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Tetrahedron: *Asymmetry* 15 (2004) 3029–3033

Enantioselective aldol condensation of *O*-silyldienolates derived from alkyl-substituted 2,2-dimethyl-[1,3]-dioxin-4-ones

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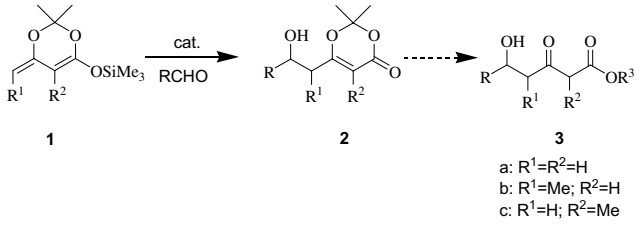
Received 27 May 2004; revised 21 July 2004; accepted 23 July 2004
Available online 15 September 2004

Abstract—Vinylogous aldol condensation of masked alkylated acetoacetates proceeds with good to excellent yields and enantiomeric excesses in the presence of a chiral Ti(O-*i*-Pr)$_4$/BINOL complex. The presence of positive nonlinear effects are also pointed out.

1. Introduction

Asymmetric Mukaiyama aldol condensation of dienolsilyl ethers of type **1** (Scheme 1) represents one of the most useful approaches for the stereoselective synthesis of C-5 polyfunctional subunits **3**, key-intermediates in the preparation of bioactive compounds.[1]



Scheme 1.

The conversion **1a** → **2a** usually takes place under chiral Lewis acid catalysis with the most relevant results being obtained by using chiral B(III),[2] Cu(II)[3] and Ti(IV)[4] catalysts.

So, for example, a chiral tartaric acid-derived acyl borane (CAB) proved to be capable of promoting the formation of aldols of type **2a**: however, high catalyst loadings (50–100 mol%) were required to reach only moderate levels of efficiency and enantioselectivity. An aldol reaction of **1a** on aldehydes bearing a suitable chelating substituent at the α-position to the carbonyl functionality proceeds in high yields and enantiomeric excesses (ee's) in the presence of reduced amounts of a chiral Cu(II)/pybox complex,[3a] while a more general, highly enantioselective procedure is based on the use of (*R*)- or (*S*)-Tol-BINAP/Cu(OTf)$_2$/*n*-Bu$_4$NPh$_3$SiF$_2$ system (2 mol%),[3c,d] although in this latter case, a poor efficiency is usually observed with aliphatic aldehydes. Furthermore, very good yields and ee's have been obtained by performing the aldol reaction of **1a** in the presence of Ti(IV)/BINOL[4] and Ti(IV)/Schiff base[4b] complexes.

Finally, a very recent report concerning the employment of a chiral Cr(Salen) complex,[5] which is particularly efficient in the promotion of the asymmetric aldol reaction on aliphatic aldehydes, while a quite different approach involves the use of a chiral bis-phosphoramide, as neutral coordinate organo-catalyst, in a $SiCl_4$-catalyzed process.[6]

In spite of this interest, it should be noted that the reactivity of silyloxydienes of type **1b** and **1c** (Scheme 1), bearing a substituent at the 5 or 6 positions, has scarcely been explored, although their successful employment could have allowed an easy access to branched polyols.

Taking advantage of the results of an intense investigation on Sato's protocol,[4a] based on the use of a Ti(O-*i*-Pr)$_4$/BINOL complex, we have achieved a significantly improved catalytic procedure for the conversion of **1a** → **2a**. Furthermore, we have clarified some interesting mechanistic aspects, such as the presence of positive nonlinear effects (NLE)[7] and the involvement of an auto-inductive process.[4h]

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0957-4166/$ - see front matter
doi:10.1016/j.tetasy.2004.07.020

Consequently, we have decided to verify the possibility of extending our procedure (optimized for silyloxydiene **1a**) to 5- and 6-substituted derivatives of type **1b** and **1c**.

2. Results and discussion

Compound **1b**, easily accessible starting from 6-ethyl-2,2-dimethyl-dioxin-4-one as an inseparable mixture of *E* and *Z* geometrical isomers (*E*/*Z* = 3:5), was chosen as representative of silyloxydiene and submitted to aldol reaction in the presence of catalytic amounts of Ti(O-*i*-Pr)$_4$/(*R*)-BINOL complex (8 mol%) under the typical conditions of the catalytic conversion **1a** → **2a** (Scheme 2).

Aldol condensation was shown to take place in good yields with aromatic, heteroaromatic and unsaturated aldehydes to afford, after in situ desilylation at −78 °C, a *syn*/*anti* diastereoisomeric mixture, with the *syn*-aldol **2b** being the major product (Table 1, entries 1–4). A much lower efficiency was observed with aliphatic aldehydes.

In entries 1–4, however, the *syn*-aldols were obtained in very good enantiomeric excesses, while the formation of *anti*-aldols were shown to occur with a reduced level of enantioselectivity. This stereochemical outcome is in agreement with a preliminary result, reported previously by Sato et al.,[4a] concerning the aldol condensation of **1b** with benzaldehyde.

The strong well-documented dependence of the catalytic properties of Ti(IV)/BINOL complex on the experimental conditions, especially with regards to the concentration[8] and the mode of preparation of the catalyst,[9] is confirmed in entry 5, using the same procedure as in entry 1 but with the exception of the use of a catalyst previously prepared in more concentrated solution (see Table 1, footnote e). In fact lower yields and ee's were observed so that *anti*-**2b** could be isolated in its almost completely racemic form.

Since positive nonlinear effects (NLE) have been detected in several processes promoted by Ti(IV)/BINOL complexes,[7b,10] benzaldehyde, chosen as the representative substrate, was submitted to reaction with **1b** in the presence of an enantiomerically enriched Ti(O-*i*-Pr)$_4$/BINOL system under the standard conditions while the presence of a positive NLE was observed for both *syn*- and *anti*-**2b** (Fig. 1).

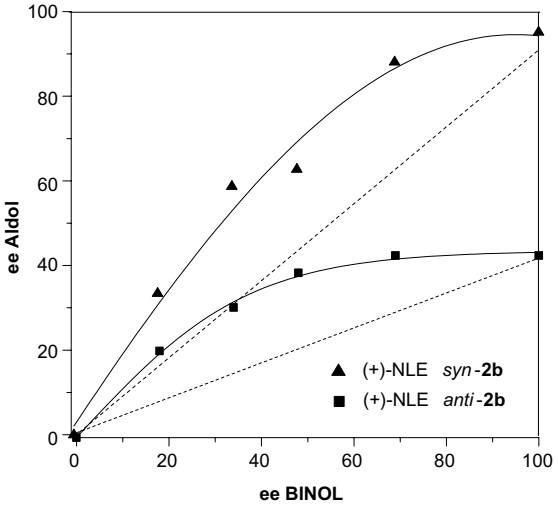
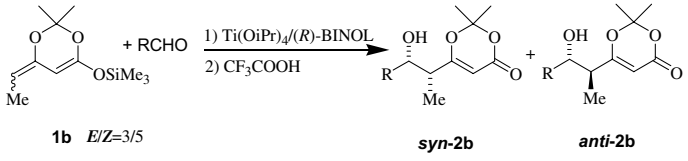


Figure 1.

The degree of the asymmetric amplification proved once again to be strongly influenced by the mode of catalyst preparation: in fact, when the aldol condensation was



Scheme 2.

Table 1. Ti(O-*i*-Pr)$_4$/(*R*)-BINOL-catalyzed aldol reaction of **1b**

Entry	R	2	Yield (%)[a]	*syn*/*anti*[b]	*syn* Ee (%)[c,d]	*anti* Ee (%)[c,d]
1	Ph–	**2ba**	75	80:20	94	42
2	PhCH=CH–	**2bb**	81	85:15	86	16
3	2-Furyl–	**2bc**	98	85:15	94	56
4	Ph–CH_2CH_2–	**2bd**	26	87:13	99	54
5[e]	Ph–	**2ba**	68	79:21	89	∼0

[a] All the yields refer to isolated chromatographically pure compounds.
[b] The relative configurations and diastereomeric ratios were determined by ^{1}H NMR analysis.
[c] Ee's were determined by HPLC analysis using a CHIRALPAK AD column.
[d] The absolute configuration in Scheme 2 was established by comparison of the specific rotation to literature values[4] for **2ba** or by conversion to the corresponding MTPA esters for **2bc**. The absolute configurations of products **2bb** and **2bd** have been assigned (see Section 4) by assuming the same asymmetric induction by Ti(O-*i*-Pr)$_4$/(*R*)-BINOL complex as in entries 1 and 3.
[e] The catalytic system was initially prepared in 1 mL. The final volume of the reaction was 6 mL.

carried out by employing enantioenriched catalysts previously prepared in concentrated solutions (according the procedure depicted in Table 1, entry 5) a very poor deviation from linearity was observed until a value of 35% ee was reached for (*R*)-BINOL, after which a positive NLE could be again detected until enantiopure (*R*)-BINOL was used (Fig. 2).

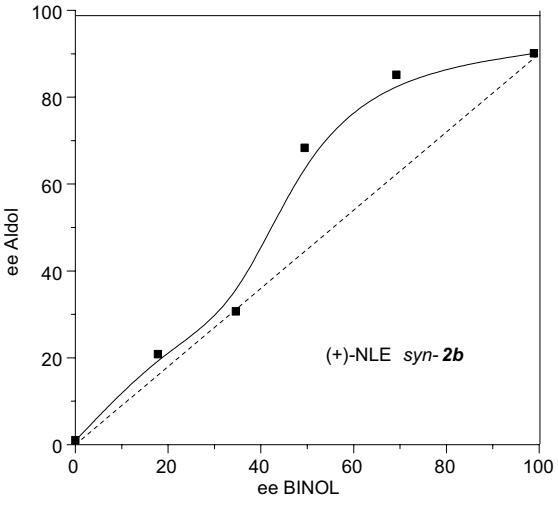


Figure 2.

Successively, the reactivity of silyloxydiene **1c** (easily accessible from *t*-butyl 2-methyl-3-oxo-butanoate)[4a,11] was investigated and, rather surprisingly, the optimized procedure for unsubstituted derivatives **1a** was found to be completely unsuccessful in the first attempt of an aldol condensation on benzaldehyde (Table 2, entry 1).

Table 2. Ti(O-*i*-Pr)$_4$/(*R*)-BINOL-catalyzed aldol reaction of **1c**[d]

Entry	R	2	Yield (%)[a]	Ee (%)[b,c]
1	Ph–	**2ca**	—	—
2	Ph–	**2ca**	14	>99
3	Ph–	**2ca**	57	84
4	*p*-$NO_2C_6H_4$–	**2cb**	74	66
5	2-Furyl–	**2cc**	62	71
6	*p*-CNC_6H_4–	**2cd**	76	>99
7	Ph–CH_2CH_2–	**2ce**	21	72
8	*p*-$OMeC_6H_4$–	**2cf**	62	22

[a] All the yields refer to isolated chromatographically pure compounds.
[b] Ee's were determined by HPLC analysis using a CHIRALPAK AD column.
[c] Absolute configuration of **2ca** was established as *R* by conversion to the corresponding MTPA esters. The absolute configurations of products **2cb**–**cf** have been assigned (see Section 4) by assuming the same asymmetric induction by Ti(IV)/(*R*)-BINOL complex as in entries 2–3.
[d] The catalytic system was initially prepared in 5 mL of THF (entry 1) or in 0.5 mL of THF (entries 2–8). The final volume of the reaction was 6 mL in entries 1 and 2, while it was 1 mL in entries 3–8.

Reagents and catalyst concentration proved once again to be an important factor both for the efficiency and enantioselectivity of the process. In fact, when the catalytic system was prepared in very concentrated solution (Table 2, entry 2) and the reaction performed under the same conditions used in entry 1 (Table 2), in regards to the final concentration of the catalyst and the reagents, the corresponding aldol was obtained in a very poor yield (14%) and high ee (>99%). A more satisfactory preparative result (57% yield) was obtained by reducing drastically the overall solvent volume (entry 3), although a not neglectable decrease of the level of enantioselectivity (84% ee) was observed.

The same procedure has afforded promising results with other aromatic and heteroaromatic aldehydes (entries 4–6), while in the case of aliphatic aldehydes (entry 7), aldol condensation showed to proceed in low yield and good ee.

3. Conclusions

Through an appropriate choice of experimental conditions, the aldol condensation of *O*-silyldienolates derived from masked alkylated acetoacetates **1b** and **1c** took place in the presence of a chiral Ti(O-*i*-Pr)$_4$/BINOL complex to afford the corresponding aldols with very satisfactory efficiency and enantioselectivity. In the case of **1b** the reaction proceeded in good diastereoselectivity affording *syn*-aldols **2b** as the far more predominant diastereoisomers. Furthermore, experiments performed in the presence of enantioenriched catalytic species pointed out the presence of a positive NLE, whose size was found to strongly depend on the mode of the catalyst preparation.

4. Experimental

4.1. General methods

All reactions were performed using oven dried glassware under an atmosphere of dry nitrogen. Tetrahydrofuran (THF) was distilled from CaH_2 and then from $LiAlH_4$. *i*-Pr_2NH was freshly distilled from CaH_2. ^1H NMR and ^{13}C NMR spectra were recorded in solutions of $CDCl_3$ with Bruker DRX 400 (400.135 MHz for ^1H and 100.03 MHz for ^{13}C) spectrometers. Data for ^1H are reported as follows: chemical shift (δ in ppm), multiplicity (s singlet, d doublet, t triplet, dd doublet of doublets, m multiplet) and coupling constant (*J* in Hz). Optical rotations were measured on a JASCO DIP-1000 polarimeter operating at the sodium D line at room temperature. Concentration is given in g/100 mL. The mass spectra were recorded on a VG TRIO 2000 spectrometer. Column chromatographic purification of products was carried out using Silica gel 60 (70–230 mesh, Merck). HPLC analyses were performed with Waters Associates equipment and a Hewlett–Packard SP4400 Chromojet integrator using a CHIRALPAK AD column with solvent mixtures of hexane/isopropanol and flow rates as indicated.

4.2. General procedure for the enantioselective dienolates 1b and 1c addition to aldehydes

A mixture of (*R*)-(+)-1,1′-bi-2-naphthol (23 mg, 0.08 mmol), titanium tetraisopropoxide (24 μL,

0.08 mmol) and molecular sieves 3 Å (350 mg) in THF (5 mL for **1b**, 0.5 mL for **1c**) was stirred at room temperature under an inert atmosphere for 1 h to yield a red-brown solution. The mixture was cooled to −78 °C and the aldehyde (1 mmol) added dropwise followed, after 20 min, by a solution of the dioxinone derivative dienolate (2 mmol) in THF (1 mL for **1b**, 0.5 mL for **1c**). The whole mixture was then stirred at −78 °C for 2 h and then at rt for 16 h. After cooling the mixture at −78 °C, TFA (0.4 mL) was added and the solution warmed to rt stirring for 1 h. A saturated aqueous solution of $NaHCO_3$ was added until the evolution of gas ceased. After stirring for 30 min, it was extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated in vacuo. Purification by chromatography on silica gel using 9:1 $CHCl_3/Et_2O$ afforded the aldol adducts.

4.2.1. 6-((1*R*,2*R*)-2-Hydroxy-1-methyl-2-phenyl-ethyl)-2,2-dimethyl-[1,3]dioxin-4-one *syn*-2ba and 6-((1*S*,2*R*)-2-hydroxy-1-methyl-2-phenyl-ethyl)-2,2-dimethyl-[1,3]dioxin-4-one *anti*-2ba. The physical and spectroscopic data of compounds **2ba** match those described in literature.[4a]

Compound *syn*-**2ba**: $[\alpha]_D^{25} = -10.5$ (*c* 1.0, $CHCl_3$), ee 96% (*R*) determined by HPLC analysis (CHIRALPACK AD column, hexane/isopropanol 9:1, 0.5 mL/min, (*R*)-enantiomer 21.51 min, (*S*) enantiomer 33.45 min; *anti*-**2ba**: $[\alpha]_D^{25} = +19.6$ (*c* 0.6, $CHCl_3$), ee 40% determined by HPLC analysis (CHIRALPACK AD column, hexane/isopropanol 9:1, 0.5 mL/min, (*R*) enantiomer 29.27 min, (*S*) enantiomer 35.78 min.

4.2.2. 6-((*E*)-(1*R*,2*S*)-2-Hydroxy-1-methyl-4-phenyl-but-3-enyl)]-2,2-dimethyl-[1,3]dioxin-4-one *syn*-2bb. [Found: C, 70.95; H, 7.06; $C_{17}H_{20}O_4$ requires C, 70.81; H, 6.99%]; $[\alpha]_D^{25} = -13.2$ (*c* 0.6, $CHCl_3$), ee 86% determined by HPLC analysis (hexane/isopropanol 9:1, 0.8 mL/min, major enantiomer 19.46 min, minor enantiomer 24.52 min; δ_H (400 MHz, $CDCl_3$) 7.36–7.24 (m, 5H), 6.63 (d, 1H, $J = 15.8$ Hz), 6.19 (dd, 1H, $J = 6.6$, 15.8 Hz), 5.34 (s, 1H), 4.44 (t, 1H, $J = 5.8$ Hz), 2.55 (m, 1H), 1.66 (s, 3H), 1.65 (s, 3H), 1.22 (d, 3H, $J = 7.0$); δ_C (100.03 MHz, $CDCl_3$) 172.8, 161.5, 136.3, 132.3, 129.2, 128.3, 126.7, 106.7, 94.2, 73.7, 44.4, 25.6, 25.0, 12.3; *m*/*z* (EIMS) 288 (M^+).

4.2.3. 6-((*E*)-(1*S*,2*S*)-2-Hydroxy-1-methyl-4-phenyl-but-3-enyl)-2,2-dimethyl-[1,3]dioxin-4-one *anti*-2bb. The aldol *anti*-**2bb** could not be isolated as a pure compound but in mixture with *syn*-**2bb**; ee 16% determined by HPLC analysis (hexane/isopropanol 9:1, 0.8 mL/min, major enantiomer 24.52 min, minor enantiomer 32.10 min); δ_H (400 MHz, $CDCl_3$) 7.39–7.24 (m, 5H), 6.63 (d, 1H, $J = 15.8$ Hz), 6.16 (dd, 1H, $J = 7.3$, 15.7 Hz), 5.36 (s, 1H), 4.34 (t, 1H, $J = 7.5$ Hz), 2.55 (m, 1H), 1.65 (s, 6H), 1.16 (d, 3H, $J = 7.2$); δ_C (100.03 MHz, $CDCl_3$) 173.5, 161.9, 136.2, 132.6, 129.4, 128.9, 127.9, 126.6, 106.7, 94.7, 74.2, 44.8, 25.2, 24.1, 13.4; *m*/*z* (EIMS) 288 (M^+).

4.2.4. 6-((1*R*,2*R*)-2-Furan-2-yl-2-hydroxy-1-methyl-ethyl)-2,2-dimethyl-[1,3]dioxin-4-one *syn*-2bc. [Found: C 61.77; H 6.50; $C_{13}H_{16}O_5$ requires C, 61.90; H, 6.39%]; $[\alpha]_D^{25} = -2.8$ (*c* 1.0, $CHCl_3$), ee 94% determined by HPLC analysis (hexane/isopropanol 95:5, 0.8 mL/min, major enantiomer 26.63 min, minor enantiomer 36.01 min; δ_H (400 MHz, $CDCl_3$) 7.37 (d, 1H, $J = 1.5$ Hz), 6.33 (t, 1H, $J = 3.1$ Hz), 6.28 (d, 1H, $J = 3.2$ Hz), 5.25 (s, 1H), 4.83 (d, 1H, $J = 6.8$ Hz), 2.87 (m, 1H), 1.48 (s, 3H), 1.60 (s, 3H), 1.26 (d, 3H, $J = 5.0$ Hz); δ_C (100.03 MHz, $CDCl_3$) 172.5, 161.7, 154.5, 142.4, 110.5, 107.5, 106.7, 94.0, 68.9, 43.5, 25.1, 12.9; *m*/*z* (EIMS) 252 (M^+).

4.2.5. 6-((1*S*,2*R*)-2-Furan-2-yl-2-hydroxy-1-methyl-ethyl)-2,2-dimethyl-[1,3]dioxin-4-one *anti*-2bc. [Found: C 61.81; H 6.47; $C_{13}H_{16}O_5$ requires C, 61.90; H, 6.39%]; $[\alpha]_D^{25} = +27.2$ (*c* 1.0, $CHCl_3$), ee 56% determined by HPLC analysis (hexane/isopropanol 95:5, 0.8 mL/min, major enantiomer 31.62 min, minor enantiomer 36.01 min); δ_H (400 MHz, $CDCl_3$) 7.40 (s, 1H); 6.35 (s, 1H), 6.32 (d, 1H, $J = 3.8$ Hz), 5.36 (s, 1H), 4.71 (d, 1H, $J = 11.7$ Hz), 2.88 (m, 1H), 1.43 (s, 3H), 1.25 (s, 3H), 1.00 (d, 3H, $J = 9.36$ Hz); δ_C (100.03 MHz, $CDCl_3$) 173.0, 162.0, 154.3, 142.4, 110.5, 107.8, 106.9, 93.9, 69.0, 44.5, 24.8, 13.3; *m*/*z* (EIMS) 252 (M^+).

4.2.6. 6-((1*R*,2*S*)-2-Hydroxy-1-methyl-4-phenyl-butyl)-2,2-dimethyl-[1,3]dioxin-4-one *syn*-2bd and 6-((1*S*,2*S*)-2-hydroxy-1-methyl-4-phenyl-butyl)-2,2-dimethyl-[1,3]dioxin-4-one *anti*-2bd. The diastereoisomers are recovered as an inseparable mixture after the usual purification on silica gel column; [Found: C 70.45; H 7.73; $C_{17}H_{22}O_4$ requires C, 70.33; H, 7.64%]; δ_H (400 MHz, $CDCl_3$) 7.31–7.18 (m, 10H), 5.30 (s, 1H, *anti*-**2bd**), 5.28 (s, 1H, *syn*-**2bd**), 3.75–3.79 (m, 1H, *syn*-**2bd**), 3.70–3.66 (m, 1H, *anti*-**2bd**), 2.86–2.79 (m, 2H), 2.72–2.66 (m, 2H), 2.36–2.40 (m, 2H), 1.83–1.78 (m, 4H), 1.65 (s, 6H), 1.61 (s, 6H), 1.16 (d, 3H, $J = 9.3$ Hz), 1.15 (d, 3H, $J = 8.6$ Hz); δ_C (100.03 MHz, $CDCl_3$) 173.8, 161.7, 141.6, 129.26, 128.6, 128.4, 127.9, 126.2, 106.6, 93.6, 93.0, 72.0, 71.5, 44.1, 36.9, 32.5, 25.3, 24.6, 11.5; *m*/*z* (EIMS) 290 (M^+).

4.2.7. 6-((*R*)-2-Hydroxy-2-phenyl-ethyl)-2,2,5-trimethyl-[1,3]dioxin-4-one 2ca. The physical and spectroscopic data of compounds **2ca** match those described in literature.[4f]

$[\alpha]_D^{25} = +25.8$ (*c* 1.3, $CHCl_3$), ee 84% (*R*), HPLC analysis (hexane/isopropanol 90:10, 0.8 mL/min, minor enantiomer 11.82 min, major enantiomer 12.95 min.

4.2.8. 6-[(*R*)-2-(4-Nitro-phenyl)-2-hydroxy-ethyl]-2,2,5-trimethyl-[1,3]dioxin-4-one 2cb. The physical and spectroscopic data of compounds **2cb** match those described in literature.[4f]

$[\alpha]_D^{25} = +33.6$ (*c* 0.3, $CHCl_3$), ee 66% (*R*), HPLC analysis (hexane/isopropanol 95:5, 0.8 mL/min, minor enantiomer 59.16 min, major enantiomer 62.37 min.

4.2.9. 6-((*R*)-2-Furan-2-yl-2-hydroxy-ethyl)-2,2,5-trimethyl-[1,3]dioxin-4-one 2cc. [Found: C 61.77; H 6.46; $C_{13}H_{16}O_5$ requires C, 61.90; H, 6.39%]; $[\alpha]_D^{25} = +16.2$ (*c* 1.2, $CHCl_3$), ee 73% (*R*), HPLC analysis (hexane/isopropanol 90:10, 0.5 mL/min, minor enantiomer 22.92 min, major enantiomer 22.44 min); ^{1}H NMR ($CDCl_3$) δ 7.32 (s, 1H), 6.27 (s, 1H), 6.2 (s, 1H), 4.92 (m, 1H), 2.85 (dd, 1H, $J = 14.1$, 7.9 Hz), 2.74 (dd, 1H, $J = 14.2$, 6.1 Hz), 1.72 (s, 3H), 1.57 (s, 3H), 1.52 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 162.78, 161.72, 155.05, 142.06, 110.24, 106.43, 104.94, 102.46, 64.7, 37.1, 25.05, 24.76, 9.93; *m*/*z* (EIMS) 252 (M^+).

4.2.10. 4-[(*R*)-1-Hydroxy-2-(2,2,5-trimethyl-6-oxo-6*H*-[1,3]dioxin-4-yl)-ethyl]-benzonitrile 2cd. [Found: C 67.01; H 6.07; N 5.01; $C_{16}H_{17}NO_4$ requires C, 66.89; H, 5.96; N 4.88%]; $[\alpha]_D^{25} = +25.9$ (*c* 1.3, $CHCl_3$), ee >99% (*R*) determined by HPLC analysis (hexane/isopropanol 90:10, 0.8 mL/min, only enantiomer 21.52 min; ^{1}H NMR ($CDCl_3$) δ 7.67 (d, 2H, $J = 8.2$ Hz), 7.52 (d, 2H, $J = 8.1$ Hz), 5.08 (m, 1H), 2.85 (dd, 1H, $J = 14.3$, 8.9 Hz), 2.59 (dd, 1H, $J = 14.4$, 4.4 Hz), 1.78 (s, 3H), 1.66 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 162.95, 161.99, 149.10, 132.39, 126.57, 118.75, 111.36, 105.22, 102.73, 70.58, 40.61, 25.66, 24.59, 10.28; *m*/*z* (EIMS) 287 (M^+).

4.2.11. 6-((*S*)-2-Hydroxy-4-phenyl-butyl)-2,2,5-trimethyl-[1,3]dioxin-4-one 2ce. [Found: C 70.19; H 7.71; $C_{17}H_{22}O_4$ requires C, 70.32; H, 7.64%]; $[\alpha]_D^{25} = +3.0$ (*c* 1.2, $CHCl_3$), ee 72% (*S*) determined by HPLC analysis (hexane/isopropanol 95:5, 0.8 mL/min, minor enantiomer 24.63 min, major enantiomer 26.02 min); ^{1}H NMR ($CDCl_3$) δ 7.17–7.29 (m, 5H), 3.93 (m, 1H), 2.81 (m, 1H), 2.69 (m, 1H), 2.52 (dd, 1H, $J = 14.1$, 8.1 Hz), 2.41 (dd, 1H, $J = 14.1$, 4.2 Hz), 1.82 (s, 3H), 1.62 (s, 3H), 1.6 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 163.22, 162.91, 141.61, 128.58, 128.50, 126.13, 105.04, 102.26, 68.81, 39.16, 39.08, 32.01, 25.33, 25.07, 10.49, *m*/*z* (EIMS) 290 (M^+).

4.2.12. 6-[(*R*)-2-Hydroxy-2-(4-methoxy-phenyl)-ethyl]-2,2,5-trimethyl-[1,3]dioxin-4-one 2cf. [Found: C 65.61; H 6.98; $C_{16}H_{20}O_5$ requires C, 65.74; H, 6.90%]; $[\alpha]_D^{25} = +5.2$ (*c* 1.1, $CHCl_3$), ee 22% (*R*) determined by HPLC analysis (hexane/isopropanol 90:10, 0.8 mL/min, minor enantiomer 22.47 min, major enantiomer 24.25 min); ^{1}H NMR ($CDCl_3$) δ 7.29 (d, 2H, $J = 8.6$ Hz), 6.89 (d, 2H, $J = 8.6$ Hz), 4.94 (m, 1H), 3.81 (s, 3H), 2.83 (dd, 1H, $J = 14.1$, 8.3 Hz), 2.61 (dd, 1H, $J = 14.2$, 5.3 Hz), 1.76 (s, 3H), 1.62 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 162.96, 162.63, 159.43, 135.41, 127.12, 113.97, 105.03, 102.26, 71.2, 55.35, 40.57, 25.58, 24.69, 10.20; *m*/*z* (EIMS) 292 (M^+).

Acknowledgements

We thank MIUR for financial support.

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