

Electronic Supplementary Information

for

Multicomponent reactions involving tricycloxonium ylide intermediate: Diastereoselective synthesis of mono- and bisalkoxyoctahydro-1,4- benzodioxocin-6(5H)-one frameworks

Sengodagounder Muthusamy,*^a Janagiraman Krishnamurthi^a and Eringathodi Suresh^b

^a School of Chemistry, Bharathidasan University, Tiruchirappalli, Tamilnadu – 620 024 India. Fax: 91-431-2407043; Tel: 91-431-2407053; E-mail: muthu@bdu.ac.in

^b Central Salt & Marine Chemicals Research Institute, Bhavnagar - 364 002, India; Fax: +91 278 2567562; Tel: +91 278 2567760; E-mail: suresh@csmcri.org

List of contents

General procedure	Page S2-3
Characterization data for all new compounds 1 , 4 , 5a-f , 7a-f , 8-10 , 11a-e and 12a-e	Pages S4-S24
X-ray data for compound 11d	Pages S25-S28
¹ H NMR and ¹³ C NMR spectra of compound 5b	Page S29
¹ H NMR and ¹³ C NMR spectra of compound 7b	Page S30
¹ H NMR and ¹³ C NMR spectra of compound 9	Page S31
¹ H NMR and ¹³ C NMR spectra of compound 10	Page S32
¹ H NMR and ¹³ C NMR spectra of compound 11a	Page S33
DEPT-135 NMR spectrum of compound 11a	Page S34
¹ H NMR and ¹³ C NMR spectra of compound 12d	Page S35
¹ H NMR and ¹³ C NMR spectra of compound 12e	Page S36

Experimental Section

General Procedure. The melting points are uncorrected. The FT-IR spectra were recorded using KBr method. ^1H NMR and ^{13}C NMR spectra (200 MHz and 50.3 MHz, respectively) were referenced to TMS. Carbon types were determined from DEPT ^{13}C NMR experiments. The diastereomeric purity was determined based on the crude NMR data. Mass analyses were performed with an ionizing voltage of 70 eV method unless otherwise stated. High resolution mass analyses were performed using electrospray ionization technique. All reactions were carried out under an argon atmosphere and glasswares were dried in an oven before using for catalytic diazo decomposition reaction. Dry solvents have freshly been prepared for every reaction. Analytical thin layer chromatography (TLC) was performed on alumina plates and components were visualized by observation under iodine and UV-Light. Column chromatography was performed on a silica gel (100-200 mesh) column.

Typical Procedure, Method A: To an oven-dried flask, a mixed solution containing an excess amount of the appropriate alcohol and rhodium(II) acetate (0.3 mol %) in dry dichloromethane (20 mL, dried over phosphorous pentoxide) was taken under N_2 atmosphere. After the mixture was stirred for 2 min, a CH_2Cl_2 solution (2 mL) of α -diazo ketone (1.1 mmol) **1** was added through a syringe pump over 2h at 10 °C. After completion of the addition, the reaction mixture was washed with 15 mL of aqueous NaHCO_3 . The aqueous phase was extracted with CH_2Cl_2 (3x15 mL) and combined organic phase was dried over anhydrous NaSO_4 . The solvent was removed under reduced pressure and the resulting residue purified using silica gel flash column chromatography (hexane/EtOAc) to afford the respective product.

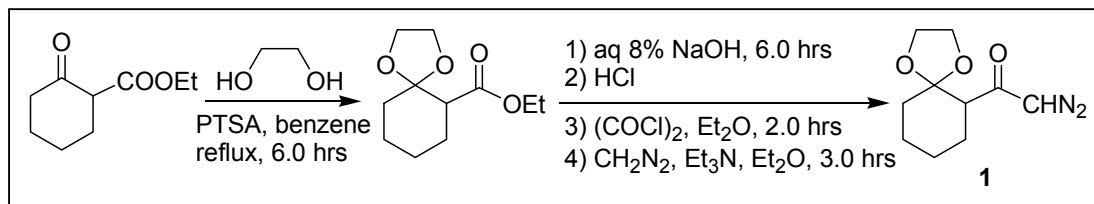
Method B: To an oven-dried flask, a mixed solution containing rhodium(II) acetate (0.3 mol %), titanium(IV) isopropoxide (1.1 mmol) and the appropriate aldehyde (1.0 mmol) in

dry dichloromethane (20 mL, dried over phosphorous pentoxide) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (4 mL) of α -diazo ketone (1.1 mmol) **1** was added through a syringe pump over 2h at rt. The reaction mixture was washed with 20 mL of aqueous NaHCO₃. The aqueous phase was extracted with CH₂Cl₂ (3x25 mL) and the procedure further followed as described above.

Method C: To an oven-dried flask, a mixed solution containing an excess amount of appropriate alcohol, rhodium(II) acetate (0.3 mol %), titanium(IV) isopropoxide (1.0 mmol) and the appropriate aldehyde (1.0 mmol) in dry dichloromethane (20 mL, dried over phosphorous pentoxide) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (4 mL) of α -diazo ketone (1.1 mmol) **1** was added through a syringe pump over 3h at 10 °C. The procedure was further followed as described above.

Method D: To an oven-dried flask, a mixed solution containing an appropriate alcohol, rhodium(II) acetate (0.5 mol %), titanium(IV) isopropoxide (2.4 mmol) and the appropriate dialdehyde (1.0 mmol) in dry dichloromethane (25 mL, dried over phosphorous pentoxide) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (10 mL) of α -diazo ketone (2.1 mmol) **1** was added through a syringe pump over 5h at 5 °C. After completion of the addition, the reaction mixture was warmed to attain the room temperature and the reaction mixture washed with 35 mL of aqueous NaHCO₃. The aqueous phase was extracted with CH₂Cl₂ (4x25 mL), and the procedure further followed as described above.

All new compounds exhibited spectral data consistent with their structures.



2-Diazo-1-(1,4-dioxaspiro[4.5]dec-6-yl)ethanone (1):

The diazo ketone **1** was prepared from 2-oxocyclohexanecarboxylic acid ethyl ester according to the above scheme by utilizing conventional method: i.e., acetalization,¹ alkaline hydrolysis, acid chloride formation and diazomethylation.² Overall yield of diazo ketone **1** from the corresponding starting ester was 70%.

¹H NMR (200 MHz, CDCl₃) δ 1.46-1.22 (m, 3H), 1.84-1.51 (m, 5H), 2.62 (t, $J = 7.4$ Hz, 1H, CH), 3.97-3.90 (m, 4H), 5.59 (s, 1H, CHN₂).

¹³C NMR (50.3 MHz, CDCl₃) δ 22.8 (CH₂), 23.3 (CH₂), 26.4 (CH₂), 54.9 (CH), 55.9 (CH), 108.7 (quat-C), 194.1 (C=O).

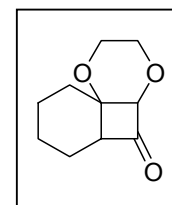
ν_{\max} (KBr)/cm⁻¹ 2939, 2891, 2865, 2101, 1730, 1636, 1446, 1368, 1339, 1140, 929.

Thick yellow oil.

1. A Daignault, and E. L. Eliel, *Organic Syntheses* 1973, Col. Vol. **5**, 303.
2. S. Muthusamy, S. A. Babu, C. Gunanathan, E. Suresh, P. Dastidar and R. V. Jasra, *Tetrahedron*, 2000, **56**, 6307.

Hexahydro-4aH-benzo[1,4]cyclobuta[1,2-b][1,4]dioxin-5(5aH)-one (4):

A solution containing rhodium(II) acetate (2.0 mg, 0.3 mol %) in dry dichloromethane (20 mL) was added a CH₂Cl₂ solution (2 mL) of 2-diazo-1-(1,4-dioxaspiro[4.5]dec-6-yl)ethanone (**1**) (200 mg, 0.95 mmol) under N₂ atmosphere afforded the product **4** (152 mg, in 88%) as thick oil.



^1H NMR (200 MHz, CDCl_3) δ 1.31-1.15 (m, 3H), 1.73-1.53 (m, 2H), 2.12-1.87 (m, 2H), 2.65-2.54 (m, 1H), 3.61-3.51 (m, 2H), 3.94-3.84 (m, 2H), 3.88 (s, 1H, CH), 4.91 (d, J = 1.7 Hz, 1H, CH).

^{13}C NMR (50.3 MHz, CDCl_3) δ 22.0 (CH_2), 22.7 (CH_2), 24.1 (CH_2), 26.6 (CH_2), 56.6 (CH), 60.6 (CH_2), 62.7 (CH_2), 81.0 (CH), 98.8 (*quat-C*), 206.4 ($\text{C}=\text{O}$).

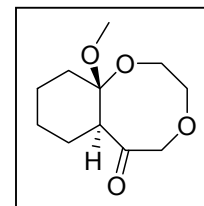
$\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 2933, 2863, 1787, 1452, 1337, 1280, 1167, 1083, 881.

HRMS (ESI^+ , LCMS) for $\text{C}_{10}\text{H}_{14}\text{O}_3$ [$(\text{M}+\text{Na})^+$] calcd 205.0919, Found 205.0945.

10a-Methoxyoctahydro-1,4-benzodioxocin-6(5H)-one (5a): A mixed solution containing rhodium(II) acetate (3.5 mg, 0.3 mol %) and an excess amount of methanol (0.150 mL, 5.0 mmol) in dry dichloromethane (20 mL) was taken under N_2 atmosphere. After the mixture was stirred for 2 min, a CH_2Cl_2 solution (4 mL) of 2-diazo-1-(1,4-dioxaspiro[4.5]dec-6-yl)ethanone (**1**) (200 mg, 0.95 mmol) was added through a syringe pump over 2h at 10 °C to afford the product **5a** (173 mg, in 85%) as a single diastereomer based on method A; Colourless thick oil.

^1H NMR (200 MHz, CDCl_3) δ 1.26-1.12 (m, 2H), 1.52-1.35 (m, 2H), 1.81-1.62 (m, 2H), 2.20-2.10 (m, 2H), 3.14 (s, 3H, CH_3), 3.45-3.25 (m, 3H), 3.72-3.60 (m, 2H), 4.14-4.03 (m, 2H).

^{13}C NMR (50.3 MHz, CDCl_3) δ 22.0 (CH_2), 24.2 (CH_2), 25.8 (CH_2), 32.4 (CH_2), 47.7 (CH_3), 53.5 (CH), 57.5 (CH_2), 71.1 (CH_2), 75.1 (CH_2), 102.6 (*quat-C*), 214.4 ($\text{C}=\text{O}$).

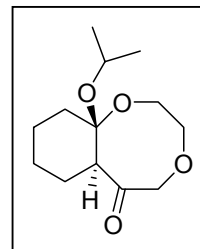


$\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 2937, 2863, 1711, 1624, 1587, 1448, 1253, 1126, 1073, 923.

HRMS (ESI^+ , LCMS) for $\text{C}_{11}\text{H}_{18}\text{O}_4$ [$(\text{M}+\text{Na})^+$] calcd 237.1181, Found 237.1197.

10a-Isopropoxyoctahydro-1,4-benzodioxocin-6(5H)-one (5b):

A mixed solution containing rhodium(II) acetate (3.5 mg, 0.3 mol %) and an excess amount of isopropanol (0.300 mL, 5.0 mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 2 min, a CH₂Cl₂ solution (5 mL) of 2-diazo-1-(1,4-dioxaspiro[4.5]dec-6-yl)ethanone (**1**) (250 mg, 1.2 mmol) was



added through a syringe pump over 2h at 10 °C to afford the product **5b** (202 mg, in 70%) as a single diastereomer based on method A; Colourless thick oil.

¹H NMR (200 MHz, CDCl₃) δ 1.12 (d, *J* = 6.0 Hz, 3H, CH₃), 1.18 (d, *J* = 6.0 Hz, 3H, CH₃), 1.71-1.25 (m, 5H), 2.12-1.77 (m, 3H), 3.46-3.23 (m, 4H), 3.83-3.62 (m, 2H), 4.13-3.90 (m, 2H).

¹³C NMR (50.3 MHz, CDCl₃) δ 22.6 (CH₂), 23.4 (CH₃), 23.9 (CH₃), 24.4 (CH₂), 25.8 (CH₂), 33.9 (CH₂), 53.8 (CH₂), 59.0 (CH), 63.5 (CH), 73.5 (CH₂), 75.4 (CH₂), 103.1 (*quat-C*), 213.9 (*C=O*).

ν_{\max} (KBr)/cm⁻¹ 2935, 2863, 172, 1622, 1584, 1448, 1253, 1124, 1072, 924.

HRMS (ESI⁺, LCMS) for C₁₃H₂₂O₄ [(M+Na)⁺] calcd 265.1494, Found 265.1497.

10a-(Allyloxy)octahydro-1,4-benzodioxocin-6(5*H*)-one (5c):

A mixed solution containing rhodium(II) acetate (3.5 mg, 0.3 mol %) and an excess amount of allyl alcohol (0.300 mL, 5.0 mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 2 min, a CH₂Cl₂ solution (5 mL) of α-diazo ketone **1** (250 mg, 1.2 mmol) was added through a syringe pump over 2h at 10 °C to furnish the product **5c** (213 mg, in 74%) as a single diastereomer based on method A. Colourless thick oil.

^1H NMR (200 MHz, CDCl_3) δ 1.78-1.28 (m, 6H), 2.11-1.98 (m, 2H), 3.44-3.24 (m, 3H), 3.75-3.66 (m, 2H), 3.95-3.86 (m, 2H), 4.16-4.02 (m, 2H), 5.09 (dd, $J_1 = 10.4$ Hz, $J_2 = 1.7$ Hz, 1H), 5.35-5.25 (m, 1H), 5.86-5.81 (m, 1H).

^{13}C NMR (50.3 MHz, CDCl_3) δ 22.2 (CH_2), 24.3 (CH_2), 25.8 (CH_2), 33.5 (CH_2), 53.8 (CH), 57.9 (CH_2), 60.7 (CH_2), 71.1 (CH_2), 75.2 (CH_2), 102.6 (*quat-C*), 115.3 (CH_2), 134.1 (CH), 213.8 ($\text{C}=\text{O}$).

$\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 2933, 2870, 1712, 1450, 1356, 1252, 1127, 1079, 953.

MS (EI, 70 eV): m/z (%) 240 (M^+ , 42), 199 (22), 183 (78), 141 (24), 125 (32), 81 (33) 68 (42), 55 (100).

HRMS (ESI $^+$, LCMS) for $\text{C}_{13}\text{H}_{20}\text{O}_4$ [$(\text{M}+2)+\text{Na}$] $^+$] calcd 265.1338, Found 265.1356.

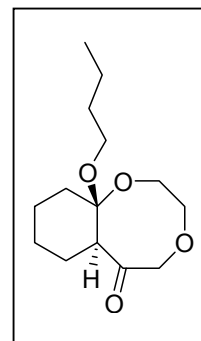
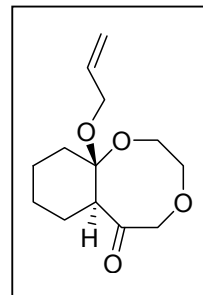
10a-Butoxyoctahydro-1,4-benzodioxocin-6(5H)-one (5d):

A mixed solution containing rhodium(II) acetate (3.5 mg, 0.3 mol %) and an excess amount of n-butanol (0.300 mg, 4.0 mmol) in dry dichloromethane (20 mL) was taken under N_2 atmosphere. After the mixture was stirred for 2 min, a CH_2Cl_2 solution (3 mL) of 2-diazo-1-(1,4-dioxaspiro[4.5]dec-6-yl)ethanone (**1**) (200 mg, 0.95 mmol) was added through a syringe pump over 2h at 10 $^\circ\text{C}$ to afford the product **5d** (176 mg, in 72%) as a single diastereomer based on method A.

Colourless solid: mp 79-81 $^\circ\text{C}$ (Chloroform/Hexane).

^1H NMR (200 MHz, CDCl_3) δ 0.91 (t, $J = 7.1$ Hz, 3H, CH_3), 1.77-1.21 (m, 9H), 2.13-1.93 (m, 3H), 3.44-3.20 (m, 4H), 3.81-3.59 (m, 3H), 4.14-4.02 (m, 2H).

^{13}C NMR (50.3 MHz, CDCl_3) δ 13.7 (CH_3), 19.4 (CH_2), 22.2 (CH_2), 22.8 (CH_2), 24.3 (CH_2), 25.8 (CH_2), 31.5 (CH_2), 33.2 (CH_2), 53.9 (CH), 57.6 (CH_2), 59.5 (CH_2), 71.1 (CH_2), 75.2 (CH_2), 102.3 (*quat-C*), 213.8 ($\text{C}=\text{O}$).

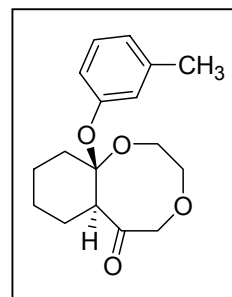


$\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 2941, 2859, 1710, 1624, 1587, 1446, 1253, 1236, 1126, 1073, 924.

HRMS (ESI⁺, LCMS) for C₁₄H₂₄O₄ [(M+Na)⁺] calcd 279.1651, Found 279.1688.

10a-(3-Methylphenoxy)octahydro-1,4-benzodioxocin-6(5H)-one (5e):

A mixed solution containing rhodium(II) acetate (3.5 mg, 0.3 mol %) and an excess amount of *m*-cresol (0.300 mL, 2.7 mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 2 min, a CH₂Cl₂ solution (2 mL) of α -dialdo ketone **1** (150 mg, 0.7 mmol) was added through a syringe



pump over 2h at 10 °C to afford the product **5e** (133 mg, in 64%) as a single diastereomer based on method A.

Colourless solid: mp 88-90 °C (Chloroform/Hexane).

¹H NMR (200 MHz, CDCl₃) δ 1.35-1.25 (m, 2H), 1.65-1.45 (m, 2H), 1.85-1.73 (m, 2H), 2.30 (s, 3H, CH₃), 2.35-2.15 (m, 2H), 3.67-3.35 (m, 3H), 4.00-3.76 (m, 2H), 4.20-4.11 (m, 2H), 6.82 (d, *J* = 7.1 Hz, 1H, ArH), 6.70-6.94 (m, 1H, ArH), 7.10 (d, *J* = 7.1 Hz, 1H, ArH), 7.26 (s, 1H, ArH).

¹³C NMR (50.3 MHz, CDCl₃) δ 21.3 (CH₃), 21.7 (CH₂), 24.1 (CH₂), 26.1 (CH₂), 32.9 (CH₂), 54.3 (CH), 58.8 (CH₂), 71.2 (CH₂), 75.3 (CH₂), 104.8 (*quat*-C), 117.0 (=CH), 120.9 (=CH), 123.3 (=CH), 128.7 (=CH), 139.0 (*quat*-C), 153.8 (*quat*-C), 213.8 (C=O).

MS (EI, 70 eV): *m/z* (%) 290 (M⁺, 5), 183 (100), 154 (8), 125 (24), 108 (43), 81 (25) 69 (27), 55 (55).

HRMS (ESI⁺, LCMS) for C₁₇H₂₂O₄ [(M+Na)⁺] calcd 313.1494, Found 313.1528.

6-Oxoctahydro-1,4-benzodioxocin-10a(5H)-yl 4-methylbenzoate (5f):

A mixed solution containing rhodium(II) acetate (3.5 mg, 0.3 mol %) and an excess amount of *p*-methylbenzoic acid (0.400 mg, 3.1 mmol) in dry dichloromethane (20 mL)

was taken under N₂ atmosphere. After the mixture was stirred for 2 min, a CH₂Cl₂ solution (4 mL) of α -diazo ketone **1** (200 mg, 0.95 mmol) was added through a syringe pump over 2h at 10 °C to attain the product **5f** (206 mg, in 68%) as a single diastereomer based on method A.

Colourless solid: mp 117-119 °C (Chloroform/Hexane).

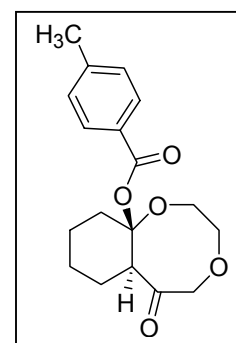
¹H NMR (200 MHz, CDCl₃) δ 1.42-1.26 (m, 2H), 1.80-1.59 (m, 4H), 2.32-2.13 (m, 2H), 2.43 (s, 3H, CH₃), 3.48-3.35 (m, 2H), 3.83-3.62 (m, 3H), 4.15-4.04 (m, 2H), 7.38 (s, 2H, ArH), 7.93 (s, 2H, ArH).

¹³C NMR (50.3 MHz, CDCl₃) δ 21.2 (CH₃), 22.3 (CH₂), 23.9 (CH₂), 25.8 (CH₂), 34.1 (CH₂), 54.0 (CH), 60.0 (CH₂), 71.1 (CH₂), 75.6 (CH₂), 106.5 (quat-C), 126.9 (=CH), 128.3 (=CH), 130.3 (=CH), 133.9 (=CH), 138.0 (quat-C), 164.0 (quat-C), 213.7 (C=O).

MS (EI, 70 eV): m/z (%) 318 (M⁺, 5), 182 (25), 136 (26), 119 (55), 91 (57), 84 (62) 68 (60), 49 (100).

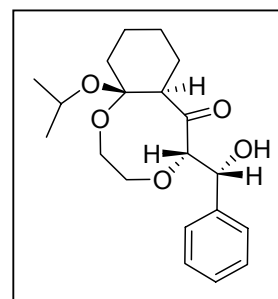
ν_{\max} (KBr)/cm⁻¹ 2979, 2983, 2946, 1745, 1709, 1598, 1446, 1250, 1152, 1131, 991, 883.

HRMS (ESI⁺, LCMS) for C₁₈H₂₂O₅ [(M+Na)⁺] calcd 341.1443, Found 341.1438.



10a-Isopropoxy-5-[hydroxy(phenyl)methyl]octahydro-1,4-benzodioxocin-6(5H)-one

(7a): A mixed solution containing rhodium(II) acetate (3.5 mg, 0.3 mol %), titanium(IV) isopropoxide (0.330 mL, 1.2 mmol) and benzaldehyde (110 mg, 1.0 mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (8 mL) of 2-diazo-1-(1,4-



dioxaspiro[4.5]dec-6-yl)ethanone (**1**) (250 mg, 1.2 mmol) was added through a syringe pump over 2.5h at room temperature to furnish the product **7a** (327 mg, in 79%) as a single diastereomer based on method B.

Colourless solid: mp 138-140 °C (chloroform/hexane).

^1H NMR (200 MHz, CDCl_3) δ 1.10 (d, $J = 6.0$ Hz, 3H, CH_3), 1.12 (d, $J = 6.0$ Hz, 3H, CH_3), 2.05-1.38 (m, 6H), 2.79 (d, 1H, $J = 6.2$ Hz), 3.34-3.19 (m, 4H), 3.73-3.65 (m, 2H), 4.09-3.93 (m, 3H), 4.86 (bs, 1H), 7.34-7.27 (m, 5H, ArH).

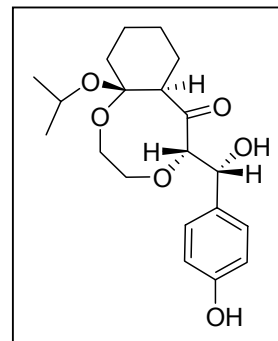
^{13}C NMR (50.3 MHz, CDCl_3) δ 22.8 (CH_2), 23.5 (CH_3), 24.0 (CH_3), 24.6 (CH_2), 26.1 (CH_2), 34.1 (CH_2), 55.2 (CH), 59.2 (CH_2), 63.6 (CH), 71.5 (CH_2), 75.2 (CH_2), 87.4 (CH), 103.5 (*quat-C*), 126.3 (=CH), 127.8 (=CH), 128.2 (=CH), 140.3 (*quat-C*), 214.7 (C=O).

ν_{max} (KBr)/ cm^{-1} 3465, 2978, 294, 1711, 1610, 1444, 1250, 1152, 1133, 991.

HRMS (ESI⁺, LCMS) for $\text{C}_{20}\text{H}_{28}\text{O}_5$ [(M+Na)⁺] calcd 371.1913, Found 371.1920.

5-[Hydroxy(4-hydroxyphenyl)methyl]-10a-isopropoxyoctahydro-1,4-benzodioxocin-

6(5H)-one (7b): A mixed solution containing rhodium(II) acetate (4.0 mg, 0.3 mol %), titanium(IV) isopropoxide (0.260 mL, 0.8 mmol) and 4-hydroxybenzaldehyde (87 mg, 0.7 mmol) in dry dichloromethane (20 mL) was taken under N_2 atmosphere. After the mixture was stirred for 5 min, a CH_2Cl_2 solution (4 mL) of 2-diazo-1-(1,4-dioxaspiro[4.5]dec-6-yl)ethanone (**1**) (150 mg, 0.7



mmol) was added through a syringe pump over 3h at room temperature to furnish the product **7b** (226 mg, in 87%) as a single diastereomer based on method B.

Colourless solid: mp 142-144 °C (chloroform/hexane).

^1H NMR (CDCl_3 , 200 MHz) δ 1.10 (br s, 3H, CH_3), 1.17 (br s, 3H, CH_3), 1.93-1.26 (m, 6H), 2.12-2.05 (m, 2H), 3.33-3.25 (m, 3H), 3.74-3.61 (m, 2H), 4.14-3.97 (m, 3H), 4.75 (s, 1H), 5.32 (broad-s, 1H), 6.80-6.76 (m, 2H, ArH), 7.21 (s, 2H, ArH).

^{13}C NMR ($\text{CDCl}_3+\text{CD}_3\text{OD}$, 50.3 MHz) δ 22.7 (CH_2), 23.2 (CH_3), 23.7 (CH_3), 24.4 (CH_2), 26.0 (CH_2), 34.0 (CH_2), 55.0 (CH), 59.0 (CH_2), 63.5 (CH), 71.1 (CH_2), 74.8 (CH) 87.8

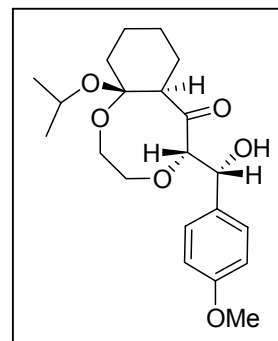
(CH), 103.5 (*quat-C*), 114.7 (=CH), 127.5 (=CH), 131.8 (*quat-C*), 156.2 (*quat-C*), 215.6 (C=O).

$\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 3495, 2971, 2931, 1705, 1611, 1448, 1248, 1147, 1131, 994, 825.

HRMS (ESI⁺, LCMS) for C₂₀H₂₈O₆ [(M+Na)⁺] calcd 387.1794, Found 387.1818.

5-[Hydroxy(4-methoxyphenyl)methyl]-10a-isopropoxyoctahydro-1,4-benzodioxcin-

6(5*H*)-one (7c): A mixed solution containing rhodium(II) acetate (3.5 mg, 0.3 mol %), titanium(IV) isopropoxide (0.260 mL, 0.8 mmol) and 4-methoxybenzaldehyde (95 mg, 0.7 mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (4 mL) of α -diazo ketone **1** (150 mg, 0.7 mmol) was added through a syringe



pump over 2h at room temperature to afford the product **7c** (243 mg, in 90%) as a single diastereomer based on method B.

Colourless solid: mp 134-136 °C (chloroform/hexane).

¹H NMR (CDCl₃, 200 MHz) δ 1.11 (d, *J* = 6.0 Hz, 3H CH₃), 1.31 (d, *J* = 6.0 Hz, 3H CH₃), 1.95-1.20 (m, 6H), 2.10-2.02 (m, 2H), 3.30-3.19 (m, 3H), 3.68-3.60 (m, 2H), 3.78 (s, 3H, OCH₃), 4.15-3.89 (m, 3H), 4.77 (bs, 1H), 6.84 (d, *J* = 8.6 Hz, 2H arom-*H*), 7.27 (d, *J* = 8.6 Hz, 2H arom-*H*).

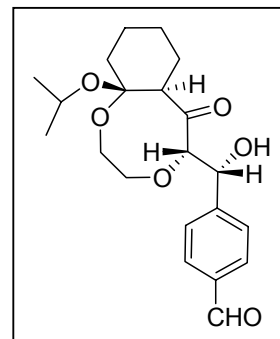
¹³C NMR (CDCl₃, 50.3 MHz) δ 22.7 (CH₂), 23.3 (CH₃), 23.9 (CH₃), 24.4 (CH₂), 26.0 (CH₂), 34.0 (CH₂), 55.0 (OCH₃), 59.0 (CH₂), 63.4 (CH), 71.2 (CH₂), 74.7 (CH), 87.5 (CH), 103.3 (*quat-C*), 113.4 (CH), 127.5 (CH) 132.4 (*quat-C*), 159.0 (*quat-C*), 214.7 (C=O).

$\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 3508, 2968, 2933, 1705, 1613, 1514, 1447, 1253, 1151, 1134, 995, 826.

HRMS (ESI⁺, LCMS) for C₂₁H₃₀O₆ [(M+Na)⁺] calcd 401.1962, Found 401.1975.

4-[Hydroxy(10a-isopropoxy-6-oxodecahydro-1,4-benzodioxocin-5-

yl)methyl]benzaldehyde (7d): A mixed solution containing rhodium(II) acetate (4 mg, 0.3 mol %), titanium(IV) isopropoxide (0.350 mL, 1.1 mmol) and terephthalaldehyde (130 mg, 1.0 mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (6 mL) of α -diazo ketone **1** (200 mg, 0.95



mmol) was added through a syringe pump over 2h at 10 °C to afford the product **7d** (279 mg, in 78%) as a single diastereomer based on method B.

Colourless solid: mp 172-174 °C (chloroform/hexane).

¹H NMR (CDCl₃, 200 MHz) δ 1.03 (d, J = 6.2 Hz, 3H, CH₃), 1.10 (d, J = 6.2 Hz, 3H, CH₃), 1.91-1.16 (m, 5H), 2.06-1.92 (m, 3H), 3.37-3.15 (m, 4H), 3.69-3.58 (m, 2H), 4.13-4.01 (m, 2H), 4.97 (brod-s, 1H, OH), 7.55 (d, J = 8.0 Hz, 2H, ArH), 7.85 (d, J = 8.0 Hz, 2H, ArH), 9.99 (s, 1H, CHO).

¹³C NMR (CDCl₃, 50.3 MHz) δ 22.1 (CH₂), 23.2 (CH₃), 23.7 (CH₃), 24.3 (CH₂), 25.9 (CH₂), 32.5 (CH₂), 54.9 (CH), 57.7 (CH₂), 63.4 (CH), 71.2 (CH₂), 74.9 (CH) 86.9 (CH), 103.2 (*quat*-C), 126.7 (=CH), 129.5 (=CH), 135.9 (*quat*-C), 147.4 (*quat*-C), 191.9 (C=O), 215.0 (C=O).

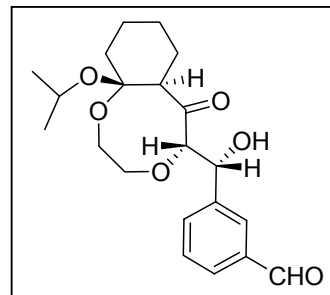
ν_{\max} (KBr)/cm⁻¹ 3390, 2943, 1698, 1609, 1450, 1423, 1266, 1096, 739, 519.

HRMS (ESI⁺, LCMS) for C₂₁H₂₈O₆ [(M+Na)⁺] calcd 399.1806, Found 399.1810.

3-[Hydroxy(10a-isopropoxy-6-oxodecahydro-1,4-benzodioxocin-5-

yl)methyl]benzaldehyde (7e): A mixed solution containing rhodium(II) acetate (4 mg, 0.3 mol %), titanium(IV) isopropoxide (0.350 mL, 1.1 mmol) and isophthalaldehyde (130, 1.0

mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (6 mL) of 2-diazo-1-(1,4-dioxaspiro[4.5]dec-6-yl)ethanone (**1**) (200 mg, 0.95 mmol) was added through a syringe pump over 2h at 10



°C to attain the product **7e** (260 mg, in 72%) as a single diastereomer based on method B. Colourless solid: mp 164-166 °C (chloroform/hexane).

¹H NMR (CDCl₃, 200 MHz) δ 1.02 (d, *J* = 6.2 Hz, 3H, CH₃), 1.09 (d, *J* = 6.2 Hz, 3H, CH₃), 1.76-1.36 (m, 6H), 2.01-1.82 (m, 2H), 3.23-3.18 (m, 3H), 3.66-3.58 (m, 2H), 4.18-3.86 (m, 3H), 4.98 (brod-s, 1H), 7.43-7.37 (m, 1H, ArH), 7.63-7.52 (m, 1H, ArH), 7.74 (d, *J* = 7.6 Hz, 1H, ArH), 7.82 (s, 1H, ArH), 9.93 (s, 1H, CHO).

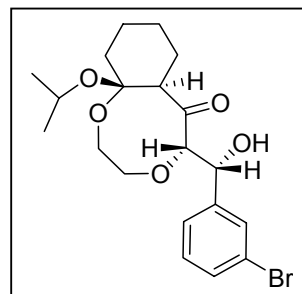
¹³C NMR (CDCl₃, 50.3 MHz) δ 22.5 (CH₂), 23.2 (CH₃), 23.7 (CH₃), 24.6 (CH₂), 34.9 (CH₂), 54.8 (CH), 58.9 (CH₂), 63.4 (CH), 71.3 (CH₂), 74.2 (CH₂), 86.9 (CH), 103.2 (*quat*-C), 127.5 (=CH), 128.5 (=CH), 132.1 (=CH), 136.0 (*quat*-C), 141.4 (*quat*-C), 191.8 (C=O), 214.0 (C=O).

ν_{\max} (KBr)/cm⁻¹ 3456, 2983, 1705, 1604, 1454, 1444, 1261, 1096, 726.

HRMS (ESI⁺, LCMS) for C₂₁H₂₈O₆ [(M+Na)⁺] calcd 399.1806, Found 399.1824.

5-[(3-Bromophenyl)(hydroxy)methyl]-10a-isopropoxyoctahydro-1,4-benzodioxocin-

6(5H)-one (7f): A mixed solution containing rhodium(II) acetate (0.3 mol %), titanium(IV) isopropoxide (0.430 mL, 1.4 mmol) and 3-bromobenzaldehyde (220 mg, 1.2 mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a



CH₂Cl₂ solution (8 mL) of α -diazo ketone **1** (250 mg, 1.2 mmol) was added through a syringe pump over 2h at room temperature to afford the product **7f** (416 mg, in 82%) as a single diastereomer based on method B.

Colourless solid: mp 181-183 °C (chloroform/hexane).

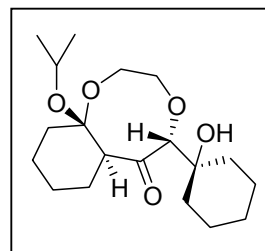
¹H NMR (CDCl₃, 200 MHz) δ 1.03 (d, J = 6.2 Hz, 3H, CH₃), 1.10 (d, J = 6.2 Hz, 3H, CH₃), 1.97-1.46 (m, 7H), 2.02-1.95 (m, 1H), 3.34-3.12 (m, 4H), 3.65-3.53 (m, 2H), 4.03-3.82 (m, 2H), 4.77 (broad-s, 1H), 7.23-7.08 (m, 2H, ArH), 7.42 (d, J = 7.6 Hz, 1H, ArH), 7.48 (s, 1H, ArH).

¹³C NMR (CDCl₃, 50.3 MHz) δ 22.73, (CH₂), 23.4 (CH₃), 23.9 (CH₃), 24.4 (CH₂), 25.9 (CH₂), 33.9 (CH₂), 55.0 (CH), 59.0 (CH₂), 63.5 (CH), 71.3 (CH₂), 74.4 (*quat*-C), 87.0 (CH), 103.4 (*quat*-C), 122.2 (*quat*-C), 124.9 (=CH), 129.3 (=CH), 129.5 (=CH), 130.6 (=CH), 143.0 (*quat*-C), 215.0 (C=O).

HRMS (ESI⁺, LCMS) for C₂₀H₂₇BrO₅ [(M+Na)⁺] calcd 449.0962, Found 449.0942.

5-(1-Hydroxycyclohexyl)-10a-isopropoxyoctahydro-1,4-

benzodioxocin-6(5H)-one (8): A mixed solution containing rhodium(II) acetate (0.3 mol %), titanium(IV) isopropoxide (0.350 mL, 1.1 mmol) and cyclohexanone (95 mg, 1.0 mmol)



in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (6 mL) of 2-diazo-1-(1,4-dioxaspiro[4.5]dec-6-yl)ethanone (**1**) (200 mg, 0.95 mmol) was added through a syringe pump over 2h at 10 °C to furnish the product **8** (226 mg, in 82%) as a single diastereomer based on method B.

Colourless solid: mp 112-114 °C (chloroform/hexane).

^1H NMR (CDCl_3 , 200 MHz) δ 1.11 (d, $J = 6.0$ Hz, 3H CH_3), 1.19 (d, $J = 6.0$ Hz, 3H CH_3), 1.98-1.25 (m, 17H), 2.14-2.02 (m, 1H), 2.56 (bs, 1H, OH), 3.55-3.17 (m, 4H), 3.81-3.67 (m, 1H), 4.07-3.92 (m, 1H), 4.24-4.10 (m, 1H).

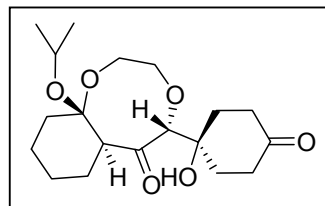
^{13}C NMR (CDCl_3 , 50.3 MHz) δ 21.2, (CH_2), 21.4 (CH_2), 22.6 (CH_2), 23.2 (CH_3), 23.8 (CH_3), 24.5 (CH_2), 25.4 (CH_2), 26.0 (CH_2), 33.1 (CH_2), 33.9 (CH_2), 34.2 (CH_2), 55.4 (CH), 58.9 (CH_2), 63.3 (CH), 71.2 (CH_2), 73.2 (*quat-C*), 89.2 (CH), 103.1 (*quat-C*), 215.0 ($\text{C}=\text{O}$).

$\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3418, 1702, 1587, 1450, 1421, 1333, 1250, 1079, 1030.

HRMS (ESI^+ , LCMS) for $\text{C}_{19}\text{H}_{32}\text{O}_5$ [$(\text{M}+\text{Na})^+$] calcd 363.2170, Found 363.2158.

5-(1-Hydroxy-4-oxocyclohexyl)-10a-isopropoxyoctahydro-1,4-benzodioxocin-6(5H)-

one (9): A mixed solution containing rhodium(II) acetate (0.3 mol %), titanium(IV) isopropoxide (0.350 mL, 1.1 mmol) and 1,4-cyclohexanedione (105 mg, 1.0 mmol) in dry dichloromethane (20 mL) was taken under N_2 atmosphere.



After the mixture was stirred for 5 min, a CH_2Cl_2 solution (6 mL) of α -diazo ketone **1** (200 mg, 0.95 mmol) was added through a syringe pump over 2h at room temperature to afford the product **9** (256 mg, in 76%) as a single diastereomer based on method B.

Colourless solid: mp 127-129 $^\circ\text{C}$ (chloroform/hexane).

^1H NMR (CDCl_3 , 200 MHz) δ 1.12 (d, $J = 6.0$ Hz, 3H, CH_3), 1.18 (d, $J = 6.0$ Hz, 3H, CH_3), 1.96-1.90 (m, 4H), 1.86-1.66 (m, 2H), 1.60-1.38 (m, 2H), 1.29-1.26 (m, 1H), 2.27-2.04 (m, 4H), 2.79-2.62 (m, 3H), 3.25-3.15 (m, 2H), 3.52-3.34 (m, 2H), 3.81-3.69 (m, 1H), 4.05-3.93 (m, 1H), 4.25-4.11 (m, 1H).

^{13}C NMR (CDCl_3 , 50.3 MHz) δ 22.6 (CH_2), 23.3 (CH_3), 23.9 (CH_3), 24.5 (CH_2), 26.1 (CH_2), 32.9 (CH_2), 33.2 (CH_2), 34.0 (CH_2), 36.3 (CH_2), 36.5 (CH_2), 55.2 (CH), 59.1

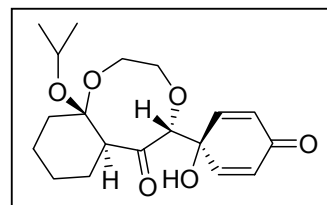
(CH₂), 63.6 (CH), 71.6 (CH₂), 72.0 (*quat*-C), 88.6 (CH), 103.2 (*quat*-C), 211.1 (C=O),
215.0 (C=O).

ν_{\max} (KBr)/cm⁻¹ 3454, 1678, 1703, 1455, 1444, 1286, 1130, 1056, 1021, 927.

HRMS (ESI⁺, LCMS) for C₁₉H₃₀O₆ [(M+Na)⁺] calcd 377.2018, Found 377.2022.

5-(1-Hydroxy-4-oxocyclohexa-2,5-dien-1-yl)-10a-isopropoxyoctahydro-1,4-

benzodioxocin-6(5*H*)-one (10): A mixed solution containing rhodium(II) acetate (0.3 mol %), titanium(IV) isopropoxide (0.260 mL, 0.9 mmol) and 1, 4-bezoquinone (75 mg, 0.7 mmol) in dry dichloromethane (20 mL) was taken under N₂



atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (4 mL) of 2-diazo-1-(1,4-dioxaspiro[4.5]dec-6-yl)ethanone (**1**) (150 mg, 0.7 mmol) was added through a syringe pump over 2h at 10 °C to attain the product **10** (210 mg, in 84%) as a single diastereomer based on method B.

Colourless solid: mp 95-97 °C (chloroform/hexane).

¹H NMR (CDCl₃, 200 MHz) δ 1.09 (d, *J* = 6.0 Hz, 3H, CH₃), 1.16 (d, *J* = 6.0 Hz, 3H, CH₃), 1.88-1.25 (m, 6H), 2.13-2.03 (m, 2H), 3.18 (dd, *J*₁ = 12.8 Hz, *J*₂ = 3.0 Hz, 1H), 3.76-3.32 (m, 5H), 4.09-3.87 (m, 1H), 4.26-4.13 (m, 1H), 6.23-6.14 (m, 2H), 6.95-6.85 (m, 2H).

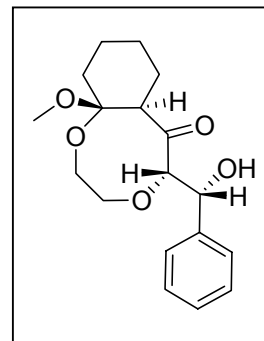
¹³C NMR (CDCl₃, 50.3 MHz) δ 22.6 (CH₂), 23.3 (CH₃), 23.8 (CH₃), 24.3 (CH₂), 25.8 (CH₂), 33.9 (CH₂), 55.1 (CH), 58.9 (CH₂), 63.7 (CH), 70.4 (*quat*-C), 71.8 (CH₂), 88.5 (CH), 103.2 (*quat*-C), 128.6 (CH), 129.1 (CH), 146.4 (CH), 147.1 (CH), 184.9 (C=O), 211.6 (C=O).

ν_{\max} (KBr)/cm⁻¹ 3476, 2986, 1696, 1711, 1478, 1435, 1252, 1133, 1041, 1020, 923.

HRMS (ESI⁺, LCMS) for C₁₉H₂₆O₆ [(M+Na)⁺] calcd 373.1649, Found 373.1682

5-[Hydroxy(phenyl)methyl]-10a-methoxyoctahydro-1,4-benzodioxocin-6(5H)-one

(11a): A mixed solution containing rhodium(II) acetate (3.5 mg, 0.3 mol %), titanium(IV) isopropoxide (0.310 mL, 1.0 mmol), an excess amount of methanol (0.200 mL, 5 mmol) and benzaldehyde (125 mg, 1.2 mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (8 mL) of 2-diazo-1-(1,4-



dioxaspiro[4.5]dec-6-yl)ethanone (**1**) (250 mg, 1.2 mmol) was added through a syringe pump over 3h at 10 °C to afford the product **11a** (310 mg, in 81%) as a single diastereomer based on method C.

Colourless solid: mp 145-147 °C (chloroform/hexane).

¹H NMR (CDCl₃, 200 MHz) δ 1.82-1.09 (m, 6H), 2.05-1.88 (m, 1H), 2.86 (d, J = 6.6 Hz, 1H), 3.11 (s, 3H, OCH₃), 3.35-3.19 (m, 4H), 3.69-3.57 (m, 2H), 4.13-4.00 (m, 1H), 4.86 (d, J = 3.2 Hz, 1H, CH), 7.35-7.29 (m, 5H, ArH).

¹³C NMR (CDCl₃, 50.3 MHz) δ 22.1 (CH₂), 24.3 (CH₂), 25.9 (CH₂), 32.5 (CH₂), 47.9 (OCH₃), 54.8 (CH), 57.7 (CH₂), 71.0 (CH₂), 75.3 (CH) 87.2 (CH), 103.0 (*quat*-C), 126.1 (=CH), 127.7 (=CH), 128.0 (=CH), 140.4 (*quat*-C), 215.5 (C=O).

ν_{\max} (KBr)/cm⁻¹ 3458, 2935, 2854, 1703, 1447, 1357, 1271, 1163, 1130, 1058, 925, 696.

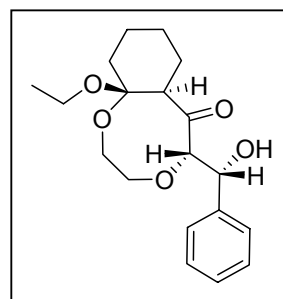
HRMS (ESI⁺, LCMS) for C₁₈H₂₄O₅ [(M+Na)⁺] calcd 343.1521, Found 343.1525.

10a-Ethoxy-5-[hydroxy(phenyl)methyl]octahydro-1,4-benzodioxocin-6(5H)-one

(11b):

A mixed solution containing rhodium(II) acetate (0.3 mol %), titanium(IV) isopropoxide (0.310 mL, 1.0 mmol), an excess amount of ethanol (0.300 mL, 5 mmol) and benzaldehyde (125 mg, 1.0 mmol) in dry dichloromethane (20 mL) was taken under N₂

atmosphere. After the mixture was stirred for 5 min, a CH_2Cl_2 solution (8 mL) of α -diazo ketone **1** (250 mg, 1.2 mmol) was added through a syringe pump over 3h at 10 °C to afford the product **11b** (305 mg, in 77%) as a single diastereomer based on method C.



Colourless solid: mp 130-132 °C (chloroform/hexane).

^1H NMR (200 MHz, CDCl_3) δ 1.10 (t, $J = 7.2$ Hz, 3H), 1.71-1.28 (m, 6H), 2.08-1.78 (m, 2H), 3.04 (d, $J = 6.0$ Hz, 1H), 3.45-3.19 (m, 4H), 3.73-3.59 (m, 2H), 4.10-3.94 (m, 2H), 4.85-4.80 (m, 1H), 7.33-7.22 (m, 5H, ArH).

^{13}C NMR (50.3 MHz, CDCl_3) δ 14.9 (CH_3), 22.3 (CH_2), 24.3 (CH_2), 25.9 (CH_2), 33.3 (CH_2), 54.9 (CH), 55.5 (CH_2), 57.6 (CH_2), 71.0 (CH_2), 75.2 (CH), 87.3 (CH), 102.8 (*quat-C*), 126.2 (CH), 127.6 (CH), 128.0 (CH), 140.3 (*quat-C*), 214.8 ($\text{C}=\text{O}$).

$\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3465, 2972, 2938, 1699, 1451, 1361, 1254, 1151, 1132, 1060, 954, 703.

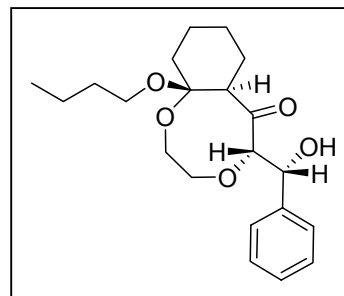
HRMS (ESI^+ , LCMS) for $\text{C}_{19}\text{H}_{26}\text{O}_5$ [$\text{M}+\text{Na}^+$] calcd 357.1700, Found 357.1738.

10a-Butoxy-5-[hydroxy(phenyl)methyl]octahydro-1,4-benzodioxocin-6(5H)-one

(11c): A mixed solution containing rhodium(II) acetate (0.3 mol %), titanium(IV) isopropoxide (0.280 mL, 1.0 mmol), an excess amount of n-butanol (350 mg, 5 mmol) and benzaldehyde (105 mg, 1.0 mmol) in dry dichloromethane (20 mL) was taken under N_2 atmosphere. After the mixture was stirred for 5 min, a CH_2Cl_2 solution (5 mL) of α -diazo ketone **1** (200 mg, 0.95 mmol) was added through a syringe pump over 3h at 10 °C to furnish the product **11c** (172 mg, in 50%) as a single diastereomer based on method C.

Colourless solid: mp 139-141 °C (chloroform/hexane).

^1H NMR (200 MHz, CDCl_3) δ 0.9 (t, $J = 7.2$ Hz, 3H), 1.81-



1.08 (m, 10H), 2.11-1.86 (m, 3H), 2.88 (d, $J = 6.0$ Hz, 1H), 3.33-3.16 (m, 4H), 3.75-3.61 (m, 2H), 4.15-4.03 (m, 1H), 4.83 (bs, 1H), 7.33-7.27 (m, 5H, arom- H).

^{13}C NMR (50.3 MHz, CDCl_3) δ 13.8 (CH_3), 19.5 (CH_2), 22.3 (CH_2), 24.4 (CH_2), 26.0 (CH_2), 31.6 (CH_2), 33.3 (CH_2), 55.5 (CH), 57.8 (CH_2), 59.7 (CH_2), 71.1 (CH_2), 75.3 (CH), 87.4 (CH), 102.7 (*quat-C*), 126.3 (CH), 127.8 (CH), 128.1 (CH), 140.2 (*quat-C*), 214.6 ($\text{C}=\text{O}$);

HRMS (ESI $^+$, LCMS) for $\text{C}_{21}\text{H}_{30}\text{O}_5$ [($\text{M}+\text{Na}$) $^+$] calcd 385.1993, Found 385.2021.

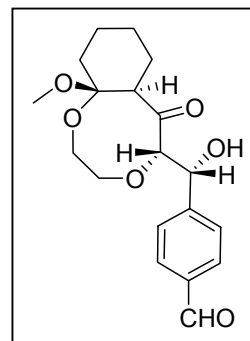
4-[Hydroxy(10a-methoxy-6-oxodecahydro-1,4-benzodioxin-5-methyl)]benzaldehyde

(11d): A mixed solution containing rhodium(II) acetate (4.0 mg, 0.3 mol %), titanium(IV) isopropoxide (0.360 mL, 1.2 mmol), an excess amount of methanol (0.200 mL, 5 mmol) and benzaldehyde (160 mg, 1.2 mmol) in dry dichloromethane (20 mL) was taken under N_2 atmosphere. After the mixture was stirred for 5 min, a CH_2Cl_2 solution (8 mL) of α -diazo ketone **1** (250 mg, 1.2 mmol) was added through a syringe pump over 3h at 10 $^\circ\text{C}$ to furnish the product **11d** (320 mg, in 78%) as a single diastereomer based on method C.

Colourless solid: mp 157-159 $^\circ\text{C}$ (chloroform/hexane).

^1H NMR (CDCl_3 , 200 MHz) δ 1.91-1.15 (m, 6H), 2.05-1.90 (m, 2H), 3.12 (s, 3H, OCH_3), 3.37-3.15 (m, 4H), 3.69-3.58 (m, 2H), 4.13-4.01 (m, 1H), 4.97 (s, 1H, CH), 7.55 (d, $J = 8.0$ Hz, 2H, ArH), 7.85 (d, $J = 8.0$ Hz, 2H, ArH), 9.99 (s, 1H, CHO).

^{13}C NMR (CDCl_3 , 50.3 MHz) δ 22.1 (CH_2), 24.3 (CH_2), 25.9 (CH_2), 32.5 (CH_2), 48.0 (OCH_3), 54.9 (CH), 57.7 (CH_2), 71.2 (CH_2), 74.9 (CH) 86.9 (CH), 103.0 (*quat-C*), 126.8 ($=\text{CH}$), 129.5 ($=\text{CH}$), 135.8 (*quat-C*), 147.4 (*quat-C*), 191.8 ($\text{C}=\text{O}$), 215.1 ($\text{C}=\text{O}$).

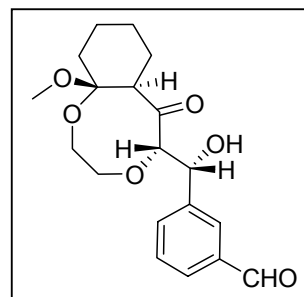


$\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 3473, 2933, 2854, 1700, 1608, 1541, 1455, 1359, 1211, 1130, 1085, 826.

HRMS (ESI⁺, LCMS) for C₁₉H₂₄O₆ [(M+Na)⁺] calcd 371.1471, Found 371.1454.

3-[Hydroxy(10a-methoxy-6-oxodecahydro-1,4-benzodioxocin-5-yl)methyl]

benzaldehyde (11e): A mixed solution containing rhodium(II) acetate (0.3 mol %), titanium(IV) isopropoxide (0.360 mL, 1.2 mmol), an excess amount of methanol (0.200 mL, 5 mmol) and benzaldehyde (160 mg, 1.2 mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere.



After the mixture was stirred for 5 min, a CH₂Cl₂ solution (8 mL) of α -diazo ketone **1** (250 mg, 1.2 mmol) was added through a syringe pump over 3h at 10 °C to afford the product **11e** (265 mg, in 64%) as a single diastereomer based on method C.

Colourless solid: mp 153-155 °C (chloroform/hexane).

¹H NMR (CDCl₃, 200 MHz) δ 1.97-1.24 (m, 6H), 2.13-2.03 (m, 2H), 3.11 (s, 3H, OCH₃), 3.47-3.15 (m, 4H), 3.76-3.58 (m, 2H), 4.13-4.01 (m, 1H), 4.98 (d, *J* = 2.8 Hz, 1H, CH), 7.54-7.47 (m, 1H, ArH), 7.66 (d, *J* = 7.6 Hz, 1H, ArH), 7.80 (d, *J* = 7.6 Hz, 1H, ArH), 7.91 (s, 1H, ArH), 9.99 (s, 1H, CHO).

¹³C NMR (CDCl₃, 50.3 MHz) δ 22.0 (CH₂), 24.3 (CH₂), 25.8 (CH₂), 32.4 (CH₂), 47.9 (OCH₃), 54.8 (CH), 57.7 (CH₂), 71.1 (CH₂), 74.6 (CH), 86.9 (CH), 102.9 (quat-C), 127.7 (=CH), 128.7 (=CH), 128.8 (=CH), 132.3 (=CH), 136.2 (quat-C), 141.8 (quat-C), 192.1 (C=O), 215.2 (C=O).

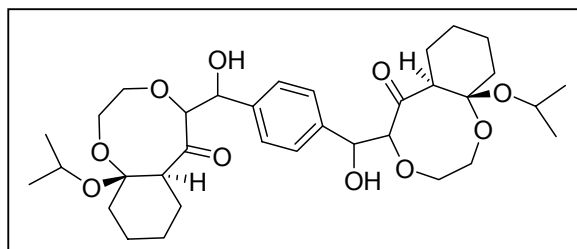
$\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 3478, 2930, 2878, 2854, 1706, 1554, 1454, 1363, 1211, 1133, 1090, 830.

HRMS (ESI⁺, LCMS) for C₁₉H₂₄O₆ [(M+Na)⁺] calcd 371.1471, Found 371.1476.

Compound 12a: A mixed solution containing rhodium(II) acetate (5.5 mg, 0.5 mol %), titanium(IV) isopropoxide (0.750 mL, 2.4 mmol) and terephthalaldehyde (134 mg, 1.0 mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (10 mL) of 2-diazo-1-(1,4-dioxaspiro[4.5]dec-6-yl)ethanone (**1**) (440 mg, 2.1 mmol) was added through a syringe pump over 5h at 5 °C to afford the product **12a** (456 mg, 82%) as

a single diastereomer based on method D.

Colourless solid: mp 193-195 °C (chloroform/hexane).



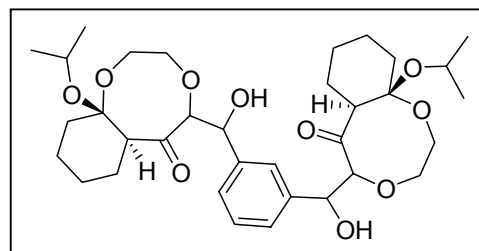
¹H NMR (CD₃OD, 200 MHz) δ 1.07 (d, J = 6.0 Hz, 6H CH₃), 1.17 (d, J = 6.0 Hz, 6H CH₃), 1.81-1.44 (m, 12H), 2.13-2.01 (m, 4H), 3.43-3.14 (m, 8H), 3.71-3.58 (m, 4H), 4.03-3.93 (m, 4H), 4.82 (bs, 2H), 7.37 (s, 2H, ArH), 7.89 (s, 2H, ArH).

¹³C NMR (50.3 MHz, CD₃OD) δ 22.2 (CH₃), 22.3 (CH₃), 22.8 (CH₂), 24.1 (CH₂), 25.6 (CH₂), 33.7 (CH₂), 54.3 (CH), 54.8 (CH₂), 63.0 (CH), 71.2 (CH₂), 74.4 (CH), 87.3 (CH), 103.1 (quat-C), 126.1 (=CH), 140.3 (quat-C), 216.4 (C=O).

ν_{\max} (KBr)/cm⁻¹ 3455, 2972, 2938, 2865, 1707, 1450, 1360, 1269, 1257, 1177, 1133, 999.

HRMS (ESI⁺, LCMS) for C₃₄H₅₀O₁₀ [(M+Na)⁺] calcd 641.3302, Found 641.3275.

Compound 12b: A mixed solution containing rhodium(II) acetate (0.5 mol %), titanium(IV) isopropoxide (0.750 mL, 2.4 mmol) and isophthalaldehyde (134 mg, 1.0 mmol) in dry



dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (10 mL) of α -diazo ketone **1** (440 mg, 2.1 mmol) was added

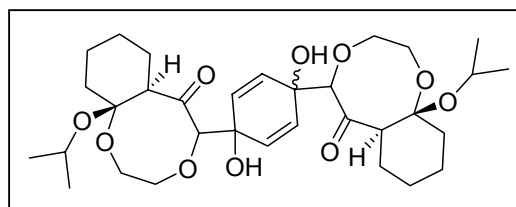
through a syringe pump over 5h at 5 °C to afford the product **12b** (389 mg, in 70%) as a single diastereomer based on method D.

Colourless solid: mp 159-161 °C (chloroform/hexane).

¹H NMR (CD₃OD, 200 MHz) δ 1.11 (d, *J* = 6.0 Hz, 6H CH₃), 1.17 (d, *J* = 6.0 Hz, 6H CH₃), 1.81-1.21 (m, 12H), 2.13-2.01 (m, 4H), 3.43-3.14 (m, 6H), 3.73-3.63 (m, 5H), 4.12-3.95 (m, 5H), 4.84 (bs, 2H), 7.32 (s, 1H) 7.32-730 (m, 3H, ArH).

¹³C NMR (50.3 MHz, CD₃OD) δ 24.3 (CH₃), 24.4 (CH₂), 24.8 (CH₃), 26.1 (CH₂), 27.6 (CH₂), 35.7 (CH₂), 56.8 (CH), 60.8 (CH₂), 65.0 (CH), 72.7 (CH₂), 76.9 (CH), 89.4 (CH), 105.1 (*quat-C*), 125.8 (CH), 126.8 (CH), 129.0 (CH), 142.9 (*quat-C*), 218.4 (C=O).
 ν_{\max} (KBr)/cm⁻¹ 3473, 2972, 2938, 2864, 1709, 1450, 1360, 1271, 1257, 1167, 1132, 998.
HRMS (ESI⁺, LCMS) for C₃₄H₅₀O₁₀ [(M+Na)⁺] calcd 641.3302, Found 641.3323.

Compound 12c: A mixed solution containing rhodium(II) acetate (0.5 mol %), titanium(IV) isopropoxide (2.4 mmol) and 1,4-benzoquinone (110 mg, 1.0 mmol) in dry



dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (10 mL) of α-diazo ketone **1** (440 mg, 2.1 mmol) was added through a syringe pump over 5h at 5 °C to furnish the product **12c** (344 mg, in 65%) as two diastereomeric mixture in the ratio of 2:1. based on method D. Colourless semi solid.

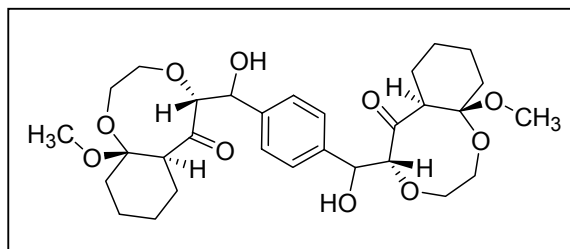
Major isomer: ¹H NMR (CDCl₃, 200 MHz) δ 1.15 (d, *J* = 6.0 Hz, 6H CH₃), 1.19 (d, *J* = 6.0 Hz, 6H CH₃), 2.36-1.45 (m, 14H), 3.45-3.23 (m, 4H), 3.82-3.69 (m, 4H), 4.28-3.86 (m, 4H), 4.30 (s, 2H), 5.30 (s, 2H), 6.00-5.97 (m, 4H).

¹³C NMR (CDCl₃, 50.3 MHz) δ 21.8, (CH₂), 22.1 (CH₂), 22.7 (CH₂), 23.4 (CH₃), 24.0 (CH₃), 24.5 (CH₂), 26.0 (CH₂), 30.2 (CH₂), 34.1 (CH₂), 55.2 (CH), 59.1 (CH₂), 61.5

(CH₂), 63.5 (CH), 68.9 (*quat*-C), 71.3 (CH₂), 71.7 (CH₂), 73.4 (CH₂), 88.2 (CH), 103.3 (*quat*-C), 129.6, (=CH), 130.3 (=CH), 213.2 (C=O).

HRMS (ESI⁺, LCMS) for C₃₂H₄₈O₁₀ [(M+Na)⁺] calcd 615.3223, Found 615.3231.

Compound 12d: A mixed solution containing rhodium(II) acetate (0.5 mol %), titanium(IV) isopropoxide (0.625 mL, 2.0 mmol), an excess amount of methanol (0.700 mL, 10 mmol) and



terephthalaldehyde (1.0 mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (10 mL) of 2-diazo-1-(1,4-dioxaspiro[4.5]dec-6-yl)ethanone (**1**) (440 mg, 2.1 mmol) was added through a syringe pump over 5h at 5 °C to attain the product **12d** (318 mg, in 63%) as a single diastereomer based on method D.

Colourless solid: mp 188-190 °C (chloroform/hexane).

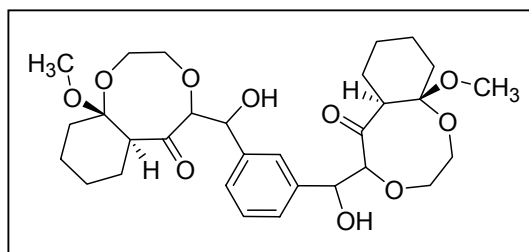
¹H NMR (CDCl₃, 200 MHz) δ 1.92-1.11 (m, 10H), 2.13-1.99 (m, 4H), 2.64 (d, *J* = 6.6 Hz, 2H), 3.12 (s, 6H, OCH₃), 3.38-3.16 (m, 6H), 3.73-3.60 (m, 4H), 4.16-4.04 (m, 2H), 4.86 (d, *J* = 3.4 Hz, 2H, *CH*), 7.35 (s, 4H, *ArH*).

¹³C NMR (CDCl₃, 50.3 MHz) δ 22.1 (CH₂), 24.3 (CH₂), 25.9 (CH₂), 32.5 (CH₂), 47.9 (OCH₃), 54.8 (CH), 57.7 (CH₂), 71.0 (CH₂), 75.1 (CH) 87.2 (CH), 103.0 (*quat*-C), 126.1 (=CH), 140.0 (*quat*-C), 215.3 (C=O).

ν_{\max} (KBr)/cm⁻¹ 3456, 2978, 2938, 2858, 1709, 1444, 1358, 1261, 1254, 1167, 1130, 998.

HRMS (ESI⁺, LCMS) for C₃₀H₄₂O₁₀ [(M+Na)⁺] calcd 585.2676, Found 585.2702.

Compound 12e: A mixed solution containing rhodium(II) acetate (0.5 mol %), titanium(IV) isopropoxide (0.625 mL, 2.0 mmol), an excess amount of methanol



(0.700 mL) and isophthalaldehyde (134 mg, 1.0 mmol) in dry dichloromethane (20 mL) was taken under N₂ atmosphere. After the mixture was stirred for 5 min, a CH₂Cl₂ solution (8 mL) of α -diazo ketone **1** (440 mg, 2.1 mmol) was added through a syringe pump over 5h at 5 °C to afford the product **12e** (273 mg, in 54%) as a single diastereomer based on method D.

Colourless solid: mp 165-167 °C (chloroform/hexane).

¹H NMR (CDCl₃, 200 MHz) δ 1.28-1.10 (m, 4H), 1.89-1.35 (m, 8H), 2.12-2.03 (m, 4H), 3.10-3.07 (m, 2H), 3.11 (s, 6H, OCH₃), 3.36-3.19 (m, 6H), 3.64-3.57 (m, 4H), 4.13-4.06 (m, 2H), 4.84 (s, 2H, CH), 7.29 (s, 1H, ArH), 7.39-7.32 (m, 3H, ArH). ¹³C NMR (CDCl₃, 50.3 MHz) δ 22.2 (CH₂), 24.4 (CH₂), 26.0 (CH₂), 32.6 (CH₂), 48.0 (OCH₃), 54.8 (CH), 57.8 (CH₂), 71.1 (CH₂), 75.3 (CH) 87.3 (CH), 103.0 (quat-C), 124.4 (=CH), 125.7 (=CH), 128.0 (=CH), 140.4 (quat-C), 140.5 (quat-C), 215.4 (C=O).

ν_{\max} (KBr)/cm⁻¹ 3473, 2972, 2938, 2864, 1709, 1450, 1360, 1271, 1257, 1167, 1132, 998.

HRMS (ESI⁺, LCMS) for C₃₀H₄₂O₁₀ [(M+Na)⁺] calcd 585.2676, Found 585.2704.

Table S1. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **11d** $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

Atom	x	y	z	U(eq)
O(11)	4737(2)	18610(18)	13441(12)	40(6)
O(1)	3170(2)	27201(19)	2688(12)	42(6)
O(13)	4154(2)	3554(2)	25650(13)	44(6)
O(4)	1926(2)	48768(19)	8830(13)	42(6)
O(15)	4053(2)	6421(2)	18644(15)	51(6)
H(15)	4469	6881	2209	76
C(6)	3824(3)	4023(3)	19108(19)	34(7)
C(6A)	4732(3)	3970(3)	12727(17)	34(7)
H(6A)	4458	4642	900	40
C(10A)	4527(3)	2806(3)	7740(18)	37(8)
C(5)	2465(3)	4768(3)	17210(18)	39(8)
H(5)	1750	4387	1977	46
C(16)	1558(3)	6867(3)	18437(19)	40(8)
C(7)	6264(3)	4157(3)	1678(2)	44(8)
H(7A)	6543	3531	2077	53
H(7B)	6356	4923	1958	53
C(10)	5522(4)	2769(3)	182(2)	50(9)
H(10A)	5251	3385	-225	60
H(10B)	5438	1997	-89	60
C(19)	-721(4)	8374(3)	1348(2)	51(9)
C(17)	1663(4)	7850(3)	1368(2)	47(9)
H(17)	2511	8007	1205	56
C(14)	2798(3)	6018(3)	2093(2)	41(8)
H(14)	2977	5936	2683	49
C(2)	1971(3)	2687(3)	654(2)	45(8)
H(2A)	2286	2536	1227	53
H(2B)	1358	2031	430	53
C(18)	531(4)	8611(3)	1127(2)	54(10)
H(18)	625	9283	815	65
O(23)	-1941(4)	1.0031(3)	665(2)	94(11)
C(3)	1152(3)	3845(3)	543(2)	49(9)
H(3A)	827	3981	-31	58

H(3B)	326	3760	786	58
C(12)	4545(4)	667(3)	1025(2)	58(10)
H(12A)	3644	609	669	86
H(12B)	4586	105	1461	86
H(12C)	5277	486	731	86
C(9)	7066(4)	2967(4)	601(2)	61(11)
H(9A)	7371	2304	966	73
H(9B)	7657	2979	197	73
C(21)	296(4)	6649(3)	2081(2)	54(10)
H(21)	210	5998	2414	65
C(8)	7248(4)	4137(4)	1071(2)	59(10)
H(8A)	7035	4809	702	71
H(8B)	8217	4215	1355	71
C(20)	-835(4)	7394(4)	1827(2)	60(11)
H(20)	-1690	7233	1981	71
C(22)	-1969(5)	9146(4)	1066(2)	67(12)
H(22)	-2818	8932	1208	81

Table S2. Bond lengths [\AA] and angles [$^\circ$] for compound **11d**

C(1)-O(11)	1.433(2)	C(10)-H(10B)	0.9700
O11-C10A	1.413(4)	C(19)-C(18)	1.359(5)
O11-C12	1.433(4)	C(19)-C(20)	1.375(5)
O(1)-C(10A)	1.423(4)	C(19)-C(22)	1.483(5)
O(1)-C(2)	1.434(4)	C(17)-C(18)	1.381(5)
O(13)-C(6)	1.206(3)	C(17)-H(17)	0.9300
O(4)-C(5)	1.413(4)	C(14)-H(14)	0.9800
O(4)-C(3)	1.429(4)	C(2)-C(3)	1.505(4)
O(15)-C(14)	1.416(4)	C(2)-H(2A)	0.9700
O(15)-H(15)	0.8200	C(2)-H(2B)	0.9700
C(6)-C(6A)	1.516(4)	C(18)-H(18)	0.9300
C(6)-C(5)	1.534(4)	O(23)-C(22)	1.198(5)
C(6A)-C(7)	1.521(4)	C(3)-H(3A)	0.9700
C(6A)-C(10A)	1.537(4)	C(3)-H(3B)	0.9700
C(6A)-H(6A)	0.9800	C(12)-H(12A)	0.9600
C(10A)-C(10)	1.515(4)	C(12)-H(12B)	0.9600
C(5)-C(14)	1.535(4)	C(12)-H(12C)	0.9600
C(5)-H(5)	0.9800	C(9)-C(8)	1.517(5)
C(16)-C(17)	1.372(5)	C(9)-H(9A)	0.9700
C(16)-C(21)	1.377(5)	C(9)-H(9B)	0.9700
C(16)-C(14)	1.521(4)	C(21)-C(20)	1.373(5)
C(7)-C(8)	1.525(5)	C(21)-H(21)	0.9300
C(7)-H(7A)	0.9700	C(8)-H(8A)	0.9700
C(7)-H(7B)	0.9700	C(8)-H(8B)	0.9700
C(10)-C(9)	1.539(5)	C(20)-H(20)	0.9300
C(10)-H(10A)	0.9700	C(22)-H(22)	0.9300
C(10A)-O(11)-C(12)	116.4(2)	O(15)-C(14)-C(5)	107.4(2)
C(10A)-O(1)-C(2)	117.6(2)	C(16)-C(14)-C(5)	111.0(3)
C(5)-O(4)-C(3)	113.3(2)	O(15)-C(14)-H(14)	108.3
C(14)-O(15)-H(15)	109.5	C(16)-C(14)-H(14)	108.3
O(13)-C(6)-C(6A)	123.0(3)	C(5)-C(14)-H(14)	108.3
O(13)-C(6)-C(5)	119.3(3)	O(1)-C(2)-C(3)	111.9(3)
C(6A)-C(6)-C(5)	117.6(3)	O(1)-C(2)-H(2A)	109.2
C(6)-C(6A)-C(7)	108.9(2)	C(3)-C(2)-H(2A)	109.2
C(6)-C(6A)-C(10A)	112.9(2)	O(1)-C(2)-H(2B)	109.2
C(7)-C(6A)-C(10A)	111.9(2)	C(3)-C(2)-H(2B)	109.2
C(6)-C(6A)-H(6A)	107.6	H(2A)-C(2)-H(2B)	107.9
C(7)-C(6A)-H(6A)	107.6	C(19)-C(18)-C(17)	119.8(4)
C(10A)-C(6A)-H(6A)	107.6	C(19)-C(18)-H(18)	120.1
O(11)-C(10A)-O(1)	110.6(2)	C(17)-C(18)-H(18)	120.1
O(11)-C(10A)-C(10)	113.7(3)	O(4)-C(3)-C(2)	114.6(3)
O(1)-C(10A)-C(10)	103.5(2)	O(4)-C(3)-H(3A)	108.6
O(11)-C(10A)-C(6A)	105.6(2)	C(2)-C(3)-H(3A)	108.6
O(1)-C(10A)-C(6A)	113.0(2)	O(4)-C(3)-H(3B)	108.6

C(10)-C(10A)-C(6A)	110.6(3)	C(2)-C(3)-H(3B)	108.6
O(4)-C(5)-C(6)	113.0(2)	H(3A)-C(3)-H(3B)	107.6
O(4)-C(5)-C(14)	109.8(2)	O(11)-C(12)-H(12A)	109.5
C(6)-C(5)-C(14)	107.5(2)	O(11)-C(12)-H(12B)	109.5
O(4)-C(5)-H(5)	108.8	H(12A)-C(12)-H(12B)	109.5
C(6)-C(5)-H(5)	108.8	O(11)-C(12)-H(12C)	109.5
C(14)-C(5)-H(5)	108.8	H(12A)-C(12)-H(12C)	109.5
C(17)-C(16)-C(21)	118.7(3)	H(12B)-C(12)-H(12C)	109.5
C(17)-C(16)-C(14)	120.9(3)	C(8)-C(9)-C(10)	111.5(3)
C(21)-C(16)-C(14)	120.4(3)	C(8)-C(9)-H(9A)	109.3
C(6A)-C(7)-C(8)	112.1(3)	C(10)-C(9)-H(9A)	109.3
C(6A)-C(7)-H(7A)	109.2	C(8)-C(9)-H(9B)	109.3
C(8)-C(7)-H(7A)	109.2	C(10)-C(9)-H(9B)	109.3
C(6A)-C(7)-H(7B)	109.2	H(9A)-C(9)-H(9B)	108.0
C(8)-C(7)-H(7B)	109.2	C(20)-C(21)-C(16)	120.0(4)
H(7A)-C(7)-H(7B)	107.9	C(20)-C(21)-H(21)	120.0
C(10A)-C(10)-C(9)	112.1(3)	C(16)-C(21)-H(21)	120.0
C(10A)-C(10)-H(10A)	109.2	C(9)-C(8)-C(7)	109.8(3)
C(9)-C(10)-H(10A)	109.2	C(9)-C(8)-H(8A)	109.7
C(10A)-C(10)-H(10B)	109.2	C(7)-C(8)-H(8A)	109.7
C(9)-C(10)-H(10B)	109.2	C(9)-C(8)-H(8B)	109.7
H(10A)-C(10)-H(10B)	107.9	C(7)-C(8)-H(8B)	109.7
C(18)-C(19)-C(20)	119.5(3)	H(8A)-C(8)-H(8B)	108.2
C(18)-C(19)-C(22)	120.8(4)	C(21)-C(20)-C(19)	120.9(4)
C(20)-C(19)-C(22)	119.7(4)	C(21)-C(20)-H(20)	119.6
C(16)-C(17)-C(18)	121.1(3)	C(19)-C(20)-H(20)	119.6
C(16)-C(17)-H(17)	119.4	O(23)-C(22)-C(19)	123.5(5)
C(18)-C(17)-H(17)	119.4	O(23)-C(22)-H(22)	118.2
O(15)-C(14)-C(16)	113.5(3)	C(19)-C(22)-H(22)	118.2

