

# Solvolytic Reactivity of 2,4-Dinitrophenolates

Mirela Matic,<sup>[a]</sup> Bernard Denegri,<sup>\*[a]</sup> and Olga Kronja<sup>\*[a]</sup>

**Keywords:** Reaction mechanisms / Solvent effects / Solvolysis / Nucleofugality scale

A series of X,Y-substituted benzhydryl 2,4-dinitrophenolates (DNP, **1–5**) were subjected to solvolysis in various methanol/water, ethanol/water, and acetone/water mixtures at 25 °C. The linear free energy relationship (LFER) equation,  $\log k = s_f(E_f + N_f)$ , was used to derive the nucleofuge-specific parameters ( $N_f$  and  $s_f$ ) for an  $S_N1$ -type reaction. The magnitudes of nucleofugalities ( $N_f$ ) are around zero, indicating that DNP falls in the middle of the established nucleofugality scale. The slope parameters ( $s_f$ ) and the Grönwald–Winstein  $m_{OTs}$  parameters obtained demonstrate that benzhydryl DNPs sol-

volyze through a late transition state (TS) in which the negative charge delocalization causes considerably diminished solvation. Because of the late TS, the nucleofuge-specific slope parameters,  $s_f$ , are relatively high, i.e., the  $\log k$  vs.  $E_f$  plots are steeper than for most of the previously investigated leaving groups. This may lead to intersection of the  $\log k$  vs.  $E_f$  plots that correspond to DNP and to some other leaving groups of similar reactivity, i.e., inversion of the relative reactivities may occur. Such inversion is shown here for DNPs and phenyl carbonates.

## Introduction

In our previous work we compared the leaving group (LG) abilities of various groups by using the recently developed electrofugality/nucleofugality scale based on solvolysis of benzhydryl derivatives.<sup>[1]</sup> According to that approach, the heterolysis rate constant for any  $S_N1$  solvolysis reaction can be expressed with the three-parameter LFER equation (1)

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

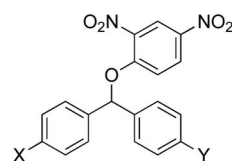
in which  $k$  is the first-order rate constant ( $s^{-1}$ ) at 25 °C,  $s_f$  is the nucleofuge-specific slope parameter,  $N_f$  is the nucleofugality parameter, and  $E_f$  is the electrofugality parameter. The latter parameter is set up as an independent variable and refers to ability of the substrate moiety to leave as a carbocation in the heterolysis reaction ( $S_N1$ ). Since the relative nucleofugalities depend not only on the substrate but also on the solvent, the nucleofuge-specific parameters ( $s_f$  and  $N_f$ ) characterize the leaving group in a given solvent. Such an approach separates the contributions of electrofuge and nucleofuge in overall solvolytic reactivity. Predefined parameters are:  $E_f = 0.00$  for dianisylcarbenium electrofuge ( $X = Y = 4\text{-OCH}_3$ ) and  $s_f = 1.00$  for chloride nucleofuge in pure ethanol.<sup>[1a]</sup> According to equation (1), the nucleofugality ( $N_f$ ) of the given leaving group is defined as the negative intercept on the abscissa of  $\log k$  vs.  $E_f$  plot.

The nucleofugality parameters in various solvents of some frequently used halides, carboxylates,<sup>[1,2]</sup> and carbon-

ates<sup>[3]</sup> have already been determined. The latter leaving groups are produced by cleavage of the C–OC(O) bond in the heterolysis step in solvolysis. Phenolates, in which cleavage of the ethereal C–OR bond occurs in heterolysis, have also been used as leaving groups in solvolytic reactions. For example, adamantyl picrate was studied to determine the solvent effects on leaving groups,<sup>[4]</sup> and 2,4-dinitrophenolate was used to compare the behavior of tertiary and secondary cation fragments.<sup>[5]</sup> Phenoxide was chosen to be the next leaving group to be placed on the nucleofugality scale, so that its reactivity could be compared with other leaving groups, particularly with those in which cleavage of the C–O bond also takes place. We intended to determine the nucleofuge-specific parameters ( $N_f$  and  $s_f$ ) for 2,4-dinitrophenolate (DNP) using its benzhydryl derivatives as substrates. DNP was the leaving group of choice here because of the convenient reactivity and solubility of its benzhydryl derivatives in the series of aqueous solvents.

## Results and Discussion

A series of benzhydryl DNPs (**1–5**), which were prepared from the corresponding benzhydrols, were subjected to solvolysis in aqueous solvents.



- 1: X = OMe, Y = Me
- 2: X = OMe, Y = H
- 3: X = Me, Y = Me
- 4: X = Me, Y = H
- 5: X = F, Y = H

[a] Faculty of Pharmacy and Biochemistry University of Zagreb, Ante Kovačića 1, 10000 Zagreb, Croatia  
Fax: +385-1-48-56-201  
E-mail: kronja@pharma.hr  
bdenegri@pharma.hr

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/ejoc.201000784>.

The solvolysis rates were measured conductometrically at 25 °C. In a few cases the rates were measured at three different temperatures and extrapolated to 25 °C. Details are given in Kinetic methods in the Supporting Information. The first-order rate constants at 25 °C (measured and extrapolated) are presented in Table 1.

Table 1. Solvolysis rate constants of X,Y-substituted benzhydryl 2,4-dinitrophenolates in various aqueous solvents at 25 °C.

| Solvent <sup>[a]</sup> | Substrate (X, Y) | $E_f^{[b]}$ | $k$ [s <sup>-1</sup> ] <sup>[c]</sup> |
|------------------------|------------------|-------------|---------------------------------------|
| 100M                   | 4 (4-Me, H)      | -4.68       | $8.20 \times 10^{-6[d,e]}$            |
|                        | 3 (4-Me, 4'-Me)  | -3.47       | $(1.81 \pm 0.04) \times 10^{-4}$      |
|                        | 2 (4-OMe, H)     | -2.06       | $(4.15 \pm 0.03) \times 10^{-3}$      |
|                        | 1 (4-OMe, 4'-Me) | -1.29       | $(2.86 \pm 0.04) \times 10^{-2}$      |
| 90M10W                 | 4 (4-Me, H)      | -4.68       | $(3.04 \pm 0.07) \times 10^{-5}$      |
|                        | 3 (4-Me, 4'-Me)  | -3.47       | $(5.70 \pm 0.10) \times 10^{-4}$      |
|                        | 2 (4-OMe, H)     | -2.06       | $(1.04 \pm 0.02) \times 10^{-2}$      |
|                        | 4 (4-Me, H)      | -4.68       | $(7.94 \pm 0.13) \times 10^{-5}$      |
| 80M20W                 | 3 (4-Me, 4'-Me)  | -3.47       | $(1.44 \pm 0.02) \times 10^{-3}$      |
|                        | 2 (4-OMe, H)     | -2.06       | $(2.35 \pm 0.03) \times 10^{-2}$      |
|                        | 4 (4-Me, H)      | -4.68       | $1.78 \times 10^{-6[d,f]}$            |
|                        | 3 (4-Me, 4'-Me)  | -3.47       | $(3.23 \pm 0.03) \times 10^{-5}$      |
| 100E                   | 2 (4-OMe, H)     | -2.06       | $(9.76 \pm 0.21) \times 10^{-4}$      |
|                        | 1 (4-OMe, 4'-Me) | -1.29       | $(7.26 \pm 0.08) \times 10^{-3}$      |
|                        | 4 (4-Me, H)      | -4.68       | $1.22 \times 10^{-5[d,g]}$            |
|                        | 3 (4-Me, 4'-Me)  | -3.47       | $(1.91 \pm 0.05) \times 10^{-4}$      |
| 90E10W                 | 2 (4-OMe, H)     | -2.06       | $(5.05 \pm 0.12) \times 10^{-3}$      |
|                        | 1 (4-OMe, 4'-Me) | -1.29       | $(3.45 \pm 0.06) \times 10^{-2}$      |
|                        | 4 (4-Me, H)      | -4.68       | $1.75 \times 10^{-6[d,h]}$            |
|                        | 3 (4-Me, 4'-Me)  | -3.47       | $(2.89 \pm 0.05) \times 10^{-5}$      |
| 80E20W                 | 2 (4-OMe, H)     | -2.06       | $(5.23 \pm 0.06) \times 10^{-4}$      |
|                        | 1 (4-OMe, 4'-Me) | -1.29       | $(1.17 \pm 0.21) \times 10^{-2}$      |
|                        | 4 (4-Me, H)      | -4.68       | $3.90 \times 10^{-6[d,i]}$            |
|                        | 3 (4-Me, 4'-Me)  | -3.47       | $(6.08 \pm 0.07) \times 10^{-5}$      |
| 70E30W                 | 2 (4-OMe, H)     | -2.06       | $(1.02 \pm 0.02) \times 10^{-3}$      |
|                        | 1 (4-OMe, 4'-Me) | -1.29       | $(1.82 \pm 0.04) \times 10^{-2}$      |
|                        | 4 (4-Me, H)      | -4.68       | $9.65 \times 10^{-6[d,j]}$            |
|                        | 3 (4-Me, 4'-Me)  | -3.47       | $(4.52 \pm 0.12) \times 10^{-4}$      |
| 90A10W                 | 2 (4-OMe, H)     | -2.06       | $(4.13 \pm 0.04) \times 10^{-5}$      |
|                        | 1 (4-OMe, 4'-Me) | -1.29       | $(3.16 \pm 0.03) \times 10^{-3}$      |
|                        | 4 (4-Me, H)      | -4.68       | $(1.00 \pm 0.02) \times 10^{-2}$      |
|                        | 3 (4-Me, 4'-Me)  | -3.47       | $(1.50 \pm 0.03) \times 10^{-3}$      |
| 80A20W                 | 2 (4-OMe, H)     | -2.06       | $(1.77 \pm 0.05) \times 10^{-5}$      |
|                        | 1 (4-OMe, 4'-Me) | -1.29       | $(3.15 \pm 0.05) \times 10^{-4}$      |
|                        | 4 (4-Me, H)      | -4.68       | $(7.29 \pm 0.07) \times 10^{-3}$      |
|                        | 3 (4-Me, 4'-Me)  | -3.47       | $(3.76 \pm 0.09) \times 10^{-2}$      |
| 70A30W                 | 2 (4-OMe, H)     | -2.06       | $(4.97 \pm 0.09) \times 10^{-5}$      |
|                        | 1 (4-OMe, 4'-Me) | -1.29       | $(7.34 \pm 0.23) \times 10^{-4}$      |
|                        | 4 (4-Me, H)      | -4.68       | $(1.21 \pm 0.04) \times 10^{-2}$      |
|                        | 3 (4-Me, 4'-Me)  | -3.47       |                                       |
| 60A40W                 | 2 (4-OMe, H)     | -2.06       |                                       |
|                        | 1 (4-OMe, 4'-Me) | -1.29       |                                       |
|                        | 4 (4-Me, H)      | -4.68       |                                       |
|                        | 3 (4-Me, 4'-Me)  | -3.47       |                                       |
| 50A50W                 | 2 (4-OMe, H)     | -2.06       |                                       |
|                        | 1 (4-OMe, 4'-Me) | -1.29       |                                       |
|                        | 4 (4-Me, H)      | -4.68       |                                       |
|                        | 3 (4-Me, 4'-Me)  | -3.47       |                                       |

[a] Binary solvents are given v/v at 25 °C. A = acetone, E = ethanol, M = methanol, W = water. [b] Electrofugality parameters are taken from Denegri et al.<sup>[1a]</sup> [c] Average rate constants from at least three runs performed at 25 °C. Errors are standard deviations. [d] Extrapolated from data at higher temperatures by using the Eyring equation. [e]  $\Delta H^\ddagger = 107.1 \pm 2.7$  kJ mol<sup>-1</sup>,  $\Delta S^\ddagger = 16.8 \pm 8.4$  J K<sup>-1</sup> mol<sup>-1</sup>. [f]  $\Delta H^\ddagger = 107.9 \pm 0.0$  kJ mol<sup>-1</sup>,  $\Delta S^\ddagger = 6.9 \pm 1.2$  J K<sup>-1</sup> mol<sup>-1</sup>. [g]  $\Delta H^\ddagger = 97.6 \pm 1.0$  kJ mol<sup>-1</sup>,  $\Delta S^\ddagger = -11.6 \pm 3.0$  J K<sup>-1</sup> mol<sup>-1</sup>. [h]  $\Delta H^\ddagger = 104.7 \pm 0.8$  kJ mol<sup>-1</sup>,  $\Delta S^\ddagger = -3.9 \pm 2.4$  J K<sup>-1</sup> mol<sup>-1</sup>. [i]  $\Delta H^\ddagger = 103.4 \pm 0.6$  kJ mol<sup>-1</sup>,  $\Delta S^\ddagger = -1.7 \pm 1.9$  J K<sup>-1</sup> mol<sup>-1</sup>. [j]  $\Delta H^\ddagger = 101.7 \pm 1.3$  kJ mol<sup>-1</sup>,  $\Delta S^\ddagger = 0.1 \pm 4.2$  J K<sup>-1</sup> mol<sup>-1</sup>. [k]  $\Delta H^\ddagger = 106.6 \pm 2.7$  kJ mol<sup>-1</sup>,  $\Delta S^\ddagger = 13.8 \pm 8.4$  J K<sup>-1</sup> mol<sup>-1</sup>.

To calculate the nucleofugality parameters ( $N_f$ ) and the slope parameters ( $s_f$ ) for DNP in various solvents, logarithms of the first-order rate constants in the given solvents were plotted against  $E_f$ . The values of  $E_f$  for all the electrofuges used have previously been determined.<sup>[1a]</sup> Plots of  $\log k$  against  $E_f$  obtained for acetone/water binary solvents are presented in Figure 1 (for correlation lines obtained in aqueous ethanol and aqueous methanol see the Supporting Information). The nucleofuge-specific parameters were calculated according to Equation (1) and are presented in Table 2.

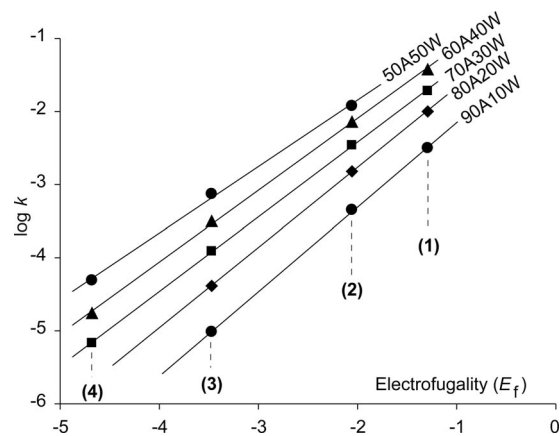


Figure 1. Plots of  $\log k$  vs.  $E_f$  for solvolysis of X,Y-substituted benzhydryl 2,4-dinitrophenolates in aqueous acetone. Solvent mixtures are given as v/v ratios; A = acetone and W = water.

Table 2. Nucleofugality parameters  $N_f$  and  $s_f$  for 2,4-dinitrophenolate in various solvents.

| Solvent <sup>[a]</sup> | $N_f^{[b]}$      | $s_f^{[b]}$     | $R^{[c]}$ ( $n$ ) <sup>[d]</sup> |
|------------------------|------------------|-----------------|----------------------------------|
| 100M                   | $-0.22 \pm 0.07$ | $1.03 \pm 0.02$ | 0.9995 (4)                       |
| 90M10W                 | $0.04 \pm 0.17$  | $0.97 \pm 0.05$ | 0.9989 (3)                       |
| 80M20W                 | $0.37 \pm 0.18$  | $0.94 \pm 0.05$ | 0.9985 (3)                       |
| 100E                   | $-0.75 \pm 0.04$ | $1.06 \pm 0.01$ | 1.0000 (4)                       |
| 90E10W                 | $-0.18 \pm 0.04$ | $1.02 \pm 0.01$ | 0.9999 (4)                       |
| 80E20W                 | $0.22 \pm 0.09$  | $1.03 \pm 0.02$ | 0.9995 (4)                       |
| 70E30W                 | $0.36 \pm 0.13$  | $0.99 \pm 0.03$ | 0.9989 (4)                       |
| 90A10W                 | $-0.85 \pm 0.06$ | $1.16 \pm 0.02$ | 0.9998 (3)                       |
| 80A20W                 | $-0.53 \pm 0.03$ | $1.10 \pm 0.01$ | 1.0000 (3)                       |
| 70A30W                 | $-0.37 \pm 0.03$ | $1.02 \pm 0.01$ | 0.9999 (4)                       |
| 60A40W                 | $-0.14 \pm 0.05$ | $0.98 \pm 0.01$ | 0.9998 (4)                       |
| 50A50W                 | $-0.03 \pm 0.12$ | $0.91 \pm 0.03$ | 0.9994 (3)                       |

[a] Binary solvents (v/v) at 25 °C. A = acetone, E = ethanol, M = methanol, W = water. [b] Errors shown are standard errors. [c] Correlation coefficient. [d] Number of data points.

The nucleofugality parameters presented in Table 2 are around zero in all solvents so, accordingly, DNP falls in the middle of the established nucleofugality scale, above phenyl carbonate and below fluorinated carboxylates, heptafluorobutyrate, and trifluoroacetate. The nucleofugalities of various leaving groups in 80% aq. ethanol and 80% aq. methanol are presented in Figure 2.

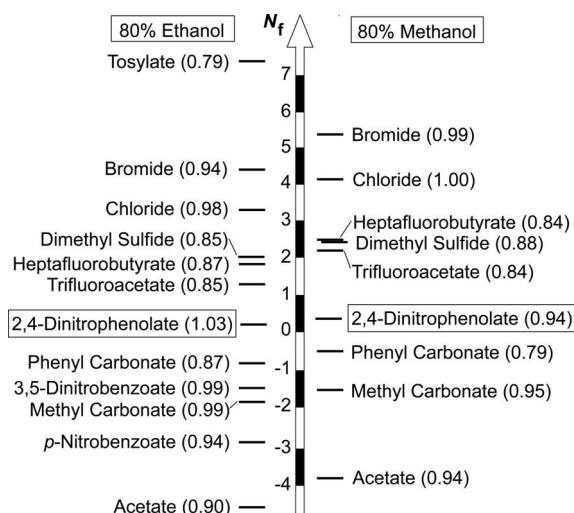


Figure 2. Nucleofugalities and the nucleofuge-specific slope parameters (in parentheses) for some leaving groups in 80% aqueous ethanol and 80% aqueous methanol.

## Discussion on the Nucleofuge-Specific Parameters of DNP

The values for the nucleofugality parameters  $N_f$  usually give correct information on the relative reactivities of the leaving groups (LGs). However, if the nucleofugalities of two LGs are close in magnitude, while the  $s_f$  parameters differ substantially, a simple comparison of nucleofugalities may be misleading because of the possible intersection of the  $\log k$  vs.  $E_f$  plots. In such cases, for correct prediction of the relative reactivities, both parameters should be taken in account, the nucleofugality and the slope parameter, i.e., Equation (1) should be applied. This is particularly important if the LG with a higher  $N_f$  value produces a lower slope because, in such cases, the intersection of the  $\log k$  vs.  $E_f$  slopes might correspond to electrofuges that are, with an appropriate LG, stable structures that solvolyze in the range of experimental reactivities or in their close vicinity. Figure 3 shows the  $\log k$  vs.  $E_f$  plots for phenyl carbonate ( $N_f = -0.84$ ,  $s_f = 0.87$ ) and DNP ( $N_f = 0.22$ ,  $s_f = 1.03$ ) obtained in 80% aqueous ethanol.

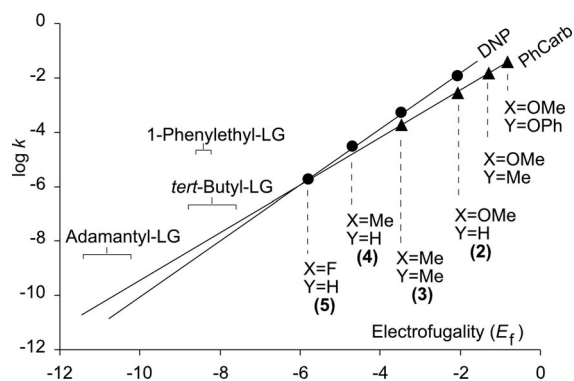


Figure 3. Comparison of  $\log k$  vs.  $E_f$  plots for 2,4-dinitrophenolate and phenyl carbonate in 80% aq. ethanol at 25 °C.

Accordingly, for more reactive substrates DNPs are more reactive than phenyl carbonates, but for less reactive substrates, i.e., those with weaker electrofuges, such as adamantyl, *tert*-butyl, or 1-phenylethyl,<sup>[1c]</sup> the carbonates may be slightly more reactive than the corresponding DNP. It should be emphasized that the intersection of the plots is reliable for two reasons: (1) it is not obtained after far extrapolation, but it is in the range of experimental data, and (2) the correlation of experimental data for both plots in Figure 3 are excellent ( $R > 0.999$ ). Thus, for example, it can be predicted that 3,3'-dichlorobenzhydryl DNP ( $E_f = -9.63$ )<sup>[1c]</sup> solvolyzes slower than the corresponding phenyl carbonate in 80% ethanol, while, for example, dianisylmethyl DNP ( $E_f = 0.00$ ) is more reactive than the corresponding phenyl carbonate.

Inversion of the relative rates of the reactions of phenyl carbonates and DNPs, as is presented in Figure 3, demonstrates another advantage of the above three-parameter LFER approach [Equation (1)] over the use of a single structure with different LGs. Thus, besides the possibility for covering a much wider range of reactivities, the cases where inversion of the reactivity between the substrates with different leaving groups occurs can also be predicted, which is not possible if the investigations are carried out with substrates in which only the leaving groups differ.

The values of the slope parameters ( $s_f$ ) obtained for DNP in various solvents are generally close to unity, as are the  $s_f$  parameters obtained with chlorides and bromides. Whereas in aqueous acetone the slopes significantly decrease as the polarity of the solvent increases, in aqueous alcohols the trend is so mild that the decrease in the  $s_f$  values is close to the limits of the experimental error (Table 2). A decrease in the slope parameters with increasing polarity of the solvent has previously been attributed to diminished solvation effects in the TS caused by additional charge delocalization in the leaving group moiety.<sup>[2a]</sup>

To extract the Grünwald–Winstein  $m$  values and to compare the sensitivity of DNP toward solvent polarity with other leaving groups, we plotted logarithms of rate constants of benzhydryl DNPs and of the corresponding chloride<sup>[6]</sup> in aqueous ethanol, aqueous methanol, and aqueous acetone, against the ionizing power ( $Y_{OTs}$ ).<sup>[7]</sup> The previously determined  $m_{OTs}$  values for phenyl carbonates were also taken for comparison.<sup>[2a]</sup> The chloride here represents the reference compound in which electron delocalization in the LG does not exist, whereas the phenyl carbonate represents the LG in which the negative charge delocalization onto three oxygen atoms occurs in the TS, due to resonance and inverse hyperconjugation.<sup>[3]</sup> Some  $m_{OTs}$  parameters are presented in Table 3.

Two major factors that determine the values of Grünwald–Winstein  $m$  parameters for limiting solvolysis presented here are solvation effects and the position of the TS; thus, an earlier TS and diminished solvation caused by charge delocalization reduce the magnitude of  $m$ .<sup>[4,8,9]</sup> The  $s_f$  parameters are, however, mostly an indication of the positive charge generated in the TS, similar to the Hammett–Brown  $\rho^+$  parameter.<sup>[10,2a]</sup> Relatively high  $s_f$  values for

Table 3. Values of  $m_{\text{OTS}}$  parameters from the Grünwald–Winstein correlations for solvolysis of X,Y-substituted benzhydryl chlorides (Cl), dinitrophenolates (DNP), and phenyl carbonates (PhCarb).

| Solvent <sup>[a]</sup> | LG                    | X,Y-Substituents on the benzhydryl ring |        |        |       |
|------------------------|-----------------------|-----------------------------------------|--------|--------|-------|
|                        |                       | MeO, Me                                 | MeO, H | Me, Me | Me, H |
| E–W                    | Cl <sup>[b]</sup>     |                                         |        |        | 0.78  |
|                        | DNP                   |                                         | 0.50   | 0.62   | 0.62  |
|                        | PhCarb <sup>[c]</sup> | 0.45                                    | 0.50   | 0.64   |       |
| M–W                    | Cl <sup>[b]</sup>     |                                         |        |        | 0.86  |
|                        | DNP                   |                                         | 0.55   | 0.64   | 0.71  |
|                        | PhCarb <sup>[d]</sup> | 0.54                                    | 0.56   | 0.67   |       |
| A–W                    | Cl <sup>[b]</sup>     |                                         |        |        | 1.13  |
|                        | DNP                   | 0.39                                    | 0.44   | 0.57   | 0.73  |
|                        | PhCarb <sup>[c]</sup> | 0.70                                    | 0.74   | 0.92   |       |

[a] A = acetone, E = ethanol, M = methanol, W = water. [b] The  $m_{\text{OTS}}$  values were calculated from rate constants published by Liu et al.<sup>[6]</sup> For details see the Supporting Information. [c] The  $m_{\text{OTS}}$  values were taken from reference 2a. [d] The  $m_{\text{OTS}}$  values were calculated from rate constants published in ref.<sup>[3]</sup> For details see the Supporting Information.

DNPs (and for chlorides) are an indication of a late TS. Lower  $m_{\text{OTS}}$  values for DNP than those for the corresponding chlorides are associated with the ability of DNP to better disperse the developing negative charge and hence diminish the solvation effect in the late TS. Table 3 shows that the  $m_{\text{OTS}}$  obtained for phenyl carbonates and DNP in aqueous alcohols are virtually the same. On the other hand, the  $s_f$  values for DNPs are higher than those for phenyl carbonates in all solvents examined (Figure 2).<sup>[3]</sup> This discrepancy indicates that, for phenyl carbonates, both the earlier TS and the delocalized partial negative charge diminish the  $m_{\text{OTS}}$  parameter in comparison to chlorides, whereas reduction of the  $m_{\text{OTS}}$  values for DNP mainly arise from the intense charge delocalization in the LG moiety of the late TS. Consequently, the solvation effect is less important for DNP than for phenyl carbonate, which is not surprising considering that two nitro groups on the phenyl ring take part in accommodating the developing negative charge in the TS by resonance.

The solvolytic behavior of DNPs in aqueous acetone is somewhat different to that in aqueous alcohols. Firstly, the decrease in the slope parameter  $s_f$  with increasing polarity of the solvent is much more pronounced (Figure 1 and Table 2), and secondly, the  $m_{\text{OTS}}$  parameters are considerably lower than those for phenyl carbonate in aqueous acetones, whereas the  $s_f$  parameters are still high. This behavior can be attributed to the lipophilicity of the developing 2,4-dinitrophenolate anion and hence to a more important role of the lipophilic acetone in the solvation of the TS.<sup>[4,11,12a]</sup> This additional solvation, which does not occur in aqueous alcohols, reduces the  $m_{\text{OTS}}$  further for DNP. The same phenomenon may be responsible for the decrease in the slope parameter  $s_f$  in more polar solvents. Increasing electrofugality in the series of benzhydryl DNPs leads to more extensive positive charge delocalization and thus less stabilization of the activated complex by more polar solvents. Thus, solvents containing a higher fraction of water enhance the rate more for substrates with a weak electrofuge than those with a strong electrofuge. The net result is convergence of the

$\log k$  vs.  $E_f$  plots (Figure 1 and Table 2), i.e., a reduction in the  $s_f$  parameters with an increase in the fraction of water in acetone.<sup>[2a]</sup>

Low  $m$  values have usually been coupled with relatively positive entropy of activation.<sup>[12]</sup> Generally, the  $\Delta S^\ddagger$  parameters obtained for DNPs are higher than those for chlorides<sup>[13]</sup> and phenyl carbonates.<sup>[2a]</sup> For example, in pure ethanol,  $\Delta S^\ddagger = +6.9 \pm 1.2 \text{ J K}^{-1} \text{ mol}^{-1}$  for **4**, whereas for the corresponding chloride  $\Delta S^\ddagger = -15.2 \pm 9.1 \text{ J K}^{-1} \text{ mol}^{-1}$ .<sup>[13]</sup> The results are consistent with intense charge delocalization of the negative charge generating in the TS of DNPs, which leads to diminished solvation and therefore to less loss of freedom of the solvent molecules in comparison with phenyl carbonates, and particularly to chlorides.

### Consideration of the Energy Profile in Solvolysis of DNPs

Nucleofugality has been linked to the basicity of the leaving groups in that a weaker base constitutes a better nucleofuge. Even though a reasonably good correlation between the reaction rates and  $\text{p}K_a$  values of the conjugated acids of the LGs for numerous substrates have been demonstrated,<sup>[14]</sup> some authors have stated that reactivity shows no correlation when wide ranges of diverse structures are examined, but exists only if the variations in the LGs are small.<sup>[15]</sup>

Figure 4a shows the correlation between the nucleofugalities ( $N_f$ ) of some leaving groups determined in 80% aq. ethanol, and the  $\text{p}K_a$  values for their corresponding conju-

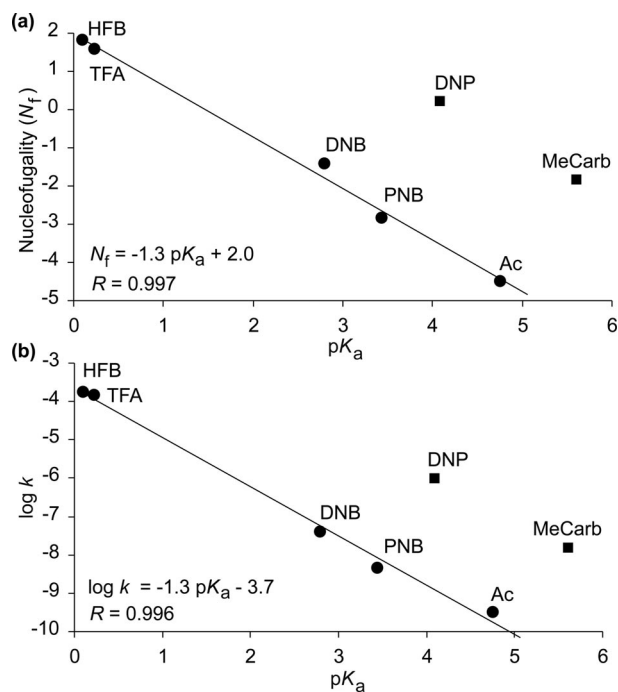


Figure 4. Plots of (a)  $N_f$  vs.  $\text{p}K_a$  and (b)  $\log k$  (25 °C) vs.  $\text{p}K_a$  in 80% aq. ethanol for some leaving groups (DNP and MeCarb are not included in the correlation) (the  $\text{p}K_a$  values and the corresponding references are given in the Supporting Information).

gated acids obtained in water; Figure 4b shows the correlation between  $\log k$  at 25 °C (measured or calculated) for unsubstituted benzhydryl derivatives with the same leaving groups obtained in 80% aq. ethanol and the  $pK_a$  values. The plots show that the correlation between the reactivity and acidity exists only within the same family of compounds. Thus, whereas the  $N_f$  values of unsubstituted benzhydryl carboxylates correlate well without exception with the  $pK_a$  values of the corresponding protonated LG ( $R = 0.997$ ), DNP turned out to be considerably more reactive than 3,5-dinitrobenzoate (DNB) and *p*-nitrobenzoate (PNB) even though both of the latter anions are weaker bases than the DNP anion. It should be emphasized that nucleofugality is a kinetic term that is derived from the rate constant, whereas acidity is a thermodynamic term derived from the equilibrium constant. Within the same group of compounds, for example carboxylates here, stabilizing effects in the TS and in the ground states are similar, so the rates increase with decreasing  $pK_a$  values. However, if the structure of the leaving group varies considerably, inversion between rate and basicity may occur. The experimental data show that DNP is an example of such a leaving group so its anion is less stabilized than DNB and PNB anions in water, and solvolyzes with a lower barrier than DNB.

Based on the approximation that the two thermodynamic terms, the endothermicity of formation of the carbocation/leaving group pair in the initial step of solvolysis, and that of deprotonation of the acid and formation the proton/leaving group (base) pair are proportional, the  $pK_a$  values reflect the relative stability of the LGs. Thus, the plot in Figure 4b essentially presents the correlation between the relative energies of the transition states and the carbocation/leaving group pairs. The fact that DNP solvolyzes faster than it would be predicted from the stability of the LG, indicates that DNPs solvolyze over a lower intrinsic barrier than carboxylates. That can be, according to principle of nonperfect synchronization, attributed to a less pronounced lag of charge delocalization behind the C–O bond cleavage in the TS of phenolates.<sup>[16]</sup> Reactions that proceed through a lower barrier, producing intermediates with higher energy, as is the case with DNPs here, have later transition states. The same conclusion regarding the later TS, in which the charge separation is already advanced, was drawn above on the basis of the relatively high  $s_f$  parameters.

According to Figure 4, a similar inversion of the reactivities can be observed between methyl carbonates and acetates in 80% aq. ethanol, indicating that benzhydryl methyl carbonate solvolyzes over a lower intrinsic barrier than acetate, which is the least reactive leaving group so far placed on the nucleofugality scale. The  $s_f$  values obtained for methyl carbonates are also relatively high and are similar to those obtained for DNP ( $s_f = 0.99$  in 80% aq. ethanol), indicating that methyl carbonates also proceed via a late TS in the rate-determining heterolysis.

In conclusion, solvolytic behavior of DNPs is somewhat different than those of carboxylates, although C–O cleavage occurs in both cases during the heterolysis process. X,Y-Substituted derivatives of benzhydryl 2,4-dinitrophenolates

solvolyze through a later TS than carboxylates, producing  $\log k$  vs.  $E_f$  plots with relatively high slope parameters.

## Experimental Section

**Substrate Preparation:** The substrates from the corresponding benzhydrols were prepared according to the substantially modified procedure presented previously.<sup>[17]</sup>

**4-Methoxybenzhydryl, 4,4'-Dimethylbenzhydryl, 4-Methylbenzhydryl, 4-Fluorobenzhydryl:** Prepared by reduction of the commercially available substituted benzophenones with sodium borohydride in methanol.

**4-Methoxy-4'-methylbenzhydryl:** Prepared according to the procedure given in ref.<sup>[3]</sup>

**4-Fluorobenzhydryl 2,4-Dinitrophenyl Ether:** Freshly cut potassium (1.0 g, 24.7 mmol) was added to a previously prepared stirring solution of 4-fluorobenzhydryl (5.0 g, 24.7 mmol) in anhydrous benzene (30 mL), and the solution was stirred for 2 h under an atmosphere of argon in an ice-cold bath. A solution of 1-fluoro-2,4-dinitrobenzene (9.2 g, 49.4 mmol) in benzene (10 mL) was then added dropwise with vigorously stirring and reaction mixture was stirred further for 1 h. The brown precipitate was filtered off and benzene was evaporated in vacuo to give a pale-yellow oil. The crude product was dissolved in diethyl ether (ca. 30 mL) and then about 50 mL of concd. aq. NaOH was added. The mixture was stirred for 12 h, then the organic layer was separated and washed with water. After drying over anhydrous sodium sulfate, the solvent was removed in vacuo to give a pale-yellow oil. Recrystallization from diethyl ether/light petroleum (4:1) afforded pale-yellow crystals (0.30 g, 30%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 6.48 (s, 1 H, Ar<sub>2</sub>CH), 7.07–7.48 [m, 10 H, ArH + (O<sub>2</sub>N)<sub>2</sub>ArH], 8.29 [dd,  $J$  = 2.8, 9.3 Hz, 1 H, (O<sub>2</sub>N)<sub>2</sub>ArH], 8.75 [d,  $J$  = 2.8 Hz, 1 H, (O<sub>2</sub>N)<sub>2</sub>ArH] ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 83.9 (Ar<sub>2</sub>CH), 116.0, 116.3, 116.4, 121.7, 126.5, 128.4, 128.6, 128.9, 129.3, 135.1, 138.8, 155.5, 161.4, 164.6 (Ar) ppm. C<sub>19</sub>H<sub>13</sub>FN<sub>2</sub>O<sub>5</sub> (368.29): calcd. C 61.96, H 3.56, N 7.60; found C 62.66, H 3.70, N 7.56.

**4-Methylbenzhydryl 2,4-Dinitrophenyl Ether, 4,4'-Dimethylbenzhydryl 2,4-Dinitrophenyl Ether, and 4-Methoxybenzhydryl 2,4-Dinitrophenyl Ether:** Prepared as pale-yellow crystals according to the procedure described for 4-fluorobenzhydryl 2,4-dinitrophenyl ether, yielding 30–40% of the desired products.

**4-Methylbenzhydryl 2,4-Dinitrophenyl Ether:** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.30 (s, 3 H, Ar-CH<sub>3</sub>), 6.44 (s, 1 H, Ar<sub>2</sub>CH), 7.15–7.46 [m, 10 H, ArH + (O<sub>2</sub>N)<sub>2</sub>ArH], 8.22 [dd,  $J$  = 2.8, 9.3 Hz, 1 H, (O<sub>2</sub>N)<sub>2</sub>ArH], 8.70 [d,  $J$  = 2.8 Hz, 1 H, (O<sub>2</sub>N)<sub>2</sub>ArH] ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 20.8 (ArCH<sub>3</sub>), 83.7 (Ar<sub>2</sub>CH), 115.8, 121.3, 125.8, 125.9, 128.0, 128.1, 128.6, 129.3, 135.4, 138.1, 138.6, 155.0 (Ar) ppm. C<sub>20</sub>H<sub>16</sub>N<sub>2</sub>O<sub>5</sub> (364.33): calcd. C 65.93, H 4.43, N 7.69; found C 65.89, H 4.57, N 7.58.

**4,4'-Dimethylbenzhydryl 2,4-Dinitrophenyl Ether:** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.31 (s, 6 H, Ar-CH<sub>3</sub>), 6.42 (s, 1 H, Ar<sub>2</sub>CH), 7.15–7.19 [m, 5 H, ArH + (O<sub>2</sub>N)<sub>2</sub>ArH], 7.34 (d,  $J$  = 8.0 Hz, 4 H, ArH), 8.25 [dd,  $J$  = 2.8, 9.3 Hz, 1 H, (O<sub>2</sub>N)<sub>2</sub>ArH], 8.72 [d,  $J$  = 2.8 Hz, 1 H, (O<sub>2</sub>N)<sub>2</sub>ArH] ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 21.1 (ArCH<sub>3</sub>), 84.1 (Ar<sub>2</sub>CH), 116.4, 121.7, 126.3, 128.6, 129.7, 136.2, 138.5, 155.7 (Ar) ppm. C<sub>21</sub>H<sub>18</sub>N<sub>2</sub>O<sub>5</sub> (378.35): calcd. C 66.66, H 4.80, N 7.40; found C 66.91, H 5.08, N 7.24.

**4-Methoxybenzhydryl 2,4-Dinitrophenyl Ether:** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.76 (s, 3 H, Ar-OCH<sub>3</sub>), 6.44 (s, 1 H, Ar<sub>2</sub>CH), 6.88 (d,  $J$  = 8.7 Hz, 2 H, ArH), 7.18–7.46 [m, 8 H, ArH]

+ (O<sub>2</sub>N)<sub>2</sub>ArH], 8.24 [dd, *J* = 2.7, 9.3 Hz, 1 H, (O<sub>2</sub>N)<sub>2</sub>ArH], 8.70 [d, *J* = 2.8 Hz, 1 H, (O<sub>2</sub>N)<sub>2</sub>ArH] ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 54.8 (ArOCH<sub>3</sub>), 83.5 (Ar<sub>2</sub>CH), 114.2, 115.9, 121.3, 125.8, 127.5, 128.0, 128.1, 128.7, 130.4, 138.7, 155.0, 159.5 (Ar) ppm. C<sub>20</sub>H<sub>16</sub>N<sub>2</sub>O<sub>6</sub> (380.33): calcd. C 63.16, H 4.24, N 7.36; found C 63.25, H 4.31, N 7.22.

**4-Methoxy-4'-methylbenzhydryl 2,4-Dinitrophenyl Ether:** Synthesized according to the procedure for 4-fluorobenzhydryl 2,4-dinitrophenyl ether, except that anhydrous diethyl ether was used instead of benzene as the solvent. From 4-methoxy-4'-methylbenzhydryl (5.0 g, 21.9 mmol), the product was obtained as pale-yellow crystals (1.7 g, ca. 19%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 2.31 (s, 3 H, Ar-CH<sub>3</sub>), 3.76 (s, 1 H, Ar-OCH<sub>3</sub>), 6.42 (s, 1 H, Ar<sub>2</sub>CH), 6.88 (d, *J* = 8.7 Hz, 2 H, ArH), 7.15–7.38 [m, 7 H, ArH + (O<sub>2</sub>N)<sub>2</sub>ArH], 8.23 [dd, *J* = 2.7, 9.3 Hz, 1 H, (O<sub>2</sub>N)<sub>2</sub>ArH], 8.69 [d, *J* = 2.7 Hz, 1 H, (O<sub>2</sub>N)<sub>2</sub>ArH] ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 21.1 (ArCH<sub>3</sub>), 55.3 (ArOCH<sub>3</sub>), 84.0 (Ar<sub>2</sub>CH), 114.7, 116.4, 121.7, 126.3, 127.9, 128.6, 129.7, 131.1, 136.4, 138.4, 155.6, 159.8 (Ar) ppm. C<sub>21</sub>H<sub>18</sub>N<sub>2</sub>O<sub>6</sub> (394.35): calcd. C 63.96, H 4.60, N 7.10; found C 64.03, H 4.69, N 6.88.

**Kinetic Methods:** Solvents were purified and dried according to standard procedures. Solvolysis rate constants were measured conductometrically. Freshly prepared solvents (30 mL) were held in a thermostatically controlled bath (± 0.1 °C) at the given temperature for several minutes prior to addition of substrate. Typically, 20–40 mg of substrate was dissolved in 0.10–0.15 mL of dichloromethane and injected into the solvent. The increase in conductivity during solvolysis was monitored automatically by means of a WTW LF 530 conductometer, using a Radiometer 2-pole Conductivity Cell (CDC641T). Individual rate constants were obtained by least-squares fitting of the conductivity data to the first-order kinetic equation for 3–4 half-lives. The rate constants were averaged from at least three measurements.

To achieve complete ionization of the liberated weak acid, the proton-sponge base [1,8-bis(dimethylamino)naphthalene] was added in a range of concentrations for each given aqueous binary mixture

Table 4. Experimental concentrations (*c*<sub>0</sub>) of base and substrates in the kinetic measurements of the solvolysis rates of the substituted benzhydryl 2,4-dinitrophenolates.

| Solvent <sup>[a]</sup> | <i>c</i> <sub>0</sub> (PSB) <sup>[b]</sup> [mM] | <i>c</i> <sub>0</sub> (PSB)/ <i>c</i> <sub>0</sub> (S) <sup>[b]</sup> |
|------------------------|-------------------------------------------------|-----------------------------------------------------------------------|
| 100M                   | 12.4–15.6                                       | 4.0–7.0                                                               |
| 90M10W                 | 7.8–26.3                                        | 4.0–10.0                                                              |
| 80M20W                 | 2.6–3.7                                         | 1.5–2.0                                                               |
| 100E                   | 84.5–137.2                                      | 20.0–30.0                                                             |
| 90E10W                 | 13.1–52.9                                       | 5.0–20.0                                                              |
| 80E20W                 | 11.0–52.6                                       | 5.0–15.0                                                              |
| 70E30W                 | 8.7–22.9                                        | 5.0–10.0                                                              |

[a] Binary solvents (v/v) at 25 °C; E = ethanol, M = methanol, W = water. [b] PSB = proton-sponge base: [1,8-bis(dimethylamino)naphthalene]; S = substrate.

presented in Table 4. Calibration showed a linear response of conductivity in the presented range of concentration of proton-sponge base and 2,4-dinitrophenol.

**Supporting Information** (see also the footnote on the first page of this article): Correlations of log *k* vs. *E*<sub>f</sub> in the series of aqueous solvents, NMR spectra (<sup>1</sup>H and <sup>13</sup>C) and rate constants for X,Y-substituted benzhydryl 2,4-dinitrophenolates at various temperatures.

## Acknowledgments

We gratefully acknowledge financial support for this research by the Ministry of Science Education and Sport of the Republic of Croatia (Grant No. 006-0982933-2963).

- [1] a) B. Denegri, A. Streiter, S. Jurić, A. R. Ofial, O. Kronja, H. Mayr, *Chem. Eur. J.* **2006**, *12*, 1648–1656; b) Correction: B. Denegri, A. Streiter, S. Jurić, A. R. Ofial, O. Kronja, H. Mayr, *Chem. Eur. J.* **2006**, *12*, 5415–5415; c) B. Denegri, A. R. Ofial, S. Jurić, A. Streiter, O. Kronja, H. Mayr, *Chem. Eur. J.* **2006**, *12*, 1657–1666; d) B. Denegri, S. Minegishi, O. Kronja, H. Mayr, *Angew. Chem. Int. Ed.* **2004**, *43*, 2302–2305.
- [2] a) B. Denegri, O. Kronja, *J. Phys. Org. Chem.* **2009**, *22*, 495–503; b) B. Denegri, O. Kronja, *Croat. Chem. Acta*, in press.
- [3] a) B. Denegri, O. Kronja, *J. Org. Chem.* **2007**, *72*, 8427–8433; b) N. Streidl, R. Branzan, H. Mayr, *Eur. J. Org. Chem.* **2010**, 4205–4210.
- [4] T. W. Bentley, K. Roberts, *J. Org. Chem.* **1985**, *50*, 4821–4828.
- [5] I. D. Page, J. R. Pritt, M. C. Whiting, *J. Chem. Soc. Perkin Trans. 2* **1972**, 906–911.
- [6] K.-T. Liu, Y.-S. Lin, M.-L. Tsao, *J. Phys. Org. Chem.* **1998**, *11*, 223–229.
- [7] T. W. Bentley, G. Llewellyn, *Prog. Phys. Org. Chem.* **1990**, *17*, 121–159.
- [8] a) D. J. McLennan, P. L. Martin, *Aust. J. Chem.* **1979**, *32*, 2361–2370; b) D. J. McLennan, P. L. Martin, *J. Chem. Soc. Perkin Trans. 2* **1982**, 1991–1998; c) R. L. Buckson, S. G. Smith, *J. Org. Chem.* **1967**, *32*, 634–639.
- [9] J. S. Lomas, J.-E. Dubois, *J. Org. Chem.* **1975**, *40*, 3303–3304.
- [10] T. W. Bentley, *Chem. Eur. J.* **2006**, *12*, 6514–6520.
- [11] M. H. Abraham, C. M. Du, J. A. Platts, *J. Org. Chem.* **2000**, *65*, 7114–7118.
- [12] a) D. N. Kevill, M. S. Bahari, S. W. Anderson, *J. Am. Chem. Soc.* **1984**, *106*, 2895–2901; b) P. R. Luton, M. C. Whiting, *J. Chem. Soc. Perkin Trans. 2* **1979**, 1507–1511.
- [13] C. Schade, H. Mayr, *Tetrahedron* **1988**, *44*, 5761–5770.
- [14] D. B. Boyd, *J. Org. Chem.* **1985**, *50*, 885–886.
- [15] a) P. Jaramillo, L. R. Domingo, P. Perez, *Chem. Phys. Lett.* **2006**, *420*, 95–99; b) D. R. Marshall, P. J. Thomas, C. J. M. Stirling, *J. Chem. Soc., Chem. Commun.* **1975**, 940–941.
- [16] C. F. Bernasconi, *Acc. Chem. Res.* **1992**, *25*, 9–16, and references cited therein.
- [17] I. D. Page, J. R. Pritt, M. C. Whiting, *J. Chem. Soc. Perkin Trans. 2* **1972**, 906–911.

Received: May 31, 2010

Published Online: September 17, 2010