JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

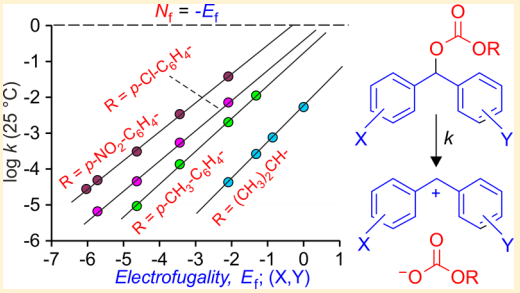
Solvolytic Behavior of Aryl and Alkyl Carbonates. Impact of the Intrinsic Barrier on Relative Reactivities of Leaving Groups

Mirela Matić, Matija Katić, Bernard Denegri,* and Olga Kronja*

University of Zagreb, Faculty of Pharmacy and Biochemistry, A. Kovačića 1, 10000 Zagreb, Croatia

Supporting Information

ABSTRACT: The effect of negative hyperconjugation on the solvolytic behavior of carbonate diesters has been investigated kinetically by applying the LFER equation log $k = s_f(E_f + N_f)$. The observation that carbonate diesters solvolyze faster than the corresponding carboxylates and that the enhancement of aromatic carbonates is more pronounced indicates that the negative hyperconjugation and π-resonance within the carboxylate moiety is operative in TS. The plots of $\Delta G^{\ddagger}$ vs approximated $\Delta_r G^{\circ}$ for solvolysis of benzhydryl aryl/alkyl carbonates and benzhydryl carboxylates reveal that a given carbonate solvolyzes over the higher Marcus intrinsic barrier and over the earlier transition state than carboxylate that produces an anion of similar stability. Due to the lag in development of the electronic effects along the reaction coordinate, the impact of the intrinsic barrier on solvolytic behavior of carbonates is more important than in the case of carboxylates and phenolates. Consequently, the solvolytic reaction constants (s_f) are generally lower for carbonates than for carboxylates. Because of considerable lower reaction constants of carbonates, an inversion of relative reactivities between aryl/alkyl carbonate and another leaving group of similar nucleofugality (N_f) may occur if the electrofuge moiety of a substrate is switched.

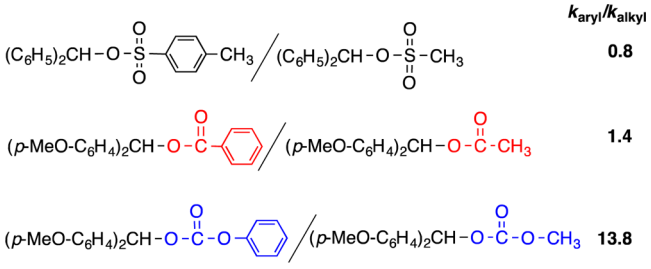


INTRODUCTION

Organic carbonates, diesters of carbonic acid, are commonly used as reagents for carbonylation, alkylation and as solvents in organic synthesis.[1] Since the oxycarbonyl group can easily be introduced and removed, they also frequently serve as protecting groups in organic synthesis.[2] Therefore, it would be useful to examine the heterolytic reactivity of various carbonate diesters as well as structural features that determine it. Furthermore, it also seems interesting to compare solvolytic behavior of carbonates and other substrates.

In our previous study we have examined the S_N1 solvolytic reactivity of benzhydryl methyl and phenyl carbonates in a series of aqueous solvents.[3] Kinetic measurements have shown that the differences in reactivity between X,Y-substituted benzhydryl phenyl carbonates (aryl ester, k_{aryl} in Scheme 1) and X,Y-substituted benzhydryl methyl carbonates (alkyl ester, k_{alkyl} in Scheme 1) are 1 order of magnitude,[3] whereas the ratio of rates of aromatic and corresponding aliphatic carboxylates[4] and sulfonates[5] are practically the same. The rate constant ratios obtained for solvolysis in 80% ethanol are presented in Scheme 1.[3−5]

Scheme 1. Rate Effect of the Aromatic Ring on the Leaving Group of Various Esters

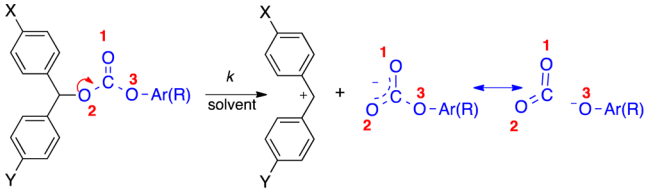


We have also investigated recently the mechanism of decomposition of a series of the model methyl aryl carbonates and methyl alkyl carbonates computationally in the gas phase as well as in the presence of the IEFPCM solvation model (water).[6] Similarly as it occurs in the rate determining heterolysis step of S_N1 solvolysis in aqueous solvents, in that study, the computed first step of the decomposition path in the gas phase and water involves heterolysis of carbonate diesters. The calculations have revealed that the negative hyperconjugation stabilizes aryl and alkyl carbonate anions toward a recombination with a cation, causing a partial transfer of the anionic charge out of the carboxylate moiety of the anions and considerable elongation and polarization of the $O_2C-OR(Ar)$ σ-bond, as depicted with the resonance structure in Scheme 2 (blue). The negative hyperconjugation occurs via two orbital interactions where lone pair orbitals of both oxygens O1 and O2, which lie in the carboxylic plane, donate electron density into the $\sigma^*(C-O3)$ antibonding orbital located between the carboxylate carbon atom and the aryloxy (alkoxy) oxygen atom O3 (Scheme S1b).[6] While the donation from O1 already exists in a neutral substrate, the donation from O2 develops along the

Received: April 13, 2017
Published: July 7, 2017

DOI: 10.1021/acs.joc.7b00885
J. Org. Chem. 2017, 82, 7820−7831

Scheme 2. Heterolytic Step in Solvolysis of Benzhydryl Carbonates



Ar = *p*-NO_2–C_6H_4, *p*-CN–C_6H_4, *p*-Cl–C_6H_4, *p*-F–C_6H_4, *p*-CH_3O–C_6H_4, *p*-CH_3–C_6H_4; **R** = CH_3CH_2, $(CH_3)_2CH$,

1: X = Y = CH_3O
2: X = CH_3O, Y = C_6H_5O
3: X = CH_3O, Y = CH_3
4: X = CH_3O, Y =H
5: X = Y = CH_3
6: X = CH_3, Y = H
7: X = F, Y = H
8: X = Y = H

heterolytic reaction coordinate and achieves its full strength in free anions.

In aryl carbonate anions, the negative hyperconjugation enables further delocalization of the anionic charge to the aromatic ring by resonance and an additional contribution to the stabilization of the anions (Scheme S1c). Calculations have also indicated that the magnitude of the negative hyperconjugation depends on the electron-accepting ability of the Ar(R) substituent attached to O3 (Scheme 2) and that the effect is somewhat suppressed in a solvent in comparison to the gas phase.

The above results prompted us to examine the solvolytic behavior of a series of benzhydryl aryl and alkyl carbonates to establish the effects of the negative hyperconjugation on their solvolytic reactivity experimentally. We have chosen to determine the leaving group abilities (nucleofugalities) of various aryl and alkyl carbonates and to examine the effects of their structural varieties by applying the special LFER approach, which was earlier used for analogous investigations of numerous leaving groups, including phenyl, methyl, and *tert*-butyl carbonates.[3,5]

Accordingly, the absolute heterolysis rate constant for S_N1 solvolysis reaction can be expressed with the following three-parameter LFER equation[5]

$$\log k = s_f(E_f + N_f) \quad (1)$$

in which k is a first-order rate constant (s^{-1}) at 25 °C, s_f (the slope parameter) and N_f (nucleofugality) are the nucleofuge-specific parameters for a given leaving group in a given solvent, and E_f is the electrofugality parameter (independent variable) of carbocation generated in heterolysis. Nucleofugality and electrofugality are kinetic terms that describe abilities of the leaving group and carbocation moieties, respectively, to depart from a substrate. The nucleofuge-specific parameters (s_f and N_f) can be determined from the log k vs E_f plot, for the series of substituted benzhydryl substrates with a given leaving group, for which s_f represents the slope parameter, and N_f corresponds to the negative intercept on the abscissa.[5] Such an approach is established to separate the contributions of an electrofuge and a nucleofuge to the overall solvolytic reactivity of a substrate. This method enables the practical application of eq 1 in estimating the solvolytic reactivity of any substrate constituted from an electrofuge and a nucleofuge of known reactivity parameters.[5,7]

RESULTS AND DISCUSSION

The series of X,Y-substituted carbonates (Scheme 2) have been prepared from the corresponding benzhydrols according to the methods presented in the Experimental Section. Substrates **1**–**8** with different aryl/alkyl carbonate leaving groups (total of 38 substrates) have been subjected to solvolysis in 80% and 60% aq. ethanol, 60% aq. acetone, and 60% aq. acetonitrile (details are given in Kinetic Methods and Tables S1–S3). First-order rate constants (measured at 25 °C and extrapolated from data obtained at higher temperatures) are presented in Table S1. The logarithms of first-order rate constants of substrates of benzhydryl series with a given aryl/alkyl carbonate leaving group were plotted against corresponding electrofugalities (E_f), and the nucleofuge-specific parameters have been extracted. The plots of log k against E_f obtained in 80% ethanol are presented in Figure 1. The nucleofuge-specific parameters,

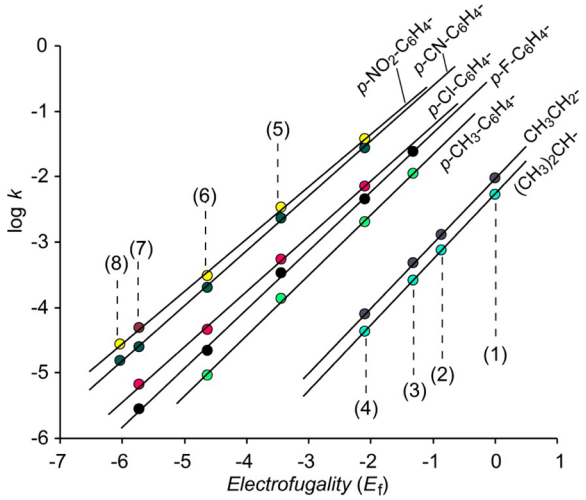


Figure 1. Plots of log k (25 °C) vs E_f for solvolyses of substituted benzhydryl aryl and alkyl carbonates in 80% ethanol (v/v). E_f parameters were taken from ref 5.

nucleofugalities (N_f), and slope parameters (s_f) along with corresponding standard errors and correlation coefficients are presented in Table 1. These parameters can further be used to estimate the solvolytic reactivity of a large number of carbonate diesters[5,7] as well as to relate the reactivities of aryl and alkyl carbonates to numerous leaving groups, whose nucleofuge-specific parameters have already been determined.[4,5,8,9]

In Figure 2 the nucleofugalities of various aryl/alkyl carbonates determined here (shown right) are compared with those of selected leaving groups on the nucleofugality scale (shown left). The scale that covers up to 12 orders of magnitude is particularly useful for easy determination of the relative reactivities of various leaving groups. For example, it is easy to observe that chloride is a more than 6 orders of magnitude more reactive leaving group than isopropyl carbonate or that *p*-nitrophenyl carbonate is more than 4 orders of magnitude more reactive than benzoate.

It should also be emphasized that due to excellent correlations (Table 1, Figure 1), the estimated solvolytic rate constants for benzhydryl derivatives are very accurate, so such calculated rate constants are reliable. Although for substrates that are not benzhydryl derivatives, the estimated rate constants are generally less accurate, eq 1 still gives good predictions of solvolytic reactivities of structurally diverse substrates in a wide

DOI: 10.1021/acs.joc.7b00885
J. Org. Chem. 2017, 82, 7820–7831

Table 1. Nucleofuge-Specific Parameters, N_f and s_f, for Some Aryl and Alkyl Carbonates in Various Solvents

leaving group	solvent[a]	N_f[b]	s_f[b]	r[c]
p-NO_2–$C_6H_4OCO_2$	80E20W	0.31 ± 0.06	0.80 ± 0.01	0.9996
	60E40W	1.05 ± 0.07	0.80 ± 0.01	0.9997
	60AN40W	0.27 ± 0.15	0.80 ± 0.03	0.9986
	60A40W	0.12 ± 0.12	0.81 ± 0.02	0.9991
p-CN–$C_6H_4OCO_2$	80E20W	0.24 ± 0.06	0.84 ± 0.01	0.9997
	60E40W	0.82 ± 0.14	0.80 ± 0.03	0.9989
	60AN40W	0.10 ± 0.15	0.80 ± 0.03	0.9986
	60A40W	−0.03 ± 0.11	0.83 ± 0.02	0.9992
p-Cl-$C_6H_4OCO_2$	80E20W	−0.46 ± 0.09	0.84 ± 0.02	0.9996
	60E40W	0.00 ± 0.11	0.80 ± 0.02	0.9993
	60AN40W	−0.62 ± 0.11	0.79 ± 0.02	0.9990
	60A40W	−0.80 ± 0.09	0.84 ± 0.02	0.9995
p-F-$C_6H_4OCO_2$	80E20W	−0.49 ± 0.07	0.90 ± 0.01	0.9996
	60E40W	−0.08 ± 0.15	0.84 ± 0.03	0.9988
	60AN40W	−0.79 ± 0.11	0.81 ± 0.02	0.9991
	60A40W	−0.94 ± 0.07	0.87 ± 0.01	0.9997
p-CH_3O–$C_6H_4OCO_2$	80E20W	−0.88 ± 0.04	0.91 ± 0.01	0.9999
	60E40W	−0.57 ± 0.07	0.82 ± 0.01	0.9996
	60AN40W	−1.24 ± 0.07	0.81 ± 0.02	0.9996
	60A40W	−1.52 ± 0.02	0.84 ± 0.01	1.0000
p-CH_3–$C_6H_4OCO_2$	80E20W	−0.80 ± 0.07	0.92 ± 0.02	0.9997
	60E40W	−0.52 ± 0.12	0.84 ± 0.03	0.9989
	60AN40W	−1.26 ± 0.08	0.80 ± 0.02	0.9994
	60A40W	−1.55 ± 0.08	0.84 ± 0.02	0.9995
$CH_3CH_2OCO_2$	80E20W	−2.04 ± 0.02	0.99 ± 0.01	1.0000
	60E40W	−1.80 ± 0.10	0.92 ± 0.03	0.9989
	60AN40W	−2.54 ± 0.17	0.90 ± 0.04	0.9978
	60A40W	−2.72 ± 0.18	0.93 ± 0.04	0.9978
$(CH_3)_2CHOCO_2$	80E20W	−2.26 ± 0.02	1.00 ± 0.01	1.0000
	60E40W	−2.03 ± 0.11	0.93 ± 0.03	0.9987
	60AN40W	−2.94 ± 0.13	0.88 ± 0.03	0.9989
	60A40W	−2.86 ± 0.12	0.97 ± 0.03	0.9991

[a]Binary solvents are v/v at 25 °C. E = ethanol, AN = acetonitrile, A = acetone, W = water. [b]Errors shown are standard errors. [c]Correlation coefficient.

range of reactivity.[5,7] Throughout this work, only in a few cases the calculated rate constants for benzhydryl derivatives have been considered.

Rate Effects. All organic carbonates measured here solvolyze about 2 or 3 orders of magnitude faster than the corresponding carboxylates (esterified with the same substituents as carbonates). Thus, the nucleofugalities (N_f) are about 1.5−3 units larger than those of the corresponding carboxylates (e.g., in 80% aq. ethanol for p-NO_2-benzoate N_f = −2.78,[5] while for p-NO_2-phenyl carbonate N_f = 0.31; for isobutyrate N_f = −3.97,[4b] while for isopropyl carbonate N_f = −2.26). In our previous investigation we have demonstrated that the solvolytic rate constants of 4-methoxybenzhydryl aryl/alkyl carbonates correlate well with the corresponding standard free energies for heterolysis, calculated at the IEFPCM-MP2/6-311+G(2d,p) level of theory (r = 0.995), indicating that the electronic effects that stabilize the free aryl and alkyl carbonate anions are operative in the transition states in solvolysis as well.[6] Hence, enhanced reactivity of carbonates in comparison to corresponding carboxylates is consistent with the previous conclusion that in aryl/alkyl carbonate anions additional electron-stabilizing effects exist, particularly the negative hyperconjugation, which delocalizes the negative charge generated on the carboxylates moiety to O3 (Scheme 2), causing additional stabilization of the TS and lowering $\Delta G^{\ddagger}$ for heterolysis.

A distinct gap between the two bottom correlation lines that belong to benzhydryl alkyl carbonates and the other lines that correspond to benzhydryl aryl carbonates, presented in Figure 1, shows that the later solvolyze noticeably faster. Therefore, in line with the rate effect of the phenyl group in carbonates observed earlier (k_{aryl}/k_{alkyl} = 13.8, Scheme 1),[3] a general rule can be set that the substrates with aromatic carbonate leaving groups solvolyze considerably faster than those with aliphatic LG. It should also be mentioned that enhancement of a substrate, if the alkyl group is replaced with the aromatic group, does not exist at both carboxylates and sulfonates,[4,5] i.e., such solvolytic behavior is a specific feature of carbonate leaving groups. The nucleofugality parameters (N_f) for the investigated aromatic carbonates are between one and three units larger than those for aliphatic carbonates, i.e., monosubstituted aromatic carbonates solvolyze 1−3 orders of magnitude faster in all solvents measured (Figure 2). The smallest rate ratios have been obtained between aliphatic carbonates and phenyl carbonates carrying electron-donating groups (p-CH_3 or p-CH_3O), and the ratios expectedly increase as the electron-accepting ability of the substituent on the aromatic ring increases. Furthermore, aromatic carbonates with very strong electron-accepting abilities, as are p-NO_2-phenyl and p-CN-

DOI: 10.1021/acs.joc.7b00885
J. Org. Chem. 2017, 82, 7820−7831

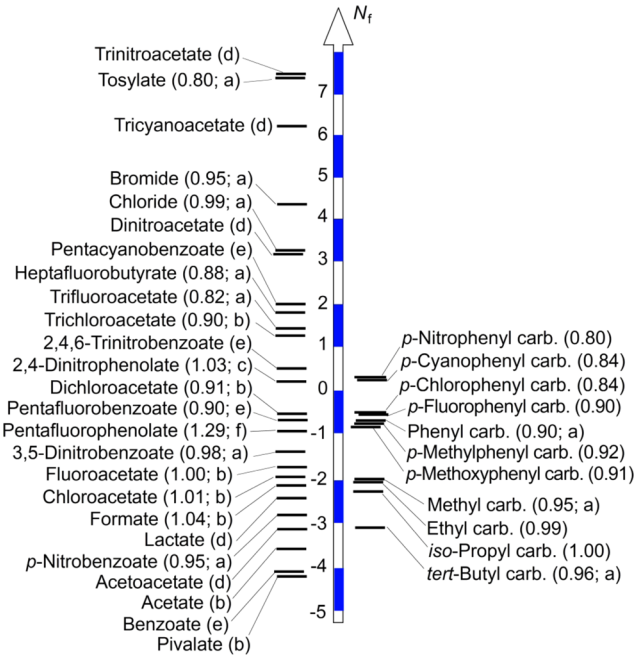


Figure 2. Carbonate leaving groups in the nucleofugality scale for 80% aqueous ethanol along with other leaving groups. Experimental s_f values are given in parentheses. Data for a, b, c, d, e, and f were taken from refs 5, 4b, 9a, 8, 4a, and 9b, respectively.

phenyl groups (the top two correlation lines), solvolyze considerably faster than other aromatic carboxylates, producing a smaller but still observable gap between the lines shown in Figure 1. Experimental rate effects are supported with previous theoretical findings about the importance of the negative hyperconjugation in TS, in which the negative charge is delocalized further by resonance into the aromatic ring, causing the rate enhancement in aromatic carbonates.[6] The degree of this delocalization, i.e. aryl carbonate anion stabilization toward the recombination with a cation, depends on the electron-accepting ability of the substituent on the aryl ring.

Accordingly, enhanced reactivity of aryl/alkyl carbonates in comparison to corresponding carboxylates indicates that additional electron stabilization occurs in the former due to the transfer of the anionic charge onto O3, i.e., out of the carboxylate moiety, while the differences in reactivities between aryl and alkyl carbonates reveal that the orbital delocalization of the negative charge to the aromatic ring occurs.

While carbonates solvolyze noticeably faster than the corresponding carboxylates, the influence of the substituents at the aromatic ring on reactivity is less pronounced than in carboxylates. For instance, in 80% ethanol, k(**1**-*p*-NO_2-phenyl carbonate)/(**1**-phenyl carbonate) = 8.2, whereas k(**1**-*p*-NO_2-benzoate)/k(**1**-benzoate) = 21.0. The similar behavior is also found for the cyano substituent; k(**1**-*p*-CN-phenyl carbonate)/k(**1**-phenyl carbonate) = 7.4 and k(**1**-*p*-CN-benzoate)/k(**1**-benzoate) = 15.5. Less pronounced substituent effects in aryl carbonates might seem surprising since they additionally delocalize the negative charge from O3 via resonance in corresponding aryl carbonate free anions,[6] while in benzoates the ring substituents stabilize both TS and free anions via generally weaker polar effects.[4a]

To examine the influence of the substituents effect in free anions in solution, standard free energies for heterolysis of three **8**-aryl carbonates and three **8**-benzoates (R = H, *p*-CN and *p*-NO_2, Scheme 2) were calculated at the M06-2X/6-311+G(3df,2pd) level of theory with the SMD solvation model that mimics water (Table S7). The energy column diagrams presented in Figure 3 correspond to differences in experimental

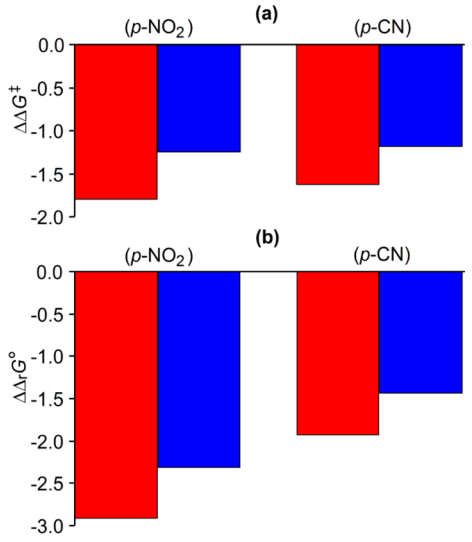


Figure 3. Impact of electron-accepting substituents (in kcal mol^{-1}) on (a) activation free energy of **1**-benzoates (red columns) and **1**-phenyl carbonates (blue columns) in 80% ethanol at 25 °C and (b) stability of free benzoate (red) and phenyl carbonate (blue) anions toward the benzhydrylium cation ($\mathbf{8}^+$), calculated at the SMD-M06-2X/6-311+G(3df,2pd) level (solvent = water). Experimental data for **1**-benzoates and **1**-phenyl carbonate were taken from refs 4a, 11, and 3. All data are presented in Tables S5, S6, and S7.

activation free energies ($\Delta\Delta G^{\ddagger}$) for solvolysis in 80% ethanol between the substrates (aryl carbonates or benzoates) with the substituted (R = *p*-CN or *p*-NO_2) and not substituted (R = H) aromatic ring (a) and to corresponding differences in calculated standard free energies ($\Delta\Delta_rG^{\circ}$) for heterolysis (b). Similar patterns of diagrams show similar modes of stabilization caused with substituents in TS and the ground state of the both substituted free anions. The calculated $\Delta\Delta_rG^{\circ}$s support the experimental findings, showing that indeed the electron-accepting substituents on the aromatic ring in benzoates lower the energy of both TS and free anion more than in aryl carbonates.

Two effects can mainly account for less pronounced substituent effects in solvolysis of carbonates: the limited orbital overlap in the transition state and the strong stabilizing effects in the TS. It has already been shown that the overlap between the O3 lone pair orbitals and the ring π-system is only partial in free aryl carbonate anions due to steric and electrostatic repulsions between the carboxylate moiety and the ring which prevents complete resonance.[6] On the contrary, the magnitude of polar effects of substituents in benzoates does not depend on dihedral angles between the moieties in both TS and free anions, so their impact on the relative solvolysis rate is larger than in carbonates. The other variable that contributes to the less pronounced substituent effect is the strong complex stabilizing mode in the TS (negative hyperconjugation and π-resonance within the carboxylate moiety, Scheme S1), which appears to cover to some extent the substituent effects, i.e., leveling occurs.[10]

Variation of the Reaction Constants. Analogously to the Hammett–Brown ρ^+ parameter, the s_f parameter (eq 1)

DOI: 10.1021/acs.joc.7b00885
J. Org. Chem. 2017, 82, 7820–7831

indicates the charge generated in heterolytic transition states of a series of related substrates ($\rho^+ \approx 4.4s_f$).[11] In our previous study, we correlated log k of 4,4′-dimethoxybenzhydryl aliphatic carboxylates (a series of carboxylates with a common electrofuge) with corresponding s_f values.[4b] The correlation has shown a slight decrease in the s_f value of a series with an increased reactivity of a carboxylate leaving group. This observation was rationalized in terms of the relative position of the transition states on the reaction. Faster reactions solvolyze over earlier transition states, in which the cleavage of a C−LG bond is less advanced; consequently, the TS is more reactant-like than those of the slower reactions, in which the charge separation is more progressed. This is, hence, consistent with the Hammond postulate that the endergonicity of solvolyses decreases within the series with increasing reactivity of a leaving group.[12]

However, when the data for s_f vs log k for aryl/alkyl carbonates are included, the correlation becomes poor (r = 0.84), due to separation of the data into two sets, the one for aryl/alkyl carbonates and the other for caraboxylates. Treatment of the data for aryl/alkyl carbonates and carboxylates individually gives much better correlation, as it is depicted in Figure 4. Although the experimental points are somewhat

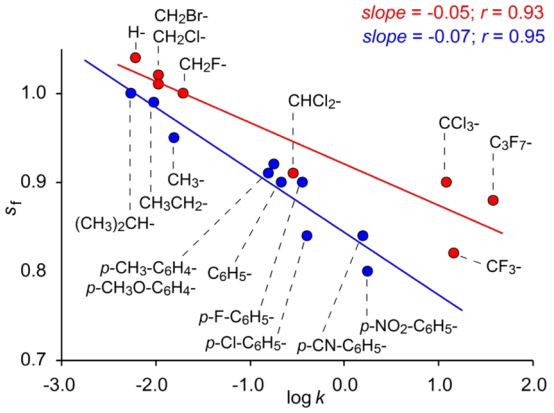


Figure 4. Correlation of s_f values of aryl/alkyl carbonates (blue circles) and aliphatic carboxylates (red circles) against log k (25 °C) for solvolysis of appropriate 4,4′-dimethoxybenzhydryl aryl/alkyl carbonates and carboxylates in 80% ethanol. The values of log k and s_f for phenyl and methyl carbonates and aliphatic carboxylates were taken from refs 3, 5, and 4b (details are given in Tables S5 and S6).

scattered and the linear correlations are not very good, the log k vs s_f plots unambiguously reveal that the trend of decreasing s_f values with increasing reactivity exists for both series, aryl/alkyl carbonates and carboxylates, and that the line that corresponds to carbonates stretches below the line for aliphatic carboxylates.

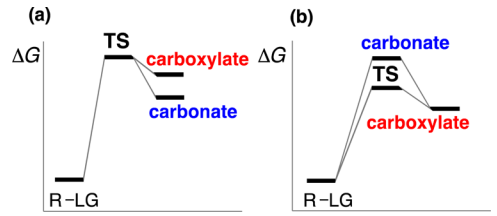
The separation of data in the log k vs s_f correlation (shown in Figure 4) implies inapplicability of both the Hammond postulate[12] and the Bell−Evans−Polanyi principle[13] if carbonates and carboxylates are considered together. Inapplicability of the Hammond postulate and the Bell−Evans−Polanyi principle was also observed with other types of organic reactions.[14] The separation of data into the two lines reveals that carboxylates and carbonates, whose rates (k) of heterolysis are similar (e.g., 4,4′-dimethoxybenzhydryl chloroacetate and 4,4′-dimethoxybenzhydryl ethyl carbonate), produce transition states with a different extent of the charge generated at the reaction center (different s_f values). This observation implies that the solvolytic reactivities in the series of benzhydryl substrates with different types of the leaving groups do not satisfactory correlate with corresponding stabilities of the free anions. Consequently, as aryl/alkyl carbonates generally have lower s_f values (Figure 4), their transition states are supposed to be earlier than those of carboxylates of similar reactivities, i.e., they solvolyze via less endergonic process.

According to Marcus theory (eq 2), the free energy of activation ($\Delta G^{\ddagger}$) depends on the free energy of reaction ($\Delta_r G^{\circ}$) and the intrinsic barrier ($\Delta G^{\ddagger}_0$).[15,16]

$$\Delta G^{\ddagger} = \Delta G_0^{\ddagger} + 0.5\Delta_r G^{\circ} + (\Delta_r G^{\circ})^2/16\Delta G_0^{\ddagger}) \quad (2)$$

Thus, when solvolysis reactions occur with the similar rates (solvolyze over the similar barrier, $\Delta G^{\ddagger}$), eq 2 predicts higher intrinsic barriers for those that produce more stable products (less endergonic processes), here for carbonates (Scheme 3a).

Scheme 3. Free Energy Profiles for Solvolysis of Aryl/Alkyl Carbonates and Carboxylates of (a) the Same Reactivities and (b) the Same Free Anion Stabilities



In both aryl/alkyl carbonates and carboxylates, leaving groups contain the carboxylate moiety, which stabilizes both TS and free anions by π-resonance (Scheme S1a), but, as mentioned above, the anionic charge is further delocalized by the negative hyperconjugation in aryl and alkyl carbonates (Scheme S1b) and additionally by resonance to the phenyl ring in aryl carbonates (Scheme S1c). Lag of developing the electronic stabilizing effects along the reaction coordinate can account for higher intrinsic barriers for solvolysis of carbonates, compared with carboxylates of similar reactivity.

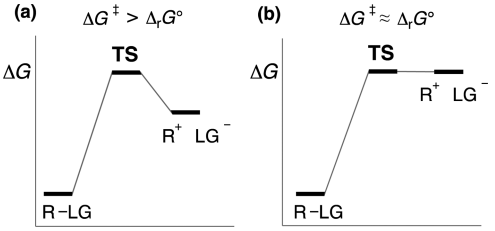
Variation in rates of development of the complex stabilizing effects along the reaction coordinate causes variation of the intrinsic barriers.[17] The lack of synchronization of resonance and polar effects has been observed and investigated at proton-transfer reactions and summarized by The Principle of Nonperfect Synchronization.[18] Accordingly, the lag in development of the charge delocalization, i.e. resonance stabilization of the transition state, leads to the increase of the intrinsic barrier. It has also been established that resonance interactions, in comparison with polar stabilization effects, develop relatively slowly during heterolysis reactions.[17,18] Since both aryloxy and alkoxy substituents attached to the carboxylate moiety at carbonates enable additional delocalization of the anionic charge by the negative hyperconjugation,[6] higher intrinsic barriers for solvolysis of carbonates may be rationalized by slower development of this stabilizing effect along the reaction coordinate in comparison with inductive effects in carboxylates. This lag of the stabilizing effects in carbonates is manifested by their additional stabilization after passing through TS, i.e. by lower free energy of a free anion (Scheme 3a). An increase in magnitude of the negative hyperconjugation, i.e. donation of electron density from O2, along the reaction coordinate does not depend only on a degree of the bond cleavage but also on a degree of the rehybridization at O2 and the change in geometry

DOI: 10.1021/acs.joc.7b00885
J. Org. Chem. 2017, 82, 7820−7831

in vicinity of O2. It appears that the complexity of developing the stabilization effect causes the lag in stabilization.

Impact of the Intrinsic Barrier on Nucleofugality. The slow heterolytic step in solvolysis of numerous compounds occurs over a barrier (Scheme 4a). However, if the backward recombination reaction between a generated nucleophile and an electrophile is a diffusion-controlled process, it occurs without the barrier; thus, according to the principle of microscopic reversibility, formation of free anions in the forward reaction is also barrierless (Scheme 4b).[5] In such a case, $\Delta G^{\ddagger}$ values obtained from the solvolytic rate constants are considered to be equal to $\Delta_r G^{\circ}$s for heterolysis.

Scheme 4. Energy Profiles for Heterolytic Step of S_N1 Reactions That Occur (a) via Barrier and (b) without Barrier



It has been shown previously that the nucleophilicities of chloride and acetate anions are similar.[19a,b] Since the 4,4′-dimethoxybenzhydrilium cation (**1**) recombines with chloride over a barrier,[19a] it can be presumed that it recombines with various carboxylate anions, which are better stabilized than acetate, also via a barrier. Furthermore, the methyl carbonate anion is a weaker nucleophile than both chloride and acetate for 1 order of magnitude.[19c] Consequently, it can also be presumed that the series of carbonate anions presented in Figure 5 combine with 4,4′-dimethoxybenzhydrilium cation (**1**) over a barrier (Scheme 4a). Further, the difference between electrophilicities of benzhydrylium cation (**8**) (E = 5.90) and 4,4′-dimethoxybenzhydrilium cation (**1**) (E = 0) indicates that the former recombines with nucleophiles approximately 6 orders of magnitude faster.[20] Even though it cannot be predicted that the anions produced in solvolyses of benzhydryl (**8**) aryl/alkyl carbonates and benzhydryl carboxylates recombine with the benzhydrylium cation (**8**) without a barrier, according to the Hammond postulate for each series (**8**-carboxylates and **8**-aryl/alkyl carbonates), the corresponding transition states should be appreciably more ion pair-like than those for heterolysis of the 4,4′-dimethoxybenzhydrilium series (energy profile similar to Scheme 4b). Consequently, the activation free energies for **8**-carboxylates and **8**-aryl/alkyl carbonates are considerably closer to the values of the corresponding standard free energies for heterolysis than those for **1**-carboxylates and **1**-aryl/alkyl carbonates; thus, for the purposes of consideration given below, the values of $\Delta G^{\ddagger}$ for **8**-carboxylates and **8**-aryl/alkyl carbonates can roughly be approximated for $\Delta_r G^{\circ}$.

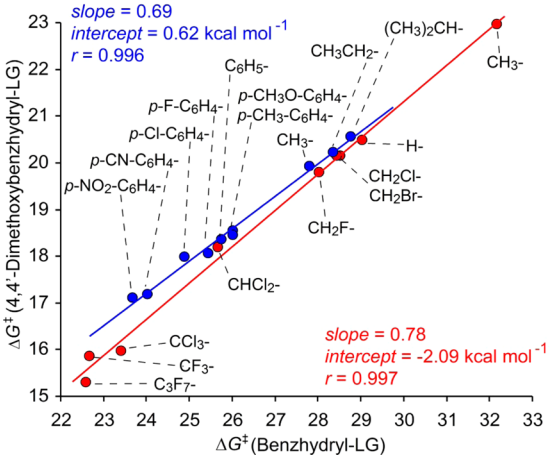


Figure 5. Correlation of activation free energies (in kcal mol^{-1}) for solvolysis of 4,4′-dimethoxybenzhydryl (**1**) aryl/alkyl carbonates (blue circles) and carboxylates (red circles) in 80% ethanol at 25 °C against activation free energies for solvolysis of corresponding benzhydryl (**8**) aryl/alkyl carbonates and carboxylates. Data for phenyl and methyl carbonates and for aliphatic carboxylates were taken from refs 3 and 4b, respectively (details are given in Tables S5 and S6).

Taking advantage from the excellent correlation according to eq 1 if using benzhydryl derivatives (Figure 1 and Table 1), we correlated the activation free energies for solvolysis of 4,4′-dimethoxybenzhydryl (**1**) aryl/alkyl carbonates and carboxylates ($\Delta G^{\ddagger}$) against the activation free energies for benzhydryl (**8**) aryl/alkyl carbonates and carboxylates ($\Delta G^{\ddagger} \approx \Delta_r G^{\circ}$) in an extended range of reactivity (Figure 5). The striking feature of the correlation is a separation of the data into two very good correlation lines, one for aryl/alkyl carbonates (blue) and the other for carboxylates (red). Because of the above-mentioned approximation of $\Delta G^{\ddagger}$ for $\Delta_r G^{\circ}$ for the benzhydryl (**8**) series of carbonates and carboxylates, the slopes of correlation lines can approximately be taken as a Hammond–Leffler α value ($\alpha = \Delta\Delta G^{\ddagger}/\Delta\Delta_r G^{\circ}$).[12] The slopes of both plots given in Figure 5 are, as expected, smaller than unity. Importantly, the slope of the line for aryl/alkyl carbonates is noticeably lower than the one for carboxylates (0.69 vs 0.78), indicating the higher exergonicity of the **1**-aryl/alkyl carbonates series and, consequently, earlier corresponding transition states. Although the slopes of the lines do not truly represent the Hammond–Leffler α value because of the approximation introduced ($\Delta G^{\ddagger} \approx \Delta_r G^{\circ}$ for benzhydryl series), they indicate that a given aryl/alkyl carbonate solvolyzes over an earlier transition state than a carboxylate of the same or similar reactivity (Scheme 3a).

The separation of the lines in this correlation also demonstrates the inapplicability of the Hammond postulate[12] and the Bell–Evans–Polanyi[13] principle if carbonates and carboxylates are treated together, which has already been concluded from the s_f vs log k correlation presented in Figure 4. The separation of data can be attributed to the impact of the height of the Marcus intrinsic barrier[15] on nucleofugality of different types of leaving groups. The lines presented in Figure 5 clearly show that if aryl/alkyl carbonates and carboxylates produce anions of similar stability (abscissa), aryl/alkyl carbonates solvolyze slower, i.e., over a higher barrier. Marcus eq 2 implies that if two substrates produce products of similar stability, the slower reaction proceeds over a higher intrinsic barrier (Scheme 3b). For example, even though $\Delta_r G^{\circ}$s for p-NO_2-phenyl carbonate and trichloroacetate are similar (the abscissa in Figure 5), the later solvolyze about 1 order of magnitude faster (the ordinate).

In summary, the existence of complex electronic stabilization in a heterolytic transition state causes carbonates to solvolyze faster than the corresponding carboxylates (e.g., methyl carbonate vs acetate) for up to 3 orders of magnitude. However, this rate enhancement is somewhat suppressed, due to the higher intrinsic barriers of carbonates caused by slower

DOI: 10.1021/acs.joc.7b00885
J. Org. Chem. 2017, 82, 7820−7831

development of the stabilizing effects along the reaction coordinate.

Relative Reactivity of Carbonates. It is well-known that relative reactivities of leaving groups vary with variation in the structure of an electrofuge, mostly due to different steric demands adjacent to the reaction center[21] and differential solvation of electrofuges.[7] However, even in the series of structurally related substrates, whose steric demands in the vicinity of the reaction center are similar (e.g., benzhydryl series), the relative reactivities of leaving groups can vary due to different contributions of both electronic effects (e.g., resonance and inductivity) and intrinsic barriers.[9b] This is also observable in the correlation shown in Figure 5. For instance, trichloroacetate is for more than 1 kcal mol^{-1} more reactive than *p*-NO_2-phenyl carbonate when an electrofuge is 4,4′-dimethoxybenzhydrilium (ordinate). Switching the electrofuge with less reactive benzhydrilium (abscissa) appreciably decreases the difference to 0.2−0.3 kcal mol^{-1}. This occurs because the transition states in slower reactions of the benzhydrylium series are more ion pair-like (the Hammond postulate), ultimately approaching the barrierless process (Scheme 4b), so the impact of the intrinsic barrier on reactivity becomes less important. In such slower processes, in which the intrinsic barrier is lower, the stability of the ions generated becomes the rate determining variable. The decrease of the intrinsic barrier in the series of the benzhydryl derivatives, which carry a common carboxylate leaving group, with decreasing electrofugality (i.e., with increasing electrophilicity of a cation generated in solvolysis) was indicated previously.[19b] Since the same conclusions have been drawn from the correlations presented in Figures 4 and 5, it is evident that information on variation of intrinsic barriers for the heterolytic step of S_N1 reactions is included in the s_f parameter of eq 1, i.e., the reaction constant.

It has been shown that phenolates solvolyze over lower intrinsic barriers than carboxylates within the same region of reactivity,[9b] so they represent an appropriate model for investigating how differences in intrinsic barriers affect the relative reactivities of the leaving groups. The nucleofugalities of *p*-NO_2-phenyl carbonate (N_f = 0.31, s_f = 0.80 in 80% aq. EtOH) and 2,4-dinitrophenolate (DNPh) (N_f = 0.22, s_f = 1.03 in 80% aq. EtOH)[9a] are almost the same, but the s_f value for the former is considerably lower. This implies a relatively higher intrinsic barrier for *p*-NO_2-phenyl carbonate in heterolysis and in the reverse combination of the ions than it is for DNPh. In Figure 6 some selected log *k* vs E_f correlation lines (eq 1) are presented. The lines that correspond to *p*-NO_2-phenyl carbonate (line A) and 2,4-dinitrophenolate (DNPh, line B)[9a] indicate similar reactivity of the two leaving groups in the region of definition of N_f value (log *k* = 0). For substrates that solvolyze with rates $k \approx 1$, the heterolytic step and its reversible recombination reaction proceed over a barrier (Scheme 4a). In the region of less reactive substrates (weaker electrofuges), divergence of the correlation lines occurs, and *p*-NO_2-phenyl carbonate becomes more reactive than DNPh. As the reaction in the series becomes slower, the intrinsic barrier becomes lower, approaching the barrierless process, in which a transition state is ion pair-like (Scheme 4b). In a slower region, the relative reactivities are mostly determined with the stability of anions generated in heterolysis. Consequently, the correlation implies that the *p*-NO_2-phenyl carbonate free anion is better stabilized than the DNPh free anion. On the other hand, in the region of faster reactions, right from the intersection of the

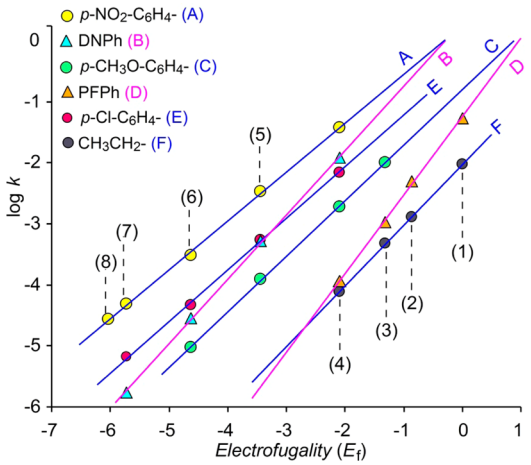


Figure 6. Plots of log *k* (25 °C) vs E_f for solvolyses of substituted benzhydryl aryl carbonates, 2,4-dinitrophenolates (DNPh),[9a] and pentafluorophenolates (PFPh)[9b] in 80% ethanol (v/v). E_f parameters were taken from ref 5.

correlation lines (higher electrofugality), the intrinsic barrier is an important variable in determining relative reactivities, rendering *p*-NO_2-phenyl carbonates in heterolysis less reactive than DNPh.

Figure 6 also reveals other cases of inversion in relative reactivities. For example, lines for *p*-CH_3O-phenyl carbonate (line C) and pentafluorophenolate (PFPh, line D)[9b] intersect in the region of electrofugality $E_f \approx 1$, while those for 2,4-dinitrophenolate (DNPh, line B)[9a] and *p*-chlorophenyl carbonate (line E) intersect at $E_f \approx -3$. An example of inversion of relative reactivities in the region of kinetic measurements is also shown with the intersection of lines of ethyl carbonate (line F) and pentafluorophenolate (line D), which intersect at $E_f \approx -2.5$. Inversion of relative reactivities in the experimental region was also observed earlier with phenolates and carboxylates.[9b] The intersections of the lines that indicate the inversion of relative reactivities of the leaving groups can be rationalized similarly as above for *p*-NO_2-phenyl carbonates and 2,4-dinitrophenolates: from the intersection point toward the more reactive region (higher electrofugality), the intrinsic barrier is important in determining the relative reactivates, while toward the region of lower heterolytic reactivities (lower electrofugality), relative reactivities are mostly determined with stabilities of generated free anions.

The difference in solvolytic intrinsic barriers of carbonates and phenolates can be attributed to the nonsynchronous development of several orbital effects in aryl and alkyl carbonate leaving groups (resonance within the carboxylate moiety, the negative hyperconjugation, and additional resonance in aryl carbonates)[6] during the heterolysis process at carbonate diesters. This behavior is consistent with the principle of nonperfect synchronization.[18] On the other hand, only resonance constitutes a dominant electronic effect at phenolate leaving groups in both transition states and free anions.

These examples do not only repeatedly demonstrate inapplicability in employing pK_a values for predicting relative reactivities of diverse leaving groups but also indicate shortcomings of the method in which the solvolysis rates of series of substrates with different leaving groups and a common electrofuge are used for determining nucleofugalities, since the inversion of reactivities cannot be predicted. The shortcomings

DOI: 10.1021/acs.joc.7b00885
J. Org. Chem. 2017, 82, 7820−7831

can be overcome if the LFER approach presented by eq 1[5] is employed.

CONCLUSION

Kinetic data revealed that the negative hyperconjugation in combination with π-resonance within the carboxylate moiety that was computationally established to stabilize free aryl and alkyl carbonate anions also exists in transition states of heterolysis of the carbonate diesters. Such mode of stabilization of the TS of carbonates contributes to their enhanced solvolytic reactivity in comparison to corresponding carboxylates. Enhancement of reactivity of aryl carbonates is even more pronounced than that of alkyl carbonates due to additional negative charge delocalization into the aromatic ring by resonance.

However, as a consequence of slower development of the complex stabilizing electronic effects during heterolysis in carbonates than in carboxylates, carbonates solvolyze over the higher intrinsic barrier, causing those that produce anions of similar stability as carboxylates to solvolyze slower. Due to the impact of the higher intrinsic barrier on the solvolytic behavior of carbonates, an increase of reactivity with increasing electrofugality is somewhat suppressed in comparison to carboxylates or phenolates. Consequently, the reaction constants (s_f) for aryl/alkyl carbonates are generally lower than those for carboxylates and particularly those for phenolates which in turn can account for the inversion of relative reactivities of aryl/alkyl carbonates and phenolates if the electrofuge moiety of a substrate is varied.

EXPERIMENTAL SECTION

Substrate Preparation. *4-Fluorobenzhydrol, 4-methylbenzhydrol, 4,4′-dimethylbenzhydrol, and 4,4′-dimethoxybenzhydrol* were prepared by the reduction of the commercially available corresponding substituted benzophenones with sodium borohydride in methanol.

4-Methoxy-4′-methylbenzhydrol and 4-methoxy-4′-phenoxybenzhydrol were prepared according to the procedure given in ref 3.

General Procedure for the Synthesis of Benzhydryl 4-Nitrophenyl Carbonates. A solution of 4-nitrophenyl chloroformate (4.2 mmol) in anhydrous benzene (10 mL) was added dropwise to the previously prepared vigorously stirring solution of appropriate benzhydrol (3.3 mmol) and pyridine (9.7 mmol) in anhydrous benzene (20 mL). The reaction mixture was stirred overnight under the atmosphere of argon at ambient temperature, except in the case of 4-methoxybenzhydryl 4-nitrophenyl carbonate, when the reaction time was 15 min. Precipitated pyridinium chloride was removed by filtration, and the excess of pyridine was removed by 10% hydrochloric acid. The benzene layer was separated and washed with 30% NaOH (3×) and water (3×). After drying over anhydrous sodium sulfate, benzene was evaporated in vacuo to give white crystals (yield 58–78%).

Benzhydryl 4-Nitrophenyl Carbonate: from benzhydrol (0.60 g; 3.3 mmol), pyridine (0.77 g; 9.7 mmol), and 4-nitrophenyl chloroformate (0.85 g; 4.2 mmol); yield 0.89 g; 78%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 6.81 (s, 1H; Ar_2CH), 7.33–7.43 (m, 12H; ArH + Ar–NO_2), 8.22 (d, J = 9.3 Hz, 2H; Ar–NO_2); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 82.4 (Ar_2CH), 121.8, 125.3, 127.1, 128.6, 128.8, 138.7, 145.4 (Ar–NO_2), 151.9 (C═O), 155.5 (Ar–NO_2); Collection of HRMS data or elemental analysis was not possible for this compound due to its limited stability.

4-Fluorobenzhydryl 4-Nitrophenyl Carbonate: from 4-fluorobenzhydrol (0.80 g; 4.0 mmol), pyridine (0.94 g; 11.9 mmol), and 4-nitrophenyl chloroformate (1.04 g; 5.2 mmol); yield 0.84 g; 58%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 6.79 (s, 1H; Ar_2CH), 7.06 (t, J = 8.7 Hz, 2H; Ar–F), 7.34–7.41 (m, 9H; ArH + Ar–F + Ar–NO_2), 8.24 (d, J = 9.3 Hz, 2H; Ar–NO_2); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 81.7 (Ar_2CH), 115.7 (d, J = 21.7 Hz, Ar–F), 121.7, 125.3, 126.9, 128.7, 128.8 (Ar), 129.1 (d, J = 8.3 Hz, Ar–F), 134.7 (d, J = 3.4 Hz, Ar–F), 138.5, 145.4 (Ar–NO_2), 151.8 (C═O), 155.4 (Ar–NO_2), 162.7 (d, J = 247.8 Hz, Ar–F); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): δ/ppm = −112.95. HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{20}H_{13}O_5NF$ 366.0777; Found 366.0794.

4-Methylbenzhydryl 4-Nitrophenyl Carbonate: from 4-methylbenzhydrol (0.80 g; 4.0 mmol), pyridine (0.96 g; 12.1 mmol), and 4-nitrophenyl chloroformate (1.06 g; 5.3 mmol); yield 0.93 g; 63%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.34 (s, 3H; Ar–CH_3), 6.78 (s, 1H; Ar_2CH), 7.18 (d, J = 8.0 Hz, 2H; Ar–CH_3), 7.29–7.42 (m, 9H; ArH + Ar–CH_3 + Ar–NO_2), 8,23 (d, J = 9.0 Hz, 2H; Ar–NO_2); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.2 (Ar–CH_3), 82.4 (Ar_2CH), 121.8, 125.2, 126.9, 127.1, 128.4, 128.7, 129.4, 135.8, 138.5, 138.9, 145.3 (Ar–NO_2), 151.9 (C═O), 155.6 (Ar–NO_2). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{21}H_{16}O_5N$ 362.1028; Found 362.1017.

4,4′-Dimethylbenzhydryl 4-Nitrophenyl Carbonate: from 4,4′-dimethylbenzhydrol (0.80 g; 3.8 mmol), pyridine (0.89 g; 11.3 mmol), and 4-nitrophenyl chloroformate (0.99 g; 4.9 mmol); yield 0.93 g; 66%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.33 (s, 6H; Ar–CH_3), 6.75 (s, 1H; Ar_2CH), 7.17 (d, J = 7.9 Hz, 4H; Ar–CH_3), 7.29 (d, J = 8.1 Hz, 4H; Ar–CH_3), 7.33 (d, J = 9.1 Hz, 2H; Ar–NO_2), 8.21 (d, J = 9.2 Hz, 2H; Ar–NO_2); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.2 (Ar–CH_3), 82.4 (Ar_2CH), 121.8, 125.2, 127.0, 129.4, 136.0, 138.3, 145.3 (Ar–NO_2), 151.9 (C═O), 155.6 (Ar–NO_2). HRMS (MALDI-TOF/TOF) m/z: $[M + (e^-)]$ Calcd for $C_{22}H_{19}O_5N$ 377.1263; Found 377.1270.

4-Methoxybenzhydryl 4-Nitrophenyl Carbonate: data are given in ref 6.

General Procedure for the Synthesis of Benzhydryl 4-Cyanophenyl Carbonates. In a solution of potassium 4-cyanophenoxide (2.6 mmol) in DMSO (15 mL), a solution of appropriate benzhydryl 4-nitrophenyl carbonate (0.9 mmol) in DMSO was added. The reaction mixture was stirred at ambient temperature for 1 h, except in the case of 4-methoxybenzhydryl 4-cyanophenyl carbonate, when the reaction time was 2 min. Fifteen milliliters of benzene was added to the mixture, and after being stirred for a few minutes, the mixture was washed with water (3×). After drying over anhydrous sodium sulfate, benzene was evaporated in vacuo to give white crystals (yield 71–89%).

Benzhydryl 4-Cyanophenyl Carbonate: from potassium 4-cyanophenoxide (0.41 g; 2.6 mmol) and benzhydryl 4-nitrophenyl carbonate (0.30 g; 0.9 mmol); yield 0.20 g; 71%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 6.79 (s, 1H; Ar_2CH), 7.28–7.42 (m, 12H; ArH + Ar–CN), 7.64 (d, J = 8.5 Hz, 2H; Ar–CN); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 82.3 (Ar_2CH), 110.0 (Ar–CN), 118.1 (Ar–<u>C</u>N), 122.1 (Ar–CN), 127.0, 128.5, 128.7 (Ar), 133.7 (Ar–CN), 138.8 (Ar), 152.0 (C═O), 154.1 (Ar–CN). Collection of HRMS data or elemental analysis was not possible for this compound due to its limited stability.

4-Fluorobenzhydryl 4-Cyanophenyl Carbonate: from potassium 4-cyanophenoxide (0.39 g; 2.5 mmol) and 4-fluorobenzhydryl 4-nitrophenyl carbonate (0.30 g; 8.2 mmol); yield 0.22 g; 79%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 6.79 (s, 1H; Ar_2CH), 7.08 (t, J = 8.5 Hz, 2H; Ar–F), 7.31–7.41 (m, 9H; ArH + Ar–F + Ar–CN), 7.67 (d, J = 8.3 Hz, 2H; Ar–CN); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 81.6 (Ar_2CH), 110.0 (Ar–CN), 115.7 (d, J = 21.7 Hz, Ar–F), 118.0 (Ar–<u>C</u>N), 122.0 (Ar–CN), 126.9, 128.6, 128.8 (Ar), 129.1 (d, J = 8.4 Hz, Ar–F), 133.7 (Ar–CN), 134.7 (d, J = 3.2 Hz, Ar–F), 138.5 (Ar), 151.9 (C═O), 154.1 (Ar–CN), 162.7 (d, J = 248.0 Hz, Ar–F); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): δ/ppm = −113.0. HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{21}H_{13}O_3NF$ 346.0880; Found 346.0872.

4-Methylbenzhydryl 4-Cyanophenyl Carbonate: from potassium 4-cyanophenoxide (0.39 g; 2.5 mmol) and 4-methylbenzhydryl 4-nitrophenyl carbonate (0.30 g; 0.8 mmol); yield 0.24 g; 86%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.34 (s, 3H; Ar–CH_3), 6.76 (s, 1H; Ar_2CH), 7.18 (d, J = 8.0 Hz, 2H; Ar–CH_3), 7.27–7.41 (m, 9H;

DOI: 10.1021/acs.joc.7b00885
J. Org. Chem. 2017, 82, 7820–7831

ArH + Ar−CH_3 + Ar−CN), 7.64 (d, J = 8.8 Hz, 2H; Ar−CN); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.2 (Ar−CH_3), 82.3 (Ar_2CH), 109.9 (Ar−CN), 118.1 (Ar−<u>C</u>N), 122.1 (Ar−CN), 126.9, 127.1, 128.4, 128.7, 129.4 (Ar), 133.7 (Ar−CN), 135.9, 138.5, 139.0 (Ar), 152.0 (C═O), 154.2 (Ar−CN). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{22}H_{16}O_3N$ 342.1130; Found 342.1133.

4,4′-Dimethylbenzhydryl 4-Cyanophenyl Carbonate: from potassium 4-cyanophenoxide (0.37 g; 2.4 mmol) and 4,4′-dimethylbenzhydryl 4-nitrophenyl carbonate (0.30 g; 0.8 mmol); yield 0.25 g; 89%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.33 (s, 6H; Ar−CH_3), 6.73 (s, 1H; Ar_2CH), 7.17 (d, J = 8.1 Hz, 4H; Ar−CH_3), 7.28 (d, 6H; J = 7.8 Hz, Ar−CH_3 + Ar−CN), 7.64 (d, J = 8.7 Hz, 2H; Ar−CN); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.2 (Ar−CH_3), 82.3 (Ar_2CH), 109.9 (Ar−CN), 118.1 (Ar−<u>C</u>N), 122.1 (Ar−CN), 127.0, 129.4 (Ar), 133.7 (Ar−CN), 136.0, 138.3 (Ar), 152.0 (C═O), 154.2 (Ar−CN). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{23}H_{18}O_3N$ 356.1286; Found 356.1283.

4-Methoxybenzhydryl 4-Cyanophenyl Carbonate: data are given in ref 6.

General Procedure for the Synthesis of Benzhydryl 4-Chlorophenyl Carbonates. The procedure for 4-chlorophenyl carbonates was almost the same as for 4-nitrophenyl carbonates, except 4-chlorophenyl chloroformate was used instead of 4-nitrophenyl chloroformate, and the reactants were used in different ratios (appropriate benzhydrol:pyridine:4-chlorophenyl chloroformate = 1.0:3.0:1.4). Furthermore, the benzene layer was separated and washed with 50% NaOH. All 4-chlorophenyl carbonates were obtained as white crystals (yield 62−80%).

4-Fluorobenzhydryl 4-Chlorophenyl Carbonate: from 4-fluorobenzhydrol (0.50 g; 2.5 mmol), pyridine (0.59 g; 7.5 mmol), and 4-chlorophenyl chloroformate (0.66 g; 3.5 mmol); yield 0.70 g; 80%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 6.76 (s, 1H; Ar_2CH), 7.02−7.10 (m, 4H; Ar−F + Ar−Cl), 7.29−7.39 (m, 9H; ArH + Ar−F + Ar−Cl); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 81.1 (Ar_2CH), 115.6 (d, J = 21.7 Hz, Ar−F), 122.4, 126.9, 128.5, 128.8 (Ar), 129.1 (d, J = 8.3 Hz, Ar−F), 129.5, 131.5, 135.0 (d, J = 3.3 Hz, Ar−F), 138.9, 149.5 (Ar), 152.7 (C═O), 162.6 (d, J = 247.6 Hz, Ar−F); ^{19}F NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = −113.3. Collection of HRMS data or elemental analysis was not possible for this compound due to its limited stability.

4-Methylbenzhydryl 4-Chlorophenyl Carbonate: from 4-methylbenzhydrol (0.50 g; 2.5 mmol), pyridine (0.60 g; 7.6 mmol), and 4-chlorophenyl chloroformate (0.67 g; 3.5 mmol); yield 0.55 g; 62%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.32 (s, 3H; Ar−CH_3), 6.75 (s, 1H; Ar_2CH), 7.08 (d, J = 8.9 Hz, 2H; Ar−Cl), 7.16 (d, J = 8.0 Hz, 2H; Ar−CH_3), 7.28−7.36 (m, 7H; ArH + Ar−Cl), 7.40 (d, J = 6.9 Hz, 2H; Ar−CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.2 (Ar−CH_3), 81.8 (Ar_2CH), 109.9, 118.1 (Ar), 122.4, 127.0, 127.2, 128.3, 128.7, 129.4, 129.5, 131.4, 136.2, 138.3, 139.3, 140.7 (Ar), 152.8 (C═O). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{21}H_{16}O_3Cl$ 351.0788; Found 351.0800.

4,4′-Dimethylbenzhydryl 4-Chlorophenyl Carbonate: from 4,4′-dimethylbenzhydrol (0.50 g; 2.4 mmol), pyridine (0.56 g; 7.1 mmol), and 4-chlorophenyl chloroformate (0.63 g; 3.3 mmol); yield 0.57 g; 65%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.32 (s, 6H; Ar−CH_3), 6.72 (s, 1H; Ar_2CH), 7.08 (d, J = 8.8 Hz, 2H; Ar−Cl), 7.15 (d, 4H; J = 8.0 Hz, Ar−CH_3), 7.28 (d, J = 8.4 Hz, 6H; Ar−Cl + Ar−CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.2 (Ar−CH_3), 81.8 (Ar_2CH), 122.4, 127.0, 129.3, 129.4, 131.3, 136.3, 138.1, 149.6 (Ar), 152.8 (C═O). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{22}H_{18}O_3Cl$ 365.0944; Found 365.0937.

4-Methoxybenzhydryl 4-Chlorophenyl Carbonate: data are given in ref 6.

4-Methoxy-4′-Methylbenzhydryl 4-Chlorophenyl Carbonate: from 4-methoxy-4′-methyl benzhydrol (0.50 g; 2.2 mmol), pyridine (0.52 g; 76.6 mmol), and 4-chlorophenyl chloroformate (0.59 g; 3.1 mmol); yield 0.53 g; 63%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C°): δ/ppm = 2.33 (s, 3H; Ar−CH_3), 3.76 (s, 3H; Ar−OCH_3), 6.72 (s, 1H; Ar_2CH), 6.87 (d, 2H, J = 8.7 Hz, Ar−OCH_3), 7.08 (d, 2H, J = 8.9 Hz, Ar−Cl), 7.16 (d, 2H, J = 7.9 Hz, Ar−CH_3), 7.27−7.34 (m, 6H; Ar−OCH_3 + Ar−CH_3 + Ar−Cl); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.2 (Ar−CH_3), 55.3 (Ar−OCH_3), 81.7 (Ar_2CH), 114.0, 122.5, 126.8, 128.7, 129.3, 129.5, 131.3, 131.4, 136.4, 138.0, 149.7, 152.8 (C═O), 159.6. Collection of HRMS data or elemental analysis was not possible for this compound due to its limited stability.

General Procedure for the Synthesis of Benzhydryl 4-Fluorophenyl Carbonate. The procedure for 4-fluorophenyl carbonates was almost the same as for 4-chlorophenyl carbonates, except 4-fluorophenyl chloroformate was used instead of the 4-chlorophenyl chloroformate. All 4-fluorophenyl carbonates were obtained as white crystals (yield 65.9−84.5%).

4-Fluorobenzhydryl 4-Fluorophenyl Carbonate: from 4-fluorobenzhydrol (0.50 g; 2.5 mmol), pyridine (0.59 g; 7.5 mmol), and 4-fluorophenyl chloroformate (0.60 g; 3.4 mmol); yield 0.71 g; 85%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 6.81 (s, 1H; Ar_2CH), 7.04−7.17 (m, 6H; Ar−F + ArH), 7.36−7.44 (m, 7H; ArH + Ar−F); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 81.1 (Ar_2CH), 115.6 (d, J = 21.7 Hz, Ar−F), 116.1 (d, J = 23.6 Hz, Ar−F), 122.5 (d, J = 8.6 Hz, Ar−F), 126.9, 128.5, 128.8 (Ar), 129.1 (d, J = 8.3 Hz, Ar−F), 135.1 (d, J = 3.2 Hz, Ar−F), 139.0 (Ar), 147.0 (d, J = 2.9 Hz, Ar−F), 153.0 (C═O), 160.3 (d, J = 244.8 Hz, Ar−F), 162.6 (d, J = 247.5 Hz, Ar−F); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): δ/ppm = −113.3, −116.4. Collection of HRMS data or elemental analysis was not possible for this compound due to its limited stability.

4-Methylbenzhydryl 4-Fluorophenyl Carbonate: from 4-methylbenzhydrol (0.50 g; 2.5 mmol), pyridine (0.60 g; 7.6 mmol), and 4-fluorophenyl chloroformate (0.62 g; 3.6 mmol); yield 0.56 g; 66%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.31 (s, 3H; CH_3Ar), 6.75 (s, 1H; Ar_2CH), 6.98 (t, 2H; J = 9.0 Hz, Ar−F), 7.07−7.10 (m, 2H; Ar−F), 7.15 (d, 2H, J = 8.1 Hz, Ar−CH_3), 7.27−7.35 (m, 5H; ArH), 7.40 (d, 2H, J = 7.4 Hz, Ar−CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.2 (Ar−CH_3), 81.8 (Ar_2CH), 116.1 (d, J = 23.6 Hz, Ar−F), 122.6 (d, J = 8.6 Hz, Ar−F), 127.0, 127.2, 128.3, 128.7, 129.4, 136.3, 138.3, 139.4 (Ar), 147.1 (d, J = 2.8 Hz, Ar−F), 153.1 (C═O), 160.3 (d, J = 244.6 Hz, Ar−F); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): δ/ppm = −116.5. HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{21}H_{16}O_3F$ 335.1084; Found 335.1100.

4,4′-Dimethylbenzhydryl 4-Fluorophenyl Carbonate: from 4,4′-dimethylbenzhydrol (0.50 g; 2.4 mmol), pyridine (0.56 g; 7.1 mmol), and 4-fluorophenyl chloroformate (0.58 g; 3.3 mmol); yield 0.59 g; 71%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.32 (s, 6H; Ar−CH_3), 6.72 (s, 1H; Ar_2CH), 6.99 (t, 2H; J = 8.9 Hz, Ar−F), 7.07−7.11 (m, 2H; Ar−F), 7.15 (d, 4H, J = 8.1 Hz, Ar−CH_3), 7.28 (d, 4H, J = 8.1 Hz, Ar−CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.2 (Ar−CH_3), 81.7 (Ar_2CH), 116.0 (d, J = 23.5 Hz, Ar−F), 122.5 (d, J = 8.6 Hz, Ar−F), 127.0, 129.3, 136.4, 138.1 (Ar), 147.0 (d, J = 3.1 Hz, Ar−F), 153.1 (C═O), 160.2 (d, J = 244.5 Hz, Ar−F); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): δ/ppm = −116.6. HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{22}H_{18}O_3F$ 349.1240; Found 349.1256.

4-Methoxybenzhydryl 4-Fluorophenyl Carbonate: data are given in ref 6.

4-Methoxy-4′-Methylbenzhydryl 4-Fluorophenyl Carbonate: from 4-methoxy-4-methylbenzhydrol (0.50 g; 2.2 mmol), pyridine (0.52 g; 6.6 mmol), and 4-fluorophenyl chloroformate (0.54 g; 3.1 mmol); yield 0.64 g; 80%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.32 (s, 3H; CH_3−Ar), 3.75 (s, 3H; Ar−OCH_3), 6.72 (s, 1H; Ar_2CH), 6.87 (d, 2H, J = 8.7 Hz, Ar−OCH_3), 6.99 (t, 2H; J = 9.0 Hz, Ar−F), 7.07−7.11 (m, 2H; Ar−F), 7.15 (d, 2H, J = 8.1 Hz, Ar−CH_3),7.27−7.32 (m, 4H; Ar−OCH_3 + Ar−CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.1 (Ar−CH_3), 55.3 (Ar−OCH_3), 81.5 (Ar_2CH), 114.0, 116.0 (d, J = 23.6 Hz, Ar−F), 122.5 (d, J = 8.6 Hz, Ar−F), 126.8, 128.7, 128.6, 129.3, 131.5, 136.4, 138.0 (Ar), 147.2 (d, J = 2.8 Hz, Ar−F), 153.1 (C═O), 159.6, 160.2 (d, J = 244.6 Hz, Ar−F); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): δ/ppm = −116.7. Collection of HRMS data or elemental analysis was not possible for this compound due to its limited stability.

General Procedure for the Synthesis of Benzhydryl 4-Methoxyphenyl Carbonate. The procedure for 4-methoxyphenyl carbonates was almost the same as for 4-chlorophenyl carbonates, except 4-methoxyphenyl chloroformate was used instead of the 4-

DOI: 10.1021/acs.joc.7b00885
J. Org. Chem. 2017, 82, 7820−7831

chlorophenyl chloroformate. All 4-methoxyphenyl carbonates were obtained as white crystals (yield 68−76%).

4-Methylbenzhydryl 4-Methoxyphenyl Carbonate: from 4-methylbenzhydrol (0.50 g; 2.5 mmol), pyridine (0.60 g; 7.6 mmol), and 4-methoxyphenyl chloroformate (0.66 g; 3.5 mmol); yield 0.67 g; 76%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.33 (s, 3H; Ar−CH_3), 3.75 (s, 3H; Ar−OCH_3), 6.75 (s, 1H; Ar_2CH), 6.84 (d, J = 9.1 Hz, 2H; Ar−OCH_3), 7.06 (d, J = 9.1 Hz, 2H; Ar−OCH_3), 7.16 (d, J = 8.0 Hz, 2H; Ar−CH_3), 7.28−7.41 (m, 7H; ArH + Ar−CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.2 (Ar−CH_3), 55.6 (Ar−OCH_3), 81.5 (Ar_2CH), 114.4, 121.9, 127.0, 127.1, 128.2, 128.6, 129.3, 136.5, 138.1, 139.5, 144.8 (Ar), 153.5 (C═O), 157.4 (Ar). Collection of HRMS data or elemental analysis was not possible for this compound due to its limited stability.

4,4′-Dimethylbenzhydryl 4-Methoxyphenyl Carbonate: from 4,4′-dimethylbenzhydrol (0.50 g; 2.4 mmol), pyridine (0.56 g; 7.1 mmol), and 4-methoxyphenyl chloroformate (0.62 g; 3.3 mmol); yield 0.60 g; 70%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.31 (s, 6H; Ar−CH_3), 3.72 (s, 3H; Ar−OCH_3), 6.73 (s, 1H; Ar_2CH), 6.82 (d, J = 9.0 Hz, 2H; Ar−OCH_3), 7.05 (d, J = 9.1 Hz, 2H; Ar−OCH_3), 7.14 (d, J = 7.9 Hz, 2H; Ar−CH_3), 7.29 (d, J = 8.1 Hz, 2H; Ar−CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.2 (Ar−CH_3), 55.6 (Ar−OCH_3), 81.5 (Ar_2CH), 114.4, 121.9, 127.0, 129.3, 136.7, 138.0, 144.9 (Ar), 153.5 (C═O), 157.4 (Ar). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{23}H_{21}O_4$ 361.1440; Found 361.1451.

4-Methoxybenzhydryl 4-Methoxyphenyl Carbonate: data are given in ref 6.

4-Methoxy-4′-Methylbenzhydryl 4-Methoxyphenyl Carbonate: from 4-methoxy-4′-methylbenzhydrol (0.50 g; 2.2 mmol), pyridine (0.52 g; 6.6 mmol), and 4-methoxyphenyl chloroformate (0.57 g; 3.1 mmol); yield 0.59 g; 72%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.37 (s, 3H; Ar−CH_3), 3.79 (s, 3H; Ar−OCH_3), 3.81 (s, 3H; Ar−OCH_3), 6.76 (s, 1H; Ar_2CH), 6.87−6.92 (m, 4H, Ar−OCH_3), 7.10 (d, J = 9.1 Hz, 2H; Ar−OCH_3), 7.20 (d, J = 8.1 Hz, 2H; Ar−CH_3), 7.31−7.37 (m, 4H; Ar−OCH_3 + Ar−CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.2 (Ar−CH_3), 55.3 (Ar−OCH_3), 55.6 (Ar−OCH_3), 81.3 (Ar_2CH), 113.9, 114.4, 121.9, 126.9, 128.7, 129.2, 131.7, 136.6, 137.9, 144.8 (Ar), 153.5 (C═O), 157.3, 159.5 (Ar). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{23}H_{21}O_5$ 377.1389; Found 377.1377.

4-Methoxy-4′-Phenoxybenzhydryl 4-Methoxyphenyl Carbonate: from 4-methoxy-4′-phenoxybenzhydrol (0.50 g; 1.6 mmol), pyridine (0.39 g; 4.9 mmol), and 4-methoxyphenyl chloroformate (0.43 g; 2.3 mmol); yield 0.52 g; 70%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 3.77 (s, 3H; Ar−OCH_3), 3.79 (s, 3H; Ar−OCH_3), 6.73 (s, 1H; Ar_2CH), 6.85 (d, J = 9.2 Hz, 2H, Ar−OCH_3), 6.90 (d, J = 8.8 Hz, 2H, Ar−OCH_3), 6.97−7.03 (m, 4H; Ar−OCH_3), 7.07 (m, 3H; Ar−OCH_3 + Ar), 7.31−7.36 (m, 6H; Ar−OCH_3 + Ar); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 55.3 (Ar−OCH_3), 55.6 (Ar−OCH_3), 80.9 (Ar_2CH), 114.0, 114.4, 118.6, 119.2, 121.9, 123.6, 128.5, 128.6, 129.8, 131.5, 134.2, 144.8 (Ar), 153.4 (C═O), 156.8, 157.3, 157.4, 159.6 (Ar). Collection of HRMS data or elemental analysis was not possible for this compound due to its limited stability.

General Procedure for the Synthesis of Benzhydryl 4-Methylphenyl Carbonate. The procedure for 4-methylphenyl carbonates was almost the same as for 4-chlorophenyl carbonates, except 4-methylphenyl chloroformate was used instead of the 4-chlorophenyl chloroformate. All 4-methylphenyl carbonates were obtained as white crystals (yield 53−74%).

4-Methylbenzhydryl 4-Methylphenyl Carbonate: from 4-methylbenzhydrol (0.50 g; 2.5 mmol), pyridine (0.60 g; 7.6 mmol), and 4-methylphenyl chloroformate (0.60 g; 3.5 mmol); yield 0.50 g; 60%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.39 (s, 3H; Ar−CH_3), 2.42 (s, 3H; Ar−CH_3), 6.88 (s, 1H; Ar_2CH), 7.13 (d, J = 8.4 Hz, 2H; Ar−CH_3), 7.20−7.27 (m, 5H; ArH), 7.40−7.46 (m, 4H; Ar−CH_3), 7.52 (d, J = 7.3 Hz, 2H; Ar−CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 20.8 (Ar−CH_3), 21.2 (Ar−CH_3), 81.4 (Ar_2CH), 120.7, 127.0, 127.1, 128.1, 128.6, 129.3, 129.9, 135.6, 136.4, 138.1, 139.5, 149.0 (Ar), 153.2 (C═O). Collection of HRMS data or elemental analysis was not possible for this compound due to its limited stability.

4,4′-Dimethylbenzhydryl 4-Methylphenyl Carbonate: from 4,4′-dimethylbenzhydrol (0.50 g; 2.4 mmol), pyridine (0.56 g; 7.1 mmol), and 4-methylphenyl chloroformate (0.56 g; 3.3 mmol); yield 0.58 g; 71%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.39 (s, 3H; Ar−CH_3), 2.41 (s, 6H; Ar−CH_3), 6.84 (s, 1H; Ar_2CH), 7.12 (d, J = 8.6 Hz, 2H; Ar−CH_3), 7.20−7.25 (m, 6H; Ar−CH_3), 7.39 (d, J = 8.1 Hz, 4H; Ar−CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 20.9 (Ar−CH_3), 21.2 (Ar−CH_3), 81.4 (Ar_2CH), 120.8, 127.0, 129.3, 129.9, 135.6, 136.6, 138.0, 149.1 (Ar), 153.3 (C═O). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{23}H_{21}O_3$ 345.1491; Found 345.1491.

4-Methoxybenzhydryl 4-Methylphenyl Carbonate: data are given in ref 6.

4-Methoxy-4′-Methylbenzhydryl 4-Methylphenyl Carbonate from 4-methoxy-4′-methylbenzhydrol (0.50 g; 2.2 mmol), pyridine (0.52 g; 6.6 mmol), and 4-methylphenyl chloroformate (0.52 g; 3.1 mmol); yield 0.42 g; 53%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.35 (s, 3H; Ar−CH_3), 2.37 (s, 3H; Ar−CH_3), 3.81 (s, 3H; Ar−OCH_3), 6.77 (s, 1H; Ar_2CH), 6.92 (d, J = 8.8 Hz, 2H; Ar−OCH_3), 7.07 (d, J = 8.6 Hz, 2H; Ar−CH_3), 7.16−7.21 (m, 4H, Ar−CH_3), 7.32−7.38 (m, 4H; Ar−OCH_3 + Ar−CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 20.8 (Ar−CH_3), 21.2 (Ar−CH_3), 55.3 (Ar−OCH_3), 81.2 (Ar_2CH), 113.9, 120.7, 126.8, 128.7, 129.2, 129.9, 131.7, 135.6, 136.6, 137.9, 149.0 (Ar), 153.3 (C═O), 159.5 (Ar). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{23}H_{21}O_4$ 361.1440; Found 361.1432.

4-Methoxy-4′-Phenoxybenzhydryl 4-Methylphenyl Carbonate: from 4-methoxy-4′-phenoxybenzhydrol (0.50 g; 1.6 mmol), pyridine (0.39 g; 4.9 mmol), and 4-methylphenyl chloroformate (0.39 g; 2.3 mmol); yield 0.41 g; 57%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 2.32 (s, 3H; Ar−CH_3), 3.79 (s, 3H; Ar−OCH_3), 6.74 (s, 1H; Ar_2CH), 6.9 (d, J = 8.8 Hz, 2H; Ar−OCH_3), 6.97−7.04 (m, 6H, Ar−CH_3 + ArH), 7.14 (d, J = 8.6 Hz, 2H; Ar−CH_3), 7.31−7.36 (m, 7H; Ar−OCH_3 + ArH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 20.9 (Ar−CH_3), 55.3 (Ar−OCH_3), 80.9 (Ar_2CH), 114.0, 118.6, 119.2, 120.7, 123.6, 128.5, 128.6, 129.8, 129.9, 131.5, 134.2, 135.7, 149.0 (Ar), 153.3 (C═O), 156.8, 157.3 (Ar). Collection of HRMS data or elemental analysis was not possible for this compound due to its limited stability.

General Procedure for the Synthesis of Benzhydryl Ethyl Carbonate. The procedure for ethyl carbonates was almost the same as for 4-chlorophenyl carbonates, except ethyl chloroformate was used instead of the 4-chlorophenyl chloroformate. All ethyl carbonates were obtained as white crystals (yield 55−70%).

4-Methoxybenzhydryl Ethyl Carbonate: data are given in ref 6.

4-Methoxy-4′-Methylbenzhydryl Ethyl Carbonate: from 4-methoxy-4′-methylbenzhydrol (0.70 g; 3.1 mmol), pyridine (0.73 g; 9.2 mmol), and ethyl chloroformate (0.47 g; 4.3 mmol); yield 0.57 g; 62%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 1.29 (t, J = 7.1 Hz, 3H; $C\underline{H}_3CH_2O$−), 2.32 (s, 3H; Ar−CH_3), 3.77 (s, 3H; Ar−OCH_3), 4.18 (q, J = 7.1 Hz, 2H; $CH_3C\underline{H}_2O$−), 6.64 (s, 1H; Ar_2CH), 6.86 (d, J = 8.8 Hz, 2H; ArH), 7.14 (d, J = 7.9 Hz, 2H; ArH), 7.23−7.30 (m, 4H; ArH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 14.6 ($\underline{C}H_3CH_2O$−), 21.5, 55.6 (Ar−OCH_3), 64.4 ($CH_3\underline{C}H_2O$−), 80.6, 114.2, 127.1, 128.9, 129.5, 132.5, 137.4, 138.0 (Ar), 155.0 (C═O), 159.7 (Ar). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{18}H_{19}O_4$ 299.1283; Found 299.1295.

4-Methoxy-4′-Phenoxybenzhydryl Ethyl Carbonate: from 4-methoxy-4′-phenoxybenzhydrol (0.70 g; 2.3 mmol), pyridine (0.54 g; 6.8 mmol), and ethyl chloroformate (0.35 g; 3.2 mmol); yield 0.48 g; 55%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 1.29 (t, J = 7.1 Hz, 3H; $C\underline{H}_3CH_2O$−), 3.78 (s, 3H; Ar−OCH_3), 4.19 (q, J = 7.1 Hz, 2H; $CH_3C\underline{H}_2O$−), 6.65 (s, 1H; Ar_2CH), 6.88 (d, J = 8.8 Hz, 2H; ArH), 6.94−7.12 (m, 5H; ArH), 7.28−7.35 (m, 6H; ArH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 14.6 ($\underline{C}H_3CH_2O$−), 55.6 (ArOCH_3), 64.5 ($CH_3\underline{C}H_2O$−), 80.3, 114.3, 118.9, 119.5, 123.8, 128.8, 130.1, 132.3, 135.1 (Ar), 154.9 (C═O), 157.2, 157.5, 159.8 (Ar). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{23}H_{21}O_5$ 377.1389; Found 377.1394.

4,4′-Dimethoxybenzhydryl Ethyl Carbonate: from 4,4′-dimethoxybenzhydrol (1.00 g; 4.1 mmol), pyridine (0.97 g; 12.3 mmol), and

DOI: 10.1021/acs.joc.7b00885
J. Org. Chem. 2017, 82, 7820−7831

ethyl chloroformate (0.62 g; 5.7 mmol); yield 0.90 g; 70%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = δ/ppm = 1.30 (t, J = 7.1 Hz, 3H; $C\underline{H}_3CH_2O-$), 3.79 (s, 3H; $Ar-OCH_3$), 4.20 (q, J = 7.1 Hz, 2H; $CH_3C\underline{H}_2O-$), 6.65 (s, 1H; Ar_2CH), 6.88 (d, J = 8.7 Hz, 4H; ArH), 7.29 (d, J = 8.8 Hz, 4H; ArH);

^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 14.3 ($\underline{C}H_3CH_2O-$), 55.2 ($ArOCH_3$), 64.1 ($CH_3\underline{C}H_2O-$), 80.1, 113.8, 128.4, 132.2 (Ar), 154.6 (C═O), 159.3 (Ar). Collection of HRMS data or elemental analysis was not possible for this compound due to its limited stability.

General Procedure for the Synthesis of Benzhydryl Isopropyl Carbonate. The procedure for isopropyl carbonates was almost the same as for 4-chlorophenyl carbonates, except 1 M isopropyl chloroformate in toluene was used instead of the 4-chlorophenyl chloroformate. All isopropyl carbonates were obtained as white crystals (yield 58−86%).

4-Methoxybenzhydryl Isopropyl Carbonate: data are given in ref 6.

4-Methoxy-4′-Methylbenzhydryl Isopropyl Carbonate: from 4-methoxy-4′-methylbenzhydrol (0.70 g; 3.1 mmol), pyridine (0.73 g; 9.2 mmol), and isopropyl chloroformate (3.83 g; 4.3 mmol); yield 0.56 g; 58%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 1.27 (d, J = 6.3 Hz, 6H; $-CH(C\underline{H}_3)_2$), 2.32 (s, 3H; $Ar-CH_3$), 3.77 (s, 3H; $Ar-OCH_3$), 4.87 (sep, J = 6.3 Hz, 1H; $-C\underline{H}(CH_3)_2$), 6.63 (s, 1H; Ar_2CH), 6.85 (d, J = 8.7 Hz, 2H; ArH), 7.14 (d, J = 8.2 Hz, 2H; ArH),7.23−7.29 (m, 4H; ArH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.5 ($Ar-CH_3$), 22.2 ($-CH(\underline{C}H_3)_2$), 55.6 ($Ar-OCH_3$), 72.4 ($-\underline{C}H(CH_3)_2$), 80.5, 114.2, 127.1, 128.8, 129.5, 132.6, 137.6, 137.9 (Ar), 154.5 (C═O), 159.7 (Ar). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{19}H_{21}O_4$ 313.1439; Found 313.1443.

4-Methoxy-4′-Phenoxybenzhydryl Isopropyl Carbonate: from 4-methoxy-4′-phenoxybenzhydrol (0.70 g; 2.3 mmol), pyridine (0.54 g; 6.8 mmol), and isopropyl chloroformate (2.85 g; 3.2 mmol); yield 0.60 g; 67%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = 1.28 (d, J = 6.3 Hz, 6H; $-CH(C\underline{H}_3)_2$), 3.76 (s, 3H; $Ar-OCH_3$), 4.87 (sep, J = 6.3 Hz, 1H; $-C\underline{H}(CH_3)_2$), 6.65 (s, 1H; Ar_2CH), 6.86 (d, J = 8.7 Hz, 2H; ArH), 6.94−7.10 (m, 5H; ArH), 7.28−7.32 (m, 6H; ArH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 21.8 ($-CH(\underline{C}H_3)_2$), 55.3 ($Ar-OCH_3$), 72.2 ($-\underline{C}H(CH_3)_2$), 79.8, 113.9, 118.6, 119.1, 123.5, 128.5, 129.8, 132.1, 134.9 (Ar), 154.1 (C═O), 156.9, 157.1, 159.4 (Ar). HRMS (MALDI-TOF/TOF) m/z: $[M - H]^-$ Calcd for $C_{24}H_{23}O_5$ 391.1545; Found 391.1552.

4,4′-Dimethoxybenzhydryl Isopropyl Carbonate: from 4,4′-dimethoxybenzhydrol (0.70 g; 2.9 mmol), pyridine (0.68 g; 8.6 mmol), and isopropyl chloroformate (3.58 g; 4.0 mmol); yield 0.56 g; 59%; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ/ppm = δ/ppm = 1.27 (d, J = 6.3 Hz, 6H; $-CH(C\underline{H}_3)_2$), 3.77 (s, 6H; $Ar-OCH_3$), 4.87 (sep, J = 6.3 Hz, 1H; $-C\underline{H}(CH_3)_2$), 6.62 (s, 1H; Ar_2CH), 6.86 (d, J = 8.8 Hz, 4H; ArH), 7.28 (d, J = 8.5 Hz, 4H; ArH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ/ppm = 22.1 ($-CH(\underline{C}H_3)_2$), 55.6 ($ArOCH_3$), 72.4 ($-\underline{C}H(CH_3)_2$), 80.3, 114.2, 128.7, 132.7 (Ar), 154.5 (C═O), 159.6 (Ar). Collection of HRMS data or elemental analysis was not possible for this compound due to its limited stability.

KINETIC METHODS

Solvolysis rate constants were measured conductometrically. Freshly prepared solvents (30 mL) were thermostated (±0.1 °C) at a given temperature for several minutes prior to addition of a substrate. Typically, the substrate (10−40 mg) was dissolved in dichloromethane (0.10 mL) and injected into the solvent. An increase of the conductivity during solvolysis was monitored automatically by means of a WTW LF 530 conductometer and use of a Radiometer 2-pole Conductivity Cell (CDC641 T). Individual rate constants were obtained by least-squares fitting of the conductivity data (three and four half-lives) to the first-order kinetic eq 3

$$G_t = a(1 - e^{-kt}) + b \quad (3)$$

in which G_t is the conductivity of the reaction mixture (mS cm^{-1}), a is the total change of conductivity of the solution from the start of the reaction (t = 0) to complete solvolysis of the substrate (mS cm^{-1}), k is the first-order rate constant (s^{-1}), t is time (s), and b represents the conductivity of the solution (solvent and organic base) before addition of a substrate (mS cm^{-1}).

The determined rate constants were averaged from at least three measurements (Tables S1 and S3). In order to achieve a complete ionization of a liberated acid, a proton sponge base [1,8-bis(dimethylamino)naphthalene] and triethylamine (TEA) were added in a range of concentration for each given aqueous binary mixture presented in Table S4.

COMPUTATIONAL METHODS

All calculations were carried out using the Gaussian 09 program suite.[22] Geometry optimizations were performed without any symmetry constrains at the M06-2X/6-311+G(3df,2pd) level of theory[23] using the SMD solvation model[24] that mimics water as a solvent. The most stable conformation found for a given ground state structure was used for calculation of standard free energies for heterolysis of benzhydryl derivatives (Table S7). Stationary points were characterized as minima (NImag = 0) by the SMD-M06-2X/6-311+G(3df,2pd) level frequency calculations, which were also used to calculate the thermal corrections to free energies at 1 atm and 298 K. Cartesian coordinates for all optimized geometries as well as corresponding energies are given in the Supporting Information.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00885.

Solvolysis rate constants of substituted benzhydryl aryl/alkyl carbonates in various solvents, activation parameters, standard free energies for heterolysis of benzhydryl aryl carbonates and benzoates calculated at the M06-2X/6-311+G(3df,2pd) level using the SMD solvation model, optimized geometries and energies, NMR spectra, conductivity vs time raw data for solvolyses of benzhydryl aryl/alkyl carbonates, Eyring plots, a scheme of delocalization of the anionic charge in aryl carbonate anions (Scheme S1) (PDF)

AUTHOR INFORMATION

Corresponding Authors

*E-mail: bdenegri@pharma.hr.

*E-mail: okronja@pharma.hr.

ORCID

Olga Kronja: 0000-0002-4070-1667

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The authors gratefully acknowledge financial support of this research by the Croatian Science Foundation (under the project number IP-1021). Computational resources provided by Isabella cluster (isabella.srce.hr) at Zagreb University Computing Centre (Srce) were used for this research.

REFERENCES

(1) Shaikh, A.-A. G.; Sivaram, S. *Chem. Rev.* **1996**, *96*, 951−976.

(2) (a) Kocienski, P. J. *Protecting Groups*, 3rd ed.; Thieme: Stuttgart, 2005. (b) Wuts, P. G. M.; Greene, T. W. *Greene's Protective Groups in Organic Synthesis*, 4th ed.; John Wiley & Sons: Hoboken, NJ, 2007.

(3) Denegri, B.; Kronja, O. *J. Org. Chem.* **2007**, *72*, 8427−8433.

(4) (a) Matić, M.; Denegri, B.; Kronja, O. *J. Org. Chem.* **2012**, *77*, 8986−8998. (b) Matić, M.; Denegri, B.; Kronja, O. *Eur. J. Org. Chem.* **2014**, *2014*, 1477−1486.

DOI: 10.1021/acs.joc.7b00885
J. Org. Chem. 2017, 82, 7820−7831

(5) Streidl, N.; Denegri, B.; Kronja, O.; Mayr, H. *Acc. Chem. Res.* **2010**, *43*, 1537−1549.
(6) Denegri, B.; Matić, M.; Kronja, O. *ChemistrySelect* **2016**, *1*, 5250−5259.
(7) Denegri, B.; Ofial, A. R.; Jurić, S.; Streiter, A.; Kronja, O.; Mayr, H. *Chem. - Eur. J.* **2006**, *12*, 1657−1666.
(8) Denegri, B.; Matić, M.; Kronja, O. *Org. Biomol. Chem.* **2014**, *12*, 5698−5709.
(9) (a) Matić, M.; Denegri, B.; Kronja, O. *Eur. J. Org. Chem.* **2010**, *2010*, 6019−6024. (b) Matić, M.; Bebek, N.; Denegri, B.; Kronja, O. *Croat. Chem. Acta* **2016**, *89*, 355−362.
(10) Vatsadze, S. Z.; Loginova, Y. D.; dos Passos Gomes, G.; Alabugin, I. V. *Chem. - Eur. J.* **2017**, *23*, 3225−3245.
(11) Denegri, B.; Streiter, A.; Jurić, S.; Ofial, A. R.; Kronja, O.; Mayr, H. *Chem. - Eur. J.* **2006**, *12*, 1648−1656.
(12) (a) Leffler, J. E. *Science* **1953**, *117*, 340−341. (b) Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963. (c) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334−338.
(13) Dewar, M. J. S.; Dougherty, R. C. *The PMO Theory of Organic Chemistry*; Plenum: New York, 1975.
(14) Mayr, H.; Ofial, A. R. *Angew. Chem., Int. Ed.* **2006**, *45*, 1844−1854.
(15) Marcus, R. A. *J. Phys. Chem.* **1968**, *72*, 891−899.
(16) (a) Schindele, C.; Houk, K. N.; Mayr, H. *J. Am. Chem. Soc.* **2002**, *124*, 11208−11214. (b) Mayr, H.; Breugst, M.; Ofial, A. R. *Angew. Chem., Int. Ed.* **2011**, *50*, 6470−6505.
(17) (a) Richard, J. P. *Tetrahedron* **1995**, *51*, 1535−1573. (b) Richard, J. P.; Amyes, T. L.; Toteva, M. M. *Acc. Chem. Res.* **2001**, *34*, 981−988.
(18) Bernasconi, C. F. *Acc. Chem. Res.* **1992**, *25*, 9−16.
(19) (a) Minegishi, S.; Loos, R.; Kobayashi, S.; Mayr, H. *J. Am. Chem. Soc.* **2005**, *127*, 2641−2649. (b) Schaller, H. F.; Tishkov, A. A.; Feng, X.; Mayr, H. *J. Am. Chem. Soc.* **2008**, *130*, 3012−3022. (c) Streidl, N.; Branzan, R.; Mayr, H. *Eur. J .Org. Chem.* **2010**, *2010*, 4205−4210.
(20) (a) Mayr, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A. R.; Remennikov, G.; Schimmel, H. *J. Am. Chem. Soc.* **2001**, *123*, 9500−9512. (b) Mayr, H.; Kempf, B.; Ofial, A. R. *Acc. Chem. Res.* **2003**, *36*, 66−77.
(21) (a) Fry, J. L.; Lancelot, C. J.; Lam, L. K. M.; Harris, J. M.; Bingham, R. C.; Raber, D. J.; Hall, R. E.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1970**, *92*, 2538−2540. (b) Schleyer, P. v. R.; Bingham, R. C. *J. Am. Chem. Soc.* **1971**, *93*, 3189−3199. (c) Slutsky, J.; Bingham, R. C.; Schleyer, P. v. R.; Dickason, W. C.; Brown, H. C. J. *J. Am. Chem. Soc.* **1974**, *96*, 1969−1970. (d) Lomas, J. S.; Dubois, J. E. *J. Org. Chem.* **1975**, *40*, 3303−3304. (e) Lomas, J. S. *Tetrahedron Lett.* **1978**, *19*, 1783−1786.
(22) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, Revision D.01; Gaussian, Inc.: Wallingford, CT, 2013.
(23) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215−241.
(24) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2009**, *113*, 6378−6396.

DOI: 10.1021/acs.joc.7b00885
J. Org. Chem. 2017, 82, 7820−7831