After completion of the reaction was confirmed by TLC analysis, the reaction was quenched with saturated
aqueous NH₄Cl, and the mixture was extracted with EtOAc. The combined organic extracts were successively washed with brine, and dried over anhydrous MgSO₄. Filtration and evaporation in vacuo furnished the crude product, which was purified by column chromatography to give inseparable mixture of diazo compound 12 and azide 13.

**Methyl 2-[(methoxycarbonyl)(phenyl)amino]phenyl)diazoacetate (12b) and methyl azido-2-[(methoxycarbonyl)(phenyl)amino]phenyl)acetate (13b)**

Arylacetic acid 11b (500 mg, 1.67 mmol), C₄F₉SO₂N₃ (814 μL, 2.51 mmol), DBU (375 μL, 2.51 mmol), and MeCN (17 mL) were used (reaction time: 3 h). The crude product was purified by column chromatography (silica gel, 4:1 n-hexane/EtOAc) to give a 15:1 mixture of 12b and 13b (233 mg, 43%) as a yellow oil: IR (CHCl₃) ν 3026, 3014, 2955, 2099, 1703, 1595 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 3.67 (3H, s), 3.74 (3H, s), 5.28 (1/15H, s), 7.09-7.16 (1H, m), 7.17-7.31 (4H, m), 7.33-7.44 (3H, m), 7.52-7.60 (1H, m); ¹³C NMR (100 MHz, CDCl₃): δ 52.0, 53.3, 59.6, 124.0, 124.4, 125.4, 128.1, 128.7, 129.3, 130.3, 132.0, 140.2, 141.3, 154.9, 165.7; MS (ESI) m/z (%) 348 ([M+Na]+, 12), 320 (33), 299 (21), 298 (100), 266 (14), 239 (12), 238 (74), 194 (12); HRMS (ESI) calcd for C₁₇H₁₅N₃O₄ [M+Na]+ 348.0960, found 348.0956.

**Methyl 2-[(tert-butoxycarbonyl)(methoxycarbonyl)amino]phenyl)diazoacetate (12c) and methyl azido-2-[(tert-butoxycarbonyl)(methoxycarbonyl)amino]phenyl)acetate (13c)**

Arylacetic acid 11c (500 mg, 1.55 mmol), C₄F₉SO₂N₃ (603 μL, 1.86 mmol), DBU (324 μL, 2.17 mmol), and MeCN (15 mL) were used (reaction time: 3 h). The crude product was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc) to give a 6:1 mixture of 12c and 13c (262 mg, 49%) as a yellow oil: IR (CHCl₃) ν 3030, 2099, 1789, 1750, 1703 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.37 (9H, s), 3.73 (3H, s), 3.81 (3H, s), 5.29 (1/6H, s), 7.17-7.22 (1H, m), 7.33-7.47 (2H, m), 7.52-7.58 (1H, m); ¹³C NMR (100 MHz, CDCl₃): δ 27.6 (CH₃×3), 52.2, 53.9, 83.7, 124.2, 128.7, 129.16, 129.19, 131.3, 137.2, 150.6, 153.0, 165.7 (C×2); MS (FAB) m/z (%) 350 ([M+H]+, 13), 307 (18), 294 (15), 189 (11), 266 (56), 265 (30), 248 (11), 222 (48), 221 (14), 220 (12), 206 (13), 190 (45), 162 (20), 155 (26), 154 (100), 146 (17), 139 (12), 138 (30), 137 (55), 136 (65), 120 (13), 107 (21), 91 (14), 89 (17), 57 (63); HRMS (FAB) calcd for C₁₆H₂₀N₃O₆ [M+H]+ 350.1352, found 350.1356.

**Methyl 2-[(bis(methoxycarbonyl)amino]phenyl)diazoacetate (12d) and methyl azido-2-[(bis(methoxycarbonyl)amino]phenyl)acetate (13d)**

Arylacetic acid 11d (300 mg, 1.07 mmol), C₄F₉SO₂N₃ (416 μL, 1.28 mmol), DBU (223 μL, 1.49 mmol), and MeCN (11 mL) were used (reaction time: 16 h). The crude product was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc) to give a 22:1 mixture of 12d and 13d (71 mg, 22%) as a yellow oil: IR (CHCl₃) ν 3034, 3020, 2957, 2099, 1794, 1758, 1703 cm⁻¹; ¹H NMR (400 MHz, CDCl₃):
δ 3.74 (6H, s), 3.78 (3H, s), 5.28 (1/2H, s), 7.19-7.31 (1H, m), 7.34-7.66 (3H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 52.2, 54.0, 72.7, 124.2, 129.1, 129.4, 129.5, 131.4, 136.8, 152.5, 165.4; MS (ESI) $m/z$ (% 330 ([M+Na]$^+$, 43), 303 (18), 280 (25), 274 (18), 162 (11); HRMS (ESI) calcd for C$_{13}$H$_{13}$N$_3$NaO$_6$ [M+Na]$^+$ 330.0702, found 330.0701.


Arylacetae 11e (300 mg, 1.13 mmol), C$_4$F$_9$SO$_2$N$_3$ (441 µL, 1.36 mmol), DBU (237 µL, 1.58 mmol), and MeCN (11 mL) were used (reaction temperature: 0 °C, reaction time: 1.5 h). The crude product was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc) to give a 2.5:1 mixture of 12e and 13e (262 mg, 50%) as a yellow oil: IR (CHCl$_3$) ν 3030, 2098, 1748, 1708, 1439 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ 2.62 (3H, s), 3.70 (3H, s), 3.80 (3H, s), 5.26 (2/5H, s), 7.10-7.20 (1H, m), 7.35-7.52 (2H, m), 7.53-7.58 (1H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 20.3, 26.0, 52.0, 53.7, 72.0, 124.0, 128.8, 129.5, 131.1, 136.6, 153.9, 165.3, 172.3; MS (EI) $m/z$ (% 291 ([M]$^+$, 0.3), 263 (41), 221 (17), 220 (12), 205 (14), 204 (100), 146 (47), 144 (29); HRMS (EI) calcd for C$_{13}$H$_{13}$N$_3$O$_5$ [M]$^+$ 291.0855, found 291.0853.


Arylacetae 11f (500 mg, 1.33 mmol), C$_4$F$_9$SO$_2$N$_3$ (517 µL, 1.59 mmol), DBU (277 µL, 1.86 mmol), and MeCN (13 mL) were used (reaction time: 23 h). The crude product was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc) to give a 6:1 mixture of 12f and 13f (216 mg, 41%) as a yellow oil: IR (CHCl$_3$) ν 3040, 3023, 2956, 2100, 1741, 1700 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): δ 2.47 (3H, s), 3.66 (3H, s), 3.81 (3H, s), 5.01 (1/6H, s), 7.14 (1H, dd, $J$ = 1.2, 7.8 Hz), 7.35 (2H, d, $J$ = 8.4 Hz), 7.38 (1H, dt, $J$ = 1.5, 7.8 Hz), 7.49 (1H, dt, $J$ = 1.2, 7.5 Hz), 7.64 (1H, dd, $J$ = 1.5, 7.8 Hz), 7.92 (2H, d, $J$ = 8.7 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 21.7, 52.3, 54.2, 60.4, 126.8, 129.1, 129.2, 129.5, 130.1, 130.3, 131.4, 134.5, 135.7, 145.2, 152.4, 165.5; MS (FAB) $m/z$ (%) 404 ([M+H]$^+$, 1), 403 ([M]$^+$, 0.4), 376 (22), 307 (25), 187 (31), 155 (58), 154 (100), 138 (30), 137 (68), 136 (69), 107 (21), 91 (28), 89 (17); HRMS (FAB) calcd for C$_{18}$H$_{18}$N$_3$O$_6$S [M+H]$^+$ 404.0916, found 404.0913.

6. **Procedure for the Rh$_2$(OAc)$_4$-catalyzed reaction of methyl [2-(methoxycarbonylamino)phenyl]diazoacetate (12a).**

To a solution of 12a (50 mg, 0.201 mmol) and DMAD (49 µL, 0.401 mmol) in toluene (2.0 mL) was added Rh$_2$(OAc)$_4$ (0.8 mg, 0.002 mmol). After stirring for 20 min at 50 °C, the whole mixture was concentrated in vacuo to furnish the crude product, which was purified by column chromatography (silica gel, 3:1 n-hexane/EtOAc) to give 15 (8.2 mg, 18%) as a yellow oil: IR (CHCl$_3$) ν 2956, 1755, 1645, 1601 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): δ 3.76 (3H, s), 4.00 (3H, s), 5.82 (1H, s), 7.00-7.15 (2H, m),
7.20-7.25 (1H, m), 7.28-7.32 (1H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 53.0, 55.9, 77.2, 118.4, 123.7, 124.7, 125.3, 130.1, 140.1, 155.7, 168.9; MS (EI) m/z (%) 221 ([M]+, 21), 162 (100), 130 (24); HRMS (EI) calcd for C$_{11}$H$_{11}$NO$_4$ [M]+ 221.0688, found 221.0687.


To a solution of DMAD (68 $\mu$L, 0.550 mmol) and Rh$_2$(OAc)$_4$ (0.8 mg, 0.002 mmol), and MS 4Å (100 mg) in refluxing CH$_2$Cl$_2$ (0.50 mL), a solution of 12b (39.4 mg, 0.121 mmol) in CH$_2$Cl$_2$ (1.5 mL) was added over 1 h using syringe pump, and the mixture was further stirred for 1 h at the same temperature. After the completion of the reaction, the whole mixture was filtered through a pad of Celite, and the filtrate was concentrated in vacuo to furnish the crude product, which was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc) to give 16 (18.4 mg, 51%) as a yellow oil: IR (CHCl$_3$) $\nu$ 3027, 1764, 1721 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 3.46 (3H, s), 3.55 (3H, s), 6.96 (1H, t, $J$ = 6.8 Hz), 7.10 (1H, d, $J$ = 8.3 Hz), 7.24-7.33 (1H, m), 7.36-7.46 (4H, m), 7.52 (1H, dt, $J$ = 7.3, 1.4 Hz), 7.68 (1H, d, $J$ = 7.8 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 51.5, 52.9, 94.4, 111.7, 119.8, 120.5, 124.2, 125.2, 126.7, 129.6, 138.2, 138.3, 159.7, 165.1, 194.6; MS (EI) m/z (%) 297 ([M]+, 9), 239 (16), 238 (100), 195 (35), 167 (15), 166 (10); HRMS (EI) calcd for C$_{17}$H$_{15}$NO$_4$ [M]+ 297.1001, found 297.1002.

8. Typical procedure for the cycloaddition of methyl [2-(methoxycarbonyl-amino)phenyl]diazoacetates (12) and n-butyl vinyl ether.

To a solution of La(OTf)$_3$ (0.01 equiv), Rh$_2$(OAc)$_4$ (0.01 equiv), and MS 4Å (100 mg) in refluxing CH$_2$Cl$_2$ (0.50 mL), a solution of 12 (1 equiv) and n-butyl vinyl ether (5 equiv) in CH$_2$Cl$_2$ (1.5 mL) was added over 1 h using syringe pump, and the mixture was further stirred for 1 h at the same temperature. After the completion of the reaction, the whole mixture was filtered through a pad of Celite, and the filtrate was concentrated in vacuo to furnish the crude product, which was purified by column chromatography.

Methyl 4-butoxy-2-methoxy-1-phenyl-1,2,3,4-tetrahydro-5$H$-2,5-epoxybenzo[b]azepine-5-carboxylate (17b)

A mixture of 12b and 13b (15:1, 50 mg) was used. The crude product was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc and CH$_2$Cl$_2$ only) to give 17b (20 mg, 35%) as a yellow solid: mp 79–82 °C (EtOAc); IR (CHCl$_3$) $\nu$ 2955, 2932, 1741, 1596 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.69 (3H, t, $J$ = 7.3 Hz), 0.93-1.05 (2H, m), 1.07-1.22 (2H, m), 2.42 (1H, d, $J$ = 13.7 Hz), 2.51 (1H, dd, $J$ = 13.7, 5.2 Hz), 3.07-3.15 (1H, m), 3.23 (3H, s), 3.29-3.37 (1H, m), 3.88 (3H, s), 5.28 (1H, d, $J$ = 5.2 Hz), 6.86 (1H, dt, $J$ = 8.3, 1.0 Hz), 7.05 (1H, d, $J$ = 8.7 Hz), 7.13 (1H, tt, $J$ = 6.8, 1.9 Hz), 7.23 (1H, dt, $J$ = 7.3, 1.0 Hz), 7.29-7.48 (5H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 13.6 (CH$_3$), 18.8 (CH$_3$), 31.3 (CH$_2$), 40.3 (CH$_2$), 51.6 (CH$_3$), 52.9 (CH$_3$), 66.9 (CH$_2$), 92.7 (C), 104.8 (CH), 107.7 (C), 109.4 (CH), 119.4 (CH),...
122.0 (CHx2), 124.0 (CH), 126.3 (CH), 128.0 (C), 129.1 (CHx2), 130.0 (CH), 140.5 (C), 148.5 (C), 169.9 (C); MS (EI) m/z (%) 397 ([M]+, 100), 324 (13), 321 (20), 310 (10), 266 (10), 264 (21), 238 (24), 236 (13), 204 (14), 195 (12), 193 (11), 192 (42), 133 (14); HRMS (EI) calcd for C_{23}H_{27}NO_{5} [M]+ 397.1889, found 397.1888.

**Dimethyl 4-butoxy-2-methoxy-1H-2,5-epoxybenzo[b]azepine-1,5(2H)-dicarboxylate (17d)**

A mixture of 12d and 13d (22:1, 140 mg) was used. The crude product was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc and CH_{2}Cl_{2} only) to give 17d (7.8 mg, 5%) as a colorless oil: IR (CHCl_{3}) ν 3025, 2956, 1733, 1718, 1704 cm^{-1}; ¹H NMR (400 MHz, CDCl_{3}): δ 0.80 (3H, t, J = 7.3 Hz), 1.07-1.30 (2H, m), 1.30-1.52 (2H, m), 2.71 (1H, dd, J = 13.9, 4.6 Hz), 2.98 (1H, dd, J = 13.9, 4.7 Hz), 3.35-3.60 (2H, m), 3.17 (3H, s), 3.78 (3H, s), 3.79 (3H, s), 5.86 (1H, t, J = 4.6 Hz), 7.15 (1H, dt, J = 7.9, 1.3 Hz), 7.27-7.42 (2H, m), 7.54 (1H, d, J = 7.9 Hz); ¹³C NMR (100 MHz, CDCl_{3}): δ 13.7, 19.0, 31.4, 37.1, 52.9, 53.17, 53.24, 56.1, 67.3, 80.6, 124.5, 125.3, 127.0, 128.0, 128.2, 134.6, 154.8, 170.2, 170.8; MS (EI) m/z (%) 380 ([M+H]+, 13), 379 ([M]+, 64), 306 (55), 246 (100), 232 (33), 202 (15), 189 (22), 144 (12); HRMS (EI) calcd for C_{19}H_{25}NO_{7} [M]+ 379.1631, found 379.1632.

**Methyl 1-acetyl-4-butoxy-2-methoxy-1,2,3,4-tetrahydro-5H-2,5-epoxybenzo[b]azepine-5-carboxylate (17e)**

A mixture of 12e and 13e (2.5:1, 20 mg) was used. The crude product was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc and CH_{2}Cl_{2} only) to give 17e (trace) as a colorless oil: IR (CHCl_{3}) ν 2957, 2930, 1872, 1770, 1744, 1701, 1604 cm^{-1}; ¹H NMR (400 MHz, CDCl_{3}, 50 °C): δ 0.62 (3H, s), 0.65-1.02 (4H, m), 1.57 (3H, brs), 2.19 (1H, dd, J = 14.1, 4.9 Hz), 3.12 (2H, dt, J = 6.6, 2.2 Hz), 2.80-3.30 (1H, m), 3.80 (3H, s), 3.89 (3H, s), 5.37 (1H, d, J = 5.1 Hz), 7.03 (1H, t, J = 7.5 Hz), 7.25-7.40 (2H, m), 7.54-8.02 (1H, brd); ¹³C NMR (100 MHz, CDCl_{3}, 50 °C): δ 13.6, 14.0, 18.9, 29.7, 31.2, 52.4, 52.6, 66.9, 104.9, 115.8, 122.8, 125.2, 130.1, 152.9, 170.6; MS (EI) m/z (%) 364 ([M+H]+, 13), 379 ([M]+, 64), 306 (55), 246 (100), 232 (33), 202 (15), 189 (22), 144 (12); HRMS (EI) calcd for C_{19}H_{25}NO_{7} [M]+ 379.1631, found 379.1632.

**Methyl 4-butoxy-2-methoxy-1-tosyl-1,2,3,4-tetrahydro-5H-2,5-epoxybenzo[b]azepine-5-carboxylate (17f)**

A mixture of 12f and 13f (6:1, 90 mg) was used. The crude product was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc and CH_{2}Cl_{2} only) to give 17f (9.4 mg, 10%) as a colorless oil: IR (CHCl_{3}) ν 3791, 2955, 1767, 1734, 1601 cm^{-1}; ¹H NMR (300 MHz, CDCl_{3}): δ 0.78 (3H, t, J = 7.1 Hz), 1.02-1.21 (2H, m), 1.28-1.45 (2H, m), 2.16 (1H, dd, J = 14.1, 2.6 Hz), 2.38 (3H, s), 2.83 (1H, dd, J = 14.1, 3.3 Hz), 3.35-3.54 (1H, m), 3.58 (3H, s), 3.66 (3H, s), 3.60-3.80 (1H, m), 5.67 (1H, t, J = 3.1 Hz), 7.13 (1H, dt, J = 7.9, 1.3 Hz), 7.22 (2H, d, J = 7.9 Hz), 7.28-7.40 (2H, m), 7.52 (2H, d, J = 8.4 Hz), 7.54 (1H, d, J = 7.9 Hz), 7.60 (1H, s).
Hz), 7.93 (1H, dd, J = 8.3, 0.9 Hz); 13C NMR (100 MHz, CDCl3): δ 13.6, 18.9, 21.5, 31.1, 32.7, 52.8, 53.1, 54.7, 67.4, 82.3, 123.6, 124.1, 124.5, 127.3, 128.7, 129.7, 130.3, 133.3, 135.9, 143.9, 170.2, 170.9; MS (EI) m/z (%) 476 ([M+H]+, 17), 475 ([M]+, 62), 402 (25), 342 (29), 320 (23), 202 (100), 188 (62), 156 (10), 155 (17), 144 (13), 91 (23); HRMS (EI) calcd for C24H29NO7 [M]+ 475.1665, found 475.1663.

9. Procedure for the cycloaddition of methyl [(2-(methoxycarbonyl)(phenyl)-amino)phenyl]diazoacetates (12b) and cyclohexyl vinyl ether.

To a solution of La(OTf)3 (1.8 mg, 3.07 × 10⁻³ mmol), Rh2(OAc)4 (1.4 mg, 3.07 × 10⁻³ mmol), and MS 4Å (100 mg) in refluxing CH2Cl2 (0.75 mL), a solution of 12b (100 mg, 12b:13b = 15:1) and cyclohexyl vinyl ether (218 μL, 1.54 mmol) in CH2Cl2 (2.25 mL) was added over 1 h using syringe pump, and the mixture was further stirred for 1 h at the same temperature. After the completion of the reaction, the whole mixture was filtered through a pad of Celite, and the combined filtrate was concentrated in vacuo to furnish the crude product, which was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc and CH2Cl2 only) to give 17g (24 mg, 19%) as a colorless oil: IR (CHCl3) ν 2935, 2858, 1741, 1595 cm⁻¹; 1H NMR (400 MHz, CDCl3, 50 °C): δ 0.75-1.68 (10H, m), 2.37 (1H, d, J = 13.5 Hz), 2.49 (1H, dd, J = 13.5, 5.2 Hz), 3.23 (3H, s), 3.25-3.37 (1H, m), 3.86 (3H, s), 5.44 (1H, d, J = 5.2 Hz), 6.83 (1H, dt, J = 7.6, 0.9 Hz), 7.00 (1H, d, J = 8.0 Hz), 7.08-7.17 (1H, m), 7.20 (1H, dt, J = 8.2, 1.1 Hz), 7.30-7.43 (5H, m); 13C NMR (100 MHz, CDCl3, 50 °C): δ 23.75 (CH2), 23.84 (CH2), 25.7 (CH2), 31.3 (CH2), 32.9 (CH2), 40.8 (CH2), 51.6 (CH3), 52.7 (CH3), 74.2 (CH2), 92.8 (C), 102.7 (CH), 108.0 (C), 109.3 (CH), 119.3 (CH), 122.7 (CH×2), 124.1 (CH), 126.4 (CH), 128.3 (C), 129.1 (CH×2), 129.9 (CH), 140.7 (C), 148.9 (C), 170.0 (C); MS (EI) m/z (%) 424 ([M+H]+, 27), 423 ([M]+, 100), 340 (39), 324 (16), 264 (12), 250 (12); HRMS (EI) calcd for C25H29NO5 [M]+ 423.2046, found 423.2042.

10. Procedure for the cycloaddition of methyl [(2-(methoxycarbonyl)(phenyl)-amino)phenyl]diazoacetates (12b) and trimethylsilyl vinyl ether.

To a solution of La(OTf)3 (1.8 mg, 3.07 × 10⁻³ mmol), Rh2(OAc)4 (1.4 mg, 3.07 × 10⁻³ mmol), and MS 4Å (100 mg) in refluxing CH2Cl2 (0.75 mL), a solution of 12b (100 mg, 12b:13b = 15:1) and trimethylsilyl vinyl ether (229 μL, 1.54 mmol) in CH2Cl2 (2.25 mL) was added over 1 h using syringe pump, and the mixture was further stirred for 1 h at the same temperature. After the completion of the reaction, the whole mixture was filtered through a pad of Celite, and the combined filtrate was concentrated in vacuo to furnish the crude product, which was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc and CH2Cl2 only) to give 17h (1.2 mg, trace) as a colorless oil: IR (CHCl3) ν 2954, 1741, 1595, 1499 cm⁻¹; 1H NMR (300 MHz, CDCl3): δ 0.00 (9H, s), 2.59 (1H, d, J = 13.3 Hz), 2.73 (1H, dd, J = 13.3, 5.0 Hz), 3.42 (3H, s), 4.08 (3H, s), 5.86 (1H, d, J = 5.0 Hz), 7.06 (1H, t, J = 7.3 Hz), 7.18-7.90 (8H, m); MS (EI) m/z (%) 414 ([M+H]+, 28), 413 ([M]+, 100), 266 (14), 265 (25), 264 (68), 238 (22), 236
11. Procedure for the cycloaddition of methyl [(2-(methoxycarbonyl)(phenyl)-amino)phenyl]diazoacetates (12b) and 1-(tert-butyldimethylsilyloxy)-1-methoxyethene.

To a solution of La(OTf)$_3$ (1.5 mg, 2.58 $\times$ $10^{-3}$ mmol), Rh$_2$(OAc)$_4$ (1.1 mg, 2.58 $\times$ $10^{-3}$ mmol), and MS 4Å (100 mg) in refluxing CH$_2$Cl$_2$ (0.65 mL), a solution of 12b (84 mg, 12b:13b = 15:1) and 1-(tert-butyldimethylsilyloxy)-1-methoxyethene (282 µL, 1.29 mmol) in CH$_2$Cl$_2$ (1.95 mL) was added over 1 h using syringe pump, and the mixture was further stirred for 1 h at the same temperature. After the completion of the reaction, the whole mixture was filtered through a pad of Celite, and the combined filtrate was concentrated in vacuo to furnish the crude product, which was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc and CH$_2$Cl$_2$ only) to give 17i (9 mg, 8%) as a colorless solid: mp 131–132 °C (EtOAc); IR (CHCl$_3$) ν 2952, 2930, 2857, 1741, 1596, 1500 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ –0.46 (3H, s), –0.02 (3H, s), 0.63 (9H, s), 2.44 (1H, d, $J$ = 13.6 Hz), 2.69 (1H, d, $J$ = 13.2 Hz), 3.20 (3H, s), 3.49 (3H, s), 3.87 (3H, s), 6.87 (1H, td, $J$ = 7.3, 1.0 Hz), 7.06-7.18 (2H, m), 7.23 (1H, td, $J$ = 7.3, 1.4 Hz), 7.32-7.47 (5H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): δ –4.3 (CH$_3$), –3.6 (CH$_3$), 17.7 (C), 25.7 (CH$_3$ × 3), 40.7 (CH$_2$), 51.4 (CH$_3$), 51.7 (CH$_3$), 52.7 (CH$_3$), 91.6 (C), 105.8 (C), 109.2 (CH), 119.7 (CH), 121.3 (C), 121.4 (CH × 2), 123.7 (CH), 126.7 (CH), 127.4 (C), 129.1 (CH × 2), 130.1 (CH), 139.8 (C), 148.6 (C), 169.7 (C); MS (EI) m/z (%) 485 ([M]$^+$, 22), 470 (11), 428 (27), 339 (11), 338 (24), 298 (18), 297 (100), 294 (12), 280 (10), 238 (14), 236 (11), 205 (10); HRMS (EI) calcd for C$_{26}$H$_{35}$NO$_6$Si [M]$^+$ 485.2234, found 485.2236.

12. Procedure for the cycloaddition of methyl [(2-(methoxycarbonyl)(phenyl)-amino)phenyl]diazoacetates (12b) and 2,3-dihydrofuran.

To a solution of La(OTf)$_3$ (1.7 mg, 2.83 $\times$ $10^{-3}$ mmol), Rh$_2$(OAc)$_4$ (1.3 mg, 2.83 $\times$ $10^{-3}$ mmol), and MS 4Å (100 mg) in refluxing CH$_2$Cl$_2$ (0.70 mL), a solution of 12b (92 mg, 12b:13b = 15:1) and 2,3-dihydrofuran (107 µL, 1.41 mmol) in CH$_2$Cl$_2$ (2.1 mL) was added over 1 h using syringe pump, and the mixture was further stirred for 1 h at the same temperature. After the completion of the reaction, the whole mixture was filtered through a pad of Celite, and the combined filtrate was concentrated in vacuo to furnish the crude product, which was purified by column chromatography (silica gel, 5:1 n-hexane/EtOAc and CH$_2$Cl$_2$ only) to give 17j (12 mg, 12%) as a colorless solid: mp 130–133 °C (EtOAc); IR (CHCl$_3$) ν 3017, 2954, 1733, 1596, 1495 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): δ 1.56-1.75 (1H, m), 2.05-2.23 (1H, m), 3.60 (3H, s), 3.65-3.78 (2H, m), 3.89 (3H, s), 3.80-4.04 (1H, m), 5.51 (1H, d, $J$ = 8.1 Hz), 6.89-7.10 (3H, m), 7.10-7.40 (6H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 28.1 (CH$_2$), 49.0 (CH), 53.0 (CH$_3$), 53.2 (CH$_3$), 60.2 (C), 66.7 (CH$_2$), 89.8 (CH), 120.7 (CH × 2), 120.8 (CH), 122.0 (CH), 122.9 (CH), 127.4 (CH), 127.8 (C), 139.8 (C), 148.6 (C), 169.7 (C); MS (EI) m/z (%) 485 ([M]$^+$, 22), 470 (11), 428 (27), 339 (11), 338 (24), 298 (18), 297 (100), 294 (12), 280 (10), 238 (14), 236 (11), 205 (10); HRMS (EI) calcd for C$_{26}$H$_{35}$NO$_6$Si [M]$^+$ 485.2234, found 485.2236.
128.8 (CH), 129.1 (CH×2), 142.2 (C), 145.9 (C), 169.5 (C), 171.2 (C); MS (EI) m/z (%) 368 ([M+H]+, 23), 367 ([M]+, 100), 308 (37), 278 (22), 276 (18), 248 (19), 220 (10); HRMS (EI) calcd for C_{21}H_{21}NO_{5} [M]+ 367.1420, found 367.1414.

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