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A New Stereocontrolled Access to Angularly Disubstituted *cis*-Decalins *via* Tandem Radical Ring Expansion and Cyclization

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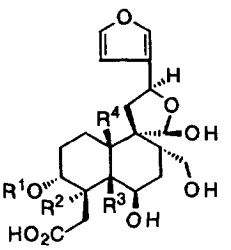
Abstract: The complete stereocontrolled access to angularly disubstituted *cis*-decalins based on the tandem radical ring expansion and cyclization process of α-iodomethylcyclopentanones **1** and **6** is described. The compounds **2–5** and **7–13** thus prepared could be versatile intermediates for the synthesis of biologically important compounds. Copyright © 1996 Elsevier Science Ltd

Angularly disubstituted *cis*-decalins constitute basic framework of many types of biologically important compounds[1] including neo-clerodane diterpenes musabalbisianes **A**, **B** and **C** (I–III)[2] isolated from the seeds of *Musa balbisiana* which show amoebicidal activity *in vitro* (Figure 1).

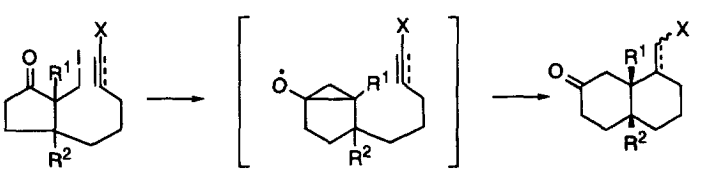
Figure 1



	R^1	R^2	R^3	R^4
I	H	CO_2H	CHO	CHO
II	H	CHO	CO_2H	CH_2OH
III	Ang	CH_2OH	CH_2OH	CH_2OH

We now communicate a novel stereocontrolled synthesis of angularly disubstituted *cis*-decalins **C**. This approach is stemmed from the tandem radical ring expansion and cyclization process[3] of α-iodomethyl substituted cyclopentanones **A** *via* cyclopropyl alkoxy radical **B**, by taking advantage of easy access to **A** which was recently developed by us[4] (Chart 1).

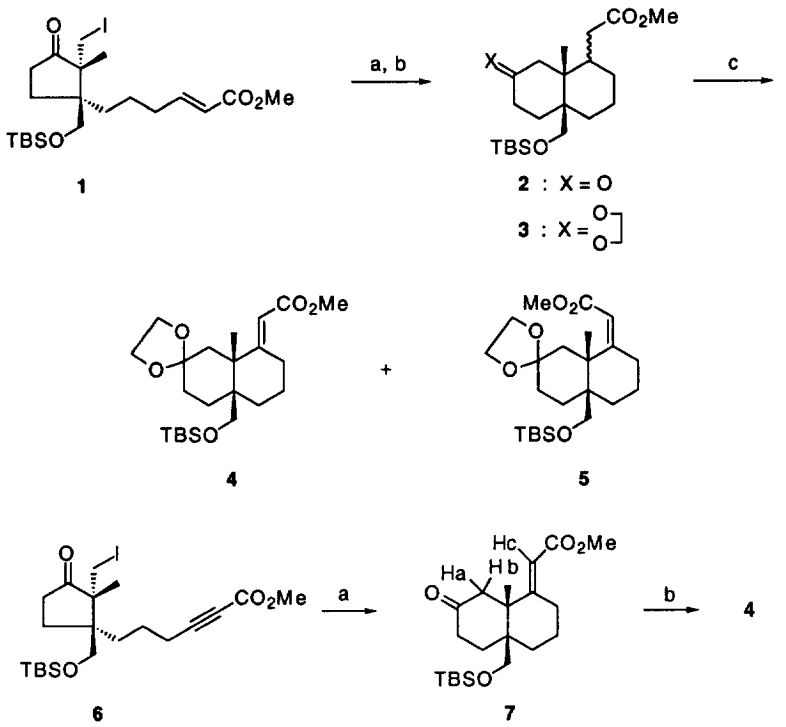
Chart 1



A **B** **C**

The tandem reaction of **1**[4] was effectively proceeded under radical conditions to give the *cis*-decalins **2** (1: 1 mixture of diastereomers) in 97% yield. The ketal **3** derived (85%) from **2** was converted to the easily separable mixture (1:4) of E (**4**)[5] and Z (**5**)[5] unsaturated esters in 67% yield by phenylselenylation-oxidative elimination sequences. The acetylenic iodide **6**[4] was also subjected to the same conditions for **1** to afford the *cis*-decalin **7** selectively in 85% yield. On ketalization **7** furnished the ketal **4** (66%) identical with that described above (Scheme 1).

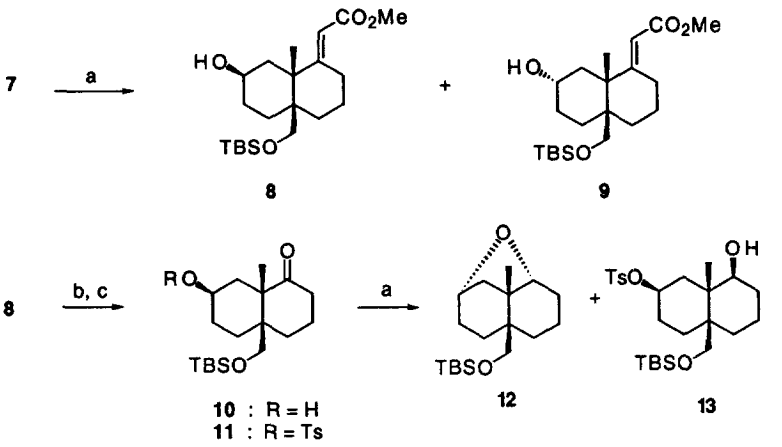
Scheme 1



[a]Steps: (a) $^{n}Bu_3SnH$, AIBN, benzene, reflux, 5 h; (b) $HOCH_2CH_2OH$, *p*-TsOH, benzene,reflux, 9 h; (c) (1) LDA, PhSeBr, THF, –78 °C, 4.5 h; (2) 30% H_2O_2, $NaHCO_3$, THF, rt, 2 h.

Although the E-geometry of **7**[5] was confirmed by the observation of definite nOe between Ha and Hb [2.21 and 2.82 ppm (each 1H, each d, J = 15.0 Hz)], and Hc [5.68 ppm (1H, s)] in its NMR (500 MHz) spectrum the *cis* ring juncture of **7** was determined unambiguously giving the suitably functionalized *cis*-decalins for further elaboration as follows. Reduction of the ketone **7** afforded the alcohols **8** and **9** (4:1) in 69% yield, the former of which was then subjected to ozonolysis to give the keto alcohol **10** (55%). Finally, the tosylate **11** derived (81%) from **10** was reduced to furnish the tricyclic compound **12** (59%) together with the alcohol **13** (38%) confirming the *cis* ring juncture of **7** (Scheme 2).

Scheme 2



[a]Steps: (a) $NaBH_4$, MeOH, 0 °C, 15 min; (b) O_3, CH_2Cl_2, –78 °C, 3 h then Me_2S; (c) *p*-TsCl, pyridine, DMAP, 0 °C, 24 h.

Thus, we could provide an efficient pathway to disubstituted *cis*-decalins which could be potential intermediates for the synthesis of biologically important compounds.

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3. For reviews in this area, see: (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergamon Press, New York, 1986. (b) Fossey, J.; Lefort, D.; Sorba, J. *Free Radicals in Organic Chemistry*, John Wiley & Sons, Paris, 1995. (c) Curran, D. P. *Synthesis* **1988**, 417-439 and 489-513. (d) Jasperse, C. P. Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237-1286. (e) Porter, N. A.; Giese, B.; Curran, D. P. *Acc. Chem. Res.* **1991**, *24*, 296-306. (f) Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091-2115. (g) Smadja, W. *Synlett* **1994**, 1-26. For some recent studies, see: (h) Dowd, P.; Choi, S.-C. *J. Am. Chem. Soc.* **1987**, *109*, 3493-3494 and 6548-6549. (i) Beckwith, A. L. J.; O'Shea, D. M.; Gerba, S.; Westwood, S. W. *J. Chem. Soc., Chem. Commun.* **1987**, 666-667. (j) Beckwith, A. L. J.; O'Shea, D. M.; Westwood, S. W. *J. Am. Chem. Soc.* **1988**, *110*, 2565-2575. (k) Ellwood, C. W.; Pattenden, G. *Tetrahedron Lett.* **1991**, *32*, 1591-1594. (l) Nishida, M.; Ueyama, E.; Hayashi, H.; Ohtake, Y.; Yamamura, Y.; Yanaginuma, E.; Yonemitsu, O.; Nishida, A.; Kawahara, N. *J. Am. Chem. Soc.* **1994**, *116*, 6455-6456. (m) Curran, D. P.; Qi, H.; DeMello, N. C.; Lin, C.-H. *ibid.* **1994**, *116*,

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5. Selected data for **4**: IR ν max (neat) cm^{-1} 1710, 1630; ^{1}H-NMR (500 MHz, $CDCl_3$) δ –0.04 (3H, s), –0.03 (3H, s), 0.83 (9H, s), 1.15 (3H, s), 1.42–1.88 (10H, m), 2.08–2.19 (1H,, m), 2.26 (1H, d, J = 14.0 Hz), 3.22 and 3.43 (each 1H, each d, J = 9.8 Hz), 3.66 (3H, s), 3.73–3.97 (4H, m), 5.72 (1H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ –5.6, –5.5, 18.2, 20.3, 21.7, 25.1, 25.8, 29.4, 30.4, 41.9, 43.1, 44.4, 50.9, 63.6, 64.5, 66.0, 109.2, 113.9, 167.7, 167.9; MS m/z 424 (M^+); HRMS (M^+) calcd for $C_{23}H_{40}O_5Si$ 424.2645. found 424.2652. For **5**: IR ν max (neat) cm^{-1} 1710, 1640; ^{1}H-NMR (500 MHz, $CDCl_3$) δ –0.02 (3H, s), –0.01 (3H, s), 0.84 (9H, s), 1.20 (3H, s), 1.41–2.04 (9H, m), 2.04–2.12 (1H, m), 2.19 (1H, d, J = 14.0 Hz), 2.38–2.49 (1H, m), 3.25 and 3.56 (each 1H, each d, J = 9.8 Hz), 3.67 (3H, s), 3.79–3.98 (4H, m), 5.59 (1H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ –5.5, –5.4, 18.3, 19.6, 21.9, 25.9, 26.0, 28.8, 30.4, 35.4, 41.5, 41.9, 44.2, 51.6, 63.7, 64.5, 65.8, 109.2, 117.0, 153.2, 170.0; MS m/z 424 (M^+); HRMS m/z (M^+) calcd for $C_{23}H_{40}O_5Si$ 424.2645. found 424.2621. For **7**: IR ν max (neat) cm^{-1} 1720, 1710, 1630; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.03 (6H, s), 0.87 (9H, s), 1.11 (3H, s), 1.21–1.95 (6H, m), 2.21 and 2.82 (each 1H, each d, J = 15.0 Hz), 2.39 (2H, t, J = 7.0 Hz), 2.91–3.05 (2H, m), 3.55 and 3.62 (each 1H, each d, J = 9.9 Hz), 3.67 (3H, s), 5.68 (1H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ –5.6, –5.4, 18.2, 21,8, 25.1, 25.9, 26.7, 28.1, 30.4, 37.7, 42.3, 47.4, 50.0, 51.1, 66.5, 114.5, 165.0, 167.3, 210.9; MS m/z 323 (M^+ –57); HRMS m/z (M^+ –57) calcd for $C_{17}H_{27}O_4Si$ 323.1679. found 323.1642.

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