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Synthesis of C_2-symmetric 1,4-diketones from tartaric acid dichloride

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Abstract

Cross-coupling reactions of tartaric acid dichloride with organocopper reagents, derived from Grignard reagents, cuprous bromide and lithium bromide, provide a simple and straightforward method for the synthesis of C_2-symmetric 1,4-diketones.

Keywords: Organocopper reagents; Ketones; Cross-coupling

1. Introduction

Tartaric acid is a very important starting material for a variety of highly selective chiral agents including chiral ligands as well as C_2-symmetrical molecules [1–4]. In many synthetic processes where tartaric acid is used as a chiral precursor, frequently, only the backbone is left unchanged while the OH and/or the COOH groups are protected or transformed to give various derivatives. However, to our knowledge, the transformation of tartaric acid and its derivatives into C_2-symmetric 1,4-diketones does not appear widely investigated [5]. Moreover, the organometallic coupling reaction on tartaric acid derivatives, which represents one of the most direct and convenient methods for this purpose, has been carried out in a very few cases [6–9] and sometimes has been considered unsuitable [5].

In fact, only recently, McNulty and coworkers have reported a more extensive investigation of the coupling reaction of Grignard reagents with 2,3-O-isopropylidene-1,4-bis-Weinreb amide derivative of tartaric acid, to give C_2-symmetrical 1,4-diketones [10]. However, the coupling reactions become sluggish as the alkyl group of Grignard reagent increases from primary to secondary and an excess of Grignard reagent with sonication was necessary to ensure the progress of the reaction. It is worth noting that this restriction of the Weinreb amides has been found by others authors [11].

These results prompted us to disclose our own results in this field. As a part of our extensive work in the area of direct acylation of organometallics [12], we have recently shown that organocopper reagents derived from Grignard reagents, cuprous bromide and lithium bromide are highly chemoselective reagents [13,14]. Thus, a chemoselective cross-coupling of these reagents with monoesters of dicarboxylic acid chlorides [13], and with α-acetoxy carboxylic acid chlorides [14], enabled us to achieve a simple and straightforward method for synthesizing a variety of ketoesters and enantiopure α-acetoxy ketones respectively. As an extension of this work we now wish to report a simple and effective method for the synthesis of C_2-symmetric 1,4-diketones, which are valuable precursors of C_2-symmetric molecules including chiral ligands [4] and of polyfunctional compounds having more asymmetric centres [9,10], based upon the reaction of organocopper reagents with tartaric acid dichloride.

2. Results and discussion

We first studied the influence of the protective group on the coupling of 2.4 equiv. of Grignard reagents, in the presence of CuBr and LiBr, with tartaric acid dichloride, protected as benzoylester [15] (Scheme 1) or by

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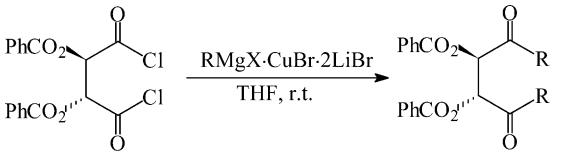
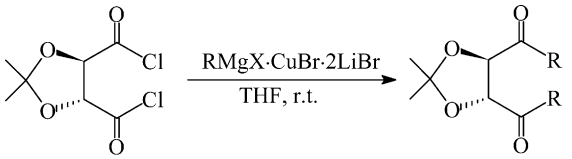


1 2 (62-89%)

Scheme 1.



3 4 (68-76%)

Scheme 2.

the cyclic ketal function [16] (Scheme 2), in THF at room temperature.

We screened several Grignard reagents (Table 1) and found that both protective groups, the ester or the cyclic ketal function, were tolerated. The diketones **2** and **4** were obtained in similar yields, whereas the best enantiomeric excess (up to >99%) was obtained for the diketones **2** with the benzoyl group as protective group.

As illustrated in Table 1, the procedure works well with aromatic (diketones **2a–d** and **4a–d**), aliphatic and alicyclic (**2e–h** and **4e–h**) Grignard reagents, including secondary and tertiary alkyl reagents. Therefore, the procedure can be applied successfully to the synthesis of various diketones **2** and **4** with isolated yields in the range 62–89% and with excellent enantiomeric purities (up to >99%) for the diketones **2** and 94–97% for the diketones **4**. In all the cases examined the cross-coupling reactions were very clean, leading to essentially pure diketones **2** and **4**, which were contaminated only by small amounts of homocoupling products. All the products were easily purified by chromatography on a silica gel column and the structures were confirmed on the basis of their spectral data.

In conclusion, a simple and convenient method to obtain C_2-symmetric 1,4-diketones directly from tartaric acid dichloride is now available. This new approach appears to be of general use (aromatic and primary, secondary, tertiary aliphatic Grignard reagents can be efficiently employed) and competitive with/or superior to others methods previously reported. The ready availability of the starting material along with the experimental simplicity of the process are further points to note.

3. Experimental

Macherey–Nagel silica gel (60, particle size 0.040–0.063 mm) for flash column chromatography and Macherey–Nagel aluminum sheets with silica gel 60 F_{254} for TLC were used. GC analysis was performed on a Hewlett-Packard 5890 series II gas chromatograph equipped with a SE-30 (methylsilicone, 30 m × 0.25 mm id) capillary column. GC/mass-spectrometry analysis was performed on a Shimadzu GCMS-QP5000 gas chromatograph-mass spectrometer equipped with a MDN-1 capillary column (methylsilicone, 30 m × 0.25 mm id). ^{1}H-NMR spectra were recorded in deuterochloroform on a Bruker AM 500 spectrometer at 500 MHz. ^{13}C NMR spectra were recorded in deuterochloroform on a Bruker AM 500 spectrometer at 125.7 MHz. IR spectra were recorded on a Perkin–Elmer FT-IR 1710 spectrometer. Optical rotations were measured at 589 nm with a Perkin–Elmer 343 polarimeter. Enantiomeric excesses were evaluated using HPLC with a Chiralcel OD-H column (Daicel) on an HP 1050 instrument, or using GC with a β-DEX 120 capillary column (Supelco) on an HP 6890 GC instrument or by ^{1}H-NMR spectroscopy with the chiral shift reagent Europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] Eu(hfc)$_3$, compared with corresponding racemic products. Melting points (uncorrected) were

Table 1
Synthesis of protected diketones **2** and **4**

R	Diketones **2**	Yields (%)[a]	e.e. (%)[b]	Diketones **4**	Yields (%)[a]	e.e. (%)[b]
Phenyl	**2a**	89	>99	**4a**	76	97
o-Tolyl	**2b**	83	>99	**4b**	74	96
2,6-Dimethylphenyl	**2c**	85	>99	**4c**	76	96
2-Thienyl	**2d**	62	>99	**4d**	71	96
n-Nonyl	**2e**	76	>98[c]	**4e**	76	94[c]
i-Propyl	**2f**	85	>99	**4f**	68	95[d]
Cyclohexyl	**2g**	81	>99	**4g**	70	94[c]
t-Butyl	**2h**	82	>99	**4h**	73	94[c]

[a] Yields refer to products purified by column chromatography.
[b] e.e. determined by HPLC.
[c] e.e. determined by ^{1}H-NMR spectroscopy with Eu(hfc)$_3$.
[d] e.e. determined by GC analysis.

determined on a Reichert Microscope. Solvents were dried before use as follows: methylene chloride was distilled over phosphorus pentoxide, tetrahydrofuran was distilled from sodium.

3.1. (1R,2R)-2-(benzoyloxy)-3-chloro-1-(chlorocarbonyl)-3-oxopropyl benzoate (dibenzoyl-L-tartaric acid dichloride) (1) [15]

A CH_2Cl_2 (50 ml) solution of $(COCl)_2$ (4.0 ml, 46.55 mmol) was added dropwise at room temperature, under nitrogen, to a solution of dibenzoyl-L-tartaric acid (4.050 g, 11.16 mmol) in CH_2Cl_2 (100 ml) in the presence of DMF (0.2 ml). After reaction completion (5 h at room temperature), the solvent was removed under vacuum and THF (50 ml) was added to the crude product. The resulting heterogeneous mixture was stirred for 5 min, filtered and the resulting solution was evaporated to give compound **1** as a viscous pale yellow oil (4.416 g, 99% yield) that was employed without further purification in the subsequent reactions.

ν_{max} (neat) 3066, 2951, 2873, 1806, 1741, 1602, 1453, 1264, 1238, 1179, 1137, 1090, 1052, 1025, 953, 909, 818, 708 cm^{-1}.

3.1.1. General procedure for the synthesis of 2,3-dibenzoyloxy-1,4-diketones

A THF solution (5 ml) of LiBr (0.42 g, 4.88 mmol) was added at room temperature, under nitrogen, to a stirred suspension of CuBr (0.35 g, 2.44 mmol) in THF (5 ml). A freshly prepared THF solution of Grignard reagent (2.44 mmol) and soon afterwards dibenzoyl-L-tartaric acid dichloride **1** (0.40 g, 1.012 mmol) in THF (15 ml) were quickly added to the stirred solution of salts. The mixture was stirred at room temperature for 10 min, quenched with aqueous NH_4Cl and extracted with ethyl acetate. The organic extracts were dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography and by crystallization.

3.2. (1R,2R)-1-benzoyl 2-(benzoyloxy)-3-oxo-3-phenylpropyl benzoate (2a)

Compound **2a** was prepared from **1** (0.407 g) in accordance with general procedure. Purification by percolation on florisil column (chloroform as eluent) followed by flash chromatography (50% ethyl acetate/petroleum ether to 80%) afforded 0.437 g of **2a** (89% yield, >99% e.e. determined by HPLC, hexane/2-propanol 90/10, 0.5 ml/min). The residual solid was crystallized from ethyl acetate/petroleum ether (white solid, mp 181–182 °C), $[\alpha]_D^{20} = -9.3°$ ($c = 3.9$, $CHCl_3$).

ν_{max} (KBr) 3060, 2984, 1718, 1707, 1698, 1597, 1451, 1365, 1318, 1263, 1250, 1232, 1118, 1098, 1072, 958, 727, 715, 690 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.05–7.99 (m, 4H), 7.94–7.89 (m, 4H), 7.61–7.56 (m, 2H), 7.54–7.44 (m, 6H), 7.36 (t like, $J = 7.9$ Hz, 4H), 6.81 (s, 2H); δ_C (125.7 MHz, $CDCl_3$) 192.9, 165.3, 134.7, 133.9, 133.6, 129.9, 128.9, 128.6, 128.4, 73.6. Anal. Found: C, 75.15; H, 4.60. Calc. for $C_{30}H_{22}O_6$: C, 75.30; H, 4.63%.

3.3. (1R,2R)-2-(benzoyloxy)-1-(2-methylbenzoyl)-3-(2-methylphenyl)-3-oxopropyl benzoate (2b)

Compound **2b** was prepared from **1** (0.396 g) in accordance with general procedure. Purification by percolation on florisil column (chloroform as eluent) afforded 0.419 g of **2b** (83% yield, >99% e.e. determined by HPLC, hexane/2-propanol 90/10, 0.5 ml/min). The residual solid was crystallized from ethyl acetate/hexane (white solid, mp 199–200 °C), $[\alpha]_D^{20} = -94.7°$ ($c = 1.9$, $CHCl_3$).

ν_{max} (KBr) 3066, 2952, 2927, 1727, 1714, 1600, 1451, 1348, 1289, 1266, 1233, 1103, 1092, 705 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.99–7.94 (m, 4H), 7.77 (d like, $J = 7.6$ Hz, 2H), 7.60–7.54 (m, 2H), 7.45–7.38 (m, 6H), 7.30 (t like, $J = 7.5$ Hz, 2H), 7.27–7.22 (m, 2H), 6.52 (s, 2H), 2.32 (s, 6H); δ_C (125.7 MHz, $CDCl_3$) 194.9, 165.1, 138.9, 134.8, 133.6, 132.2, 132.1, 129.9, 128.5, 127.8, 125.8, 75.3, 20.2. Anal. Found: C, 75.80; H, 5.15. Calc. for $C_{32}H_{26}O_6$: C, 75.88; H, 5.17%.

3.4. (1R,2R)-2-(benzoyloxy)-1-(2,6-dimethylbenzoyl)-3-(2,6-dimethylphenyl)-3-oxopropyl benzoate (2c)

Compound **2c** was prepared from **1** (0.400 g) in accordance with general procedure. Purification by column chromatography (50% ethyl acetate/petroleum ether) afforded 0.462 g of **2c** (85% yield, >99% e.e. determined by HPLC, hexane/2-propanol 90/10, 0.5 ml/min). The residual solid was crystallized from ethyl acetate/hexane (white solid, mp 148–149 °C), $[\alpha]_D^{20} = -108.4°$ ($c = 2.1$, $CHCl_3$).

ν_{max} (KBr) 3063, 2958, 1731, 1718, 1594, 1462, 1450, 1346, 1294, 1264, 1228, 1177, 1137, 1106, 1096, 710 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.08–8.03 (m, 4H), 7.62–7.56 (m, 2H), 7.46 (t like, $J = 7.8$ Hz, 4H), 7.14 (t, $J = 7.6$ Hz, 2H), 6.95 (d, $J = 7.6$ Hz, 4H), 6.48 (s, 2H), 2.15 (s, 12H); δ_C (125.7 MHz, $CDCl_3$) 200.8, 164.9, 135.9, 134.6, 133.6, 129.9, 129.8, 128.6, 128.5, 128.1, 77.1, 19.3. Anal. Found: C, 76.30; H, 5.60. Calc. for $C_{34}H_{30}O_6$: C, 76.39; H, 5.66%.

3.5. (1R,2R)-2-(benzoyloxy)-3-oxo-3-(thien-2-yl)-1-(thien-2-ylcarbonyl)propyl benzoate (2d)

Compound **2d** was prepared from **1** (0.410 g) in accordance with general procedure. Purification by percolation on florisil column (chloroform as eluent) followed by flash chromatography (50% ethyl acetate/petroleum ether to 80%) afforded 0.316 g of **2d** (62%

yield, >99% e.e. determined by HPLC, hexane/2-propanol 85/15, 0.5 ml/min). The residual solid was crystallized from ethyl acetate/hexane (pale brown solid, mp 187–189 °C), $[\alpha]_D^{20} = -69.9°$ ($c = 0.5$, $CHCl_3$).

ν_{max} (KBr) 3112, 1722, 1675, 1412, 1273, 1256, 1241, 1107, 1059, 754, 718, 710 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.04 (dd, $J = 3.9$, 1.0 Hz, 2H), 8.01–7.97 (m, 4H), 7.71 (dd, $J = 4.9$, 1.0 Hz, 2H), 7.58–7.52 (m, 2H), 7.43–7.37 (m, 4H), 7.17 (dd, $J = 4.9$, 3.9 Hz, 2H), 6.66 (s, 2H); δ_C (125.7 MHz, $CDCl_3$) 185.2, 165.3, 140.5, 135.6, 133.9, 133.7, 130.0, 128.5, 74.8. Anal. Found: C, 63.60; H, 3.68; S, 13.02. Calc. for $C_{26}H_{18}O_6S_2$: C, 63.66; H, 3.70; S 13.07%.

3.6. (1R,2R)-2-(benzoyloxy)-1-decanoyl-3-oxododecyl benzoate (2e)

Compound **2e** was prepared from **1** (0.409 g) in accordance with general procedure. Purification by column chromatography (90% petroleum ether/ethyl acetate) afforded 0.457 g of **2e** as a pale yellow-orange oil (76% yield, >98% e.e. determined by ^{1}H-NMR shift reagent experiment), $[\alpha]_D^{20} = -48.4°$ ($c = 2.4$, $CHCl_3$).

ν_{max} (neat) 3070, 2926, 2855, 1728, 1453, 1261, 1244, 1177, 1093, 1069, 1026, 712 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.09–8.03 (m, 4H), 7.63–7.57 (m, 2H), 7.46 (t like, $J = 7.8$ Hz, 4H), 5.92 (s, 2H), 2.66 (dt, $J = 17.7$, 7.3 Hz, 2H), 2.52 (dt, $J = 17.7$, 7.4 Hz, 2H), 1.61–1.50 (m, 4H), 1.28–1.09 (m, 24H), 0.83 (t, $J = 7.2$ Hz, 6H); δ_C (125.7 MHz, $CDCl_3$) 203.6, 165.3, 133.8, 129.9, 128.6, 128.5, 76.9, 39.1, 31.8, 29.3, 29.2, 29.0, 22.9, 22.6, 14.1. Anal. Found: C, 74.69; H, 8.68. Calc. for $C_{36}H_{50}O_6$: C, 74.71; H, 8.71%.

3.7. (1R,2R)-2-(benzoyloxy)-4-methyl-1-(2-methylpropanoyl)-3-oxopentyl benzoate (2f)

Compound **2f** was prepared from **1** (0.399 g) in accordance with general procedure. Column chromatography (80% petroleum ether/ethyl acetate) afforded 0.350 g of **2f** (85% yield, >99% e.e. determined by HPLC, hexane/2-propanol 98/2, 0.5 ml/min). The residue was crystallized from hexane (white solid, mp 105–106 °C), $[\alpha]_D^{20} = -121.1°$ ($c = 2.0$, $CHCl_3$).

ν_{max} (KBr) 3068, 2975, 2934, 2874, 1735, 1724, 1713, 1601, 1466, 1454, 1318, 1277, 1238, 1179, 1111, 1094, 1070, 1026, 993, 715 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.08–8.01 (m, 4H), 7.61–7.55 (m, 2H), 7.45 (t like, $J = 7.8$ Hz, 4H), 6.13 (s, 2H), 3.05–2.94 (m, 2H), 1.21 (d, $J = 7.2$ Hz, 6H), 1.04 (d, $J = 6.7$ Hz, 6H); δ_C (125.7 MHz, $CDCl_3$) 207.0, 165.2, 133.7, 129.9, 128.6, 75.5, 37.1, 18.6, 17.6; MS m/z 297 (2), 106 (8), 105 (100), 77 (17), 71 (7), 51 (4), 43 (36), 41 (5%). Anal. Found: C, 70.20; H, 6.35. Calc. for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38%.

3.8. (1R,2R)-2-(benzoyloxy)-3-cyclohexyl-1-(cyclohexylcarbonyl)-3-oxopropyl benzoate (2g)

Compound **2g** was prepared from **1** (0.396 g) in accordance with general procedure. Column chromatography (60% petroleum ether/ethyl acetate) afforded 0.397 g of **2g** (81% yield, >99% e.e. determined by HPLC, hexane/2-propanol 98/2, 0.5 ml/min). The residue was crystallized from hexane (white solid, mp 129–130 °C), $[\alpha]_D^{20} = -107.2°$ ($c = 2.0$, $CHCl_3$).

ν_{max} (KBr) 3065, 2928, 2854, 1743, 1723, 1601, 1451, 1289, 1260, 1247, 1108, 1097, 714, 705 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.06–8.01 (m, 4H), 7.61–7.55 (m, 2H), 7.45 (t like, $J = 7.8$ Hz, 4H), 6.07 (s, 2H), 2.78–2.67 (m, 2H), 2.11–2.02 (m, 2H), 1.83–1.56 (m, 8H), 1.46–1.10 (m, 10H); δ_C (125.7 MHz, $CDCl_3$) 205.9, 165.2, 133.7, 129.9, 128.6, 128.5, 75.4, 47.1, 29.0, 27.5, 25.7, 25.6, 25.2. Anal. Found: C, 73.50; H, 6.93. Calc. for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99%.

3.9. (1R,2R)-2-(benzoyloxy)-4,4-dimethyl-1-(2,2-dimethylpropanoyl)-3-oxopentyl benzoate (2h)

Compound **2h** was prepared from **1** (0.398 g) in accordance with general procedure. Purification by column chromatography (90% petroleum ether/ethyl acetate) afforded 0.362 g of **2h** (82% yield, >99% e.e. determined by HPLC, hexane/2-propanol 98/2, 0.5 ml/min). The residual solid was crystallized from hexane (white solid, mp 126–128 °C), $[\alpha]_D^{20} = +21.2°$ ($c = 1.8$, $CHCl_3$).

ν_{max} (KBr) 3068, 2974, 2932, 2907, 2869, 1739, 1722, 1601, 1477, 1466, 1455, 1354, 1293, 1268, 1250, 1235, 1179, 1113, 1070, 1050, 1031, 974, 800, 715, 684 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.98–7.93 (m, 4H), 7.55–7.49 (m, 2H), 7.38 (t like, $J = 7.9$ Hz, 4H), 6.39 (s, 2H), 1.25 (s, 18H); δ_C (125.7 MHz, $CDCl_3$) 207.3, 165.1, 133.5, 129.9, 128.6, 128.4, 72.4, 44.1, 26.6. MS m/z 381 (M^+-57, <1), 227 (4), 175 (3), 105 (100), 85 (4), 77 (19), 57 (43), 51 (5), 41 (15%). Anal. Found: C, 71.15; H, 6.92. Calc. for $C_{26}H_{30}O_6$: C, 71.21; H, 6.90%.

3.9.1. General procedure for the synthesis of 2,3-O-isopropylidene-1,4-diketones

A THF solution (5 ml) of LiBr (0.551 g, 6.34 mmol) was added at room temperature, under nitrogen, to a stirred suspension of CuBr (0.454 g, 3.17 mmol) in THF (5 ml). A freshly prepared THF solution of Grignard reagent (3.17 mmol) and soon afterwards 2,3-O-isopropylidene-L-tartaric acid dichloride **3** [16] (0.30 g, 1.32 mmol) in THF (15 ml) were quickly added to the stirred solution of salts. The mixture was stirred at room temperature for 10 min, quenched with aqueous NH_4Cl and extracted with ethyl acetate. The organic extracts were dried over Na_2SO_4 and concentrated under vacuum.

The residue was purified by column chromatography [17].

3.10. [(4R,5R)-5-benzoyl-2,2-dimethyl-1,3-dioxolan-4-yl]-(phenyl)methanone (**4a**) [7]

Compound **4a** was prepared from **3** (0.304 g) in accordance with general procedure. Purification by column chromatography (90% petroleum ether/ethyl acetate) afforded 0.315 g of **4a** (76% yield, 97% e.e. determined by HPLC, hexane/2-propanol 98/2, 0.5 ml/min). After crystallization from hexane, compound **4a** was obtained as a white solid (mp 58–59 °C, lit. [7] mp 57–58 °C), $[\alpha]_D^{r.t.} = -75.9°$ ($c = 0.9$, $CHCl_3$), lit. [7] $[\alpha]_D^{r.t.} = -78.4°$ ($c = 1.0$, $CHCl_3$).

ν_{max} (KBr) 3060, 2989, 2944, 1691, 1681, 1597, 1580, 1449, 1376, 1320, 1282, 1243, 1205, 1143, 1091, 1004, 832, 704 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.15–8.05 (m, 4H), 7.65–7.53 (m, 2H), 7.52–7.40 (m, 4H), 5.83 (s, 2H), 1.40 (s, 6H); δ_C (125.7 MHz, $CDCl_3$) 196.2, 134.7, 133.7, 129.5, 128.6, 113.2, 79.0, 26.7; MS *m/z* 295 (M^+-15, <1), 205 (13), 147 (15), 105 (100), 91 (10), 77 (25), 69 (4), 65 (3), 51 (16), 43 (10%).

3.11. [(4R,5R)-2,2-dimethyl-5-(2-methylbenzoyl)-1,3-dioxolan-4-yl](2-methylphenyl)methanone (**4b**)

Compound **4b** was prepared from **3** (0.302 g) in accordance with general procedure. Purification by column chromatography (90% petroleum ether/ethyl acetate) afforded 0.333 g of **4b** (74% yield, 96% e.e. determined by HPLC, hexane/2-propanol 98/2, 0.5 ml/min). After crystallization from hexane, compound **4b** was obtained as a white solid (mp 100–102 °C), $[\alpha]_D^{20} = -54.1°$ ($c = 1.4$, $CHCl_3$).

ν_{max} (KBr) 3059, 2985, 2928, 1679, 1598, 1566, 1454, 1378, 1269, 1240, 1211, 1141, 1092, 832, 765, 726, 649 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.82–7.78 (m, 2H), 7.41–7.35 (m, 2H), 7.29–7.22 (m, 4H), 5.67 (s, 2H), 2.50 (s, 6H), 1.35 (s, 6H); δ_C (125.7 MHz, $CDCl_3$) 199.6, 139.3, 134.9, 132.0, 131.9, 130.1, 125.5, 112.9, 80.2, 26.5, 21.3; MS *m/z* 219 (7), 161 (4), 119 (100), 105 (3), 91 (27), 65 (9), 43 (6%). Anal. Found: C, 74.60; H, 6.50. Calc. for $C_{21}H_{22}O_4$: C, 74.54; H, 6.55%.

3.12. [(4R,5R)-2,2-dimethyl-5-(2,6-dimethylbenzoyl)-1,3-dioxolan-4-yl](2,6-dimethylphenyl)methanone (**4c**)

Compound **4c** was prepared from **3** (0.310 g) in accordance with general procedure. Purification by column chromatography (90% petroleum ether/ethyl acetate) afforded 0.382 g of **4c** (76% yield, 96% e.e. determined by HPLC, hexane/2-propanol 97/3, 0.5 ml/min). After crystallization from hexane, compound **4c** was obtained as a white solid (mp 97–98 °C), $[\alpha]_D^{20} = -17.2°$ ($c = 1.9$, $CHCl_3$).

ν_{max} (KBr) 3060, 2994, 2924, 2867, 1703, 1595, 1464, 1385, 1265, 1213, 1199, 1155, 1092, 1063, 875, 857, 777, 714 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.17 (t like, $J = 7.6$ Hz, 2H), 6.99 (d like, $J = 7.6$ Hz, 4H), 5.17 (s, 2H), 2.19 (s, 12H), 1.41 (s, 6H); δ_C (125.7 MHz, $CDCl_3$) 206.0, 138.5, 133.9, 129.4, 127.8, 113.6, 82.5, 26.6 19.6; MS *m/z* 133 (100), 105 (19), 91 (3), 85 (4), 79 (7), 78 (3), 77 (7), 43 (6), 41 (3%). Anal. Found: C, 75.30; H, 7.12. Calc. for $C_{23}H_{26}O_4$: C, 75.38; H, 7.15%.

3.13. [(4R,5R)-2,2-dimethyl-5-(thien-2-ylcarbonyl)-1,3-dioxolan-4-yl](thien-2-yl)methanone (**4d**)

Compound **4d** was prepared from **3** (0.318 g) in accordance with general procedure. Purification by column chromatography (80% petroleum ether/ethyl acetate) afforded 0.321 g of **4d** as a yellow oil (71% yield, 96% e.e. determined by HPLC, hexane/2-propanol 95/5, 0.5 ml/min), $[\alpha]_D^{20} = -153.2°$ ($c = 2.6$, $CHCl_3$).

ν_{max} (neat) 3101, 2988, 2936, 1661, 1515, 1412, 1383, 1373, 1357, 1250, 1213, 1152, 1081, 1057, 858, 728 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.02 (dd, $J = 3.9$, 1.0 Hz, 2H), 7.68 (dd, $J = 4.9$, 1.0 Hz, 2H), 7.12 (dd, $J = 4.9$, 3.9 Hz, 2H), 5.57 (s, 2H), 1.44 (s, 6H); δ_C (125.7 MHz, $CDCl_3$) 189.3, 141.0, 135.1, 134.8, 128.3, 113.6, 80.2, 26.6; MS *m/z* 236 (1), 211 (7), 153 (18), 125 (3), 111 (100), 97 (15), 85 (6), 83 (6), 69 (4), 53 (4), 45 (6), 43 (10), 41 (4%). Anal. Found: C, 55.80; H, 4.35; S, 19.85. Calc. for $C_{15}H_{14}O_4S_2$: C, 55.88; H, 4.38; S, 19.89%.

3.14. 1-[(4R,5R)-5-decanoyl-2,2-dimethyl-1,3-dioxolan-4-yl]decan-1-one (**4e**)

Compound **4e** was prepared from **3** (0.302 g) in accordance with general procedure. Purification by column chromatography (95% petroleum ether/ethyl acetate) afforded 0.413 g of **4e** as a pale yellow oil (76% yield, 94% e.e. determined by ^{1}H-NMR shift reagent experiment), $[\alpha]_D^{20} = +3.3°$ ($c = 5.2$, $CHCl_3$).

ν_{max} (neat) 2930, 2855, 1723, 1465, 1375, 1259, 1211, 1153, 1083, 861, 722 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 4.51 (s, 2H), 2.65–2.52 (m, 4H), 1.59–1.51 (m, 4H), 1.38 (s, 6H), 1.29–1.15 (m, 24H), 0.83 (t, $J = 6.9$ Hz, 6H); δ_C (125.7 MHz, $CDCl_3$) 208.6, 112.3, 81.5, 39.1, 31.8, 29.4, 29.2, 29.1, 26.2, 23.1, 22.6, 14.1; MS *m/z* 255 (18), 197 (5), 155 (100), 95 (13), 85 (24), 81(12), 71 (44), 69 (11), 67 (8), 57 (62), 55 (32), 43 (89), 41 (35%). Anal. Found: C, 73.20; H, 11.23. Calc. for $C_{25}H_{46}O_4$: C, 73.12; H, 11.29%.

3.15. 1-[(4R,5R)-2,2-dimethyl-5-(2-methylpropanoyl)-1,3-dioxolan-4-yl]-2-methylpropan-1-one (**4f**)

Compound **4f** was prepared from **3** (0.307g) in accordance with general procedure. Purification by column chromatography (95% petroleum ether/ethyl

acetate) afforded 0.221 g of **4f** as a pale yellow oil (68% yield, 95% e.e. determined by GC analysis, isothermal at 80 °C, 1.2 ml/min), $[\alpha]_D^{20} = +51.1°$ ($c = 2.8$, $CHCl_3$).

ν_{max} (neat) 2975, 2937, 2876, 1717, 1468, 1384, 1259, 1212, 1156, 1099, 1073, 1021, 864 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 4.66 (s, 2H), 3.11–2.98 (m, 2H), 1.34 (s, 6H), 1.09 (d, $J = 6.9$ Hz, 6H), 1.04 (d, $J = 6.7$ Hz, 6H); δ_C (125.7 MHz, $CDCl_3$) 212.2, 112.1, 80.1, 37.0, 26.1, 18.3, 17.4; MS *m/z* 171 (5), 113 (4), 85 (5), 71 (70), 59 (3), 55 (3), 43 (100), 41 (19%). Anal. Found: C, 64.40; H, 9.10. Calc. for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15%.

*3.16. [(4R,5R)-5-(cyclohexylcarbonyl)-2,2-dimethyl-1,3-dioxolan-4-yl](cyclohexyl)methanone (**4g**)*

Compound **4g** was prepared from **3** (0.307 g) in accordance with general procedure. Purification by column chromatography (95% petroleum ether/ethyl acetate) afforded 0.307 g of **4g** as a pale yellow oil (70% yield, 94% e.e. determined by ^{1}H-NMR shift reagent experiment), $[\alpha]_D^{20} = +20.8°$ ($c = 2.5$, $CHCl_3$).

ν_{max} (neat) 2931, 2856, 1714, 1450, 1378, 1256, 1212, 1153, 1081, 1001, 895, 861, 808, 730 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 4.59 (s, 2H), 2.81–2.71 (m, 2H), 1.88–1.80 (m, 2H), 1.74–1.64 (m, 6H), 1.62–1.54 (m, 2H), 1.38–1.06 (m, 16H); δ_C (125.7 MHz, $CDCl_3$) 211.0, 111.9, 79.9, 46.6, 28.4, 27.4, 25.9, 25.6, 25.5, 25.1; MS *m/z* 211 (6), 153 (3), 111(51), 83 (100), 81 (3), 55 (32), 43 (12), 41 (27%). Anal. Found: C, 70.80; H, 9.40. Calc. for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38%.

*3.17. 1-[(4R,5R)-2,2-dimethyl-5-(2,2-dimethylpropanoyl)-1,3-dioxolan-4-yl]-2,2-dimethylpropan-1-one (**4h**)*

Compound **4h** was prepared from **3** (0.298g) in accordance with general procedure. Purification by column chromatography (95% petroleum ether/ethyl acetate) afforded 0.258 g of **4h** as a pale yellow oil (73% yield, 94% e.e. determined by ^{1}H-NMR shift reagent experiment), $[\alpha]_D^{20} = -26.4°$ ($c = 1.9$, $CHCl_3$).

ν_{max} (neat) 2972, 2930, 2874, 1703, 1480, 1465, 1385, 1370, 1256, 1214, 1160, 1078, 1044, 977, 870 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 4.92 (s, 2H), 1.35 (s, 6H), 1.15 (s, 18H); δ_C (125.7 MHz, $CDCl_3$) 211.3, 112.4, 78.0, 44.3, 26.3, 26.0; MS *m/z* 185 (5), 127 (3), 85 (29), 71 (3), 57 (100), 43 (15), 41 (25%). Anal. Found: C, 66.60; H, 9.71. Calc. for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69%.

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[17] In the formation of the diketones **4** the GC-MS analysis of the crude reaction products revealed the presence of small amounts (~2–5%) of another compound which we presumed to be the *meso* diastereoisomer of **4**.