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On the stereoselectivity of the Paternò–Büchi reaction between carbonyl compounds and 2-furylmethanol derivatives. The case of aliphatic aldehydes and ketones

Maurizio D'Auria,[a,*] Lucia Emanuele,[a] Gabriella Poggi,[b] Rocco Racioppi[a] and Gianfranco Romaniello[a]

[a]*Dipartimento di Chimica, Università della Basilicata, Via N. Sauro 85, 85100 Potenza, Italy*
[b]*Dipartimento di Chimica 'G. Ciamician', Università di Bologna, Via Selmi 2, 40126 Bologna, Italy*

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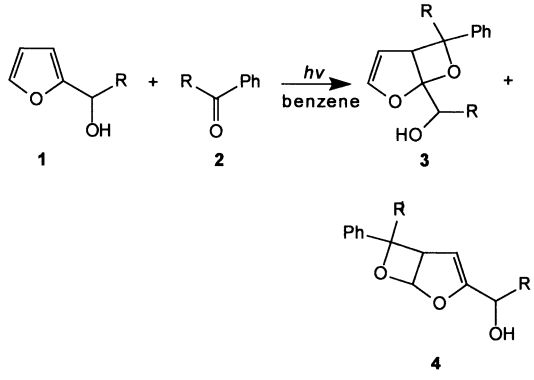
Abstract—The Paternò–Büchi reaction between 2-furylmethanol derivatives and aliphatic aldehydes and ketones induced by irradiation through Vycor at 8°C shows high regioselectivity but no stereoselectivity. This behaviour can be rationalised by assuming that this type of compound reacts through both singlet and triplet excited states. Ab initio calculations are in agreement with the formation of the 1,4-biradical. The more stable biradical accounts for the observed regioselectivity. The lack of stereoselectivity was discussed on the basis of two hypotheses. The allylic strain proposed by Adam does not account for the observed results. On the contrary, hydrogen bond interaction between (triplet excited) carbonyl oxygen and hydroxy group is able to describe the observed behaviour.

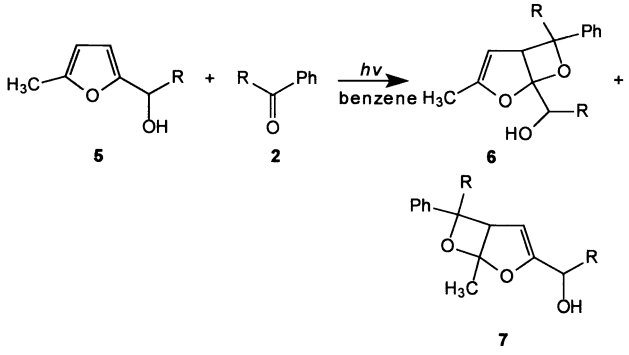
1. Introduction

The Paternò–Büchi reaction between furan derivatives and carbonyl compounds has been extensively studied and several synthetic applications have been reported.[1–44] Nevertheless, the effect of unusual substituents on the site selectivity and stereoselectivity of the reaction has not been studied. Recently we reported that the irradiation of 2-furylmethanol derivatives **1** in the presence of aromatic carbonyl compounds **2** gave the corresponding Paternò–Büchi adducts **3** or **4** (Scheme 1).[45]

The reaction showed good regioselectivity: we obtained **3** as the main product in most of the reactions tested. Furthermore, the reaction showed high stereoselectivity when R was not hydrogen or methyl. In this case only one stereoisomer (1*RS*,1′*RS*,5*RS*) was obtained. When an optically active 2-furylmethanol was used (R≠H and Me), a single enantiomer was obtained. The irradiation of (5-methyl-2-furyl)-benzylic alcohol (**5**) in the presence of aromatic carbonyl compounds gave the corresponding adducts **6** and **7** showing a lack of regioselectivity, although, when the reaction occurred on the side of the furan ring bearing the alcoholic side chain, the stereoselectivity was high (Scheme 2).[46]



Scheme 1.



Scheme 2.

Keywords: Paternò–Büchi reaction; stereoselectivity; furylmethanol derivatives.

* Corresponding author. Tel.: +39-0971-202-240; fax: +39-0971-202-223; e-mail: dauria@unibas.it

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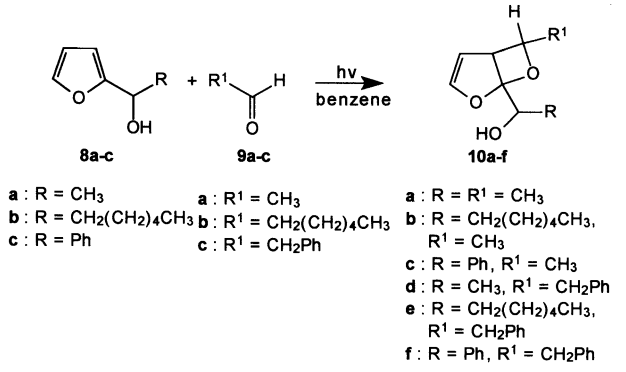
In this paper we report our results obtained on irradiating 2-furylmethanol derivatives in the presence of aliphatic aldehydes and ketones. We will show that in this case the reaction occurs with high regioselectivity but without stereoselectivity.

2. Results and discussion

We used as starting material 1-(2-furyl)-ethanol (**8a**), 1-(2-furyl)-*n*-heptanol (**8b**), and 2-furyl-benzylic alcohol (**8c**) (Scheme 3). These substrates were prepared from the furan-2-carbaldehyde and the corresponding Grignard reagent. The photochemical reactions were carried out in benzene at 8°C in the presence of a Vycor filter. The use of this filter avoids the direct irradiation of the furan derivatives.

The irradiation of **8a** in the presence of acetaldehyde (**9a**) gave **10a** in good yield (Scheme 3, Table 1). We observed the formation of only one regioisomeric product, obtained from attack on the most hindered side of the molecule. The ^{1}H NMR spectrum of **10a** clearly showed that the C-6 configuration is *exo*. In fact, we obtained a signal at δ 4.73 ppm in agreement with previous reported data.[44] The analysis of the product by using HPLC showed that **10a** is a 1:1 diastereoisomeric mixture. The reaction of **8b** with **9a** gave the corresponding adduct **10b** in lower yield (Scheme 3, Table 1). In this case we only observed the formation of the product obtained on the most hindered side of the molecule. Furthermore, we obtained good stereoselectivity at C-6 because we observed the formation of the *exo* isomer. However, HPLC showed that **10b** is a 1:1 mixture of diastereoisomers. The reaction of **8c** with **9a** gave **10c** in good yield (Scheme 3, Table 1). The previously observed trend was maintained: we obtained only one regioisomer, with high stereoselectivity at C-6, but as a 1:1 mixture of diastereoisomers.



Scheme 3.

Table 1. The photochemical reaction between aliphatic aldehydes and 2-furylmethanols

Furan	Aldehyde	Irradiation time (h)	Product	Yield (%)
8a	**9a**	8	**10a**	64
8b	**9a**	8	**10b**	42
8c	**9a**	8	**10c**	58
8a	**9b**	8	**10a**	46
8b	**9b**	8	**10b**	68
8c	**9b**	8	**10c**	56
8a	**9c**	8	**10d**	52
8b	**9c**	8	**10e**	48
8c	**9c**	8	**10f**	64

The irradiation of **8a–c** in the presence of heptanal (**9b**) gave some unexpected results. In fact, the irradiation of **8a** in the presence of **9b** gave **10a** as the only product (Scheme 3, Table 1). Also in this case the product was a single regioisomer and the *exo* stereoisomer at C-6. It was also a 1:1 mixture of diastereoisomers. Surprisingly, we obtained a product where R^1 was the methyl group and not the *n*-hexyl group as expected. The same result was obtained using **8b** and **8c** as substrates. By using **8b** as substrate we obtained **10b** as the only product (Scheme 3, Table 1), while the irradiation of **8c** gave the adduct **10c** (Scheme 3, Table 1).

Finally, the irradiation of **8a** in the presence of phenylacetaldehyde (**9c**) gave the corresponding adduct **10d** in good yield (Scheme 3, Table 1). We obtained a single regioisomeric product (from the attack on the most hindered side of the molecule) and an *exo* stereoisomer at C-6. However, HPLC showed the presence of a 1:1 mixture of diastereoisomers. The irradiation of **8b** with **9c** gave **10e** (Scheme 3, Table 1), while the same reaction between **8c** and **9c** gave **10f** as the only product (Scheme 3, Table 1).

On the basis of the above results we can draw some conclusions: (i) the reaction between 2-furylmethanol derivatives and aliphatic aldehydes showed higher regioselectivity than the reactions of the same substrates with aromatic aldehydes;[45,46] (ii) the reaction between 2-furylmethanol derivatives and aliphatic aldehydes showed lower stereoseletivity than the reactions of the same substrates with aromatic aldehydes;[45,46] (iii) the use of aliphatic aldehydes induced the formation of unexpected products (such in the reaction of **8a–c** with **9b**).

The use of aliphatic aldehydes in the Paternò–Büchi reaction is often explained by a mechanism involving an excited singlet state.[47] Acetaldehyde shows a low intensity absorption band at 290–293 nm due to a $n\rightarrow\pi^*$ transition. At this wavelength the fluorescence quantum yield (Φ_f) is in the range 0.50×10^{-3}–1.2×10^{-3};[48,49] the intersystem crossing quantum yield (Φ_{isc}) for this compound is 0.6;[48] on the basis of these data both singlet and triplet state can be involved in the reaction.

Assuming that the reaction occurs in the first excited singlet state, the 0–0 transition occurs at 29,771 cm^{-1};[50] this indicates that the energy (E_S) of the excited singlet state is ca. 356 kJ mol^{-1}. Assuming that the reaction occurs in the first excited triplet state, acetaldehyde shows a maximum in the phosphorescence spectrum at 430 nm;[51] this emission corresponds to a triplet energy (E_T) of 276 kJ mol^{-1}.

As reported earleir the reaction between furylmethanol derivatives and heptanal gave unexpected products **10a–c** where R^1 was CH_3 instead of $CH_2(CH_2)_4CH_3$ (Scheme 3). This behaviour can be explained by assuming that heptanal does not react with furan derivatives but undergoes a

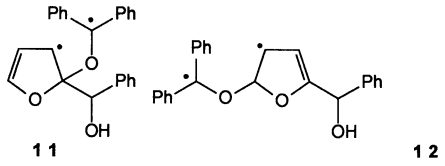


Figure 1.

Norrish type-II reaction with γ-H abstraction to give acetaldehyde and this product reacts with the furan ring. Norrish type-II reactions occur from both singlet and triplet n,π* states, but the quantum yields from the singlet state are generally lower than from the triplet state.[52] Furthermore, it is known that aliphatic aldehydes (capable of giving the Norrish type-II reaction) react with furan to give the corresponding adducts with high efficiency.[6] This results the following conclusions: (i) if the reaction between aliphatic aldehydes and furylmethanols occurs in the singlet excited state, the Norrish type-II reaction must compete with the Paternò–Büchi reaction in this excited state; in this case, β-cleavage occurred more rapidly than the Paternò–Büchi reaction; (ii) this hypothesis is in conflict with both the low efficiency of the Norrish type-II reaction in the singlet state and the energetically favoured reaction between the aliphatic aldehyde in its excited singlet state and furan as described above; (iii) if the reaction between aliphatic aldehydes and furylmethanols occurs in the triplet excited state, the Norrish type-II reaction must compete with the Paternò–Büchi reaction in both singlet and triplet excited states.

In our previous work in this field, the regioselectivity of the Paternò–Büchi reaction between carbonyl compounds and 2-furylmethanol derivatives was explained on the basis of the relative stability of the possible intermediates.[45,46] In fact, theoretical work on this reaction showed that, for reactions occurring in the triplet state, the reaction path could be predicted by the most stable biradical rule.[53] Semiempirical calculations showed that only a zwitterionic intermediate could explain the observed regiochemical behaviour.

In order to test this hypothesis we performed ab initio calculations on the triplet 1,4-biradicals **11** and **12** (Fig. 1). The structures were optimized at B3LYP/3-21G* level by means of the Gaussian94 package of programs on a K200 Pentium II/400 MHz SCSI system.[54]

The results of the calculations showed that **11** is more stable than **12** by 0.8 kJ mol^{-1}. On the basis of this result we must revise our previous hypothesis on the formation of a zwitterionic intermediate: the regioselectivity in the reaction between **1** and **2** can be explained by proposing the formation of the triplet 1,4-biradical.

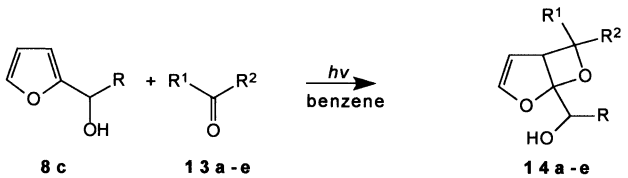
In our previous work we found that the reaction between 2-furylmethanol derivatives and aromatic aldehydes and ketones gave the corresponding products with high stereoselectivity.[45,46] In this work we found that the reaction of the same furan derivatives with aliphatic aldehydes gave high stereoselectivity at C-6 (in the dioxabicycloheptene skeleton), however, we observed that all the reactions occurred with no stereoselectivity at C-1 and C-5. In order to explain the observed stereoselectivity when aromatic carbonyl compounds were used, we assume an interaction between the hydroxyl group and the carbonyl group.[45] A similar type of interaction has been proposed in the case of the reaction of allylic alcohols with carbonyl compounds.[55,56] The lack of stereoselectivity in the experiments reported earlier can be explained by assuming that the interaction between the hydroxyl and the carbonyl groups does not exist in this case.

We could assume that, in a reaction involving an excited singlet state, this short lived state cannot interact with the hydroxyl group to give the observed stereoselectivity in the case of reaction where the triplet state is involved.

The lack of stereoselectivity has been confirmed by using chiral 2-furylmethanol derivatives.[45] *R*-(+)-**8a–c** were obtained through kinetic resolution of (±)-**8a–c** in the presence of Ti(O*i*Pr)$_4$, TBHP and L-(+)-DIPT.[57,58] The substrates thus obtained were enantiomerically pure by chiral HPLC. When the irradiation was carried out on *R*-**8a–c** in the presence of acetaldehyde we obtained the same products without any difference in the stereoisomeric composition of the products.

In order to obtain further information about the reactivity of 2-furylmethanol derivatives, we studied the Paternò–Büchi reaction of these substrates with aliphatic ketones. The irradiation of **8c** in the presence of acetone (**13a**) gave **14a** in good yields (Scheme 4, Table 2). We observed the formation of only one regioisomeric product, obtained from the attack on the most hindered side of the molecule. The analysis of the product by using HPLC showed that **14a** is a 1:1 diastereoisomeric mixture.

The irradiation of **8c** in the presence of 2,4-dimethyl-3-pentanone (**13b**) gave the same type of results. In fact, the irradiation of **8c** in the presence of **13b** gave **14b** as the only



c : R = Ph
a : $R^1 = R^2 = CH_3$
b : $R^1 = R^2 = CH(CH_3)_2$
c : R^1-R^2 = -$CH_2(CH_2)_3CH_2$-
d : R^1-R^2 = -$CH_2CH_2CH[C(CH_3)_3]CH_2CH_2$-
e : R^1-R^2 = -$CH_2(CH_2)_4CH_2$-

a : R = Ph, $R^1 = R^2 = CH_3$
b : R = Ph, $R^1 = R^2 = CH(CH_3)_2$
c : R = Ph, R^1-R^2 = -$CH_2(CH_2)_3CH_2$-
d : R = Ph, R^1-R^2 = -$CH_2CH_2CH[C(CH_3)_3]CH_2CH_2$-
e : R = Ph, R^1-R^2 = -$CH_2(CH_2)_4CH_2$-

Scheme 4.

Table 2. The photochemical reaction between aliphatic ketones and **8c**

Aldehyde	Irradiation time (h)	Solvent	Product	Yield (%)
13a	8	Benzene	**14a**	33
13a	8	Acetone	**14a**	47
13b	8	Benzene	**14b**	45
13c	8	Benzene	**14c**	30
13d	8	Benzene	**14d**	25
13e	8	Benzene	**14e**	40

product (Scheme 4, Table 2). Also in this case the product was a single regioisomer. It was also a 1:1 mixture of diastereoisomers.

The irradiation of **8c** in the presence of cyclohexanone (**13c**) gave the corresponding adduct **14c** in good yields (Scheme 4, Table 2). We obtained a single regioisomeric product (that from the attack on the most hindered side of the molecule). Furthermore, in this case HPLC again showed the presence of a 1:1 mixture of diastereoisomers.

When **8c** is irradiated in the presence of 4-*t*-butylcyclohexanone (**13d**) the product **14d** is obtained (Scheme 4, Table 2). Also in this case we obtained only one regioisomer. Furthermore, **14d** appeared as a 1:1 diastereoisomeric mixture (^{1}H NMR).

Finally, the reaction of **8c** in the presence of cycloheptanone (**13e**) gave **14e** as a single regioisomeric product but as a mixture of stereoisomeric compounds (Scheme 4, Table 2).

By using acetone as model compound for aliphatic ketones, the singlet excited acetone is converted with an efficiency of unity into triplet acetone via rapid intersystem crossing.[59]

It is noteworthy that both the reactions of 2-furylmethanols with aliphatic aldehydes and ketones do not show stereoselectivity. Furthermore, in the case of aliphatic ketones we can exclude that this effect is due to a short lived singlet excited state. Our results can not be explained on the basis of 1,3 allylic strain as reported by Adam.[55,56] In fact, the same 'allylic' substrates were used giving high stereoselectivity with aromatic aldehydes and ketones and no stereoselectivity when using aliphatic aldehydes and ketones.

Recently, Griesbeck reported that stereoselectivity in 2+2 cycloaddition reactions between carbonyl compounds and allylic alcohol derivatives can increase with the possibility of hydrogen-bonding interactions with singlet as well as triplet excited carbonyl states prior to bond formation.[60] However, aliphatic and aromatic ketones could give the same hydrogen bond interaction with the hydroxy group in the furan derivatives, while the stereoselectivity is different. In order to understand if the strength of the hydrogen bond interaction can be different in aromatic and aliphatic aldehydes and ketones, we calculated (PM3) the charge on carbonyl oxygen in the triplet state of benzophenone and acetone: while in benzophenone the charge was −0.076, in acetone we obtained −0.066. This difference could possibly justify the observed lack in stereoselectivity observed when using aliphatic aldehydes and ketones.

3. Experimental

NMR spectra were recorded on a Bruker 300 AM instrument. Elemental analyses were obtained using a Carlo Erba Elemental Analyzer 1106. 2-Furylmethanol was obtained by Aldrich. 2-Furylmethanol derivatives were prepared through the reaction of suitable Grignard reagents with furan-2-carbaldehyde.[61]

3.1. Caution

Performing the NMR spectra of cycloadducts we observed that deuterated chloroform purchased from Aldrich induced a retro-cycloaddition reaction giving, within an hour, the starting materials. We did not observe this behaviour using deuterated chloroform from Fluka or Carlo Erba. We asked Aldrich about the presence of metals or some other trace impurities in deuterated chloroform which could give this type of reaction. Until now, we did not obtain any reply from Aldrich and we think we should advice readers on this possible problem.

3.2. Cycloaddition reaction between 2-furylmethanols and carbonyl compounds—general procedure

2-Furylmethanol derivative (**8a**–**c**) (10 mmol) was dissolved in benzene (70 ml) in the presence of the carbonyl compound (15 mmol) in a quartz vessel. The mixture was flushed with nitrogen for 1 h and, then, maintained at 8°C with a Haake F3 thermostat. The mixture was irradiated with a 500 W high-pressure mercury arc (Helios–Italquartz) with Vycor filter. After 8 h, the irradiation was stopped. After this time 50% conversion of the starting material was observed. The removal of the solvent yielded a crude product that was chromatographed on silica gel. Elution with *n*-hexane/ethyl acetate 9:1 gave pure products (Table 1)

3.2.1. 1-(1-Hydroxyethyl)-6-methyl-2,7-dioxabicyclo-[3.2.0]hept-3-ene (10a). Viscous oil; ^{1}H NMR ($CDCl_3$) δ: 6.60 (dd, J_1=2.5 Hz, J_2=0.5 Hz, 1H, 3-H), 5.30 (dd, J_1=J_2=2.5 Hz, 1H, 4-H), 4.73 (m, 1H, 6-H), 3.90 (m, 1H, C*H*OH), 3.36 (m, 1H, 5-H), 2.2 (br s, 1H, OH), 1.48 (d, J=6 Hz, 3H, CH_3), 1.18 (d, J=6.6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 148.4 (C-3), 117.5 (C-1), 104.8 (C-4), 87.3 (C-6), 67.4 (CHOH), 47.6 (C-5), 21.7 (CH_3), 15.3 (CH_3). $C_8H_{12}O_3$ (156.2): calcd C 61.52, H 7.74; found C 61.55, H, 7.70.

3.2.2. 1-(1-Hydroxy-*n*-heptyl)-6-methyl-2,7-dioxabicyclo-[3.2.0]-hept-3-ene (10b). Viscous oil; ^{1}H NMR ($CDCl_3$) δ: 6.59 (dd, J_1=2.6 Hz, J_2=0.5 Hz, 1H, 3-H), 5.29 (dd, J_1=2.6 Hz, J_2=2.5 Hz, 1H, 4-H), 4.71 (m, 1H, 6-H), 3.68 (m, 1H, C*H*OH), 3.34 (m, 1H, 5-H), 2.3 (br s, 1H, OH), 1.49 (d, J=6 Hz, 3H, CH_3), 1.31 (m, 10H, CH_2), 1.31 (t, J=7 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 148.4 (C-3), 117.1 (C-1), 104.7 (C-4), 87.2 (C-6), 71.5 (CHOH), 48.2 (C-5), 32.0, 30.8, 30.1, 29.5, 25.6, 22.7, 21.7 (CH_3), 14.9 (CH_3). $C_{13}H_{22}O_3$ (226.3): calcd C 68.99, H 9.80; found C 68.89, H, 9.87.

3.2.3. 1-(1-Hydroxybenzyl)-6-methyl-2,7-dioxabicyclo-[3.2.0]-hept-3-ene (10c). Viscous oil; ^{1}H NMR ($CDCl_3$) δ: 7.5–7.2 (m, 5H, aromatic protons), 6.66 (dd,

J_1=2.7 Hz, J_2=0.5 Hz, 0.5H, 3-H), 6.46 (dd, J_1=2.7 Hz, J_2=0.5 Hz, 0.5H, 3-H), 5.29 (dd, J_1=2.7 Hz, J_2=2.5 Hz, 0.5H, 4-H), 5.14 (dd, J_1=2.7 Hz, J_2=2.5 Hz, 0.5H, 4-H), 4.85 (m, 0.5H, 6-H), 4.80 (m, 0.5H, 6-H), 4.75 (m, 0.5H, C*H*OH),), 4.61 (m, 0.5H, C*H*OH), 3.32 (m, 1H, 5-H), 2.97 (s, 0.5H, OH), 2.62 (s, 0.5H, OH), 1.50 (d, J=6.4 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 148.4 (C-3), 148.3 (C-3), 134.9, 129.8, 129.7, 127.6, 116.9 (C-1), 105.0 (C-4), 104.8 (C-4), 87.8 (C-6), 87.5 (C-6), 74.1 (CHOH), 73.0 (CHOH), 48.4 (C-5), 48.2 (C-5), 21.5 (CH_3). $C_{13}H_{14}O_3$ (218.3): calcd C 71.54, H 6.47; found C 71.76, H, 6.55.

3.2.4. 1-(1-Hydroxyethyl)-6-benzyl-2,7-dioxabicyclo-[3.2.0]hept-3-ene (10d). Viscous oil; ^{1}H NMR ($CDCl_3$) δ: 7.5–7.2 (m, 5H, aromatic protons), 6.62 (dd, J_1=2.6 Hz, J_2=0.5 Hz, 1H, 3-H), 5.28 (dd, J_1=J_2=2.6 Hz, 1H, 4-H), 4.73 (m, 1H, 6-H), 4.69 (s, H, CH_2), 4.67 (s, 1H, CH_2), 3.85 (m, 1H, C*H*OH), 3.34 (m, 1H, 5-H), 2.2 (br s, 1H, OH), 1.18 (d, J=6.6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 148.4 (C-3), 138.5, 132.9, 129.6, 126.2, 117.3 (C-1), 105.0 (C-4), 87.3 (C-6), 70.3 (CHOH), 48.2 (C-5), 29.3 (CH_2), 15.2 (CH_3). $C_{14}H_{16}O_3$ (232.3): calcd C 72.39, H 6.94; found C 72.25, H, 7.00.

3.2.5. 1-(1-Hydroxy-*n*-heptyl)-6-benzyl-2,7-dioxabicyclo-[3.2.0]-hept-3-ene (10e). Viscous oil; ^{1}H NMR ($CDCl_3$) δ: 7.5–7.2 (m, 5H, aromatic protons), 6.60 (dd, J_1=2.6 Hz, J_2=0.5 Hz, 1H, 3-H), 5.29 (dd, J_1=2.6 Hz, J_2=2.5 Hz, 1H, 4-H), 4.75 (s, 1H, CH_2), 4.73 (s, 1H, CH_2), 4.71 (m, 1H, 6-H), 3.80 (m, 1H, C*H*OH), 3.30 (m, 1H, 5-H), 2.3 (br s, 1H, OH), 1.30 (m, 10H, CH_2), 1.28 (t, J=7 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 148.4 (C-3), 138.6, 133.0, 129.4, 126.0, 117.0 (C-1), 104.6 (C-4), 87.4 (C-6), 71.5 (CHOH), 48.2 (C-5), 38.5, 32.0, 30.8, 30.0, 29.5, 25.6, 22.7, 14.1. $C_{19}H_{26}O_3$ (302.4): calcd C 75.46, H 8.67; found C 75.55, H, 8.63.

3.2.6. 1-(1-Hydroxybenzyl)-6-benzyl-2,7-dioxabicyclo-[3.2.0]hept-3-ene (10f). Viscous oil; ^{1}H NMR ($CDCl_3$) δ: 7.5–7.2 (m, 10H, aromatic protons), 6.63 (dd, J_1=2.6 Hz, J_2=0.5 Hz, 1H, 3-H), 5.31 (dd, J_1=2.6 Hz, J_2=2.5 Hz, 1H, 4-H), 4.87 (m, 1H, 6-H), 4.75 (m, 2H, CH_2), 4.60 (m, 1H, C*H*OH), 3.32 (m, 1H, 5-H), 3.0 (bs, 1H, OH). ^{13}C NMR ($CDCl_3$) δ: 148.4 (C-3), 138.4, 134.9, 132.9, 129.8, 129.6, 127.6, 126.3, 116.9 (C-1), 105.1 (C-4), 87.7 (C-6), 72.5 (CHOH), 48.4 (C-5), 30.1 (CH_2). $C_{19}H_{18}O_3$ (294.4): calcd C 77.53, H 6.16; found C 77.61, H, 6.11.

3.2.7. 1-(1-Hydroxybenzyl)-6,6-dimethyl-2,7-dioxabicyclo-[3.2.0]-hept-3-ene (14a). Viscous oil; ^{1}H NMR ($CDCl_3$) δ: 7.5–7.2 (m, 5H, aromatic protons), 6.56 (dd, J_1=J_2=3.5 Hz, 0.5H, 3-H), 5.59 (dd, J_1=J_2=3.2 Hz, 0.5H, 3-H), 5.47 (s, 0.5H, C*H*OH), 5.43 (s, 0.5H, C*H*OH), 5.36 (dd, J_1=J_2=2.5 Hz, 0.5H, 4-H), 5.27 (d, J=2.5 Hz, 0.5H, 4-H), 3.68 (m, 1H, 5-H), 2.88 (s, 1H, OH), 1.22 (s, 3H, CH_3), 1.18 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 148.4 (C-3), 148.3 (C-3), 135.2, 129.7, 127.7, 116.8 (C-1), 105.2 (C-4), 104.9 (C-4), 87.8 (C-6), 87.6 (C-6), 74.1 (CHOH), 72.9 (CHOH), 48.3 (C-5), 48.1 (C-5), 21.6 (CH_3), 20.3 (CH_3). $C_{14}H_{16}O_3$ (232.3): calcd C 72.39, H 6.94; found C 72.45, H, 6.89.

3.2.8. 1-(1-Hydroxybenzyl)-6,6-di(methylethyl)-2,7-dioxa-bicyclo-[3.2.0]hept-3-ene (14b). Viscous oil; ^{1}H NMR ($CDCl_3$) δ: 7.5–7.2 (m, 5H, aromatic protons), 6.58 (d, J=3.3 Hz, 0.5H, 3-H), 5.61 (d, J=3.5 Hz, 0.5H, 3-H), 5.31 (m, 1H, 4-H), 4.93 (d, J=2.5 Hz, 1H, C*H*OH), 3.88 (m, 1H, 5-H), 2.61 (s, 1H, OH), 1.56 (m, 2H, CH), 1.35 (m, 12H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 149.2 (C-3), 142.9 (C-3), 135.1, 129.9, 127.5, 119.5 (C-1), 112.8 (C-4), 111.1 (C-4), 104.9 (C-6), 90.4 (C-6), 73.5 (CHOH), 72.9 (CHOH), 49.5 (C-5), 30.3 (CH), 29.7 (CH) 22.7 (CH_3). $C_{18}H_{24}O_3$ (288.4): calcd C 74.97, H 8.39; found C 74.90, H, 8.45.

3.2.9. 1-(1-Hydroxybenzyl)-6,6-pentamethylene-2,7-dioxa-bicyclo-[3.2.0]hept-3-ene (14c). Viscous oil; ^{1}H NMR ($CDCl_3$) δ: 7.5–7.3 (m, 5H, aromatic protons), 6.45 (m, 0.5H, 3-H), 6.25 (d, J=3 Hz, 0.5H, 4-H), 5.62 (d, J=3 Hz, 0.5H, 3-H), 5.35 (s, 1H, C*H*OH), 5.00 (m, 0.5H, 4-H), 3.88 (m, 0.5H, 5-H), 3.38 (m, 0.5H, 5-H), 2.5 (s, 1H, OH), 1.25 (s, 10H, CH_2). ^{13}C NMR ($CDCl_3$) δ: 149.2 (C-3), 142.9 (C-3), 134.8, 129.8, 127.8, 119.5 (C-1), 112.8 (C-4), 112.4 (C-4), 104.9 (C-6), 90.4 (C-6), 73.5 (CHOH), 72.9 (CHOH), 49.5 (C-5), 30.3 (CH_2), 29.7 (CH_2), 27.7 (CH_2), 23.9 (CH_2), 22.2 (CH_2). $C_{17}H_{20}O_3$ (272.3): calcd C 74.97, H 7.40; found C 75.04, H, 7.32.

3.2.10. 1-(1-Hydroxybenzyl)-6,6-(3-*t*-butyl)pentamethyl-ene-2,7-dioxa-bicyclo[3.2.0]hept-3-ene (14d). Viscous oil; ^{1}H NMR ($CDCl_3$) δ: 7.5–7.2 (m, 5H, aromatic protons), 6.57 (dd, J_1=J_2=3.3 Hz, 0.5H, 3-H), 5.59 (dd, J_1=J_2=3.2 Hz, 0.5H, 3-H), 5.30 (m, 1H, C*H*OH), 4.94 (m, 1H, 4-H), 3.72 (m, 1H, 5-H), 2.73 (s, 1H, OH), 1.68 (m, 9H, CH_2 e CH), 1.18 (s, 9H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 149.2 (C-3), 135.2, 130.0, 127.8, 117.3 (C-1), 104.9 (C-4), 90.4 (C-6), 73.4 (CHOH), 49.5 (C-5), 47.6, 37.5, 34.3, 27.7, 15.3 (CH_3). $C_{21}H_{28}O_3$ (328.5): calcd C 76.79, H 8.59; found C 76.60, H, 8.72.

3.2.11. 1-(1-Hydroxybenzyl)-6,6-hexamethylene-2,7-dioxa-bicyclo-[3.2.0]hept-3-ene (14e). Viscous oil; ^{1}H NMR ($CDCl_3$) δ: 7.5–7.3 (m, 5H, aromatic protons), 6.45 (m, 0.5H, 3-H), 6.28 (d, J=3 Hz, 0.5H, 4-H), 5.62 (d, J=3 Hz, 0.5H, 3-H), 5.34 (m, 1H, C*H*OH), 5.00 (m, 0.5H, 4-H), 3.90 (m, 0.5H, 5-H), 3.37 (m, 0.5H, 5-H), 2.63 (s, 1H, OH), 1.28 (s, 12H, CH_2). ^{13}C NMR ($CDCl_3$) δ: 149.2 (C-3), 135.2, 129.8, 127.8, 117.8 (C-1), 112.8 (C-4), 112.4 (C-4), 104.9 (C-6), 90.4 (C-6), 73.5 (CHOH), 65.8 (CHOH), 49.5 (C-5), 34.1, 29.5, 23.9. $C_{18}H_{22}O_3$ (286.4): calcd C 75.50, H 7.74; found C 75.38, H, 7.85.

3.3. Optically active 2-furylmethanols—general procedure

A solution of Ti(O*i*Pr)$_4$ (6.84 ml, 46 mmol) in CH_2Cl_2 (112 ml) was treated at −20°C with L-(+)-DIPT (5.77 ml, 55 mmol). After 10 min at −30°C a (2-furyl)methanol derivative (46 mmol) dissolved in CH_2Cl_2 (5.5 ml) and *t*-butylhydroperoxide (4.6 ml) were added. The solution was stirred at −21°C for 40 h and then poured into a mixture of 10% tartaric acid (0.94 ml), ether (37.4 ml), and NaF (5.6 g). The mixture was stirred for 3 h at room temperature. The mixture was filtered on Celite. The organic phase was concentrated to give an oil which was dissolved in ether (187 ml) and treated with 1N NaOH (93.5 ml) for 30 min at 0°C. The ethereal phase was washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave an oil that was

chromatographed on silica gel to give pure *R*-(+)-**8** derivatives. The ee was estimated by using chiral HPLC on Chiralcel OD using as eluent *n*-hexane/*i*-propanol 95:5 at 1 ml min^{-1}. The chromatograms were detected with an UV detector at 235 nm.

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