Synthetic Methods

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Hydrocarbation of C≡C Bonds: Quantification of the Nucleophilic Reactivity of Ynamides[**]

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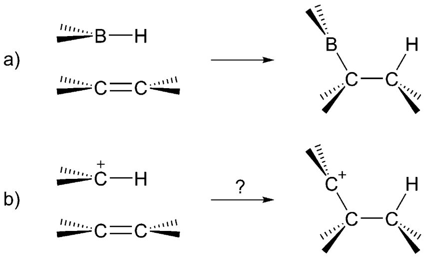
Dedicated to Professor Klaus T. Wanner on the occasion of his 60th birthday

Abstract: *Donor-substituted diarylcarbenium ions Ar_2CH^+ react with ynamides to give 1-amido-substituted allyl cations (α,β-unsaturated iminium ions). Kinetic studies show that these adducts, which correspond to the addition of a C−H bond across the C≡C bond, are formed stepwise with initial formation of keteniminium ions and subsequent 1,3-hydride shifts. The linear correlations between the second-order rate constants ($\lg k_2$, 20 °C) with the electrophilicity parameters E of the diarylcarbenium ions allow us to include ynamides in our comprehensive nucleophilicity scale and thus predict potential electrophilic reaction partners.*

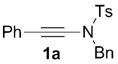
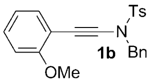
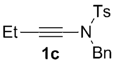
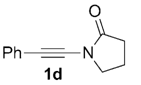
Hydroborations[1] of C=C and C≡C bonds belong to the most reliable reactions in organic synthesis (Scheme 1 a). As carbenium ions are isoelectronic with boranes, one might wonder why analogous reactions of carbenium ions (Scheme 1 b) have so far not been reported despite the potential of such reactions in organic synthesis. We now show that such reactions occur when ynamides[2] are combined with stabilized benzhydrylium ions and discuss why hydrocarbations of alkenes and alkynes do not usually take place.



Scheme 1. a) Hydroborations of alkenes compared with b) analogous hydrocarbations.

During our investigations of the nucleophilic reactivity of ynamides **1a–d**[3] (Table 1) by the benzhydrylium methodology,[4] we observed a color change to green when the blue benzhydrylium tetrafluoroborate **2c-BF$_4$** (Table 2) was combined with ynamide **1d** in CH_2Cl_2 (Figure 1). UV/Vis spectroscopic monitoring of this reaction showed that the green species was formed with the same rate with which the blue carbenium ion disappeared.

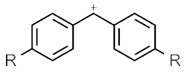
Table 1: Absorption maxima A and B of the developing α,β-unsaturated iminium ions during the reactions of benzhydrylium ions **2a–c** with ynamides **1a–d** in dichloromethane.

Ynamides	Products from **2a**		Products from **2b**		Products from **2c**	
	λ_A [nm]	λ_B [nm]	λ_A [nm]	λ_B [nm]	λ_A [nm]	λ_B [nm]
 **1a**	520	752	474	670	478	670
 **1b**	510	736	467	652	472	654
 **1c**	513	731	467	650	472	650
 **1d**	–	–	–	–	480	649

The assumption that the green species is the product of a hydrocarbation reaction was confirmed by the isolation of the allylic sulfonamide **4**, which was obtained by treatment of the reaction product **3ab** with DIBAL-H (Scheme 2).

As shown in Table 1, the UV/Vis absorption maxima of the 1-amido-3,3-diarylallyl cations (↔α,β-unsaturated imi-

Table 2: Reference electrophiles used for quantifying the nucleophilicities of **1a–d**.



$Ar_2CH^{+[a]}$	R	**2**	$\lambda_{max}{}^{[b]}$ [nm]	$E^{[c]}$
$(dpa)_2CH^+$	NPh_2	**2a**	672	−4.72
$(mfa)_2CH^+$	$N(CH_3)CH_2CF_3$	**2b**	593	−3.85
$(pfa)_2CH^+$	$N(Ph)CH_2CF_3$	**2c**	601	−3.14

[a] dpa = 4-(diphenylamino)phenyl; mfa = 4-(methyl(trifluoroethyl)amino)phenyl; pfa = 4-(phenyl(trifluoroethyl)amino)phenyl. [b] In dichloromethane. [c] Empirical electrophilicities E from Ref. [4a].

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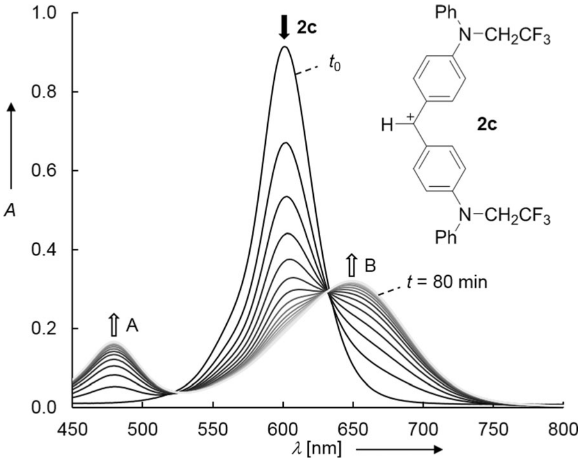
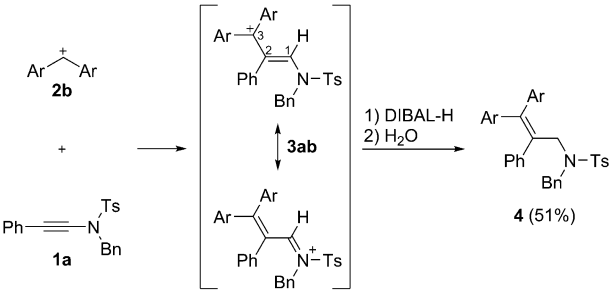


Figure 1. Time-dependent UV/Vis spectra during the reaction of ynamide **1d** ($c = 1.02\times10^{-3}$ M) with benzhydrylium salt **2c-BF$_4$** ($c = 1.13\times10^{-5}$ M) in dichloromethane at 20°C.



Scheme 2. Formation of the allylic sulfonamide **4** by treatment of the colored intermediate **3ab** with DIBAL-H (Ar see Table 2).

nium ions) **3** depend only slightly on the nature of the substituents at nitrogen and at C-2, but are strongly affected by the nature of the aryl groups at C-3. The considerably longer wavelength of the absorption maximum of **2a** (compared to **2b** and **2c**, Table 2) is in line with the bathochromic shifts of both bands of the allyl cations derived from **2a** compared to those obtained from **2b** and **2c** (Table 1). The analogous conjugation of the aryl rings with a carbenium center in the products **3**, as in the benzhydrylium ions **2**, is thus indicated.

When the kinetics of the reactions of the ynamides **1a–d** with the benzhydrylium ions **2a–c** were studied under pseudo-first order conditions ([**1a–d**] ≫ [**2a–c**]), monoexponential decays of the absorbances of the benzhydrylium ions **2** and monoexponential increases of both absorbances of the unsaturated iminium ions **3** were observed, as depicted for the reaction of **2c** with **1b** in Figure 2.

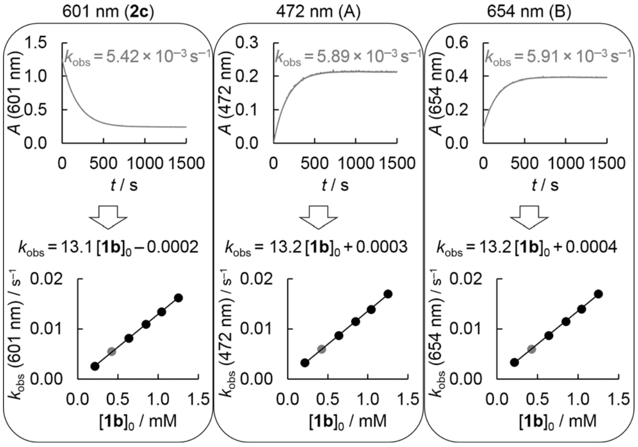


Figure 2. Upper part: From the exponential decay of the absorbance of **2c** (left) and the exponential increases of the absorbances at 472 nm (middle) and 654 nm (right) during the reaction of **1b** ($c = 4.25\times10^{-4}$ M) with **2c** ($c = 2.17\times10^{-5}$ M) at 20°C in CH_2Cl_2, the corresponding first-order rate constants k_{obs} (**2c**), k_{obs} (472 nm), and k_{obs} (654 nm) were derived. Lower part: The respective second-order rate constants k_2 (**2c**), k_2 (472 nm), and k_2 (654 nm) are obtained as the slopes of the linear correlations of the corresponding first-order rate constants k_{obs} against [**1b**]$_0$.

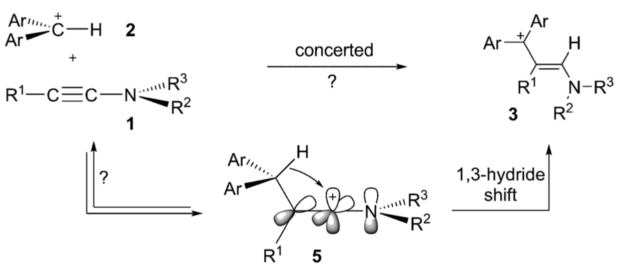
Because some of the iminium ions **3** undergo subsequent reactions, which are only slightly slower than their formations, the second-order rate constants derived from the consumption of the benzhydrylium ions **2** and from the formation of the iminium ions **3** sometimes differ slightly. While Figure 2 shows the coincidence of the different values, Table S1 of the Supporting Information also includes examples for slight deviations. As the rate constants derived from the decay of the absorbances of the benzhydrylium ions are directly related to the rates of the bimolecular reactions, only these rate constants are given in Table 3.

As depicted in Scheme 3, the formation of **3** may either be concerted or stepwise with reversible or irreversible formation of a keteniminium ion **5**, which undergoes a subsequent 1,3-hydride shift to give the observed amido allyl cation **3**.

This 1,3-hydride shift is not a [1,3]-sigmatropic process, which is subject to the orbital symmetry rules. Unlike in a [1,3]-sigmatropic shift, the involved σ_{CH} bond is in the plane of the three carbon atoms, and the Ar_2C^+-fragment must rotate to achieve conjugation between the developing carbenium center and the enamide fragment of **3**.

Table 3: Second-order rate constants k_2 (in M^{-1} s^{-1}) for the reactions of the ynamides **1a–d** with the benzhydrylium ions **2a–c** in dichloromethane at 20°C.

Ynamides	k_2 (**2a**)	k_2 (**2b**)	k_2 (**2c**)
1a	0.181	1.07	3.75
1b	0.574	2.51	13.1
1c	2.48	12.1	55.5
1d	–	–	0.963



Scheme 3. Mechanistic alternatives for the reactions of the ynamides **1** with the benzhydrylium ions **2**.

In order to differentiate these mechanistic alternatives, we have also studied the rate of the reaction of the C-1-deuterated benzhydrylium ion D-**2b** ($Ar_2C\text{-}D^+$) with the ynamide **1a**. As shown in Figure 3, the deuterated benzhydrylium ion D-**2b** reacts even faster than its ^1H isotopomer **2b**, which excludes breaking of the C–H bond in the rate-determining step.

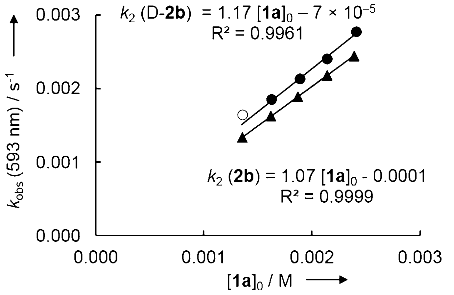


Figure 3. Comparison of the first-order rate constants k_{obs} obtained for the reactions of benzhydrylium ions $(mfa)_2CH^+$ (**2b**, triangles) and $(mfa)_2CD^+$ (D-**2b**, circles) with different amounts of ynamide **1a** (data point shown as an open circle was not used for determining k_2 (D-**2b**)).

The ratio $k_2(\mathbf{2b})/k_2(\text{D-}\mathbf{2b}) = 0.91$ rather corresponds to an inverse α-secondary kinetic isotope effect, which is typical for reactions involving rehybridization $C_{sp^2} \rightarrow C_{sp^3}$ in the rate-determining step.[5] We thus conclude that the rate constants listed in Table 3 reflect the attack of the benzhydrylium ions **2a–c** at the ynamides **1a–d** with irreversible formation of the keteniminium ions **5**. As this step corresponds to the type of reactions for which Equation (1) was derived, it is now

$$\lg k\ (20\,^\circ\mathrm{C}) = s_N(N + E) \qquad (1)$$

possible to determine the nucleophile-specific parameters N and s_N by plotting $\lg k_2$ of the rate constants in Table 3 against the electrophilicity parameters E of the benzhydrylium ions **2a–c** (Figure 4).

The linear correlations shown in Figure 4 indicate that all investigated reactions follow analogous mechanisms. As the sensitivities s_N (slopes of the correlation lines) are similar to those of related π-nucleophiles,[4g] the nucleophilicity parameters N (negative intercepts on the abscissa) can directly be employed to discuss structure–reactivity relationships.

Figure 5 shows that ynamides **1a–d** possess nucleophilicities that are comparable to those of (2-methylallyl)trimethylsilane (**6**)[4a] and butyl vinyl ether (**7**).[4f] They are significantly less reactive than enamines,[6] as shown by the comparison of the structurally related compounds **8b** and **1c**. Replacement of the alkyl substituents at the position of electrophilic attack by a phenyl group decreases the nucleophilicities of enamines (**8b**→**8a**) as well as of ynamides (**1c**→**1a**) by approximately one order of magnitude. Structurally related enamides,[7] such as **9**, were reported to possess nucleophilicities of $4.6 < N < 7.1$, that is, somewhat higher than those found for the ynamides **1a–d** in this work.

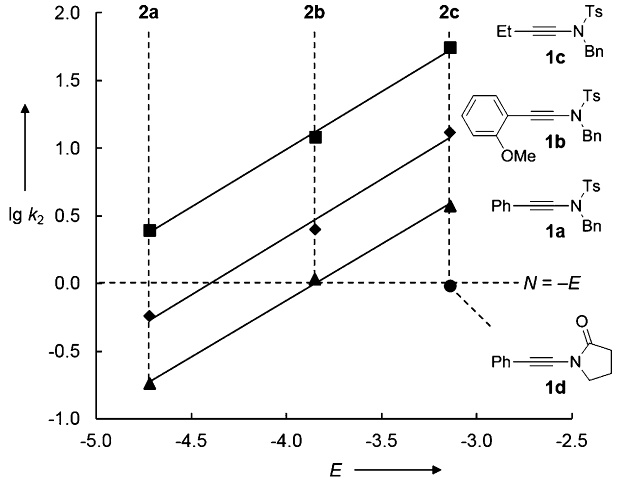


Figure 4. Plots of $\lg k_2$ for the reactions of benzhydrylium ions **2a–c** with ynamides **1a–d** in CH_2Cl_2 at 20°C versus the electrophilicity parameters E of the benzhydrylium ions.

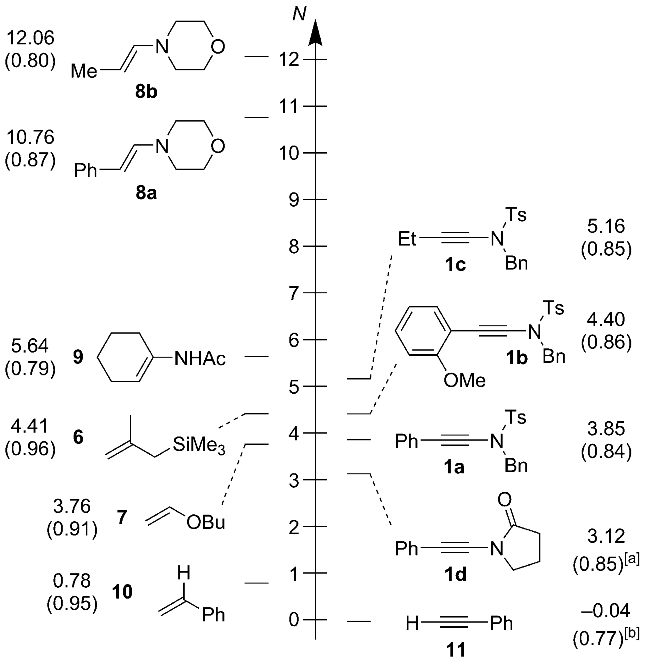
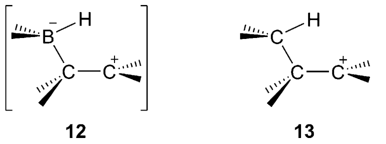


Figure 5. Comparison of the nucleophilicity N of ynamides **1a–d** (s_N in parentheses) with those of other π-nucleophiles[4g] in CH_2Cl_2 (CH_3CN for enamides; [a] estimated value of s_N; [b] nucleophilicity parameter adjusted to the revised electrophilicity parameters E of the reference electrophiles given in Ref. [4f]).

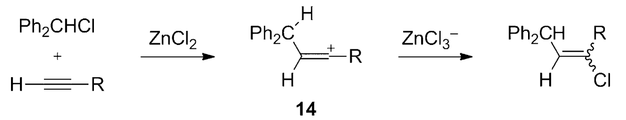
Why do hydrocarbations, as described in Scheme 1b, in contrast to hydroborations generally not take place? As B–H bonds in borohydride anions are far better hydride donors than C–H bonds,[8] the zwitterion **12** shown in Scheme 4 is not formed as an intermediate in hydroboration reactions, as it would undergo activation-less collapse to the hydroboration product (Jencks' criterion[9]). In contrast, C–H bonds are much poorer hydride donors, and 1,3-hydride migrations in carbocations are generally slow, even when the hydride transfer is exothermic.[10] As a consequence, carbocations **13**, which are formed by the addition of a carbocation to an olefin



Scheme 4. Comparison of the hypothetical intermediate **12** of a stepwise hydroboration with the intermediate **13** obtained after the addition of a carbocation to an alkene.

(Scheme 1b and 4), are usually trapped by external nucleophiles.[11]

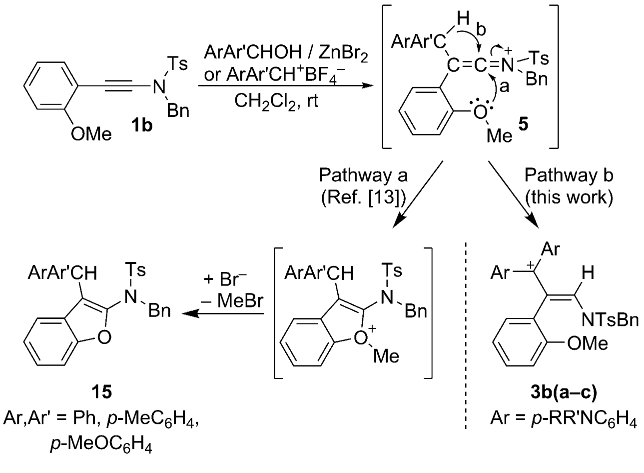
For the same reason, Lewis acid catalyzed reactions of alkyl halides to alkynes give vinyl halides in good yields (Scheme 5), thus indicating that a hydride transfer in the intermediate vinyl cation **14** cannot be a major process.[12]



Scheme 5. Lewis acid catalyzed additions of alkyl halides to alkynes.[12]

A recent report[13] on the formation of benzofurans **15** by Lewis acid catalyzed reactions of methoxy- and methyl-substituted or unsubstituted benzhydrols with ynamide **1b** (Scheme 6, pathway a) shows that hydrocarbations through hydride transfer in the intermediate keteniminium ions **5** (Scheme 6, pathway b), as observed in this work, only occur when the carbocation generated by hydride transfer is stabilized by strongly electron-donating groups.

In summary, we have shown that hydrocarbations of alkynes with carbenium ions are possible when electron-donating substituents are present in the alkynes and in the carbenium ions. The observation of an inverse α-secondary kinetic isotope effect when replacing the hydrogen atom at C-1 of a carbenium ion with deuterium showed that the irreversible electrophilic attack of the benzhydrylium ions at the ynamides is the rate-determining step of the studied reactions.



Scheme 6. The substitution pattern in the benzhydrylium moiety determines the subsequent reaction pathway of the keteniminium ion **5**.

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Keywords: iminium ions · kinetic isotope effects · kinetics · linear free energy relationships · vinyl cations

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