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FRIEDEL-CRAFTS REACTIONS OF VINYLAZIRIDINE LINKED TO AN ESTER GROUP

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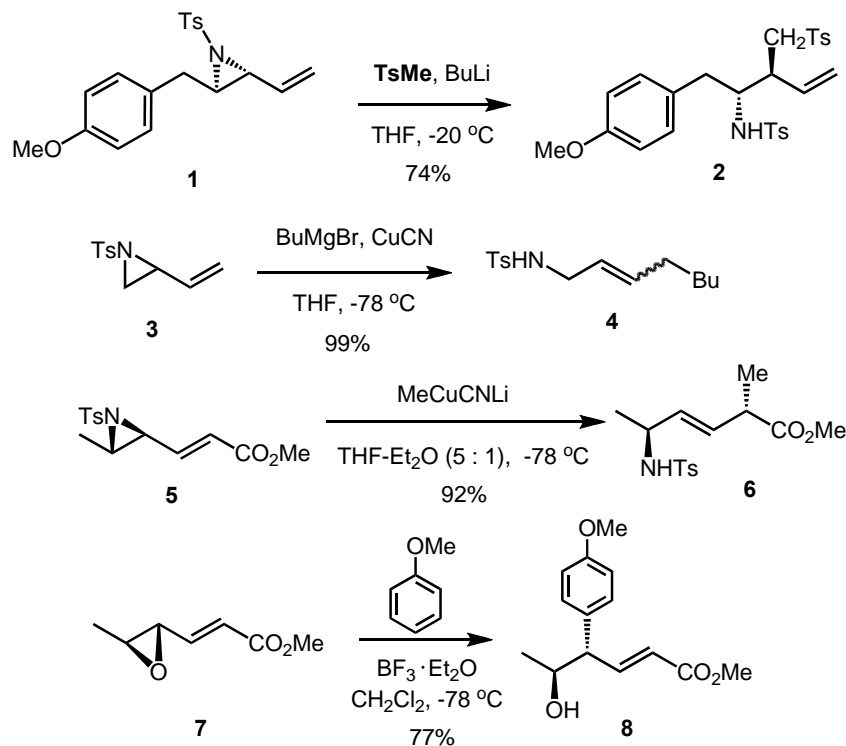
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Abstract – Intermolecular Friedel-Crafts reactions of vinylaziridines **11**, **12**, **15**, **16** and **20** linked to an ester with various benzene derivatives occurred at the C4 position selectively to afford 5-amino-4-aryl-2-hexenoate derivatives in good yields.

INTRODUCTION

Aziridine undergoes several types of reactions as well as epoxide due to its high ring strain. The ring-opening reaction, in particular, is an important transformation¹ and has widely been applied to manifold natural product syntheses.² Its synthetic value depends on the level of regiochemical selection related to both electrophilic carbons in an aziridine moiety. The issue can often be solved by using aziridines that are directly coupled with a π -electron system. Ring-opening reactions of arylaziridine with various nucleophiles such as organometal reagents and electron-rich arenes tend to proceed selectively at a benzylic position.³ Ring-opening reactions of vinylaziridine with various organometal reagents and sulfur-stabilized carbanion have also recently been reported. However, this type of reaction involves another critical issue; that is, an S_N2' -like ring-opening occurs competitively with an S_N2 -like one. The coupling of sulfur-stabilized carbanion with vinylaziridine **1** resulted in the S_N2 like ring-opening with perfect regioselectivity.⁴ In contrast, most organometal reagents have been reported to react with vinylaziridines **3** and **5** in an S_N2' fashion rather than in an S_N2 fashion.⁵ Unlike arylaziridines, there are few reports on regioselective Friedel-Crafts reaction of vinylaziridines. Akita *et al.* reported $BF_3 \cdot Et_2O$ -promoted intermolecular Friedel-Crafts reaction of vinyl epoxides **7** linked to an ester group with

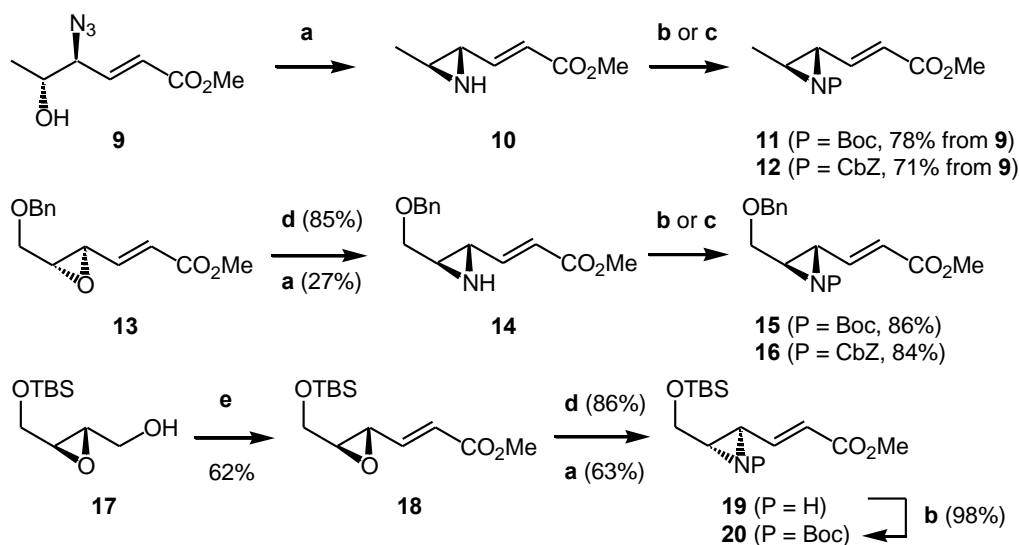
activated arenes.^{6,7} Most arenes attacked **7** in an S_N2 fashion with high regioselectivity. We thus report herein regioselective Friedel-Crafts coupling of the corresponding vinylaziridines linked to an ester group with various arenes.



Scheme 1

RESULTS AND DISCUSSION

Vinylaziridines **11**, **12**, **15**, **16** and **20** were prepared as shown in Scheme 2. Staudinger reaction⁸ of azidealcohol **9** with PPh₃ in MeCN at 90 °C provided aziridine **10**, which was converted into *N*-protected



Scheme 2. (a) PPh₃, MeCN, 90 °C; (b) Boc₂O, Et₃N, THF; (c) CbzCl, Et₃N, CH₂Cl₂, 0 °C to rt; (d) NaN₃, NH₄Cl, EtOH, 80 °C (e) Dess-Martin Periodinane, CH₂Cl₂, 0 °C then Ph₃P=CHCO₂Me, rt.

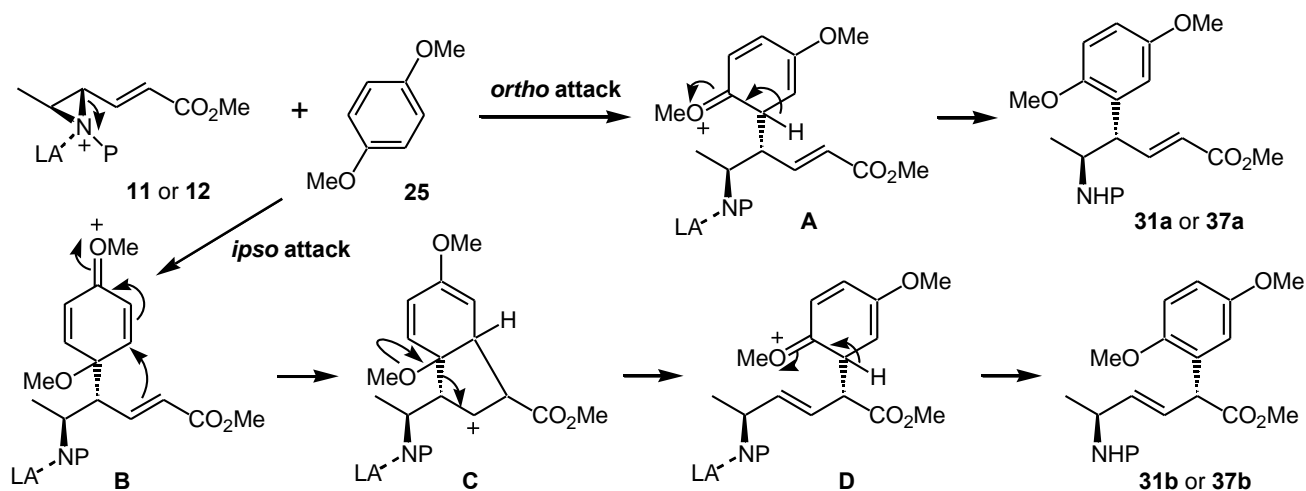
aziridine **11** and **12** by protection with Boc and Cbz groups. Dess-Martin oxidation⁹ of **17** followed by Wittig reaction afforded vinyloxy **18** in 62% yield. Treatment of **13** and **18** with NaN₃/NH₄Cl in EtOH at 80 °C followed by Staudinger reaction gave **14** and **19**, respectively, which were also converted into **15**, **16** and **20** by protection with Boc and Cbz groups.

Table 1. Friedel-Crafts Reactions of Simple Vinylaziridines

| Entry | Aziridines | Ar | R ₁ | R ₂ | R ₃ | R ₄ | Products | Yields | Ratio (a : b) |
|-------|------------|-----------|----------------|----------------|----------------|----------------|------------------|--------|---------------|
| 1 | 11 | 21 | OMe | H | H | H | 27a | 24% | |
| 2 | 11 | 22 | H | Me | H | OMe | 28a | 17% | |
| 3 | 11 | 23 | OMe | OMe | H | H | 29a | 83% | |
| 4 | 11 | 24 | OMe | H | OMe | H | 30a | 76% | |
| 5 | 11 | 25 | H | OMe | H | OMe | 31a + 31b | 76% | ca. 2 : 1 |
| 6 | 11 | 26 | OMe | H | OMe | OMe | 32a | 64% | |
| 7 | 12 | 21 | OMe | H | H | H | 33a | 71% | |
| 8 | 12 | 22 | H | Me | H | OMe | 34a | 79% | |
| 9 | 12 | 23 | OMe | OMe | H | H | 35a | 85% | |
| 10 | 12 | 24 | OMe | H | OMe | H | 36a | 81% | |
| 11 | 12 | 25 | H | OMe | H | OMe | 37a + 37b | 73% | ca. 1.5 : 1 |
| 12 | 12 | 26 | OMe | H | OMe | OMe | 38a | 99% | |

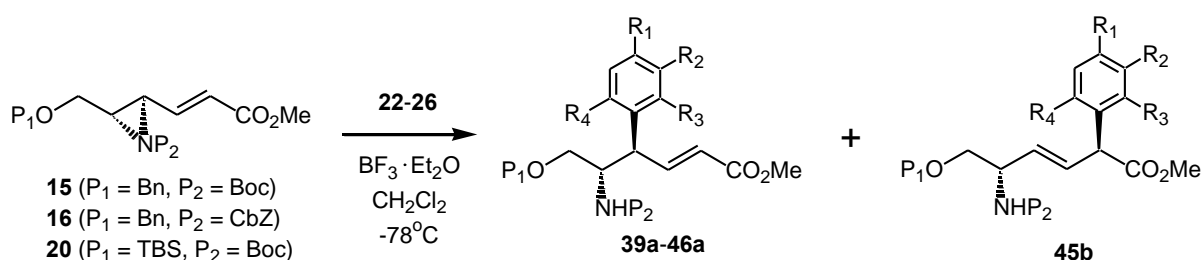
Intermolecular Friedel-Crafts reactions of vinylaziridine **11** and **12** with various kinds of arenes (**21-26**) was conducted in the presence of BF₃·Et₂O in CH₂Cl₂ for 30 min at -78 °C under an argon atmosphere (Table 1). As expected, the coupling of *N*-Boc vinylaziridine **11** with monomethoxybenzenes **21-22** occurred selectively at the C4 position to give **27a** (24%) and **28a** (17%), although their yields were low.¹⁰ The yield increased when dimethoxybenzenes or trimethoxybenzene were used. The reactions with 1,2-dimethoxybenzene (**23**), 1,3-dimethoxybenzene (**24**) and 1,3,5-trimethoxybenzene (**26**) proceeded smoothly to afford 5-amino-4-aryl-2-hexenoate **29a** (83%), **30a** (76%) and **32a** (64%), respectively. On the other hand, the reaction of 1,4-dimethoxybenzene (**25**) resulted in the formation of both S_N2-type product **31a** and S_N2'-type product **31b** as an unseparable mixture (ca. 2 : 1). The yield in the reaction with monomethoxybenzenes was drastically improved by using *N*-Cbz vinylaziridine **12** (Entries 7 and 8). Other results for the reaction of **12** are all similar to those of the reaction of **11** (Entries 9-12). These results indicate that the vinyl group exerts a strong directing effect on the regiochemical recognition of

aziridine ring-opening, which is due to selective weakening of the allylic C-N bond by $\pi\text{C}=\text{C}-\sigma^*\text{C}-\text{N}$ overlap. It was also noteworthy that $\text{S}_{\text{N}}2'$ reaction occurred to furnish 5-amino-2-aryl-4-hexenoate **31b** and **37b** only in the case of using **25** (Entries 5 and 11). This may be explained by considering the sequential mechanistic route, although further argument will be allowed (Scheme 3). Compound **25**, which is distinct from other arenes, undergoes competitive *ortho*-attack and *ipso*-attack¹¹ leading to two different types of benzenium ion **A** and **B**. The intermediate **A** is transformed to $\text{S}_{\text{N}}2$ adduct **31a** or **37a** by a simple deprotonation. On the other hand, **B** may undergo an intramolecular conjugated addition to form bicyclic cation **C**, which is converted into $\text{S}_{\text{N}}2'$ adduct **31b** or **37b** in two steps: (1) isomerization including disconnection of the C-C bond leading to **D** and (2) deprotonation. An electron-releasing effect of the methoxy group should be essential for smooth disconnection of C-C bond in **C**.



Scheme 3

Table 2. Friedel-Crafts Reactions of Vinylaziridines Having an Oxygen Group at the C6 Position



| Entry | Aziridines | P ₁ | P ₂ | Ar | R ₁ | R ₂ | R ₃ | R ₄ | Products | Yields | Ratio (a : b) |
|-------|------------|----------------|----------------|-----------|----------------|----------------|----------------|----------------|------------------|--------|---------------|
| 1 | 15 | Bn | Boc | 23 | OMe | OMe | H | H | 39a | 79% | |
| 2 | 16 | Bn | CbZ | 23 | OMe | OMe | H | H | 40a | 73% | |
| 3 | 16 | Bn | CbZ | 24 | OMe | H | OMe | H | 41a | 46% | |
| 4 | 20 | TBS | Boc | 22 | H | Me | H | OMe | 42a | 67% | |
| 5 | 20 | TBS | Boc | 23 | OMe | OMe | H | H | 43a | 91% | |
| 6 | 20 | TBS | Boc | 24 | OMe | H | OMe | H | 44a | 85% | |
| 7 | 20 | TBS | Boc | 25 | H | OMe | H | OMe | 45a + 45b | 73% | 3 : 1 |
| 8 | 20 | TBS | Boc | 26 | OMe | H | OMe | OMe | 46a | 84% | |

Next, we carried out Friedel-Crafts reactions of vinylaziridines **15**, **16** and **20** possessing an oxygen group at the C6 position because the resulting products were expected to be valuable synthetic intermediates of unnatural amino acids and nitrogen-containing natural products. As a result, also vinylaziridine possessing a benzyloxy or silyloxy group at the C6 position was found to react smoothly with activated arenes **22-26** to afford the target compounds **39a-46a** and **45b** in moderate to good yields.

In summary, intermolecular Friedel-Crafts reactions of vinylaziridines with various arenes were performed. Only in the case of using 1,4-dimethoxybenzene, S_N2' and S_N2 reactions proceeded competitively to give two types of product. In other cases, Friedel-Crafts coupling proceeded regioselectively at the C4 position to give only S_N2-type products in good yields. Synthetic transformation of the products **39-46** into unnatural amino acids is now in progress in our laboratory.

EXPERIMENTAL

General

Melting points were determined on a Yanagimoto MP-S3 micro melting point apparatus and were uncorrected. IR spectra were recorded on a JASCO FT/IR-4100 as thin films using ATR (attenuated total reflectance) or NaCl crystal. ¹H and ¹³C NMR spectra were recorded on a JEOL JNN-ECX-400 spectrometer at 400 and 100 MHz, respectively. Chemical shifts were expressed in δ parts per million with tetramethylsilane as an internal standard (δ = 0 ppm) for ¹H NMR. Chemical shifts of carbon signals were referenced to CDCl₃ (δ_C = 77.0 ppm). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. EI-mass spectra were recorded on a JEOL JMS-GCmate II. FAB and ESI-mass spectra were recorded on a JEOL JMS-700. SI-mass spectra were recorded on a Hitachi M-2000. Optical rotations were measured on a JASCO P-2200 polarimeter. Column chromatography was carried out on Merck's Silica gel 60 (70-230 mesh ASTM). Tetrahydrofuran (THF) was distilled from sodium/benzophenone before use. Acetonitrile (MeCN) was distilled from P₂O₅ immediately before use. All other reagents and solvents were purchased from commercial sources and used without further purification.

(1'E,2RS,3RS)-2-(3'-Methoxy-3'-oxo-1'-propenyl)-3-methylaziridine-1-carboxylic acid tert-butyl ester (11): To a solution of azide alcohol **9** (1.11 g, 6.00 mmol) in MeCN (25 mL) was added triphenylphosphine (1.78 g, 6.79 mmol). The reaction mixture was stirred at 90 °C for 1 h, and after cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The resulting residue was dissolved in THF (20 mL) and cooled under an ice bath. After addition of Boc₂O (2.84 mL, 12.4 mmol) and Et₃N (0.92 mL, 6.60 mmol), the reaction mixture was stirred for 4 h, then quenched with

brine, and extracted with AcOEt. The extract was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluted with *n*-hexane/AcOEt (10/1) to give Boc-aziridine **11** (1.12 g, 4.65 mmol, 78% in 2 steps) as a colorless oil. ¹H-NMR (CDCl₃) δ: 6.50 (1H, dd, *J* = 15.6, 8.4 Hz), 6.14 (1H, d, *J* = 15.6 Hz), 3.74 (3H, s), 2.79 (1H, dd, *J* = 8.8, 2.8 Hz), 2.55 (1H, dq, *J* = 5.6, 2.8 Hz), 1.46 (9H, s), 1.34 (3H, d, *J* = 5.6 Hz); ¹³C-NMR (CDCl₃) δ: 166.05 (s), 159.94 (s), 144.46 (d), 123.43 (d), 81.74 (s), 51.64 (q), 43.92 (d), 41.54 (d), 27.90 (3C, q), 16.11 (q); IR (ATR) cm⁻¹: 1712, 1655, 1137; SI-MS *m/z* 242 [M+H]⁺, 222, 204; HR-SIMS *m/z* calcd for C₁₂H₂₀NO₄ 242.1392 found 242.1371.

(1'*E*,2*RS*,3*RS*)-2-(3'-Methoxy-3'-oxo-1'-propenyl)-3-methylaziridine-1-carboxylic acid benzyl ester (12): To a solution of azide alcohol **9** (0.964 g, 5.21 mmol) in MeCN (30 mL) was added triphenylphosphine (1.50 g, 5.73 mmol). The reaction mixture was stirred at 90 °C for 1.5 h, and after cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel eluted with *n*-hexane/AcOEt (1/1, finally AcOEt only) to give aziridine **10** (2.99 g, containing Ph₃P=O). To a mixture containing aziridine **10** in CH₂Cl₂ (25 mL) was added Cbz-Cl (1.57 mL, 10.4 mmol) and Et₃N (1.46 mL, 10.4 mmol). After being stirred for 35 h at room temperature, the reaction mixture was quenched with brine and extracted with AcOEt. The extract was dried over Na₂SO₄ and concentrated under reduced pressure. The resulting residue was submitted to acetylation in order to remove benzyl alcohol. To a mixture containing Cbz-aziridine **12** in CH₂Cl₂ (25 mL) was added acetic anhydride (3.0 mL) and pyridine (5.0 mL). After being stirred for 21 h at room temperature, the reaction mixture was quenched with saturated aqueous NaHCO₃ and extracted with AcOEt. The extract was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluted with *n*-hexane/AcOEt (5/1) to give Cbz-aziridine **12** (1.02 g, 3.71 mmol, 71% in 2 steps) as a colorless oil. ¹H-NMR (CDCl₃) δ: 7.37-7.30 (5H, m), 6.51 (1H, dd, *J* = 15.6, 8.4 Hz), 6.14 (1H, d, *J* = 15.6 Hz), 5.17 (1H, d, *J* = 14.4 Hz), 5.14 (1H, d, *J* = 14.4 Hz), 3.73 (3H, s), 2.84 (1H, dd, *J* = 8.4, 2.8 Hz), 2.58 (1H, dq, *J* = 5.6, 2.8 Hz), 1.32 (3H, d, *J* = 5.6 Hz); ¹³C-NMR (CDCl₃) δ: 165.93 (s), 160.83 (s), 143.83 (d), 135.54 (s), 128.53 (2C, d), 128.34 (3C, d), 123.80 (d), 68.30 (t), 51.68 (q), 44.08 (d), 41.90 (d), 16.11 (q); IR (film) cm⁻¹: 1714, 1657, 1188; EI-MS *m/z* 275 [M]⁺, 232, 140; HR-MS *m/z* calcd for C₁₅H₁₇NO₄ 275.1158 found 275.1166.

(1'*E*,2*RS*,3*SR*)-2-Benzylloxymethyl-3-(3'-methoxy-3'-oxo-1'-propenyl)aziridine-1-carboxylic acid *tert*-butyl ester (15): To a solution of vinyloxyepoxide **13** (408 mg, 1.64 mmol) in EtOH (30 mL) was added sodium azide (314 mg, 4.83 mmol) and ammonium chloride (289 mg, 5.40 mmol). The reaction mixture was stirred at 80 °C for 3 h, then quenched with H₂O, and extracted with AcOEt. The extract was washed with H₂O, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by

column chromatography on silica gel eluted with *n*-hexane/AcOEt (4/1) to give azide alcohol (408 mg, 1.40 mmol, 85%) as a pale yellow oil. ¹H-NMR (CDCl₃) δ: 7.39-7.28 (5H, m), 6.90 (1H, dd, *J* = 15.6, 7.2 Hz), 6.09 (1H, dd, *J* = 15.6, 1.6 Hz), 4.53 (2H, s), 4.21 (1H, m), 3.84 (1H, m), 3.75 (3H, s), 3.56 (1H, dd, *J* = 9.6, 6.0 Hz), 3.51 (1H, dd, *J* = 9.6, 4.0 Hz), 2.91 (1H, m); ¹³C-NMR (CDCl₃) δ: 165.87 (s), 141.35 (d), 137.28 (s), 128.42 (2C, d), 127.92 (d), 127.79 (2C, d), 124.42 (d), 73.47 (t), 71.79 (d), 70.06 (t), 63.73 (d), 51.74 (q); IR (ATR) cm⁻¹: 3439, 2100, 1722, 1660; FAB (pos) *m/z* 292 [M+H]⁺, 264; HRMS (FAB-pos) *m/z* calcd for C₁₄H₁₈N₃O₄ 292.1297 found 292.1270. According to the conversion of **9** into **10**, **14** (91.8 mg, 0.372 mmol, 27%) was obtained from the azide alcohol. Furthermore, **15** (362 mg, 1.04 mmol, 86%, colorless oil) was obtained from **14** (300 mg, 1.22 mmol) according to the conversion of **10** into **11**. ¹H-NMR (CDCl₃) δ: 7.37-7.27 (5H, m), 6.48 (1H, dd, *J* = 15.6, 8.8 Hz), 6.17 (1H, d, *J* = 15.6 Hz), 4.57 (1H, d, *J* = 11.8 Hz), 4.52 (1H, d, *J* = 11.8 Hz), 3.75 (1H, dd, *J* = 11.2, 4.0 Hz), 3.74 (3H, s), 3.64 (1H, dd, *J* = 11.2, 4.0 Hz), 3.12 (1H, dd, *J* = 8.4, 2.8 Hz), 2.73 (1H, td, *J* = 4.0, 2.8 Hz), 1.43 (9H, s); ¹³C-NMR (CDCl₃) δ: 165.90 (s), 159.38 (s), 143.82 (d), 137.54 (s), 128.39 (2C, d), 127.76 (d), 127.61 (2C, d), 124.09 (d), 81.82 (s), 72.95 (t), 67.19 (t), 51.66 (q), 43.92 (d), 40.25 (d), 27.83 (3C, q); IR (ATR) cm⁻¹: 1714, 1658; FAB (pos) *m/z* 348 [M+H]⁺, 292; HRMS (FAB-pos) *m/z* calcd for C₁₉H₂₆NO₅ 348.1811 found 348.1810.

(1'E,2RS,3SR)-2-Benzoyloxymethyl-3-(3'-methoxy-3'-oxo-1'-propenyl)aziridine-1-carboxylic acid benzyl ester (16): Compound **16** (384 mg, 1.01 mmol, 84%, colorless oil) was obtained from **14** (297 mg, 1.20 mmol) according to the conversion of **10** into **12**. ¹H-NMR (CDCl₃) δ: 7.41-7.23 (10H, m), 6.55 (1H, dd, *J* = 15.6, 8.4 Hz), 6.16 (1H, d, *J* = 15.6 Hz), 5.10 (1H, d, *J* = 12.2 Hz), 5.06 (1H, d, *J* = 12.2 Hz), 4.42 (2H, s), 3.81 (1H, dd, *J* = 11.2, 3.2 Hz), 3.74 (1H, dd, *J* = 11.2, 3.2 Hz), 3.73 (3H, s), 3.27 (1H, dd, *J* = 8.0, 2.8 Hz), 2.72 (1H, q, *J* = 3.2 Hz); ¹³C-NMR (CDCl₃) δ: 165.92 (s), 160.46 (s), 143.55 (d), 137.42 (s), 135.49 (s), 128.48 (2C, d), 128.41 (2C, d), 128.28 (3C, d), 127.78 (d), 127.51 (2C, d), 124.12 (d), 72.88 (t), 68.22 (t), 65.86 (t), 51.69 (q), 44.48 (d), 39.34 (d); IR (ATR) cm⁻¹: 1716, 1659; FAB (pos) *m/z* 382 [M+H]⁺, 147; HRMS (FAB-pos) *m/z* calcd for C₂₂H₂₄NO₅ 382.1654 found 382.1659.

(2E,2'S,3'S)-3-[3'-(*tert*-Butyldimethylsilyloxymethyl)-oxiran-2'-yl]acrylic acid methyl ester (18): To a solution of known alcohol **17** (1.46 g, 6.70 mmol) in CH₂Cl₂ (40 mL) was added Dess-Martin Periodinane (8.53 g, 20.1 mmol) at 0 °C under Ar atmosphere for 30 min. After confirmation of production of aldehyde by TLC, (carbomethoxymethylene)triphenylphosphorane (3.58 g, 10.1 mmol) was added to the reaction mixture at room temperature. After being stirred for 17.5 h, the reaction mixture was quenched with saturated aqueous Na₂S₂O₃ (45 mL) and saturated aqueous NaHCO₃ (45 mL) and filtered through a celite pad. The resulting filtrate was extracted with AcOEt. The extract was washed with water and brine, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by

column chromatography on silica gel eluted with *n*-hexane/AcOEt (19/1) to give vinyloxyepoxide **18** (1.13 g, 4.15 mmol, 62%) as a colorless oil. ¹H-NMR (CDCl₃) δ: 6.72 (1H, dd, *J* = 15.8, 7.2 Hz), 6.16 (1H, d, *J* = 15.8 Hz), 3.89 (1H, dd, *J* = 12.4, 3.2 Hz), 3.78 (1H, dd, *J* = 12.4, 4.0 Hz), 3.75 (3H, s), 3.44 (1H, dd, *J* = 7.2, 2.0 Hz), 3.06 (1H, m), 0.90 (9H, s), 0.084 (3H, s), 0.075 (3H, s); ¹³C-NMR (CDCl₃) δ: 166.03 (s), 144.44 (d), 123.47 (d), 62.15 (t), 61.06 (d), 53.50 (d), 51.72 (q), 25.78 (3C, q), 18.30 (s), -5.39 (q), -5.41 (q); IR (film) cm⁻¹: 1729, 1660; FAB (pos) *m/z* 273 [M+H]⁺, 215, 147; HRMS (FAB-pos) *m/z* calcd for C₁₃H₂₅O₄Si 273.1522 found 273.1519; [α]_D²³ -16.17 (CDCl₃, c 1.14).

(1'*E*,2*S*,3*R*)-2-(*tert*-Butyldimethylsilyloxymethyl)-3-(3'-methoxy-3'-oxo-1'-propenyl)aziridine-1-carboxylic acid *tert*-butyl ester (20): To a solution of vinyloxyepoxide **18** (50.0 mg, 0.184 mmol) in EtOH (1 mL) was added sodium azide (36.5 mg, 0.551 mmol) and ammonium chloride (29.8 mg, 0.551 mmol). The reaction mixture was stirred at 80 °C for 4 h and then quenched with water (4.5 mL) at room temperature. The mixture was extracted with AcOEt. The extract was washed with water, dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluted with *n*-hexane/AcOEt (14/1) to give azide alcohol (50.0 mg, 0.159 mmol, 86%) as a pale yellow oil. ¹H-NMR (CDCl₃) δ: 6.96 (1H, dd, *J* = 15.6, 6.8 Hz), 6.12 (1H, dd, *J* = 15.6, 1.2 Hz), 4.19 (1H, m), 3.77 (3H, s), 3.74-3.64 (3H, m), 2.63 (1H, m), 0.91 (9H, s), 0.10 (3H, s), 0.09 (3H, s); ¹³C-NMR (CDCl₃) δ: 165.93 (s), 141.71 (d), 124.38 (d), 72.90 (d), 63.58 (d), 62.97 (t), 51.80 (q), 25.78 (3C, q), 18.20 (s), -5.48 (q), -5.50 (q); IR (film) cm⁻¹: 3460, 2106, 1730, 1662, 1257, 1118; ESI-MS (pos) *m/z* 338 [M+Na]⁺, 296; HRMS (ESI-pos) *m/z* calcd for C₁₃H₂₅N₃O₄SiNa 338.1512 found 338.1489; [α]_D²⁶ -5.69 (CDCl₃, c 1.06). To a solution of azide alcohol (0.114 g, 0.361 mmol) in MeCN (2 mL) was added triphenylphosphine (0.107 g, 0.397 mmol). The reaction mixture was stirred at 90 °C for 1 h and then concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluted with *n*-hexane/AcOEt (9/1) to give aziridine **19** (61.9 mg, 0.228 mmol, 63%) as a pale yellow oil. To a solution of aziridine **19** (0.180 g, 0.663 mmol) in THF (4 mL) was added Boc₂O (0.298 g, 1.33 mmol) and Et₃N (0.102 mL, 0.730 mmol) at 0 °C. After being stirred at room temperature for 22 h, the reaction mixture was quenched with water and extracted with AcOEt. The extract was washed with water and brine, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluted with benzene to give Boc-aziridine **20** (0.241 g, 0.650, 98%) as a colorless oil. ¹H-NMR (CDCl₃) δ: 6.50 (1H, dd, *J* = 15.6, 8.8 Hz), 6.17 (1H, d, *J* = 15.6 Hz), 3.93 (1H, dd, *J* = 11.6, 3.6 Hz), 3.76 (1H, dd, *J* = 12.6, 4.8 Hz), 3.75 (3H, s), 3.07 (1H, dd, *J* = 8.8, 2.8 Hz), 2.66 (1H, q, *J* = 3.6 Hz), 1.45 (9H, s), 0.89 (9H, s), 0.07 (3H, s), 0.06 (3H, s); ¹³C-NMR (CDCl₃) δ: 166.01 (s), 159.43 (s), 144.17 (d), 123.82 (d), 81.69 (s), 60.93 (t), 51.68 (q), 45.87 (d), 40.23 (d), 27.93 (3C, q), 25.87 (3C, q), 18.35 (s), -5.29 (q), -5.34 (q); IR (ATR) cm⁻¹: 1719, 1658, 1139; SI-MS *m/z*: 372

$[M+H]^+$, 316, 277; HR-MS m/z : calcd for $C_{18}H_{34}NO_5Si$ 372.2206 found 372.2199; $[\alpha]_D^{26} +2.36$ ($CDCl_3$, c 1.04).

General procedure for Friedel-Crafts reactions of vinylaziridines 11, 12, 15, 16, 20 and various kinds of benzene derivatives

To a solution of vinylaziridines **11, 12, 15, 16, 20** (0.4 mmol) and benzene derivatives **21-26** (0.6 mmol) in CH_2Cl_2 (3 mL) was added $BF_3 \cdot Et_2O$ (0.2 mmol) at $-78^\circ C$ under Ar atmosphere. The reaction mixture was stirred for 30 min, then quenched with saturated aqueous $NaHCO_3$, and extracted with Et_2O . The extract was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluted with *n*-hexane/ $AcOEt$ (9/1) to give coupling compounds **27-46**.

(2E,4RS,5RS)-5-tert-Butoxycarbonylamino-4-(4'-methoxyphenyl)hex-2-enoic acid methyl ester (27a): White powder; Mp $82-83^\circ C$ ($CHCl_3/ Et_2O/ Hex$); 1H -NMR ($CDCl_3$) δ : 7.17 (1H, dd, $J = 15.6, 8.8$ Hz), 7.11 (2H, d, $J = 8.6$ Hz), 6.87 (2H, d, $J = 8.6$ Hz), 5.82 (1H, dd, $J = 15.6, 0.8$ Hz), 4.37 (1H, br), 4.03 (1H, br), 3.80 (3H, s), 3.69 (3H, s), 3.35 (1H, t, $J = 8.4$ Hz), 1.43 (9H, s), 1.01 (3H, d, $J = 6.4$ Hz); ^{13}C -NMR ($CDCl_3$) δ : 166.72 (s), 158.72 (s), 155.16 (s), 149.08 (d), 131.28 (s), 129.32 (2C, d), 122.02 (d), 114.21 (2C, d), 79.45 (s), 55.25 (q), 54.79 (d), 51.45 (q), 50.07 (d), 28.30 (3C, q), 18.73 (q); IR (ATR) cm^{-1} : 3340, 1713, 1678 ; EI-MS m/z : 349 $[M]^+$; HR-MS m/z : calcd for $C_{19}H_{28}NO_5$ $[M+1]^+$ 350.1967 found 350.1970.

(2E,4RS,5RS)-5-tert-Butoxycarbonylamino-4-(2'-methoxy-5'-methylphenyl)hex-2-enoic acid methyl ester (28a): White powder; Mp $94-96^\circ C$ ($CHCl_3/ Et_2O/ Hex$); 1H -NMR ($CDCl_3$) δ : 7.21 (1H, dd, $J = 15.6, 9.2$ Hz), 7.03-6.93 (2H, m), 6.76 (1H, d, $J = 8.4$ Hz), 5.82 (1H, dd, $J = 15.6, 1.6$ Hz), 4.46 (1H, br), 4.17 (1H, br), 3.79 (3H, s), 3.75 (1H, t, $J = 8.4$ Hz), 3.68 (3H, s), 2.26 (3H, s), 1.42 (9H, s), 0.99 (3H, d, $J = 6.4$ Hz); ^{13}C -NMR ($CDCl_3$) δ : 166.89 (s), 155.30 (s), 154.84 (s), 149.13 (d), 130.01 (s), 129.50 (d), 128.37 (d), 127.69 (s), 121.98 (d), 110.89 (d), 79.19 (s), 55.69 (q), 51.35 (q), 49.35 (d), 49.09 (d), 28.27 (3C, q), 20.49 (q), 19.30 (q); IR (ATR) cm^{-1} : 3367, 1717, 1682; EI-MS m/z : 363 $[M]^+$; HR-MS m/z : calcd for $C_{20}H_{29}NO_5$ 363.2046 found 363.2017.

(2E,4RS,5RS)-5-tert-Butoxycarbonylamino-4-(3',4'-dimethoxyphenyl)hex-2-enoic acid methyl ester (29a): White powder; Mp $106-107^\circ C$ (benzene/ Hex); Anal. Calcd for $C_{20}H_{29}NO_6$: C, 63.31; H, 7.70; N, 3.69. Found: C, 63.60; H, 7.80; N, 3.65; 1H -NMR ($CDCl_3$) δ : 7.18 (1H, dd, $J = 15.6, 8.8$ Hz), 6.83 (1H, d, $J = 8.0$ Hz), 6.75 (1H, dd, $J = 8.0, 1.8$ Hz), 6.71 (1H, br s), 5.84 (1H, dd, $J = 15.6, 0.8$ Hz), 4.56 (1H, br s), 4.05 (1H, m), 3.88 (3H, s), 3.86 (3H, s), 3.70 (3H, s), 3.32 (1H, t, $J = 8.8$ Hz), 1.43 (9H, s), 1.03 (3H, d, $J = 8.8$ Hz); ^{13}C -NMR ($CDCl_3$) δ : 166.68 (s), 155.18 (s), 149.15 (s), 148.89 (d), 148.19 (s), 131.81 (s), 122.12 (d), 120.49 (d), 111.38 (d), 111.09 (d), 79.49 (s), 55.90 (q), 55.88 (q), 55.37 (d), 51.46 (q), 50.04

(d), 28.29 (3C, q), 18.89 (q); IR (ATR) cm^{-1} : 3365, 1710, 1683; EI-MS m/z : 379 $[\text{M}]^+$; HR-MS m/z : calcd for $\text{C}_{20}\text{H}_{29}\text{NO}_6$ 379.1995 found 379.1979.

(2E,4RS,5RS)-5-tert-Butoxycarbonylamino-4-(2',4'-dimethoxyphenyl)hex-2-enoic acid methyl ester (30a): White powder; Mp 93-94 °C (Et₂O/ Hex); ¹H-NMR (CDCl₃) δ : 7.20 (1H, dd, $J = 15.6, 8.8$ Hz), 7.06 (1H, d, $J = 8.0$ Hz), 6.47-6.43 (2H, m), 5.80 (1H, dd, $J = 15.6, 0.8$ Hz), 4.45 (1H, br), 4.14 (1H, m), 3.793 (3H, s), 3.789 (3H, s), 3.71 (1H, t, $J = 8.8$ Hz), 3.68 (3H, s), 1.42 (9H, s), 0.99 (3H, d, $J = 6.8$ Hz); ¹³C-NMR (CDCl₃) δ : 166.90 (s), 159.76 (s), 157.94 (s), 155.26 (s), 149.24 (d), 129.37 (d), 121.69 (d), 120.28 (s), 104.45 (d), 98.80 (d), 79.12 (s), 55.39 (q), 55.27 (q), 51.30 (q), 49.23 (d), 48.61 (d), 28.26 (3C, q), 19.16 (q); IR (ATR) cm^{-1} : 3390, 1714, 1693; EI-MS m/z : 379 $[\text{M}]^+$; HR-MS m/z : calcd for $\text{C}_{20}\text{H}_{29}\text{NO}_6$ 379.1995 found 379.1979.

(2E,4RS,5RS)-5-tert-Butoxycarbonylamino-4-(2',5'-dimethoxyphenyl)hex-2-enoic acid methyl ester (31a) & (2SR,3E,5RS)-5-tert-Butoxycarbonylamino-2-(2',5'-dimethoxyphenyl)hex-3-enoic acid methyl ester (31b): Compound **31a** and **31b** were obtained as a mixture in the ratio of 2 : 1. White powder; Mp 78-80 °C (for **31a**, CHCl₃/ Et₂O/ Hex); ¹H-NMR (C₆D₆) δ : 7.58 (1H for **31a**, dd, $J = 15.2, 8.8$ Hz), 6.81 (1H for **31a**, d, $J = 2.8$ Hz), 6.66 (1H for **31b**, dd, $J = 8.8, 3.2$ Hz), 6.62 (1H for **31a**, dd, $J = 8.8, 3.2$ Hz), 6.48 (1H for **31b**, d, $J = 9.2$ Hz), 6.42 (1H for **31a**, d, $J = 8.8$ Hz), 6.23 (1H for **31b**, s), 6.10 (1H for **31b**, ddd, $J = 15.2, 8.0, 1.2$ Hz), 5.98 (1H for **31a**, d, $J = 15.2$ Hz), 5.47 (1H for **31b**, dd, $J = 15.2, 8.0$ Hz), 4.81 (1H for **31b**, d, $J = 8.4$ Hz), 4.43 (1H for **31a**, m), 4.32 (1H for **31b**, br), 4.20-4.01 (1H for **31a** and 1H for **31b**), 3.56 (1H for **31a**, t, $J = 9.2$ Hz), 3.40 (3H for **31b**, s), 3.36 (3H for **31a**, s), 3.332 (3H for **31b**, s), 3.329 (3H for **31b**, s), 3.29 (3H for **31a**, s), 3.26 (3H for **31a**, s), 1.45 (9H for **31a**, s), 1.42 (9H for **31b**, s), 0.83 (3H for **31a** and 3H for **31b**, d, $J = 6.4$ Hz); ¹³C-NMR (CDCl₃) δ : 173.18 (s), 166.77 (s), 155.24 (s), 153.66 (s), 153.59 (s), 151.23 (s), 150.85 (s), 155.01 (s), 148.68 (d), 135.10 (d), 129.05 (s), 128.12 (s), 126.13 (d), 122.18 (d), 115.26 (d), 114.91 (d), 112.51 (d), 112.37 (d), 111.98 (d), 111.87 (d), 79.18 (s), 56.19 (q), 56.03 (q), 55.62 (q), 52.08 (q), 51.33 (q), 49.19 (d), 47.99 (d), 28.31 (3C, q), 28.23 (3C, q), 20.80 (q), 19.27 (q); IR (ATR) cm^{-1} : 3376, 1718, 1680; EI-MS m/z : 379 $[\text{M}]^+$; HR-MS m/z : calcd for $\text{C}_{20}\text{H}_{29}\text{NO}_6$ 379.1995 found 379.1979.

(2E,4RS,5RS)-5-tert-Butoxycarbonylamino-4-(2',4',6'-trimethoxyphenyl)hex-2-enoic acid methyl ester (32a): White powder; Mp 124-126 °C (Et₂O/ Hex); Anal. Calcd for $\text{C}_{21}\text{H}_{31}\text{NO}_7$: C, 61.60; H, 7.63; N, 3.42. Found: C, 61.97; H, 7.91; N, 3.42; ¹H-NMR (CDCl₃) δ : 7.38 (1H, dd, $J = 15.6, 8.8$ Hz), 6.10 (2H, s), 5.75 (1H, dd, $J = 15.6, 0.8$ Hz), 4.51-4.30 (2H, m), 3.85 (1H, t, $J = 8.8$ Hz), 3.794 (3H, s), 3.787 (6H, s), 3.67 (3H, s), 1.43 (9H, s), 0.92 (3H, d, $J = 6.4$ Hz); ¹³C-NMR (CDCl₃) δ : 167.25 (s), 160.26 (s), 158.78 (2C, s), 155.46 (s), 149.85 (d), 121.05 (d), 108.65 (s), 90.86 (2C, d), 78.90 (s), 55.65 (2C, q), 55.24 (q), 51.19 (q), 47.68 (d), 45.59 (d), 28.31 (3C, q), 19.59 (q); IR (ATR) cm^{-1} : 3381,

1710, 1177; EI-MS m/z : 409 $[M]^+$; HR-MS m/z : calcd for $C_{21}H_{32}NO_7$ $[M+1]^+$ 410.2179 found 410.2158.

(2E,4RS,5RS)-5-Benzyloxycarbonylamino-4-(4'-methoxyphenyl)hex-2-enoic acid methyl ester (33a):

White powder; Mp 81-83 °C ($CHCl_3$ / Et_2O / Hex); Anal. Calcd for $C_{22}H_{25}NO_5$: C, 68.91; H, 6.57; N, 3.65. Found: C, 68.94; H, 6.55; N, 3.60; 1H -NMR ($CDCl_3$) δ : 7.39-7.30 (5H, m), 7.15 (1H, dd, $J = 15.8, 8.8$ Hz), 7.08 (2H, d, $J = 8.8$ Hz), 6.85 (2H, d, $J = 8.8$ Hz), 5.83 (1H, dd, $J = 15.8, 1.2$ Hz), 5.09 (2H, s), 4.60 (1H, br d, $J = 8.8$ Hz), 4.10 (1H, br), 3.79 (3H, s), 3.70 (3H, s), 3.44 (1H, br t, $J = 7.6$ Hz), 1.04 (3H, d, $J = 6.8$ Hz); ^{13}C -NMR ($CDCl_3$) δ : 166.64 (s), 158.79 (s), 155.59 (s), 148.56 (d), 136.46 (s), 130.77 (s), 129.42 (2C, d), 128.52 (2C, d), 128.11 (d), 128.04 (2C, d), 122.39 (d), 114.23 (2C, d), 66.67 (t), 55.24 (q), 53.78 (d), 51.53 (q), 50.60 (d), 18.66 (q); IR (ATR) cm^{-1} : 3339, 1712, 1689; FAB-MS (pos) m/z : 384 $[M+1]^+$, 308, 206; HRMS (FAB-pos) m/z calcd for $C_{22}H_{26}NO_5$ 384.1811 found 384.1821.

(2E,4RS,5RS)-5-Benzyloxycarbonylamino-4-(2'-methoxy-5'-methylphenyl)hex-2-enoic acid methyl ester (34a):

Colorless oil; 1H -NMR ($CDCl_3$) δ : 7.38-7.29 (5H, m), 7.20 (1H, dd, $J = 15.6, 8.4$ Hz), 7.01 (1H, dd, $J = 8.4, 2.0$ Hz), 6.95 (1H, br), 6.76 (1H, d, $J = 8.0$ Hz), 5.84 (1H, dd, $J = 15.6, 0.8$ Hz), 5.08 (2H, s), 4.71 (1H, br d, $J = 8.8$ Hz), 4.23 (1H, br q, $J = 7.2$ Hz), 3.84 (1H, br t, $J = 8.8$ Hz), 3.77 (3H, s), 3.69 (3H, s), 2.26 (3H, s), 1.03 (3H, d, $J = 6.4$ Hz); ^{13}C -NMR ($CDCl_3$) δ : 166.82 (s), 155.75 (s), 154.82 (s), 148.67 (d), 136.58 (s), 130.02 (s), 129.68 (d), 128.54 (d), 128.49 (2C, d), 128.02 (d), 127.98 (2C, d), 127.26 (s), 122.27 (d), 110.92 (d), 66.55 (t), 55.52 (q), 51.46 (q), 49.92 (d), 48.26 (d), 20.50 (q), 19.20 (q); IR (film) cm^{-1} : 3334, 1722, 1689; EI-MS m/z : 397 $[M]^+$; HR-MS m/z : calcd for $C_{23}H_{27}NO_5$ 397.1889 found 397.1916.

(2E,4RS,5RS)-5-Benzyloxycarbonylamino-4-(3',4'-dimethoxyphenyl)hex-2-enoic acid methyl ester (35a):

White powder; Mp 83-85 °C ($CHCl_3$ / Et_2O / Hex); Anal. Calcd for $C_{23}H_{27}NO_6$: C, 66.81; H, 6.58; N, 3.39. Found: C, 66.58; H, 6.67; N, 3.39; 1H -NMR ($CDCl_3$) δ : 7.39-7.29 (5H, m), 7.16 (1H, dd, $J = 15.6, 8.4$ Hz), 6.81 (1H, d, $J = 8.4$ Hz), 6.72 (1H, d, $J = 8.4$ Hz), 6.67 (1H, s), 5.85 (1H, dd, $J = 15.6, 1.2$ Hz), 5.12 (1H, d, $J = 12.0$ Hz), 5.07 (1H, d, $J = 12.0$ Hz), 4.59 (1H, br d, $J = 8.4$ Hz), 4.11 (1H, m), 3.86 (3H, s), 3.84 (3H, s), 3.71 (3H, s), 3.41 (1H, t, $J = 8.0$ Hz), 1.06 (3H, d, $J = 6.4$ Hz); ^{13}C -NMR ($CDCl_3$) δ : 166.57 (s), 155.61 (s), 149.10 (d), 148.39 (s), 148.20 (s), 136.40 (s), 131.37 (s), 128.47 (2C, d), 128.07 (d), 127.98 (2C, d), 122.41 (d), 120.50 (d), 111.33 (d), 111.16 (d), 66.63 (t), 55.83 (q), 55.81 (q), 54.35 (d), 51.49 (q), 50.52 (d), 18.80 (q); IR (ATR) cm^{-1} : 3362, 1705, 1689; EI-MS m/z : 413 $[M]^+$; HR-MS m/z : calcd for $C_{23}H_{27}NO_6$ 413.1838 found 413.1823.

(2E,4RS,5RS)-5-Benzyloxycarbonylamino-4-(2',4'-dimethoxyphenyl)hex-2-enoic acid methyl ester (36a):

White powder; Mp 84-86 °C (Et_2O / Hex); Anal. Calcd for $C_{23}H_{27}NO_6$: C, 66.81; H, 6.58; N, 3.39. Found: C, 66.65; H, 6.60; N, 3.42; 1H -NMR ($CDCl_3$) δ : 7.38-7.31 (5H, m), 7.18 (1H, dd, $J = 15.8, 8.8$ Hz), 7.03 (1H, d, $J = 8.0$ Hz), 6.47-6.41 (2H, m), 5.82 (1H, dd, $J = 15.8, 0.8$ Hz), 5.08 (2H, s), 4.67 (1H,

br d, $J = 7.2$ Hz), 4.26-4.15 (1H, m), 3.84-3.74 (7H, m), 3.69 (3H, s), 1.03 (3H, d, $J = 6.8$ Hz); $^{13}\text{C-NMR}$ (CDCl_3) δ : 166.86 (s), 159.90 (s), 157.96 (s), 155.74 (s), 148.77 (d), 136.59 (s), 129.58 (d), 128.49 (2C, d), 128.02 (d), 127.99 (2C, d), 122.07 (d), 119.87 (s), 104.46 (d), 98.84 (d), 66.55 (t), 55.39 (q), 55.33 (q), 51.46 (q), 49.90 (d), 47.66 (d), 19.10 (q); IR (ATR) cm^{-1} : 3343, 1713, 1696; EI-MS m/z : 413 $[\text{M}]^+$; HR-MS m/z : calcd for $\text{C}_{23}\text{H}_{28}\text{NO}_6$ $[\text{M}+1]^+$ 414.1917 found 414.1894.

(2E,4RS,5RS)-5-Benzoyloxycarbonylamino-4-(2',5'-dimethoxyphenyl)hex-2-enoic acid methyl ester (37a) & (2SR,3E,5RS)-5-Benzoyloxycarbonylamino-2-(2',5'-dimethoxyphenyl)hex-3-enoic acid methyl ester (37b): Compound **37a** and **37b** were obtained as a mixture in the ratio of ca. 1.5 : 1 as a colorless oil. $^1\text{H-NMR}$ (CDCl_3) δ : 7.40-7.28 (5H for **37a** and 5H for **37b**, m), 7.19 (1H for **37a**, dd, $J = 15.6, 8.8$ Hz), 6.82-6.70 (3H for **37a** and 3H for **37b**, m), 5.95 (1H for **37b**, ddd, $J = 15.6, 7.6, 1.4$ Hz), 5.85 (1H for **37a**, dd, $J = 15.6, 0.8$ Hz), 5.55 (1H for **37b**, dd, $J = 15.6, 5.0$ Hz), 5.08 (2H for **37a** and 2H for **37b**, s), 4.73 (1H for **37a** and 1H for **37b**, m), 4.57 (1H for **37b**, d, $J = 8.0$ Hz), 4.33 (1H for **37b**, br), 4.23 (1H for **37a**, m), 3.87 (1H for **37a**, m), 3.75 (6H for **37a**, s), 3.74 (6H for **37b**, s), 3.69 (3H for **37a**, s), 3.67 (3H for **37b**, s), 1.24 (3H for **37b**, $J = 6.8$ Hz), 1.04 (3H for **37a**, $J = 6.4$ Hz); $^{13}\text{C-NMR}$ (CDCl_3) δ : 173.07 (s), 166.68 (s), 155.71 (s), 155.40 (s), 153.60 (s), 153.57 (s), 151.19 (s), 150.83 (s), 148.23 (d), 136.53 (s), 136.48 (s), 134.55 (d), 128.65 (s), 128.45 (5C, d), 127.97 (3C, d), 127.93 (3C, d), 126.65 (d), 122.49 (d), 115.28 (d), 115.22 (d), 112.57 (d), 112.37 (d), 111.94 (d), 111.90 (d), 66.52 (2C, t), 56.17 (q), 55.96 (q), 55.63 (q), 55.60 (q), 52.11 (q), 51.43 (q), 49.81 (d), 48.30 (d), 47.97 (d), 47.80 (d), 20.78 (q), 19.17 (q); IR (ATR) cm^{-1} : 3334, 1716, 1652, 1498; EI-MS m/z : 413 $[\text{M}]^+$; HR-MS m/z : calcd for $\text{C}_{23}\text{H}_{27}\text{NO}_6$ $[\text{M}]^+$ 413.1838 found 413.1847.

(2E,4RS,5RS)-5-Benzoyloxycarbonylamino-4-(2',4',6'-trimethoxyphenyl)hex-2-enoic acid methyl ester (38a): Colorless oil; $^1\text{H-NMR}$ (CDCl_3) δ : 7.41-7.28 (6H, m), 6.10 (2H, s), 5.77 (1H, dd, $J = 15.6, 0.8$ Hz), 5.09 (2H, s), 4.73 (1H, br d, $J = 8.4$ Hz), 4.47 (1H, m), 3.93 (1H, t, $J = 9.2$ Hz), 3.79 (6H, s), 3.78 (3H, s), 3.67 (3H, s), 0.97 (3H, d, $J = 6.4$ Hz); $^{13}\text{C-NMR}$ (CDCl_3) δ : 167.13 (s), 160.31 (s), 158.71 (2C, s), 155.82 (s), 149.49 (d), 136.72 (s), 128.40 (2C, d), 127.88 (3C, d), 121.30 (d), 108.45 (s), 90.84 (2C, d), 66.34 (t), 55.61 (q), 55.21 (2C, q), 51.25 (q), 48.47 (d), 44.68 (d), 19.61 (q); IR (film) cm^{-1} : 3345, 1716, 1650; EI-MS m/z : 443 $[\text{M}]^+$; HR-MS m/z : calcd for $\text{C}_{24}\text{H}_{29}\text{NO}_7$ $[\text{M}+1]^+$ 444.2022 found 444.2040.

(2E,4RS,5SR)-6-Benzoyloxy-5-tert-butoxycarbonylamino-4-(3',4'-dimethoxyphenyl)hex-2-enoic acid methyl ester (39a): Colorless oil; $^1\text{H-NMR}$ (CDCl_3) δ : 7.37-7.25 (5H, m), 7.20 (1H, dd, $J = 15.6, 9.2$ Hz), 6.83-6.70 (3H, m), 5.81 (1H, d, $J = 15.6$ Hz), 5.09 (1H, d, $J = 10.4$ Hz), 4.43 (1H, d, $J = 12.0$ Hz), 4.32 (1H, d, $J = 12.0$ Hz), 4.08 (1H, m), 3.85 (3H, s), 3.82 (3H, s), 3.67 (3H, s), 3.65 (1H, t, $J = 10.0$ Hz), 3.39 (1H, dd, $J = 9.2, 2.4$ Hz), 3.23 (1H, dd, $J = 9.2, 2.4$ Hz), 1.43 (9H, s); $^{13}\text{C-NMR}$ (CDCl_3) δ : 166.48 (s), 155.44 (s), 149.08 (s), 148.93 (d), 147.97 (s), 137.68 (s), 131.89 (s), 128.26 (2C, d), 127.65 (d), 127.48

(2C, d), 121.95 (d), 120.23 (d), 111.32 (d), 110.59 (d), 79.42 (s), 73.16 (t), 69.38 (t), 55.72 (2C, q), 53.93 (d), 51.22 (q), 50.90 (d), 28.10 (3C, q); IR (ATR) cm^{-1} : 3366, 1707, 1653; FAB-MS (pos) m/z : 486 $[\text{M}+1]^+$, 430, 386; HRMS (FAB-pos) m/z calcd for $\text{C}_{27}\text{H}_{36}\text{NO}_7$ 486.2492 found 486.2517.

(2E,4RS,5SR)-6-Benzoyloxy-5-benzoyloxycarbonylamino-4-(3',4'-dimethoxyphenyl)hex-2-enoic acid methyl ester (40a): Colorless oil; $^1\text{H-NMR}$ (CDCl_3) δ : 7.39-7.22 (10H, m), 7.18 (1H, dd, $J = 15.6, 8.8$ Hz), 6.79 (1H, d, $J = 8.4$ Hz), 6.74 (1H, d, $J = 8.4$ Hz), 6.71 (1H, s), 5.82 (1H, d, $J = 15.6$ Hz), 5.26 (1H, d, $J = 9.6$ Hz), 5.14 (1H, d, $J = 12.4$ Hz), 5.08 (1H, d, $J = 12.4$ Hz), 4.40 (1H, d, $J = 11.8$ Hz), 4.31 (1H, d, $J = 11.8$ Hz), 4.16 (1H, m), 3.86 (3H, s), 3.82 (3H, s), 3.69 (1H, t, $J = 9.6$ Hz), 3.68 (3H, s), 3.40 (1H, dd, $J = 9.6, 3.2$ Hz), 3.23 (1H, dd, $J = 9.6, 2.8$ Hz); $^{13}\text{C-NMR}$ (CDCl_3) δ : 166.53 (s), 156.01 (s), 149.15 (s), 148.56 (d), 148.10 (s), 137.63 (s), 136.37 (s), 131.71 (s), 128.46 (2C, d), 128.34 (2C, d), 128.03 (d), 127.92 (2C, d), 127.74 (d), 127.54 (2C, d), 122.35 (d), 120.30 (d), 111.36 (d), 110.78 (d), 73.22 (t), 69.34 (t), 66.75 (t), 55.80 (2C, q), 54.51 (d), 51.43 (q), 50.35 (d); IR (ATR) cm^{-1} : 3342, 1718, 1654; FAB-MS (pos) m/z : 520 $[\text{M}+1]^+$, 476; HRMS (FAB-pos) m/z calcd for $\text{C}_{30}\text{H}_{34}\text{NO}_7$ 520.2335 found 520.2341.

(2E,4RS,5SR)-6-Benzoyloxy-5-benzoyloxycarbonylamino-4-(2',4'-dimethoxyphenyl)hex-2-enoic acid methyl ester (41a): Colorless oil; $^1\text{H-NMR}$ (CDCl_3) δ : 7.42-7.20 (11H, m), 7.04 (1H, d, $J = 8.0$ Hz), 6.43 (1H, s), 6.42 (1H, d, $J = 7.6$ Hz), 5.78 (1H, d, $J = 15.6$ Hz), 5.22 (1H, d, $J = 9.6$ Hz), 5.12 (1H, d, $J = 12.4$ Hz), 5.07 (1H, d, $J = 12.4$ Hz), 4.43 (1H, m), 4.37 (1H, d, $J = 11.8$ Hz), 4.28 (1H, d, $J = 11.8$ Hz), 3.98 (1H, t, $J = 9.6$ Hz), 3.78 (3H, s), 3.77 (3H, s), 3.66 (3H, s), 3.42 (1H, dd, $J = 9.6, 3.2$ Hz), 3.24 (1H, dd, $J = 9.6, 2.4$ Hz); $^{13}\text{C-NMR}$ (CDCl_3) δ : 166.82 (s), 160.01 (s), 158.01 (s), 156.04 (s), 148.78 (d), 137.92 (s), 136.55 (s), 130.12 (d), 128.42 (3C, d), 128.24 (2C, d), 127.93 (d), 127.87 (d), 127.54 (d), 127.46 (2C, d), 121.92 (d), 119.73 (s), 104.47 (d), 98.85 (d), 73.12 (t), 69.82 (t), 66.58 (t), 55.26 (2C, q), 52.98 (d), 51.30 (q), 45.70 (d); IR (ATR) cm^{-1} : 3342, 1718, 1654; FAB-MS (pos) m/z : 520 $[\text{M}+1]^+$, 476, 444; HRMS (FAB-pos) m/z calcd for $\text{C}_{30}\text{H}_{34}\text{NO}_7$ 520.2335 found 520.2314.

(2E,4R,5S)-5-tert-Butoxycarbonylamino-6-tert-butyl dimethylsilyloxy-4-(2'-methoxy-5'-methylphenyl)-hex-2-enoic acid methyl ester (42a): Colorless oil; $^1\text{H-NMR}$ (CDCl_3) δ : 7.25 (1H, dd, $J = 15.6, 9.2$ Hz), 7.05-6.96 (2H, m), 6.74 (1H, d, $J = 8.4$ Hz), 5.77 (1H, d, $J = 15.6$ Hz), 4.89 (1H, d, $J = 9.6$ Hz), 4.27 (1H, br t, $J = 10.0$ Hz), 3.93 (1H, t, $J = 9.6$ Hz), 3.77 (3H, s), 3.66 (3H, s), 3.51 (1H, dd, $J = 10.0, 3.2$ Hz), 3.32 (1H, dd, $J = 10.0, 2.0$ Hz), 2.24 (3H, s), 1.42 (9H, s), 0.88 (9H, s), -0.06 (3H, s), -0.10 (3H, s); $^{13}\text{C-NMR}$ (CDCl_3) δ : 166.94 (s), 155.63 (s), 155.02 (s), 149.40 (d), 130.40 (d), 129.90 (s), 128.51 (d), 127.25 (s), 121.77 (d), 110.76 (d), 79.26 (s), 62.66 (t), 55.34 (q), 53.56 (d), 51.24 (q), 45.87 (d), 28.29 (3C, q), 25.78 (3C, q), 20.38 (q), 18.22 (s), -5.79 (q), -5.84 (q); IR (film) cm^{-1} : 3451, 3370, 1723, 1651; EI-MS m/z : 493 $[\text{M}]^+$; HR-MS m/z : calcd for $\text{C}_{26}\text{H}_{44}\text{NO}_6\text{Si}$ $[\text{M}+1]^+$ 494.2938 found 444.2918; $[\alpha]_{\text{D}}^{27} -47.53$ (CDCl_3 , c 1.04).

(2E,4R,5S)-5-tert-Butoxycarbonylamino-6-tert-butyldimethylsilyloxy-4-(3',4'-dimethoxyphenyl)hex-2-enoic acid methyl ester (43a): Colorless oil; $^1\text{H-NMR}$ (CDCl_3) δ : 7.19 (1H, dd, $J = 15.6, 9.2$ Hz), 6.82 (1H, d, $J = 8.4$ Hz), 6.77 (1H, dd, $J = 8.4, 1.6$ Hz), 6.73 (1H, d, $J = 1.6$ Hz), 5.78 (1H, dd, $J = 15.6, 1.2$ Hz), 4.90 (1H, d, $J = 9.6$ Hz), 3.99 (1H, m), 3.87 (6H, s), 3.68 (3H, s), 3.59 (1H, t, $J = 10.0$ Hz), 3.51 (1H, dd, $J = 10.0, 3.2$ Hz), 3.35 (1H, dd, $J = 10.0, 2.4$ Hz), 1.44 (9H, s), 0.91 (9H, s), -0.01 (3H, s), -0.03 (3H, s); $^{13}\text{C-NMR}$ (CDCl_3) δ : 166.63 (s), 155.57 (s), 149.35 (s), 149.17 (s), 148.11 (d), 132.03 (s), 121.97 (d), 120.47 (d), 111.43 (d), 110.89 (d), 79.53 (s), 62.22 (t), 55.84 (q), 55.81 (q), 55.06 (d), 51.32 (q), 50.38 (d), 28.23 (3C, q), 25.83 (3C, q), 18.20 (s), -5.56 (q), -5.63 (q); IR (film) cm^{-1} : 3451, 3370, 1722, 1653; EI-MS m/z : 509 $[\text{M}]^+$; HR-MS m/z : calcd for $\text{C}_{26}\text{H}_{43}\text{NO}_7\text{Si}$ $[\text{M}]^+$ 509.2809 found 509.2822; $[\alpha]_{\text{D}}^{29} -56.62$ (CDCl_3 , c 1.03).

(2E,4R,5S)-5-tert-Butoxycarbonylamino-6-tert-butyldimethylsilyloxy-4-(2',4'-dimethoxyphenyl)hex-2-enoic acid methyl ester (44a): Colorless oil; $^1\text{H-NMR}$ (CDCl_3) δ : 7.22 (1H, dd, $J = 15.6, 9.2$ Hz), 7.07 (1H, d, $J = 8.4$ Hz), 6.47-6.41 (2H, m), 5.74 (1H, d, $J = 15.6$ Hz), 4.88 (1H, d, $J = 10.0$ Hz), 4.22 (1H, m), 3.91 (1H, t, $J = 9.6$ Hz), 3.79 (3H, s), 3.77 (3H, s), 3.66 (3H, s), 3.51 (1H, dd, $J = 10.0, 3.2$ Hz), 3.35 (1H, dd, $J = 10.0, 2.0$ Hz), 1.43 (9H, s), 0.88 (9H, s), -0.06 (3H, s), -0.09 (3H, s); $^{13}\text{C-NMR}$ (CDCl_3) δ : 166.99 (s), 159.93 (s), 158.10 (s), 155.63 (s), 149.59 (d), 130.03 (d), 121.52 (d), 120.01 (s), 104.40 (d), 98.78 (d), 79.25 (s), 62.57 (t), 55.33 (q), 55.24 (q), 53.59 (d), 51.24 (q), 44.99 (d), 28.29 (3C, q), 25.80 (3C, q), 18.21 (s), -5.74 (2C, q); IR (ATR) cm^{-1} : 1714; EI-MS m/z : 509 $[\text{M}]^+$; HR-MS m/z : calcd for $\text{C}_{26}\text{H}_{43}\text{NO}_7\text{Si}$ $[\text{M}]^+$ 509.2809 found 509.2825; $[\alpha]_{\text{D}}^{27} -43.73$ (CDCl_3 , c 1.04).

(2E,4R,5S)-5-tert-Butoxycarbonylamino-6-tert-butyldimethylsilyloxy-4-(2',5'-dimethoxyphenyl)hex-2-enoic acid methyl ester (45a) & (2S,3E,5S)-5-tert-Butoxycarbonylamino-6-tert-butyldimethylsilyloxy-2-(2',5'-dimethoxyphenyl)hex-3-enoic acid methyl ester (45b): Compound **45a** and **45b** were obtained as a mixture in the ratio of 3 : 1 as a colorless oil. $^1\text{H-NMR}$ (CDCl_3) δ : 7.23 (1H for **45a**, dd, $J = 15.6, 8.8$ Hz), 6.84-6.72 (3H for **45a** and 3H for **45b**, m), 5.99 (1H for **45b**, ddd, $J = 15.6, 8.0, 1.6$ Hz), 5.77 (1H for **45a**, d, $J = 15.6$ Hz), 5.56 (1H for **45b**, dd, $J = 15.6, 5.6$ Hz), 4.89 (1H for **45a**, d, $J = 9.6$ Hz), 4.80 (1H for **45b**, br), 4.61 (1H for **45b**, d, $J = 7.6$ Hz), 4.25 (1H for **45a**, m), 4.20 (1H for **45b**, br), 3.96 (1H for **45a**, t, $J = 9.2$ Hz), 3.754 (3H for **45a** and 3H for **45b**, s), 3.750 (3H for **45a** and 3H for **45b**, s), 3.672 (3H for **45b**, s), 3.665 (3H for **45a**, s), 3.65-3.55 (2H for **45b**, m), 3.52 (1H for **45a**, dd, $J = 10.0, 3.2$ Hz), 3.36 (1H for **45a**, dd, $J = 10.0, 2.4$ Hz), 1.44 (9H for **45b**, s), 1.43 (9H for **45a**, s), 0.87 (9H for **45a**, s), 0.85 (9H for **45b**, s), 0.01 (3H for **45b**, s), 0.00 (3H for **45b**, s), -0.06 (3H for **45a**, s), -0.09 (3H for **45a**, s); $^{13}\text{C-NMR}$ (CDCl_3) δ : 173.12 (s), 166.88 (s), 155.59 (s), 155.26 (s), 153.65 (s), 153.27 (s), 151.39 (s), 150.87 (s), 149.02 (d), 131.54 (d), 128.56 (s), 128.08 (s), 127.67 (d), 121.98 (d), 115.50 (d), 115.32 (d), 112.74 (d), 112.62 (d), 111.84 (d), 79.31 (s), 65.24 (t), 62.67 (t), 56.19 (q), 55.79 (q), 55.68

(q), 55.65 (q), 53.54 (d), 52.07 (q), 51.28 (q), 48.06 (d), 45.70 (d), 28.35 (3C, q), 28.28 (3C, q), 25.79 (3C, q), 18.22 (s), -5.55 (2C, q), -5.78 (2C, q); IR (ATR) cm^{-1} : 1714, 1498, 1222, 1167; EI-MS m/z : 509 $[\text{M}]^+$, 396, 274; HR-MS m/z : calcd for $\text{C}_{26}\text{H}_{43}\text{NO}_7\text{Si}$ $[\text{M}]^+$ 509.2809 found 509.2801; $[\alpha]_{\text{D}}^{26}$ -32.91 (CDCl_3 , c 1.03).

(2E,4R,5S)-5-tert-Butoxycarbonylamino-6-tert-butyldimethylsilyloxy-4-(2',4',6'-trimethoxyphenyl)-hex-2-enoic acid methyl ester (46a): Colorless oil; $^1\text{H-NMR}$ (CDCl_3) δ 7.30 (1H, dd, $J = 15.6, 8.4$ Hz), 6.08 (2H, s), 5.73 (1H, d, $J = 15.6$ Hz), 4.87 (1H, d, $J = 10.0$ Hz), 4.54 (1H, m), 4.19 (1H, t, $J = 9.2$ Hz), 3.80 (3H, s), 3.76 (6H, s), 3.65 (3H, s), 3.50 (1H, dd, $J = 10.0, 2.8$ Hz), 3.31 (1H, dd, $J = 10.0, 2.0$ Hz), 1.43 (9H, s), 0.85 (9H, s), -0.09 (3H, s), -0.14 (3H, s); $^{13}\text{C-NMR}$ (CDCl_3) δ : 167.32 (s), 160.29 (s), 158.96 (2C, s), 155.75 (s), 149.69 (d), 120.90 (d), 107.81 (s), 90.61 (d), 78.92 (s), 62.85 (t), 55.48 (2C, q), 55.26 (q), 52.29 (d), 51.14 (q), 40.45 (d), 28.32 (3C, q), 25.75 (3C, q), 18.20 (s), -5.83 (q), -5.89 (q); IR (film) cm^{-1} : 3450, 3379, 1720, 1650; SI-MS m/z : 540 $[\text{M}+\text{H}]^+$, 440, 265; HR-SIMS m/z : calcd for $\text{C}_{26}\text{H}_{46}\text{NO}_7\text{Si}$ $[\text{M}+1]^+$ 540.2993 found 540.2982; $[\alpha]_{\text{D}}^{26}$ -41.89 (CDCl_3 , c 1.06).

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 11. Arenes **21**, **23**, **24** and **26** cannot undergo *ipso*-attack since the *para* position of a methoxy group is not substituted. On the other hand, *ipso*-attack of **22** might occur to form the **B** type of benzenium ion. However, a methyl group would be incapable of promoting the isomerization of the benzenium ion **C**.