Alkylations of (*R*,*R*)-2-*t*-Butyl-6-methyl-1,3-dioxan-4-ones which are not Possible with Lithium Amides may be Achieved with a Schwesinger P4 Base

Thomas Pietzonka[1] **and Dieter Seebach***

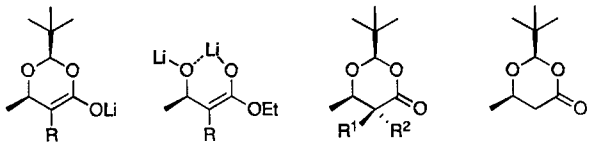
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule, ETH-Zentrum, Universitätstraße 16, CH-8092 Zürich

Rcceived March 30, 1991

Key Words: β-Hydroxycarboxylic acids, α-alkylation of / EPC synthesis / 1,3-Dioxan-4-ones, enolates of / Enolates, naked / Schwesinger's base / Phosphazene P4 base

Enolates **A** of the dioxanones specified in the title, when generated with lithium amide bases, can only be alkylated with highly reactive electrophiles, and only once. With Schwesinger's *t*-Bu-P4 base (a very strong, so-called neutral base, containing 4P and 13N atoms capable of bearing a positive charge in the conjugate $P4H^+$ cation) the dioxanone **1** can be doubly alkylated even with iodobutane (products **16**, **17**). The 5,6-dimethyl- and 5-benzyl-6-methyldioxanone **2** and **3** can be alkylated diastereoselectively with the formation of quaternary centers at C(5) (products **4**, **8**–**14**). In one case, the configuration of the product **4** obtained was determined by conversion to a β-lactone **6** and an olefin **7** (a previous assignment had to be revised). Even the 2,5,6,6-tetraalkyl-substituted dioxanone **19** could be further alkylated (→ **20** + **21**). Five of the new alkylation products were hydrolyzed to the parent 3-hydroxycarboxylic acids **5**, **22**–**25**. The enormous reactivities achieved with the inherently labile enolates and the $P4H^+$ counterions are discussed.

β-Hydroxycarboxylic acids can be α-alkylated by lithium enolates **A** of dioxanones[2]. The advantage over the use of the lithioxy lithium enolate **B**[3–5] is that only one equivalent of base is required and that the diastereoselectivities of the reactions are usually higher. A disadvantage is the low stability of enolates of type **A**[2b], which is the reason for the fact that, so far, only the more reactive electrophilic reagents such as iodomethane, allyl and benzyl bromide, aldehydes, acid chlorides or phenyl selenyl halides have been employed[2,6–8]. This is especially true when attempts were made to prepare 5,5-disubstituted derivatives **C** (R ≠ H in the enolate **A**)[2b,9]. We describe here the application of a new method of generating and alkylating enolates with non-metal-containing extremely strong, so-called PN bases (Schwesinger's bases)[10–12], see the formula of the *t*-Bu-P4 base in Scheme 1. After only a brief experience with this base it is not risky for us to predict that this type of bases will adopt a paramount role in organic synthesis. The bases are readily prepared, soluble in non-polar media (even at low temperatures), nontoxic, nonnucleophilic[10–14], and they generate anionic species of extraordinary reactivity[15].

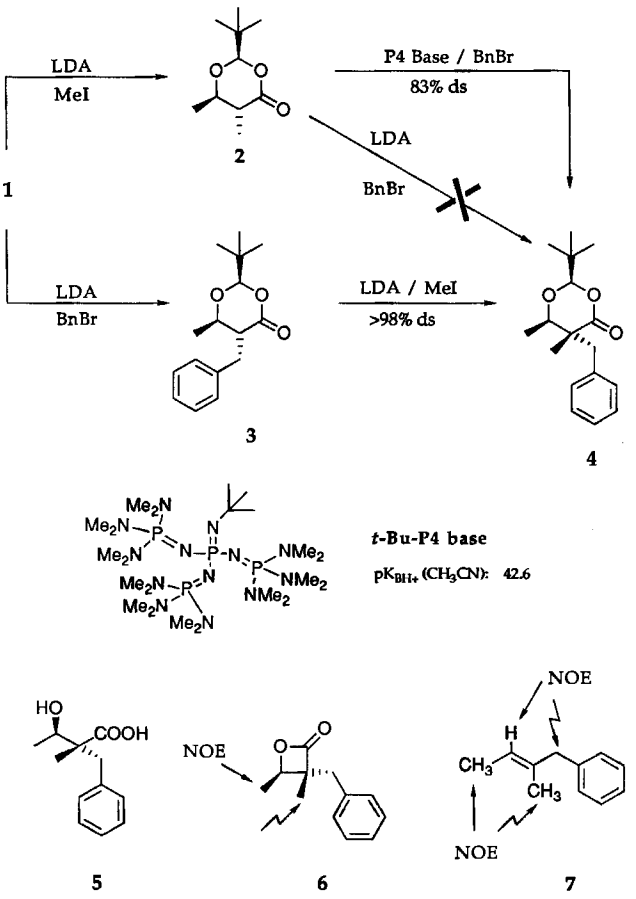


A **B** **C** **1**

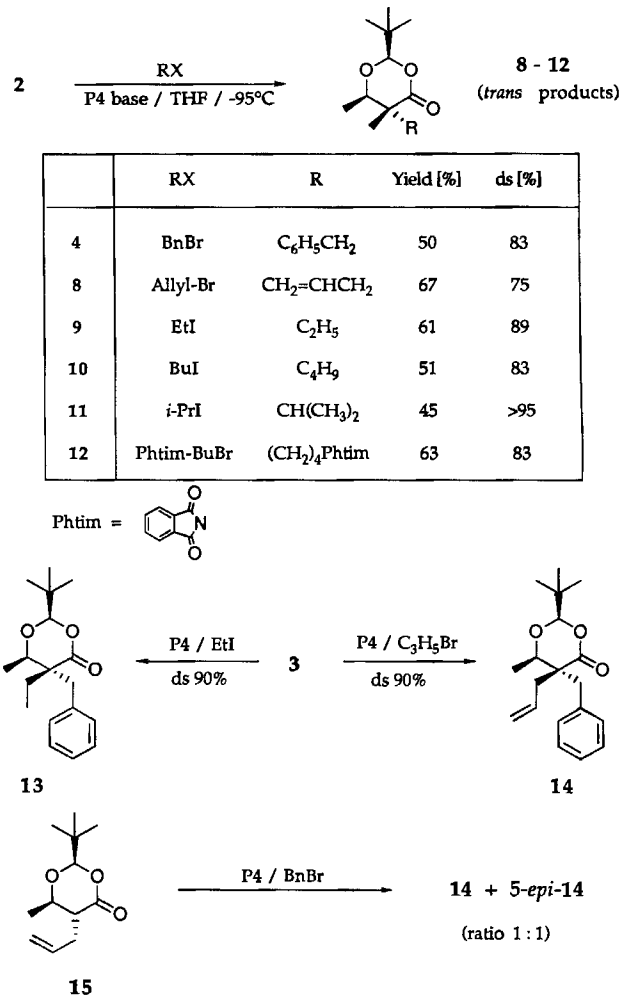
We first used the *t*-Bu-P4 base for the benzylation of dimethyl-dioxanone **2**: Curiously, this dioxanone cannot be benzylated[16] through the lithium enolate (**A**, R = CH_3) while the corresponding benzyl-methyl-dioxanone **3** is readily methylated under the usual conditions (→ **4**), and since Schwesinger's base had been shown before to be applicable to elimination-prone enolates[10b], we tested it on **2**. Indeed, the reaction gave in ca. 50% yield a product of benzylation. Although the sequence of alkylation steps had been reversed, we were surprised to find that the same major product **4** was formed on the two routes **1** → **2** → **4** (83% ds) and **1** → **3** → **4** (> 98% ds). Before drawing any mechanistic conclusions, we had to determine the configuration of **4** unambiguously, which we had assigned, solely on the basis of nuclear Overhauser effects with the one and only diastereomer obtained via **3**, to be 5*S* in our previous paper[2b]. Thus, we hydrolyzed the dioxanone to the 3-hydroxy acid **5**, which was cyclized to the β-lactone **6** (Ph-SO_2Cl/Py)[17], and this in turn was decarboxylated to the olefin **7**. Nuclear Overhauser effects on the latter two products clearly established the configuration at C-5 of the dioxanone **4** to be *R*, in contrast to our previous assignment[2b,18]. We were now left with the conclusion that either the 5-benzyl- and the 5-methyl-enolate react with the corresponding electrophiles from the diastereotopic *Si* and *Re* faces, respectively, or that the $P4H^+$ enolate and the lithium enolate react from opposite faces. Since the *t*-Bu-P4 base cannot be used for methylations[13,14] we ethylated the benzyl derivative **3** (vide infra) to find that ethylation with the P4 base takes the same course (rel. topicity *ul*-1,2) as methylation with the lithium enolate. This is confirmed by allylation of the benzyl derivative described below. Thus, with the P4 base the steric course reverses from *lk*-1,2 to *ul*-1,2 on going from the 5-methyl to the 5-benzyl derivative – just like in the case of protonation of the corresponding lithium enolates (see our previous paper[7b] and references cited therein).

  0009–2940/91/0808–1837 $ 3.50+.25/0

Scheme 1. Benzylation of the dimethyl-dioxanone **2** is possible with *t*-Bu-P4 base, but not with LDA. Structure determination of the product **4** — a correction.



Scheme 2. Diastereoselective alkylations of 5-alkyl-dioxanones with alkyl bromides and iodides by using the P4 base. The yields refer to purified major diastereomers.



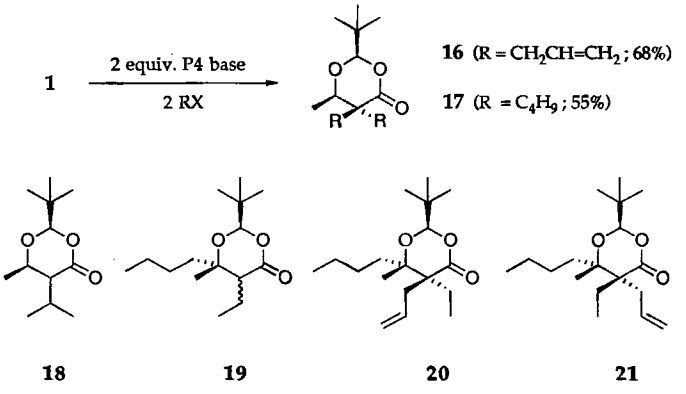
	RX	R	Yield [%]	ds [%]
4	BnBr	$C_6H_5CH_2$	50	83
8	Allyl-Br	CH_2=$CHCH_2$	67	75
9	EtI	C_2H_5	61	89
10	BuI	C_4H_9	51	83
11	*i*-PrI	$CH(CH_3)_2$	45	>95
12	Phtim-BuBr	$(CH_2)_4$Phtim	63	83

We next checked which other alkylating reagents could be used to introduce a quaternary center into the dioxanone **2**. The results are shown in Scheme 2; we, indeed, isolated in reasonable yields (45–67%) of major diastereomers not only the products **4** and **8** of benzylation and allylation, but also those of ethylation and butylation (**9** and **10**, respectively), and even of isopropylation (**11**!), and a functionalized bromide could also be successfully employed (→ **12**). On the other hand, the use of the following electrophiles did not lead to the isolation of products: 2-bromo- and 2-iodobutane, iodocyclohexane, 2-(2-bromoethyl)dioxolane, 2-phenyl-bromo-ethane, and methyl-oxirane which are known to be sluggish alkylating reagents.

Two groups, both of which larger than methyl, can be introduced as well: ethylation of **3** gave 66% of the *gem*-benzyl-ethyl derivative **13**, the configuration of which follows from NMR comparison with the corresponding *gem*-benzyl-methyl compound **4** (**13** like **4** shows a large shift difference between the diastereotopic benzylic hydrogen, while in 5-*epi*-**4** the signals of these hydrogen atoms appear much closer to each other). Also, allylation of the benzyl-dioxanone **3** with the P4 base occurs with the same relative topicity *ul*-1,2 (see **3** → **14**) as judged from the same feature in the ^{1}H-NMR spectrum described above. It is intriguing that the reversal of the sequence of alkylation steps (benzylation of the allyl derivative[2] with P4 base, see **15** → **14**) gave totally unselectively **14** and *epi*-**14**!

Monoalkylations of **1** are not possible with *t*-Bu-P4: it is so vigorous a base[14] that it does not select between the 5-unsubstituted and the 5-monoalkyl derivatives; mixtures of

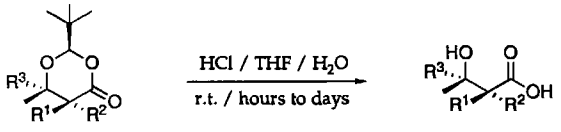
Scheme 3. Double alkylations of dioxanones in the 5-position by using the P4 base, including formation of pentasubstituted dioxanones **20**, **21**.



starting material, mono- und *gem*-disubstituted products arise. With two equivalents each of the base and alkylating agent good yields of 5,5-dialkyldioxanones (**16**, **17**) can be obtained (see Scheme 3). With 2-iodopropane there is no overalkylation; a 2:1 mixture of diastereomers **18** is formed in 40% yield (the major isomer was separated and characterized). Surprisingly, even the tetraalkyldioxanone **19** (from the Michael addition of dibutyl cuprate to the corresponding dioxinone)[7b] could be allylated by using the P4 base to give 16% of the epimers **20** and **21** (ratio 1.5:1), containing two adjacent persubstituted carbon atoms (configurational assignment see next paragraph).

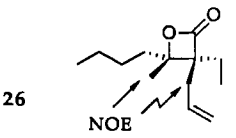
As shown in Scheme 4, we have hydrolyzed five of the dioxanones with geminal disubstitution in the 5-position to the corresponding carboxylic acids, including the one which also contains a tertiary alcohol. With reaction times of up to 7 days in aqueous THF/HCl at room temperature the acids were formed in high yields, the purification being, however, complicated by their glassy consistency. The 3-hydroxy acid **25** formed from the major diastereomer **20** by allylation of **19** was cyclized, as described for the conversion **5** → **6** above, to give the β-lactone **26**, NOE measurements of which proved unambiguously the configuration pictured in Scheme 4.

Scheme 4. Hydrolysis of (up to pentasubstituted) dioxanones to the parent 3-hydroxycarboxylic acids (single enantiomers and diastereomers).



4, 8, 14, 15, 18 **5, 22 - 25**

Acid	5	22	23	24	25
R^1	CH_3	CH_3	C_4H_9	$CH_2CH{=}CH_2$	$CH_2CH{=}CH_2$
R^2	$CH_2C_6H_5$	$CH_2CH{=}CH_2$	C_4H_9	$CH_2CH{=}CH_2$	C_2H_5
R^3	H	H	H	H	C_4H_9
Yield [%]	88	94	90	95	90



26

The P4 base has been shown to accomplish conversions of dioxanones which have otherwise not been possible at all. The reactivity of the $P4H^+$ enolates is so high that the S_N2 substitution reaction, which involves a highly ordered, intermolecularly formed transition state, competes successfully with the β-elimination[2,7], a unimolecular step which should also be accelerated in the case of a "naked" as compared to a lithiated enolate anion!? Maybe, the base can span the distance between the disappearing O^- of the enolate and the developing X^- of the leaving group — each phosphorus and each nitrogen of $P4H^+$ bearing a partial positive charge (17 resonance structures can be drawn), see the model in Figure 1.

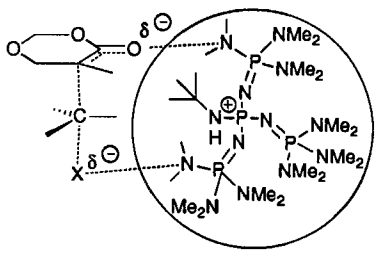


Figure 1. Speculation about the possible lowering of the S_N2-transition state by the $P4H^+$ cation. Modelling shows that the cation is large enough to reach from O^- to X^-, the sites at which the charge disappears and evolves in the alkylation of an enolate.

Further applications of Schwesinger's PN bases (up to seven phosphorus atoms have been incorporated) to synthetic problems are being investigated in our laboratory and will be reported shortly.

We thank Dr. *Schwesinger* and Dr. *Schlemper*[11] for accepting one of us (T.P.) as an apprentice in their laboratory to learn about the secrets of PN bases.

Experimental

General. — *Abbreviations*: GP (general procedure), FC (flash chromatography), HV [high vacuum (10^{-1} to 10^{-3} Torr)], concd. (concentrated), soln. (solution), RT (room temperature). — All reactions requiring anhydrous conditions were performed in oven-dried glassware. — Melting points were determined in open capillaries in a Büchi 510 apparatus equipped with an Anschütz thermometer set and are uncorrected. — TLC: Analytical plates Merck 60 F_{254}, detection either by UV light or by dipping into a soln. of 9.2 ml of anisaldehyde, 3.75 ml of AcOH, 12.5 ml of concd. H_2SO_4 and 338 ml of EtOH (techn.) followed by heating. — FC: Kieselgel 60 (Merck), 230–400 mesh. — Optical rotations $[\alpha]_D$ were measured in soln. at 589 nm (Na-D line) with a Perkin-Elmer 241 polarimeter in a 1.0-dm cell at RT (ca. 22°C); concentration *c* (in g/100 ml) and solvent in parentheses. — ^{1}H-NMR and ^{13}C-NMR spectra: Recorded in $CDCl_3$ with a Bruker AM-400, Bruker WM-300, Varian XL 300, and Varian Gemini 200 NMR spectrometer (*J* is given in Hz). — Mass spectra: Hitachi-Perkin-Elmer-RMU-6M. — The infrared spectra of crystalline compounds were recorded with a Perkin-Elmer 983 spectrophotometer (chloroform solutions), oily compounds as films on NaCl plates with a Perkin-Elmer 782 spectrophotometer (wave numbers in cm^{-1}). — Elemental analyses were performed by Mikrolaboratorium der ETH Zürich. — THF was freshly destilled from Na wire under argon.

General Procedure for the Alkylation with P4 Base (GP1): Unless stated otherwise, the following procedure was used: To a soln. of 1.0 mmol of substrate in 5 ml of THF under argon an excess of alkyl halide (3 to 5 equivalents) was added. After cooling to −100°C, a soln. of 1.1 mmol of P4 base[19] in 2 ml of dry THF was added dropwise with stirring by means of a syringe, so that the temperature of the mixture did not increase above −95°C. A precipitation occurred, and after stirring for 1 h at −95°C the reaction mixture was warmed up to RT. The solvent was then evaporated and the oily residue taken up with ether. The resulting precipitate was filtered through a G4 sintered glass filter, and concentration of the filtrate gave the crude product which was purified.

General Procedure for the Double Alkylation with P4 Base (GP2): To a soln. of 1.0 mmol of substrate in 5 ml of THF under argon an excess of alkyl halide (5 to 8 equivalents) was added. After cool-

ing to −100°C, a soln. of 2.1 mmol of P4 base in 5 ml of dry THF was added dropwise by means of a syringe, so that the temperature of the reaction mixture did not increase above −95°C. Precipitation occurred, and, after stirring for 1 h at −95°C, the reaction mixture was allowed to warm up to RT. The solvent was then evaporated and the oily residue taken up with ether. The resulting precipitate was filtered through a G4 sintered glass filter, and evaporation of the filtrate gave the crude product which was purified.

General Procedure for the Hydrolysis of the Dioxanone Derivatives (GP3): To a soln. of 1 mmol of the dioxanone derivative in 10 ml of THF 3 N HCl was added to maintain a homogenous solution. The reaction mixture was stirred at RT until the hydrolysis was complete (as monitored by TLC). After several extractions with ether, the combined organic layers were dried with $MgSO_4$, filtered, and the solvent was evaporated. To remove organic impurities the residue was dissolved in 30 ml of ether and extracted three times with saturated Na_2CO_3 solution. The aqueous phase was acidified with 6 N HCl to pH = 2 and extracted several times with ether. The combined organic layers were then dried ($MgSO_4$), and the solvent was evaporated. The solid hydroxy acids (**5**, **25**) were recrystallized from ether/hexane, the glassy ones (**23**–**25**) were characterized and for the elemental analyses converted tho the corresponding methyl esters.

(2R,5R,6R)-5-Benzyl-2-(tert-butyl)-5,6-dimethyl-1,3-dioxan-4-one (**4**): As described in GP1, 186 mg (1.0 mmol) of **2** and 0.25 ml (2.3 mmol) of benzyl bromide were treated with 0.69 g (1.10 mmol) of P4 base. The crude product (diastereomeric ratio 5:1) was purified by FC (pentane/ether, 10:1), and 137 mg (50%) of **4** was obtained as a colorless oil. – $[\alpha]_D$ = −103.3 (*c* = 0.3 in $CHCl_3$). – ^{1}H NMR (300 MHz): δ = 0.90 [s, 9H, 2-C(CH_3)$_3$], 1.25 (d, 3H, *J* = 6.3, 6-CH_3), 1.34 (s, 3H, CH_3), 2.45 (d, 1H, *J* = 14.1, 1′-H_A), 3.60 (d, 1H, *J* = 14.1, 1′-H_B), 3.73 (q, 1H, *J* = 6.4, 6-H), 4.61 (s, 1H, 2-H), 7.16–7.30 (m, 5H, arom.). – ^{13}C NMR (100 MHz): δ = 14.25, 21.13, 23.78, 35.27, 41.00, 48.92, 74.11, 108.34, 126.81, 128.60, 129.93, 137.02, 174.47. – IR (KBr): $\tilde{\nu}$ = 3080 cm^{-1}, 3040 (w), 2990 (m), 2970 (m), 2890 (m), 1730 (s), 1490 (m), 1450 (m), 1390 (m), 1340 (m), 1270 (m), 1180 (m), 1140 (m), 1120 (m), 990 (s). – MS (70 eV): *m/z* (%) = 277 (3) [M^+ +1], 219 (12), 190 (68), 173 (81), 146 (66), 145 (92), 131 (83), 91 (100), 83 (15).

(2R,3R)-2-Benzyl-3-hydroxy-2-methylbutanoic Acid (**5**): As described in GP3, from 3 g (10.8 mmol) of **4**, 2.1 g (88%) of the acid **5** was obtained after recrystallization as colorless crystals, m.p. 76°C. – $[\alpha]_D$ = +22.8 (*c* = 1.0 in $CHCl_3$). – ^{1}H NMR (400 MHz): δ = 1.09 (s, 2-CH_3), 1.26 (d, *J* = 6, 4-CH_3), 3.00 (dd, J_1 = 13.3, J_2 = 48.4), 3.84 (q, *J* = 6, 3-H), 7.19–7.29 (m, 5H, phenyl). – ^{13}C NMR (100 MHz): δ = 17.2, 18.4, 42.2, 52.2, 71.3, 126.8, 128.2, 130.2, 136.5, 181.5. – IR (KBr): $\tilde{\nu}$ = 3440 cm^{-1} (br), 3030 (w), 2980 (s), 2950 (m), 2930 (m), 2880 (s), 1730 (s), 1240 (s), 1180 (s), 1145 (s), 1135 (s), 990 (s), 770 (s), 705 (s). – MS (70 eV): *m/z* (%) = 190 (23) [$M^+ - H_2O$], 173 (33), 146 (44), 145 (58), 131 (75), 91 (100), 83 (10), 65 (14), 57 (24), 43 (14), 41 (34), 29 (21).

$C_{12}H_{16}O_3$ (208.3) Calcd. C 69.21 H 7.74
Found C 69.47 H 7.81

(3R,4R)-3-Benzyl-3,4-dimethyloxetan-4-one (**6**): 200 mg (1 mmol) of **5** was dissolved in 4 ml of pyridine and cooled to 0°C. After addition of 0.32 ml (2.5 mmol) of benzenesulfonyl chloride, the soln. was allowed to stand at 4°C for 4d. The reaction mixture was poured onto 10 g of ice, extracted three times with dichloromethane, and the excess pyridine removed by extraction with $CuSO_4$ solution. After drying of the dichloromethane extract with $MgSO_4$, traces of copper could be removed by washing with a 2.5% aqueous ammonia solution. The crude product obtained by evaporation of the solvent was recrystallized from ether/pentane to yield 150 mg (80%) of **6** as colorless crystals, m.p. 69°C. – $[\alpha]_D$ = −16.9 (*c* = 1.1 in $CHCl_3$). – ^{1}H NMR (300 MHz): δ = 1.25 (s, 2-CH_3), 1.37 (d, *J* = 6, 3-CH_3), 2.86 (d, *J* = 14, 1′-H_A), 3.12 (d, *J* = 14, 1′-H_B), 4.59 (q, *J* = 6, 3-H), 7.15–7.34 (m, 5H, phenyl). – ^{1}H-NOE NMR (300 MHz): Irradiation of the double doublet at δ = 3.0 causes an NOE on the quadruplet at δ = 4.59, irradiation of the doublet at δ = 1.37 causes an NOE on the quadruplet at δ = 4.59, irradiation of the singlet at δ = 1.25 causes an NOE of the double doublet at δ = 3.0 and doublet at δ = 1.3. – ^{13}C NMR (75 MHz): δ = 15.1, 15.7, 41.4, 58.0, 76.5, 127.2, 128.7, 129.7, 135.6, 174.6. – IR (KBr): $\tilde{\nu}$ = 3440 cm^{-1} (br), 3020 (w), 2990 (w), 2920 (w), 1800 (s), 1600 (m), 1500 (m), 1030 (s), 825 (s), 770 (m), 700 (s). – MS (70 eV): *m/z* (%) = 190 (1.2) [M^+], 146 (56), 131 (100), 118 (19, 117 (25), 91 (76), 65 (23), 39 (25), 27 (13).

$C_{12}H_{14}O_2$ (190.2) Calcd. C 75.76 H 7.42
Found C 75.41 H 7.42

(E)-2-Methyl-1-phenyl-2-butene (**7**): 60 mg (0.31 mmol) of **6** in a bomb tube was heated to 160°C for 25 min. After cooling, 30 mg (67%) of **7** was obtained as a colorless liquid. – ^{1}H NMR (300 MHz): δ = 1.55 (s, 2-CH_3), 1.62 (dd, J_1 = 6.7, J_2 = 1, 4-H_3), 3.29 (s, 1-H_2), 5.28–5.36 (m, 3-H), 7.16–7.34 (m, 5H, phenyl). – ^{1}H-NOE NMR (300 MHz): Irradiation of the singlet at δ = 3.29 causes an NOE on the multiplet at δ = 5.3, irradiation of the singlet at δ = 1.55 causes an NOE on the singlet at δ = 3.29.

(2R,5R,6R)-5-Allyl-2-(tert-butyl)-5,6-dimethyl-1,3-dioxan-4-one (**8**): According to GP1, 186 mg (1.0 mmol) of **2** and 0.2 ml (2.4 mmol) of allyl bromide were treated with 0.69 g (1.10 mmol) of P4 base. The crude product (diastereomeric ratio 3:1) was purified by FC (pentane/ether, 10:1), and 158 mg (70%) of **8** was obtained as a colorless oil. – $[\alpha]_D$ = −71.9 (*c* = 1.1 in $CHCl_3$). – ^{1}H NMR (300 MHz): δ = 0.97 [s, 9H, 2-C(CH_3)$_3$], 1.20 (d, *J* = 6.4, 6-CH_3), 1.23 (s, 5-CH_3), 1.99 (dd, *J* = 14, 1H, 1′-H), 2.79–2.87 (m, 1H, 1′-H), 3.96 (q, *J* = 6.4, 6-H), 4.92 (s, 2-H), 5.05–5.12 (m, 3′-H_2), 5.67–5.81 (m, 2′-H). – ^{13}C NMR (90 MHz): δ = 13.9, 20.1, 23.9, 35.3, 39.7, 47.1, 74.7, 108.7, 118.7, 133.5, 174.2. – IR (film): $\tilde{\nu}$ = 3090 cm^{-1}, 2990 (s), 2890 (s), 1740 (s), 1240 (s), 1170 (s), 1140 (s), 1000 (s). – MS (70 eV): *m/z* (%) = 227 (11) [M^+], 141 (21), 123 (22), 95 (84), 81 (100), 71 (31), 67 (28), 57 (36), 55 (33), 43 (70), 41 (65), 29 (39).

(2R,5R,6R)-2-(tert-Butyl)-5-ethyl-5,6-dimethyl-1,3-dioxan-4-one (**9**): According to GP1, 500 mg (2.7 mmol) of **2** and 0.90 ml (1.11 mmol) of ethyl iodide were treated with 1.88 g (2.9 mmol) of P4 base. The crude product (diastereomeric ratio 8:1) was purified by FC (pentane/ether, 10:1), and 350 mg (61%) of **9** was obtained as a colorless oil. – $[\alpha]_D$ = −6.7 (*c* = 1.0 in $CHCl_3$). – ^{1}H NMR (300 MHz): δ = 0.94 (t, *J* = 7.6, C′-H_3), 0.97 [s, 9H, 2-C(CH_3)$_3$], 1.16 (s, 5-CH_3), 1.26 (d, *J* = 6.5, 6-CH_3), 1.56–1.80 (m, *J* = 7.6 and 6.5, CH_2), 3.80 (q, *J* = 6.5, 6-H), 4.93 (s, 2-H). – ^{13}C NMR (75 MHz): δ = 9.9, 14.3, 20.2, 24.0, 27.3, 35.2, 47.0, 79.1, 108.8, 174.0. – IR (film): $\tilde{\nu}$ = 2980 cm^{-1}, 2880 (m), 1740 (s), 1460 (m), 1390 (m), 1240 (s), 1170 (s), 1135 (m), 1085 (m), 990 (m). – MS (70 eV): *m/z* (%) = 215 (4) [M^+ +1], 84 (100), 83 (40), 69 (53), 57 (26), 56 (18), 55 (29), 45 (21), 43 (30), 41 (44), 39 (33), 27 (20).

$C_{12}H_{22}O_3$ (214.3) Calcd. C 67.26 H 10.35
Found C 67.29 H 10.43

(2R,5R,6R)-5-Butyl-2-(tert-butyl)-5,6-dimethyl-1,3-dioxan-4-one (**10**): According to GP1, 270 mg (1.45 mmol) of **2** and 0.5 ml (4.38 mmol) of butyl iodide were treated with 1.01 g (1.60 mmol) of P4 base. The crude product (diastereomeric ratio 5:1) was purified by FC (pentane/ether, 10:1), and 180 mg (51%) of **10** was obtained as

a colorless oil. – $[\alpha]_D$ = –7.3 (*c* = 1.1 in $CHCl_3$). – ^1H NMR (400 MHz): δ = 0.88 (t, 4′-H_3), 0.97 [s, 9H, 2-C(CH_3)$_3$], 1.17 (s, 5-CH_3), 1.25 (d, *J* = 6.5, 6-CH_3), 1.2–1.75 (m, 6H, 3 CH_2), 3.78 (q, *J* = 6.5, 6-H), 4.92 (s, 2-H). – ^{13}C NMR (100 MHz): δ = 13.8, 14.4, 20.6, 23.3, 24.0, 27.4, 34.3, 35.2, 46.6, 79.1, 108.8, 174.2. – IR (film): $\tilde{\nu}$ = 2980 cm^{-1}, 2880 (s), 1740 (s), 1485 (w), 1460 (w), 1210 (m), 1170 (m), 990 (m). – MS (70 eV): *m/z* (%) = 243 (2.6) [M^+ +1], 112 (87), 111 (49), 83 (26), 71 (38), 70 (100), 69 (64), 57 (34), 55 (47), 53 (12), 45 (20), 43 (45), 41 (61), 39 (20), 29 (40) 27 (24), 18 (16).

$C_{14}H_{26}O_3$ (242.4) Calcd. C 69.38 H 10.81
Found C 69.45 H 10.87

(2R,5R,6R)-2-(tert-Butyl)-5-isopropyl-5,6-dimethyl-1,3-dioxan-4-one (**11**): According to GP1, 250 mg (1.34 mmol) of **2** and 1.0 ml (10.0 mmol) of isopropyl iodide were treated with 0.93 g (1.47 mmol) of P4 base. The crude product (diastereomeric ratio >10:1) was purified by FC (pentane/ether, 10:1), and 125 mg (45%) of **11** was obtained as colorless crystals, m.p. 44°C. – $[\alpha]_D$ = +9.0 (*c* = 1.0 in $CHCl_3$). – ^1H NMR (300 MHz): δ = 0.97 [s, 9H, 2-C(CH_3)$_3$], 1.03 (dd, *J* = 6.8, 6H, 1′-(CH_3)$_2$), 1.19 (s, 3H, 5-CH_3), 1.31 (d, *J* = 6.6, 6-CH_3), 1.98 (m, *J* = 6.8, 1H, 1′-H), 3.83 (q, *J* = 6.6, 6-H), 4.89 (s, 2-H). – ^{13}C NMR (75 MHz): δ = 14.9, 19.3, 20.6, 20.7, 24.2, 32.1, 35.1, 49.2, 81.2, 108.7, 172.8. – IR (film): $\tilde{\nu}$ = 2980 cm^{-1}, 2880 (s), 1740 (s), 1460 (m), 1390 (m), 1350 (m), 1240 (s), 1230 (s), 1170 (s), 990 (s), 770 (w). – MS (70 eV): *m/z* (%) = 229 (4.3) [M^+ +1], 98 (100), 97 (72), 83 (93), 71 (23), 69 (13), 57 (21), 55 (44), 43 (33), 41 (36), 29 (21), 28 (14), 18 (10).

$C_{13}H_{24}O_3$ (228.3) Calcd. C 68.38 H 10.59
Found C 68.74 H 10.50

(2R,5R,6R)-2-(tert-Butyl)-5,6-dimethyl-5-(4-phthalimidobutyl)-1,3-dioxan-4-one (**12**): According to GP1, 350 mg (1.90 mmol) of **2** and 1.0 g (4.5 mmol) of phthalimidobutyl bromide were treated with 1.32 g (2.09 mmol) of P4 base. The crude product (diastereomeric ratio 5:1) was purified by FC (pentane/ether, 10:1), and 253 mg (45%) of not diastereomerically pure **12** was obtained as a glassy oil. – $[\alpha]_D$ = –4.2 (*c* = 1.3 in $CHCl_3$). – ^1H NMR (200 MHz): δ = 0.92 [s, 9H, 2-C(CH_3)$_3$], 1.2 (s, 3H, 5-CH_3), 1.25 (d, 3H, 6-CH_3), 1.2–1.8 (m, 6H, 3CH_2), 3.65 (t, 2H, 4′-H_2), 3.70 (q, 1H, 6-H), 4.9 (s, 1H, 2-H), 7.6–7.9 (m, 5H, arom.). – ^{13}C NMR (50 MHz): δ = 14.54, 20.81, 22.68, 24.15, 29.17, 34.30, 35.33, 37.79, 46.71, 79.26, 109.11, 123.44, 132.40, 134.20, 168.60, 174.30. – IR ($CHCl_3$): $\tilde{\nu}$ = 3010 cm^{-1}, 2990 (m), 2980 (m), 1720 (s), 1480 (m), 1400 (s), 1360 (m), 1170 (m), 990 (m). – MS (70 eV): *m/z* (%) = 387 (1) [M^+], 257 (68), 202 (24), 188 (20), 160 (100), 148 (41), 110 (50), 109 (43), 69 (21), 41 (45), 28 (55), 18 (38).

(2R,5R,6R)-5-Benzyl-2-(tert-butyl)-5-ethyl-6-methyl-1,3-dioxan-4-one (**13**): According to GP1, 455 mg (1.73 mmol) of **3** and 0.50 ml (6.1 mmol) of ethyl iodide were treated with 1.21 g (1.91 mmol) of P4 base. The crude product (diastereomeric ratio >10:1) was purified by FC (pentane/ether, 10:1), and 390 mg (66%) of **13** was obtained as a colorless oil. – $[\alpha]_D$ = –57.8 (*c* = 0.9 in $CHCl_3$). – ^1H NMR (300 MHz): δ = 0.89 [s, 9H, 2-C(CH_3)$_3$], 1.03 (t, 3H, *J* = 7.5, 2″-H_3), 1.29 (d, 3H, *J* = 6.5, 5-CH_3), 1.82 (q, 2H, *J* = 7, 1″-H_2), 2.38 (d, 1H, *J* = 14, 1′-H_A), 3.56 (d, 1H, *J* = 14, 1′-H_B), 3.79 (q, 1H, *J* = 6.5, 5-H), 4.52 (s, 1H, 2-H), 7.15–7.31 (m, 5H, arom.). – ^{13}C NMR (75 MHz): δ = 10.33, 14.24, 23.93, 29.45, 35.09, 41.01, 52.25, 75.20, 108.44, 126.80, 128.64, 130.00, 137.28, 173.28. – IR (film): $\tilde{\nu}$ = 3030 cm^{-1}, 3980 (s), 2960 (s), 2940 (m), 2880 (m), 1735 (s), 1490 (m), 1220 (s), 1000 (s). – MS (70 eV): *m/z* (%) = 291 (10) [M^+ +1], 205 (20), 204 (61), 187 (49), 160 (50), 159 (65), 145 (21), 131 (85), 117 (26), 91 (100), 57 (24), 43 (23), 41 (35).

(2R,5R,6R)-5-Allyl-5-benzyl-2-(tert-butyl)-6-methyl-1,3-dioxan-4-one (**14**): According to GP1, 421 mg (1.60 mmol) of **15** and 0.5 ml (5.9 mmol) of allyl bromide were treated with 1.60 g (2.52 mmol) of P4 base. The crude product (diastereomeric ratio 10:1) was purified by FC (pentane/ether, 10:1), and 250 mg (52%) **14** was obtained as a colorless oil. – ^1H NMR (200 MHz): δ = 0.88 [s, 9H, 2-C(CH_3)$_3$], 1.33 (d, 3H, 6-CH_3), 2.42 (d, *J* = 14, 1H, benzyl-H_A), 2.40–2.65 (m, 2H, allyl-H_2), 3.59 (d, *J* = 14, 1H, benzyl-H_B), 3.80 (q, 1H, 6-H), 4.55 (s, 1H, 2-H), 5.02–5.18 (m, 2H, allyl-H_2), 5.78–6.04 (m, 1H, allyl-H). Minor diastereomer 5-*epi*-**14**: ^1H NMR (200 MHz): δ = 0.88 [s, 9H, 2-C(CH_3)$_3$], 1.28 (d, 3H, 6-CH_3), 2.00 (dd, *J* = 14, 1H, allyl-H_A), 2.75 (d, *J* = 14, 1H, benzyl-H_A), 2.89 (dd, 1H, allyl-H_B), 3.13 (d, *J* = 14, 1H, benzyl-H_B), 4.12 (q, 1H, 6-H), 4.61 (s, 1H, 2-H), 5.03–5.18 (m, 2H, allyl-H_2), 5.55–5.85 (m, 1H, allyl-H).

(2R,6R)-5,5-Diallyl-2-(tert-butyl)-6-methyl-1,3-dioxan-4-one (**16**): According to GP2, 250 mg (1.45 mmol) of **1** and 0.5 ml (5.9 mmol) of allyl bromide were treated with 1.93 g (3.04 mmol) of P4 base. After FC (pentane/ether, 10:1), 250 mg (68%) of **16** was obtained as a colorless oil. – $[\alpha]_D$ = –72.6 (*c* = 1.2 in $CHCl_3$). – ^1H NMR (300 MHz): δ = 0.96 [s, 9H, 2-C(CH_3)$_3$], 1.28 (d, *J* = 6.5 Hz, 6-CH_3), 1.94 (dd, J_1 = 14.2, J_2 = 9.4, 1H, 1′-H_2), 2.29 (dd, J_1 = 14.0, J_2 = 8.1, 1H, 1′-CH_2), 2.50 (dd, J_1 = 14.0, J_2 = 6.7, 1″-H_2), 2.85 (dd, J_1 = 14.2, J_2 = 5.3, 1″-H_2), 4.05 (q, *J* = 6.5, 6-CH_3), 4.90 (s, 2-H), 5.03–5.13 (m, 4H, 3 CH_2), 5.68–5.88 (m, 2H, 2 CH). – ^{13}C NMR (75 MHz): δ = 14.1, 24.0, 35.2, 38.6, 38.7, 50.7, 75.4, 108.9, 118.0, 119.0, 133.5, 133.6, 172.1. – IR (film): $\tilde{\nu}$ = 3180 cm^{-1}, 2980 (m), 2880 (m), 1740 (s), 1640 (m), 1485 (m), 1220 (s), 1160 (m), 1000 (m), 920 (m). – MS (70 eV): *m/z* (%) = 253 (2) [M^+ +1], 208 (2), 195 (14), 166 (24), 149 (24), 138 (10), 121 (45), 107 (63), 93 (100), 79 (82), 57 (31), 41 (70), 29 (31).

$C_{15}H_{24}O_3$ (252.3) Calcd. C 71.39 H 9.59
Found C 71.18 H 9.64

(2R,6R)-2-(tert-Butyl)-5,5-dibutyl-6-methyl-1,3-dioxan-4-one (**17**): According to GP2, 234 mg (1.36 mmol) of **1** and 0.7 ml (6.0 mmol) of butyl iodide were treated with 1.82 g (2.86 mmol) of P4 base. After FC (pentane/ether, 10:1), 248 mg (64%) of **15** was obtained as a colorless oil. – $[\alpha]_D$ = –19.5 (*c* = 1.0 in $CHCl_3$). – ^1H NMR (400 MHz): δ = 0.85–0.92 (m, 6H, 4′, 4″-H_3), 0.96 [s, 9H, 2-C(CH_3)$_3$], 1.25 (d, *J* = 6.5, 6-CH_3), 1.21–2.53 (m, 12H, 6 CH_2), 4.03 (q, *J* = 6.5, 1H, 6-H), 4.91 (s, 1H, 2-H). – ^{13}C NMR (100 MHz): δ = 13.79, 13.85, 14.27, 23.30, 23.97, 27.35, 27.57, 34.88, 35.18, 35.87, 50.55, 75.67, 108.66, 173.51. – IR ($CHCl_3$): $\tilde{\nu}$ = 2980 cm^{-1}, 2920 (s), 2870 (m), 1730 (s), 1485 (w), 1230 (m). – MS (70 eV): *m/z* (%) = 569 (49) [2 M^+ +1], 286 [M^+ +2] (95), 285 [M^+ +1] (99), 239 (48), 200 (73), 199 (100), 181 (81), 154 (91), 143 (86), 112 (79), 87 (48), 70 (80), 57 (76), 55 (77), 43 (85).

$C_{17}H_{32}O_3$ (284.4) Calcd. C 71.79 H 11.34
Found C 71.67 H 11.50

(2R,5R,6R)-2-(tert-Butyl)-5-isopropyl-6-methyl-1,3-dioxan-4-one (**18**): According to GP2, 233 mg (1.35 mmol) of **1** and 0.6 ml (6 mmol) of isopropyl iodide were treated with 1.80 g (2.83 mmol) of P4 base. The crude product (diastereomeric ratio 2:1) was purified by FC (pentane/ether, 10:1). 113 mg (40%) of **18** was obtained as colorless crystals, m.p. 40°C. – $[\alpha]_D$ = –24.2 (*c* = 1.3 in $CHCl_3$). – ^1H NMR (300 MHz): δ = 0.96 [s, 9H, 2-C(CH_3)$_3$], 1.01 (d, *J* = 7, 3H, 1′-CH_3), 1.15 (d, *J* = 7, 3H, 1′-CH_3), 1.34 (d, *J* = 6, 3H, 6-CH_3), 2.06 (m, 1H, 5-H), 2.34 (dd, J_1 = 9, J_2 = 3.6, 1H, 1′-H), 2.34 (qd, J_1 = 9, J_2 = 6, 1H, 6-H), 4.85 (s, 1H, 2-H). – ^{13}C NMR (75 MHz): δ = 19.39, 21.04, 21.59, 23.89, 29.20, 35.15, 54.45, 73.51, 107.41, 170.37. – IR ($CHCl_3$): $\tilde{\nu}$ = 2980 cm^{-1}, 2970 (s), 2940 (m), 2900 (m), 2880 (m), 1730 (s), 1345 (m), 1240 (s), 1080 (m), 1000

(s). – MS (70 eV): *m/z* (%) = 215 (7) [M^+ +1], 157 (38), 111 (100), 84 (84), 69 (66), 57 (32), 55 (20), 43 (29), 41 (31).

$C_{12}H_{22}O_3$ (214.3) Calcd. C 67.26 H 10.35
Found C 67.33 H 10.23

(2R,5S,6S)-5-Allyl-6-butyl-2-(tert-butyl)-5-ethyl-6-methyl-1,3-dioxan-4-on (**20**): According to GP2, 320 mg (1.25 mmol) of **19** and 0.72 ml (8.5 mmol) of allyl bromide were treated with 0.99 g (1.56 mmol) of P4 base. The crude product (diastereomeric ratio 3:2) was purified by repeated FC (pentane/ether, 10:1) and 20 mg (6%) of **20** and 37 mg (10%) of **21** were obtained as colorless oils. Diastereomer **20**: $[\alpha]_D$ = –54.9 (*c* = 1.0 in $CHCl_3$) – ^{1}H NMR (300 MHz): δ = 0.80–1.10 (m, 6H, 2 CH_3), 0.96 [s, 9H, 2-C(CH_3)$_3$], 1.23 (s, 3H, 6-H), 1.20–2.10 (m, 8H, various CH_2), 2.40 (dd, 1H, CH), 2.65 (dd, 1H, CH). – ^{13}C NMR (75 MHz); δ = 9.84, 14.13, 20.56, 23.11, 23.34, 24.08, 24.48, 33.60, 35.35, 35.87, 54.81, 79.43, 102.71, 118.02, 134.18, 173.57. – IR ($CHCl_3$): $\tilde{\nu}$ = 2950 cm^{-1} (s), 2850 (m), 1720 (s), 1480 (m), 1400 (m), 1360 (m), 1160 (m), 990 (s), 860 (m). – MS (70 eV): *m/z* (%) = 297 (1) [M^+ +1], 165 (50), 153 (40), 113 (32), 110 (58), 95 (43), 83 (45), 69 (57), 55 (71), 43 (100), 41 (61), 29 (43). – 5-*epi*-Diastereomer **21**: $[\alpha]_D$ = –30.2 (*c* = 1.2 in $CHCl_3$). – ^{1}H NMR (300 MHz): δ = 0.92–1.00 (m, 6H, 2 CH_3), 0.96 [s, 9H, 2-C(CH_3)$_3$], 1.18 (s, 3H, 6-H), 1.15–2.05 (m, 8H, various CH_2), 2.21 (dd, 1H, CH), 2.78 (m, 1H, CH). – ^{13}C NMR (75 MHz): δ = 9.52, 14.11, 19.84, 23.08, 24.02, 24.40, 33.76, 33.80, 35.35, 54.93, 79.47, 102.94, 117.34, 135.15, 173.58.

$C_{18}H_{32}O_3$ (296.4) Calcd. C 72.97 H 11.22
Found C 73.03 H 11.23

(1'R,2R)-2-(1'-Hydroxyethyl)-2-methyl-4-pentenoic Acid (**22**): According to GP3, from 277 mg (1.22 mmol) of **8**, 180 mg (94%) of **22** was obtained as colorless crystals, m.p. 48°C. – $[\alpha]_D$ = +14.2 (*c* = 1.4 in EtOH). – ^{1}H NMR (300 MHz): δ = 1.15 (s, 3H, 2-CH_3), 1.21 (d, *J* = 6.4, 3H, 2'-H_3), 2.29–2.48 (m, 2H, 3-H_2), 3.93 (q, *J* = 6.4, 1H, 1'-H), 5.09–5.15 (m, 2H, 5-H_2), 5.69–5.83 (m, 1H, 4-H), 5.2–6.5 (s, br., 2H, COOH, OH). – ^{13}C NMR (75 MHz): δ = 16.86, 17.77, 40.93, 51.07, 71.28, 118.80, 133.01, 181.51. – IR ($CHCl_3$): $\tilde{\nu}$ = 3600–2200 cm^{-1} (s, br), 3090 (s), 2990 (s), 2940 (s), 1710 (s), 1230 (m), 1190 (m), 920 (m). – MS (70 eV): *m/z* (%) = 317 [2 M^+ +1] (6), 159 [M^+ +1] (60), 141 (63), 123 (33), 114 (100), 95 (60), 81 (27), 69 (93), 55 (20), 43 (41).

$C_8H_{14}O_3$ (158.2) Calcd. C 60.74 H 8.92
Found C 60.49 H 8.83

(1'R)-2-Butyl-2-(1'-hydroxyethyl)hexanoic Acid (**23**): According to GP3, from 150 mg (0.53 mmol) of **17**, 102 mg (90%) of **23** was obtained as a glassy oil. – $[\alpha]_D$ = –3.3 (*c* = 0.8 in EtOH). – ^{1}H NMR (200 MHz): δ = 0.87–0.93 (m, 6H, 2 CH_3), 1.10–1.82 (m, 12H, 6 CH_2), 3.98 (q, *J* = 6.8, 1'-H), 5.2–7.0 (s, br, 2H, OH and COOH). – ^{13}C NMR (75 MHz): δ = 14.12, 18.10, 23.45, 23.68, 26.30, 26.55, 31.29, 33.30, 53.43, 70.50, 182.18. – IR ($CHCl_3$): $\tilde{\nu}$ = 3600–2300 cm^{-1} (s, br), 2990 (s), 2970 (s), 2920 (s), 1700 (s), 1440 (m), 1390 (m), 1040 (m), 915 (s). – MS (70 eV): *m/z* (%) = 217 (9) [M^+ + 1], 199 (48), 172 (56), 154 (41), 129 (78), 115 (35), 111 (44), 98 (56), 87 (65), 83 (51), 81 (51), 69 (70), 55 (77), 45 (57), 43 (100), 41 (57), 29 (56).

Methylester of **23**: $C_{13}H_{26}O_3$ (230.4) Calcd. C 67.79 H 11.38
Found C 67.53 H 11.40

(1'R)-2-Allyl-2-(1'-hydroxyethyl)-4-pentenoic Acid (**24**): According to GP3, from 123 mg (0.50 mmol) of **16**, 87 mg (95%) of **24** was obtained as a glassy oil. – $[\alpha]_D$ = –6.1 (*c* = 1.1 in EtOH). – ^{1}H NMR (300 MHz): δ = 1.26 (d, *J* = 6.4, 3H, 2'-H_3), 2.27–2.58 (m, 4H, 3-H_2), 3.95 (q, *J* = 6.4, 1H, 1'-H), 5.10–5.17 (m, 4H, 5-H_2), 5.73–5.95 (m, 2H, 4-H), 5.7–6.4 (s, br, 2H, COOH, OH). – ^{13}C NMR (75 MHz): δ = 18.19, 36.06, 37.57, 53.86, 70.60, 118.51, 118.70, 133.46, 133.72, 179.74. – IR ($CHCl_3$): $\tilde{\nu}$ = 3700–2200 cm^{-1} (s, br), 3090 (m), 3000 (s), 2980 (s), 2940 (s), 1700 (s), 1450 (m), 1400 (m), 1280 (m), 925 (s). – MS (70 eV): *m/z* (%) = 369 (16) [2 M^+ +1], 185 (77) [M^+ +1], 167 (82), 149 (63), 140 (87), 121 (91), 107 (69), 95 (100), 81 (91), 67 (69), 53 (45), 43 (72), 41 (62), 39 (54).

Methylester of **24**: $C_{11}H_{18}O_3$ (198.3) Calcd. C 66.64 H 9.15
Found C 66.37 H 9.22

(2S,3S)-2-Allyl-2-ethyl-3-methylheptanoic Acid (**25**): According to GP3, from 104 mg (0.35 mmol) of **20**, after 7 d of stirring at RT, 72 mg (90%) of **25** was obtained as a glassy oil. – **25**: $[\alpha]_D$ = –7.8 (*c* = 0.7 in EtOH) – ^{1}H NMR (200 MHz): δ = 0.90 (m, 6H, 2 CH_3), 1.26 (s, 3H, 3-CH_3) 1.15–2.12 (m, 8H, 4 CH_2), 1.44 (m, 1H, C'-H_A), 1.80–2.10 (m, 1H, C'-H_B), 4.98–5.15 (m, 2H, C'-H_2), 5.80–6.05 (m, 1H, C'-H). – ^{13}C NMR (50 MHz): δ = 10.18, 14.28, 23.41, 23.49, 24.74, 25.55, 36.37, 37.08, 58.33, 76.88, 117.63, 136.40, 180.46. – IR ($CHCl_3$): $\tilde{\nu}$ = 3600–2700 cm^{-1} (br), 2980 (s), 2920 (m), 2880 (m), 1730 (s), 1460 (m), 1380 (s), 1040 (s), 915 (m), 880 (m). – MS (70 eV): *m/z* (%) = 229 (4) [M^+ +1], 171 (53), 101 (51), 83 (50), 57 (56), 55 (65), 43 (100), 29 (42), 18 (24). – Diastereomer 2-*epi*-**25**: ^{1}H NMR (200 MHz): δ = 0.80–1.00 (m, 6H, 2 CH_3), 1.21 (s, 3H, 3-CH_3) 1.15–2.3 (m, 10H, 4 CH_2 + C'-H_2), 4.98–5.15 (m, 2H, C'-H_2), 5.80–6.10 (m, 1H, C'-H). – ^{13}C NMR (50 MHz): δ = 9.57, 13.81, 21.85, 22.93, 24.13, 25.13, 36.02, 37.84, 57.65, 76.49, 116.87, 135.75, 179.09.

Methylester of **25**: $C_{14}H_{26}O_3$ (242.4) Calcd. C 69.38 H 10.81
Found C 69.68 H 10.69

(3S,4S)-3-Allyl-4-butyl-3-ethyl-4-methyloxetan-2-one (**26**): According to the procedure described for **6**, from 34 mg (0.15 mmol) of **25**, 23 mg (73%) of **26** was obtained. – ^{1}H NMR (400 MHz): δ = 0.93 (t, 3H, *J* = 7.2, CH_3), 1.01 (t, 3H, *J* = 7.4, 3-CH_3), 1.20–1.45 (m, var. CH_2), 1.53 (s, 3H, 3-CH_3), 1.70–2.05 (m, var. CH_2), 2.48–2.70 (m, 2H, allyl-H_2), 5.13–5.22 (m, CH_2), 5.65–5.78 (m, 1H, CH). – ^{1}H-NOE NMR (300 MHz): irradiation of the multiplet at δ = 2.48–2.70 causes an NOE on the singlet at δ = 1.53. – ^{13}C NMR (75 MHz): δ = 8.37, 13.91, 20.95, 21.07, 23.07, 26.21, 32.04, 35.88, 60.93, 85.88, 119.08, 131.94, 174.25.

CAS Registry Numbers

1: 100017-18-3 / **2**: 107312-93-6 / **3**: 107289-11-2 / **4**: 134528-85-1 / **5**: 134528-86-2 / **6**: 134528-87-3 / **7**: 3968-90-9 / **8**: 134528-88-4 / **9**: 134528-89-5 / **10**: 134528-90-8 / **11**: 134528-91-9 / **12**: 134528-92-0 / **13**: 134528-93-1 / **14**: 134528-94-2 / 5-*epi*-**14**: 134529-03-6 / **15**: 107289-10-1 / **16**: 134528-95-3 / **17**: 134528-96-4 / (2*R*5*R*,6*R*)-**18**: 129287-66-7 / (2*R*,5*S*,6*R*)-**18**: 134529-06-9 / **19**: 134566-47-5 / **20**: 134528-97-5 / **21**: 134529-04-7 / **22**: 134528-98-6 / **23**: 134528-99-7 / **24**: 134529-00-3 / **25**: 134529-01-4 / 2-*epi*-**25**: 134529-05-8 / **26**: 134529-02-5 / **P4**: 111324-04-0 / Phtim-BuBr: 5394-18-3 / BnBr: 100-39-0 / AllylBr: 106-95-6 / EtI: 75-03-6 / BuI: 542-69-8 / *i*-PrI: 75-30-9

---

[1] Part of the projected *Ph. D. Thesis* of T. Pietzonka, ETH Zürich.

[2] [2a] D. Seebach, J. Zimmermann, *Helv. Chim. Acta* **69** (1986) 1147. – [2b] J. Zimmermann, D. Seebach, T. Ha, *Helv. Chim. Acta* **71** (1988) 1143.

[3] Alkylations of **B** using the cosolvent HMPA: G. Fráter, *Helv. Chim. Acta* **62** (1979) 2825, 2829.

[4] Methylation of **B**, R = H in THF, with iodomethane and iodoethane on a 20–40 g scale: M. Sutter, D. Seebach, *Liebigs Ann. Chem.* **1983**, 939; D. Seebach, H. Chow, R. Jackson, M. Sutter, S. Thaisrivongs, J. Zimmermann, *ibid.* **1986**, 1281.

[5] Alkylation of the lithioxy-lithium enolates generated from diethyl malonate: D. Seebach, D. Wasmuth, *Helv. Chim. Acta* **63** (1980) 197; D. Seebach, J. Aebi, D. Wasmuth, *Organic Syntheses* **63** (1984) 109.

[6] B. Herradon, D. Seebach, *Helv. Chim. Acta* **72** (1989) 690.

[7] Aldol condensation products of the dioxanone **1** (→ 5-alkylidene derivatives) followed by double bond isomerization (→ 5-alkyldioxinones) gives Michael acceptors the reactions of which eventually lead to 5-alkyl dioxanones. – [7a] W. Amberg, D. Seebach, *Chem. Ber.* **123** (1990) 2413. – [7b] W. Amberg, D. Seebach, *Chem. Ber.* **123** (1990) 2429. – [7c] W. Amberg, D. Seebach, *Chem. Ber.* **123** (1990) 2439.

[8] D. Seebach, U. Misslitz, P. Uhlmann, *Angew. Chem.* **101** (1989) 484; *Angew. Chem., Int. Ed. Engl.* **28** (1989) 472; Idem, *Chem. Ber.* **124** (1991), 1845 following publication.

[9] The reagents and products **A** – **C** are derived from (*R*)-3-hydroxybutanoic acid (see **1**), but the reactivities studied in this paper and in previous investigations are of course also applicable to dioxanones derived from other β-hydroxycarboxylic acids. 3-Hydroxy pentanoic acid: J. Zimmermann, D. Seebach, *Helv. Chim. Acta* **70** (1987) 1104. Trifluoro- and trichloro-3-hydroxybutanoic acid: A. Beck, M. Gautschi, D. Seebach, *Chimia* **44** (1990) 291; A. Beck, A. Brunner, V. Montanari, D. Seebach, *Chimia*, paper in preparation. See the general access to (*R*)- or (*S*)-hydroxycarboxylic acids by enantioselective catalytic hydrogenation: M. Kitamura, T. Ohkuma, N. Sayo, H. Kumobayashi, S. Akutagawa, T. Ohta, H. Takaya, R. Noyori, *J. Am. Chem. Soc.* **109** (1987) 5856. – M. Kitamura, T. Ohkuma, S. Inoue, N. Sayo, H. Kumobayashi, S. Akutagawa, T. Ohta, H. Takaya, R. Noyori, *J. Am. Chem. Soc.* **110** (1988) 629.

[10] [10a] R. Schwesinger, H. Schlemper, *Chimia* **39** (1985) 269. – [10b] R. Schwesinger, M. Missfeldt, K. Peters, H. G. von Schnering, *Angew. Chem.* **99** (1987), 1209, 1210; *Angew. Chem., Int. Ed. Engl.* **26** (1987) 1164, 1165; R. Schwesinger, H. Schlemper, *Angew. Chem.* **99** (1987) 1212; *Angew. Chem., Int. Ed. Engl.* **26** (1987) 1167.

[11] R. Schwesinger, *Habilitationsschrift*, Universität Freiburg 1990. – H. Schlemper, *Dissertation*, Universität Freiburg 1990.

[12] For a recent review article see: R. Schwesinger, *Nachr. Chem. Tech. Lab.* **38** (1990) 1214.

[13] The *t*-Bu-P4 base used here is not hindered enough so that it will undergo methylation by CH_3I; therefore it cannot be used for methylations of too weakly acidic compounds (see also the following footnote).

[14] Some other P4 bases have been prepared[11,12], in which the imino nitrogen is more hindered, so that better selectivities, for instance between mono- and dialkylation, can be achieved.

[15] The generated anions may be regarded as the first really "naked" anions, due to the size and extreme charge delocalization of the corresponding cation, the protonated P4 base!

[16] Stilbene and bromo-diphenylethane were identified as typical undesired products from base treatments of benzyl bromide!

[17] W. Adam, J. Baeza, *J. Am. Chem. Soc.* **94** (1972) 2000.

[18] G. Schewerowsky and M. Sefkow have also observed that the sequence of benzylation/methylation of **1** leads to the trisubstituted dioxanone with the 5-benzyl and the 5-methyl group *trans* to each other: hitherto unpublished results, Institut für Organische Chemie der Technischen Universität Berlin, 1990. We thank *M. Sefkow* for private communication of his results.

[19] Preparation as indicated in ref.[10b]; all the material used was prepared by T. Pietzonka and H. Schlemper (University of Freiburg).

[148/91]