J. Phys. Chem. A **2005,** *109,* 6279−6289

Ab Initio Study of the Substituent Effects on the Relative Stability of the *E* and *Z* Conformers of Phenyl Esters. Stereoelectronic Effects on the Reactivity of the Carbonyl Group

Helmi Neuvonen,*,† Kari Neuvonen,† Andreas Koch,‡ and Erich Kleinpeter‡

Department of Chemistry, University of Turku, FIN-20014 Turku, Finland, and University of Potsdam, D-14415 Potsdam, POB 691553, Germany

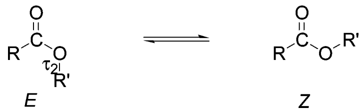
Received: December 22, 2004; In Final Form: May 9, 2005

Equilibria between the *Z* ($\tau_1 = 0°$) and *E* ($\tau_1 = 180°$) conformers of *p*-substituted phenyl acetates **4** and trifluoroacetates **5** (X = OMe, Me, H, Cl, CN, NO_2) were studied by ab initio calculations at the HF/6-31G* and MP2/6-31G* levels of theory. The preference for the *Z* conformer, ΔE(HF), was calculated to be 5.36 kcal mol^{-1} and 7.50 kcal mol^{-1} for phenyl acetate and phenyl trifluoroacetate (i.e., with X = H), respectively. The increasing electron-withdrawing ability of the phenyl substituent X increases the preference of the *Z* conformer. An excellent correlation with a negative slope was observed for both series between ΔE of the *E*−*Z* equilibrium and the Hammett σ constant. By using an appropriate isodesmic reaction, it was shown that electron-withdrawing substituents decrease the stability of both conformers, but the effect is higher with the *E* conformer. Electron-withdrawing phenyl substituents decrease the delocalization of the lone pair of the ether oxygen to the C═O antibonding orbital ($n_O \rightarrow \pi^*_{C=O}$) in both the *E* and *Z* forms and in both series studied; this effect is higher in the *E* conformer than in the *Z* conformer. The $n_O \rightarrow \pi^*_{C=O}$ electron donation has a minimum value with $\tau_1 = 90°$ and a maximum value with $\tau_1 = 0°$ (the *Z* conformer), the value with $\tau_1 = 180°$ (the *E* conformer) being between these two values, obviously due to steric hindrance. The effects of the phenyl substituents on the reactivity of the esters studied are discussed in terms of molecular orbital interactions. ED/EW substituents adjust the availability of the $\pi^*_{C=O}$ antibonding orbital to interact with the lone pair orbital of the attacking nucleophile and therefore affect the reactivity: EW substituents increase and ED substituents decrease it. Excellent correlations were observed between the rate coefficients of nucleophilic acyl substitutions and $\pi^*_{C=O}$ occupancies of the ester series **4** and **5**.

Introduction

One of the conformational equilibria of carboxylic acid esters is due to the rotation around the single C(═O)−O bond. In general the most stable conformations correspond to the planar *Z* ($\tau_1 = 0°$) and *E* ($\tau_1 = 180°$) conformers; the *Z* conformer being clearly favored (Scheme 1).[1−3] Several different aspects have been considered to explain the higher stability of the *Z* conformer. These include for instance steric effects, dipole−dipole interactions, lone pair-lone pair repulsion effects, and hyperconjugative interactions.[1−6] When R is methyl or a larger group unfavorable steric interactions between R and R′ are obvious in the *E* conformer. However, for esters of formic acid (R = H) the main steric interactions are between the carbonyl oxygen and R′. This is seen for instance when compared the *E*−*Z* free energy differences 2.5, 1.67, 1.36, and 0.48 kcal mol^{-1}, respectively, determined for methyl, ethyl, isopropyl and *tert*-butyl formates (in acetone-d_6 − DMF, 1:1).[7] In the gas phase the *Z* conformer of *tert*-butyl formate is highly preferred over the *E* conformer [5.11 kcal mol^{-1} (RHF)].[8] Although the *Z* conformer is more stable than the *E* conformer in each case its preference decreases when the size of R′ increases.

SCHEME 1



Increasing electronegativity of R′ in the order methyl < vinyl ≈ phenyl ≈ cyclopropyl < hydrogen < ethynyl in esters of formic acid, HCOOR′, has been suggested to favor the *E* relative to the *Z* conformer.[9] Ab initio calculations, recently performed by Noe et al.[10] for trichloromethyl formate **1** and trifluoromethyl formate **2**, show that, although also for these compounds the rotational *E* isomer is calculated to have a higher free energy in the gas phase [the free energy difference 0.857 kcal mol^{-1} for **1** and 1.14 kcal mol^{-1} for **2** at the MP2/6-311G (df, pd) level], the *E*−*Z* free energy difference is much smaller than that for methyl formate **3** (5.16 kcal mol^{-1} at MP2/6-31+G** level).[11] The relatively low free-energy differences between the *E* and *Z* conformers for **1** and **2** was attributed to a combination of steric effects and the near-equality of the dipole moments for the two conformers.[10] A recent study by Uchimaru et al.[12] shows that the preference of the *Z* conformer over the *E* conformer (CBS-APNO enthalpy differences) is decreased in the series of methyl formate (5.03 kcal mol^{-1}), fluoromethyl formate (3.05 kcal mol^{-1}), difluoromethyl formate (2.58 kcal mol^{-1}), and trifluoromethyl formate (1.14 kcal mol^{-1}). Changes in geometry were discussed in terms of an interplay of orbital interactions ($n_O \rightarrow \pi^*_{C=O}$ vs $n_O \rightarrow \sigma^*_{C-F}$).[12]

Despite the large amount of both the experimental and theoretical studies concerning the stability of ester conformations

---

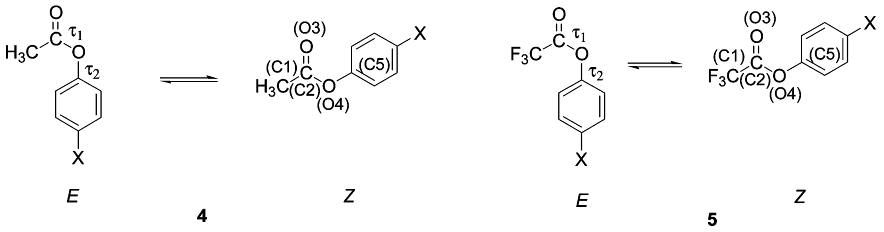
* Corresponding author. Fax: +358-2-3336700. E-mail: helmi.neuvonen@utu.fi

† University of Turku.

‡ University of Potsdam.

10.1021/jp044172k CCC: $30.25

SCHEME 2



X = OMe (**a**), Me (**b**), H (**c**), Cl (**d**), CN (**e**), NO_2(**f**)

TABLE 1: Calculated Energies for the *Z* and *E* Conformers of Phenyl Acetates 4a−f and the Energy Differences between the *Z* and *E* Conformers[a]

X	σ[b]	HF/6-31G* *Z*	HF/6-31G* *E*	HF/6-31G* Δ*E*[c]	MP2/6-31G* *Z*	MP2/6-31G* *E*	MP2/6-31G* Δ*E*[c]
OMe	−0.27	−571.2260	−571.21748	−5.35	−572.8945	−572.888	−4.08
Me	−0.17	−496.38383	−496.37536	−5.32	−497.8781	−497.8714	−4.20
H	0	−457.34688	−457.33833	−5.36	−458.7074	−458.7007	−4.20
Cl	0.23	−916.24591	−916.23657	−5.86	−917.7392	−917.7318	−4.64
CN	0.66	−549.08168	−549.07155	−6.36	−550.7211	−550.7129	−5.15
NO_2	0.78	−660.81813	−660.80772	−6.53	−662.7171	−662.7087	−5.27

[a] The energies are given in hartrees and they are calculated for the local minima which are *Z*_60 (cf. Table 3) and *E*_90. [b] Hammett substituent constants from ref 20. [c] In kcal mol^{-1}.

the reasons of the general preference of just the planar *Z* and *E* forms, i.e., $\tau_1 = 0°$ (*Z*) and 180° (*E*) (τ_1 defined as O3═C2−O4−C5 torsional angle), are not totally understood.[1−12] In addition, the research reports discussing reactivity of ester functions seldom even consider the status of the preferential conformation, even though it is possible that the spatial arrangement of the molecular framework can have a significant role in the reaction pathway. However, ester functional group is of high importance in organic synthesis, and it is the functional group of several lipid structures and that of the intermediates of some enzyme catalyzed processes.

Our ^{13}C NMR and theoretical studies have recently shown that the shielding of the carbonyl carbon of para-substituted phenyl acetates, dichloroacetates, and trifluoroacetates clearly and systematically depends on the electron-withdrawing (EW) ability of the phenyl substituent. The same is true also for substituted phenyl benzoates.[13−15] This suggests that the remote phenyl substituents can adjust the electron distribution around the carbonyl unit. Furthermore, by the isodesmic energy calculations evaluating the stability of the esters, we have shown on PM3 level that the EW substituents at the phenyl group destabilize phenyl acetates, dichloroacetates, and trifluoroacetates while the electron donating (ED) substituents affect them inversely.[14] As mentioned already, there are some indications that the electron-withdrawing ability of alkyl substituents of alkyl formates can affect the relative stability of the *Z* and *E* conformers.[10−12] To clarify the effect of the EW/ED ability of the phenyl substituent in that respect, we decided to study by ab initio calculations the effect of phenyl substituent on the structure and on the relative stability of the conformational isomers of phenyl acetates **4** and trifluoroacetates **5** (Scheme 2). Changes in substitution X should result in only minimal changes in the steric effects permitting evaluation of the electronic component.

Computational Methods

The calculations were carried out with the GAUSSIAN 98 program.[16] Ab initio calculations were performed at the Hartree−Fock (HF) level of theory and with the second-order Møller−Plesset (MP2) perturbation theory. The split valence 6-31G* basis set were used for all calculations.[17] All conformations were optimized without any restrictions. The rotational barriers and the energy surface (HF/6-31G*) were obtained by rotation of the torsional angles τ_1 (O3═C2−O4−C5) and τ_2 (C2−O4−C5−C6) in 30° steps. All internal coordinates except τ_1 and τ_2 were optimized.

The NBO 5.0 program[18] was used for analysis of Wiberg bond order indices (the sum of squares of off-diagonal density matrix elements between atoms).[19] Occupancy of orbitals (bonding, antibonding and lone pairs) is obtained as the result of the NBO population analysis. The program Excel was used for graphical presentation of the results.

Results and Discussion

The energy values calculated for the most stable *Z* and *E* conformers of **4a**−**f** and **5a**−**f** are shown in Tables 1 and 2. Table 3 collects the most stable conformers (those denoted by Z_60, i.e., $\tau_1 = 0°$; τ_2 ca. 60 ° or by Z_90, i.e., $\tau_1 = 0°$; $\tau_2 = 90$ °) for the derivatives of series **4** and **5** in terms of τ_2. In Table 4 are given the relative energies of the *Z* and *E* conformations of phenyl acetate (**4c**; X = H) at different values of τ_2. In Tables S1−S18 in the Supporting Information are given the bond order and bond length data of the relevant bonds as well as the relevant orbital occupancy data of the *Z*_60, *Z*_90, and *E*_90 conformations of **4a**−**f** and **5a**−**f**. In the Supporting Information are also given the bond order, bond length, orbital occupancy, and energy data for **4c** with different values of τ_1 when τ_2 is 90° (Table S19).

Stability Difference between the *Z* and *E* Conformers. In Figure 1 is shown the energy *E*(HF) with respect to the global minimum conformation surface for phenyl acetate **4c** (Scheme 3). The figure clearly shows that the most stable conformation of phenyl acetate is the *Z* conformation, i.e., that with $\tau_1 = 0°$ (τ_1 defined as the torsional angle O3═C2−O4−C5). The most stable *E* conformation ($\tau_1 = 180°$, $\tau_2 = 90°$; τ_2 defined as the torsional angle C2−O4−C5−C6) corresponds to a local minimum only because its energy is clearly higher than those of any of the Z conformations. Cross sections of the energy surface at these two values of the torsional angle τ_1 (0 and 180°) are shown in Figure 2, parts a and b. The varying of the dihedral

TABLE 2: Calculated Energies for the *Z* and *E* Conformers of Phenyl Trifluoroacetates 5a−f and the Energy Differences between the *Z* and *E* Conformers[a]

		HF/6-31G*			MP2/6-31G*		
X	σ^b	*Z*	*E*	ΔE^c	*Z*	*E*	ΔE^c
OMe	−0.27	−867.7916[d]	−867.77983	−7.39	−869.9622	−869.9538	−5.27
Me	−0.17	−792.94929[d]	−792.93743	−7.44	−794.9457	−794.9373	−5.27
H	0	−753.91207[d]	−753.90012	−7.50	−755.7748	−755.7663	−5.33
Cl	0.23	−1212.810	−1212.7979	−7.61	−1214.806	−1214.797	−5.38
CN	0.66	−845.64452	−845.63211	−7.79	−847.7865	−847.7778	−5.46
NO_2	0.78	−957.38047	−957.36793	−7.87	−959.7822	−959.7736	−5.40

[a] The energies are given in hartrees, and they are calculated for the local minima which are Z__60 (cf. Table 3) and E__90 if not otherwise stated. [b] Hammett substituent constants from ref 20. [c] In kcal mol^{-1}. [d] For Z__90.

TABLE 3: Degree Values of τ_2 Corresponding to the Most Stable *Z* Conformers of Phenyl Acetates (4a−f) and Phenyl Trifluoroacetates (5a−f)

	4a	4b	4c	4d	4e	4f	5a	5b	5c	5d	5e	5f
HF/6-31G*	77.2	72.8	73.6	64.3	57.6	55.6	90.0	90.0	90.0	79.0	61.9	59.9
MP2/6-31G*	67.7	64.0	63.4	60.2	56.9	56.1	72.4	67.8	67.4	62.9	59.5	59.0

TABLE 4: Relative Energies at HF/6-31G* Level for *Z* (τ_1 = 0°) and *E* (τ_1 = 180°) Conformations of Phenyl Acetate 4c at Different Values of τ_2 (i.e., for Rotation around the $CH_3(C{=}O)O{-}Ph$ Bond)

	$\tau_2 = 0°$	$\tau_2 = 30°$	$\tau_2 = 60°$	$\tau_2 = 90°$	$\tau_2 = 120°$	$\tau_2 = 150°$	$\tau_2 = 180°$
$\tau_1 = 0°$	1.01[a]	0.61	0.03	0.00	0.01	0.51	1.01
Z	(−457.34525)[b]	(−457.34589)	(−457.34681)	(−457.34686)	(−457.34684)	(−457.34604)	(−457.34525)
$\tau_1 = 180°$	12.69	10.56	7.00	5.36	6.57	10.03	12.62
E	(−457.32664)	(−457.33003)	(−457.3357)	(−457.33832)	(−457.33639)	(−457.33087)	(−457.32675)

[a] In kcal mol^{-1}. [b] In hartrees.

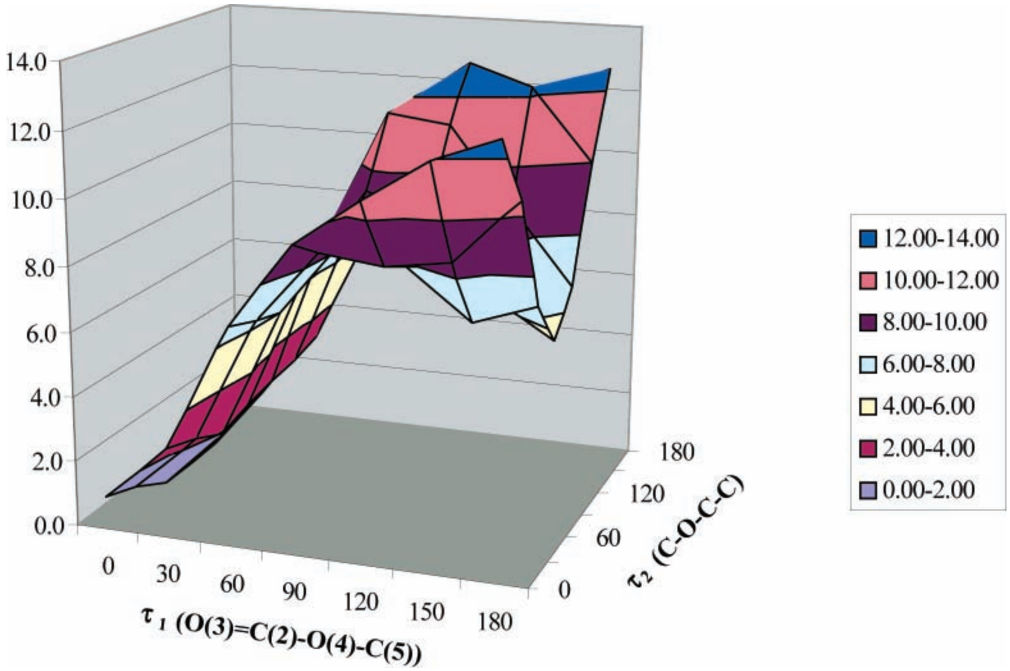
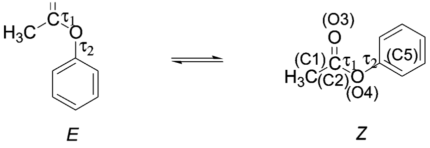


Figure 1. Energy (HF/6-31G*; in kcal mol^{-1}) with respect to the global minimum conformation surface for phenyl acetate (**4c**).

angle τ_2 corresponds to the rotation of the plane of the phenyl group with respect to the plane of the (O═C)−O−group. The corresponding energies are given in Table 4. For the *Z* conformation the minimum is very shallow (Figure 2a). The orientation of the plane of the phenyl ring affects only slightly on the stability and the energies vary within ca. 1 kcal mol^{-1} with varying $\tau_{2.}$ In contrast, as regards the *E* conformations, there is observed a clear local minimum at τ_2 = 90° (Figure 2b). This indicates that while the steric hindrance is significant in the *E* conformations, it is not crucial in the *Z* conformations.

SCHEME 3



4c

The preference of the planar *Z* and *E* conformers over the other ones is illustrated by Figure 3 where the cross section at τ_2 = 90° when varying τ_1 is shown for **4c**. The diagram gives an estimate of the location of the transition state at 103° and of the barrier height of 9.7 kcal mol^{-1} for the transition from *Z* to *E*. For methyl acetate, the corresponding values of 105° and

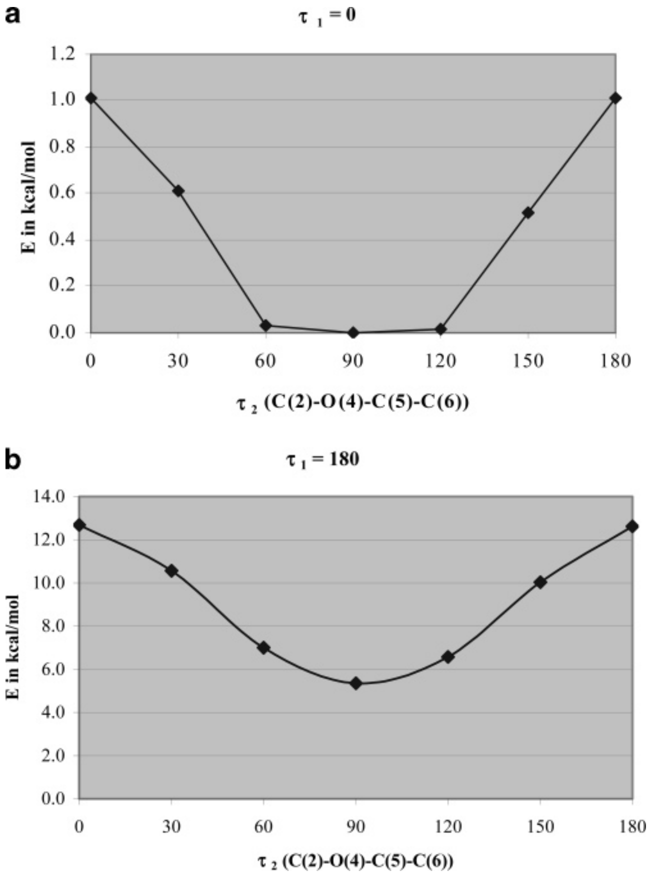


Figure 2. (a) Changes in energy (HF/6-31G*) for **4c** when varying τ_2 with $\tau_1 = 0°$. (b) Changes in energy (HF/6-31G*) for **4c** when varying τ_2 with $\tau_1 = 180°$.

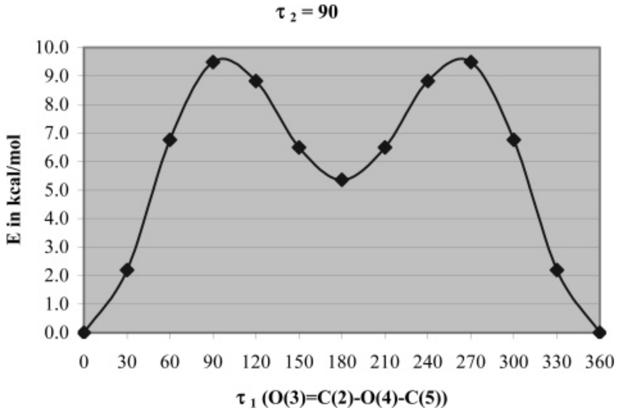


Figure 3. Changes in energy (HF/6-31G*) for **4c** when varying τ_1 with $\tau_2 = 90°$.

13.5 kcal mol^{-1}, respectively, have been recently reported in the gas phase.[21] Alike character of the energy values of the *Z* and *E* conformers was observed for all of the esters studied.

In accordance with the literature data concerning carboxylic acid esters,[1−12,21] in **4** and **5** the *E* conformers are calculated to have in the gas phase a remarkably higher energy than their Z conformers have (Tables 1 and 2). The high preference of the *Z* form over the *E* form can be partially attributed to the lower steric hindrance in the Z form (cf. the discussion above). In most cases the *Z*_60 conformer [$\tau_1 = 0°$; $\tau_2 = 55.6{-}77.2°$ (HF) and $56.1{-}67.7°$ (MP2) for derivatives of the series **4**; cf. Table 3] owns the lowest energy, i.e., represents the global minimum. However, as discussed above the energies of the different *Z* conformations corresponding to the different τ_2 values are very close to each other (cf. Figures 1 and 2a).

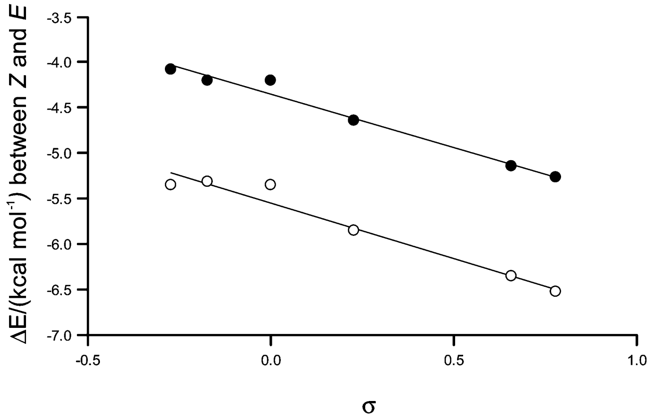


Figure 4. Energy difference between the *Z* and *E* conformers for phenyl substituted phenyl acetates (**4**) vs Hammett substituent constant σ^{20}: HF/6-31G* values (○); MP2/6-31G* values (●).

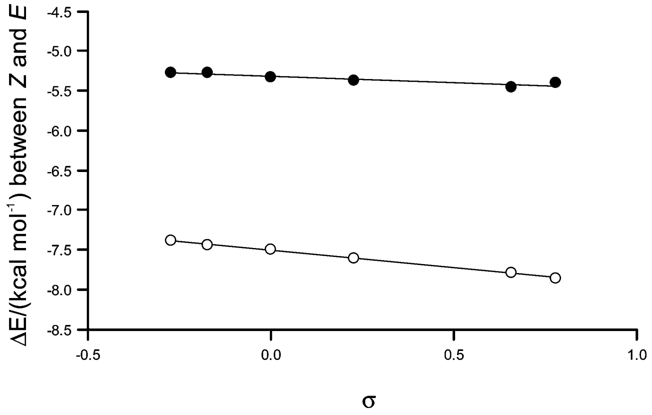


Figure 5. Energy difference between the *Z* and *E* conformers for phenyl substituted phenyl trifluoroacetates (**5**) vs Hammett substituent constant σ^{20}: HF/6-31G* values (○); MP2/6-31G* values (●).

According to HF energies, for three (X = MeO, Me or H) of the six trifluoroacetic acid esters *Z*_90 is the most stable *Z* conformer (Table 3). Also in these cases, however, the energy difference between *Z*_60 and *Z*_90 is only 0.09−0.12 kcal mol^{-1}. The stability differences between the *E* and *Z* conformers for the phenyl ester studied (Tables 1 and 2) are on average somewhat lower than those previously observed for methyl acetate (8.5 kcal mol^{-1})[11] but on the same level or higher than those observed for methyl, fluoromethyl, difluoromethyl, or trifluoromethyl formates (1.14−5.03 kcal mol^{-1} enthalpy differences).[12] The higher preference of the *Z* over the *E* conformer in series **5** as compared with series **4** obviously is due to the higher steric hindrance in series **5**. A clear dependence of the stability difference between the *Z* and *E* conformers (ΔE) on substitution is seen in both series **4** and **5** and at both HF/6-31G* and MP2/6-31G* levels (Tables 1, 2, and 5; Figures 4 and 5). *Electron-withdrawing phenyl substituents systematically increase the preference of the Z isomer*. This result is just opposite to the conclusions drawn previously in the literature for alkyl formates: electron-withdrawing alkyl groups have been suggested to prefer the *E* conformer.[9,10,12] In our compounds the substituent situates at the remote *para*-position of the phenyl group. Any steric effects, heavy atom effects or adjacent polar bond effects which can contribute to the *E*−*Z* energy difference of halogen substituted alkyl formates can be excluded in the present case. Therefore, the substituent effect on the *E*−*Z* stability difference observed for series **4** and **5** can be attributed to the electronic effects only. This conclusion is convincingly supported by the excellent correlations between the ΔE energy

TABLE 5: Statistical Data for the Correlations of the $E-Z$ Energy Difference ΔE and Hammett Substituent Constant σ for Phenyl Acetates 4a−f and Phenyl Trifluoroacetates 5a−f

	HF/6-31G*		MP2/6-31G*	
series	slope	R^a	slope	R^a
4	-1.23 ± 0.12	0.9812	-1.18 ± 0.09	0.9894
5	-0.45 ± 0.01	0.9987	-0.16 ± 0.03	0.9204

[a] Correlation coeffcient.

SCHEME 4

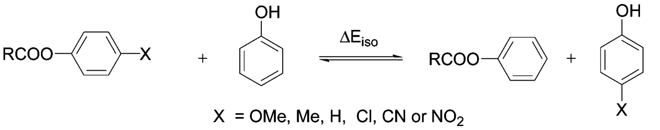


TABLE 6: Calculated Energies, ΔE_{Iso}, of the Isodesmic Reaction Shown in Scheme 4 for $RCOOC_6H_4$-*p*-X (Series 4, R = CH_3; Series 5, R = CF_3)[a,b]

ΔE_{iso} for Series **4**

	Z_60		E_90	
X	in hartrees	in kcal mol^{-1}	in hartrees	in kcal mol^{-1}
OMe	0.0020244	1.270	0.0020544	1.289
Me	0.0006057	0.380	0.0006857	0.430
H	0	0	0	0
Cl	−0.0003777	−0.237	−0.0011671	−0.732
CN	−0.0023552	−1.478	−0.0039352	−2.469
NO_2	−0.0031893	−2.001	−0.0050493	−3.168

ΔE_{iso} for Series **5**

	Z_most stable[c]		E_90	
X	in hartrees	in kcal mol^{-1}	in hartrees	in kcal mol^{-1}
OMe	0.0024344	1.528	0.0026144	1.641
Me	0.0008757	0.550	0.0009657	0.606
H	0	0	0	0
Cl	−0.0014771	−0.927	−0.0016271	−1.021
CN	−0.0047052	−2.953	−0.0051652	−3.241
NO_2	−0.0060393	−3.790	−0.0066293	−4.160

[a] A negative value indicates the substituted derivative to be less stable than the parent compound. [b] The heat of formation energies for the substituted phenols are given in the Supporting Information. The heat of formation energies for the esters are given in Tables 1 and 2. [c] Z_90 for X = OMe, Me, H; Z_60 for X = Cl, CN, NO_2.

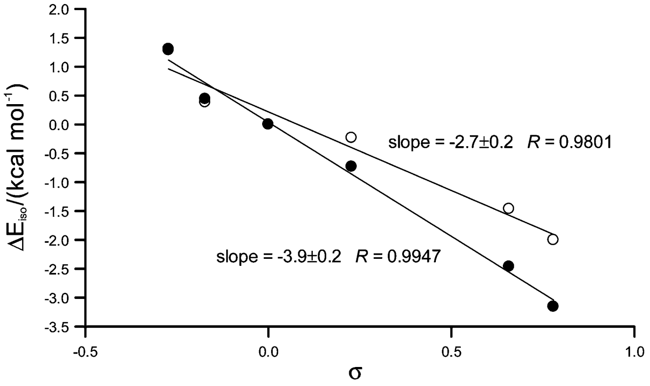


Figure 6. Energies (HF/6-31G*) of the isodesmic reaction (Scheme 4) for series **4** vs Hammett substituent constant σ. The notations are as follows: *Z*_60 (○); *E*_90 (●).

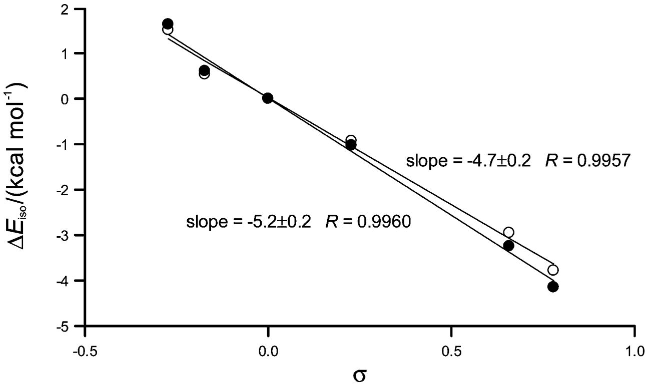


Figure 7. Energies (HF/6-31G*) of the isodesmic reaction (Scheme 4) for series **5** vs Hammett substituent constant σ. The notations are as follows: Z_most stable (Z_90 for X = OMe, Me, H; Z_60 for X = Cl, CN, NO_2) (○); *E*_90 (●).

values and the Hammett substituent constants σ of the phenyl substituents (Table 5, Figures 4 and 5—for series **4** the correlation is better at the MP2/6-31G* level while for series **5** the correlation is better at the HF/6-31G* level). In both series, the sensitivity of the ΔE(HF/6-31G*) values to substitution is higher than the sensitivity of ΔE(MP2/6-31G*) values. Further, the dependence of the energy difference ΔE on substitution is remarkably more significant for phenyl acetates (**4**) than for phenyl trifluoroacetates (**5**) at both levels of the calculations.

Isodesmic Reaction Energies. That the EW substituents increase the preference of the *Z* conformer can mean that they influence only on the stability of the *Z* conformer or on that of the *E* conformer or on the stabilities of both of them. We have previously shown by the isodesmic calculations on PM3 level that EW phenyl substituents decrease the stability of the *Z* conformer of phenyl acetates, dichloroacetates and trifluoroacetates.[14] Now we have verified this effect by ab initio calculations and studied the influence of the phenyl substituent X (relative to X = H) on the stabilities of ester series **4** and **5** (cf. Scheme 4). For both ester series and for both the *Z* and *E* forms unambiguous results are obtained (Table 6; Figures 6 and 7). The electron-donating substituents stabilize the ester structure relative to the unsubstituted one while the electron-withdrawing phenyl substituents clearly destabilize it. The slopes for the correlations of ΔE_{iso} vs Hammett substituent constant σ are for the *E* conformers *clearly higher* than those for the Z conformers in both series **4** (Figure 6) and **5** (Figure 7). This means that the stabilizing/destabilizing effect of the phenyl substituent is on the *E* conformer stronger than on the *Z* conformer. This behavior explains the observed substituent effect on the stability difference between the two conformers: EW substituents increase the preference of the *Z* conformer (Tables 1 and 2; Figures 4 and 5).

Effect of Substitution on Bond Lengths, Bond Orders, and Orbital Occupancies. To better understand (i) the preference for *Z* ($\tau_1 = 0°$) and *E* ($\tau_1 = 180°$) conformations over the other ones ($0° < \tau_1 < 180°$), (ii) the preference of *Z* over *E*, and (iii) the effect of substituents on the stability of these two conformers as well as (iv) the substituent effect on the relative stability of the most stable *E* and *Z* forms with respect to τ_2, we analyzed the effect of phenyl substitution on the C2=O3, C2−O4 and O4−C5 bond lengths and bond orders as well as on the occupancies of some relevant orbitals. Bond length, bond order, and orbital occupancy data are collected in Tables S1−S18 in the Supporting Information. The statistical data concerning the correlations of bond lengths are given in Table 7, and those concerning bond orders are given in Table 8. For both phenyl acetates (**4**) and phenyl trifluoroacetates (**5**) and for both their *E* and *Z* conformers the bond lengths C2−O4, C2=O3 and O4−C5 studied correlate nicely with the Hammett substituent constant σ (Table 7). Excellent correlations are observed in each case. Negative slopes are observed for C2=O3 and O4−C5

TABLE 7: Statistical Data for the Correlations of Some Bond Lengths with Hammett Substituent Constants *σ* for Series 4a−f and 5a−f

line	series/conformation	bond length vs *σ*	slope ± s^a	R^b
1	**4**/*Z*_60	*r*(C2═O3)	−0.0018 ± 0.0001	0.9948
2	**4**/*E*_90	*r*(C2═O3)	−0.0035 ± 0.0002	0.9960
3	**5**/*Z*_most stable[c]	*r*(C2═O3)	−0.0015 ± 0.0001	0.9931
4	**5**/*E*_90	*r*(C2═O3)	−0.0030 ± 0.0002	0.9949
5	**4**/*Z*_60	*r*(C2−O4)	0.0078 ± 0.0005	0.9932
6	**4**/*E*_90	*r*(C2−O4)	0.0096 ± 0.0005	0.9950
7	**5**/*Z*_most stable[c]	*r*(C2−O4)	0.0060 ± 0.0004	0.9893
8	**5**/*E*_90	*r*(C2−O4)	0.0090 ± 0.0007	0.9880
9	**4**/*Z*_60	*r*(O4−C5)	−0.0122 ± 0.0007	0.9937
10	**4**/*E*_90	*r*(O4−C5)	−0.0114 ± 0.0005	0.9963
11	**5**/*Z*_most stable[c]	*r*(O4−C5)	−0.0117 ± 0.0008	0.9911
12	**5**/*E*_90	*r*(O4−C5)	−0.0111 ± 0.0005	0.9957

[a] Standard deviation. [b] Correlation coefficient. [c] Z_90 for X = OMe, Me, H; Z_60 for X = Cl, CN, NO_2.

TABLE 8: Statistical Data for the Correlations of Bond Orders with Hammett Substituent Constants *σ* for Series 4a−f and 5a−f

line	series/conformation	bond order vs *σ*	slope ± s^a	R^b
1	**4**/*Z*_60	*b-o*(C2═O3)	0.0106 ± 0.0008	0.9891
2	**4**/*E*_90	*b-o*(C2═O3)	0.0213 ± 0.0010	0.9954
3	**5**/*Z*_most stable[c]	*b-o*(C2═O3)	0.0104 ± 0.0011	0.9796
4	**5**/*E*_90	*b-o*(C2═O3)	0.0201 ± 0.0012	0.9932
5	**4**/*Z*_60	*b-o*(C2−O4)	−0.023 ± 0.001	0.9952
6	**4**/*E*_90	*b-o*(C2−O4)	−0.026 ± 0.001	0.9965
7	**5**/*Z*_most stable[c]	*b-o*(C2−O4)	−0.020 ± 0.001	0.9939
8	**5**/*E*_90	*b-o*(C2−O4)	−0.024 ± 0.001	0.9956
9	**4**/*Z*_60	*b-o*(O4−C5)	0.025 ± 0.002	0.9926
10	**4**/*E*_90	*b-o*(O4−C5)	0.020 ± 0.0009	0.9958
11	**5**/*Z*_most stable[c]	*b-o*(O4−C5)	0.023 ± 0.002	0.9886
12	**5**/*E*_90	*b-o*(O4−C5)	0.019 ± 0.001	0.9943

[a] Standard deviation. [b] Correlation coefficient. [c] Z_90 for X = OMe, Me, H; Z_60 for X = Cl, CN, NO_2.

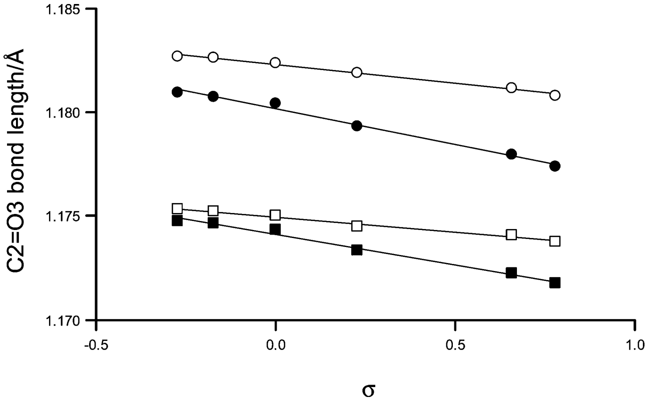
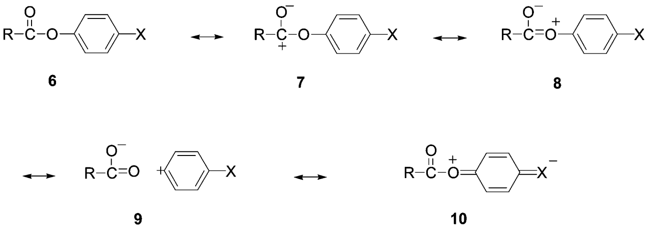


Figure 8. Correlation of the C2═O3 bond length for the most stable *Z* (*Z*_60 for **4a**−**f** and for **5d**−**f**; *Z*_90 for **5a**−**c**) and *E* (*E*_90) conformers for series **4** and **5** vs Hammett substituent constant *σ*. The notations are as follows: *Z* for series **4** (○); *E* for series **4** (●); *Z* for series **5** (□); *E* for series **5** (■).

SCHEME 5



bonds (Table 7, lines 1−4 and 9−12) and positive ones for the C2−O4 bond (Table 7, lines 5−8). In other words, EW substituents affect elongation of the bond between the carbonyl carbon and the ether oxygen while they affect shortening of the bond between the carbonyl carbon and the carbonyl oxygen and that between the ether oxygen and the phenyl ring (cf. also Figure 8). When the corresponding bond orders are correlated with *σ*, opposite signs of the slopes are observed (Table 8). So for instance the bond order between the ether oxygen and the carbonyl carbon is increased by ED substituents while it is decreased by EW substituents (Table 8, lines 5−8). The C═O bond (C2═O3) behaves oppositely, its bond order is decreased by ED substituents and increased by EW substituents (Table 8, lines 1−4). A like shortening of the C(═O)−O bond by electron donating alkyl groups has been previously observed for the *Z* conformer of alkyl acetates; gas electron diffraction data and ab initio calculations were consistent with the preferential *Z* form for these compounds.[8,22] The observed decrease of the C2═O3 and increase of the C2−O4 bond order respond elongation of the C2═O3 bond (cf. Figure 8) and shortening of the C2−O4 bond, respectively, when the ED ability of the phenyl substituent increases and suggest the increase of the contribution of the resonance structures **8** and/or **9** (Scheme 5). When considering in addition the occupancies of the antibonding orbitals around the (C═O)−O−Ph system, the highest occupancies are observed for the π^*(C2═O3) orbitals (Table S7, S9, S11, S13, S15, and S17; Tables 9 and 10), e.g., 0.141 and 0.134 electrons for *Z*_60 and *E*_90 of phenyl acetate (**4c**), respectively. The extent of the σ^*(C2−O3) occupancy is only ca. 12% of that of the π^*(C2═O3) occupancy. Furthermore, the π^*(C2═O3) occupancy is clearly increased along the elongation of the C2═O3 bond while, especially for the *Z* conformer, the occupancy of the σ^*(C2═O3) orbital varies only slightly (Tables 9 and 10). These observations indicate that the main stereoelectronic effect in operation is not the $n_O \rightarrow \sigma^*$(C2═O3) electron donation as suggested previously[3,4] but rather the $n_O \rightarrow \pi^*$(C2═O3) electron donation. The increase of the contribution of the resonance structures **8** and/or **9** (Scheme 5) is equivalent with this molecular orbital view where the lone pair orbital of the ether oxygen and/or σ(O4−C5) donates electron density into π^* orbital of the C2═O3 bond ($n_O \rightarrow \pi^*_{C=O}$ and/or $\sigma \rightarrow \pi^*_{C=O}$ electron donation, respectively).[23,24] This equivalence is convincingly supported by the excellent correlations with negative slopes between π^*(C2═O3) orbital occupancies and Hammett substituent constant *σ* (cf. Table 11) and those with positive slopes between π^*(C2═O3) orbital occupancies and the bond length of the C2═O3 bond (Table 12).

Effect of Phenyl Substituent on the Stability Difference between *E* and *Z* Conformers. When the substituent sensitivity of the bond length of the C2═O3 or C2−O4 bond is compared between the *E* and *Z* conformers (cf. Table 7, lines 1−8) it is seen that for the *E* form the substituent sensitivity is higher than that for the *Z* form in both series **4** and **5**. For the O4−C5 bond, the effects are closer to each other for the *E* and *Z* conformers and the order is reversed. When the substituent sensitivity of the π^*(C2═O3) occupancy is compared between the two conformers a clear difference is also observed. As shown in Figure 9, the substituent sensitivity is with the *E* conformer higher than with the *Z* conformer in both series **4** and **5**. The electron donation to π^*(C2═O3) orbital means electron delocalization and increase in the stability of the molecule structure. Therefore, the observed substituent sensitive difference of the stability between the *E* and *Z* conformers (Table 5, Figures 4

TABLE 9: Oxygen Lone Pair, σ*(C2=O3), and π*(C2=O3) Antibonding Orbital Occupancies for the *Z*_60 and *E*_90 Conformers of Substituted Phenyl Acetates (Series 4)

		*Z*_60					*E*_60				
X	σ[a]	ΣLPO3[b]	ΣLPO4[c]	σ*(C2=O3)	π*(C2=O3)	*r*(C2=O3)	ΣLPO3[b]	ΣLPO4[c]	σ*(C2=O3)	π*(C2=O3)	*r*(C2=O3)
OMe	−0.27	3.8529	3.8179	0.01756	0.14201	1.18267	3.8560	3.8143	0.01412	0.13521	1.18096
Me	−0.17	3.8525	3.8156	0.01759	0.14250	1.18261	3.9561	3.8128	0.01409	0.13542	1.18075
H	0	3.8524	3.8162	0.01755	0.14136	1.18234	3.8560	3.8131	0.01407	0.13434	1.18040
Cl	0.23	3.8514	3.8147	0.01755	0.13993	1.18190	3.8542	3.8144	0.01390	0.13190	1.17932
CN	0.66	3.8509	3.8120	0.01755	0.13694	1.18117	3.8526	3.8141	0.01376	0.12866	1.17796
NO$_2$	0.78	3.8499	3.8104	0.01750	0.13602	1.18077	3.8513	3.8136	0.01368	0.12781	1.17738

[a] Hammett substituent constants from ref 20. [b] The sum of the O3 lone pair occupancies. [c] The sum of the O4 lone pair occuopancies.

TABLE 10: Oxygen Lone Pair, σ*(C2=O3), and π*(C2=O3) Antibonding Orbital Occupancies for the *Z*_Most Stable[a] and *E*_90 Conformers of Substituted Phenyl Trifluoroacetates (Series 5)

		*Z*_most stable[a]					*E*_90				
X	σ[b]	ΣLPO3[c]	ΣLPO4[d]	σ*(C2=O3)	π*(C2=O3)	*r*(C2=O3)	ΣLPO3[c]	ΣLPO4[d]	σ*(C2=O3)	π*(C2=O3)	*r*(C2=O3)
OMe	−0.27	3.8484	3.8013	0.01649	0.14202	1.175327	3.8540	3.7986	0.01313	0.13550	1.174770
Me	−0.17	3.8479	3.8000	0.01642	0.14250	1.175220	3.8534	3.7969	0.01308	0.13593	1.174620
H	0	3.8482	3.8001	0.01638	0.14113	1.174990	3.8534	3.7975	0.01305	0.13451	1.174320
Cl	0.23	3.8475	3.8023	0.01621	0.13844	1.174500	3.8522	3.7999	0.01283	0.13121	1.173310
CN	0.66	3.8471	3.7981	0.01625	0.13656	1.174083	3.8507	3.7999	0.01264	0.12832	1.172212
NO$_2$	0.78	3.8461	3.7971	0.01615	0.13573	1.173750	3.8496	3.7995	0.01253	0.12749	1.171740

[a] Z_90 for X = OMe, Me, H; Z_60 for X = Cl, CN, NO$_2$. [b] Hammett substituent constants from ref 20. [c] The sum of the O3 lone pair occupancies. [d] The sum of the O4 lone pair occuopancies.

TABLE 11: Statistical Data for the Correlations of the Occupancy of the π*(C2=O3) Antibonding Orbital with Hammett Substituent Constants σ for Series 4a−f and 5a−f

line	series/conformation	slope ± *s*[a]	*R*[b]
1	**4**/*Z*_60	−0.0062 ± 0.0005	0.9879
2	**4**/*E*_90	−0.0076 ± 0.0005	0.9924
3	**5**/*Z*_most stable[c]	−0.0065 ± 0.0006	0.9823
4	**5**/*E*_90	−0.0084 ± 0.0007	0.9869

[a] Standard deviation. [b] Correlation coefficient. [c] Z_90 for X = OMe, Me, H; Z_60 for X = Cl, CN, NO$_2$.

TABLE 12: Statistical Data for the Cross-correlations of the Occupancy of the π* (C2=O3) Antibonding Orbital vs the Bond Length *r*(C2=O3) for Series 4a−f and 5a−f

line	series/conformation	slope ± *s*[a]	*R*[b]
1	**4**/*Z*_60	3.44 ± 0.18	0.9946
2	**4**/*E*_90	2.21 ± 0.08	0.9971
3	**5**/*Z*_most stable[c]	4.48 ± 0.31	0.9903
4	**5**/*E*_90	2.85 ± 0.15	0.9947

[a] Standard deviation. [b] Correlation coefficient. [c] Z_90 for X = OMe, Me, H; Z_60 for X = Cl, CN, NO$_2$.

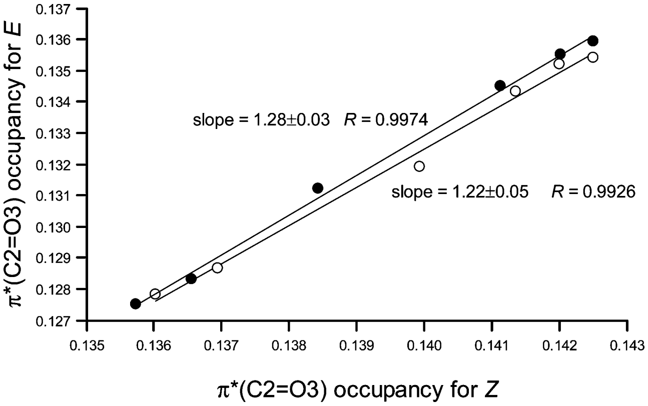


Figure 9. Cross-correlations between the occupancy of the π*(C2=O3) antibonding orbital for the most stable *E* conformer (*E*_90) vs that for the most stable *Z* conformer (*Z*_60 for series **4a−f** and for **5 d−f**; *Z*_90 for **5a−c**): series **4** (○); series **5** (●).

and 5) can be attributed to the aforementioned difference between the *E* and *Z* conformers: EW substituents decrease the electron delocalization with both the *E* and *Z* conformers but they do that *more* with the *E* conformer than with the *Z* conformer. As discussed above, the difference in the substituent effect on the stability of the *E* and *Z* conformers is distinctly seen by the isodesmic results in Figures 6 and 7. The slopes for the correlations of ΔE_{iso} vs Hammett substituent constant σ are for the *E* conformer *clearly higher* than for the Z conformer in both series **4** (Figure 6) and **5** (Figure 7).

The Effect of Phenyl Substitution on τ_2. The magnitude of the π*(C2=O3) occupancy is somewhat higher with the *Z* conformers than with the *E* conformers (Tables 9 and 10; Figure 9). The corresponding difference is seen in the bond lengths. For instance, for phenyl acetate (**4c**), the C2=O3 bond length is 1.18234 Å for *Z*_60 (Table S1) while it is 1.18040 Å for *E*_90 (Table S2). As discussed above, destabilizing steric effects in the *E* conformations obviously are significant for the stability difference between the *E* and *Z* conformers. In light of the present data, the more efficient electron delocalization in the *Z* conformer also is significant. One interesting point is that the most favorable orientation of the phenyl ring (value of τ_2) for the *Z* conformer ($\tau_1 = 0°$) systematically depends on the Hammett substituent constant σ (Figure 10). The value of τ_2 is the higher the higher is the electron-donating ability of the phenyl substituent. Further, the two lone pair orbitals of both the carbonyl oxygen (O3) and the ether oxygen (O4) are differently occupied suggesting nonequivalence of the lone pair orbitals in the case of the two oxygens and for the both conformers (Tables S6, S8, S10, S12, S14, and S16). That is to say, the present results give support for the previous suggestions that the ether oxygen is not sp^3 hybridized.[25,26] When the phenyl substituent effect on the sum of LPO4's is considered (Tables 9 and 10) it is seen that despite the increase in the occupancy of the π*(C2=O3) antibonding orbital by ED substituents also the sum of the occupancies of the lone pair orbitals of both the ether oxygen and the carbonyl oxygen in most cases systematically increase. Obviously the net effect is that electron density from the substituted aromatic ring is donated to the ester moiety to a greater amount the more electron donating the phenyl substituent is. The gained electron density is seen in the

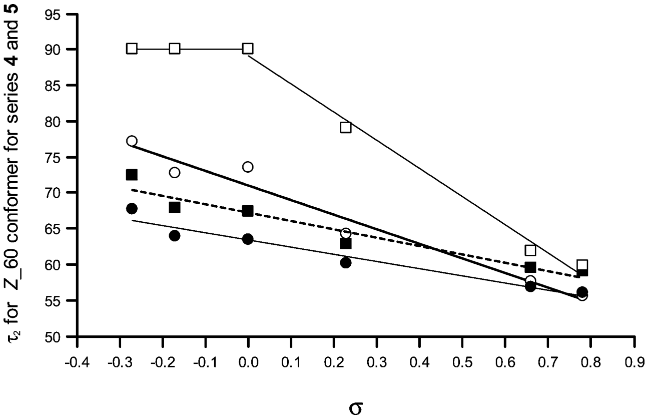


Figure 10. Values of the torsional angle τ_2 for vs the Hammett substituent constant σ: series **4** HF/6-31G* values (○); series **4** MP2/6-31G* values (●); series **5** HF/6-31G* values (□); series **5** MP2/6-31G* values (■).

increased occupancy of the oxygens and of the π^*(C2═O3) antibonding orbital.

We still studied in more detail the difference between the activity of stereoelectronic effects in the *Z* and *E* conformers. It has been observed that in general there prevails a stereoelectronic preference for conformations in which the best donor lone pair or bond is antiperiplanar to the best acceptor bond.[3,26,27] The following (i) donor capability order: $n_N > n_O > \sigma_{C-C}, \sigma_{C-H} > \sigma_{C-X}$ (X = N > O > S > halogens) and (ii) decreasing order of reactivity for the acceptor orbitals: π^*(C═O) > σ^*(C−X) > σ^*(C−O) > σ^*(C−N) > σ^*(C−C), σ^*(C−H) have been observed.[27] If we assume that the ether oxygen is sp^2 hybridized there are four modes of stereoelectronic effects to be considered between lone pair/bonding orbitals and antibonding orbitals in the *Z* conformation: n_O(π-type) → π^*(C2═O3), n_O(σ-type) → σ^*(C2═O3), σ(C1−C2) → σ^*(O4−C5), and σ(O4−C5) → σ^*(C1−C2) electron donations. In the *E* conformation there are four possible modes of stereoelectronic effects: n_O(π-type) → π^*(C2═O3), n_O(σ-type) → σ^*(C1−C2), σ(O4−C5) → σ^*(C2═O3), and σ(C2═O3) → σ^*(O4−C5) electron donations. Excellent correlations with the slope of −1 were observed when correlating π^*(C2═O3) antibonding occupancy with the occupancy of one of the lone pairs of the ether oxygen (LPO4b) for both the *E*_90 and *Z*_90 conformations and in both series **4** and **5** (cf. Table 13, lines 8 and 14, and Table 14, lines 8 and 14). Good correlations are also observed between σ^*(C2═O3) occupancy and LPO4b for *Z*_90 and between σ^*(C1−C2) occupancy and LPO4b for *E*_90, but the numerical values for the slopes are very small. For the other possible electron donations any other relevant correlations were not observed.

We interpret these observations so that when the plane of the carbonyl group and that of the phenyl ring are orthogonal the ether oxygen has sp^2 character and the π-type lone pair can interact with the π^*(C2═O3) antibonding orbital while its interaction with the phenyl ring is interrupted. In both the *Z* and *E* conformations obviously prevails a balance between the steric demand, electron pair-electron pair repulsion, dipole−dipole interactions *and* the favorable electron delocalization. In the *E* conformation the steric effects obviously dominate adjusting the most stable conformation to $\tau_2 = 90°$, the aforementioned electronic interactions prevailing. In the *Z* conformations the planar form with $\tau_2 = 0°$ is the sterically most restricted. The presence of a hydrogen bond between the carbonyl carbon and the *o*-hydrogen of the phenyl group could not be verified. If a hydrogen bond existed, it could adjust τ_2 but its strength should depend on the electron-donating ability of the substituent, and this should affect the distance between the *o*-carbon and *o*-hydrogen. The lengths of the $C_{ortho}-H_{ortho}$ bonds stayed, however, constant in both series when substitution was varied (Table S21). The trends in the changes in $C5-C_{ortho}-H_{ortho}$ angles with varying substitution are also quite similar for series **4** and **5** (Table S22). The balance between the other effects and the most favorable electron delocalization (including both the interaction of the ether oxygen lone pairs with the phenyl ring and with the carbonyl group) is achieved with τ_2 ca. 60°. There seems to prevail a substituent dependent interplay of conjugation of the oxygen lone pairs with C═O and the phenyl ring. Therefore, there obviously occurs a change in the hybridization of the ether oxygen between the sp^3 and sp^2 hybridizations when the electron-donating ability of the phenyl substituent is changed; the change in τ_2 is the consequence. Figure 10 highly corroborates these conclusions and further shows that series **4** and **5** behave quite similarly in that respect, especially when MP2/6-31G* values are considered. The value

TABLE 13: Slopes and Correlation Coefficients *R* for Different Possible Electron Donations for the *Z*_60,[a] *Z*_90, and *E*_90 Conformations for Phenyl Substituted Phenyl Acetates 4

	correlation	slope	R^b
1	π^*(C2−O3) vs n(LPO4a) for *Z*_60	−2.5 ± 1.7	0.5986
2	π^*(C2−O3) vs n(LPO4b) for *Z*_60	0.83 ± 0.13	0.9559
3	σ^*(C2−O3) vs n(LPO4a) for *Z*_60	−0.018 ± 0.021	0.3935
4	σ^*(C2−O3) vs n(LPO4b) for *Z*_60	0.006 ± 0.003	0.6951
5	σ^*(O4−C5) vs σ(C1−C2) for *Z*_60	9.7 ± 1.2	0.9694
6	σ^*(C1−C2) vs σ(O4−C5) for *Z*_60	−3.4 ± 0.3	0.9837
7	π^*(C2−O3) vs n(LPO4a) for *Z*_90	1.5 ± 0.2	0.9709
8	π^*(C2−O3) vs n(LPO4b) for *Z*_90	**−0.99 ± 0.02**	**0.9992**
9	σ^*(C2−O3) vs n(LPO4a) for *Z*_90	0.10 ± 0.02	0.9531
10	σ^*(C2−O3) vs n(LPO4b) for *Z*_90	−0.068 ± 0.004	0.9917
11	σ^*(O4−C5) vs σ(C1−C2) for *Z*_90	20 ± 6	0.8582
12	σ^*(C1−C2) vs σ(O4−C5) for *Z*_90	−5.0 ± 0.6	0.9689
13	π^*(C2−O3) vs n(LPO4a) for *E*_90	1.07 ± 0.16	0.9590
14	π^*(C2−O3) vs n(LPO4b) for *E*_90	**−1.08 ± 0.04**	**0.9971**
15	σ^*(C1−C2) vs n(LPO4a) for *E*_90	0.17 ± 0.01	0.9898
16	σ^*(C1−C2) vs n(LPO4b) for *E*_90	−0.16 ± 0.007	0.9958
17	σ^*(C2−O3) vs σ(O4−C5) for *E*_90	−1.25 ± 0.17	0.9644
18	σ^*(O4−C5) vs σ(C2−O3) for *E*_90	−25 ± 7	0.8724

[a] The value of τ_2 varies with substitution; cf. Table 3. [b] Correlation coefficient.

TABLE 14: Slopes and Correlation Coefficients *R* for Different Possible Electron Donations for the *Z*_60,[a] *Z*_90, and *E*_90 Conformations for Phenyl Substituted Phenyl Trifluoroacetates 5

	correlation	slope	R^b
1	π^*(C2−O3) vs n(LPO4a) for *Z*_60	2.6 ± 0.8	0.8580
2	π^*(C2−O3) vs n(LPO4b) for *Z*_60	−0.71 ± 0.32	0.7434
3	σ^*(C2−O3) vs n(LPO4a) for *Z*_60	0.24 ± 0.05	0.9258
4	σ^*(C2−O3) vs n(LPO4b) for *Z*_60	−0.069 ± 0.021	0.8540
5	σ^*(O4−C5) vs σ(C1−C2) for *Z*_60	6.6 ± 0.9	0.9681
6	σ^*(C1−C2) vs σ(O4−C5) for *Z*_60	−0.32 ± 0.17	0.6939
7	π^*(C2−O3) vs n(LPO4a) for *Z*_90	2.0 ± 0.4	0.9270
8	π^*(C2−O3) vs n(LPO4b) for *Z*_90	**−1.04 ± 0.04**	**0.9976**
9	σ^*(C2−O3) vs n(LPO4a) for *Z*_90	0.17 ± 0.03	0.9579
10	σ^*(C2−O3) vs n(LPO4b) for *Z*_90	−0.086 ± 0.005	0.9940
11	σ^*(O4−C5) vs σ(C1−C2) for *Z*_90	7.1 ± 0.7	0.9800
12	σ^*(C1−C2) vs σ(O4−C5) for *Z*_90	−0.92 ± 0.25	0.8806
13	π^*(C2−O3) vs n(LPO4a) for *E*_90	1.3 ± 0.3	0.9360
14	π^*(C2−O3) vs n(LPO4b) for *E*_90	**−1.07 ± 0.03**	**0.9983**
15	σ^*(C1−C2) vs n(LPO4a) for *E*_90	0.082 ± 0.018	0.9135
16	σ^*(C1−C2) vs n(LPO4b) for *E*_90	−0.064 ± 0.008	0.9684
17	σ^*(C2−O3) vs σ(O4−C5) for *E*_90	−1.51 ± 0.16	0.9790
18	σ^*(O4−C5) vs σ(C2−O3) for *E*_90	−14 ± 6	0.7830

[a] The value of τ_2 varies with substitution; cf. Table 3. [b] Correlation coefficient.

TABLE 15: Energy, Bond Length, and Orbital Occupancy Data for Phenyl Acetate (4c) at Different Values of τ_1 with the Value of τ_2 = 90°

conformation	energy[a]	C2═O3 bond length	C2−O4 bond length	σ^*(C2═O3) occupancy	π^*(C2═O3) occupancy
0_90[b]	−457.346864	1.18222	1.34215	0.01738	0.14137
30_90	−457.343300	1.18136	1.34713	0.01854	0.12998
60_90	−457.335949	1.17919	1.35963	0.02078	0.10080
90_90	−457.331507	1.17786	1.36667	0.02400	0.08099
120_90	−457.332400	1.17853	1.36008	0.02564	0.09228
150_90	−457.336207	1.17991	1.35123	0.02159	0.11793
180_90[c]	−457.338326	1.18041	1.34799	0.01405	0.13470

[a] In hartrees. [b] Z_90. [c] *E*_90.

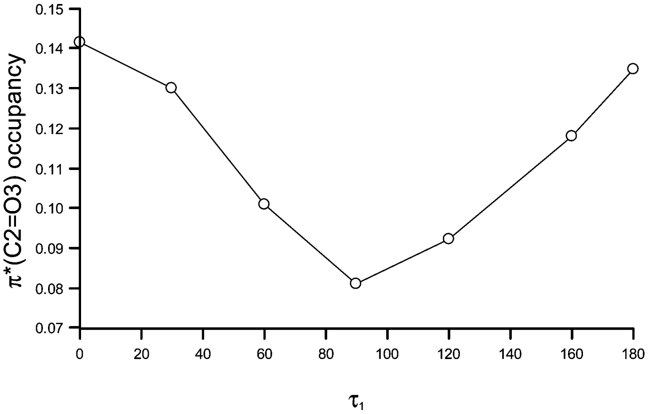


Figure 11. Occupancy of the π^*(C2═O3) antibonding orbital as a function of the dihedral angle τ_1 for phenyl acetate **4c** with $\tau_2 = 90°$.

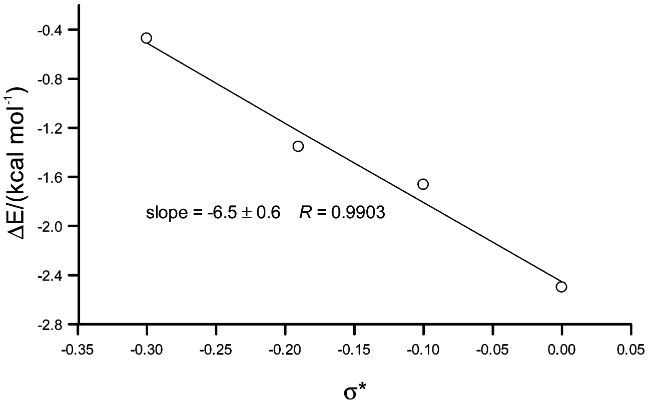


Figure 12. Energy difference between the *Z* and *E* conformers of alkyl formates in acetone-d_6−DMF, 1:1. The energy values are from ref 7.

of τ_2 systematically increases when the electron donating ability of the phenyl substituent increases. With the HF/6-31G* values the orthogonal conformation $\tau_2 = 90°$ is achieved for series **5** with X = H ($\sigma = 0$), and it does not change anymore even if the electron donating ability of the phenyl substituent increases.

τ_1 and the Relative Stability of the Ester Structure. We also analyzed the preference of the *Z* and *E* conformations, i.e., $\tau_1 = 0°$ and $\tau_1 = 180°$, respectively, within the interval $0° \le \tau_1 \le 180°$, with phenyl acetate **4c** used as an example. In Figure 3 are shown the energies of the corresponding conformations as a function of τ_1 ($\tau_2 = 90°$). Table 15 collects the numerical energy values, the bond lengths of C2═O3 and C2−O4 as well the occupancies of the σ^*(C2═O3) and π^*(C2═O3) antibonding orbitals at different values of τ_1. Further data concerning these rotational changes are given in the Supporting Information. Table 15 shows a clear minimum of the π^*(C2═O3) occupancy at $\tau_1 = 90°$ (cf. Figure 11). The highest value is observed for the *Z* conformer ($\tau_1 = 0°$) while the extent of this stereoelectronic effect ($n_O \rightarrow \pi^*_{C=O}$ electron donation) for the *E* conformer ($\tau_1 = 180°$) is only intermediate, obviously due to steric hindrance. The other parameters, energy and bond lengths of the C2═O3 and C2−O4, nicely coincide the variation of the occupancy of the π^*(C2═O3) antibonding orbital. For instance, the maximum π^*(C2═O3) occupancy corresponds to the shortest C2−O4 bond, the most elongated C2═O3 bond and, due to the efficient electron delocalization, also the lowest energy (Table 15). The data also show that in the 90_90 conformation, which possess the least efficient overlap of the lone pair orbital of the ether oxygen with the π^*(C2═O3) antibonding orbital and for which the oxygen lone pair orbital is antiperiplanar with the C2═O3 bond, the $n_O \rightarrow \sigma^*_{C=O}$ electron donation is close to its maximum value even if the extent of that process is considerably lower than the $n_O \rightarrow \pi^*_{C=O}$ electron donation. These results allow us to assume that one *significant factor which prefers the Z and E conformations over the other τ_1 values is the efficient $n_O \rightarrow \pi^*_{C=O}$ electron donation*. This effect seems to compete successfully with the steric hindrance obviously active in the planar *Z* and *E* conformations.

Substituent Effects on Alkyl Formates. As already discussed in the Introduction section, for alkyl esters of formic acid it has been shown that although the *Z* conformer is more stable than the *E* conformer the *E*−*Z* free energy differences (in acetone-d_6−DMF, 1:1) decreases in the order of methyl, ethyl, isopropyl, and *tert*-butyl formates, the values being, respectively, 2.5, 1.67, 1.36, and 0.48 kcal mol^{-1}.[7] This result has been interpreted in terms of steric effects between the alkyl group and the carbonyl oxygen, which decrease the preference of the *Z* conformer when the size of the alkyl group increases. Because we observed for the phenyl esters that the EW/ED properties of the phenyl substituents systematically affect the *E*−*Z* energy difference of these derivatives we also decided to check the situation with the alkyl formates. Interestingly, an excellent correlation (R = 0.9903) is observed between the aforementioned energy values and the polar substituent constant σ^* of the alkyl group (Figure 12). At the same time as the size of the alkyl group increases also its ability to donate electrons increases. The same trend as with the phenyl esters is seen. Increase in the electron donating ability of the alkyl group decreases the preference of the *Z* conformer. With the steric constants E_S the *E*−*Z* energy difference gave the correlation coefficient R = 0.9160 only. We also tried the dual substituent parameter approach by taking into consideration both the electronic (σ^*) and the steric effects (E_S) but the correlation was poor only. Gas electron diffraction data and ab initio calculations have shown for the Z conformer of these same alkyl acetates the shortening of the C(═O)−O bond when the ED ability of the alkyl group increases.[8,22] So we can conclude that also *for the alkyl formates, the ED alkyl groups increase the $n_O \rightarrow \pi^*_{C=O}$ electron donation*. The dependence of ΔE on σ^* (Figure 12) further suggests that like with the phenyl esters the effect is higher on the *E* conformer than on the *Z* conformer.

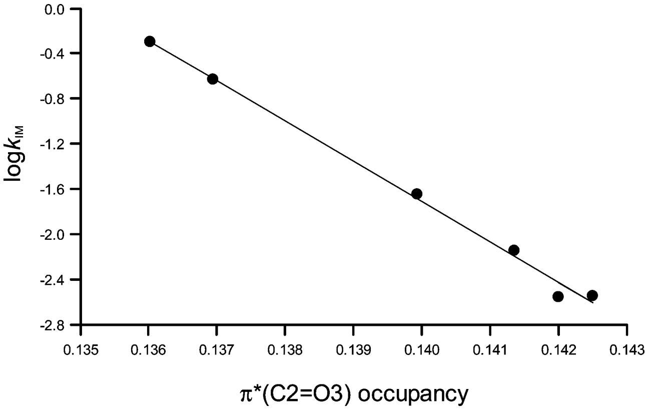
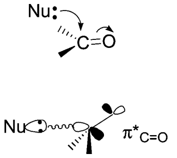


Figure 13. Rate coefficients for the nucleophilic reaction of imidazole with substituted phenyl acetates in aqueous solution at 298.2 K (values from ref 33) vs the π*(C2═O3) occupancy for the *Z* conformer of phenyl acetates.

SCHEME 6



Reactivity Considerations. In nuclephilic acyl substitution reactions of phenyl esters, EW phenyl substituents increase the reactivity while the ED ones decrease it, and positive Hammett reaction constants ρ are observed by eq 1.[13,14,28−32] In eq 1

$$\log(k/k_o) = \rho\sigma \tag{1}$$

k_o is the rate coefficient for the reaction of the unsubstituted derivative and k that for the substituted one. Without excluding the substituent effects on the transition state stability, we have recently suggested that the ground state stabilization of the esters by ED substituents significantly contributes to the observed decrease in reactivity by this type of substituents. Increase in the stability of the ground state leads to increase in $\Delta G^{\neq}$.[13,14] The present study excellently supports that conclusion. The ab initio calculations clearly show that ED substituents stabilize the ester structures studied while EW ones destabilize it. However, the decrease in reactivity can also be understood by a novel way on the molecular orbital basis in terms of stereoelectronic effects. When a nucleophile attacks the carbonyl carbon the decisive interaction is between the HOMO of the nucleophile, which is the lone pair orbital of the nucleophile, and the LUMO of the reacting compound, which is the $\pi^*_{C=O}$ (Scheme 6).[27] Because the ED phenyl substituents increase the efficiency of the $n_O \rightarrow \pi^*_{C=O}$ electron donation we can conclude that they decrease the ability of $\pi^*_{C=O}$ to interact with the nucleophile lone pair orbital: decrease in reactivity is the consequence. The EW substituents affect oppositely. By decreasing the interaction between the ether oxygen lone pair and $\pi^*_{C=O}$ orbitals they make the interaction between the lone pair orbital of the attacking nucleophile and the $\pi^*_{C=O}$ orbital of the reacting compound easier and thereby increase the reaction rate. This suggestion is unequivocally supported by the correlations shown in Figures 13 and 14. Rate coefficients of the nucleophilic reaction of imidazole with phenyl substituted phenyl acetates[33] excellently correlate with the π*(C2═O3) occupancy of the ester substrate (Figure 13) as do the rate coefficients of the neutral hydrolysis of phenyl substituted phenyl trifluoroacetates[31,34] with the π*(C2═O3) occupancy of the corresponding esters (Figure 14). *In both nucleophilic acyl substitution reactions, the higher the π*(C2═O3) occupancy of the reacting ester is the lower is the reaction rate*. The Hammett substituent constants have been originally determined via the substituent effects on the acidity of benzoic acid[35] and used thereafter to correlate a countless amount of experimental parameters of aromatic derivatives.[29,30,36] The now observed excellent correlation of the computational data as well with the Hammett σ makes understandable the universality of these substituent constants.

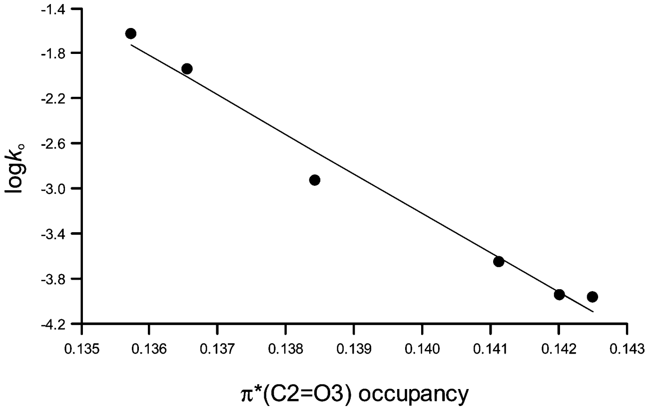


Figure 14. Rate coefficients for the neutral hydrolysis of phenyl substituted phenyl trifluoroacetates in 3.89 M water in acetonitrile at 298.2 K (values from refs 31 and 34) vs the π*(C2═O3) occupancy for the *Z* conformer of phenyl trifluoroacetates.

Conclusions

It has been shown by ab initio calculations that the stability of the *Z* conformer is significantly higher than that of the *E* conformer for phenyl substituted phenyl acetates (**4**) and phenyl trifluoroacetates (**5**). In both series EW substituents still increase the preference of the Z conformer. The reason for that was shown by the isodesmic reaction applied. The EW substituents decrease the stability of both the *E* and *Z* conformers, but the substituent effect on the stability of the *E* conformer is higher than on that of the *Z* conformer due to τ_2 conformational variations in the latter case. The molecular orbital view of these effects mainly is the two electron−two orbital interaction: $n_O \rightarrow \pi^*_{C=O}$ electron donation. The extent of that stereoelectronic effect is diminished by EW substituents and it is enhanced by ED substituents, substituent dependence of that process being for the *E* conformer higher than for the *Z* conformer. The dependence of the efficiency of the $n_O \rightarrow \pi^*_{C=O}$ electron donation on τ_1 reveals the significance of this stereoelectronic interaction for the preference of the planar *Z* ($\tau_1 = 0°$) and *E* ($\tau_1 = 180°$) conformations over the other ones ($0° < \tau_1 < 180°$).

These results also can be used to explain the well-known decrease in reactivity of the esters by ED substituents in nucleophilic acyl substitution reactions. ED substituents increase the stability of the esters and therefore increase the value of $\Delta G^{\neq}$. On the basis of the present results still another explanation can be given. ED/EW substituents adjust the availability of the $\pi^*_{C=O}$ antibonding orbital to interaction with the attacking nucleophile lone pair orbital and therefore affect the reactivity: EW substituents increase and ED substituents decrease it. Excellent correlations with experimental rate coefficient data support this conclusion. Several quite recent studies have shown that stereoelectronic effects are not anomalous but common in all organic molecules.[26,37] We therefore predict that future investigations will show that also the substituent effects on reactivity more often than not can be explained on the basis of substituent effects on orbital interactions.

Supporting Information Available: The bond-order and bond length data of the relevant bonds as well as the relevant orbital occupancy data of the *Z*_60, *Z*_90, and *E*_90 conformations of **4a−f** and **5a−f** (Tables S1−S18). The bond-order, bond length, orbital occupancy and energy data for **4c** with different values of τ_1 when τ_2 is 90° (Table S19). Heat of formation values for the substituted phenols (Table S20). Values for the $C_{ortho}-H_{ortho}$ distances (Table S21) and for the $C5-C_{ortho}-H_{ortho}$ angles (Table S22) for series **4** and **5**. Cartesian coordinates and structures for the relevant ester structures. The ester structures are collected in the zip file named as Structures.zip. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Jones; G. I. L.; Owen, N. L. *J. Mol. Struct.* **1973**, *18*, 1.

(2) Exner, O. In *The Chemistry of Double-Bonded Functional Groups*; Patai, S., Ed.; Interscience: London, 1977; p 1.

(3) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley-Interscience: New York, 1994; pp 618−621.

(4) Larson, J. R.; Epiotis, N. D.; Bernardi, F. *J. Am. Chem. Soc.* **1978**, *100*, 5713.

(5) Wang, X.; Houk, K. N. *J. Am. Chem. Soc.* **1988**, *110*, 1870.

(6) Wiberg, K. B.; Laidig, K. E. *J. Am. Chem. Soc.* **1988**, *110*, 1872.

(7) Grindley, T. B. *Tetrahedron Lett.* **1982**, *23*, 1757.

(8) Takeuchi, H.; Matsuoka, T.; Tsuji, T.; Takshima, H.; Ito. M.; Konaka, S. *J. Mol. Srtuct.* **1998**, *471*, 275.

(9) Pawar, D. M.; Khalil, A. A.; Hooks, D. R.; Collins, K.; Elliot, T.; Stafford, J.; Smith, L.; Noe, E, A. *J. Am. Chem. Soc.* **1998**, *120*, 2108.

(10) Pawar, D. M.; Sims, Y. S.; Moton, D. M.; Noe, E. A. *J. Mol. Struct. (THEOCHEM)* **2003**, *626*, 159.

(11) Wiberg, K. B.; Wong, M. W. *J. Am. Chem. Soc.* **1993**, *115*, 1078.

(12) Uchimaru, T.; Tsuzuki, S.; Sugie, M.; Sekiya, A. *Chem. Phys.* **2004**, *299*, 25.

(13) Neuvonen, H.; Neuvonen, K. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1497.

(14) Neuvonen, H.; Neuvonen, K.; Koch, A.; Kleinpeter, E.; Pasanen, P. *J. Org. Chem.*, **2002**, *67*, 6995.

(15) Neuvonen, H.; Neuvonen, K.; Pasanen, P. *J. Org. Chem.* **2004**, *69*, 3794.

(16) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A. 11.3; Gaussian, Inc.: Pittsburgh, PA, 1998.

(17) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A., *Ab initio Molecular Orbital Theory*; Wiley: New York, 1986.

(18) NBO 5.0. Glendening, E. D.; Badenhoop, J. K.; Reed, A. E.; Carpenter, J. E.; Bohmann, J. A.; Morales, C. M.; Weinhold, F. Theoretical Chemistry Institute, University of Wisconsin: Madison, WI, 2001.

(19) Wiberg, K. B. *Tetrahedron* **1968**, *24*, 1083.

(20) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

(21) Byun, K.; Mo, Y.; Gao, J. *J. Am. Chem. Soc.* **2001**, *123*, 3974.

(22) Takeuchi, H.; Enmi, J.; Onozaki, M.; Egawa, T.; Konaka, S. *J. Phys. Chem.* **1994**, *98*, 8632.

(23) Kallies, B.; Mitzner, R. *J. Chem. Soc., Perkin Trans. 2* **1996**, *1397*, 1403.

(24) Kallies, B.; Kleinpeter, E.; Koch, A.; Mitzner, R. *J. Mol. Struct.* **1997**, *435*, 123.

(25) Juaristi, E.; Cuevas, G. *Tetrahedron* **1992**, 5019 and references therein.

(26) Alabugin, I. V.; Manoharan, M.; Zeidan, T. A. *J. Am. Chem. Soc.* **2003**, *125*, 14014.

(27) Kirby, A. J. *Stereoelectronic Effects*; Oxford University Press: Oxford, England, 1996; p 13.

(28) Bruice, C.; Mayahi, F. *J. Am. Chem. Soc.* **1960**, *82*, 3067.

(29) Kirby, A. J. In *Comprehensive Chemical Kinetics*; Bamford, C. H., Tipper, C. F. H., Eds.; Elsevier Publishing Company: Amsterdam, 1980; Vol. 10; Chapter 2, p 161.

(30) Connors, K. A. *Structure Reactivity Relationships: the Study of Reaction Rates in Solution*; VCH Publishers: New York, 1990; Chapter 7, p 311.

(31) Neuvonen, H. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1141.

(32) Neuvonen, H. *J. Chem. Soc., Perkin Trans. 2* **1987**, 159.

(33) Williams, A.; Naylor, R. A. *J. Chem. Soc. B* **1971**, 1967.

(34) Neuvonen, H. Unpublished results.

(35) Hammett, L. P. *Chem. Rev.* **1935**, *11*, 125. Hammett, L. P. *Physical Organic Chemistry*, McGraw-Hill: New York, 1940.

(36) Exner, O. In *Advances in Linear Free Energy Relationships*; Chapman, N. B., Shorter, J., Eds.; Plenum Press: London, 1972; p 1.

(37) See for example: Alabugin, A. V. *J. Org. Chem.* **2000**, *65*, 3910. Kleinpeter, E.; Taddei, F.; Wacker, P. *Chem.−Eur. J.*, **2003**, *9*, 1360. Alabugin, I. V.; Manoharan, M.; Peabody, S.; Weihold, F. *J. Am. Chem. Soc.* **2003**, *125*, 5973. Martínez-Mayorga, K.; Juaristi, E.; Cuevas, G. *J. Org. Chem.* **2004**, *126*, 7266.