77. Stereocontrolled Syntheses of Polysubstituted 2,3-Dihydro-4*H*-pyran-4-ones by Cyclocondensation of β-Acyloxy-ketones

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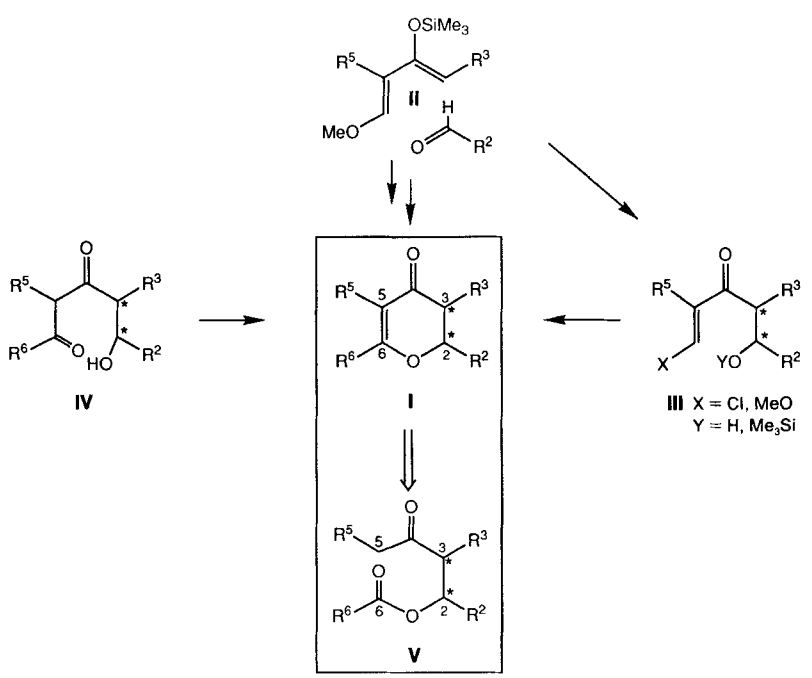
(4.III.93)

syn-β-Acyloxy-ketones **6** and an *anti*-β-acyloxy-ketone **17** undergo smooth intramolecular enolate/ester condensations **6** → **18** and **17** → **19** when treated with $TiCl_4/EtN(i\text{-}Pr)_2$. Thus, tri- and tetrasubstituted *cis*- or *trans*-2,3-dihydro-4*H*-pyran-4-ones are easily prepared in a stereoselective manner.

Introduction. – Dihydropyranones **I** (*Scheme 1*) are versatile intermediates for the synthesis of tetrahydropyrans, carbohydrates, and acyclic polypropionate segments [1]. Furthermore, several natural products, such as serricorole [2], stegobiol [3], stegobinone [4], vallartanones A and B [5], maurenone [6], and hepialone [7] contain the dihydropyranone ring **I** as an integral structural element. To date, the best known method to assemble ring system **I** is the *Lewis*-acid-catalyzed cyclocondensation of 1,3-dioxygenated butadienes **II** with aldehydes [1] [8]. Other routes to dihydropyranones **I** rely either on cyclizations of β-(chlorovinyl)- [9] and β-(methoxyvinyl)-3-hydroxy-ketone [10] derivatives **III** or on intramolecular condensations of 5-hydroxy-1,3-diones **IV** [7b] (*Scheme 1*).

Scheme 1



An alternative, potentially more attractive approach to polyfunctionalized dihydropyranones **I**, involving the ring closure of β-acyloxy-ketones **V**, suffered in the past from intolerably poor yields [2b] [3]. However, in the preceding article, we describe an efficient synthesis of the dihydropyranone pheromone (−)-serricorole (**3**) which hinges on a new Ti-mediated cyclization **1** → **2** (*Scheme 2*) [11].

Scheme 2

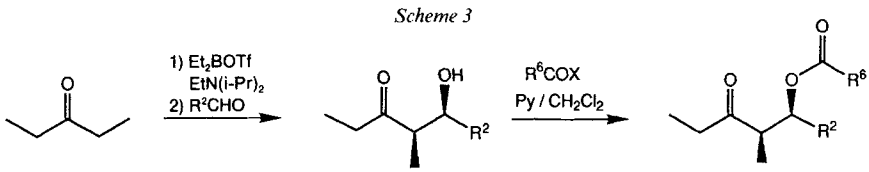
1

2 R = TBDMS
3 R = H, (−)-Serricorole

We were interested in applying the conditions of reaction **1** → **2** to the ring closure of various β-acyloxy-ketones thereby exploring the scope and limitations of this route to multifunctional dihydropyranones.

Preparation of Acyclic β-Acyloxyketones. – Treatment of diethyl ketone (**4**) with (*in situ* prepared) diethylboryl triflate/EtN(i-Pr)$_2$ [12], followed by condensation of the resulting boryl enolate with an aldehyde, gave the expected [13] *syn*-aldols (±)-**5** with 90:10 to 96:4 diastereoselectivity. *O*-Acylation of these aldols **5** provided a series of racemic *syn*-β-acyloxy-ketones **6** (*Scheme 3*, *Table 1*).

Scheme 3



4

(±)-**5**

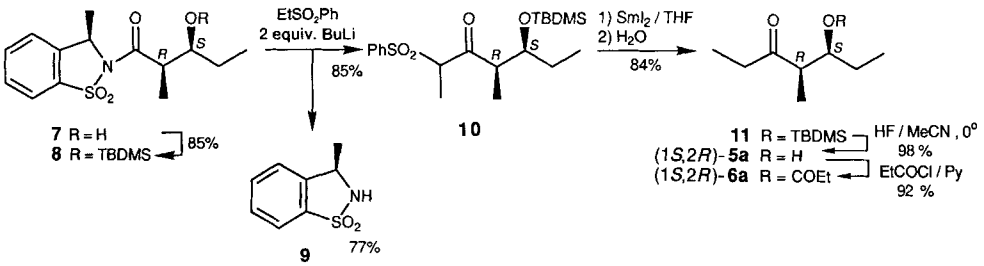
(±)-**6**

Table 1. *Conversion of Diethyl Ketone* (**4**) *to Racemic* syn-*β-Acyloxy-ketones*: **4** → (±)-**5** → (±)-**6**

Entry	Aldehyde R^2	Racemic aldol	Yield [%]	*syn*/*anti*-Ratio	Acyl chloride R^6	Racemic β-acyloxy-ketone	Yield [%]
1	Et	**5a**	71	96:4	Et	**6a**	87
2	Et	**5a**	71	96:4	i-Pr	**6b**	84
3	Et	**5a**	71	96:4	Ph	**6c**	84
4	Et	**5a**	71	96:4	$PhCH_2$	**6d**	92
5	Et	**5a**	71	96:4	H	**6e**	85
6	Ph	**5b**	81	96:4	Et	**6f**	87
7	(*E*)-MeCH=CH	**5c**	69	90:10	Et	**6g**	83

Enantiomerically pure oxopentyl propionate (1*S*,2*R*)-**6a** was obtained from crystalline *syn*-aldol **7** [11] [14] by a reaction sequence similar to that employed for the synthesis of (−)-serricorole (**3**) [11] (*Scheme 4*).

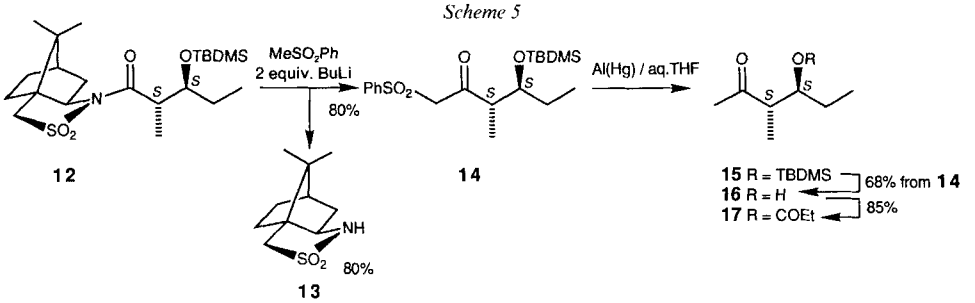
Scheme 4



Thus, *O*-silylation **7** → **8**, nucleophilic displacement of the sultam auxiliary with dilithiated ethyl phenyl sulfone **8** → **9** + **10**, reductive removal of the sulfone group **10** → **11**, desilylation **11** → **5a**, and *O*-acylation of **5a** provided (1*S*,2*R*)-**6a**.

The *anti*-oxobutyl propionate (1*S*,2*S*)-**17** was similarly prepared *via* cleavage of crystalline *N*-(silyloxyacyl)sultam **12** [11] [15] with dilithiated methyl phenyl sulfone[1]), C,S-hydrogenolysis (Al/Hg, aq. THF), desilylation, and *O*-acylation (*Scheme 5*).

Scheme 5

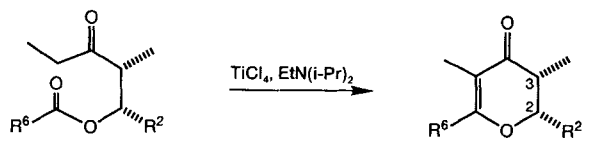


Cyclization. – The stage was now set to probe the generality of the β-acyloxy-ketone/dihydropyranone cyclization method. Our results are summarized in *Schemes 6* and *7* and in *Table 2*.

Thus, $TiCl_4$ (1.5 mmol), followed by $EtN(i\text{-}Pr)_2$ (3 mmol) were added to a solution of oxopentyl propionate (±)-**6a** (1 mmol) in CH_2Cl_2 (10 ml) at −78°. The mixture was stirred at −78° for 1 h, then warmed slowly to −10° and kept at that temperature for 16 h. Workup and chromatography provided racemic *cis*-dihydropyranone **18a** in 81% yield

[1]) The cleavage of *N*-acylbornane-10,2-sultams with dilithiated ethyl phenyl sulfone is relatively slow and accompanied by partial epimerization at C(α). *N*-Acyltoluenesultams, on the other hand, undergo smooth displacement of the sultam group by a variety of alkyl phenyl sulfones [16].

Scheme 6



6 **18**

Table 2. *Transformation of* syn-*β-Acyloxy-ketones* **6** *to* cis-*2,3-Substituted Dihydropyranones* **18** *by Intramolecular Ti Enolate/Ester Condensation*

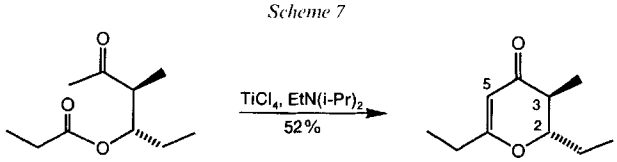
Entry	Series	R^2	R^6	Conc. of **6**	Yield of **18** [%]	Config. of **18**	$[\alpha]_D$ of **18**
1	**a**	Et	Et	0.10M	81	(2*RS*,3*SR*)	–
2	**a**	Et	Et	0.10M	82	(2*S*,3*R*)	–232.7
3	**b**	Et	i-Pr	0.10M	83	(2*RS*,3*SR*)	–
4	**c**	Et	Ph	0.08M	89	(2*RS*,3*SR*)	–
5	**d**	Et	$PhCH_2$	0.07M	41	(2*RS*,3*SR*)	–
6	**e**	Et	H	0.07M	58	(2*RS*,3*SR*)	–
7	**f**	Ph	Et	0.05M	68	(2*RS*,3*RS*)	–
8	**g**	(*E*)-MeCH=CH	Et	0.05M	52	(2*RS*,3*SR*)	–

(*Entry 1*). Compound (2*S*,3*R*)-**18a** was obtained from the enantiomerically pure precursor **6a** in an analogous fashion (82%; *Entry 2*). Employing a similar protocol[2]), a variety of *cis*-dihydropyranones **18** were generally obtained in good yields from acyloxy-ketones **6**, the modest yield of dihydropyranone **18d** being possibly due to facile ester enolate formation of the *O*-phenacetyl derivative **6d**. Yields of **18** increased with increasing bulk of the ester substituent (*Entries 6* < *1* < *3* < *4*). Ph- and propenyl-substituted oxo-esters **6f** and **6g** were preferably cyclized at higher dilution (*Entries 7* and *8*).

The *cis*-products **18** were accompanied by minor amounts of *trans*-isomers in proportions which correspond to the *syn*/*anti* ratios of the acyloxy-ketone precursors **6**. Hence, cyclizations **6** → **18** proceed without noticable C(α)-epimerization.

Analogous ring closure of enantiomerically pure *anti*-oxobutyl propionate **17** gave C(2)/C(3)-*trans*-substituted pyranone **19** (52%) carrying no substituent at C(5) (*Scheme 7*).

Scheme 7

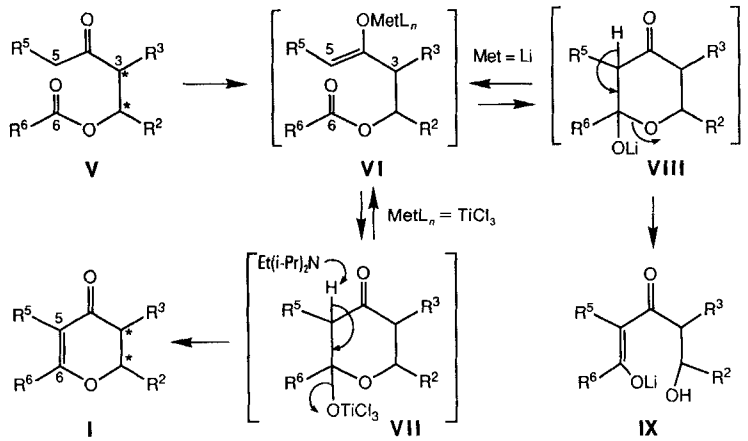


17 **19**

[2]) It was of little relevance whether $TiCl_4$ and $EtN(i\text{-}Pr)_2$ were added to the acyl-ketone (*Entries 1* and *3–5*), or whether $TiCl_4$ was added to a mixture of oxo-ester and $EtN(i\text{-}Pr)_2$ (*Entries 2* and *6–8*). The cyclization **1** → **2** required 5 mol-equiv. of $TiCl_4$ and 8 mol-equiv. of $EtN(i\text{-}Pr)_2$ to ensure complete consumption of starting material [11].

The decisive role of $TiCl_4$ in the cyclocondensations **V** → **I** may be rationalized as depicted in *Scheme 8*.

Scheme 8



Coordination of Ti^{IV} with the ester C=O group should accelerate the cyclization of enolates **VI** (Met = Ti^{IV}) to give tetrahedral intermediates **VII** which undergo irreversible elimination to the dihydropyranone products **I** by facile departure of $OTiCl_3$[3]). The poor yields of dihydropyranone **2** previously obtained by successive treatment of acyloxy-ketone **1** with lithium hexamethyldisilazide and aqueous acid [2b] [11] may be ascribed to a tetrahedral intermediate **VIII** which eliminates with departure of the endocylic O-atom rather than with departure of the poor lithium-alkoxide leaving group. Resulting 1,3-dione enolate **IX** could undergo various side reactions prior to its acid-promoted conversion to **I**.

Conclusion. – A series of tri- and tetrasubstituted 2,3-dihydro-4*H*-pyran-4-ones were readily obtained in a single step from *β*-acyloxy-ketones. To our knowledge, this is the first general process providing tetrasubstituted 2,3-dihydro-4*H*-pyran-4-ones in good yield and in a stereocontrolled manner. The ready availability of stereochemically pure *β*-acyloxy-ketone precursors by established asymmetric aldolization methodology renders this approach particularly attractive.

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[3]) For *Dieckmann* and aldol condensations *via* Ti enolates, see [17].

Experimental Part

General. See [11].

Preparation of β-Acyloxy-ketones. – *(4RS,5SR)-5-Hydroxy-4-methylheptan-3-one* ((±)-**5a**). A soln. of $EtN(i\text{-}Pr)_2$ (10.8 ml, 62 mmol) in CH_2Cl_2 (20 ml), followed by diethyl ketone (**4**; 6 ml, 56.4 mmol) were added at −78° to a 1M soln. of *in situ* prepared diethylboryl triflate [12] in hexane (57.7 ml). Stirring of the mixture at −78° for 30 min, addition of propanol (8 ml, 112 mmol), stirring of the mixture for 1 h, addition of aq. phosphate buffer (pH 7), extraction (Et_2O), and FC (hexane/AcOEt 6:1) furnished (±)-**5a** (oil, 5.8 g, 71%) as a 96:4 mixture of s-*cis*/s-*trans*-isomers (^{1}H-NMR of s-*trans*-isomer: H–C(5) at 3.65 (*m*, 1 H)). IR: 3571, 3024, 2976, 2939, 2879, 1698, 1460, 1409, 1379. ^{1}H-NMR (major s-*cis*-isomer): 0.95 (*t*, *J* = 7.5, 3 H); 1.06 (*t*, *J* = 7.0, 3 H); 1.13 (*d*, *J* = 7.0, 3 H); 1.38 (*m*, 1 H); 1.53 (*m*, 1 H); 2.47 (*q*, *J* = 7, 1 H); 2.51 (*q*, *J* = 7, 1 H); 2.66 (*q*, *J* = 7, 1 H); 2.76 (*d*, *J* = 3, 1 H); 3.82 (*m*, 1 H). ^{13}C-NMR: 216.71 (*s*); 72.56 (*d*); 49.29 (*d*); 35.07 (*t*); 26.84 (*t*); 10.39 (*q*); 9.90 (*q*); 7.57 (*q*).

(1RS,2RS)-1-Hydroxy-2-methyl-1-phenylpentan-3-one ((±)-**5b**). Following the procedure described for the preparation of (±)-**5a**, **4** (2.45 ml, 23.2 mmol) was treated successively with $EtN(i\text{-}Pr)_2$ (4.45 ml, 25.5 mmol), diethylboryl triflate (24.36 mmol), and benzaldehyde (2.8 ml, 27.84 mmol). FC (hexane/AcOEt 4:1) gave (±)-**5b** (oil, 3.62 g, 81%) as a 96:4 mixture of s-*cis*/s-*trans* (^{1}H-NMR of s-*trans*-isomer: H–C(1) at 4.74 (*dd*, *J* = 8, 4, 1 H)). IR: 3514, 3024, 3027, 3009, 2982, 2940, 1698, 1494, 1452, 1408, 1379, 1224. ^{1}H-NMR: 0.99 (*t*, *J* = 7.0, 3 H); 1.08 (*d*, *J* = 7.0, 3 H); 2.32 (*dq*, *J* = 18, 7.0, 1 H); 2.49 (*dq*, *J* = 18, 7.0, 1 H); 2.84 (*dq*, *J* = 4.0, 7.0, 1 H); 3.21 (*d*, *J* = 2.5, 1 H); 5.03 (*dd*, *J* = 2.5, 4.0, 1 H). ^{13}C-NMR: 216.12 (*s*); 141.82 (*s*); 128.20 (*d*); 127.30 (*d*); 125.90 (*d*); 73.30 (*d*); 52.30 (*d*); 35.38 (*t*); 10.60 (*q*); 7.40 (*q*).

(4RS,5SR,E)-5-Hydroxy-4-methyloct-6-en-3-one ((±)-**5c**). Following the procedure described for the preparation of (±)-**5a**, **4** (2.45 ml, 23.2 mmol) was treated successively with $EtN(i\text{-}Pr)_2$ (4.45 ml, 25.5 mmol), diethylboryl triflate (24.36 mmol), and (*E*)-crotonaldehyde (2.8 ml, 34.8 mmol). FC (hexane/AcOEt 4:1) gave (±)-**5c** (oil, 2.49 g, 69%) as a 90:10 mixture of s-*cis*/s-*trans*-isomers (^{1}H-NMR of s-*trans*-isomer: H–C(5) at 4.15 (*m*, H). IR: 3603, 3507, 3024, 3011, 2980, 2940, 2280, 1698, 1459, 1408, 1378, 1356, 1224. ^{1}H-NMR: 1.04 (*t*, *J* = 7.0, 3 H); 1.13 (*d*, *J* = 7.0, 3 H); 1.69–1.71 (3 H); 2.44–2.60 (2 H); 2.66 (*m*, 1 H); 4.41 (*m*, 1 H); 5.45 (*ddq*, *J* = 7.0, 15, 2.0, 1 H); 5.69 (*m*, 1 H). ^{13}C-NMR: 215.73 (*s*); 130.60 (*d*); 128.00 (*d*); 72.80 (*d*); 50.60 (*d*); 35.47 (*t*); 17.70 (*q*); 11.11 (*q*); 7.50 (*q*).

(1RS,2SR)-1-Ethyl-2-methyl-3-oxopentyl Propanoate ((±)-**6a**). Propanoyl chloride (0.4 ml, 4.32 mmol) was added at 0° to a soln. of (±)-**5a** (0.5 g, 3.46 mmol) in CH_2Cl_2/pyridine (5:1, 12 ml). Stirring of the mixture at 0° for 20 h, addition of 1M aq. HCl, and workup gave crude ester (±)-**6a**. GC (80/5/10/270): 9.78 (91), 9.94 (3.8, s-*trans*-isomer). FC (hexane/AcOEt 10:1) gave pure (±)-**6a** (oil, 602 mg, 87%) as 96:4-mixture of s-*cis*/s-*trans*-isomers. IR: 3028, 2977, 2941, 2881, 1728, 1716, 1461, 1380, 1350, 1275, 1231, 1193. ^{1}H-NMR: 0.89 (*t*, *J* = 7.0, 3 H); 1.04 (*t*, *J* = 7.0, 3 H); 1.07 (*d*, *J* = 7.0, 3 H); 1.14 (*t*, *J* = 7.0, 3 H); 1.56 (*quint.*, *J* = 7.0, 2 H); 2.32 (*q*, *J* = 7.0, 2 H); 2.43 (*dq*, *J* = 18, 7.0, 1 H); 2.57 (*dq*, *J* = 18, 7.0, 1 H); 2.77 (*dq*, *J* = 5.5, 7.0, 1 H); 5.13 (br. *q*, *J* = 6.0, 1 H). ^{13}C-NMR: 212.07 (*s*); 173.99 (*s*); 74.96 (*d*); 49.05 (*d*); 35.17 (*t*); 27.65 (*t*); 25.12 (*t*); 11.36 (*q*); 10.00 (*q*); 9.20 (*q*); 7.66 (*q*). MS: 171 (8, $[C_{11}H_{20}O_3 - C_2H_5]^+$), 143 (10), 126 (32), 97 (18), 86 (10), 70 (15), 57 (100). HR-MS: 171.10395 ($[C_{11}H_{20}O_3 - C_2H_5]^+$; calc. 171.1021).

(1RS,2SR)-1-Ethyl-2-methyl-3-oxopentyl 2-Methylpropanoate ((±)-**6b**). 2-Methylpropionic acid (250 ml, 2.70 mmol), dicyclohexylcarbodiimide (557 mg, 2.70 mmol) and DMAP (330 mg, 2.7 mmol) were added to a soln. of (±)-**5a** (0.4 g, 2.70 mmol) in CH_2Cl_2 (10 ml) at r.t. Addition of 1M aq. HCl, workup and FC (hexane/AcOEt 9.1) gave (±)-**6b** (491 mg, 84%). GC (80/5/10/270): 11.22 (96), 11.48 (3.95, s-*trans*-isomer). IR: 3028, 2977, 2941, 2939, 2879, 1723, 1460, 1387, 1349, 1265, 1233, 1195, 1160, 1094, 1071. ^{1}H-NMR: 0.89 (*t*, *J* = 7.50, 3 H); 1.04 (*t*, *J* = 7.0, 3 H); 1.08 (*d*, *J* = 7.0, 3 H); 1.16 (*d*, *J* = 7.0, 6 H); 1.57 (*quint.*, *J* = 7.0, 2 H); 2.44 (*dq*, *J* = 18, 7.0, 1 H); 2.50–2.63 (2 H); 2.77 (*dq*, *J* = 5.5, 7.0, 1 H); 5.12 (*dt*, *J* = 5, 6.5, 1 H). ^{13}C-NMR: 211.09 (*s*); 176.50 (*s*); 74.71 (*d*); 49.08 (*d*); 35.05 (*t*); 34.17 (*d*); 25.14 (*t*); 18.99 (*q*); 18.96 (*q*); 11.26 (*q*); 9.96 (*q*); 7.64 (*q*). MS: 185 (2, $[C_{12}H_{22}O_3 - C_2H_9]^+$), 145 (11), 126 (5), 97 (32), 86 (8), 71 (100), 57 (58). HR-MS: 185.11738 ($[C_{12}H_{22}O_3 - C_2H_9]^+$; calc. 185.11818).

(1RS,2SR)-1-Ethyl-2-methyl-3-oxopentyl Benzoate ((±)-**6c**). Benzoyl chloride (443 ml, 3.81 mmol) was added at 0° to a soln. of (±)-**5a** (0.5 g, 3.46 mmol) in CH_2Cl_2/pyridine (5:1, 12 ml). Stirring of the mixture at 0° for 20 h, addition of 1M aq. HCl, workup, and FC (hexane/AcOEt 10:1) gave ester (±)-**6c** (oil, 716 mg, 83.50%). GC (100/5/10/270): 11.47 (96.5%). IR: 3031, 2975, 2940, 2880, 1787, 1712, 1601, 1584, 1491, 1452, 1409, 1381, 1348, 1314, 1271, 1176, 1115, 1094, 1026. ^{1}H-NMR: 0.95 (*t*, *J* = 7.0, 3 H); 1.04 (*t*, *J* = 7.0, 3 H); 1.07 (*d*, *J* = 7.0, 3 H); 1.18 (*d*, *J* = 7.0, 3 H); 1.65–1.75 (2 H); 2.49 (*dq*, *J* = 18, 7.0, 1 H); 2.59 (*dq*, *J* = 18, 7.0, 1 H); 2.93 (*m*, 1 H); 5.38 (*dt*, *J* = 7.5, 5.5, 1 H); 7.42–7.47 (2 H); 7.55 (*m*, 1 H); 8.0–8.04 (2 H). ^{13}C-NMR: 211.97 (*s*); 166.05 (*s*); 132.96 (*d*); 130.19 (*s*); 129.6 (*d*, 2 C); 128.4 (*d*, 2 C); 67.94 (*d*); 49.12 (*d*); 35.24 (*t*); 25.21 (*t*); 11.80 (*q*); 10.10 (*q*); 7.70 (*q*). MS: 219 (8, $[C_{15}H_{20}O_3 - C_2H_5]^+$), 179 (32), 105 (100), 77 (25), 57 (29).

(1RS,2SR)-1-Ethyl-2-methyl-3-oxopentyl 2-Phenylacetate ((±)-**6d**). 2-Phenylacetyl chloride (1.65 ml, 12.4 mmol) was added at 0° to a soln. of (±)-**5a** (1.5 g, 10.4 mmol) in CH_2Cl_2/pyridine (5:1, 24 ml). Stirring of the

mixture at 0° for 20 h, addition of 1M aq. HCl, workup, and FC (hexane/AcOEt 9:1) gave (±)-**6d** (oil, 2.5 g, 92%). GC (100/5/10/270): 8.7 (98%). IR: 3024, 2975, 2940, 2880, 1728, 1715, 1642, 1601, 1496, 1455, 1409, 1381, 1347, 1261, 1228, 1162, 1097, 1030. ^{1}H-NMR: 0.80 (*t*, *J* = 7.5, 3 H); 0.95 (*t*, *J* = 7.5, 3 H); 1.01 (*d*, *J* = 7.0, 3 H); 1.48 (*m*, 1 H); 2.20–2.51 (2 H); 2.71 (*dq*, *J* = 5.4, 7.0, 1 H); 3.59 (*s*, 2 H); 5.08 (*dt*, *J* = 7.0, 5.8, 1 H); 7.20–7.40 (5 H). ^{13}C-NMR: 212.07 (*s*); 171.10 (*s*); 134.01 (*s*); 129.25 (*d*, 2 C); 128.5 (*d*); 127.0 (*d*, 2 C); 75.90 (*d*); 48.93 (*d*); 41.61 (*t*); 35.19 (*t*); 24.94 (*t*); 11.52 (*q*); 9.95 (*q*); 7.61 (*q*). MS: 262 (20, $[C_{16}H_{22}O_3]^+$), 193 (100), 119 (15), 97 (30), 91 (100), 85 (57). HR-MS 262.15615 ($[C_{16}H_{22}O_3]^+$, calc. 262.15685).

(1RS,2SR)-1-Ethyl-2-methyl-3-oxopentyl Formate ((±)-**6e**). Acetic formic anhydride (600 ml, 6.74 mmol) was added to a soln. of (±)-**5a** (0.6 g, 4.16 mmol) in CH_2Cl_2/pyridine (5:1, 24 ml). Stirring of the mixture at 0° for 20 h, addition of 1M aq. HCl, workup, and FC (hexane/AcOEt 8:1) gave (±)-**6e** (oil, 610 mg, 85%). GC (70/5/10/270): 6.38 (98%). IR: 3028, 2976, 2939, 2882, 1720, 1460, 1409, 1380, 1230, 1186, 1095, 1026, 975. ^{1}H-NMR: 0.91 (*t*, *J* = 7.0, 3 H); 1.05 (*t*, *J* = 7.0, 3 H); 1.12 (*d*, *J* = 7.0, 3 H); 1.60 (*quint.*, *J* = 7.0, 3 H); 2.42–2.61 (2 H); 2.79 (*m*, 1 H); 5.24 (*q*, *J* = 6.0, 1 H); 8.1 (*s*, 1 H). ^{13}C-NMR: 211.80 (*s*); 166.66 (*s*); 75.40 (*d*); 48.90 (*d*); 35.23 (*t*); 25.17 (*t*); 11.70 (*q*); 10.00 (*q*); 7.60 (*q*).

(1RS,2RS)-1-Phenyl-2-methyl-3-oxopentyl Propanoate ((±)-**6f**). Propionyl chloride (0.4 ml, 4.32 mmol) was added at 0° to a soln. of (±)-**5b** (0.5 g, 2.60 mmol) in CH_2Cl_2/pyridine (5:1, 12 ml). Stirring of the mixture at 0° for 20 h, addition of 1M aq. HCl, workup, and FC (hexane/AcOEt 9:1) gave (±)-**6d** (oil, 560 mg, 87%). GC (70/5/10/270): 9.34 (96), 9.40 (3.8, s-*trans*-isomer). IR: 3031, 2983, 2941, 2880, 1736, 1715, 1494, 1456, 1408, 1379, 1352, 1274, 1228, 1186, 1081, 1006. ^{1}H-NMR: 0.87 (*t*, *J* = 7.0, 3 H); 1.13 (*t*, *J* = 7.0, 3 H); 1.16 (*d*, *J* = 7.0, 3 H); 2.12 (*dq*, *J* = 18, 7.0, 1 H); 2.29–2.44 (3 H); 3.06 (*m*, 1 H); 5.99 (*d*, *J* = 8.0, 1 H); 7.23–7.36 (5 H). ^{13}C-NMR: 211.63 (*s*); 173.21 (*s*); 139.14 (*s*); 128.40 (*d*, 2 C); 128.0 (*d*); 126.60 (*d*, 2 C); 75.90 (*d*); 51.94 (*d*); 35.84 (*t*); 27.68 (*t*); 12.76 (*q*); 9.03 (*q*); 7.34 (*q*). MS: 248 (0.2, $[C_{15}H_{20}O_3]^+$), 191 (22), 174 (8), 145 (8), 118 (20), 105 (30), 86 (13), 57 (100).

(1RS,2SR)-2-Methyl-3-oxo-1-[(E)-prop-1-enyl]pentyl Propanoate ((±)-**6g**). Propionyl chloride (0.4 ml, 4.32 mmol) was added at 0° to a soln. of (±)-**5c** (0.5 g, 3.2 mmol) in CH_2Cl_2/pyridine (5:1, 12 ml). Stirring of the mixture at 0° for 20 h, addition of 1M aq. HCl, workup, and FC (hexane/AcOEt 10:1) gave (±)-**6g** (oil, 562 mg, 83%). IR: 3026, 2982, 2941, 2881, 1728, 1673, 1461, 1409, 1379, 1274, 1228, 1081, 1001. ^{1}H-NMR: 1.03 (*t*, *J* = 7.0, 3 H); 1.08 (*d*, *J* = 7.0, 3 H); 1.13 (*t*, *J* = 7.0, 3 H); 1.67–1.70 (3 H); 2.32 (*q*, *J* = 7.0, 2 H); 2.40–2.57 (2 H); 2.83 (*m*, 1 H); 5.30–5.45 (2 H); 5.73 (*m*, 1 H). ^{13}C-NMR: 211.72 (*s*); 173.32 (*s*); 130.60 (*d*); 126.90 (*d*); 75.00 (*d*); 49.80 (*d*); 37.77 (*t*); 27.70 (*t*); 17.67 (*q*); 12.24 (*q*); 9.03 (*q*); 7.51 (*q*). MS: 155 (5, $[C_{12}H_{20}O_3 - C_3H_5O]^+$), 82 (42), 67 (18), 57 (100).

*(3R)-N-{(2R,3S)-3-[(*tert*-Butyl)dimethylsilyloxy]-2-methylpentanoyl}-2,3-dihydro-3-methyl-1,2-benzothiazole 1,1-Dioxide* (**8**). 2,6 Lutidine (0.92 ml, 7.90 mmol) and (*tert*-butyl)dimethylsilyl triflate (1.09 ml, 4.76 mmol) were added at r.t. to a soln. of aldol **7** [11] (1.18 g, 3.97 mmol) in CH_2Cl_2 (10 ml). Stirring for 30 min, workup (2N HCl), and crystallization (EtOH) furnished **8** (1.39 g, 85%). M.p. 104–105. IR: 3022, 2963, 2932, 2856, 1688, 1461, 1384, 1327, 1255, 1228, 1158, 1228, 1158, 1130, 1110, 1054. ^{1}H-NMR: 0.074 (*s*, 3 H); 0.077 (*s*, 3 H); 0.92 (*s*, 9 H); 0.94 (*t*, *J* = 7.5, 3 H); 1.37 (*d*, *J* = 7.0, 3 H); 1.55–1.63 (2 H); 1.64 (*d*, *J* = 6.5, 3 H); 3.42 (*quint.*, *J* = 7, 1 H); 4.12 (*dt*, *J* = 7.5, 1 H); 5.42 (*q*, *J* = 6.5, 1 H); 7.45 (*d*, *J* = 7.5, 1 H); 7.59 (*t*, *J* = 7.5, 1 H); 7.71 (*t*, *J* = 7.5, 1 H); 7.82 (*t*, *J* = 7.5, 1 H). ^{13}C-NMR: 173.68 (*s*); 137.19 (*s*); 134.05 (*d*); 133.76 (*s*); 129.59 (*d*); 124.26 (*d*); 121.73 (*d*); 73.41 (*d*); 55.50 (*d*); 45.58 (*d*); 28.52 (*t*); 25.94 (*q*, 3 C); 21.13 (*q*); 18.17 (*s*); 15.61 (*q*); 8.52 (*q*); −4.15 (*q*); −4.48 (*q*). MS: 354 (32.8, $[C_{20}H_{33}NO_4SSi - C_4H_9]^+$), 296 (34), 199 (15), 173 (18), 171 (22), 115 (17), 103 (19), 97 (18), 77 (24), 75 (100), 57 (53).

*(3R,4S)-5-[(*tert*-Butyl)dimethylsilyloxy]-3-methyl-2-(phenylsulfonyl)heptan-3-one* (**10**). A 1.6M soln. of BuLi (hexane, 1.82 ml) followed by TMEDA (440 µl, 2.92 mmol) were added to a soln. of ethyl phenyl sulfone (248 mg, 1.46 mmol) in THF (3 ml) at −78°. Stirring of the mixture at 0° for 1 h, cooling to −78°, addition of a soln. of acylsultam **8** (500 mg, 1.2 mmol) in THF (2 ml), stirring for 5 h, addition of sat. aq. NH_4Cl soln., acidification to pH 1 with HCl, extraction with Et_2O, and FC (hexane/AcOEt 6:1→2:1) gave toluenesultam **9** (372 mg, 77%) and the less polar **10** (164 mg, 85%) as a 87:13 mixture of C(2)-epimers (^{1}H-NMR). IR: 3028, 2957, 2932, 2858, 1712, 1463, 1448, 1463, 1448, 1378, 1318, 1309, 1259, 1154, 1082, 1052, 1003. ^{1}H-NMR: 0.1 (*s*, 3 H); 0.19 (*s*, 3 H); 0.89 (*t*, *J* = 7.0, 3 H); 0.92 (*s*, 9 H); 1.05 (*d*, *J* = 7.0, 3 H); 1.31 (*d*, *J* = 7.0, 3 H); 1.43–1.55 (2 H); 2.97 (*dq*, *J* = 5, 7, 0.13 H); 3.48 (*dq*, *J* = 3.5, 7, 0.87 H); 3.68 (*m*, 0.87 H); 3.87 (*m*, 0.13 H); 4.56 (*q*, *J* = 7.0, 0.13 H); 4.78 (*d*, *J* = 7.0, 0.87 H); 7.53–7.59 (2 H); 7.68 (*m*, 1 H); 7.73–7.76 (2 H). ^{13}C-NMR: 204.46 (*s*); 135.96 (*s*); 134.09 (*d*); 129.65 (*d*, 2 C); 128.90 (*d*, 2 C); 76.60 (*d*); 70.00 (*d*); 53.90 (*d*); 26.50 (*t*); 25.90 (*q*, 3 C); 18.04 (*s*); 12.30 (*q*); 11.90 (*q*); 10.90 (*q*); −4.10 (*q*); −4.60 (*q*). MS: 369 (3, $[C_{20}H_{34}O_4SSi]^+$), 361 (15), 283 (12), 199 (100), 173 (10), 135 (45), 75 (47).

*(4R,5S)-5-[(*tert*-Butyl)dimethylsilyloxy]-4-methylheptan-3-one* (**11**). A 0.1M soln. of SmI_2 in THF (20 ml) was added at −78° to a soln. of **10** (400 mg, 1 mmol) in THF (10 ml). Stirring for 15 min, workup and FC (hexane/AcOEt, 20:1) gave **11** (215 mg, 83.5%). GC (100/5/10/270): 8.01 (99.8). IR: 3024, 3059, 2931, 2881, 2857, 1708, 1417, 1462, 1379, 1256, 1223, 1101, 1053, 1004. ^{1}H-NMR: 0.045 (*s*, 3 H); 0.061 (*s*, 3 H); 0.87 (*t*, *J* = 7.0, 3 H);

0.89 (*s*, 9 H); 1.03 (*t*, *J* = 7.0, 3 H); 1.07 (*d*, *J* = 7.0, 3 H); 1.35 (*m*, 1 H); 1.50 (*m*, 1 H); 2.45 (*dq*, *J* = 18, 7.0, 1 H); 2.59 (*dq*, *J* = 18, 7.0, 1 H); 2.67 (*m*, 1 H); 3.84 (*q*, *J* = 5.5, 1 H). ^{13}C-NMR: 213.99 (*s*); 74.85 (*d*); 50.66 (*d*); 35.76 (*t*); 27.44 (*t*); 25.86 (*q*, 3 C); 18.04 (*s*); 12.13 (*q*); 9.72 (*q*); 7.59 (*q*); –4.31 (*q*); –4.52 (*q*).

(4R,5S)-5-Hydroxy-4-methylheptan-3-one (**5a**). A 45% aq. soln. of HF (150 µl, 3.5 mmol) was added at 0° to a soln. of **11** (180 mg, 0.7 mmol) in MeCN (5 ml). Stirring of the mixture at 0° for 6 h, dilution with Et_2O, washing with sat. aq. $NaHCO_3$, soln., and drying ($MgSO_4$) gave **5a** (98 mg, 98%) which was subjected to the subsequent acylation step without further purification. ^{1}H-NMR: identical to that of (±)-**5a**.

(1S,2R)-1-Ethyl-2-methyl-3-oxopentyl Propanoate (**6a**). Propanoyl chloride (74 µl, 0.8 mmol) was added at 0° to a soln. of (4*R*,5*S*)-aldol **5a** (100 mg, 0.67 mmol) in CH_2Cl_2/pyridine (5:1, 2.4 ml). Stirring of the mixture at 0° for 20 h, addition of 1M aq. HCl workup, and FC (hexane/AcOEt 10:1) gave pure (4*R*,5*S*)-**6a** (oil, 112 mg, 92%). GC (80/5/10/270): 7.7 (99.5). ^{1}H-NMR: identical to that of (±)-**6a**.

*(3S,4S)-4-[(*tert*-Butyl)dimethylsilyloxy]-3-methyl-1-(phenylsulfonyl)hexan-2-one* (**14**). A 1.6M soln. of BuLi (hexane, 3.10 ml) followed by TMEDA (748 µl, 4.96 mmol) were added to a soln. of methyl phenyl sulfone (388 mg, 2.48 mmol) in THF (5 ml) at –78°. Stirring of the mixture at 0° for 1 h, cooling to –78°, addition of a soln. of *N*-acylsultam **12** [11] (1.0 g, 2.25 mmol) in THF (3 ml), stirring for 4 h, addition of sat. aq. NH_4Cl soln., acidification to pH 1 with HCl, extraction with Et_2O, and FC (hexane/AcOEt 6:1→2:1) gave bornanesultam **13** (382 mg, 80%) and the less polar **14** (691 mg, 80%). GC (150/5/10/270): 13.44 (94) 13.50 (1.5, s-*cis*-isomer). IR: 3016, 2957, 2931, 2883, 2858, 1716, 1463, 1448, 1463, 1448, 1361, 1324, 1309, 1257, 1157, 1070, 1001. ^{1}H-NMR: 0.099 (*s*, 3 H); 0.005 (*s*, 3 H); 0.82 (*s*, 9 H); 0.86 (*t*, *J* = 7.0, 3 H); 0.99 (*d*, *J* = 7.0, 3 H); 1.36–1.58 (2 H); 3.09 (*quint.*, *J* = 7.0, 1 H); 3.75 (*dt*, *J* = 7.5, 4.5, 1 H); 4.06 (*d*, *J* = 14, 1 H); 4.48 (*d*, *J* = 14, 1 H); 7.50–7.73 (3 H); 7.87–7.93 (2 H). ^{13}C-NMR: 202.51 (*s*); 139.02 (*s*); 134.11 (*d*); 129.22 (*d*, 2 C); 128.33 (*d*, 2 C); 75.98 (*d*); 68.19 (*t*); 50.57 (*d*); 26.68 (*t*); 25.81 (*q*, 3 C); 17.96 (*s*); 12.77 (*q*); 7.34 (*q*); –4.63 (*q*); –4.95 (*q*). MS: 384 (0.3, $[C_{20}H_{34}O_4SSi]^{+\cdot}$), 327 (9), 269 (50), 185 (14), 173 (54), 143 (18), 135 (70), 125 (18), 115 (18), 113 (17), 77 (100), 75 (93), 73 (95).

(3S,4S)-4-Hydroxy-3-methylhexan-2-one (**16**). Al foil (4.21 g, 150 mmol) was dipped into a 2% aq. $HgCl_2$ soln. and then added to a soln. of **14** (1.0 g, 2.6 mmol) in THF/H_2O (10:1, 66 ml). Heating of the mixture at reflux for 20 h, filtration, drying ($MgSO_4$), addition of a 48% aq. THF soln. (400 µl, 10.4 mmol) at 0°, stirring at 0° for 6 h, extraction with Et_2O, washing with a sat. aq. $NaHCO_3$ soln., and FC (hexane/AcOEt 3:1) furnished (–)-**16** (230 mg, 68% from **14**). $[\alpha]_D$ = –27.6 (*c* = 1.63, *T* = 22°, $CHCl_3$). IR: 3590, 3514, 3020, 3008, 2969, 2937, 2878, 1702, 1458, 1377, 1235, 1172, 967. ^{1}H-NMR: 0.94 (*t*, *J* = 7.0, 3 H); 1.09 (*d*, *J* = 7.0, 3 H); 1.30–1.66 (2 H); 2.16 (*s*, 3 H); 2.48–2.70 (2 H); 3.59 (*m*, 1 H). ^{13}C-NMR: 214.01 (*s*); 74.64 (*d*); 51.76 (*d*); 29.77 (*q*); 27.28 (*t*); 13.82 (*q*); 9.74 (*q*).

(1S,2S)-1-Ethyl-2-methyl-3-oxobutyl Propanoate (**17**). Propanoyl chloride (154 µl, 1.66 mmol) was added at 0° to a soln. of (4*S*,5*S*)-aldol **16** (180 mg, 1.39 mmol) in CH_2Cl_2/pyridine (5:1, 5 ml). Stirring of the mixture at 0° for 20 h, addition of 1M aq. HCl workup, and FC (hexane/AcOEt 6:1) gave ester (1*S*,2*S*)-**17** (oil, 219 mg, 85%). GC (80/5/10/270): 5.36 (100). IR: 3026, 2976, 2942, 2881, 1723, 1462, 1381, 1357, 1276, 1230, 1190, 1100, 1081. ^{1}H-NMR: 0.84 (*t*, *J* = 7.0, 3 H); 1.02 (*d*, *J* = 7.0, 3 H); 1.09 (*t*, *J* = 7.0, 3 H); 1.40–1.70 (2 H); 2.12 (*s*, 3 H); 2.21–2.26 (2 H); 2.80 (*quint.*, *J* = 7.0, 1 H); 5.03 (*dt*, *J* = 4.0, 7.5, 1 H). ^{13}C-NMR: 209.63 (*s*); 173.82 (*s*); 75.22 (*d*); 50.06 (*d*); 28.61 (*q*); 27.66 (*t*); 23.70 (*t*); 21.00 (*q*); 9.18 (*q*, 2 C). MS: 186 (0.2, $[C_{10}H_{18}O_3]^{+\cdot}$), 113 (32), 70 (23), 57 (100).

Cyclocondensation of Oxo-esters to Dihydropyranones. – *(2RS,3SR)-2,6-Diethyl-2,3-dihydro-3,5-dimethyl-4H-pyran-4-one* (**18a**). $TiCl_4$ (172 µl, 1.5 mmol), followed by EtN(i-Pr)$_2$ (523 µl, 3.0 mmol) were added at –78° to a soln. of (±)-**6a** (200 mg, 1.0 mmol) in CH_2Cl_2 (10 ml). The mixture was stirred at –78° for 1 h, then allowed to warm up to –10° and stirred at –78° for 16 h. Addition of a sat. aq. NH_4Cl soln. and workup gave crude (±)-**18a**. GC (80/5/10/270): 11.04 (87), 12.47 (4.5). FC (hexane/AcOEt 10:1) furnished the minor *trans*-isomer (4.8 mg, 2.6%, ^{1}H-NMR: H–C(2) at 3.83 (*m*, 1 H)) and the pure *cis*-dihydropyranone (±)-**18a** (148 mg, 81%). GC: 11.06 (99.5%). IR: 3030, 2977, 2940, 2880, 1715, 1648, 1601, 1462, 1398, 1378, 1348, 1140, 1091. ^{1}H-NMR: 0.99 (*t*, *J* = 7.5, 3 H); 1.01 (*t*, *J* = 7.5, 3 H); 1.13 (*t*, *J* = 7.5, 3 H); 1.55 (*m*, 1 H); 1.72 (*s*, 3 H); 1.82 (*m*, 1 H); 2.28–2.41 (3 H); 4.11 (*ddd*, *J* = 3.0, 6.0, 8.5, 1 H). ^{13}C-NMR: 197.94 (*s*); 173.55 (*s*); 107.37 (*s*); 81.94 (*d*); 42.35 (*d*); 25.51 (*t*); 23.49 (*t*); 10.84 (*q*); 9.74 (*q*); 9.50 (*q*); 9.10 (*q*). MS: 182 (30, $[C_{11}H_{18}O_2]^{+\cdot}$), 153 (5), 113 (100), 97 (10), 83 (28), 70 (10), 57 (22). HR-MS: 183.13484 ($[C_{11}H_{18}O_2 - C_2H_5]^+$; calc. 183.1340).

(2RS,3SR)-2-Ethyl-2,3-dihydro-6-isopropyl-3,5-dimethyl-4H-pyran-4-one (**18b**). $TiCl_4$ (79.5 µl, 0.69 mmol), followed by EtN(i-Pr)$_2$ (242 µl, 1.38 mmol) were added at –78° to a soln. of (±)-**6b** (100 mg, 0.46 mmol) in CH_2Cl_2 (5 ml). The mixture was stirred at –78° for 1 h, then allowed to warm up to –10° and stirred at –78° for 16 h. Addition of a sat. aq. NH_4Cl soln. and workup gave crude (±)-**18b**. GC (80/5/10/270): 12.03 (92). FC (hexane/AcOEt 10:1) furnished the minor *trans*-isomer (2.3 mg, 2.5%, ^{1}H-NMR: H–C(2) at 3.8 (*m*, 1 H)) and pure (±)-**18b** (76 mg, 83%). GC: 12.02 (98). IR: 3030, 2975, 2938, 2878, 1714, 1647, 1596, 1460, 1399, 1378, 1348, 1230, 1139. ^{1}H-NMR: 1.01 (*t*, *J* = 7.0, 6 H); 1.12 (*t*, *J* = 7.0, 6 H); 1.54 (*m*, 1 H); 1.73 (*s*, 3 H); 1.82 (*m*, 1 H); 2.31 (*dq*, *J* = 3.0,

7.0, 1 H); 2.92 (*sept.*, J = 7.0, 1 H); 4.11 (*ddd*, J = 3.0, 5.0, 8.5, 1 H). ^{13}C-NMR: 190.03 (*s*); 175.85 (*s*); 106.33 (*s*); 81.88 (*d*); 42.61 (*d*); 30.42 (*d*); 23.53 (*t*); 19.22 (*q*); 19.16 (*q*); 9.81 (*q*); 9.57 (*q*); 8.81 (*q*). MS: 196 (43, $[C_{12}H_{20}O_2]^{+\cdot}$), 181 (5), 139 (5), 127 (100), 83 (28), 71 (10), 55 (8). HR-MS: 197.15029 ($[C_{12}H_{20}O_2]^{+\cdot}$; calc. 197.1542).

*(2RS,3SR)-2-Ethyl-2,3-dihydro-3,5-dimethyl-6-phenyl-4*H*-pyran-4-one* (**18c**). A 1M soln. of $TiCl_4$ in CH_2Cl_2 (1.29 ml), followed by $EtN(i\text{-}Pr)_2$ (422 µl, 2.42 mmol) were added at −78° to a soln. of (±)-**6c** (200 mg, 0.8 mmol) in CH_2Cl_2 (8 ml). The mixture was stirred at −78° for 1 h, then allowed to warm up to −10° and stirred at −78° for 16 h. Addition of a sat. aq. NH_4Cl soln. and workup gave crude (±)-**18c**. GC (100/5/10/270): 12.35 (95.4). FC (hexane/AcOEt 10:1) furnished the *trans*-isomer (2.2 mg, 2%, ^{1}H-NMR: H–C(2) at 4.05 (*m*, 1 H)) pure (±)-**18c** (164 mg, 89%). GC: 11.82 (98.8). IR: 3080, 2976, 2940, 2939, 2880, 1650, 1606, 1591, 1574, 1493, 1457, 1445, 1388, 1372, 1347, 1237, 1164, 1138, 1015. ^{1}H-NMR: 1.09 (*t*, J = 7.0, 3 H); 1.12 (*d*, J = 7.0, 3 H); 1.64 (*m*, 1 H); 1.86 (*s*, 3 H); 1.92 (*m*, 1 H); 2.45 (*dq*, J = 3.0, 7.0, 1 H); 4.37 (*ddd*, J = 8, 5, 3, 1 H); 7.40–7.45 (3 H); 7.51–7.55 (2 H). ^{13}C-NMR: 198.60 (*s*); 167.06 (*s*); 134.37 (*s*); 130.19 (*d*); 128.99 (*d*, 2 C); 128.14 (*d*, 2 C); 109.07 (*s*); 82.56 (*d*); 42.76 (*d*); 23.61 (*t*); 11.48 (*q*); 9.97 (*q*); 9.43 (*q*). MS: 230 (30, $[C_{15}H_{18}O_2]^{+\cdot}$), 161 (65), 132 (20), 105 (100), 77 (40). HR-MS: 230.13018 ($[C_{15}H_{18}O_2]^{+\cdot}$; calc. 230.13068).

*(2RS,3SR)-6-Benzyl-2-ethyl-2,3-dihydro-3,5-dimethyl-4*H*-pyran-4-one* (**18d**). A 1M soln. of $TiCl_4$ in CH_2Cl_2 (1.22 ml), followed by $EtN(i\text{-}Pr)_2$ (398 µl, 2.28 mmol) were added at −78° to a soln. of (±)-**6c** (200 mg, 0.76 mmol) in CH_2Cl_2 (10 ml). The mixture was stirred at −78° for 1 h, then allowed to warm up to −10° and stirred at −78° for 16 h. Addition of a sat. aq. NH_4Cl soln., workup, and FC (hexane/AcOEt 9:1) furnished pure (±)-**18d** (79 mg, 43%). IR: 3011, 2976, 2938, 2879, 1715, 1652, 1609, 1591, 1494, 1455, 1391, 1372, 1348, 1134. ^{1}H-NMR: 0.92 (*t*, J = 7.0, 3 H); 1.02 (*d*, J = 7.0, 3 H); 1.47–1.57 (2 H); 1.78 (*s*, 3 H); 2.35 (*dq*, J = 3.0, 7.0, 1 H); 3.62 (*d*, J = 14, 1 H); 3.68 (*d*, J = 14, 1 H); 4.12 (*ddd*, J = 8, 6, 3, 1 H); 7.20–7.35 (5 H). ^{13}C-NMR: 197.89 (*s*); 169.96 (*s*); 136.43 (*s*); 130.11 (*d*); 128.60 (*d*); 128.50 (*d*); 126.7 (*d*, 2 C); 108.96 (*s*); 82.26 (*d*); 42.50 (*d*); 38.99 (*t*); 23.46 (*t*); 9.68 (*q*, 2 C); 9.51 (*q*). MS: 244 (30, $[C_{16}H_{20}O_2]^{+\cdot}$), 175 (60), 105 (15), 83 (100), 77 (40), 57 (22). HR-MS: 244.145248 ($[C_{16}H_{20}O_2]^{+\cdot}$; calc. 244.14633).

*(2RS,3SR)-2-Ethyl-2,3-dihydro-3,5-dimethyl-4*H*-pyran-4-one* (**18e**). A 0.5M soln. of $TiCl_4$ in CH_2Cl_2 (1.86 ml) was added to a soln. of (±)-**6e** (100 mg, 0.58 mmol) and $EtN(i\text{-}Pr)_2$ (303 µl, 1.74 mmol) in CH_2Cl_2 (6 ml). The mixture was stirred at −78° for 1 h, then allowed to warm up to −10° and stirred at −78° for 16 h. Addition of a sat. aq. NH_4Cl soln., workup, and FC (hexane/AcOEt 10:1) furnished pure (±)-**18e** (52 mg, 58%). GC (70/5/10/270): 11.82 (95). IR: 3019, 2976, 2939, 2880, 1721, 1461, 1382, 1185. ^{1}H-NMR: 0.99 (*t*, J = 7.0, 3 H); 1.05 (*d*, J = 7.0, 3 H); 1.57 (*m*, 1 H); 1.66 (*s*, 3 H); 1.83 (*m*, 1 H); 2.37 (*dq*, J = 3.0, 7.0, 1 H); 4.20 (*ddd*, J = 9, 6, 3, 1 H); 7.21 (*s*, 1 H). ^{13}C-NMR: 197.92 (*s*); 159.10 (*d*); 112.02 (*s*); 83.30 (*d*); 43.30 (*d*); 23.43 (*t*); 10.60 (*q*); 9.70 (*q*); 9.50 (*q*). MS: 154 (28 $[C_9H_{14}O_2]^{+\cdot}$), 85 (100), 70 (28), 55 (35).

*(2RS,3RS)-6-Ethyl-2,3-dihydro-3,5-dimethyl-2-phenyl-4*H*-pyran-4-one* (**18f**). A 0.5M soln. of $TiCl_4$ in CH_2Cl_2 (2.58 ml) was added to a soln. of (±)-**6f** (200 mg, 0.8 mmol) and $EtN(i\text{-}Pr)_2$ (422 µl, 2.42 mmol) in CH_2Cl_2 (15 ml). The mixture was stirred at −78° for 1 h, then allowed to warm up to −10° and stirred at −78° for 16 h. Addition of a sat. aq. NH_4Cl soln. and workup gave crude (±)-**18f**. GC (80/5/10/270): 14.33 (6, **6f**), 15.39 (2.9), 15.51 (80.2). FC (hexane/AcOEt 6:1) furnished pure (±)-**18f** (126 mg, 68%). GC: 14.49 (98). IR: 3030, 2979, 2940, 2937, 2877, 1650, 1606, 1585, 1498, 1453, 1395, 1196, 1142, 1122. ^{1}H-NMR: 0.87 (*d*, J = 7.5, 3 H); 1.22 (*t*, J = 7.0, 3 H); 1.80 (*s*, 3 H); 2.47 (*q*, J = 7.0, 2 H); 2.56 (*dq*, J = 3.0, 7.0, 1 H); 5.40 (*d*, J = 3.0, 1 H); 7.36 (5 H). ^{13}C-NMR: 197.47 (*s*); 173.05 (*s*); 128.40 (*d*, 2 C); 127.73 (*d*); 125.38 (*d*, 2 C); 107.77 (*s*); 81.44 (*d*); 44.97 (*d*); 25.54 (*t*); 10.91 (*q*); 9.95 (*q*); 9.18 (*q*). MS: 230 (10, $[C_{15}H_{18}O_2]^{+\cdot}$), 183 (10), 134 (10), 118 (60), 105 (100), 91 (12), 77 (52), 57 (35). HR-MS: 230.12962 ($[C_{15}H_{18}O_2]^{+\cdot}$; calc. 230.1307).

*(2RS,3SR)-6-Ethyl-2,3-dihydro-3,5-dimethyl-2-[(*E*)-prop-1-enyl]-4*H*-pyran-4-one* (**18g**). A 0.5M soln. of $TiCl_4$ in CH_2Cl_2 (3.0 ml) was added to a soln. of (±)-**6g** (200 mg, 0.94 mmol) and $EtN(i\text{-}Pr)_2$ (494 µl, 2.83 mmol) in CH_2Cl_2 (15 ml). The mixture was stirred at −78° for 1 h, then allowed to warm up to −10° and stirred at −78° for 16 h. Addition of a sat. aq. NH_4Cl soln., workup, and FC (hexane/AcOEt 6:1) furnished pure (±)-**18g** (96 mg, 52%). GC (70/5/10/270): 10.76 (95). IR: 3026, 2984, 2942, 2877, 1716, 1650, 1602, 1456, 1379. ^{1}H-NMR: 1.03 (*d*, J = 7.0, 3 H); 1.14 (*t*, J = 7.0, 3 H); 1.73 (*s*, 3 H); 1.75–1.78 (3 H); 2.31–2.42 (3 H); 4.69 (*m*, 1 H); 5.60 (*ddq*, J = 7.0, 15, 2.0, 1 H); 5.85 (*ddq*, J = 15, 1.0, 6.5, 1 H). ^{13}C-NMR: 197.13 (*s*); 172.81 (*s*); 130.71 (*d*); 125.70 (*d*); 107.35 (*s*); 81.31 (*d*); 43.50 (*d*); 25.62 (*t*); 17.89 (*q*); 10.85 (*q*); 10.03 (*q*); 9.11 (*q*). MS: 194 (10, $[C_{12}H_{18}O_2]^{+\cdot}$), 155 (5), 137 (10), 109 (8), 82 (40), 67 (30), 57 (100).

*(2S,3R)-2,6-Diethyl-2,3-dihydro-3,5-dimethyl-4*H*-pyran-4-one* (**18a**). $TiCl_4$ (86 µl, 0.75 mmol), followed by $EtN(i\text{-}Pr)_2$ (260 µl, 1.5 mmol) were aded at −78° to a soln. of (1*S*,2*R*)-**6a** (100 mg, 0.5 mmol) in CH_2Cl_2 (5 ml). The mixture was stirred at −78° for 1 h, then allowed to warm up to −10° and stirred at −78° for 16 h. Addition of a sat. aq. NH_4Cl soln., workup, and FC (hexane/AcOEt 6:1) furnished pure **18a** (75 mg, 82%). GC: (80/5/10/270): 8.42

(99.5). $[\alpha]_D = -232.7$, $[\alpha]_{578} = -245.8$, $[\alpha]_{546} = -288.48$, $[\alpha]_{436} = -625.7$, $[\alpha]_{365} = -1714$ ($c = 3.30$, $T = 22°$, $CHCl_3$). ^{1}H-NMR: identical with that of (±)-**18a**.

(2S,3S)-2,6-Diethyl-2,3-dihydro-3-methyl-4H-pyran-4-one (**19**). A 0.5M soln. of $TiCl_4$ in CH_2Cl_2 (1.72 ml) was added to a soln. of **17** (100 mg, 0.53 mmol) and EtN(i-Pr)$_2$ (281 µl, 1.61 mmol) in CH_2Cl_2 (5 ml). The mixture was stirred at −78° for 1 h, then allowed to warm up to −40° and stirred at −78° for 16 h. Addition of a sat. aq. NH_4Cl soln., workup, and FC (hexane/AcOEt 10:1) furnished pure **19** (46 mg, 52%). $[\alpha]_D = -146.47$ ($c = 0.71$, $T = 22°$, $CHCl_3$). IR: 3015, 2975, 2938, 2890, 1654, 1608, 1462, 1404, 1380, 1343. ^{1}H-NMR: 0.95–1.15 (9 H); 1.52–1.58 (2 H); 2.20–2.40 (2 H); 3.95 (*ddd*, $J = 11, 7, 3$, 1 H); 5.30 (*s*, 1 H). ^{13}C-NMR: 195.77 (*s*); 117.71 (*s*); 101.94 (*d*); 84.72 (*d*); 42.34 (*d*); 27.79 (*t*); 25.26 (*t*); 10.71 (*q*); 10.58 (*q*); 8.89 (*q*). MS: 169 (9, $[C_{10}H_{16}O_2]^{+\cdot}$), 99 (100), 70 (28), 55 (63). HR-MS: 168.1154 ($[C_{10}H_{16}O_2]^{+\cdot}$; calc. 168.1150).

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