

## How Nucleophilic Are Diazo Compounds?

Thorsten Bug, Manfred Hartnagel, Clemens Schlierf, and Herbert Mayr\*<sup>[a]</sup>

Dedicated to Professor Gernot Boche on the occasion of his 65th birthday

**Abstract:** The kinetics of the reactions of benzhydryl cations with eight diazo compounds **1a–g** were investigated photometrically in dichloromethane. The nucleophilicity parameters  $N$  and slope parameters  $s$  of these diazo compounds were derived from the equation  $\log k(20^\circ\text{C}) = s(E+N)$  and compared with the nucleophilicities of other  $\pi$  systems (alkenes, arenes, silyl enol ethers, silyl ketene acetals). It is shown that the nucleophilic reactivities of diazo compounds cover more than ten orders of magnitude, being comparable to that of styrene on the low reactivity end and to that of enamines on the high reactivity end. The rate-determining step of these reactions is the electrophilic attack at the diazo-carbon atom to yield diazonium ions, which rapidly lose nitrogen.

**Keywords:** carbocations • C–C coupling • diazo compounds • kinetics • structure–activity relationships

### Introduction

Diazo compounds are ambiphilic (ambivalent) reagents<sup>[1]</sup> and their chemistry has been extensively reviewed.<sup>[2]</sup> While electrophiles usually attack at the carbon atom,<sup>[3]</sup> the terminal nitrogen atom is the preferred site of attack by nucleophiles.<sup>[4]</sup> Their ambiphilic behavior is also observed in [3+2] cycloadditions with dipolarophiles (Huisgen reactions).<sup>[5]</sup> Methyl diazoacetate, for example, reacts rapidly with strong nucleophiles (e.g., enamines) as well as with strong electrophiles (e.g., unsaturated esters and nitriles), while its cycloadditions with enol ethers and alkyl-substituted ethylenes proceed rather slowly.<sup>[6]</sup> Perturbational molecular orbital theory has been employed to rationalize this behavior.<sup>[6, 7, 8]</sup>

In 1994 we reported that absolute rate constants of electrophile nucleophile combination reactions can be predicted by the three-parameter Equation (1), where  $s$  = nucleophile-specific slope parameter,  $N$  = nucleophilicity parameter, and  $E$  = electrophilicity parameter, if only one new bond is formed in the rate-determining step.<sup>[9]</sup>

$$\log k(20^\circ\text{C}) = s(E+N) \quad (1)$$

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Supporting information for this article is available on the WWW under <http://www.wiley-vch.de/home/chemeurj.org/> or from the author. Procedures and characterized products of reactions of diazo compounds with benzhydryl cations, and tables containing the concentrations and rate constants of the individual runs of the kinetic experiments are available.

In the case of ionic cycloadditions, deviations from Equation (1) have been interpreted as a measure for the energy of concert.<sup>[10]</sup>

Recently, we have recommended benzhydryl cations  $\text{Ar}_2\text{CH}^+$  as reference electrophiles (Table 1) for the determi-

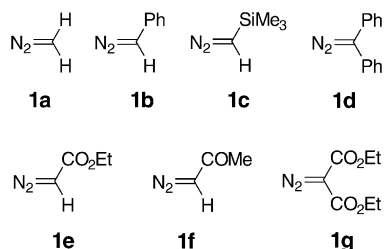
Table 1. Abbreviations and electrophilicity parameters  $E$  of the employed reference electrophiles in  $\text{CH}_2\text{Cl}_2$  for determining the nucleophilicities of diazo compounds.

$\text{Ar}_2\text{CH}^+$	X	Y	$E^{[a]}$	$\lambda_{\text{max}} [\text{nm}]^{[a]}$
(ani) <sub>2</sub> CH <sup>+</sup>	OMe	OMe	0.00	512
(fur) <sub>2</sub> CH <sup>+</sup>			– 1.36	533
fc(Ph)CH <sup>+</sup>		Ph	– 2.64	410
(pfa) <sub>2</sub> CH <sup>+</sup>	N(Ph)CH <sub>2</sub> CF <sub>3</sub>	N(Ph)CH <sub>2</sub> CF <sub>3</sub>	– 3.14	601
(mfa) <sub>2</sub> CH <sup>+</sup>	N(CH <sub>3</sub> )CH <sub>2</sub> CF <sub>3</sub>	N(CH <sub>3</sub> )CH <sub>2</sub> CF <sub>3</sub>	– 3.85	593
(dpa) <sub>2</sub> CH <sup>+</sup>	NPh <sub>2</sub>	NPh <sub>2</sub>	– 4.72	672
(mpa) <sub>2</sub> CH <sup>+</sup>	N(Ph)CH <sub>3</sub>	N(Ph)CH <sub>3</sub>	– 5.89	622
(dma) <sub>2</sub> CH <sup>+</sup>	N(CH <sub>3</sub> ) <sub>2</sub>	N(CH <sub>3</sub> ) <sub>2</sub>	– 7.02	613
(pyr) <sub>2</sub> CH <sup>+</sup>	N(CH <sub>2</sub> ) <sub>4</sub>	N(CH <sub>2</sub> ) <sub>4</sub>	– 7.69	620
(thq) <sub>2</sub> CH <sup>+</sup>			– 8.22	628
(jul) <sub>2</sub> CH <sup>+</sup>			– 9.45	642

[a] From ref. [11].

nation of the nucleophilic reactivities of aromatic and aliphatic  $\pi$  systems,<sup>[11]</sup> carbanions,<sup>[12]</sup> hydride donors,<sup>[11, 13a]</sup> and *n*-nucleophiles.<sup>[13b]</sup>

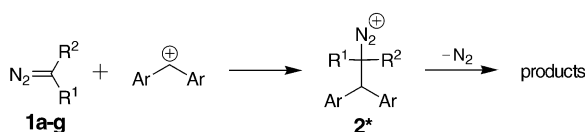
It was the goal of this work to determine the nucleophilicity parameters *N* and *s* of the diazo compounds **1a–g** according



to Equation (1), in order to compare the nucleophilicities of diazo compounds quantitatively with those of other  $\pi$  nucleophiles and to predict possible reactions with one-bond electrophiles. These data may subsequently be employed for the analysis of the kinetics and mechanisms of diazo compound cycloadditions.

### Preparative Investigations

**Reaction products:** The reactions of the diazo compounds **1a–g** with the benzhydrylium salts  $\text{Ar}_2\text{CH}^+\text{X}^-$  can be assumed initially to produce the diazonium salts **2\***, from which the isolated products are derived (Scheme 1, Table 2).<sup>[14]</sup>



Scheme 1. Reactions of benzhydrylium ions with diazo compounds.

Since the substitution pattern of the benzhydrylium ions was found to have little influence on the types of reaction products, product studies have not been performed for all electrophile nucleophile combinations studied kinetically. However, each diazo compound has been investigated with at least one benzhydrylium ion.

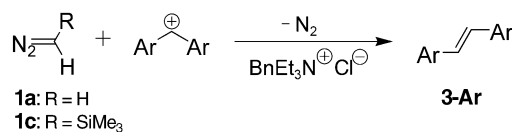
**Abstract in German:** Die Kinetik der Reaktionen von Benzhydrylkationen mit acht Diazoverbindungen **1a–g** wurde photometrisch in Dichlormethan untersucht. Die Nucleophilieparameter *N* und die Steigungsparameter *s* dieser Diazoverbindungen wurden aus der Gleichung  $\log k(20^\circ\text{C}) = s(E+N)$  abgeleitet und mit der Nucleophilie anderer  $\pi$ -Systeme verglichen. Wir zeigen, dass sich die nucleophilen Reaktivitäten von Diazoverbindungen über mehr als zehn logarithmische Einheiten erstrecken. Die wenig reaktiven Verbindungen besitzen eine ähnliche Nucleophilie wie Styrol, während die nucleophilsten Diazoverbindungen Enaminen entsprechen. Der geschwindigkeitsbestimmende Schritt ist der elektrophile Angriff am Diazo-Kohlenstoff, wobei Diazonium-Ionen entstehen, die rasch Stickstoff abspalten.

Table 2. Yields of the reactions of diazo compounds **1a** and **1c–g** with benzhydryl salts  $\text{Ar}_2\text{CH}^+\text{X}^-$ .

Diazo compound <b>1</b>	$\text{Ar}_2\text{CH}^+\text{X}^-$	Product <sup>[a]</sup>	Yield [%]
diazomethane ( <b>1a</b> )	$(\text{dma})_2\text{CH}^+\text{OTf}^-$	<b>3-dma</b>	32 <sup>[b]</sup>
	$(\text{thq})_2\text{CH}^+\text{BF}_4^-$	<b>3-thq</b>	57 <sup>[b]</sup>
	$(\text{jul})_2\text{CH}^+\text{BF}_4^-$	<b>3-jul</b>	26 <sup>[b]</sup>
(trimethylsilyl)diazomethane ( <b>1c</b> )	$(\text{dma})_2\text{CH}^+\text{OTf}^-$	<b>3-dma</b>	60 <sup>[b]</sup>
	$(\text{mpa})_2\text{CH}^+\text{BF}_4^-$	<b>3-mpa</b>	36 <sup>[b]</sup>
	$(\text{fc}(\text{Ph}))_2\text{CH}^+\text{ZnCl}_3^-$	<b>6e</b>	76
diphenyldiazomethane ( <b>1d</b> )	$(\text{dma})_2\text{CH}^+\text{OTf}^-$	<b>4d-dma</b>	43
ethyl diazoacetate ( <b>1e</b> )	$(\text{dma})_2\text{CH}^+\text{OTf}^-$	<b>5e-dma</b>	37 <sup>[c]</sup>
	$(\text{fur})_2\text{CH}^+\text{OTf}^-$	<b>5e-fur</b>	31
	$(\text{dma})_2\text{CH}^+\text{OTf}^-$	<b>5f-dma</b>	26
diethyl diazomalonate ( <b>1g</b> )	$(\text{fur})_2\text{CH}^+\text{OTf}^-$	<b>4g-fur</b>	31
	$(\text{ani})_2\text{CH}^+\text{ZnCl}_3^-$	<b>4g-ani</b>	29

[a] Abbreviations see Table 1. [b] In the presence of five equivalents of benzyltriethylammonium chloride. [c] **5e-dma** is the main product in a 9:1 mixture of isomers.

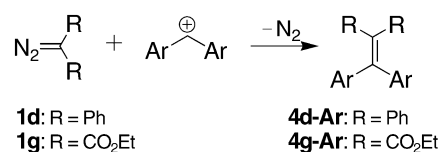
When solutions of benzhydrylium tetrafluoroborates or triflates in dichloromethane were combined with diazomethane (**1a**), phenyldiazomethane (**1b**), or (trimethylsilyl)diazomethane (**1c**), only insoluble polymeric material was produced, analogously to the  $\text{BF}_3$ -catalyzed formation of polymethylene from diazomethane (**1a**).<sup>[15]</sup> The *trans*-stilbenes **3-Ar** were formed, however, when the reactions of benzhydrylium salts with **1a** or **1c** were carried out under analogous conditions, but in the presence of 5 equivalents of benzyltriethylammonium chloride ( $\text{BnEt}_3\text{N}^+\text{Cl}^-$ ), which acts as a base (Scheme 2, Table 2).



Scheme 2. Reaction products from the reaction of benzhydrylium salts with **1a** or **1c**.

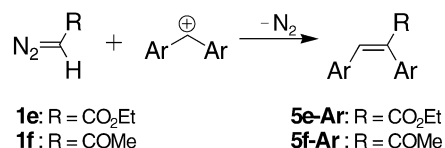
Compound **3-dma**<sup>[16b,c]</sup> was identical to a product that we obtained from 4-(dimethylamino)benzaldehyde through a McMurry reaction by a literature procedure.<sup>[16a]</sup> Analogous spectral data were obtained for the *trans*-stilbenes **3-thq**,<sup>[16d]</sup> **3-jul**,<sup>[16a]</sup> and **3-mpa**. However, we were not able to isolate any pure products from benzhydrylium salts with phenyldiazomethane (**1b**), though a GC/MS analysis indicated the presence of a diarylphenylethene.

Diarylethenes **4\***, in which the original benzhydryl fragment is retained, were obtained from the reactions of benzhydrylium salts with the two disubstituted diazo compounds diphenyldiazomethane (**1d**) and diethyl diazomalonate (**1g**) (Scheme 3). The observation of two <sup>13</sup>C NMR resonances for the olefinic carbon atoms is in accord with the suggested structures **4\***.



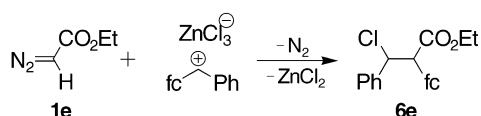
Scheme 3. Reaction products from the reaction of benzhydrylium salts with **1d** or **1g**.

When the benzhydrylium tetrafluoroborates or triflates were combined with 1–2 equivalents of ethyl diazoacetate (**1e**) or diazoacetone (**1b**), the compounds **5\*** were obtained. (Scheme 4).



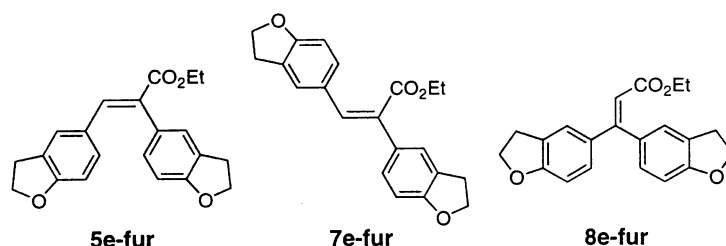
Scheme 4. Reaction products from the reaction of benzhydrylium salts with **1e** or **1f**.

In the reaction of  $\text{fc}(\text{Ph})\text{CH}^+\text{ZnCl}_3^-$  with ethyl diazoacetate (**1e**), the chloro-substituted compound **6e** was isolated (Scheme 5). The  $^1\text{H}$  and  $^{13}\text{C}$  NMR signals of the compound



Scheme 5. Reaction product from **1e** and 1-ferrocenylbenzyl chloride/ $\text{ZnCl}_3^-$ .

obtained from  $(\text{fur})_2\text{CH}^+\text{OTf}^-$  and ethyl diazoacetate (**1e**) indicate the formation of either **5e-fur**, **7e-fur**, or **8e-fur**.



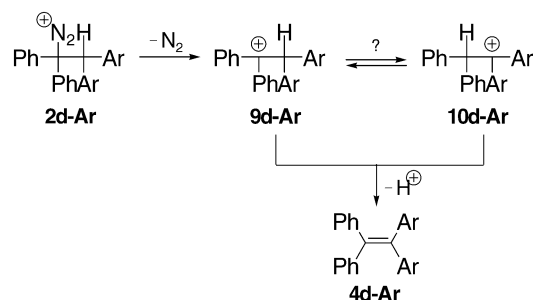
In the NOESY-NMR spectrum, weak cross-peaks were obtained between the vinylic hydrogen and all protons of the ethoxy group. Structure **7e-fur** can therefore be excluded, because of the large distance between these protons. Compound **8e-fur** is ruled out by the observation of  $^3J$  couplings between the vinylic CH-carbon atom and some aromatic protons (gHSQC and gHMBC methods). Structure **5e-fur** is thus derived. Simulation of the  $^1\text{H}$  NMR spectrum by the ACD/LABS NMR Spectrum Generator gave chemical shifts of  $\delta = 7.84$ ,  $7.02$ , and  $6.39$  ppm for the vinylic hydrogens of **5e-fur**, **7e-fur**, and **8e-fur**, respectively, close to those observed experimentally for the corresponding diphenyl-substituted ethyl acrylates ( $\delta = 7.79$ ,<sup>[17]</sup>  $7.02$ ,<sup>[18]</sup> and  $6.37$  ppm<sup>[19]</sup>). The structural assignment for **5e-fur** is thus corroborated by the observed chemical shift of the singlet at  $\delta = 7.72$  ppm.

The structure of **5f-dma** was assigned analogously to that of **5e-fur** (NOESY, gHSQC, gHMBC, NMR spectrum simulation).

**Reaction mechanism:** Table 2 indicates that the products obtained from diazomethane (**1a**) and the monosubstituted

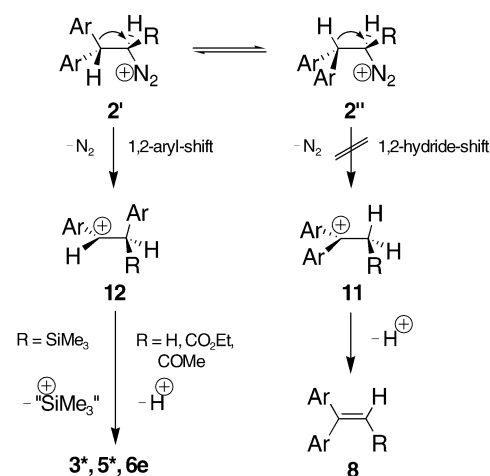
diazomethanes (**1c**, **1e**, **1f**) arise from a 1,2-aryl shift, while the formation of compounds **4\*** from the disubstituted diazomethanes **1d** and **1g** proceeds without aryl migration. A rationalization of this behavior is given in Scheme 6, Scheme 7, and Scheme 8.

Dediazoniation of the diazonium ion (**2d-Ar**) obtained from diphenyldiazomethane (**1d**) and  $\text{Ar}_2\text{CH}^+\text{X}^-$  yields the diaryl-substituted carbenium ion **9d-Ar**. This is deprotonated prior to or after hydride migration ( $\rightarrow$  **10d-Ar**) to give **4d-Ar** (Scheme 6).



Scheme 6. Dediazoniation of the diazonium ion **2d-Ar**.

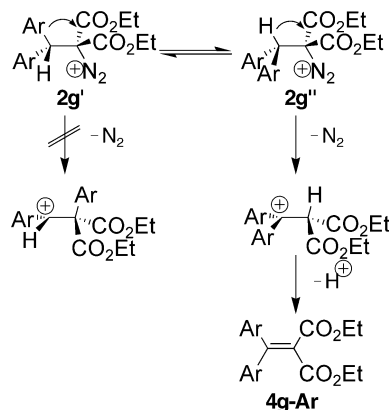
In all other cases, the loss of  $\text{N}_2$  is accompanied by migration of hydride or an aryl group to yield more stabilized carbocations. Although 1,2-hydride migration would give rise to better stabilized carbocations (**11**) than 1,2-aryl migration ( $\rightarrow$  **12**) (Scheme 7), the latter process is usually kinetically preferred, as indicated by the formation of compounds **3\***, **5\***, and **6e** from benzhydrylium ions  $\text{Ar}_2\text{CH}^+\text{X}^-$  and **1a**, **1c**, **1e**, and **1f**. Obviously, the transition state of the dediazoniation step can be stabilized by a bridging aryl group (phenonium ion)<sup>[20]</sup> in accord with observations in solvolysis reactions of  $\beta$ -arylalkyl systems.<sup>[21]</sup>



Scheme 7. Dediazoniation accompanied by 1,2-aryl migration.

Why does 1,2-aryl migration not occur in the reactions of benzhydrylium ions with diethyl diazomalonate (**1g**)?

The 1,2-aryl migration requires a conformation with the aryl group *anti* to N<sub>2</sub> (**2'** in Scheme 7). Since the corresponding conformation **2g'** (Scheme 8) suffers from conformational strain, conformation **2g''** is preferred, and undergoes dediazonation accompanied by hydride migration, finally resulting in the formation of the tetrasubstituted alkene **4g-Ar**.<sup>[22]</sup>



Scheme 8. Dediazonation accompanied by 1,2-hydride migration.

**Kinetic investigations:** The rates of the reactions of the benzhydrylium ions Ar<sub>2</sub>CH<sup>+</sup> with the diazo compounds **1a–g** were followed photometrically. Colorless products arise from the blue or red benzhydrylium ions. For slow reactions ( $\tau_{1/2} > 10$  s), the decrease in the absorbances of the benzhydrylium ions was followed in a thermostated flask with an immersion UV/Vis probe and a working station as described in ref. [23]. Faster reactions were followed with a stopped-flow spectrophotometer system as described recently.<sup>[11]</sup> All reactions reported in this article followed second-order kinetics, first order with respect to the carbocation (Ar<sub>2</sub>CH<sup>+</sup>X<sup>-</sup>) concentration and first order with respect to diazo compound **1a–g** concentration. Since the diazo compounds were usually

employed in large excess over the carbocations (10–120 equivalents), their concentrations can be considered to be constant, and the second-order rate constants given in Table 3, Table 4, and Table 5 were obtained by dividing the pseudo first-order rate constants by the initial concentrations of the diazo compounds.

**Counterion effects:** According to Table 3, (dma)<sub>2</sub>CH<sup>+</sup>OTf<sup>-</sup> reacts twice as rapidly as (dma)<sub>2</sub>CH<sup>+</sup>BF<sub>4</sub><sup>-</sup> with ethyl diazoacetate (**1e**), probably because of a weak stabilizing Lewis acid–base interaction of the intermediate diazonium ion (**2**) with the triflate anion, analogous to the nucleophilic solvation of the diazonium ions discussed in the next section.

Table 3. Influence of the counterion on the reaction rates of the benzhydrylium ions with diphenyldiazomethane (**1d**) or ethyl diazoacetate (**1e**) in CH<sub>2</sub>Cl<sub>2</sub> at 20 °C.

Diazo compound	Ar <sub>2</sub> CH <sup>+</sup>	Counterion	<i>k</i> [L mol <sup>-1</sup> s <sup>-1</sup> ]
ethyl diazoacetate ( <b>1e</b> )	(dma) <sub>2</sub> CH <sup>+</sup>	OTf <sup>-</sup>	(2.88 ± 0.13) × 10 <sup>-2</sup>
	(dma) <sub>2</sub> CH <sup>+</sup>	BF <sub>4</sub> <sup>-</sup>	(1.40 ± 0.03) × 10 <sup>-2</sup>
diphenyldiazomethane ( <b>1d</b> )	(mpa) <sub>2</sub> CH <sup>+</sup>	OTf <sup>-</sup>	(3.16 ± 0.17) × 10 <sup>-1</sup>
	(mpa) <sub>2</sub> CH <sup>+</sup>	BF <sub>4</sub> <sup>-</sup>	(2.88 ± 0.18) × 10 <sup>-1</sup>

The identical reactivity of (mpa)<sub>2</sub>CH<sup>+</sup> tetrafluoroborate and triflate with diphenyldiazomethane (**1d**), within experimental error, is analogous to the counterion-independent rate constants of the reactions of carbocations with alkenes and enol ethers.<sup>[23, 24]</sup> Since the counterion effects are small in comparison with the rate effects caused by variation in structures, we have not investigated them in detail.

The minor importance of counterion effects in these reactions is also reflected by the fact that all reaction series depicted in Figure 1 include benzhydrylium salts with different counterions.

**Solvent effects:** The variation of solvent has been reported to have only a small influence on the rates of the reactions of

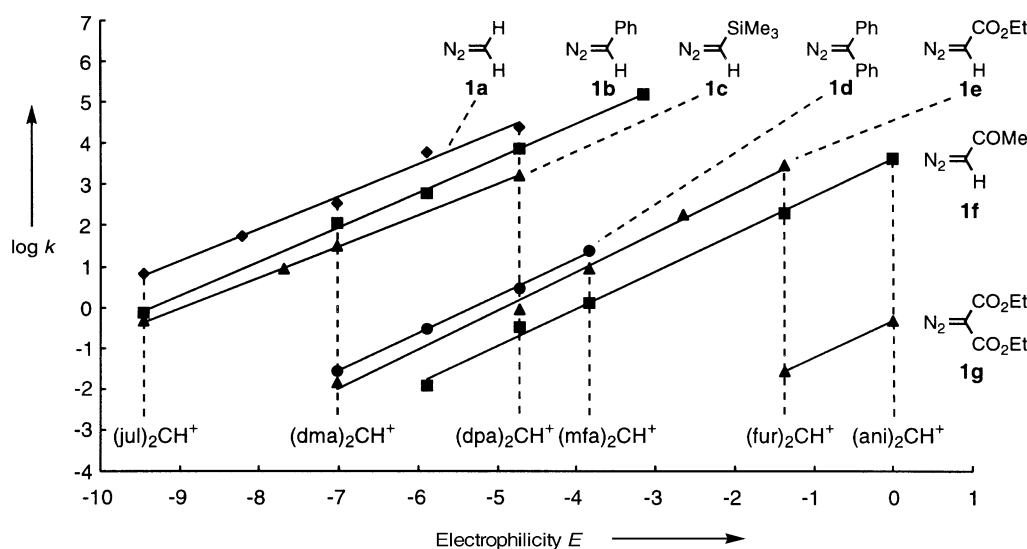


Figure 1. Correlations of the rate constants ( $\log k$ , 20 °C, CH<sub>2</sub>Cl<sub>2</sub>) for the reactions of diazo compounds **1** with benzhydryl cations Ar<sub>2</sub>CH<sup>+</sup> versus their electrophilic reactivities *E*.

benzhydrylium ions with alkenes (C–C bond formation) and trialkylsilanes (hydride abstractions). While the rate for the reaction of  $(\text{ani})_2\text{CH}^+\text{BCl}_4^-$  with 2-methyl-1-pentene increased by less than a factor of 5 with increasing solvent polarity ( $\text{CHCl}_3 \rightarrow \text{CH}_2\text{Cl}_2 \rightarrow (\text{CH}_2\text{Cl})_2 \rightarrow \text{CH}_3\text{CH}_2\text{NO}_2 \rightarrow \text{CH}_3\text{NO}_2$ ),<sup>[23]</sup> the rate of hydride abstraction from dimethylphenylsilane by the same carbocation  $(\text{ani})_2\text{CH}^+\text{OTf}^-$  increased by a factor of only 1.5 in a similar series of solvents ( $\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_3\text{CN} \rightarrow \text{CH}_3\text{NO}_2$ ).<sup>[25]</sup>

In contrast, a significant solvent effect was found in the reactions of  $(\text{dma})_2\text{CH}^+$  with ethyl diazoacetate (**1e**) (Table 4).

The observation that the reaction was noticeably faster in ethyl acetate and tetrahydrofuran than in dichloromethane and acetonitrile indicates that solvent polarity as measured by  $E_T$  cannot be responsible for the observed reactivity order. The moderate correlation between  $\log k$  and Gutmann's donor numbers (DNs) suggests a stabilization of the intermediate diazonium ion **2** by interaction with donor solvents.

In accord with this interpretation, the reverse relationship between rate constants and Gutmann's donor numbers of the solvents was found for azo couplings, because there the interaction between diazonium ions and donor solvents stabilizes the reactants.<sup>[27]</sup> Because of the small number of entries in Table 4, a more detailed discussion of solvent effects does not appear appropriate.

Table 4. Rate constants of the reactions of  $(\text{dma})_2\text{CH}^+\text{OTf}^-$  with ethyl diazoacetate (**1e**) in different solvents.

Solvent	DN <sup>[a,b]</sup>	$E_T(30)$ <sup>[a,b]</sup>	$k$ [ $\text{L mol}^{-1} \text{s}^{-1}$ ]
dichloromethane	0.0	40.7	$2.88 \times 10^{-2}$
acetonitrile	14.1	45.6	$4.98 \times 10^{-2}$
ethyl acetate	17.1	38.1	$9.92 \times 10^{-1}$
tetrahydrofuran	20.0	37.4	$4.55 \times 10^{-1}$

[a] From ref. [26]. [b] Gutmann's donor number.

**Structure-reactivity relationships:** Depending on the nucleophilicities of the diazo compounds, different benzhydrylium ions have been employed for the kinetic investigations (Table 5).

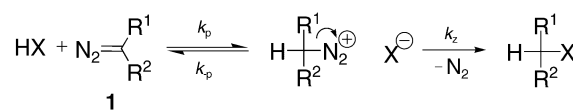
When the rate constants ( $\log k$ ) for the reactions of diazo compounds **1a–g** with  $\text{Ar}_2\text{CH}^+$  are plotted against the  $E$  parameters of the benzhydryl cations (from Table 1), linear correlations are obtained (Figure 1), from which  $N$  and  $s$  can be determined according to Equation (1).

Table 5. Second-order rate constants and activation parameters for the reaction of diazo compounds (**1**) with benzhydrylium ions in  $\text{CH}_2\text{Cl}_2$ .

Diazo compound	$\text{Ar}_2\text{CH}^+\text{X}^-$	$k$ (20 °C) [ $\text{L mol}^{-1} \text{s}^{-1}$ ]	$\Delta H^\ddagger$ [ $\text{kJ mol}^{-1}$ ]	$\Delta S^\ddagger$ [ $\text{J K}^{-1} \text{mol}^{-1}$ ]
diazomethane ( <b>1a</b> )	$(\text{jul})_2\text{CH}^+ \text{BF}_4^-$	6.64	–	–
	$(\text{thq})_2\text{CH}^+ \text{BF}_4^-$	$5.57 \times 10^1$	35.9	–88.9
	$(\text{dma})_2\text{CH}^+ \text{OTf}^-$	$3.59 \times 10^2$	28.1	–100.1
	$(\text{mpa})_2\text{CH}^+ \text{BF}_4^-$	$5.88 \times 10^3$	–	–
	$(\text{dpa})_2\text{CH}^+ \text{BF}_4^-$	$2.43 \times 10^4$	–	–
phenyldiazomethane ( <b>1b</b> )	$(\text{jul})_2\text{CH}^+ \text{BF}_4^-$	$7.56 \times 10^{-1}$	–	–
	$(\text{dma})_2\text{CH}^+ \text{OTf}^-$	$1.19 \times 10^2$	34.6	–87.0
	$(\text{mpa})_2\text{CH}^+ \text{BF}_4^-$	$5.80 \times 10^2$	–	–
	$(\text{dpa})_2\text{CH}^+ \text{BF}_4^-$	$6.85 \times 10^3$	–	–
	$(\text{pfa})_2\text{CH}^+ \text{BF}_4^-$	$1.45 \times 10^5$	–	–
(trimethylsilyl)diazomethane ( <b>1c</b> )	$(\text{jul})_2\text{CH}^+ \text{BF}_4^-$	$4.50 \times 10^{-1}$	–	–
	$(\text{pyr})_2\text{CH}^+ \text{BF}_4^-$	8.72	40.3	–89.2
	$(\text{dma})_2\text{CH}^+ \text{OTf}^-$	$3.10 \times 10^1$	35.7	–94.4
	$(\text{dpa})_2\text{CH}^+ \text{BF}_4^-$	$1.62 \times 10^3$	–	–
	$(\text{dma})_2\text{CH}^+ \text{OTf}^-$	$2.71 \times 10^{-2}$	–	–
diphenyldiazomethane ( <b>1d</b> )	$(\text{mpa})_2\text{CH}^+ \text{BF}_4^-$	$2.88 \times 10^{-1}$	–	–
	$(\text{dpa})_2\text{CH}^+ \text{BF}_4^-$	2.93	–	–
	$(\text{mfa})_2\text{CH}^+ \text{BF}_4^-$	$2.30 \times 10^1$	–	–
	$(\text{dma})_2\text{CH}^+ \text{OTf}^-$	$1.40 \times 10^{-2}$	–	–
	$(\text{dpa})_2\text{CH}^+ \text{BF}_4^-$	$8.46 \times 10^{-1}$	–	–
ethyl diazoacetate ( <b>1e</b> )	$(\text{mfa})_2\text{CH}^+ \text{BF}_4^-$	8.56	–	–
	$\text{fc}(\text{Ph})\text{CH}^+ \text{OTf}^-$	$1.80 \times 10^2$	33.1	–88.7
	$(\text{fur})_2\text{CH}^+ \text{OTf}^-$	$2.72 \times 10^3$	21.7	–105.0
	$(\text{mpa})_2\text{CH}^+ \text{BF}_4^-$	$1.21 \times 10^{-2}$	–	–
	$(\text{dpa})_2\text{CH}^+ \text{BF}_4^-$	$3.25 \times 10^{-1}$	–	–
diazoacetone ( <b>1f</b> )	$(\text{mfa})_2\text{CH}^+ \text{BF}_4^-$	1.30	–	–
	$(\text{fur})_2\text{CH}^+ \text{OTf}^-$	$1.98 \times 10^2$	19.9	–133.1
	$(\text{ani})_2\text{CH}^+ \text{OTf}^-$	$4.06 \times 10^3$	–	–
	$(\text{fur})_2\text{CH}^+ \text{OTf}^-$	$2.63 \times 10^{-2}$	–	–
	$(\text{ani})_2\text{CH}^+ \text{OTf}^-$	$4.77 \times 10^{-1}$	–	–

## Discussion

Brønsted acid catalyzed decompositions of diazo compounds have been reported to proceed through different mechanisms.<sup>[2a, 28, 29]</sup> Protonation of the diazo compounds can either be rate-determining ( $k_z > k_{-p}$ ) or occur in a rapid pre-equilibrium (Scheme 9), followed by rate-determining dediazonation ( $k_{-p} > k_z$ ).



Scheme 9. Brønsted acid-catalyzed decompositions of diazo compounds **1a–g**.

Analogously, the reactions described in this article may proceed either with rate-determining C–C bond formation or by fast reversible C–C bond formation and consecutive slow cleavage of the C–N<sub>2</sub> bond.

The absence of breaking points in the linearity of the correlations depicted in Figure 1 indicates that in none of these reaction series does a change in the mechanism take place (i.e., each of these diazo compounds reacts with all benzhydrylium ions either with rate-determining C–C bond formation or with rate-determining dediazonation).

The slopes of the correlation lines, which are comparable to those of enol ethers<sup>[11]</sup> and enamines,<sup>[30]</sup> indicate rate-determining formation of the carbon–carbon bonds. If the reactions were to proceed with rapid reversible formation of diazonium ions followed by slow dediazonation ( $k_{-p} \gg k_2$ ), slopes of  $s \approx 1.33$  would be expected,<sup>[31]</sup> since in this case transition states with essentially uncharged benzhydryl carbons would be involved.

Since the slopes  $s$  do not differ widely ( $0.75 < s < 0.95$ ), the  $N$  parameters can be used for a direct comparison of the nucleophilicities of the diazo compounds **1a–g** with one another as well as with those of other nucleophiles.

More than 80 years ago, Staudinger observed different decomposition rates of diazo compounds in the presence of unsubstituted and halogenated acetic acids.<sup>[32]</sup> The reported reactivity order **1a** > **1b** > **1d** > **1e** > **1g** corresponds to the nucleophilic reactivities of these diazo compounds shown in Figure 2.

Variation of the substituents has a large influence on the nucleophilicity of diazo compounds, and the reactivities of **1a–g** cover more than 10 orders of magnitude. Diazomethane (**1a**) is the most reactive compound in this series.

As previously observed for furans and thiophenes, the presence of a trimethylsilyl group at the position of electrophilic attack affects the nucleophilicity of the  $\pi$ -system only slightly.<sup>[33]</sup> Phenyldiazomethane (**1b**) is only one order of magnitude less nucleophilic than diazomethane (**1a**). Considerably stronger deactivation is caused by the second phenyl group, as demonstrated by the  $N$  value of diphenyldiazo-

methane (**1d**), which is 5 logarithmic units smaller than  $N$  of diazomethane (**1a**), probably due to steric shielding.

The retarding effect of the inductively and mesomerically electron-withdrawing ethoxycarbonyl group is demonstrated by the comparison of diazomethane (**1a**) ( $N = 10.48$ ) with ethyl diazoacetate (**1e**) ( $N = 4.91$ ) and diethyl diazomalonate (**1g**) ( $N = -0.35$ ), which indicates a rate decrease of approximately  $10^5$  for each ester group.

In accord with the larger Hammett substituent constant of the acetyl group ( $\sigma_p^- = 0.82$ )<sup>[34]</sup> in relation to ethoxycarbonyl ( $\sigma_p^- = 0.74$ ),<sup>[34]</sup> diazoacetone (**1f**) is one order of magnitude less nucleophilic than ethyl diazoacetate (**1e**).

Figure 2 furthermore shows that diazomethane (**1a**), phenyldiazomethane (**1b**), and (trimethylsilyl)diazomethane (**1c**) are comparable in reactivity to ketene acetals. The less reactive compounds diphenyldiazomethane (**1d**), ethyl diazoacetate (**1e**), and diazoacetone (**1f**), with  $N$  parameters of around 4–5, are comparable to typical silyl enol ethers and activated allylsilanes. Two ester groups deactivate so strongly that the nucleophilicity of diethyl diazomalonate (**1g**) corresponds to that of 1,1-dialkylethylenes or styrenes.

**Consequences:** In previous work,<sup>[9]</sup> we derived the rule of thumb that electrophile nucleophile combinations can be expected to be observable at 20 °C if  $E + N > -5$  (i.e., if the nucleophile is located below the electrophile in an arrangement as shown in Figure 3).

The applicability of this rule to reactions of diazo compounds with electrophiles results from the fact that all diazo

compounds investigated in this work are characterized by slope parameters close to the average value of  $s = 0.87$ , from which one derives a combination rate constant of  $\log k = -5 \times 0.87 = -4.35$  for electrophiles and nucleophiles at equal levels in Figure 3 ( $E + N = -5$ ). Assuming equal initial concentrations of 0.1 M for both reactants, one calculates a half-life of  $\tau_{1/2} = 1/(kc_0) = 3$  days: a slow reaction at 20 °C.

In accord with the location of **13** and **14** above **1a** in Figure 3, Whitlock reported that diazomethane (**1a**) reacted with xanthylium perchlorate (**13**) to give **15** and with  $N$ -methylacridinium iodide (**14**) to give a mixture of **16** and **17** (Scheme 10).<sup>[35]</sup>

Though Equation (1) is not recommended for application to reactions of tritylium ions with  $\pi$ -nucleophiles (steric effects),<sup>[13, 36]</sup> the position of  $\text{Ph}_3\text{C}^+$  (**18**) far above ethyl diazoacetate (**1e**) ( $E + N = 5.42$ ), diphenyldiazomethane (**1d**) ( $E$

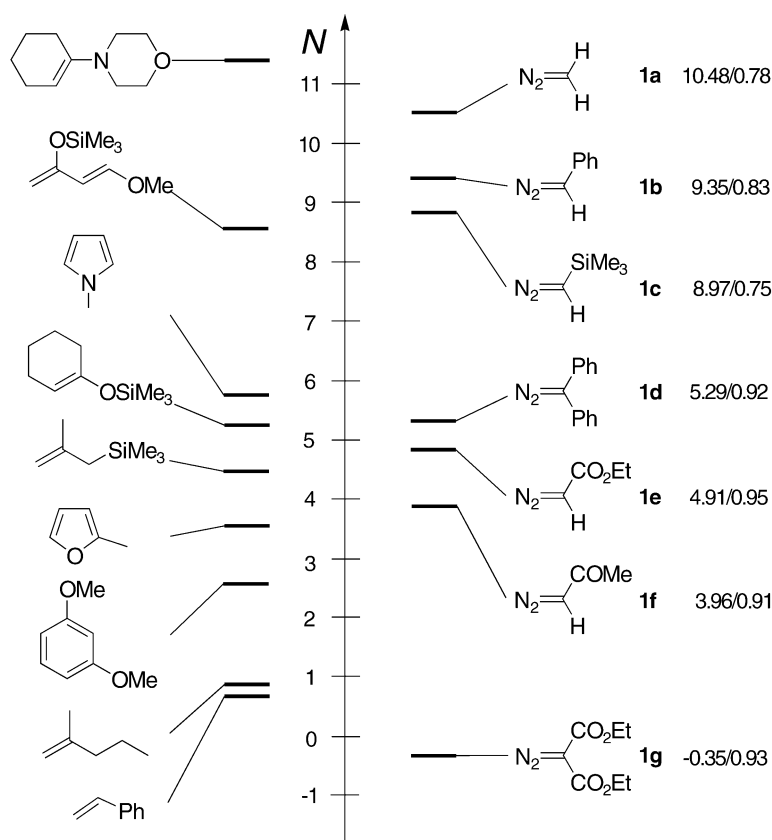


Figure 2. Nucleophilicity and slope parameters  $N$ s of diazo compounds **1a–g** in comparison with other  $\pi$ -systems ( $N$  parameters from ref. [11]).

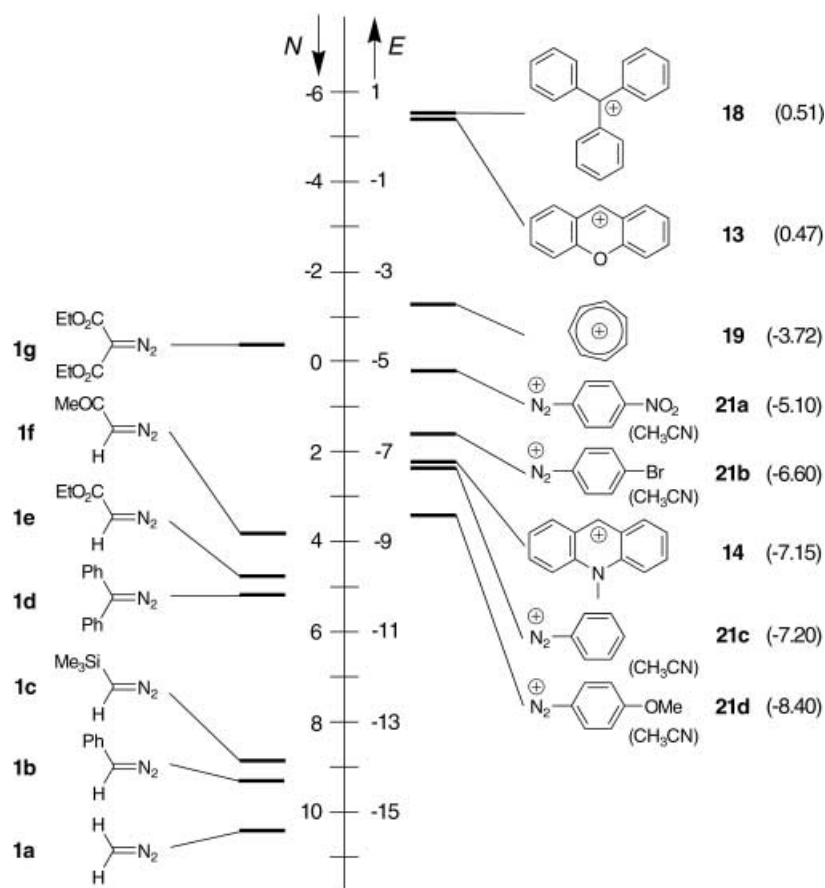
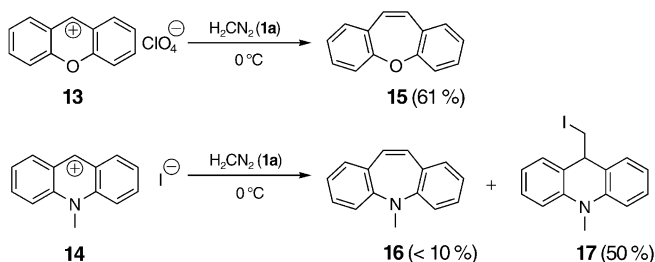


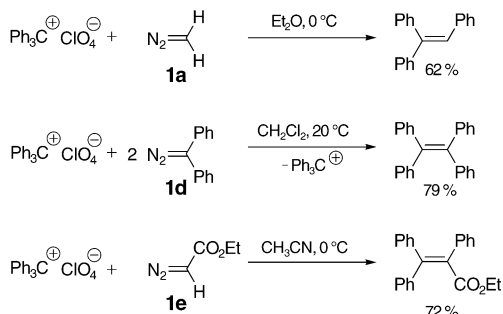
Figure 3. Analysis of literature reports on reactions of diazo compounds with electrophiles on the basis of Equation (1).  $E$  parameters (in parentheses) from reference [13b] (**13** and **18**), reference [9b] (**14** and **19**), and reference [27b] (**21a–d**).

+  $N=5.80$ ), and diazomethane (**1a**) ( $E + N=11.0$ ) is in accord with reports by Whitlock<sup>[37]</sup> and Olah<sup>[20]</sup> (Scheme 11).

The reaction of  $\text{Ph}_3\text{C}^+\text{ClO}_4^-$  with phenyldiazomethane (**1b**) gave a mixture of compounds, including 10% of *trans*-stilbene



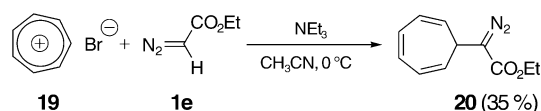
Scheme 10. Reactions of diazomethane (**1a**) with heteroaromatic cations.<sup>[35]</sup>



Scheme 11. Reactions of the tritylium ion (**18**) with diazo compounds.<sup>[20, 37]</sup>

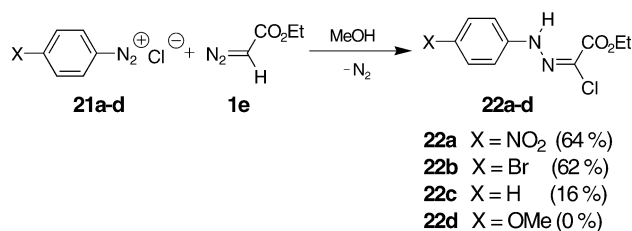
and 6% of tetraphenylethylene.<sup>[37]</sup> Accordingly, in the reaction of phenyldiazomethane (**1b**) with  $(\text{dma})_2\text{CH}^+\text{OTf}^-$ , we observed a complex mixture of products, from which individual compounds could not be isolated. In agreement with Equation (1), Regitz and co-workers observed that the reaction of tropylium bromide (**19**) with ethyl diazoacetate (**1e**) ( $E + N=1.19$ ) in the presence of triethylamine yielded ethyl (cycloheptatrienyl)diazoacetate (**20**) (Scheme 12).<sup>[38]</sup> To achieve reactions with weaker electrophiles such as 2,4,6-trialkylpyrylium ions, metallated diazo compounds have been employed.<sup>[3]</sup>

Because of the reported solvent dependence of the electrophilicities of diazonium ions,<sup>[27]</sup> only a qualitative comparison with the results of azo couplings can be made. The reactions of aryldiazonium chlorides (**21a–d**) with ethyl diazoacetate (**1e**) in methanol show a remarkable agreement with the expectations from Figure 3.<sup>[39]</sup> Huisgen



Scheme 12. Reaction of tropylium bromide (**19**) with ethyl diazoacetate (**1e**).<sup>[38]</sup>

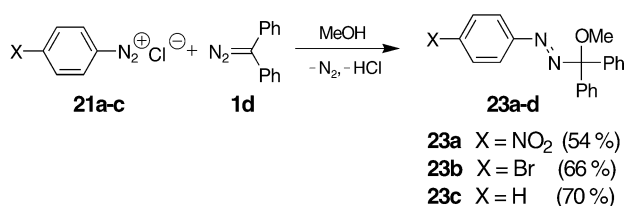
and Koch reported that **1e** reacts with *p*-nitrobenzene diazonium chloride (**21a**) within a few minutes at 0°C to give a 64% yield of **22a** (Scheme 13). After 24 h at room temperature, a 62% yield of coupling product **22b** could be isolated from **1e** and **21b**, whereas 14 h at 15°C were needed for the reaction of **1e** with **21c** to obtain a yield of 16%, whilst the least electrophilic *p*-methoxybenzenediazonium chloride (**21d**) did not react at all with **1e**.



Scheme 13. Reactions of diazonium ions **21a–d** with ethyl diazoacetate (**1e**).<sup>[39]</sup>

On the assumption that the nucleophilicity of dibenzoyldiazomethane resembles that of diethyl diazomalonate (**1g**), Figure 3 explains why this compound does not even react with the *p*-nitrobenzenediazonium ion (**21a**).<sup>[39]</sup> Since the 2,4-dichlorobenzenediazonium ion can be expected to have an electrophilicity parameter similar to that of the *p*-nitrobenzenediazonium ion (based on Hammett's  $\sigma$ ), its reported azo coupling with diazoacetone<sup>[39]</sup> is also in agreement with Figure 3.

The higher nucleophilicity of diphenyldiazomethane (**1d**) than of ethyl diazoacetate (**1e**) is in agreement with the report that the benzenediazonium ions **21a–c** react with **1d** within a few minutes to give the  $\alpha$ -phenylazobenzhydryl ethers **23a–c** in 54–70% yield<sup>[39]</sup> (Scheme 14).



Scheme 14. Reactions of the diazonium ions **21a–c** with diphenyldiazomethane (**1d**).<sup>[39]</sup>

As predicted by Figure 3, the *p*-nitrobenzenediazonium ion (**21a**) reacts rapidly with phenyldiazomethane (**1b**), but as in reactions with tritylium and benzhydrylium ions, identification of the products was not possible.<sup>[39]</sup>

The highly nucleophilic diazomethane (**1a**) (see Figure 3) was found to react both with *p*-nitro- and with the unsubstituted benzenediazonium ion.<sup>[39]</sup> Since product studies indicated a different type of mechanism in these reactions ([3+2] cycloadditions), application of Equation (1) is not possible. In future work, the rates of 1,3-dipolar cycloaddition reactions will be compared with the rates predicted by Equation (1), in order to gain further insight in the mechanisms of these reactions.

## Experimental Section

The benzhydryl salts Ar<sub>2</sub>CH<sup>+</sup> (see Table 1) were prepared as described.<sup>[11]</sup> (Trimethylsilyl)diazomethane (**1c**, 2M in hexane) and ethyl diazoacetate (**1e**, ≤10% in CH<sub>2</sub>Cl<sub>2</sub>) were purchased from Fluka. Diazomethane (**1a**) was prepared from *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide with KOH in CH<sub>2</sub>Cl<sub>2</sub>/*n*-butanol instead of by using ether and ethanol as solvents as described.<sup>[40]</sup> The reaction flask was kept at 60°C and diazomethane distilled off immediately after formation. For the preparative investigations, diazomethane was distilled directly into the solution of the benzhydrylium salts through a condenser, which keeps back the refluxing solvent. For the kinetic experiments, **1a** was used as a solution in CH<sub>2</sub>Cl<sub>2</sub>. The concentrations of the solutions of **1a**, **1c**, and **1e** were determined directly before use by titration as described.<sup>[41]</sup>

Phenyldiazomethane (**1b**)<sup>[42]</sup> (from benzaldehyde *p*-toluenesulfonylhydrazonate<sup>[42]</sup>) diphenyldiazomethane (**1d**)<sup>[43]</sup> (from commercially available benzhydrylidene hydrazine), diazoacetone (**1f**)<sup>[44]</sup> (from acetyl chloride and diazomethane), and diethyl diazomalonate (**1g**)<sup>[45]</sup> (from diethyl malonate and tosyl azide<sup>[46]</sup>) were prepared as described in the literature. Products of the reactions of the diazo compounds **1** with the benzhydrylium salts Ar<sub>2</sub>CH<sup>+</sup>X<sup>-</sup> were synthesized by addition of the diazo compounds to

stirred solutions of the benzhydrylium salts in dry CH<sub>2</sub>Cl<sub>2</sub>. After fading of the color, the reaction mixture was stirred with water or NH<sub>3</sub>, the layers were separated, and the organic solvent was removed in vacuo. The residue was purified by crystallization or column chromatography.

For details and characterization of the products see the Supporting Information.

Concentrations and rate constants for the individual kinetic experiments for the reactions of diazo compounds with benzhydryl cations are given in the Supporting Information.

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- [1] R. Huisgen in *1,3-Dipolar Cycloaddition Chemistry*, (Ed.: A. Padwa), J. Wiley, New York, **1984**, pp. 1–31.
- [2] a) M. Regitz, *Diazoalkane: Eigenschaften und Synthesen*, Thieme, Stuttgart, **1977**; b) H. Zollinger, *Diazo Chemistry I*, VCH, Weinheim, **1994**; c) H. Zollinger, *Diazo Chemistry II*, VCH, Weinheim, **1995**; d) T. Ye, M. A. McKervey, *Chem. Rev.* **1994**, *94*, 1091–1160.
- [3] J. Fink, M. Regitz, *Synthesis* **1985**, 569–585.
- [4] R. Huisgen, *Angew. Chem.* **1955**, *67*, 439–461.
- [5] a) A. Ledwith, Y. Shih-Lin, *J. Chem. Soc. B* **1967**, 83–84; b) R. Huisgen, *Angew. Chem.* **1963**, *75*, 742–754; *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 633–645; c) R. Huisgen, *Angew. Chem.* **1963**, *75*, 604–637; *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 565–598.
- [6] W. Bihlmaier, R. Huisgen, H.-U. Reissig, S. Voss, *Tetrahedron Lett.* **1979**, 2621–2624.
- [7] K. Fukui, *Angew. Chem.* **1982**, *94*, 852–861; *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 801–809.
- [8] K. N. Houk in *Pericyclic Reactions*, (Eds.: A. P. Marchand, R. E. Lehr), Vol. 2, Academic Press, **1977**, pp. 181–271.
- [9] a) H. Mayr, M. Patz, *Angew. Chem.* **1994**, *106*, 990–1010; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 938–957; b) H. Mayr, B. Kempf, A. R. Ofial, *Acc. Chem. Res.* **2003**, *36*, 66–77.
- [10] a) M. Hartnagel, K. Grimm, H. Mayr, *Liebigs Ann.* **1997**, 71–80; b) H. Mayr, J. Henninger, *Eur. J. Org. Chem.* **1998**, 1919–1922; c) H. Mayr, A. R. Ofial, J. Sauer, B. Schmied, *Eur. J. Org. Chem.* **2000**, 2013–2020; d) C. Fichtner, H. Mayr, *J. Chem. Soc. Perkin Trans. 2* **2002**, 1441–1444.
- [11] H. Mayr, T. Bug, M. F. Gotta, N. Hering, B. Irrgang, B. Janker, B. Kempf, R. Loos, A. R. Ofial, G. Remennikov, H. Schimmel, *J. Am. Chem. Soc.* **2001**, *123*, 9500–9512.
- [12] a) R. Lucius, H. Mayr, *Angew. Chem.* **2000**, *112*, 2086–2089; *Angew. Chem. Int. Ed.* **2000**, *39*, 1995–1997; b) R. Lucius, R. Loos, H. Mayr, *Angew. Chem.* **2002**, *114*, 97–102; *Angew. Chem. Int. Ed.* **2002**, *41*, 91–95.
- [13] a) H. Mayr, G. Lang, A. R. Ofial, *J. Am. Chem. Soc.* **2002**, *124*, 4076–4083; b) S. Minegishi, H. Mayr, *J. Am. Chem. Soc.* **2003**, *125*, 286–295.
- [14] Though the following discussion considers diazonium ions as intermediates, our results are also in accord with mechanisms in which cleavage of the C–N<sub>2</sub> bond starts before the electrophilic addition is complete. Quantum chemical calculations indicate that the benzyl-diazonium ion does not exist: a) R. Glaser, C. J. Horan, E. D. Nelson, M. K. Hall, *J. Org. Chem.* **1992**, *57*, 215–228; b) R. Glaser, D. Farmer, *Chem. Eur. J.* **1997**, *3*, 1244–1253.
- [15] a) H. Meerwein, *Angew. Chem.* **1948**, *60*, 78; b) S. W. Kantor, R. C. Osthoff, *J. Am. Chem. Soc.* **1953**, *75*, 931–932.
- [16] a) J.-F. Létard, R. Lapouyade, W. Rettig, *Chem. Phys. Lett.* **1994**, *222*, 209–216; b) M. Singh, K. N. Singh, R. A. Misra, *Ind. J. Chem.* **1994**, *33 B*, 173–176; c) W. Tadros, L. Ekladius, A. B. Sakla, *J. Chem. Soc.* **1954**, 2351–2353; d) F. H. C. Stewart, *J. Org. Chem.* **1961**, *26*, 3604–3605.
- [17] G. R. Newkome, J. M. Robinson, *J. Org. Chem.* **1976**, *41*, 2536–2540
- [18] R. Rossi, A. Carpita, P. Cossi, *Tetrahedron* **1992**, *48*, 8801–8824.



- [19] M.-H. Le Tadic-Biadatti, A.-C. Callier-Dublanchet, J. H. Horner, B. Quiclet-Sire, S. Z. Zard, M. Newcomb, *J. Org. Chem.* **1997**, *62*, 559–563.
- [20] G. A. Olah, M. Alemayehu, A. Wu, O. Farooq, G. K. S. Prakash, *J. Am. Chem. Soc.* **1992**, *114*, 8042–8045.
- [21] C. J. Lancelot, D. J. Cram, P. v. R. Schleyer in *Carbonium Ions*, (Eds.: G. A. Olah, P. v. R. Schleyer), Volume 3, Wiley, New York, **1972**, pp. 1347–1483.
- [22] Strictly speaking, this analysis violates the Curtin–Hammett principle. One can, however, assume that the transition states arising from **2g'** and **2g''** partially reflect the conformational strain in **2g'** and **2g''**.
- [23] H. Mayr, R. Schneider, C. Schade, J. Bartl, R. Bederke, *J. Am. Chem. Soc.* **1990**, *112*, 4446–4454.
- [24] J. Burfeindt, M. Patz, M. Müller, H. Mayr, *J. Am. Chem. Soc.* **1998**, *120*, 3629–3634.
- [25] H. Mayr, N. Basso, G. Hagen, *J. Am. Chem. Soc.* **1992**, *114*, 3060–3066.
- [26] C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry*, 3rd ed., Wiley-VCH Weinheim, **2003**.
- [27] H. Mayr, M. Hartnagel, K. Grimm, *Liebigs Ann.* **1997**, 55–69.
- [28] a) W. Jugelt, L. Berseck, *Tetrahedron* **1970**, *26*, 5581–5586; b) W. Jugelt, L. Berseck, *Tetrahedron* **1970**, *26*, 5557–5579.
- [29] W. J. Albery, M. H. Davies, *Trans. Faraday Soc.* **1969**, *65*, 1066–1073.
- [30] B. Kempf, N. Hampel, A. R. Ofial, H. Mayr, *Chem. Eur. J.* **2003**, *9*, 2209–2218.
- [31] For Brønsted's  $\alpha = 1.0$  from Equation (1) in: C. Schindele, K. N. Houk, H. Mayr, *J. Am. Chem. Soc.* **2002**, *124*, 11208–11214.
- [32] H. Staudinger, A. Gaule, *Ber. Dtsch. Chem. Ges.* **1916**, *49*, 1897–1918.
- [33] M. Herrlich, N. Hampel, H. Mayr, *Org. Lett.* **2001**, *3*, 1629–1632.
- [34] O. Exner, *Correlation Analysis of Chemical Data*, Plenum, New York, **1988**.
- [35] H. W. Whitlock, *Tetrahedron Lett.* **1961**, *17*, 593–595.
- [36] *Ionic Polymerizations and Related Processes*, H. Mayr (Eds.: J. E. Puskas, A. Michel, S. Barghi, C. Paulo), *NATO ASI Series E (Applied Sciences)* **1999**, Vol. 359, pp. 99–115.
- [37] H. W. Whitlock, *J. Am. Chem. Soc.* **1962**, *84*, 2807–2811.
- [38] W. Bethäuser, B. Weber, H. Heydt, M. Regitz, *Chem. Ber.* **1985**, *118*, 1315–1328.
- [39] R. Huisgen, H.-J. Koch, *Liebigs Ann. Chem.* **1955**, *591*, 200–231.
- [40] T. J. DeBoer, H. J. Backer, *Org. Synth.* **1956**, *36*, 16–19.
- [41] E. K. Marshall, S. F. Acree, *Ber. Dtsch. Chem. Ges.* **1910**, *43*, 2323–2330.
- [42] D. G. Farnum, *J. Org. Chem.* **1963**, *28*, 870–872.
- [43] L. I. Smith, K. L. Howard, *Org. Synth. Coll. Vol. 3*, **1955**, 351–352.
- [44] F. Arndt, J. Amende, *Ber. Dtsch. Chem. Ges.* **1928**, *61*, 1122–1124.
- [45] M. Regitz, *Chem. Ber.* **1966**, *99*, 3128–3147.
- [46] L. F. Tietze, T. Eicher, *Reaktionen und Synthesen*, Thieme, Stuttgart, **1981**.

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