Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry


# Supporting Information-I

## Observation of Neighboring *ortho*-Hydroxyl Group Participation in Organocatalytic Asymmetric Sequential Michael-Lactonization Reactions: Synthesis of Highly Substituted Chiral Spirodihydrocoumarins

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**General Methods:** The $^{1}H$ NMR and $^{13}C$ NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts are reported in ppm downfield to TMS ($\delta = 0$) for $^{1}H$ NMR and relative to the central $CDCl_3$ resonance ($\delta = 77.0$) for $^{13}C$ NMR. *In the $^{13}C$ NMR spectra, the nature of the carbons (C, CH, $CH_2$ or $CH_3$) was determined by recording the DEPT-135 experiment, and is given in parentheses.* The coupling constants *J* are given in Hz. Column chromatography was performed using Acme's silica gel (particle size 0.063-0.200 mm). High-resolution mass spectra were recorded on micromass ESI-TOF MS. GCMS mass spectrometry was performed on Shimadzu GCMS-QP2010 mass spectrometer. IR spectra were recorded on JASCO FT/IR-5300. Elemental analyses were recorded on a Thermo Finnigan Flash EA 1112 analyzer. Mass spectra were recorded on either VG7070H mass spectrometer using EI technique or Shimadzu-LCMS-2010 A mass spectrometer. The X-ray diffraction measurements were carried out at 298 K on an automated Enraf-Nonious MACH 3 diffractometer using graphite monochromated, Mo-Kα (λ = 0.71073 Å) radiation with CAD4 software or the X-ray intensity data were measured at 298 K on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube (λ = 0.71073 Å). For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used and compounds were visualized by

irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. $H_2SO_4$ (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating.

The enantiomeric excess (*ee*) of the sequential *M-L* products was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H, Chiralcel OJ-H, Chiralpak AD-H, Chiralpak AS-H or Lux 5u Amylose-2 columns and hexane/2-propanol as the eluent. Retention times and solvent ratios are indicated in the respective entries.

**Materials:** All solvents and commercially available chemicals were used as received.

**Preparation of β-keto esters:** β-keto ester **1a** is commercially available and **1b**, **1c** and **1d** were prepared according to literature procedures.[1-3]

1. A. M. R. Smith, D. Billen and K. Kuok (Mimi) Hii, *Chem. Commun*., 2009, 3925–3927.
2. V. Justribo, S. C. Pellegrinet and M. I. Colombo, *J. Org. Chem.,* 2007, **72**, 3702-3712.
3. D. A. May, Jr and T. D. Lash, *J. Org. Chem.,* 1992, **57**, 4820-4828.

## *General Experimental Procedures for the Sequential M-L Reactions:*

**Procedure A:** ***General procedure for amine-catalyzed racemic Michael reaction of keto-esters 1 with 2-(2-nitrovinyl)phenols 2:*** In an ordinary glass vial equipped with a magnetic stirring bar, to the 1:1 mixture of **3a**/**3d** (each 5 mol%) in DCM (1.0 mL), were added **1a** (0.4 mmol, 1.33 equiv.) and 2-(2-nitrovinyl)phenols **2a-i** (0.3 mmol). After stirring the reaction mixture at 25 °C as shown in Table S1, the crude reaction mixture was concentrated and pure racemic products **4/5** were obtained by quick filtration (silica gel, mixture of hexane/ethyl acetate).

**Procedure B:** ***General procedure for quinine-NH-thiourea-catalyzed asymmetric Michael reaction of keto-esters 1 with 2-(2-nitrovinyl)phenols 2:*** In an ordinary glass vial equipped with a magnetic stirring bar, to the **3f** or **3h** (10 mol%) in DCM (1.0 mL), were added **1a-d** (0.4 mmol, 1.33 equiv.) and 2-(2-nitrovinyl)phenols **2a-i** (0.3 mmol). After stirring the reaction mixture at 25 °C as shown in Tables 1-2, the crude reaction mixture was concentrated and pure chiral products **4/5** were obtained by quick filtration (silica gel, mixture of hexane/ethyl acetate).

**Procedure C:** ***General procedure for amine-/p-TSA-catalyzed racemic sequential Michael-lactonization reaction of keto-esters 1 with 2-(2-nitrovinyl)phenols 2:*** In an ordinary glass vial equipped with a magnetic stirring bar, to the 1:1 mixture of **3a**/**3d** (each 5 mol%) in DCM (1.0 mL), were added **1a-c** (0.4

mmol, 1.33 equiv.) and 2-(2-nitrovinyl)phenols **2a-i** (0.3 mmol). After stirring the reaction mixture at 25 °C as shown in Tables S1, the crude reaction mixture was quickly filtered through silica gel, concentrated and taken into a oven dried round bottom flask equipped with a magnetic stirring bar, to this add dry DCE (4.0 mL) and *p*-TSA (0.03 mmol, 10 mol%). After stirring the reaction mixture at 80 °C for 3-4 h, the crude reaction mixture was worked up with aqueous $NaHCO_3$ solution and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were dried ($Na_2SO_4$), filtered and concentrated. Pure racemic products **6** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

**Procedure D:** ***General procedure for quinine-NH-thiourea-/p-TSA-catalyzed asymmetric sequential Michael-lactonization reaction of keto-esters 1 with 2-(2-nitrovinyl)phenols 2:*** In an ordinary glass vial equipped with a magnetic stirring bar, to the **3f** or **3h** (10 mol%) in DCM (1.0 mL), were added **1a-c** (0.4 mmol, 1.33 equiv.) and of 2-(2-nitrovinyl)phenols **2a-i** (0.3 mmol). After stirring the reaction mixture at 25 °C as shown in Tables 1-2, the crude reaction mixture was filtered through silica gel, concentrated and taken into a oven dried round bottom flask equipped with a magnetic stirring bar, to this add dry DCE (4.0 mL) and *p*-TSA (0.03 mmol, 10 mol%). After stirring the reaction mixture at 80 °C for 4 h, the crude reaction mixture was worked up with aqueous $NaHCO_3$ solution and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were dried ($Na_2SO_4$), filtered and concentrated. Pure chiral products **6** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

**Procedure E:** ***General procedure for quinine-NH-thiourea-/PCC-mediated asymmetric sequential Michael-oxidation reaction of keto-ester 1d with 2-(2-nitrovinyl)phenols 2:*** In an ordinary glass vial equipped with a magnetic stirring bar, to the **3f** or **3h** (10 mol%) in DCM (1.0 mL), were added **1d** (0.4 mmol, 1.33 equiv.) and 2-(2-nitrovinyl)phenols **2a** or **2d** (0.3 mmol). After stirring the reaction mixture at 25 °C as shown in Table 2, the crude reaction mixture was filtered through silica gel, concentrated and taken into a oven dried round bottom flask equipped with a magnetic stirring bar, to this added dry DCM (3.0 mL), silica gel (3 equiv.) and PCC (0.9 mmol, 3 equiv.). After stirring the reaction mixture at room temperature for 24 h, the crude reaction mixture was passed through a pad of celite and concentrated to dryness. Pure chiral products **6da** or **6dd** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

**Procedure F:** ***Lewis acid-induced hydrolysis of cascade Michael products 4/5:*** In an oven dried round bottomed flask, to the compound **4aa/5aa** (90 mg, 0.3 mmol), added dry DCM (0.1 M) under $N_2$ through syringe and $BF_3.Et_2O$ (1.1 equiv.) at 0 °C. This reaction mixture was stirred for 1.5 h at same temperature, brought the reaction to room temperature and worked up with $H_2O$ and the aqueous layer was extracted

with DCM (3 x 10 mL). The combined organic layers were dried ($Na_2SO_4$), filtered and concentrated. Pure product 7**aa** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

**Procedure G:** ***Protection of Michael products 4/5:*** In a dry oven dried round bottom flask, to the compound **4aa/5aa** (0.3 mmol) in dry DCM (3.0 mL) were added successively dry triethylamine (70 µL, 0.6 mmol) and acetyl chloride (0.6 mmol) at 0 °C. The resulting mixture was stirred at 25 °C for 12 h and then worked up with aqueous $NH_4Cl$ and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were dried ($Na_2SO_4$), filtered and concentrated. Pure acetyl protected product **8aa** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

**Procedure H:** ***Hydrogenation of protected Michael products 8:*** The product **8aa** was taken in an oven dried round bottom flask which contains activated 10% Pd/C (7 mg, 10 mol-%), and dry EtOAc (3.0 mL) were added and stirred under $H_2$ atmosphere at 25 °C for 24 h. The reaction mixture was passed through a pad of celite and concentrated to dryness. Pure product (+)-**9aa** was obtained by quick column chromatography (silica gel, mixture of hexane/ethyl acetate).

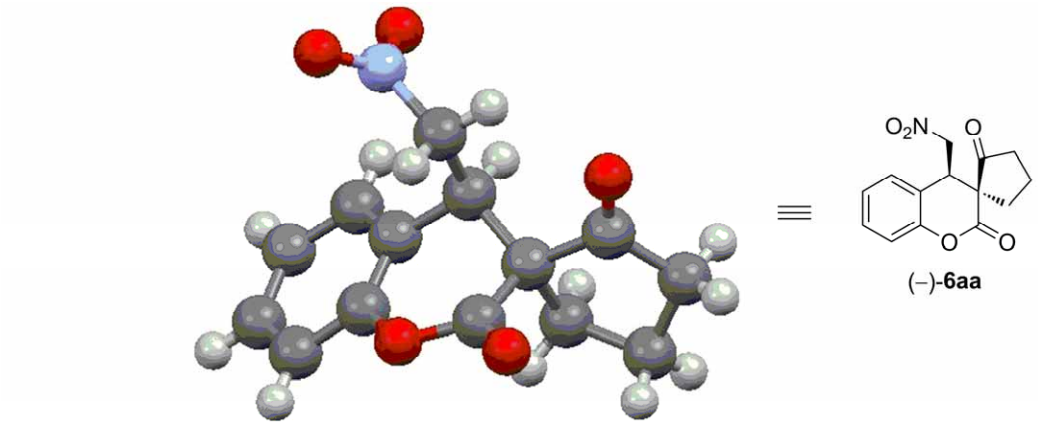
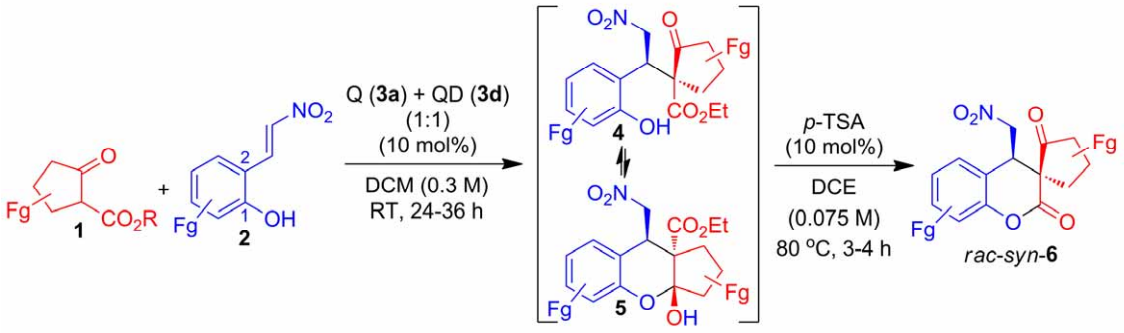
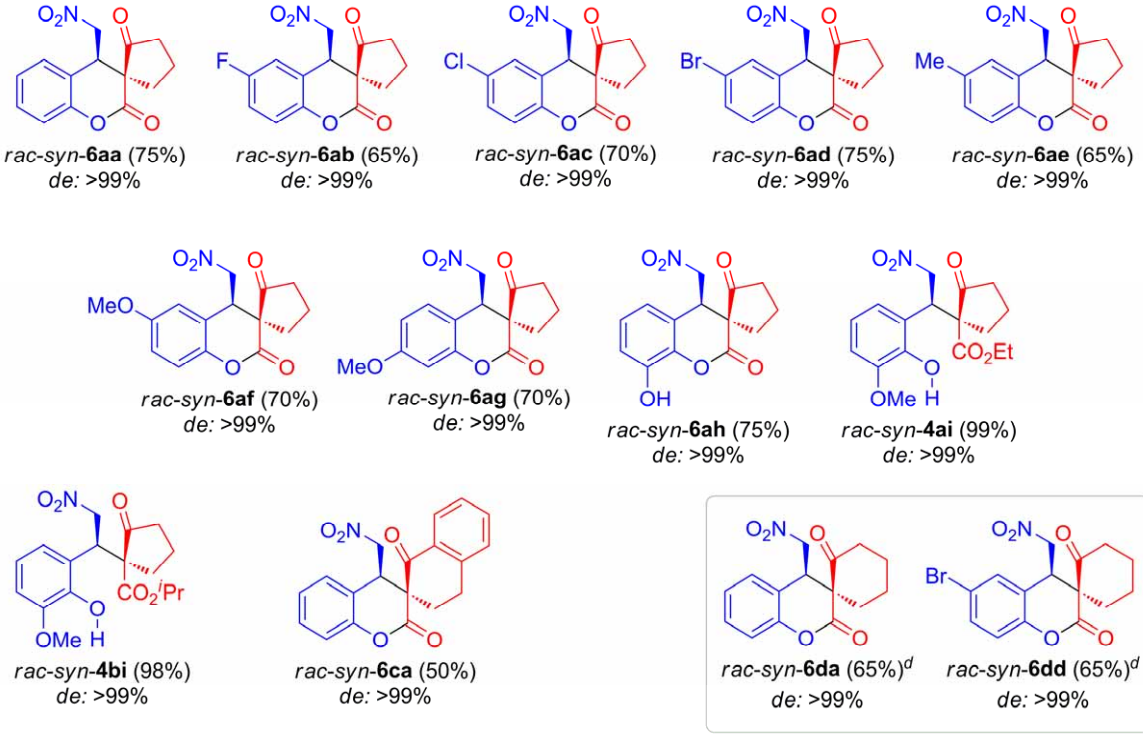


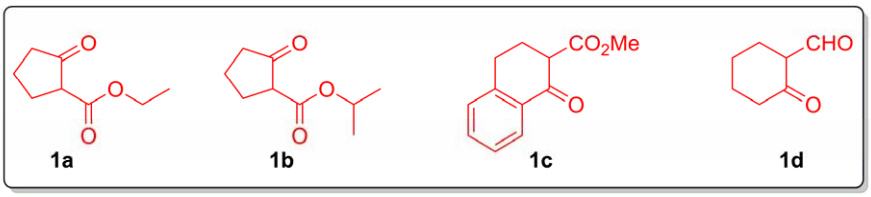

***Figure S1.*** X-Ray crystal structure of chiral (1'*S*,4*R*)-4-(nitromethyl)spiro[chroman-3,1'-cyclopentane]-2,2'-dione (**6aa**).

***Table S1:*** Synthesis of racemic *spirodihydrocoumarin* products **6**[a-c]

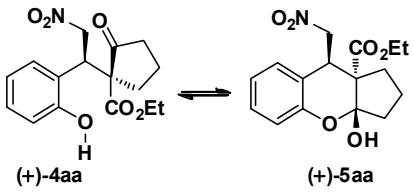


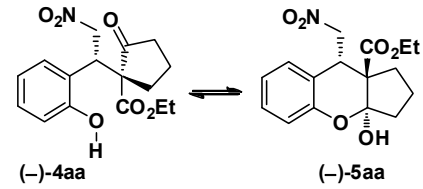

[a] Reactions were carried out in DCM (0.3 M) with 1.3 equiv. of **1a** relative to the **2a-i** (0.3 mmol) in the presence of 10-mol% of catalyst **3a** + **3d** [1:1]. After one quick filtration, resulting products **4/5** were treated with 10 mol% of *p*-TSA in DCE (0.075 M) for 3-4 h at 80 °C. [b] Yield refers to the column purified product. [c] Ratio or *de* is based on HPLC analysis. [d] 2-oxocyclohexanecarbaldehyde **1d** used as substrate and PCC mediated oxidation utilized for the cyclization reaction.



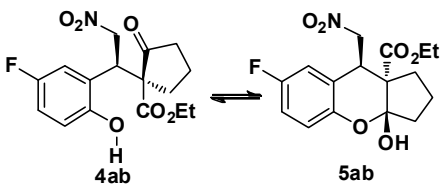
**(*S*)-ethyl 1-[(*R*)-1-(2-hydroxyphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate [(+)-4aa] and (3a*S*,9*R*,9a*S*)-ethyl 3a-hydroxy-9-(nitromethyl)-1,2,3,3a,9,9a-hexahydrocyclopenta[b]chromene-9a-carboxylate [(+)-5aa]:** Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid. **$[\alpha]_D^{25}$ = +20.3° (*c* = 0.42 g/100 mL, $CHCl_3$, >99.9% *ee*)**. IR (Neat): $\nu_{max}$ 3449 (O-*H*), 2980, 2257, 1730 (C=O), 1726 (C=O), 1555 (*$NO_2$*), 1379 (*$NO_2$*), 1231, 1015, 860, 733 and 648 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 1:1 ratio of **4aa** and **5aa**) δ 7.24-7.20 (2H, m), 7.15-7.09 (2H, m), 7.00 (1H, t, *J* = 7.6 Hz), 6.93 (1H, d, *J* = 8.0 Hz), 6.88 (1H, t, *J* = 7.6 Hz), 6.81 (1H, d, *J* = 8.0 Hz), 6.61 (1H, br s, OH, phenolic-OH), 5.22 (1H, dd, *J* = 13.6, 4.0 Hz), 5.11 (1H, dd, *J* = 13.6, 10.0 Hz), 4.76 (1H, dd, *J* = 13.6, 6.4 Hz), 4.57 (1H, dd, *J* = 12.8, 5.6 Hz), 4.56 (1H, br s, *tert*-OH), 4.46-4.40 (2H, m), 4.31-4.17 (4H, m, 2 x $OCH_2CH_3$), 2.44-2.38 (2H, m), 2.29-2.22 (2H, m), 2.12-1.88 (6H, m), 1.82-1.71 (1H, m), 1.59-1.51 (1H, m), 1.33 (3H, t, *J* = 7.2 Hz, $OCH_2CH_3$), 1.27 (3H, t, *J* = 7.2 Hz, $OCH_2CH_3$); $^{13}C$ NMR ($CDCl_3$, DEPT-135, 1:1 ratio of **4aa** and **5aa**) δ 214.4 (C, C=O), 174.0 (C, O-C=O), 169.6 (C, O-C=O), 154.4 (C), 150.7 (C), 130.1 (CH), 129.4 (CH), 129.0 (CH), 126.3 (CH), 122.6 (C), 122.5 (CH), 121.1 (CH), 120.1 (C), 118.4 (CH), 117.3 (CH), 106.3 (C, O-*C*-OH), 77.4 ($CH_2$), 76.2 ($CH_2$), 63.1 (C), 62.6 ($CH_2$), 62.4 ($CH_2$), 56.4 (C), 39.8 (CH), 37.8 ($CH_2$), 36.7 ($CH_2$), 36.4 (CH), 31.7 ($CH_2$), 27.6 ($CH_2$), 19.3 ($CH_2$), 19.1 ($CH_2$), 13.9 ($CH_3$), 13.8 ($CH_3$); LRMS m/z 322.15 ($M + H^+$), calcd for $C_{16}H_{19}NO_6$ 321.1212; Anal. calcd for $C_{16}H_{19}NO_6$ (321.1212): C, 59.81; H, 5.96; N, 4.36. Found: C, 59.75; H, 5.89; N, 4.41%.




**(*R*)-ethyl 1-[(*S*)-1-(2-hydroxyphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate [(−)-4aa] and (3a*R*,9*S*,9a*R*)-ethyl 3a-hydroxy-9-(nitromethyl)-1,2,3,3a,9,9a-hexahydrocyclopenta[b]chromene-9a-carboxylate [(−)-5aa]:** Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid. **$[\alpha]_D^{25}$ = −19.2° (*c* = 0.42 g/100 mL, $CHCl_3$, 98% *ee*);** IR (Neat): $\nu_{max}$ 3435 (O-*H*), 2966, 1720 (C=O), 1552 (*$NO_2$*), 1455, 1375 (*$NO_2$*), 1226, 1051, 1014 and 755 $cm^{-1}$.

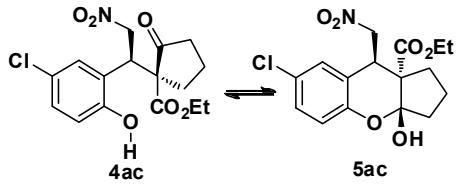



**(*S*)-ethyl 1-[(*R*)-1-(5-fluoro-2-hydroxyphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate (4ab) and (3a*S*,9*R*,9a*S*)-ethyl 7-fluoro-3a-hydroxy-9-(nitromethyl)-1,2,3,3a,9,9a-hexahydrocyclopenta[b]chromene-9a-carboxylate (5ab):** Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid; **$[\alpha]_D^{25}$ = −3.0° (*c* = 0.70 g/100 mL, $CHCl_3$);** IR (Neat): $\nu_{max}$ 3430 (O-*H*), 2982, 1725 (C=O), 1718 (C=O), 1557 (*$NO_2$*), 1377 (*$NO_2$*), 1233, 1169, 1016



and 820 $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$, 1:1 ratio of **4ab** and **5ab**) δ 7.05-6.98 (1H, m), 6.96-6.88 (2H, m), 6.87-6.82 (2H, m), 6.80-6.76 (1H, m), 6.46 (1H, br s, Ph-O*H*), 5.20 (1H, dd, *J* = 13.8, 3.9 Hz), 5.06 (1H, dd, *J* = 13.7, 10.3 Hz), 4.71 (1H, dd, *J* = 14.0, 6.7 Hz), 4.58 (1H, dd, *J* = 14.0, 5.2 Hz), 4.50 (1H, br s, *tert-OH*), 4.41 (2H, br t, *J* = 6.2 Hz), 4.29 (2H, q, *J* = 6.8 Hz, $OCH_2CH_3$), 4.22 (2H, q, *J* = 6.8 Hz, $OCH_2CH_3$), 2.51-2.36 (2H, m), 2.33-2.23 (2H, m), 2.16-2.08 (1H, m), 2.06-1.98 (2H, m), 1.97-1.84 (2H, m), 1.82-1.71 (1H, m), 1.56-1.48 (1H, m), 1.33 (3H, t, *J* = 7.1 Hz, $OCH_2CH_3$), 1.28 (3H, t, *J* = 7.1 Hz, $OCH_2CH_3$), 0.91-0.83 (1H, m); $^{13}C$ NMR ($CDCl_3$, DEPT-135, 1:1 ratio of **4ab** and **5ab**) δ 214.3 (C, C=O), 173.8 (C, O-C=O), 169.5 (C, O-C=O), 157.9 (C, d, *J* = 239.7 Hz, *C*-F), 156.9 (C, d, *J* = 238.0 Hz, *C*-F), 150.4 (C, d, *J* = 2.2 Hz), 146.7 (C, d, *J* = 2.2 Hz), 124.3 (C, d, *J* = 7.1 Hz), 121.7 (C, d, *J* = 7.2 Hz), 119.6 (CH, d, *J* = 8.2 Hz), 118.4 (CH, d, *J* = 8.1 Hz), 116.0 (CH, d, *J* = 18.1 Hz), 115.8 (CH, d, *J* = 18.2 Hz), 113.0 (CH), 112.8 (CH), 106.7 (C, O-*C*-O), 77.0 ($CH_2$), 76.0 ($CH_2$), 62.9 (C), 62.7 ($CH_2$, $OCH_2CH_3$), 62.5 ($CH_2$, $OCH_2CH_3$), 56.3 (C), 39.2 (CH), 37.7 ($CH_2$), 36.7 (CH), 36.7 ($CH_2$), 31.7 ($CH_2$), 27.7 ($CH_2$), 19.3 ($CH_2$), 19.1 ($CH_2$), 13.8 ($CH_3$), 13.8 ($CH_3$); HRMS m/z 362.1016 (M + Na), calcd for $C_{16}H_{18}FNO_6Na$ 362.1016; Anal. calcd for $C_{16}H_{18}FNO_6$ (339.1118): C, 56.63; H, 5.35; N, 4.13. Found: C, 56.71; H, 5.31; N, 4.19%.

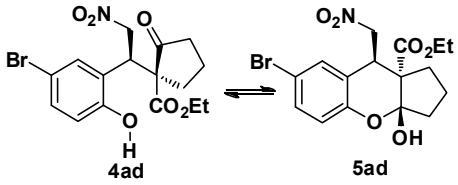
**(*S*)-ethyl 1-[(*R*)-1-(5-chloro-2-hydroxyphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate (4ac) and (3a*S*,9*R*,9a*S*)-ethyl 7-chloro-3a-hydroxy-9-(nitromethyl)-1,2,3,3a,9,9a-hexahydrocyclopenta[b]chromene-9a-carboxylate (5ac):**




Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid; **$[\alpha]_D^{25}$ = –5.90° (*c* = 1.00 g/100 mL, $CHCl_3$);** IR (Neat): $\nu_{max}$ 3428 (O-*H*), 2982, 1742 (C=O), 1724 (C=O), 1554 ($NO_2$), 1379 ($NO_2$), 1231, 1169, 1018 and 820 $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$, 1:1 ratio of **4ac** and **5ac**) δ 7.24 (1H, d, *J* = 2.0 Hz), 7.19 (1H, dd, *J* = 8.4, 1.6 Hz), 7.11-7.08 (2H, m), 6.87 (1H, d, *J* = 8.8 Hz), 6.76 (1H, d, *J* = 8.8 Hz), 6.80-6.70 (1H, br s, Ph-O*H*), 5.22 (1H, dd, *J* = 13.6, 4.0 Hz), 5.06 (1H, dd, *J* = 13.6, 10.4 Hz), 4.72 (1H, dd, *J* = 14.0, 6.4 Hz), 4.58 (1H, dd, *J* = 14.0, 5.6 Hz), 4.53 (1H, br s, *tert-OH*), 4.40 (1H, t, *J* = 6.0 Hz), 4.38-4.30 (1H, m), 4.30-4.18 (4H, m, 2 x $OCH_2CH_3$), 2.50-2.38 (2H, m), 2.35-2.23 (2H, m), 2.19-2.10 (1H, m), 2.06-1.98 (3H, m), 1.95-1.85 (2H, m), 1.82-1.71 (1H, m), 1.55-1.47 (1H, m), 1.33 (3H, t, *J* = 7.2 Hz, $OCH_2CH_3$), 1.28 (3H, t, *J* = 7.2 Hz, $OCH_2CH_3$); $^{13}C$ NMR ($CDCl_3$, DEPT-135, 1:1 ratio of **4ac** and **5ac**) δ 214.2 (C, C=O), 173.7 (C, O-C=O), 169.5 (C, O-C=O), 153.1 (C), 149.3 (C), 129.7 (CH), 129.4 (CH), 129.1 (CH), 127.3 (C), 126.3 (CH), 125.8 (C), 124.6 (C), 121.7 (C), 119.7 (CH), 118.5 (CH), 106.5 (C, O-*C*-O), 77.0 ($CH_2$), 75.9 ($CH_2$), 62.8 (C), 62.7 ($CH_2$), 62.5 ($CH_2$), 56.0 (C), 37.6 ($CH_2$), 36.5 ($CH_2$), 36.3 (2 x CH), 31.9 ($CH_2$), 27.5 ($CH_2$), 19.2 ($CH_2$), 18.9 ($CH_2$), 13.9 ($CH_3$), 13.8 ($CH_3$); HRMS m/z

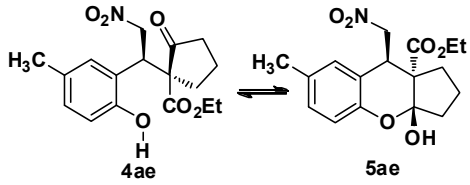
378.0721 (M + Na), calcd for $C_{16}H_{18}ClNO_6Na$ 378.0720; Anal. calcd for $C_{16}H_{18}ClNO_6$ (355.0823): C, 54.02; H, 5.10; N, 3.94. Found: C, 54.12; H, 5.16; N, 3.89%.

**(*S*)-ethyl 1-[(*R*)-1-(5-bromo-2-hydroxyphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate (4ad) and (3a*S*,9*R*,9a*S*)-ethyl 7-bromo-3a-hydroxy-9-(nitromethyl)-1,2,3,3a,9,9a-hexahydrocyclopenta[b]chromene-9a-carboxylate (5ad):**




Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid; **$[\alpha]_D^{25}$ = –1.82° (*c* = 0.71 g/100 mL, $CHCl_3$);** IR (Neat): $\nu_{max}$ 3447 (O-*H*), 2959, 1742 (C=O), 1721 (C=O), 1614, 1557 (*$NO_2$*), 1379 (*$NO_2$*), 1233, 1122, 1092, 937, 858 and 733 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 1:1 ratio of **4ad** and **5ad**) δ 7.37-7.31 (2H, m), 7.26-7.23 (2H, m), 6.82 (1H, d, *J* = 8.4 Hz), 6.73 (1H, d, *J* = 8.8 Hz), 5.21 (1H, dd, *J* = 14.0, 4.0 Hz), 5.05 (1H, dd, *J* = 14.0, 10.4 Hz), 4.73 (1H, dd, *J* = 14.0, 6.4 Hz), 4.58 (1H, dd, *J* = 14.4, 5.6 Hz), 4.41 (1H, br t, *J* = 5.6 Hz), 4.40-4.30 (1H, m), 4.27 (2H, q, *J* = 7.2 Hz, $OCH_2CH_3$), 4.22 (2H, q, *J* = 7.2 Hz, $OCH_2CH_3$), 2.48-2.39 (2H, m), 2.35-2.25 (2H, m), 2.20-2.11 (1H, m), 2.07-1.98 (3H, m), 1.94-1.89 (2H, m), 1.80-1.77 (1H, m), 1.56-1.49 (1H, m), 1.34 (3H, t, *J* = 7.2 Hz, $OCH_2CH_3$), 1.29 (3H, t, *J* = 7.2 Hz, $OCH_2CH_3$); $^{13}C$ NMR ($CDCl_3$, DEPT-135, 1:1 ratio of **4ad** and **5ad**) δ 214.2 (C, C=O), 173.7 (C, O-C=O), 169.5 (C, O-C=O), 153.6 (C), 149.9 (C), 132.6 (CH), 132.3 (CH), 132.0 (CH), 129.2 (CH), 125.1 (C), 122.2 (C), 120.2 (CH), 119.1 (CH), 114.6 (C), 113.1 (C), 106.4 (C, O-*C*-O), 77.0 ($CH_2$), 75.9 ($CH_2$), 62.9 ($CH_2$), 62.8 ($CH_2$), 62.6 (C), 55.9 (C), 37.6 ($CH_2$), 36.5 ($CH_2$), 36.2 (2 x CH), 31.9 ($CH_2$), 27.5 ($CH_2$), 19.2 ($CH_2$), 18.9 ($CH_2$), 13.9 ($CH_3$), 13.8 ($CH_3$); HRMS m/z 422.0215 (M + Na), calcd for $C_{16}H_{18}BrNO_6Na$ 422.0215; Anal. calcd for $C_{16}H_{18}BrNO_6$ (399.0317): C, 48.02; H, 4.53; N, 3.50. Found: C, 48.12; H, 4.49; N, 3.56%.

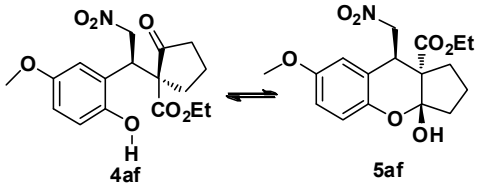
**(*S*)-ethyl 1-[(*R*)-1-(2-hydroxy-5-methylphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate (4ae) and (3a*S*,9*R*,9a*S*)-ethyl 3a-hydroxy-7-methyl-9-(nitromethyl)-1,2,3,3a,9,9a-hexahydrocyclopenta[b]chromene-9a-carboxylate (5ae):**




Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid; **$[\alpha]_D^{25}$ = –1.82° (*c* = 0.71 g/100 mL, $CHCl_3$);** IR (Neat): $\nu_{max}$ 3434 (O-*H*), 2924, 1742 (C=O), 1724 (C=O), 1555 (*$NO_2$*), 1377 (*$NO_2$*), 1232, 1119, 1018 and 818 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 1:1 ratio of **4ae** and **5ae**) δ 7.03 (1H, br d, *J* = 8.0 Hz), 6.98 (1H, br s), 6.94 (1H, br d, *J* = 8.0 Hz), 6.90 (1H, br s), 6.84 (1H, d, *J* = 8.4 Hz), 6.72 (1H, d, *J* = 8.0 Hz), 6.25 (1H, br s, Ph-*OH*), 5.19 (1H, dd, *J* = 13.6, 4.4 Hz), 5.09 (1H, dd, *J* = 13.2, 10.0 Hz), 4.77 (1H, dd, *J* = 14.0, 6.8 Hz), 4.56 (1H, dd, *J* = 14.0, 5.6 Hz), 4.47 (1H, br s, *tert*-O*H*), 4.40 (2H, t,

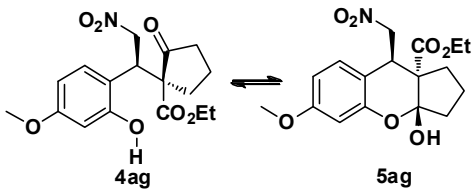
*J* = 6.0 Hz), 4.34-4.25 (2H, m, OC*H*$_2$CH$_3$), 4.21 (2H, q, *J* = 6.8 Hz, OC*H*$_2$CH$_3$), 2.47-2.39 (2H, m), 2.33-2.22 (1H, m), 2.29 (3H, s, ArC*H*$_3$), 2.24 (3H, s, ArC*H*$_3$), 2.13-2.09 (2H, m), 2.01-1.94 (3H, m), 1.93-1.76 (3H, m), 1.59-1.52 (1H, m), 1.34 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.28 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); $^{13}$C NMR (CDCl$_3$, DEPT-135, 1:1 ratio of **4ae** and **5ae**) δ 214.3 (C, C=O), 174.0 (C, O-C=O), 169.5 (C, O-C=O), 152.0 (C), 148.4 (C), 131.9 (C), 130.3 (C), 130.0 (CH), 129.6 (CH), 126.6 (2 x CH), 122.3 (C), 119.7 (C), 118.2 (CH), 117.3 (CH), 106.2 (C, O-*C*-O), 77.3 (CH$_2$), 76.1 (CH$_2$), 63.1 (C), 62.5 (CH$_2$), 62.3 (CH$_2$), 56.4 (C), 37.7 (CH$_2$), 36.7 (CH$_2$), 36.5 (2 x CH), 31.5 (CH$_2$), 27.6 (CH$_2$), 20.7 (CH$_3$, ArC*H*$_3$), 20.6 (CH$_3$, ArC*H*$_3$), 19.2 (CH$_2$), 19.0 (CH$_2$), 13.9 (CH$_3$, OCH$_2$C*H*$_3$), 13.8 (CH$_3$, OCH$_2$C*H*$_3$); HRMS m/z 358.1267 (M + Na), calcd for $C_{17}H_{21}NO_6Na$ 358.1267; Anal. calcd for $C_{17}H_{21}NO_6$ (335.1369): C, 60.89; H, 6.31; N, 4.18. Found: C, 60.75; H, 6.38; N, 4.12%.

**(*S*)-ethyl 1-[(*R*)-1-(2-hydroxy-5-methoxyphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate (4af) and (3a*S*,9*R*,9a*S*)-ethyl 3a-hydroxy-7-methoxy-9-(nitromethyl)-1,2,3,3a,9,9a-hexahydrocyclopenta[b]chromene-9a-carboxylate (5af):**



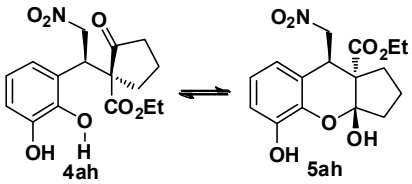

Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid; **$[\alpha]_D^{25}$ = –15.47° (*c* = 0.28 g/100 mL, CHCl$_3$);** IR (Neat): $\nu_{max}$ 3434 (O-*H*), 2961, 2484, 1742 (C=O), 1723 (C=O), 1557 (*NO*$_2$), 1377 (*NO*$_2$), 1231, 1180, 1020 and 818 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 1:1 ratio of **4af** and **5af**) δ 6.90 (1H, d, *J* = 8.8 Hz), 6.84-6.78 (3H, m), 6.73 (1H, dd, *J* = 8.8, 2.8 Hz), 6.66 (1H, d, *J* = 2.4 Hz), 5.75 (1H, br s, Ph-*OH*), 5.13 (1H, dd, *J* = 13.6, 4.4 Hz), 5.05 (1H, dd, *J* = 13.6, 10.0 Hz), 4.75 (1H, dd, *J* = 14.0, 6.8 Hz), 4.57 (1H, dd, *J* = 13.6, 5.6 Hz), 4.49-4.44 (1H, m, *tert*-OH), 4.39 (1H, t, *J* = 6.4 Hz), 4.35-4.32 (1H, m), 4.31-4.26 (2H, m, OC*H*$_2$CH$_3$), 4.25-4.19 (2H, m, OC*H*$_2$CH$_3$), 3.77 (3H, s, OC*H*$_3$), 3.75 (3H, s, OC*H*$_3$), 2.48-2.40 (2H, m), 2.31-2.18 (2H, m), 2.15-2.06 (2H, m), 2.05-1.93 (3H, m), 1.92-1.83 (1H, m), 1.81-1.71 (1H, m), 1.59-1.51 (1H, m), 1.35 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.29 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); $^{13}$C NMR (CDCl$_3$, DEPT-135, 1:1 ratio of **4af** and **5af**) δ 214.4 (C, C=O), 174.0 (C, O-C=O), 169.5 (C, O-C=O), 155.1 (C), 154.0 (C), 148.0 (C), 144.6 (C), 124.0 (C), 121.4 (C), 119.3 (CH), 118.9 (CH), 115.3 (CH), 114.5 (CH), 114.4 (CH), 111.6 (CH), 106.7 (C, O-*C*-O), 77.2 (CH$_2$), 76.1 (CH$_2$), 63.3 (C), 62.6 (CH$_2$), 62.5 (CH$_2$), 56.8 (C), 55.74 (CH$_3$, O*CH*$_3$), 55.70 (CH$_3$, O*CH*$_3$), 37.7 (CH$_2$), 37.3 (2 x CH), 36.8 (CH$_2$), 31.3 (CH$_2$), 28.0 (CH$_2$), 19.4 (CH$_2$), 19.3 (CH$_2$), 13.9 (CH$_3$), 13.9 (CH$_3$); HRMS m/z 374.1216 (M + Na), calcd for $C_{17}H_{21}NO_7Na$ 374.1216; Anal. calcd for $C_{17}H_{21}NO_7$ (351.1318): C, 58.11; H, 6.02; N, 3.99. Found: C, 58.25; H, 6.08; N, 3.91%.

**(*S*)-ethyl 1-[(*R*)-1-(2-hydroxy-4-methoxyphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate (4ag) and (3a*S*,9*R*,9a*S*)-ethyl 3a-hydroxy-6-methoxy-9-(nitromethyl)-1,2,3,3a,9,9a-hexahydrocyclopenta[b]chromene-9a-carboxylate (5ag):**




Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid; **$[\alpha]_D^{25}$ = –4.21° (*c* = 0.43 g/100 mL, $CHCl_3$);** IR (Neat): $\nu_{max}$ 3428 (O-*H*), 2965, 2224, 1739 (C=O), 1723 (C=O), 1618, 1555 ($NO_2$), 1379 ($NO_2$), 1231, 1167, 1033, 839 and 733 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 1:1 ratio of **4ag** and **5ag**) δ 7.11 (1H, d, *J* = 8.8 Hz), 7.00 (1H, dd, *J* = 8.4, 0.8 Hz), 6.59 (1H, dd, *J* = 8.8, 2.8 Hz), 6.50 (1H, d, *J* = 2.8 Hz), 6.46 (1H, dd, *J* = 8.8, 2.4 Hz), 6.40 (1H, d, *J* = 2.8 Hz), 5.10 (1H, dd, *J* = 13.6, 4.8 Hz), 5.04 (1H, dd, *J* = 13.2, 10.0 Hz), 4.72 (1H, dd, *J* = 14.0, 6.4 Hz), 4.55 (1H, dd, *J* = 14.0, 5.6 Hz), 4.39-4.32 (2H, m), 4.31-4.26 (2H, m, $OCH_2CH_3$), 4.21 (2H, qd, *J* = 7.2, 1.2 Hz, $OCH_2CH_3$), 3.78 (3H, s, $OCH_3$), 3.74 (3H, s, $OCH_3$), 2.47-2.39 (2H, m), 2.31-2.25 (1H, m), 2.21-2.11 (2H, m), 2.08-1.96 (3H, m), 1.92-1.73 (3H, m), 1.62-1.54 (1H, m), 1.34 (3H, t, *J* = 7.2 Hz, $OCH_2CH_3$), 1.28 (3H, t, *J* = 7.2 Hz, $OCH_2CH_3$); $^{13}C$ NMR ($CDCl_3$, DEPT-135, 1:1 ratio of **4ag** and **5ag**) δ 214.7 (C, C=O), 174.2 (C, O-C=O), 169.7 (C, O-C=O), 160.4 (C), 160.1 (C), 155.4 (C), 151.6 (C), 133.8 (CH), 127.1 (CH), 114.5 (C), 111.5 (C), 109.4 (CH), 107.1 (CH), 106.1 (C, O-*C*-O), 103.2 (CH), 103.1 (CH), 77.5 ($CH_2$), 76.2 ($CH_2$), 63.4 (C), 62.6 ($CH_2$), 62.4 ($CH_2$), 55.9 (C), 55.3 ($CH_3$, $OCH_3$), 55.2 ($CH_3$, $OCH_3$), 37.7 ($CH_2$), 36.6 ($CH_2$), 36.0 (2 x CH), 31.4 ($CH_2$), 27.2 ($CH_2$), 19.3 ($CH_2$), 18.7 ($CH_2$), 13.9 ($CH_3$), 13.8 ($CH_3$); HRMS m/z 374.1216 (M + Na), calcd for $C_{17}H_{21}NO_7Na$ 374.1216; Anal. calcd for $C_{17}H_{21}NO_7$ (351.1318): C, 58.11; H, 6.02; N, 3.99. Found: C, 58.23; H, 6.08; N, 4.05%.

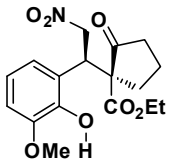
**(*S*)-ethyl 1-[(*R*)-1-(2,3-dihydroxyphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate (4ah) and (3a*S*,9*R*,9a*S*)-ethyl 3a,5-dihydroxy-9-(nitromethyl)-1,2,3,3a,9,9a-hexahydrocyclopenta[b]chromene-9a-carboxylate (5ah):**




Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid; **$[\alpha]_D^{25}$ = –15.47° (*c* = 0.28 g/100 mL, $CHCl_3$);** IR (Neat): $\nu_{max}$ 3447 (O-*H*), 2982, 2564, 1740 (C=O), 1721 (C=O), 1620, 1595 ($NO_2$), 1551, 1379 ($NO_2$), 1231, 1165, 914, 831 and 737 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 3:1 ratio of **4ah** and **5ah**) δ 6.95-6.85 (2H, m), 6.84-6.77 (2H, m), 6.71-6.63 (2H, m), 5.04 (1H, dd, *J* = 14.0, 5.2 Hz), 4.99 (1H, dd, *J* = 14.0, 10.0 Hz), 4.77 (1H, dd, *J* = 14.0, 6.8 Hz), 4.58-4.51 (2H, m), 4.43 (1H, t, *J* = 6.4 Hz), 4.37-4.27 (2H, m, $OCH_2CH_3$), 4.22 (2H, q, *J* = 7.6 Hz, $OCH_2CH_3$), 2.48-2.44 (3H, m), 2.32-2.27 (1H, m), 2.21-2.05 (3H, m), 2.02-1.91 (3H, m), 1.86-1.69 (1H, m), 1.60-1.51 (1H, m), 1.34 (3H, t, *J* = 7.2 Hz, $OCH_2CH_3$), 1.28 (3H, t, *J* = 7.2 Hz, $OCH_2CH_3$); $^{13}C$ NMR

($CDCl_3$, DEPT-135, 3:1 ratio of **4ah** and **5ah**) δ 215.7 (C, C=O), 173.8 (C, O-C=O), 169.5 (C, O-C=O), 146.0 (C), 145.7 (C), 142.1 (C), 137.8 (C), 123.1 (C), 122.8 (CH), 121.4 (CH), 120.8 (C), 117.1 (CH), 114.9 (2 x CH), 114.5 (CH), 107.3 (C, O-*C*-O), 77.0 ($CH_2$), 75.7 ($CH_2$), 63.8 (C), 62.7 (2 x $CH_2$), 56.9 (C), 39.2 (CH), 37.7 ($CH_2$), 36.8 ($CH_2$), 36.8 (CH), 30.8 ($CH_2$), 27.8 ($CH_2$), 19.4 ($CH_2$), 19.2 ($CH_2$), 13.8 ($CH_3$, $OCH_2\mathit{CH_3}$), 13.8 ($CH_3$, $OCH_2\mathit{CH_3}$); HRMS m/z 360.1109 (M + Na), calcd for $C_{16}H_{19}NO_7Na$ 360.1059; Anal. calcd for $C_{16}H_{19}NO_7$ (337.1162): C, 56.97; H, 5.68; N, 4.15. Found: C, 56.85; H, 5.62; N, 4.19%.

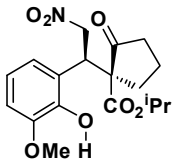
**(*S*)-ethyl 1-[(*R*)-1-(2-hydroxy-3-methoxyphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate (4ai):**



(+)-4ai

Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 80:20, flow rate 0.5 mL/min, λ = 254 nm), $t_R$ = 18.89 min (minor), $t_R$ = 20.45 min (major). **$[\alpha]_D^{25}$ = +4.8° (*c* = 0.42 g/100 mL, $CHCl_3$, 98% *ee*);** IR (Neat): $\nu_{max}$ 3450 (O-*H*), 2961, 1740 (C=O), 1725, 1555 ($\mathit{NO_2}$), 1379 ($\mathit{NO_2}$), 1283, 1081, and 1022 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 6.90-6.88 (1H, m), 6.82-6.76 (2H, m), 5.94 (1H, br s, OH), 5.35 (1H, dd, *J* = 13.6, 3.6 Hz), 5.22 (1H, dd, *J* = 13.6, 10.4 Hz), 4.36 (1H, dd, *J* = 10.8, 4.0 Hz), 4.20 (2H, q, *J* = 7.2 Hz, $OC\mathit{H_2}CH_3$), 3.87 (3H, s, $OC\mathit{H_3}$), 2.40-2.32 (3H, m), 2.08-2.01 (2H, m), 1.95-1.89 (1H, m), 1.28 (3H, t, *J* = 7.2 Hz, $OCH_2C\mathit{H_3}$); $^{13}C$ NMR ($CDCl_3$, DEPT-135) δ 213.0 (C, C=O), 169.3 (C, O-C=O), 146.4 (C), 144.3 (C), 121.8 (CH), 121.7 (C), 120.0 (CH), 110.0 (CH), 76.2 ($CH_2$), 62.5 (C), 61.9 ($CH_2$, $OCH_2CH_3$), 55.9 ($CH_3$, $OCH_3$), 39.7 (CH), 37.9 ($CH_2$), 32.2 ($CH_2$), 19.2 ($CH_2$), 14.0 ($CH_3$, $OCH_2\mathit{CH_3}$); LRMS m/z 352.10 ($M + H^+$), calcd for $C_{17}H_{21}NO_7$ 351.1318; Anal. calcd for $C_{17}H_{21}NO_7$ (351.1318): C, 58.11; H, 6.02; N, 3.99. Found: C, 58.23; H, 5.96; N, 4.07%.

**(*S*)-isopropyl 1-[(*R*)-1-(2-hydroxy-3-methoxyphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate (4bi):** Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane

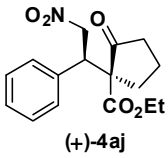


(+)-4bi

and isolated as liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), $t_R$ = 23.07 min (minor), $t_R$ = 26.96 min (major). **$[\alpha]_D^{25}$ = +5.6° (*c* = 0.143 g/100 mL, $CHCl_3$, 99% *ee*);** IR (Neat): $\nu_{max}$ 3468 (O-*H*), 2926, 1742 (C=O), 1723, 1615, 1555 ($\mathit{NO_2}$), 1377 ($\mathit{NO_2}$), 1254, 1101, and 1026 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 6.92-6.88 (1H, m), 6.79-6.76 (2H, m), 5.99 (1H, br s, OH), 5.34 (1H, dd, *J* = 13.6, 3.6 Hz), 5.20 (1H, dd, *J* = 13.6, 10.8 Hz), 5.07-5.01 (1H, m, $OC\mathit{H}(CH_3)_2$), 4.36 (1H, dd, *J* = 10.8, 4.0 Hz), 3.84 (3H, s, $OC\mathit{H_3}$), 2.38-2.28 (3H, m), 2.07-1.97 (2H, m), 1.92-1.87 (1H, m), 1.25 (3H, d, *J* = 6.0 Hz, $OCH(C\mathit{H_3})_2$), 1.22 (3H, d, *J* = 6.4 Hz, $OCH(C\mathit{H_3})_2$); $^{13}C$ NMR ($CDCl_3$, DEPT-135) δ 213.1 (C, C=O),

168.9 (C, O-C=O), 146.4 (C), 144.3 (C), 122.0 (C), 121.8 (CH), 120.0 (CH), 110.0 (CH), 76.3 ($CH_2$), 69.8 (CH, O*C*H($CH_3$)$_2$), 62.5 (C), 56.0 ($CH_3$, O*C*$H_3$), 39.6 (CH), 37.8 ($CH_2$), 32.3 ($CH_2$), 21.6 ($CH_3$), 21.5 ($CH_3$), 19.2 ($CH_2$); LRMS m/z 366.15 (M + $H^+$), calcd for $C_{18}H_{23}NO_7$ 365.1475; Anal. calcd for $C_{18}H_{23}NO_7$ (365.1475): C, 59.17; H, 6.34; N, 3.83. Found: C, 59.25; H, 6.41; N, 3.76%.

**(*S*)-ethyl 1-[(*R*)-2-nitro-1-phenylethyl]-2-oxocyclopentanecarboxylate (4aj):** Prepared by procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 90:10, flow rate 0.7 mL/min, λ = 254 nm), $t_R$ = 15.05 min (major), $t_R$ = 22.10 min (minor). **$[\alpha]_D^{25}$ = +31.2° (*c* = 1.42 g/100 mL, $CHCl_3$, 79% *ee* and 89% *de*);** IR (Neat): $\nu_{max}$ 2979, 1748 (C=O), 1721, 1552 (*$NO_2$*), 1378 (*$NO_2$*), 1225, 1147, 1025 and 752 $cm^{-1}$; $^1$H NMR ($CDCl_3$, **89% *de*, major isomer**) δ 7.32-7.28 (3H, m), 7.27-7.24 (2H, m), 5.17 (1H, dd, *J* = 14.0, 4.0 Hz), 5.01 (1H, dd, *J* = 13.5, 11.0 Hz), 4.21 (2H, q, *J* = 8.0, 2.0 Hz, OC*H*$_2$CH$_3$), 4.07 (1H, dd, *J* = 11.5, 4.0 Hz), 2.40-2.31 (2H, m), 2.05-1.88 (3H, m), 1.84-1.77 (1H, m), 1.27 (3H, t, *J* = 7.0 Hz, OCH$_2$C*H*$_3$); $^{13}$C NMR ($CDCl_3$, DEPT-135, **89% *de*, major isomer**) δ 212.3 (C, C=O), 169.3 (C, O-C=O), 135.4 (C), 129.3 (2 x CH), 128.8 (2 x CH), 128.2 (CH), 76.5 ($CH_2$), 62.4 (C), 62.2 ($CH_2$, O*C*H$_2$CH$_3$), 46.2 (CH), 37.9 ($CH_2$), 31.2 ($CH_2$), 19.3 ($CH_2$), 13.9 ($CH_3$, OCH$_2$*C*H$_3$); LRMS m/z 306.20 (M + $H^+$), calcd for $C_{16}H_{19}NO_5$ 305.1263; Anal. calcd for $C_{16}H_{19}NO_5$ (305.1263): C, 62.94; H, 6.27; N, 4.59. Found: C, 62.85; H, 6.32; N, 4.51%.

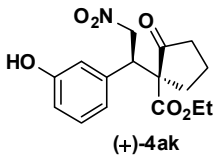


(+)-4aj

**Configuration assignment:** The absolute stereochemistry of (+)-**4aj** was assigned as (*S*, *R*) by correlation with other examples and also by comparison of the retention time of HPLC with the literature data.[4]

Reference 4: (a) H. Y. Bae, S. Some, J. S. Oh, Y. S. Lee and C. E. Song, *Chem. Commun*., 2011, **47**, 9621-9623; (b) J. Luo, L. –W. Xu, R. A. S. Hay and Y. Lu, *Org. Lett.,* 2009, **11**, 437-440;

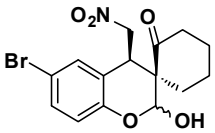
**(*S*)-ethyl 1-[(*R*)-1-(3-hydroxyphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate (4ak):** Prepared by procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 7.42 min (major), $t_R$ = 9.08 min (minor). **$[\alpha]_D^{25}$ = +26.1° (*c* = 1.35 g/100 mL, $CHCl_3$, 78% *ee* and 73% *de*);** IR (Neat): $\nu_{max}$ 3343 (O-*H*), 2977, 1716 (C=O), 1552 (*$NO_2$*), 1378 (*$NO_2$*), 1228, 1147, 1023 908, 785 and 703 $cm^{-1}$; $^1$H NMR ($CDCl_3$, **73%**



(+)-4ak

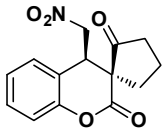
***de*, major isomer**) δ 7.14 (1H, t, *J* = 7.5 Hz), 6.78-6.74 (3H, m), 6.29 (1H, br s, OH), 5.13 (1H, dd, *J* = 14.0, 4.0 Hz), 4.97 (1H, dd, *J* = 13.5, 11.0 Hz), 4.19 (2H, q, *J* = 7.5 Hz, $OCH_2CH_3$), 4.03 (1H, dd, *J* = 11.0, 4.0 Hz), 2.40-2.31 (2H, m), 2.04-1.97 (2H, m), 1.93-1.87 (1H, m), 1.83-1.79 (1H, m), 1.25 (3H, t, *J* = 7.0 Hz, $OCH_2CH_3$); $^{13}$C NMR ($CDCl_3$, DEPT-135, **73% *de*, major isomer**) δ 213.0 (C, C=O), 169.4 (C, O-C=O), 156.1 (C), 136.9 (C), 129.9 (CH), 121.2 (CH), 116.5 (CH), 115.4 (CH), 76.4 ($CH_2$), 62.4 (C), 62.3 ($CH_2$, $OCH_2CH_3$), 46.0 (CH), 37.9 ($CH_2$), 31.0 ($CH_2$), 19.3 ($CH_2$), 13.9 ($CH_3$, $OCH_2CH_3$); LRMS m/z 322.25 ($M + H^+$), calcd for $C_{16}H_{19}NO_6$ 321.1212; Anal. calcd for $C_{16}H_{19}NO_6$ (321.1212): C, 59.81; H, 5.96; N, 4.36. Found: C, 59.76; H, 5.91; N, 4.42%.

**(1'*R*,4*R*)-6-bromo-2-hydroxy-4-(nitromethyl)spiro[chroman-3,1'-cyclohexan]-2'-one (5dd):** Prepared by procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as liquid. **$[\alpha]_D^{25}$ = –9.9° (*c* = 0.38 g/100 mL, $CHCl_3$);** IR (Neat): $\nu_{max}$ 3427 (O-*H*), 2952, 1705 (C=O), 1552 (*NO*$_2$), 1481, 1377 (*NO*$_2$), 1223, 1018 and 904 $cm^{-1}$; $^1$H NMR ($CDCl_3$, **3:1 ratio of isomers, major isomer**) δ 7.33 (1H, dd, *J* = 8.8, 2.4 Hz), 7.18 (1H, d, *J* = 2.0 Hz), 6.79 (1H, d, *J* = 8.8 Hz), 5.62 (1H, s, O-C*H*-O), 4.78 (1H, dd, *J* = 14.4, 8.4 Hz), 4.62 (1H, dd, *J* = 14.4, 2.4 Hz), 4.10-4.08 (1H, m), 3.94 (1H, br s, OH), 2.69-2.51 (2H, m), 2.18-2.09 (1H, m), 1.93-1.83 (2H, m), 1.81-1.73 (3H, m); $^{13}$C NMR ($CDCl_3$, DEPT-135, **3:1 ratio of isomers, major isomer**) δ 212.8 (C, C=O), 148.1 (C), 132.6 (CH), 131.7 (CH), 122.7 (C), 119.4 (CH), 114.3 (C), 94.0 (CH, O-*C*H-O), 79.1 ($CH_2$), 53.0 (C), 40.1 ($CH_2$), 36.8 (CH), 34.8 ($CH_2$), 28.6 ($CH_2$), 20.4 ($CH_2$); LRMS m/z 370.15 ($M + H^+$), calcd for $C_{15}H_{16}BrNO_5$ 369.0212; Anal. calcd for $C_{15}H_{16}BrNO_5$ (369.0212): C, 48.67; H, 4.36; N, 3.78. Found: C, 48.56; H, 4.41; N, 3.73%.



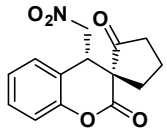
(–)-5dd

**(1'*S*,4*R*)-4-(nitromethyl)spiro[chroman-3,1'-cyclopentane]-2,2'-dione (6aa):** Prepared by procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 142-145 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 20.99 min (major), $t_R$ = 26.44 min (minor). **$[\alpha]_D^{25}$ = –36.5° (*c* = 0.34 g/100 mL, $CHCl_3$, >99.9% *ee*);** IR (Neat): $\nu_{max}$ 2954, 1762 (C=O), 1726, 1666 (*NO*$_2$), 1366 (*NO*$_2$), 1171, 1016, 911, 811 and 754 $cm^{-1}$; $^1$H NMR ($CDCl_3$) δ 7.42-7.38 (1H, m), 7.22-7.17 (2H, m), 7.15-7.13 (1H, m), 5.56 (1H, dd, *J* = 10.8, 4.0 Hz), 4.42 (1H, dd, *J* = 10.8, 8.0 Hz), 3.78 (1H, dd, *J* = 8.0, 4.0 Hz), 2.73-2.67 (1H, m), 2.51-2.45 (1H, m), 2.22-2.19 (1H, m), 2.10-1.99 (3H, m); $^{13}$C NMR ($CDCl_3$, DEPT-135) δ 212.6 (C, C=O), 166.6 (C, O-C=O), 150.3 (C), 130.4 (CH), 128.8 (CH), 125.6 (CH), 120.6 (C), 117.2 (CH), 75.5 ($CH_2$), 54.9 (C), 41.6 (CH), 39.1 ($CH_2$), 35.7 ($CH_2$), 18.7 ($CH_2$); LRMS m/z 276.15 ($M + H^+$), calcd for $C_{14}H_{13}NO_5$ 275.0794; Anal. calcd for $C_{14}H_{13}NO_5$ (275.0794): C, 61.09; H, 4.76; N, 5.09. Found: C, 61.13; H, 4.68; N, 5.17%.



(–)-6aa

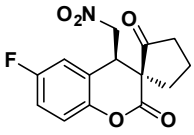
**(1'*R*,4*S*)-4-(nitromethyl)spiro[chroman-3,1'-cyclopentane]-2,2'-dione (6aa):** Prepared by procedure **D**



(+)-6aa

and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 143-145 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 20.52 min (minor), $t_R$ = 25.46 min (major). **$[\alpha]_D^{25}$ = +28.7° (*c* = 0.42 g/100 mL, $CHCl_3$, 98% *ee*);** IR (Neat): $\nu_{max}$ 2962, 1758 (C=O), 1736, 1546 (*$NO_2$*), 1375 (*$NO_2$*), 1258, 1087, 1011 and 793 $cm^{-1}$.

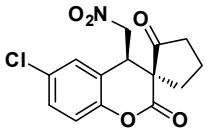
**(1'*S*,4*R*)-6-fluoro-4-(nitromethyl)spiro[chroman-3,1'-cyclopentane]-2,2'-dione (6ab):** Prepared by



(–)-6ab

procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 125-127 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 23.46 min (major), $t_R$ = 33.42 min (minor). **$[\alpha]_D^{25}$ = –22.8° (*c* = 0.63 g/100 mL, $CHCl_3$, 88% *ee*);** IR (Neat): $\nu_{max}$ 2953, 1762 (C=O), 1725, 1552 (*$NO_2$*), 1366 (*$NO_2$*), 1191, 1016, 911, 811 and 754 $cm^{-1}$; $^1$H NMR ($CDCl_3$) δ 7.12-7.10 (2H, m), 6.96 (1H, br dd, *J* = 7.6, 2.0 Hz), 5.58 (1H, dd, *J* = 13.6, 4.8 Hz), 4.42 (1H, dd, *J* = 13.6, 10.0 Hz), 3.77 (1H, dd, *J* = 10.0, 4.8 Hz), 2.74-2.67 (1H, m), 2.54-2.44 (1H, m), 2.22-2.18 (1H, m), 2.12-1.99 (3H, m); $^{13}$C NMR ($CDCl_3$, DEPT-135) δ 212.1 (C, C=O), 166.1 (C, O-C=O), 159.3 (C, d, *J* = 245.6 Hz), 146.4 (C, d, *J* = 3.1 Hz), 122.3 (C, d, *J* = 8.0 Hz), 118.7 (CH, d, *J* = 8.3 Hz), 117.2 (CH, d, *J* = 23.4 Hz), 115.7 (CH, d, *J* = 24.5 Hz), 75.0 ($CH_2$), 54.4 (C), 41.5 (CH), 39.0 ($CH_2$), 35.6 ($CH_2$), 18.6 ($CH_2$); LRMS m/z 294.25 (M + $H^+$), calcd for $C_{14}H_{12}FNO_5$ 293.0700; Anal. calcd for $C_{14}H_{12}FNO_5$ (293.0700): C, 57.34; H, 4.12; N, 4.78. Found: C, 57.25; H, 4.19; N, 4.71%.

**(1'*S*,4*R*)-6-chloro-4-(nitromethyl)spiro[chroman-3,1'-cyclopentane]-2,2'-dione (6ac):** Prepared by

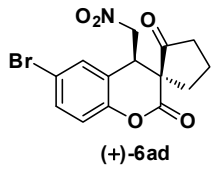


(–)-6ac

procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 116-118 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 24.85 min (major), $t_R$ = 34.65 min (minor). **$[\alpha]_D^{25}$ = –12.1° (*c* = 0.28 g/100 mL, $CHCl_3$, 87% *ee*);** IR (Neat): $\nu_{max}$ 2957, 1767 (C=O), 1742, 1549 (*$NO_2$*), 1375 (*$NO_2$*), 1292, 1134, 826 and 660 $cm^{-1}$; $^1$H NMR ($CDCl_3$) δ 7.37 (1H, dd, *J* = 8.4, 2.4 Hz), 7.22 (1H, d, *J* = 2.4 Hz), 7.09 (1H, d, *J* = 8.8 Hz), 5.57 (1H, dd, *J* = 14.0, 4.8 Hz), 4.42 (1H, dd, *J* = 14.0, 10.0 Hz), 3.76 (1H, dd, *J* = 10.0, 4.8 Hz), 2.74-2.67 (1H, m), 2.54-2.44 (1H, m), 2.22-2.17 (1H, m), 2.10-1.98 (3H, m); $^{13}$C NMR ($CDCl_3$, DEPT-135) δ 212.0 (C, C=O), 165.9 (C, O-C=O), 148.9 (C), 130.8 (C), 130.6 (CH), 128.7 (CH), 122.3 (C), 118.6 (CH), 75.0 ($CH_2$), 54.5 (C), 41.4 (CH), 39.0 ($CH_2$), 35.7 ($CH_2$), 18.7 ($CH_2$); LRMS m/z 310.00 (M + $H^+$), calcd for $C_{14}H_{12}ClNO_5$

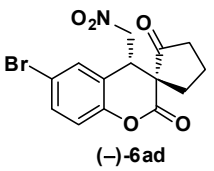
309.0404; Anal. calcd for $C_{14}H_{12}ClNO_5$ (309.0404): C, 54.29; H, 3.91; N, 4.52. Found: C, 54.19; H, 3.96; N, 4.48%.

**(1'*S*,4*R*)-6-bromo-4-(nitromethyl)spiro[chroman-3,1'-cyclopentane]-2,2'-dione (6ad):** Prepared by procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 120-122 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 27.45 min (major), $t_R$ = 38.37 min (minor). **$[\alpha]_D^{25}$ = +14.0° (*c* = 0.27 g/100 mL, $CHCl_3$, >99.9% *ee*);** IR (Neat): $\nu_{max}$ 2921, 1759 (C=O), 1734, 1547 ($NO_2$), 1380 ($NO_2$), 1342, 1221, 1145, 941, 785 and 761 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 7.52 (1H, dd, *J* = 8.8, 2.4 Hz), 7.37 (1H, d, *J* = 2.4 Hz), 7.03 (1H, d, *J* = 8.4 Hz), 5.54 (1H, dd, *J* = 14.0, 4.8 Hz), 4.42 (1H, dd, *J* = 14.0, 9.6 Hz), 3.76 (1H, dd, *J* = 9.6, 4.8 Hz), 2.75-2.67 (1H, m), 2.54-2.44 (1H, m), 2.22-2.17 (1H, m), 2.11-1.97 (3H, m); $^{13}C$ NMR ($CDCl_3$, DEPT-135) δ 211.9 (C, C=O), 165.8 (C, O-C=O), 149.4 (C), 133.5 (CH), 131.5 (CH), 122.7 (C), 118.9 (CH), 118.2 (C), 74.9 ($CH_2$), 54.4 (C), 41.2 (CH), 39.0 ($CH_2$), 35.7 ($CH_2$), 18.7 ($CH_2$); LRMS m/z 353.20 ($M + H^+$), calcd for $C_{14}H_{12}BrNO_5$ 352.9899; calcd for $C_{14}H_{12}BrNO_5$ (352.9899): C, 47.48; H, 3.42; N, 3.95. Found: C, 47.56; H, 3.37; N, 3.89%.



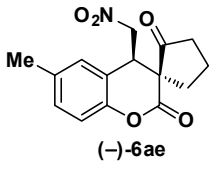
(+)-6ad

**(1'*R*,4*S*)-6-bromo-4-(nitromethyl)spiro[chroman-3,1'-cyclopentane]-2,2'-dione (6ad):** Prepared by procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 118-119 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 28.22 min (minor), $t_R$ = 38.36 min (major). **$[\alpha]_D^{25}$ = –12.9° (*c* = 0.28 g/100 mL, $CHCl_3$, 96% *ee*);** IR (Neat): $\nu_{max}$ 2924, 1761 (C=O), 1729, 1551 ($NO_2$), 1455, 1376 ($NO_2$), 1336, 1223, 1180, 1031 and 756 $cm^{-1}$.



(–)-6ad

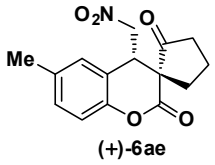
**(1'*S*,4*R*)-6-methyl-4-(nitromethyl)spiro[chroman-3,1'-cyclopentane]-2,2'-dione (6ae):** Prepared by procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 130-133 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 17.14 min (major), $t_R$ = 22.10 min (minor). **$[\alpha]_D^{25}$ = –18.3° (*c* = 0.28 g/100 mL, $CHCl_3$, 96% *ee*);** IR (Neat): $\nu_{max}$ 2921, 1758 (C=O), 1735, 1550 ($NO_2$), 1379 ($NO_2$), 1221, 1145, 897 and 760 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 7.17 (1H, d, *J* = 8.0 Hz), 7.01 (1H, d, *J* = 8.0 Hz), 6.98 (1H, br s), 5.54 (1H, dd, *J* = 13.6, 4.8 Hz), 4.40 (1H, dd, *J* = 13.2, 10.0 Hz), 3.73 (1H, dd, *J* = 9.6, 4.8 Hz), 2.72-2.65 (1H, m), 2.52-2.43 (1H, m), 2.33 (3H, s, $CH_3$), 2.21-2.17 (1H, m), 2.10-1.97 (3H, m); $^{13}C$ NMR ($CDCl_3$, DEPT-135) δ 212.6 (C, C=O),



(–)-6ae

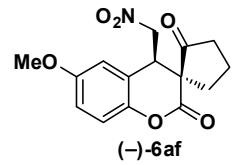
166.7 (C, O-C=O), 148.2 (C), 135.5 (C), 130.9 (CH), 129.0 (CH), 120.2 (C), 116.9 (CH), 75.5 ($CH_2$), 54.9 (C), 41.6 (CH), 39.1 ($CH_2$), 35.7 ($CH_2$), 20.7 ($CH_3$), 18.7 ($CH_2$); LRMS m/z 290.05 ($M + H^+$), calcd for $C_{15}H_{15}NO_5$ 289.0950; Anal. calcd for $C_{15}H_{15}NO_5$ (289.0950): C, 62.28; H, 5.23; N, 4.84. Found: C, 62.35; H, 5.28; N, 4.79%.

**(1'*R*,4*S*)-6-methyl-4-(nitromethyl)spiro[chroman-3,1'-cyclopentane]-2,2'-dione (6ae):** Prepared by procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 126-128 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 15.72 min (minor), $t_R$ = 19.32 min (major). **$[\alpha]_D^{25}$ = +26.0° (*c* = 0.42 g/100 mL, $CHCl_3$, 99% *ee*);** IR (Neat): $\nu_{max}$ 2962, 1759 (C=O), 1736, 1546 ($NO_2$), 1375 ($NO_2$), 1258, 1086, 1011 and 793 $cm^{-1}$.



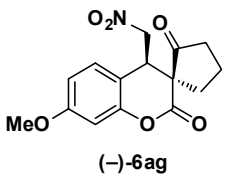
(+)-6ae

**(1'*S*,4*R*)-6-methoxy-4-(nitromethyl)spiro[chroman-3,1'-cyclopentane]-2,2'-dione (6af):** Prepared by procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 23.94 min (major), $t_R$ = 32.88 min (minor). **$[\alpha]_D^{25}$ = –35.2° (*c* = 0.30 g/100 mL, $CHCl_3$, 84% *ee*);** IR (Neat): $\nu_{max}$ 2924, 1762 (C=O), 1733, 1551 ($NO_2$), 1475, 1374 ($NO_2$), 1221, 1161 and 816 $cm^{-1}$; $^1$H NMR ($CDCl_3$) δ 7.06 (1H, d, *J* = 9.2 Hz), 6.89 (1H, dd, *J* = 9.2, 3.2 Hz), 6.71 (1H, d, *J* = 2.8 Hz), 5.55 (1H, dd, *J* = 13.6, 4.8 Hz), 4.41 (1H, dd, *J* = 13.6, 10.0 Hz), 3.79 (3H, s, $OCH_3$), 3.73 (1H, dd, *J* = 10.0, 4.8 Hz), 2.72-2.65 (1H, m), 2.52-2.45 (1H, m), 2.22-2.18 (1H, m), 2.10-1.98 (3H, m); $^{13}$C NMR ($CDCl_3$, DEPT-135) δ 212.6 (C, C=O), 166.7 (C, O-C=O), 156.8 (C), 144.0 (C), 121.5 (C), 118.0 (CH), 115.4 (CH), 113.7 (CH), 75.4 ($CH_2$), 55.7 ($CH_3$, $OCH_3$), 54.8 (C), 41.8 (CH), 39.1 ($CH_2$), 35.6 ($CH_2$), 18.7 ($CH_2$); LRMS m/z 306.15 ($M + H^+$), calcd for $C_{15}H_{15}NO_6$ 305.0899; Anal. calcd for $C_{15}H_{15}NO_6$ (305.0899): C, 59.01; H, 4.95; N, 4.59. Found: C, 59.11; H, 5.03; N, 4.52%.



(–)-6af

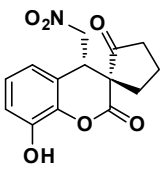
**(1'*S*,4*R*)-7-methoxy-4-(nitromethyl)spiro[chroman-3,1'-cyclopentane]-2,2'-dione (6ag):** Prepared by procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 13.50 min (major), $t_R$ = 17.75 min (minor). **$[\alpha]_D^{25}$ = –41.1° (*c* = 0.29 g/100 mL, $CHCl_3$, 90% *ee*);** IR (Neat): $\nu_{max}$ 2953, 1764 (C=O), 1737, 1545 ($NO_2$), 1386 ($NO_2$), 1222, 1140, 893 and 816 $cm^{-1}$; $^1$H NMR ($CDCl_3$) δ 7.08 (1H, d, *J* = 8.4 Hz), 6.69 (1H, dd, *J* = 8.4, 2.8 Hz), 6.66 (1H, d, *J* = 2.8 Hz) 5.46 (1H, dd, *J* = 13.2, 4.8 Hz), 4.39 (1H, dd, *J* = 13.6, 10.0



(–)-6ag

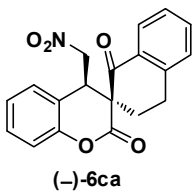
Hz), 3.81 (3H, s, OC*H*$_3$), 3.71 (1H, dd, *J* = 10.0, 5.2 Hz), 2.71-2.63 (1H, m), 2.52-2.43 (1H, m), 2.22-2.18 (1H, m), 2.09-1.99 (3H, m); $^{13}$C NMR ($CDCl_3$, DEPT-135) δ 212.6 (C, C=O), 166.5 (C, O-C=O), 161.1 (C), 151.1 (C), 129.3 (CH), 112.2 (C), 111.3 (CH), 102.9 (CH), 75.8 ($CH_2$), 55.6 ($CH_3$, O*C*H$_3$), 55.2 (C), 41.0 (CH), 39.1 ($CH_2$), 35.7 ($CH_2$), 18.7 ($CH_2$); LRMS m/z 306.15 (M + H$^+$), calcd for $C_{15}H_{15}NO_6$ 305.0899; Anal. calcd for $C_{15}H_{15}NO_6$ (305.0899): C, 59.01; H, 4.95; N, 4.59. Found: C, 59.11; H, 4.92; N, 4.51%.

**(1'*R*,4*S*)-8-hydroxy-4-(nitromethyl)spiro[chroman-3,1'-cyclopentane]-2,2'-dione (6ah):** Prepared by procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), $t_R$ = 66.89 min (minor), $t_R$ = 76.20 min (major). **$[\alpha]_D^{25}$ = +15.4° (*c* = 0.143 g/100 mL, $CHCl_3$, 76% *ee*);** IR (Neat): $\nu_{max}$ 3419 (O-*H*), 2961, 1763 (C=O), 1736, 1555 (*NO*$_2$),1480, 1342 (*NO*$_2$), 1262, 1033, and 734 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 7.08-7.00 (2H, m), 6.73 (1H, dd, *J* = 7.2, 1.6 Hz), 6.00 (1H, br s, OH), 5.46 (1H, dd, *J* = 13.6, 5.2 Hz), 4.44 (1H, dd, *J* = 13.6, 9.2 Hz), 3.80 (1H, dd, *J* = 9.6, 5.2 Hz), 2.72-2.65 (1H, m), 2.56-2.47 (1H, m), 2.26-2.22 (1H, m), 2.12-2.04 (3H, m); $^{13}$C NMR ($CDCl_3$, DEPT-135) δ 212.3 (C, C=O), 165.8 (C, O-C=O), 143.8 (C), 137.7 (C), 126.1 (CH), 121.0 (C), 119.7 (CH), 117.5 (CH), 75.4 ($CH_2$), 55.0 (C), 41.6 (CH), 39.1 ($CH_2$), 35.8 ($CH_2$), 18.8 ($CH_2$); LRMS m/z 292.10 (M + H$^+$), calcd for $C_{14}H_{13}NO_6$ 291.0743; Anal. calcd for $C_{14}H_{13}NO_6$ (291.0743): C, 57.73; H, 4.50; N, 4.81. Found: C, 57.62; H, 4.58; N, 4.76%.



(+)-6ah

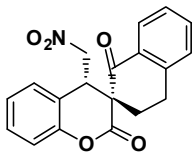
**(2'*S*,4*R*)-4-(nitromethyl)-3',4'-dihydro-1'*H*-spiro[chroman-3,2'-naphthalene]-1',2-dione (6ca):** Prepared by procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 167-169 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AS-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 18.96 min (major), $t_R$ = 26.08 min (minor). **$[\alpha]_D^{25}$ = –193.4° (*c* = 0.057 g/100 mL, $CHCl_3$, >99.9% *ee*);** IR (Neat): $\nu_{max}$ 2921, 1756 (C=O), 1734, 1550 (*NO*$_2$), 1456, 1377 (*NO*$_2$), 1340, 1221, 1146, and 759 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 8.11 (1H, d, *J* = 8.0 Hz), 7.55 (1H, t, *J* = 7.2 Hz), 7.43-7.38 (2H, m), 7.26-7.20 (2H, m), 7.22-7.10 (2H, m), 5.56 (1H, dd, *J* = 13.5, 5.0 Hz), 4.51 (1H, dd, *J* = 13.5, 10.0 Hz), 4.02 (1H, dd, *J* = 9.5, 5.0 Hz), 2.98 (2H, t, *J* = 6.0 Hz), 2.34 (1H, td, *J* = 14.0, 5.0 Hz), 2.12 (1H, td, *J* = 14.5, 7.0 Hz); $^{13}$C NMR ($CDCl_3$, DEPT-135) δ 193.3 (C, C=O), 165.8 (C, O-C=O), 150.2 (C), 142.1 (C), 134.5 (CH), 132.2 (C), 130.4 (CH), 129.1 (CH), 128.6 (CH), 128.5 (CH), 127.5 (CH), 125.8 (CH), 120.8 (C), 117.1 (CH), 77.3 ($CH_2$), 53.7 (C), 41.3 (CH), 30.9 ($CH_2$), 25.4 ($CH_2$); LRMS m/z 338.25 (M + H$^+$),



(–)-6ca

calcd for $C_{19}H_{15}NO_5$ 337.0950; Anal. calcd for $C_{19}H_{15}NO_5$ (337.0950): C, 67.65; H, 4.48; N, 4.15. Found: C, 67.56; H, 4.52; N, 4.21%.

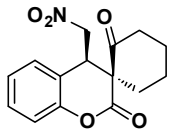
**(2'*R*,4*S*)-4-(nitromethyl)-3',4'-dihydro-1'*H*-spiro[chroman-3,2'-naphthalene]-1',2-dione (6ca):**



(+)-6ca

Prepared by procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 172-173 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AS-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 19.19 min (minor), $t_R$ = 26.06 min (major). **$[\alpha]_D^{25}$ = +157.3° (*c* = 0.25 g/100 mL, $CHCl_3$, 97% *ee*);** IR (Neat): $\nu_{max}$ 2924, 1759 (C=O), 1734, 1547 (*$NO_2$*), 1493, 1375 (*$NO_2$*), 1257, 1011, and 815 $cm^{-1}$.

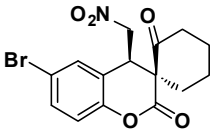
**(1'*S*,4*R*)-4-(nitromethyl)spiro[chroman-3,1'-cyclohexane]-2,2'-dione (6da):** Prepared by procedure **E**



(–)-6da

and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 142-145 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OJ-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), $t_R$ = 17.04 min (major), $t_R$ = 19.30 min (minor). **$[\alpha]_D^{25}$ = –43.7° (*c* = 0.128 g/100 mL, $CHCl_3$, 99% *ee*);** IR (Neat): $\nu_{max}$ 2931, 1759 (C=O), 1710, 1512 (*$NO_2$*), 1370 (*$NO_2$*), 1244, 1036, 811 and 767 $cm^{-1}$; $^1$H NMR ($CDCl_3$) δ 7.37 (1H, t, *J* = 7.6 Hz), 7.22 (1H, d, *J* = 7.2 Hz), 7.15 (1H, t, *J* = 7.6 Hz), 7.10 (1H, d, *J* = 8.0 Hz), 5.41 (1H, dd, *J* = 12.8, 4.0 Hz), 4.21 (1H, dd, *J* = 12.4, 10.4 Hz), 3.90 (1H, dd, *J* = 10.4, 4.0 Hz), 3.39-3.31 (1H, m), 2.62-2.58 (1H, m), 2.17-2.14 (2H, m), 1.75-1.67 (3H, m), 1.50 (1H, td, *J* = 12.0, 3.6 Hz); $^{13}$C NMR ($CDCl_3$, DEPT-135) δ 206.9 (C, C=O), 166.1 (C, O-C=O), 150.0 (C), 130.2 (CH), 129.2 (CH), 125.6 (CH), 121.4 (C), 116.5 (CH), 76.7 ($CH_2$), 56.3 (C), 41.8 ($CH_2$), 41.77 (CH), 36.3 ($CH_2$), 27.7 ($CH_2$), 21.9 ($CH_2$); LRMS m/z 290.05 ($M + H^+$), calcd for $C_{15}H_{15}NO_5$ 289.0950; Anal. calcd for $C_{15}H_{15}NO_5$ (289.0950): C, 62.28; H, 5.23; N, 4.84. Found: C, 62.14; H, 5.27; N, 4.75%.

**(1'*S*,4*R*)-6-bromo-4-(nitromethyl)spiro[chroman-3,1'-cyclohexane]-2,2'-dione (6dd):** Prepared by

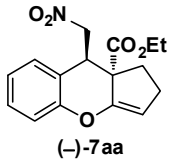


(–)-6dd

procedure **E** and purified by column chromatography using EtOAc/hexane and isolated as white solid. Mp 120 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OJ-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 240 nm), $t_R$ = 25.34 min (major), $t_R$ = 30.76 min (minor). **$[\alpha]_D^{25}$ = –4.2° (*c* = 0.21 g/100 mL, $CHCl_3$, 79% *ee*);** IR (Neat): $\nu_{max}$ 2918, 1764 (C=O), 1718, 1552 (*$NO_2$*), 1380 (*$NO_2$*), 1242, 1029 and 822 $cm^{-1}$; $^1$H NMR ($CDCl_3$) δ 7.49 (1H, dd, *J* = 8.4, 2.0 Hz), 7.38 (1H, d, *J* = 2.4 Hz), 7.00 (1H, d, *J* = 8.8 Hz), 5.37 (1H, dd, *J* = 13.2, 4.4 Hz), 4.22 (1H, dd, *J* = 13.2, 10.4 Hz), 3.87 (1H, dd, *J* = 10.4, 4.0 Hz), 3.38-3.29 (1H, m), 2.62-2.58 (1H, m), 2.20-2.11 (2H, m), 1.77-1.60 (3H, m), 1.52 (1H, td, *J* = 13.6, 3.6 Hz); $^{13}$C NMR ($CDCl_3$, DEPT-135) δ 206.5 (C,

C=O), 165.4 (C, O-C=O), 149.2 (C), 133.2 (CH), 131.9 (CH), 123.7 (C), 118.2 (C), 118.2 (CH), 76.3 ($CH_2$), 56.0 (C), 41.7 ($CH_2$), 41.4 (CH), 36.4 ($CH_2$), 27.7 ($CH_2$), 21.9 ($CH_2$); LRMS m/z 368.10 ($M + H^+$), calcd for $C_{15}H_{14}BrNO_5$ 367.0055; Anal. calcd for $C_{15}H_{14}BrNO_5$ (367.0055): C, 48.93; H, 3.83; N, 3.80. Found: C, 48.85; H, 3.76; N, 3.85%.

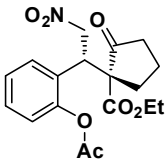
**(9*R*,9a*S*)-ethyl 9-(nitromethyl)-1,2,9,9a-tetrahydrocyclopenta[b]chromene-9a-carboxylate (7aa):**



(–)-7aa

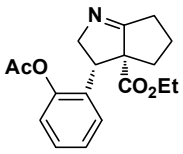
Prepared following the procedure **F** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), $t_R$ = 12.26 min (major), $t_R$ = 13.12 min (minor). **$[\alpha]_D^{25}$ = –142.5° (*c* = 0.085 g/100 mL, $CHCl_3$, 60% *ee* and >99% *de*);** IR (Neat): $\nu_{max}$ 2926, 1736 (C=O), 1678, 1557 (*$NO_2$*), 1375 (*$NO_2$*), 1246, 862, 804 and 756 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 7.22 (1H, dt, *J* = 8.8, 1.6 Hz), 7.08 (1H, dd, *J* = 7.2, 1.2 Hz), 6.96-6.91 (2H, m), 5.37 (1H, t, *J* = 2.4 Hz, olefinic-*H*), 4.68 (1H, dd, *J* = 11.2, 4.4 Hz), 4.32-4.23 (2H, m), 4.04-3.98 (2H, m, $OCH_2CH_3$), 2.56-2.47 (1H, m), 2.39-2.28 (2H, m), 2.13-2.07 (1H, m), 0.99 (3H, t, *J* = 6.8 Hz, $OCH_2CH_3$); $^{13}C$ NMR ($CDCl_3$, DEPT-135) δ 172.4 (C, O-C=O), 152.1 (C), 148.7 (C), 129.9 (CH), 129.8 (CH), 122.7 (CH), 120.6 (C), 116.7 (CH), 105.7 (CH), 77.8 ($CH_2$), 61.6 ($CH_2$, $OCH_2CH_3$), 54.6 (C), 40.5 (CH), 30.0 ($CH_2$), 25.9 ($CH_2$), 13.8 ($CH_3$, $OCH_2CH_3$); LRMS m/z 304.15 ($M + H^+$), calcd for $C_{16}H_{17}NO_5$ 303.1107; Anal. calcd for $C_{16}H_{17}NO_5$ (303.1107): C, 63.36; H, 5.65; N, 4.62. Found: C, 63.18; H, 5.71; N, 4.56%.

**(*R*)-ethyl 1-[(*S*)-1-(2-acetoxyphenyl)-2-nitroethyl]-2-oxocyclopentanecarboxylate (8aa):** Prepared following the procedure **G** and purified by column chromatography using EtOAc/hexane and isolated as Liquid; **$[\alpha]_D^{25}$ = –16.7° (*c* = 1.32 g/100 mL, $CHCl_3$, 98% *ee*);** IR (Neat): $\nu_{max}$ 2931, 1764 (C=O), 1726, 1551 (*$NO_2$*), 1381 (*$NO_2$*), 1211, 1014, and 915 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 7.49 (1H, d, *J* = 6.4 Hz), 7.32 (1H, t, *J* = 5.6 Hz), 7.22 (1H, t, *J* = 6.0 Hz), 7.14 (1H, d, *J* = 6.4 Hz), 5.34 (1H, dd, *J* = 11.2, 2.8 Hz), 4.95 (1H, dd, *J* = 11.2, 7.6 Hz), 4.33 (1H, dd, *J* = 7.6, 3.2 Hz), 4.21 (2H, q, *J* = 6.0 Hz, $OCH_2CH_3$), 2.50-2.40 (2H, m), 2.38 (3H, s, $O=CCH_3$), 2.33-2.23 (1H, m), 2.00-1.94 (2H, m), 1.92-1.86 (1H, m), 1.27 (3H, t, *J* = 6.0 Hz, $OCH_2CH_3$); $^{13}C$ NMR ($CDCl_3$, DEPT-135) δ 212.4 (C, C=O), 169.6 (C, O-C=O), 168.9 (C, O-C=O), 149.2 (C), 129.0 (CH), 128.8 (CH), 128.7 (C), 126.4 (CH), 123.3 (CH), 77.0 ($CH_2$), 62.2 (C), 62.18 ($CH_2$, $OCH_2CH_3$), 38.1 (CH), 37.6 ($CH_2$), 32.6 ($CH_3$), 21.1 ($CH_2$), 19.2 ($CH_2$), 13.9 ($CH_3$, $OCH_2CH_3$); LRMS m/z 364.40 ($M + H^+$), calcd for $C_{18}H_{21}NO_7$ 363.1318; Anal. calcd for $C_{18}H_{21}NO_7$ (363.1318): C, 59.50; H, 5.83; N, 3.85. Found: C, 59.41; H, 5.87; N, 3.79%.



(–)-8aa

**(3*S*,3a*R*)-ethyl 3-(2-acetoxyphenyl)-2,3,3a,4,5,6-hexahydrocyclopenta[b]pyrrole-3a-carboxylate (9aa):** Prepared following the procedure **H** and purified by column chromatography using EtOAc/hexane and isolated as oil; **$[\alpha]_D^{25}$ = +160.2° (*c* = 1.21 g/100 mL, $CHCl_3$, 98% *ee*);** IR (Neat): $\nu_{max}$ 2930, 1761 (C=O), 1736, 1655 (*$NO_2$*), 1493, 1370 (*$NO_2$*), 1207, 1017, 912, 812 and 756 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 7.30 (1H, t, *J* = 8.0 Hz), 7.26 (1H, d, *J* = 8.4 Hz), 7.18 (1H, t, *J* = 7.6 Hz), 7.11 (1H, d, *J* = 8.0 Hz), 5.19 (1H, t, *J* = 12.0 Hz), 4.24 (1H, dd, *J* = 12.4, 8.8 Hz), 4.05 (1H, dd, *J* = 10.8, 8.4 Hz), 3.83 (2H, q, *J* = 7.2 Hz, $OCH_2CH_3$), 2.76-2.61 (2H, m), 2.33 (3H, s, $O{=}CCH_3$), 2.27-2.16 (1H, m), 2.14-1.99 (2H, m), 1.71-1.63 (1H, m), 0.97 (3H, t, *J* = 7.2 Hz, $OCH_2CH_3$); $^{13}C$ NMR ($CDCl_3$, DEPT-135) δ 169.3 (C, O-C=O), 168.6 (C, O-C=O), 154.1 (C), 149.3 (C), 129.0 (CH), 127.1 (CH), 126.3 (C), 125.8 (CH), 122.9 (CH), 69.8 ($CH_2$), 67.8 (C), 61.7 ($CH_2$, $OCH_2CH_3$), 45.4 (CH), 35.3 ($CH_2$), 26.5 ($CH_2$), 21.9 ($CH_2$), 21.2 ($CH_3$, $O{=}CCH_3$), 13.7 ($CH_3$, $OCH_2CH_3$); LRMS m/z 316.10 ($M + H^+$), calcd for $C_{18}H_{21}NO_4$ 315.1471; Anal. calcd for $C_{18}H_{21}NO_4$ (315.1471): C, 68.55; H, 6.71; N, 4.44. Found: C, 68.46; H, 6.67; N, 4.51%.



(+)-9aa

# Check CIF/PLATON (standard) for (–)-6aa: Data block: dbr22

Bond precision: C-C = 0.0037 A Wavelength=1.54184

Cell: a=6.0553(2) b=13.8095(5) c=15.5347(5)

alpha=90 beta=90 gamma=90

Temperature: 293 K

| | Calculated | Reported |
|---|---|---|
| Volume | 1299.02(8) | 1299.02(8) |
| Space group | P 21 21 21 | P2(1)2(1)2( |
| Hall group | P 2ac 2ab | ? |
| Moiety formula | C14 H13 N O5 | ? |
| Sum formula | C14 H13 N O5 | C14 H13 N O5 |
| Mr | 275.25 | 275.28 |
| Dx,g cm-3 | 1.407 | 1.418 |
| Z | 4 | 4 |
| Mu (mm-1) | 0.911 | 0.912 |
| F000 | 576.0 | 576.0 |
| F000' | 578.04 | |
| h,k,lmax | 7,17,19 | 7,16,18 |
| Nref | 1496[ 2547] | 2486 |
| Tmin,Tmax | 0.769,0.864 | 0.955,1.000 |
| Tmin' | 0.720 | |

Correction method= MULTI-SCAN

Data completeness= 1.66/0.98 Theta(max)= 71.760

R(reflections)= 0.0438( 2093) wR2(reflections)= 0.1146( 2486)

S = 1.075 Npar= 181

## **Data block dbr22** - ellipsoid plot