Reactivity and Selectivity of Captodative Olefins as Dienes in Hetero-*Diels–Alder* Reactions

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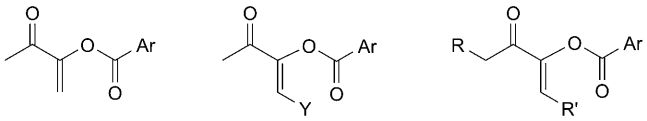
The reactivity and selectivity of the the captodative olefins 1-acylvinyl benzoates **1a**–**1f** and **3a** as heterodienes in hetero-*Diels–Alder* reactions in the presence of electron-rich dienophiles is described. Heterodienes **1** undergo regioselective cycloaddition with the alkyl vinyl etherdienophiles **6a**,**b** and **9** to give the corresponding dihydro-2*H*-pyrans **7**, **8**, and **10** under thermal conditions. The reactivity of these cycloadditions depends, to a large extent, on the electronic demand of the substituent in the aroyloxy group of the heterodiene. Frontier-molecular-orbital (FMO; *ab initio*) and density-functional-theory (DFT) calculations of the ground and transition states account for the reactivity and regioselectivity observed in these processes.

1. Introduction. – Hetero-*Diels–Alder* reactions have found wide synthetic application as a highly convergent and selective methodology for building functionalized heterocyclic rings [1]. Enones have attracted particular attention as heterodienes in this process due to their potential for the preparation of dihydro-2*H*-pyrans as versatile precursors in the synthesis of carbohydrates [2]. An extension of this process is the asymmetric version that employs either chiral auxiliaries in the heterodiene or chiral catalysts [3]. It has been established that, in general, the hetero-*Diels–Alder* reaction of enones follows a concerted pathway, and the reactivity is subjected to inverse-electron-demand (IED) conditions [1–3].

The reactivity and selectivity of these processes are substantially enhanced with the introduction of electron-withdrawing groups at C(3) of the '1-oxabuta-1,3-dienes' [2a][4]. This is explained in terms of frontier-molecular-orbital (FMO) theory by the fact that a *Diels–Alder* cycloaddition under IED is controlled by the heterodiene E_{LUMO}, and the presence of this kind of group will lower further this energy [1]. As

expected, the number of cycloadditions with heterodienes substituted by electron-donating groups at C(3) is limited, because their reactivity is decreased [5]. However, some of these heterodienes have proven to be reactive enough [6], probably as a result of the increased stability of the *cisoid* diene conformation required for the [4+2] approach.

Owing to the opposite electronic demand and to the synthetic potential displayed by their geminally substituted functional groups, captodative olefins have attracted special interest [7]. We have described the behavior of 1-acetylvinyl benzoates **1**, which show high reactivity and selectivity in cycloaddition reactions, with diverse dienes [8] and 1,3-dipoles [9]. These captodative olefins have also proved to be useful synthons in natural product synthesis [10]. However, 1-acetylvinyl benzoates **2** functionalized with a third substituent at the C=C bond, such as a Br-atom, a dialkylamino group, or a, thioether moiety, reacted very inefficiently in *Diels–Alder* cycloadditions [11]. In contrast, β-substituted captodative olefin derivatives **3a**–**3c** added to nitrones to yield the corresponding heterocycles, with a regioselectivity opposite to that observed for the unsubstituted alkene derivatives **1** [12].



1

2a Y = Br
2b Y = R^1R^2N
2c Y = RS
Ar = 4-$NO_2C_6H_4$

3a R = H, R' = Me
3b R = H, R' = Et
3c R = R' = Me
Ar = 4-$NO_2C_6H_4$

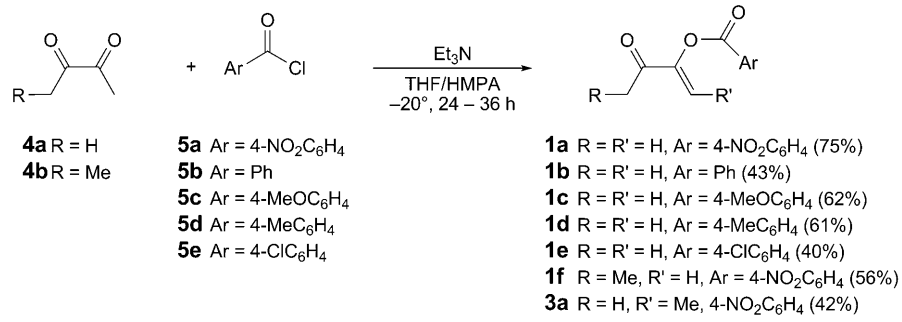
It has been shown that the aroyloxy (=(arenecarbonyl)oxy) group in these series of alkene derivatives does not have a significant electron-donating effect on the C=C bond, which, if present, would increase the electron density of the π system [13]. This inhibition of the delocalization of the lone pairs of the O-atom of the aroyloxy group is probably due to the conformational preference of the molecule. However, the aroyloxy group does exert a σ-acceptor effect upon the C=C bond, reinforcing the electron-withdrawing effect of the acetyl group [14]. This explains the fact that olefin derivative **1a** (Ar = 4-$NO_2C_6H_4$) is as reactive as methyl vinyl ketone in *Diels–Alder* additions [15], and much more reactive in conjugate *Friedel–Crafts* reactions [10f].

Moreover, in spite of the fact that compounds **1** bear the aroyloxy group, these '1-oxabuta-1,3-dienes' can be considered as potential heterodienes in hetero-*Diels–Alder* reactions under IED. We report herein the study on the reactivity and regioselectivity of the cycloaddition of a series of compounds **1** and **3** with alkyl vinyl ethers under thermal conditions. *Ab initio* and density-functional-theory (DFT) calculations were also carried out to account for the behavior of the heterodienes in these reactions.

2. Results and Discussion. – 2.1. *Preparation of Captodative Olefins.* The series of olefin derivatives **1a**–**1f**, and **3a** were prepared in accordance with the reported method [10b][12][14], by reacting the α-diketones **4a** or **4b** with the corresponding aroyl chlorides **5** (*Scheme 1*). The yield of the new olefin derivative **1c** was improved when

the addition of the reagents was carried out at $-40°$. In particular, we found that when the reaction with **4b** was carried out at $-20°$, not only was the yield increased with respect to those trials at higher temperatures, but a mixture of the kinetic and thermodynamic products **1f** and **3a** was obtained in a 57:43 ratio, respectively, which was readily separated by column chromatography (silica gel). As previously observed [12], the β-substituted olefin derivative **3a** was produced as the (Z) stereoisomer, exclusively. The new alkenyl esters **1c** and **1f** were isolated as thermally stable white powders, which were characterized by spectroscopy and elemental analysis. Spectroscopic data of alkenyl ester **3a** agreed with those obtained when this compound was prepared by the *Negishi* procedure starting from **2a** [16].

Scheme 1



2.2. *Hetero*-Diels–Alder *Reactions of Captodative Olefins with Alkyl Vinyl Ethers.* The *Diels–Alder* cycloadditions between ethyl vinyl ether (**6a**) and olefin derivatives **1a**–**1e** were carried out under thermal conditions (*Scheme 2*), providing the corresponding 2-ethoxy-3,4-dihydro-2*H*-pyran-5-yl adducts **7a**–**7e** (*Table 1*). No evidence of the C(3) substituted regioisomer was found either by chromatography or by ^{1}H-NMR, even after stopping the reaction before the heterodiene had disappeared. This regioselectivity corresponds to that expected for the cycloaddition between enones acting as heterodienes activated with electron-withdrawing substituents at the conjugated π-system [1a][2], and monosubstituted or unsubstituted captodative olefins [6b][6c][17]. In the case of heterodiene **1a**, its dimeric [4 + 2] adduct was the main by-product, as previously reported for the thermal attempt of a *Diels–Alder* reaction with a hindered diene [18].

Long reaction times were observed in all the additions up to the comparably high temperature of 115°. A further increase of temperature shortened the reaction time, but the yields were decreased. Severe conditions (high temperatures and pressures) are frequently used to ensure the conversion to the desired adducts in almost all cases of cycloadditions involving analogous heterodienes [1][6][19], which indicates that our molecules have a comparable reactivity. Even though the reaction times were decreased by carrying out the cycloaddition of **1a** and **6a** under different power levels of microwave irradiation at the same temperature (100°), the yields were also decreased (*Table 1*, *Entries 1–3*). We observed that the modest yields obtained in these

Scheme 2

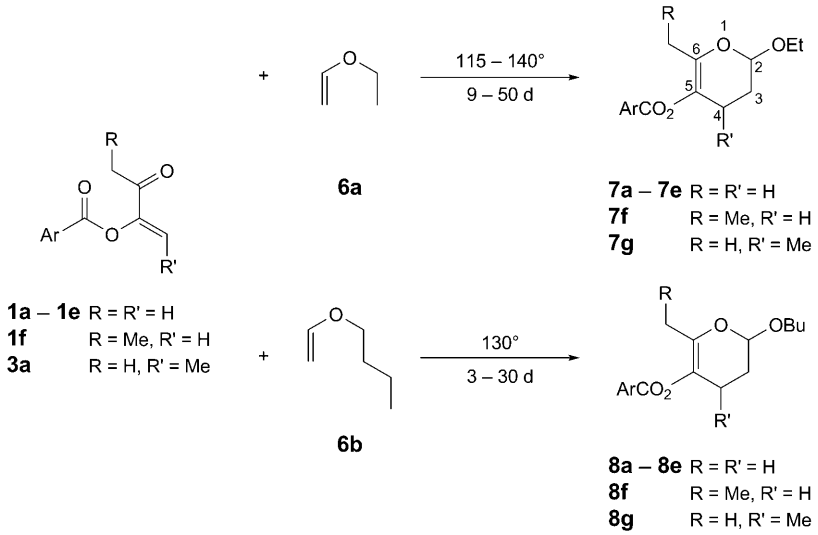


Table 1. *Preparation of 3,4-Dihydro-2*H*-pyran-5-yl Benzoates* **7a**–**7g**[a])

Entry	**1**	Ar	*T* [°]	Time	**7**	Yield [%][b])
1	**1a**	4-$NO_2C_6H_4$	100	16 d	**7a**	61
2	**1a**	4-$NO_2C_6H_4$	100[c])	24 h	**7a**	42
3	**1a**	4-$NO_2C_6H_4$	100[d])	12 h	**7a**	44
4	**1a**	4-$NO_2C_6H_4$	115	10 d	**7a**	76
5	**1b**	Ph	115	11 d	**7b**	46
6	**1c**	4-$MeOC_6H_4$	115	30 d	**7c**	48
7	**1d**	4-MeC_6H_4	115	35 d	**7d**	59
8	**1e**	4-ClC_6H_4	115	47 d	**7e**	57
9	**1f**	4-$NO_2C_6H_4$	115	9 d	**7f**	89
10	**3a**	4-$NO_2C_6H_4$	140	50 d	**7g**	27[c])

[a]) Under N_2, with ethyl vinyl ether (**6a**; 20 mol-equiv.) and hydroquinone (0.04 mol-equiv.). [b]) After column chromatography. [c]) Under microwave irradiation (100 W). [d]) Under microwave irradiation (200 W). [e]) As a 78 : 22 mixture of stereoisomers.

reactions were mostly due to decomposition of the starting materials. *Lewis* acid catalysis was also employed, but the yields in these cases were even lower (< 10%).

It is noteworthy that there seems to be a correlation between the reaction time and the electronic demand of the substituent in the aroyloxy group of the heterodiene. Thus, compound **1a**, which has an electron-withdrawing group (*p*-nitro), was more reactive than compound **1c**, where the aroyloxy group has an electron-donating group (*p*-methoxy). With the aim of evaluating the effect of the electronic demand on the reactivity, the cycloadditions of heterodienes **1a** (Ar = 4-$NO_2C_6H_4$), **1b** (Ar = Ph), and **1c** (Ar = 4-$MeOC_6H_4$) were monitored periodically by ^{1}H-NMR measurements, under

identical reaction conditions. After 48 h, the relative degree of conversion was found to be as follows: **1a** (100%), **1b** (88%), and **1c** (40%). Indeed, the reactivity was enhanced by the presence of an electron-withdrawing group [20]. This is in agreement with previous results where the enones acted as dienophiles in *Diels–Alder* additions under conditions of normal electron-demand [15]. Such a behavior in enones **1** was mostly associated with the remote inductive effect (*I*) of the substituent in the aroyloxy group, in which the reactivity is increased with $-I$ groups [14]. This is probably due to the fact that the electron-donating effect of the lone-pairs of the aroyloxy group on the heterodiene moiety, which would exert the opposite effect over reactivity, is inhibited [13].

The reactivity of heterodiene **1f** (Ar = 4-$NO_2C_6H_4$, R = Me, R′ = H) was comparable to that of **1a** (Ar = 4-$NO_2C_6H_4$, R = R′ = H) (*Table 1*, *Entries 4* and *9*). This suggests that, from the point of view of inductive and steric effects, there is no significant difference in reactivity between the heterodienes with an Et or Me at C(2). In contrast, in the presence of a Me group at C(4) of the heterodiene, such as in compound **3a**, the reactivity was massively affected [21]. The reaction took place only after heating up to 140° and required a longer reaction time (*Table 1*, *Entry 10*), giving adduct **7g** in low yield as a 78:22 mixture of *trans*/*cis*-forms resulting from the *exo*- and *endo*-approach. Although the relative configuration of the components of the mixture was not unambiguously established, it was tentatively assigned according to the coupling constants in the ^{1}H-NMR spectra (see *Exper. Part*) and to our transition state calculations (*vide infra*). The decomposition of **3a** and the polymerization of ethyl vinyl ether under such severe reaction conditions account for the resulting low yield.

The structure of adducts **7** was established by spectroscopy and elemental analysis or high-resolution mass spectrometry (HR-MS). This was also supported by the X-ray diffraction analysis of the structure of **7a** (*Fig. 1*), where it was found that the dihydro-2*H*-pyran ring adopts a half-chair conformation, the aroyloxy group keeps an almost orthogonal conformation with respect to the C=C bond of the cycle, and the EtO group is in the equatorial position. It was also found that the Me group at C(6) was disordered, with two distinct orientations readily apparent from the *Fourier* peak map; both Me geometries were refined assuming equal occupancies (one is shown in *Fig. 1*).

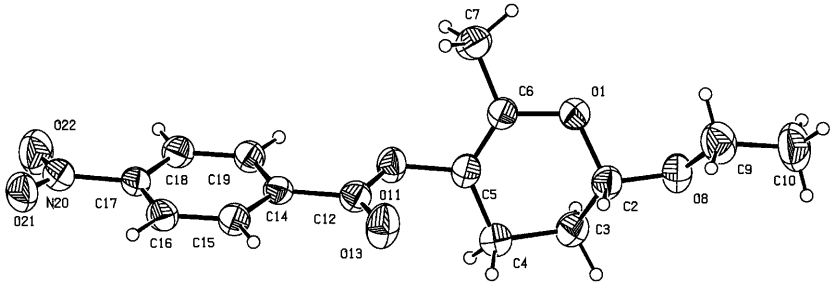


Fig. 1. *X-Ray structure of* **7a** (ellipsoids with 30% probability)

The solution and gas-phase conformational preference of the EtO group in the dihydro-2*H*-pyran ring was investigated by ^{1}H-NMR spectroscopy and by DFT calculations (B3LYP/6-31G(d)) [22] of **7a**. The energies of three of the most stable

geometries for both axial and equatorial conformations are summarized in *Table 2*. From these geometries (*Fig. 2*) and from the corresponding dihedral angles for H–C(2), H_{ax}–C(3), and H_{eq}–C(3) at the dihydro-2*H*-pyran ring, the coupling constants were calculated with the *Altona* equation [23] as implemented in the MestRe-J program [24] (*Table 2*). As expected from a stabilizing anomeric effect, the axial conformations A-1 and A-3 were the most stable conformations in the gas phase. Moreover, in solution, the axial conformation was also the most stable, as shown by the fact that the calculated coupling constants for this conformation are similar to those found by ^{1}H-NMR measurement. The signal due to H–C(2) appears as a very narrow *t*-like pattern (line width 3.2 Hz), which is closer to the expected signal arising from the calculated coupling constants for the axial conformer. Therefore, the fact of finding the less stable equatorial conformation in the X-ray crystallographic analysis of **7a** is probably due to a molecular packing effect within the crystal lattice.

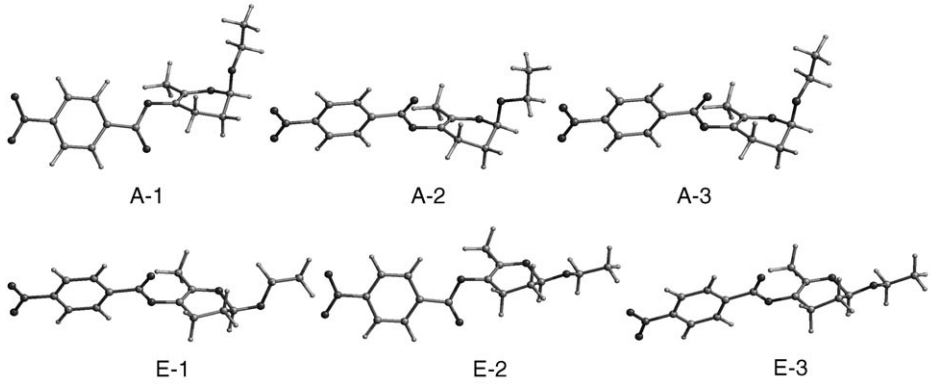


Fig. 2. *Calculated geometries [B3LYP/6-31G(d,p)] of some of the most stable axial* (A-1, A-2, and A-3) *and equatorial* (E-1, E-2, and E-3) *conformers of dihydro-2*H*-pyran* **7a**

Table 2. *B3LYP/6-31G(d,p) Relative Energies*[a]*, Calculated Dihedral Angles* (θ)*, and Calculated Coupling Constants* (J) *of the Most Stable Conformers of Adduct* **7a**

Conformer	E [kcal/mol]	θ [°]		J [Hz]	
		H–C(2)–C(3)–H_{ax}	H–C(2)–C(3)–H_{eq}	H–C(2), H_{ax}–C(3)	H–C(2), H_{eq}–C(3)
A-1	0.00	–53.9	63.5	3.6	2.5
A-2	3.87	–54.7	62.2	3.5	2.6
A-3	0.13	–53.5	63.8	3.6	2.5
E-1	3.48	–176.9	65.2	10.6	2.5
E-2	0.83	–178.0	65.2	10.7	2.5
E-3	1.22	–178.3	64.9	10.7	2.6

[a]) Relative energies including zero-point energy corrections.

In general, better yields were found for the reactions leading to the 2-butoxy-3,4-dihydro-2*H*-pyran-5-yl adducts **8a**–**8f** (*Table 3*), when the thermal cycloadditions were

carried out between butyl vinyl ether (**6b**) and olefin derivatives **1a**–**1f** (*Scheme 2*). This is probably due to the fact that the higher boiling point and stability under thermal conditions of **6b**, with respect to **6a**, allowed us to increase the temperature and, as a result, to reduce reaction times. An analogous result was obtained in the case of heterodiene **3a**, which yielded **8g** as a mixture of stereoisomers in a lower ratio (57:43; *Table 3*, *Entry 7*) than that observed for **7g**, under similar reaction conditions, but in a shorter reaction time. The hypothesis of the higher stability of **6b** to polymerization was supported by monitoring the reaction mixture by ^{1}H-NMR, which revealed that the decrease of the concentration of **6a** was faster than that for **6b**.

Table 3. *Preparation of 3,4-Dihydro-2*H*-pyran-5-yl Benzoates* **8a**–**8g**[a])

Entry	**1**	Ar	*T* [°]	Time	**8**	Yield [%][b])
1	**1a**	4-$NO_2C_6H_4$	130	3 d	**8a**	65
2	**1b**	Ph	130	3 d	**8b**	85
3	**1c**	4-$MeOC_6H_4$	130	4 d	**8c**	76
4	**1d**	4-MeC_6H_4	130	3 d	**8d**	59
5	**1e**	4-ClC_6H_4	130	6 d	**8e**	80
6	**1f**	4-$NO_2C_6H_4$	130	4 d	**8f**	81
7	**3a**	4-$NO_2C_6H_4$	140	30 d	**8g**	75[c])

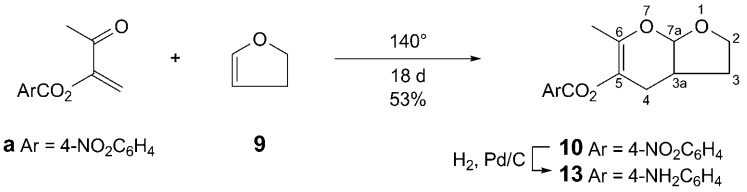
[a]) Under N_2, with butyl vinyl ether (**6b**; 20 mol-equiv.) and hydroquinone (0.02 mol-equiv.). [b]) After column chromatography. [c]) As a 57:43 mixture of stereoisomers.

Adducts **8a**–**8g** were isolated after purification by column chromatography as oily compounds, hence we were unable to determine their structure by X-ray crystallographic analysis. However, they were fully characterized by spectroscopy and HR-MS. The ^{1}H-NMR spectra of all the adducts **8** showed a signal pattern for H–C(2) in the anomeric position similar to that found for adducts **7**, which is consistent with the preferred axial conformation of the BuO group at C(2).

2.3. *Hetero*-Diels–Alder *Reaction of Captodative Olefin Derivative* **1a** *with 2,3-Dihydrofuran* (**9**). To evaluate the reactivity of **1a** in a hetero-*Diels–Alder* cycloaddition with a vicinal disubstituted dienophile, the corresponding reaction with 2,3-dihydrofuran (**9**) was carried out under thermal conditions (*Scheme 3*). After heating at 140° for 19 days, a single isomeric adduct, **10**, was identified by ^{1}H-NMR measurements. Although the yield was modest, it is noteworthy that an olefin derivative **1** adds to this kind of cyclic dienophiles [4a][6c][25]. It is also interesting to notice that the signal of the anomeric H–C(7a) of adduct **10** appeared at δ 5.41 as a *d* ($J = 3.9$) in the ^{1}H-NMR spectrum. According to MestRe-J calculations [24], the value of the coupling constant suggests that the main conformation of the bicycle is such that the dihedral angle between the angular H–C(3a) and H–C(7a) is close to 45°. Calculation (B3LYP/6-31G(d,p)) of the most stable geometries of **10** provided two sets of two conformations. In the lowest-energy set, corresponding to conformers in which the $-OCH_2-$ fragment of the furan ring adopts the equatorial position, the difference in energies is only 0.03 kcal/mol (the energy of the third most stable conformation, with an axial $-OCH_2-$ fragment, is 2.59 kcal/mol higher in energy than the lowest-energy conformer). The average dihedral angle between protons H–C(3a) and H–C(7a) in

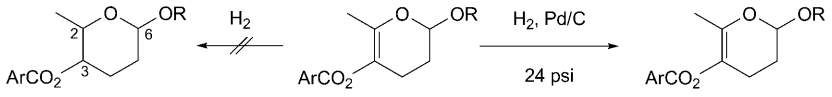
these two conformations is 46.1°, which corresponds to a calculated (MestRe-J [24]) coupling constant of $J = 3.8$ Hz, which is close to that found experimentally.

Scheme 3



2.4. *Application to the Synthesis of Tetrahydro-2*H*-pyranyl Compounds.* The conversion of adducts **7** and **8** to the tetrahydro-2*H*-pyranyl derivatives **11** could represent a novel synthetic approach to carbohydrates, with the convergent introduction of two O-functionalities at C(3) and C(6) in the cycloaddition step, and an alkyl group at C(2) (*Scheme 4*). Therefore, the Pd-catalyzed (10% Pd/C) hydrogenation of adducts **7a** and **8a** was carried out at low pressure (24 psi) for 24 h. However, the C=C bond was not hydrogenated; instead reduction of the nitro group took place to furnish the amino compounds **12a** and **12b**, respectively. A similar outcome resulted from the hydrogenation of cycloadduct **10**, yielding the corresponding amino compound **13** in 54% yield (*Scheme 3*). Despite the use of other catalysts (*Raney*-Ni, PtO_2, and $Pd(OH)_2$) the hydrogenation of the C=C bond failed.

Scheme 4



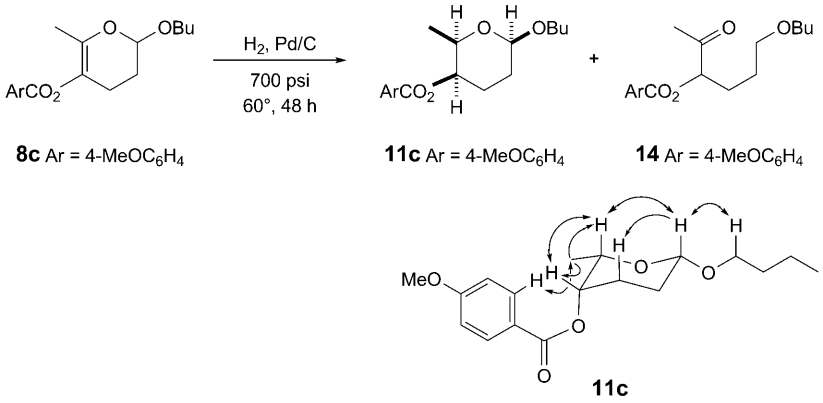
11a R = Et, Ar = 4-$NO_2C_6H_4$
11b R = Bu, Ar = 4-$NO_2C_6H_4$

7a R = Et, Ar = 4-$NO_2C_6H_4$
8a R = Bu, Ar = 4-$NO_2C_6H_4$

12a R = Et, Ar = 4-$NH_2C_6H_4$ (77%)
12b R = Bu, Ar = 4-$NH_2C_6H_4$ (63%)

To avoid the interference of the nitro group, adduct **8c** was submitted to similar hydrogenation conditions; however, the substrate was recovered without change. Only after increasing the pressure up to 700 psi and the temperature to 60° for 48 h, the desired product **11c** was obtained in 36% yield, along with a second product, corresponding to the hydrogenolysis compound **14** (*Scheme 5*), in 29% yield. It is interesting to notice that the hydrogenated product **11c** appeared as a single stereoisomer, whose relative configuration was established by NOE experiments (*Scheme 5*). These spectra suggested a chair conformation for the pyrane ring, with the benzoyloxy group in the axial position, and both the Me and the BuO groups in the equatorial position. At the same time, this structure also suggests that the hydrogenation took place on the *anti*-face of the heterocycle with respect to the BuO group.

Scheme 5



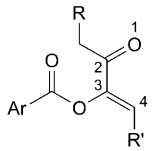
8c Ar = 4-$MeOC_6H_4$ **11c** Ar = 4-$MeOC_6H_4$ **14** Ar = 4-$MeOC_6H_4$

11c

2.5. *Evaluation of the Reactivity and Selectivity of the Hetero*-Diels–Alder *Cycloadditions by Calculation of FMO Energies and Coefficients, and DFT Calculations of Transition States.* The reactivity and regioselectivity of alkenyl esters **1** as dienophiles in *Diels–Alder* cycloadditions has been accounted for satisfactorily by the FMO theory [8a]. Therefore, this model should also be useful to correlate the energies and coefficients of the frontier molecular orbitals of heterodienes **1** and **3a**, with those of dienophiles **6a**,**b** and **9** [13]. Frontier orbitals of heterodienes **1a**–**1c** were obtained from *ab initio* HF/6-31G(d) calculations [14]. The structures of these alkenyl esters were fully optimized at the same level of theory, showing that the most stable geometry for all of them corresponded to the nonplanar conformation of the aroyloxy group with respect to the enone moiety, and to the s-*trans* conformation of the latter. However, we chose the geometries with the s-*cis* conformation of the enone moiety because it is expected that these heterodienes react with this conformation. The corresponding MO energies and coefficients are summarized in *Tables 4* and *5*.

As expected [26], the inverse-electron-demand interaction, LUMO-diene/HOMO-dienophile, is largely preferred (about 4 eV or more for all interactions). In the heterodiene, both HOMO and LUMO are stabilized when an electron-withdrawing group (NO_2) is present at the arene ring of the heterodiene, **1a** (*Table 4*), and they are destabilized in the presence of electron-donor groups (MeO), **1c**, with respect to the unsubstituted arene in olefin derivatiave **1b** [26][27]. Therefore, heterodiene **1a** should be more reactive than heterodiene **1b** and still more reactive than **1c**. The β-substituted heterodiene **3a** should be the least reactive because of the largest destabilization of its LUMO. This order of reactivity is in agreement with the experimental findings with both dienophiles **6a** and **6b** (*Tables 1* and *3*). Due to the decomposition and, consequently, to the variation of the concentration of the dienophile in the reaction mixture, particularly in the case of **6a**, it is not possible to establish a clear correlation between the HOMO energies and the reactivity of the three dienophiles used, *i.e.*, **6a**, **6b**, and **9**. However, it is noteworthy that **9** was the least reactive dienophile even though its HOMO was the highest lying, and the energy gap was the smallest. It is likely that the fact that **9** is a disubstituted dienophile plays an additional role in the reactivity.

Table 4. Ab initio *HF/6-31G(d) Calculated Energies* [eV] *of the Frontier Molecular Orbitals of Heterodienes* **1a**–**1c**, **1f**, *and* **3a**, *and Dienophiles* **6a**, **6b**, *and* **9**[a]). Energy gaps [eV] of FMOs for dienes and dienophiles **6a**, **6b**, and **9**.



1a R = R' = H, Ar = 4-$NO_2C_6H_4$
1b R = R' = H, Ar = Ph
1c R = R' = H, Ar = 4-$MeOC_6H_4$
1f R = Me, R' = H, Ar = 4-$NO_2C_6H_4$
3a R = H, R' = Me, Ar = 4-$NO_2C_6H_4$

6a R = Et
6b R = Bu

9

Compound[b])	E_{HOMO}[c])	E_{LUMO}[d])	HOMO – LUMO[e])	LUMO – HOMO[f])	Gap diff[g])
1a	– 10.7222	2.2196	16.2508 (16.3517)	11.2489 (11.4466)	5.0019 (4.9051)
1b	– 10.3619	2.6311	15.8905 (15.9914)	11.6604 (11.8581)	4.2301 (4.1333)
1c	– 10.2765	2.7103	15.8051 (15.9060)	11.7396 (11.9373)	4.0655 (3.9687)
1f	– 10.8596	2.5443	16.3882 (16.4891)	11.5736 (11.7713)	4.8146 (4.7178)
3a	– 10.4041	2.7116	15.9327 (16.0336)	11.7409 (11.9386)	4.1918 (4.0950)
6a	– 9.0293	5.5286			
6b	– 9.2270	5.6295			
9	– 8.7025	5.6257	16.3479[h])	10.9221[i])	5.4258

[a]) Energies of the first FMO with significant coefficient contributions at the enone moiety or at the C=C bond of the dienophiles. [b]) For the most stable nonplanar (between aroyloxy group and enone moiety) s-*cis* conformation of the dienes. [c]) Energies of the 2 NHOMO of dienes **1a**–**1f** and **3a**, and of the HOMO of dienophiles **6a**, **6b**, and **9**. [d]) Energies of the NLUMOs of derivatives **1a**–**1f** and **3a**, and of the LUMO of dienophiles **6a**, **6b**, and **9**. [e]) HOMO-diene/LUMO-dienophile **1a**–**1f** and **3a**/**6a**; in parentheses HOMO-diene/LUMO-dienophile **1a**–**1f** and **3a**/**6b**. [f]) LUMO-diene/HOMO-dienophile **1a**–**1f** and **3a**/**6a**; in parentheses LUMO-diene/HOMO-dienophile **1a**–**1f** and **3a**/**6b**. [g]) **1a**–**1f** and **3a**/**6a**; in parentheses **1a**–**1f** and **3a**/**6b**. [h]) HOMO-diene/LUMO-dienophile **1a**/**9**. [i]) LUMO-diene/HOMO-dienophile **1a**/**9**.

The observed regioselectivity is also anticipated from the analysis of the coefficients (*Table 5*). In terms of FMO theory, the strongest interaction of the reactants will correspond to the approach of the atoms with the largest coefficients of the LUMO-diene (C(4)) and the HOMO-dienophile (C(2)), which in our case leads to the C(2) orientation (*ortho*), in agreement with the experimental results.

In spite of the fact that the FMO model accounts for the correct reactivity and regioselectivity, it is based on the analysis of the properties of the ground-state of the reactants and not of the transition state (TS), the energy of which is directly related to reactivity and selectivity under conditions of kinetic control. For this reason, we carried out the theoretical determination of the TSs of the cycloadditions between heterodienes **1a** and **3a** and dienophile **6a** at the HF/3-21G and HF/6-31G(d,p) *ab initio*, and B3LYP/6-31G(d,p) DFT levels of theory. We considered several relative geometries for the approach of the cycloaddends, namely the *ortho*/*meta* and *endo*/*exo* orientations. In addition, two more conformational variations were taken into account. First, due to the

Table 5. Ab initio *HF/6-31G(d)* p_z *Coefficients* (C_i) *of the Frontier Molecular Orbitals of Heterodienes* **1a**–**1c**, **1f**, *and* **3a**, *and of Dienophiles* **6a**, **6b**, *and* **9**[a])[b])

	HOMO[c])				LUMO[d])			
	C(1)	C(2)	C(3)	C(4)	C(1)	C(2)	C(3)	C(4)
1a	– 0.1932	– 0.0342	0.3123	0.2969	0.2525	– 0.2859	– 0.2105	0.2890
1b	– 0.2246	– 0.0369	0.3580	0.3435	0.2627	– 0.3009	– 0.2140	0.2914
1c	– 0.2241	– 0.0362	0.3587	0.3460	0.2570	– 0.2951	– 0.2091	0.2835
1f	– 0.1916	– 0.0353	0.3498	0.3293	0.2618	– 0.2876	– 0.2300	0.2945
3a	– 0.1969	– 0.0256	0.3679	0.3150	0.2460	– 0.2764	– 0.1999	0.2983
6a	0.2998	0.3808			0.3753	– 0.3053		
6b	0.3002	0.3856			0.4092	– 0.3161		
9	0.2899	0.3689			0.3881	– 0.3091		

[a]) Coefficients of the FMOs of the most stable nonplanar s-*cis* conformation for the heterodienes. Only the p_z coefficients are shown; the $p_{z'}$ coefficients follow a similar trend. [b]) For formulae, see *Table 4* (arbitrary atom numbering). [c]) Coefficients of the 2 NHOMO of dienes **1a**–**1f** and **3a**, and of HOMO of dienophiles **6a**, **6b**, and **9**. [d]) Coefficients of the NLUMOs of derivatives **1a**–**1f** and **3a**, and of the LUMO of dienophiles **6a**, **6b**, and **9**.

fact that in captodative olefin derivatiaves **1a** and **3a** the (4-nitrobenzoyl)oxy group is perpendicular to the enone moiety, **6a** can approach to the enone fragment from the side of the O-atom of the ester carbonyl group, or from the opposite side ('*syn*'/'*anti*', resp.; *vide infra*). Second, the conformation of the alkoxy group in the dienophile can be either s-*cis* or s-*trans* with respect to the C=C bond; so, the search for transition states also considered these geometrical possibilities. The geometry of the heterodiene was kept in the s-*cis* conformation, in accordance with a concerted transition state. The results corresponding to the first cycloaddition (**1a**/**6a**, data not shown) support the FMO prediction (*vide supra*); the *meta* adducts and transition states are less stable than the corresponding *ortho* geometries for at least 10 kcal/mol. Concerning the second cycloaddition, **3a**/**6a**, the results followed a similar trend; thus *Table 6* and *Fig. 3* summarize the relative energies and geometries of the *ortho* TSs for this system.

The geometries of all the calculated TSs shown in *Fig. 3*, as well as the normal modes corresponding to the associated imaginary vibrational frequencies, support the idea of a concerted asynchronous cycloaddition process. In all cases, the incipient bond forming between C(β) of the enol ether and C(β) of the captodative olefin is shorter than the bond forming between C(α) of **6a** and the carbonyl O-atom of **3a**. A higher degree of C–C bond-formation in the TS can be anticipated from the polarization of the π-systems in both heterodiene and dienophile, evidenced by the FMO data shown in *Table 5*, where the C(4) of the former is the most electrophilic center and C(2) of the latter is the most nucleophilic center. In both *endo* and *exo* approaches, the TSs in which **6a** adopts the s-*trans* conformation are more stable than the corresponding TSs with the s-*cis* conformation by more than 4 kcal/mol. This difference can be attributed essentially to the energy difference between the s-*cis* and s-*trans* conformations of the enol ether. Comparison between the '*syn*' and '*anti*' TSs shows that the former series is the most stable, suggesting the possibility of a stabilizing interaction between the O-atom of the carbonyl group in the heterodiene, and the H–C(β) of the C=C bond of

Table 6. Ab initio *HF/6-31G(d,p) and DFT [B3LYP/6-31G(d,p)] Relative Energies Including ZPE Corrections* (ΔE_0, [kcal/mol]) *of the TSs for the Cycloaddition of Heterodiene* **3a** *to Dienophile* **6a** *at Eight Different Geometries*[a])

Transition state	Geometry	HF/6-31G(d,p)	B3LYP/6-31G(d,p)
TS-7g-1	'*ortho-endo-syn*-s-*cis*'	6.07	5.43
TS-7g-2	'*ortho-endo-syn*-s-*trans*'	1.94	1.16
TS-7g-3	'*ortho-exo-syn*-s-*cis*'	5.40	4.71
TS-7g-4	'*ortho-exo-syn*-s-*trans*'	0.00	0.00
TS-7g-5	'*ortho-endo-anti*-s-*cis*'	8.38	7.18
TS-7g-6	'*ortho-endo-anti*-s-*trans*'	2.80	1.79
TS-7g-7	'*ortho-exo-anti*-s-*cis*'	7.74	6.34
TS-7g-8	'*ortho-exo-anti*-s-*trans*'	2.23	1.61

[a]) The '*syn*' geometry corresponds to the approach of **6a** to the heterodiene from the same side as that of the CO group of the C(3) aroyloxy group; the '*anti*' geometry corresponds to the approach from the opposite side. The *endo* and *exo* approaches correspond to the orientation of the ethoxy group in the dienophile '*in*' or '*out*' with respect to the heterodiene moiety. The s-*cis* and s-*trans* conformations of the Et–O bond of the ethoxy group of the dienophile are with respect to the C=C bond.

the dienophile '*syn*' to the heterodiene. The distance between these two atoms ranges from 2.47 to 2.73 Å, which is suitable for H-bonding. In addition, all the *exo* TSs are more stable than the corresponding *endo* geometries. It is likely that the *exo* preference is the result of steric repulsion between the EtO group of the dienophile and the Me group at C(2) of the heterodiene in the *endo* TSs (*Fig. 3*). This hypothesis seems to be supported by the fact that the length of the forming C–O bond is slightly shorter in all *exo* TSs, with respect to the corresponding *endo* geometries. Even though we were unable to establish unambiguously the structure of the major stereoisomer of the reaction between **3a** and **6a**; it is likely that, in accordance with our calculations, the *trans*-isomer of **7g** is the major adduct.

3. Conclusions. – Captodative olefin derivatives **1a**–**1f** have proved to be efficient heterodienes in *Diels–Alder* cycloadditions under inverse electron-demand conditions. The reaction with the alkyl vinyl ethers **6a** and **6b** furnished the corresponding dihydro-2*H*-pyrans **7** and **8** as a single regioisomer. The reactivity of these processes depends, to a large extent, on the inductive effect (*I*) of the substituent in the aroyloxy group in the heterodiene. Thus, the presence of a nitro group in **1a** enhances the reactivity, being more reactive than heterodiene **1b** with the unsubstituted benzoyloxy group, and still more reactive than **1c**, which has an electron-releasing MeO group at the aroyloxy moiety. The X-ray diffraction analysis of adduct **7a** showed the conformational preference of the EtO group in the solid state to be equatorial. ^{1}H-NMR Measurements and theoretical calculations indicate that this preference is probably due to a molecular-packing effect in the crystal lattice, since the axial conformation turned out to be more stable in solution and in the gas phase. Compound **3a** was found to be the least reactive heterodiene, due to the presence of the Me substituent at the β-position, which increases the electron density at the conjugate π-system. Upon high pressure

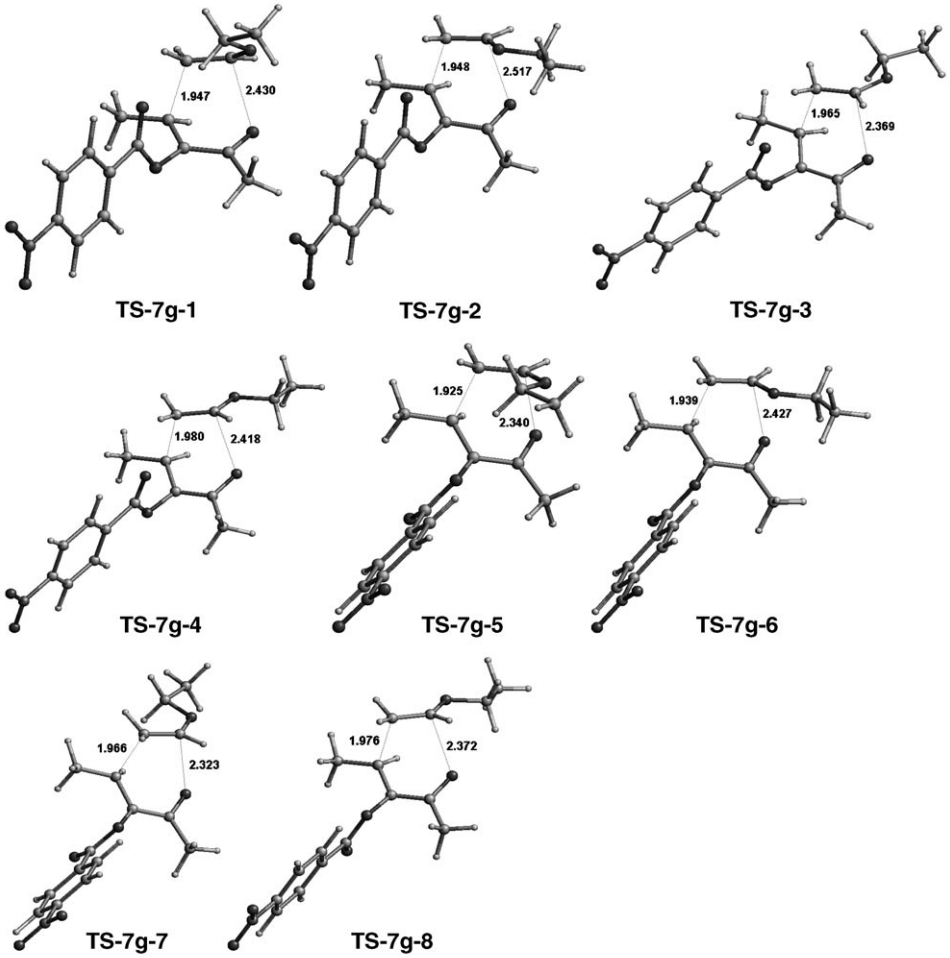


Fig. 3. *Calculated geometries [B3LYP/6-31G(d,p)] of the most stable transition states for the cycloaddition of heterodiene* **3a** *and dienophile* **6a**

hydrogenation, adduct **8c** was transformed stereoselectively into tetrahydro-2*H*-pyran **11c**.

The reactivity and regioselectivity of these reactions were rationalized by the FMO theory; the effects of heterodiene substitution were described fairly well by a correlation with the LUMO energies, showing a reduction of the latter with a stronger electron-withdrawing effect of the substituent of the aroyloxy group, which increased the reactivity. The observed *ortho* regiochemistry of the cycloaddition matched that predicted by the magnitude of the coefficients in both reactants. DFT Calculations of the TSs supported the FMO predictions about regioselectivity, and showed that, for heterodiene **3a**, the *exo* approach for the cycloaddition with dienophile **6a** is energetically favored.

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Experimental Part

General. All air-moisture-sensitive reactions were carried out under N_2 with oven-dried glassware. THF was freshly distilled over Na, and CH_2Cl_2 over CaH_2 prior to use. Et_3N was distilled over NaOH. All other reagents were used without further purification. Microwave irradiation: *SEV/MIC-1* (Puebla, Mexico) microwave reactor [28]. Anal. TLC: silica-gel-*60-F*$_{254}$-coated plates (*E. Merck*), visualized by long- and short-wavelength UV lamps. Column chromatography (CC): silica gel (230–400 mesh; *Natland International Co.*). M.p.: uncorrected; *Electrothermal* capillary melting-point apparatus. IR Spectra: *Perkin-Elmer 1600* spectrophotometer; in cm^{-1} (only strong bands are reported). ^{1}H-(300 MHz) and ^{13}C-NMR (75.4 MHz) Spectra: *Varian Mercury-300* instrument; in $CDCl_3$ as solvent with Me_4Si as internal standard; δ in ppm, *J* in Hz. MS: *Hewlett-Packard 5971A* spectrometer for EI mode (70 eV); *Jeol JMS-AX-505-HA* spectrometer for HR in the FAB mode (*m*NBA), in *m*/*z* (rel %). X-Ray analysis: *Siemens P4* diffractometer. Microanalyses: *M-H-W Laboratories* (Phoenix, AZ), and Centro de Investigaciones Químicas, Universidad Autónoma de Hidalgo (Pachuca, Hgo., Mexico).

Alkenyl Esters **1a**–**1f** *and* **3a**: *General Procedure 1 (G.P. 1)*. Under N_2 and vigorous magnetic stirring, a soln. of Et_3N (21.412 g, 0.212 mol) in a mixture of dry THF/hexamethylphosphoric triamide (HMPA) 94:6 (100 ml) was cooled to $-20°$ or $-40°$, and a soln. of the acid chloride **5** (0.127 mol) in dry THF (80 ml) was added dropwise. At the same temp., a soln. of dione **4** (0.106 mol) in dry THF (15 ml) was slowly added, and the temp. was allowed to increase up to r.t. The mixture was stirred for 24–36 h, the solvent evaporated, and the residue diluted with cold CH_2Cl_2 (100 ml). Then, the org. soln. was successively washed with cold 5% aq. HCl soln. (3 × 25 ml), cold sat. aq. $NaHCO_3$ soln. (3 × 25 ml), and cold sat. NaCl soln. (3 × 30 ml), dried (Na_2SO_4), and concentrated. The residue was successively purified by CC (SiO_2 conditioned with Et_3N (10%) in hexane (30 g/1 g of crude), hexane/AcOEt 90:10). The solid product was dried and recrystallized from hexane/AcOEt or hexane/CH_2Cl_2. Spectroscopic data of compounds **1a**, **1b**, **1d**, and **1e** agreed with those previously described [10b][12][14].

4-Methoxybenzoic Acid 1-Methylene-2-oxopropyl Ester (**1c**). According to the *G.P. 1*, at $-40°$ with **4a** (9.116 g), **5c** (21.65 g), and stirring for 24 h: 14.44 g (62%) of **1c** (with hexane/CH_2Cl_2 9:1). White powder. R_f 0.43 (hexane/AcOEt 7:3). M.p. 56–57°. IR (CH_2Cl_2): 1729, 1696, 1605, 1511, 1253, 1124, 1081, 1025, 847, 764. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.40 (*s*, MeCO); 3.88 (*s*, MeO); 5.71 (*d*, *J* = 2.1, 1 H, CH_2=); 6.02 (*d*, *J* = 2.1, 1 H, CH_2=); 6.91–6.98 (*m*, 2 arom. H); 8.02–8.10 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 25.6 (*Me*CO); 55.5 (MeO); 113.7 (CH_2=); 113.8 (2 arom. C); 120.8 (arom. C_{ipso}); 132.4 (2 arom. C); 151.8 (C(1)); 164.0 (arom. *C*–OMe); 164.3 (Ar*C*O_2); 192.0 (Me*C*O). EI-MS (70 eV): 220 (1, M^+), 135 (100), 107 (8), 92 (15), 77 (13), 64 (5). Anal. calc. for $C_{12}H_{12}O_4$: C 65.45, H 5.49; found: C 65.23, H 5.29.

4-Nitrobenzoic Acid 1-Methylene-2-oxobutyl Ester (**1f**) *and 4-Nitrobenzoic Acid (1Z)-1-Acetylprop-1-en-1-yl Ester* (**3a**). According to the *G.P. 1*, at $-20°$ with, **4b** (10.6 g), **5a** (23.55 g), and stirring for 24 h: 14.86 g (56%) of **1f** (with hexane/AcOEt 9:1) as a white powder and 11.07 g (42%) of **3a** (with hexane/AcOEt 85:15) as a white powder.

Data of **1f**: R_f 0.57 (hexane/AcOEt 7:3). M.p. 60–62°. IR (CH_2Cl_2): 1743, 1698, 1529, 1349, 1272, 1246, 1093, 717. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.18 (*t*, *J* = 7.1, *Me*CH_2CO); 2.80 (*q*, *J* = 7.1, MeCH_2CO); 5.82 (*d*, *J* = 3.0, 1 H, CH_2=); 6.10 (*d*, *J* = 3.0, 1 H, CH_2=); 8.27–8.36 (*m*, 4 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 7.8 (C(4)); 30.9 (C(3)); 113.9 (*C*H_2=C(1)); 123.7 (2 arom. C); 131.3 (2 arom. C); 134.1 (C_{ipso}); 151.0 (arom. C–NO_2); 151.3 (C(1)); 162.8 (Ar*C*O_2); 194.0 (C(2)). EI-MS (70 eV): 249 (1, M^+), 220 (1), 150 (100), 120 (5), 104 (18), 92 (8), 76 (14). HR-FAB-MS: 250.0731 (M^+, $C_{12}H_{12}NO_5^+$; calc. 250.0715).

Data of **3a**: R_f 0.57 (hexane/AcOEt 7:3). M.p. 103–104° ([12]: 104–106°). IR (CH_2Cl_2): 1742, 1687, 1528, 1349, 1260, 1095, 715. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.40 (*s*, MeCO); 1.89 (*d*, *J* = 7.2, *Me*CH=); 6.73 (*q*, *J* = 7.2, MeC*H*=); 8.30–8.37 (*m*, 4 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 12.0 (C(3)); 25.1 (*Me*CO); 123.7 (2 arom. C); 131.4 (2 arom. C); 134.2 (arom. C_{ipso}); 147.1 (C(1)); 150.9 (arom. C–NO_2); 162.4 (Ar*C*O_2); 190.4 (Me*C*O). EI-MS (70 eV): 249 (1, M^+), 150 (100), 134 (2), 120 (6), 104 (37), 92 (8), 76 (13).

Adducts **7a**–**7g**: *General Procedure 2 (G.P. 2)*. Under N_2 and vigorous magnetic stirring, a mixture of the alkenyl ester **1a**–**1g** or **3a** (1.0 g), ether **6a** (20 mol-equiv), and hydroquinone (20 mg), was placed in a threaded *ACE-Glass* pressure tube with a sealed *Teflon* screw cap, and kept in the dark. The mixture was heated to 115° for 9–50 d. The excess of **6a** was removed under vacuum, and the crude was purified by CC (SiO_2 conditioned with Et_3N (10%) in hexane (30 g/1 g of crude), hexane/AcOEt 90:10): corresponding adducts **7a**–**7g**.

*2-Ethoxy-3,4-dihydro-6-methyl-2*H*-pyran-5-yl 4-Nitrobenzoate* (**7a**). According to the *G. P. 2*, with **1a** (4.26 mmol), **6a** 6.13 g, 0.085 mol), and heating for 10 d: 1.0 g (76%) of **7a** (with hexane/AcOEt 95:5). Yellow crystalline solid. R_f 0.60 (hexane/AcOEt 7:3). M.p. 87–89°. IR (CH_2Cl_2): 1737, 1529, 1349, 1271, 1169, 1130, 1053, 1013, 863, 718. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.22 (*t*, *J* = 7.0, *Me*CH_2O); 1.72 (*dd*, *J* = 3.3, 2.1, Me–C(6)); 1.94–2.02 (*m*, 2 H–C(3)); 2.16–2.28 (*m*, 1 H–C(4)); 2.37–2.51 (*m*, 1 H–C(4)); 3.60 (*dq*, *J* = 9.7, 7.0, 1 H, MeCH_2O); 3.85 (*dq*, *J* = 9.7, 7.0, 1 H, MeCH_2O); 5.00–5.05 (*m*, H–C(2)); 8.22–8.32 (*m*, 4 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 14.1 (*Me*–C(6)); 15.1 (*Me*CH_2O); 20.0 (C(4)); 26.9 (C(3)); 63.9 (Me*C*H_2O); 96.6 (C(2)); 123.6 (2 arom. C); 126.8 (C(5)); 131.0 (2 arom. C); 135.1 (arom. C); 140.0 (C(6)); 150.6 (arom. C); 163.2 (Ar*C*O_2). EI-MS (70 eV): 307 (14, M^+), 262 (15), 157 (83), 150 (68), 111 (28), 104 (37), 72 (96), 43 (100). HR-FAB-MS: 307.1067 (M^+, $C_{15}H_{17}NO_6^+$; calc. 307.1056).

*2-Ethoxy-3,4-dihydro-6-methyl-2*H*-pyran-5-yl Benzoate* (**7b**). According to the *G. P. 2*, with **1b** (5.26 mmol), **6a** (7.58 g, 0.105 mol), and heating for 11 d: 0.634 g (46%) of **7b**. Colorless oil. R_f 0.74 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 1730, 1448, 1373, 1264, 1168, 1117, 1054, 972, 923, 858, 710. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.26 (*t*, *J* = 6.6, *Me*CH_2O); 1.75 (br. *s*, Me–C(6)); 1.94–2.06 (*m*, 2 H–C(3)); 2.21–2.33 (*m*, 1 H–C(4)); 2.37–2.52 (*m*, 1 H–C(4)); 3.50–3.70 (*m*, 1 H, MeCH_2O); 3.80–3.96 (*m*, 1 H, MeCH_2O); 5.01–5.07 (*m*, H–C(2)); 7.42–7.51 (*m*, 2 arom. H); 7.55–7.64 (*m*, 1 arom. H); 8.06–8.14 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 14.1 (*Me*–C(6)); 15.2 (*Me*CH_2O); 20.2 (C(4)); 27.0 (C(3)); 63.8 (Me*C*H_2O); 96.7 (C(2)); 126.7 (C(5)); 128.4 (2 arom. C); 129.7 (arom. C); 129.9 (2 arom. C); 133.2 (arom. C); 139.7 (C(6)); 165.1 (Ar*C*O_2). EI-MS (70 eV): 262 (5, M^+), 217 (4), 157 (8), 105 (100), 77 (22). HR-FAB-MS: 262.1191 (M^+, $C_{15}H_{18}O_4^+$; calc. 262.1205).

*2-Ethoxy-3,4-dihydro-6-methyl-2*H*-pyran-5-yl 4-Methoxybenzoate* (**7c**). According to the *G. P. 2*, with **1c** (4.54 mmol), **6a** (6.54 g, 0.091 mol), and heating for 30 d: 0.64 g (48%) of **7c**. Colorless oil. R_f 0.66 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 1723, 1605, 1510, 1258, 1165, 1128, 1051, 1018, 972, 852, 767. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.15 (*t*, *J* = 7.2, *Me*CH_2O); 1.64 (br. *s*, Me–C(6)); 1.84–1.96 (*m*, 2 H–C(3)); 2.10–2.22 (*m*, 1 H–C(4)); 2.28–2.41 (*m*, 1 H–C(4)); 3.52 (*dq*, *J* = 9.7, 7.2, 1 H, MeCH_2O); 3.75 (*s*, MeO); 3.79 (*dq*, *J* = 9.7, 7.0, 1 H, MeCH_2O); 4.92–4.96 (*m*, H–C(2)); 6.80–6.86 (*m*, 2 arom. H); 7.93–8.00 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 14.1 (*Me*–C(6)); 15.1 (*Me*CH_2O); 20.3 (C(4)); 27.0 (C(3)); 55.4 (MeO); 63.8 (Me*C*H_2O); 96.7 (C(2)); 113.7 (2 arom. C); 122.1 (arom. C); 126.6 (C(5)); 131.9 (2 arom. C); 139.6 (C(6)); 163.6 (arom. C or Ar*C*O_2); 164.8 (Ar*C*O_2 or arom. C). EI-MS (70 eV): 292 (4, M^+), 247 (3), 135 (100), 107 (5), 92 (12), 77 (13). HR-FAB-MS: 292.1304 (M^+, $C_{16}H_{20}O_5^+$; calc. 292.1311).

*2-Ethoxy-3,4-dihydro-6-methyl-2*H*-pyran-5-yl 4-Methylbenzoate* (**7d**). According to the *G. P. 2*, with **1d** (4.9 mmol), **6a** (7.06 g, 0.098 mol), and heating for 35 d: 0.797 g (59%) of **7d**. Colorless oil. R_f 0.76 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 1713, 1528, 1375, 1350, 1270, 1130, 1052, 1015, 857, 749, 718. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.21 (*t*, *J* = 6.9, *Me*CH_2O); 1.74 (*t*, *J* = 1.8, Me–C(6)); 1.97–2.04 (*m*, 2 H–C(3)); 2.22–2.32 (*m*, 1 H–C(4)); 2.38–2.50 (*m*, 1 H–C(4)); 2.42 (*s*, *Me*C_6H_4); 3.61 (*dq*, *J* = 9.6, 7.1, 1 H, MeCH_2O); 3.89 (*dq*, *J* = 9.6, 7.1, 1 H, MeCH_2O); 5.04 (*t*, *J* = 3.3, H–C(2)); 7.22–7.29 (*m*, 2 arom. H); 7.97–8.02 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 14.0 (*Me*–C(6)); 15.1 (*Me*CH_2O); 20.2 (C(4)); 21.6 (*Me*C_6H_4); 26.9 (C(3)); 63.8 (Me*C*H_2O); 96.7 (C(2)); 126.6 (C(5)); 129.1 (2 arom. C); 129.9 (2 arom.

C); 139.6 (C(6)); 143.9 (arom. C); 151.6 (arom. C); 165.1 (Ar*C*O_2). EI-MS (70 eV): 276 (5, M^+), 231 (3), 157 (2), 119 (100), 91 (29), 65 (14). HR-FAB-MS: 276.1370 (M^+, $C_{18}H_{24}O_4^+$; calc. 276.1362).

*2-Ethoxy-3,4-dihydro-6-methyl-2*H*-pyran-5-yl 4-Chlorobenzoate* (**7e**). According to the *G. P. 2*, with **1e** (4.45 mmol), **6a** (6.41 g, 0.089 mol), and heating for 47 d: 0.75 g (57%) of **7e**. Colorless oil. R_f 0.75 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 1730, 1593, 1528, 1484, 1441, 1372, 1265, 1167, 1125, 1048, 1009, 971, 927, 852, 755. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.26 (*t*, *J* = 7.2, *Me*CH_2O); 1.74 (*t*, *J* = 1.9, Me–C(6)); 1.97–2.05 (*m*, 2 H–C(3)); 2.20–2.32 (*m*, 1 H–C(4)); 2.38–2.52 (*m*, 1 H–C(4)); 3.64 (*dq*, *J* = 9.6, 7.2, 1 H, MeC*H*$_2$O); 3.87 (*dq*, *J* = 9.6, 7.2, 1 H, MeC*H*$_2$O); 5.03–5.07 (*m*, H–C(2)); 7.41–7.47 (*m*, 2 arom. H); 8.01–8.07 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 14.0 (*Me*–C(6)); 15.4 (*Me*CH_2O); 20.1 (C(4)); 26.9 (C(3)); 67.8 (Me*C*H_2O); 96.6 (C(2)); 126.7 (C(5)); 128.1 (2 arom. C); 128.7 (2 arom. C); 131.2 (2 arom. C); 139.6 (C(6) or arom. C); 139.7 (arom. C or C(6)); 164.2 (Ar*C*O_2). EI-MS (70 eV): 298 (2, $[M+2]^+$), 296 (5, M^+), 251 (3), 157 (13), 141 (32), 139 (100), 113 (28), 111 (7), 72 (18). HR-FAB-MS: 296.0816 (M^+, $C_{15}H_{17}ClO_4^+$; calc. 296.0815).

*2-Ethoxy-6-ethyl-3,4-dihydro-2*H*-pyran-5-yl 4-Nitrobenzoate* (**7f**). According to the *G. P. 2*, with **1f** (4.02 mmol), **6a** (5.78 g, 0.08 mol), and heating for 9 d: 1.146 g (89%) of **7f**. Yellow oil. R_f 0.71 (hexane/AcOEt 8:2). IR (CH_2Cl_2): 1736, 1529, 1348, 1269, 1165, 1124, 1047, 718. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.05 (*t*, *J* = 7.4, *Me*CH_2–C(6)); 1.27 (*t*, *J* = 7.2, *Me*CH_2O); 1.97–2.06 (*m*, 2 H–C(3)); 2.06–2.20 (*m*, MeC*H*$_2$–C(6)); 2.20–2.32 (*m*, 1 H–C(4)); 2.43–2.56 (*m*, 1 H–C(4)); 3.64 (*dq*, *J* = 9.6, 7.2, 1 H, MeC*H*$_2$O); 3.91 (*dq*, *J* = 9.6, 7.2, 1 H, MeC*H*$_2$O); 5.07 (*t*, *J* = 3.2, H–C(2)); 8.26–8.36 (*m*, 4 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 11.3 (*Me*CH_2–C(6)); 15.1 (*Me*CH_2O); 19.9 (C(4)); 21.5 (Me*C*H_2–C(6)); 26.8 (C(3)); 63.7 (Me*C*H_2O); 96.4 (C(2)); 123.6 (2 arom. C); 126.0 (C(5)); 131.0 (2 arom. C); 135.2 (arom. C); 144.4 (C(6)); 150.6 (arom. C); 163.3 (Ar*C*O_2). EI-MS (70 eV): 321 (18, M^+), 276 (15), 275 (11), 246 (2), 171 (84), 150 (75), 125 (28), 104 (50), 92 (17), 72 (60), 57 (100). HR-FAB-MS: 321.1220 (M^+, $C_{16}H_{19}NO_6^+$; calc. 321.1212).

*2-Ethoxy-3,4-dihydro-4,6-dimethyl-2*H*-pyran-5-yl 4-Nitrobenzoate* (**7g**). According to the *G. P. 2*, with **1g** (4.02 mmol), **6a** (5.78 g, 0.08 mol), and heating for 50 d: 0.35 g (27%) of **7g**, 78:22 mixture of epimers. Yellow powder. R_f 0.69 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 1736, 1604, 1529, 1502, 1445, 1376, 1347, 1268, 1213, 1127, 1048, 943, 868, 843, 718. ^{1}H-NMR (300 MHz, $CDCl_3$): major epimer: 1.08 (*d*, *J* = 6.9, Me–C(4)); 1.27 (*t*, *J* = 7.0, *Me*CH_2O); 1.69–1.81 (*m*, 1 H–C(3)); 1.75 (*d*, *J* = 3.8, Me–C(6)); 2.19 (*ddd*, *J* = 13.5, 6.9, 2.2, 1 H–C(3)); 2.77–2.92 (*m*, H–C(4)); 3.56–3.69 (*m*, 1 H, MeC*H*$_2$O); 3.85–4.01 (*m*, 1 H, MeC*H*$_2$O); 5.06 (*dd*, *J* = 7.7, 2.2, H–C(2)); 8.26–8.36 (*m*, 4 arom. H); selected signals of the minor epimer: 1.02 (*d*, *J* = 6.9, Me–C(4)); 1.26 (*t*, *J* = 7.0, *Me*CH_2O); 1.72 (*d*, *J* = 2.2, Me–C(6)); 2.10 (*ddd*, *J* = 13.2, 6.3, 3.8, H–C(3)); 5.03 (*dd*, *J* = 3.8, 2.4, H–C(2)). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 14.3 (*Me*–C(6)); 15.2 (*Me*CH_2O); 17.8 (*Me*–C(4)); 27.8 (C(4)); 36.4 (C(3)); 64.9 (Me*C*H_2O); 98.6 (C(2)); 123.7 (2 arom. C); 130.6 (C(5)); 131.0 (2 arom. C); 135.0 (arom. C); 140.5 (C(6)); 150.7 (arom. C); 163.2 (Ar*C*O_2); selected signals of the minor epimer: 17.5 (*Me*–C(4)); 25.3 (C(4)); 35.7 (C(3)); 63.9 (Me*C*H_2O); 96.2 (C(2)). EI-MS (70 eV): 321 (9, M^+), 276 (11), 275 (18), 171 (60), 150 (100), 125 (17), 104 (36), 72 (91). HR-FAB-MS: 321.1202 (M^+, $C_{16}H_{19}NO_6^+$; calc. 321.1212).

Adducts **8a**–**8g**: *General Procedure 3 (G. P. 3)*. Under N_2 and vigorous magnetic stirring, a mixture of alkenyl ester **1a**–**1g** or **3a** (1.0 g), ether **6b** (20 mol-equiv), and hydroquinone (20 mg), was placed in a threaded *ACE–Glass* pressure tube with a sealed *Teflon* screw cap, and kept in the dark. The mixture was heated to 130° for 3–17 d. The excess of **6b** was removed under vacuum, and the crude was purified by CC (SiO_2 conditioned with Et_3N (10%) in hexane (30 g/1 g of crude), hexane/AcOEt 95:5): corresponding adducts **8a**–**8g**.

*2-Butoxy-3,4-dihydro-6-methyl-2*H*-pyran-5-yl 4-Nitrobenzoate* (**8a**). According to the *G. P. 3*, with **1a** (4.25 mmol), **6b** (8.51 g, 0.085 mol), and heating for 3 d: 0.927 g (65%) of **8a**. Yellow oil. R_f 0.75 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 2929, 2868, 1735, 1605, 1528, 1448, 1347, 1266, 1164, 1114, 1054, 1010, 928, 858, 715. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.94 (*t*, *J* = 7.5, *Me*$(CH_2)_3O$); 1.35–1.48 (*m*, MeC*H*$_2$-$(CH_2)_2O$); 1.56–1.68 (*m*, $MeCH_2CH_2CH_2O$); 1.73–1.78 (*m*, Me–C(6)); 1.97–2.06 (*m*, 2 H–C(3)); 2.18–2.30 (*m*, 1 H–C(4)); 2.42–2.57 (*m*, 1 H–C(4)); 3.56 (*dt*, *J* = 9.8, 6.4, 1 H, Me$(CH_2)_2$C*H*$_2O$); 3.83 (*dt*, *J* = 9.8, 6.4, 1 H, Me$(CH_2)_2$C*H*$_2O$); 5.04 (*t*, *J* = 3.0, H–C(2)); 8.18–8.40 (*m*, 4 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 13.8 (*Me*$(CH_2)_3O$); 14.1 (*Me*–C(6)); 19.1 (Me*C*$H_2(CH_2)_2O$); 19.9 (C(4)); 26.8 (C(3)); 31.6 ($MeCH_2CH_2CH_2O$); 68.1 (Me$(CH_2)_2$*C*H_2O); 96.7 (C(2)); 123.5 (2 arom. C); 126.9 (C(5));

130.9 (2 arom. C); 135.1 (arom. C); 139.9 (C(6)); 150.6 (arom. C); 163.1 (Ar*C*O$_2$). EI-MS (70 eV): 335 (11, M^+), 262 (16), 185 (51), 150 (100), 129 (18), 111 (50), 104 (51), 100 (31), 85 (53), 76 (36), 57 (73). HR-FAB-MS: 335.1376 (M^+, $C_{17}H_{21}NO_6^+$; calc. 335.1369).

*2-Butoxy-3,4-dihydro-6-methyl-2*H*-pyran-5-yl Benzoate* (**8b**). According to the *G. P. 3*, with **1b** (5.26 mmol), **6b** (10.53 g, 0.105 mol), and heating for 3 d: 1.297 g (85%) of **8b**. Colorless oil. R_f 0.81 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 2929, 1730, 1597, 1500, 1450, 1370, 1264, 1166, 1126, 1055, 1013, 926, 857. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.93 (*t*, *J* = 7.5, *Me*(CH$_2$)$_3$O); 1.31–1.45 (*m*, MeC*H*$_2$(CH$_2$)$_2$O); 1.52–1.65 (*m*, MeCH$_2$C*H*$_2$CH$_2$O); 1.70–1.76 (*m*, Me–C(6)); 1.92–2.04 (*m*, 2 H–C(3)); 2.17–2.31 (*m*, 1 H–C(4)); 2.37–2.52 (*m*, 1 H–C(4)); 3.54 (*dt*, *J* = 9.7, 6.4, 1 H, Me(CH$_2$)$_2$C*H*$_2$O); 3.82 (*dt*, *J* = 9.7, 6.4, 1 H, Me(CH$_2$)$_2$C*H*$_2$O); 5.02 (*t*, *J* = 3.3, H–C(2)); 7.40–7.50 (*m*, 2 arom. H); 7.54–7.62 (*m*, 1 arom. H); 8.06–8.13 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 13.8 (*Me*(CH$_2$)$_3$O); 14.0 (*Me*–C(6)); 19.2 (MeCH$_2$(CH$_2$)$_2$O); 20.1 (C(4)); 26.9 (C(3)); 31.7 (MeCH$_2$*C*H$_2$CH$_2$O); 68.1 (Me(CH$_2$)$_2$*C*H$_2$O); 96.8 (C(2)); 126.7 (C(5)); 128.4 (2 arom. C); 129.8 (arom. C); 129.9 (2 arom. C); 133.2 (arom. C); 139.6 (C(6)); 165.1 (Ar*C*O$_2$). EI-MS (70 eV): 290 (5, M^+), 217 (4), 185 (5), 129 (4), 111 (9), 105 (100), 77 (22), 57 (9). HR-FAB-MS: 290.1532 (M^+, $C_{17}H_{22}O_4^+$; calc. 290.1518).

*2-Butoxy-3,4-dihydro-6-methyl-2*H*-pyran-5-yl 4-Methoxybenzoate* (**8c**). According to the *G. P. 3*, with **1c** (4.54 mmol), **6b** (9.09 g, 0.091 mol), and heating for 4 d: 1.10 g (76%) of **8c**. Colorless oil. R_f 0.68 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 2931, 1725, 1605, 1504, 1458, 1376, 1315, 1257, 1163, 1119, 1061, 1021, 923, 848, 765. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.94 (*t*, *J* = 7.5, *Me*(CH$_2$)$_3$O); 1.33–1.47 (*m*, MeC*H*$_2$-(CH$_2$)$_2$O); 1.50–1.65 (*m*, MeCH$_2$C*H*$_2$CH$_2$O); 1.74 (br. *s*, Me–C(6)); 1.92–2.02 (*m*, 2 H–C(3)); 2.16–2.31 (*m*, 1 H–C(4)); 2.37–2.52 (*m*, 1 H–C(4)); 3.50–3.59 (*m*, 1 H, Me(CH$_2$)$_2$C*H*$_2$O); 3.77–3.86 (*m*, 1 H, Me(CH$_2$)$_2$C*H*$_2$O); 3.85 (*s*, MeO); 4.97–5.03 (*m*, H–C(2)); 6.88–6.97 (*m*, 2 arom. H); 8.01–8.08 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 13.7 (*Me*(CH$_2$)$_3$O); 13.9 (*Me*–C(6)); 19.1 (MeCH$_2$-(CH$_2$)$_2$O); 20.1 (C(4)); 26.9 (C(3)); 31.6 (MeCH$_2$*C*H$_2$CH$_2$O); 55.2 (MeO); 67.9 (Me(CH$_2$)$_2$*C*H$_2$O); 96.7 (C(2)); 113.5 (2 arom. C); 122.0 (arom. C); 126.6 (C(5)); 131.8 (2 arom. C); 139.4 (C(6)); 163.5 (arom. C or Ar*C*O$_2$); 164.6 (Ar*C*O$_2$ or arom. C). EI-MS (70 eV): 320 (3, M^+), 247 (2), 135 (100), 107 (4), 92 (8), 77 (8). HR-FAB-MS: 320.1611 (M^+, $C_{18}H_{24}O_5^+$; calc. 320.1624).

*2-Butoxy-3,4-dihydro-6-methyl-2*H*-pyran-5-yl 4-Methylbenzoate* (**8d**). According to the *G. P. 3*, with **1d** (4.90 mmol), **6b** (9.80 g, 0.098 mol), and heating for 3 d: 0.878 g (59%) of **8d**. Colorless oil. R_f 0.77 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 2930, 1727, 1609, 1503, 1452, 1374, 1267, 1166, 1120, 1062, 1014, 924, 855, 747. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.93 (*t*, *J* = 7.5, *Me*(CH$_2$)$_3$O); 1.29–1.47 (*m*, MeC*H*$_2$(CH$_2$)$_2$O); 1.48–1.64 (*m*, MeCH$_2$C*H*$_2$CH$_2$O); 1.73 (br. *s*, Me–C(6)); 1.93–2.02 (*m*, 2 H–C(3)); 2.17–2.29 (*m*, 1 H–C(4)); 2.37–2.51 (*m*, 1 H–C(4)); 2.40 (*s*, *Me*C$_6$H$_4$); 3.53 (*dt*, *J* = 9.7, 6.7, 1 H, Me(CH$_2$)$_2$C*H*$_2$O); 3.82 (*dt*, *J* = 9.7, 6.7, 1 H, Me(CH$_2$)$_2$C*H*$_2$O); 5.00 (*t*, *J* = 3.3, H–C(2)); 7.20–7.28 (*m*, 2 arom. H); 7.95–8.01 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 13.8 (*Me*(CH$_2$)$_3$O); 14.0 (*Me*–C(6)); 19.2 (MeCH$_2$-(CH$_2$)$_2$O); 20.1 (C(4)); 21.6 (*Me*C$_6$H$_4$); 26.9 (C(3)); 31.6 (MeCH$_2$*C*H$_2$CH$_2$O); 68.0 (Me(CH$_2$)$_2$*C*H$_2$O); 96.8 (C(2)); 126.7 (C(5)); 127.0 (arom. C); 129.1 (2 arom. C); 129.9 (2 arom. C); 139.5 (C(6)); 143.9 (arom. C); 165.1 (Ar*C*O$_2$). EI-MS (70 eV): 304 (3, M^+), 231 (3), 119 (100), 111 (3), 91 (12), 65 (4), 57 (8). HR-FAB-MS: 304.1669 (M^+, $C_{18}H_{24}O_4^+$; calc. 304.1675).

*2-Butoxy-3,4-dihydro-6-methyl-2*H*-pyran-5-yl 4-Chlorobenzoate* (**8e**). According to the *G. P. 3*, with **1e** (4.45 mmol), **6b** (8.91 g, 0.089 mol), and heating for 6 d: 1.16 g (80%) of **8e**. Colorless oil. R_f 0.81 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 2928, 1732, 1593, 1483, 1454, 1367, 1265, 1165, 1122, 1058, 1011, 853, 755. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.94 (*t*, *J* = 7.5, *Me*(CH$_2$)$_3$O); 1.33–1.48 (*m*, MeC*H*$_2$(CH$_2$)$_2$O); 1.52–1.68 (*m*, MeCH$_2$C*H*$_2$CH$_2$O); 1.70–1.76 (*m*, Me–C(6)); 1.94–2.03 (*m*, 2 H–C(3)); 2.17–2.28 (*m*, 1 H–C(4)); 2.37–2.52 (*m*, 1 H–C(4)); 3.55 (*dt*, *J* = 9.6, 6.9, 1 H, Me(CH$_2$)$_2$C*H*$_2$O); 3.82 (*dt*, *J* = 9.6, 6.9, 1 H, Me(CH$_2$)$_2$C*H*$_2$O); 5.02 (*t*, *J* = 3.3, H–C(2)); 7.41–7.48 (*m*, 2 arom. H); 8.00–8.07 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 13.8 (*Me*(CH$_2$)$_3$O); 14.0 (*Me*–C(6)); 19.2 (MeCH$_2$(CH$_2$)$_2$O); 20.0 (C(4)); 26.9 (C(3)); 31.6 (MeCH$_2$*C*H$_2$CH$_2$O); 68.1 (Me(CH$_2$)$_2$*C*H$_2$O); 96.8 (C(2)); 126.7 (C(5)); 128.2 (arom. C); 128.7 (2 arom. C); 131.2 (2 arom. C); 139.7 (C(6) and arom. C); 164.2 (Ar*C*O$_2$). EI-MS (70 eV): 326 (2, $[M + 2]^+$), 324 (5, M^+), 251 (3), 185 (9), 141 (33), 139 (100), 111 (40), 75 (13), 57 (10). HR-FAB-MS: 324.1118 (M^+, $C_{17}H_{21}ClO_4^+$; calc. 324.1128).

*2-Butoxy-6-ethyl-3,4-dihydro-2*H*-pyran-5-yl 4-Nitrobenzoate* (**8f**). According to the *G. P. 3*, with **1f** (4.02 mmol), **6b** (8.03 g, 0.08 mol), and heating for 4 d: 1.135 g (81%) of **8f**. Yellow oil. R_f 0.71 (hexane/

AcOEt 7:3). IR (CH_2Cl_2): 2933, 1735, 1605, 1528, 1458, 1346, 1266, 1161, 1121, 1045, 937, 869, 842, 717. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.95 (*t*, *J* = 7.3, *Me*$(CH_2)_3O$); 1.05 (*t*, *J* = 7.6, *Me*CH_2–C(6)); 1.35–1.49 (*m*, Me*C*$H_2(CH_2)_2O$); 1.56–1.68 (*m*, $MeCH_2CH_2CH_2O$); 1.96–2.06 (*m*, 2 H–C(3)); 2.07–2.18 (*m*, Me*C*H_2–C(6)); 2.18–2.30 (*m*, 1 H–C(4)); 2.44–2.58 (*m*, 1 H–C(4)); 3.55 (*dt*, *J* = 9.6, 6.6, 1 H, $Me(CH_2)_2CH_2O$); 3.84 (*dt*, *J* = 9.6, 6.6, 1 H, $Me(CH_2)_2CH_2O$); 5.02–5.08 (*m*, H–C(2)); 8.22–8.39 (*m*, 4 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 11.4 (*Me*CH_2–C(6)); 13.9 (*Me*$(CH_2)_3O$); 19.3 (Me*C*H_2-$(CH_2)_2O$); 19.9 (C(4)); 21.5 (Me*C*H_2–C(6)); 26.8 (C(3)); 31.7 ($MeCH_2CH_2CH_2O$); 68.0 ($Me(CH_2)_2$-*C*H_2O); 96.6 (C(2)); 123.6 (2 arom. C); 126.1 (C(5)); 131.0 (2 arom. C); 135.2 (arom. C); 144.4 (C(6)); 150.6 (arom. C); 163.4 (Ar*C*O_2). EI-MS (70 eV): 349 (4, M^+), 276 (8), 275 (6), 199 (31), 150 (67), 143 (18), 125 (27), 104 (31), 100 (21), 85 (41), 76 (18), 57 (100). HR-FAB-MS: 349.1522 (M^+, $C_{18}H_{23}NO_6^+$; calc. 349.1525).

*2-Butoxy-3,4-dihydro-4,6-dimethyl-2*H*-pyran-5-yl 4-Nitrobenzoate* (**8g**). According to the *G. P. 3*, with **1g** (4.02 mmol), **6b** (8.03 g, 0.08 mol), and heating for 30 d: 1.05 g (75%) of **8g**, 53:43 mixture of epimers. Yellow oil. R_f 0.77 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 2956, 2929, 1737, 1605, 1528, 1457, 1347, 1266, 1132, 1044, 971, 866, 845, 717. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.94 (*t*, *J* = 7.3, *Me*$(CH_2)_3O$); 1.02 (*d*, *J* = 6.9, Me–C(4)); 1.35–1.49 (*m*, Me*C*$H_2(CH_2)_2O$); 1.56–1.67 (*m*, $MeCH_2CH_2CH_2O$); 1.73 (*d*, *J* = 1.9, Me–C(6)); 1.71–1.82 (*m*, 1 H–C(3)); 2.09 (*ddd*, *J* = 13.3, 6.1, 3.6, 1 H–C(3)); 2.77–2.96 (*m*, H–C(4)); 3.50–3.62 (*m*, 1 H, $Me(CH_2)_2CH_2O$); 3.79–3.95 (*m*, 1 H, $Me(CH_2)_2CH_2O$); 5.01–5.03 (*m*, H–C(2)); 8.30–8.40 (*m*, 4 arom. H); selected signals of the minor epimer: 1.09 (*d*, *J* = 6.9, Me–C(4)); 1.75 (*d*, *J* = 1.6, Me–C(6)); 2.20 (*ddd*, *J* = 13.4, 6.9, 2.3, H–C(3)); 5.05 (*dd*, *J* = 7.1, 2.2, H–C(2)). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 13.8 (*Me*$(CH_2)_3O$); 14.3 (*Me*–C(6)); 17.4 (*Me*–C(4)); 19.2 (Me*C*$H_2(CH_2)_2O$); 25.2 (C(4)); 31.7 ($MeCH_2CH_2CH_2O$); 35.7 (C(3)); 68.1 ($Me(CH_2)_2CH_2O$); 94.4 (C(2)); 123.6 (2 arom. C); 130.6 (C(5)); 131.0 (2 arom. C); 135.0 (arom. C); 139.5 (C(6)); 150.7 (arom. C); 163.1 (Ar*C*O_2); selected signals of the minor epimer: 17.9 (*Me*–C(4)); 20.2 (Me*C*$H_2(CH_2)_2O$); 27.7 (C(4)); 36.1 (C(3)); 68.8 ($Me(CH_2)_2CH_2O$); 98.7 (C(2)); 140.4 (C(6)). EI-MS (70 eV): 349 (3, M^+), 275 (16), 199 (31), 150 (100), 134 (10), 125 (30), 104 (40), 100 (62), 85 (70), 76 (22), 56 (71). HR-FAB-MS: 349.1519 (M^+, $C_{18}H_{23}NO_6^+$; calc. 349.1525).

*3,3a,4,7a-Tetrahydro-6-methyl-2*H*-furo[2,3-*b*]pyran-5-yl 5-Nitrobenzoate* (**10**). According to the *G. P. 3*, with **1a** (4.25 mmol), **9** (5.96 g, 0.085 mol) instead of **6b**, and heating to 140° for 18 d: 0.69 g (53%) of **10**. Yellow powder. R_f 0.47 (hexane/AcOEt 7:3). M.p. 121–122°. IR (CH_2Cl_2): 2921, 1737, 1529, 1350, 1270, 1127, 718. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.75 (br. *s*, Me–C(6)); 2.00–2.22 (*m*, 2 H–C(3)); 2.31 (br. *d*, *J* = 16.8, 1 H–C(4)); 2.52–2.64 (*m*, H–C(3a)); 2.75–2.87 (*m*, 1 H–C(4)); 4.00 (*q*, *J* = 8.4, 1 H–C(2)); 4.25 (*ddd*, *J* = 8.6, 8.1, 3.1, 1 H–C(2)); 5.41 (*d*, *J* = 3.9, H–C(7a)); 8.21–8.37 (*m*, 4 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 14.3 (*Me*–C(6)); 24.1 (C(4)); 28.1 (C(3)); 37.9 (C(3a)); 68.3 (C(2)); 99.2 (C(7a)); 123.7 (2 arom. C); 124.3 (C(5)); 131.0 (2 arom. C); 134.9 (arom. C); 140.7 (C(6)); 150.7 (arom. C); 163.4 (Ar*C*O_2). EI-MS (70 eV): 305 (8, M^+), 150 (38), 138 (11), 120 (5), 104 (20), 95 (10), 70 (100), 43 (23). Anal. calc. for $C_{15}H_{15}NO_6$: C 59.02, H 4.95, N 4.59; found: C 58.86, H 4.84, N 4.32.

*2-Ethoxy-3,4-dihydro-6-methyl-2*H*-pyran-5-yl 4-Aminobenzoate* (**12a**). Under H_2 (24 psi) and vigorous magnetic stirring, a mixture of **7a** (0.50 g, 1.63 mmol) and 10% Pd/*C* (0.05 g, 0.048 mmol) in AcOEt (4 ml) was treated at r.t. for 24 h. The mixture was filtered over *Celite*, the *Celite* washed with AcOEt (3 × 10 ml), the solvent evaporated, and the crude purified by CC (SiO_2 (30 g/1 g of crude), hexane/AcOEt 90:10): 0.35 g (77%) of **12a**. White powder. R_f 0.32 (hexane/AcOEt 7:3). M.p. 95–96°. IR (CH_2Cl_2): 3468, 3368, 1704, 1603, 1311, 1274, 1169, 1129, 1051, 1014, 853, 768. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.25 (*t*, *J* = 7.0, *Me*CH_2O); 1.72–1.75 (*m*, Me–C(6)); 1.90–2.06 (*m*, 2 H–C(3)); 2.19–2.31 (*m*, 1 H–C(4)); 2.34–2.48 (*m*, 1 H–C(4)); 3.61 (*dq*, *J* = 9.8, 7.1, 1 H, Me*C*H_2O); 3.89 (*dq*, *J* = 9.8, 7.1, 1 H, Me*C*H_2O); 4.12 (br. *s*, NH_2); 5.03 (*t*, *J* = 3.3, H–C(2)); 6.61–6.69 (*m*, 2 arom. H); 7.88–7.95 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 14.0 (*Me*–C(6)); 15.2 (*Me*CH_2O); 20.4 (C(4)); 27.0 (C(3)); 63.8 (Me*C*H_2O); 96.8 (C(2)); 113.7 (2 arom. C); 119.0 (arom. C); 126.6 (C(5)); 132.0 (2 arom. C); 139.5 (C(6)); 151.2 (arom. C); 165.1 (Ar*C*O_2). EI-MS (70 eV): 277 (1, M^+), 140 (28), 137 (26), 120 (100), 95 (28), 92 (16), 65 (8), 57 (8). Anal. calc. for $C_{15}H_{19}NO_4$: C 64.97, H 6.91, N 5.05; found: C 64.97, H 6.92, N 4.86.

*2-Butoxy-3,4-dihydro-6-methyl-2*H*-pyran-5-yl 4-Aminobenzoate* (**12b**). As described for **12a**, with **8a** (0.93 g, 2.78 mmol), 10% Pd/C (0.093 g, 0.087 mmol), and stirring for 24 h: 0.53 g (63%) of **12b**. White

powder. R_f 0.40 (hexane/AcOEt 7:3). M.p. 58–59°. IR (CH_2Cl_2): 3470, 3367, 2956, 2931, 1711, 1697, 1604, 1594, 1516, 1439, 1310, 1273, 1168, 1133, 1007, 842, 767. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.93 (*t*, *J* = 7.4, *Me*(CH_2)$_3$O); 1.33–1.46 (*m*, MeC*H*$_2$(CH_2)$_2$O); 1.54–1.65 (*m*, MeCH_2C*H*$_2$CH_2O); 1.73 (br. *s*, *Me*–C(6)); 1.93–2.03 (*m*, 2 H–C(3)); 2.17–2.30 (*m*, 1 H–C(4)); 2.34–2.48 (*m*, 1 H–C(4)); 3.54 (*dt*, *J* = 9.6, 6.6, 1 H, Me(CH_2)$_2$C*H*$_2$O); 3.82 (*dt*, *J* = 9.6, 6.6, 1 H, Me(CH_2)$_2$C*H*$_2$O); 4.21 (br. *s*, NH_2); 5.01 (*t*, *J* = 3.3, H–C(2)); 6.63–6.69 (*m*, 2 arom. H); 7.88–7.94 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 13.8 (*Me*(CH_2)$_3$O); 14.0 (*Me*–C(6)); 19.2 (Me*C*H$_2$(CH_2)$_2$O); 20.3 (C(4)); 26.9 (C(3)); 31.6 (MeCH_2*C*H$_2$CH_2O); 68.1 (Me(CH_2)$_2$*C*H$_2$O); 96.9 (C(2)); 113.7 (2 arom. C); 118.9 (arom. C); 126.6 (C(5)); 132.0 (2 arom. C); 139.4 (C(6)); 151.2 (arom. C); 165.2 (Ar*C*O$_2$). EI-MS (70 eV): 305 (1, M^+), 288 (1), 168 (10), 137 (7), 120 (100), 95 (23), 92 (18), 65 (18), 57 (19). Anal. calc. for $C_{17}H_{23}NO_4$: C 66.86, H 7.59, N 4.59; found: C 67.02, H 7.64, N 4.71.

*3,3a,4,7a-Tetrahydro-6-methyl-2*H*-furo[2,3-*b*]pyran-5-yl 4-Aminobenzoate* (**13**). As described for **12a**, with **10** (0.3 g, 0.98 mmol), 10% Pd/C (0.03 g, 0.028 mmol), and stirring for 22 h: 0.14 g (54%) of **13**. White powder. R_f 0.22 (hexane/AcOEt 7:3). M.p. 136–137°. IR (CH_2Cl_2): 3366, 2940, 1710, 1690, 1631, 1601, 1440, 1314, 1273, 1168, 1123, 1038, 989, 885, 836, 769. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.73 (*t*, *J* = 1.8, Me–C(6)); 2.04–2.16 (*m*, 2 H–C(3)); 2.27 (br. *d*, *J* = 16.8, 1 H–C(4)); 2.48–2.60 (*m*, H–C(3a)); 2.70–2.81 (*m*, 1 H–C(4)); 3.98 (*dt*, *J* = 8.4, 8.1, 1 H–C(2)); 4.12 (br. *s*, NH_2); 4.23 (*ddd*, *J* = 8.1, 7.8, 4.5, 1 H–C(2)); 5.39 (*d*, *J* = 3.9, H–C(7a)); 6.63–6.70 (*m*, 2 arom. H); 7.86–7.92 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 14.2 (*Me*–C(6)); 24.3 (C(4)); 28.1 (C(3)); 38.0 (C(3a)); 68.2 (C(2)); 99.1 (C(7a)); 113.7 (2 arom. C); 118.7 (arom. C); 124.2 (C(5)); 131.9 (2 arom. C); 140.0 (C(6)); 151.3 (arom. C); 165.3 (Ar*C*O$_2$). EI-MS (70 eV): 275 (2, M^+), 258 (1), 138 (10), 120 (100), 92 (16), 65 (20). Anal. calc. for $C_{15}H_{17}NO_4$: C 65.44, H 6.22, N 5.09; found: C 65.42, H 6.16, N 5.16.

rel-*(2*R*,3*R*,6*R*)-6-Butoxytetrahydro-2-methyl-2*H*-pyran-3-yl 4-Methoxybenzoate* (**11c**) *and 1-Acetyl-4-butoxybutyl 4-Methoxybenzoate* (**14**). Under H_2 (700 psi) and vigorous magnetic stirring, a mixture of **7a** (0.208 g, 0.650 mmol) and 10% Pd/C (0.022 g, 0.021 mmol) in AcOEt (40 ml) and glacial AcOH (5 drops) was treated at 60° for 48 h. The mixture was filtered over *Celite*, the *Celite* washed with AcOEt (3 × 30 ml) and CH_2Cl_2 (3 × 20 ml), the solvent evaporated, and the crude purified by CC (SiO_2 (30 g/1 g of crude), hexane/AcOEt 90:10): 0.075 g (36%) of **11c** and 0.06 g (29%) of **14**.

Data of **11c**: Pale yellow oil. R_f 0.66 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 2955, 2934, 1710, 1606, 1511, 1455, 1372, 1313, 1260, 1210, 1668, 1106, 1073, 1026, 940, 850, 771. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.94 (*t*, *J* = 7.3, *Me*(CH_2)$_3$O); 1.32–1.47 (*m*, MeC*H*$_2$(CH_2)$_2$O); 1.57–1.67 (*m*, MeCH_2C*H*$_2$CH_2O); 1.67–1.82 (*m*, 2 H–C(5)); 1.74 (*d*, *J* = 6.5, Me–C(2)); 1.80–1.86 (*m*, 1 H–C(4)); 2.10–2.19 (*m*, 1 H–C(4)); 3.47 (*dt*, *J* = 9.4, 7.0, 1 H, Me(CH_2)$_2$C*H*$_2$O); 3.80 (*qd*, *J* = 6.5, 1.3, H–C(2)); 3.87 (*s*, MeO); 3.96 (*dt*, *J* = 9.4, 6.7, 1 H, Me(CH_2)$_2$C*H*$_2$O); 4.48–4.56 (*m*, H–C(6)); 4.88–5.05 (*m*, H–C(3)); 6.90–6.96 (*m*, 2 arom. H); 8.06–8.13 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 13.9 (*Me*(CH_2)$_3$O); 17.2 (*Me*–C(2)); 19.2 (Me*C*H$_2$(CH_2)$_2$O); 26.2 (C(5)); 27.5 (C(4)); 31.7 (MeCH_2*C*H$_2$CH_2O); 55.4 (MeO); 68.5 (C(3)); 68.9 (Me(CH_2)$_2$*C*H$_2$O); 72.7 (C(2)); 102.2 (C(6)); 113.5 (2 arom. C); 122.5 (arom. C); 131.9 (2 arom. C); 163.4 (arom. C or Ar*C*O$_2$); 166.0 (Ar*C*O$_2$ or arom. C). EI-MS (70 eV): 249 (3, $[M - C_4H_9O]^+$), 135 (66), 107 (12), 92 (14), 87 (33), 77 (88), 63 (31), 43 (56), 41 (100). HR-FAB-MS: 321.1700 ($[M - H]^+$, $C_{18}H_{25}O_5^+$; calc. 321.1702).

Data of **14**: Pale yellow oil. R_f 0.57 (hexane/AcOEt 7:3). IR (CH_2Cl_2): 2932, 2862, 1714, 1606, 1511, 1459, 1360, 1316, 1258, 1669, 1103, 1029, 848, 771, 696. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.92 (*t*, *J* = 7.3, *Me*(CH_2)$_3$O); 1.28–1.44 (*m*, MeC*H*$_2$(CH_2)$_2$O); 1.49–1.61 (*m*, MeCH_2C*H*$_2$CH_2O); 1.70–1.82 (*m*, 2 H–C(3)); 1.86–2.09 (*m*, 2 H–C(2)); 2.22 (*s*, *Me*CO); 3.41 (*t*, *J* = 6.6, Me(CH_2)$_2$C*H*$_2$O); 3.46 (*t*, *J* = 6.2, 2 H–C(4)); 3.88 (*s*, MeO); 5.22 (*dd*, *J* = 8.3, 4.4, H–C(1)); 6.88–6.98 (*m*, 2 arom. H); 7.99–8.10 (*m*, 2 arom. H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 13.9 (*Me*(CH_2)$_3$O); 19.3 (Me*C*H$_2$(CH_2)$_2$O); 25.5 (C(3)); 26.1 (*Me*CO); 27.3 (C(2)); 31.7 (MeCH_2*C*H$_2$CH_2O); 55.4 (MeO); 69.8 (Me(CH_2)$_2$*C*H$_2$O); 70.7 (C(4)); 78.6 (C(1)); 113.7 (2 arom. C); 121.6 (arom. C); 131.9 (2 arom. C); 163.7 (arom. C or Ar*C*O$_2$); 165.8 (Ar*C*O$_2$ or arom. C); 205.8 (*C*OMe). EI-MS (70 eV): 323 (3, $[M + 1]^+$), 135 (100), 107 (13), 92 (16), 77 (87), 63 (21), 43 (48), 41 (40). HR-FAB-MS: 323.1856 ($[M + H]^+$, $C_{18}H_{27}O_5^+$; calc. 323.1858).

Single-Crystal X-Ray Crystallography. Adduct **7a** was obtained as white crystals. These were mounted on glass fibers. Crystallographic measurements were performed on a *CCD-Smart-6000* diffractometer with MoK_α radiation (graphite crystal monochromator, λ 0.7107 Å) at r.t. Data were

integrated, scaled, sorted, and averaged with the Smart software package. The structures were solved by direct methods, with SHELXTL, version 5.10, and refined by full-matrix least squares against F^2 [29]. An empirical absorption correction based on the multiple measurement of equivalent reflections was applied by using the program SADABS [30]. The displacement parameters of non-H-atoms were refined anisotropically. The positions of the H-atoms were kept fixed with a common isotropic displacement parameter. Data for **7a**: Formula $C_{15}H_{17}NO_6$; M_r 307.30; crystal size $0.1 \times 0.3 \times 0.4$ mm; crystal system triclinic; space group *P*-1; unit cell parameters: $a = 7.8575(6)$, $b = 10.1281(8)$, $c = 10.3925(8)$ Å; $\alpha = 86.287(2)$, $\beta = 78.957(2)$, $\gamma = 72.879(2)^\circ$; $V = 775.73(10)$ Å^3; temp. 293(2) K; $Z = 2$; $D_x = 1.316$ Mg/m^3; absorption coefficient = 0.103 mm^{-1}; θ scan range 2.00–23.26°; reflections collected 4028; independent reflections 2204; reflections observed 2204; data collection range: $4.0 < 2\theta < 46.52^\circ$; $R = 0.0420$; $wR = 0.1068$; *G.o.f.:* 0.992.

CCDC-680887 contains the supplementary crystallographic data (excluding structure factors) for the structure of **7a**. These data can be obtained, free of charge, *via* www.ccdc.ac.uk/data_request/cif.

Calculation Methods. All the calculations described in this work were carried out with the Gaussian 94 program package [22] and personal computers running under the Linux operating system. All optimizations were first carried out at the HF/3-21G level of theory, and the resulting geometries were employed as starting points for further optimizations at the HF/6-31G(d) and B3LYP/6-31G(d) levels. In all optimizations (minima and transition states), the OPT = TIGHT keyword was employed; in addition, all the DFT calculations were carried out with the INT(GRID = 99590) keyword, to obtain better energies and vibrational frequencies by means of a finer integration grid. For each one of the approaches of the reactants described in the main text, geometries were generated for the corresponding products out of chemical intuition (in most cases, a single conformer was optimized, no particular attempt was made to carry out a conformational search). From these geometries, and those of the reactants, the transition states were obtained employing the QST2 (QST3 at the highest levels, with the geometries of TSs obtained at lower levels of theory) option of the OPT keyword. For all stationary points, vibrational analyses were carried out at each level of theory; each point was characterized by the appropriate number of imaginary vibrational frequencies. Each transition state was further characterized by visual inspection of the normal mode corresponding to its single imaginary frequency. Relative energies were obtained by subtracting the energy of the lowest-energy structures (TSs or minima) from the energies of all the other geometries, and converting these differences into kcal/mol.

REFERENCES

[1] a) D. L. Boger, S. M. Weinreb, 'Hetero Diels–Alder Methodology in Organic Synthesis', Academic Press, San Diego, 1987; b) D. L. Boger, 'Heterodiene Additions', in 'Comprehensive Organic Synthesis', Eds. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, Vol. 5, pp. 451–512; c) F. Fringuelli, A. Taticchi, 'Dienes in the Diels–Alder Reaction', John Wiley & Sons, New York, 1990; d) G. Desimoni, G. Tacconi, *Chem. Rev.* **1975**, *75*, 651.

[2] a) K. A. Jørgensen, *Eur. J. Org. Chem.* **2004**, 2093; b) D. L. Boger, K. D. Robarge, *J. Org. Chem.* **1988**, *53*, 5793; c) A. Dondoni, L. Kniezo, M. Martinkova, *J. Chem. Soc., Chem. Commun.* **1994**, 1963; d) L. De Gaudenzi, S. Apparao, R. R. Schmidt, *Tetrahedron* **1990**, *46*, 277.

[3] H. Waldmann, *Synthesis* **1994**, 535; K. A. Jørgensen, *Angew. Chem., Int. Ed.* **2000**, *39*, 3558; K. Juhl, K. A. Jørgensen, *Angew. Chem., Int. Ed.* **2003**, *42*, 1498.

[4] a) L.-F. Tietze, K.-H. Glüsenkamp, *Angew. Chem., Int. Ed.* **1983**, *22*, 887; b) L.-F. Tietze, K.-H. Glüsenkamp, W. Holla, *Angew. Chem., Int. Ed.* **1982**, *21*, 793; c) S. L. Schreiber, A. H. Hoveyda, H. J. Wu, *J. Am. Chem. Soc.* **1983**, *105*, 660.

[5] W. E. Gore, G. T. Pearce, R. M. Silverstein, *J. Org. Chem.* **1976**, *41*, 603; K. B. Lipkowitz, S. Scarpone, B. P. Mundy, W. G. Bornmann, *J. Org. Chem.* **1979**, *44*, 486.

[6] a) S. Murai, I. Ryu, Y. Kadono, H. Katayama, K. Kondo, N. Sonoda, *Chem. Lett.* **1977**, 1219; b) R. R. Schmidt, M. Maier, *Tetrahedron Lett.* **1985**, *26*, 2065; c) K. Takani, M. Yamada, K. Negoro, *J. Org. Chem.* **1982**, *47*, 5246; d) S. Apparao, M. E. Maier, R. R. Schmidt, *Synthesis* **1987**, 900.

[7] H. G. Viehe, Z. Janousek, R. Merényi, L. Stella, *Acc. Chem. Res.* **1985**, *18*, 148; J.-L. Boucher, L. Stella, *Tetrahedron* **1986**, *42*, 3871; D. Döpp, H. Libera, *Tetrahedron Lett.* **1983**, *24*, 885; A. Y. Rulev,

Russ. Chem. Rev. **2002**, *71*, 195; P. Seneci, I. Leger, M. Souchet, G. Nadler, *Tetrahedron* **1997**, *53*, 17097; P. M. T. Ferreira, H. L. S. Maia, L. S. Monteiro, *Tetrahedron Lett.* **2002**, *43*, 4491; H. R. Memarian, M. Dehghani, G. Henkel, D. Döpp, *Monatsh. Chem.* **2004**, *135*, 425; A. Avenoza, J. H. Busto, N. Canal, J. M. Peregrina, M. Pérez-Fernández, *Org. Lett.* **2005**, *7*, 3597; C. Bonauer, T. Walenzyk, B. König, *Synthesis* **2006**, 1; M. Lasa, C. Cativiela, *Synlett* **2006**, 2517; A. Sakakura, K. Suzuki, K. Ishihara, *Adv. Synth. Catal.* **2006**, *348*, 2457.

[8] a) A. Reyes, R. Aguilar, A. H. Muñoz, J. C. Zwick, M. Rubio, J. L. Escobar, M. Soriano, R. Toscano, J. Tamariz, *J. Org. Chem.* **1990**, *55*, 1024; b) R. Aguilar, A. Reyes, J. Tamariz, J.-L. Birbaum, *Tetrahedron Lett.* **1987**, *28*, 865; c) O. García de Alba, J. Chanona, F. Delgado, G. Zepeda, F. Labarrios, R. W. Bates, S. Bott, E. Juaristi, J. Tamariz, *Anal. Quím., Int. Ed.* **1996**, *92*, 108.

[9] A. Nagarajan, G. Zepeda, J. Tamariz, *Tetrahedron Lett.* **1996**, *37*, 6835; R. Jiménez, L. Pérez, J. Tamariz, H. Salgado, *Heterocycles* **1993**, *35*, 591; R. Herrera, A. Nagarajan, M. A. Morales, F. Méndez, H. A. Jiménez-Vázquez, L. G. Zepeda, J. Tamariz, *J. Org. Chem.* **2001**, *66*, 1252.

[10] a) R. M. Andrade, A. H. Muñóz, J. Tamariz, *Synth. Commun.* **1992**, *22*, 1603; b) A. Orduña, L. G. Zepeda, J. Tamariz, *Synthesis* **1993**, 375; c) Z. Dienes, P. Vogel, *J. Org. Chem.* **1996**, *61*, 6958; d) M. E. Ochoa, M. S. Arias, R. Aguilar, F. Delgado, J. Tamariz, *Tetrahedron* **1999**, *55*, 14535; e) R. Aguilar, A. Reyes, A. Orduña, G. Zepeda, R. W. Bates, J. Tamariz, *Rev. Soc. Quím. Méx.* **2000**, *44*, 91; f) R. Aguilar, A. Benavides, J. Tamariz, *Synth. Commun.* **2005**, *34*, 2719.

[11] J. Peralta, J. P. Bullock, R. W. Bates, S. Bott, G. Zepeda, J. Tamariz, *Tetrahedron* **1995**, *51*, 3979.

[12] R. Herrera, J. A. Mendoza, M. A. Morales, F. Méndez, H. A. Jiménez-Vázquez, F. Delgado, J. Tamariz, *Eur. J. Org. Chem.* **2007**, 2352.

[13] H. A. Jiménez-Vázquez, M. E. Ochoa, G. Zepeda, A. Modelli, D. Jones, J. A. Mendoza, J. Tamariz, *J. Phys. Chem. A* **1997**, *101*, 10082.

[14] J. A. Mendoza, E. García-Pérez, H. A. Jiménez-Vázquez, J. Tamariz, *J. Mex. Chem. Soc.* **2006**, *45*, 47.

[15] J. Tamariz, P. Vogel, *Helv. Chim. Acta* **1981**, *64*, 188.

[16] L. Villar, J. P. Bullock, M. M. Khan, A. Nagarajan, R. W. Bates, S. G. Bott, G. Zepeda, F. Delgado, J. Tamariz, *J. Organomet. Chem.* **1996**, *517*, 9.

[17] F. Leyendecker, M.-T. Comte, *Tetrahedron Lett.* **1982**, *23*, 5031.

[18] J. D. Dudones, P. Sampson, *J. Org. Chem.* **1997**, *62*, 7508.

[19] G. Berti, G. Catelani, F. Colonna, L. Monti, *Tetrahedron* **1982**, *38*, 3067.

[20] A. C. Coda, G. Desimoni, P. P. Righetti, G. Tacconi, A. Buttafava, F. M. Faucitano, *Tetrahedron* **1983**, *39*, 331, and ref. cit. therein.

[21] W. G. Dauben, H. O. Krabbenhoft, *J. Org. Chem.* **1977**, *42*, 282.

[22] M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez, J. A. Pople, Gaussian 94, Revision E.2, *Gaussian, Inc.*, Pittsburgh, PA, 1995.

[23] C. A. G. Haasnoot, F. A. A. M. de Leeuw, C. Altona, *Tetrahedron* **1980**, *36*, 2783.

[24] MestRe-J 1.0, Mestrelab Research SL, Xosé Pasín 6-5C, E-15706 Santiago de Compostela; A. Navarro-Vázquez, J. C. Cobas, F. J. Sardina, J. Casanueva, E. Díez, *J. Chem. Inf. Comput. Sci.* **2004**, *44*, 1680.

[25] R. Paul, S. Tchelitcheff, *Bull. Soc. Chim. Fr.* **1954**, *21*, 672.

[26] I. Fleming, 'Frontier Orbitals and Organic Chemical Reactions', John Wiley & Sons, Chichester, 1976.

[27] K. N. Houk, *Acc. Chem. Res.* **1975**, *8*, 361; O. Eisenstein, J. M. Lefour, N. T. Anh, R. F. Hudson, *Tetrahedron* **1977**, *33*, 523; C. Spíno, M. Pesant, Y. Dory, *Angew. Chem., Int. Ed.* **1998**, *37*, 3262.

[28] Web page: www.sevmexico.com.

[29] SHEXTL 5.10, *Bruker AXS, Inc.*, Madison, WI, USA, 1998.

[30] SADABS, Area-Detector Absorption Correction, *Siemens Industrial Automation, Inc.*, Madison, WI, 1996.

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