Reductive Elimination of Acetonides, Cyclic Carbonates, or Cyclic Sulfites of γ,δ-Dihydroxy (*E*)-α,β-Unsaturated Esters: An Efficient Route to δ-Hydroxy (*E*)-β,γ-Unsaturated Esters and δ-Hydroxy Esters

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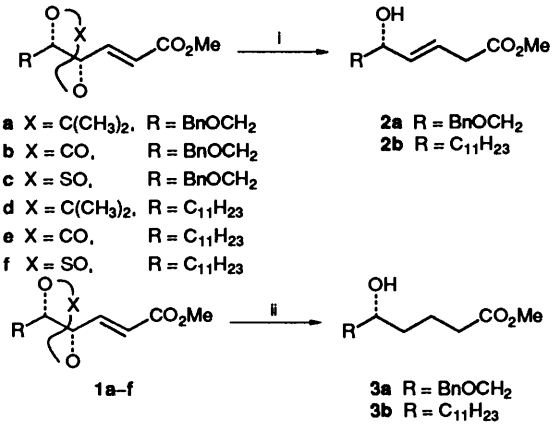
The acetonides, cyclic carbonates, or cyclic sulfites of γ,δ-dihydroxy (*E*)-α,β-unsaturated esters have been found to undergo facile reductive cleavage with samarium diiodide or magnesium in methanol to provide δ-hydroxy (*E*)-β,γ-unsaturated esters or δ-hydroxy esters, respectively. Using the δ-hydroxy ester **3b** as a chiral synthon, (−)-5-hexadecanolide, the pheromone of the oriental hornet *Vespa orientalis* was synthesized.

Samarium diiodide[1] and magnesium[2] in methanol are known reducing reagents. In the literature, samarium diiodide reduction of γ,δ-epoxy α,β-unsaturated esters as a route to δ-hydroxy (*E*)-β,γ-unsaturated esters has been described.[3] In connection with our current research programs on the synthesis of optically active insect pheromones which have a lactone moiety, we have examined the reduction of the acetonides, carbonates or sulfites of γ,δ-dihydroxy α,β-unsaturated esters with samarium diiodide and magnesium and the results are depicted in Scheme 1.



Scheme 1 *Reagents and conditions:* i, Method A: SmI_2, THF, MeOH, −78 °C; ii, Method B: Mg, MeOH, reflux

The acetonide **1a** underwent smooth reductive elimination by treatment with samarium diiodide (8 equiv.) in THF (tetrahydrofuran) and MeOH at −78 °C for 30 min to afford the β,γ-unsaturated ester **2a** as a single (*E*)-isomer (entry 1, Method A, Table 1). The (*E*)-stereochemistry of the compound **2a** was confirmed by the 300 MHz ^1H NMR coupling constants of the two olefinic protons. Treatment of **1a** with magnesium (5 equiv.) in refluxing methanol for 2.5 h afforded δ-hydroxy ester **3a** as the only isolated product (entry 2, Method B, Table 1). It is presumed that the β,γ-unsaturated ester **2a** is the intermediate in the above reduction, and the ester **2a** formed transiently is subsequently isomerized to the α,β-unsaturated ester, which is in turn subjected to double bond reduction. The reductive cleavage of carbonate **1b** was more easily carried out with samarium diiodide (8 equiv.) to give **2a** (entry 3). It is notable that the carbonate **1b** was more effectively reduced than the acetonide **1a**. The carbonate **1b** was also readily converted into **3a** with magnesium (entry 4). These methods were applied to the sulfite **1c** (entry 5). The acetonide of γ,δ-dihydroxy (*E*)-α,β-enoate **1d** was readily prepared from 2-deoxy-D-ribose acetonide[4] **4**. Condensation of **4** with nonyltriphenylphosphorane followed by catalytic hydrogenation provided the saturated alcohol **5**, $[\alpha]_D^{25}$ +23.03 (*c* 0.17, $CHCl_3$). The alcohol **5** was oxidized and then condensed with methyl (triphenylphosphoranylidene)acetate to afford the unsaturated ester **1d**. Treatment of **1d** with magnesium (5 equiv.) in refluxing methanol for 0.5 h provided **3b** in 93% yield (entry 7).† The δ-hydroxy ester **3b** was subjected to lactonization with TFA (trifluoroacetic acid) in benzene to afford (*S*)-5-hexadecanolide **6**,[5] m.p. 38–39 °C, $[\alpha]_D^{23}$ −41.3 (*c* 1.27, THF) [lit.,[5j] $[\alpha]_D^{21.5}$ −40.2 (THF)], which is the pheromone of the oriental hornet *Vespa orientalis*[6] (Scheme 2).

Table 1 Reductive elimination of acetonides, cyclic carbonates, or cyclic sulfites of γ,δ-dihydroxy (*E*)-α,β-unsaturated esters

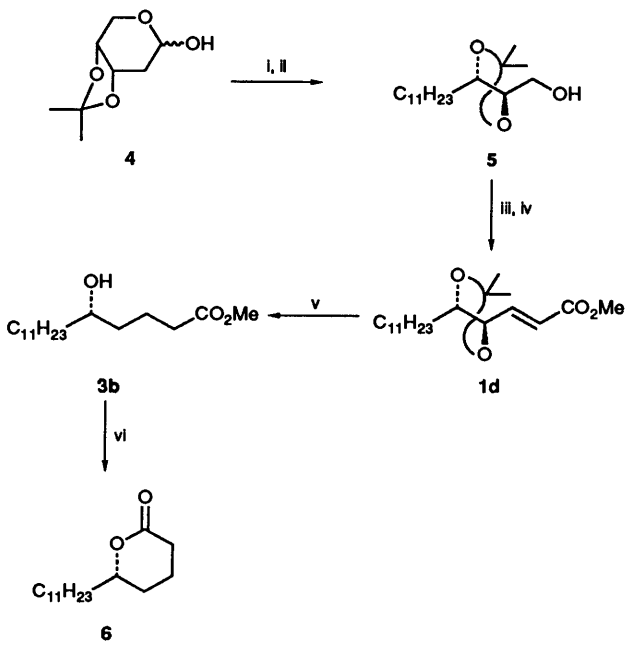
Entry	Substrate	Reaction conditions[a] (reaction time, yield %)	Product[b]
1	**1a**	A(0.5 h, 52%)	**2a**
2	**1a**	B(2.5 h, 83%)	**3a**
3	**1b**	A(10 min, 90%)	**2a**
4	**1b**	B(45 min, 63%)	**3a**
5	**1c**	A(2 h, 60%)	**2a**
6	**1d**	A(0.5 h, 49%)	**2b**
7	**1d**	B(0.5 h, 93%)	**3b**
8	**1e**	A(10 min, 95%)	**2b**
9	**1e**	B(45 min, 65%)	**3b**
10	**1f**	A(1 h, 73%)	**2b**

[a] A (Method A): SmI_2 (8 equiv.), THF, MeOH, −78 °C; B (Method B): Mg (5 equiv.), CH_3OH, reflux. [b] The specific rotations, $[\alpha]_D^{25}$ values in $CHCl_3$: **2a**: −6.5 (*c* 0.20); **2b**: +3.27 (*c* 0.25); **3a**: −4.18 (*c* 2.40); **3b**: −12.0 (*c* 0.05).

These reduction procedures were applied to the acetonides, carbonates or sulfites **1d–f** and the products and isolated yields are tabulated (entries 6–10). The results are summarized in Table 1.

Typical Procedures.—Method A. To a stirred solution of SmI_2 (0.5 mol dm^{-3} in THF, 5 cm^3, 8 equiv.) at −78 °C, was added the carbonate **1e** (97.9 mg, 0.30 mmol) in dry methanol

† When the reaction mixture was stirred with silica gel at room temperature for 4 h after treatment with magnesium in refluxing methanol, the lactone **6** was obtained directly.



Scheme 2 *Reagents and conditions:* i, $(C_6H_5)_3P^+(CH_2)_8CH_3Br^-$, BuLi, THF, 25 °C, 12 h, (90%); ii, H_2, Pd/C, EtOAc, 1 atm, 25 °C, 12 h, (95%); iii, $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −70 °C, 1 h, (89%); iv, $Ph_3P{=}CHCO_2Me$, toluene, reflux, 1 h, (95%); v, Mg, MeOH, reflux, 0.5 h, (93%); vi, TFA, PhH, room temp., 2 h, (82%)

(0.3 cm^3). The reaction mixture was stirred at −78 °C for 10 min and then triturated with hexane (10 cm^3). The solvents were evaporated and the crude product was purified by SiO_2 column chromatography (eluent ethyl acetate–hexanes, 1:3, R_f = 0.45) to afford **2b** (81 mg, 95%).

Method B. To a stirred solution of the acetonide **1d** (102 mg, 0.30 mmol) in dry MeOH (2 cm^3) was added magnesium turnings (36.5 mg, 1.5 mmol, 5 equiv.). The reaction mixture was heated at reflux for 30 min. MeOH was evaporated under reduced pressure and the reaction mixture was extracted with ether. The ether layer was dried ($MgSO_4$) and then evaporated. The crude product was purified by SiO_2 column chromatography (eluent ethyl acetate–hexanes, 1:3, R_f = 0.36) to afford **3b** (79.9 mg, 93%).

Acknowledgements

We acknowledge financial support by Korea Science Engineering Foundation (KOSEF) and the Organic Chemistry Research Center (OCRC)-KOSEF.

References

1 (*a*) G. A. Molander, *Chem. Rev.*, 1992, **92**, 29; (*b*) J. A. Soderquist, *Aldrichim. Acta*, 1991, **24**, 15.
2 I. K. Youn, G. H. Yon and C. S. Pak, *Tetrahedron Lett.*, 1986, **27**, 2409.
3 G. A. Molander, B. E. La Belle and G. Hahn, *J. Org. Chem.*, 1986, **51**, 5259.
4 E. J. Corey, A. Marfat, G. Goto and F. Brion, *J. Am. Chem. Soc.*, 1980, **102**, 1985.
5 For previous enantioselective routes to 5-hexadecanolide, see: (*a*) J. L. Coke and A. B. Richon, *J. Org. Chem.*, 1976, **41**, 3516; (*b*) W. H. Pirkle and P. E. Adams, *J. Org. Chem.*, 1979, **44**, 2169; (*c*) G. Solladie and F. M. Moghadam, *J. Org. Chem.*, 1982, **44**, 91; (*d*) S. Servi, *Tetrahedron Lett.*, 1983, **24**, 2023; (*e*) N. Naoshima, H. Ozawa, H. Kondo and S. Hayashi, *Agric. Biol. Chem.*, 1983, **47**, 1431; (*f*) M. Larcheveque and J. Ladonde, *Tetrahedron*, 1984, **40**, 1016; (*g*) T. Kikukawa and A. Tai, *Chem. Lett.*, 1984, 1935; (*h*) T. Fujisawa, T. Itoh, M. Nakai and T. Sato, *Tetrahedron Lett.*, 1985, **26**, 771; (*i*) H. Yamamoto and A. Mori, *J. Org. Chem.*, 1985, **50**, 5444; (*j*) K. Mori and T. Otsuka, *Tetrahedron*, 1985, **41**, 547; (*k*) H. Kosugi, H. Konta and H. Uda, *J. Chem. Soc., Chem. Commun.*, 1985, 211; (*l*) A. Takeda, M. Utaka and H. Watabu, *Chem. Lett.*, 1985, 1475; (*m*) D. B. Gerth and B. Giese, *J. Org. Chem.*, 1986, **51**, 3726; (*n*) A. Sakamoto, Y. Yamamoto and J. Oda, *J. Am. Chem. Soc.*, 1987, **109**, 7188; (*o*) D. F. Taber, P. B. Deker and M. D. Gaul, *J. Am. Chem. Soc.*, 1987, 7488.
6 For the isolation and structure of 5-hexadecanolide, see: R. Ikan, R. Gottlieb, E. D. Bergman and J. Ishay, *J. Insect Physiol.*, 1969, **15**, 1709.

Paper 2/05414K
Received 9*th October* 1992
Accepted 30*th October* 1992