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LITHIUM DERIVATIVES FROM ENANTIOMERICALLY PURE 2-(2´-HALOETHYL) DIOXOLANES: FORMATION AND USE AS CHIRAL PROPANAL HOMOENOLATE SYNTHONS.

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Abstract: Condensation of acetals of 3-chloro- and 3-bromopropanal with (-)-1,4-di-O-benzyl-L-threitol and (-)-cis-2,3-bornanediol leads to the corresponding 2-(2'-chloroethyl-)- and 2-(2'-bromoethyl)dioxolanes that were converted into the Li-derivatives by transhalometallation with t-butyllithium in excellent yields. These chiral propanal homoenolates react with benzaldehyde and acetophenone yielding carbinols in moderate chemical yields and low diastereomeric excesses.

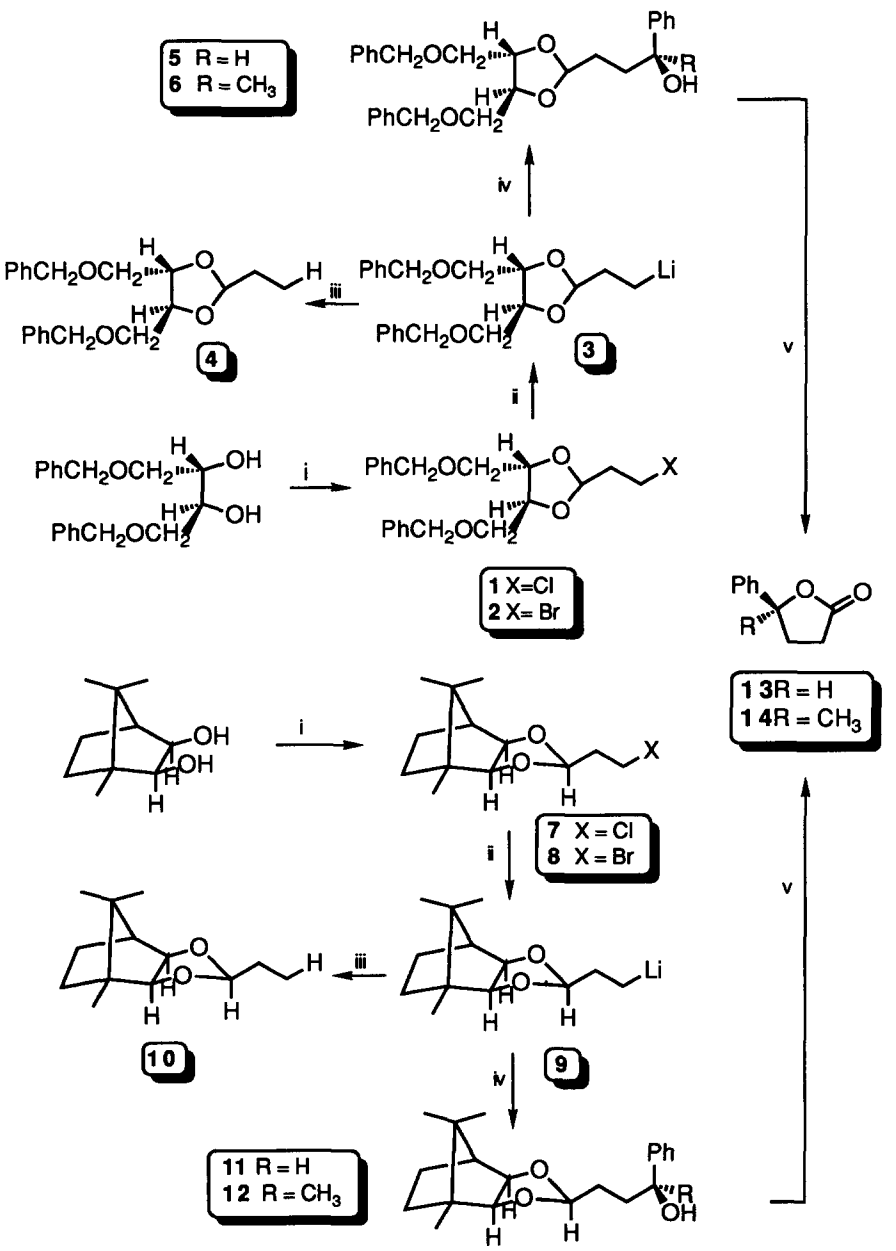
The usefulness of chiral cyclic acetals in asymmetric synthesis has been widely reported during the last ten years. The stereoselective ring cleavage by a diversity of nucleophiles is the transformation that has attracted more attention because its excellent level of stereoselectivity; whereas nucleophilic additions to a carbonyl group next to the chiral acetal, acting as a chelating substituent, have also deserved a lot of work.[1]

On the contrary, the use of nucleophilic chirons bearing an acetal appendage is scarce, being limited to the application as enolates,[2-4] and a few examples of orthometallated acetals derived from benzaldehyde,[5,6] but there are no antecedents to the preparation of non-stabilized chiral masked lithium homoenolates derived from propanal, and there are only a few examples on the synthetic application of these non-chiral species.[7-9]

We have explored the preparation of the chiral 2-(2´-chloroethyl)- (**1** and **7**) and 2-(2´-bromoethyl) dioxolanes (**2** and **8**), and their transformation into the lithium derivatives **3** and **9** by transhalometallation in different conditions.

The classical method of preparation of the starting dioxolanes by reaction of the corresponding acetal or aldehyde with 1,2-diols, catalyzed by p-toluenesulfonic acid or pyridinium tosylate, in benzene or toluene with azeotropic removal of water[10] led to the desired products, but in yields under 50 per cent. Instead, the preparation of **1** (83%) and **7** (84%) was carried out by transacetalization, in the presence of boron trifluoride etherate, of 3-chloro-1,1-diethoxypropane with (-)-1,4-di-O-benzyl-L-threitol,[11] and (-)-(1R,2S,3S,4S)-1,7,7-trimethyl [2.2.1]heptane-2,3-diol[12] respectively, whereas **2** (70%) and **8** (62%) was obtained in the same way from 2-(2´-bromoethyl) dioxolane.

It is worth noting that the formation of dioxolanes **7** and **8** is highly stereoselective (d.e. better than 96%),[13] and the absolute configurations of the new stereogenic centers at C-4 are (R), and coincident with those previously reported for related compounds.[14]



Scheme 1. *Reagents and conditions*: i) for **1** and **7**: 3-chloro-1,1-diethoxypropane, $BF_3.Et_2O$, benzene, R.T., 30 min. For **2** and **8**: 2-(2'-bromoethyl)-1,3-dioxolane, $BF_3.Et_2O$, benzene, R.T., 30 min. ii) *tert*-BuLi, THF or Et_2O, -78 °C. iii) H_2O. iv) For **5** and **11**: C_6H_5CHO, -78°C to 20°C, then aqueous sat. NH_4Cl solution. For **6** and **12**: $C_6H_5COCH_3$, -78°C to 20°C, then H_2O. v) MCPBA, CH_2Cl_2, $BF_3.OEt_2$, R.T., 12 h., then aqueous $NaHCO_3$.

Our first attempts to promote the additions of Li-derivatives formed by treatment of chloro compounds **1** and **7** with *tert*-butyllithium were not very promising; in all cases the reaction mixtures were very complex, and a lot of unreacted products were recovered. Then, we directed our attention to find the experimental conditions that allowed the efficient generation of lithium intermediates **3** and **9** by treating chloro- (**1** and **7**) or bromo-derivatives (**2** and **8**) with different lithium alkyls, followed by quenching with water to the propanal dioxolanes **4** and **10** (The best results were obtained with *tert*-butyllithium, and some of them are summarized in Table 1).

Table 1. Formation of Li-derivatives of dioxolanes **1, 2, 7,** and **8** and hydrolysis to **4** and **10**

Entry	Dioxolane	Base	Solvent	Temperature (°C)	Time (min)	Product (%)
1	**1**	t-Bu-Li	Et_2O	-78	10	**4** (5)
2	**2**	t-Bu-Li	Et_2O	-78	10	**4** (63)
3	**2**	t-Bu-Li	THF	-78	10	**4** (43)
4	**7**	Naph-Li	THF	-78	360	-
5	**7**	t-Bu-Li	THF	-78	10	**10** (5)
6	**7**	t-Bu-Li	THF	-78	90	**10** (55)
7	**8**	t-Bu-Li	THF	-78	10	**10** (60)
8	**8**	t-Bu-Li	Et_2O	-78	10	**10** (78)

In fact, the transhalometallation of chloroderivatives occurs in only 5 per cent yield after treatment with *tert*-butyllithium for 10 minutes (entries 1 and 5), whereas a moderate yield of 55 per cent was reached after 90 minutes (entry 6), and chloro-derivative **7** was recovered unchanged after stirring for 6 hours at -78°C with 2 equivalents of lithium naphthalenide (entry 4). Instead, lithium intermediates **3** and **9** were easily prepared in 63 and 78% yields (entries 2 and 8) from bromo-compounds **2** and **8** respectively. Otherwise, it has been shown that diethyl ether was a better solvent than THF in these transhalometallation reactions.

We have explored the reactions of **3** and **9**, prepared from bromoderivatives **2** and **8**, with benzaldehyde and acetophenone directed to the diastereoselective preparation of carbinols **5, 6, 11** and **12**, and the results are collected in table 2. In the course of considerable experimentation we found that **3** and **9** did not react with the carbonyl derivatives at -78°C, being necessary to heat to room temperature to promote the reactions. Then, we standarized our experimental conditions as follows: The formation of Li-derivatives was carried out at -78°C, the electrophile was added, and the reaction mixture was allowed to reach the room temperature and stirred for 6 h. In these conditions both organolithiums cleanly reacted with benzaldehyde and acetophenone affording the expected addition products in good chemical yields (60-85%).

The data collected in table 2 shown that the higher chemical yields were obtained by using diethyl ether as solvent instead THF, and that these were slight better in the reactions with benzaldehyde than with acetophenone. Otherwise, the stereochemical outcome of the additions was quite similar to previously described for aryllithium derivatives bearing a chiral dioxolane.[5]

Thus, lithium dioxolane **3**, derived from L-threitol, is unable to discriminate the faces of the carbonyl compounds, yielding an equimolar mixture of epimeric carbinols **5** (entries 1-4 in table 2). The facial discrimination, in favour of the *si* face of the carbon-oxygen double bond, of the camphanediol derivative **9** is very modest, in these reactions the major isomer was the carbinol with the new stereocenter S-configurated, but the d.e.'s were low. Once again the best stereochemical results were obtained when the reactions were carried out in diethyl ether as solvent (compare entries 5 and 7 versus 6 and 8 in table 2).

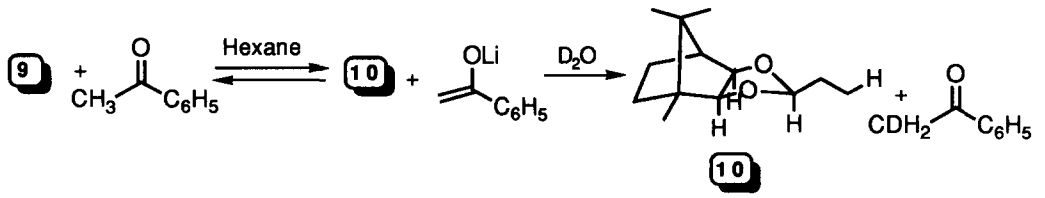
Table 2. Reactions of Li-derivatives **3** and **9** with benzaldehyde and acetophenone.

Entry	Li-Deriv.	Electrophile	Solvent	Temperature (°C)[a]	Time (min)	Product (%)[b]	Conf.(d.e.%)[c]
1	**3**	PhCHO	Et_2O	-78 to 20	360	**5** (51)[81]	- -
2	**3**	PhCHO	THF	-78 to 20	360	**5** (36)[81]	- -
3	**3**	PhCOMe	Et_2O	-78 to 20	360	**6** (49)[78]	- -
4	**3**	PhCOMe	THF	-78 to 20	360	**6** (26)[60]	- -
5	**9**	PhCHO	Et_2O	-78 to 20	360	**11** (64)[82]	S (9)
6	**9**	PhCHO	THF	-78 to 20	360	**11** (50)[85]	S (3)
7	**9**	PhCOMe	Et_2O	-78 to 20	360	**12** (51)[65]	S (26)
8	**9**	PhCOMe	THF	-78 to 20	360	**12** (36)[60]	S (8)
9	**9**	PhCOMe	Hexane	-78 to 20	360	**10** (75)	- -
10	**9**	PhCOMe	Hexane	0	360	**10** (90)	- -

[a] -78°C correspond to the temperature of formation of the Li-derivative, then the electrophile was added, and the mixture allowed to rise to 20°C. [b]Numbers in square brackets reflect the chemical yields with respect to the Li-derivative formed by transhalometallation. [c] The d.e. was determined by integration of the NMR signals in the mixtures of the reactions.

Carbinols **11** and **12** were easily transformed into chiral γ-substituted butyrolactones **13** and **14** by oxidation with m-chloroperbenzoic acid.[9] These transformations allowed us to determine both the configuration at the newly created stereocenter and the e.e.'s by comparison of the sign and the value of the previously described specific rotation for these compounds.[16, 17]

Finally, it is worth noting the behaviour of lithium derivative **9** towards acetophenone in hexanes as solvent (entries 9 and 10 in table 2). In fact, the generation of **9** by treatment of bromoderivative **8** with *tert*-butyllithium, followed by the addition of acetophenone in hexane, led, after the corresponding hydrolysis to the propanal dioxolane **10** in 75% yield, if the reaction was carried out in the general experimental conditions, or in 90% yield if the formation of lithium derivative and the addition of the ketone was performed at 20°C. This fact, that could be interpreted as the unreactivity of **9** in this solvent, is a consequence of the behaviour of lithium dioxolane as a base and not as a nucleophile in hexane. This behaviour was proved by the incorporation of the deuterium into the acetophenone instead of the dioxolane **10** when the reaction was quenched with deuterium oxide, proving the enolization of the carbonyl compound as shown in scheme 2.



Scheme 2

Experimental.

General. All the reactions were carried out in anhydrous solvents, under argon atmosphere and in oven-dried glassware. 3-Chloro-1,1-diethoxypropane and 2-(2'-bromoethyl)-1,3-dioxolane are commercially available, and they were distilled immediately before use. (-)-*Exo*-camphanediol[12] and (-)-1,4-di-O-benzyl-L-threitol[11] were prepared from camphorquinone[15] and L-tartaric acid respectively. The ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75 MHz) spectra were registered on a Bruker AC 300, using TMS as internal standard and $CDCl_3$ as solvent. IR spectra were recorded on a Philips PU 9706 Spectrometer as film. Optical rotations were measured on a Perkin-Elmer 241 Polarimeter in a 1 dm. cell, and concentrations are given in g/100ml. Mass spectra were recorded on a Hewlett-Packard 5988-A mass spectrometer by Electronic Impact. Microanalyses were performed with a Perkin-Elmer 2400-CHN elemental analyzer at the Deparment of Inorganic Chemistry.

General procedure for the synthesis of 2-(2'-haloethyl)-1,3-dioxolanes. To a solution of diol (1 mmol) and 3-chloro-1,1-diethoxypropane or 2-(2'-bromoethyl)-1,3-dioxolane (1 mmol) in 10 ml of benzene was added $BF_3.Et_2O$ (3 mmol). The reaction mixture was stirred at room temperature for 30 min. The mixture was neutralized with a saturated $NaHCO_3$ solution, the organic layer was extracted with ethyl acetate, dried over anhydrous Na_2SO_4 and filtered. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography using hexane/ethyl acetate as eluent.

Transhalometallation of **1**, **2**, **7** *and* **8**, *and hydrolisis to* **4** *and* **10**. *General Procedure.* To a solution of dioxolane (0.4 mmol) in dry solvent (10 ml) under Ar atmosphere at -78°C was added *tert*-BuLi (1.7M, 0.8 mmol). The reaction was stirred at this temperature for the time indicated in table 1, and then quenched with a saturated solution of NH_4Cl. The mixture was extracted with diethyl ether, dried over anhydrous Na_2SO_4 and filtered. The solvents were removed in vacuo and the residue was purified by flash chromatography using hexane/ethyl acetate as eluent.

Addition of Lithium derivatives **3** *and* **9** *to benzaldehyde and acetophenone. General Procedure.* To a solution of dioxolane (0.4 mmol) in dry solvent (10 ml) under Ar atmosphere at -78°C was added *tert*-BuLi (1.7M in pentane, 0.8 mmol). The mixture was stirred at this temperature for 10 min. Then, the carbonyl compound (0.44 mmol) was added and the mixture was allowed to gradually raise the room temperature for 4 h. The reaction was hydrolized with a saturated aqueous NH_4Cl solution and extracted with diethyl ether. The organic layer was dried over anhydrous Na_2SO_4, filtered and the solvents were eliminated under reduced pressure. The oily residue was purified by flash cromatographywith hexane/ethyl acetate as solvent.

Synthesis of γ-butyrolactones **13** *and* **14**.[9] To a solution of dioxolanes **11** or **12** (0.4 mmol) in dichloromethane (5 ml) was added MCPBA (0.45 mmol), and $BF_3.Et_2O$ (0.08 mmol). The mixture was stirred overnight at room temperature. The resulting suspension was hydrolised with water, neutralized with $NaHCO_3$

and extracted with diethyl ether. The extracts were washed and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by distillation *in vacuo*.

(4S,5S)-4,5-Bis(Benzyloxymethyl)-2-(2'-chloroethyl)-1,3-dioxolane (1). Colorless oil. $[\alpha]_D^{23}$ = -16.7 (c = 1.0, acetone). IR (neat, cm^{-1}): 3080, 3040, 3020, 1490, 1450, 730, 690. MS (m/z, %): 376(M^+, 0.6), 91 (100). ^{1}H-NMR : 2.00-2.23 (m, 2H, H-1'), 3.50-3.70 (m, 6H), 3.90-4.06 (m, 2H, H-4 and H-5), 4.54 (s, 4H, Ar-C$\underline{H_2}$), 5.20 (t, 1H, H-2, J= 4.4 Hz), 7.27-7.35 (m, 10H, H_{Arom}). ^{13}C-NMR : 37.0 (C-1'), 39.5 (C-2'), 70.1(CH_2), 70.2 (CH_2), 73.4 (Ar-$\underline{C}H_2$), 77.3 (CH), 78.0 (CH), 102.0 (C-2), 127.6 (CH_{Arom}), 127.7 (CH_{Arom}), 128.4 (CH_{Arom}), 137.8 (C_{Arom}). Anal. Calcd. for $C_{21}H_{25}ClO_4$: C, 66.93; H, 6.64; Cl, 9.43. Found: C, 66.68; H, 6.91; Cl, 9.22.

(4S,5S)-4,5-Bis(Benzyloxymethyl)-2-(2'-bromoethyl)-1,3-dioxolane (2). Colorless oil. $[\alpha]_D^{23}$ = -11.6 (c =1.0, acetone). IR(neat, cm^{-1}): 3090, 3060, 3030, 1500, 1450, 1365, 740, 700. MS (m/z,%): 422 (M^+, 1), 420 (M^+-2, 1), 181 (100). ^{1}H-NMR : 2.17-2.26 (m, 2H, H-1'), 3.46 (t, 2H, H-2', J= 7.2 Hz),3.55-3.59 (m, 4H), 3.83-4.10 (m, 2H, H-4 and H-5), 4.56 (s, 4H, Ar-C$\underline{H_2}$), 5.19 (t, 1H, H-2, J= 4.4 Hz), 7.23-7.36 (m, 10H, H_{Arom}). ^{13}C-NMR : 27.0 (C-2'), 37.2 (C-1'), 70.1 (CH_2), 70.2 (CH_2), 73.4 (Ar-$\underline{C}H_2$), 77.3 (CH), 77.4 (CH), 102.7 (C-2), 127.5 (CH_{Arom}), 127.6 (CH_{Arom}), 128.3 (CH_{Arom}), 129.6 (CH_{Arom}), 137.7 (C_{Arom}). Anal. Calcd. for $C_{21}H_{25}BrO_4$: C, 59.85; H, 5.94; Br, 19.00. Found: C, 59.62; H, 6.21; Br, 19.23.

(4S,5S)-4,5-Bis(Benzyloxymethyl)-2-ethyl-1,3-dioxolane (4). Colorless oil. $[\alpha]_D^{23}$ = -6.6 (c = 0.75, acetone). IR (neat, cm^{-1}): 3090, 3060, 3030, 1500, 1450, 1365. MS (m/z, %): 342 (M^+, 1.75), 181(100). ^{1}H-NMR : 0.96 (t, 3H, H-2', J= 7.54 Hz), 1.67-1.71 (m, 2H, H-1'), 3.53-3.63 (m, 4H), 3.97-4.07 (m, 2H, H-4 and H-5), 4.56-4.57 (m, 4H, Ar-C$\underline{H_2}$), 5.03 (t, 1H, H-2, J= 4.5 Hz), 7.23-7.33 (m, 10H, H_{Arom}). ^{13}C-NMR : 7.7 (C-2'), 26.9 (C-1'), 70.3 (CH_2), 70.5 (CH_2), 73.3 (Ar-$\underline{C}H_2$), 77.2 (CH), 77.8 (CH), 105.4 (C-2), 127.5 (CH_{Arom}), 127.6 (CH_{Arom}), 128.3 (CH_{Arom}), 137.9 (C_{Arom}). Anal. Calcd. for $C_{21}H_{26}O_4$: C, 73.68; H, 7.60. Found: C, 73.89; H, 7.51.

(4S,5S)-4,5-Bis(Benzyloxymethyl)-2-(3'-hydroxy-3'-phenylpropyl)-1,3-dioxolane (5). Colorless oil. IR (neat, cm^{-1}): 3430. MS (m/z, %): 448 (M^+, 0.65), 147 (100). ^{1}H-NMR : 1.50-1.90 (m, 2H, H-1' and H-2'), 2.45 (broad s, 1H, OH), 3.51-3.63 (m, 4H), 3.96-4.08 (m, 2H, H-4 and H-5), 4.52-4.55 (m, 4H, Ar-C$\underline{H_2}$), 4.70 (t, 1H, H-3', J= 5.3), 5.08-5.12 (m, 1H, H-2), 7.17-7.35 (m, 15H, H_{Arom}). ^{13}C-NMR: 29.4 (C-1'), 32.8 (C-2'), 70.2 (CH_2), 73.4 (Ar-$\underline{C}H_2$), 74.0 (C-3'), 77.2 (CH), 77.9 (CH), 104.2 (C-2), 125.8 (CH_{Arom}), 127.0 (CH_{Arom}), 127.3 (CH_{Arom}),127.5 (CH_{Arom}), 127.7 (CH_{Arom}), 128.0 (CH_{Arom}), 128.4 (CH_{Arom}), 137.8 (C_{Arom}), 144.5 (C_{Arom}). Anal. Calcd. for $C_{28}H_{32}O_5$: C, 75.00; H, 7.14. Found: C, 74.81; H, 7.32.

(4S,5S)-4,5-Bis(Benzyloxymethyl)-2-(3'-hydroxy-3'-phenylbutyl)-1,3-dioxolane (6). Colorless oil. IR (neat, cm^{-1}): 3440. MS (m/z, %): 447 (M^+-15, 0.5), 91 (100). ^{1}H-NMR : 1.52 (s, 3H, H-4'), 1.59-1.66 (m, 2H), 1.94-1.98 (m, 2H), 2.50-2.55 (broad s, 1H, OH), 3.52-3.62 (m, 4H), 3.94-4.05 (m, 2H, H-4 and H-5), 4.53-4.54 (m, 2H, Ar-C$\underline{H_2}$), 5.04 (t, 1H, H-2, J= 4.2 Hz), 7.17-7.43 (m, 15H, H_{Arom}). ^{13}C-NMR: 28.3 (C-1'), 30.6 (C-4'), 37.1 (C-2'), 70.2 (CH_2), 70.3 (CH_2), 73.4 (Ar-$\underline{C}H_2$), 73.9 (C-3'), 77.3 (CH), 77.9 (CH), 104.4 (C-2), 124.8 (CH_{Arom}), 126.4 (CH_{Arom}), 127.5 (CH_{Arom}),127.6 (CH_{Arom}), 128.1 (CH_{Arom}), 128.3 (CH_{Arom}), 137.8 (C_{Arom}), 147.7 (CH_{Arom}). Anal. Calcd. for $C_{29}H_{34}O_5$: C, 75.32; H, 7.36. Found: C, 75.52; H, 7.58.

(1R,2S,4R,6S,7S)-4-(2'-Chloroethyl)-1,10,10-trimethyl-3,5-dioxa-tricyclo [3.2.1.$0^{2,6}$] decane (7). Colorless oil. B.p. 100-102°C/ 0.5 Torr. $[\alpha]_D^{23}$ = -11.6 (c = 1.0, acetone). IR (neat, cm^{-1}):

1470, 1430, 1410, 1380, 1360, 1335. MS (m/z, %): 246 (M^++2, 0.3), 244 (M^+, 1), 134 (100). ^{1}H-NMR : 0.73 (s, 3H), 0.80-0.89 (m, 2H), 0.94 (s, 3H), 1.06 (s, 3H), 1.35-1.49 (m, 1H), 1.60-1.78 (m, 1H), 1.92 (d, 2H, J = 5.0 Hz), 2.10-2.40 (m, 2H, H-1'), 3.48 (t, 2H, H-2', J= 6.8), 3.76 (d, 1H, J= 6.7), 3.96 (d, 1H, J = 6.7 Hz), 4.80 (t, 1H, H-4, J =5.3 Hz). ^{13}C-NMR : 11.0 (CH_3), 19.9 (CH_3), 22.5 (CH_3), 23.4 (CH_2), 31.7 (CH_2), 33.1 (C-1'), 40.3 (C-2'), 46.0 (C quat.), 47.2 (C quat.), 47.3 (CH), 83.5 (CH), 87.6 (CH), 101.5 (C-4). Anal. Calcd. for $C_{13}H_{21}ClO_2$: C, 63.80; H, 8.59; Cl, 14.52. Found: C, 63.61; H, 8.42; Cl, 14.69.

(1R,2S,4R,6S,7S)-4-(2'-Bromoethyl)-1,10,10-trimethyl-3,5-dioxa-tricyclo [3.2.1.$0^{2,6}$] decane (8). Colorless oil. B.p. 123-125°C/0.5 Torr. $[\alpha]_D^{23}$ = - 9.3 (c = 1.0, EtOH). IR (neat, cm^{-1}): 1720, 1480, 1440, 1415, 1390, 1370, 1345. MS (m/z, %): 289 (M^+-1, 31), 287 (M^+-3, 31), 178 (100), 180 (100). ^{1}H-NMR : 0.79 (s, 3H), 0.81-0.90 (m, 2H), 0.96 (s, 3H), 1.05 (s, 3H), 1.34-1.51 (m, 1H), 1.60-1.78 (m, 1H), 1.96 (d, 1H, J = 4.9 Hz), 2.25-2.31 (m, 2H, H-1'), 3.48 (t, 2H, H-2', J = 7.0 Hz), 3.77 (d, 1H, J = 6.6 Hz), 3.95 (d, 1H, J = 6.6 Hz), 4.80 (t, 1H, H-4, J = 5.3 Hz). ^{13}C-NMR: 10.9 (CH_3), 19.9 (CH_3), 22.4 (CH_3), 23.4 (CH_2), 27.9 (C-2'), 31.8 (CH_2), 35.8 (C-1'), 46.0 (C quat.), 47.3 (C quat.), 47.3 (CH), 83.6 (CH), 87.8 (CH), 101.7 (C-4). Anal. Calcd. for $C_{13}H_{21}BrO_2$: C, 53.98; H, 7.27; Br, 27.68. Found: C, 54.19; H, 7.12; Br, 27.78.

(1R,2S,4R,6S,7S)-4-Ethyl-1,10,10-trimethyl-3,5-dioxa-tricyclo [3.2.1.$0^{2,6}$] decane (10). Colorless oil. B.p. 123-124°C/10 Torr. $[\alpha]_D^{23}$ = -15 (c = 1.0, EtOH). IR (neat, cm^{-1}): 1450, 1410, 1380, 1360, 1340, 1300. MS (m/z, %): 210 (M^+, 4), 181 (100), 100 (72). ^{1}H-NMR : 1.74 (s, 3H), 1.83-1.90 (m, 2H), 0.95-1.03 (m, 6H), 1.11 (s, 3H), 1.35-1.49 (m, 1H), 1.60-1.81 (m, 3H), 1.92 (d, 1H, J = 4.9 Hz), 3.75 (d, 1H, J = 6.7 Hz), 3.93 (d, 1H, J= 6.7), 4.58 (t, 1H, H-4, J = 5.5 Hz). ^{13}C-NMR : 9.4 (C-2'), 11.0 (CH_3), 20.0 (CH_3), 22.5 (CH_3), 23.5 (CH_2), 25.9 (C-1'), 31.9 (CH_2), 46.1 (C quat.), 47.3 (C quat.), 47.5 (CH), 83.6 (CH), 87.8 (CH), 105.4 (C-4). Anal. Calcd. for $C_{13}H_{22}O_2$: C, 74.28; H, 10.47. Found: C, 74.52; H, 10.76.

(1R,2S,3'S,4R,6S,7S)-4-(3'-hydroxy-3'-phenylpropyl)-1,10,10-trimethyl-3,5-dioxa-tricyclo [3.2.1.$0^{2,6}$] decane (11). Colorless oil. B.p. 179-180°C/2 Torr. $[\alpha]_D^{23}$ = -13.5 (c = 1.0, $CHCl_3$) (d.e. 9%). IR (neat, cm^{-1}): 3380. MS (m/z,.%): 315 (M^+-1, 0.66), 194 (61), 147 (100). ^{1}H-NMR: 0.80 (s, 3H), 0.82-0.90 (m, 2H), 0.99 (s, 3H), 1.09 (s, 3H), 1.31-1.50 (m, 1H), 1.59-1.96 (m, 6H), 2.50-2.75 (broad s, 1H, OH), 3.73-3.76 (m, 1H), 3.90-3.93 (m, 1H), 4.65-4.71 (m, 2H, H-4 and H-3'), 7.24-7.35 (m, 5H). ^{13}C-NMR: 10.9 (CH_3), 19.9 (CH_3), 22.4 (CH_3), 23.3 (CH_2), 28.9 (C-1'), 31.7 (CH_2), 34.3 (C-2'), 45.9 (C quat.), 47.1 (C quat.), 47.2 (CH), 73.6 (C-3'), 83.5 (CH), 87.6 (CH), 104.0 (C-4), 127.7 (CH_{Arom}), 127.1 (CH_{Arom}), 128.1 (CH_{Arom}), 144.3 (C_{Arom}). Anal. Calcd. for $C_{20}H_{28}O_3$: C, 75.95; H, 8.86. Found: C, 75.72; H, 8.71.

(1R,2S,3'S,4R,6S,7S)-4-(3'-hydroxy-3'-phenylbutyl)-1,10,10-trimethyl-3,5-dioxa-tricyclo [3.2.1.$0^{2,6}$] decane (12). Colorless oil. B.p. 180-181°C/2 Torr. $[\alpha]_D^{23}$ = -34.8 (c = 1.5, $CHCl_3$) (d.e. 26%). IR (neat, cm^{-1}): 3410. MS (m/z, %): 329 (M^+-1, 0.48), 194 (83), 121 (100). ^{1}H-NMR: 0.77 (s, 3H), 1.81-1.90 (m, 2H), 0.96 (s, 3H), 1.03 (s, 3H), 1.38-1.50 (m, 1H), 1.52 (s, 3H), 1.65-1.81 (m, 3H), 1.89-2.11(m, 3H), 3.20-3.29 (broad s, 1H, OH), 3.71-3.76 (m, 1H), 3.88-3.92 (m, 1H), 4.59-4.65 (m, 1H, H-4), 7.17-7.43 (m, 5H). ^{13}C-NMR: 11.3 (CH_3), 20.2 (CH_3), 22.7 (CH_3), 23.7 (CH_2), 27.9 (C-1'), 31.1 (C-4'), 32.1 (CH_2), 39.3 (C-2'), 46.3 (C quat.), 47.6 (C quat.), 47.6 (CH), 74.5 (C-3'), 83.9 (CH), 88.2 (CH),

104.7 (C-4), 125.1 (CH_{Arom}), 125.2 (CH_{Arom}), 126.6 (CH_{Arom}), 128.3 (CH_{Arom}), 147.8(C_{Arom}). Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.36; H, 9.09. Found: C, 76.54; H, 9.36.

(S)-4-Phenylbutanolide (13). Colorless oil. B.p. 95-97°C/10^{-1} Torr. $[\alpha]_D^{23}$ = −2.92 (c = 1.0, $CHCl_3$) (lit.[16] $[\alpha]_D$ = -32.5 (c= 4.3, $CHCl_3$)). IR (neat, cm^{-1}): 1755. MS (m/z, %): 162 (M^+, 94), 107 (100). ^{1}H-NMR : 2.10-2.50 (m, 4H, H-2 and H-3), 3.06 (dd, 1H, H-4, J = 8.0 Hz and 6.2 Hz), 7.30-7.41 (m, 5H). ^{13}C-NMR: 28.9 (C-2), 30.9 (C-3), 81.2 (C-4), 125.2 (CH_{Arom}), 128.3 (CH_{Arom}), 128.7 (CH_{Arom}), 139.3 (C_{Arom}), 176.9 (C-1).

(S)-4-Methyl-4-phenylbutanolide (14). Colorless oil. B.p. 55-56°C/10^{-4} Torr. $[\alpha]_D^{23}$ = -18.8 (c = 1.3, $CHCl_3$) (lit.[17] $[\alpha]_D$ = -72.4 (c = 1.3, $CHCl_3$)). IR (neat, cm^{-1}): 1765. MS (m/z, %): 176 (M^+, 15), 161 (100). ^{1}H-NMR: 1.72 (s, CH_3), 2.39-2.71 (m, 4H, H-2 and H-3), 7.27-7.40 (m, 5H). ^{13}C-NMR : 28.9 (C-2), 29.3 (CH_3), 36.1 (C-3), 86.8 (C-4), 124.0 (CH_{Arom}), 127.6 (CH_{Arom}), 128.5 (CH_{Arom}), 144.2 (C_{Arom}), 176.5 (C-1).

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