

Electronic Supplementary Information (ESI)

**Quantification of the Hydride Donor Abilities of  
NADH, NADPH and  $\text{BH}_3\text{CN}^-$  in Water**

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## General

**Materials.** NADH (Reduced  $\beta$ -Nicotinamide adenine dinucleotide, reduced disodium salt hydrate), NADPH (Roche;  $\beta$ -Nicotinamide adenine dinucleotide 2'-phosphate reduced tetrasodium salt hydrate) and sodium cyanoborohydride (PharmaGrade) were purchased from Sigma-Aldrich and their purity was determined by quantitative NMR spectroscopy. Benzhydrylium ions **E1-6** were obtained from the group of Prof. Herbert Mayr and Dr. Armin Ofial (LMU Munich) where they were prepared using published procedures.<sup>S1</sup>

Phosphate buffer (1 M) was prepared by mixing 1 M solutions of  $\text{KH}_2\text{PO}_4$  (ReagentPlus®, Sigma-Aldrich) and  $\text{K}_2\text{HPO}_4$  (ACS reagent,  $\geq 98\%$ , Sigma-Aldrich) to pH 7 as monitored by a calibrated pH meter. Water used for preparation of buffers or all other solutions was obtained from a Sartorius Arium purification system (18 M $\Omega$ cm).

**NMR Spectroscopy.** NMR spectra were recorded on a Bruker 400 MHz spectrometer at a sample temperature maintained at 20 °C.

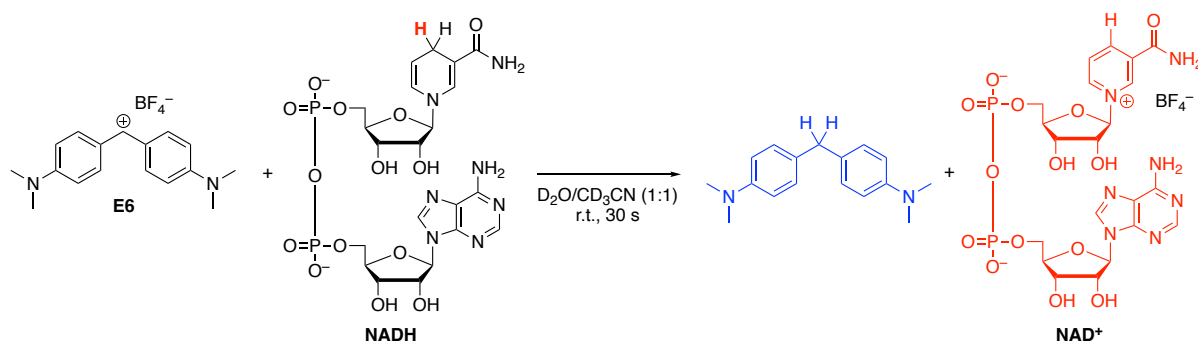
**UV/Vis Kinetics.** Spectra and kinetics were measured on a Jasco V-670 spectrophotometer equipped with a Peltier-cooled PAC-743 sample changer and an integrated magnetic stirrer at 20 °C. For measurements, Hellma 10 mm quartz glass cuvettes were employed containing a small magnetic stirring bar. Fast kinetics (< 10 min) were followed by continuously monitoring a single sample, while for slower measurements the parallel kinetic mode was employed where the sample-changer was used to continuously measure up to four samples simultaneously.

**Kinetic Analysis.** Concentration-time profiles were fitted to the single exponential  $A \exp(-k_{\text{obs}} t) + C$ .

**Error Analysis.** All reported errors correspond to standard errors calculated from regression analyses.

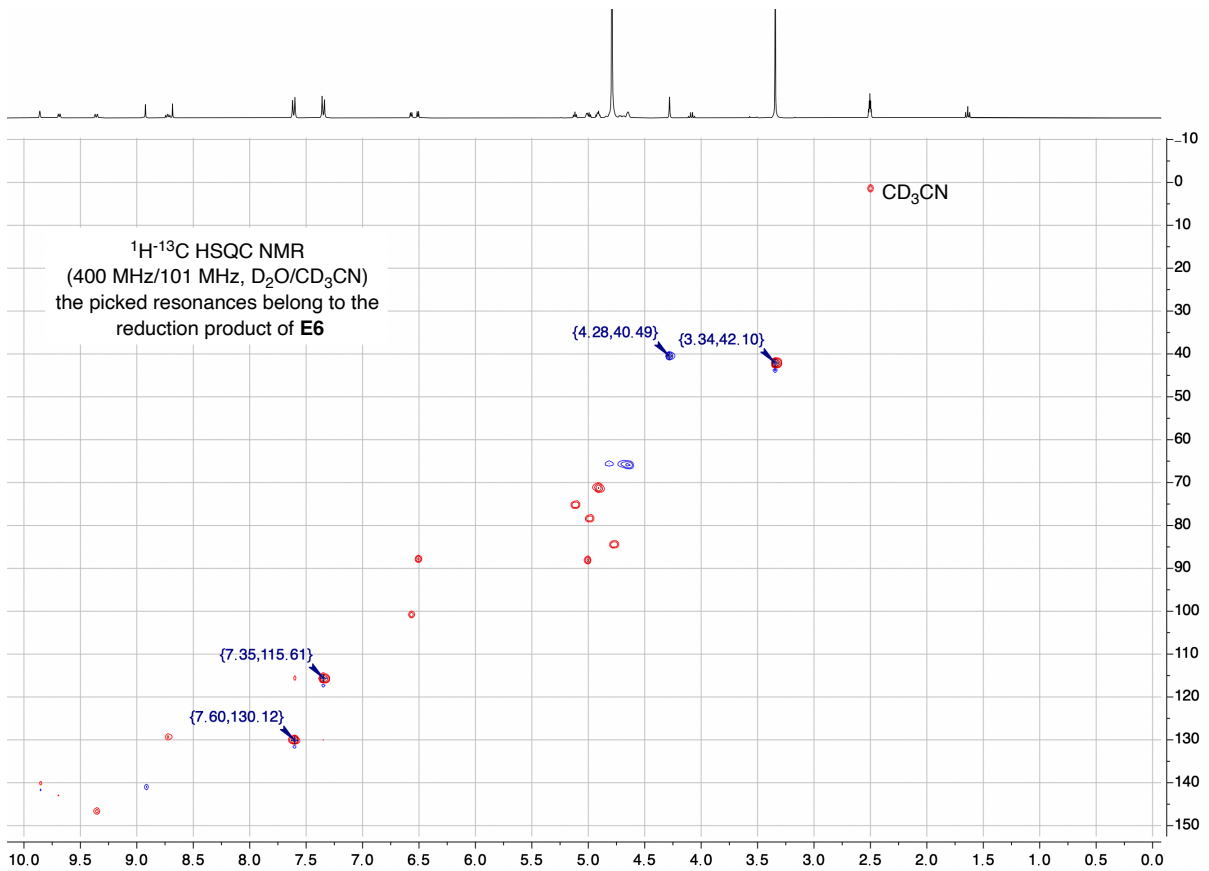
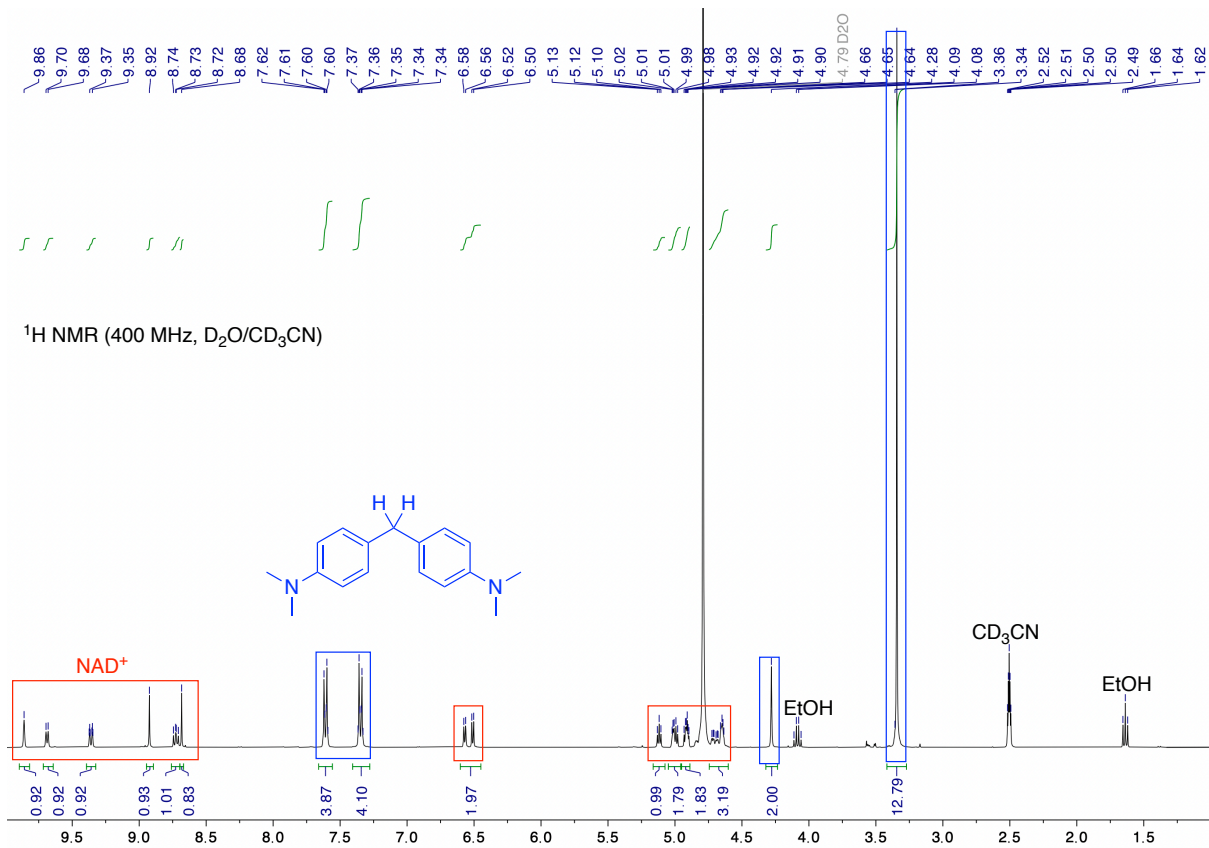
## Analysis of the Products of Hydride Donors with Benzhydrylium Ion **E6**

### Product analysis of the reaction of NADH with benzhydrylium salt **E6-BF<sub>4</sub>** (**RM03-390**)

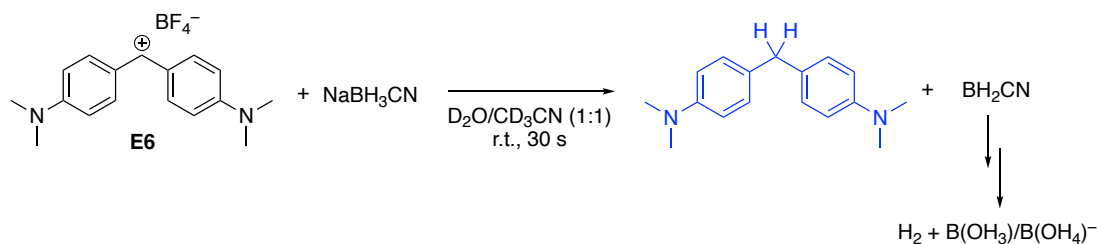


The benzhydrylium salt **E6-BF<sub>4</sub>** (2.23 mg, 0.0066 mmol, 1 equiv) was dissolved in  $\text{CD}_3\text{CN}$  (300  $\mu\text{L}$ ). NADH (4.65 mg, 0.0066 mol, 1 equiv) was dissolved in  $\text{D}_2\text{O}$  (300  $\mu\text{L}$ ) and added by means of a pipette to the solution of **E6-BF<sub>4</sub>**. The resulting deep blue solution was mixed by pipetting up and down and decolorized within 30 seconds. Thereafter, the solution was transferred to an NMR tube and subjected to analysis by  $^1\text{H}$  and  $^1\text{H}$ - $^{13}\text{C}$  HSQC NMR. The products NAD<sup>+</sup> and 4,4'-methylenebis(*N,N*-dimethylaniline) were identified by comparison with known spectra.<sup>S2</sup> The successful reduction of **E6** is most clearly seen by the presence of a  $\text{CH}_2$  group in the HSQC spectra (blue resonance at 4.28 ppm/40.5 ppm).

*Note:*  $\text{CD}_3\text{CN}$  was used as non-nucleophilic co-solvent as both the benzhydrylium salt **E6-BF<sub>4</sub>** and the reaction product are not sufficiently soluble in pure water at the concentrations needed to record NMR spectra. EtOH is present as an impurity in the commercial NADH sample.

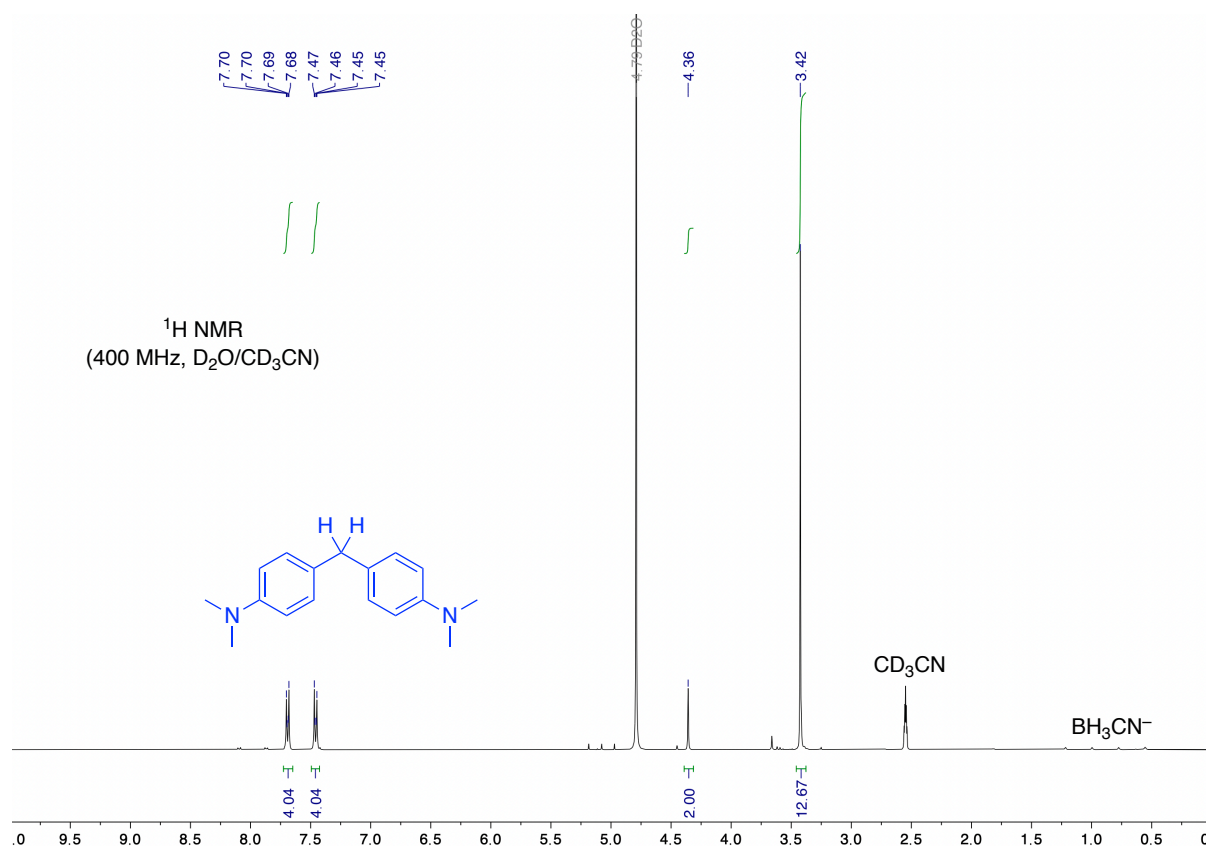


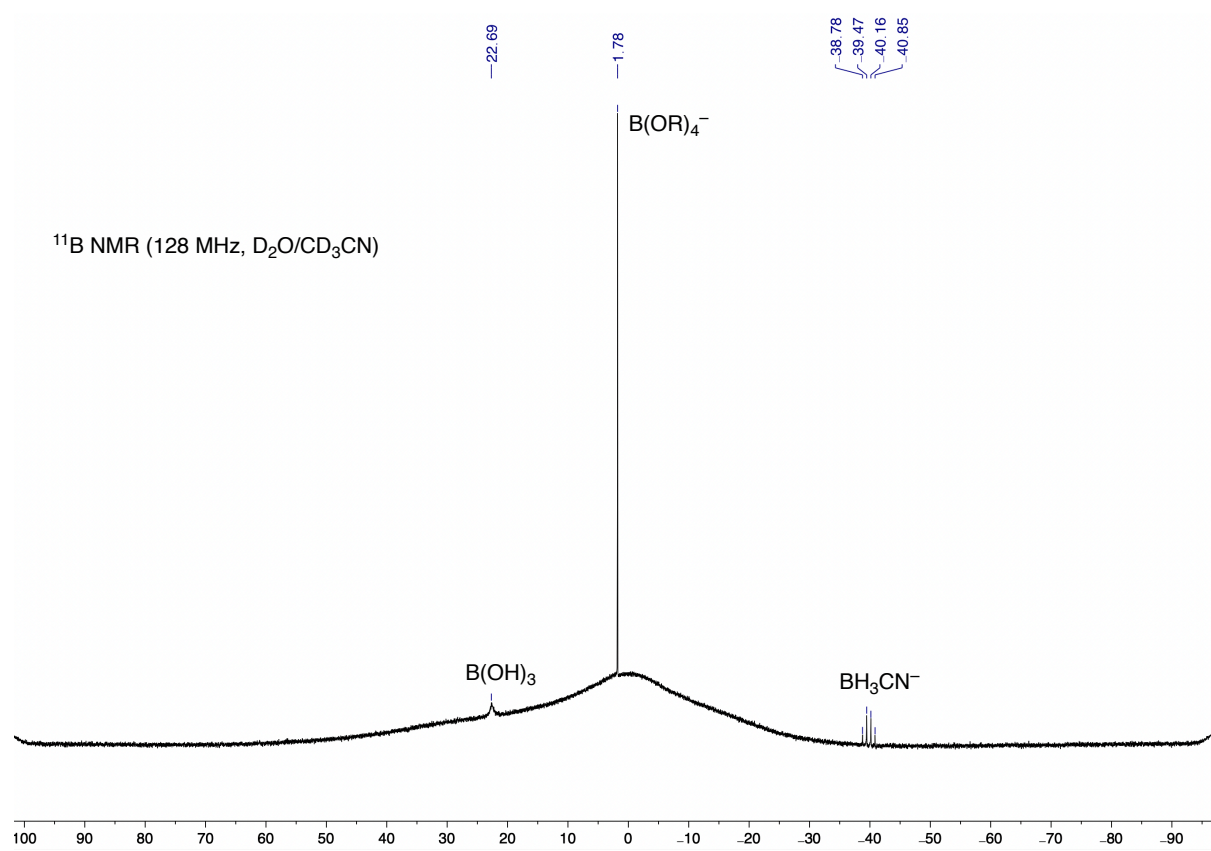
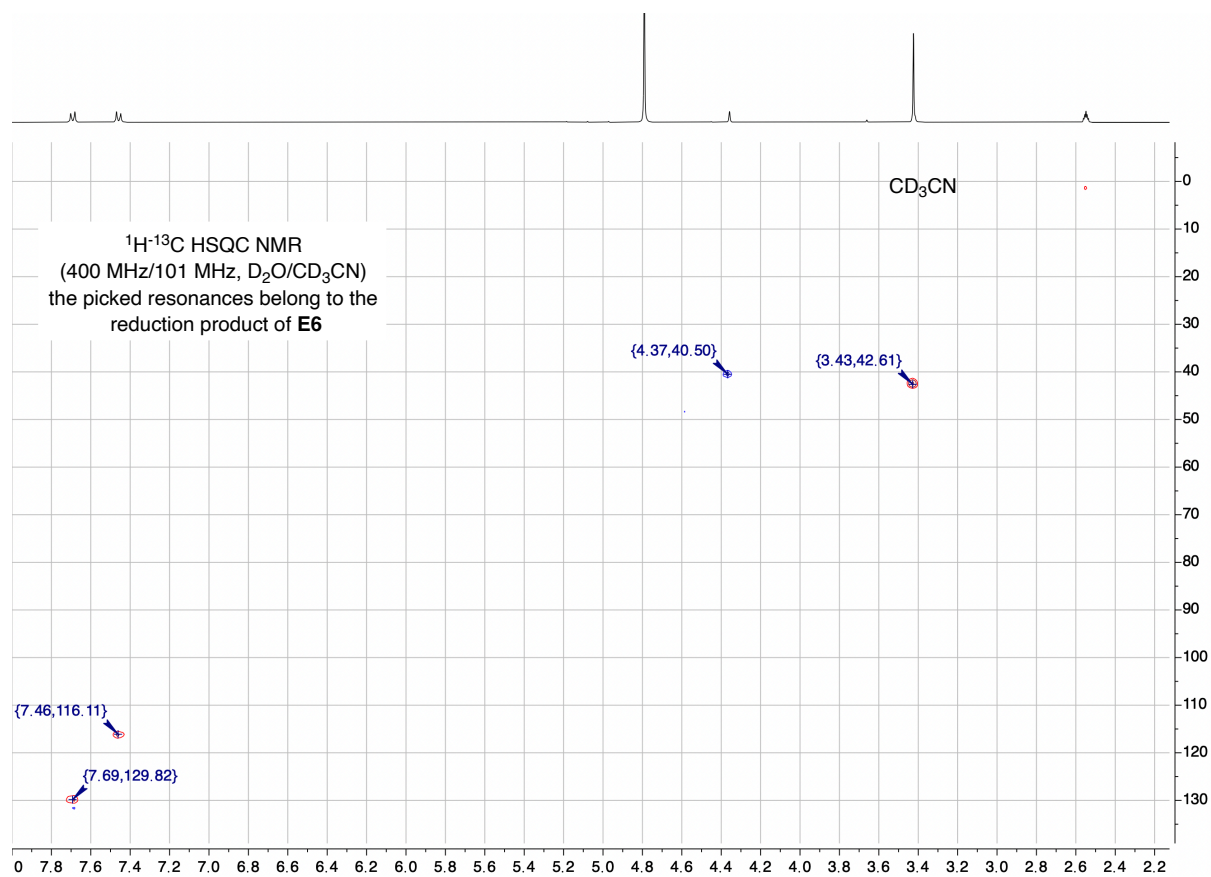
### Product analysis of the reaction of NaBH<sub>3</sub>CN with benzhydrylium salt **E6**-BF<sub>4</sub> (RM03-394)



The benzhydrylium salt **E6** (2.40 mg, 0.0071 mmol, 1 equiv) was dissolved in CD<sub>3</sub>CN (300  $\mu$ L). NaBH<sub>3</sub>CN (0.44 mg, 0.0071 mol, 1 equiv) was dissolved in D<sub>2</sub>O (300  $\mu$ L) and added by means of a pipette to the solution of **E6**. The resulting deep blue solution was mixed by pipetting up and down and decolorized within 30 seconds. Thereafter, the solution was transferred to an NMR tube and subjected to analysis by <sup>1</sup>H and <sup>1</sup>H-<sup>13</sup>C HSQC NMR. The product 4,4'-methylenebis(*N,N*-dimethylaniline) was identified by comparison with known NMR data and is most clearly characterized by the presence of a CH<sub>2</sub> group in the HSQC spectra (blue resonance at 4.28 ppm/40.5 ppm).<sup>S2b</sup>

*Note:* CD<sub>3</sub>CN was used as non-nucleophilic co-solvent as both the benzhydrylium salt **E6** and the reaction product are not sufficiently soluble in pure water at the concentrations needed to record NMR spectra. The direct reaction product BH<sub>2</sub>CN could not be detected due to rapid hydrolysis. <sup>11</sup>B NMR, however, showed the characteristic resonance of boric acid (22.7 ppm) and a sharp resonance at 1.8 ppm for a tetracoordinated boron species, most likely a borate ion.



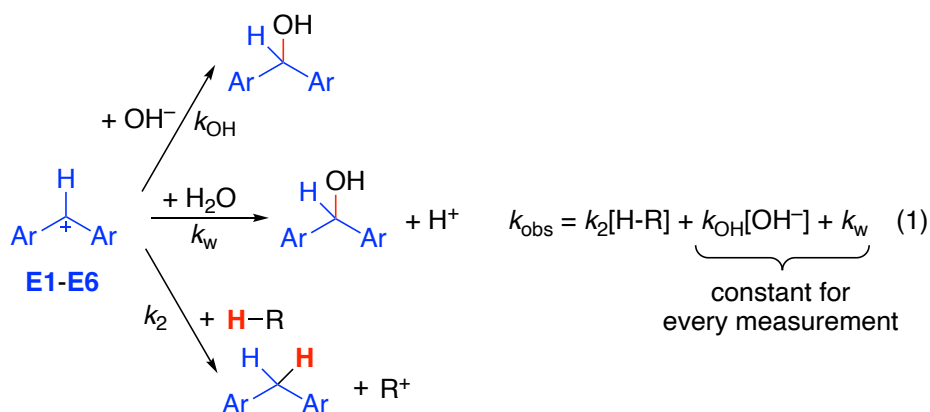


# Determination of the Nucleophilicity Parameter of NADH and $\text{BH}_3\text{CN}^-$

## Procedure and Kinetic Analysis

A stock solution of the hydride donor was prepared in a 5 mL volumetric flask in MilliQ  $\text{H}_2\text{O}$ . 500  $\mu\text{L}$  of the stock solution were added to a precisely weighed amount of qNMR-grade dimethyl sulfone, 100  $\mu\text{L}$   $\text{D}_2\text{O}$  was added and the well mixed solution transferred to an NMR tube. The sample was analyzed by quantitative  $^1\text{H}$  NMR spectroscopy ( $d_1 = 50$  s) to determine the absolute concentration of the hydride donor. After having determined the precise concentration, the same stock solution was used for the kinetic measurements. All measurements with one stock solutions were performed within a time-frame of approx. 4-6 h and the stock solutions were stored at 4  $^\circ\text{C}$  in between measurements. NMR analysis indicates that no significant decomposition could be observed during this time.

UV/Vis kinetics were followed at 20.0  $^\circ\text{C}$ . A quartz cuvette was charged with a stirring bar, phosphate buffer (pH 7), water, and the corresponding amount of a stock solution of the hydride donor (for concentrations, see the tables below; all measurements were performed with a total volume of 2000  $\mu\text{L}$  of all species). The background was recorded, the measurement started, and the reference electrophile added from a stock solution in MeCN (typically 8-20  $\mu\text{L}$ ; MeCN is necessary to dissolve the benzhydrylium salts) to the stirred solution. Such small amounts of a non-nucleophilic co-solvent were commonly found to not have an impact on the kinetics. In the following, the time-dependent decay of the absorbance of the benzhydrylium ions was recorded with, depending on the reaction time, a sampling interval of 0.2 s – 1 s.



Due to the large excess ( $> 10$  equiv) of the hydride donors H-R over the electrophiles **E**, generally pseudo-first order kinetics resulted. The time-dependent decay of the absorbances of **E** were analyzed by least-squares fitting to afford the pseudo-first order rates  $k_{\text{obs}}$ . In aqueous solution, the observed kinetics for the disappearance of **E** are due to three competing reactions: The hydrolysis with either hydroxide or water and the actual reaction with the nucleophile of interest (eq 1). As the kinetics were measured in 0.05 M phosphate buffered solution, the concentration of hydroxide and water are identical for every measurement within a series of measurements where the concentration of the nucleophile is varied. Accordingly, a correlation of  $k_{\text{obs}}$  with  $[\text{H-R}]$  will be linear with the slope corresponding to  $k_2$  and the intercept with the ordinate to  $k_{\text{OH}}[\text{OH}^-] + k_w$  (see the correlations below). All reported errors correspond to standard errors.



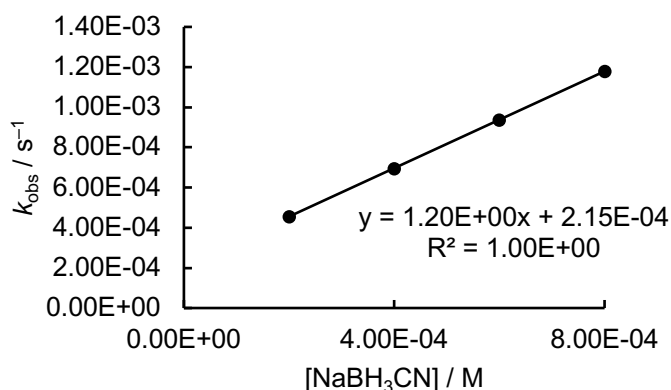
## Nucleophilicity of $\text{BH}_3\text{CN}^-$

### Reaction of $\text{NaBH}_3\text{CN}$ with E1

Kinetics of the reaction of  $\text{lil}_2\text{CH}^+\text{BF}_4^-$  (**E1**) with  $\text{NaBH}_3\text{CN}$  followed by UV/Vis spectroscopy (630 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in  $\text{H}_2\text{O}$  containing 0.20% MeCN (RM03-466).

[E1] / M	[NaBH <sub>3</sub> CN] / M	$k_{\text{obs}}$ / s <sup>-1</sup>
$1.50 \times 10^{-5}$	$2.00 \times 10^{-4}$	$4.57 \times 10^{-4}$
$1.50 \times 10^{-5}$	$4.00 \times 10^{-4}$	$6.95 \times 10^{-4}$
$1.50 \times 10^{-5}$	$6.00 \times 10^{-4}$	$9.37 \times 10^{-4}$
$1.50 \times 10^{-5}$	$8.00 \times 10^{-4}$	$1.18 \times 10^{-3}$

$$k_2 = (1.20 \pm 0.01) \text{ L mol}^{-1} \text{ s}^{-1}$$

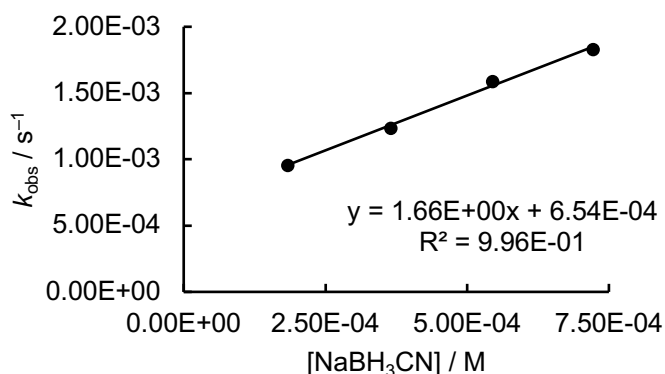


### Reaction of $\text{NaBH}_3\text{CN}$ with E2

Kinetics of the reaction of  $\text{jul}_2\text{CH}^+\text{BF}_4^-$  (**E2**) with  $\text{NaBH}_3\text{CN}$  followed by UV/Vis spectroscopy (634 nm) at 20 °C in pH 7 phosphate solution (0.1 M) in  $\text{H}_2\text{O}$  containing 0.07% MeCN (RM01-168).

[E2] / M	[NaBH <sub>3</sub> CN] / M	$k_{\text{obs}}$ / s <sup>-1</sup>
$1.60 \times 10^{-5}$	$1.83 \times 10^{-4}$	$9.56 \times 10^{-4}$
$1.15 \times 10^{-5}$	$3.64 \times 10^{-4}$	$1.24 \times 10^{-3}$
$1.17 \times 10^{-5}$	$5.44 \times 10^{-4}$	$1.59 \times 10^{-3}$
$1.18 \times 10^{-5}$	$7.21 \times 10^{-4}$	$1.83 \times 10^{-3}$

$$k_2 = (1.66 \pm 0.08) \text{ L mol}^{-1} \text{ s}^{-1}$$

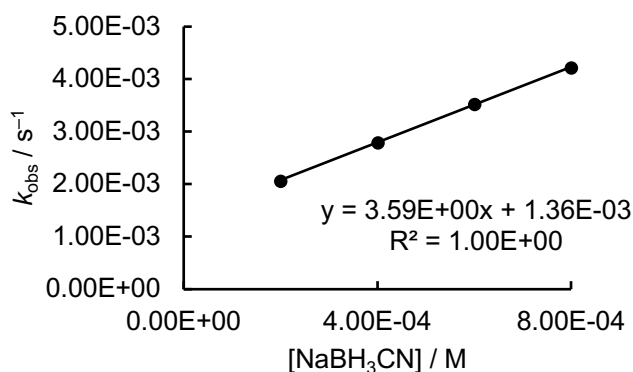


### Reaction of $\text{NaBH}_3\text{CN}$ with E3

Kinetics of the reaction of  $\text{ind}_2\text{CH}^+\text{BF}_4^-$  (**E3**) with  $\text{NaBH}_3\text{CN}$  followed by UV/Vis spectroscopy (614 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in  $\text{H}_2\text{O}$  containing 0.07% MeCN (RM03-466).

[E3] / M	[NaBH <sub>3</sub> CN] / M	$k_{\text{obs}}$ / s <sup>-1</sup>
$1.50 \times 10^{-5}$	$2.00 \times 10^{-4}$	$2.07 \times 10^{-3}$
$1.50 \times 10^{-5}$	$4.00 \times 10^{-4}$	$2.80 \times 10^{-3}$
$1.50 \times 10^{-5}$	$6.00 \times 10^{-4}$	$3.53 \times 10^{-3}$
$1.50 \times 10^{-5}$	$8.00 \times 10^{-4}$	$4.22 \times 10^{-3}$

$$k_2 = (3.59 \pm 0.03) \text{ L mol}^{-1} \text{ s}^{-1}$$

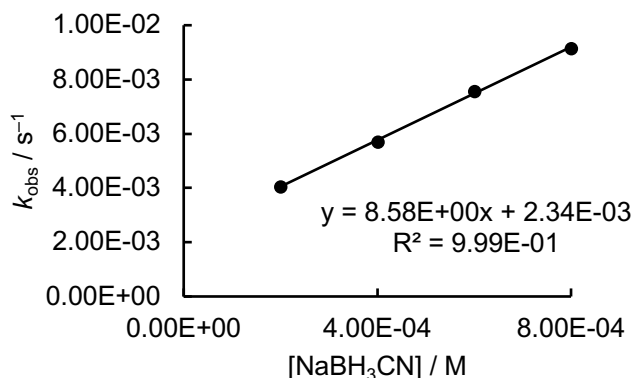


### Reaction of NaBH<sub>3</sub>CN with E4

Kinetics of the reaction of thq<sub>2</sub>CH<sup>+</sup>BF<sub>4</sub><sup>-</sup> (**E4**) with NaBH<sub>3</sub>CN followed by UV/Vis spectroscopy (618 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in H<sub>2</sub>O containing 0.14% MeCN (RM03-466).

[E4] / M	[NaBH <sub>3</sub> CN] / M	k <sub>obs</sub> / s <sup>-1</sup>
1.50 × 10 <sup>-5</sup>	2.00 × 10 <sup>-4</sup>	4.06 × 10 <sup>-3</sup>
1.50 × 10 <sup>-5</sup>	4.00 × 10 <sup>-4</sup>	5.71 × 10 <sup>-3</sup>
1.50 × 10 <sup>-5</sup>	6.00 × 10 <sup>-4</sup>	7.57 × 10 <sup>-3</sup>
1.50 × 10 <sup>-5</sup>	8.00 × 10 <sup>-4</sup>	9.16 × 10 <sup>-3</sup>

$$k_2 = (8.58 \pm 0.18) \text{ L mol}^{-1} \text{ s}^{-1}$$

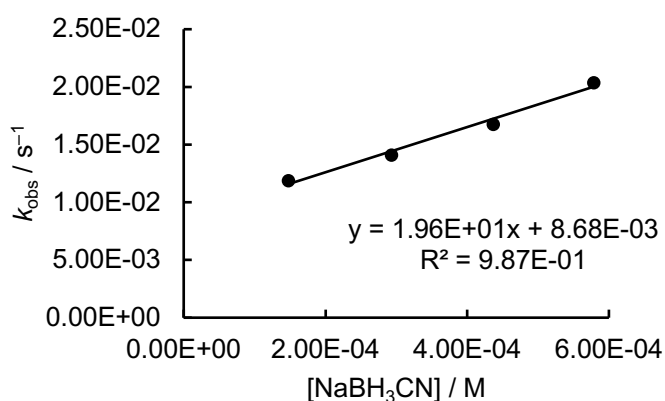


### Reaction of NaBH<sub>3</sub>CN with E5

Kinetics of the reaction of pyr<sub>2</sub>CH<sup>+</sup>BF<sub>4</sub><sup>-</sup> (**E5**) with NaBH<sub>3</sub>CN followed by UV/Vis spectroscopy (610 nm) at 20 °C in pH 7 phosphate solution (0.1 M) in H<sub>2</sub>O containing 0.04% MeCN (RM01-168).

[E5] / M	[NaBH <sub>3</sub> CN] / M	k <sub>obs</sub> / s <sup>-1</sup>
1.06 × 10 <sup>-5</sup>	1.47 × 10 <sup>-4</sup>	1.19 × 10 <sup>-2</sup>
1.03 × 10 <sup>-5</sup>	2.92 × 10 <sup>-4</sup>	1.41 × 10 <sup>-2</sup>
1.07 × 10 <sup>-5</sup>	4.36 × 10 <sup>-4</sup>	1.68 × 10 <sup>-2</sup>
1.03 × 10 <sup>-5</sup>	5.78 × 10 <sup>-4</sup>	2.04 × 10 <sup>-2</sup>

$$k_2 = (1.96 \pm 0.16) \times 10^1 \text{ L mol}^{-1} \text{ s}^{-1}$$

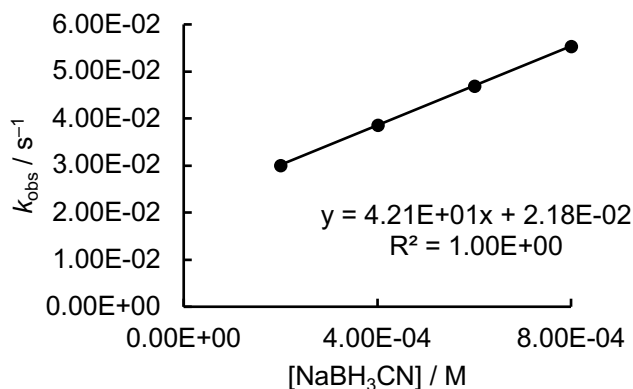


### Reaction of NaBH<sub>3</sub>CN with E6

Kinetics of the reaction of dma<sub>2</sub>CH<sup>+</sup>BF<sub>4</sub><sup>-</sup> (**E6**) with NaBH<sub>3</sub>CN followed by UV/Vis spectroscopy (604 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in H<sub>2</sub>O containing 0.05% MeCN (RM03-466).

[E6] / M	[NaBH <sub>3</sub> CN] / M	k <sub>obs</sub> / s <sup>-1</sup>
1.50 × 10 <sup>-5</sup>	2.00 × 10 <sup>-4</sup>	3.01 × 10 <sup>-2</sup>
1.50 × 10 <sup>-5</sup>	4.00 × 10 <sup>-4</sup>	3.87 × 10 <sup>-2</sup>
1.50 × 10 <sup>-5</sup>	6.00 × 10 <sup>-4</sup>	4.69 × 10 <sup>-2</sup>
1.50 × 10 <sup>-5</sup>	8.00 × 10 <sup>-4</sup>	5.54 × 10 <sup>-2</sup>

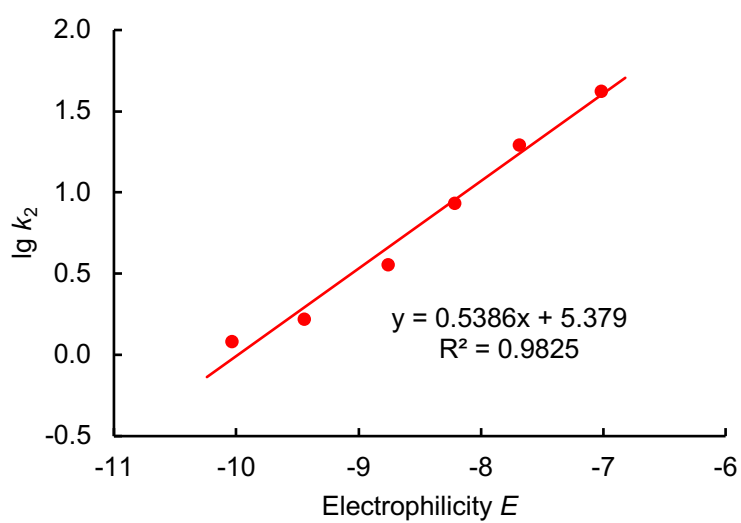
$$k_2 = (42.1 \pm 0.3) \text{ L mol}^{-1} \text{ s}^{-1}$$



### Determination of the Nucleophilicity Parameter of $\text{BH}_3\text{CN}^-$

**Table S1.** Electrophiles and associated electrophilicity  $E$  as well as their rates  $k_2$  for the reaction with  $\text{BH}_3\text{CN}^-$  used for the determination of the nucleophilicity of  $\text{BH}_3\text{CN}^-$ .

Electrophile	Electrophilicity $E$	$k_2 / \text{L mol}^{-1}\text{s}^{-1}$	$\lg k_2$
E1	-10.04	$1.20 \pm 0.01$	$8.28 \times 10^{-2}$
E2	-9.45	$1.66 \pm 0.08$	$2.20 \times 10^{-1}$
E3	-8.76	$3.59 \pm 0.03$	$5.55 \times 10^{-1}$
E4	-8.22	$8.58 \pm 0.18$	$9.33 \times 10^{-1}$
E5	-7.69	$19.6 \pm 1.6$	1.29
E6	-7.02	$42.1 \pm 0.3$	1.62



$$N = 9.99$$

$$s_N = 0.54$$

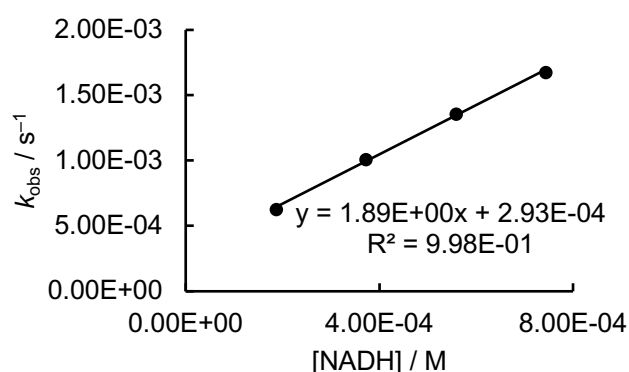
## Nucleophilicity of NADH

### Reaction of NADH with E1

Kinetics of the reaction of  $\text{IiI}_2\text{CH}^+\text{BF}_4^-$  (**E1**) with NADH followed by UV/Vis spectroscopy (630 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in  $\text{H}_2\text{O}$  containing 0.4% MeCN (RM03-467).

[E1] / M	[NADH] / M	$k_{\text{obs}}$ / $\text{s}^{-1}$
$1.50 \times 10^{-5}$	$1.86 \times 10^{-4}$	$6.28 \times 10^{-4}$
$1.50 \times 10^{-5}$	$3.72 \times 10^{-4}$	$1.01 \times 10^{-3}$
$1.50 \times 10^{-5}$	$5.57 \times 10^{-4}$	$1.36 \times 10^{-3}$
$1.50 \times 10^{-5}$	$7.42 \times 10^{-4}$	$1.68 \times 10^{-3}$

$$k_2 = (1.89 \pm 0.05) \text{ L mol}^{-1} \text{ s}^{-1}$$

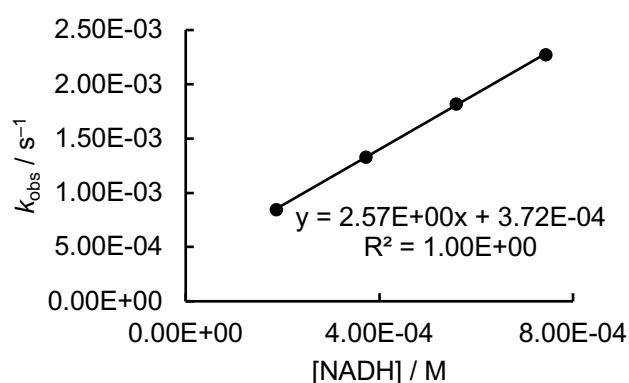


### Reaction of NADH with E2

Kinetics of the reaction of  $\text{IuI}_2\text{CH}^+\text{BF}_4^-$  (**E2**) with NADH followed by UV/Vis spectroscopy (634 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in  $\text{H}_2\text{O}$  containing 0.8% MeCN (RM03-467).

[E2] / M	[NADH] / M	$k_{\text{obs}}$ / $\text{s}^{-1}$
$1.50 \times 10^{-5}$	$1.86 \times 10^{-4}$	$8.42 \times 10^{-4}$
$1.50 \times 10^{-5}$	$3.72 \times 10^{-4}$	$1.33 \times 10^{-3}$
$1.50 \times 10^{-5}$	$5.57 \times 10^{-4}$	$1.82 \times 10^{-3}$
$1.50 \times 10^{-5}$	$7.42 \times 10^{-4}$	$2.27 \times 10^{-3}$

$$k_2 = (2.57 \pm 0.04) \text{ L mol}^{-1} \text{ s}^{-1}$$

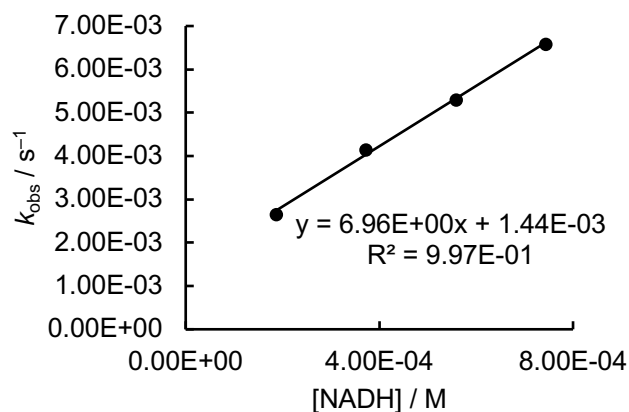


### Reaction of NADH with E3

Kinetics of the reaction of  $\text{Ind}_2\text{CH}^+\text{BF}_4^-$  (**E3**) with NADH followed by UV/Vis spectroscopy (614 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in  $\text{H}_2\text{O}$  containing 1.0% MeCN (RM03-467).

[E3] / M	[NADH] / M	$k_{\text{obs}}$ / $\text{s}^{-1}$
$1.50 \times 10^{-5}$	$1.86 \times 10^{-4}$	$2.66 \times 10^{-3}$
$1.50 \times 10^{-5}$	$3.72 \times 10^{-4}$	$4.15 \times 10^{-3}$
$1.50 \times 10^{-5}$	$5.57 \times 10^{-4}$	$5.30 \times 10^{-3}$
$1.50 \times 10^{-5}$	$7.42 \times 10^{-4}$	$6.59 \times 10^{-3}$

$$k_2 = (6.96 \pm 0.25) \text{ L mol}^{-1} \text{ s}^{-1}$$

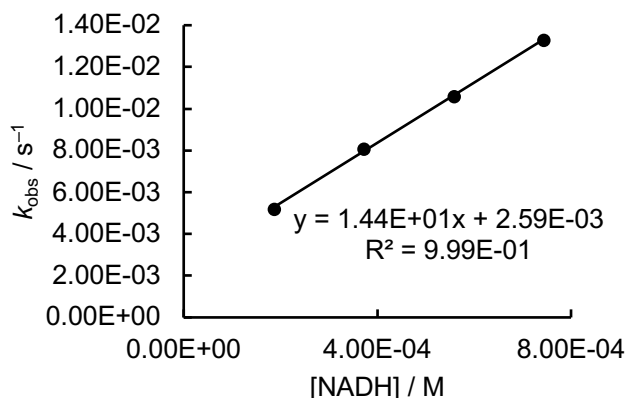


### Reaction of NADH with E4

Kinetics of the reaction of  $\text{thq}_2\text{CH}^+\text{BF}_4^-$  (**E4**) with NADH followed by UV/Vis spectroscopy (618 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in H<sub>2</sub>O containing 0.4% MeCN (RM03-467).

[E4] / M	[NADH] / M	$k_{\text{obs}}$ / s <sup>-1</sup>
$1.50 \times 10^{-5}$	$1.86 \times 10^{-4}$	$5.20 \times 10^{-3}$
$1.50 \times 10^{-5}$	$3.72 \times 10^{-4}$	$8.09 \times 10^{-3}$
$1.50 \times 10^{-5}$	$5.57 \times 10^{-4}$	$1.06 \times 10^{-2}$
$1.50 \times 10^{-5}$	$7.42 \times 10^{-4}$	$1.33 \times 10^{-2}$

$$k_2 = (14.4 \pm 0.3) \text{ L mol}^{-1} \text{ s}^{-1}$$

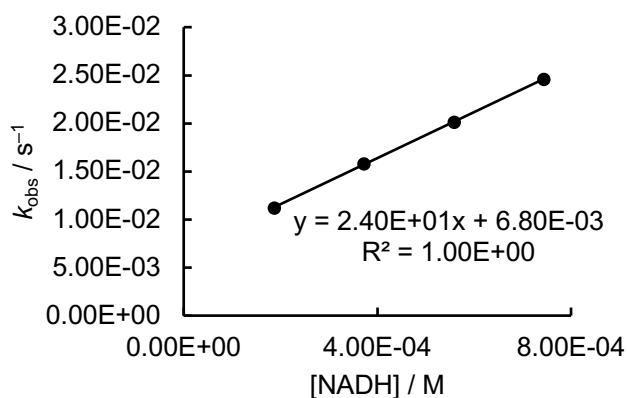


### Reaction of NADH with E5

Kinetics of the reaction of  $\text{pyr}_2\text{CH}^+\text{BF}_4^-$  (**E5**) with NADH followed by UV/Vis spectroscopy (610 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in H<sub>2</sub>O containing 1.1% MeCN (RM03-467).

[E5] / M	[NADH] / M	$k_{\text{obs}}$ / s <sup>-1</sup>
$1.50 \times 10^{-5}$	$1.86 \times 10^{-4}$	$1.12 \times 10^{-2}$
$1.50 \times 10^{-5}$	$3.72 \times 10^{-4}$	$1.58 \times 10^{-2}$
$1.50 \times 10^{-5}$	$5.57 \times 10^{-4}$	$2.01 \times 10^{-2}$
$1.50 \times 10^{-5}$	$7.42 \times 10^{-4}$	$2.46 \times 10^{-2}$

$$k_2 = (24.0 \pm 0.2) \text{ L mol}^{-1} \text{ s}^{-1}$$

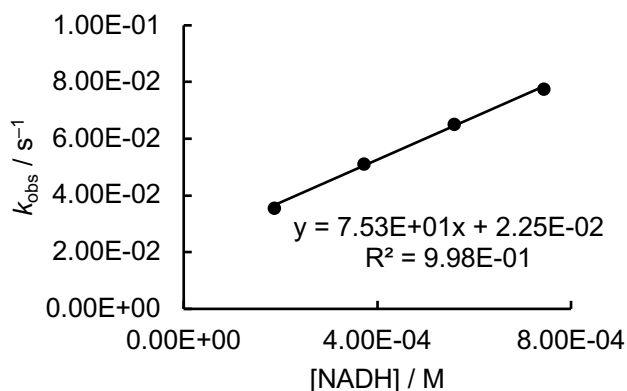


### Reaction of NADH with E6

Kinetics of the reaction of  $\text{dma}_2\text{CH}^+\text{BF}_4^-$  (**E6**) with NADH followed by UV/Vis spectroscopy (604 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in H<sub>2</sub>O containing 0.8% MeCN (RM03-467).

[E6] / M	[NADH] / M	$k_{\text{obs}}$ / s <sup>-1</sup>
$1.50 \times 10^{-5}$	$1.86 \times 10^{-4}$	$3.57 \times 10^{-2}$
$1.50 \times 10^{-5}$	$3.72 \times 10^{-4}$	$5.13 \times 10^{-2}$
$1.50 \times 10^{-5}$	$5.57 \times 10^{-4}$	$6.52 \times 10^{-2}$
$1.50 \times 10^{-5}$	$7.42 \times 10^{-4}$	$7.77 \times 10^{-2}$

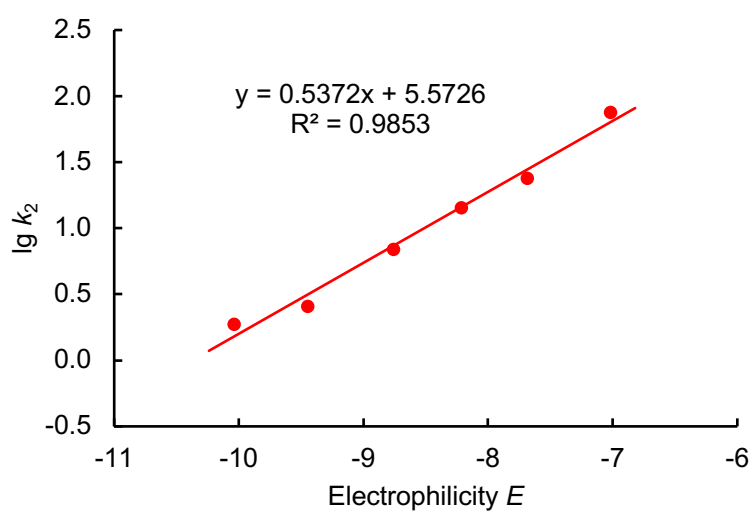
$$k_2 = (75.3 \pm 2.6) \text{ L mol}^{-1} \text{ s}^{-1}$$



### Determination of the Nucleophilicity Parameter of NADH

**Table S2.** Electrophiles and associated electrophilicity  $E$  as well as their rates  $k_2$  for the reaction with NADH used for the determination of the nucleophilicity of NADH.

Electrophile	Electrophilicity $E$	$k_2 / \text{L mol}^{-1} \text{s}^{-1}$	$\lg k_2$
E1	-10.04	$1.89 \pm 0.05$	$2.76 \times 10^{-1}$
E2	-9.45	$2.57 \pm 0.04$	$4.10 \times 10^{-1}$
E3	-8.76	$6.96 \pm 0.25$	$8.43 \times 10^{-1}$
E4	-8.22	$14.4 \pm 0.3$	1.16
E5	-7.69	$24.0 \pm 0.2$	1.38
E6	-7.02	$75.3 \pm 2.6$	1.88



$$N = 10.37$$

$$s_N = 0.54$$

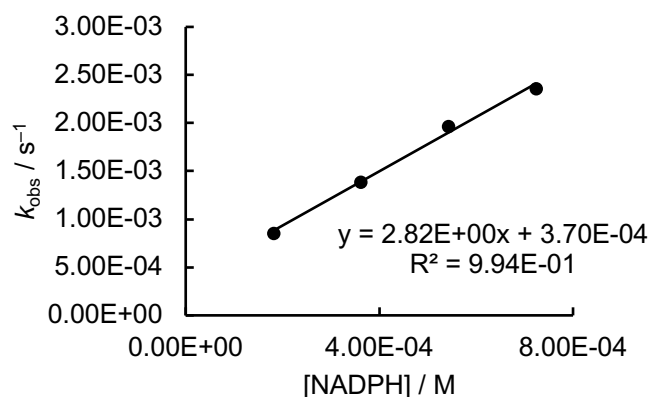
## Nucleophilicity of NADPH

### Reaction of NADPH with E1

Kinetics of the reaction of  $\text{Ii}_2\text{CH}^+\text{BF}_4^-$  (**E1**) with NADPH followed by UV/Vis spectroscopy (630 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in  $\text{H}_2\text{O}$  containing 0.4% MeCN (RM03-475).

[E1] / M	[NADPH] / M	$k_{\text{obs}}$ / $\text{s}^{-1}$
$1.50 \times 10^{-5}$	$1.81 \times 10^{-4}$	$8.55 \times 10^{-4}$
$1.50 \times 10^{-5}$	$3.61 \times 10^{-4}$	$1.39 \times 10^{-3}$
$1.50 \times 10^{-5}$	$5.42 \times 10^{-4}$	$1.97 \times 10^{-3}$
$1.50 \times 10^{-5}$	$7.22 \times 10^{-4}$	$2.36 \times 10^{-3}$

$$k_2 = (2.82 \pm 0.16) \text{ L mol}^{-1} \text{ s}^{-1}$$

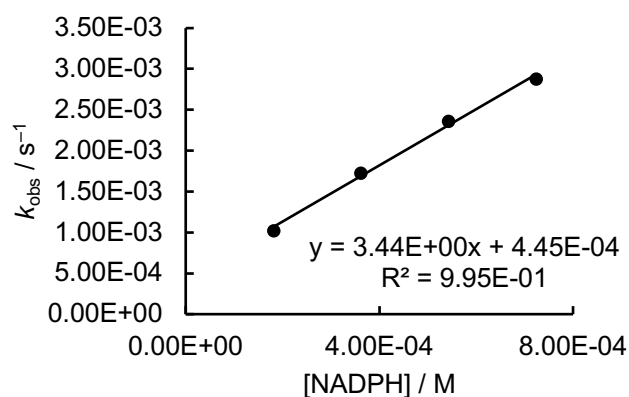


### Reaction of NADPH with E2

Kinetics of the reaction of  $\text{Iu}_2\text{CH}^+\text{BF}_4^-$  (**E2**) with NADPH followed by UV/Vis spectroscopy (634 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in  $\text{H}_2\text{O}$  containing 0.9% MeCN (RM03-475).

[E2] / M	[NADH] / M	$k_{\text{obs}}$ / $\text{s}^{-1}$
$1.50 \times 10^{-5}$	$1.81 \times 10^{-4}$	$1.02 \times 10^{-3}$
$1.50 \times 10^{-5}$	$3.61 \times 10^{-4}$	$1.73 \times 10^{-3}$
$1.50 \times 10^{-5}$	$5.42 \times 10^{-4}$	$2.36 \times 10^{-3}$
$1.50 \times 10^{-5}$	$7.22 \times 10^{-4}$	$2.88 \times 10^{-3}$

$$k_2 = (3.44 \pm 0.17) \text{ L mol}^{-1} \text{ s}^{-1}$$

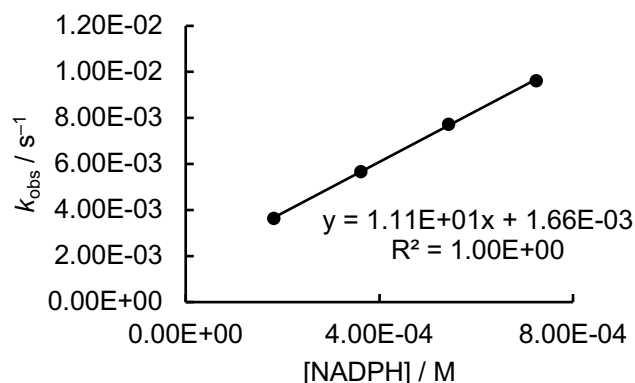


### Reaction of NADPH with E3

Kinetics of the reaction of  $\text{Ind}_2\text{CH}^+\text{BF}_4^-$  (**E3**) with NADPH followed by UV/Vis spectroscopy (614 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in  $\text{H}_2\text{O}$  containing 1.0% MeCN (RM03-475).

[E3] / M	[NADH] / M	$k_{\text{obs}}$ / $\text{s}^{-1}$
$1.50 \times 10^{-5}$	$1.81 \times 10^{-4}$	$3.63 \times 10^{-3}$
$1.50 \times 10^{-5}$	$3.61 \times 10^{-4}$	$5.67 \times 10^{-3}$
$1.50 \times 10^{-5}$	$5.42 \times 10^{-4}$	$7.72 \times 10^{-3}$
$1.50 \times 10^{-5}$	$7.22 \times 10^{-4}$	$9.62 \times 10^{-3}$

$$k_2 = (11.1 \pm 0.1) \text{ L mol}^{-1} \text{ s}^{-1}$$

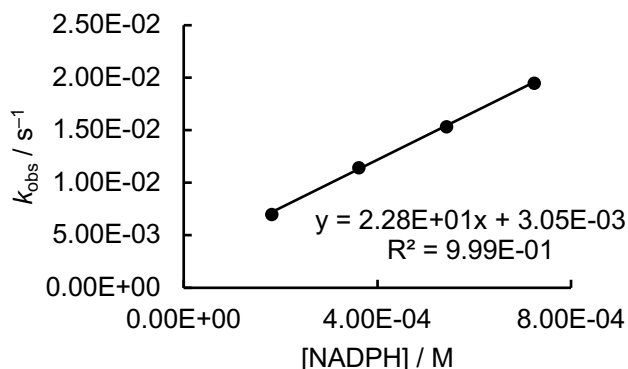


### Reaction of NADPH with E4

Kinetics of the reaction of  $\text{thq}_2\text{CH}^+\text{BF}_4^-$  (**E4**) with NADPH followed by UV/Vis spectroscopy (618 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in H<sub>2</sub>O containing 0.20% MeCN (RM03-475).

[E4] / M	[NADH] / M	$k_{\text{obs}}$ / s <sup>-1</sup>
$1.50 \times 10^{-5}$	$1.81 \times 10^{-4}$	$7.02 \times 10^{-3}$
$1.50 \times 10^{-5}$	$3.61 \times 10^{-4}$	$1.15 \times 10^{-2}$
$1.50 \times 10^{-5}$	$5.42 \times 10^{-4}$	$1.54 \times 10^{-2}$
$1.50 \times 10^{-5}$	$7.22 \times 10^{-4}$	$1.95 \times 10^{-2}$

$$k_2 = (22.8 \pm 0.4) \text{ L mol}^{-1} \text{ s}^{-1}$$

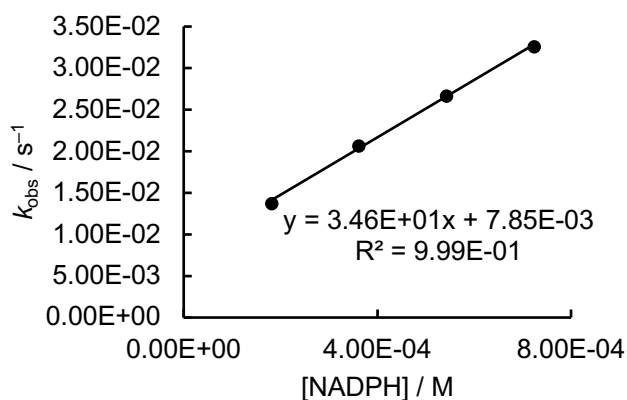


### Reaction of NADPH with E5

Kinetics of the reaction of  $\text{pyr}_2\text{CH}^+\text{BF}_4^-$  (**E5**) with NADPH followed by UV/Vis spectroscopy (610 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in H<sub>2</sub>O containing 1.1% MeCN (RM03-475).

[E5] / M	[NADH] / M	$k_{\text{obs}}$ / s <sup>-1</sup>
$1.50 \times 10^{-5}$	$1.81 \times 10^{-4}$	$1.38 \times 10^{-2}$
$1.50 \times 10^{-5}$	$3.61 \times 10^{-4}$	$2.07 \times 10^{-2}$
$1.50 \times 10^{-5}$	$5.42 \times 10^{-4}$	$2.67 \times 10^{-2}$
$1.50 \times 10^{-5}$	$7.22 \times 10^{-4}$	$3.26 \times 10^{-2}$

$$k_2 = (34.6 \pm 0.9) \text{ L mol}^{-1} \text{ s}^{-1}$$

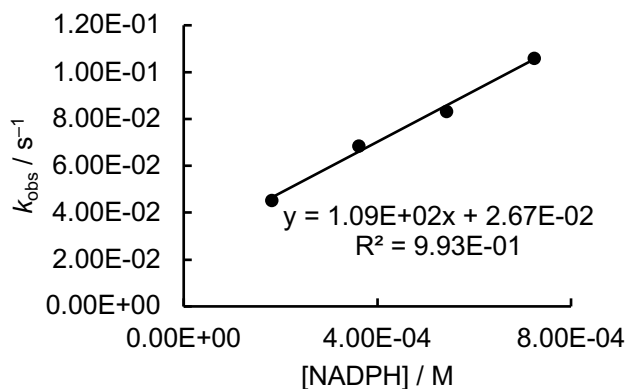


### Reaction of NADPH with E6

Kinetics of the reaction of  $\text{dma}_2\text{CH}^+\text{BF}_4^-$  (**E6**) with NADPH followed by UV/Vis spectroscopy (604 nm) at 20 °C in pH 7 phosphate solution (0.05 M) in H<sub>2</sub>O containing 0.4% MeCN (RM03-475).

[E6] / M	[NADH] / M	$k_{\text{obs}}$ / s <sup>-1</sup>
$1.50 \times 10^{-5}$	$1.81 \times 10^{-4}$	$4.54 \times 10^{-2}$
$1.50 \times 10^{-5}$	$3.61 \times 10^{-4}$	$6.86 \times 10^{-2}$
$1.50 \times 10^{-5}$	$5.42 \times 10^{-4}$	$8.34 \times 10^{-2}$
$1.50 \times 10^{-5}$	$7.22 \times 10^{-4}$	$1.06 \times 10^{-1}$

$$k_2 = (109 \pm 6) \text{ L mol}^{-1} \text{ s}^{-1}$$

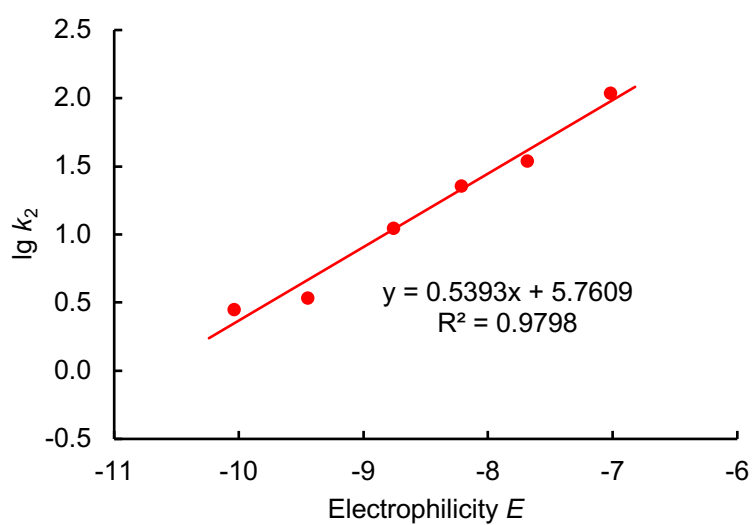




### Determination of the Nucleophilicity Parameter of NADPH

**Table S3.** Electrophiles and associated electrophilicity  $E$  as well as their rates  $k_2$  for the reaction with NADPH used for the determination of the nucleophilicity of NADPH.

Electrophile	Electrophilicity $E$	$k_2 / \text{L mol}^{-1} \text{s}^{-1}$	$\lg k_2$
E1	-10.04	$2.82 \pm 0.16$	$4.50 \times 10^{-1}$
E2	-9.45	$3.44 \pm 0.17$	$5.37 \times 10^{-1}$
E3	-8.76	$11.1 \pm 0.1$	1.05
E4	-8.22	$22.8 \pm 0.4$	1.36
E5	-7.69	$34.6 \pm 0.9$	1.54
E6	-7.02	$109 \pm 6$	2.04



$$N = 10.68$$

$$s_N = 0.54$$

## References

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- (S1) R. J. Mayer, N. Hampel, P. Mayer, A. R. Ofial and H. Mayr, *Eur. J. Org. Chem.*, 2019, **2019**, 412-421.
- (S2) a) for NADH: Biological Magnetic Resonance Data Bank (BMRB), entry bmse000053, doi:10.13018/BMSE000053; b) for the diarylmethane: K. Takaishi, H. Kosugi, R. Nishimura, Y. Yamada and T. Ema, *Chem. Commun.*, 2021, **57**, 8083-8086.