76. An Efficient Enantioselective Synthesis of (−)-Serricorole[1])

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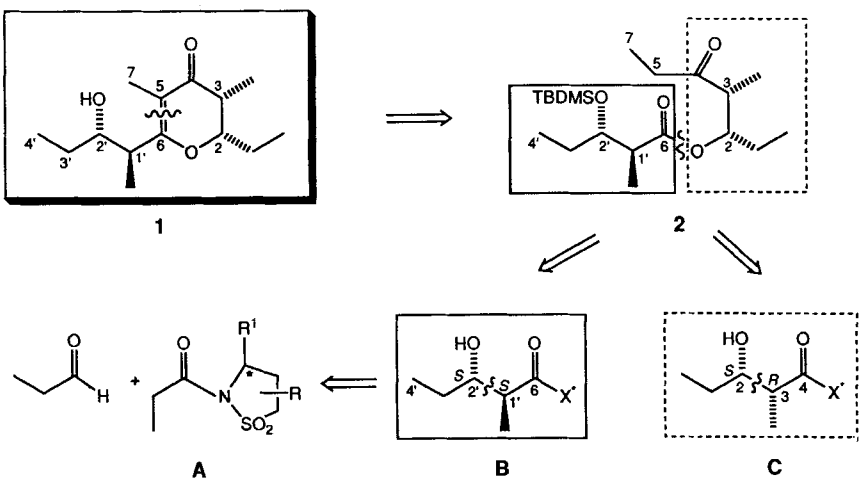
The cigarette beetle pheromone (−)-serricorole (**1**) has been synthesized in 23% overall yield by an eight-step sequence starting from *N*-propionylsultam **3**. The synthesis features asymmetric *anti*- and *syn*-aldolizations **3** → **4** and **8** → **9**, a non-destructive *N*-acylsultam cleavage with lithiated ethylphenylsulfone (**10** → **12**), and the smooth, Ti-mediated cyclization of β-acyloxy-ketone **2** to dihydropyranone **14**.

Introduction. – (−)-Serricorole, is a sex pheromone component of the cigarette beetle (*Lasioderma serricorne* F.) [1]. Its constitution and relative configuration **1** has been assigned *via* a synthesis of the racemate [2] and the depicted absolute configuration follows from an enantiospecific 16-step synthesis carried out by *Mori et al.* [3].

Mori's approach to (−)-**1** starts with the (*R*)- and (*S*)-antipodes of methyl 3-hydroxypentanoate and features an intramolecular condensation of the β-acyloxy-ketone **2** [3] (*Scheme 1*). However, the crucial step **2** → **1** was reported to proceed in low yield (18%) which could not even be reproduced in our hands (*vide infra*).

Scheme 1

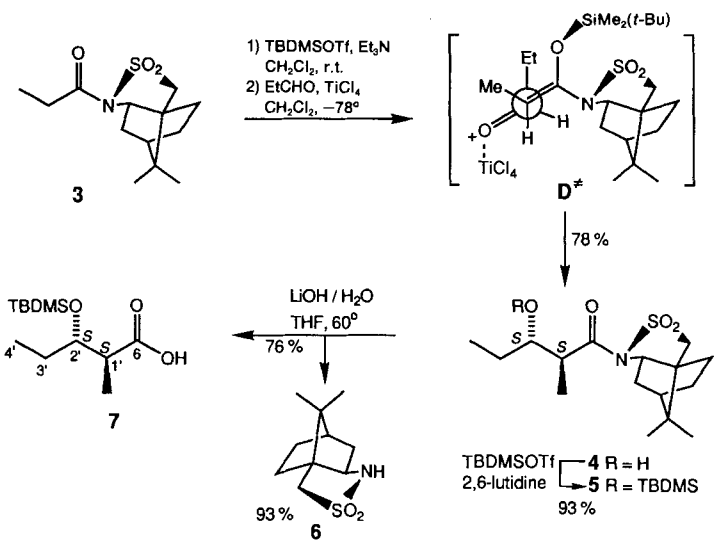


[1]) Presented at the Annual Autumn Meeting of the New Swiss Chemical Society, Bern, October 1992.

Planning a shorter and more practical synthesis of (−)-serricorole, we, nevertheless, centered our strategy on the C(5)=C(6) disconnection[2]) **1** → **2**. Apart from the challenge of developing new reaction conditions for an efficient cyclization **2** → **1**, this leads to an attractive molecular simplification. Thus, key intermediate **2** should be readily assembled from stereochemically pure *anti*- and *syn*-aldols **B** and **C**. These segments, in turn, are readily accessible by aldol condensation of propionaldehyde with chiral *N*-propionylsultams **A**, which can be directed either in an *anti*- (**A** → **B**) [4] or *syn*-sense (**A** → **C**) [5].

Preparation of the Aldol Segments. – To prepare the *anti*-aldol segment C(4')–C(6), *N*-propionylsultam **3** was treated with (*t*-butyl)dimethylsilyl triflate (TBDMSOTf)/NEt_3 at room temperature (*Scheme 2*).

Scheme 2



$TiCl_4$-Mediated condensation of the resulting crude *O*-silyl-*N*,*O*-ketene acetal with propionaldehyde at −78° gave pure *anti*-aldol **4** in 78% yield after direct crystallization [5]. The C(α)-*Re*/'*anti*'-topicity of this *Mukaiyama*-type aldolization is consistent with an 'open' transition state **D**≠ featuring attack of the *Lewis*-acid-coordinated aldehyde opposite to the O–Si bond.

A related transition state can be ascribed to the aldol condensation of the *O*-diethylboryl enolate of **3** with propionaldehyde (2 mol-equiv.) *in the presence of* $TiCl_4$ (4 mol-equiv.) which afforded the same *anti*-aldol **4** (77% after crystallization) [6].

O-Silylation of **4** (93%) and saponification of the crystalline *N*-(O-silylacyl)sultam **5** with LiOH provided recovered auxiliary **6** (93%) and pure (2*S*,3*S*)-carboxylic acid **7** (76%).

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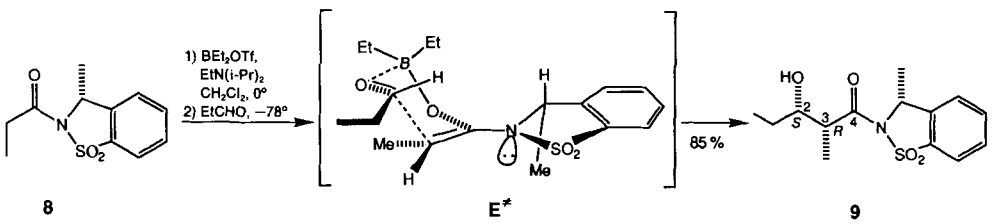
[2]) The numbering of **1** corresponds to [2] and is used also for all intermediates; systematic names are given in the *Exper. Part.*

We then proceeded to assemble the C(2)–C(4) segment. The corresponding, crystalline *syn*-aldol **C** was easily obtained from the same *N*-propionylbornanesultam **3** *via* conventional borylenolate/propionaldehyde condensation (in the absence of a *Lewis* acid) [5a]. However, in view of our intention to displace the auxiliary group ultimately by a C-nucleophile (to introduce the C(5)–C(7) segment, *vide infra*), we employed the more readily removable toluenesultam auxiliary (*Scheme 3*) [5b].

Scheme 3

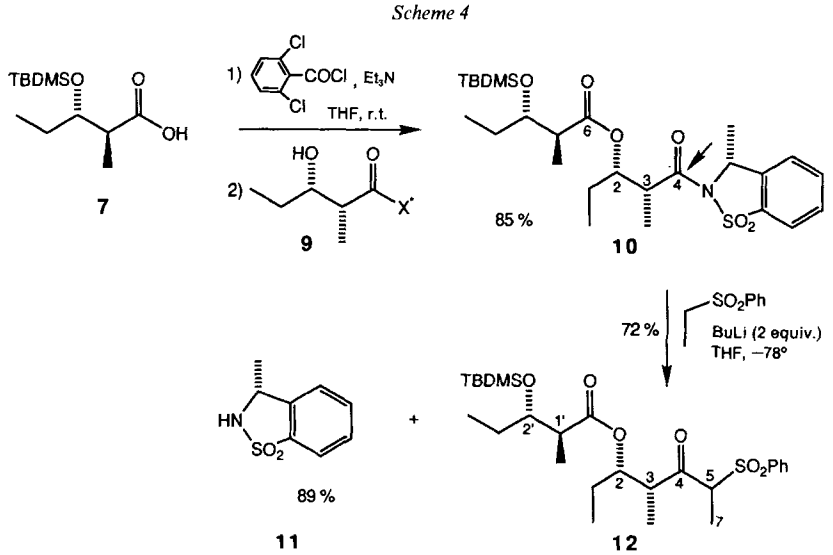


Thus, successive treatment of *N*-propionyltoluenesultam **8** with (*in situ* prepared) diethylboryl triflate/EtN(i-Pr)$_2$ at 0° and propionaldehyde at –78° yielded pure *syn*-aldol **9** (85% after crystallization). The observed double-face selectivity of condensation **8** → **9** conforms to the closed transition-state model **E**$^{\neq}$.

Coupling of the C(2)–C(4), C(4')–C(6), and C(5)–C(7) Segments. – Activation of carboxylic acid **7** with 2,6-dichlorobenzoyl chloride/NEt$_3$ and *O*-acylation of aldol **9** with the resulting mixed anhydride/DMAP [7] furnished ester **10** in 85% yield after crystallization (*Scheme 4*).

Displacement of the sultam moiety in **10** by an ethyl equivalent was accomplished by reaction with dilithiated ethyl phenyl sulfone [8]. Thus, deprotonation of ethyl phenyl

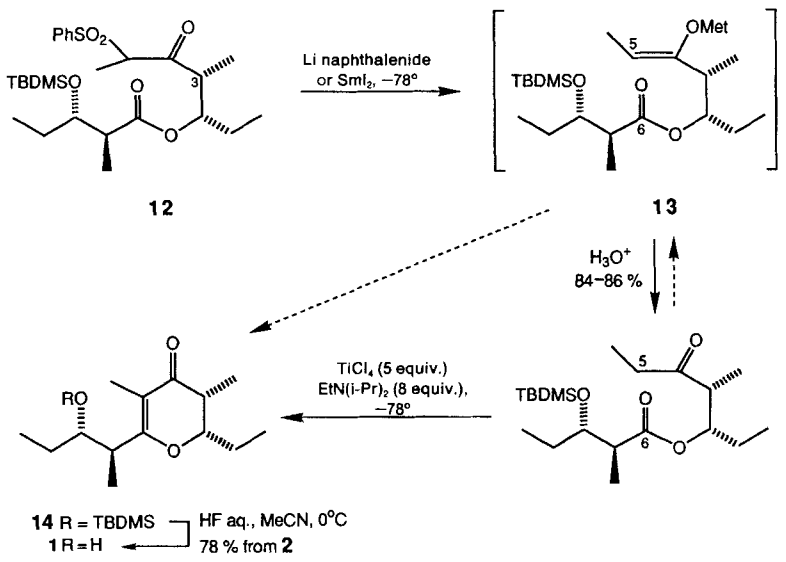
Scheme 4



sulfone with BuLi/TMEDA (2 mol-equiv.) at 0° in THF, addition of *N*-acyltoluenesultam **10** at −78° and stirring the mixture at −78° for 3 h gave sultam auxiliary **11** (89%) and *β*-oxo-sulfone **12** (72%) as a 93:7 mixture of C(5)-epimers. It is remarkable that the $MeCLi_2SO_2Ph$ reagent attacks selectively the C(4)-imide C=O group in preference to the C(6)-ester C=O group[3]) and without epimerization at C(3) or C(1′).

Intramolecular Enolate/Ester Condensation: Dihydropyranone Formation. – Reductive cleavage of the *β*-oxo-sulfone **12** was initially expected to yield dihydropyranone **14** directly *via* a spontaneous cyclization of the regioselectively generated enolate **13** (*Scheme 5*).

Scheme 5



Desulfonation of **12** with lithium naphthalenide [10] and aqueous workup gave oxopentyl ester **2** in 84% yield, but to our disappointment, not even a trace of **14**. All further attempts to cyclize the transient enolate **13**, including transmetallation of **13**, Met = Li with $TiCl_4$, $(i\text{-}PrO)_3TiCl$, $CeCl_3$, Me_2AlCl, and $ZnCl_2$ failed to produce dihydropyranone **14**. Reduction of **12** with SmI_2 [11] also yielded **2** (84–86%) but no dihydropyranone.

With ester **2** in hand, we then tried to reproduce the reported cyclization conditions **2** → **1** [3]. Deprotonation of **2** with LiHDMS (2 mol-equiv.) in THF/TMEDA at −78° to 0° under Ar, pouring of the mixture into a 10% solution of $ClCH_2COOH$ in THF/H_2O 1:1, stirring for 20 h at r.t., workup, and desilylation gave at best 4% (−)-serricorole (**1**) together with its C(3)-epimer (4%).

Systematic exploration of various reaction conditions led to the following cyclization protocol. A 0.02M solution of **2** in CH_2Cl_2 was treated with $TiCl_4$ (5 mol-equiv.) and

[3]) For the cleavage of carboxylates with lithiated alkylsulfones, see [9].

EtN(i-Pr)$_2$ (8 mol-equiv.) at −78° (1 h) and then at 0° (20 h). Workup and desilylation of crude cyclization product **14** (HF/MeCN, 0°) provided pure (−)-serricorole (**1**) in 67% yield (from **2**). Thus obtained **1** shows ^{1}H-NMR, ^{13}C-NMR, and mass spectra in agreement with reported data and a slightly higher optical rotation $[\alpha]_D = -124$ compared to the previously recorded value $[\alpha]_D = -113$ [3].

Conclusion. – In summary, pure (−)-serricorole (**1**) has been prepared from *N*-propionylsultam **3** by an eight-step sequence in 23% overall yield. All four stereocenters of **1** were perfectly controlled *via* sultam-directed *syn*- or *anti*-aldolizations, which once again highlights the synthetic value of chiral sultam auxiliaries [4] [12]. The cleavage of an *N*-acylsultam using a lithiated alkylsulfone as a C-nucleophile (**10** → **12**) represents a general approach to chiral alkyl ketones [8]. A convenient and efficient route to optically pure, polysubstituted γ-dihydropyranones by Ti-mediated cyclization[4]) of β-acyloxyketones is exemplified by the key step **2** → **14**. The scope and limitations of this cyclization are the subject of the following contribution.

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Experimental Part

General. All reactions were carried out under Ar with magnetic stirring, unless otherwise specified. Solvents were dried by distillation from drying agents as follows: Et_2O, THF (Na-benzophenone), toluene (Na), CH_2Cl_2, hexane, pentane, TMEDA (CaH_2), MeOH (Mg). Workup denotes extraction with an org. solvent, washing of the org. phase with sat. aq. NH_4Cl soln., drying ($MgSO_4$), and evaporation *in vacuo*. Column flash chromatography (FC): SiO_2 (*Merck*, *Kieselgel 60*, 0.040–0.060 mm). GC: *Hewlett-Packard 5790A*, integrator *HP 3390A*, capillary column (fused silica, *OV-1*, 0.2 mm i.d., 12 m), 10 psi H_2; t_R in min (area −%). M.p.: *Kofler* hot stage; uncorrected. $[\alpha]_D$: *Perkin-Elmer 241* polarimeter, in $CHCl_3$, unless otherwise specified. IR: *Polaris Matteson Instruments* or *Perkin-Elmer 681* in $CHCl_3$, unless otherwise specified. NMR Spectra (*Bruker AMX-400* or *Bruker WH-360* or *Varian XL-200*), in $CDCl_3$, unless otherwise specified; standard $CHCl_3$ ($\delta = 7.27$ ppm), *J* in Hz. MS: *Varian CH-4* or *Finnigan 4023* at 70 eV, *m/z* (rel.-%). HR-MS: *VG 707-E*.

N-[(2S,3S)-3-Hydroxy-2-methylpentanoyl]bornane-10,2-sultam (**4**). (*t*-Butyl)dimethylsilyl triflate (4.65 ml, 20.29 mmol) and Et_3N (3.1 ml, 22.14 mmol) were added to a soln. of *N*-propionylsultam **3** [5a] (5 g, 18.45 mmol) in CH_2Cl_2 (15 ml). Stirring of the mixture at r.t. for 16 h, evaporation, trituration of the residue with pentane under Ar, decantation of the clear pentane soln. under Ar, and evaporation gave the corresponding *O*-silyl-*N*,*O*-ketene acetal as a solid residue. A soln. of this residue in CH_2Cl_2 (15 ml) was added at −78° to a mixture of $TiCl_4$ (2.54 ml, 22.14 mmol) and propionaldehyde (1.6 ml, 22.14 mmol) in CH_2Cl_2 (20 ml) at −78°. Stirring of the mixture at −78° for 5 min, addition of sat. aq. NH_4Cl soln., and workup gave crude **4**. HPLC (hexane/AcOEt 6:1, 1 ml/min): 6.43 min (14%, **5**), 9.6 min (3%, **3**), 21.2 min (82%, **4**). FC (hexane/AcOEt 6:1) and crystallization (Et_2O/pentane) furnished aldol **4** (4.75 g, 78%). M.p. 76–77°. $[\alpha]_D = -64.8$, $[\alpha]_{578} = -65.0$, $[\alpha]_{546} = -75.5$, $[\alpha]_{463} = -123.9$, $[\alpha]_{365} = -189.4$, ($c = 1.32$, $T = 22°$). IR: 3530, 2950, 1680, 1450, 1380, 1330, 1270, 1240, 1160, 1140, 1050, 960. ^{1}H-NMR: 0.97 (*s*, 3 H); 0.99 (*t*, *J* = 7.5, 3 H); 1.18 (*s*, 3 H); 1.23 (*d*, *J* = 7, 3 H); 1.32–1.44 (3 H); 1.65 (*m*, 1 H); 1.85–1.98 (3 H); 2.08 (*m*, 1 H); 2.17 (*m*, 1 H); 2.37 (*d*, *J* = 10, 1 H); 3.19 (*m*, 1 H); 3.45 (*d*, *J* = 14, 1 H); 3.53 (*d*, *J* = 14, 1 H); 3.55 (*m*, 1 H); 3.90 (*dd*, *J* = 5, 8, 1 H). ^{13}C-NMR: 175.5 (*s*); 77.0 (*d*); 65.5 (*d*); 53.2 (*t*); 48.3 (*s*); 47.8 (*s*); 45.1 (*d*); 44.8 (*d*); 38.5 (*t*); 33.0 (*t*); 28.5 (*t*); 26.4 (*t*); 20.7 (*q*); 19.9 (*q*); 14.2 (*q*); 9.8 (*q*).

N-[(2S,3S)-3-[(tert-Butyl)dimethylsilyloxy]-2-methylpentanoyl]bornane-10,2-sultam (**5**). 2,6-Lutidine (3.2 ml, 27.34 mmol) and (*tert*-butyl)dimethylsilyl triflate (3.76 ml, 16.4 mmol) were added to a soln. of **4** (4.5 g, 13.67 mmol) in CH_2Cl_2 (15 ml). Stirring of the mixture at r.t. for 30 min, workup, and crystallization (EtOH) furnished **5** (5.66 g, 93%). GC (150, 5, 10, 270): 15.25 (99%). M.p. 144–145°. IR: 3027, 2953, 2888, 2858, 1691, 1472, 1456,

[4]) For the use of Ti enolates in *Dieckmann* condensations and in aldolizations, see [13] and [14], respectively.

1328, 1258, 1162, 1125, 1060. ^{1}H-NMR: 0.07 (*s*, 3 H); 0.09 (*s*, 3 H); 0.88 (*s*, 12 H); 0.97 (*s*, 3 H); 1.11 (*d*, *J* = 6.5, 3 H); 1.15 (*s*, 3 H); 1.26–1.55 (4 H); 1.83–1.97 (3 H); 1.97–2.1 (2 H); 3.30 (*m*, 1 H); 3.43 (*d*, *J* = 13, 1 H); 3.50 (*d*, *J* = 13, 1 H); 3.89 (*dd*, *J* = 5, 7, 1 H); 4.07 (*m*, 1 H). ^{13}C-NMR: 174.23 (*s*); 73.88 (*d*); 65.38 (*d*); 53.10 (*d*); 48.10 (*s*); 45.96 (*d*); 44.66 (*d*); 38.57 (*t*); 32.81 (*t*); 26.47 (*t*); 25.88 (*q*); 25.06 (*t*); 20.72 (*q*); 19.85 (*q*); 18.08 (*s*); 10.68 (*q*); 9.24 (*q*); −4.39 (*q*); −5.00 (*q*). MS: 443 (0.5, $[C_{22}H_{41}NO_4SSi]^+$). 387 (17), 386 (36), 328 (11), 188 (18), 173 (35), 170 (13), 135 (48), 115 (20), 93 (31), 79 (21), 75 (62), 73 (100), 57 (35). HR-MS: 386.1767 ($[C_{22}H_{30}NO_2SSI]^+$; calc. 386.1734).

*(2S,3S)-3-[(*tert*-Butyl)dimethylsilyloxy]-2-methylpentanoic Acid* (**7**). A soln. of **5** (4 g, 9.02 mmol) in a mixture of THF (108 ml) and 1N aq. soln. of LiOH (36 ml) was stirred at 60° for 20 h. Evaporation of the THF *in vacuo*, acidification (2N aq. HCl) of the aq. phase to pH 1, extraction (CH_2Cl_2), evaporation, and crystallization (pentane) of the residue furnished the auxiliary **6** (1.55 g). FC (hexane/AcOEt 8:1→4:1) of the mother liquors gave another 255 mg of **6** (total 93%) and **7** (oil, 1.68 g, 76%). GC (100, 5, 10, 270): 8.38 (99%). $[\alpha]_D$ = +13.08, $[\alpha]_{578}$ = +13.75, $[\alpha]_{546}$ = +15.8, $[\alpha]_{463}$ = +26.54, $[\alpha]_{365}$ = +40.8 (*c* = 1.36, *T* = 22°). IR: 3100, 2953, 2930, 2899, 2856, 1744, 1707, 1461, 1402, 1381, 1360, 1253, 1119, 1082, 1050, 1012. ^{1}H-NMR: 0.06 (*s*, 3 H); 0.07 (*s*, 3 H); 0.86–0.90 (12 H); 1.14 (*d*, *J* = 7, 3 H); 1.48–1.58 (2 H); 2.65 (*dq*, *J* = 5.5, 7, 1 H); 3.82–3.87 (*q*, *J* = 5.5, 1 H). ^{13}C-NMR: 179.66 (*s*); 74.88 (*d*); 44.47 (*d*); 26.68 (*t*); 25.73 (*q*, 3 C); 17.98 (*s*); 13.11 (*q*); 8.79 (*q*); −4.45 (*q*); −5.01 (*q*). MS: 217 (0.6, $[C_{12}H_{26}O_3Si - C_4H_9]^+$), 189 (17), 173 (4.0), 133 (22.8), 115 (8.4), 75 (100), 73 (29.1), 69 (5.9), 59 (5.9). HR-MS: 189.0941 ($[C_8H_{17}O_3Si]^+$; calc. 189.0949).

*(3R)-2,3-Dihydro-*N*-[(2R,3S)-3-hydroxy-2-methylpentanoyl]-3-methyl-1,2-benzothiazole-1,1-dioxide* (**9**). CF_3SO_3H (1.87 ml, 21.23 mmol) was added at r.t. to a 1M soln. of BEt_3 in hexane (21.5 ml, 21.44 mmol), and the mixture was stirred at 40° for 15 min. Successive addition of a soln. of *3-methyl-2-propionyltoluenesultam* (**8** [5b]; 2.5 g, 10.46 mmol) in CH_2Cl_2 (10 ml) and a 1M soln. of EtN(i-Pr)$_2$ in CH_2Cl_2 (20.9 ml) at 0°, stirring of the mixture at 0° for 30 min, cooling to −78°, addition of propionaldehyde (1.52 ml, 20.9 mmol), stirring for 90 min at −78°, addition of aq. phosphate buffer (pH 7), extraction (CH_2Cl_2), and evaporation gave crude aldol **9**. HPLC (hexane/AcOEt 6:1, 2 ml/min): 24.36 min (99.2%). FC (hexane/AcOEt 3:1) and crystallization (Et_2O/hexane) gave pure **9** (2.56 g, 85%). M.p. 95–96°. $[\alpha]_D$ = −25.98, $[\alpha]_{578}$ = −27.67, $[\alpha]_{546}$ = −31.02, $[\alpha]_{463}$ = −48.92, $[\alpha]_{365}$ = −64.64 (*c* = 2.24, *T* = 22°). IR: 3600, 3017, 2995, 2963, 2931, 2878, 1675, 1450, 1381, 1328, 1231, 1162, 1130. ^{1}H-NMR: 1.00 (*t*, *J* = 7.5, 3 H); 1.37 (*d*, *J* = 7, 3 H); 1.51 (*m*, 1 H); 1.63 (*m*, 1 H); 1.65 (*d*, *J* = 7, 3 H); 3.03 (*s*, 1 H); 3.42 (*dq*, *J* = 3, 7, 1 H); 3.94 (*m*, 1 H); 5.47 (*q*, *J* = 7, 1 H); 7.46 (*m*, 1 H); 7.61 (*m*, 1 H); 7.73 (*m*, 1 H); 7.81 (*m*, 1 H). ^{13}C-NMR: 175.80 (*s*); 136.96 (*d*); 134.32 (*d*); 133.30 (*s*); 129.76 (*d*); 124.35 (*d*); 121.77 (*d*); 72.67 (*d*); 55.37 (*d*); 44.04 (*d*); 26.8 (*t*); 21.11 (*q*); 11.38 (*q*); 10.33 (*q*).

*(1′S,2′R)-3′-[(3″R)-2″,3″-dihydro-3′-methyl-1″,1″-dioxo-1″,2″-benzothiazol-2″-yl]-1′-ethyl-2′-methyl-3′-oxopropyl (2S,3S)-3-[(*tert*-Butyl)dimethylsilyloxy]-2-methylpentanoate* (**10**). A mixture of **7** (1 g, 4.06 mmol), 2,6-dichlorobenzoyl chloride (0.61 ml, 4.26 mmol), NEt_3 (0.62 ml, 4.46 mmol), and THF (6 ml) was stirred at r.t. for 20 h. Then, the mixture was filtered under N_2, the filtrate was evaporated and the residue dissolved in toluene (30 ml). Addition of **9** (1.14 g, 3.85 mmol) followed by a soln. of DMAP (496 mg, 4.06 mmol) in CH_2Cl_2 (5 ml), stirring at r.t. for 20 h, filtration, evaporation of the filtrate, FC (hexane/AcOEt 6:1), and crystallization (Et_2O/hexane) furnished pure **10** (1.81 g, 85%). GC (150, 5, 10, 270): 18.94 (98.5%). M.p. 83–84°. IR: 3019, 2953, 2921, 2855, 1817, 1725, 1686, 1461, 1378, 1328, 1251. ^{1}H-NMR: 0.08 (*s*, 3 H); 0.09 (*s*, 3 H); 0.88–0.94 (15 H); 1.15 (*d*, *J* = 7, 3 H); 1.35 (*d*, *J* = 6, 3 H); 1.44–1.52 (2 H); 1.63 (*d*, *J* = 6, 3 H); 1.65–1.74 (2 H); 2.70 (*dq*, *J* = 5, 7, 1 H); 3.54 (*quint.*, *J* = 6, 1 H); 3.98 (*q*, *J* = 5, 1 H); 5.33 (*m*, H); 5.42 (*q*, *J* = 6, 1 H); 7.37 (*m*, 1 H); 7.45 (*m*, 1 H); 7.59 (*m*, 1 H); 7.73 (*m*, 1 H); 7.81 (*m*, 1 H). ^{13}C-NMR: 173.89 (*s*); 172.12 (*s*); 137.20 (*s*); 134.17 (*d*); 133.42 (*s*); 129.61 (*d*); 124.32 (*d*); 121.67 (*d*); 74.97 (*d*); 74.20 (*d*); 55.60 (*d*); 45.56 (*d*); 43.93 (*d*); 25.85 (*q*, 3 C); 25.77 (*t*); 25.61 (*t*); 18.05 (*s*); 14.16 (*q*); 11.05 (*q*); 9.86 (*q*); 9.70 (*q*); −4.59 (*q*); −4.64 (*q*). MS: 468 (1, $[C_{26}H_{43}O_6NSSi - C_4H_9]^+$), 327 (15), 280 (63), 173 (100), 145 (19), 97 (20), 75 (38). HR-MS: 354.1158 ($C_{16}H_{24}O_4NSSi$; calc. 354.1195).

*(2′S,3′R)-1′-Ethyl-2′-methyl-3′-oxo-4′-(phenylsulphonyl)pentyl (2S,3S)-3-[(*tert*-Butyl)dimethylsilyloxy]-2-methylpentanoate* (**12**). A 1.6M soln. of BuLi (hexane, 2.60 ml) followed by TMEDA (0.63 ml, 4.18 mmol) were added to a soln. of ethyl phenyl sulfone (355 mg, 2.09 mmol) in THF (20 ml) at −78°. Stirring of the mixture at 0° for 1 h, cooling to −78°, addition of a soln. of **10** (1 g, 1.90 mmol) in THF (10 ml), stirring for 3 h, addition of sat. aq. NH_4Cl soln., neutralization with HCl, extraction with Et_2O and FC (hexane/AcOEt 20:1→2:1) gave **11** (309 mg, 89%) and the less polar **12** (93:7 mixture of C(4′)-epimers (^{1}H-NMR), 699 mg, 72%). M.p. 86–91°. IR: 3010, 3018, 2957, 2925, 2879, 2859, 1719, 1459, 1448, 1381, 1316, 1309, 1257, 1214, 1142, 1110, 1080. ^{1}H-NMR (major epimer): 0.05 (*s*, 3 H); 0.06 (*s*, 3 H); 0.45–0.85 (12 H); 0.95 (*t*, *J* = 7.5, 3 H); 1.05 (*d*, *J* = 7, 3 H); 1.12 (*d*, *J* = 6.5, 3 H); 1.32 (*d*, *J* = 7, 3 H); 1.15–1.45 (2 H); 1.61–1.69 (2 H); 2.58 (*dq*, *J* = 4.5, 7, 1 H); 3.49 (*dq*, *J* = 2.5, 7, 1 H); 3.82 (*quint.*, *J* = 4, 1 H); 4.6 (*q*, *J* = 6.5, 1 H); 5.18 (*m*, 1 H); 7.52–7.57 (2 H); 7.69 (*m*, 1 H); 7.74–7.78 (2 H). ^{13}C-NMR: 202.23 (*s*); 173.78 (*s*); 135.67 (*s*); 134.25 (*d*); 129.45 (*d*); 129.01 (*d*); 74.32 (*d*); 73.63 (*d*); 68.47 (*d*); 50.80 (*d*); 45.58 (*d*); 25.79 (*q*); 25.60 (*t*); 25.42 (*t*); 18.02 (*s*); 12.22 (*q*); 10.60 (*q*); 10.42 (*q*); 10.07 (*q*); 9.12 (*q*); −4.57 (*q*); −4.75 (*q*).

MS: 455 (0.4, $[C_{26}H_{44}O_6SSi - C_4H_9]^+$), 267 (15), 189 (68), 125 (100), 97 (43), 75 (88). HR-MS: 455.19219 ($[C_{26}H_{44}O_6SSi - C_4H_9]^+$; calc. 455.19239).

*(1'S,2'R)-1'-Ethyl-2'-methyl-3'-oxopentyl (2S,3S)-3-[(*tert*-Butyl)dimethylsilyloxy]-2-methylpentanoate* (**2**). *Reduction with Li/Naphthalenide.* A 1M soln. of lithium naphthalenide in THF (0.6 ml) was added at −78° to a soln. of **12** (150 mg, 1.29 mmol) in THF (3 ml), and the mixture was stirred at −78° for 15 min. Addition of sat. aq. NH_4Cl soln., extraction with Et_2O and FC (hexane/AcOEt 100:0–10:1) yielded **2** (oil, 90.5 mg, 84%). GC (150, 5, 10, 270): 9.45 (98%).

Reduction with SmI_2. CH_2I_2 (0.47 ml, 5.85 mmol) was added under N_2 at 0° in one portion to a suspension of Sm powder (1.1 g, 7.30 mmol) in THF (58 ml), and the mixture was stirred at 0° for 30 min, then at r.t. for 2 h. 30 ml of the resulting dark-blue soln. of SmI_2 was added at −78° to a soln. of **12** (0.50 g, 0.97 mmol) in THF (5 ml). Addition of sat. aq. $NaHCO_3$ soln., extraction with Et_2O and FC (hexane/AcOEt 30:1) gave **2** (oil, 309 mg, 86%). GC (150, 5, 10, 270): 9.30 (98.5%). IR: 2963, 2931, 2878, 2856, 1726, 1715, 1456, 1253, 1183, 1109, 1050, 1012. ^{1}H-NMR: 0.07 (*s*, 3 H); 0.08 (*s*, 3 H); 0.87–0.92 (15 H); 1.04 (*t*, *J* = 7, 3 H); 1.09 (*d*, *J* = 7, 3 H); 1.10 (*d*, *J* = 7, 3 H); 1.33–1.51 (2 H); 1.52–1.62 (2 H); 2.44 (*dq*, *J* = 7, 18, 1 H); 2.57 (*dq*, *J* = 7, 18, 1 H); 2.64 (*ddd*, *J* = 5, 7, 14, 1 H); 2.77 (*ddd*, *J* = 5, 7, 14, 1 H); 3.90 (*m*, 1 H); 5.13 (*m*, 1 H). ^{13}C-NMR: 211.83 (*s*); 173.80 (*s*); 75.09 (*d*); 74.28 (*d*); 48.88 (*d*); 45.51 (*d*); 35.09 (*t*); 25.82 (*q*); 25.62 (*t*); 25.06 (*t*); 18.06 (*s*); 11.46 (*q*); 11.06 (*q*); 10.00 (*q*); 9.79 (*q*); 7.67 (*q*); −4.60 (*q*); −4.70 (*q*). MS: 343 (1, $[C_{20}H_{40}O_4Si - C_2H_5]^+$), 315 (4), 189 (100), 127 (15), 75 (80), 57 (80). HR-MS: 343.22929, ($[C_{20}H_{40}O_4Si - C_2H_5]^+$; calc. 343.23045).

*(2S,3R)-2-Ethyl-2,3-dihydro-6-[(1S,2S)-2-hydroxy-1-methylbutyl]-3,5-dimethyl-4*H*-pyran-4-one* (= *(−)-Serricorole*; **1**). A 0.5M soln. of $TiCl_4$ in CH_2Cl_2 (4 ml, 2.0 mmol) was added dropwise at −78° to a mixture of **2** (150 mg, 0.4 mmol) and $EtN(i\text{-}Pr)_2$ (0.5 ml, 3.20 mmol) in CH_2Cl_2 (18 ml). The mixture was stirred at −78° for 1 h, then allowed to warm up over 2 h to −10° and stirred at −10° for 20 h. Addition of sat. aq. NH_4Cl soln. and workup gave *O*-silylated dihydropyranone 14 which was dissolved in MeCN (5 ml). Addition of a 45% aq. soln. of HF (10 drops), stirring of the mixture at 0° for 20 h, dilution with Et_2O, washing with sat. aq. $NaHCO_3$ soln., drying ($MgSO_4$), and FC (hexane/Et_2O 1:2) gave pure **1** (64.3 mg, 67%).

Following the same protocol, **2** (40 mg, 0.1 mmol) gave **1** (20.2 mg, 78%). $[\alpha]_D = -124$ ($c = 2.34$, $T = 22°$) ([3]: $[\alpha]_D = -113$ ($c = 0.15$, $T = 24°$)). IR: 3573, 3476, 3029, 2997, 2973, 2936, 2879, 1654, 1602, 1460, 1392, 1378, 1348, 1133, 1114, 968, 909. ^{1}H-NMR: 1.01 (*t*, *J* = 7, 6 H); 1.02 (*d*, *J* = 7, 3 H); 1.19 (*d*, *J* = 7, 3 H); 1.42 (*m*, 1 H); 1.52–1.63 (2 H); 1.75 (*s*, 3 H); 1.82 (*m*, 1 H); 1.95 (*d*, *J* = 7, 1 H); 2.38 (*dq*, *J* = 3, 7, 1 H); 2.89 (*quint.*, *J* = 6.5, 1 H); 3.59 (*m*, 1 H); 4.17 (*m*, 1 H). ^{13}C-NMR: 197.42 (*s*); 173.06 (*s*); 109.40 (*s*); 81.98 (*t*); 75.37 (*d*); 28.20 (*t*); 23.37 (*t*); 14.77 (*q*); 10.03 (*q*); 9.88 (*q*); 9.51 (*q*); 9.26 (*q*). MS: 240 (12, $[C_{14}H_{24}O_3]^+$), 182 (54), 153 (19), 141 (11), 124 (18), 112 (100), 109 (28), 101 (14), 97 (14), 83 (89), 69 (32), 67 (26), 59 (82), 55 (82). HR-MS: 240.1768 ($[C_{14}H_{24}O_3]^+$; calc. 240.1726). The ^{1}H- and ^{13}C-NMR and mass spectra match the reported spectra [3].

REFERENCES

[1] T. Chuman, K. Mochizuki, K. Kato, M. Ono, A. Okubo, *Agric. Biol. Chem.* **1983,** *47,* 1413.

[2] T. Chuman, K. Mochizuki, M. Mori, M. Kohono, K. Kato, M. Noguchi, *J. Chem. Ecol.* **1985,** *11,* 417.

[3] T. Ebata, K. Mori, *Agric. Biol. Chem.* **1987,** *51,* 2925.

[4] W. Oppolzer, C. Starkemann, I. Rodriguez, G. Bernardinelli, *Tetrahedron Lett.* **1991,** *32,* 61.

[5] a) W. Oppolzer, J. Blagg, I. Rodriguez, E. Walther, *J. Am. Chem. Soc.* **1990,** *112,* 2767; b) W. Oppolzer, I. Rodriguez, C. Starkemann, E. Walther, *Tetrahedron Lett.* **1990,** *31,* 5019.

[6] W. Oppolzer, P. Lienard, *Tetrahedron Lett.* **1993,** *34,* in press.

[7] J. Inanaga, K. Hirata, H. Saeki, T. Katsuki, M. Yamaguchi, *Bull. Chem. Soc. Jpn.* **1979,** *52,* 1989.

[8] W. Oppolzer, J.-E. Ancel, G. Poli, publication in preparation.

[9] a) P. A. Bartlett, F. R. Green III, E. H. Rose, *J. Am. Chem. Soc.* **1978,** *100,* 4852; b) K. Kondo, D. Tunemoto, *Tetrahedron Lett.* **1975,** 1397.

[10] a) D. Crich, L. B. L. Lim, *Tetrahedron Lett.* **1990,** *31,* 1897; b) L. Zhu, R. M. Wehmeyer, R. D. Rieke, *J. Org. Chem.* **1991,** *56,* 1445.

[11] a) G. A. Molander, G. Hahn, *J. Org. Chem.* **1986,** *51,* 1135; b) G. A. Molander, *Chem. Rev.* **1992,** *92,* 29.

[12] a) W. Oppolzer, *Tetrahedron* **1987,** *43,* 1969; b) W. Oppolzer, *Pure Appl. Chem.* **1990,** *62,* 1241; B. H. Kim, D. P. Curran, *Tetrahedron* **1993,** *49,* 293.

[13] a) Y. Tanabe, T. Mukayiama, *Chem. Lett.* **1984,** 1867; b) Y. Tanabe, *Bull. Chem. Soc. Jpn.* **1989,** *62,* 1917.

[14] D. A. Evans, D. L. Rieger, M. T. Bilodeau, F. Urpi, *J. Am. Chem. Soc.* **1991,** *113,* 1047.