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New 2-acyl-1,3-dioxane derivatives from (1*R*)-(−)-myrtenal: stereochemical effect on their relative ability as chiral auxiliaries

Elvia Becerra-Martínez,[a] Pedro Velázquez-Ponce,[a] Miguel A. Sánchez-Aguilar,[a] Alfredo Rodríguez-Hosteguín,[a] Pedro Joseph-Nathan,[b] Joaquín Tamariz[a] and L. Gerardo Zepeda[a,*]

[a]*Departamento de Química Orgánica, Escuela Nacional de Ciencias Biológicas, Instituto Politécnico Nacional, Prol. de Carpio y Plan de Ayala, México, DF 11340, Mexico*
[b]*Departamento de Química, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Apartado 14-740, México, DF 07000, Mexico*

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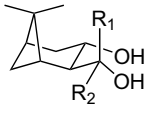
Abstract—Four 3,10-pinanediol derivatives **1a**–**d**, prepared in 50–72% global yields from (1*R*)-(−)-myrtenal **2**, were treated with $(RO)_2CHCOR_3$ ($R_3 = CH_3$, Ph) to afford 2-acyl-1,3-dioxanes **3a**–**f**. The latter were submitted to nucleophilic additions using several Grignard reagents to mainly afford carbinols generated by *re* diastereofacial attack (85–99% yield, ⩾88:12 dr). The lowest diastereoselectivity was observed when PhLi or hydrides were used as nucleophiles. Only an equatorial substituent at C-3 modifies the diastereoselectivity of the nucleophilic additions.

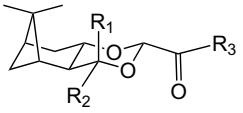
1. Introduction

The preparation of enantiomerically pure 2-substituted-1,3-dioxanes continues to be a particular challenge in asymmetric synthesis due to the scarce availability of chiral 1,3-diols which normally are their immediate precursors.[1,2] The former are usually employed in diastereoselective nucleophilic and electrophilic additions, both of which are carried out on the pro-chiral center present in the 2-substituent.[1,2] S_N2-type reactions at the ketal/acetal carbon, with concomitant dioxane ring cleavage, also occur.[1–4] A literature search revealed a scarce number of studies describing the synthesis of chiral 2-substituted-1,3-dioxanes from natural sources,[1,2,5] this being an encouraging reason to prepare them in enantiomerically pure forms. Accordingly, we visualized 3,10-pinanediols **1a**–**d** as key precursors for a variety of enantiomerically pure 2-substituted-1,3-dioxane derivatives, which might be of significance in asymmetric synthesis.[2] Since such precursors can easily be prepared from commercially available (1*R*)-(−)-myrtenal **2**, the present work deals with the construction of 2-acyl-1,3-dioxane derivatives **3a**–**f** from (1*R*)-(−)-myrtenal **2**, and its treatment with several nucleophilic reagents, this being the first application of pinane based 2-acyldiox-

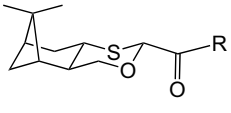
chart 1



1a $R_1 = R_2 = H$
1b $R_1 = CH_3$; $R_2 = H$
1c $R_1 = H$; $R_2 = CH_3$
1d $R_1 = R_2 = CH_3$



3a $R_1 = R_2 = H$; $R_3 = CH_3$
3b $R_1 = R_3 = CH_3$; $R_2 = H$
3c $R_2 = R_3 = CH_3$; $R_1 = H$
3d $R_1 = CH_3$; $R_2 = H$; $R_3 = Ph$
3e $R_1 = H$; $R_2 = CH_3$; $R_3 = Ph$
3f $R_1 = R_2 = R_3 = CH_3$



4a R = CH_3
4b R = Ph

* Corresponding author. Fax: +52 55 5396 3503; e-mail: lzepeda@woodward.encb.ipn.mx

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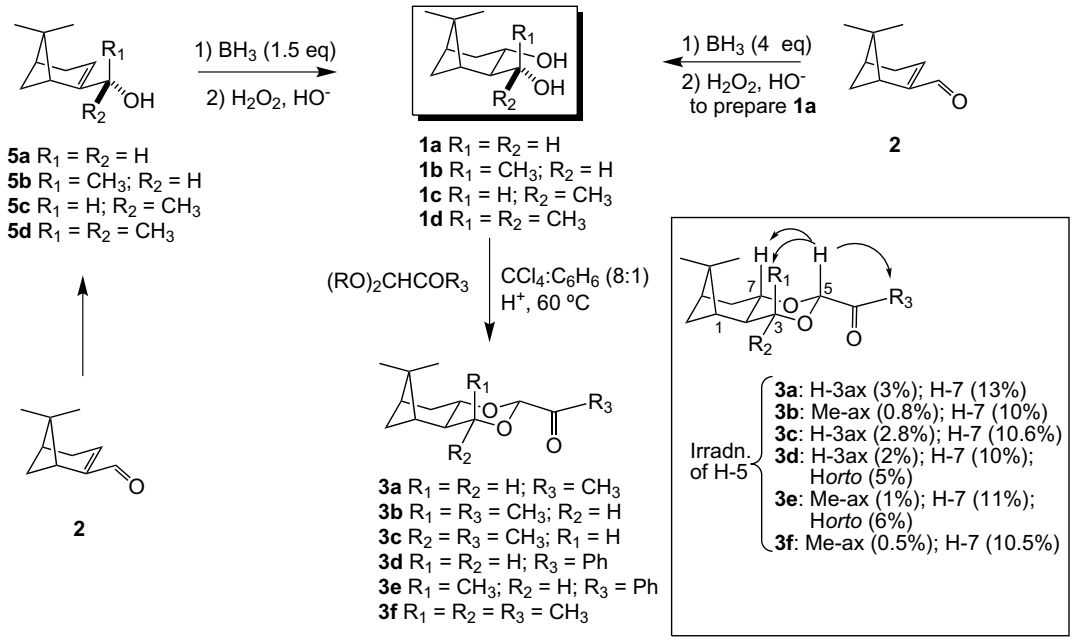
anes as chiral auxiliaries. In addition, the stereochemical outcome of the nucleophilic addition on **3a**–**f** allowed us to compare their relative diastereoselectivities with those obtained when using structurally analogous 2-acyl-1,3-oxathianes **4a** and **4b**.[6–8]

2. Results and discussion

Our early synthesis started with the preparation of 3,10-pinanediol **1a** by hydroboration–oxidation of (1*R*)-(−)-myrtenol **5a** in 74% yield (Scheme 1), as described.[9,10] However due to the proven capability of BH_3 to reduce carbonyl groups, we decided to use (1*R*)-(−)-myrtenal **2** as the starting material to prepare 3,10-pinanediol **1a** in a one-pot protocol. Thus, the treatment of (1*R*)-(−)-myrtenal **2** with excess $H_3B{\cdot}SMe_2$ in THF at rt for 24 h, followed by oxidation with H_2O_2 in the presence of NaOH, afforded diol **1a** in 78% yield as a white crystalline solid. This yield was substantially higher than that described in a similar protocol.[9,10] In turn, the preparation of diols **1b**, **1c**, and **1d** began by reacting (1*R*)-(−)-myrtenal **2** with MeMgBr to afford an epimeric mixture of 10-methylmyrtenols **5b**:**5c** (63:37) in 98% yield, from which the former compound was efficiently purified by fractionated crystallization and the latter by column chromatography. The above epimeric mixture was also oxidized with CrO_3 in pyridine to give 10-methylmyrtenone (82%), which was subsequently treated with MeMgBr to yield tertiary carbinol **5d** (88%). Hydroboration–oxidation of alcohols **5b**–**d** gave diols **1b** (80%), **1c** (82%), and **1d** (87%), respectively.

Suitable crystals of diols **1a**,**b**,**d** were analyzed by X-ray diffraction to give the ORTEP structures shown in Figure 1, in which a *trans* relationship of the substituents at the two newly formed stereogenic centers (C-2 and C-3) is visualized. Unexpectedly, in the three cases, mutual interatomic distances between the hydroxyl groups in the solid state structures preclude any type of intramolecular hydrogen bonding interaction.

To prepare 2-acyl-1,3-dioxanes **3a**–**f**, a transacetalization protocol was used. Thus, the initial treatment of 3,10-pinanediol **1a** with pyruvaldehyde dimethyl acetal in benz-



Scheme 1.

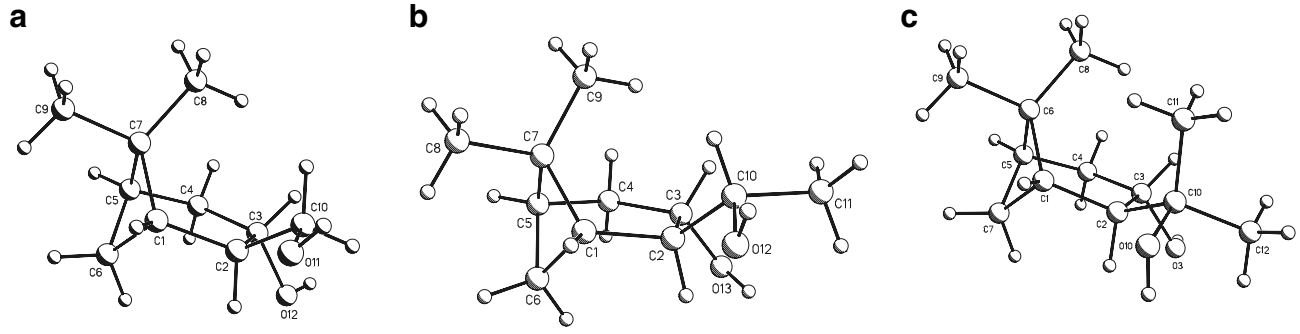


Figure 1. ORTEP X-ray projections of 3,10-pinanediols: (a) **1a**, (b) **1b**, and (c) **1d**.

ene, using *p*-TsOH as the catalyst, at 75 °C for 4 h gave acetyldioxane **3a** in 38% yield after silica gel column chromatography. To minimize the hydrolysis of the acetal group, the silica gel should be previously alkalinized with triethylamine. The low yield could be attributable to the strong tendency of pyruvaldehyde dimethyl acetal to be polymerized under the reaction conditions. The yield was significantly improved by using a benzene–CCl_4 solvent mixture and camphorsulfonic acid as the catalyst at 60 °C for 72 h, giving **3a** in 54% yield after column chromatography. Presumably, the lower polarity of CCl_4 and its consequent lower water-affinity, combined with the lower acidity of camphorsulfonic acid, as compared to *p*-TsOH, might contribute to the higher yield, since a lower degree of polymerization of pyruvaldehyde dimethyl acetal was noticeable. A similar protocol was used to prepare dioxanes **3b–f**, whose yields were in the 35–60% range.

The stereochemical outcome of these transacetalization reactions showed a very similar behavior than those observed in the preparation of 2-acyl-1,3-oxathianes,[6,7] giving in all cases a major predominance for the equatorial isomer of acyldioxanes **3a–f**, as was confirmed by NOE diff. experiments (Scheme 1). As a result, the respective ^{1}H NMR signals of H-3ax (2.0–3.5%) and H-7 (10–11%) were enhanced upon irradiation of the acetalic hydrogen (H-5). The stereochemical information obtained from NOE experiments was further supported by X-ray diffraction analysis of a crystal of benzoyldioxane **3e** (Fig. 2), where the C-3 (*S*)- and C-5 (*R*)-configurations can be appreciated, and a well-defined chair-like conformation of the dioxane ring is evident.

The evaluation of 2-acetyl-1,3-dioxane **3a** to induce diastereofacial nucleophilic additions was tested using a representative series of nucleophiles. The diastereoselective ratios are presented in Table 1. As can be observed, the nucleophilic addition proceeded in good to excellent chemical yields at −78 °C in THF as the solvent, giving carbinol derivatives **6a–h** and **7a–h**. Concerning the stereoselectivity, Grignard reagents (entries 1–7) were the most diastereoselective, followed by PhLi (entry 10), while reduction reactions with $LiAlH_4$ and $NaBH_4$ (entries 8 and 9) lack stereoselectivity. Additions of PhMgBr (entry 4) and PhLi (entry 10) afforded epimer **6d** as the major diastereoisomer, denoting the same diastereofacial attack. In turn, the addition of MeMgBr to benzoyldioxane **3d** gave carbinols **6d** and **7d** in a 13:87 ratio (entry 13), which is essentially the inverse ratio obtained by the addition of PhMgBr to acetyldioxane **3a** (entry 4). The absolute configuration of the new stereogenic center of major carbinol **7d** is *S* as revealed by X-ray diffraction analysis (Fig. 2), denoting the preferred *re* diastereofacial attack of the nucleophile.

To complement this, the addition of PhMgBr on acetyldioxane **3b** gave a mixture of carbinols **6i**:**7i** (entry 11) almost

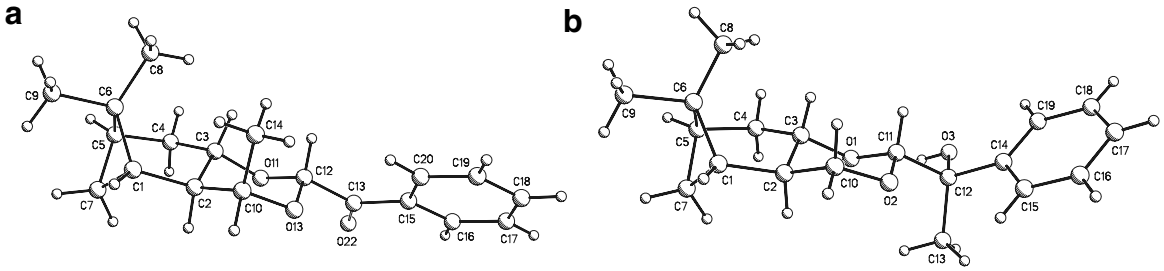


Figure 2. ORTEP X-ray projections of (a) benzoyldioxane **3e** and (b) carbinol **7d**.

Table 1. Chemical yields and diastereomeric ratios of **6**:**7** mixtures obtained from nucleophilic additions on acyldioxanes **3a–f** (Scheme 2)

Entry	Acyldioxane	Reagent	R_4	Yield[a] (%)	Ratio[b]
1	**3a**	EtMgBr	Et	90	98:02 (**6a**:**7a**)
2	**3a**	*i*-PrMgBr	*i*-Pr	86	90:10 (**6b**:**7b**)
3	**3a**	*i*-BuMgBr	*i*-Bu	70	85:15 (**6c**:**7c**)
4	**3a**	PhMgBr	Ph	82	89:11 (**6d**:**7d**)
5	**3a**	$PhCH_2MgCl$	$PhCH_2$	73	80:20 (**6e**:**7e**)
6	**3a**	$CH_2{=}CHMgBr$	$CH_2{=}CH$	85	80:20 (**6f**:**7f**)
7	**3a**	$CH_3C{\equiv}CMgBr$	$CH_3C{\equiv}C$	80	83:17 (**6g**:**7g**)
8	**3a**	$LiAlH_4$	H	95	50:50 (**6h**:**7h**)
9	**3a**	$NaBH_4$	H	93	50:50 (**6h**:**7h**)
10	**3a**	PhLi	Ph	95	70:30 (**6d**:**7d**)
11	**3b**	PhMgBr	Ph	90	88:12 (**6i**:**7i**)
12	**3c**	PhMgBr	Ph	90	67:33 (**6j**:**7j**)
13	**3d**	MeMgBr	Me	98	13:87 (**6d**:**7d**)
14	**3e**	MeMgBr	Me	88	11:89 (**6i**:**7i**)
15	**3f**	PhMgBr	Ph	95	77:23 (**6k**:**7k**)
16	**3f**	PhLi	Ph	92	50:50 (**6k**:**7k**)

[a] Calculated after column chromatography purification as mixture of **6** and **7**.
[b] Determined by ^{1}H NMR integration of H-5 on the crude reaction mixture.

in the same ratio as obtained by the addition of PhMgBr on acetyldioxane **3a** (entry 4). Furthermore, similar ratios from the addition of MeMgBr on benzoyldioxanes **3d** (entry 13) and **3e** (entry 14) were obtained. These results clearly suggest that *axial* substituents at C-3 (or eventually at C-7) do not affect the stereochemical course of the nucleophile, essentially preserving the same diastereoisomeric ratio of their corresponding carbinols as compared with those obtained from acyldioxanes **3a** or **3d** unsubstituted at the C-3 position. In contrast, the addition of PhMgBr was noticeably lower when acetyldioxanes **3c** (entry 12, **6j**:**7j** 67:33) and **3f** (entry 15, **6k**:**7k** 77:23), both bearing an equatorial methyl group at C-3, were used. In turn, the addition of PhLi to **3f** yielded the respective diastereoisomeric mixture in ca. 50:50 ratio (entry 16). These results demonstrate the capability of the equatorial substituent in C-3 (R_2) to modulate the diastereoselectivity of the nucleophilic addition.

The diastereoselectivity can be explained by considering a Cram-type chelated transition state where the metal coordination is shown between O4 (O2 in the X-ray structure) and the oxygen of the carbonyl group (Fig. 3), as was described by Bailey et al.[11] in a similar series of 2-acyl-1,3-dioxanes formed from 2,3-butanediol. In this sense, the coordination capability of both dioxane oxygen atoms is mainly differentiated by the unequal substitution pattern placed at C-3 and C-7, where the equatorial substituent exerts the decisive steric effect that drives the stereochemical course of the incoming nucleophile (Scheme 2). On the other hand, in comparison with 2-acyl-1,3-oxathianes **4a** and **4b**,[6,7] the lower diastereoselectivity observed in 2-acyldioxanes **3a** and **3d** is due to a similar coordination capability of the dioxane oxygen atoms for the metal of the nucleophile, despite the aforementioned unequal substitution pattern. In addition, it is very stimulating to obtain reasonable to good stereoinductions in good yields by using non-sulfur containing molecules.

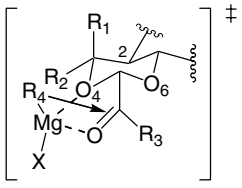
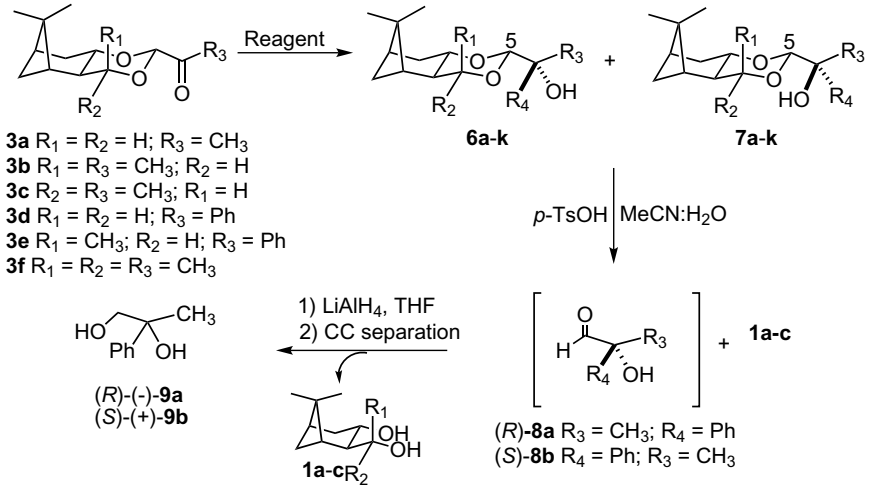


Figure 3. Cram-type chelated transition state showing the preferred coordination site of the Grignard reagents as well as the favored *re* face attack on the carbonyl group.

The diastereofacial preference of the nucleophile was confirmed by hydrolyzing some representative mixtures of carbinols (Scheme 2). Thus, the mixtures of carbinols **6d**:**7d**, obtained by the addition of PhMgBr to **3a** (entry 4), and MeMgBr addition on **3d** (entry 13), were hydrolyzed using a catalytic amount of *p*-TsOH in a CH_3CN–H_2O mixture to give 3,10-pinanediol **1a** and aldehydes **8a** and **8b**, respectively (Scheme 2). A similar protocol was followed to hydrolyze the mixtures of carbinols **6i**:**7i** obtained from the addition of PhMgBr on **3b** (entry 11), or MeMgBr addition on **3d** (entry 13), giving also aldehydes **8a** and **8b**, respectively. Finally, the mixture of carbinols **6i**:**7i**, obtained according to entry 14, was also hydrolyzed to give aldehyde **8b** as the major enantiomer. All the above crude reaction mixtures were treated with $NaBH_4$ in MeOH to afford the more stable 1-phenyl-1,2-ethanodiols **9a** and **9b**, along with the corresponding 3,10-pinanediol. In turn, these mixtures were separated by column chromatography to provide (*R*)-(−)-**9a** as the major enantiomer (64–70% yield, 72–76% ee from mixtures of entries 4 and 11, and 54% ee from entry 15), and (*S*)-(+)-**9b** (72% yield, 72% ee from mixtures of entries 13 and 14), while the corresponding pinanediols were recovered in good yield (70–80%) preserving their original enantiomeric purity.

3. Conclusions

Herein we have reported a very easy protocol to synthesize 3,10-pinanediols **1a**–**d** from (1*R*)-(−)-myrtenal and show for the first time their potential synthetic utility as chiral auxiliaries. Although (*R*)-1,3-butanediol and (*R*,*R*)-2,4-



Scheme 2.

pentanediol are two of the most preferred 1,3-diols to be used as chiral auxiliaries, high costs seriously limit their utilization in multigram scales. Therefore, 3,10-pinanediols **1a–d** offer a practical alternative. Furthermore, X-ray diffraction studies of carbinol **7d** and chemical correlation revealed that nucleophilic additions on acyldioxanes proceeded mainly through the *re*-face of the carbonyl group, a preference which is clearly modulated by the presence of equatorial substituents at C-3. The poorer diastereoselectivities found in acyldioxanes **3a** and **3d**, as compared to acyloxathianes **4a** and **4b**,[6–8] could be due to the similar coordinating capability of both dioxane oxygen atoms for the metal of the nucleophilic reagent. Despite the lower diastereoselectivities obtained, as compared to those obtained using 3-acyl-1,3-oxathianes,[6–8] the present results are a good approach for improving diastereoselectivities in myrtenal-derived acyldioxanes by implementing the proper structural changes.

4. Experimental

4.1. General

Melting points were determined on an electrothermal capillary melting point apparatus and are uncorrected. Optical rotations were measured at 589 nm using a 1 dm cell on a JASCO DIP-370 polarimeter. Infrared spectra were recorded on a Perkin–Elmer Spectrum 2000 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury-300 spectrometer using $CDCl_3$ as solvent and TMS as the internal standard. Chemical shifts are reported in parts per million (δ) downfield from TMS for ^{1}H, and relative to the central line of the triplet of $CDCl_3$ at 77.00 ppm for ^{13}C. The low-resolution mass spectra (LRMS) were recorded on a Varian Saturn 2000 GC/Ion Trap Detector, using either EI (70 eV) or CI, as specified. The high-resolution electron impact mass spectra (HREIMS) were recorded on a VG 7070 high-resolution mass spectrometer at the UCR Mass Spectrometry Facility, University of California, Riverside, CA. Thin-layer chromatograms were done on precoated TLC sheets of silica gel 60 F_{254} (E. Merck). Flash chromatography was carried out using Merck silica gel (230–400 mesh). THF used in the nucleophilic addition reactions was distilled from Na immediately prior to use, and all other reagents were used as received.

4.2. (1*S*,2*R*,3*S*)-2-Hydroxymethyl-6,6-dimethylbicyclo-[3.1.1]heptan-3-ol 1a

A 500-mL oven-dried two-necked round-bottom flask, equipped with a pressure-equalizing addition funnel, was cooled in an ice-water bath and charged with 170 mL of anhydrous THF and 10 mL (9.7 g, 65.7 mmol) of (1*R*)-(−)-myrtenal **2** under a nitrogen atmosphere. A solution of 13.5 mL of 10–10.2 M (136.4 mmol) BH_3–Et_2O in 30 mL of THF was added dropwise through the addition funnel during 30 min. The resulting mixture was stirred at 0–4 °C for 3 h and further 24 h at room temperature. The mixture was cooled again in an ice-water bath and 10 mL of water was added dropwise over 30 min and stirring was continued for 2 h at the above temperature. Once the reaction reached room temperature, 45 mL of 3 M NaOH were added at once, followed by the dropwise addition of 30 mL of 30% H_2O_2 over 30 min, the mixture was stirred for an additional 1.5 h. Excess THF was eliminated in a rotary evaporator, the residue was extracted with CH_2Cl_2 (2 × 60 mL) and the organic layer was dried with anhydrous Na_2SO_4, filtered, and evaporated to dryness. The solid residue was washed with hexane (2 × 25 mL) and dissolved in 250 mL of a mixture of hexane–CH_2Cl_2 (3:1). The organic layer was washed with water (5 × 20 mL), dried with anhydrous Na_2SO_4, and evaporated to dryness. The solid was recrystallized from hexane–$CHCl_3$, giving 8.75 g (78%) of 3,10-pinanediol **1** as colorless crystals (mp 78–80 °C; R_f 0.39, hexane–EtOAc 9:1). $[\alpha]_D^{25} = +14.4$ (*c* 0.12, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 4.31 (dt, 1H, $J = 9.5$, $J = 5.1$ Hz, H-3), 3.62–3.78 (m, 2H, H-10a and H-10b), 2.37–2.58 (m, 3H, H-7e, H-2, H-4e), 1.96 (m, 1H, H-5), 1.89 (br t, 1H, $J = 5.5$ Hz, H-1), 1.74 (ddd, 1H, $J = 13.8$, 4.8, 2.4 Hz, H-4a), 1.65 (br s, 2H, OH), 1.21 (s, 3H, Me-9), 1.14 (d, 1H, $J = 9.6$ Hz, H-7a), 0.88 (s, 3H, Me-8). ^{13}C NMR ($CDCl_3$): δ 68.2 (C-3), 67.0 (C-1′), 55.4 (C-2), 43.4 (C-1), 41.8 (C-5), 38.0 (C-6), 37.7 (C-4), 34.1 (C-7), 27.4 (C-9), 23.9 (C-8). IR ($CHCl_3$): 3449, 3018, 2934, 1638, 1544, 1427, 1336, 1234, 1137, 933, 762, 453 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.41; H, 10.50.

4.3. (1*R*)-10,10-Dimethylmyrtenol 5d

To a cooled solution (−78 °C) of 2 g (12.17 mmol) of 10-methylmyrtenone[12] in 20 mL of anhydrous THF was added 1.3 equiv of MeMgBr, and the resulting mixture was stirred at the same temperature for 2 h under an N_2 atmosphere. The crude reaction mixture was poured into ice-water and was extracted (2 × 70 mL) with CH_2Cl_2, washed with brine, dried with anhydrous Na_2SO_4, filtered, and concentrated to dryness. The residue was purified through column chromatography (hexane–EtOAc 4:1) giving 1.93 g (88%) of carbinol **5d** as a colorless syrup. R_f 0.36, hexane–EtAOc 4:1. $[\alpha]^{23} = -38.3$ (*c* 1.71, MeOH). ^{1}H NMR ($CDCl_3$): δ 5.46 (m, 1H, H-3), 2.41 (m, 1H, H-7eq), 2.33 (m, 1H, H-5), 2.26 (m, 2H, H-4eq, H4ax), 2.09 (m, 1H, H-1), 1.48 (s, 1H, OH), 1.30 (s, 3H, Me-9), 1.26–1.25 (s, 6H, Me-11a, Me-11b), 1.13 (d, 1H, $J = 8.8$ Hz, H-7ax), 0.82 (s, 3H, Me-8). ^{13}C NMR ($CDCl_3$): δ 153.9 (C-10), 113.4 (C-3), 72.0 (C-2), 42.7 (C-5), 40.7 (C-1), 37.5 (C-6), 31.7 (C-7), 30.9 (C-4), 27.9 (C-11), 27.6 (C-12), 26.2 (C-9), 21.2 (C-8). MS *m*/*z* (rel. int.): 162 (M^+−18, 22), 147 (17), 133 (4), 119 (79), 105 (46), 91 (100), 77 (29), 65 (10), 53 (7), 41 (16), 27 (5). HRFABMS calcd for $C_{12}H_{20}O$+H 181.2945. Found 181.2939.

4.4. (1*S*,2*R*,3*S*,10*S*)-2-(1-Hydroxyethyl)-6,6-dimethylbicyclo[3.1.1]heptan-3-ol 1b

Obtained as described in Section 4.2, in 50% yield, after column chromatography, from the hydroboration–oxidation of the epimeric mixture of **5b** and **5c**, as colorless crystals, mp 105–107 °C. $[\alpha]^{23} = +30.4$ (*c* 0.21, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 4.05 (dt, 1H, $J = 10.8$, 5.0 Hz, H-3), 3.81 (dc, 1H, $J = 10.2$, 7.0 Hz, H-10eq), 2.60–2.42 (m,

2H, H-7eq, H-2), 2.30 (m, 1H, H-4eq), 1.95 (m, 1H, H-1), 1.75 (m, 2H, H-4a H-5), 1.35 (d, 3H, $J = 7.0$ Hz, Me-11), 1.25 (s, 3H, Me-9), 1.09 (d, 1H, $J = 10.5$ Hz, H-7ax), 0.90 (s, 3H, Me-8). ^{13}C NMR ($CDCl_3$): δ 70.1 (C-3), 66.2 (C-1′), 50.8 (C-2), 42.0 (C-1), 41.6 (C-5), 38.3 (C-4), 37.8 (C-6), 33.3 (C-7), 27.4 (C-9), 23.9 (C-8), 22.6 (C-11). IR ($CHCl_3$): 3604, 3450, 3020, 2990, 2930, 1470, 1244, 1088, 788 cm^{-1}. The structure of **1b** was fully characterized by single crystal X-ray analysis as shown in Figure 1.

4.5. (1*S*,2*R*,3*S*,10*R*)-2-(1-Hydroxyethyl)-6,6-dimethylbicyclo[3.1.1]heptan-3-ol 1c

Obtained as described in Section 4.2, in 30% yield, after column chromatography, from the hydroboration–oxidation of the epimeric mixture of **5b** and **5c**, as colorless needles, mp 58–59 °C. $[\alpha]^{23} = +25.1$ (c 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 4.47 (s, 1H, H-3), 3.84 (m, 1H, H-10), 3.26 (s, 1H, –OH), 3.08 (s, 1H, –OH), 2.49 (m, 1H, H-4ec), 2.39 (M, H1-7ec), 1.99–1.90 (m, 2H, H-1, H-5), 1.78 (m, 1H, H-4ax), 1.74 (m, 1H, H-2), 1.20 (s, 3H, Me-9), 1.19 (d, 3H, $J = 6$ Hz, Me-11), 1.09 (d, 1H, $J = 10$ Hz), 0.89 (s, 3H, Me-8). ^{13}C NMR ($CDCl_3$): δ 72.0 (C-10), 68.6 (C-3), 60.9 (C-2), 43.5 (C-1), 41.9 (C-5), 38.2 (C-6), 37.2 (C-4), 34.1 (C-7), 27.8 (C-9), 24.2 (C-8), 22.8 (C-11). MS m/z (rel. int.): 285 (M^++1, 0.3), 149 (10), 123 (179), 109 (10), 107 (41), 105 (22), 96 (20), 95 (35), 92 (23), 90 (30), 80 (89), 79 (75), 78 (29), 77 (15), 71 (100), 70 (17), 69 (12), 67 (41), 55 (29), 43 (35), 41 (33), 39 (18). HRES-I/APCI MS calcd for $C_{11}H_{20}O_2$+NH_4 202.1807. Found 202.1804.

4.6. (1*S*,2*S*,3*S*)-2-(1-Hydroxy-1-methylethyl)-6,6-dimethylbicyclo[3.1.1]heptan-3-ol 1d

Obtained as described in Section 4.2 in 87% yield by hydroboration–oxidation of **5d**, as colorless crystals, mp 60–61 °C. $[\alpha]^{23} = +33.6$ (c 1.28, MeOH). ^{1}H NMR ($CDCl_3$): δ 4.59 (dt, 1H, $J = 7.7$, 6.6 Hz, H-3), 3.14 (s, 1H, OH), 2.55 (m, 1H, H-7eq), 2.52 (m, 1H, H-4eq), 2.11 (dd, 1H, $J = 7.7$ Hz, H-2), 1.98 (m, 2H, $J = 6.6$ Hz, H-1, H-5), 1.73 (ddd, 1H, $J = 13.2$, 5.5, 6.6 Hz, H-4ax), 1.28 (s, 3H, Me-9), 1.23–1.21 (s, 6H, H-11a, H-11b), 1.08 (d, 1H, $J = 9.9$ Hz, H-7ax), 0.97 (s, 3H, Me-8). ^{13}C NMR ($CDCl_3$): δ 74.1 (C-10), 65.6 (C-3), 62.7 (C-2), 44.5 (C-5), 42.5 (C-1), 38.3 (C-6), 37.8 (C-7), 37.1 (C-4), 31.4 (C-9), 28.4 (C-12), 26.6 (C-11), 26.0 (C-8). IR ($CHCl_3$): 3337, 2929, 1464, 1385, 1367 cm^{-1}. MS m/z (rel. int.): 180 (M^+−18, 0.6), 165 (2), 147 (2), 137 (6), 129 (14), 107 (26), 95 (23), 79 (100), 78 (44), 59 (73), 43 (53), 41 (51), 39 (20), 27 (9). HRFABMS calcd for $C_{12}H_{22}O_2$+H 199.1698. Found 199.1691.

4.7. General procedure for the preparation of acyldioxanes 3a–f

These compounds can be obtained using either of the following methods.

4.7.1. Method A. A 100 mL oven-dried two-necked round-bottom flask equipped with a Dean–Stark trap and a magnetic stirring bar, containing a solution of 0.93 mmol of diols **1a–d** and 1.39 mmol of *p*-TsOH in 25 mL of anhydrous benzene, was placed in an oil bath and warmed to 74–78 °C. Then, 1.7 mmol of α,α-dialkoxyacetal were added dropwise, and the resulting mixture was stirred at the above temperature under a nitrogen atmosphere for 3.5 h. The reaction mixture was allowed to reach room temperature and 40 mL of hexane was added. The organic layer was washed with 10 mL of a 5% aqueous solution of $NaHCO_3$, dried with anhydrous Na_2SO_4, filtered, and evaporated to dryness in a rotary evaporator at 40–45 °C under a reduced pressure. The oily residue was purified by column chromatography using silica gel alkalinized with Et_3N and a mixture of hexane–EtOAc (99:1) to give acyldioxanes **3a–f**.

4.7.2. Method B. In a 100 mL oven-dried two-necked round-bottom flask equipped with a magnetic stirring bar, thermometer, and condenser were dissolved 1.8 mmol of diol **1a–c** and 30 mg of camphorsulfonic acid in 6 mL of benzene under gentle warming. A solution of 3.22 mmol of α,α-dialkoxyacetal in 20 mL of CCl_4 was added and the resulting mixture was warmed at 60–62 °C for 48 h. An additional 0.2 mL (190 mg, 161.0 mmol) of pyruvic aldehyde dimethyl acetal was added and stirring continued at the above temperature for further 24 h. After the reaction mixture was allowed to reach room temperature, it was filtered through 2 g of silica gel alkalinized with Et_3N, which was washed with 10 mL of hexane. The crude reaction mixture was evaporated to dryness in a rotary evaporator at 40–45 °C under reduced pressure. The residue was purified by column chromatography packed with silica gel alkalinized with Et_3N and using hexane–EtOAc 99:1 as mobile phase.

4.7.3. (1*S*,2*R*,5*R*,7*S*,9*R*)-5-Acetyl-10,10-dimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 3a. Obtained using either method A (38%) or method B (54%). Colorless syrup (R_f 0.33, hexane–EtOAc 10:1). $[\alpha]_D^{25} = -2.0$ (c 0.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 4.97 (s, 1H, H-5), 4.45 (br q, 1H, $J = 9.3$ Hz, H-7), 4.12 (dd, 1H, $J = 12.0$, 4.0 Hz, H-3eq), 3.80 (t, 1H, $J = 12.0$ Hz, H-3ax), 2.63 (m, 1H, H-11eq), 2.46–2.3 (m, 2H, H-8eq, H-2), 2.28 (s, 3H, Me-2′), 2.14 (m, 1H, H-9), 1.94–1.83 (m, 2H, H-1, H-8ax), 1.30 (s, 3H, Me-13), 1.12 (s, 3H, Me-12), 1.08 (d, 1H, $J = 11.5$ Hz, H-11ax). ^{13}C NMR ($CDCl_3$): δ 201.8 (C=O), 101.9 (C-5), 77.7 (C-7), 73.2 (C-3), 48.6 (C-2) 43.7 (C-1), 43.1 (C-9), 40.4 (C-11), 38.9 (C-10), 32.9 (C-8), 29.8 (C-13), 25.1 (C-12), 25.0 (C-2′). IR ($CHCl_3$): 2925, 1756, 1466, 1353, 1196, 1138, 1090, 996, 932, 881, 830, 769, 600 cm^{-1}. MS m/z (rel. int.) 224 (M^+, 0.1), 181 (50), 135 (56), 107 (50), 105 (13), 93 (54), 91 (47), 81 (16), 79 (61), 67 (38), 53 (20), 43 (100), 39 (25).

4.7.4. (1*S*,2*R*,3*S*,5*R*,7*S*,9*R*)-5-Acetyl-3,10,10-trimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 3b. Obtained using method A (45%) as a colorless syrup. $[\alpha]_D^{23} = -36$ (c 0.15, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.17 (s, 1H, H-5), 4.70 (br q, 1H, $J = 9.7$ Hz, H-7), 4.38 (dq, 1H, $J = 6.3$, 5.4 Hz, H-3), 2.71 (dd, 1H, $J = 4.3$, 9.7 Hz, H-2), 2.65 (m, 1H, H-11eq), 2.40 (m, 1H, H-8eq), 2.25 (s, 3H, Me-2′), 2.13 (m, 1H, H-9), 1.85 (m, 2H, H-1, H-8ax), 1.35 (d, 3H, $J = 6.3$ Hz, Me-14), 1.28 (s, 3H, Me-13), 1.12 (d, 1H,

$J = 7.8$ Hz, H-11ax), 1.11 (s, 3H, Me-12). ^{13}C NMR ($CDCl_3$): δ 202.5 (C=O), 95.9 (C-5), 74.6 (C-3), 70.0 (C-7), 51.5 (C-2), 44.2 (C-1), 43.4 (C-9), 41.5 (C-11), 39.4 (C-10), 32.8 (C-8), 29.9 (C-13), 25.8 (C-12), 25.0 (C-2′), 13.4 (C-14). IR ($CHCl_3$): 2925, 1721, 1190, 1145, 1088 cm^{-1}. MS *m/z* (rel. int.): 237 (M^++1, 0.1), 195 (32), 149 (40), 107 (63), 91 (37), 79 (57), 43 (100).

4.7.5. (1*S*,2*R*,3*R*,5*R*,7*S*,9*R*)-5-Acetyl-3,10,10-trimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 3c. Obtained using method A (63%) as a colorless syrup. $[\alpha]_D^{23} = -28.4$ (*c* 0.44, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.0 (s, 1H, H-5), 4.42 (dd, 1H, H-7), 3.88 (m, 1H, H-3), 2.59 (m, 1H, H-11eq), 2.39 (m, 1H, H-8eq), 2.26 (s, 3H, Me-16), 2.12 (m, 1H, H-9), 2.02 (m, 1H, H-1), 1.89 (m, 2H, H-8ax, H-2), 1.29 (s, 3H, Me-13), 1.25 (d, 3H, $J = 6$ Hz, Me-14), 1.10 (s, 3H, Me-12), 1.02 (d, 1H, $J = 9.6$ Hz, H-11ax). ^{13}C NMR ($CDCl_3$): δ 202.3 (C-15), 101.9 (C-5), 79.4 (C-3), 76.8 (C-7), 55.3 (C-2), 43.2 (C-9), 43.1 (C-1), 40.2 (C-11), 39.1 (C-10), 33.1 (C-8), 30.1 (Me-13), 25.4 (Me-12), 30.1 (Me-16), 18.7 (Me-14). IR ($CHCl_3$): 2982, 2936, 1744, 1272, 1228, 1174 cm^{-1}. MS *m/z* (rel. int.): 239 (M^++1, 66), 316 (M^+, 2.26), 167 (30), 149 (100), 123 (8), 107 (13), 93 (13). HRES-I/APCI MS calcd for $C_{14}H_{22}O_3$+Na 261.1467. Found 261.1462.

4.7.6. (1*S*,2*R*,5*R*,7*S*,9*R*)-5-Benzoyl-10,10-dimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 3d. Obtained using method A (60%) as a colorless syrup. $[\alpha]_D^{25} = -6.3$ (*c* 0.74, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.14 (d, 2H, $J = 7.1$ Hz, H-*ortho*), 7.60 (t, 1H, $J = 7.4$ Hz, H-*para*); 7.50 (t, 2H, $J = 7.3$ Hz, H-*meta*), 5.71 (s, 1H, H-5), 4.62 (br q, 1H, $J = 9.4$ Hz, H-7), 4.22 (dd, 1H, $J = 10.1$, 3.7 Hz, H-3eq), 3.94 (t, 1H, $J = 10.1$ Hz, H-3ax), 2.64 (m, 1H, H-11eq), 2.69–2.39 (m, 2H, H-8eq and H-2), 2.16 (m, 1H, H-9), 2.01–1.89 (m, 2H, H-1 and H-8ax), 1.31 (s, 3H, CH_3-13), 1.18 (s, 3H, CH_3-12), 1.13 (d, 1H, $J = 9.8$ Hz, H-11ax). ^{13}C NMR ($CDCl_3$): δ 181.1 (C=O); 133.9 (C-*ipso*); 133.6 (C-*para*); 130.0 (C-*ortho*); 128.4 (C-*meta*), 102.0 (C-5), 78.5 (C-7), 73.8 (C-3), 48.9 (C-2), 43.9 (C-1), 43.0 (C-9), 40.5 (C-11), 39.0 (C-10), 33.0 (C-8), 30.0 (C-12). IR ($CHCl_3$): 2970, 1719, 1595, 1460, 1384, 1255, 1177 cm^{-1}. Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.42; H, 7.74. Found: C, 75.29; H, 7.64.

4.7.7. (1*S*,2*R*,3*S*,5*R*,7*S*,9*R*)-5-Benzoyl-3,10,10-trimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 3e. Obtained using method A (50%) as a colorless crystals, mp 85–86 °C. $[\alpha]_D^{28} = -36.4$ (*c* 0.44, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.14 (d, 2H, $J = 8.1$ Hz, H-*ortho*), 7.56 (t, 1H, $J = 6.4$ Hz, H-*meta*), 7.45 (dd, 2H, $J = 8.4$, 6.4 Hz, H-*para*), 5.93 (s, 1H, H-5), 4.85 (br q, 1H, $J = 9.8$ Hz, H-7), 4.48 (dq, 1H, $J = 7.1$, 5.4 Hz, H-3), 2.89 (dd, 1H, $J = 9.8$, 5.4 Hz, H-2), 2.68 (m, 1H, H-11eq), 2.44 (m, 1H, H-8eq), 2.25 (m, 1H, H-9), 1.92 (s, 2H, H-1, H-8ax), 1.46 (d, 3H, $J = 7.1$ Hz, Me-14), 1.30 (s, 3H, Me-13), 1.18 (d, 1H, $J = 10.4$ Hz, H-11ax), 1.16 (s, 3H, M-12). ^{13}C NMR ($CDCl_3$): δ 191.5 (C=O), 133.9 (C-*ipso*). 133.4 (C-*meta*), 129.9 (C-*para*), 128.3 (C-*ortho*), 95.7 (C-5), 75.0 (C-3), 70.7 (C-7), 51.6 (C-2), 44.3 (C-1), 43.4 (C-9), 41.5 (C-11), 39.4 (C-10), 32.8 (C-8), 29.9 (C-13), 25.8 (C-12), 13.4 (C-14). Anal. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.97; H, 8.14.

4.7.8. (1*S*,2*S*,5*R*,7*S*,9*R*)-5-Acetyl-3,3,10,10-tetramethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 3f. Obtained using method B (45%) as a colorless syrup. $[\alpha]_D^{25} = +16.5$ (*c* 0.34, CH_3OH). ^{1}H NMR ($CDCl_3$): δ 5.09 (s,1H, H-5), 4.59 (br q, 1H, $J = 9.3$ Hz, H-7), 2.67 (m 1H, H-11eq), 2.40 (m, 1H, H-8eq), 2.24 (m, 1H, H-2), 2,21 (s, 3H, Me-2′), 2.11 (q, 1H, $J = 6.1$ Hz, H-9), 1.97 (t, 1H, $J = 6.0$ Hz, H-1), 1.83 (m, 1H, H-8ax), 1.30 (s, 3H, Me-15), 1.28 (s, 6H, Me-13, Me-14), 1.09 (s, 3H, Me-12), 1.08 (d, 1H, $J = 9.6$ Hz, H-11ax). ^{13}C NMR ($CDCl_3$): δ 202.8 (C=O), 96.8 (C-5), 78.1 (C-3), 71.0 (C-7), 57.8 (C-2), 43.3 (C-1), 43.2 (C-9), 41.4 (C-11), 39.3 (C-10), 32.9 (C-8), 29.9 (C-13) 29.2 (C-15), 25.5 (C-12), 24.8 (C-2′), 19.0 (C-14). IR ($CHCl_3$): 2926, 1736, 1457, 1389, 1234, 1148, 1078, 919 cm^{-1}.

4.8. General procedure for the addition of Grignard reagents to acyldioxanes 3a–e

To a solution of acyldioxanes **3a**–**f** (1 equiv) in anhydrous THF was added the Grignard reagent (1.5–2 equiv) at −78 °C in an N_2 atmosphere. After stirring for 2 h at the same temperature, the reaction mixture was allowed to warm up to room temperature and stirred for a further 1 h. The reaction mixture was quenched with 10 mL of a saturated solution of ammonium chloride, the THF was eliminated by evaporation under reduced pressure, and the remaining emulsion was extracted with ethyl ether. The organic layer was washed with a saturated solution of ammonium chloride, dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness, to give the corresponding mixture of carbinols as colorless oils. Column chromatographic separations were unsuccessful due to the very close R_f of the resulting mixture of diastereoisomers; therefore, specific rotations are not reported. Only spectroscopic data for the major diastereomers **6a**–**k**, **7d**, and **7i**, obtained from the spectra of their corresponding mixtures, are described.

4.8.1. (1*S*,2*R*,5*R*,7*S*,9*R*,2′*R*)-5-(2′-Hydroxybut-2′-yl)-10,10-dimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 6a. Obtained following the general procedure, compound **3a** (111 mg, 0.49 mmol) in anhydrous THF (10 mL) was treated with 3 M EtMgBr (0.49 mL, 1.48 mmol) in diethyl ether. After workup 114 mg (90%) of a diastereoisomeric mixture of carbinols **6a**:**7a** (49:1) was obtained as a colorless syrup (R_f 0.44, hexane–EtOAc 9:1). ^{1}H NMR ($CDCl_3$): δ 4.55 (s, 1H, H-5), 4.35 (br q, 1H, $J = 9.3$ Hz, H-7), 4.02 (dd, 1H, $J = 10.1$, 3.8 Hz, H-3eq), 3.72 (dd, 1H, $J = 10.1$, 9.8 Hz, H-3ax), 2.61 (m, 1H, H-11eq), 2.33 (m, 1H, H-8eq), 2.25–2.08 (m, 3H, H-2, OH, H-9), 1.88–1.80 (m, 2H, H-1, H-8ax), 1.58 (m, 2H, H-3′a, H-3′b), 1.27 (s, 3H, Me-1′), 1.16 (s, 3H, Me-13), 1.11 (s, 3H, Me-12), 1.04 (d, 1H, $J = 9.7$ Hz, H-11ax), 0.93 (t, 3H, $J = 7.5$ Hz, CH_3-4′). ^{13}C NMR ($CDCl_3$): δ 106.5 (C-5), 77.4 (C-7), 73.6 (C-2′), 73.1 (C-3), 49.1 (C-2), 43.1 (C-1), 43.4 (C-9), 40.6 (C-11), 39.1 (C-10), 33.3 (C-8), 30.2 (C-1′), 29.8 (C-3′), 25.4 (C-12), 21.3 (C-13), 7.7 (C-4′). IR ($CHCl_3$): 3585, 2936, 1457, 1368, 1140, 1093 cm^{-1}. MS *m/z* (rel. int.): 254 (M^++1, 1), 153 (24), 135 (100), 125 (14), 107 (12), 93 (8). HRCIMS calcd for $C_{15}H_{26}O_3$+NH_4 272.2226. Found 272.2227.

4.8.2. (1*S*,2*R*,5*R*,7*S*,9*R*,2′*R*)-5-(3′-Methyl-2′-hydroxybut-2′-yl)-10,10-dimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 6b. Obtained following the general procedure, compound **3a** (174 mg, 0.77 mmol) in anhydrous Et_2O (10 mL) was treated with freshly prepared *i*PrMgBr (1.54 mmol) in diethyl ether. After workup 179 mg (86%) of a diastereoisomeric mixture of carbinols **6b**:**7b** (9:1) was obtained as a colorless syrup (R_f 0.33, hexane–EtOAc 9:1). ^{1}H NMR ($CDCl_3$): δ 4.65 (s, 1H, H-5), 4.36 (br q, 1H, $J = 9.6$ Hz, H-7), 4.04 (dt, 1H, $J = 9.9$, 3.3 Hz, H-3eq), 3.72 (br t, 1H, $J = 10.0$ Hz, H-3ax), 2.58 (m, 1H, H-11eq), 2.33 (m, 1H, H-8eq), 2.26–2.16 (m, 2H, OH, H-2), 2.11 (br q, 1H, $J = 5.6$ Hz, H-9), 1.95 (m, 1H, H-3′), 1.90–1.80 (m, 2H, H-1, H-8a), 1.27 (s, 3H, Me-1′), 1.12 (s, 3H, Me-13), 1.10 (s, 3H, Me-12), 1.04 (d, 1H, $J = 9.6$ Hz, H-11ax), 0.96 (d, $J = 6.9$ Hz, CH_3-4′), 0.91 (d, $J = 6.9$ Hz, CH_3-5′). ^{13}C NMR ($CDCl_3$): δ 105.3 (C-5), 77.6 (C-7), 75.4 (C-2′), 73.2 (C-3), 49.2 (C-2), 44.0 (C-1), 43.4 (d, C-9), 40.7 (C-11), 39.2 (C-10), 33.3 (C-8), 33.2 (C-3′), 30.2 (C-1′), 25.4 (C-13), 18.1 (C-12), 17.0 (C-4′), 16.9 (C-5′). IR ($CHCl_3$): 3584, 2936, 1466, 1367, 1091, 919 cm^{-1}. MS *m*/*z* (rel. int.): 269 (M^++1, 0.1), 251 (1), 225 (3), 181 (37), 153 (8), 135 (98), 107 (41), 93 (52), 82 (100), 67 (22), 43 (25). HRESIMS calcd for $C_{16}H_{28}O_3$+Na 291.1936. Found 291.1949.

4.8.3. (1*S*,2*R*,5*R*,7*S*,9*R*,2′*R*)-5-(4′-Methyl-2′-hydroxypent-2′-yl)-10,10-dimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 6c. Obtained following the general procedure, compound **3a** (148 mg, 0.66 mmol) in anhydrous THF (10 mL) was treated with *i*BuMgBr (0.99 mL, 1.98 mmol) in diethyl ether. After workup 130 mg (70%) of a diastereoisomeric mixture of carbinols **6c**:**7c** (85:15) was obtained as a colorless syrup (R_f 0.39, hexane–EtOAc 9:1). ^{1}H NMR ($CDCl_3$): δ 4.49 (s, 1H, H-5), 4.34 (br q, 1H, $J = 9.4$ Hz, H-7), 4.02 (dd, 1H, $J = 10.0$, 3.7 Hz, H-3eq), 3.71 (dd, 1H, $J = 11.3$, 10.1 Hz, H-3ax), 2.58 (m, 1H, H-11eq), 2.33 (m, 1H, H-8eq), 2.25–2.15 (m, 3H, H-2, OH, H-9), 1.92–1.78 (m, 3H, H-1, H-8ax, H-4′), 1.45 (m, 2H, H-3′a, H-3′b), 1.27 (s, 3H, CH_3-1′), 1.19 (s, 3H, Me-13), 1.11 (s, 3H, Me-12), 1.05 (d, 1H, $J = 9.7$ Hz, H-11ax), 0.98 (d, 3H, $J = 6.6$ Hz, CH_3-5′), 0.95 (d, 3H, $J = 6.7$ Hz, CH_3-6′). ^{13}C NMR ($CDCl_3$): δ 106.9 (C-5), 77.2 (C-7), 73.8 (C-2′), 72.9 (C-3), 48.9 (C-2), 44.9 (C-3′), 43.8 (C-1), 43.2 (C-9), 40.4 (C-11), 38.9 (C-10), 33.0 (C-8), 29.9 (C-1′), 25.1 (C-12), 25.1 (C-6′), 24.5 (C-5′), 23.5 (C-4′), 21.8 (C-13). IR ($CHCl_3$): 3585, 2950, 1466, 1367, 1092, 958 cm^{-1}. MS *m*/*z* (rel. int.): 282 (M^+−1, 2), 181 (41), 135 (100), 107 (41), 93 (48), 82 (76), 79 (39), 67 (13), 57 (10), 43 (13). HRESIMS calcd for $C_{30}H_{30}O_3$+Na 305.2092. Found 305.2102.

4.8.4. (1*S*,2*R*,5*R*,7*S*,9*R*,1′*R*)-5-(1′-Hydroxy-1′-phenyleth-1′-yl)-10,10-dimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 6d. This compound was prepared according to the following procedures.

4.8.4.1. Method A. A well-stirred cooled (−78 °C) solution of 120 mg (0.53 mmol) of acetyloxathiane **3a** in 8 mL of anhydrous THF was treated with 0.89 mmol of 1.8 M PhLi in cyclohexane and stirred under an N_2 atmosphere for 2 h. The mixture was quenched with 1.5 mL of a saturated soln. of ammonium chloride and allowed to warm up to room temperature. The THF was evaporated and the residue extracted with 70 mL of ethyl ether. The organic layer was washed with 5% aq HCl (3 × 30 mL) and brine (1 × 30 mL), dried over anhyd Na_2SO_4, filtered, and evaporated to dryness. The crude reaction outcome was purified through a Chromatotron system using a mixture of hexane–EtOAc (99:1) as the eluent to give 154 mg (95%) of a mixture of **6d**:**7d** (7:3) as a colorless syrup.

4.8.4.2. Method B. Following the general procedure described in 4.8, the addition of PhMgBr on acetyldioxane **3a** gave an 82% of a mixture of **6d**:**7d** (89:11) as a colorless syrup (R_f 0.37, hexane–EtOAc 9:1). ^{1}H NMR ($CDCl_3$): δ 7.55 (d, 2H, $J = 8.6$ Hz, H-*ortho*), 7.34 (dd, 2H, $J = 8.6$, 7.2 Hz, H-*meta*), 7.27 (t, 1H, $J = 7.2$ Hz, H-*para*), 4.85 (s, 1H, H-5), 4.36 (br q, 1H, $J = 9.4$ Hz, H-7), 4.01 (dd, 1H, $J = 10.0$, 3.7 Hz, H-3eq), 3.69 (dd, 1H, $J = 11.3$, 10.2 Hz, H-3ax), 3.04 (s, 1H, OH), 2.58 (m, 1H, H-11eq), 2.40–2.20 (m, 2H, H-2, H-8eq), 2.11 (br q, 1H, $J = 5.6$ Hz, H-9), 1.85 (m, 2H, H-8ax, H-1), 1.56 (s, 3H, Me-2′), 1.27 (s, 3H, Me-13), 1.09 (s, 3H, Me-12), 1.05 (d, 1H, $J = 9.7$ Hz, H-11ax). ^{13}C NMR ($CDCl_3$): δ 144.6 (C-*ipso*), 127.8 (C-*meta*), 126.7 (C-*para*), 125.5 (C-*ortho*), 106.1 (C-5), 77.2 (C-7), 74.8 (C-1′), 73.0 (C-3), 48.7 (C-2), 43.7 (C-9), 43.1 (C-1), 40.3 (C-11), 38.9 (C-10), 32.9 (C-8), 29.9 (C-13), 25.1 (C-12), 25.0 (C-2′). IR ($CHCl_3$): 3585, 2927, 1495, 1447, 1367, 1091, 699 cm^{-1}. MS *m*/*z* (rel. int.): 301 (M^+−1, 1), 285 (7), 181 (4), 135 (100), 133 (28), 107 (11), 93 (11), 67 (14), 55 (14). HRCIMS calcd for $C_{19}H_{26}O_3$+NH_4 320.2226. Found 320.2228.

4.8.5. (1*S*,2*R*,5*R*,7*S*,9*R*,2′*R*)-5-(2′-Hydroxy-3-phenylpropane-2′-yl)-10,10-dimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 6e. Obtained following the general procedure, compound **3a** (210 mg, 0.93 mmol) in anhydrous THF (12 mL) was treated with $PhCH_2MgCl$ (1.40 mL, 2.81 mmol) in diethyl ether. After workup 216 mg (73%) of a diastereoisomeric mixture of carbinols **6e**:**7e** (4:1) was obtained as a colorless syrup (R_f 0.39, hexane–EtOAc 9:1). ^{1}H NMR ($CDCl_3$): δ 7.27 (m, 5H, Ar-H), 4.48 (s, 1H, H-5), 4.31 (br q, 1H, $J = 9.4$ Hz, H-7), 4.06 (dd, 1H, $J = 9.9$, 3.9 Hz, H-3eq), 3.71 (dd, 1H, $J = 11.2$, 10.1 Hz, H3ax), 2.85 (d, 1H, $J = 13.5$ Hz, H-3′a), 2.82 (d, 1H, $J = 13.5$ Hz, H-3′b), 2.59 (m, 1H, H-11eq), 2.29–2.19 (m, 3H, H-8eq, OH, H-2), 2.11 (m, 1H, H-9), 1.85 (m, 2H, H-1, 8ax), 1.27 (s, 3H, Me-1′), 1.14 (s, 3H, Me-13), 1.09 (s, 3H, Me-12), 1.04 (d, 1H, $J = 9.8$ Hz, H-11ax). ^{13}C NMR ($CDCl_3$): δ 137.6 (C-*ipso*), 131.0 (C-*meta*), 128.1 (C-*ortho*), 126.4 (C-*para*), 105.8 (C-5), 77.5 (C-7), 73.7 (C-2′), 73.1 (C-3), 49.1 (C-2), 44.0 (C-1), 43.4 (C-9), 43.3 (C-3′), 40.7 (C-11), 39.2 (C-10), 33.3 (C-8), 30.2 (C-1′), 25.4 (C-12), 22.1 (C-13). IR ($CHCl_3$): 3501, 2924, 1492, 1454, 1367, 1140, 701 cm^{-1}. MS *m*/*z* (rel. int.): 298 (M^+−18, 1), 224 (3), 135 (100), 107 (39), 91 (37), 67 (20), 43 (13), 41 (12), 39 (14). HRCIMS calcd for $C_{20}H_{28}O_3$+NH_4 334.2382. Found 334.2389.

4.8.6. (1*S*,2*R*,5*R*,7*S*,9*R*,2′*R*)-5-(2′-Hydroxy-3′-buten-2′-yl)-10,10-dimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 6f. Obtained following the general procedure, compound **3a** (120 mg, 0.53 mmol) in anhydrous THF (10 mL) was treated with CH_2=CHMgBr (1.60 mL, 1.52 mmol) in diethyl ether. After workup 114 mg (85%) of a diastereoisomeric

mixture of carbinols **6f**:**7f** (4:1) was obtained as a colorless syrup (R_f 0.39, hexane–EtOAc 9:1). ^{1}H NMR ($CDCl_3$): δ 6.06 (dd, 1H, $J = 17.4$, 10.8 Hz, H-3′), 5.38 (d, 1H, $J = 17.3$ Hz, H-4′), 5.15 (d, 1H, $J = 10.8$ Hz, H-4′), 4.58 (s, 1H, H-5), 4.36 (br q, 1H, $J = 9.3$ Hz, H-7); 4.04 (dd, 1H, $J = 10.8$, 3.6 Hz, H-3eq), 3.72 (dd, 1H, $J = 10.8$ Hz, H-3ax), 2.58 (m, 1H, H-11eq), 2.46 (br s, 1H, OH), 2.33 (m, 1H, H-8eq), 2.20 (m, 1H, H-2), 2.10 (m, 1H, H-9), 1.86–1.80 (m, 2H, H-1 and H-8a), 1.28 (s, 3H, Me-1′), 1.27 (s, 3H, Me-13), 1.10 (s, 3H, Me-12), 1.04 (d, 1H, $J = 9.6$ Hz, H-11ax). ^{13}C NMR ($CDCl_3$): δ 140.9 (C-3′), 113.2 (C-4′), 106.1 (C-5), 77.3 (C-7), 73.0 (C-2′), 72.0 (C-3), 48.8 (C-2), 43.7 (C-1), 43.2 (C-9), 40.3 (C-11), 38.9 (C-10), 32.9 (C-8), 29.9 (C-13), 25.1 (C-12), 22.8 (C-1′). IR ($CHCl_3$): 3501, 2930, 1456, 1368, 1140, 1091 cm^{-1}. MS *m*/*z* (rel. int.): 252 (M^+, 1), 234 (1), 181 (11), 136 (12), 135 (100), 107 (73), 93 (75), 82 (90), 67 (86), 55 (35), 43 (55), 41 (40), 39 (39). HRCIMS calcd for $C_{15}H_{24}O_3$+H 253.1804. Found 253.1795.

4.8.7. (1*S*,2*R*,5*R*,7*S*,9*R*,2′*R*)-5-(2′-Hydroxy-3-pentin-2′-yl)-10,10-dimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 6g. Obtained following the general procedure, compound **3a** (149 mg, 0.61 mmol) in anhydrous THF (10 mL) was treated with 0.5 M $CH_3CCMgBr$ (3.69 mL, 1.84 mmol) in diethyl ether. After workup 141 mg (80%) of a diastereoisomeric mixture of carbinols **6g**:**7g** (83:17) was obtained as a colorless syrup (R_f 0.39, hexane–EtOAc 9:1). ^{1}H NMR ($CDCl_3$): δ 4.63 (s, 1H, H-5), 4.39 (br q, 1H, $J = 9.4$ Hz, H-7), 4.10 (dd, 1H, $J = 10.0$, 3.7 Hz, H-3eq), 3.80 (dd, 1H, $J = 11.3$, 10.2 Hz, H-3ax), 2.80 (s, 1H, OH), 2.60 (m, 1H, H-11eq), 2.41–2.21 (m, 2H, H-2 and H-8eq), 2.12 (br q, 1H, $J = 5.5$ Hz, H-9), 1.96–1.83 (m, 2H, H-1, 8ax); 1.86 (s, 3H, Me-5′), 1.47 (s, 3H, Me-1′), 1.28 (s, 3H, Me-13), 1.11 (s, 3H, Me-12), 1.07 (d, 1H, $J = 9.7$ Hz, H-11ax). ^{13}C NMR ($CDCl_3$): δ 105.3 (C-5), 80.5 (C-3′), 80.5 (C-4′), 77.5 (C-7), 73.4 (C-3) 69.3 (C-2′), 48.8 (C-2), 43.9 (C-1), 43.4 (C-9), 40.5 (C-11), 39.2 (C-10), 33.1 (C-8), 30.4 (C-13), 25.4 (C-12), 25.1 (C-1′), 4.2 (C-5′). IR ($CHCl_3$): 3501, 2920, 2250, 1456, 1367, 1141, 1092. MS *m*/*z* (rel. int.): 263 (M^+−1, 3), 247 (3), 181 (35), 135 (100), 107 (49), 93 (61), 82 (89), 79 (53), 67 (31), 69 (32), 43 (19). HRESIMS calcd for $C_{16}H_{24}O_3$+Na 287.1623. Found 287.1619.

4.8.8. (1*S*,2*R*,5*R*,7*S*,9*R*,1′*S*)-5-(1′-Hydroxyethane-1′-yl)-10,10-dimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 6h. This compound was prepared according to the following procedures.

4.8.8.1. Method A. To a cooled (−78 °C) suspension of 60 mg (1.58 mmol) of $LiAlH_4$ in 5 mL of anhydrous THF and under an N_2 atmosphere was added a solution of 180 mg (0.80 mmol) of dioxane **3a** in 5 mL of anhydrous THF, and the resulting mixture was stirred at the above temperature for 3 h. Then, 10 mL of a saturated solution of ammonium chloride was added, the remaining THF was evaporated and the crude reaction mixture was extracted (3 × 30 mL) with ethyl ether. The organic layer was washed with brine, dried with anhydrous Na_2SO_4, filtered, and evaporated to dryness. The residue was purified through column chromatography using silica gel alkalinized with triethylamine and a mixture of hexane–EtOAc 19:1 as eluent, yielding 172 mg (95%) of carbinols **6h**:**7h** (1:1) as a colorless syrup.

4.8.8.2. Method B. To a cooled (−78 °C) solution of 120 mg (0.53 mmol) of acetyldioxane **3a** in 10 mL of MeOH was added 60 mg (1.58 mmol) of $NaBH_4$ and the resulting mixture was stirred for 3 h. The reaction was quenched with 10 mL of a saturated solution of NH_4Cl, stirred for 30 min, then methanol was added and the solvents were evaporated. The crude reaction mixture was extracted with Et_2O (3 × 50 mL) and the solution washed with water. The organic layer was dried with anhydrous Na_2SO_4, filtered, and evaporated to dryness. The residue was purified by column chromatography (silica gel 230–400 mesh) using hexane–AcOEt (99:1) as eluent, giving 172 mg (93%) of carbinols **6h**:**7h** (1:1) as a colorless syrup. (R_f 0.14, hexane–EtOAc 9:1). ^{1}H NMR ($CDCl_3$): δ 4.57 (d, 1H, $J = 2.3$ Hz, H-5), 4.42 (br q, 1H, $J = 9.3$ Hz, H-7), 4.03 (dd, 1H, $J = 9.9$, 3.5 Hz, H-3eq), 3.74 (m, 1H, H-1′), 3.73 (t, 1H, $J = 9.9$ Hz, H-3ax), 2.58 (m, 1H, H-11eq), 2.36 (m, 2H, H-8eq, OH), 2.22 (m, 1H, H-2), 2.11 (br q, 1H, $J = 5.5$ Hz, H-9), 1.89–1.75 (m, 2H, H-1 and H-8a), 1.28 (s, 3H, Me-13), 1.21 (d, 3H, $J = 6.3$ Hz, Me-2′), 1.11 (s, 3H, Me-12), 1.04 (d, 1H, $J = 9.6$ Hz, H-11a). ^{13}C NMR ($CDCl_3$): δ 105.4 (C-5), 77.5 (C-7), 73.1 (C-1′), 68.9 (C-3), 49.2 (C-2), 44.0 (C-1), 43.4 (C-9) 40.7 (C-11), 39.2 (C-10), 33.2 (C-8), 30.2 (C-13), 25.4 (C-12), 17.7 (C-2′). IR ($CHCl_3$): 3479, 2928, 1456, 1367, 1141, 1091 cm^{-1}. MS *m*/*z* (rel. int.): 225 (M^+−1, 1), 181 (5), 153 (14), 135 (100), 107 (32), 93 (23), 82 (30), 67 (27), 55 (9), 41 (16). HRCIMS calcd for $C_{13}H_{22}O_3$+NH_4 244.1913. Found 244.1913.

4.8.9. (1*S*,2*R*,3*S*,5*R*,7*S*,9*R*,1′*R*)-5-(1′-Hydroxy-1′-phenyl-eth-1′-yl)-3,10,10-trimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 6i. Obtained following the general procedure, compound **3b** (110 mg, 0.46 mmol) in anhydrous THF (10 mL) was treated with 1 M PhMgBr (1.15 mL, 1.15 mmol) in diethyl ether. After workup 131 mg (90%) of a diastereoisomeric mixture of carbinols **6i**:**7i** (22:3) was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$): δ 7.50 (d, 2H, $J =$ 8.3 Hz, H-*ortho*), 7.30 (dd, 2H, $J = 8.3$, 6.2 Hz, H-*meta*), 7.22 (d, 1H, $J = 6.2$ Hz, H-*para*), 5.14 (s, 1H, H-5), 4.70 (br q, 1H, $J = 9.3$ Hz, H-7), 4.43 (dq, 1H, $J = 6.9$, 5.4 Hz, H-3e), 2.61 (m, 2H, H-11e, H-2), 2.31 (m, 1H, H-8e), 2.09 (m, 1H, H-9), 1.80 (m, 2H, H-8a, H-1), 1.50 (s, 3H, Me-2′), 1.24 (s, 3H, Me-13), 1.22 (d, 3H, $J = 6.9$ Hz, Me-14), 1.10 (d, 1H, $J = 11.7$ Hz, H-11a), 1.09 (s, 3H, Me-12). ^{13}C NMR ($CDCl_3$): δ 144.9 (C-*ipso*), 127.7 (C-*meta*), 126.6 (C-*para*), 125.5 (C-*ortho*), 99.4 (C-5), 74.9 (C-3), 74.1 (C-1′), 69.7 (C-7), 51.5 (C-2), 44.1 (C-1), 43.3 (C-9), 41.4 (C-11), 39.4 (C-10), 32.7 (C-8), 29.9 (C-13), 25.7 (C-12), 25.0 (C-2′), 13.6 (C-14). MS *m*/*z* (rel. int.): 315 (M^+, 0.1), 195 (33), 149 (54), 121 (34), 107 (100), 93 (33), 79 (47), 77 (25), 67 (15), 43 (73), 39 (7).

4.8.10. (1*S*,2*R*,5*R*,7*S*,9*R*,1′*S*)-5-(1′-Hydroxy-1′-phenyleth-1′-yl)-10,10-dimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 7d. Obtained following the general procedure, compound **3d** (100 mg, 0.35 mmol) in anhydrous THF (10 mL) was treated with MeMgBr (0.17 mL, 0.52 mmol) 3 M in diethyl

ether. After workup 103 mg (98%) of a diastereoisomeric mixture of carbinols **6d**:**7d** (13:87) was obtained as a colorless oil. A small amount of **7d** was obtained as a white solid by crystallization from CH_2Cl_2–hexane, mp 75–76 °C. ^{1}H NMR ($CDCl_3$): δ 7.5 (d, 2H, $J = 8.4$ Hz, H-*ortho*), 7.32 (t, 2H, $J = 8.4$ Hz, H-*meta*), 7.27 (d, 1H, $J = 8.4$ Hz, H-*para*); 4.79 (s, 1H, H-5), 4.35 (br q, 1H, $J = 9.4$ Hz, H-7), 3.99 (dd,1H, $J = 10.0$, 3.7 Hz, H-3eq), 3.66 (t, 1H, $J = 10.0$ Hz, H-3a), 2.91 (br s, 1H, OH), 2.56 (m, 1H, H-11eq), 2.5 (m, 2H, H-2 and H-8eq), 2.08 (m, 1H, H-9), 1.83 (m, 2H, H-8a and H-1), 1.56 (s, 3H, CH_3-2′), 1.25 (s, 3H, CH_3-13), 1.06 (s, 3H, CH_3-12), 1.02 (d, 1H, $J = 9.6$ Hz, H-11ax). ^{13}C NMR ($CDCl_3$): δ 144.3 (C-*ipso*), 127.8 (C-*meta*), 126.9 (C-*para*), 126.0 (C-*ortho*), 106.5 (C-5), 77.1 (C-7), 75.0 (C-1′), 73.0 (C-3), 48.9 (C-2), 43.8 (C-9), 43.3 (C-1), 40.6 (C-11), 39.0 (C-10), 33.2 (C-8), 30.0 (q, C-2′), 25.2 (q, C-12), 24.4 (q, C-13). IR ($CHCl_3$): 3450, 2930, 1603, 1450, 1370, 1140, 1090, 1005, 700 cm^{-1}. MS *m*/*z* (rel. int.): 302 (M+1, 0.1); 181 (47); 135 (60); 122 (8); 120 (75); 105 (80); 93 (70); 91 (64); 79 (100); 67 (50); 55 (30).

4.8.11. (1*S*,2*R*,3*S*,5*R*,7*S*,9*R*,1′*S*)-5-(1′-Hydroxy-1′-phenyleth-1′-yl)-3,10,10-trimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 7i. Obtained following the general procedure, compound **3e** (130 mg, 0.43 mmol) in anhydrous THF (10 mL) was treated with MeMgBr (0.23 mL, 0.69 mmol) in diethyl ether. After workup 120 mg (88%) of a diastereoisomeric mixture of carbinols **6i**:**7i** (11:89) was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$): δ 7.52 (d, 2H, $J = 8.3$ Hz, H-*ortho*), 7.33 (dd, 2H, $J = 8.3$, 6.2 Hz, H-*meta*), 7.25 (d, 1H, $J = 6.2$ Hz, H-*para*), 5.06 (s, 1H, H-5), 4.62 (br q, 1H, $J = 9.4$ Hz, H-7), 4.26 (dq, 1H, $J = 7.0$, 5.3 Hz, H-3e), 2.96 (s, 1H, OH), 2.62 (m, 2H, H-11e, H-2), 2.32 (m, 1H, H-8e), 2.08 (m, 1H, H-9), 1.81 (m, 2H, H-8a, H-1), 1.53 (s, 3H, Me-2′), 1.26 (s, 3H, Me-13), 1.25 (d, 3H, $J = 7.0$ Hz, Me-14), 1.11 (d, 1H, $J = 11.8$ Hz, H-11a), 1.08 (s, 3H, Me-12). ^{13}C NMR ($CDCl_3$): δ 144.5 (C-*ipso*), 127.7 (C-*meta*), 126.7 (C-*para*), 125.8 (C-*ortho*), 99.7 (C-5), 75.0 (C-1′), 73.9 (C-3), 69.8 (C-7), 51.6 (C-2), 44.1 (C-1), 43.3 (C-9), 41.5 (C-11), 39.3 (C-10), 32.8 (C-8), 29.9 (C-13), 25.8 (C-12), 24.9 (C-2′), 13.8 (C-14). MS *m*/*z* (rel. int.): 315 (M$^+$, 0.1), 195 (33), 149 (54), 121 (34), 107 (100), 93 (33), 79 (47), 77 (25), 67 (15), 43 (73), 39 (7).

4.8.12. (1*S*,2*R*,3*R*,5*R*,7*S*,9*R*,1′*R*)-5-(1′-Hydroxy-1′-phenyleth-1′-yl)-3,10,10-trimethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 6j. Obtained following the general procedure, compound **3c** (450 mg, 1.88 mmol) in anhydrous THF (20 mL) was treated with PhMgBr (1.25 mL, 3.77 mmol) in diethyl ether. After workup 537 mg (90%) of a diastereoisomeric mixture of carbinols **6j**:**7j** (67:33) was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$): δ 7.54 (m, 2H, H-*ortho*), 7.32 (m, 2H, H-*meta*), 7.23 (m, 1H, H-*para*), 4.79 (s, 1H, H-5), 4.32 (dd, 1H, $J = 17$, 9 Hz, H-7), 3.76 (m, 1H, H-3), 2.96 (s, 1H, –OH), 2.56 (m, 1H, H-11eq), 2.29 (m, 1H, H-8eq), 2.07 (q, 1H, $J = 5$ Hz, H-9), 1.98 (t, 1H, $J = 6$ Hz, H-1), 1.80 (m, 2H, H-8ax, H-2), 1.55 (s, 3H, Me-16), 1.25 (s, 3H, Me-13), 1.17 (d, 3H, $J = 6$ Hz, Me-14), 1.04 (s, 3H, Me-12), 0.99 (d, 1H, $J = 10$ Hz, H-11ax). ^{13}C NMR ($CDCl_3$): δ 144.6 (C-*ipso*), 127.8 (C-*ortho*), 126.9 (C-*para*), 126.1 (C-*meta*), 105.8 (C-5), 78.5 (C-3), 76.5 (C-7), 75.0 (C-15), 55.4 (C-2), 43.3 (C-9), 43.1 (C-1), 40.1 (C-11), 39.1 (C-10), 33.2 (C-8), 30.2 (Me-13), 25.4 (Me-12), 24.7 (Me-16), 18.8 (Me-14). IR ($CHCl_3$): 3494, 2934, 1496, 1448, 1366, 1338, 1266, 1222, 1134, 1094, 796 cm^{-1}. MS *m*/*z* (rel. int.): 316 (M$^+$, 0.38), 299 (7), 195 (9), 165 (12), 149 (75), 121 (24), 107 (100), 105 (15), 93 (35), 91 (12), 79 (33), 43 (14). HRESI/APCI MS calcd for $C_{20}H_{28}O_3$+Na 339.1936. Found 339.1935.

4.8.13. (1*S*,2*R*,5*R*,7*S*,9*R*,1′*R*)-5-(1′-Hydroxy-1′-phenyleth-1′-yl)-3,3,10,10-tetramethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane 6k. Obtained using either procedure described in Section 4.8.4.1 or 4.8.4.2. An enriched sample of **6k** was obtained by using the latter procedure as follows: compound **3f** (140 mg, 0.55 mmol) in anhydrous THF (10 mL) was treated with 1 M PhMgBr (1.23 mL, 1.23 mmol) in diethyl ether. After workup 172 mg (95%) of a diastereoisomeric mixture of carbinols **6k**:**7k** (77:23) was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$): δ 7.54 (d, 2H, $J = 8$,47 Hz, H-*ortho*), 7.31 (dd, 2H, $J = 7.04$, 8.76 Hz, H-*meta*), 7.24 (d, 1H, $J = 7.24$ Hz, H-*para*), 4.92 (s, 1H, H-5), 4.47 (br q, 1H, $J = 8.70$ Hz, H-7), 3.07 (s, 1H, OH), 2.62 (m, 1H, H-11e), 2.30 (m, 1H, H-8e), 2.09 (m, 2H, H-2, H-9), 1.92 (t, 1H, $J = 6.98$ Hz, H-1), 1.78 (m, 1H, H-8a), 1.52 (s, 3H, Me-2′), 1.24 (s, 3H, Me-15), 1.19 (s, 6H, Me-13, Me-14), 1.05 (d, 1H, $J = 9.6$ Hz, H-11a), 1.04 (s, 3H, Me-12). ^{13}C NMR ($CDCl_3$): δ 145.2 (C-*ipso*) 127.9 (C-*meta*), 126.8 (C-*para*), 126.2 (C-*ortho*), 100.5 (C-5), 77.5 (C-3), 74.9 (C-1′), 71.1 (C-7), 58.1 (C-2), 43.6 (C-1), 43.5 (C-9), 41.7 (C-11), 39.6 (C-10), 33.2 (C-8), 30.3 (C-15), 29.6 (C-13) 25.9 (C-12), 24.6 (C-2′), 19.6 (C-14). MS *m*/*z* (rel. int.): 330 (M$^+$, 0.28), 163 (46), 135 (16), 121 (51), 107 (72), 91 (68), 79 (100), 67 (48).

4.9. General procedure for the hydrolysis of carbinols 6d and 7d

To a solution of carbinols **6d** or **7d** (0.33 mmol) in 10 mL of CH_3CN–H_2O (9:1) was added 10 mg of *p*-TsOH and the resulting mixture was stirred for 1 h. Then, 5 mL of a saturated solution of $NaHCO_3$ was added and the mixture stirred for 15 min. The organic layer was separated, the aqueous layer was extracted with ethyl ether (3 × 20 mL) and the combined organic layers were dried with anhydrous Na_2SO_4, filtered, and concentrated to dryness to give a colorless oil, whose ^{1}H NMR spectrum showed the presence of aldehydes (*R*)-**8a** and (*S*)-**8b**. The crude reaction mixture was submitted to reduction without further purification.

4.10. General procedure for the preparation of diols 9a and 9b

The above crude reaction mixture was dissolved in anhydrous ethyl ether, cooled in an ice-water bath, treated with 4 equiv of $LiAlH_4$, and the resulting mixture stirred for 1.5 h at room temperature. After the usual workup, a mixture of pinanediol **1** and diols (*S*)-**9a**, or (*R*)-**9b**, was obtained, which was separated by column chromatography using hexane–EtOAc (5:1) as the mobile phase, giving the title diols in 66–74% yield. All spectroscopic data of diols (*S*)-**9a** and (*R*)-**9b** are in agreement with the published

data.[13] Lit.[13] $[\alpha]_D^{23} = -5.8$ (*c* 0.17, EtOH) for (*R*)-**9b**. Data for (*S*)-**9a**: $[\alpha]_D^{25} = +4.1$ (*c* 0.18, EtOH) obtained from mixture **6d**:**7d** (Table 1, entry 13). Data for (*R*)-**9b**: $[\alpha]_D^{25} = -4.3$ (*c* 0.16, EtOH) obtained from a mixture of **6d**:**7d** (Table 1, entry 4) and $[\alpha]_D^{25} = -3.2$ (*c* 0.14, EtOH) from a mixture of **6j**:**7j** (Table 1, entry 15).

4.11. X-ray analysis of 1a–c, 3e, and 7d

Crystal data were collected on a Siemens P4 diffractometer using Mo Kα monochromated radiation ($\lambda = 0.71073$ Å), excepting **1c** whose data were collected on a Nonius Bruker CAD4 diffractometer using Cu Kα monochromated radiation ($\lambda = 1.54184$ Å). The structures were solved by direct methods using SHELXS97. Data for **1a** are: $C_{10}H_{18}O_2$, $M = 170.25$, monoclinic, space group $P2_1$, $a = 6.563(1)$, $b = 11.217(2)$, $c = 13.829(2)$, $\beta = 98.18(1)^\circ$, crystal size: $0.21 \times 0.52 \times 0.68$ mm, $V = 1007.7(2)$, $\rho_{calcd} = 1.122$ g/cm^3, $Z = 4$, $F(000)e^- = 376$. Collected reflections: 3213 within a θ range of 2.35–27.00°, unique reflections: 2546, observed reflections: 2080 with $[I > 2\sigma(I)]$, $R = 3.7\%$, CCDC deposition no. 663927. Data for **1b** are: $C_{11}H_{20}O_2$, $M = 184.27$, orthorhombic, space group $P2_12_12_1$, $a = 6.8217(5)$, $b = 11.6941(7)$, $c = 13.62(1)$, crystal size: $0.6 \times 0.6 \times 0.9$ mm, $V = 1086.3(2)$, $\rho_{calcd} = 1.127$ g/cm^3, $Z = 4$, $F(000)e^- = 408$, collected reflections: 2018 within a θ range of 2.30–28.50°, unique reflections: 1917, observed reflections: 1649 with $[I > 2\sigma(I)]$, $R = 5.3\%$, CCDC deposition no. 663928. Data for **1c** are: $C_{12}H_{22}O_2$, $M = 198.30$, orthorhombic, space group $P2_12_12_1$, $a = 7.0330(6)$, $b = 9.125(2)$, $c = 18.668(1)$, crystal size: $0.42 \times 0.40 \times 0.38$ mm, $V = 1198.0(3)$, $\rho_{calcd} = 1.099$ g/cm^3, $Z = 4$, $F(000)e^- = 440$. Collected reflections: 925 within a θ range of 4.74–54.87°, unique reflections: 902, observed reflections: 883 with $[I > 2\sigma(I)]$, $R = 3.3\%$, CCDC deposition no. 663929. Data for **3e** are: $C_{19}H_{24}O_3$, $M = 300.38$, triclinic, space group $P1$, $a = 8.128(1)$, $b = 9.5291(5)$, $c = 11.0837(6)$, $\alpha = 91.843(5)$, $\beta = 90.49(1)$, $\gamma = 107.58(1)$, $V = 816.05(9)$, $\rho_{calcd} = 1.222$ g/cm^3, $Z = 2$, $F(000)e^- = 324$ crystal size: $0.18 \times 0.26 \times 0.8$ mm, collected reflections: 4185 within a θ range of 1.73–28.00°, unique reflections: 4184, observed reflections: 3262 with $[I > 2\sigma(I)]$, $R = 7.6\%$, CCDC deposition no. 663930. Data for **7d** are: $C_{19}H_{26}O_3$, $M = 302.40$, hexagonal, space group $P6_3$, $a = 13.580(1)$, $b = 13.580(1)$, $c = 18.130(2)$, $\gamma = 120^\circ$, $V = 2895.5(4)$, $\rho_{calcd} = 1.041$ g/cm^3, $Z = 6$, $F(000)e^- = 984$, crystal size: $0.5 \times 0.4 \times 0.4$ mm, collected reflections: 5908 within a θ range of 1.73–28.00°, unique reflections: 2538, observed reflections: 1603 with $[I > 2\sigma(I)]$, $R = 8.2\%$, CCDC deposition no. 663931. Crystallographic data are deposited with the Cambridge Crystallographic Data Center. Copies of the data can be obtained, free of charge, on applications to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk.

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