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New Captodative Olefins: 3-(2-Furoyloxy)-3-buten-2-one and Alkyl 2-(2-Furoyloxy)-2-propenoates, and their Reactivity in Addition Reactions

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Abstract. A new series de captodative olefins 3-(2-furoyloxy)-3-buten-2-one and alkyl 2-(2-furoyloxy)-2-propenoates, **3a**-**3c**, has been prepared with the aim of evaluating the effect of a heterocycle in the *electron-donating* moiety on the reactivity of these compounds in Diels-Alder and conjugate additions. In the former reactions, their behavior has been evaluated by reacting under thermal and catalyzed conditions with cyclopentadiene (**9**) and cyclohexadiene (**12**) as the dienes, showing a comparable reactivity, but a lower stereoselectivity, with respect to the reference captodative olefins **1a** and **2a**. In the case of conjugate additions, the Friedel-Crafts reaction of the highly activated benzene ring of 1,2,4-trimethoxybenzene (**7**) led to the corresponding adduct **8** only for olefin **3a**. *Ab initio* calculations (HF/6-31G*) of the energies and coefficients of the FMOs were carried out to explain the experimental reactivity in both processes. The results suggest that both the electron-withdrawing and the 2-furoyloxy groups are involved in controlling the reactivity and selectivity of olefins **3**.
Keywords: Captodative olefins, 2-furoyloxy group, Diels-Alder, Friedel-Crafts, FMO.

Resumen. Se describe la preparación de una nueva serie de olefinas captodativas 3-(2-furoiloxi)-3-buten-2-ona y 2-(2-furoiloxi)-2-propenoatos de alquilo, **3a**–**3c**, con el fin de evaluar el efecto del heterociclo en la parte *electro-donadora* de la olefina sobre su reactividad en reacciones de Diels-Alder y de adiciones conjugadas. En el primer caso, se evaluó su comportamiento bajo condiciones térmicas y catalizadas empleando ciclopentadieno (**9**) y ciclohexadieno (**12**) como los dienos, encontrándose una reactividad comparable, aunque menor estereoselectividad, con respecto a las olefinas captodativas de referencia **1a** and **2a**. Para el caso de la adición conjugada, la reacción de Friedel-Crafts del compuesto 1,2,4-trimetoxibenceno (**7**), el cual posee un anillo bencénico muy activado, condujo solamente al aducto correspondiente, **8**, de la olefina **3a**. Se llevaron a cabo cálculos *ab initio* (HF/6-31G*) de energías y coeficientes de los FMOs para explicar la reactividad experimental en ambos procesos. Estos resultados sugieren que la reactividad y selectividad de las olefinas **3** están controladas tanto por el grupo electroatractor como por el grupo 2-furoiloxi.
Palabras clave: Olefinas captodativas, grupo 2-furoiloxi, Diels-Alder, Friedel-Crafts, OMF.

Introduction

Owing to the opposite electronic demand and to the synthetic potential displayed by their geminally substituted double bond, captodative olefins have captured special interest [1], since the electron-releasing effect of the electron-donor group should counterbalance the effect of the electron-withdrawing group, leading to a low reactivity and selectivity in pericyclic reactions [2]. Captodative olefins 1-acetylvinyl *p*-arenecarboxylates **1** have proved to be highly reactive and selective in Diels-Alder [3] and 1,3-dipolar cycloadditions [4], and in Friedel-Crafts reactions [5]. As versatile synthons, they have been employed in natural product synthesis [6]. Moreover, captodative alkyl 2-aroyloxy acrylates **2a**-**2b** have shown high reactivity and selectivity in Diels-Alder reactions as well [7].

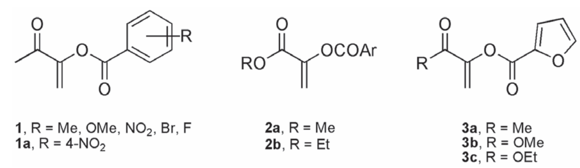


Fig. 1

Structural and theoretical studies of olefin **1a** revealed that the delocalization of the oxygen lone pair of the electron-releasing group toward the π-system is inhibited by a conformational preference [8]. However, recently, we have established by FMO theory calculations that the reactivity of olefins **1** is also controlled by a long-range inductive effect of the substituents at the phenyl ring of the aroyloxy group [9], as suggested by kinetic data [10]. This inductive effect also contributes to the dominant effect of the acetyl electron-withdrawing group on the polarization of the double bond and explains the high reactivity and regioselectivity observed in Diels-Alder reactions [8]. In contrast, the highly regioselective 1,3-dipolar additions shown by olefins **1** to nitrones and nitrile oxides was better accounted for by DFT/HSAB theory [4c], which suggests that the electron-donor group plays an important role in controlling the interaction of the cycloaddends.

Herein, we describe the synthesis of new captodative olefins 3-(2-furoyloxy)-3-buten-2-one and alkyl 2-(2-furoyloxy)-2-propenoates, **3a**-**3c**, with the aim of evaluating the effect of the electronic and structural properties of the heterocycle on their reactivity in Diels-Alder and conjugate additions. This study was supported by conformational and FMO calculations in order to rationalize such reactivity.

Results and Discussion

Synthesis and conformational analysis of the new captodative olefins 3a-3d.

In contrast with the series of substituted olefins **1** and **2**, which are prepared in fairly good yields, olefins **3a**–**3c** were obtained in low yields (29-38%), due to the decomposition during the purification process by column chromatography. Their preparation was carried out by using the reported methods [7, 9, 11], by reacting either diacetyl (**4a**) or the alkyl pyruvic acids **4b**-**4c** with 2-furoyl chloride (**5**) (Figure 2). Although the optimized conditions were applied by lowering the temperature to -20 ºC and the reaction time was controlled, the yields were not improved. Olefin **3a** was isolated as a solid with a low *mp* (48-49 ºC), and derivatives **3b** and **3c** were obtained as oily products, which were fully characterized by spectroscopy.

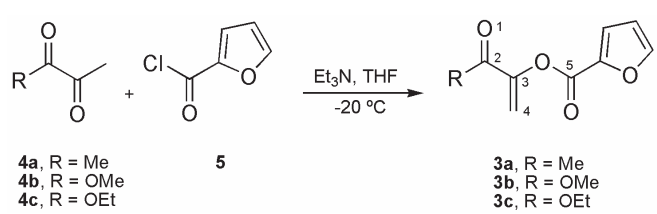


Fig. 2

Calculations (HF/6-31G*) of the minimum energy conformations of **3a** shows that the non-planar conformer of the 2-furoyloxy group, with respect to the plane formed by the enone moiety, was preferred (Table 1). This is in agreement with previous calculations obtained for captodative olefins **1** and **2** [7-9]. Among the four most stable conformations, **3a-A** [*s-cis*(enone)-*s-cis*(furoyl)], **3a-B** [*s-cis*(enone)-*s-trans*(furoyl)], **3a-C** [*s-trans*(enone)-*s-cis*(furoyl)], and **3a-D** [*s-trans*(enone)-*s-trans*(furoyl)], the conformer **3a-B** was the most stable (Figure 3). In particular for the enone moiety, the *s-trans*(enone) conformers were less stable than the *s-cis*(enone). This is in contrast with the most stable conformation of the closely related structure **1a**, which prefers the *s-trans*(enone) [8]. Concerning the conformation of the furoyl moiety, we found that the *s-trans*(furoyl) was more stable with respect to the *s-cis*(furoyl). This is probably due to the presence of the oxygen atoms of the furan ring and the carbonyl group, which increase the destabilizing dipole interactions in the latter conformation.

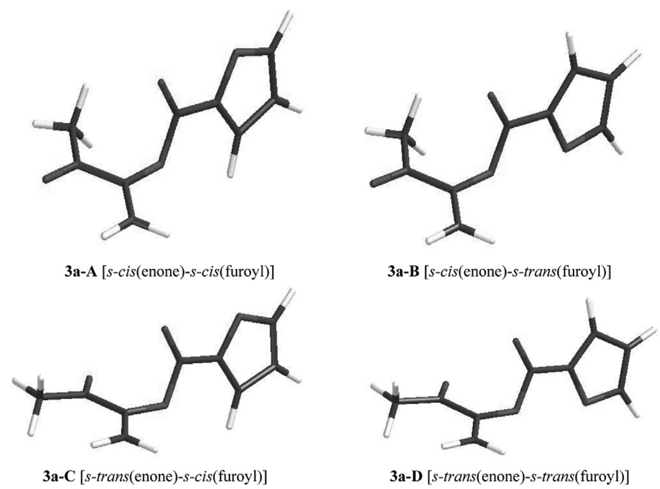
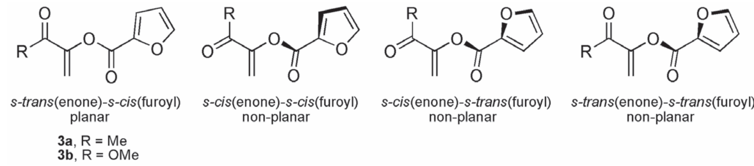


Fig. 3. Optimized geometries (HF/6-31G*) of olefin **3a** for the non-planar conformations **A**-**D**.

Similar minimum-energy conformations and relative energies were found for olefin **3b** (Table 1). The non-planar conformation of the furoyloxy group (with respect to the plane formed by the conjugate π-system of the acrylate), the *s-cis* conformation of the acrylate moiety, and the *s-trans* conformation of the furoyl moiety, were the most stable conformations.

With the aim of evaluating the effect of a third substituent in the double bond [12], we investigated the synthesis of **3d** by functionalization of **3a** with a bromine atom. Thus, bromination of the double bond of the latter provided the dibromo compound **6** in an almost quantitative yield (Figure 4). The treatment of this compound with triethylamine at 10 ºC for 3 h, furnished the desired product **3d** in a quantitative yield. The (*Z*) stereochemistry of the double bond was established by NOE experiments, in which an enhancement of the signal of the olefinic proton is produced by irradiation of the methyl group. No signals of the (*E*) stereoisomer were detected in the crude reaction mixture.

Table 1. *Ab initio* (HF/6-31G*) energies (HA) of the minimum-energy conformations of olefins **3a** and **3b**.



3	Planar (*HA*)	Non-planar (*HA*)	Δ*E (kcal/mol)*[a]	Δ*E (kcal/mol)*[b]
3a-A [*s-cis*(enone)-*s-cis*(furoyl)]	-644.8827565	-644.8845305	1.098	0.265
3a-B [*s-cis*(enone)-*s-trans*(furoyl)]	-644.8842722	-644.8849531	0.427	0.000
3a-C [*s-trans*(enone)-*s-cis*(furoyl)]	-644.8812251	-644.8844844	2.046	0.294
3a-D [*s-trans*(enone)-*s-trans*(furoyl)]	-644.8790318	-644.8846998	3.558	0.159
3b-A [*s-cis*(enone)-*s-cis*(furoyl)]	-719.753529	-719.7572113	2.309	0.145
3b-B [*s-cis*(enone)-*s-trans*(furoyl)]	-719.7528021	-719.7574428	2.912	0.000
3b-C [*s-trans*(enone)-*s-cis*(furoyl)]	-719.7539666	-719.7569856	1.895	0.287
3b-D [*s-trans*(enone)-*s-trans*(furoyl)]	-719.7519746	-719.7571877	3.268	0.160

[a] Considered for the difference: planar-non-planar for each conformer. [b] Considered as the relative stability of the four non-planar conformers of each olefin **3a** and **3b**.

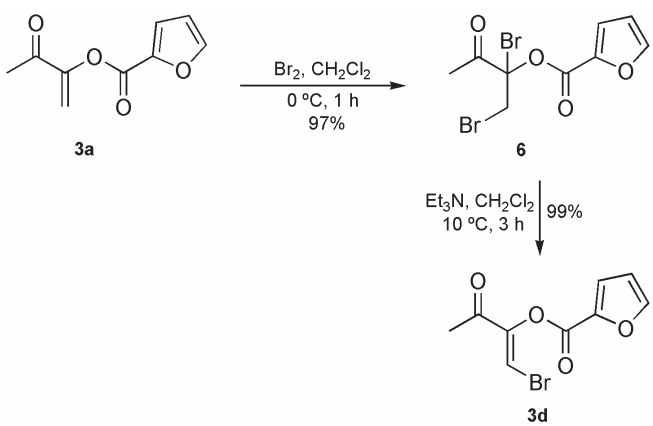


Fig. 4

Reactivity of captodative olefins 3a–3d in the Friedel-Crafts reaction.

We have shown in a previous study that olefin **1a** undergoes a readily efficient conjugate addition of activated benzene rings in the presence of Lewis acids [5]. When a mixture of olefin **3a** and 1,2,4-trimethoxybenzene (**7**) was catalyzed with BF_3·Et_2O in methylene chloride at 0 ºC, the corresponding adduct **8** was obtained in 79% yield (Figure 5).

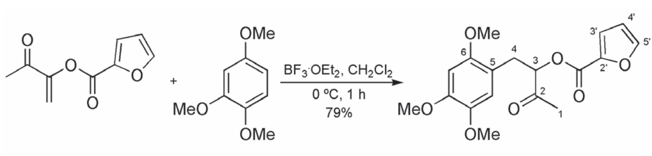


Fig. 5

In contrast with these results, the reaction with the highly activated benzene ring of **7** and the captodative olefins **3b** and **3c** failed, even though the reaction conditions used were similar or more drastic (60 ºC). The use of other Lewis acids ($ZnCl_2$, $AlCl_3$) provided similar results. Analogous unsuccessful results were obtained when the reaction was carried out with the β-substituted captodative olefin **3d**, which is in agreement with the low reactivity of the β-functionalized captodative olefins derived from **1a** [12].

The X-ray diffraction structure of adduct **8** was carried out and it is depicted in Figure 6 [13]. It is interesting to notice that, in the preferred conformation at the solid state, the groups are staggered around the C_3-C_4 bond, where the trimethoxybenzene and the 2-furoyloxy substituents are *gauche*, whilst the former and the acetyl group are *anti* periplanar (C_2-C_3-C_4-C_5 -177.6º)

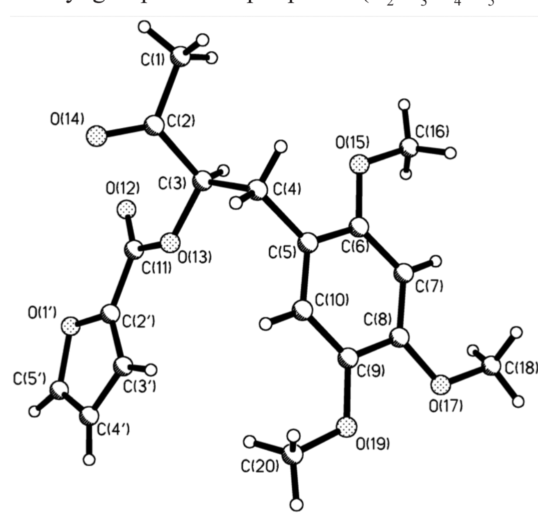


Fig. 6. X-ray structure of captodative olefin **8** (ellipsoids with 30% probability)

Reactivity of captodative olefins 3a–3c in Diels-Alder additions.

The reactivity and stereoselectivity of the thermal Diels-Alder cycloaddition of **1a** with cyclopentadiene (**9**) was drastically enhanced by Lewis acid catalysis [3c]. When the process of **3a** was carried out in the presence of BF_3Et_2O in methylene chloride at -78 ºC, the reaction took place in only 0.5 h (Figure 7). In spite of the high reactivity displayed by this olefin, the steroisomeric ratio of the *endo/exo* adducts **10a**/**11a** was low (68:32) (entry 1, Table 2), but higher than that obtained with **1a** (60:40) [3c]. The *endo* selectivity of **1a** was highly increased in the presence of $TiCl_4$ [3c], hence the catalyzed addition of **9** to **3a** was also carried out (entry 2, Table 2). Nevertheless, the *endo/exo* adducts **10a**/**11a** was lower (60:40) than that observed with the first catalyst. Unlike **1a**, olefin **3a** has a heterocycle with a complexing center (the oxygen atom) that might be attached to the Lewis acid. Then, the possible complexes may generate additional steric interactions at the *endo* and *exo* transition states, impeding a better stereoselectivity.

The solvent-free thermal (40 ºC) reaction between the same cycloaddends yielded a 1:1 ratio of **10a**/**11a** (entry 3, Table 2). This is in contrast with the *endo/exo* ratio (30:70) of **1a**, under the same conditions, where the stereoselectivity was reversed with respect to the catalyzed trials, since the *exo* adduct was the major product. The structure of adducts **10a** and **11a** was established by ^{1}H and ^{13}C NMR spectroscopy, which was supported by the previous and unambiguous NMR and X-ray analyses on closely related adducts [3c].

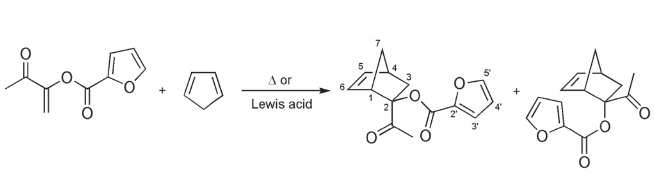


Fig. 7

A considerable effect of the polarity of the solvent upon both reactivity and stereoselectivity of the Diels-Alder reaction has been found [14]. Consequently, we investigated the reaction of **3a** with **9** in a mixture of MeOH/H_2O (9:1) (entry 4, Table 2). Although the reaction proceeded at room temperature, the reaction time and stereoselectivity were not improved with respect to the thermal trial.

Table 2 summarizes the cycloadditions carried out between olefin **3b** and cyclopentadiene (**9**) (Figure 8). The thermal and solvent-free reaction yielded the expected mixture of *endo/exo* adducts **10b**/**11b** in a low ratio (41:59), where the *exo* isomer was the major product (entry 5, Table 2). It is worth noticing that the reaction failed in the presence of catalysts such as $BF_3 Et_2O$ and $AlCl_3$ (entries 7 and 8), and only $TiCl_4$ was effective (entry 6, Table 2), albeit with very low stereoselectivity. In contrast to olefin **3a**, where the major isomer was the *endo* adduct, in the case of **3b**, the major isomer was the *exo*, though by a slight margin. The low *exo* preference in these cycloadditions is comparable to that shown by olefin **2a**, though, in this case the stereoselectivity was improved when the reactions were catalyzed by $AlCl_3$ and $TiCl_4$ [7].

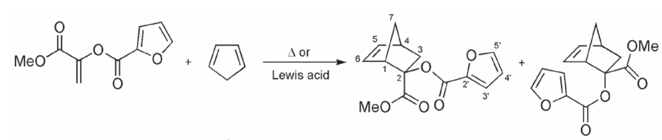


Fig. 8

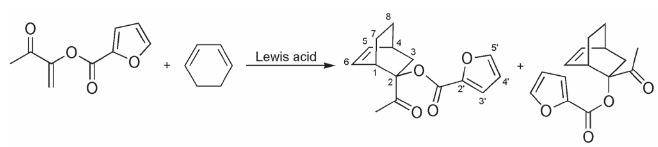
Owing to the fact that reactivity and steric interactions at the transition state can be significantly changed in the case of cyclohexadiene (**12**) [15], we evaluated these factors in the cycloaddition with olefin **3a** (Figure 9). Thus, the catalyzed reactions furnished a mixture of *endo/exo* adducts **13**/**14** in different stereoisomeric ratios, depending on the Lewis acid used ($BF_3 Et_2O$ or $AlCl_3$) (Table 2). Although in both cases the *endo* isomer was the major adduct, the highest reactivity and stereoselectivity were found by using $BF_3 Et_2O$ (entry 9, Table 2).

Table 2. Diels-Alder cycloadditions of olefins **3a** and **3b** with dienes **9** and **12**.[a]

Entry	Alkene	Diene	Solvent	Catalyst (mol equiv.)	T (ºC)	t (h)	Products (ratio)[b]	Yield (%)[c]
1	**3a**	**9**	CH_2Cl_2	$BF_3 Et_2O$ (0.1)	-78	0.5	**10a**/**11a** (68:32)	93
2	**3a**	**9**	CH_2Cl_2	$TiCl_4$ (0.096)	-15	4	**10a**/**11a** (60:40)	90
3	**3a**	**9**	–	–	40	16	**10a**/**11a** (50:50)	55
4	**3a**	**9**	MeOH/H_2O (9:1)	–	25	24	**10a**/**11a** (50:50)	58
5	**3b**	**9**	–	–	40	24	**10b**/**11b** (41:59)	84
6	**3b**	**9**	CH_2Cl_2	$TiCl_4$ (0.1)	-50	6	**10b**/**11b** (46:54)	67
7	**3b**	**9**	CH_2Cl_2	$BF_3 Et_2O$ (0.1)	-78	7	(*d*)	(*d*)
8	**3b**	**9**	CH_2Cl_2	$AlCl_3$ (1.5)	25	48	(*d*)	(*d*)
9	**3a**	**12**	CH_2Cl_2	$BF_3 Et_2O$ (0.1)	-78	0.5	**13**/**14** (70:30)	82
10	**3a**	**12**	CH_2Cl_2	$AlCl_3$ (1.5)	25	48	**13**/**14** (57:43)	68

[a] All under N_2 atmosphere. Thermal trials in the presence of 1-2% hydroquinone. [b] Proportions (*endo*/exo) as determined by ^{1}H NMR of the crude reaction mixtures. [c] As a mixture of isomers after column and radial chromatography. [d] No reaction was observed.

It appears that the latter promotes the cycloaddition efficiently, since the reaction took place at -78 ºC in a short time (30 min). The fact that mainly the *endo* isomer was obtained suggests that a hindered complex is formed between the Lewis acid and the oxygen atom of the acetyl group, leading to a preferred *endo* transition state. In this approach the complex avoids the largest steric interactions with the two methylene groups of the bridge (Figure 10). The preference for a ML3 complexed dienophile and not for a chelate (formed between the Lewis acid and the oxygen atoms of acetyl and furoyloxy groups [3c]) may be due to the less energetic *s-cis* conformation of the enone moiety. Although the mixture of adducts **13**/**14** was very difficult to separate by chromatographic techniques, a pure fraction of the *endo* adduct **13** allowed for the establishment of its structure by nOe and 2D NMR experiments, in agreement with the unambiguously established structure of the *endo* adduct of olefin **1a** [16].



3a **12** **13** (*endo*) **14** (*exo*)

Fig. 9

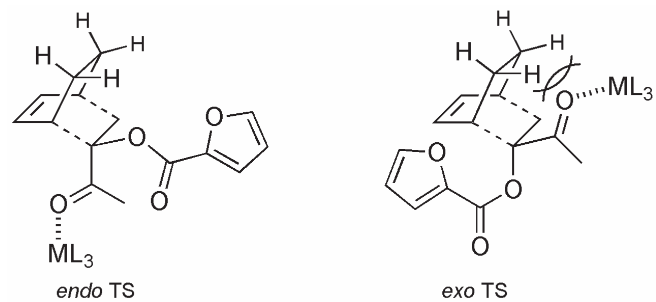


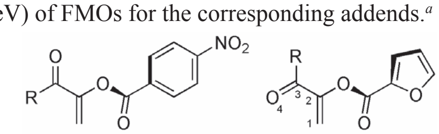
Fig. 10. Possible steric interactions at the *endo* and *exo* transition states (TS) in the Diels-Alder cycloadditions of olefin **3a** and cyclohexadiene (**12**).

FMO calculations of captodative olefins 3.

Considering that the Diels-Alder reaction is mostly controlled by MO interactions [17], we decided to investigate the role of the FMO energies and coefficients on the reactivity of these molecules. Tables 3 and 4 summarize the calculated (HF/6-31G*) FMO energies and the coefficients of the key atoms for captodative olefin **3a** and **3b**, for the already studied olefins **1a** and **2a**, and for 1,2,4-trimethoxybenzene (**7**) and cyclopentadiene (**9**). The FMO data corresponded to the lowest energy geometries of these olefins after optimization at the same level of theory (Table 1). As shown before, the most stable geometry for all of them corresponded to the non-planar conformation of the aroyloxy group with respect to the enone moiety, and to the *s-cis* and *s-trans* conformations of the latter for **3a**-**3b** and for the already studied olefins **1a**-**2a**, respectively. FMO calculations indicate that captodative olefins **1**-**3** react with dienes and electron-rich benzenes under *normal electronic demand* in Diels-Alder [8, 17] and Friedel-Crafts [17a] reactions, respectively. Therefore, the stronger perturbation is given by the interaction between the HOMO of the diene or benzene ring and the LUMO of the olefin.

Both HOMO and LUMO are energetically destabilized in olefins **3a** and **3b** with respect to olefins **1a** and **2a** (Table 3). This suggests that the furoyl group is not exerting a comparable electron-withdrawing effect to that of the latter olefins [9]. This is probably due to the electron-donor effect of the lone-pairs of the oxygen atom of the furan ring towards the carbonyloxy group attached to the double bond. The difference in reactivity between olefins **1a** and **3a** parallels with that of LUMO energies, since under identical non-catalyzed conditions, the cycloaddition of **1a** to **9** is fivefold more reactive than that of **3a** [3c]. Of course, it is very difficult to compare the processes carried out under Lewis acid catalysis, because the complexation sites and the strength of the interaction are completely different depending on the structure of the olefin.

Table 3. *Ab initio* (HF/6-31*) calculated energies (eV) of the Frontier Molecular Orbitals of olefins **1a**, **2a**, **3a**, and **3b**, and 1,2,4-trimethoxybenzene (**7**) and cyclopentadiene (**9**). Energy gaps (eV) of FMOs for the corresponding addends.[a]

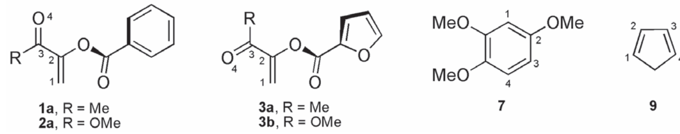


1a, R = Me
2a, R = OMe
3a, R = Me
3b, R = OMe

Compd[b]	E_{HOMO}[c]	E_{LUMO}[d]	HOMO-LUMO[e]	LUMO-HOMO[f]	Gap diff
1a[g]	-11.0123	2.4588	10.0272 (10.7793)	15.2976 (14.9386)	5.2704 (4.1593)
2a[g]	-10.9921	2.8080	10.3764 (11.1285)	15.2774 (14.9184)	4.9010 (3.7899)
3a	-10.5042	2.8849	10.4533 (11.2054)	14.7895 (14.4305)	4.3362 (3.2251)
3b	-10.5573	3.2330	10.8014 (11.5535)	14.8426 (14.4836)	4.0412 (2.9301)
7	-7.5684	4.2853			
9	-8.3205	3.9263			

[a]Energies of the first FMO with significant coefficient contributions at the enone moiety or at the double bond of the olefins. [b] For the most stable non-planar (between aroyloxy or furoyloxy groups and enone moiety) *s-trans* and *s-cis* conformations of the olefins **1a-2a** and **3a-3b**, respectively. [c] Energies of 2NHOMO of olefins **1a-2a**, NHOMO of olefins **3a-3b**, and of HOMO of **7** and **9**. [d] Energies of NLUMOs of olefins **1a-2a** and **3a-3b**, and of LUMO of of **7** and **9**. [e] HOMO-**7**/LUMO-olefins **1a-2a** and **3a-3b**, or (HOMO-**9**/LUMO-olefins **1a-2a** and **3a-3b**). [f] LUMO-**7**/HOMO-olefins **1a-2a** and **3a-3b**, or (LUMO-**9**/HOMO- olefins **1a-2a** and **3a-3b**). [g] Ref. 7.

Table 4. *Ab initio* (HF/6-31*) p_z Coefficients (C_i) of the Frontier Molecular Orbitals of the olefins **1a**, **2a**, **3a**, and **3b**, and compounds **7** and **9**.[a]



	HOMO					LUMO				
Compd	C_1	C_2	C_3	C_4	ΔC_i^b	C_1	C_2	C_3	C_4	ΔC_i^b
1a[c]	0.3593	0.3565	-0.0237	-0.1675	0.0028	0.2940	-0.2386	-0.2888	0.2800	0.0554
2a[d]	0.3452	0.3530	-0.0089	-0.1358	-0.0078	0.3028	-0.2585	-0.2740	0.2349	0.0443
3a	0.3413	0.3571	-0.0328	-0.1956	-0.0158	0.2597	-0.1997	-0.2509	0.2280	0.0600
3b	0.3530	0.3693	-0.0177	-0.1767	-0.0163	0.2922	-0.2482	-0.2659	0.2087	0.0440
7	-0.0347	-0.2552	-0.2451	0.1316		0.2781	-0.0498	-0.1987	0.2985	
9	0.3161	0.2372	-0.2372	-0.3161		0.2842	-0.2064	-0.2064	0.2842	

[a] Coefficients of the FMOs reported in Table 3. Only the p_z coefficients are shown, and the $p_{z'}$ coefficients follow a similar trend. [b] Carbon 1 – carbon 2 for the olefins. [c] Ref. 9. [d] Ref. 16.

This is also applicable for the Friedel-Crafts reaction, which takes place only by catalysis. Nevertheless, in principle, from the HOMO-LUMO interaction of the respective components **7** and **9** and olefins **1**-**3**, one could expect the following reactivity sequence: **1a** > **2a** > **3a** > **3b** (Figure 11). Although we have not similar reaction conditions for comparing all these olefins, and only a rough estimation can be made, the thermal Diels-Alder reaction of these olefins with **9** shows a parallel sequence of reactivity with respect to that furnished by the FMO calculations [3c, 7]. However, even though olefins **1a** and **3a** reacted very fast with **7**, it is not clear why olefins **2a** and **3b** did not react at all.

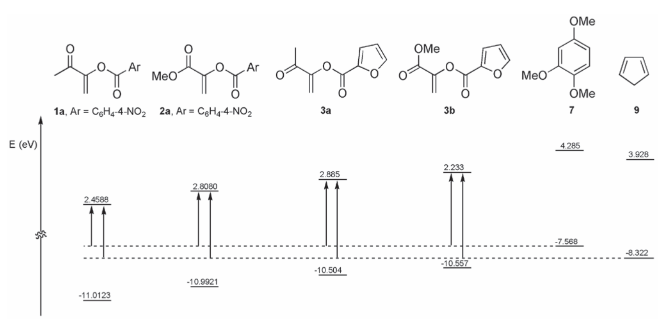


Fig. 11. Energy gaps for the FMO interactions between olefins **1a**, **2a**, **3a**, and **3b** with **7** and **12**.

The calculations show that the relative value of the coefficient on the unsubstituted carbon C-1 is greater than that on the captodative carbon C-2 for the LUMO of olefins **1**-**3** (Table 4). Therefore, the predicted main interaction is that between carbon C-1 of alkenes and the nucleophile (i.e., the benzene ring). Actually, for the unsubstituted carbon centers of compound **7**, the larger coefficient in the HOMO corresponds to that located at the carbon C-3, which is, indeed, the center that reacts with olefin **3a** in the Friedel-Crafts reaction to give adduct **8** (Figure 5).

Although the inductive effect of the aroyloxy substituent is relatively weak on the overall electron density of the carbon atoms of the double bond, the trend is significant for olefins **1**, showing that an electron-withdrawing group such as the nitro group reduces the charge at the unsubstituted methylenic carbon, while an electron-donor group (Me or *p*-OMe groups) has the opposite effect [9]. This correlation is reversed in the captodative carbon. The analysis of the HOMO coefficients of the captodative and the methylenic carbons for the same alkenes **1** showed a trend that is in agreement with that found for the charges at these atoms [9]. It is interesting that a larger difference in coefficients (ΔC_i) in the HOMOs of the new olefins **3a** and **3b** with respect to olefins **1a** and **2a** reflects the electron-withdrawing effect of the furoyloxy group. This is also supported by the fact that the ΔC_i values in the LUMOs are comparable between the four olefins. Hence, and in spite of the expected electron-donating effect of the furan ring, the inductive and electrostatic effects of the furoyloxy group control the reactivity of this kind of new olefins, in agreement with our previous investigations [9].

Conclusions

We describe the synthesis of the new furoyloxy captodative olefins **3a**–**3d**. Only captodative olefin **3a** was reactive enough to undergo conjugate addition from the activated benzene derivative **7**. The Diels-Alder cycloadditions between these olefins and cyclic dienes **9** and **12** produced the corresponding *endo/exo* adducts. Unlike olefin **3a**, which led to a preferential *endo* selectivity in both dienes, olefin **3b** added to **9** to give a slight preference for the *exo* adduct. The effect of the electron-demand and the lone-pairs of the oxygen atom of the furoyl group of the new captodative olefins strongly modify the reactivity and stereoselectivity in Diels-Alder additions. The Lewis acid interactions with the oxygen atoms seem to lead to the formation of crowded complexes, which perturb the stability of the *endo/exo* transition states, leading to a lower stereoselectivity in comparison to that found in the case of olefins **1a** and **2a**. FMO calculations account for some of the experimental findings, showing that the LUMO energies of the captodative olefins control the reactivity in these processes. Moreover, the inductive and electrostatic effects exerted by the furoyloxy substituent enhance the reactivity of these processes, in cooperation with the electron-withdrawing group (acetyl or alkoxycarbonyl) of these geminally substituted olefins.

Experimental Section

General. Melting points (uncorrected) were determined with an Electrothermal capillary melting point apparatus. IR spectra were recorded on a Perkin-Elmer 1600 spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained on a Varian Mercury-300 (300 MHz and 75.4 MHz) instrument, with $CDCl_3$ as solvent and TMS as internal standard. Mass spectra (MS) and high resolution mass spectrometry were taken, in electron impact (70 eV) and fast atom bombardment (FAB) modes, on Hewlett-Packard 5971A and Thermo-Finnigan Polaris Q, and on a Jeol JMS-AX 505 HA spectrometers. X-Ray crystallographic measurements were collected on a Siemens P4 diffractometer with Mo Kα radiation (graphite crystal monochromator, λ = 0.7107 Å). Microanalyses were performed by M-H-W Laboratories (Phoenix, AZ). Analytical thin-layer chromatography was carried out using E. Merck silica gel 60 F_{254} coated 0.25 plates, visualizing by long- and short-wavelength UV lamps. Flash column chromatography was performed on silica gel (230-400 mesh, Natland Int.). Radial chromatography was performed on a Chromatotron of Harrison Research Instruments. All air moisture sensitive reactions were carried out under nitrogen using oven-dried glassware. THF was freshly distilled from sodium, and methylene chloride from calcium hydride, prior to use. Triethylamine was freshly distilled from NaOH. All other reagents were used without further purification.

3-(2-Furoyloxy)-3-buten-2-one (3a). Under N_2 atmosphere at 0 ºC and vigorous magnetic stirring, a solution of 1.0 g (7.66 mmol) of **5** in dry THF (3.5 mL) was added dropwise to a solution of 1.414 g (1.40 mmol) of triethylamine in dry THF (5.6 mL). At the same temperature, a solution of 0.507 g (5.90 mmol) of **4a** in dry THF (1.7 mL) was slowly added, the temperature was allowed to increase until reaching room temperature, and the mixture was stirred for 24 h. The mixture was diluted with CH_2Cl_2 (85 mL) and successively washed with a cold 5% aqueous solution of HCl (2 × 25 mL) and a cold 5% aqueous solution of $NaHCO_3$ (2 × 25 mL) until neutral. The organic layer was dried (Na_2SO_4), and the solvent was evaporated under vacuum. The residue was purified by column chromatography over silica gel (60 g, hexane/EtOAc, 95:5), to give 0.37 g (35%) of **3a** as a pale yellow solid: R_f 0.27 (hexane/EtOAc, 8:2); mp 48–49 ºC (hexane/CH_2Cl_2, 6:4); IR (CH_2Cl_2) 1738, 1696, 1642, 1574, 1472, 1393, 1287, 1173, 1103, 766 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.41 (s, 3H, CH_3CO), 5.77 (d, *J* = 2.4 Hz, 1H, HC=), 6.05 (d, *J* = 2.4 Hz, 1H, HC=), 6.58 (dd, *J* = 3.5, 1.8 Hz, 1H, H-4'), 7.35 (dd, *J* = 3.5, 0.9 Hz, 1H, H-3'), 7.66 (dd, *J* = 1.8, 0.9 Hz, 1H, H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 25.5 ($\mathit{C}H_3$CO), 112.2 (C-4'), 114.7 (C-4), 120.0 (C-3'), 143.1 (C-2'), 147.4 (C-5'), 150.9 (C-3), 156.1 (*C*O_2), 191.4 (CH_3*C*O); MS (70 eV) 180 (M^+, 3), 152 (12), 95 (100), 67 (3), 43 (11). Anal. Calcd for $C_9H_8O_4$: C, 60.00; H, 4.48. Found: C, 59.91; H, 4.60.

General Procedure for the Preparation of Olefins 3b–3c. Under N_2 atmosphere and vigorous magnetic stirring, a solution of 0.619 g (6.13 mmol) of triethylamine in dry THF (20 mL) was cooled to -20 ºC, and a solution of **5** (4.09 mmol) in dry THF (15 mL) was added dropwise. At the same temperature, a solution of the alkyl pyruvate (**4b** or **4c**) (4.09 mmol) in 10 mL of dry THF was slowly added, and the temperature was allowed to increase until reaching room temperature. The mixture was stirred for 16-36 h, the solvent was removed under vacuum, and the reaction crude was diluted with cold CH_2Cl_2 (50 mL). Then, the organic solution was successively washed with a cold 5% aqueous solution of HCl (2 × 25 mL), a cold aqueous saturated solution of NH_4Cl (3 × 25 mL), a cold 10% aqueous solution of $NaHCO_3$ (3 × 25 mL), and with a cold saturated solution of NaCl (2 × 25 mL). The organic layer was dried (Na_2SO_4), and the solvent was evaporated under vacuum. The residue was successively purified by column chromatography on silica gel (30 g/1 g of crude, hexane/EtOAc, 95:5), to give **3b** or **3c** as oils.

Methyl 2-(2-Furoyloxy)-2-propenoate (3b). According to the general procedure, with 0.417 g of **4b** and 0.534 g of **5**, and after stirring for 24 h, 0.23 g (29%) of **3b** were obtained as a pale yellow oil: R_f 0.31 (hexane/EtOAc, 8:2); IR (CH_2Cl_2) 1735, 1650, 1575, 1471, 1441, 1393, 1294, 1154, 1100, 1017, 765 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.81 (s, 3H, CO_2CH_3), 5.64 (d, *J* = 2.0 Hz, 1H, HC=), 6.18 (d, *J* = 2.0 Hz, 1H, HC=), 6.59 (dd, *J* = 3.6, 1.8 Hz, 1H, H-4'), 7.36 (dd, *J* = 3.6, 0.9 Hz, 1H, H-3'), 7.68 (dd, *J* = 1.8, 0.9 Hz, 1H, H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 52.4 ($CO_2\mathit{C}H_3$), 112.1 (C-4'), 114.6 (C-3), 119.9 (C-3'), 142.8 (C-2'), 143.7 (C-2), 147.3 (C-5'), 155.9 (*C*O_2), 161.5 (*C*O_2CH_3); MS (70 eV) 196 (M^+, 2), 165 (1), 95 (100), 67 (2). Anal. Calcd for $C_9H_8O_5$: C, 55.11; H, 4.11. Found: C, 55.27; H, 4.34.

Ethyl 2-(2-Furoyloxy)-2-propenoate (3c). According to the general procedure, with 0.474 g of **4c** and 0.534 g of **5**, and after stirring for 36 h, 0.33 g (38%) of **3c** were obtained as a pale yellow oil: R_f 0.39 (hexane/EtOAc, 8:2); IR (CH_2Cl_2) 1732, 1650, 1575, 1471, 1393, 1291, 1154, 1097, 1017, 761 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (t, *J* = 7.2 Hz, 3H, $\mathit{C}H_3CH_2O$), 4.28 (q, *J* = 7.2 Hz, 2H, $CH_3\mathit{CH}_2O$), 5.63 (d, *J* = 2.0 Hz, 1H, HC=), 6.16 (d, *J* = 2.0 Hz, 1H, HC=), 6.58 (dd, *J*

= 3.5, 1.9 Hz, 1H, H-4'), 7.35 (dd, *J* = 3.5, 0.8 Hz, 1H, H-3'), 7.67 (dd, *J* = 1.9, 0.8 Hz, 1H, H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 13.9 ($CO_2CH_2CH_3$), 61.8 ($CO_2CH_2CH_3$), 112.2 (C-4'), 114.4 (C-3), 119.9 (C-3'), 143.0 (C-2'), 144.2 (C-2), 147.4 (C-5'), 156.1 (CO_2), 161.1 ($CO_2CH_2CH_3$); MS (70 eV) 210 (M^+, 1), 182 (2), 165 (3), 95 (100), 67 (2). HRMS (FAB, MH^+) (*m*NBA) Calcd for $C_{10}H_{11}O_5$: 211.0606. Found: 211.0606.

3,4-Dibromo-3-(2-furoyloxy)-2-butanone (6). Under N_2 atmosphere at 0 ºC and vigorous magnetic stirring, a solution of 3.46 g (21.65 mmol) of Br_2 in dry CH_2Cl_2 (25 mL) was added dropwise to a solution of 1.0 g (5.55 mmol) of **3a** in dry CH_2Cl_2 (30 mL). The mixture was stirred at 0 ºC for 1 h. The mixture was diluted with CH_2Cl_2 (100 mL) and successively washed with a cold saturated aqueous solution of $Na_2S_2O_4$ (5 x 50 mL) and cold brine (2 × 50 mL). The organic layer was dried (Na_2SO_4), and the solvent was evaporated under vacuum. The residue was purified by column chromatography over silica gel (30 g, hexane/EtOAc, 90:10), to give 1.83 g (97%) of **6** as a pale yellow oil: R_f 0.46 (hexane/EtOAc, 8:2); IR (CH_2Cl_2) 1738, 1467, 1397, 1358, 1294, 1256, 1234, 1167, 1076, 1014, 762 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.57 (s, 3H, CH_3CO), 4.39 (d, *J* = 11.0 Hz, 1H, H-4), 4.75 (d, *J* = 11.0 Hz, 1H, H-4), 6.59 (dd, *J* = 3.6, 1.8 Hz, 1H, H-4'), 7.36 (dd, *J* = 3.6, 0.8 Hz, 1H, H-3'), 7.70 (dd, *J* = 1.8, 0.8 Hz, 1H, H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 24.4 (CH_3CO), 32.6 (C-4), 86.2 (C-3), 112.5 (C-4'), 120.8 (C-3'), 142.8 (C-2'), 148.1 (C-5'), 154.4 (CO_2), 195.7 (CH_3CO); HRMS (FAB, M^+) (*m*NBA) Calcd for $C_9H_8Br_2O_4$: 340.8813. Found: 340.8820.

(*Z*)-4-Bromo-3-(2-furoyloxy)-3-buten-2-one (3d). Under N_2 atmosphere at 10 ºC, a solution of 0.59 g (5.88 mmol) of triethylamine in dry CH_2Cl_2 (5 mL) was added dropwise to a solution of 1.0 g (2.94 mmol) of **6** in dry CH_2Cl_2 (20 mL), and the mixture was stirred at the same temperature for 3 h. The mixture was diluted with CH_2Cl_2 (50 mL) and successively washed with a cold 5% aqueous solution of HCl (2 × 50 mL) and cold brine (2 × 50 mL) until neutral. The organic layer was dried (Na_2SO_4), and the solvent was evaporated under vacuum. The residue was purified by column chromatography over silica gel (30 g, hexane/EtOAc, 9:1), to give 0.75 g (99%) of **3d** as a pale brown solid: R_f 0.28 (hexane/EtOAc, 8:2); mp 78–79 ºC (hexane/ CH_2Cl_2, 3:7); IR (CH_2Cl_2) 1743, 1694, 1616, 1573, 1470, 1392, 1281, 1171, 1101, 1015, 764 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.39 (s, 3H, CH_3CO), 6.61 (dd, *J* = 3.7, 1.8 Hz, 1H, H-4'), 7.42 (dd, *J* = 3.7, 1.0 Hz, 1H, H-3'), 7.50 (s, 1H, H-4), 7.70 (dd, *J* = 1.8, 1.0 Hz, 1H, H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 25.6 (CH_3CO), 112.3 (C-4'), 114.9 (C-4), 120.7 (C-3'), 142.5 (C-2'), 147.8 (C-5'), 148.9 (C-3), 154.5 (CO_2), 188.6 (CH_3CO); MS (70 eV) 179 (M^+-80, 6), 95 (100), 67 (2). Anal. Calcd for $C_9H_7BrO_4$: C, 41.73; H, 2.72. Found: C, 41.96; H, 2.80.

3-(2-Furoyloxy)-4-(2,4,5-trimethoxyphenyl)-2-butanone (8). Under N_2 atmosphere and at 0 ºC, 0.113 g (0.67 mmol) of **7** and 0.008 g (0.056 mmol) of $BF_3{\cdot}Et_2O$ were successively added dropwise to a solution of 0.1 g (0.56 mmol) of **3a** in dry CH_2Cl_2 (3 mL). The mixture was stirred at 0 ºC for 1 h. The mixture was diluted with EtOAc (75 mL) and successively washed with H_2O (2 × 10 mL), with an aqueous saturated solution of $NaHCO_3$ (3 × 50 mL), and with H_2O until neutral. The organic layer was dried (Na_2SO_4), and the solvent was evaporated under vacuum. The residue was purified by column chromatography over silica gel (10 g, hexane/EtOAc, 9:1), to give 0.153 g (79%) of **8** as a white solid: R_f 0.15 (hexane/EtOAc, 7:3); mp 86–87 ºC (EtOAc/MeOH, 7:3); IR (CH_2Cl_2) 1719, 1611, 1577, 1467, 1397, 1298, 1205, 1176, 1116, 1033, 763 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.19 (s, 3H, CH_3CO), 2.98 (dd, *J* = 14.0, 8.1 Hz, 1H, H-4), 3.29 (dd, *J* = 14.0, 5.1 Hz, 1H, H-4), 3.79 (s, 3H, MeO), 3.80 (s, 3H, MeO), 3.88 (s, 3H, MeO), 5.42 (dd, *J* = 8.1, 5.1 Hz, 1H, H-3), 6.49 (s, 1H, H-7), 6.51 (dd, *J* = 3.6, 1.6 Hz, 1H, H-4'), 6.76 (s, 1H, H-10), 7.19 (dd, *J* = 3.6, 0.8 Hz, 1H, H-3'), 7.58 (dd, *J* = 1.6, 0.8 Hz, 1H, H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 26.8 (CH_3CO), 31.0 (C-4), 55.9 (MeO), 56.0 (MeO), 56.5 (MeO), 78.4 (C-3), 96.8 (C-7), 111.9 (C-4'), 114.8 (C-5), 115.2 (C-10), 118.6 (C-3'), 142.5 (C-2' or C-9), 144.0 (C-9 or C-2'), 146.6 (C-5'), 148.7 (C-8), 151.6 (C-6), 157.8 (CO_2), 204.9 (CH_3CO); MS (70 eV) 348 (M^+, 1), 237 (2), 151 (15), 108 (14), 107 (18), 95 (100), 91 (46), 79 (50), 77 (37), 67 (24), 43 (58). Anal. Calcd for $C_{18}H_{20}O_7$: C, 62.06; H, 5.79. Found: C, 61.93; H, 5.86.

(1*R,2*R**,4*R**)-2-Acetyl-2-(2-furoyloxy)bicyclo[2.2.1]-5-heptene (10a). (1*R**,2*S**,4*R**)-2-Acetyl-2-(2-furoyloxy)bicyclo[2.2.1]-5-heptene (11a). Method A.** To a solution of 0.10 g (0.56 mmol) of **3a** in dry CH_2Cl_2 (4 mL), under N_2 atmosphere and at -78 ºC, 0.183 g (2.77 mmol) of **9** and 0.008 g (0.056 mmol) of $BF_3{\cdot}Et_2O$ were successively added. The mixture was stirred at -78 ºC for 30 min, diluted with CH_2Cl_2 (40 mL), and successively washed with H_2O (2 × 10 mL), with a 5% aqueous solution of $NaHCO_3$ (2 × 15 mL), and with H_2O until neutral. The organic layer was dried (Na_2SO_4), and the solvent was evaporated under vacuum. The residue was purified by column chromatography over silica gel (10 g, hexane/EtOAc, 9:1), to give 0.127 g (93%) of a mixture of **10a**/**11a** (68:32) as a pale yellow oil.

Method B. To a solution of 0.10 g (0.56 mmol) of **3a** in dry CH_2Cl_2 (4 mL), under N_2 atmosphere at -15 ºC, were successively added 0.183 g (2.77 mmol) of **9** and 0.01 g (0.053 mmol) of $TiCl_4$. The mixture was stirred at -15 ºC for 4 h, extracted and purified following method A, to give 0.122 g (90%) of a mixture of **10a**/**11a** (60:40) as a pale yellow oil.

Method C. A mixture of 0.03 g (0.17 mmol) of **3a** and 0.11 g (1.67 mmol) of **9** was stirred at 40 ºC for 16 h, and purified by column chromatography over silica gel (10 g, hexane/EtOAc, 9:1), to give 0.023 g (55%) of a mixture of **10a**/**11a** (1:1) as a pale yellow oil.

Method D. A mixture of 0.06 g (0.34 mmol) of **3a** and 0.11 g (1.67 mmol) of **9** in 5 mL of a mixture of MeOH/H_2O (9:1) was stirred at 20 ºC for 24 h. The solvent was removed under vacuum, and the residue was purified by column chromatography over silica gel (10 g, hexane/EtOAc, 9:1), to give 0.048

g (58%) of a mixture of **10a**/**11a** (1:1) as a pale yellow oil, which was separated by column chromatography over silica gel (10 g, hexane/EtOAc, 98:2). Data of **10a**: 0.01 g (13%) as a pale yellow oil: R_f 0.37 (hexane/EtOAc, 8:2); IR (CH_2Cl_2) 1717, 1576, 1471, 1392, 1308, 1255, 1235, 1175, 1114, 1080, 1017, 766 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.69-1.77 (m, 2H, H-3x, H-7s), 2.01 (br d, *J* = 8.7 Hz, 1H, H-7a), 2.16 (s, 3H, CH_3CO), 2.41 (dd, *J* = 13.2, 3.0 Hz, 1H, H-3n), 2.98 (br s, 1H, H-4), 3.17 (br s, 1H, H-1), 5.81 (dd, *J* = 5.6, 3.0 Hz, 1H, H-6), 6.40 (dd, *J* = 5.6, 3.0 Hz, 1H, H-5), 6.56 (dd, *J* = 3.6, 1.8 Hz, 1H, H-4'), 7.27 (dd, *J* = 3.6, 0.8 Hz, 1H, H-3'), 7.63 (dd, *J* = 1.8, 0.8 Hz, 1H, H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 25.7 ($\mathit{C}H_3CO$), 37.3 (C-3), 42.2 (C-4), 49.2 (C-7), 51.2 (C-1), 92.9 (C-2), 112.0 (C-4'), 118.9 (C-3'), 129.7 (C-6), 141.7 (C-5), 144.1 (C-2'), 146.9 (C-5'), 158.4 ($\mathit{C}O_2$), 203.6 ($CH_3\mathit{C}O$); MS (70 eV) 247 (M^++1, 10), 203 (3), 135 (14), 134 (23), 106 (3), 95 (100), 66 (67), 43 (68). Data of **11a**: 0.02 g (26%) as a pale yellow oil: R_f 0.40 (hexane/EtOAc, 8:2); IR (CH_2Cl_2) 1721, 1472, 1393, 1310, 1239, 1177, 1115, 1046, 1017, 768 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (dd, *J* = 12.9, 3.9 Hz, 1H, H-3n), 1.47 (dm, *J* = 9.0 Hz, 1H, H-7s), 1.67 (br d, *J* = 9.0 Hz, 1H, H-7a), 2.21 (s, 3H, CH_3CO), 2.70 (dd, *J* = 12.9, 3.6 Hz, 1H, H-3x), 2.94 (br s, 1H, H-4), 3.21-3.25 (m, 1H, H-1), 6.16 (dd, *J* = 5.7, 3.0 Hz, 1H, H-6), 6.43 (dd, *J* = 5.7, 3.0 Hz, 1H, H-5), 6.52 (dd, *J* = 3.6, 1.8 Hz, 1H, H-4'), 7.17 (dd, *J* = 3.6, 0.8 Hz, 1H, H-3'), 7.60 (dd, *J* = 1.8, 0.8 Hz, 1H, H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 24.7 ($\mathit{C}H_3CO$), 38.2 (C-3), 42.0 (C-4), 46.7 (C-7), 49.5 (C-1), 93.5 (C-2), 111.9 (C-4'), 118.8 (C-3'), 132.5 (C-6), 140.6 (C-5), 143.9 (C-2'), 146.9 (C-5'), 158.4 ($\mathit{C}O_2$), 205.4 ($CH_3\mathit{C}O$); MS (70 eV) 247 (M^++1, 6), 203 (2), 135 (11), 134 (12), 95 (100), 66 (56), 43 (43).

(1*R,2*R**,4*R**)-2-(2-Furoyloxy)-2-methoxycarbonylbicyclo[2.2.1]-5-heptene (10b). (1*R**,2*S**,4*R**)-2-(2-Furoyloxy)-2-methoxycarbonylbicyclo[2.2.1]-5-heptene (11b). Method A.** To a solution of 0.05 g (0.255 mmol) of **3b** in dry CH_2Cl_2 (4 mL), under N_2 atmosphere and at -50 ºC, 0.183 g (2.77 mmol) of **9** and 0.005 g (0.026 mmol) of $TiCl_4$ were successively added. The mixture was stirred at -50 ºC for 6 h, and extracted following method A of **10a**/**11a**. The residue was purified by column chromatography over silica gel (10 g, hexane/EtOAc, 98:2), to give 0.045 g (67%) of a mixture of **10b**/**11b** (46:54) as a pale yellow oil.

Method B. A mixture of 0.04 g (0.204 mmol) of **3b** and 0.067 g (1.02 mmol) of **9** was stirred at 40 ºC for 24 h, and purified by column chromatography over silica gel (10 g, hexane/EtOAc, 98:2), to give 0.045 g (84%) of a mixture of **10b**/**11b** (41:59) as a pale yellow oil, which was separated by column chromatography over silica gel (15 g, hexane/EtOAc, 98:2). Data of **10b**: 0.014 g (21%) as a pale yellow oil: R_f 0.36 (hexane/EtOAc, 8:2); IR (CH_2Cl_2) 1729, 1577, 1471, 1393, 1308, 1175, 1116, 1053, 1014, 765 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.72 (dm, *J* = 8.9 Hz, 1H, H-7s), 1.85 (dd, *J* = 13.2, 3.8 Hz, 1H, H-3x), 1.97 (br d, *J* = 8.9 Hz, 1H, H-7a), 2.41 (dd, *J* = 13.2, 3.1 Hz, 1H, H-3n), 2.98 (br s, 1H, H-4), 3.24 (br s, 1H, H-1), 3.68 (s, 3H, CO_2CH_3), 5.90 (dd, *J* = 5.6, 3.0 Hz, 1H, H-6), 6.42 (dd, *J* = 5.7, 3.3 Hz, 1H, H-5), 6.52 (dd, *J* = 3.6, 1.7 Hz, 1H, H-4'), 7.23 (dd, *J* = 3.6, 0.9 Hz, 1H, H-3'), 7.60 (dd, *J* = 1.7, 0.9 Hz, 1H, H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 39.3 (C-3), 42.0 (C-4), 49.0 (C-7), 51.8 (C-1), 52.4 ($CO_2\mathit{C}H_3$), 86.8 (C-2), 111.9 (C-4'), 118.7 (C-3'), 130.3 (C-6), 141.7 (C-5), 144.3 (C-2'), 146.7 (C-5'), 158.2 ($\mathit{C}O_2$), 171.1 ($\mathit{C}O_2CH_3$); MS (70 eV) 263 (M^++1, 2), 231 (3), 151 (5), 137 (13), 107 (8), 95 (100), 79 (14), 66 (42). Data of **11b**: 0.021 g (31%) as a pale yellow oil: R_f 0.42 (hexane/EtOAc, 8:2); IR (CH_2Cl_2) 1734, 1577, 1472, 1438, 1394, 1310, 1176, 1117, 1054, 1014, 766 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (dd, *J* = 13.2, 3.6 Hz, 1H, H-3n), 1.55 (dm, *J* = 9.0 Hz, 1H, H-7s), 1.87 (d, *J* = 9.0 Hz, 1H, H-7a), 2.75 (dd, *J* = 13.2, 3.6 Hz, 1H, H-3x), 2.98 (br s, 1H, H-4), 3.41 (br s, 1H, H-1), 3.76 (s, 3H, CO_2CH_3), 6.15 (dd, *J* = 5.6, 3.0 Hz, 1H, H-6), 6.42 (dd, *J* = 5.6, 3.0 Hz, 1H, H-5), 6.49 (dd, *J* = 3.6, 1.8 Hz, 1H, H-4'), 7.14 (dd, *J* = 3.6, 0.9 Hz, 1H, H-3'), 7.57 (dd, *J* = 1.8, 0.9 Hz, 1H, H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 40.1 (C-3), 42.1 (C-4), 47.4 (C-7), 51.1 (C-1), 52.7 ($CO_2\mathit{C}H_3$), 87.2 (C-2), 111.8 (C-4'), 118.5 (C-3'), 132.8 (C-6), 140.2 (C-5), 144.2 (C-2'), 146.6 (C-5'), 158.1 ($\mathit{C}O_2$), 172.8 ($\mathit{C}O_2CH_3$); MS (70 eV) 263 (M^++1, 2), 231 (2), 151 (2), 137 (14), 107 (8), 95 (100), 91 (8), 79 (13), 66 (45).

(1*R,2*R**,4*R**)-2-Acetyl-2-(2-furoyloxy)bicyclo[2.2.2]-5-octene (13). (1*R**,2*S**,4*R**)-2-Acetyl-2-(2-furoyloxy)bicyclo[2.2.2]-5-octene (14). Method A.** To a solution of 0.10 g (0.56 mmol) of **3a** in dry CH_2Cl_2 (4 mL), under N_2 atmosphere and at -78 ºC, 0.067 g (0.84 mmol) of **12** and 0.008 g (0.056 mmol) of $BF_3 \cdot Et_2O$ were successively added. The mixture was stirred at -78 ºC for 30 min, diluted with CH_2Cl_2 (30 mL), and successively washed with with H_2O (2 × 15 mL), with a 5% aqueous solution of $NaHCO_3$ (2 × 15 mL), and with H_2O until neutral. The organic layer was dried (Na_2SO_4), and the solvent was evaporated under vacuum. The residue was purified by column chromatography over silica gel (15 g, hexane/EtOAc, 98:2), to give 0.118 g (82%) of a mixture of **13**/**14** (70:30) as a pale yellow oil.

Method B. To a solution of 0.10 g (0.56 mmol) of **3a** in dry CH_2Cl_2 (4 mL), under N_2 atmosphere and at 20 ºC, 0.067 g (0.84 mmol) of **12** and 0.11 g (0.83 mmol) of $AlCl_3$ were successively added. The mixture was stirred at 20 ºC for 48 h, extracted and purified following method A, to give 0.098 g (68%) of a mixture of **13**/**14** (57:43) as a pale yellow oil. Adduct **13** was separated pure by column chromatography over silica gel (15 g, hexane/EtOAc, 99:1), to give 0.033 g (23%) of the product as a pale yellow oil: R_f 0.32 (hexane/EtOAc, 8:2); IR (CH_2Cl_2) 1719, 1575, 1470, 1392, 1357, 1305, 1230, 1173, 1114, 1084, 1049, 1015, 981, 764, 711 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16-1.40 (m, 2H, H-7s, H-8s), 1.55 (dd, *J* = 14.1, 2.7 Hz, 1H, H-3x),1.58-1.70 (m, 1H, H-8a), 2.13 (s, 3H, CH_3CO), 2.14-2.21 (m, 1H, H-7a), 2.41 (dt, *J* = 14.1, 3.0 Hz, 1H, H-3n), 2.71-2.78 (m, 1H, H-4), 3.02-3.08 (m, 1H, H-1), 6.10 (dd, *J* = 8.1, 6.9 Hz, 1H, H-6), 6.35 (dd, *J* = 7.8, 6.9 Hz, 1H, H-5), 6.55 (dd, *J* = 3.3, 1.8 Hz, 1H, H-4'), 7.25 (dd, *J* = 3.3, 0.9 Hz, 1H, H-3'), 7.62 (dd, *J* = 1.8, 0.9 Hz, 1H, H-5'); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 19.9 (C-7), 23.7 (C-8), 24.4 (CH_3CO), 30.0 (C-4), 36.1 (C-3), 36.2 (C-1), 88.5 (C-2), 112.0 (C-4'), 118.8 (C-3'), 129.6 (C-6), 135.7 (C-5), 144.3 (C-2'), 146.9 (C-5'), 158.1 (CO_2), 203.9 (CH_3CO); MS (70 eV) 260 (M^+, 1), 217 (2), 145 (2), 105 (3), 95 (100), 79 (11), 77 (12), 43 (21).

Single-Crystal X-Ray Crystallography [13]**.** Compound **8** was obtained as white crystals. These were mounted in glass fibers. Crystallographic measurements were performed on a Siemens P4 diffractometer with Cu Kα radiation (λ = 1.5418 Å; graphite monochromator) at room temperature. Two standard reflections were monitored periodically; they showed no change during data collection. Unit cell parameters were obtained from least-square refinement of 38 reflections in the range 10.91 < θ < 28.08°. Intensities were corrected for Lorentz and polarization effects. No absorption correction was applied. Anisotropic temperature factors were introduced for all non-hydrogen atoms. Hydrogen atoms were placed in idealized positions and their atomic coordinates refined. Unit weights were used in the refinement. The structure was solved using SHELX-97 [19], and the structure was visualized and plotted with the PLATON program package [20]. Data of **8**: Formula: $C_{18}H_{20}O_7$: molecular weight: 348.34; cryst. syst.: monoclinic; space group: $P2_1/n$; unit cell parameters: *a*, 7.0577(4), *b*, 11.3816(8), *c*, 22.847(2) (Å); α, 90, β, 93.322(6), γ, 90 (deg); temp. (°K): 293 (2); volume: 1832.1(2) (Å^3); Z: 4; density: 1.263 (mg/m^3); No. of reflections collected: 3557; no. of independent reflections: 2474; no. of reflections observed: 2464; data collection range: 3.88 < θ < 56.95°; *R*: 0.0582; GOF: 1.070.

Calculations. The *ab initio* SCF/HF calculations were carried out with the 6-31G* basis sets using Gaussian 94 [21] in personal computers running under Linux operating system. Geometries were fully optimized at the HF/3-21G* level of theory and these were employed as the starting point for optimization, at the HF/6-31G* level. Optimization of conformers was followed by frequency analysis to insure the correct nature of the stationary points. Relative energies were obtained by subtracting the energy of the lowest-energy conformer from the energies of all conformers in each system, and converting these differences into kcal/mol (Table 1). In all cases the reactive HOMOs and LUMOs were located by visual inspection of the corresponding MO wavefunctions; the atomic charges, MO energies, and coefficients were extracted from the output of HF/6-31G* single point calculations on the minimum-energy conformers employing the POP=REG Gaussian keyword.

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Director Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

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