The Paternò-Büchi Reaction of 2-Furylmethanols

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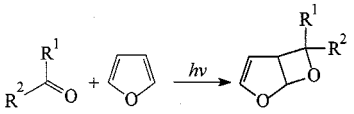
The Paternò-Büchi reaction between 2-furylmethanol derivatives and aromatic carbonyl compounds shows good regioselectivity and high stereoselectivity. The regio- and stereoselectivity of the reaction can be explained by assuming a role of both the substituent on the 2-furylmethanol derivative and the hydroxy group in order to favor the approach of the carbonyl group towards a prochiral face of the furan. Electrochemical and kinetic properties of 2-furylmethanols are in agreement with an electron-transfer mechanism. The stereoselectivity of the reaction was confirmed using chiral 2-furylmethanols: These substrates gave the corresponding Paternò-Büchi adducts with high enantiomeric excess.

Introduction

The photochemical reaction of furan with carbonyl compounds to give the corresponding oxetanes (Scheme 1) has been extensively studied in organic chemistry[1] and several synthetic applications of this method have been reported.[2]

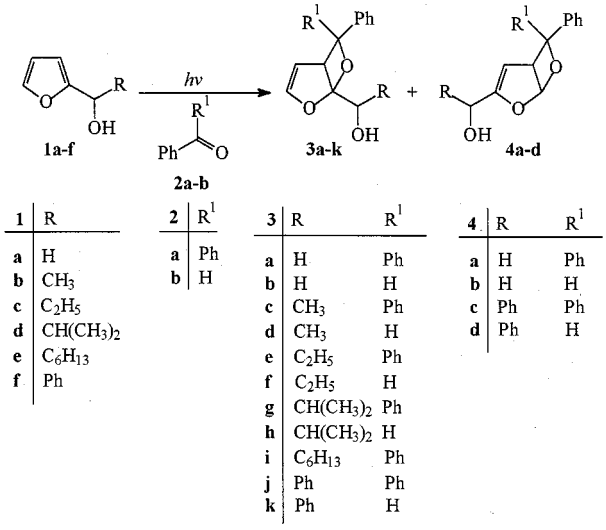


Scheme 1

Some years ago Carless found that 2-acetylfurans showed remarkable selectivity in cycloaddition reactions with aromatic aldehydes.[3] In this paper we want to report our results obtained using 2-furylmethanols as substrates. In the literature, only the reaction of 2-furylmethanol with benzaldehyde was described and, in this case, low selectivity was observed.[3]

Results and Discussion

The irradiation of 2-furylmethanol (**1a**) in the presence of benzophenone (**2a**) gave a 3:1 mixture of regioisomeric products **3a** and **4a** (Scheme 2, Table 1). The yields refer to isolated products and they did not change when the reaction mixtures were monitored by ^{1}H NMR spectroscopy.



1	R
a	H
b	CH_3
c	C_2H_5
d	$CH(CH_3)_2$
e	C_6H_{13}
f	Ph

2	R^1
a	Ph
b	H

3	R	R^1
a	H	Ph
b	H	H
c	CH_3	Ph
d	CH_3	H
e	C_2H_5	Ph
f	C_2H_5	H
g	$CH(CH_3)_2$	Ph
h	$CH(CH_3)_2$	H
i	C_6H_{13}	Ph
j	Ph	Ph
k	Ph	H

4	R	R^1
a	H	Ph
b	H	H
c	Ph	Ph
d	Ph	H

Scheme 2

Table 1. The photochemical reaction between aromatic carbonyl compounds and 2-furylmethanols

Furan	Carbonyl compound	Irradiation time [h]	Product	Yield [%]
1a	**2a**	96	**3a**	65
			4a	20
	2b	15	**3b**	50
			4b	26
1b	**2a**	36	**3c**	71
	2b	48	**3d**	7
1c	**2a**	36	**3e**	73
	2b	36	**3f**	78
1d	**2a**	30	**3g**	69
	2b	48	**3h**	60
1e	**2a**	96	**3i**	61
	2b	48	**–**	–
1f	**2a**	18	**3j**	73
			4c	7
	2b	24	**3k**	25
			4d	43

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When the reaction was performed in the presence of benzaldehyde (**2b**), we observed the formation of a 2:1 mixture of the same type of regioisomeric products (**3b** and **4b**) (Scheme 2, Table 1). The ^{1}H NMR spectrum of **3b** showed that the phenyl group was in an *exo* position,[1a] in agreement with previously reported results on this compound.[3]

The same reaction was carried out using 2-furylethanol (**1b**) as substrate: In this case we observed a large increase in the regioselectivity of the reaction. In fact, when benzophenone was used as a reagent, only **3c** was obtained as an inseparable mixture of stereoisomers (Scheme 2, Table 1).

The reaction of **1b** with benzaldehyde gave only the compound **3d**. In this case, however, we obtained the product in a very low yield (Scheme 2, Table 1). Nevertheless, **3d** was obtained as a single diastereoisomer. The analysis of the NOE effects of this compound showed that it was the (1*RS*,1′*RS*,5*RS*,6*R,S*) diastereoisomer. Irradiation at δ = 3.83 (5-H) caused a sharp increase (8%) in the signals for the *ortho* protons of the phenyl ring (δ = 7.25) and a negative NOE for the CHOH proton at δ = 4.01. This negative NOE can be understood by considering that the most stable conformation of (1*R*,1′*R*,5*R*,6*R*)-**3d** is that represented in Figure 1. This assignment is supported by PM3 semiempirical calculations. The distance between an *ortho* proton on the phenyl ring and the hydrogen atom at the hydroxy-bearing carbon atom is approximately 3.60 Å. The most stable conformation of the diastereoisomer (1*R*,1′*S*,5*R*,6*R*)-**3d** does not show the same distance between the phenyl *ortho* protons and the CHOH proton.

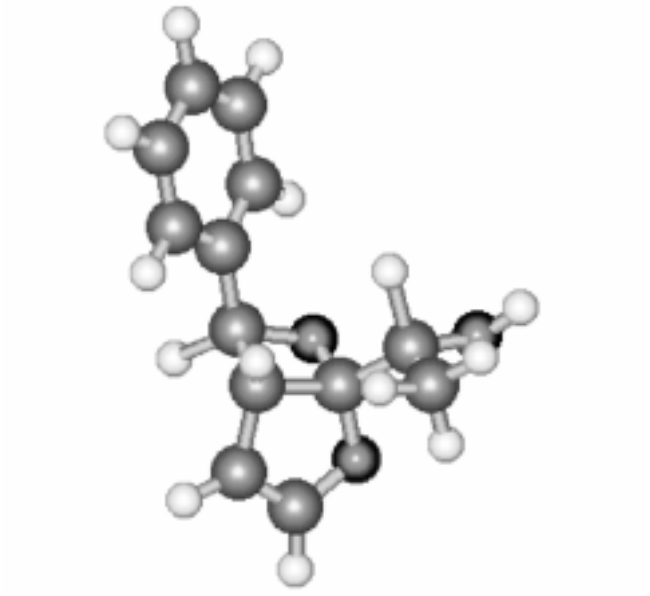


Figure 1. The most stable conformation of (1*R*,1′*R*,5*R*,6*R*)-**3d**

The same results were obtained when **1c** and **1d** were used as substrates. In this case we obtained only the regioisomers **3e** and **3g**, when irradiated in the presence of benzaldehyde, and the regioisomers **3f** and **3h**, when irradiated with benzophenone (Scheme 2, Table 1).

In order to study the effect of an extended side-chain on the regiochemistry of the reaction, we tested the photochemical behavior of 1-(2-furyl)heptanol (**1e**). In the presence of benzophenone, we obtained only **3i** as a single diastereoisomer (Scheme 2, Table 1). The NOE of this molecule showed that we obtained the (1*RS*,1′*RS*,5*RS*) diastereoisomer, the effect being similar to that reported for **3d**. In this case we observed a high stereoselectivity in the photochemical reaction, which has never been described before. When the reaction was carried out in the presence of benzaldehyde, no product was observed (Table 1). These results demonstrated that both regio- and stereoselectivity increase in the presence of bulky substituents on the side-chain of 2-furylmethanols. In all cases, the most favored product was derived from the attack of the carbonyl group at the most hindered side of the furan ring. Finally, benzaldehyde showed a lower reactivity than benzophenone towards our substrates.

A slightly different behavior was observed with 1-(2-furyl)benzylic alcohol (**1f**) as substrate. In this case, the reaction with benzophenone gave a 10:1 mixture of **3j** and **4c** (Scheme 2, Table 1). We also obtained **3j** as a single pair of enantiomers. The analysis of NOE allows us to assign a (1*RS*,1′*RS*,5*RS*) stereochemistry to the stereogenic centers. When benzaldehyde was used, the photochemical reaction took place in reasonable yields (Scheme 2, Table 1). However, we obtained a 3:2 mixture of **4d** and **3k**: In this case, the regiochemistry of the reaction was completely reversed. Compound **4d** appeared as a mixture of stereoisomers, while **3k** was a 2:1 mixture of the (1*RS*,1′*RS*,5*RS*,6*RS*) and (1*RS*,1′*SR*,5*RS*,6*RS*) diastereoisomers.

On the basis of the above data we can formulate the following conclusions:

1) 2-Furylmethanol derivatives react with aromatic carbonyl compounds in variable yields.

2) Benzaldehyde shows a lower reactivity towards 2-furylmethanols than benzophenone.

3) The reaction shows a good regioselectivity and in some cases we observed regiospecific reactions.

4) In most of the reported examples, the reaction occurs at the more substituted double bond of the furan derivative.

5) The reaction is stereoselective and when the reagent is benzaldehyde, the *exo* isomer is favored, in agreement with reported data.

6) The presence of a hydroxy group in the furan derivatives leads to different results depending on the nature of the side chain R. In particular: a) When R = CH_3, the reaction is not affected by the presence of the alcohol; in fact we obtained a 1:1 mixture of two diastereoisomers. b) When R = CH_2CH_3, $CH(CH_3)_2$, and *n*-C_6H_{13}, we observed complete stereoselectivity. In these cases, the configuration of the carbon atom bearing the alcohol group determines the configuration of the other chiral centers on the molecule. c) When R = phenyl, we observed the same behavior as **1b**, with complete stereoselectivity.

The Paternò-Büchi reaction can occur starting from the first excited singlet state or from the first excited triplet state of the carbonyl compound. Furthermore, photo-induced electron transfer has been invoked.[4] The reactions de-

scribed above occur from the triplet state of both benzophenone and benzaldehyde because they show $\Phi_{isc} = 1$.[5] The reaction follows second-order kinetics. We studied the kinetic behavior of **1b** in the presence of **2a**. The reaction followed first-order kinetics when the disappearance of benzophenone was monitored by UV at 360 nm (Figure 2). The same behavior was observed following the disappearance of **1b** by ^{1}H NMR spectroscopic analysis (Figure 3). This datum allows us to know that both the carbonyl compound and the furan derivative participate in the rate-determining step (the primary photochemical process).

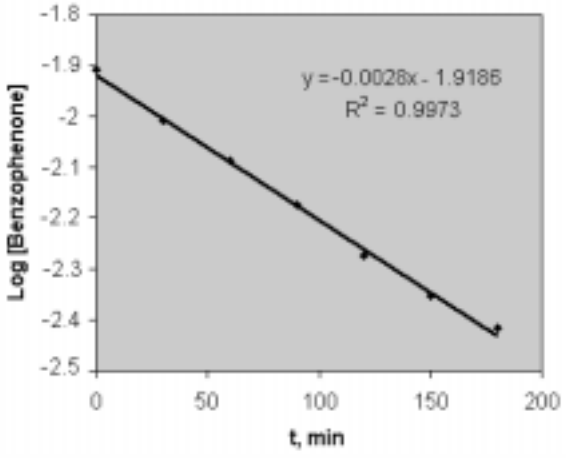


Figure 2. Kinetics of the photochemical reaction between **1b** and **2a**: disappearance of **2a**

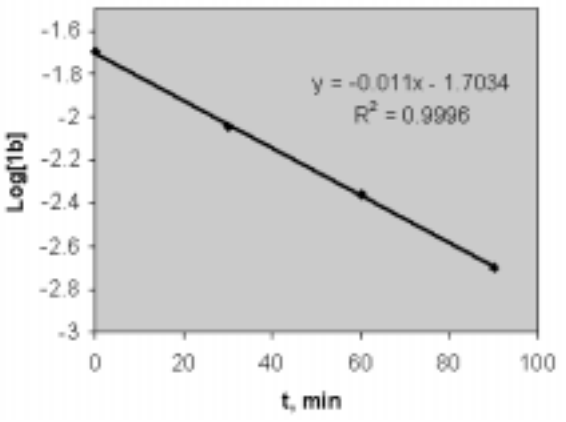


Figure 3. Kinetics of the photochemical reaction between **1b** and **2a**: disappearance of **1b**

The regiochemical behavior of the reactions described above is similar to that reported in related reactions.[3] The only exception is the photochemical behavior of compound **1f** in the presence of benzaldehyde.

In order to explain the observed regioselectivity, we calculated the total electronic energy of the adducts **5** and **6** obtained from the reaction between the triplet benzophenone and **1f** (Figure 4), by the PM3 semiempirical method. The Polak−Ribiere algorithm with gradient calculations was adopted for geometry optimizations. The open-shell states were treated at the same level of accuracy as the closed-state states. By calculating the frequencies of the optimized structures, we verified that the obtained structures were minima on the potential energy surfaces

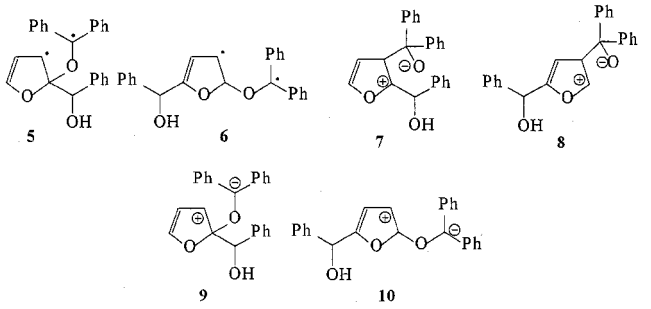


Figure 4. The possible adducts deriving from the reaction between triplet benzophenone and **1f**

We found that the formation of the diradical intermediate **6** shows a lower energy than **5** (8 kcal mol^{-1}) and is thus favored. Considering that this result is not in agreement with experimental results, we tested the capability of our reagents to engage in a photo-induced electron-transfer reaction. In this case, the reaction has to follow the Weller Equation (1) where $E^{Ox}_{1/2}$(D) is the oxidation potential of the donor, $E^{Red}_{1/2}$(A) is the reduction potential of the acceptor, ΔE_{exc} is the excitation energy, F = 96490 C, e = 1.602×10^{-19} C, $\varepsilon_0 = 8.854 \times 10^{-12}$ F m^{-1}, ε is the dielectric constant of the solvent, and a is the encounter distance 7 Å.[6]

$$\Delta G = F\left[E^{Ox}_{1/2}(D) - E^{Red}_{1/2}(A)\right] - \Delta E_{exc} + \frac{e^2 N}{4\pi\varepsilon_o a}\left(\frac{1}{\varepsilon} - \frac{2}{37.5}\right) \quad (1)$$

The excited-state reduction potential $E_{1/2}$*(A) = ΔE_{exc} + $E^{Red}_{1/2}$(A) for benzophenone is 1.7 eV.[7] The triplet energy E_T for benzaldehyde is 3.17 eV.[8] The $E^{Red}_{1/2}$ for benzaldehyde is 1.80 V relative to the SCE in DMF.[9] The dielectric constant for benzene was assumed to be 2.27.[10] The E^{Ox} for **1a** was determined through cyclic voltammetry in acetonitrile relative to Ag/AgCl and was 0.93 ± 0.05 V. The same determination for **1f** gave 0.88 ± 0.05 V and 1.07 ± 0.05 V for **1b**. With these results, we could calculate the ΔG values reported in Table 2. In all cases, the electron-transfer process

Table 2. ΔG of formation of solvent-separated radical pairs between 2-furylmethanols and aromatic carbonyl compounds

Reaction[a]	ΔG [eV]
1a + **2a**	−0.03
1a + **2b**	0.3
1b + **2a**	0.11
1b + **2b**	0.44
1f + **2a**	−0.08
1f + **2b**	0.25

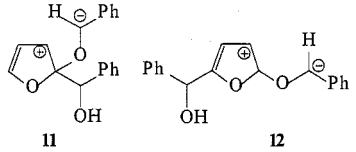
[a] We suppose an electron ransfer reaction between the excited triplet state of **2** and **1**.

is possible, but it is favored when benzophenone is used as reagent. All the results are negative or rather positive: this is in agreement with the formation of solvent-separated radical pairs (in the case of negative values) or of tight radical pairs. These results can explain the observation that the reactivity of benzaldehyde is lower than benzophenone as well as the low yields of the reaction between **1b** and benzaldehyde.

Provided that an electron-transfer process is taking place, we calculated the total electronic energy of the possible intermediates **7** and **8** (Figure 4). We assumed that after the electron-transfer process, radical coupling occurred between a β carbon atom on the furan and the carbonyl carbon atom of benzophenone. The results do not allow us to explain the observed regiochemical behavior. In fact we also found that the formation of the zwitterion **8** on the less substituted double bond of the furan is favored in this case. In fact, it showed a total electronic energy of 2 kcal mol^{-1} lower than that of **7**.

A solution to this problem could be offered by the study of spin density of the radical cation derived from the furan derivative **1f**. We found that α carbon atoms on the furan showed higher spin density than β carbon atoms. On the other hand, the spin density on the oxygen and carbonyl carbon atoms of the benzophenone radical anion are similar. We thus propose that the coupling reaction between the radical cation of **1f** and the radical anion of benzophenone occurs between the α carbon atom of furan and the oxygen atom of benzophenone. In the resulting zwitterions **9** and **10**, the phenyl groups can stabilize the negative charge (Figure 4).

The results of our calculations on the total electronic energy of **9** and **10** showed that in this case the most stable intermediate was **9** (7 kcal mol^{-1} lower than that of **10**). The most favored intermediate is that formed at the more substituted double bond of the furan, in agreement with experimental results. Furthermore, we can rationalize the change in the regioselectivity observed when using **1f** in the presence of benzaldehyde. In fact, in this case, the difference between the total electronic energies of the intermediates **11** and **12** (−2 kcal mol^{-1}) are in agreement with the observed regioselectivity showing that **12** is the most favored intermediate (Figure 5).



11 **12**

Figure 5. The possible intermediates **11** and **12**

To confirm this hypothesis we tested the photochemical behavior of our reactions in different solvents and the sensitivity of the reaction to the change of *para* substituents on the benzophenone. In this case the photochemical behavior of **1f** in the presence of **2a** was studied.

The use of different solvents shows that ethyl acetate ($E_N^T = 0.228$)[11] is the best solvent for this type of reaction. The use of polar solvents, in contrast, does not lead to an increase in the quantum yields: In fact, methanol (E_N^T = 0.762), acetonitrile (E_N^T = 0.46), and acetone (E_N^T = 0.355) gave quantum yields of 0.04, 0.12, and 0.10, respectively (Figure 6). It hence appears that the reaction is not favored in solvents able to lead to solvent-separated radical pairs.

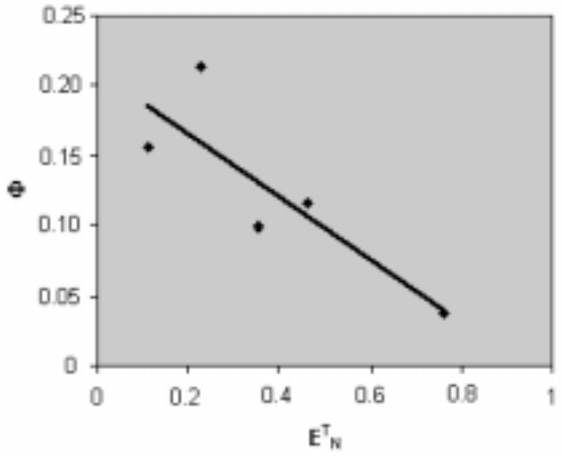


Figure 6. Quantum yields vs. the polarity of solvents

The effect of the substituents on the benzophenone was studied using benzophenone, 4,4′-dimethoxybenzophenone and 4,4′-dichlorobenzophenone. The effect of these substituents on the quantum yields of the reaction with **1f** is depicted in Figure 7.

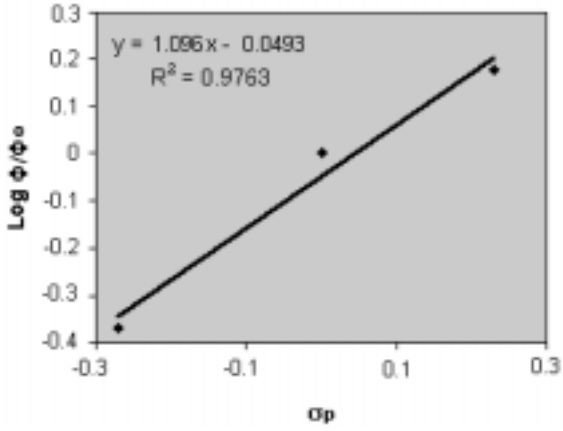


Figure 7. Correlation between quantum yields and σ_p

We observe a clear correlation between the quantum yields and the electronic properties of the substituents. The use of an electron-releasing substituent (OMe) leads to a decrease in the quantum yields of the reaction, while the electron-withdrawing substituent (Cl) gives an increase in Φ. Furthermore, the δ value (1.096) is in agreement with the hypothesis of a negative charge on the carbon atom bearing the substituted phenyl groups.

A problem we have to solve is the high stereoselectivity observed when R in compounds **1** is ethyl, isopropyl, *n*-hexyl or phenyl. In fact, when R was methyl we did not observe an effect of the side-chain on the stereoselectivity of the reaction. We can assume that, in the presence of bulky substituents, the side-chain of the furan prefers a conformer

with the bulky substituent oriented in order to minimize steric interactions.

We carried out some ab initio calculations on the different conformations of **1b** and **1c**. Using a 6−31G* basis set on HyperChem. We found that in **1b**, conformation **B** is favored over **A** with a difference of 0.32 kcal mol^{-1} (Figure 8), while the same conformation in **1c** is favored with a difference of 3.02 kcal mol^{-1} (Figure 8).

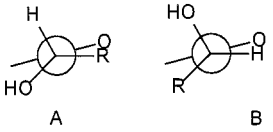


Figure 8. Preferential conformations of some 2-furylmethanols

Thus **1b** does not prefer a particular conformation, while **1c** shows a preferential conformation **B**.

Furthermore, we can assume that the approach of the carbonyl group to the furan moiety is assisted by the formation of an interaction between the hydroxy group and the carbonyl compound. In this way, the configuration of the carbon atom bearing the hydroxy group can determine the configuration of the oxetane ring (Figure 9). The interaction could be the formation of a hydrogen bond or the polar interaction following an electron-transfer process.

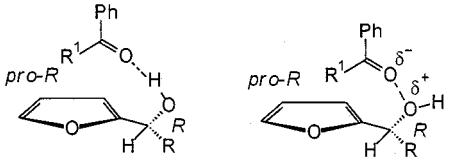
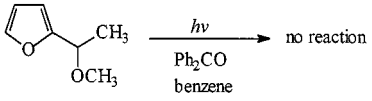


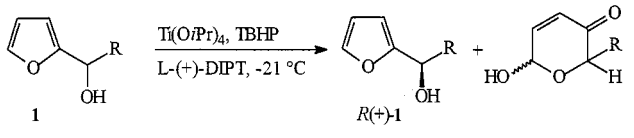
Figure 9. Schematic view of the possible effect of the hydroxy group in order to induce stereoselectivity in the Paternò-Büchi reaction

To test this hypothesis, we performed the photochemical reaction on the methyl ether **5** (Scheme 3). In this case the reaction failed. This result does not rule out the hypotheses depicted above: In fact the absence of the photochemical reaction can probably be due to the different oxidation potential of **5** that does not allow the electron-transfer process.



Scheme 3

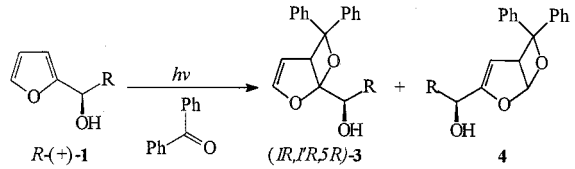
In order to test the synthetic utility of the reaction described above, we carried out some reactions by using chiral 2-furylmethanols. *R*-(+)-**1b**−**f** were obtained through kinetic resolution of (±)-**1b**−**f** in the presence of Ti(O*i*Pr)$_4$, TBHP and L-(+)-DIPT (Scheme 4).[12] The substrates thus obtained were enantiomerically pure as shown by chiral HPLC.



a: R = CH_3
b: R = $CH_2(CH_2)_4CH_3$
c: R = Ph

Scheme 4

The reaction of *R*(+)-**1b** with benzophenone gave the corresponding adduct (Scheme 5). In agreement with the results reported above, the analysis of the product on Chiralcel OD showed that it was a 1:1 mixture of two diastereoisomers: each of these was enantiomerically pure. On the basis of the above results, they can be identified as (1*R*,1′*R*,5*R*)-**3c** and (1*S*,1′*R*,5*S*)-**3c**. The reaction of *R*(+)-**1e** with benzophenone gave an adduct showing α_D = −269.5 (c = 1, $CHCl_3$). The analysis of this product through ^{1}H NMR spectroscopy using Eu(hfc)$_3$ showed that (1*R*,1′*R*,5*R*)-**3i** obtained in this way has an *ee* ≥ 98%. The reaction of *R*(+)-**1f** with benzophenone gave an adduct that showed α_D = −195.4 (c = 1, $CHCl_3$). The product can be identified as (1*R*,1′*R*,5*R*)-**3j** and the ^{1}H NMR spectrum in the presence of Eu(hfc)$_3$ showed an *ee* ≥ 98%.



Scheme 5

Conclusion

In conclusion we have demonstrated that 2-furylmethanol derivatives can be used as substrates in the Paternò-Büchi reaction with aromatic carbonyl compounds. We observed a good regioselectivity and a high stereoselectivity. The regioselectivity cannot be explained assuming the formation of the diradical via the triplet state of the carbonyl compound. Nevertheless, it cannot be explained postulating an electron-transfer process where the coupling between the resulting radicals occurs between a β carbon atom on the furan ring and the carbonyl carbon atom. Furthermore, it is obvious that changes in the frontier orbitals involved in the reaction cannot be invoked in order to justify the regiochemistry of the reaction. The regiochemical behavior of the reaction can be explained by assuming a single-electron transfer between the reagent followed by radical coupling between an α carbon atom on the furan and the oxygen atom on the carbonyl group.

Furthermore, the high stereoselectivity of the reaction can be explained assuming that substituents on the carbon atom bearing the hydroxy group are able to determine a more stable conformation of the substrate. The hydroxy group also influences the approach of the carbonyl group to a prochiral face of the furan.

Finally, the high stereoselectivity of the reaction can be used in the synthesis of enantiomerically pure compounds.

Experimental Section

General Remarks: NMR spectra were recorded with a Bruker 300 AM instrument. When the NMR spectra of cycloadducts were measured, we observed that deuterated chloroform purchased from Aldrich induced a retro-cycloaddition reaction giving, within 1 h, the starting materials. We have no information on the presence of metals or some other trace impurities in the chloroform which may be able to give this type of reaction. We did not observe this behavior using deuterated chloroform from Fluka or Carlo Erba. − Elemental analyses were carried out with a Carlo Erba Elemental Analyzer 1106. − 2-Furylmethanol was obtained by Aldrich. 2-Furylmethanol derivatives were prepared by the reaction of suitable Grignard reagents with furan-2-carbaldehyde.[13]

Cycloaddition Reaction between 2-Furylmethanols and Carbonyl Compounds. − General Procedure: The 2-furylmethanol derivative (**1a−d**) (10 mmol) was dissolved in benzene (70 mL) in the presence of the carbonyl compound (15 mmol). The mixture was flushed with nitrogen for 1 h and then irradiated with a 125-W high-pressure mercury arc (Helios-Italquartz). At the end of the reaction (Table 1), the removal of the solvent yielded a crude product that was purified by chromatography on silica gel. Elution with *n*-hexane/ethyl acetate mixtures gave pure products (Table 1).

(1*RS*,5*RS*)-1β-Hydroxymethyl-6,6-diphenyl-2,7-dioxabicyclo[3.2.0]-hept-3-ene (3a): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.5−7.1 (m, 10 H, aromatic protons), 5.80 (d, ^1J = 4 Hz, 1 H, 3-H), 4.96 (d, ^1J = 4 Hz, 1 H, 4-H), 4.24 (s, 1 H, 6-H), 3.33 (d, ^1J = 12 Hz, 1 H, C$H_a$$H_b$OH), 3.18 (d, ^1J = 12 Hz, 1 H, C$H_a$$H_b$OH), 2.5 (br. s, 1 H, OH). − ^{13}C NMR ($CDCl_3$): δ = 148.2 (C-3), 113.1 (C-1), 103.2 (C-4), 92.9 (C-6), 65.1 (CH_2OH) 54.3 (C-5). − $C_{18}H_{16}O_3$ (280.3): calcd. C 77.12, H 5.75; found C, 77.24, H 5.80.

(1*RS*,5*RS*)-3-Hydroxymethyl-6,6-diphenyl-2,7-dioxabicyclo[3.2.0]-hept-3-ene (4a): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.6−7.2 (m, 10 H, aromatic protons), 6.30 (m, 0.5 H, 1-H), 6.25 (m, 0.5 H, 1-H), 5.68 (m, 0.5 H, 4-H), 5.48 (d, ^1J = 4 Hz, 0.5 H, 4-H), 4.58 (s, 2 H, CH_2OH), 4.36 (s, 1 H, 5-H), 2.6 (br s, 1 H, OH). − ^{13}C NMR ($CDCl_3$): δ = 147.5 (C-3), 112.1 (C-1), 110.0 (C-1), 107.5 (C-4), 97.3 (C-6), 68.7 (CH_2OH), 57.4 (C-5). − $C_{18}H_{16}O_3$ (280.3): calcd. C 77.12, H 5.75; found C, 77.05, H 5.82.

(1*RS*,5*RS*,6*RS*)-1β-Hydroxymethyl-6β-phenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (3b): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.45 (m, 5 H, aromatic protons), 6.70 (m, 1 H, 3-H), 5.62 (d, ^1J = 4 Hz, 1 H, 6-H), 5.48 (m, 1 H, 4-H), 4.0 (br s, 1 H, OH), 3.85 (m, 3 H, 5-H, CH_2OH). − ^{13}C NMR ($CDCl_3$): δ = 148.9 (C-3), 116.0 (C-1), 104.9 (C-4), 90.1 (C-6), 63.3 (CH_2OH), 50.5 (C-5). − $C_{12}H_{12}O_3$ (204.2): calcd. C 70.57, H 5.92; found C 70.49, H 6.01.

(1*RS*,5*RS*,6*RS*)-3-Hydroxymethyl-6β-phenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (4b): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.5−7.3 (m, 5 H, aromatic protons), 6.57 (d, ^1J = 6 Hz, 1 H, 1-H), 5.60 (d, ^1J = 4 Hz, 1 H, 4-H), 5.40 (m, 1 H, 6-H), 4.38 (s, 2 H, CH_2OH), 3.67 (m, 1 H, 5-H), 2.4 (br s, 1 H, OH). − ^{13}C NMR ($CDCl_3$): δ = 160.3 (C-3), 108.8 (C-1), 100.2 (C-4), 92.6 (C-6), 58.2 (CH_2OH), 53.3 (C-5). − $C_{12}H_{12}O_3$ (204.2): calcd. C 70.57, H 5.92; found C 70.47, H 5.89.

(1*RS*,1′*RS*,5*RS*)- and (1*RS*,1′*SR*,5*RS*)-1β-(1-Hydroxyethyl)-6,6-diphenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (3c): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.5−7.1 (m, 10 H, aromatic protons), 6.43 (m, 1 H, 3-H), 4.88 (m, 1 H, 4-H), 4.46 (m, 0.6 H, 5-H), 4.42 (m, 0.4 H, 5-H), 3.86 (m, 1 H, C*H*OH), 2.5 (br s, 1 H, OH), 1.18 (d, ^1J = 6.5 Hz, 1.8 H, CH_3), 1.12 (d, ^1J = 6.5 Hz, 1.2 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 148.4 (C-3), 115.4 (C-1), 103.0 (C-4), 102.7 (C-4), 92.9 (C-6), 68.3 (CHOH), 67.7 (CHOH), 53.4 (C-5), 53.0 (C-5), 16.2 (CH_3), 15.6 (CH_3). − $C_{19}H_{18}O_3$ (294.4): calcd. C 77.53, H 6.16; found C 77.48, H 6.10.

(1*RS*,1′*RS*,5*RS*,6*RS*)-1β-(1-Hydroxyethyl)-6β-phenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (3d): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.4−7.2 (m, 5 H, aromatic protons), 6.72 (dd, $^1J_1$ = 2.8 Hz, $^1J_2$ = 0.7 Hz, 1 H, 3-H), 5.60 (d, ^1J = 4 Hz, 1 H, 6-H), 5.47 (m, 1 H, 4-H), 4.01 (q, ^1J = 6.5 Hz, 1 H, C*H*OH), 3.83 (m, 1 H, 5-H), 2.18 (s, 1H, OH), 1.21 (d, ^1J = 6.5 Hz, 3 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 149.1 (C-3), 104.9 (C-4), 118.0 (C-1), 89.9 (C-6), 67.9 (CHOH), 50.0 (C-5), 15.4 (CH_3). − $C_{13}H_{14}O_3$ (218.3): calcd. C 71.54, H 6.47; found C 71.50, H 6.45.

(1*RS*,1′*RS*,5*RS*)-1β-(1-Hydroxypropyl)-6,6-diphenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (3e): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.5−7.0 (m, 10 H, aromatic protons), 6.41 (m, 1 H, 3-H), 4.90 (m, 1 H, 4-H), 4.41 (m, 1 H, 5-H), 3.90 (m, 1 H, C*H*OH), 2.5 (br s, 1 H, OH), 1.18 (m, 2 H, CH_2), 1.02 (t, ^1J = 7 Hz, 3 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 148.4 (C-3), 115.6 (C-1), 103.0 (C-4), 92.8 (C-6), 68.3 (CHOH), 53.2 (C-5), 15.6 (CH_2), 11.7 (CH_3). − $C_{20}H_{20}O_3$ (308.4): calcd. C 77.90, H 6.54; found C 78.10, H, 6.61.

(1*RS*,1′*RS*,5*RS*,6*RS*)-1β-(1-Hydroxypropyl)-6β-phenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (3f): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.5−7.2 (m, 5 H, aromatic protons), 6.70 (dd, $^1J_1$ = 3 Hz, $^1J_2$ = 0.7 Hz, 1 H, 3-H), 5.57 (d, ^1J = 4 Hz, 1 H, 6-H), 5.43 (m, 1 H, 4-H), 4.05 (t, ^1J = 7 Hz, 1 H, C*H*OH), 3.90 (m, 1 H, 5-H), 2.2 (s, 1H, OH), 1.22 (m, 2 H, CH_2), 1.03 (t, ^1J = 7 Hz, 3 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 149.1 (C-3), 105.0 (C-4), 118.1 (C-1), 89.9 (C-6), 67.8 (CHOH), 50.1 (C-5), 15.4 (CH_2), 11.7 (CH_3). − $C_{14}H_{16}O_3$ (232.3): calcd. C 72.39, H 6.94; found C 72.50, H 6.97.

(1*RS*,1′*RS*,5*RS*)-1β-(1-Hydroxy-2-methylpropyl)-6,6-diphenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (3g): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.4−7.0 (m, 10 H, aromatic protons), 6.38 (m, 1 H, 3-H), 4.93 (m, 1 H, 4-H), 4.50 (m, 1 H, 5-H), 3.90 (m, 1 H, CHOH), 2.5 (br s, 1 H, OH), 1.25 (m, 1 H, CH), 1.02 (d, ^1J = 7 Hz, 6 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 148.4 (C-3), 115.7 (C-1), 103.1 (C-4), 92.9 (C-6), 68.5 (CHOH), 53.3 (C-5), 16.1 (CH), 11.6 (CH_3), 11.3 (CH_3). − $C_{21}H_{22}O_3$ (322.4): calcd. C 78.23, H 6.88; found C 78.18, H, 6.83.

(1*RS*,1′*RS*,5*RS*,6*RS*)-1β-(1-Hydroxy-2-methylpropyl)-6β-phenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (3h): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.5−7.2 (m, 5 H, aromatic protons), 6.65 (dd, $^1J_1$ = 3 Hz, $^1J_2$ = 0.7 Hz, 1 H, 3-H), 5.62 (d, ^1J = 4 Hz, 1 H, 6-H), 5.40 (m, 1 H, 4-H), 4.0 (t, ^1J = 7 Hz, 1 H, C*H*OH), 3.92 (m, 1 H, 5-H), 2.5 (s, 1H, OH), 1.28 (m, 1 H, CH), 1.06 (d, ^1J = 7 Hz, 6 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 149.2 (C-3), 105.1 (C-4), 118.0 (C-1), 89.9 (C-6), 67.6 (CHOH), 50.2 (C-5), 15.4 (CH), 11.7 (CH_3), 11.5 (CH_3). − $C_{15}H_{18}O_3$ (246.3): calcd. C 73.15, H 7.37; found C 73.24, H 6.40.

(1*RS*,1′*RS*,5*RS*)-1β-(1-Hydroxy-*n*-heptyl)-6,6-diphenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (3i): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.5−7.1 (m, 10 H, aromatic protons), 6.43 (m, 1 H, 3-H), 4.90 (m, 1 H, 4-H), 4.44 (m, 1 H, 5-H), 3.68 (m, 1 H, C*H*OH), 1.5 (br s, 1 H, OH), 1.33 (m, 10 H, CH_2), 0.86 (t, ^1J = 7 Hz, 3 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 148.4 (C-3), 111.3 (C-1), 103.1 (C-4), 92.8 (C-6), 71.7 (CHOH), 53.7 (C-5). − $C_{24}H_{28}O_3$ (364.5): calcd. C, 79.09, H 7.74; found C 79.17, H 7.68.

(1*RS*,1′*RS*,5*RS*)-1β-(α-Hydroxybenzyl)-6,6-diphenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (3j): ^{1}H NMR ($CDCl_3$, 300 MHz): δ =

7.6−7.1 (m, 15 H, aromatic protons), 6.28 (d, ^1J = 3 Hz, 1 H, 3-H), 4.80 (s, 1 H, C*H*OH), 4.73 (dd, $^1J_1 = {}^1J_2$ = 3 Hz, 1 H, 4-H), 4.49 (d, ^1J = 3 Hz, 1 H, 5-H), 2.5 (br s, 1 H, OH). − ^{13}C NMR ($CDCl_3$): δ = 148.5 (C-3), 107.4 (C-1), 103.0 (C-4), 93.1 (C-6), 73.3 (CHOH), 53.6 (C5). − $C_{24}H_{20}O_3$ (356.4): calcd. C 80.88, H 5.66; found C 81.00, H 5.59.

3-(α-Hydroxybenzyl)-6,6-diphenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (4c): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.5−7.0 (m, 15 H, aromatic protons), 6.29 (d, ^1J = 3 Hz, 1 H, 1-H), 5.18 (m, 1 H, 4-H), 4.72 (m, 1 H, C*H*OH), 4.36 (m, 1 H, 5-H), 2.5 (br s, 1 H, OH). − ^{13}C NMR ($CDCl_3$): δ = 148.5 (C-3), 105.8 (C-1), 99.6 (C-4), 94.7 (C-6), 70.0 (CHOH), 56.4 (C-5). − $C_{24}H_{20}O_3$ (356.4): calcd. C 80.88, H 5.66; found C 80.96, H 5.71.

(1*RS*,1′*RS*,5*RS*,6*RS*)-1β-(α-Hydroxybenzyl)-6β-phenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (3k): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.5−7.1 (m, 10 H, aromatic protons), 6.73 (d, ^1J = 2.8 Hz, 1 H, 3-H), 5.60 (d, ^1J = 3.9 Hz, 1 H, 6-H), 5.44 (m, 1 H, 4-H), 4.89 (s, 1 H, C*H*OH), 3.87 (m, 1 H, 5-H), 2.91 (br s, 1 H, OH). − ^{13}C NMR ($CDCl_3$) δ = 149.2 (C-3), 117.6 (C-1), 104.7 (C-4), 90.5 (C-6), 74.6 (CHOH), 50.0 (C-5). − $C_{18}H_{16}O_3$ (280.3): calcd. C 77.12, H 5.75; found C 77.02, H 5.68.

(1*RS*,1′*SR*,5*RS*,6*RS*)-1β-(α-Hydroxybenzyl)-6β-phenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (3k): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.5−7.1 (m, 10 H, aromatic protons), 6.60 (dd, $^1J_1$ = 2.9 Hz, $^1J_2$ = 0.9 Hz, 1 H, 3-H), 5.62 (d, ^1J = 4 Hz, 1 H, 6-H), 5.33 (dd, $^1J_1 = {}^1J_2$ = 2.9 Hz, 1 H, 4-H), 4.97 (s, 1 H, C*H*OH), 3.89 (m, 1 H, 5-H), 2.66 (s, 1 H, OH). − ^{13}C NMR ($CDCl_3$): δ = 149.1 (C-3), 117.2 (C-1), 104.8 (C-4), 90.4 (C-6), 73.4 (CHOH), 49.5 (C-5). − $C_{18}H_{16}O_3$ (280.3): calcd. C 77.12, H 5.75; found C 77.18, H 5.80.

3-(α-Hydroxybenzyl)-6β-phenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (4d): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.7−7.2 (m, 10 H, aromatic protons), 6.56 (m, 1 H, 1-H), 5.60 (m, 1 H, 4-H), 5.45 (m, 1 H, CHOH), 5.22 (m, 1 H, 6-H), 3.69 (m, 1 H, 5-H), 2.8 (br s, 1 H, OH). − ^{13}C NMR ($CDCl_3$): δ = 141.0 (C-3), 111.3 (C-1), 108.6 (C-4), 92.5 (C-6), 70.2 (CHOH), 53.2 (C-5). − $C_{18}H_{16}O_3$ (280.3): calcd. C 77.12, H 5.75; found C 77.20, H 5.73.

Voltammograms: All voltammograms were obtained on an Amel Model 472 (Amel, Milano, Italy) polarograph equipped with a potentiostatic control, allowing for a potential scan rate up to 200 mV s^{-1}. The Metrohm 6.0302.000 platinum electrode was used as the stationary working electrode, and a platinum button (diameter 2 mm) was used as the counter electrode. All the potential values are relative to an Ag, $AgCl/LiCl_{satd.}$ (in acetonitrile) reference electrode, whose potential value relative to the aqueous SCE is 124 mV (at 27 °C). The experiments were carried out in acetonitrile containing Bu_4N^+ ClO_4^- (0.1 M) as supporting electrolyte. All experiments were performed at room temperature (25−28 °C) on 25 mL of solution. The solution to be processed was first bubbled with nitrogen for few seconds, and then the nitrogen was maintained above the solution in order to prevent contact with air. The voltammograms were recorded at a 20 mV s^{-1} scan rate, unless otherwise specified.

Quantum Yields: The quantum yields were determined using phenylglyoxylic acid as actinometer. A solution of phenylglyoxylic acid in acetonitrile/water (3:1, 0.1 M, 10 mL) was irradiated for 600 s under nitrogen in a Pyrex tube which was surrounded by a Pyrex water-jacket connected to a Haake F3 thermostat to maintain the temperature at 25.0 ± 0.1 °C. A Rayonet apparatus with an output centered at 350 nm was used for irradiation. The mixture was then extracted with CH_2Cl_2 and dried (Na_2SO_4). The removal of the solvent gave a crude product that was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR spectroscopy. The chemical conversion was calculated from the integrated *ortho* proton signals of the phenyl ring of phenylglyoxylic acid at δ = 8.1 and of benzaldehyde at δ = 7.9 with reference to the *meta* and *para* ring proton signals at δ = 7.6. The value of Φ is assumed to be 0.7. A 0.1 M solution of the reagents in benzene was irradiated in a Pyrex tube surrounded with a Pyrex water-jacket connected to a Haake F3 thermostat to maintain the temperature at 25.0 ± 0.1 °C in a Rayonet apparatus with an output centered at 350 nm. After 600 s, the solvent was removed and the mixture was analyzed by ^{1}H NMR spectroscopy.

Optically Active 2-Furylmethanols. − General Procedure: A solution of $Ti(OiPr)_4$ (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 *tert*-butyl hydroperoxide (4.6 mL), was 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 through Celite. The organic phase was concentrated to give an oil which was dissolved in ether (187 mL) and treated with NaOH (1 N, 93.5 mL) for 30 min at 0 °C. The ether layer was washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave an oil that was purified by chromatography on silica gel to give pure *R*-(+)-**1** derivatives. The *ee* was estimated by using chiral HPLC on Chiralcel OD using *n*-hexane/2-propanol (95:5, 1 mL min^{-1}) as eluent. The chromatograms were detected with a UV detector at 235 nm.

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