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Enantiomeric 4,4a,7,7a-tetrahydro-1*H*-cyclopenta[*c*]pyran-3-ones

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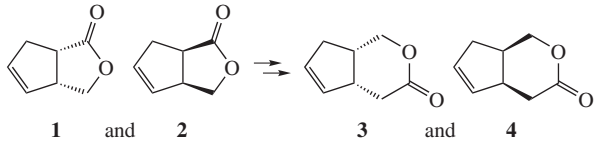
Based on γ-lactones 1 and 2, enantiomeric δ-lactones 3 and 4 were obtained and characterised.

Chiral vicinally disubstituted cyclopentene derivatives are of interest as key block synthons in the synthesis of prostaglandins, brefeldin A, cyclopentene antibiotics, *etc*.[1–5] In this work, we studied the conversion of the previously reported enantiomeric γ-lactones **1** and **2**[6] into corresponding topologically similar homologous δ-lactones **3** and **4** (Scheme 1).

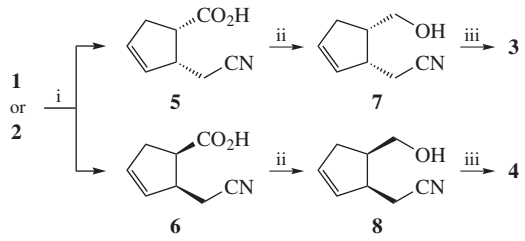


Scheme 1

Compounds **3** and **4** can find diverse applications in the synthesis of enantiomerically pure cyclopentanoids. Note that the syntheses of chiral lactone (+)-**4** and its use for the synthesis of prostaglandin precursors and next preclavulon A, isoprostanes, neuprostanes, *etc*. have been reported by Zanoni and Vidari.[7–10] Tietze *et al.* reported the sufficient labour-consuming chemoenzymatic synthesis of compounds **3** and **4**,[11] and used enantiomerically pure **4** for the synthesis of spinosyn A analogues.[12]

Thermal ring opening reactions with the cyanide ion were tested during the development of the γ-lactone → δ-lactone conversion, *i.e*., for homologation of γ-lactones **1** and **2**. These reactions smoothly occurred on heating the solutions of **1** or **2** with KCN in DMSO to 180 °C. Cyanoacids **5** and **6** containing ~5–10% of the corresponding *trans*-cyanoacids (epimers at the carboxyl-carrying centre) were converted without separation into mixed anhydrides by treatment with ethyl carbonate chloride and then reduced with sodium borohydride. Finally, acidic hydrolysis of cyanoalcohols **7** and **8** gave δ-lactones **3** and **4**. Simultaneously, the by-products – *trans*-cyanoacids formed during the preparation of compounds **5** and **6** – were also converted into corresponding *trans*-cyanoalcohols, which remained unchanged during the hydrolysis stage and were easily removed by column chromatography on SiO_2 from the target lactones (Scheme 2).

Enantiomeric δ-lactones **3**† and **4**‡ are colourless crystalline compounds that melt in a narrow temperature range (67.5–68.5 and 65.5–66.5 °C, respectively) and have specific rotations of –73.1 (*c* 1.15, CH_2Cl_2) for compound **3** and +72.8 (*c* 1.125, CH_2Cl_2) for compound **4**. Zanoni *et al.*[8] did not report the mp for compound (+)-**4** but did report $[\alpha]_D^{20}$ +77.8 (*c* 1.25, CH_2Cl_2), Tietze *et al.*[11] reported $[\alpha]_D^{20}$ +51.0 (*c* 0.30, CH_2Cl_2) for **4**.



Scheme 2 *Reagents and conditions*: i, KCN, DMSO, 180 °C, 1 h, 85%; ii, ClCOOEt, Et_3N, THF, 15 min, then $NaBH_4$, THF, 20 °C, 2 h, 95%; iii, dioxane–9 N H_2SO_4, reflux, 4 h, 85%.

References

1 M. T. Crimmins, *Tetrahedron*, 1998, **54**, 9229.
2 E. J. Corey, R. H. Wollenberg and D. R. Williams, *Tetrahedron Lett.*, 1977, **26**, 2243.
3 R. M. Scarboround, Jr., B. H. Toder and A. B. Smith, *J. Am. Chem. Soc*., 1980, **102**, 3904.
4 S. M. Roberts, M. Santoro and E. Sickle, *J. Chem. Soc., Perkin Trans. 1*, 2002, 1735.
5 R. E. Parker and N. S. Isaacs, *Chem. Rev*., 1959, **59**, 737.
6 A. M. Gimazetdinov, N. S. Vostrikov and M. S. Miftakhov, *Tetrahedron Asymmetry*, 2008, **19**, 1094.
7 G. Zanoni, S. Re, A. Merrigi, F. Castranovo and G. Vidari, *Tetrahedron Asymmetry*, 2001, **12**, 1785.
8 G. Zanoni, A. Porta, E. Brunoldi and G. Vidari, *J. Org. Chem*., 2006, **71**, 8459.
9 G. Zanoni, A. Porta, F. Castranovo and G. Vidari, *J. Org. Chem*., 2003, **68**, 6005.
10 G. Zanoni, E. Brunoldi, A. Porta and G. Vidari, *J. Org. Chem*., 2007, **72**, 9698.
11 L. F. Tietze, C. Stadler, N. Boehnke, G. Brashe and A. Grube, *Synlett*, 2007, **3**, 485.
12 L. F. Tietze, G. Brashe, A. Grube, N. Boehnke and C. Stadler, *Chem. Eur. J*., 2007, **13**, 8543.

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† *(4a*R*,7a*S*)-4,4a,7,7a-tetrahydro-1*H*-cyclopenta[*c*]pyran-3-one* **3**: colourless crystals, yield 85%, mp 67.5–68.5 °C; $[\alpha]_D^{20}$ –73.1 (*c* 1.15, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.21–2.43 (m, 2H, H-4, H-7), 2.60–2.85 (m, 3H, H-4, H-7, H-7a), 3.29–3.37 (m, 1H, H-4a), 4.00–4.10 (dd, 1H, H-1, *J* 9.2 and 11.6 Hz), 4.25–4.35 (dd, 1H, H-1, *J* 9.2 and 11.6 Hz), 5.54–5.59 (m, 1H, H-5), 5.73–5.79 (m, 1H, H-6). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 33.96 [C(4)], 33.98 [C(7a)], 36.23 [C(7)], 41.33 [C(4a)], 70.32 [C(1)], 130.94 [C(6)], 131.66 [C(5)], 173.33 [C(3)]. IR (KBr, ν/cm^{-1}): 3051, 2920, 1743 (C=O), 1622 (C=C), 1483, 1433, 1386, 1274, 1138, 1078, 991. MS (ACPI), *m*/*z* (%): 139 [MH$^+$] (100), 80 (43). Found (%): C, 69.23; H, 6.98. Calc. for $C_8H_{10}O_2$ (%): C, 69.55; H, 7.30.

‡ *(4a*S*,7a*R*)-4,4a,7,7a-tetrahydro-1*H*-cyclopenta[*c*]pyran-3-one* **4**: colourless crystals, yield 85%, mp 65.5–66.5 °C; $[\alpha]_D^{20}$ +72.8 (*c* 1.125, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.18–2.39 (m, 2H, H-4, H-7), 2.60–2.83 (m, 3H, H-4, H-7, H-7a), 3.28–3.37 (m, 1H, H-4a), 3.99–4.08 (dd, 1H, H-1, *J* 9.3 and 11.5 Hz), 4.25–4.33 (dd, 1H, H-1, *J* 9.3 and 11.5 Hz), 5.52–5.58 (m, 1H, H-5), 5.72–5.78 (m, 1H, H-6). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 33.93 [C(4)], 33.99 [C(7a)], 36.13 [C(7)], 41.36 [C(4a)], 70.23 [C(1)], 130.65 [C(6)], 131.81 [C(5)], 173.34 [C(3)]. IR (KBr, ν/cm^{-1}): 3043, 2922, 1746 (C=O), 1624 (C=C), 1485, 1427, 1383, 1273, 1131, 1072, 989. MS (ACPI), *m*/*z* (%): 139 [MH$^+$] (100), 80 (32). Found (%): C, 69.16; H, 6.93. Calc. for $C_8H_{10}O_2$ (%): C, 69.55; H, 7.30.

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