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Diastereoselective Synthesis of *cis*-2,6-Disubstituted Perhydro-4-pyranones Using Elevated Pressure Hydrogenation

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Summary. A diastereoselective strategy for the synthesis of γ-pyrons was developed, starting from the Mg diacetonedicarboxylate complex. Initial cyclization with suitable anhydrides or acid chlorides, followed by hydrolytic decarboxylation leads to 2,6-disubstituted pyrans. Elevated pressure hydrogenation using Pd/C affords the title compounds in high diastereoselectivity. Scope and limitations of the method are outlined on selected examples.

Keywords. Reduction; γ-Pyrons; Magnesium diacetonedicarboxylate complex; Cyclization.

Introduction

In the context of our recent research program aimed at the application of recombinant whole-cell biocatalysts in enantioselective *Baeyer-Villiger* oxidations [1, 2], we optimized access to various prochiral cyclic ketones, previously [3–5]. As we became interested in the microbial oxidation of several heterocyclic precursors [6, 7], we required an efficient strategy for the preparation of an array of 2,6-disubstituted tetrahydropyran-4-ones.

In recent literature a number of methods are available for the synthesis of γ-pyrons [8, 9], and this served as a starting point to enter this area. According to our initial experiences, these approaches lacked generality and simplicity, which represent key aspects for the generation of a small library of precursors suitable for subsequent biotransformation studies. Consequently, development of a simple and robust procedure for the preparation of substituted γ-pyrons was our first goal.

As desymmetrization of prochiral compounds is a most efficient strategy for the generation of chiral products with a 100% theoretical yield, we focused our interest

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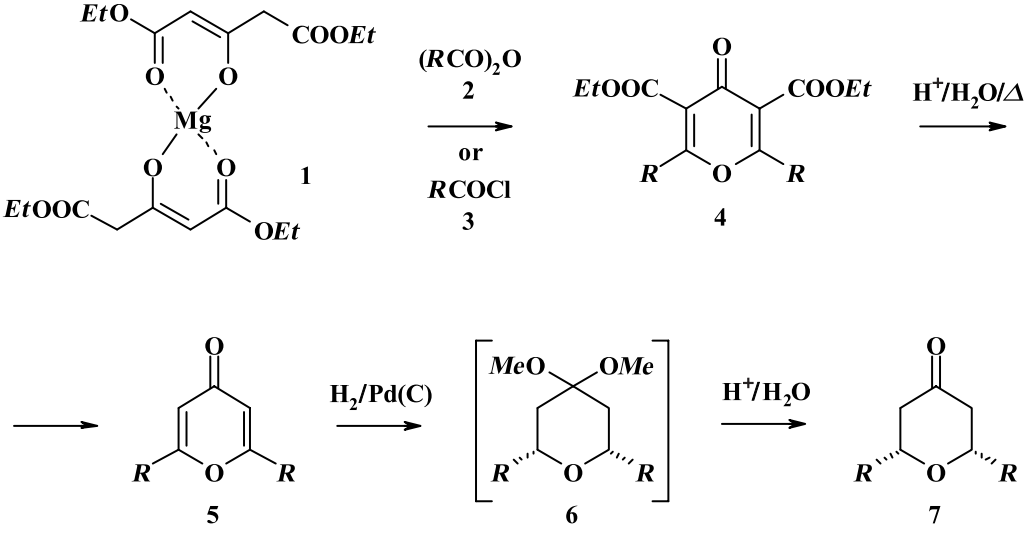
on perhydro-heterocycles with a *cis*-2,6-substitution pattern. According to our general pathway this required a diastereoselective hydrogenation of the γ-pyrons. Stereoselectivity can be achieved when performing the reaction under conditions of heterogeneous catalysis [10]. In this case, attack of the hydrogen commences from the surface of the catalyst, and stereoselectivity is ensured due to the orientation of the planar substrate *vis-à-vis* the catalytic entity.

Results and Discussion

Based on previous work by *Yamato et al.* [11], a Mg diacetonedicarboxylate ($(DADC)_2Mg$) complex [12, 13] seemed to be a suitable reagent to allow for a versatile entry into the required heterocyclic system. *Yamato* and coworkers reported suitable reaction conditions to favor formation of cyclic compounds *vis-à-vis* open chain products. The one-pot transformation is initiated by an acylation reaction, followed by cyclization towards the pyrane core using either anhydrides **2** or acid chlorides **3** (Scheme 1, Table 1).

Initially, we compared both strategies for the formation of diester **4a** with a slightly modified protocol. When using anhydrides, the reaction of **1** is carried out in an excess of the reagent simultaneously acting as solvent at reflux temperature. Conversions with acid chlorides required the presence of a base such as pyridine, with reagents mixed under ice cooling and subsequent stirring at room temperature. For the model reaction to **4a** no significant difference of both methods was observed and the pure product was obtained in similar yields after chromatographic purification.

Cyclization to diethyl substituted **4b** *via* the anhydride method gave a decreased yield, which might be attributed to the higher reflux temperature. This hypothesis is supported to some extent by the excellent yield for the preparation of **4f** using trifluoroacetic anhydride. Hence, conversion to products bearing longer side chains was performed utilizing the acid chloride protocol. Cyclizations are summarized in Table 1 and gave acceptable yields of pyranones **4a**–**4f** after



Scheme 1

Table 1. Synthetic sequence towards perhydro-pyranones **7**

R	Acylation precursor	**4**	**5**	**6**	**7**
Me	**2a**	45%	87%	65%	65%
	3a	46%			
Et	**2b**	34%	80%	81%	70%
n-Pr	**3c**	44%	86%		56%[a]
i-Pr	**3d**	59%	53%		71%[b]
n-Bu	**3e**	52%	79%	46%	76%
CF_3	**2f**	73%	0%	n.a.[c]	n.a.[c]

[a] no formation of intermediate ketone **6** observed; [b] direct hydrolysis to ketone **7**; [c] not applicable

chromatographic purification for a variety of substituents *R*. The reaction seems only limited by sterical aspects, as pivaloyl chloride **3g** (*R* = *tert.-Bu*) gave a spectrum of various mono-acylated and acyclic intermediates.

Thermal treatment of pyranones **4** under aqueous acidic conditions has given the expected products **5a**–**5e** in a hydrolysis/decarboxylation sequence [14]. As a prerequisite to ensure success of this conversion, diesters **4** are required to allow formation of a tautomer. Consequently, a proton in α-position of substituents *R* must be present. Such an enol species cannot be formed by CF_3-substituted **4f**, which prohibits the decarboxylation reaction. Apart from this limitation, pyranones **5a**–**5e** were obtained in good quality without the need for further purification. It should be noted, that reaction times increased with chain length and sterical demands of alkyl substituents.

Initially, the hydrogenation reaction was attempted at ambient or slightly elevated pressure (3–4 bar, *Parr* apparatus). In contrast to previous reports [10], only mixtures of partially reduced compounds were obtained. In addition, the stereochemistry of fully reduced products was ambiguous. While initial experiments were carried out in *Et*O*Ac* as non-polar solvent, we observed accelerated reductions when using dry *Me*OH.

In order to further increase the reaction rate and to improve the diastereoselectivity of the transformation, reactions were carried out at an elevated pressure of 20–25 bar in a steel autoclave. Under these reaction conditions, only *cis*-substituted reaction products were obtained and double bonds were generally fully reduced. However, in some cases ketal **6** was obtained after crude work-up of the hydrogenation mixture. Usually, this intermediate was not purified, but directly submitted to a deprotection step using standard conditions in a modified work-up protocol. The target compounds **7a**–**7e** were finally purified by flash column chromatography and obtained in moderate to good yields.

Conclusion

We have developed a facile synthetic route to a variety of prochiral 2,6-disubstituted tetrahydropyranones **7** starting from $(DADC)_2$Mg complex **1**. The reported high pressure hydrogenation is highly diastereoselective and provides access to several substrates suitable for subsequent enantioselective *Baeyer-Villiger* oxidation, as has been demonstrated recently [6].

Experimental

Unless otherwise noted, chemicals were purchased from commercial suppliers and used without further purification. All solvents were distilled prior to use. Flash column chromatography was performed on silica gel 60 from Merck (40–63 μm). *Kugelrohr* distillation was carried out using a Büchi GKR-51 apparatus. Melting points were determined using a *Kofler*-type Leica Galen III micro hot stage microscope and are uncorrected. NMR spectra were recorded from $CDCl_3$ solutions on a Bruker AC 200 (^{1}H 200 MHz, ^{13}C 50 MHz) spectrometer and chemical shifts are reported in ppm using *TMS* as internal standard. Abbreviations, LP = light petroleum (bp 40–60°C).

General Procedure for γ-Pyranone Cyclization – Method A

The (*DADC*)$_2$Mg complex **1** (1 equiv) was dissolved in the corresponding acid anhydride **2** (10% solution) and heated to reflux for 30–120 min. The heterogeneous reaction mixture was cooled to rt and concentrated *in vacuo*. The residue was taken up in CH_2Cl_2, washed with satd. $NaHCO_3$ solution, and the aqueous layers were re-extracted with CH_2Cl_2. The combined organic phases were dried (Na_2SO_4), decolorized (charcoal), filtered, and concentrated.

General Procedure for γ-Pyranone Cyclization – Method B

The (*DADC*)$_2$Mg complex (1 equiv) was dissolved in dry pyridine (20% solution) under N_2 and cooled with an external ice/H_2O bath. The corresponding acid chloride **3** (4.4 equiv) was added at 0–5°C and the resulting mixture was stirred at room temperature for 1–2 days. After hydrolysis with ice/HCl (2*N*) the mixture was extracted repeatedly with CH_2Cl_2. The combined organic layers were washed with satd. $NaHCO_3$ solution, dried (Na_2SO_4), decolorized (charcoal), filtered, and concentrated.

2,6-Dimethyl-4-oxo-4H-pyran-3,5-dicarboxylic acid diethyl ester (**4a**)

(*DADC*)$_2$Mg complex **1** (2.00 g, 4.69 mmol) was converted with acetic anhydride according to method A to give 1.13 g **4a** [11] (45%) as yellow crystals after flash column chromatography (silica gel, LP/*Et*OA*c* = 4/1); conversion of 1.00 g **1** (2.34 mmol) with acetyl choride following method B gave 0.58 g (46%) **4a** after chromatographic purification; physical data matching those of Ref. [11]; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.0 (q), 18.4 (q), 61.7 (t), 121.6 (s), 164.0 (s), 165.2 (s), 171.7 (s) ppm.

2,6-Diethyl-4-oxo-4H-pyran-3,5-dicarboxylic acid diethyl ester (**4b**, $C_{15}H_{20}O_6$)

Complex **1** (2.00 g, 4.69 mmol) was converted with propionic anhydride according to method A to give 0.95 g **4b** (34%) as yellow oil after flash column chromatography (silica gel, LP/*Et*OA*c* = 3/1); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.20–1.40 (m, 6H), 2.65 (q, J = 7 Hz, 4H), 4.35 (q, J = 7 Hz, 4H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.4 (q), 14.0 (q), 25.7 (t), 61.7 (t), 120.9 (s), 163.9 (s), 168.9 (s), 172.2 (s) ppm.

4-Oxo-2,6-dipropyl-4H-pyran-3,5-dicarboxylic acid diethyl ester (**4c**, $C_{17}H_{24}O_6$)

Complex **1** (3.00 g, 7.03 mmol) was converted with butanoyl chloride according to method B to give 2.00 g **4c** (44%) as colorless oil after flash column chromatography (silica gel, LP/*Et*OA*c* = 5/1); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.00 (t, J = 6 Hz, 6H), 1.35 (t, J = 6 Hz, 6H), 1.70 (sex, J = 6 Hz, 4H), 2.60 (t, J = 6 Hz, 4H), 4.35 (q, J = 6 Hz, 4H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.4 (q), 14.1 (q), 20.6 (t), 33.9 (t), 61.8 (t), 121.6 (s), 164.1 (s), 167.9 (s), 172.2 (s) ppm.

2,6-Diisopropyl-4-oxo-4H-pyran-3,5-dicarboxylic acid diethyl ester (**4d**, $C_{17}H_{24}O_6$)

Complex **1** (5.00 g, 11.7 mmol) was converted with isobutanoyl chloride according to method B to give 4.13 g **4d** (59%) as yellow oil after flash column chromatography (silica gel, LP/*Et*OAc = 5/1); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.30$–1.50 (m, 18H), 2.90–3.10 (m, 2H), 4.35 (q, $J = 7$ Hz, 4H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.0$ (q), 19.7 (q), 31.7 (d), 61.8 (t), 120.1 (s), 164.0 (s), 170.8 (s), 172.5 (s) ppm.

2,6-Dibutyl-4-oxo-4H-pyran-3,5-dicarboxylic acid diethyl ester (**4e**, $C_{19}H_{28}O_6$)

Complex **1** (5.14 g, 12.0 mmol) was converted with pentanoyl chloride according to method B to give 8.14 g **4e** (52%) as yellow oil after flash column chromatography (silica gel, LP/*Et*OAc = 7/1); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.95$ (t, $J = 7$ Hz, 6H), 1.20–1.45 (m, 10H), 1.55–1.70 (m, 4H), 2.60 (t, $J = 7$ Hz, 4H), 4.35 (q, $J = 7$ Hz, 4H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.0$ (q), 22.0 (t), 22.1 (q), 29.1 (t), 31.8 (t), 61.7 (t), 121.4 (s), 164.0 (s), 168.1 (s), 172.1 (s) ppm.

2,6-Trifluoromethyl-4-oxo-4H-pyran-3,5-dicarboxylic acid diethyl ester (**4f**)

Complex **1** (3.00 g, 7.03 mmol) was converted with trifluoroacetic anhydride according to method A to give 3.86 g **4f** [15] (73%) as colorless crystals after flash column chromatography (silica gel, LP/*Et*OAc = 7/1); mp 92–94°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.37$ (t, $J = 7$ Hz, 6H), 4.42 (q, $J = 7$ Hz, 4H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 13.8$ (q), 63.6 (t), 117.5 (q, $J_{CF} = 275$ Hz), 124.7 (q, $J_{CF} = 1.5$ Hz), 149.0 (q, $J_{CF} = 41$ Hz), 158.9 (s), 170.5 (s) ppm.

General Procedure for the Decarboxylation

Diester **4** was dissolved in a 5/1 mixture of 2*N* HCl and acetic acid (5%) and refluxed for 5–30 h until TLC indicated complete conversion. The reaction was hydrolyzed with satd. $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered, and evaporated to give **5** without further purification.

2,6-Dimethyl-4H-pyran-4-one (**5a**)

Decarboxylation of 0.50 g **4a** (1.86 mmol) gave 0.20 g **5a** [16] (87%) as colorless crystals; physical data matching those of Ref. [16].

2,6-Diethyl-4H-pyran-4-one (**5b**)

Decarboxylation of 0.50 g **4b** (1.67 mmol) gave 0.20 g **5b** [8] (87%) as colorless oil; physical data matching those of Ref. [8]; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 10.5$ (q), 26.4 (t), 111.7 (d), 170.0 (s), 180.4 (s) ppm.

2,6-Dipropyl-4H-pyran-4-one (**5c**)

Decarboxylation of 2.00 g **4c** (6.17 mmol) gave 0.95 g **5c** [9] (86%) as colorless crystals; mp 56–58°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.10$ (t, $J = 7$ Hz, 6H), 1.60–1.80 (m, 4H), 2.45 (t, $J = 7$ Hz, 4H), 6.05 (s, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 13.3$ (q), 20.5 (t), 35.3 (t), 113.1 (d), 168.9 (s), 180.4 (s) ppm.

2,6-Diisopropyl-4H-pyran-4-one (**5d**, $C_{11}H_{16}O_2$)

Decarboxylation of 2.23 g **4d** (6.80 mmol) gave 0.64 g **5d** (53%) as colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.25$ (d, $J = 7$ Hz, 12H), 2.70–2.80 (m, 4H), 6.05 (2H, s) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.0$ (q), 32.6 (d), 110.7 (d), 173.5 (s), 181.0 (s) ppm.

2,6-Dibutyl-4H-pyran-4-one (**5e**, $C_{13}H_{20}O_2$)

Decarboxylation of 4.10 g **4e** (11.60 mmol) according to the above procedure gave 1.89 g **5e** (79%) as colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.95$ (t, $J = 7$ Hz, 6H), 1.30–1.40 (m, 4H), 1.50–1.70 (m, 4H), 2.45 (t, $J = 7$ Hz, 4H), 6.05 (s, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 13.6$ (q), 22.1 (t), 29.1 (t), 31.8 (t), 112.9 (s), 169.1 (s), 180.4 (s) ppm.

Elevated Pressure Hydrogenation

Starting material **5** was dissolved in dry *Me*OH (5% solution) and charged into a *Büchi* steel autoclave with mechanical stirring. Pd catalyst (10% on C, 5%-*w*/*w*) was added and hydrogenation was accomplished at room temperature and 25 bar H_2 pressure. After complete conversion (18–48 h) the reaction mixture was filtered through a pad of Celite® and concentrated.

cis-Tetrahydro-4,4-dimethoxy-2,6-dimethyl-2H-pyrane (**6a**, $C_9H_{18}O_3$)

Hydrogenation of 5.00 g **5a** (40.3 mmol) gave 4.53 g **6a** [10] (65%) as colorless liquid; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.20$ (d, $J = 7$ Hz, 6H), 1.85–2.00 (m, 4H), 3.15 (s, 3H), 3.20 (s, 3H), 3.50–3.70 (m, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 21.5$ (q), 39.8 (t), 46.9 (q), 47.3 (q), 69.7 (d), 98.7 (s) ppm.

cis-2,6-Diethyltetrahydro-4,4-dimethoxy-2H-pyrane (**6b**, $C_{11}H_{22}O_3$)

Hydrogenation of 4.50 g **5b** (29.6 mmol) gave 4.85 g **6b** (81%) as colorless liquid; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.95$ (t, $J = 7$ Hz, 6H), 1.11–1.30 (m, 2H), 1.32–1.65 (m, 4H), 1.89–2.12 (m, 2H), 3.19 (s, 3H), 3.23 (s, 3H), 3.26–3.41 (m, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 10.0$ (q), 28.8 (t), 38.4 (t), 47.2 (q), 47.5 (q), 75.3 (d), 99.3 (s) ppm.

cis-Tetrahydro-2,6-dipropyl-4H-pyran-4-one (**7c**, $C_{11}H_{20}O_2$)

Hydrogenation of 0.90 g **5c** (5.3 mmol) gave 0.68 g **7c** (56%) as beige oil after flash column chromatography (silica gel, LP/*Et*OAc = 10/1); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.90$ (t, $J = 7$ Hz, 6H), 1.30–1.80 (m, 8H), 2.15–2.40 (m, 4H), 3.60–3.75 (m, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.3$ (q), 19.0 (t), 38.9 (t), 48.4 (t), 77.1 (d), 207.9 (s) ppm.

cis-Tetrahydro-2,6-diisopropyl-4H-pyran-4-one (**7d**, $C_{11}H_{20}O_2$)

Hydrogenation of 1.59 g **5d** (8.8 mmol) gave a mixture of ketal and ketone, which was treated with *THF*/2*N* HCl (5/1, 25 cm^3) at rt overnight. The deprotection was hydrolyzed with satd. $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Pure **7d** (1.16 g, 71%) was obtained as colorless oil after *Kugelrohr* distillation; bp 90–95°C/0.1 mbar (KRD); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.90$ (d, $J = 6$ Hz, 6H), 0.95 (d, $J = 6$ Hz, 6H), 1.60–1.80 (m, 2H), 2.10–2.45 (m, 4H), 3.20–3.30 (m, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 18.1$ (q), 33.4 (d), 45.2 (t), 81.8 (d), 208.8 (s) ppm.

cis-2,6-Dibutyltetrahydro-4,4-dimethoxy-2H-pyrane (**6e**, $C_{15}H_{30}O_3$)

Hydrogenation of 1.89 g **5e** (9.09 mmol) gave 1.07 g **6e** (46%) as yellow oil; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.85$ (t, $J = 7$ Hz, 6H), 1.20–1.60 (m, 12H), 1.85–2.00 (m, 4H), 3.15 (s, 3H), 3.20 (s, 3H), 3.32–3.47 (m, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 13.9$ (q), 22.5 (t), 27.7 (t), 35.6 (t), 38.7 (t), 47.1 (q), 47.4 (q), 73.8 (d), 99.1 (s) ppm.

Deketalization

A solution of ketal **6** in *THF*/2*N* HCl (5/1, 10%) was stirred at rt overnight. The mixture was hydrolyzed with satd. $NaHCO_3$ solution and extracted with Et_2O. The combined organic layers were dried (Na_2SO_4), filtered, and concentrated.

cis-Tetrahydro-2,6-dimethyl-4H-pyran-4-one (**7a**)

Deketalization of 4.53 g **6a** (23 mmol) gave 2.17 g **7a** [10] (65%) as colorless liquid after extraction with CH_2Cl_2 and vacuum distillation; bp 62–65°C/12 mbar; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.35$ (d, $J = 7$ Hz, 6H), 2.10–2.45 (m, 4H), 3.61–3.80 (m, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 21.9$ (q), 48.8 (t), 72.9 (d), 207.2 (s) ppm.

cis-2,6-Diethyltetrahydro-4H-pyran-4-one (**7b**, $C_9H_{16}O_2$)

Deketalization of 4.78 g **6b** (23.6 mmol) gave 2.59 g **7b** (70%) as colorless liquid after vacuum distillation; bp 81–83°C/11 mbar; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.00$ (t, $J = 7$ Hz, 6H), 1.43–1.81 (m, 4H), 2.11–2.45 (m, 4H), 3.39–3.55 (m, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 9.6$ (q), 29.3 (t), 47.5 (t), 78.2 (d), 207.7 (s) ppm.

cis-2,6-Dibutyltetrahydro-4H-pyran-4-one (**7e**, $C_{13}H_{24}O_2$)

Deketalization of 1.07 g **6e** (4.1 mmol) gave 0.66 g **7e** (76%) as beige oil after flash column chromatography (silica gel, LP/*Et*OAc = 10/1); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.90$–1.00 (m, 6H), 1.20–1.80 (m, 12H), 2.10–2.40 (m, 4H), 3.40–3.55 (m, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.4$ (q), 22.9 (t), 27.9 (t), 36.5 (t), 48.8 (t), 77.4 (d), 208.4 (s) ppm.

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References

[1] For general reviews on *Baeyer-Villiger* oxidations see: Mihovilovic MD, Rudroff F, Grötzl B (2004) Curr Org Chem **8**: 1057; Renz M, Meunier B (1999) Eur J Org Chem 737
[2] For recent reviews on enzymatic *Baeyer-Villiger* oxidations see: Kamerbeek NM, Janssen DB, van Berkel WJH, Fraaije MW (2003) Adv Synth Catal **345**: 667; Mihovilovic MD**,** Müller B, Stanetty P (2002) Eur J Org Chem 3711
[3] Mihovilovic MD, Adelwöhrer C, Stanetty P (2001) Arkivoc **2**: 1082
[4] Mihovilovic MD, Müller B, Kayser MM, Stanetty P (2002) Synlett 700
[5] Mihovilovic MD, Müller B, Schulze A, Stanetty P, Kayser MM (2003) Eur J Org Chem 2243
[6] Mihovilovic MD, Rudroff F, Kandioller W, Grötzl B, Stanetty P, Spreitzer H (2003) Synlett 1973
[7] Mihovilovic MD, Müller B, Kayser MM, Stewart JD, Fröhlich J, Stanetty P, Spreitzer H (2001) J Mol Catal B Enzym **11**: 349
[8] Yates P, Hand ES, Singh P, Roy SK, Still IWJ (1969) J Org Chem **34**: 4046
[9] Sear RP, Frenkel D (1996) J Chem Phys **105**: 10632
[10] Sato M, Kuroda H, Kaneko C, Furuya T (1994) J Chem Soc Chem Commun 687
[11] Yamato M, Kusunoki Y (1981) Chem Pharm Bull **29**: 1214
[12] Yamato M, Uenishi J-I, Hashigaka K (1978) Chem Pharm Bull **26**: 1973
[13] Yamato M, Uenishi J-I, Hashigaka K (1978) Chem Pharm Bull **26**: 1459
[14] Feist F (1890) Liebigs Ann Chem **257**: 253
[15] Lee LF, Miller ML (1986) Eur Pat Appl EP 182769, Chem Abstr **105**: 190960
[16] Gold V, Mah T (1981) J Chem Soc Perkin Trans 2, 812