Deconjugation of α,β-Unsaturated Esters and an Intramolecular Michael Reaction of Bis-α,β-unsaturated Esters with Trialkylsilyl Trifluoromethanesulfonate in the Presence of Tertiary Amine: Synthesis of (±)-Ricciocarpin A

Masataka Ihara, Shuichi Suzuki, Nobuaki Taniguchi and Keiichiro Fukumoto*
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan

Treatment of the α,β-unsaturated esters **1**, **6** and **8** with trialkylsilyl trifluoromethanesulfonate in the presence of a tertiary amine gave, *via* silyl dienol ethers, the corresponding deconjugated esters **3**, **7** and **9** as the major products, respectively. Reaction of bis-α,β-unsaturated esters **12a** and **12b** with a trialkylsilyl trifluoromethansulfonate in the presence of a tertiary amine caused an intramolecular Michael reaction to produce the cyclopentanes **14a** and **20a** and the cyclohexanes **14b** and **20b**. Bicyclic compounds **21a** and **21b** formed by tandem Michael–Dieckmann or intramolecular Diels–Alder reaction were concurrently obtained. The cyclohexane derivative **14b** was converted into the racemate of a sesquiterpene, (±)-ricciocarpin A **22**.

Formation of enolates and their selective reactions are among the most important processes in organic synthesis.[1] Stereoselective aldol and Michael reactions have been developed utilizing several metal enolates, such as lithium, boron, aluminium, silicon, titanium, tin and zinc. Among them, silyl enolates are superior to other metal enolates in isolation, regioselective formation, and inherent reactivities under mild conditions.[2] Trialkylsilyl trifluoromethanesulfonates are known as the most potent silylating agent, smoothly converting a wide range of ketones, diketones and esters directly into their silyl enol ethers or silyl ketene acetals.[2,3] In the course of our studies of tandem reactions using trialkylsilyl trifluoromethanesulfonates,[4–6] the ready formation of silyl dienol ethers from α,β-unsaturated esters was observed. We here report the deconjugation of α,β-unsaturated esters and an intramolecular Michael reaction of bis-α,β-unsaturated esters based on the creation of the silyl dienol ethers together with an application of the method to a synthesis of a natural product.[7]

Results and Discussion

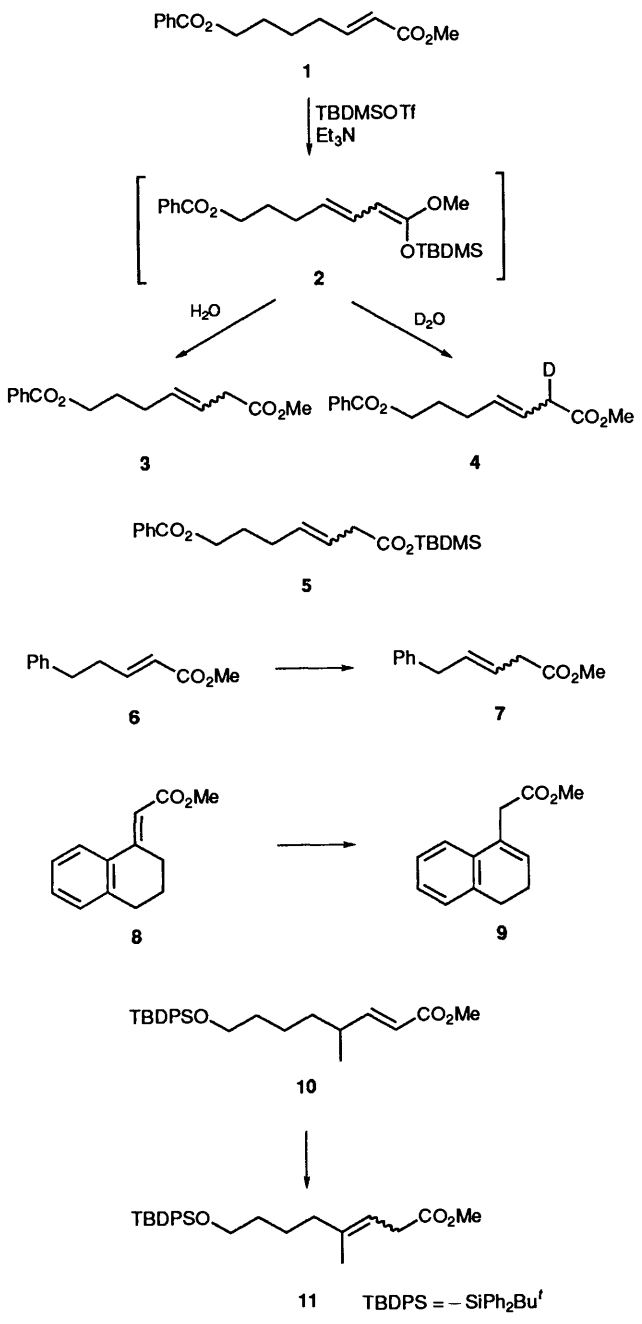
Deconjugation Reaction of α,β-Unsaturated Esters.—Treatment of the (*E*)-unsaturated ester **1**, which was prepared by benzoylation of methyl (*E*)-7-hydroxyhept-2-enoate,[8] with an excess of *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBDMSOTf) in the presence of triethylamine in dichloromethane at room temperature followed by work-up provided the deconjugated esters **3** as major products. It was revealed from 500 MHz ^{1}H NMR spectrum that the deconjugated esters **3** were composed of two isomers in a 1:1.3 ratio. When the reaction mixture of **1** with TBDMSOTf and triethylamine was quenched with deuterium oxide, the α-deuteriated esters **4** were obtained. The fact was supported by spectroscopic evidence: reduction of the integration of the resonance due to the α-hydrogens in the 500 MHz ^{1}H NMR spectrum and the molecular ion peak observed at *m/z* 263. The result indicates a formation of the silyl dienol ether **2**. The deconjugated ester **3** must be formed by a kinetic protonation of **2** (Scheme 1).

The deconjugation of α,β-unsaturated esters was examined under various conditions and the results are shown in Table 1. The reaction proceeded in the presence of a tertiary amine such as triethylamine or diisopropylethylamine (Entries 1 and 2), but the use of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), pyridine and hexamethyldisilazane as a base did not give the deconjugated product **3** (Entries 3–5). Among the solvents tested, the silyl dienol ether **2** was quickly formed in dichloromethane (Entry 1) and dichloroethane (Entry 6). Considerable exchange of methyl group of the ester function with the *tert*-butyldimethylsilyl group was observed during the reaction in dichloroethane over 1 h (Entry 6). The reaction was sluggish in chloroform (Entry 7), carbon tetrachloride (Entry 8), tetrahydrofuran (THF) (Entry 9), benzene (Entry 11) and hexane (Entry 12), and in diethyl ether for 1 h, no deconjugation was detected (Entry 10).

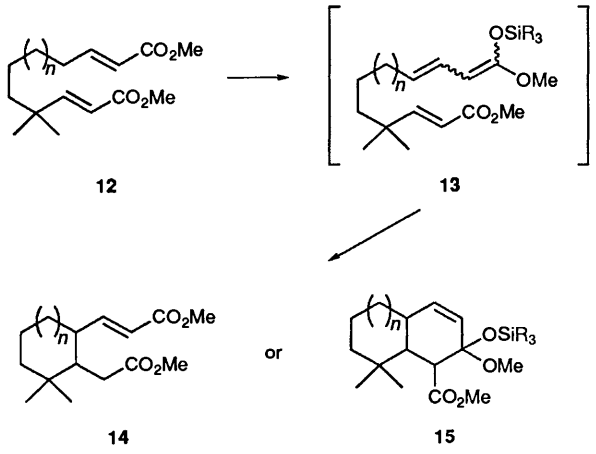
Treatment of the ester **6** with both TBDMSOTf and triisopropylsilyl trifluoromethanesulfonate (TIPSOTf) in the presence of triethylamine produced mainly the deconjugated products **7** (Entries 13 and 14). The silyl dienol ether formed by the reaction with TIPSOTf was rather stable and the product was decomposed by the acetic acid (Entries 14 and 16). The deconjugated ester **9** was exclusively produced from the conjugated ester **8** although the yield was low (Entry 15). It was interesting that the formation of the deconjugated ester **11** from the conjugated ester **10** possessing a substituent at the γ position was poor (Entry 16).

Intramolecular Michael Reaction of Bis-α,β-unsaturated Esters.—The intramolecular Michael reaction provides a powerful tool for the construction of ring systems.[9] The above observation about the facile formation of silyl dienol ethers from α,β-unsaturated esters led us to investigate a novel intramolecular Michael reaction of bis-α,β-unsaturated esters. The intramolecular conjugate addition of the bis-α,β-unsaturated esters **12** to form the cyclic compound **14** would take place through the silyl dienol ethers **13** under the given reaction conditions (Scheme 2). It was further expected that the bicyclic compounds **15** would be assembled by the tandem Michael–Dieckmann reaction[10] or by the intramolecular Diels–Alder reaction of **13**.

Two substrates **12a** and **12b** for the key reaction were effectively prepared starting from 2-methylpropanal dimethylhydrazone. The reaction of the hydrazone with the alkyl bromides **16a**[11] and **16b**, in the presence of lithium diisopropylamide (LDA) proceeded through elimination[12] to afford the nitriles **17a** and **17b** (Scheme 3). Reduction of the latter with diisobutylaluminium hydride (DIBALH), followed by treatment of the products with silica gel provided the

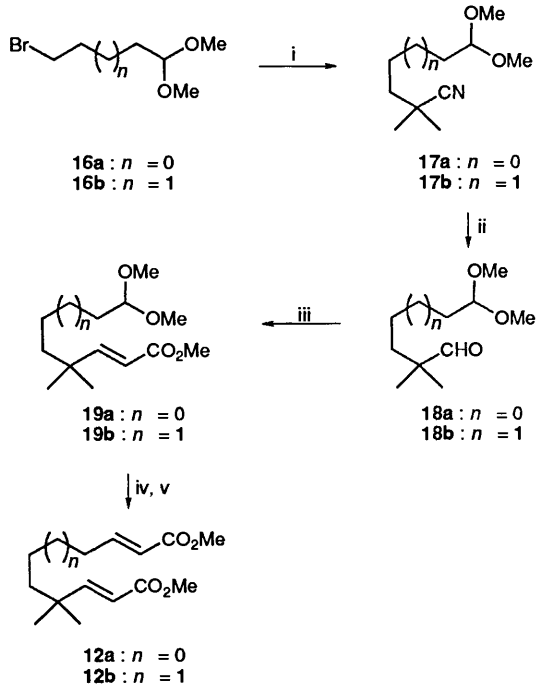


Scheme 1



Scheme 2

aldehydes **18a** and **18b**. These reacted with trimethyl phosphonoacetate in the presence of sodium hydride to yield the (*E*)-unsaturated esters **19a** and **19b**. After deprotection of the acetal groups of **19a** and **19b** using pyridinium toluene-*p*-sulfonate (PPTS), condensation with methyl triphenylphosphoranylideneacetate in acetonitrile gave the required bis-(*E*,*E*)-unsaturated esters **12a** and **12b**.



Scheme 3 *Reagents:* i, 2-methylpropanal dimethylhydrazone, LDA; ii, DIBALH then silica gel; iii, $(MeO)_2P(O)CH_2CO_2Me$, NaH; iv, PPTS; v, $Ph_3P{=}CHCO_2Me$

The outcome of the reaction of the bis-(*E*,*E*)-unsaturated esters **12a** and **12b** with various trialkylsilyl trifluoromethanesulfonates in the presence of triethylamine in dichloromethane is summarised in Table 2. An inseparable mixture of the cyclopentane derivatives **14a** and **20a** and cyclohexane derivatives **14b** and **20b** were obtained from **12a** and **12b**, respectively. The cyclopentane **14a** having the (*E*)-conjugated ester was obtained as a single stereoisomer, while two isomeric cyclohexanes **14b** were obtained. It was later established by the equilibration of the aldehydes **24** derived from **14b** that the major isomer was the *trans*-substituted cyclohexane and the minor was the *cis*-substituted one. The (*E*)-structures of the deconjugated esters **20a** and **20b** were tentatively assigned, mainly on the basis of their thermodynamic stability. It was noteworthy that the bicyclic compounds **21a** and **21b** were obtained only by the reactions carried out with TBDMSOTf (Entries 1 and 3), although it is difficult to determine the precise mechanism: the tandem Michael–Dieckmann or the intramolecular cycloaddition process. The products **21a** and **21b** were each formed as a single stereoisomer. The stereostructure of **21a** was uncertain, but the *trans*-fused structure of **21b** was established by the coupling constants of the signal due to the angular 4a-H observed as a doublet, *J* 12.8 and 11.4 Hz.

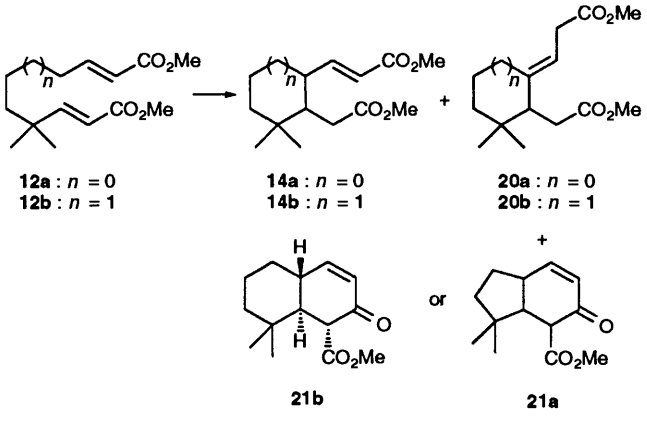
On the other hand, it was observed that treatment of bis-(*E*,*E*)-unsaturated esters **12a** and **12b** with various bases did not effectively induce the desired intramolecular Michael reaction. Thus, compounds **14a** and **14b** were obtained in very poor yield by the reaction with a base such as LDA or sodium hydride.

Synthesis of (±)-*Ricciocarpin A*.—Ricciocarpin A **22**, which was isolated from *Ricciocarpos natans* by Becker[12] in 1990, exhibits potent molluscicidal activity.[14] Recently, Eicher and

Table 1 Reaction of α,β-unsaturated esters with trialkylsilyl trifluoromethanesulfonate in the presence of amine for 1 *h* at 18 °C

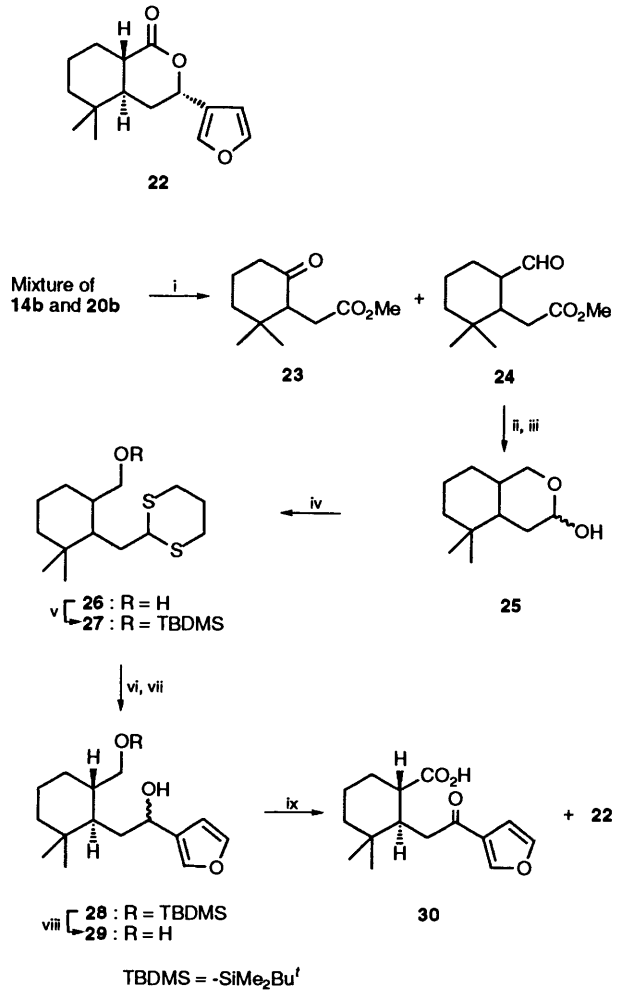
Entry	Substrate	$R_3SiOSO_2CF_3$	Amine	Solvent	Product	Yield (%)	Recovered (%)
1	**1**	TBDMSOTf	Et_3N	CH_2Cl_2	**3**	82	14
2	**1**	TBDMSOTf	Pr^i_2NEt	CH_2Cl_2	**3**	80	16
3	**1**	TBDMSOTf	DBU	CH_2Cl_2	**3**	0	98
4	**1**	TBDMSOTf	Pyridine	CH_2Cl_2	**3**	0	98
5	**1**	TBDMSOTf	$(Me_3Si)_2NH$	CH_2Cl_2	**3**	0	98
6	**1**	TBDMSOTf	Et_3N	$ClCH_2CH_2Cl$	**3**	56	4
					5	20	
7	**1**	TBDMSOTf	Et_3N	$CHCl_3$	**3**	14	84
8	**1**	TBDMSOTf	Et_3N	CCl_4	**3**	12	86
9	**1**	TBDMSOTf	Et_3N	THF	**3**	16	82
10	**1**	TBDMSOTf	Et_3N	Et_2O	**3**	0	98
11	**1**	TBDMSOTf	Et_3N	Benzene	**3**	11	87
12	**1**	TBDMSOTf	Et_3N	Hexane	**3**	11	87
13	**6**	TBDMSOTf	Et_3N	CH_2Cl_2	**7**	90	5
14	**6**	TIPSOTf	Et_3N	CH_2Cl_2	**7**	93	5
15	**8**	TBDMSOTf	Et_3N	CH_2Cl_2	**9**	38	0
16	**10**	TIPSOTf	Et_3N	CH_2Cl_2	**11**	15	75

Table 2 Reaction of the diesters **12** with trialkylsilyl trifluoromethanesulfonate in the presence of Et_3N



Entry	Substrate	$R_3SiOSO_2CF_3$	Yield (%) of **14** and **20** (ratio)	Yield (%) of **21**
1	**12a**	TBDMSOTf	53 (3 : 1)	12
2	**12a**	TMSOTf	81 (2 : 1)	0
3	**12b**	TBDMSOTf	89 (5 : 3)	3.8
4	**12b**	TMSOTf	80 (1 : 1.7)	0
5	**12b**	TIPSOTf	77 (8 : 5)	0

co-workers synthesised the racemate of **22**.[15] Therefore, we were interested in the conversion of the above Michael product **14b** into the natural product **22**. The mixture of the cyclohexanes **14b** and **20b**, obtained by the above method (Entry 3) was subjected to ozonolysis to give the ketone **23** and the aldehydes **24**, which were composed of two isomers in a 1.5 : 1 ratio. The ratio of two isomers of **24** was changed to 7.5 : 1 by their treatment with DBU in dichloromethane at room temperature. Reduction of the equilibrated products with sodium borohydride produced the cyclic hemiacetals **25**, which consisted of the *trans*- and *cis*-fused isomers in a 7.5 : 1 ratio. Since the coupling reaction of the hemiacetals **25** with 3-furyllithium gave a poor result, they were transformed into the thioacetals **26** by the action of propane-1,3-dithiol in the presence of boron trifluoride–diethyl ether. After the protection of the hydroxy group with the *tert*-butyldimethylsilyl group, deprotection of the thioacetal group of **27**, followed by the reaction of the resulting aldehyde with 3-furyllithium smoothly produced the epimeric mixture of the alcohols **28**. Removal of the protecting group of **28** provided a 1.3 : 1 mixture of the diols **29**. It was interesting that oxidation of the mixture of diols **29** with pyridinium dichromate (PDC) in dimethylformamide (DMF)



Scheme 4 *Reagents:* i, O_3; then Et_3N; ii, DBU; iii, $NaBH_4$; iv, $(HSCH_2)_2CH_2$, $BF_3{\cdot}OEt_2$; v, TBDMSOTf, 2,6-dimethylpyridine; vi, MeI, $NaHCO_3$; vii, 3-bromofuran, BuLi; viii, Bu_4NF; ix, PDC, DMF

produced the keto acid **30**, m.p. 130–131 °C (lit.,[15] 131–132 °C), together with (±)-ricciocarpin A **22**, m.p. 92.5–93 °C (lit.,[15] 95–96 °C). The keto acid **30** had been stereoselectively transformed into (±)-ricciocarpin A **22**.[15] The ^{1}H NMR spectrum of the synthetic **22** was identical with that of the natural product.

Experimental

General Methods.—M.p.s were determined on a Yanako micromelting point apparatus and are uncorrected. IR spectra were recorded on a JASCO-IR-Report-100 spectrophotometer, with the sample prepared as a neat film or in chloroform solution. The assignable absorptions are reported. ^{1}H NMR spectra were recorded on the following instruments: Hitachi R-1200 (60 MHz), Hitachi R-3000 (300 MHz) and JEOL GX-500 (500 MHz). Chemical shifts (δ) are measured relative to tetramethylsilane, using either $SiMe_4$ or the solvent as internal reference. All J values are given in Hz and only characteristic signals are recorded. The ratio of products was determined by *integrations in* the 500 MHz NMR spectra. Mass spectra were recorded on either a JEOL DX-300 or a JEOL DX-303 instrument. Ordinary chromatography was performed on Merck Kieselgel 60 Art 7734, while flash chromatography was carried out using Merck Kieselgel 60 Art 9385. HPLC was carried out with a Gilson HPLC system Model 320/303 and monitored by UV absorption and refractive-index measurements. All reactions were carried out under N_2 or Ar atmospheres. Solvents were distilled prior to use: THF, Et_2O and benzene were distilled from sodium–benzophenone, CH_2Cl_2 and DME were distilled from CaH_2 and stored over molecular sieves 4 Å. All extracts were dried over $MgSO_4$ unless otherwise stated, and solvents were removed on a rotary evaporator at 30–40 °C. Oily NaH was washed with dry hexane three times prior to use. All new compounds described in this Experimental section were homogeneous on TLC and HPLC.

Methyl (E)-7-*Benzoyloxyhept*-2-*enoate* **1**.—To a solution of methyl (*E*)-7-hydroxyhept-2-enoate[8] (500 mg, 3.16 mmol) in dry pyridine (10 cm^3) was added benzoyl chloride (1.5 cm^3, 12.9 mmol) at 0 °C and the mixture was stirred for 2.5 h at room temp. After addition of MeOH (1 cm^3), the mixture was stirred for 10 min at the same temperature and then diluted with benzene. The resulting mixture was washed with 10% HCl, saturated aq. $NaHCO_3$ and brine, dried, and evaporated to give a residue which was subjected to chromatography on silica gel. Elution with hexane–EtOAc (9:1 v/v) afforded the methyl ester **1** (785 mg, 95%) as an oil; ν_{max}(neat)/cm^{-1} 1720–1715 (C=O) and 1655 (C=C); δ_H(300 MHz, $CDCl_3$) 1.60–1.69 (2 H, m), 1.76–1.86 (2 H, m), 2.29 (2 H, ddt, J 7.3, 7.3 and 1.5, CH_2CH=), 3.73 (3 H, s, OMe), 4.33 (2 H, t, J 6.4, CH_2O), 5.86 (1 H, dt, J 15.3 and 1.5, CHCO_2Me), 6.98 (1 H, dt, J 15.3 and 7.3, CH=CHCO_2Me), 7.39–7.47 (3 H, m, 3 × ArH) and 7.52–7.58 (2 H, m, 2 × ArH); m/z 262 (M$^+$).

Methyl (E)-8-tert-*Butyldiphenylsiloxy*-4-*methyloct*-2-*enoate* **10**.—According to the reported procedure,[5] 2-methyl-ε-caprolactone (200 mg, 1.56 mmol) was reduced with DIBALH in hexane (0.93 mol dm^{-3}; 1.84 cm^3, 1.71 mmol) to give the aldehyde, which was used in the following reaction without purification. A mixture of the aldehyde and methyl triphenylphosphoranylideneacetate (782 mg, 2.34 mmol) in dry MeCN (6 cm^3) was stirred for 16 h at room temp. and heated for 5 h at 60 °C. Evaporation of the solvent gave a residue, which was subjected to chromatography on silica gel. Elution with hexane–EtOAc (3:1 v/v) provided methyl 8-hydroxy-4-methyloct-2-enoate (225 mg, 77% overall yield) as a mixture of two (*E*)- and (*Z*)-isomers; ν_{max}(neat)/cm^{-1} 3380 (OH) and 1710 (C=O) and 1645 (C=C); δ_H(60 MHz, $CDCl_3$) 1.05 (3 H, d, J 6.6, CHMe), 3.72 (3 H, s, OMe), 5.76 (1 H, dd, J 15.7 and 0.9, CHCO_2Me) and 6.88 (1 H, dd, J 15.7 and 7.6, CH=CHCO_2Me); m/z 186 (M$^+$) and 168 (M$^+$ − H_2O) (Found: M$^+$ − H_2O, 168.1149, $C_{10}H_{16}O_2$ requires m/z, 168.1131).

A mixture of the alcohols (54 mg, 0.29 mmol), imidazole (45 mg, 0.66 mmol) and *tert*-butyldiphenylsilyl chloride (TBDPSCl) (0.11 cm^3, 0.43 mmol) in dry DMF (1 cm^3) was stirred for 2 h at room temp. After being poured into water, the mixture was extracted with Et_2O. The extract was washed with brine, dried and evaporated to give a residue, which was chromatographed on silica gel with hexane–Et_2O (30:1 v/v) as the eluent to afford the (Z)-*unsaturated ester* (6 mg, 5%) as an oil; ν_{max}(neat)/cm^{-1} 1721 (C=O) and 1650 and 1641 (C=C); δ_H(300 MHz, $CDCl_3$) 0.89 (3 H, d, J 6.6, CHMe), 1.04 (9 H, s, SiBu^t), 3.42–3.55 (1 H, m, CHCH=CH), 3.63 (2 H, t, J 6.6, OCH_2), 3.69 (3 H, s, OMe), 5.71 (1 H, dd, J 11.4 and 0.8, CHCO_2Me), 5.95 (1 H, dd, J 11.4 and 10.3, CH=CHCO_2Me), 7.31–7.45 (6 H, m, 6 × ArH) and 7.62–7.70 (4 H, m, 4 × ArH); m/z 393 (M$^+$ − OMe) and 367 (M$^+$ − Bu^t) (Found: M$^+$ − Bu^t, 367.1725. $C_{22}H_{27}O_3Si$ requires m/z, 367.1729).

Further elution gave the (E)-*unsaturated ester* **10** (98 mg, 80%) as an oil; ν_{max}(neat)/cm^{-1} 1721 (C=O) and 1652 (C=C); δ_H(300 MHz, $CDCl_3$), 1.02 (3 H, d, J 6.6, CHMe), 1.04 (9 H, s, SiBu^t), 2.21–2.33 (1 H, m, CHCH=CH), 3.64 (2 H, t, J 6.7, OCH_2), 3.72 (3 H, s, OMe), 5.67 (1 H, dd, J 15.7 and 1.1, CHCO_2Me), 6.85 (1 H, dd, J 15.7 and 8.1, CH=CHCO_2Me), 7.34–7.45 (6 H, m, 6 × ArH) and 7.64–7.67 (4 H, m, 4 × ArH); m/z 393 (M$^+$ − OMe) (Found: M$^+$ − OMe, 393.2232. $C_{25}H_{32}O_2Si$ requires m/z, 393.2250).

Typical Procedures for Deconjugation Reaction.—(*A*). To a stirred solution of the α,β-unsaturated ester **1** (27 mg, 0.10 mmol) and Et_3N (0.12 cm^3, 0.86 mmol) in dry CH_2Cl_2 (2 cm^3) was added dropwise TBDMSOTf (0.12 cm^3, 0.52 mmol) at 18 °C and the mixture was stirred for 1 h at the same temperature. After dilution with Et_2O, the resulting mixture was washed with saturated aq. $NaHCO_3$ and brine, dried and evaporated. The residue was subjected to column chromatography on silica gel with hexane–EtOAc (9:1 v/v) as the eluent to give a 6:1 mixture of the deconjugated ester **3** and the recovered starting material **1** (26 mg, 96%) as an oil. The deconjugated ester **3** was composed of two isomers in a 1:1.3 ratio; ν_{max}(neat)/cm^{-1} 1735 (C=O); δ_H(500 MHz, $CDCl_3$) 3.03–3.06 and 3.10–3.12 [2 H(1:1.3), each m, CH_2CO_2Me], 3.67 and 3.68 [3 H (1.3:1), each s, OMe] and 5.59–5.65 (2 H, m, CH=CH); m/z 262 (M$^+$).

(*B*). To a stirred solution of the α,β-unsaturated ester **6** (21 mg, 0.11 mmol) and Et_3N (0.12 cm^3, 0.88 mmol) in dry CH_2Cl_2 (0.65 cm^3) was added dropwise at 18 °C TIPSOTf (0.12 cm^3, 0.45 mmol). After being stirred for 1 h at 18 °C, followed by addition of AcOH (0.063 cm^3, 1.10 mmol) whilst being cooled with ice, the resulting mixture was stirred for 2 h at 18 °C. After dilution with Et_2O, the mixture was washed with water saturated aq. $NaHCO_3$ and brine, dried and evaporated. Chromatography of the residue on silica gel with hexane–Et_2O (15:1 v/v) as the eluent afforded an 18:1 mixture of the deconjugated esters **7** and the starting material **6** (20.5 mg, 98%) as an oil. The deconjugated esters **7** were composed of two isomers in a 1.9:1 ratio; ν_{max}(neat)/cm^{-1} 1735 (C=O); δ_H(300 MHz, $CDCl_3$) 3.07 (0.69 H, d, J 5.9, PhCH_2), 3.21 (1.31 H, d, J 6.6, PhCH_2), 3.38 (0.69 H, d, J 6.9, CH_2CO_2Me), 3.41 (1.31 H, d, J 6.6, CH_2CO_2Me), 3.69 (1.03 H, s, OMe), 3.71 (1.97 H, s, OMe), 5.59–5.87 (2 H, m, CH=CH) and 7.16–7.32 (5 H, m, Ph).

6,6-*Dimethoxy*-2,2-*dimethylhexanenitrile* **17a**.—To a stirred solution of LDA [prepared from diisopropylamine (0.65 cm^3, 4.64 mmol) and BuLi in hexane (1.56 mol cm^{-3}; 2.76 cm^3,

4.31 mmol) in dry THF (5 cm^3)] was added a solution of 2-methylpropanal dimethylhydrazone (410 mg, 3.59 mmol) at −78 °C in dry THF (2 cm^3) and the mixture was stirred for 2 h at 0 °C. After addition of a solution of the bromide **16a**[11] (630 mg, 3.21 mmol) in dry THF (2 cm^3), the resulting mixture was further stirred for 50 min at 0 °C and then poured into saturated aq. NH_4Cl. After extraction with Et_2O, the extract was washed with brine, dried and evaporated to give a residue, which was chromatographed on silica gel. Elution with hexane–EtOAc (9 : 1 v/v) provided the *nitrile* **17a** (450 mg, 76%) as an oil (Found: C, 64.8; H, 10.35; H, 7.45. $C_{10}H_{19}NO_2$ requires C, 64.8; H, 10.35; N, 7.55%); ν_{max}(neat)/cm^{-1} 2230 (C≡N); δ_H(500 MHz, $CDCl_3$) 1.34 (6 H, s, CMe_2), 3.33 (6 H, s, 2 × OMe) and 4.38 [1 H, t, *J* 5.3, C*H*(OMe)$_2$]; *m*/*z* 184 (M^+ − 1).

7,7-*Dimethoxy*-2,2-*dimethylheptanenitrile* **17b**.—To a solution of ethyl 5-bromovalerate (10.0 g, 47.9 mmol) in a mixture of dry CH_2Cl_2 (25 cm^3) and DME (25 cm^3) was added dropwise DIBALH in hexane (0.99 mol cm^{-3}; 53.2 cm^3, 52.7 mmol) at −78 °C and the mixture was stirred for 30 min at the same temperature. After dilution with Et_2O, followed by addition of water (40 cm^3), the resulting mixture was stirred for 1 h and then filtered through Celite. Evaporation of the filtrate gave the aldehyde, which was used in the next reaction without purification.

A mixture of the above aldehyde and NH_4Cl (200 mg) in MeOH (100 cm^3) was heated for 12 h under reflux. After concentration, the residue was partitioned between saturated aq. $NaHCO_3$ and Et_2O. The organic layer was washed with brine, dried and evaporated to give a residue, which was distilled to give the acetal **16b** (6.7 g, 67%) as an oil, b.p. 97–107 °C/25 mmHg (Found: C, 40.2; H, 7.2; Br, 37.4. $C_7H_{15}BrO_2$ requires C, 40.0; H, 7.2; Br, 37.6%); *m*/*z* 209 and 211 (M^+ − 1).

To a solution of LDA [prepared from diisopropylamine (0.38 cm^3, 2.68 mmol) and BuLi in hexane (1.56 dm^{-3}; 1.58 cm^3, 2.47 mmol) in dry THF (1 cm^3)] was added a solution of the hydrazone (258 mg, 2.26 mmol) at −78 °C in dry THF (1 cm^3) and the mixture was stirred for 40 min at 0 °C. After addition of a solution of the above bromide **16b** (432 mg, 2.06 mmol) in dry THF (1 cm^3), the resulting mixture was stirred for 1 h at 0 °C. After being poured into saturated aq. NH_4Cl, the resulting mixture was thoroughly extracted with Et_2O. The extract was washed with brine, dried and evaporated to give a residue, which was subjected to chromatography on silica gel. Elution with hexane–EtOAc (9 : 1 v/v) afforded the *nitrile* **17b** (287 mg, 70%) as an oil (Found: C, 66.25; H, 10.3; N, 7.4. $C_{11}H_{21}NO_2$ requires C, 66.3; H, 10.65; N, 7.05%); ν_{max}(neat)/cm^{-1} 2230 (C≡N); δ_H(500 MHz, $CDCl_3$) 1.34 (6 H, s, CMe_2), 1.37–1.42 (2 H, m), 1.50–1.53 (4 H, m), 1.61–1.66 (2 H, m), 3.32 (6 H, s, 2 × OMe) and 4.37 [1 H, t, *J* 5.5, C*H*(OMe)$_2$]; 198 (M^+ − 1).

6,6-*Dimethoxy*-2,2-*dimethylhexanal* **18a**.—To a stirred solution of the nitrile **17a** (178 mg, 0.96 mmol) in dry CH_2Cl_2 (5 cm^3) was added DIBALH in hexane (0.99 mol dm^{-3}; 1.07 cm^3, 1.06 mmol) at −78 °C and the mixture was stirred for 1 h at −78 °C. After addition of further DIBALH in hexane (0.99 mol dm^{-3}, 0.1 cm^3, 0.099 mmol), the mixture was further stirred for 20 min at −78 °C. After dilution with Et_2O, followed by addition of water (0.9 cm^3), the mixture was stirred for 30 min at room temp. and then filtered through Celite. Evaporation of the filtrate gave a residue, which was adsorbed on silica gel. After being allowed to stand for 1.5 h at room temperature, elution with hexane–EtOAc (9 : 1 v/v) provided the *aldehyde* **18a** (168 mg, 93%) as an oil; ν_{max}(neat)/cm^{-1} 1725 (C=O); δ_H(60 MHz, $CDCl_3$) 1.06 (6 H, s, CMe_2), 3.32 (6 H, s, 2 × OMe) and 9.48 (1 H, s, CHO); *m*/*z* 157 (M^+ − OMe) (Found: M^+ − OMe, 157.1241. $C_9H_{17}O_2$ requires *m*/*z* 157.1229.

7,7-*Dimethoxy*-2,2-*dimethylheptanal* **18b**.—The nitrile **17b** (1.50 g, 7.53 mmol) was similarly converted as above into the aldehyde **18b** (1.40 g, 92%) as an oil; ν_{max}(neat)/cm^{-1} 1725 (C=O); δ_H(60 MHz, $CDCl_3$) 1.05 (6 H, s, CMe_2), 3.32 (6 H, s, 2 × OMe) and 9.48 (1 H, s, CHO); *m*/*z* 201 (M^+ − 1) (Found: M^+ − 1, 201.1489. $C_{11}H_{21}O_3$ requires *m*/*z* 201.1491).

Methyl (E)-8,8-*Dimethoxy*-4,4-*dimethyloct*-2-*enoate* **19a**.—To a suspension of NaH (60 w/w% in oil; 438 mg, 11.0 mmol) in dry DME (30 cm^3) was added trimethyl phosphonoacetate (1.86 cm^3, 11.5 mmol) at room temp. After being stirred for 15 min, a solution of the aldehyde **18a** (1.03 g, 5.48 mmol) in dry DME (8 cm^3) was added to the mixture. After being stirred for 22 h at room temp, the resulting mixture was diluted with water and then extracted with Et_2O. The extract was washed with brine, dried and evaporated. Chromatography of the residue on silica gel with hexane–EtOAc (9 : 1 v/v) as the eluent gave the *ester* **19a** (1.10 g, 83%) as an oil (Found: C, 63.95; H, 9.9. $C_{13}H_{24}O_4$ requires C, 64.0; H, 9.9%); ν_{max}(neat)/cm^{-1} 1720 (C=O) and 1650 (C=C); δ_H(500 MHz, $CDCl_3$) 1.05 (6 H, s, CMe_2), 3.31 (6 H, s, 2 × OMe), 3.73 (3 H, s, CO_2Me), 4.34 [1 H, t, *J* 5.8, C*H*(OMe)$_2$], 5.72 (1 H, d, *J* 15.9 Hz, C*H*CO_2Me) and 6.92 (1 H, d, *J* 15.9, C*H*=CHCO_2Me); *m*/*z* 243 (M^+ − 1).

Methyl (E)-9,9-*Dimethoxy*-4,4-*dimethylnon*-2-*enoate* **19b**.—The aldehyde **18b** (1.37 g, 6.78 mmol) was similarly transformed into the *ester* **19b** (1.66 g, 95%) as an oil (Found: C, 65.05; H, 10.15. $C_{14}H_{26}O_4$ requires C, 64.95; H, 10.1%); ν_{max}(neat)/cm^{-1} 1722 (C=O) and 1650 (C=C); δ_H(500 MHz, $CDCl_3$) 1.04 (6 H, s, CMe_2), 3.31 (6 H, s, 2 × OMe), 3.73 (3 H, s, CO_2Me), 4.33 [1 H, t, *J* 5.5, C*H*(OMe)$_2$], 5.71 (1 H, d, *J* 15.9, C*H*CO_2Me) and 6.91 (1 H, d, *J* 15.9, C*H*=CHCO_2Me); *m*/*z* 257 (M^+ − 1).

Dimethyl (2E,8E)-4,4-*Dimethyldec*-2,8-*dienedicarboxylate* **12a**.—A solution of the acetal **19a** (86 mg, 0.35 mmol) and PPTS (440 mg, 1.75 mmol) in a mixture of THF (2 cm^3) and water (2 cm^3) was stirred for 30 min at room temp and for 1.5 h at 45 °C. After neutralisation with saturated aqueous $NaHCO_3$ whilst being cooled with ice, the mixture was thoroughly extracted with CH_2Cl_2. The extract was washed with brine, dried and evaporated to give the aldehyde; ν_{max}(neat)/cm^{-1} 1720 (C=O) and 1640 (C=C), which was used in the following reaction without purification.

A mixture of the above aldehyde and methyl triphenylphosphoranylideneacetate (235 mg, 0.70 mmol) in dry MeCN (5 cm^3) was stirred for 7 h at room temp. and for 1 h at 40 °C. After evaporation of the solvent, the residue was subjected to chromatography on silica gel. Elution with hexane–EtOAc (9 : 1 v/v) afforded the *diester* **12a** (87 mg, 97%) as an oil; ν_{max}(neat)/cm^{-1} 1720 (C=O) and 1650 (C=C); δ_H(500 MHz, $CDCl_3$) 1.05 (6 H, s, CMe_2), 1.35–1.39 (4 H, m), 2.13–2.21 (2 H, m, 7-H_2), 3.73 (3 H, s, OMe), 3.74 (3 H, s, OMe), 5.72 (1 H, d, *J* 15.9, 2-H), 5.81 (1 H, br, d, *J* 15.3, 9-H), 6.90 (1 H, d, *J* 15.9, 3-H) and 6.93 (1 H, dt, *J* 15.3 and 6.7, 8-H); *m*/*z* 239 (M^+ − Me) (Found: M^+ − Me, 239.1300. $C_{13}H_{19}O_4$ requires *m*/*z*, 239.1283).

Dimethyl (2E,9E)-4,4-*Dimethylundeca*-2,9-*dienedicarboxylate* **12b**.—The acetal **19b** (604 mg, 2.34 mmol) was similarly transformed *via* the corresponding aldehyde [ν_{max}(neat)/cm^{-1} 1720 (C=O) and 1648 (C=C); δ_H(300 MHz, $CDCl_3$), 1.04 (6 H, s, CMe_2), 2.42 (2 H, dt, *J* 7.3 and 1.8 CH_2CHO), 3.74 (3 H, s, OMe), 5.71 (1 H, d, *J* 16.0, C*H*CO_2Me), 6.90 (1 H, t, *J* 16.0, C*H*=CHCO_2Me) and 9.75 (1 H, t, *J* 1.8, CHO)] into the diester **12b** (621 mg, 99%) as an oil; ν_{max}(neat)/cm^{-1} 1720 (C=O) and 1650 (C=C); δ_H(500 MHz, $CDCl_3$) 1.04 (6 H, s, CMe_2), 2.16–2.21 (2 H, m, 8-H_2), 3.73 (3 H, s, OMe), 3.74 (3 H, s, OMe), 5.72 (1 H, d, *J* 15.9, 2-H), 5.81 (1 H, dr, *J* 15.3 and 1.2, 10-H), 6.91

(1 H, d, *J* 15.9, 3-H) and 6.94 (1 H, dt, *J* 15.3 and 7.3, 9-H); *m/z* 268 (M^+) (Found: M^+, 268.1681. $C_{15}H_{24}O_4$ requires *M*, 268.1675).

Reaction of Dimethyl (2E,8E)-4,4-*Dimethyldeca*-2,8-*dienedicarboxylate* **12a** *with Trialkylsilyl Trifluoromethanesulfonate in the Presence of Triethylamine.*—(A) To a stirred solution of the diester **12a** (19 mg, 0.075 mmol) and Et_3N (0.085 cm^3, 0.61 mmol) in dry CH_2Cl_2 (1 cm^3) was added TBDMSOTf (0.085 cm^3, 0.37 mmol) at 18 °C and the mixture was stirred for 3 h at the same temperature. After being poured into 10% aq. $KHSO_4$, the mixture was thoroughly extracted with Et_2O. The extract was washed with brine, dried and evaporated to give a residue, which was dissolved in THF (1 cm^3) and then treated with 10% aq. $HClO_4$ (1 cm^3) for 2 h at 18 °C. The resulting mixture was thoroughly extracted with $CHCl_3$. The extract was washed with brine, dried and evaporated. The residue was chromatographed on silica gel with hexane–EtOAc (9:1 v/v) as the eluent to give a 3:1 mixture of the cyclopentanes **14a** and **20a** (10 mg, 53%) as an oil; ν_{max}(neat)/cm^{-1} 1735 and 1725 (C=O) and 1650 (C=C); δ_H(500 MHz, $CDCl_3$) 0.72 and 0.84 [3 H (1:3), each s, C*Me*Me], 1.00 and 1.02 [3 H (1:3), each s, CMe*Me*], 2.14 (0.75 H, dd, *J* 14.6 and 8.5, C*H*HCO$_2$Me), 2.29 (0.25 H, dd, *J* 15.3 and 8.6, CH*H*CO$_2$*Me*), 2.30 (0.75 H, dd, *J* 14.6 and 6.1, CH*H*CO$_2$Me), 2.35 (0.25 H, dd, *J* 15.3 and 5.5, CH*H*CO$_2$Me), 2.39–2.47 (0.75 H, m, C*H*CH=CH), 2.51–2.56 (0.25 H, m), 3.02 (0.5 H, br, d, *J* 7.3, C=CHC*H*$_2$CO$_2$Me), 3.59 and 3.67 [3 H (3:1), each s, OMe], 3.70 and 3.72 [3 H (1:3), each s, OMe], 5.22–5.28 (0.25 H, m, C=CH), 5.74 (0.75 H, br d, *J* 15.9, CH=C*H*CO$_2$Me), 6.82 (0.75 H, dd, *J* 15.9 and 9.8, C*H*=CHCO$_2$Me); *m/z* 254 (M^+) (Found: M^+, 254.1516. $C_{14}H_{22}O_4$ requires *M*, 254.1518).

Further elution provided the *indane derivative* **21a** (2 mg, 12%) as an oil; ν_{max}(neat)/cm^{-1} 1725 and 1703 (C=O) and 1652 (C=C); δ_H(500 MHz, $CDCl_3$) 0.94 (3 H, s, CMe), 1.04 (3 H, s, CMe), 2.56–2.64 (1 H, m, C*H*CH=CH), 3.44 (1 H, d, *J* 8.5, C*H*CO$_2$Me), 3.73 (3 H, s, OMe), 5.89 (1 H, dd, *J* 15.9 and 1.2, CH=C*H*CO) and 6.96 (1 H, dd, *J* 15.9 and 7.9, C*H*=CHCO); *m/z* 221 ($M^+ - 1$).

(B) To a stirred solution of the diester **12a** (36 mg, 0.14 mmol) and Et_3N (0.14 cm^3, 0.97 mmol) in dry CH_2Cl_2 (1.5 cm^3) was added TMSOTf (0.14 cm^3, 0.70 mmol) at 18 °C and the mixture was stirred for 2.5 h at 18 °C. The same work-up, followed by purification as above, gave a 2:1 mixture of the cyclopentanes **14a** and **20a** (26 mg, 81%).

Reaction of Dimethyl (2E,9E)-4,4-*Dimethylundeca*-2,9-*dienedicarboxylate* **12b** *with Trialkylsilyl Trifluoromethanesulfonate in the presence of Triethylamine.*— (A) To a stirred solution of the diester **12b** (150 mg, 0.56 mmol) and Et_3N (0.6 cm^3, 4.31 mmol) in dry CH_2Cl_2 (5 cm^3) was added TBDMSOTf (0.6 cm^3, 2.61 mmol) at 0 °C and the mixture was stirred for 1 h at 0 °C. After being poured into 10% HCl, the mixture was thoroughly extracted with Et_2O. The extract was washed with saturated aq. $NaHCO_3$ and brine, dried and evaporated. Chromatography of the residue on silica gel with hexane–EtOAc (9:1 v/v) as the eluent afforded a 5:3 mixture of the *cyclohexanes* **14b** and **20b** (133 mg, 89%) as an oil; ν_{max}(neat)/cm^{-1} 1738 and 1660 (C=O), 1650 and 1645 (C=C); δ_H(500 MHz, $CDCl_3$) 0.81 (2.25 H, s, CMe), 0.83 (0.75 H, s, CMe), 0.92, 0.93 and 1.04 [3 H (1.5:1.5:1), each s, CMe], 1.76 (0.38 H, ddd, *J* 16.6, 7.9 and 3.1, C*H*CH$_2$CO$_2$Me), 1.99 (0.38 H, dd, *J* 16.5 and 7.9, C*H*HCO$_2$Me). 2.34 (0.38 H, dd, *J* 16.5 and 3.1, CH*H*CO$_2$Me), 2.44 (0.38 H, dd, *J* 14.0 and 11.0, CH*H*CO$_2$Me), 2.50 (0.38 H, dd, *J* 14.0 and 4.9, CH*H*CO$_2$Me), 2.66–2.72 (0.25 H, m, C*H*CH=CH), 3.04 and 3.08 (each 0.38 H, each dd, each *J* 16.0 and 7.3, =CHC*H*$_2$CO$_2$Me), 3.57, 3.62 and 3.64 [3 H (1.5:1.5:1), each s, OMe], 3.66, 3.70 and 3.72 [3 H (1.5:1.5:1), each s, OMe], 5.23 (0.38 H, br, dd, *J* 7.3 and 7.3, C=CH), 5.77 (0.25 H, dd, *J* 15.9 and 1.8, CH=C*H*CO$_2$Me), 5.78 (0.38 H, d, *J* 15.3, CH=C*H*CO$_2$Me), 6.68 (0.38 H, dd, *J* 15.3 and 9.8, C*H*=CHCO$_2$Me) and 6.99 (0.25 H, dd, *J* 15.9 and 5.5, C*H*=CHCO$_2$Me); *m/z* 268 (M^+) (Found: M^+, 268.1664. $C_{15}H_{24}O_4$ requires *M*, 268.1675).

Further elution gave the trans-*decalone derivative* **21b** (2.5 mg, 4%) as an oil; ν_{max}(neat)/cm^{-1} 1737 (C=O) and 1670 (C=C); δ_H(300 MHz, $CDCl_3$) 0.85 (3 H, s, 5-Me), 0.99 (3 H, s, 5-Me), 1.91–2.00 (1 H, m), 2.17 (1 H, dd, *J* 12.8 and 11.4, 4a-H), 2.28–2.40 (1 H, m, 8a-H), 3.28 (1 H, d, *J* 12.8, 4-H), 3.74 (3 H, s, OMe), 6.03 (1 H, dd, *J* 9.9 and 3.6, 1-H) and 6.76 (1 H, dd, *J* 9.9 and 1.8, 2-H); *m/z* 236 (M^+) (Found: M^+, 236.1414. $C_{14}H_{20}O_3$ requires *M*, 236.1412).

(B) Reaction of the diester **12b** (30 mg, 0.11 mmol) with TMSOTf (0.086 cm^3, 0.45 mmol) in the presence of Et_3N (0.125 cm^3, 0.90 mmol) in dry CH_2Cl_2 (1 cm^3) as above, followed by the similar work-up and purification, provided a 1:1.7 mixture of cyclohexanes **14b** and **20b** (24 mg, 80%).

(C) Reaction of the diester **12b** (30 mg, 0.11 mmol) with TIPSOTf (0.12 cm^3, 0.45 mmol) in the presence of Et_3N (0.12 cm^3, 0.86 mmol) in dry CH_2Cl_2 (1 cm^3) as above, followed by the similar work-up and purification, gave an 8:5 mixture of cyclohexanes **14b** and **20b** (23 mg, 77%).

Methyl (2,2-*Dimethyl*-6-*oxocyclohexyl*)*acetate* **23** *and Methyl* (6-*Formyl*-2,2-*dimethylcyclohexyl*)*acetate* **24**.—The mixture of the cyclohexanes **14b** and **20b** (429 mg, 1.60 mmol), prepared by the method A, was dissolved in dry CH_2Cl_2 (12 cm^3) and an excess of O_3 was introduced into the solution at −78 °C over 20 min. After the removal of O_3 with N_2, to the resulting mixture was added Et_3N (1.8 cm^3, 12.91 mmol) at −78 °C the whole was stirred for 6 h at room temp.; it was then poured into water. The mixture was extracted with Et_2O and the extract was washed with brine, dried and evaporated. Chromatography of the residue on silica gel with hexane–EtOAc (95:5 v/v) as the eluent gave the *ester* **23** (85 mg, 27%) as an oil; ν_{max}(neat)/cm^{-1} 1735 and 1705 (C=O); δ_H(500 MHz, $CDCl_3$) 0.74 (3 H, s, C-Me), 1.07 (3 H, s, CMe), 2.24 (1 H, dd, *J* 16.7 and 3.7, C*H*CH$_2$CO$_2$Me), 2.35–2.41 (2 H, m, CH$_2$CO), 2.71 (1 H, dd, *J* 16.5 and 10.4, C*H*HCO$_2$Me), 2.85 (1 H, dd, *J* 10.4 and 3.7, C*H*HCO$_2$Me) and 3.67 (3 H, s, OMe); *m/z* 198 (M^+) (Found: M^+, 198.1260. $C_{11}H_{18}O_3$ requires *M*, 198.1256.

Further elution provided a 1.5:1 mixture of the formyl esters **24** (151 mg, 44%) as an oil; ν_{max}(neat)/cm^{-1} 1730 and 1718 (C=O); δ_H(300 MHz, $CHCl_3$) 0.82 and 0.84 [3 H (1.5:1), each s, CMe], 0.95 and 1.05 [3 H (1.5:1), each s, CMe], 3.65 and 3.67 [3 H (1.5:1), each s, OMe], 9.44 (0.6 H, d, *J* 3.8, CHO) and 9.75 (0.4 H, s, CHO); *m/z* 213 ($M^+ + 1$) (Found: $M^+ + 1$, 213.1469. $C_{12}H_{21}O_3$ requires *m/z* 213.1491).

Isomerization of Methyl (6-*Formyl*-2,2-*dimethylcyclohexyl*)-*acetate* **24**.—The 1.5:1 mixture of the above esters **24** (151 mg, 0.71 mmol) was dissolved in dry CH_2Cl_2 (8 cm^3) and then treated with DBU (0.13 cm^3, 0.87 mmol) for 6 h at room temp. The resulting mixture was partitioned between 10% aq. $KHSO_4$ and Et_2O. The organic layer was washed with brine, dried and evaporated to give a residue, which was purified by chromatography on silica gel. Elution with hexane–EtOAc (95:5 v/v) yielded the 7.5:1 mixture of the formyl esters **24** (118 mg, 78%).

5,5-*Dimethyl*-4a,5,6,7,8,8a-*hexahydroisochroman*-3-*ol* **25**.—To a solution of the 7.5:1 mixture of the aldehydes **24** (108 mg, 0.51 mmol) in EtOH (3 cm^3) was added $NaBH_4$ (20 mg, 0.53 mmol) portionwise at −8 °C and the mixture was stirred for 10 min at −8 °C. After dilution with Et_2O, the mixture was treated with 5% aq. oxalic acid. The aqueous layer was thoroughly extracted with Et_2O and the combined organic layers were

washed with brine, dried and evaporated. The residue was subjected to chromatography on silica gel with hexane–Et_2O (2:1 v/v) as the eluent to afford a diastereoisomeric mixture of cyclic hemiacetals **25** (93 mg, 99%) as an oil; ν_{max}(neat)/cm^{-1} 3420–3380 (OH); δ_H(500 MHz, $CDCl_3$) 0.80 and 0.82 [3 H (1:1.4), each s, CMe], 0.87 and 0.88 [3 H (1:1.4), each s, CMe], 2.48 (0.42 H, br s, OH), 2.98–3.03 (0.58 H, m, OH), 3.08 (0.58 H, dd, *J* 11.0 and 11.0 CH_{ax}HO), 3.44 (0.42 H, dd, *J* 11.0 and 4.2, CHH_{eq}O), 3.59 (0.42 H, dd, *J* 11.0 and 11.0, CH_{ax}HO), 3.84 (0.58 H, dd, *J* 11.0 and 4.2, CHH_{eq}O) 4.70 and 5.37 [1 H (1.4:1), br d, *J* 8.4 and br s, respectively, C*H*OH]; *m/z* 184 (M^+) (Found: $M^+ - 1$, 183.1367. $C_{11}H_{19}O_2$ requires *m/z*, 183.1385).

3,3-*Dimethyl*-2-(1,3-*dithian*-2-*ylmethyl*)-1-*hydroxymethylcyclohexane* **26**.—To a stirred solution of the hemiacetals **25** (27 mg, 0.15 mmol) and propane-1,3-dithiol (0.044 cm^3, 0.44 mmol) in dry CH_2Cl_2 (1 cm^3) was added BF_3·OEt_2 (0.09 cm^3, 0.73 mmol) at 0 °C and the mixture was stirred for 1 h at room temp. After dilution with Et_2O, the mixture was washed with saturated aq. $NaHCO_3$ and brine, dried and evaporated. The residue was chromatographed on silica gel with hexane–Et_2O (2:1 v/v) as the eluent to give a 7:1 mixture of the *alcohols* **26** (39 mg, 97%) as an oil; ν_{max}(neat)/cm^{-1} 3440 (OH); δ_H(300 MHz, $CDCl_3$) 0.78 and 0.94 [3 H (7:1), each s, CMe], 0.98 and 1.03 [3 H (7:1), each s, CMe], 2.77–2.96 (4 H, m, 2 × SCH_2), 3.52–3.73 (2 H, m, CH_2OH) and 3.86 and 4.01 [1 H (1:7), each dd, each *J* 9.5 and 4.8, S_2CH]; *m/z* 274 (M^+) (Found: M^+, 274.1417. $C_{14}H_{26}OS_2$ requires *M*, 274.1425).

1-tert-*Butyldimethylsiloxymethyl*-3,3-*dimethyl*-2-(1,3-*dithian*-2-*ylmethyl*)*cyclohexane* **27**.—To a solution of the alcohols **26** (112 mg, 0.41 mmol) and 2,6 dimethylpyridine (0.19 cm^3, 1.63 mmol) in dry CH_2Cl_2 (3 cm^3) was added TBDMSOTf (0.19 cm^3, 0.82 mmol) at 18 °C and the mixture was stirred for 25 min at the same temperature. After dilution with Et_2O, the mixture was washed with saturated aq. $NaHCO_3$ and brine, dried and evaporated. Chromatography of the residue on silica gel with hexane–Et_2O (10:1 v/v) as the eluent afforded a 7:1 mixture of the *silyl ethers* **27** (159 mg, 100%) as an oil; δ_H(300 MHz, $CDCl_3$) 0.01 (0.12 H, s, SiMe), 0.02 (0.12 H, s, SiMe), 0.07 (0.88 H, s, SiMe), 0.08 (0.88 H, s, SiMe), 0.74 and 0.87 [3 H (8:1), each s, CMe], 0.91 and 0.94 [9 H (1:8), each s, SiBu^t], 0.97 and 0.99 [3 H (8:1), each s, CMe], 2.71–2.93 (4 H, m, 2 × SCH_2). 3.39–3.67 (2 H, m, CH_2O), 4.05 (0.12 H, dd, *J* 11.9 and 6.5, S_2CH) and 4.11 (0.88 H, br d, *J* 9.5, S_2CH); *m/z* 388 (M^+) (Found: 388.2303. $C_{20}H_{40}OS_2Si$ requires *m/z*, 388.2290).

3-[2-(2-*Hydroxymethyl*-6,6-*dimethylcyclohexyl*)-1-*hydroxyethyl*]*furan* **29**.—To a solution of the silyl ethers **27** (20 mg, 0.052 mmol) and $NaHCO_3$ (22 mg, 0.26 mmol) in a mixture of MeCN (1 cm^3) and water (0.13 cm^3) was added MeI (0.032 cm^3, 0.51 mmol) at 18 °C and the mixture was heated at 45 °C for 23 h. After partition of the reaction mixture between water and Et_2O, the organic phase was washed with brine, dried and evaporated to give a residue, which was subjected to chromatography on silica gel. Elution with hexane–Et_2O (10:1 v/v) yielded the aldehyde; ν_{max}(neat)/cm^{-1} 1720.

To a stirred solution of 3-bromofuran (0.032 cm^3, 0.36 mmol) in dry THF (0.5 cm^3) was added BuLi in hexane (1.56 mol dm^{-3}; 0.165 cm^3, 0.257 mmol) at −78 °C. After being stirred for 30 min at this temperature, to the resulting mixture was added at −78 °C a solution of the above aldehyde in dry THF (0.5 cm^3) and the mixture was stirred for 30 min at −78 °C. After dilution with Et_2O, the mixture was neutralised with saturated aq. NH_4Cl whilst being cooled with ice. The aqueous layer was thoroughly extracted with Et_2O and the combined organic extracts were washed with brine, dried and evaporated to give the alcohols **28** as a yellowish oil, ν_{max}(neat)/cm^{-1} 3430 (OH), which was subjected to the following reaction without purification.

A mixture of the above alcohols and Bu_4NF in THF (1 mol dm^{-3}; 0.1 cm^3, 0.1 mmol) in THF (0.6 cm^3) was stirred for 1 h at 0 °C. The mixture was partitioned between water and Et_2O and the organic phase was separated, washed with brine, dried and evaporated to give a residue, which was chromatographed on silica gel. Elution with hexane–EtOAc (1:1 v/v) afforded a 1.3:1 mixture of the *diols* **29** (8.1 mg, 62% overall yield from **27**) as an oil; ν_{max}(neat)/cm^{-1} 3330–3270 (OH); δ_H(300 MHz, $CDCl_3$) 0.79 (3 H, s, CMe), 0.89 and 0.93 [3 H (1.3:1), each s, CMe], 3.35–3.70 (1.6 H, m, CH_2OH), 4.02–4.07 (0.4 H, m, CH_2OH), 4.61–4.66 and 4.73–4.80 [1 H (1:1.3), each m, C*H*OH), 6.41 (1 H, br s, C*H*=CHO) and 7.39 (2 H, m, CHOCH); *m/z* 252 (M^+) (Found: M^+, 252.1723. $C_{15}H_{24}O_3$ requires *M*, 252.1725).

2-[2-(3-*Furyl*)-2-*oxoethyl*]-2,2-*dimethylcyclohexanecarboxylic Acid* **30** *and* (±)-*Ricciocarpin A* **22**.—To a mixture of PDC (300 mg, 0.797 mmol) in dry DMF (1 cm^3) was added a solution of the diols **29** (25 mg, 0.099 mmol) at room temp. in dry DMF (1 cm^3) and the mixture was stirred for 70 h at the same temperature. After being poured into 10% aq. HCl, the mixture was thoroughly extracted with EtOAc. The extract was washed with brine, dried and evaporated. Chromatography of the residue on silica gel with hexane–Et_2O (3:1 v/v) as the eluent provided a syrup, which was further purified by HPLC on Si 80-125-C5 (4 × 250 mm) with hexane–Et_2O (3:1 v/v, 0.5 cm^3 min^{-1}) as the eluent to afford (±)-ricciocarpin A **22** (4 mg, 16%) as crystals (from Pr^{i}OH), m.p. 92.5–93 °C (lit.,[15] 95–96 °C), whose ^{1}H NMR (500 MHz, $CDCl_3$) spectrum was identical with that of the natural product.

Further elution of the above chromatography on silica gel with $CHCl_3$–MeOH (95:5 v/v) as the eluent gave the acid **30** (6.1 mg, 23%) as crystals (from MeOH), m.p. 130–131 °C (lit.,[15] 131–132 °C), whose IR ($CHCl_3$) and ^{1}H NMR (500 MHz, $CDCl_3$) spectra were consistent with the reported data.

Acknowledgements

We thank Professor H. Becker of University of Saarlandes for his generous gift of sample and spectral data of ricciocarpin A.

References

1 H. B. Mekelburger and C. S. Wilcox, in *Comprehensive Organic Synthesis*, ed. B. M. Trost, Pergamon, Oxford, 1991, vol. 2, p. 99.
2 E. W. Colvin, *Silicon in Organic Synthesis*, Butterworths, London, 1981, p. 198; W. P. Weber, *Silicon Reagents for Organic Synthesis*, Springer–Verlag, Berlin, 1983, p. 206.
3 H. Emde, D. Domsch, H. Feger, U. Frick, A. Götz, H. H. Hergott, K. Hofmann, W. Kober, K. Krägeloh, T. Oesterle, W. Steppan, W. West and G. Simchen, *Synthesis*, 1982, 1.
4 M. Ihara and K. Fukumoto, *J. Synth. Org. Chem. Jpn.*, 1986, **44**, 96; M. Ihara, M. Tsuruta, K. Fukumoto and T. Kametani, *J. Chem. Soc., Chem. Commun.*, 1985, 1159; M. Ihara, Y. Takino, K. Fukumoto and T. Kametani, *Tetrahedron Lett.*, 1988, **29**, 4135; M. Ihara, Y. Takino, M. Tomotake and K. Fukumoto, *J. Chem. Soc., Perkin Trans. 1*, 1990, 2287.
5 M. Ihara, S. Suzuki, N. Taniguchi, K. Fukumoto and C. Kabuto, *J. Chem. Soc., Chem. Commun.*, 1991, 1168; *J. Chem. Soc., Perkin Trans. 1*, 1992, 2527.
6 M. Ihara, M. Ohnishi, M. Takano, K. Makita, N. Taniguchi and K. Fukumoto, *J. Am. Chem. Soc.*, 1992, **114**, 4408.
7 A part of this work has been published as preliminary communication: M. Ihara, S. Suzuki, N. Taniguchi and K. Fukumoto, *J. Chem. Soc., Chem. Commun.*, 1993, 755
8 J. P. Yardley and R. W. Rees, *Can. J. Chem.*, 1985, **63**, 1013.
9 Reviews: D. A. Oare and C. H. Heathcock, in *Topics in Stereochemistry*, ed. E. L. Eliel and S. H. Wilen, John Wiley, New York, vol. 19, p. 227; P. Perlmutter, *Conjugate Addition Reactions in Organic Synthesis*, Pergamon, Oxford, 1992. Recent examples: G.

Stork and N. A. Saccomano, *Tetrahedron Lett.*, 1987, **28**, 2087; T. Terada and T. Yamazaki, *J. Am. Chem. Soc.*, 1988, **110**, 958; Y. Yokoyama and K. Tsuchikura, *Tetrahedron Lett.*, 1992, **33**, 2823.
10 M. J. Aurell, P. Gaviña, S. Gil, M. Parra, A. Tortajada and R. Mestres, *Synth. Commun.*, 1991, **21**, 1825; G. H. Posner and E. M. Shulman-Roskes, *J. Org. Chem.*, 1989, **54**, 3514.
11 M. Ihara, T. Kakahashi, N. Shimizu, Y. Ishida, I. Sudow, K. Fukumoto and T. Kemetani, *J. Chem. Soc., Perkin Trans. 1*, 1989, 529.
12 T. Cuvigny, J. F. DeBorgne, M. Larchevêque and H. Normant, *Synthesis*, 1976, 237.
13 G. Wurzel and H. Becker, *Phytochemistry*, 1990, **29**, 2565.
14 G. Wurzel, H. Becker, T. Eicher and K. Tiefensee, *Planta Med.*, 1990, **56**, 444; H. D. Zinsmeister, H. Becker and T. Eicher, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 130.
15 T. Eicher, K. Massonne and M. Herrmann, *Synthesis*, 1991, 1173.

Paper 3/03566B
Received 21*st June* 1993
Accepted 28*th June* 1993