A DFT-based model for calculating solvolytic reactivity. The nucleofugality of aliphatic carboxylates in terms of $N_f$ parameters

Bernard Denegri,* Mirela Matić and Olga Kronja

The most comprehensive nucleofugality scale, based on the correlation eqn (1) and solvolytic rate constants of benzhydrylium derivatives, has recently been proposed by Mayr and co-workers (Acc. Chem. Res., 2010, 43, 1537–1549). In this work, the possibility of employing quantum chemical calculations in further determination of nucleofugality ($N_f$) parameters of leaving groups is explored. Whereas the heterolytic transition state of benzhydryl carboxylate cannot be optimized by quantum chemical calculations, the possibility of an alternative model reaction is examined in order to obtain nucleofugality parameters of various aliphatic carboxylates, which can properly be included in the current nucleofugality scale. For that purpose, ground and transition state structures have been optimized for the proposed model reaction, which includes anchimerically assisted heterolytic dissociation of cis-2,3-dihydroxycyclopropyl trans-carboxylates. The validity of the model reaction as well as of applied DFT methods in the presence of the IEFPCM solvation model is verified by correlating calculated free energies of activation of the model reaction with literature experimental data for solvolysis of reference dianisylmethyl carboxylates. For this purpose the ability of several functionals (including popular B3LYP) is examined, among which the M06-2X gives the best results. The very good correlation indicates acceptable accurate relative reactivities of aliphatic carboxylates, and enables the estimation of rate constants for solvolysis of other dianisylmethyl carboxylates in aqueous ethanol mixtures, from which the corresponding $N_f$ parameters are determined using mentioned Mayr’s equation. In addition, DFT calculations confirm the previous experimental observation that the abilities of aliphatic carboxylate leaving groups in solution are governed by the inductive effect of substituents attached to the carboxyl group.

Introduction

Carboxylate derivatives have wide applications in synthetic chemistry, and they are involved in many metabolic processes. Aliphatic carboxylates, as well as substituted benzoates and sulfonates, solvolyze in a weakly basic and neutral medium via the $S_N_1$ mechanism if a stabilized carbocation intermediate is produced in the heterolytic step. Under these conditions, the reactivity of leaving groups (nucleofugality) is one of the crucial parameters that determines heterolytic rates for esters in general.

The wider knowledge of the nucleofugality of aliphatic carboxylates would not only provide a better understanding of the mechanism of solvolysis of these esters but could also be utilized in everyday laboratory practice for planning organic syntheses. Nucleofugalities of 11 aliphatic carboxylates in various solvents have already been examined experimentally.

In general, the reactivity of leaving groups (nucleofugality) plays a very important role in defining the rate of heterolytic bond dissociation, which is the rate determining step of many organic reactions. Therefore, this is one of the unavoidable subjects of all general textbooks on organic chemistry as well as of mechanistically oriented textbooks. Nevertheless, little attention has been paid to the quantification of nucleofugalities, mostly due to the fact that a wide variation of leaving groups in the same type of substrate (e.g. 1-adamantly-LG or 1-phenylethyl-LG) exceeds the range of the heterolytic reactivity which is accessible by kinetic measurements.

†Electronic supplementary information (ESI) available: Calculated nucleofugalities of various carboxylates in ethanol-water mixtures and other reactivity data, correlation plots of model $\Delta G^\ddagger$ versus the corresponding solvolysis $\Delta G^\ddagger$, optimized geometries of cis-2,3-dihydroxycyclopropyl carboxylates and of related heterolytic transition states, coordinates and calculated energies for optimized geometries, literature data and references on reactivity and acidity. See DOI: 10.1039/c4ob00563e
the qualitative rule that abilities of leaving groups are arranged according to acidities of their conjugate Brønsted acids. The basic flaw of such an approach arises from the fact that the variability of the intrinsic barriers in heterolysis of substrates with different types of leaving groups is neglected (e.g. halide, carboxylate, carbonate, phenolate, etc.).

To extend the range of quantifying the leaving group ability, which is fairly limited by using the single type of substrate, an electrofugality scale based on 39 benzhydrylium carbocations, which cover 18 orders of magnitude in reactivity, has recently been established. Employing that scale and the special LFER equation [eqn (1)], abilities of structurally diverse leaving groups have been determined in the range of 12 orders of magnitude for a certain solvent. In this equation, established by Mayr, the contributions of an electrofuge (the alkyl/aryl part of a substrate that in the heterolytic process gives a carbocation) and a nucleofuge to the overall solvolytic reactivity of a substrate are separated. This enables the main practical application of the scales; the estimation of reactivities of substrates that consist of any combination of an electrofuge and a nucleofuge in a given solvent at 25 °C.

\[
\log k (25 \, ^\circ C) = s_f (E_f + N_f) \tag{1}
\]

Parameters in eqn (1) are the solvolytic rate constant of a substrate at 25 °C \(k\), the nucleofuge-specific parameters \(N_f\) (the negative intercept on the abscissa of the \(\log k \) versus \(E_f\) correlation line) and \(s_f\) (the slope of the correlation line), and the electrofugality parameter \(E_f\) (the independent variable that quantifies the reactivity of an electrofuge). Using the reference electrofuges, leaving groups of a wide range of reactivity can further be included in the nucleofugality scale. From the solvolytic rate constants of a series of benzhydrylium derivatives (which contain a leaving group of interest) measured in a given solvent, the nucleofuge-specific parameters for a certain combination of a leaving group and a solvent can be determined from the log \(k \) versus \(E_f\) correlation line.

Nevertheless, a general scale of nucleofugality, which implies exclusively intrinsic abilities of leaving groups, cannot exist since it is not possible to separate completely the reactivity of a leaving group from the influences of solvation effects and structural features of electrofuges. In this LFER model influences of solvation effects are associated with the nucleofugality, defined by two nucleofuge-specific parameters \((N_f\) and \(s_f\)), which specify the reactivity of a certain leaving group in a given solvent. In fact, the \(N_f\) parameter determines the basic reactivity of the certain combination, while the \(s_f\) parameter for diverse leaving group/solvent combinations varies within a limited range and does not affect solvolytic rate constants significantly. However, the slope parameter \(s_f\) can be employed as a useful tool for observing fine influences of general solvation effects on relative reactivities, as well as influences of the structure of a leaving group on the relative position of TS on the reaction coordinate.

An analogous model has already been applied by Mayr and co-workers in developing the scales of electrophilicity and nucleophilicity, providing a simple method for estimating the rates of combination reactions between various types of electrophiles and nucleophiles, in which a bond is formed. Since the unassisted bond fission and bond formation often determine the reaction rates, these two analogous models can be utilized for planning organic syntheses.

In order to make the electrofugality/nucleofugality model broadly used, two major tasks should be accomplished. One is that diverse types of electrofuges must be included in the electrofugality scale. The abundance of literature data on solvolytic rates of various chlorides and bromides enables determination of electrofugality \((E_f\) parameters) for many aromatic and non-aromatic electrofuges. Independently from that, due to variation in structures, there is an enormous number of possible leaving groups that should be included in the nucleofugality scale. However, since insufficient literature data are available to support that work, it implies extensive experimental work and high material cost. Consequently, the inclusion of quantum-chemical calculations in determining nucleofugalties appears to be an eligible way for further developing the \(N_f\) scale at this stage. From the theoretical point of view, the nucleofugality as the property of a leaving group has already been investigated and described by some authors. In this work, we utilize DFT calculations and the transition state theory in order to obtain \(N_f\) parameters of many aliphatic carboxylates.

**Results and discussion**

**A model reaction based on heterolysis of cyclopropyl carboxylates**

The transition state of a pure heterolysis reaction that produces a positively charged electrofuge (carbocation) and a negatively charged nucleofuge (leaving group) can be optimized neither in the gas phase nor in the presence of the solvation model. Therefore, our primary aim here has been to establish a suitable model reaction whose calculated rate is determined by the heterolytic displacement of the aliphatic carboxylate leaving group. In such a case, the series of optimized model aliphatic carboxylates and their heterolytic transition states should yield calculated barriers which correlate acceptably well with experimental barriers for solvolyses of the corresponding carboxylates. Good candidates for providing experimental solvolytic barriers for such correlation are dianisylmethyl carboxylates because substrates constituted from this common electrofuge undergo \(S_{N1}\) reactions, in which the heterolytic alkyl-oxygen bond fission occurs, determining the overall reaction rate. Additionally, dianisylmethyl is a reference electrofuge in the electrofugality scale with the electrofugality value being zero \((E_f = 0)\). For that purpose, all available literature data on the solvolytic reactivity of dianisylmethyl carboxylates in various aqueous ethanol mixtures at 25 °C were collected (Scheme 1, Table S5†). Thus, 11 aliphatic carboxylates constitute the experimental set of reference substrates.
whose solvolytic free energies of activation cover the range of reactivity of as much as 10 kcal mol$^{-1}$. Furthermore, we have searched for an appropriate model whose computed barriers for displacement of the carboxylate leaving groups correlate well with the experimental barriers for solvolysis of the reference dianisylmethyl carboxylates presented in Scheme 1. To enable the optimization of the heterolytic transition state, which is characterized as a first-order saddle point on the PES, the departure of a leaving group in a model reaction is concerted with the anchimeric assistance of a neighboring group. Despite the concerted process instead of pure heterolysis, the structure of leaving groups should remain a major structural feature that determines relative reactivities of modeled substrates.$^{1,15}$

It has already been shown in the literature that in solvolysis of cyclopropyl derivatives the departure of the leaving group is concerted with the ring opening, i.e. the backside σ-participation occurs.$^6$ In those reactions, the opening of the cyclopropyl ring is controlled by the orbital symmetry rules. Thus, disrotatory ring opening occurs, moving outward the ring substituents on C2 and C3, which in the ground state are in the trans-position toward the leaving group (Scheme 2).

Consequently, 2,3-dihydroxycyclopropyl carboxylates (diOHCP-$\text{R}$-carboxylates) were examined as candidates for the model reaction. Two hydroxyl groups were placed onto the cyclopropyl ring (C2 and C3), both in the trans position toward the leaving group (Scheme 2). It turned out that these $\text{meso}$-derivatives ($\text{cis}$-2,3-dihydroxycyclopropyl $\text{trans}$-carboxylates) constituted good substrates for the model reaction since the absolute values of the imaginary frequencies of the transition states optimized with different DFT methods, as well as intrinsic reaction coordinate (IRC) calculations, indicated that indeed the heterolytic transition structures were located on the PES. The role of the hydroxyl substituents here is to increase the reactivities of modeled cyclopropyl carboxylates in order to obtain pure transition state structures rather than loose cation–anion complexes on the potential energy maximum, characterized by the low absolute value of the imaginary mode (see the Computational methods section).

Quantum chemical calculations for the model reactions have been performed by the GAUSSIAN 09 suite of programs,$^{16}$ utilizing four DFT methods (M06-2X$^{17}$, B3LYP$^{18}$, mPW3PBE$^{19}$ and B97D$^{20}$) in combination with several basis sets. The ground state structures of eleven 2,3-dihydroxycyclopropyl carboxylates and the corresponding transition state structures given in Scheme 2 have been optimized. Influences of solvation effects are included by employing the IEFPCM$^{21}$ solvation model in both optimization and frequency calculations. The important role of the solvation model here is to diminish strong electrostatic interactions caused by the charge separation inside the transition states and thus facilitate their optimizations. Furthermore, experiments have already shown that the nature of the electronic effects exerted by substituents attached to the carboxyl group is not the same in the gas phase and in protic solvents.$^3,6,^b,22$ Consequently, the additional role of IEFPCM is to suppress the intrinsic polarizability effect of the substituents that dominates the stabilization of carboxylate free anions in the gas phase.$^{22}$

The optimized structures of the starting diOHCP-$\text{R}$–fluoroacetate and diOHCP-$\text{R}$–trichloroacetate as well as of the corresponding transition state structures obtained at the M06-2X/AUG-cc-pVTZ level of theory are presented in Fig. 1. Other geometries optimized at this level are presented in the ESL.$^\dagger$ The structures of the transition states obtained with all DFT methods used indicate that the model substrates indeed react...
in a concerted process, in which simultaneous elongation of the C1–O and C2–C3 bonds occurs, due to anchimeric assistance of the σ-electrons of the C2–C3 bond. The C1–O and C2–C3 distances in the transition state structures increase gradually as the reactivity of the leaving group decreases (Table S4†), which is in accordance with the concept of the later transition states for the less reactive substrates. In a later transition state the cleavage of the C1–O bond is more advanced, as well as the cyclopropyl ring opening. For example, in the TS of diOHCP–heptafluorobutanoate (at the M06-2X/AUG-cc-pVTZ level), which is the most reactive carboxylates among the 11 reference diOHCP–carboxylates, the C1–O distance is 1.78 Å and the C2–C3 distance is 1.93 Å, whereas in the TS of diOHCP–2,2-dimethylpropanoate (the least reactive carboxylate in the series) those distances are 1.84 Å and 2.04 Å, respectively.

Intrinsic reaction coordinate (IRC) calculations have been utilized to verify that the transition state structures are associated with the given processes. The disrotatory ring opening process is unambiguously supported with the disrotatory cyclopropyl ring closure observed on the path from the corresponding TS to the starting cis-2,3-dihydroxycyclopropyl trans-carboxylates. On the reaction coordinate, TS leads to the ground state structure in which the hydroxyl groups are in the cis position exclusively, and the LG is trans toward the hydroxyl groups. In the opposite direction, IRC calculations follow the downward energy path, affording the dihydroxyallyl cation and a carboxylate anion.

**Correlation of the experimental and computed barriers**

Only substrates which contain leaving groups of the same type, i.e. with the identical functional group and structural features that exert the same type of stabilizing effect in free anions in solution, are included in the correlation between experimental and calculated barriers. Due to complex specific solvation effects in the region of the reaction site, the lack of discrete solvent molecules can affect the calculated relative reactivities (i.e. the correlation) among different types of substrates (e.g. halides, sulfonates, carboxylates, etc.). At this stage, the aim with the model reaction is to obtain relative reactivities of the leaving groups, which are as accurate as possible rather than to establish the universal model reaction with significant deviations from experimental values. The practical reasons for this approach are given in the Introduction. Furthermore, much more available experimental data are required for investigating and establishing the universal application of the model reaction. Consequently, in this work only the series of aliphatic carboxylates is considered.

Using thermochemical data calculated by four DFT methods under standard conditions in the combination with various basis sets, free energies of activation (ΔG‡model) were obtained for the model reaction with 11 reference carboxylate leaving groups (Scheme 2). The model reaction barrier heights are given in Table S3†. Expectedly, the barriers calculated by the M06-2X functional are higher than those calculated by other three functionals. In any case, for the further analysis, a systematic underestimation of the model reaction barrier heights does not play a significant role because relative, but not absolute, heterolytic reactivities are considered.

At this point, results obtained by DFT methods in combination with several basis sets are evaluated by correlating the calculated ΔG‡ of the model reaction (ΔG‡model) for various carboxylate leaving groups (given in Table S3†) with the literature ΔG‡ obtained in solvolysis of the corresponding diansilylmethyl carboxylates in 80% ethanol at 25 °C (Table S5†). The correlation plot in which ΔG‡model values are calculated at the M06-2X/AUG-cc-pVTZ level of theory is shown in Fig. 2. Other correlation plots are presented in the ESI (Fig. S1–S8†). The performances of different methods in correlating with the experimental data are compared in Table 1.

Although 11 reference aliphatic carboxylates were chosen for the correlation, in some cases less data points were included in the correlation (column n of Table 1) because those heterolytic transition states of the model reaction had been characterized as second-order saddle points and, finally, were not taken into account for obtaining ΔG‡model. The presence of an additional imaginary mode affects the thermochemistry calculations significantly, causing inconsistencies in the correlation with the experimental data. The imaginary frequency in these cases is associated with the rotation of moieties about the partially broken C1–O bond. Whenever it was possible, the next lowest-energy conformation of such diOHCP–carboxylate and the corresponding heterolytic transition state were included in the model reaction in order to calculate ΔG‡model for a certain carboxylate. Such an exception is diOHCP–heptafluorobutrate calculated at the M06-2X/AUG-cc-pVTZ level of theory.

**Fig. 2** Correlation of experimental free energies of activation (in kcal mol⁻¹) for solvolyses of diansilylmethyl carboxylates in 80% ethanol versus free energies of activation (in kcal mol⁻¹) for heterolysis of cis-2,3-dihydroxycyclopropyl carboxylates calculated at the M06-2X/AUG-cc-pVTZ level of theory in the presence of the IEPCM solvation model (solvent = water).
Several transition states in the series of reference carboxylates optimized by the B3LYP and mPW3PBE functionals have been characterized as first-order saddle points. On the other hand, all but one of the transition state structures optimized by the M06-2X functional in combination with all basis sets used have afforded only the expected imaginary mode associated with stretching of the partially broken C1–O bond. The exception is dIOHCPr-trichloroacetate optimized using the AUG-cc-pVDZ basis set. In addition, all transition state structures optimized with the B97D functional have also been characterized as first-order saddle points. Nevertheless, the statistical data in Table 1 reveal that the quality of the correlation is the best with barriers calculated by the M06-2X hybrid functional (Fig. 2). Despite the differences in the quality of the correlations, all employed DFT methods in the combination with the IEFPCM solvation model yield relative reactivities of carboxylates very close to experimental ones (i.e. the slopes of the correlation plots range from 0.8 to 1.3), additionally demonstrating the applicability of the model reaction for calculating leaving group abilities. Furthermore, the impact of Pople-type basis sets and Dunning’s correlation consistent basis sets on the quality of the correlation has briefly been examined. Data presented in Table 1 show that the choice of the basis set does not influence the quality of the correlation to the extent which the choice of the DFT method does.

Since the model reaction gives the best results with the M06-2X functional, we have also examined the possibility of employing the SMB model as a continuum solvation model for mimicking solvation effects of water. However, $\Delta G^1$ (dianisylmethyl carboxylates) versus $\Delta G^\text{model}$ correlation reveals that heterolytic free energies of activation for some model carboxylates, calculated using this solvation model, deviate considerably from the correlation line (Fig. S9 and S10†). Thus, the IEFPCM model has been used as the appropriate solvation model for the model reaction.

Along with the uncharged 2,3-dihydroxycyclopropyl carboxylate model, we have also examined the applicability of a negatively charged 2-oxyethyl carboxylate model in the same manner using the M06-2X and B3LYP methods. It has been reported elsewhere that a suitable model reaction for determining the reactivity of differently substituted benzoates is the epoxy ring formation reaction, starting from 2-oxyethyl benzoates (−OCH₂CH₂–Bz), in which the intramolecular backside $n$-electron attack of the negatively charged oxygen is a driving force for the carbon–benzoate bond fission. Unlike with substituted benzoates, both optimized ground states and heterolytic transition states of several reference 2-oxyethyl carboxylates afforded the additional imaginary mode, affecting the thermodynamics data and preventing the construction of the adequate correlation line. For these reasons, the model reaction with 2-oxyethyl carboxylates was abandoned. Although the 2,3-dihydroxycyclopropyl carboxylate model also suffers from similar problems (but to a substantial lesser extent), affording the additional imaginary mode for some transition states, second-order saddle points are avoided with the proper choice of the DFT method.

Since the best regression line had been obtained with the data for the model reaction calculated at the M06-2X/AUG-cc-pVTZ level of theory (Table 1), the same set of $\Delta G^\text{model}$ was further correlated with the literature barriers (given in Table S5†) for solvolyses of the corresponding dianisylmethyl carboxylates in 90%, 70% and 60% binary mixtures of ethanol and water. The correlation parameters are presented in Table 2. In analyzing the mean absolute errors (MAE) of statistical data for the correlation between experimental free energies of activation for solvolysis of dianisylmethyl carboxylates in 80% ethanol at 25 °C and free energies of activation for heterolysis of cis-2,3-dihydroxycyclopropyl carboxylates calculated with different methods under standard conditions.

<table>
<thead>
<tr>
<th>Methoda</th>
<th>Basis set</th>
<th>Slopeb</th>
<th>Interceptc</th>
<th>rde</th>
<th>MAEf</th>
<th>nfi</th>
</tr>
</thead>
<tbody>
<tr>
<td>M06-2X</td>
<td>AUG-cc-pVTZ</td>
<td>0.89 ± 0.03</td>
<td>−6.85 ± 0.85</td>
<td>0.996</td>
<td>0.25</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>AUG-cc-pVDZ</td>
<td>0.90 ± 0.04</td>
<td>−7.91 ± 1.34</td>
<td>0.991</td>
<td>0.31</td>
<td>10</td>
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<td></td>
<td>6-311+G(3df,2p)</td>
<td>0.93 ± 0.04</td>
<td>−8.70 ± 1.10</td>
<td>0.993</td>
<td>0.30</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>6-31+G(d)</td>
<td>0.83 ± 0.03</td>
<td>−6.44 ± 0.98</td>
<td>0.994</td>
<td>0.30</td>
<td>11</td>
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<tr>
<td>B3LYP</td>
<td>AUG-cc-pVTZ</td>
<td>1.27 ± 0.06</td>
<td>−4.48 ± 1.06</td>
<td>0.994</td>
<td>0.33</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>6-311+G(3df,2p)</td>
<td>1.24 ± 0.06</td>
<td>−4.25 ± 1.13</td>
<td>0.992</td>
<td>0.31</td>
<td>9</td>
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<tr>
<td></td>
<td>6-31+G(d)</td>
<td>1.10 ± 0.11</td>
<td>−5.15 ± 2.61</td>
<td>0.968</td>
<td>0.66</td>
<td>7</td>
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<tr>
<td>mPW3PBE</td>
<td>AUG-cc-pVTZ</td>
<td>1.23 ± 0.06</td>
<td>2.36 ± 0.87</td>
<td>0.989</td>
<td>0.39</td>
<td>11</td>
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<tr>
<td></td>
<td>6-311+G(3df,2p)</td>
<td>1.25 ± 0.06</td>
<td>1.62 ± 0.89</td>
<td>0.990</td>
<td>0.38</td>
<td>11</td>
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</tbody>
</table>

a All calculations were carried out using the IEFPCM solvation model (solvent = water). Free energies of activation used in correlations are given in Table S3 ($\Delta G^\text{model}$) and Table S5 (experimental $\Delta G$ with literature references). Correlation plots are presented in the ESI (Fig. S1–S8). b Errors shown are standard errors. c In kcal mol$^{-1}$. d Correlation coefficient. e Mean absolute error; in kcal mol$^{-1}$. f The number of correlation data points.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Slopeb</th>
<th>Interceptc</th>
<th>rde</th>
<th>MAEf</th>
<th>nfi</th>
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<td>90E10W</td>
<td>0.89 ± 0.02</td>
<td>−6.61 ± 0.75</td>
<td>0.997</td>
<td>0.24</td>
<td>11</td>
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<tr>
<td>70E30W</td>
<td>0.90 ± 0.03</td>
<td>−7.46 ± 0.90</td>
<td>0.995</td>
<td>0.25</td>
<td>11</td>
</tr>
<tr>
<td>60E40W</td>
<td>0.90 ± 0.03</td>
<td>−7.86 ± 0.95</td>
<td>0.994</td>
<td>0.30</td>
<td>11</td>
</tr>
</tbody>
</table>

a Binary solvents are v/v at 25 °C. E = ethanol, W = water. Free energies of activation used in correlations are given in Table S3 ($\Delta G^\text{model}$) and Table S5 (experimental $\Delta G$ with literature references). Correlation plots are presented in the ESI (Fig. S11–S13). b Errors shown are standard errors. c In kcal mol$^{-1}$. d Correlation coefficient. e Mean absolute error; in kcal mol$^{-1}$. f The number of correlation data points.
regression for these solvents (0.24–0.30 kcal mol$^{-1}$), including 80% ethanol (Table 1), it must be borne in mind that both the set of barriers used in the correlation (experimental $\Delta G^0$ and $\Delta G^{\text{model}}$) cover the ranges of as much as 10 kcal mol$^{-1}$. Interestingly, the quality of the regression slightly decreases as the water content of the binary mixture increases even though water has been set as the solvent in the IEFPCM solvation model. Anyhow, the role of the solvation model here is not to mimic the specific solvent, but to facilitate the optimization of TS, as well as to induce electronic effects of the substituents which operate in a real solution. Since the electrostatic component of the solvation model is crucial for this purpose, water has been chosen as the solvent due to its high dielectric constant.

**Calculated $N_f$ parameters of the reference aliphatic carboxylates**

The main purpose of the model reaction and the above presented correlation plots is to obtain nucleofugality parameters of various carboxylate leaving groups, which can be included in Mayr’s nucleofugality scale. The applicability of this approach can finally be verified by comparing calculated $N_f$ parameters of 11 reference carboxylates ($N_f^{\text{calc}}$) with previously published experimental $N_f$ parameters.

From the given $\Delta G^0$ (dianisylmethyl carboxylates) versus $\Delta G^{\text{model}}$ (M06-2X/AUG-cc-pVTZ level) plots, free energies of activation ($\Delta G^{\text{calc}}$) for solvolyses of the reference dianisylmethyl carboxylates in four mentioned ethanol–water binary mixtures were calculated. Data for $\Delta G^{\text{calc}}$ and the corresponding log $k^{\text{calc}}$ for 80% ethanol are given in Table 3, whereas data for 90%, 70% and 60% ethanol are given in Table S1.$^\dagger$

Although log $k$ versus $E_t$ plots have originally been established for determining $N_t$ and $s_t$ parameters of any leaving group, a certain $N_t$ parameter can also be determined from a single log $k$ of an appropriate benzhydryl substrate and a good guess for an $s_t$ value using eqn (1).$^{3,5}$ It has previously been shown that a linear correlation exists between $s_t$ values and the corresponding log $k$ for solvolysis of dianisylmethyl carboxylates in aqueous ethanol mixtures, which is in accordance with the Hammond postulate.$^3$ Using a certain log $k^{\text{calc}}$ given in Table 3 (or Table S1$^\dagger$) and an appropriate $s_t$ value estimated from the $s_t$ versus log $k$ plots ($s_t^{\text{estim}}$) given in ref. 3, the $N_t$ parameter of each reference carboxylic acid leaving group ($N_t^{\text{calc}}$) was calculated for each given aqueous ethanol mixture. Results are presented and compared with literature experimental data in Tables 3 and S1.$^\dagger$

Comparisons of the calculated with previously published experimental data for solvolysis of dianisylmethyl carboxylates as well as for nucleofugalities of the reference aliphatic carboxylate leaving groups are presented in parentheses as individual deviations from the experimental values. The average deviation for free energies of activation for each solvent (each correlation line) is already expressed in terms of the mean absolute error (MAE) in Tables 1 and 2 (the M06-2X/AUG-cc-pVTZ level of theory). Individual deviations of $\Delta G^{\text{calc}}$ are reflected in the deviations of log $k^{\text{calc}}$ in smaller values due to a smaller range of the corresponding log $k$ values in general. On the other hand, since the units for both log $k^{\text{calc}}$ and $N_f^{\text{calc}}$ represent the orders of magnitude in reactivity, their deviations can be compared. To make the comparison easier, from the individual deviations given in parentheses of Tables 3 and S1.$^\dagger$ mean absolute errors have been calculated for both log $k^{\text{calc}}$ and $N_f^{\text{calc}}$ values for each aqueous ethanol mixture. MAEs for log $k^{\text{calc}}$ are as follows: 0.17 in 90% ethanol, 0.18 in 80% ethanol, 0.18 in 70% ethanol and 0.21 in 60% ethanol, while for $N_f^{\text{calc}}$ they are 0.16, 0.16, 0.18 and 0.23, respectively.

Comparison of the MAE of log $k^{\text{calc}}$ with that of $N_f^{\text{calc}}$ for each binary mixture reveals the similarity of these values as well as their similar trends in the series of 4 mixtures, which unambiguously verifies that reliable $s_t$ parameters ($s_t^{\text{estim}}$) were

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**Table 3** Calculated solvolytic reactivities for the reference dianisylmethyl carboxylates and the corresponding calculated nucleofugalities of carboxylate leaving groups in 80% ethanol

<table>
<thead>
<tr>
<th>Carboxylate</th>
<th>$\Delta G^{\text{calc}}$</th>
<th>$\log k^{\text{calc}}$</th>
<th>$N_f^{\text{estim}}$</th>
<th>$N_f^{\text{calc}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formate</td>
<td>21.06 (+0.59)</td>
<td>$-2.64 (-0.43)$</td>
<td>1.05 (+0.01)</td>
<td>-2.52 (-0.39)</td>
</tr>
<tr>
<td>Acetate</td>
<td>23.26 (+0.29)</td>
<td>$-4.26 (-0.22)$</td>
<td>1.12$^f$</td>
<td>-3.80 (+0.08)</td>
</tr>
<tr>
<td>2-Methylpropanoate</td>
<td>23.36 (-0.12)</td>
<td>$-4.48 (+0.08)$</td>
<td>1.15$^f$</td>
<td>-3.89 (+0.10)</td>
</tr>
<tr>
<td>2,2-Dimethylpropanoate</td>
<td>24.14 (-0.17)</td>
<td>$-4.90 (+0.12)$</td>
<td>1.17$^f$</td>
<td>-4.19 (+0.10)</td>
</tr>
<tr>
<td>Fluoroacetate</td>
<td>20.22 (+0.43)</td>
<td>$-2.03 (-0.32)$</td>
<td>1.02 (+0.02)</td>
<td>-1.99 (-0.27)</td>
</tr>
<tr>
<td>Chloroacetate</td>
<td>19.82 (-0.33)</td>
<td>$-1.73 (+0.24)$</td>
<td>1.01 (+0.00)</td>
<td>-1.72 (+0.23)</td>
</tr>
<tr>
<td>Bromoacetate</td>
<td>20.04 (-0.10)</td>
<td>$-1.90 (+0.07)$</td>
<td>1.01 (+0.01)</td>
<td>-1.88 (+0.05)</td>
</tr>
<tr>
<td>Dichloroacetate</td>
<td>18.11 (-0.08)</td>
<td>$-0.48 (+0.06)$</td>
<td>0.94 (+0.03)</td>
<td>-0.51 (+0.08)</td>
</tr>
<tr>
<td>Trifluoroacetate</td>
<td>15.62 (-0.24)</td>
<td>1.34 (+0.18)</td>
<td>0.85 (+0.03)</td>
<td>1.58 (+0.16)</td>
</tr>
<tr>
<td>Trichloroacetate</td>
<td>16.18 (+0.21)</td>
<td>0.93 (+0.16)</td>
<td>0.87 (+0.03)</td>
<td>1.07 (-0.14)</td>
</tr>
<tr>
<td>Heptfluorobutanoate</td>
<td>15.49 (+0.20)</td>
<td>1.44 (-0.14)</td>
<td>0.85 (-0.03)</td>
<td>1.69 (-0.11)</td>
</tr>
</tbody>
</table>

$^a$ In kcal mol$^{-1}$. Obtained from $\Delta G^0$ (dianisylmethyl carboxylates) versus $\Delta G^{\text{model}}$ (M06-2X/AUG-cc-pVTZ level) plots given in Tables 1 and 2. Deviations from experimental values ($\Delta G^{\text{calc}} - \Delta G^0$) are given in parentheses. $^b$ Logarithms of solvolytic first-order rate constants at 25 °C obtained from $\Delta G^{\text{calc}}$. Deviations from experimental values (log $k^{\text{calc}}$ – log $k$) are given in parentheses. $^c$’$s_t$ parameters estimated from the correlation of $s_t$ versus log $k$ (25 °C) for solvolysis of dianisylmethyl carboxylates in an appropriate solvent. The correlation plots are presented in ref. 3. Deviations from experimental $s_t$ values ($s_t^{\text{estim}} - s_t$) are given in parentheses. $^d$ Calculated from the log $k^{\text{calc}}$ and appropriate $s_t^{\text{estim}}$ using eqn (1). The $E_t$ value for the dianisylmethyl electrofuge is 0.00. Deviations from experimental values ($N_f^{\text{calc}} - N_f$) are given in parentheses. $^e$ Experimental data are given in ref. 5 and 3. $^f$ $s_t$ parameters were previously obtained from the $s_t$ versus log $k$ (25 °C) correlation plots and presented in ref. 3.
obtained using the \( n_i \) versus \( \log k \) (25 °C) correlation plots given in ref. 3, also indicating the reliable method for estimating these parameters. Moreover, the deviations of \( \Delta G^\text{calc} \) values given in parentheses (Tables 3 and S1†) are in the range of those determined experimentally from the genuine log \( k/E \) correlation plots.\(^3\) It follows that the main source of an error in the \( N_i^\text{calc} \) parameter lies in an error of \( \Delta G^\text{calc} \), and, consequently, in the quality of the \( \Delta G^\text{calc} \) (dianisylmethyl carboxylates) versus \( \Delta G^\text{model} \) regression line, in general (Tables 1 and 2).

To assess the significance of the MAE in \( N_i^\text{calc} \) parameters for these four series of aqueous ethanol mixtures, the range of \( N_i^\text{calc} \) values of the reference carboxylates must be taken into account. For example, MAE of 0.16 unit for 80% ethanol refers to the range of as much as 6 units of \( N_i \). The significance of these errors is further diminished if the whole range of the current \( N_i \) scale, consisting of diverse types of nucleofuges, is taken into account (about 12 units for 80% ethanol).\(^3,5\) Of course, the use of experimentally obtained \( N_i \) and \( s_i \) parameters is recommended, but this analysis of the errors provides additional verification for both the model reaction and the \( \Delta G^\text{calc} \) (dianisylmethyl carboxylates) versus \( \Delta G^\text{model} \) correlation, based on computations at the M06-2X/AUG-cc-pVTZ level of theory, in determining solvolytic reactivities and \( N_i^\text{calc} \) parameters of other aliphatic carboxylates.

**Calculated solvolytic reactivities of other aliphatic carboxylates**

Geometries of 34 other 2,3-dihydroxycyclopropyl carboxylates and of the corresponding heterolytic transition state structures were optimized at the M06-2X/AUG-cc-pVTZ level of theory in the presence of the IEFPCM solvation model. Using the same method, frequency calculations on these stationary points were carried out in order to obtain heterolytic \( \Delta G^\text{calc} \) values for the model reaction. Diverse carboxylates were included in the model reaction: unsubstituted and unsaturated carboxylates, variously halogenated acetates, propanoates and butanoates; nitro-, cyano-, hydroxy- and oxo-substituted carboxylates, as well as alkyl dicarboxylates and dicarboxylates. Geometries, coordinates and energies of the substrates and the heterolytic transition states are presented in the ESI.\(^†\) From the correlation plots based on the M06-2X/AUG-cc-pVTZ data (given in Tables 1 and 2, as well as in Fig. 2, S11–S13†), in the same manner as for the reference carboxylates, \( \Delta G^\text{calc} \) values for solvolyses of other dianisylmethyl carboxylates in 90%, 80%, 70% and 60% ethanol at 25 °C were obtained. \( \Delta G^\text{calc} \) and the corresponding log \( k^\text{calc} \) are given in Table S2.†

As mentioned above, for reliability of \( N_i^\text{calc} \) values it is crucial that errors of the \( \Delta G^\text{calc} \) values are not significant. In the absence of experimental data the quality of the \( \Delta G^\text{calc} \) values for solvolyses of these carboxylates can be verified only in general. For that purpose two correlations presented in ref. 3 can be used in assessing the calculated results. In order to investigate the influence of the stability of free carboxylate anions in solution on the solvolytic reactivity of carboxylate substrates, the Gibbs free energies of activation of 11 reference dianisylmethyl carboxylates were correlated with standard free energies for dissociations of the corresponding carboxylic acids in water (obtained from literature \( pK_a \) values). A satisfactory good fit with \( r = 0.988 \) and the root mean square error (RMSE) of 0.47 kcal mol\(^{-1}\) was obtained.\(^3\) The correlation plot has a slope of 1.23 and an intercept of 15.27 kcal mol\(^{-1}\). To verify the accuracy of the here obtained \( \Delta G^\text{calc} \), the same type of correlation has been made by employing \( \Delta G^\text{calc} \) of 11 reference carboxylates (Table 3) along with additional \( \Delta G^\text{calc} \) values of 18 other carboxylates (from Table S2†). The standard free energies for dissociations of the corresponding carboxylic acids in water have been taken from the literature (values and references are given in Table S6†). The correlation plot is presented in Fig. 3. The comparison of these two correlation plots reveals that the slopes and intercepts on the ordinate, as well as the correlation coefficients and RMSE (root mean square error) are almost indistinguishable, although different sources of free energies of activation for solvolysis of dianisylmethyl carboxylates are used. The cause of dispersion of the points from the regression line cannot be ascribed only to errors incorporated in \( \Delta G^\text{calc} \), but also to possible errors in \( pK_a \) values (different literature sources) as well as to possible inconsistencies in the variability of intrinsic barriers. In general, the correlation confirms that relative reactivities of aliphatic carboxylates are mainly determined by relative stabilities of free anions in solution, \textit{i.e.} by stabilizing effects present in carboxylate anions in solution. Moreover, the slope larger than unity might indicate that the range of relative Lewis basicities of the carboxylate anions is expanded when the proton counterion is replaced by the benzhydrylum ions.\(^3\)
In one different type of correlation, it has been shown that the logarithms of rate constants for solvolysis of dianisylmethylic acids, substituted with halogens and methyl substituents, correlate satisfactorily well with the Hammett $\sigma_{meta}$ values and $\Sigma \sigma_{meta}$, indicating that the inductive effect on the carboxylate moiety of the transition states plays a major role in determining the relative reactivities of these substrates in solution. The correlation plot has been constructed using data for 9 reference dianisylmethyl carboxylates, affording a slope of 4.73 and an intercept of $-3.85$ ($r = 0.993$; RMSE = 0.24). To examine whether the theory at this level also confirms the influence of the inductive effect on the relative reactivity of this compound, log $k^{calc}$ of 9 reference carboxylates (from Table 3) along with additional log $k^{calc}$ of 11 other carboxylates from Table S2† have been correlated with Hammett $\sigma_{meta}$ values. The correlation is not only extended in reactivity, but also enriched in structures with substituents on the acetate core, which are not present in the correlation with the experimental data. The plot is shown in Fig. 4. The comparison of these plots also does not reveal significant differences between the corresponding regression parameters, which leads to the conclusion that the theory, as well as the experiment, confirms domination of the inductive effects in determining the relative reactivities of aliphatic carboxylates in solution. This is important because it is well known that the intrinsic polarizability of the substituent is the major stabilizing effect on carboxylate ions in the gas phase. Nevertheless, in solution polarizability is overcome by inductive and solvation effects, which is manifested in the inversion of acidities of some carboxylic acids.

Although some inconsistencies can be observed by comparing experimental and calculated log $k$ of dianisylmethyl carboxylates of close solvolytic reactivities, in general, the solvation model utilized here mimics a real solvent reasonably well, which is obvious from this and other correlation plots presented here. In addition, unusually high slope ($\rho = 4.46$) of the plot shown in Fig. 4 does not only indicate that solvolyses of these compounds undergo limited $S_N1$ reaction, but also shows a substantially stronger impact of the inductive effects of substituents on relative reactivities of the aliphatic carboxylates than on relative reactivities of both substituted benzoates ($\rho \approx 1.7$) and benzenesulfonates ($\rho \approx 1.8$). Such behavior is not surprising since the structural variations occur noticeably closer to the reaction center in the series of aliphatic carboxylates, rendering their reactivity significantly more sensitive to the substituent changes.

Calculated $N_f$ parameters of other aliphatic carboxylates

After verification of $\Delta G^{calc}$ and the corresponding log $k^{calc}$ values for solvolyses of dianisylmethyl carboxylates, $N_f^{calc}$ parameters of other 34 carboxylates have been determined for the aqueous ethanol mixtures by inserting the appropriate log $k^{calc}$ and $\sigma_f^{estim}$ values into eqn (1). As with the reference carboxylates, $\sigma_f^{estim}$ parameters have been estimated using the $s_i$ versus log $k$ (dianisylmethyl carboxylates) correlation plots given in ref. 3 and appropriate log $k^{calc}$. $N_f^{calc}$ parameters of other carboxylates are presented in Table S2† along with the corresponding $s_i^{estim}$, log $k^{calc}$ and $\Delta G^{calc}$ values.

Now, the current nucleofugality scale is extended with other variously substituted carboxylates, and the procedure for the fast determination of $N_f^{calc}$ parameters for simple aliphatic carboxylates is established. Nucleofugalities of some carboxylates calculated here in 80% ethanol are compared with literature nucleofugalities of various leaving groups in Fig. 5. The overall nucleofugality of the aliphatic carboxylates for a certain solvent spans the range of 12 orders of magnitude. Although previous examinations have showed that heptafluorobutyrate and trifluoroacetate leaving groups are almost two orders of magnitude less reactive than chloride, the calculations predict that carboxylates can reach the nucleofugality of the most reactive leaving groups – sulfonates. Nevertheless, the nucleofugality of most of the carboxylates is in the range of $-5$ to $2$, which is also the region of reactivity of benzoates, carbonates and substituted phenolates. Analyzing the order of carboxylates on the $N_f$ scale, the influence of the inductive effect becomes also evident at the qualitative level. The more inductive heteroatom or group in the vicinity of the reaction site and the larger number of heteroatoms, as well as their closer position to the reaction site, increase the nucleofugality of a carboxylate leaving group, and the reactivity of a corresponding substrate in general (Tables 3, S1 and S2†). In contrast, the positive inductive effect of alkyl groups (unsubstituted carboxylates) or the negative charge already present in a leaving group (malonate and oxalate) decreases the nucleofugality, positioning such carboxylates to the lower region of the $N_f$ scale.

Although the nucleofugality scale provides useful information on heterolytic reactivities (nucleofugalities) of diverse
leaving groups, the possibility of practical application of \( N_f \) parameters in predicting solvolytic reactivities of various substrates, by employing eqn (1), makes the further development of the scale even more worthwhile. The insight into the range and potency of the \( N_f \) and \( E_f \) scales can be simply illustrated in the following example. Using the \( E_f \) value of \(-8.48\) for the 1-phenylethyl electrofuge and appropriate nucleofugality parameters from Table S2,† half-lives for solvolysis of 1-phenylethyl trinitroacetate (\( N_f^{calc} = 7.49, s_f^{estim} = 0.67 \)) and 1-phenylethyl malonate (\( N_f^{calc} = -4.59, s_f^{estim} = 1.19 \)) in 80% ethanol at 25 °C can be estimated using eqn (1). The half-lives amount to 3 seconds and about 80 million years, respectively. Obviously, the first substrate is very unstable in protic solvents, whereas the \( s_f^{estim} \) value of the latter never occurs. Nevertheless, if the 1-phenylethyl electrofuge in the negatively charged malonate is replaced by a considerably more reactive electrofugality scale, the \( N_f \) value of 2-oxyethyl benzoates, which significantly improved the correlation (calculated \( \Delta G^\dagger \) affects the correlation). Similar behavior of the model was observed when the M06-2X method was utilized. Exp5

Experimental data for carboxylates, as opposed to benzoates, have shown that variation in \( \Delta G^\dagger \) for solvolysis of the series of benzhydryl carboxylates is influenced by both \( \Delta H^\dagger \) and \( \Delta S^\dagger \). In this work, we also observed that experimental \( \Delta G^\dagger \) for solvolyses of the series of dianisylmethyl benzoates correlates better with \( \Delta G_{model}^\dagger \) of diOHCPr–carboxylates than with the corresponding \( \Delta H_{model}^\dagger \) (from Table S3†). Consequently, no approximation was used in the correlation for aliphatic carboxylates. Whereas the 2-oxyethyl model, as mentioned above, shows significant shortcomings when applied to aliphatic carboxylates, the 2,3-dihydroxypropyl model can be definitively considered as the better model for aliphatic carboxylates. In addition, benzoates are not included in this work in order to avoid multiplication of calculated \( N_f^{calc} \) parameters in the situation when the quality of the existed ones cannot be improved. Also, inclusion of other types of substrates in the correlation cannot reduce the errors of \( \Delta G^{calc} \). Consequently, the errors of \( \log k^{calc} \) for solvolysis of dianisylmethyl carboxylates.

Despite the shown shortcomings, the advantage of the 2-oxyethyl model lies in its simple structure, which provides facile geometry optimization, and it should not be rejected in further investigations. On the other hand, the application of 2,3-dihydroxypropyl as the universal model electrofuge in determining \( \log k^{calc} \) and \( N_f^{calc} \) values requires more solvolytic experimental data on other types of leaving groups.

**Comparison of the model reactions**

As mentioned above, the 2-oxyethyl benzoate model and the B3LYP method were utilized for determining calculated nucleofugalities of substituted benzoates. Comparison of the results reveals smaller errors for solvolytic \( \log k^{calc} \) of benzoates than for solvolytic \( \log k^{calc} \) of aliphatic carboxylates (from Tables 3 and S1†). Nevertheless, it indicates neither the generally more suitable model reaction nor the superior DFT method for determining calculated reactivities. In the first place, somewhat different procedure was applied for benzoates. Experimental data had shown that variation in \( \Delta G^\dagger \) for solvolyses of the series of benzhydryl benzoates with the same electrofuge (e.g. dianisylmethyl) in a certain solvent are mostly determined with the changes in the enthalpies of activation (\( \Delta H^{\dagger} \)), while the contributions of the entropy of activation (\( \Delta S^{\dagger} \)) are essentially the same regardless of the benzoate leaving group investigated. This observation was used as the approximation to correlate solvolytic \( \Delta G^\dagger \) of dianisylmethyl benzoates with calculated \( \Delta H^{\dagger} \) of 2-oxyethyl benzoates, which

**Conclusions**

The absolute rate constant for pure heterolytic of a neutral substrate can be calculated neither in the gas phase nor in the presence of a solvation model because it is not possible to optimize the corresponding heterolytic transition state structure. On the other hand, the relative heterolytic reactivity of a series of substrates constituted from the same electrofuge and various aliphatic carboxylate leaving groups can be calculated

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**Fig. 5** Comparison of calculated abilities of some aliphatic carboxylates on the nucleofugality scale (right) with experimentally determined nucleofugalities of some leaving groups (left; data for a, b, c and d were taken from ref. 5, 3, 30 and 9a, respectively.)
using an appropriate anchimerically assisted heterolytic model reaction. The suitable model substrate for that purpose is cis-2,3-dihydroxycyclopropyl trans-carboxylate, optimized at the M06-2X/AUG-cc-pVTZ level of theory using the IEFPCM solvation model. The correlation of calculated free energies of activation of the model reaction ($\Delta G^{model}$), which includes the series of reference aliphatic carboxylate leaving groups, with literature experimental free energies of activation for solvolysis of the corresponding reference dianisylmethyl carboxylates in a given aqueous ethanol mixture affords a very good linear fit, with the slope close to unity, verifying the acceptable precision of the model reaction in calculating the solvolytic reactivity of carboxylates. Although $\Delta G^{model}$ values calculated by other DFT methods in combination with the IEFPCM solvation model also afford the correlation plots with the slope close to unity, the best quality of the linear fit is obtained by utilizing the M06-2X functional. Moreover, B3LYP18 and mPW3PBE19 functionals exhibit difficulties in optimizing some transition state structures. Employing the correlation, absolute solvolytic reactivities of other dianisylmethyl carboxylates ($\Delta G^{calc}$ and the corresponding $k^{calc}$) can be obtained from the barriers of the model reaction ($\Delta G^{model}$) calculated by the appropriate DFT method.

Since the satisfactorily accurate $\log k^{calc}$ for solvolysis of dianisylmethyl carboxylates in the series of aqueous ethanol mixtures have been obtained, they can be further used in determining nucleofugality parameters ($N_t^{calc}$) of various aliphatic carboxylates according to previously established Mayr’s eqn (1). The acceptable error of $N_t^{calc}$ parameters of reference carboxylates justifies the inclusion of the calculated parameters ($N_t^{calc}$) of other carboxylates on the regular nucleofugality scale, which is constituted from diverse leaving groups, and based on experimental solvolytic data. The $N_t^{calc}$ values in combination with electrofugality ($E_t^f$) values from the electrofugality scale can be applied in estimating solvolysis rate constants (and half-lives) of various carboxylate substrates using eqn (1).

Calculated solvolytic reactivities of dianisylmethyl carboxylates ($\log k^{calc}$) confirm earlier experimental observations that the inductive effect of the substituents on the carboxylate moiety of the transition state is the major stabilizing effect which influences relative reactivities of aliphatic carboxylates in solution. The IEFPCM solvation model, in general, suppresses the intrinsic polarizability effect of the substituents that dominates the stabilization of carboxylate free anions in the gas phase.

The good linear correlation between the calculated and the corresponding experimental reactivities of aliphatic carboxylates presented here, as well as a good linear correlation for substituted benzoate substrates presented elsewhere, implies the possibility of broader utilization of this approach on other types of substrates. Since the goal is to obtain both calculated solvolytic reactivities of substrates and calculated nucleofugalties of leaving groups close to experimental ones, it appears that the crucial points are to establish an appropriate heterolytic model reaction for a certain type of leaving groups and to apply an adequate DFT method for calculating heterolytic barriers.

Computational methods

All calculations were carried out with the GAUSSIAN 09 suite of programs. Geometries of cis-2,3-dihydroxycyclopropyl trans-carboxylates (diOHCPr–carboxylates) and of the corresponding heterolytic transition states were fully optimized using the M06-2X, B3LYP18 and mPW3PBE19 hybrid functionals, as well as the B97D20 pure functional with the D2 dispersion scheme included. The DFT methods were combined with Pople-type basis sets and Dunning’s correlation consistent basis sets. Polarizable continuum model IEFPCM for solvation by water was used in most calculations. Other calculations were performed using the SMDO28 solvation model (results are presented in the ESI†). The ultrasoft grid and tight convergence criteria were applied in all computations.

The frequency calculation was performed for each optimized geometry at the same level of theory as its optimization in order to characterize the stationary point either as a ground state (Nimag = 0) or as a heterolytic transition state (Nimag = 1). Along with frequencies, thermal corrections were calculated under standard conditions (1.00 atm and 298.15 K). Coordinates of optimized structures with the corresponding energies are given in the ESL†.

The imaginary frequency mode of heterolytic transition states is associated with stretching of the partially broken C1–O bond. The value of imaginary frequency depends slightly on the reactivity of a modeled carboxylate, and for the transition state structures of the reference diOHCPr–carboxylates, calculated at the IEFPCM-M06-2X/AUG-cc-pVTZ level of theory, varies from 380i cm$^{-1}$ (diOHCPr–pivalate) to 450i cm$^{-1}$ (diOHCPr–heptafluorobutyrate). Other utilized methods and basis sets afforded analogous variations in the values. In addition, intrinsic reaction coordinate (IRC) calculations have been performed to verify that the transition state structures are associated with the C2–C3 σ-bond assisted heterolytic C1–O cleavage.

For some substrates, the structure of a leaving group determines the existence of more conformations of a certain substrate. In such cases, the lowest energy conformation and a corresponding heterolytic transition state structure have been taken for calculating the Gibbs energy of activation. Exceptions have been made for diOHCPr–heptafluorobutyrate, diOHCPr–trinitroacetate and diOHCPr–methyl malonate calculated at the M06-2X/AUG-cc-pVTZ level of theory. For the two former substrates the heterolytic transition state structure of the most stable conformation has an additional imaginary frequency, which is associated with the rotation of the moieties about the partially broken C1–O bond of diOHCPr–carboxylate, whereas for the third one the transition state structure cannot be fully optimized under the tight convergence criteria. Thus, the next lowest-energy conformation has been taken for calculating the free energy of activation for each of three mentioned carboxylates.
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Notes and references


