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HIGHLY EFFICIENT PREPARATION OF BOTH ENANTIOMERS OF VERSATILE CHIRAL SYNTHON FOR 1,2-DIAMINES VIA THE Fe(III)-CATALYZED OXIDATION OF 2-IMIDAZOLONE

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Abstract – A new method was established for the preparation of both of the enantiomers of *trans*-4,5-dimethoxy-2-imidazolidinone (DMIm) *via* the Fe(III)-catalyzed oxidation of 2-imidazolone by H_2O_2-urea, which allowed the subsequent achievement of optical resolution via the introduction of a MAC moiety and a 2-mesitylenesulfonyl group at the two nitrogen positions of DMIm, which then were easily removed. The two enantiomers are useful as versatile chiral synthons for 1,2-diamines.

INTRODUCTION

1,2-Diamine is a fundamental component of a substantial number of compounds that are of biological and medicinal importance.[1,2] Also, in asymmetric reaction systems 1,2-diamine and its derivatives, imidazoline and Schiff base, function as chiral ligands.[3]

Until now, there have been a number of methodologies for the synthesis of chiral 1,2-diamines such as derivatization from amino acids,[4] substitutional induction of nitrogen nucleophiles to haloalkanes,[5] conjugate addition of nitrogen nucleophiles to nitroalkenes and aziridines,[6] diamination of 1,2-dilos,[7] and the coupling reaction of imines,[8] and most of these are primarily for the construction of a specific side chain structure and/or a stereocenter. Therefore, the need remains for a versatile method for the chiral syntheses of various types of C_2-symmetric and unsymmetric1,2-diamines.

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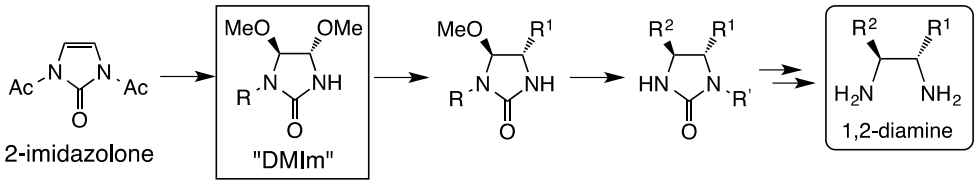
* Dedicated to Professor Victor Snieckus, Queen's University, on the occasion of his 77th birthday.

We previously reported that optically active *trans*-4,5-dimethoxy-2-imidazolidinone (DMIm), the enantiomers of which were both readily available, functioned as a versatile chiral synthon for the construction of various types of symmetric ($R^1 = R^2$) and unsymmetric ($R^1 \neq R^2$) 1,2-diamines, including the stepwise and stereoselective conversion of two aminal moieties to other substituents followed by ring-opening (Scheme 1).[9] This methodology has an advantage over other methods, in that various types of symmetric and unsymmetric 1,2-diamines and their enantiomers can be easily prepared. The construction of a chemical library in the field of medicinal research would be easier with this methodology.



Scheme 1

Both of the optically pure enantiomers of DMIm were provided from a simple 5-membered heterocycle. 1,3-Diacetyl-2-imidazolone underwent the smooth electrophilic addition of bromine to give *trans*-1,3-diacetyl-4,5-dibromo-2-imidazolidinone and that was methanolyzed to the corresponding (4*RS*,5*RS*)-1-acetyl-DMIm followed by *N*-acylation with (1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl chloride (MAC-Cl), which proved to be a versatile auxiliary of choice for optical resolution,[10] and led to the subsequent optical resolution of both diastereomers.[9] However, this synthetic methodology includes some drawbacks: i) bromine is harmful and difficult to handle, and it was needed for the first step; and, ii) the direct optical resolution of the diastereomers of 1-MAC-DMIm was impossible, which necessitated a somewhat lengthy and tedious process that included the replacement of one methoxy moiety with a benzyloxy moiety in the presence of a large amount of benzyl alcohol (that was difficult to remove from the reaction mixture), and the subsequent optical resolution of their diastereomers had to be followed by the re-methoxylation of the benzyloxy moiety. Therefore, the need remains for a more practical and facile method for the preparation of both enantiomers (diastereomers) of DMIm.

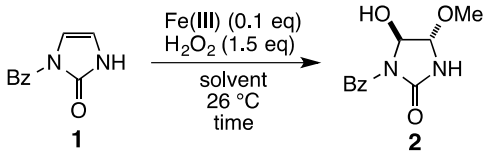
Meanwhile, we recently attempted to oxidize the olefinic moiety of a 2-imidazolone heterocycle to obtain its epoxide as a DMIm equivalent and unexpectedly found that the $FeCl_3$-catalyzed oxidation of 2-imidazolone using aqueous hydrogen peroxide (30%) as an oxidant yielded hydroxy/alkoxy-functionalized 2-imidazolidinones in place of its epoxide.[11] This accidental result prompted us to conceive of this new strategy for DMIm without the use of bromine. Concurrently, during the course of other research, we also discovered that the racemic DMIm were optically resolved by the introduction of a MAC moiety and a specific arylsulfonyl group at the *N*-position of DMIm. Herein, we describe an

efficient method for the preparation of both enantiomers of DMIm using the Fe(III)-catalyzed oxidation of 2-imidazolone followed by the optical resolution of the *N*-arylsulfonyl derivatives using MAC acid.

RESULTS AND DISCUSSION

1. Exploration of a simple method for the preparation of racemic DMIm using Fe(III)-catalyzed oxidation:

Table 1. The Fe(III)-catalyzed oxidation of 1-benzoyl-2-imidazolone by hydrogen peroxide



1 **2**

Entry	Fe(III) complex	Oxidant	Solvent	Time (h)	Yield (%)[a]
1	$FeCl_3$•$6H_2O$ (0.1) dipicolinic acid (0.1) *i*-Pr_2NH (0.2)	30% H_2O_2 aq	MeOH/CH_2Cl_2 (5:5)	2	4[b]
2	$FeCl_3$•$6H_2O$ (0.1) dipicolinic acid (0.1) *i*-Pr_2NH (0.2)	30% H_2O_2 aq	$MeC(OMe)_3$/CH_2Cl_2 (5:5)	24	30 (56)[c]
3	$FeCl_3$•$6H_2O$ (0.1) dipicolinic acid (0.1) *i*-Pr_2NH (0.2)	H_2O_2 urea	$MeC(OMe)_3$/CH_2Cl_2 (5:5)	24	58 (33)[c]
4	FeCl(dipic)$(H_2O)_2$ (0.1) *i*-Pr_2NH (0.2)	H_2O_2 urea	$MeC(OMe)_3$/CH_2Cl_2 (5:5)	24	18 (48)[c]
5	FeCl(dipic)$(H_2O)_2$ (0.1) *i*-Pr_2NH (0.1)	H_2O_2 urea	$MeC(OMe)_3$/CH_2Cl_2 (5:5)	24	41 (14)[c]
6	FeCl(dipic)$(H_2O)_2$ (0.1) *i*-Pr_2NH•HCl (0.1)	H_2O_2 urea	$MeC(OMe)_3$/CH_2Cl_2 (5:5)	6	49 (21)[c]
7	FeCl(dipic)$(H_2O)_2$ (0.1) *i*-Pr_2NH•HCl (0.1)	H_2O_2 urea	$MeC(OMe)_3$/CH_2Cl_2 (1:9)	3	69[b]
8	FeCl(dipic)$(H_2O)_2$ (0.1) *i*-Pr_2NH•HCl (0.1)	H_2O_2 urea	$MeC(OMe)_3$/CH_2Cl_2 (3:7)	3	85[b]

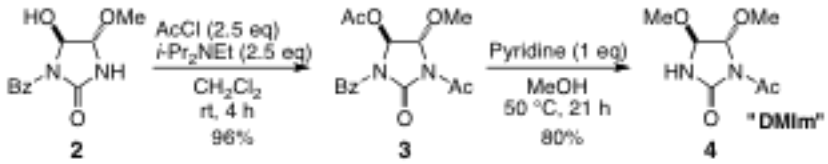
a) *cis*-Product was not observed from ^1H NMR spectroscopy.
b) Isolated yields.
c) Calculated yields based on ^1H NMR. The values in parentheses show the recovered yield of starting material **1**.

According to our preliminary results,[11] we first examined the efficient functionalization of 2-imidazolone to a DMIm precursor using Fe(III)-catalyzed oxidation (Table 1). Using methanol rather than *t*-butanol as the solvent, the reaction did not proceed well and gave the corresponding 4-methoxy-5-hydroxy-2-imidazolone **2** in a poor yield (entry 1). We speculated that this was the result of the oxidation of methanol, and chose trimethyl orthoacetate as the next candidate for a methoxy donor. However, the

hydrolysis of trimethyl orthoacetate with aqueous hydrogen peroxide solution resulted in methanol, which resulted in lower reactivity (entry 2). Compared with previous trials, the use of a hydrogen peroxide-urea complex, instead of aqueous hydrogen peroxide, induced a higher yield of 4-methoxy derivative **2** (entry 3).

A similar moderate yield of **2** (entry 5) was obtained when we tried a pre-synthesized Fe(III)-dipicolinate complex ($FeCl(dipic)(H_2O)_2$) in order to simplify the reaction procedure and maintain uniformity of the catalyst: the combination of $FeCl(dipic)(H_2O)_2$, 0.1 equivalent of diisopropylamine, and a hydrogen peroxide-urea complex. Intriguingly, the addition of diisopropylammonium chloride in place of diisopropylamine also activated the reaction to give a higher yield of **2** (entry 6). This reaction system was also greatly affected by the amount of trimethyl orthoacetate. The 30% trimethyl orthoacetate solvent system showed the highest reactivity, and produced an 85% yield of **2** (entry 8).

With 5-hydroxy-4-methoxy-2-imidazolidinone **2** thus obtained, the conversion to (4*RS*,5*RS*)-DMIm **4** resulted in a 77% yield that was easily accomplished in two steps: i) diacetylation of **2**, and ii) the regioselective cleavage of a 1-benzoyl group followed by the substitution of the acetoxy group with a methoxy group (Scheme 2).



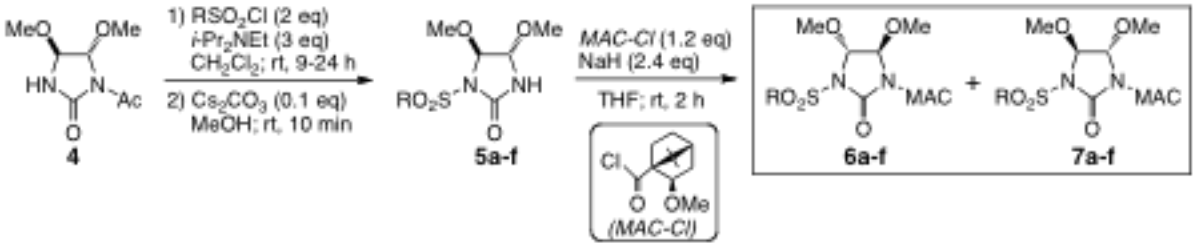
Scheme 2

2. Effective optical resolution of racemic DMIm:

As mentioned above, a lengthy and tedious process was required for the production of both enantiomers of DMIm using MAC acid. The process included the conversion of methoxy to a benzyloxy group in the presence of a large amount of benzyl alcohol. Therefore, the investigation of a more facile method for the optical resolution of DMIm is needed.

During the course of our recent research, we found that the introduction of some arylsulfonyl moieties to the nitrogen position of *N*-MAC-DMIm changed the separability of diastereomers during silicagel column chromatography. Thus, several types of 1-arylsulfonyl-3-MAC-DMIm were examined and 1-benzenesulfonyl and 1-(2-mesitylenesulfonyl) derivatives could be effectively separated to the diastereomers **6** and **7** (Table 2, entries 5, 6).[12]

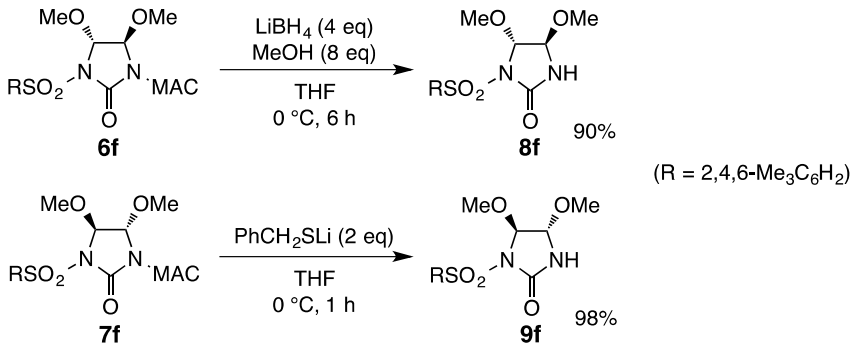
Table 2. Trials for the optical resolution of 1-arylsulfonyl-3-MAC-DMIm



Entry	R	Yield (%)[a] 5	6	7	separability of diastereomers
1	Tol (**a**)	97	0 (48)	0 (48)	X
2	*p*-$NO_2C_6H_4$ (**b**)	94	2 (37)	10 (41)	X
3	*o*-$NO_2C_6H_4$ (**c**)	67	2 (47)	20 (51)	X
4	*p*-ClC_6H_4 (**d**)	92	29 (37)	21 (50)	Δ
5	Ph (**e**)	99	39 (48)	47 (51)	O
6	2,4,6-$Me_3C_6H_2$ (**f**)	96	38 (46)	47 (52)	O

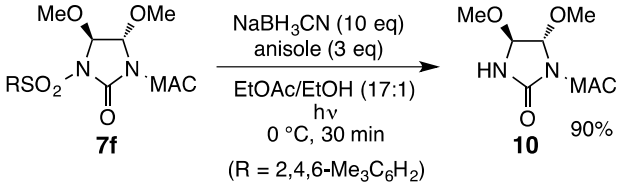
a) Isolated yields. The values in parentheses are calculated yields based on ^{1}H-NMR.

There are two ways to transform these diastereomers into chiral synthons for 1,2-diamines. Desulfonylation and deacylation are the valid routes for mono-*N*-substituted DMIm, with a methoxy group at the "NH" side that can be converted into another substituent. As a result of our examinations, the selective removal of both groups, arylsulfonyl and MAC, was accomplished. Thus, the diastereomers of 1-(2-mesitylenesulfonyl)-3-MAC-DMIm, **6f** and **7f**, were treated with $LiBH_4$/MeOH (1:2) and $PhCH_2SLi$, respectively, to yield a pair of deacylated DMIm enantiomers, **8f** and **9f**, in excellent yields (90 and 98%, respectively; Scheme 3).[13] The same trials using 1-benzenesulfonyl derivatives **6e** and **7e** gave inferior results (72% of **8e** and 68% of **9e**).



Scheme 3

On the other hand, UV-irradiation to 1-(2-mesitylenesulfonyl)-3-MAC-DMIm **7f** in the presence of sodium cyanoborohydride and anisole gave the corresponding desulfonylated DMIm **10** in a 90% yield (Scheme 4). The compound **6f** also gave similar results under the same conditions.



Scheme 4

In conclusion, we established a complementary method for the preparation of both of the enantiomers of DMIm, using the Fe(III)-catalyzed oxidation of 2-imidazolone *via* a H_2O_2-urea complex with subsequent optical resolution *via* the introduction of a MAC moiety and a 2-mesitylenesulfonyl group at the two nitrogen positions of DMIm, which were then selectively removed. Compared with the previous method, this new procedure required neither hazardous bromine, which is difficult to handle, nor the multi-step conversion of the alkoxy moiety, which requires the use of a large amount of benzyl alcohol that is difficult to remove from the reaction mixture. This new method features ease of handling and a simple attach-detach process, and, therefore, is more suitable for the multi-gram scale preparation of both enantiomers of chiral DMIm.

EXPERIMENTAL

Melting points were determined using a Yanaco micro melting point apparatus and were uncorrected. Optical rotations were measured with a JASCO P-1010 polarimeter. ^{1}H NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard using JEOL ALPHA 500 (500 MHz), JEOL JNM-GX400 (400 MHz) and JEOL JNM-AL300 (300 MHz) spectrometers. ^{13}C NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard using JEOL ALPHA 500 (125 MHz), JEOL JNM-GX400 (100 MHz) and JEOL JNM-AL300 (75 MHz) spectrometers with broad-band proton decoupling. Infrared spectra were measured with a JEOL JIR-6500W and JASCO FT/IR-410 FT-IR spectrometer. MS and HRMS (EI or FAB) were obtained with a JEOL JMS-700 mass spectrometer. Fuji silysia silica gel (PSQ60B) was used for flash chromatography. Fe(III)-dipicolinate complex ($FeCl(dipic)(H_2O)_2$) was prepared following a previously reported procedure.[14]

Fe(III)-catalyzed oxidation of 1-benzoyl-2-imidazolone (1) by hydrogen peroxide (Table 1):

i) Typical procedure using $FeCl_3$•$6H_2O$/dipicolinic acid/*i*-Pr_2NH and 30% H_2O_2 aq (entry 2). To a

suspension of $FeCl_3$•$6H_2O$ (7.2 mg, 0.1 eq) and dipicolinic acid (4.4 mg, 0.1 eq) in CH_2Cl_2 (1 mL) was added *i*-Pr_2NH (7.5 μL) and the suspension was stirred at 26 °C for 30 min. After the addition of a solution of 1-benzoyl-2-imidazolone (**1**) (50 mg, 0.2657 mmol)in CH_2Cl_2 (1.4 mL) to the catalyst mixture with stirring for 10 min at 26 °C, trimethyl orthoacetate (2.4 mL) was added along with an aqueous H_2O_2 solution (30%) in trimethyl orthoacetate (0.48 mL), which were added to the reaction mixture over 1 h using a syringe pump at 0 °C followed by stirring for 24 h at 0 °C. The reaction mixture was passed through SiO_2 pad (EtOAc as eluent) to quench the reaction and the eluent was evaporated *in vacuo* followed by flash column chromatography on silica gel (hexane/EtOAc; 5/5 to 2/8) to yield a mixture of (4*RS*,5*RS*)-*tran*s-1-benzoyl-5-hydroxy-4-methoxy-2-imidazolidinone (**2**) (18.8 mg, 0.0795 mmol, 30%) and the starting material (**1**) (27.9 mg, 0.1484 mmol, 56%) as a colorless amorphous solid, the ratio of which was determined by ^{1}H NMR spectrometry.

ii) Typical procedure using FeCl(dipic)$(H_2O)_2$/*i*-Pr_2NH•HCl and H_2O_2 urea (entry 8). A suspension of FeCl(dipic)$(H_2O)_2$ (7.8 mg, 0.1 eq) and *i*-Pr_2NH•HCl (3.7 mg, 0.1 eq) in CH_2Cl_2 (2.3 mL) was stirred at 26 °C for 30 min. After the addition of a solution of 1-benzoyl-2-imidazolone (**1**) in CH_2Cl_2 (1.4 mL) to the catalyst mixture with stirring for 10 min at 26 °C, trimethyl orthoacetate (1.59 mL) and H_2O_2-urea (37.5 mg) were subsequently added at 0 °C and then stirred at 26 °C for 3 h. The reaction mixture was passed through a SiO_2 pad (EtOAc as eluent) to quench the reaction and the eluent was evaporated *in vacuo* followed by flash column chromatography on silica gel (hexane/EtOAc; 5/5 to 2/8) to yield (4*RS*,5*RS*)-*tran*s-1-benzoyl-5-hydroxy-4-methoxy-2-imidazolidinone (**2**) (53.3 mg, 0.2256 mmol, 85%) as colorless crystals; mp 145-148 °C (CH_2Cl_2); IR (KBr) ν 3410, 3207, 3128, 2935, 2916, 2835, 1741, 1680, 1448, 1427, 1404 cm^{-1}; ^{1}H NMR (300 MHz), $CDCl_3$) d 3.42 (3H, s), 4.29(1H, d, *J* = 2.6 Hz), 4.68 (1H, d, *J* = 2.6 Hz), 5.73 (1H, d, *J* = 1.1 Hz), 6.00 (1H, br s), 7.40-7.45 (2H, m), 7.53-7.58 (1H, m), 7.66-7.69 (2H, m); ^{13}C-NMR (75 MHz, CD_3CN) d 53.1, 81.9, 85.7, 126.6, 127.7, 130.6, 133.6, 152.6, 169.0. MS (FAB) *m/z* 237 (MH^+, 52), 105 (PhCO, 100), 77 (Ph, 23); HRMS (FAB) Calcd for $C_{11}H_{13}N_2O_4$ (MH^+): *m/z* 237.0875. Found: *m/z* 237.0875.

(4*RS*,5*RS*)-*trans*-5-Acetoxy-3-acetyl-1-benzoyl-4-methoxy-2-imidazolidinone (3). To a solution of (4*RS*,5*RS*)-*tran*s-1-benzoyl-5-hydroxy-4-methoxy-2-imidazolidinone (**2**) (340 mg, 1.439 mmol) in CH_2Cl_2 (14 mL) were added *i*-Pr_2NEt (0.63 mL, 3.598 mmol, 2.5 eq) and acetyl chloride (0.26 mL, 3.598 mmol, 2.5 eq) at 0 °C with stirring at room temperature for 4 h. The reaction mixture was passed through a SiO_2 pad (EtOAc as eluent) to quench the reaction and the eluent was evaporated *in vacuo* followed by flash column chromatography on silica gel (hexane/CH_2Cl_2 (2/8) - CH_2Cl_2 - EtOAc/CH_2Cl_2 (2/8)) to yield **3** (440.4 mg, 1.375 mmol, 96%) as a pale yellow oil; IR (KBr) ν 3014, 2943, 2846, 1782, 1753, 1716, 1699, 1373 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.16 (3H, s), 2.50 (3H, s), 3.65 (3H, s), 5.30 (1H, s), 6.54 (1H, s), 7.44 (2H, m), 7.57-7.66 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.7, 24.3, 58.0, 79.6, 85.7, 128.0,

128.8, 132.7, 132.8, 150.2, 168.6, 169.3, 170.3. MS (FAB) *m/z* 321 (MH^+, 4), 289 (M^+-OMe, 3), 261 (M^+-OAc, 10), 105 (PhCO, 100), 77 (Ph, 7); HRMS (FAB) Calcd for $C_{15}H_{17}N_2O_6$ (MH^+): *m/z* 321.1087. Found: *m/z* 321.1066.

(4*RS*,5*RS*)-*trans*-1-Acetyl-4,5-dimethoxy-2-imidazolidinone (4). To a solution of (4*RS*,5*RS*)-*trans*-5-acetoxy-3-acetyl-1-benzoyl-4-methoxy-2-imidazolidinone (**3**) (271 mg, 0.846 mmol) in MeOH (17 mL) was added pyridine (0.067 mL, 0.846 mmol, 1.0 eq) with stirring at 50 °C for 21 h. The reaction mixture was concentrated *in vacuo* and the residue was purified by flash column chromatographed on silica gel (CH_2Cl_2/EtOAc (9/1 to 7/3)) to obtain **4** (127 mg, 0.677 mmol, 80%) as colorless crystals; mp 100-102 °C (hexane); IR (KBr) ν 3248, 3145, 3014, 2985, 2941, 2846, 2825, 1732, 1707, 1464, 1406 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.52 (3H, s), 3.36 (3H, s), 3.53 (3H, s), 4.57 (1H, d, *J* = 1.3 Hz), 5.34 (1H, d, *J* = 1.3 Hz), 6.77 (1H, br s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.0, 54.2, 57.3, 85.6, 88.2, 155.4, 170.9. MS (FAB) *m/z* 189 (MH^+, 100), 157 (M^+-OMe, 20), 115 (MH^+-OMe-OAc, 37); HRMS (FAB) Calcd for $C_7H_{13}N_2O_4$ (MH^+): *m/z* 189.0875. Found: *m/z* 189.0868.

Typical procedure for the preparation of (4*RS*,5*RS*)-1-arylsulfonyl-4,5-dimethoxy-2-imidazolidinones 5a-f. (4*RS*,5*RS*)-4,5-dimethoxy-1-toluenesulfonyl-2-imidazolidinone (5a). To a solution of (4*RS*,5*RS*)-*trans*-1-acetyl-4,5-dimethoxy-2-imidazolidinone (**4**) (200 mg, 1.06 mmol) in CH_2Cl_2 (11 mL) were added diisopropylethylamine (0.56 mL, 3.18 mmol, 3 eq), *p*-toluenesulfonyl chloride (0.405 g, 2.12 mmol, 2 eq) and DMAP (0.013 g, 0.106 mmol, 0.1 eq) with stirring at room temperature for 18 h. The reaction mixture was passed through a SiO_2 pad (EtOAc as eluent) to quench the reaction, and the eluent was evaporated *in vacuo* followed by flash chromatography on silica gel (hexane/EtOAc (19/1 to 8/2)) to yield (4*RS*,5*RS*)-3-acetyl-4,5-dimethoxy-1-(*p*-toluenesulfonyl)-2-imidazolidinone (355 mg, 1.04 mmol) as a colorless oil, which was subsequently dissolved in MeOH (10.4 mL) and Cs_2CO_3 (34 mg, 0.104 mmol, 0.1 eq) with stirring for 10 min at room temperature. Citric acid (20 mg, 0.104 mmol, 0.1 eq) was added to the reaction mixture to quench the reaction and the mixture was concentrated *in vacuo* followed by flash column chromatography on silica gel (hexane/EtOAc (6/4 to 5/5)) to yield (4*RS*,5*RS*)-4,5-dimethoxy-1-(*p*-toluenesulfonyl)-2-imidazolidinone (309 mg, 1.03 mmol, 97% from **4**) as a colorless solid; mp 143.5-144.0 °C; IR (KBr) ν 3356, 3228, 2947, 1763, 1338, 1165, 1107, 933, 667, 601, 544 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.43 (3H, s), 3.31 (3H, s), 3.53 (3H, s), 4.58 (1H, d, *J* = 1.5 Hz), 5.31(1H, d, *J* = 1.5 Hz), 5.74 (1H, br s), 7.32 (2H, d, *J* = 8.1Hz), 7.93 (2H, d, *J* = 8.1Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 54.1, 56.0, 85.9, 91.6, 128.2, 129.5, 135.9, 144.9, 154.1. MS (FAB) *m/z* 301 (MH^+, 39), 269 (M^+-OMe, 100), 91 ($CH_3C_6H_5^+$, 22); HRMS (FAB) Calcd for $C_{12}H_{17}N_2O_5S$ (MH^+): *m/z* 301.0858. Found: *m/z* 301.0873.

(4*RS*,5*RS*)-4,5-Dimethoxy-1-(*p*-nitrobenzenesulfonyl)-2-imidazolidinone (5b): a colorless solid; mp 138-139 °C; IR (KBr) ν 3251, 3140, 2939, 1743, 1531, 1377, 1184, 949, 856, 744, 621 cm^{-1}; ^1H NMR

(300 MHz, $CDCl_3$) δ 3.33 (3H, s), 3.54 (3H, s), 4.60 (1H, d, *J* = 1.3 Hz), 5.28 (1H, d, *J* = 1.3 Hz), 6.61 (1H, br s), 8.23 (2H, d, *J* = 9.1 Hz), 8.35 (2H, d, *J* = 9.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.5, 56.4, 85.9, 91.8, 124.1, 129.7, 144.2, 150.7, 153.6. MS (FAB) *m/z* 332 (MH^+, 3), 300 (M^+-OMe, 4), 154 (100); HRMS (FAB) Calcd for $C_{11}H_{13}N_3O_7SNa$ (MNa^+): *m/z* 354.0372. Found (MNa^+): *m/z* 354.0382.

(4*RS*,5*RS*)-4,5-Dimethoxy-1-(*o*-nitrobenzenesulfonyl)-2-imidazolidinone (5c): a colorless solid; mp 161-162 °C; IR (KBr) ν 3313, 3124, 2951, 1751, 1543, 1369, 1180, 1088, 602 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.41 (3H, s), 3.61 (3H, s), 4.64 (1H, s), 5.40 (1H, s), 5.95 (1H, br s), 7.67-7.84 (3H, m), 8.42-8.44 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.7, 56.9, 87.4, 91.6, 124.6, 131.6, 132.1, 134.4, 135.0, 148.1, 153.1. MS (FAB) *m/z* 332 (MH^+, 3), 300 (M^+-OMe, 29), 154 (100); HRMS (FAB) Calcd for $C_{11}H_{14}N_3O_7S$ (MH^+): *m/z* 332.0552. Found: *m/z* 332.0564.

(4*RS*,5*RS*)-1-(*p*-Chlorobenzenesulfonyl)-4,5-dimethoxy-2-imidazolidinone (5d): a colorless solid; mp 119.5-120.5 °C; IR (KBr) ν 3356, 3105, 2943, 2839, 1755, 1577, 1365, 1176, 1095, 945, 764, 633 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.30 (3H, s), 3.52 (3H, s), 4.58 (1H, s), 5.27 (1H, s), 6.50 (1H, br s), 7.47-7.50 (2H, d, *J* = 8.6 Hz), 7.96-7.99 (2H, d, *J* = 8.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 54.1, 56.2, 85.9, 91.6, 129.2, 129.8, 137.3, 140.5, 153.5. MS (FAB) *m/z* 321 (MH^+, 43), 323 ($(M+2)H^+$, 18), 289 (M^+-OMe, 100), 291 ($(M+2)^+$-OMe, 39); HRMS (FAB) Calcd for $C_{11}H_{14}ClN_2O_5S$ (MH^+): *m/z* 321.0312. Found: *m/z* 321.0307.

(4*RS*,5*RS*)-1-Benzenesulfonyl-4,5-dimethoxy-2-imidazolidinone (5e): a colorless solid; mp 161-162 °C; IR (KBr) ν 3602, 3305, 2951, 1763, 1724, 1430, 1365, 1173, 1099, 945, 605 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.28 (3H, s), 3.51 (3H, s), 4.58 (1H, d, *J* = 1.1 Hz), 5.30 (1H, d, *J* = 1.1 Hz), 6.48 (1H, br s), 7.49-7.54 (2H, m), 7.59-7.65 (1H, m), 8.02-8.06 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 54.0, 56.1, 85.9, 91.5, 128.2, 128.8, 133.8, 138.9, 153.7. MS (FAB) *m/z* 287 (MH^+, 43), 255 (M^+-OMe, 100), 77 ($C_6H_5^+$, 21); HRMS (FAB) Calcd for $C_{11}H_{15}N_2O_5S$ (MH^+): *m/z* 287.0702. Found: *m/z* 287.0707.

(4*RS*,5*RS*)-4,5-Dimethoxy-1-(2-mesitylenesulfonyl)-2-imidazolidinone (5f): a colorless solid; mp 179-182 °C; IR (KBr) ν 3317, 2951, 1755, 1601, 1450, 1400, 1353, 1288, 1168, 1072, 941, 852, 660, 598, 536 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.29 (3H, s), 2.65 (6H, s), 3.28 (3H, s), 3.61 (3H, s), 4.56 (1H, s), 5.33 (1H, s), 6.28 (1H, br s), 6.95 (2H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 22.6, 54.5, 56.2, 86.8, 91.5, 132.0, 132.3, 141.3, 143.7, 154.1. MS (FAB) *m/z* 329 (MH^+, 28), 297 (M^+-OMe, 81), 183 ($Me_3C_6H_2SO_2$, 72), 119 ($Me_3C_6H_2$, 100); HRMS (FAB) Calcd for $C_{14}H_{21}N_2O_5S$ (MH^+): *m/z* 329.1171. Found: *m/z* 329.1176.

Typical procedure for the conjunction of (4*RS*,5*RS*)-1-arylsulfonyl-4,5-dimethoxy-2-imidazolidinones 5a-f with MAC-Cl. Optical resolution of 6a and 7a. To a solution of (4*RS*,5*RS*)-4,5-dimethoxy-1-toluenesulfonyl-2-imidazolidinone (**5a**) (251 mg, 0.837 mmol) in THF (4.2 mL) was added NaH (60% in oli, 81 mg, 2.4 eq) at 0 °C with stirring for 15 min at room temperature

followed by the addition of MAC-Cl, prepared from MAC acid (200 mg, 1 mmol, 1.2 eq) and thoinyl chloride (0.293 mL, 4 mmol, 4.8 eq) under reflux for 1 h with the subsequent removal of the remaining thoinyl chloride, HCl and SO_2 by toluene-azeotrope, and further stirring for 2 h. The reaction was quenched by the addition of satd. NH_4Cl aq., and the product was extracted (EtOAc, 40 mL x 3), washed (brine, 30 mL x 3) and dried (anhyd. Na_2SO_4). After the concentration of the organic layer i*n vacuo*, the residue was purified by flash column chromatography on silica gel (hexane/EtOAc (6/4 to 5/5)) to afford a colorless amorphous solid of a 1:1 mixture of **6a** and **7a** (386 mg, 0.804 mmol, 96%), the elements of which were scarcely separable on SiO_2. Absolute configurations of both products were estimated based on comparisons of the ^{1}H NMR spectroscopies of **6f** and **7f**.[15]

(4*S*,5*S*)-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(*p*-toluenesulfonyl)-2-imidazolidinone (7a, higher polarity): IR (neat) ν 3664, 3521, 3020, 2877, 1766, 1697, 1597, 1454, 1373, 1180, 1092, 945, 814, 733, 667 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05-1.11 (1H, m), 1.11 (3H, s), 1.19 (3H, s), 1.54-1.65 (2H, m), 1.76-1.80 (3H, m), 2.27-2.33 (1H, m), 2.42 (3H, s), 2.78 (3H, s), 3.45 (3H, s), 3.48 (3H, s), 4.11 (1H, dd, *J* = 3.7, 7.7 Hz), 5.21 (1H, s), 5.30 (1H, s), 7.33 (2H, d, *J* = 8.4 Hz), 7.95 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 21.7, 21.8, 27.0, 28.5, 37.2, 45.4, 50.7, 55.5, 55.7, 56.8, 62.1, 83.0, 87.1, 88.9, 128.8, 129.5, 135.3, 145.2, 148.7, 173.2. MS (FAB) *m/z* 481 (MH^+, 4), 449 (M^+-OMe, 14), 181 (MAC moiety, 100); HRMS (FAB) Calcd for $C_{23}H_{32}N_2O_7SNa$ (MNa^+): *m/z* 503.1828. Found (MNa^+): *m/z* 503.1793.

(4*R*,5*R*)-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(*p*-toluenesulfonyl)-2-imidazolidinone (6a, lower polarity): IR (neat) ν 3687, 2943, 1766, 1697, 1597, 1454, 1373, 1184, 1107, 941, 818, 744, 667 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (3H, s), 1.04-1.08 (1H, m), 1.25 (3H, s), 1.59-1.69 (5H, m), 2.04-2.09 (1H, m), 2.42 (3H, s), 2.92 (3H, s), 3.40 (3H, s), 3.54 (3H, s), 4.37 (1H, dd, *J* = 3.7, 7.9 Hz), 5.18 (1H, s), 5.41 (1H, s), 7.32 (2H, d, *J* = 7.9 Hz), 7.92 (2H, d, *J* = 7.9 Hz) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 21.5, 21.7, 26.65, 26.67, 37.9, 45.4, 50.7, 56.1, 56.3, 56.8, 62.0, 84.4, 86.7, 89.2, 128.7, 129.5, 135.3, 145.2, 148.6, 173.1. MS (FAB) *m/z* 481 (MH^+, 4), 449 (M^+-OMe, 8), 181 (MAC moiety, 100); HRMS (FAB) Calcd for $C_{23}H_{32}N_2O_7SNa$ (MNa^+): *m/z* 503.1828. Found (MNa^+): *m/z* 503.1865.

***trans*-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(*p*-nitrobenzenesulfonyl)-2-imidazolidinone (6b, 7b)**: From 277 mg (0.837 mmol) of **5b**, a colorless amorphous solid of a mixture of **6b** and **7b** (331 mg, 0.65 mmol, 78%), both of which were slightly separable on SiO_2, was obtained. Absolute configurations of both products were estimated based on comparisons of the ^{1}H NMR spectroscopies of **6f** and **7f**.[15]

(4*S*,5*S*)-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(*p*-nitrobenzenesulfonyl)-2-imidazolidinone (7b, higher polarity): IR (neat) ν 3656, 3109, 3001, 2881, 1770, 1701, 1608, 1535,

1458, 1377, 1188, 1088, 945, 856, 741, 621, 567 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.10 (3H, s), 1.04-1.14 (1H, m), 1.19 (3H, s), 1.53-1.64 (3H, m), 1.71-1.84 (2H, m), 2.16-2.28 (1H, m), 2.79 (3H, s), 3.47 (3H, s), 3.53 (3H, s), 4.07 (1H, dd, *J* = 7.7, 3.7 Hz), 5.20 (1H, s), 5.34 (1H, s), 8.27 (2H, d, *J* = 9.1 Hz), 8.38 (2H, d, *J* = 9.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 21.5, 26.8, 28.4, 37.0, 45.2, 50.7, 55.4, 56.0, 57.2, 62.1, 83.0, 87.1, 89.2, 124.0, 130.2, 143.6, 148.4, 150.8, 173.0. MS (FAB; +NaI) *m/z* 534 (MNa^+, 45), 181 (MAC moiety, 100); HRMS (FAB) Calcd for $C_{22}H_{29}N_3O_9SNa$ (MNa^+): *m/z* 534.1522. Found (MNa^+): *m/z* 534.1537.

(4*R*,5*R*)-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(*p*-nitrobenzenesulfonyl)-2-imidazolidinone (6b, lower polarity): IR (neat) ν 3599, 3109, 2943, 1770, 1701, 1608, 1535, 1458, 1373, 1188, 1092, 945, 856, 741, 621, 567 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.04 (3H, s), 1.02-1.16 (1H, m), 1.25 (3H, s), 1.55-1.75 (3H, m), 1.78-1.88 (1H, m), 1.95-2.03 (1H, m), 2.99 (3H, s), 3.43 (3H, s), 3.56 (3H, s), 4.34 (1H, dd, *J* = 7.9, 3.7 Hz), 5.19 (1H, s), 5.46 (1H, s), 8.26 (2H, d, *J* = 9.2 Hz), 8.38 (2H, d, *J* = 9.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 21.4, 26.6, 26.7, 37.7, 45.3, 50.7, 56.0, 56.4, 57.0, 62.0, 84.2, 86.3, 89.3, 124.0, 130.1, 143.7, 148.3, 150.8, 173.0. MS (FAB; +NaI) *m/z* 534 (MNa^+, 100), 181 (MAC moiety, 97); HRMS (FAB) Calcd for $C_{22}H_{29}N_3O_9SNa$ (MNa^+): *m/z* 534.1522. Found (MNa^+): *m/z* 534.1534.

***trans*-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(*o*-nitrobenzenesulfonyl)-2-imidazolidinone (6c, 7c)**: From 277 mg (0.837 mmol) of **5c**, a colorless amorphous solid of a mixture of **6c** and **7c** (418 mg, 0.82 mmol, 98%), both of which were slightly separable on SiO_2, was obtained. Absolute configurations of both products were estimated based on comparisons of the ^1H NMR spectroscopies of **6f** and **7f**.[15]

(4*S*,5*S*)-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(*o*-nitrobenzenesulfonyl)-2-imidazolidinone (7c, lower polarity): IR (neat) ν 3575, 3101, 2943, 1766, 1701, 1547, 1454, 1377, 1188, 1092, 945, 737 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.12 (3H, s), 1.05-1.16 (1H, m), 1.24 (3H, s), 1.60-1.87 (5H, m), 2.15-2.24 (1H, m), 3.18 (3H, s), 3.55 (3H, s), 3.57 (3H, s), 4.20 (1H, dd, *J* = 7.6, 3.8 Hz), 5.28 (1H, s), 5.30 (1H, s), 7.77-7.80 (3H, m), 8.44-8.47 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 21.7, 27.1, 28.6, 37.3, 45.4, 50.9, 56.2, 56.3, 57.1, 62.1, 83.0, 88.7, 89.0, 124.9, 131.3, 132.1, 134.4, 135.3, 148.3, 148.5, 172.9. MS (FAB; +NaI) *m/z* 534 (MNa^+, 86), 181 (MAC moiety, 100); HRMS (FAB) Calcd for $C_{22}H_{29}N_3O_9SNa$ (MNa^+): *m/z* 534.1522. Found (MNa^+): *m/z* 534.1530.

(4*R*,5*R*)-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(*o*-nitrobenzenesulfonyl)-2-imidazolidinone (6c, higher polarity): IR (neat) ν 3683, 3105, 2943, 1766, 1701, 1547, 1454, 1377, 1188, 1095, 945, 737 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.07 (3H, s), 1.07-1.12 (1H, m), 1.26 (3H, s), 1.56-1.87 (5H, m), 2.05-2.15 (1H, m), 2.86 (3H, s), 3.48 (3H, s), 3.59 (3H, s), 4.31 (1H, dd, *J* = 7.7, 3.8 Hz), 5.26 (1H, s), 5.38 (1H, s), 7.76-7.80 (3H, m), 8.49-8.43 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 21.2, 21.4, 26.6, 26.9, 37.8, 45.3, 50.7, 55.9, 56.9, 57.0, 62.0, 84.5, 87.9, 89.3, 124.7, 131.2, 131.9, 133.8, 135.0, 148.1, 148.3, 172.7. MS (FAB; +NaI) *m/z* 534 (MNa^+, 100), 181 (MAC moiety, 92); HRMS (FAB) Calcd for $C_{22}H_{29}N_3O_9SNa$ (MNa^+): *m/z* 534.1522. Found (MNa^+): *m/z* 534.1531.

***trans*-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(*p*-chlorobenzenesulfonyl)-2-imidazolidinone (6d, 7d)**: From 162 mg (0.505 mmol) of **5d**, a mixture of **6d** and **7d** (218 mg, 0.44 mmol, 87%), both of which were partly separable on SiO_2, was obtained. Absolute configurations of both products were estimated based on comparisons of the ^{1}H NMR spectroscopies of **6f** and **7f**.[15]

(4*S*,5*S*)-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(*p*-chlorobenzenesulfonyl)-2-imidazolidinone (7d, higher polarity): colorless crystals; mp 102-103 °C (from hexane-CH_2Cl_2); $[\alpha]_D^{30}$ -9.5 (*c* 1.01, $CHCl_3$); IR (KBr) ν 3390, 2966, 1770, 1693, 1581, 1466, 1377, 1188, 1092, 945, 764, 629, 567 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04-1.13 (1H, m), 1.11 (3H, s), 1.20 (3H, s), 1.55-1.65 (2H, m), 1.71-1.85 (3H, m), 2.20-2.30 (1H, m), 2.79 (3H,s), 3.46 (3H, s), 3.49 (3H, s), 4.09 (1H, dd, *J* = 7.9, 3.8 Hz), 5.18 (1H, s), 5.32 (1H, s), 7.51 (2H, d, *J* = 8.7 Hz), 8.01 (2H, d, *J* = 8.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 21.6, 26.9, 28.4, 37.2, 45.3, 50.7, 55.4, 55.8, 56.9, 62.1, 83.0, 87.0, 89.0, 129.1, 130.2, 136.7, 140.8, 148.6, 173.1. MS (FAB) *m/z* 501 (MH^+, 4), 469 (M^+-OMe, 7), 181 (MAC moiety, 100); HRMS (FAB) Calcd for $C_{22}H_{29}ClN_2O_7SNa$ (MNa^+): *m/z* 523.1282. Found (MNa^+): *m/z* 523.1291.

(4*R*,5*R*)-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(*p*-chlorobenzenesulfonyl)-2-imidazolidinone (6d, lower polarity): colorless crystals; mp 118-118.5 °C (from hexane-CH_2Cl_2); $[\alpha]_D^{30}$ -35.1 (*c* 1.00, $CHCl_3$); IR (KBr) ν 3429, 2947, 1766, 1701, 1581, 1466, 1377, 1184, 1095, 945, 760, 629, 575 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (3H, s), 1.04-1.11 (1H, m), 1.25 (3H, s), 1.59-1.75 (4H, m), 1.78-1.86 (1H, m), 2.00-2.07 (1H, m), 2.96 (3H, s), 3.41 (3H, s), 3.54 (3H, s), 4.36 (1H, dd, *J* = 7.7, 3.7 Hz), 5.17 (1H, s), 5.43 (1H, s), 7.51 (2H, d, *J* = 8.7 Hz), 7.99 (2H, d, *J* = 8.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 21.4, 26.61, 26.64, 37.8, 45.3, 50.7, 56.0, 56.3, 56.8, 62.0, 84.3, 86.6, 89.3, 129.1, 130.1, 136.6, 140.8, 148.5, 173.0. MS (FAB) *m/z* 501 (MH^+, 5), 469 (M^+-OMe, 6), 181 (MAC moiety, 100); HRMS (FAB) Calcd for $C_{22}H_{29}ClN_2O_7SNa$ (MNa^+): *m/z* 523.1282. Found (MNa^+): *m/z* 523.1267.

***trans*-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-benzenesulfonyl-2-imidazolidinone (6e, 7e)**: From 140 mg (0.489 mmol) of **5e**, a mixture of **6e** and **7e** (218 mg, 0.44 mmol, 87%), both of which were almost separable on SiO_2, was obtained. Absolute configurations of both products were estimated based on comparisons of the ^{1}H NMR spectroscopies of **6f** and **7f**.[15]

(4*S*,5*S*)-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-benzenesulfonyl-2-imidazolidinone (7e, higher polarity): colorless crystals; mp 163-164 °C (from hexane-CH_2Cl_2); $[\alpha]_D^{30}$ -3.8 (*c* 1.01, $CHCl_3$); IR (KBr) ν 3440, 2943, 1774, 1697, 1454, 1381, 1180, 1107, 945, 764, 725, 606, 571 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04-1.11 (1H, m), 1.11 (3H, s), 1.19 (3H, s), 1.53-1.62 (2H, m), 1.69-1.84 (3H, m), 2.26-2.33 (1H, m), 2.72 (3H, s), 3.45 (3H, s), 3.48 (3H, s), 4.09 (1H, dd, *J* = 7.7, 3.7

Hz), 5.22 (1H, s), 5.32 (1H, s), 7.52-7.57 (2H, m), 7.60-7.66 (1H, m), 8.07-8.10 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 21.6, 26.9, 28.4, 37.1, 45.3, 50.6, 55.4, 55.6, 56.8, 62.0, 83.0, 87.0, 88.8, 128.7, 128.8, 134.0, 138.3, 148.6, 173.1. MS (FAB) *m/z* 467 (MH^+, 8), 435 (M^+-OMe, 16), 181 (MAC moiety, 100), 77 ($C_6H_5^+$, 13); HRMS (FAB) Calcd for $C_{22}H_{30}N_2O_7SNa$ (MNa^+): *m/z* 489.1671. Found (MNa^+): *m/z* 489.1682.

(4*R*,5*R*)-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-benzenesulfonyl-2-imidazolidinone (6e, lower polarity): colorless crystals; mp 108-109 °C (from hexane-CH_2Cl_2); $[\alpha]_D^{30}$ -35.3 (*c* 1.00, $CHCl_3$); IR (KBr) ν 3444, 2947, 1774, 1701, 1454, 1373, 1180, 1103, 949, 756, 602 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02-1.09 (1H, m), 1.04 (3H, s) 1.24 (3H, s), 1.57-1.72 (4H, m), 1.76-1.84 (1H, m), 2.02-2.09 (1H, m), 2.89 (3H, s), 3.40 (3H, s), 3.56 (3H, s), 4.35 (1H, dd, *J* = 7.7, 3.7 Hz), 5.20 (1H, s), 5.42 (1H, s), 7.51-7.56 (2H, m), 7.60-7.66 (1H, m), 8.04-8.07 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 21.4, 26.6, 37.9, 45.4, 50.6, 56.0, 56.3, 56.7, 62.0, 84.3, 86.8, 89.3, 128.6, 128.8, 134.0, 138.3, 148.5, 173.1. MS (FAB) *m/z* 467 (MH^+, 4), 435 (M^+-OMe, 8), 181 (MAC moiety, 100), 77 ($C_6H_5^+$, 12); HRMS (FAB) Calcd for $C_{22}H_{30}N_2O_7SNa$ (MNa^+): *m/z* 489.1671. Found (MNa^+): *m/z* 489.1677.

***trans*-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(2-mesitylenesulfonyl)-2-imidazolidinone (6f, 7f)**: From 135 mg (0.411 mmol) of **5f**, the mixture of **6f** and **7f** (205 mg, 0.40 mmol, 98%), both of which were almost separable on SiO_2, was obtained. The absolute configuration of **7f** was assigned based on the fact that the optical rotation and ^{1}H NMR data of desulfonylated compound **10** identified it as the same compound that was previously reported.[9]

(4*S*,5*S*)-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(2-mesitylenesulfonyl)-2-imidazolidinone (7f, higher polarity): colorless crystals; mp 152-153 °C (from hexane-CH_2Cl_2); $[\alpha]_D^{30}$ -27.4 (*c* 1.00, $CHCl_3$); IR (KBr) ν 3440, 2947, 1763, 1697, 1604, 1458, 1362, 1196, 1176, 1088, 941, 733, 663, 586, 528 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04-1.12 (1H, m), 1.12 (3H, s), 1.21 (3H, s), 1.58-1.85 (5H, m), 2.12-2.19 (1H, m), 2.31 (3H, s), 2.69 (6H, s), 3.13 (3H, s), 3.48 (3H, s), 3.58 (3H, s), 4.13 (1H, dd, *J* = 7.7, 3.7 Hz), 5.23 (1H, s), 5.30 (1H, s), 6.98 (2H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 21.1, 21.8, 22.7, 27.0, 28.7, 37.2, 45.3, 50.7, 55.8, 56.1, 57.1, 61.9, 82.9, 88.1, 88.8, 131.8, 132.0, 141.6, 143.9, 148.9, 173.4. MS (FAB) *m/z* 509 (MH^+, 4), 477 (M^+-OMe, 6), 181 (MAC moiety, 100); HRMS (FAB) Calcd for $C_{25}H_{36}N_2O_7SNa$ (MNa^+): *m/z* 531.2141. Found (MNa^+): *m/z* 531.2176.

(4*R*,5*R*)-4,5-Dimethoxy-3-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-1-(2-mesitylenesulfonyl)-2-imidazolidinone (6f, lower polarity): colorless crystals; mp 135-135.5 °C (from hexane-CH_2Cl_2); $[\alpha]_D^{30}$ -19.4 (*c* 1.00, $CHCl_3$); IR (KBr) ν 3001, 1763, 1697, 1601, 1458, 1365, 1192, 1173, 1111, 1080, 937, 741, 663, 586, 528 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03-1.11 (1H, m), 1.08 (3H, s), 1.21 (3H, s), 1.54-1.64 (2H, m), 1.68-1.77 (3H, m), 2.10-2.16 (1H, m), 2.28 (3H, s), 2.67 (3H, s), 2.69 (6H, s), 3.44 (3H, s), 3.61 (3H, s), 4.15 (1H, dd, *J* = 7.7, 3.7 Hz), 5.21 (1H, s), 5.42 (1H, s), 6.95 (2H, s); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 21.0, 21.6, 22.7, 26.7, 27.1, 37.8, 45.3, 50.6, 55.8, 56.4, 57.3, 61.8, 84.1, 87.4, 88.8, 131.6, 131.8, 141.7, 143.8, 148.4, 173.2. MS (FAB) *m/z* 509 (MH^+, 4), 477 (M^+-OMe, 5), 181 (MAC moiety, 100); HRMS (FAB) Calcd for $C_{25}H_{36}N_2O_7SNa$ (MNa^+): *m/z* 531.2141. Found (MNa^+): *m/z* 531.2162.

Removal of the MAC moiety from 6f. (4*R*,5*R*)-4,5-dimethoxy-1-(2-mesitylenesulfonyl)-2-imidazolidinone (8f). To a solution of **6f** (170 mg, 0.334 mmol) in THF (3.4 mL) under an argon atmosphere were subsequently added $LiBH_4$ (1.0 M in THF; 0.67 mL, 1.336 mmol, 4 eq) and MeOH (0.11 mL, 2.67 mmol, 8 eq; dissolved in THF (1 mL)) at 0 °C with stirring for 6 h at 0 °C. The reaction was quenched by the addition of satd. NH_4Cl aq., and the product was extracted (EtOAc, 40 mL x 3), washed (brine, 30 mL x 3) and dried (anhyd. Na_2SO_4). After concentration of the organic layer i*n vacuo*, the residue was purified by flash column chromatography on silica gel (hexane/EtOAc (8/2 to 5/5)) to afford **6f** (5 mg, 3%) and **8f** (99 mg, 0.301 mmol, 90%) as a colorless solid along with an oily amount (50 mg, 80%) of 2-*exo*-methoxy-l-apocamphanemethanol. **8f**: a colorless crystals; mp 158.5-159 °C (from hexane/CH_2Cl_2); $[\alpha]_D^{29}$ -67.9 (*c* 0.72, $CHCl_3$); IR (KBr) ν 3320, 2950, 2839, 1755, 1605, 1450, 1354, 1288, 1169, 1074, 941, 852, 775, 660, 590, 525 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.29 (3H, s), 2.65 (6H, s), 3.28 (3H, s), 3.61 (3H, s), 4.56 (1H, s), 5.33 (1H, s), 6.26 (1H, br s), 6.95 (2H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 22.6, 54.5, 56.2, 86.8, 91.5, 132.0, 141.3, 143.7, 154.1. MS (FAB) *m/z* 329 (MH^+, 48), 297 (M^+-OMe, 88), 183 ($Me_3C_6H_2SO_2$, 62), 119 ($Me_3C_6H_2$, 72); HRMS (FAB) Calcd for $C_{14}H_{20}N_2O_5SNa$ (MNa^+): *m/z* 351.0991. Found: *m/z* 351.0992.

Removal of the MAC moiety from 7f. (4*S*,5*S*)-4,5-dimethoxy-1-(2-mesitylenesulfonyl)-2-imidazolidinone (9f). To a solution of $PhCH_2SH$ (42 μL, 0.358 mmol, 2 eq) in THF (1.8 mL) was added *n*-BuLi (2.66 M in *n*-hexane; 0.10 mL, 0.268 mmol, 1.5 eq) at 0 °C under an argon atmosphe re with stirring for 10 min to form $PhCH_2SLi$, to which was added **7f** (91 mg, 0.18 mmol) in THF (1.8 mL) at 0 °C with stirring for 1 h at 0 °C. The reaction was quenched by the addition of satd. NH_4Cl aq. and the product was extracted (EtOAc, 20 mL x 3), washed (brine, 10 mL x 3) and dried (anhyd. Na_2SO_4). After concentration of the organic layer i*n vacuo*, the residue was purified by flash column chromatography on silica gel (hexane/EtOAc (19/1 to 5/5)) to afford, in addition to the oily thiobenzyl ester of MAC acid (54 mg, 98%), **9f** (58 mg, 0.178 mmol, 98%) as colorless crystals; mp 159-160 ℃ (from hexane/CH_2Cl_2); $[\alpha]_D^{30}$ 68.8 (*c* 0.90, $CHCl_3$); IR (KBr) ν 3316, 2950, 1755, 1600, 1340, 1282, 1160, 1085, 941, 852, 775, 597, 536 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.28 (3H, s), 2.64 (6H, s), 3.21 (3H, s), 3.60 (3H, s), 4.56 (1H, s), 5.31 (1H, s), 6.83 (1H, br s), 6.93 (2H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 22.6, 54.5, 56.2, 86.8, 91.5, 132.0, 141.3, 143.7, 154.1. MS (FAB) *m/z* 329 (MH^+, 41), 297 (M^+-OMe, 92), 183 ($Me_3C_6H_2SO_2$, 74), 119 ($Me_3C_6H_2$, 98); HRMS (FAB) Calcd for $C_{14}H_{20}N_2O_5SNa$ (MNa^+): *m/z* 351.0991. Found: *m/z* 351.0997.

Removal of the mesitylenesulfonyl moiety from 7f. (4*S*,5*S*)-4,5-dimethoxy-1-[(1*S*,2*R*)-2-*exo*-methoxyapocamphanecarbonyl]-2-imidazolidinone (10). A mixture of **7f** (87 mg, 0.17 mmol), $NaBH_3CN$ (107 mg, 1.7 mmol, 10 eq) and anisole (56 μL, 0.51 mmol, 3 eq) in EtOAc (17 mL) and *t*-BuOH (1 mL) was placed into a 30 mL quartz flask under an argon atmosphere and was irradiated with a 100 W high-pressure Hg lamp (Ushio Inc.) at 0 °C for 30 min under vigorous stirring. The reaction mixture was passed through SiO_2 pad (EtOAc as eluent), and the eluent was evaporated *in vacuo* followed by flash chromatography on silica gel (hexane/EtOAc (8/2 to 6/4)) to yield **10** (50 mg, 0.154 mmol, 90%) as colorless crystals; mp 84.5-85.0 ℃ (from hexane); $[\alpha]_D^{28}$ -64.8 (*c* 1.00, $CHCl_3$); IR (KBr) ν 3460, 3178, 3012, 2831, 1755, 1685, 1454, 1396, 1323, 1238, 1095, 945, 818, 729 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.09-1.17 (1H, m), 1.13 (3H, s), 1.29 (3H, s), 1.61-1.67 (2H, m), 1.75-1.92 (3H, m), 2.39-2.47 (1H, m), 3.15 (3H, s), 3.32 (3H, s), 3.49 (3H, s), 4.40 (1H, dd, *J* = 3.8, 7.7 Hz), 4.59 (1H, d, *J* = 1.7 Hz), 5.45 (1H, d, *J* = 1.7 Hz), 6.08 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 21.6, 26.8, 28.2, 37.4, 45.5, 50.4, 53.1, 55.9, 56.7, 61.9, 83.6, 85.2, 89.4, 154.3, 173.4. Anal. Calcd for $C_{16}H_{26}N_2O_5$: C, 58.88; H, 8.03; N, 8.58. Found: C, 58.65; H, 8.27; N, 8.50.

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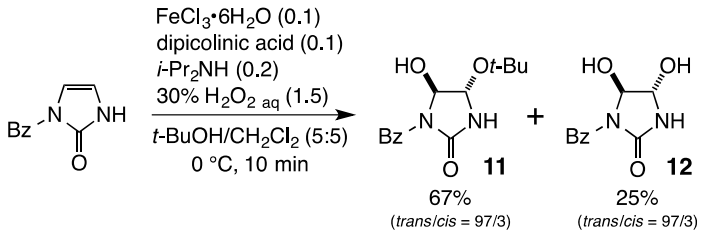
11. Unpublished data. Following Beller's procedure,[16] the treatment of *N*-benzoyl-2-imidazolone with aqueous hydrogen peroxide solution (30%) in the presence of catalytic amount of $FeCl_3$•$6H_2O$, dipicolinic acid and diisopropylamine in *t*-BuOH/CH_2Cl_2 (1:1) mixture as solvent yielded 4-*tert*-butoxy-5-hydroxy- and 4,5-dihydroxy-2-imidazolidinone (**11**, **12**) (Sheme 5).



Scheme 5

12. Absolute configulation of **7f** was assigned from the fact that the optical rotation and ^{1}H NMR data of desulfonylated compound **10** was identical as the same compound which was previously reported.[9]
13. Selective removal of MAC group of **6f** using $PhCH_2SLi$ had also tried and only 13% yield of **8f** was obtained, accompanying 59% recovered yield of the starting material **6f**.
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15. The chemical shifts of 2-*endo* protons at MAC moieties (1H, dd) of **6** and **7** were mainly compared. (4*R*,5*R*)-**6f** showed 4.15 ppm (lower field) and (4*S*,5*S*)-**7f** showed 4.13 ppm (higher field). Alternatively, two methyl signals (3H, s) of MAC group appeared at 1.08 and 1.21 ppm in (4*R*,5*R*)-**6f** (differential of each δ values (*Δ*δ): 0.13 ppm, larger value than **7f**) and also appeared at 1.12 and 1.21 ppm in (4*S*,5*S*)-**7f** (*Δ*δ: 0.09 ppm, smaller value than **6f**). Other diastereomers showed similar larger/smaller δ and *Δ*δ values.

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