

A Laser Flash Photolysis Study on 2-Azido-*N,N*-diethylbenzylamine – The Reactivity of Iminoquinone Methides in Solution

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Dedicated to the memory of Professor Lennart Eberson

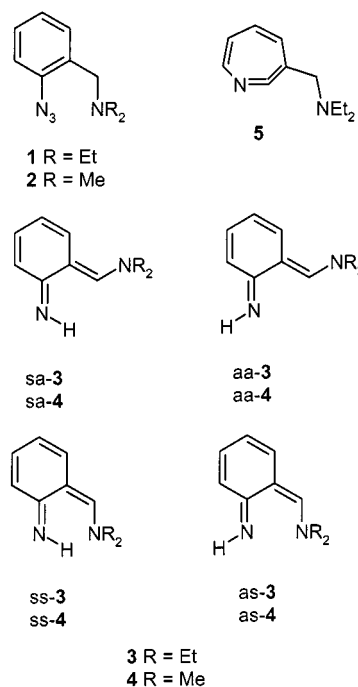
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Photolysis of 2-azido-*N,N*-diethylbenzylamine (**1**) in acetonitrile solution in the presence of various quenchers yields products of common nitrene chemistry (that is, derived from a didehydroazepine or a triplet nitrene), together with products arising from trapping of stereoisomeric iminoquinone methides. These intermediates are formed in a monophotonic process, by dediazotation of the precursor combined with a 1,4-hydrogen shift. The reactivity of the iminoquinone methides (IQM) towards a variety of quenchers, including dienophiles and various nucleophiles, has been explored, using acetonitrile, DMF, and *n*-hexane as solvents. IQM reacts efficiently with electron deficient dienophiles [k_q (maleic anhydride) = $2.4 \cdot 10^7 \text{ M}^{-1} \text{ s}^{-1}$], but not with simple olefins such as cyclohexene. IQM shows low to medium reactivity towards simple primary or secondary amines [k_q (*n*-propylamine) = $6.4 \cdot 10^4 \text{ M}^{-1} \text{ s}^{-1}$], medium reactivity with sterically unhindered simple alcohols [k_q (methanol) = $4.6 \cdot 10^6 \text{ M}^{-1} \text{ s}^{-1}$], and high to very high reactivity towards thiols [k_q (*n*-dodecanethiol) = $1.1 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$], diols, and triols [k_q (glycerol) = $1.5 \cdot 10^8 \text{ M}^{-1} \text{ s}^{-1}$], and sugars [k_q (D-glucose) = $1.0 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$]. IQM also reacts rapidly with cytosine: k_q (cytosine) = $3.4 \cdot 10^8 \text{ M}^{-1} \text{ s}^{-1}$, while the reaction with adenine or thymine is less efficient [k_q (adenine) = $6.4 \cdot 10^7 \text{ M}^{-1} \text{ s}^{-1}$, k_q (thymine) = $7.7 \cdot 10^6 \text{ M}^{-1} \text{ s}^{-1}$].

Introduction

The preceding contribution^[1] describes the photochemistry of matrix-isolated aryl azides bearing π -donor substituents in *ortho*-benzylic positions. It was found that almost any π -donor in this position will enable a photochemical 1,4-hydrogen shift to take place, yielding iminoquinone methides. Quinone methides and iminoquinone methides are a current focus of research. A number of papers have dealt with their use as reactive dienes in preparative organic chemistry.^[2–7] Other work has been devoted to stabilizing these highly reactive species by complexation to transition metals,^[8–11] and to elucidating their properties and reactivity by using time-resolved techniques,^[12–14] photoelectron spectroscopy,^[15,16] or matrix isolation spectroscopy.^[17–19] Quinone methides have received attention for their role in the metabolism of a number of preservatives,^[20] for their potential use as anti-cancer agents and as active component of insecticides,^[21,22] and for their ability to alkylate DNA efficiently.^[21,23] The reactions between parent *o*-quinone methide and DNA bases have been investigated in detail by Pande et al.^[23] In their study, *o*-quinone methide was liberated from a silylated 2-bromomethylphenol by fluoride-induced desilylation followed by bromide elimination. It was found, if the free bases were used as targets, that *o*-quinone methide reacted preferentially with cytosine, while, if duplex DNA was employed, reaction with dC was suppressed. The

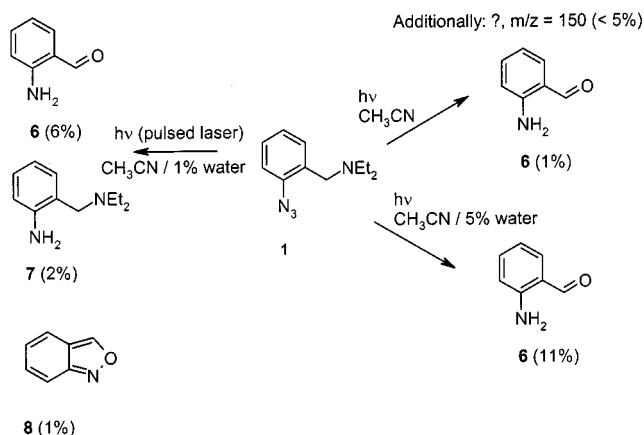
relative reactivity determined was 6200:520:210 for dC/dG/dA (dT trapping was not observed) if deoxynucleosides were used, with 310:38:8.4 for single-strand DNA, and 1.7:19:1.0 for duplex DNA.^[23] In order to obtain absolute kinetic data on this interesting system, an efficient photochemical precursor for *o*-quinone methide would be required. The hydroxybenzyl alcohols used by Wan et al.,^[12,13,24,25] however, require excitation with $\lambda_{\text{exc}} = 248$ or



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266 nm, which precludes quenching studies with DNA bases. Aryl azides, on the other hand, may be conveniently excited using the 3rd harmonic of an Nd-YAG laser at $\lambda_{\text{exc}} = 355$ nm. The observation of a highly efficient 1,4-hydrogen shift in 2-[(dialkylamino)methyl]phenylnitrenes, as described in the preceding contribution,^[1] offers the promise that, at least in this case, laser flash photolysis of the corresponding azides should result in the detection of iminoquinone methides. The work reported here was undertaken with this aim in mind. It describes studies on the photochemistry of 2-azido-*N,N*-diethylbenzylamine (**1**). This precursor was shown in the preceding contribution^[1] to undergo a highly efficient 1,4-hydrogen shift when photolyzed under matrix isolation conditions.



Scheme 1

Results

Product Studies

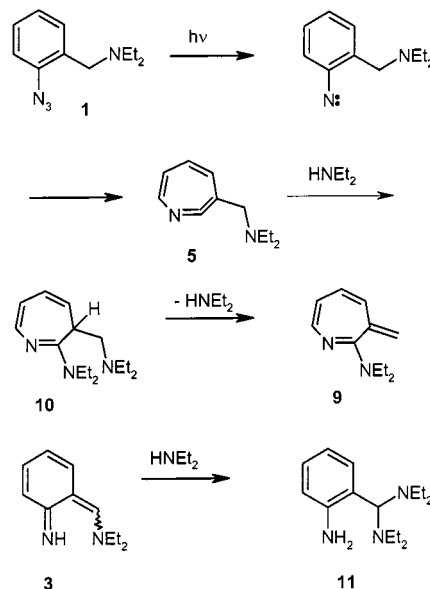
The primary products of the photolysis of **1** at very low temperature could be unequivocally identified as sa-**3** + aa-**3**, by IR spectroscopy on matrix-isolated samples.^[1] Didehydroazepine **5**, on the other hand, was only formed in minute amounts. Low-temperature photochemistry of **1** in argon thus represents a very clean reaction, yielding a well-defined set of products. In contrast to this, photolysis of **1** in solution at ambient temperature gave rise to complex mixtures.

Three quenchers – water, diethylamine, and acrylonitrile – were employed to test the photochemistry of **1**. The photolysis of **1** was performed using acetonitrile as solvent, and both steady-state and pulsed-laser excitation were used. For product identification, several compounds suspected as possible photoproducts were synthesized independently. If a reference compound was not available, only tentative product assignments were made, on the basis of the MS decay patterns.

GC-MS analysis of the products formed by steady-state photolysis ($\lambda = 320$ nm, 30 min) of **1** in acetonitrile solution showed that only a small amount (< 15%) of volatile products had been formed. As the main product (< 5%), an as yet unidentified species with $m/z = 150$ was formed.^[26] The product mixture also contained small amounts (ca. 1%) of 2-aminobenzaldehyde (**6**). Addition of 1 or 5% water to the solvent resulted in a significantly increased yield (8% or 11%, respectively) of **6**.

If a pulsed laser (Nd-YAG, 355 nm or XeCl-excimer, 308 nm) was used for irradiation of a sample of **1** in $\text{CH}_3\text{CN}/1\%$ H_2O , the composition of the product mixture did not change significantly. As a new product, 2,1-benzisoxazole (**8**) (1%) was identified, in addition to 6% of 2-aminobenzaldehyde (**6**), 2% of the aniline **7**, and three different unidentified products ($\Sigma = 13\%$), with molecular masses of $M = 176$ (twice) or 150. The products formed by photolysis of **1** in acetonitrile or in acetonitrile/water are given in Scheme 1.

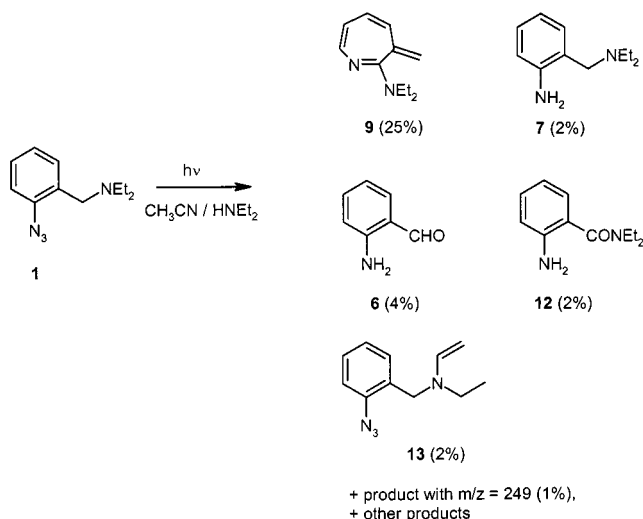
Steady-state photolysis ($\lambda = 320$ nm, 30 min) of **1** in $\text{CH}_3\text{CN}/\text{HNEt}_2$ (9:1) with ^1H NMR spectroscopic analysis, yielded a mixture consisting mainly of the methyleneazepine **9** and unchanged precursor. Methyleneazepine **9** had previously been synthesized in this laboratory^[27] and was available as a reference sample. It is formed by elimination of diethylamine from azepine **10**, which in turn is formed from didehydroazepine **5** (Scheme 2). Aminoal **11**, the product expected from trapping of iminoquinone methides by diethylamine, was not found to be a major constituent of the mixture. Aminoal **11** would have to show a characteristic methine ^1H resonance (singlet) between $\delta \approx 3.3$ and 4.4,^[28,29] and this was not detected as a major peak in the ^1H NMR spectrum of the mixture.



Scheme 2

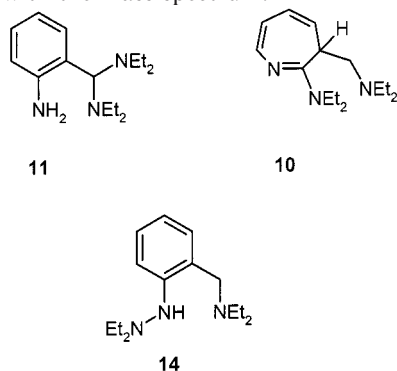
If the analysis of the photolyzed sample (solvent: 1% diethylamine in acetonitrile) was performed by GC/MS, however, small amounts (1%) of a compound with $m/z = 249$ were detected in addition to methyleneazepine **9** (25%), 2-amino-*N,N*-diethylbenzylamine (**7**)^[30] (2%), 2-aminobenzal-

dehyde (**6**) (4%), 2-amino-*N,N*-diethylbenzamide (**12**) (2%), enamine **13** (2%, tentative assignment based on MS decay pattern), and a multitude of other, unidentified products present in small concentrations. Peaks with $m/z = 249$ correspond to products of reactions between the nitrene – or rearranged intermediates derived from it – and diethylamine. Three products with $m/z = 249$ can be conceived of, corresponding to diethylamine trapping of singlet nitrene, iminoquinone methide, or didehydroazepine. Scheme 3 depicts the products formed upon photolysis of **1** in acetonitrile in the presence of diethylamine.

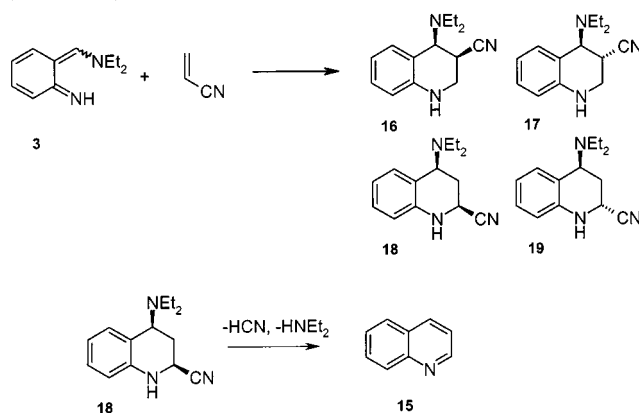


Scheme 3

Given the fact that methyleneazepine **9** is formed as a major product, the elimination of diethylamine from azepine **10** must occur readily. For that reason, it appears unlikely that this compound would survive the high temperatures in the injector block of the gas chromatograph. Insertion of a singlet nitrene into an N–H bond of a secondary amine, producing hydrazine derivatives such as **14**, has been observed before.^[31] This reaction, however, seems to be limited to highly reactive nitrenes activated by electron-withdrawing substituents such as nitro groups^[31] or fluorine atoms, in which cases C–H insertion and addition to C=C double bonds has been observed.^[32–34] Hence, amination **11** appears to be the most likely candidate. The structure is in agreement with the mass spectrum.^[35]



Pulsed-laser (355 or 308 nm) irradiation of solutions of **1** in acetonitrile containing diethylamine produced results that did not differ substantially from those obtained using steady-state irradiation. Again, methyleneazepine **9** was detected as the main volatile product. As an additional photoproduct, small amounts of 2,1-benzisoxazole (**8**, 1%) were detected. Steady-state photolysis of **1** in acetonitrile containing 1% acrylonitrile yielded 4% of 2-aminobenzaldehyde (**6**), 1% of quinoline (**15**), 2% of the aniline **7**, and a total of 7% (1% + 2% + 3% + 1%) of compounds with $m/z = 229$, in addition to a total of 16% of various unidentified products. A molecular mass of 229 is to be expected for the products of trapping of iminoquinone methides or 2-(diethylaminomethyl)phenylnitrene with acrylonitrile (Scheme 4).



Scheme 4

Among the four products with $m/z = 229$, there are two subsets of two compounds, each exhibiting very similar mass spectra. This observation might point towards the formation of a mixture of the four isomeric cyanotetrahydroquinolines depicted in Scheme 4, as the mass spectra of the *cis* and *trans* isomers of each of the two regioisomers may be anticipated to be similar. The formation of small amounts of quinoline (**15**) as a side product would support this notion, as quinoline can be formed from **16–19** by elimination of both diethylamine and HCN. As a caveat it has to be noted that in Diels–Alder reactions between electron-rich dienes and electron-deficient olefins, the outcome is predominantly such that the substituents (here diethylamino and cyano) end up located *ortho* (or *para*, if the diene is substituted in 3-position) to each other. Thus, it would appear very surprising, that an iminoquinone methide **3** should show so little selectivity.

Laser Flash Photolysis: Transient Identification

Laser flash photolysis ($\lambda_{\text{exc}} = 266$ or 355 nm) of **1** in acetonitrile gave a transient spectrum (transient X, see Figure 1), which was not affected by purging the solution with oxygen. Apart from the absolute transient intensity, there was no difference between data recorded using 266- or 355-nm excitation. A plot of transient intensity vs. laser power ($\lambda_{\text{exc}} = 266$ nm) reveals a linear power dependence (Figure 2), which means that the transient observed is formed

in a monophotonic process. Figure 1 shows that $\lambda_{\max}$ shifted from an initial 450 nm to 410 nm within 10 μs . After 150 μs , $\lambda_{\max}$ was 370 nm. Fitting of the transient trace of transient X ($\lambda = 450$ nm) with a first-order rate law gave a lifetime of $\tau = 33$ μs . However, close examination of the fitting revealed a systematic deviation in the residuals (Figure 3). This observation, together with the time-dependent $\lambda_{\max}$, suggests more complex transient behavior. Figure 3 suggests, that at least three different transient species contribute to the decay measured at $\lambda = 450$ nm. Furthermore, a first-order growth ($\tau = 1.4$ μs) was detected at $\lambda = 370$ nm (Figure 4).

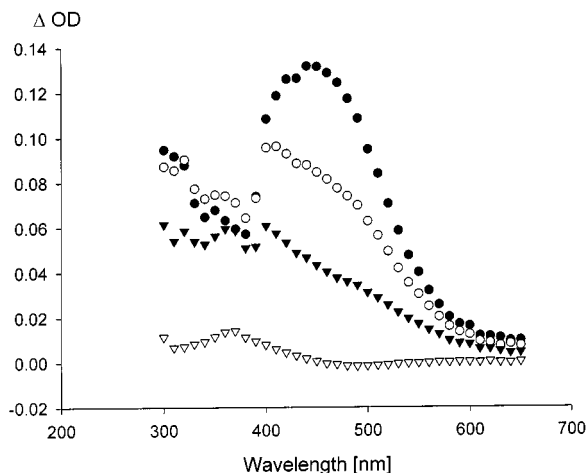


Figure 1. Transient spectrum obtained after LFP (355 nm) of **1** in acetonitrile, room temp., Ar purge; black dots: 2.2 μs after LFP; light dots: 10.7 μs after LFP; black triangles: 34 μs after LFP; light triangles: 150 μs after LFP

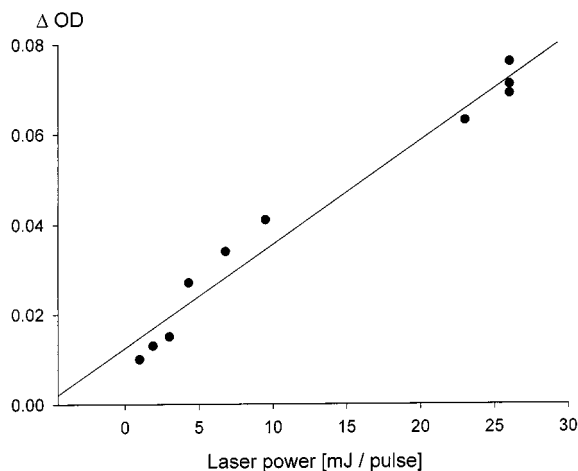


Figure 2. Plot of the initial transient intensity at $\lambda = 450$ nm, observed after LFP (266 nm) of **1** in ACN, versus the laser power (measured at the place of the sample); the straight line represents a linear fit to the experimental data points

Some LFP experiments were performed with DMF as solvent. The transient spectra and lifetimes were virtually identical to those obtained in acetonitrile, while the quenching rate constants may differ (see below). If cyclohexane or *n*-hexane were used as solvent, the transient behavior detected upon LFP ($\lambda_{\text{exc}} = 355$ nm) of **1** was again very sim-

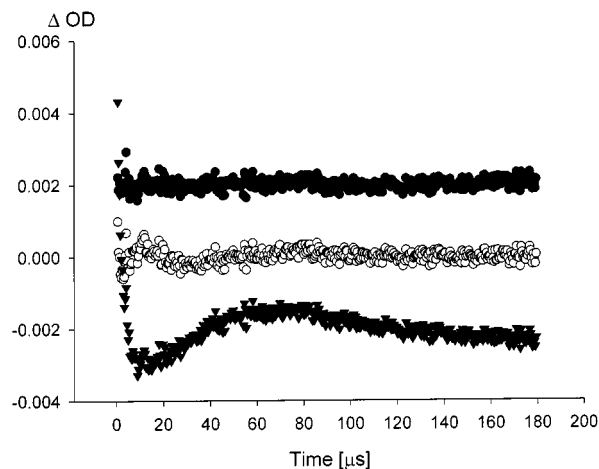


Figure 3. Plot of the residuals of a trace fitting; trace obtained by LFP (266 nm) of **1** in ACN, $\lambda = 460$ nm; bottom: first-order fitting (monoexponential); center: $2 \times$ first-order fitting (biexponential); top: $3 \times$ first-order fitting (triexponential)

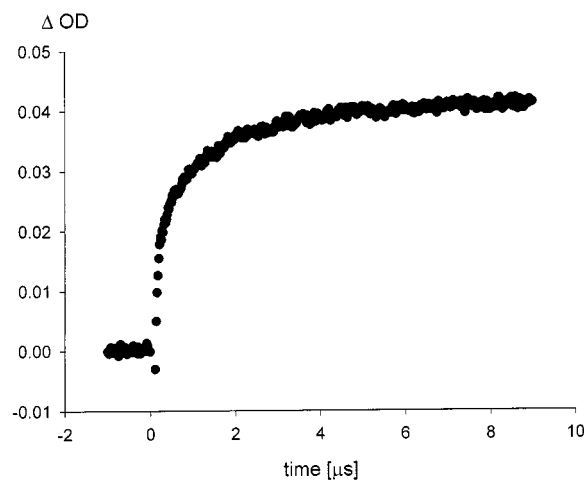


Figure 4. Transient trace, monitored at $\lambda = 360$ nm after LFP (266 nm) of **1** in ACN

ilar to the behavior detected when using acetonitrile. Again, a transient with $\lambda_{\max} = 450$ nm was detected, with a lifetime τ of the order of 30 μs (Figure 5).

The transient spectrum of transient X obtained by LFP of **1** is very similar to the UV/Vis spectrum assigned to iminoquinone methide **sa-3**, matrix-isolated in Ar.^[1] For **sa-3**, the reactivity of a reactive diene, undergoing facile Diels–Alder cycloadditions and addition of nucleophiles, was anticipated. Quenching experiments were therefore performed, using dienophiles such as 2-chloroacrylonitrile (CAN) and nucleophiles such as methanol. Indeed, the 450-nm transient was quenched both by methanol and by CAN. Hence an assignment of transient X to **sa-3**, possibly plus another stereoisomer of **3**, appears to be a plausible working hypothesis.

The traces recorded at $\lambda_{\text{mon}} = 450$ nm reveal the presence of more than one transient species. In order to identify the transients observed, it was therefore necessary to deconvolute the superposition of transient traces observed. This

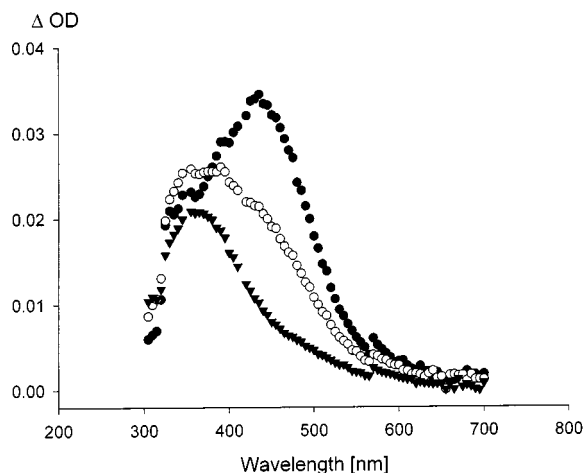


Figure 5. Transient spectra, measured during different time windows after LFP (355 nm) of **1** in cyclohexane purged with argon; dark dots: 3 μ s after LFP; light dots: 11 μ s after LFP; black triangles: 30 μ s after LFP

could partially be achieved by selective quenching of some of the transients. While approximate fitting of the traces according to first-order kinetics was possible at low quencher concentrations, further addition of quencher led to traces that could be much better fitted using biexponential kinetics. In typical quenching experiments (using methanol as quencher, for example), two components of the transient signal monitored at $\lambda = 450$ nm were quenched, while one slow component was not affected. The decay rate constant of this slow third component was an invariant $k_{\text{slow}} = 2 \cdot 10^4 \text{ s}^{-1}$. The identity of the slow component cannot be deduced from comparison with matrix data; however, a broad λ_{max} at $\lambda < 400$ nm is characteristic of didehydroazepines.^[36] The possibility that the slow component can be attributed to such a seven-membered ring is supported by the observation that it is quenched by diethylamine. In the case of this quencher, the lifetime of the slow component proved not to be independent of quencher concentration.^[37] The rate constant for the reaction between the slow component and diethylamine was obtained as $k_{\text{q}} = 5.8 \cdot 10^4 \text{ M}^{-1} \text{ s}^{-1}$, which is in a typical range.^[36] One possible structure for the slow component is therefore didehydroazepine **5**.

As far as the growth at $\lambda = 370$ nm is concerned, a clear assignment cannot be made. The rate constant of the 370-nm growth is nearly independent of quencher concentration; addition of 7% triethylamine merely changed it from an initial $k = 7.1 \cdot 10^5 \text{ s}^{-1}$ to $k = 7.5 \cdot 10^5 \text{ s}^{-1}$. Addition of 1% thiophenol, however, resulted in efficient quenching. One possible interpretation might be the formation of *trans*-2,2'-bis(diethylaminomethyl)azobenzene by dimerization of two molecules of triplet 2-(diethylaminomethyl)phenylnitrene.

Laser Flash Photolysis: Quenching Studies in Polar Solvents

The reactivity of **X** was examined using a series of quenchers, including dienophiles and a variety of different nucleophiles. As the decay at $\lambda = 450$ nm obeyed complex kinet-

ics, a standardized technique was employed to obtain consistent and reproducible results. At low quencher concentrations, traces were fitted according to first-order kinetics. Upon addition of quencher, the decay rate constants for the two faster components increased, reducing the quality of the first-order fit, and allowing a biexponential fit (which is very difficult if both k_{decay} are similar). This point was usually reached when $k_{1\text{st}(450)} = 6 \cdot 10^4 \text{ s}^{-1}$. As the rate constant k_{slow} for decay of the slow component **5** proved to be independent of quencher concentration (with the exception of amines used as quenchers: see above), a typical value of $k_{\text{slow}} = 2 \cdot 10^4 \text{ s}^{-1}$ was used in fitting the traces, thereby reducing the number of parameters to be fitted. Starting from $k_{\text{fast}} = 6 \cdot 10^5 \text{ s}^{-1}$, the traces could again be fitted according to first-order kinetics, as the slow component was practically stable in this time regime.

The quenching plots measured in this study can be divided into two categories. Quenching plots obtained when employing non-hydroxy quenchers (that is, dienophiles and amines) proved to be linear (Figure 6). If the quencher contained at least one hydroxy functionality, on the other hand, the plots were nonlinear, consisting of an initial section in which k_{decay} was almost independent of quencher concentration, and a second, linear part, in which efficient quenching was observed. Figure 7 shows quenching plots obtained using water and $[\text{D}_2]\text{water}$. The concentration needed for the onset of efficient quenching was dependent on the nature of the quencher employed. It is interesting that deuterium oxide reproducibly required a slightly higher concentration than water, while the slope of the linear section was identical in both isotopomers (Figure 7). No such observation was made when comparing the quenching plots obtained using CH_3OH vs. CH_3OD . In this case, however, the slopes of the linear sections differed by a factor of two (Figure 8).

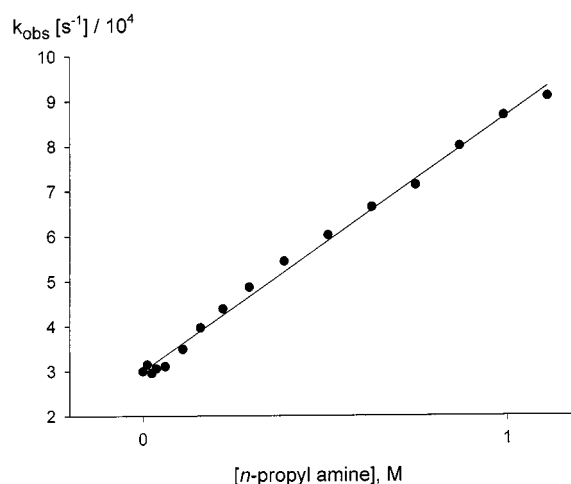


Figure 6. Plot of the decay rate constant after LFP (266 nm) of **1** in acetonitrile, monitored at $\lambda = 450$ nm, versus the concentration of *n*-propylamine added; the line represents the linear fitting of the data

Another detail deserving mention is the observation that the addition of small concentrations of relatively unreactive

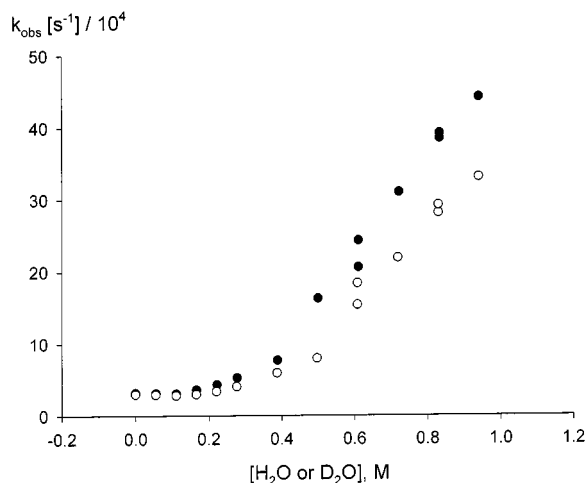


Figure 7. Plots of the decay rate constant at $\lambda = 450$ nm, LFP (266 nm) of **1** in acetonitrile, versus quencher concentration; black dots: quenching with water; light dots: quenching with deuterium oxide

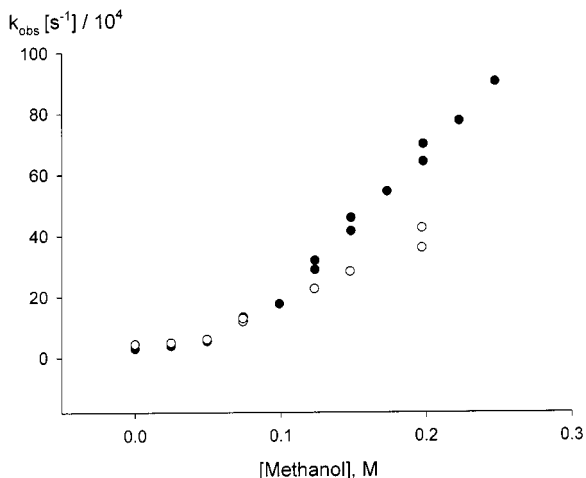


Figure 8. Plots of the decay rate constant at $\lambda = 450$ nm, LFP (266 nm) of **1** in acetonitrile, versus quencher concentration; black dots: quenching with MeOH; light dots: quenching with MeOD

hydroxy quenchers such as 2-propanol or *tert*-butyl alcohol led to a small, but reproducible *decrease* in k_{decay} (see Figure 9). With phenol as quencher, the quenching plot obtained was curved downward, reaching a plateau at $[\text{phenol}] = 0.03$ M. Similar effects were observed with thiols and the DNA bases as quenchers. Here the plateau was reached very early ($[\text{R-SH}] > 0.2$ mM, $[\text{cytosine}] > 1$ mM) (Figure 10). The implications of these observations are discussed below. The pseudo first-order rate constants obtained in the quenching studies are summarized in Table 1.

Some conclusions from Table 1:

(1) **X** is quenched by electron-deficient dienophiles such as maleic anhydride, but not by simple olefins such as cyclohexene or tetramethylethylene.

(2) Particularly efficient quenching is found with thiols, or if the quencher has two or more hydroxy groups in close proximity. Introduction of steric hindrance reduces the quenching rate constant.

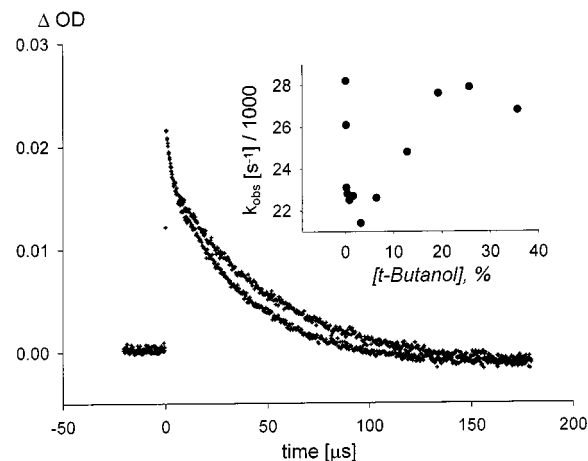


Figure 9. Transient traces, recorded after LFP (266 nm) of **1** in ACN; lower trace: in pure acetonitrile; upper trace: 3.2% *tert*-butyl alcohol added; inset: plot of the decay rate constant, monitored at $\lambda = 450$ nm, vs. $[\text{tBuOH}]$

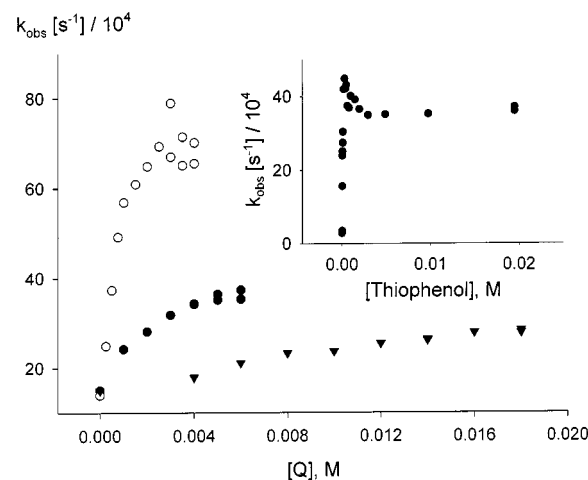


Figure 10. Plots of the decay rate constant at $\lambda = 450$ nm, LFP (355 nm) of **1** in DMF, versus quencher concentration; light dots: quenching with cytosine; black dots: quenching with adenine; black triangles: quenching with thymine; inset: plot of the decay rate constant after LFP (266 nm) of **1** in acetonitrile, monitored at $\lambda = 450$ nm, versus the concentration of thiophenol added

(3) Deuterium kinetic isotope effects are small (methanol) or not detectable (water). No ^{18}O -isotope effect was observed for water quenching.

(4) Reactions with methanol are significantly more rapid in cyclohexane and acetonitrile than in DMF.

Quenching Studies Using Cyclohexane as Solvent

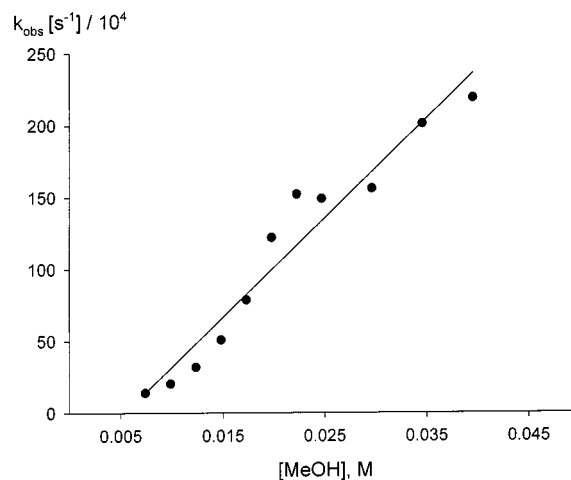
The reactivity of transient **X** was also examined using cyclohexane as solvent. Here, the kinetics of the transient decay, monitored at $\lambda = 450$ nm, are no longer triexponential, but can be fitted in terms of a biexponential decay. This made it possible to obtain individual quenching rate constants for both species absorbing at $\lambda = 450$ nm. In the case of methanol quenching, k_{fast} was determined as $6.9 \cdot 10^7 \text{ M}^{-1} \text{ s}^{-1}$ (Figure 11) and $k_{\text{slow}} = 1.4 \cdot 10^5 \text{ M}^{-1} \text{ s}^{-1}$. The number for k_{slow} may not be significant, as $k_{\text{decay,slow}}$ varied only

Table 1. Second order rate constants for reactions between transient **X** ($\lambda_{\text{mon}} = 450$ nm) and various quenchers

Quencher	Rate constant ($10^4 \text{ M}^{-1} \text{ s}^{-1}$) ^[a]
2-Chloroacrylonitrile	1400
Maleic anhydride	2400
Cyclohexene	no quenching
Tetramethylethylene	no quenching
Acetonitrile	< 0.15 ^[b]
Acetone	no quenching
Methanol	460, 95 ^[c] , 850 ^[d]
[D ₁]Methanol ^[e]	230
Ethanol	180
Isopropyl alcohol	33
<i>tert</i> -Butyl alcohol	no quenching ^[f]
Water	66
[D ₂]Water	68
[¹⁸ O]Water ^[g]	68
Phenol	1400 ^[h]
Ethylene glycol	2300
1,3-Propanediol	2900
<i>trans</i> -1,2-Cyclohexanediol	1900
Glycerol	15000
D-Glucose	100000
Triethylamine	29
Diethylamine	110
<i>n</i> -Propylamine	6.4
Ethylenediamine	130
2-Aminoethanol	510
Aniline	14
Pyridine	0.37
Pyridine <i>N</i> -oxide	780
Adenine	6400 ^[c] ^[i]
Cytosine	34000 ^[c] ^[j]
Thymine	770 ^[c] ^[k]
Thiophenol	120000 ^[l]
<i>n</i> -Dodecanethiol	110000 ^[l]
1,3-Dimercaptopropane	130000 ^[l]
Oxygen (³ O ₂)	no quenching

^[a] Measured at room temp. in acetonitrile, unless otherwise noted. Because of the multiexponential decay, the accuracy of the numbers given is generally limited to $\pm 10\%$. Very low rate constants, such as measured for pyridine quenching, are less accurate ($\pm 20\%$). If the quenching plot is strongly curved as in footnotes^[d,f-i], the accuracy is estimated to $\pm 30\%$. The rate constants given refer to the bulk concentration of quencher. No distinction is made between reactions with monomeric quenchers, and reactions in which clusters of quencher may be involved. — ^[b] k_{decay} (**X**) divided by the molarity of pure acetonitrile. This value therefore represents an upper limit. — ^[c] In DMF, room temp. — ^[d] In cyclohexane, room temp., first order fit of the traces. — ^[e] CH₃OD. — ^[f] See Figure 8. — ^[g] 90% isotopic enrichment. — ^[h] Quenching plot curved downward (see text). This value corresponds to the slope of the plot at [phenol] < 0.03 M. — ^[i] Quenching plot curved downward (see text). This value corresponds to the slope of the plot at [adenine] < 3 mM. — ^[j] Quenching plot curved downward (see text). This value corresponds to the slope at [cytosine] < 1 mM. — ^[k] Quenching plot curved downward (see text). This value corresponds to the slope at [thymine] < 16 mM. — ^[l] Quenching plot curved downward (see text). This value corresponds to the slope at [R-SH] < 0.2 mM.

between $4 \cdot 10^4 \text{ s}^{-1}$ and $6 \cdot 10^4 \text{ s}^{-1}$ within the limited concentration range available for methanol in cyclohexane. First order fitting of the traces gave a value between these figures ($k = 8.5 \cdot 10^6 \text{ M}^{-1} \text{ s}^{-1}$). This value is higher than that obtained when using acetonitrile or DMF as solvent.

Figure 11. Plot of the rate constant of the fast component of the decay at $\lambda = 450$ nm, observed after LFP (266 nm) of **1** in cyclohexane, versus methanol concentration

Calculations

In order to obtain further evidence for the hypothesis that transient **X** might be a mixture of stereoisomers of iminoquinone methide **3**, transition state geometries for some representative reactions of stereoisomers of **4** were optimized using DFT calculations [B3LYP/6-31G(d); **4** was chosen rather than **3** in order to reduce computation time]. The energies are summarized in Table 2. As reference points, a number of complexes formed from isomers of **4** and the corresponding quencher molecules were optimized.

Some conclusions from Table 2:

(1) In Diels–Alder reactions, *sa*-**4** is predicted to show a prominent preference for electron-deficient dienophiles such as acrylonitrile. The calculations predict a preferential *ortho* orientation of the substituents in the product.

(2) With simple olefins, reaction rates are predicted to be considerably lower. Additional alkyl substituents are predicted to lead to an increase in the barrier.

(3) The reactivity of the iminoquinone methides is predicted to depend sensitively on the orientation of the imino hydrogen atom and the dialkylamino functionality. In reactions with ethylene, the *anti-anti* isomer *aa*-**4** is predicted to show the highest reactivity. According to preliminary AM1 calculations, this statement also holds if *as*-**4** is included in the consideration.

(4) In the TS of the reaction between *sa*-**4** and ethylene, both the new C–C bond ($r = 235.7$ pm) and the new C–N bond ($r = 214.1$ pm) are formed to a comparable degree, indicating, that the reaction is both concerted and synchronous. Similar geometries were computed for the TSs of other IQM + olefin reactions.

(5) The TS of the reaction between *aa*-**4** and water was also optimized at the B3LYP/6-31G(d) level of theory. In the TS, the new N–H bond is more fully developed than the new C–O bond [$r(\text{N–H}) = 130.5$ pm, $r(\text{H–O}) = 119.1$ pm, $r(\text{C–O}) = 213.5$ pm]. It is characterized by one mode with negative force constant, which may be described as the

Table 2. Reactions of iminoquinone methides; calculated energies of reactants, reactant complexes, and transition states; activation energies and enthalpies of complex formation

Substrate	Quencher	Energy of separate reactants [H]	Energy of precursor complex [H]	Energy of TS [H]	Barrier [kcal/mol]	$\Delta H(\text{complex})$ [kcal/mol]	Dipole moment (complex) [D]	Dipole moment (TS) [D]
sa-4	Ethylene	−537.967596	−537.970756	−537.939573	19.6	−2.0	6.027	4.513
aa-4	Ethylene	−538.219781	not calculated	−538.198401	15.4 ^[a]	—	—	2.678
ss-4	Ethylene	−538.213891	not calculated	−538.182500	21.7 ^[a]	—	—	4.123
sa-4	Tetramethylethylene	−695.484327	−695.486128	−695.442498	28.4	−0.8	6.238	4.122
sa-4	Acrylonitrile ^[b]	−630.212071	−630.216468	−630.184455	20.1	−2.8	9.788	7.278
sa-4	Acrylonitrile ^[c]	−630.212071	−630.216468	−630.200122	10.3	−2.8	9.788	6.170
aa-4	Water	−536.041281	−536.065314	−536.045137	10.2	−12.3	3.953	3.438
aa-4	Water dimer	−612.220592	−612.249587	−612.237014	7.9	−18.2 ^[d]	4.264	4.359
aa-4	Methanol	−575.346752	−575.370719	−575.351688	9.0	−13.1	3.911	3.371
aa-4	Ethylene glycol	−689.587951	−689.609028	−689.602043	4.4	−13.2	3.910	6.244
aa-4	Ammonia	−515.950129	−515.961708	−516.170127	15.9	−7.3	2.773	5.602

^[a] Assuming a $\Delta H(\text{complex})$ of −2.0 kcal/mol as in the case of sa-4. — ^[b] TS leading to 4-(dimethylamino)tetrahydroquinoline-2-carbonitrile, cyano group *exo*. — ^[c] TS leading to 4-(dimethylamino)tetrahydroquinoline-3-carbonitrile, cyano group *exo*. — ^[d] Reaction enthalpy for aa-4 + water dimer → complex.

migration of a proton from water to the imino nitrogen atom of aa-4. The calculated activation energy is 10.2 kcal/mol (in this system, the TS energy has to be compared with the energy of the complex [aa-4 × H₂O], which is calculated to be lower in energy than aa-4 + H₂O by 12.3 kcal/mol). A similar situation is encountered when the reaction between aa-4 and methanol is calculated. Here, the barrier starting from [aa-4 × MeOH] is predicted to amount to 9.0 kcal/mol, slightly less than the activation energy calculated for water as quencher.

(6) The barrier for the reaction between sa-4 and ethylene glycol is calculated to be significantly smaller than the barrier for the reaction with methanol or water. In the transition state, $r(\text{C}–\text{O})$ is 241.4 pm, while $r(\text{O}–\text{H})$ is calculated as 129.3 pm and $r(\text{N}–\text{H})$ as 121.1 pm. Unlike the reaction between sa-4 and water or methanol, the reaction between sa-4 and ethylene glycol predominantly has the character of a protonation of the imino group. The second hydroxy group of ethylene glycol forms a hydrogen bond with the attacking hydroxy functionality [$r(\text{O} \cdots \text{H}) = 210.7$ pm].

(7) The barrier calculated for reaction with dimeric water is calculated to be significantly smaller than the barrier for reaction with monomeric water.

(8) For the reaction with ammonia, a significant barrier of 15.9 kcal/mol is predicted.

The relative Diels–Alder reactivities of the dialkylamino-substituted iminoquinone methides predicted by DFT are in qualitative accord with the experimental findings, where high reactivity towards electron-deficient dienophiles such as maleic anhydride was observed, and no reactivity towards olefins such as cyclohexene or tetramethylethylene. As far as the reactions with nucleophiles are concerned, the relative reactivities calculated for the reactions between aa-4 and water or methanol are in agreement with the experimental findings (methanol being more reactive).

Additionally, the geometries of a number of relevant stationary points on the C₉H₁₂N₂ surface were optimized and characterized as minima or transition states by calculating

vibrational spectra [all calculations B3LYP/6-31G(d)]. Table 3 gives the relevant energies, and Figure 12 shows the results in graphic form. The zero-point was set as the energy of the triplet nitrene plus 18.3 kcal/mol, which is the singlet-triplet energy gap determined experimentally for parent phenylnitrene.^[38,39] The triplet energy of sa-4 is obtained as $\Delta E_{S-T} = 25.5$ kcal/mol [(U)B3LYP/6-31G(d)].

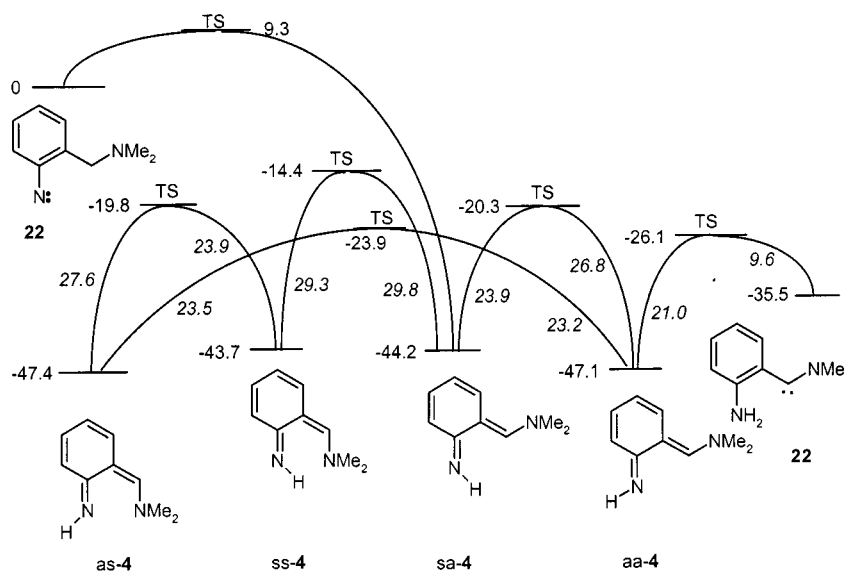
Discussion

Identification of Transient X

Iminoquinone methides sa-3 and aa-3 are formed photochemically ($\lambda_{\text{exc}} = 320$ nm) from azide **1**, matrix-isolated in Ar at $T = 10$ K.^[1] While the data obtained with matrix isolation spectroscopy thus draw a clear picture, the situation is definitely less obvious when looking at the product studies, LFP data, and calculations presented in this contribution. Certainly, a significant part of the photochemistry of **1** runs via the well-established pathways of conventional singlet nitrene chemistry, eventually yielding methylenazepine **9**. This statement is supported both by the results obtained by LFP and by the product studies. Most probably, some of the products obtained from irradiation of **1**, such as the aniline **7**, derive from triplet nitrene chemistry. There is also some evidence, from the LFP studies, that a triplet nitrene may be involved, as the growth at $\lambda = 370$ nm may be assigned to formation of an azo dye. Many of the products identified (such as 2-aminobenzaldehyde), however, cannot be formed by these conventional routes. The reactivity pattern found with transient X (high reactivity towards electron-deficient dienophiles and nucleophiles) limits the choice of possible structures to a number of reactive molecules. These are iminoquinone methides **3**, 2-(diethylaminomethyl)(phenyl)nitrene (**20**) (singlet or triplet), and (2-aminophenyl)(diethylamino)carbene (**21**). Scheme 5 depicts the pathways by which the intermediates should be formed.

Table 3. Energies (in Hartrees) and dipole moments of stationary points relevant to this study

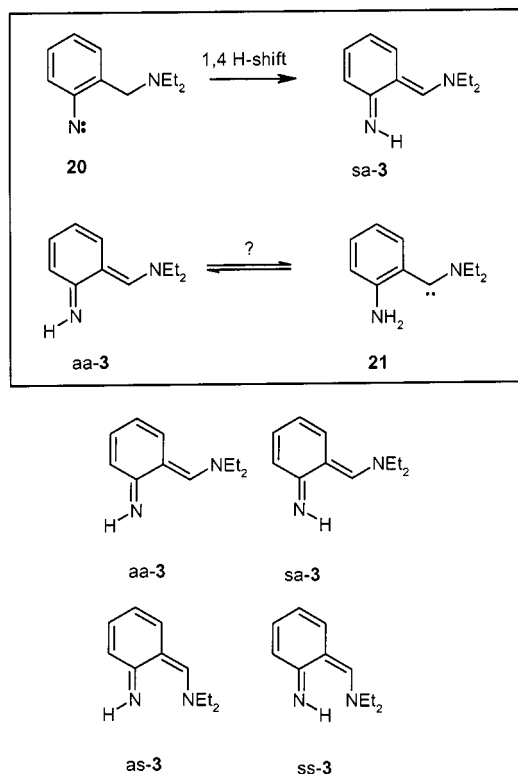
Stationary point	Energy [H]	Energy + ZPC [H]	Dipole moment [D]
sa-4	-459.627618	-459.431370	6.122
aa-4	-459.633110	-459.436668	4.153
ss-4	-459.626510	-459.430473	5.036
as-4	-459.632777	-459.436514	3.261
TS aa-4/sa-4	-459.586720	-459.393392	5.755
TS sa-4/ss-4	-459.576891	-459.383755	9.951
TS ss-4/as-4	-459.585313	-459.392397	4.982
TS aa-4/as-4	-459.593840	-459.399773	6.630
Carbene 22	-459.613308	-459.417478	2.006
TS aa-4/carbene 22	-459.593662	-459.402446	3.289
sa-4 triplet	-459.583425	-459.390683	4.014
sa-3	-538.256879	-538.003088	6.377
aa-3	-538.032909	-537.778861	3.798

Figure 12. Schematic representation showing the relative energies of important stationary points and calculated activation energies on the $C_9H_{12}N_2$ surface

Nitrene **20** can be ruled out as a possible candidate. Singlet nitrenes are known to be very short-lived, with a lifetime in the ps range.^[40–44] Triplet nitrenes, on the other hand, react sluggishly in intermolecular reactions, preferentially decaying through H abstraction or dimerization.^[45] In this study, a transient growth ($\lambda = 370$ nm) has tentatively been assigned to dimerization of triplet nitrene **20**, yielding an azo dye. This growth, however, does not correlate with the decay of transient **X**, which represents a further argument against an assignment of **X** as triplet nitrene **20**.

The case against carbene **21** is not as evident. This species would have to be formed by transfer of a second hydrogen atom to the imine nitrogen atom. The second 1,4-H shift required for the formation of carbene **22** ($R = NMe_2$ instead of NEt_2) is calculated by B3LYP/6-31G(d) + ZPE [MP2/6-31G(d) + ZPE gives similar results] to be endothermic by 11.9 kcal/mol, requiring an activation energy of $E_a = 24.3$ kcal/mol (Figure 12, Table 3). For this reason, formation of carbene **21** can be ruled out.

The iminoquinone methides **3** represent intermediates that should be quenched by dienophiles and by nucleophiles. Reaction between **3** and water should eventually yield 2-aminobenzaldehyde (**6**), which is indeed formed in significant amounts if **1** is photolyzed in wet acetonitrile. With acrylonitrile as quencher, 4-(diethylamino)tetrahydroquinoline-3-carbonitriles should be formed, and these are in fact probably detected. Further support for the observation of **3** comes from the fact that the UV/Vis spectrum of sa-3/aa-3 in argon matrix^[1] and the transient spectrum observed immediately after the laser pulse are very similar. It thus appears very likely that transient **X** can indeed be assigned as a mixture of probably two stereoisomers of neutral iminoquinone methide **3**. These intermediates are therefore, in fact, surprisingly short-lived species ($\tau \approx 30$ μ s),^[46] much shorter lived than *o*-quinone methide,^[12,13] and even shorter lived than didehydroazepine **5**. This was also observed in the low-temperature studies presented previously.^[1] If an organic glass containing both the didehy-



Scheme 5

droazepine **5** and iminoquinone methides sa-3 + aa-3 is thawed, sa-3 and aa-3 disappear before **5**.

Product Studies

A number of open questions remain to be discussed. As far as the product studies are concerned, the following observations deserve comment:

(1) Small amounts of 2,1-benzisoxazole (**8**) are formed upon pulsed-laser irradiation of **1**. This compound is probably formed by photolysis of 2-azidobenzaldehyde. 2-Azidobenzaldehyde is in turn formed in three steps from the radical cation of **1**.^[47] The observation that **8** is detected in small yield only if **1** is irradiated using a pulsed laser indicates that direct photoionization of **1** requires at least two photons.

(2) Four isomeric products with $m/z = 229$ are formed upon photolysis of **1** in the presence of acrylonitrile. Only *cis*- and *trans*-4-diethylamino-1,2,3,4-tetrahydroquinoline-3-carbonitrile, however, can be expected to be formed in a concerted [4 + 2] cycloaddition, as the pathways yielding *cis*- or *trans*-4-diethylamino-1,2,3,4-tetrahydroquinoline-2-carbonitrile are calculated to have a prohibitively high barrier (see Table 2). At this point, it should be noted that non-regiospecific cycloadditions have been observed before for cycloadditions involving iminoquinone methides. Ito et al.^[3] obtained a mixture of both regioisomeric tetrahydroquinoline carbonitriles upon generation of *N*-benzyl-*o*-iminoquinone methide in the presence of acrylonitrile. Given this precedent, it seems reasonable to assign structures **16–19** to

the four products with $m/z = 229$. However, the mechanistic scenario still requires clarification.

Curved Quenching Plots

In the quenching studies, curved quenching plots were very often observed. Upon addition of small concentrations of hydroxy quenchers such as methanol or water, the lifetime of the iminoquinone methide mixture hardly changed. Starting from a certain threshold of quencher concentration, a linear rise in k_{decay} was observed (quenching plot curved upward, see Figure 7). In certain cases, such as quenching by phenol, thiols, or DNA bases, a plateau region was reached (quenching plot curved downward, see Figure 10). If relatively unreactive hydroxy quenchers such as 2-propanol or *tert*-butyl alcohol were employed, a decrease in k_{decay} was observed upon addition of relatively small concentrations of quencher (see Figure 9).

The quenching plots could reflect several factors complicating the system studied: complex formation between quencher and iminoquinone methide, complex formation between azide and quencher, and dimerization or oligomerization of the quenchers themselves.

Quenching Plots Involving Hydroxy Quenchers

Alcohols dimerize or oligomerize in aprotic solvents. If the alcohol is small, the dimer is usually more reactive than the monomer, producing quenching plots that are curved upward. Such quenching plots have frequently been observed for reactions between carbenes and alcohols.^[48–51] In a study on the reactions between silyloxycarbenes and alcohols, conducted in acetonitrile, Kirmse, Guth, and Steenken pointed out, that in this particular polar solvent, methanol oligomerization plays no role up to methanol concentrations of 0.4 M.^[52] In the case of reactions between silyloxycarbenes and weakly acidic alcohols, the quenching plots were curved upward. For these reactions, the authors suggested a mechanism in which one molecule of alcohol forms a complex with the carbene, while the second molecule of alcohol then assists in the conversion of the carbene–alcohol complex to the final ether product.^[52] According to Kirmse et al., more acidic alcohols such as 2-chloroethanol do not require activation in a ternary carbene/alcohol dimer complex. The downward-curved quenching plots observed for these quenchers thus have to be due to alcohol association.^[52]

Most of the peculiarities found with the quenching plots presented in this study can be explained in terms of the model presented by Kirmse, Guth, and Steenken. According to the calculations presented above (Table 2), aa-4 forms complexes with water or methanol, which gives rise to a significant stabilization ($\Delta H_{\text{complex}} = -13.05$ kcal/mol for aa-4 + methanol in the gas phase) of the iminoquinone methide. If the complexing alcohol is bulky, such as *tert*-butyl alcohol, complex formation may in fact result in a kinetic stabilization of **3**, since dimerization of the iminoquinone methide/*tert*-butyl alcohol complex will be impeded relative to the uncomplexed iminoquinone methide.

This explains the decrease in k_{decay} observed upon addition of small to medium concentrations of *tert*-butyl alcohol or 2-propanol. If the alcohol concentration is increased further, product formation through the ternary iminoquinone methide/alcohol dimer complex becomes more significant, resulting in an increase in k_{decay} (see Figure 9). In quenching plots with deuterium oxide, the onset of efficient quenching requires a higher quencher concentration than in quenching plots obtained using water as quencher (Figure 7). This can be explained in terms of slightly different dimerization (and probably complex formation) properties in the two isotopomers, due to subtle entropic effects.^[53] The idea that water dimers react more efficiently than monomeric water with **3** is confirmed by the calculations presented above (barrier for reaction between aa-**4** and water: 10.2 kcal/mol; for reaction with dimeric water: 7.9 kcal/mol, see Table 2).

Quenching Plots Involving DNA Bases and Thiols

Figure 10 shows quenching plots measured for the reactions between **3** and DNA bases and thiophenol. DNA bases are well known to form dimeric complexes. Dimeric DNA bases can be expected to react more slowly with **3** than the free bases, which should result in downward curved quenching plots.

Dimer formation is unlikely to be of any importance in the case of dilute solutions of thiols in acetonitrile. At least here, the downward curvature and plateau formation observed in the quenching plot shown in Figure 10 are in all likelihood not due to any kind of association phenomenon. The only explanation that can be offered is protonation of azide **1** by the relatively acidic thiols. This would probably result in completely different transient phenomena at high thiol concentrations.

Reactions of Iminoquinone Methides

The iminoquinone methides show pronounced reactivity towards thiols, compounds containing at least two close hydroxy functionalities, cytosine, and adenine. If one compares the figures obtained for cytosine, adenine, and thymine quenching (Table 1) with the relative reactivities for reactions between deoxynucleosides and *o*-quinone methide as published by Pande et al.,^[23] one finds that the relative reactivities determined in this work ($C/A/T = 44:8:1$) parallel the results published for reactions of *o*-quinone methide ($dC/dG/dA = 30:2.5:1$; no reaction found with dT). Overall, the iminoquinone methides **3** are less selective than *o*-quinone methide, which is in agreement with the much shorter lifetime of **3**. Given the very high reactivity of **3** towards polyhydroxy quenchers, reaction of **3** with the sugar backbone of DNA would probably compete with DNA alkylation. What makes diols, glycerol, and glucose so reactive towards **3**? In reactions between (silyloxy)carbenes and simple alcohols, a second alcohol molecule catalyzes the conversion of a carbene–alcohol complex to the ether product.^[52] A similar mechanism may be invoked for the analogous reactions undergone by the iminoquinone

methides generated in this work. If the alcohol already contains a second hydroxy functionality to catalyze the reaction, no second alcohol molecule is required, and the activation entropy is more favorable. The calculated geometry of the transition state of the reaction between sa-**4** and ethylene glycol indicates the presence of a hydrogen bond formed by the second hydroxy group – which is not directly involved in the reaction – and the attacking hydroxy group. In the reaction with 1,3-propanediol, this hydrogen bond would be part of a six-membered ring, which is more favorable than the five-membered ring hydrogen bond present in the reaction with ethylene glycol. The hydrogen bond most probably increases the acidity of the attacking alcohol. A similar mechanism may operate for compounds containing one hydroxy group and one amino functionality (2-aminoethanol) or two amino functionalities (ethylenediamine).

Finally, the extremely high reactivity of the iminoquinone methides **3** towards thiols is to be expected on the basis of the weak S–H bond, and the high acidity and nucleophilicity of these quenchers. The N–H bond in aniline is also relatively weak, it is a good nucleophile, and yet the rate constant of its reaction with **3** is lower by four orders of magnitude. The crucial difference probably lies in the very different acidities; the pK_a of unprotonated aniline (in DMSO) is 30.6,^[54] while thiophenol in the same solvent has a pK_a of 10.3.^[54] Thus, thiols probably act primarily as Brønsted acids, first protonating the basic imine moiety in **3**. In reactions with good nucleophiles that are very weak acids, the quencher has to act primarily as a nucleophile, attacking at the sterically congested methylene site of **3**. The order of reactivity found with *n*-propylamine vs. diethylamine vs. triethylamine ($6.4 \cdot 10^4 \text{ M}^{-1} \text{ s}^{-1}$ vs. $1.1 \cdot 10^6 \text{ M}^{-1} \text{ s}^{-1}$ vs. $2.9 \cdot 10^5 \text{ M}^{-1} \text{ s}^{-1}$) reflects the increase in nucleophilicity upon going from a primary amine to a secondary amine, while the reactivity of the tertiary amine is reduced by steric constraints. In the reaction of the tertiary amine, a zwitterion is the logical primary product.

Why are the iminoquinone methides presented in this work such extraordinarily reactive compounds? The reactivity of dienes is a function of the HOMO–LUMO gap. This gap is calculated for sa-**4** [B3LYP/6-31G(d)] as 3.31 eV, compared with 3.59 eV calculated for *o*-quinone methide, 3.91 eV calculated for cyclopentadienone, and 5.49 eV calculated for cyclopentadiene. The very low calculated triplet energy of 25.5 kcal/mol for sa-**4** is in agreement with this picture. Furthermore, the stereoisomers of **3** and **4** are polar molecules (Table 3). The calculated dipole moments are of the order of 3.8 D (aa-**3**) or 6.4 D (sa-**3**). Reactions with electrophiles (acids) or nucleophiles should be facilitated by this dipolar character.

The high reactivity of **3** holds promise that azidobenzylamines might find application in photoaffinity labelling. To make the reaction useful for preparative chemistry, the competing ring expansion of the singlet nitrene to didehydroazepine **5** has to be suppressed, which might be achieved by introduction of additional substituents in the 6-position. Studies directed towards this goal are in progress.

Conclusion

Photolysis of 2-azido-*N,N*-diethylbenzylamine in acetonitrile (or DMF, *n*-hexane) solution results in formation of stereoisomeric iminoquinone methides, which can be trapped with water to yield up to 10% of 2-aminobenzaldehyde (**6**). In addition, the formation of significant amounts of methyleneazepine **9** in the presence of diethylamine is indicative of typical singlet nitrene–didehydroazepine ring-expansion chemistry. The iminoquinone methides were characterized by time-resolved laser flash photolysis. They show high reactivity towards electron-deficient dienophiles, but do not react measurably with simple olefins. In reactions with nucleophiles, particularly high reactivity was found towards thiols, polyhydroxylated compounds (glycerol, glucose), and cytosine, while simple alcohols, amines, and thymine quenched the iminoquinone methides less efficiently.

Experimental Section

Product Studies: In a typical experiment, **1** (10 mg) was dissolved in solvent (40 mL) and placed in a quartz vessel. Oxygen was removed by purging the sample with Ar for 30 min. The sample was then irradiated for 15 min with $\lambda_{\text{exc}} = 320$ nm, using a Hg low-pressure lamp with filter (Grüntzel, Germany). After removal of the solvent, 1-bromonaphthalene (10 mg) was added as external standard, the sample was dissolved in ca. 1 mL of CH_2Cl_2 , and analyzed by GC/MS (Hewlett–Packard, column: OV1, 29.5 m). If a reference sample of a given product was available, its peak integral was calibrated against 1-bromonaphthalene by injecting 1:1 mixtures with 1-bromonaphthalene. In several experiments, pulsed lasers [355 nm from the Nd-YAG laser used in the LFP studies (130 mJ/pulse), and 308 nm from a Lambda-Physik EMG 100 excimer laser operated with He/Xe/HCl, 80 mJ/pulse] were used as excitation light sources. – Laser flash photolysis (LFP): A standard LFP set-up was used. The apparatus consisted of a Spectra-Physics Quanta-Ray Lab 130 Nd-YAG laser operated at 1 Hz repetition rate and 266 nm (50 mJ/pulse, 10 ns, used whenever possible) or 355 nm (130 mJ/pulse, 10 ns, used if the quencher absorbed at $\lambda = 266$ nm), a pulsed Xe high-pressure lamp (Müller, Germany), and a Spex Minimate monochromator coupled to a photoelectron multiplier tube. The sample was irradiated at a 90° angle relative to the monitoring beam. To avoid depletion of starting material and product build-up, a flow system was used. Data acquisition was performed using a LeCroy 9361 digital oscilloscope. The entire system was programmed using LabView software. Solutions of **1** were ca. $4\text{--}6 \cdot 10^{-5}$ M in acetonitrile (spectroscopic grade, used as received) for 266-nm excitation and 3 mM in acetonitrile (or DMF) for 355-nm excitation. They were purged with argon for 30 min before starting the experiment. The alkenes and amines used as quenchers were freshly distilled immediately prior to use. With the exceptions of glycerol, phenol, 1,2-cyclohexanediol, pyridine *N*-oxide, glucose, maleic anhydride, and the DNA bases, the quenchers were injected into the flow tank neat. Glycerol was injected as a 0.4 M solution in THF, *trans*-1,2-cyclohexanediol as a 0.2 M solution in CH_2Cl_2 , pyridine *N*-oxide, phenol, and maleic anhydride as 1 M solutions in acetonitrile, and glucose as a 1 M solution in water. The DNA bases were insufficiently soluble in acetonitrile. Experiments involving them were conducted using DMF as solvent, preparing the stock solution separately for each point on a quenching plot.

Guanine proved to be too sparingly soluble even in DMF.^[55] Deuterium and ^{18}O kinetic isotope effects were determined by measurement of the rate constants for both labeled and unlabeled quencher on a single afternoon, keeping all experimental parameters exactly the same for both isotopomers. – Azide **1** was obtained as described in the previous contribution.^[1] – Calculations were performed using Gaussian 98^[56] or Titan^[57] software, using the hybrid B3LYP method.^[58] All optimized structures were characterized as minima or transition states by calculating vibrational spectra. All calculated reaction barriers given are corrected for zero point vibrational energy.

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- [1] G. Bucher, *Eur. J. Org. Chem.* **2001**, 0000–0000, preceding paper.
- [2] H. Steinhagen, E. J. Corey, *Angew. Chem.* **1999**, *111*, 2054–2056; *Angew. Chem. Int. Ed.* **1999**, *38*, 1928–1931.
- [3] Y. Ito, E. Nakajo, T. Saegusa, *Synth. Commun.* **1986**, *16*, 1073–1080.
- [4] K. Wojciechowski, *Tetrahedron* **1993**, *49*, 10017–10026.
- [5] M. Lancaster, D. J. H. Smith, *Chem. Commun.* **1980**, 471–472.
- [6] K. Wojciechowski, *Tetrahedron* **1993**, *49*, 7277–7286.
- [7] K. Wojciechowski, *Pol. J. Chem.* **1997**, *71*, 1375–1400.
- [8] A. Vigalok, D. Milstein, *J. Am. Chem. Soc.* **1997**, *119*, 7873–7874.
- [9] A. Vigalok, L. J. W. Shimon, D. Milstein, *J. Am. Chem. Soc.* **1998**, *120*, 477–483.
- [10] O. Rabin, A. Vigalok, D. Milstein, *J. Am. Chem. Soc.* **1998**, *120*, 7119–7120.
- [11] O. Rabin, A. Vigalok, D. Milstein, *Chem. Eur. J.* **2000**, *6*, 454–462.
- [12] [12a] L. Diao, C. Yang, P. Wan, *J. Am. Chem. Soc.* **1995**, *117*, 5369–5370. [12b] B. Barker, L. Diao, P. Wan, *J. Photochem. Photobiol. A* **1997**, *104*, 91–96.
- [13] [13a] Y. Chiang, A. J. Kresge, Y. Zhu, *J. Am. Chem. Soc.* **2000**, *122*, 9854–9855. [13b] E. Modica, R. Zanaletti, M. Freccero, M. Mella, *J. Org. Chem.* **2001**, *66*, 41–52.
- [14] P. Wan, B. Barker, L. Diao, M. Fischer, Y. Shi, C. Yang, *Can. J. Chem.* **1996**, *74*, 465–475.
- [15] G. Pfister-Gouillouzo, F. Gracian, A. Senio, M. Letulle, J.-L. Ripoll, *Tetrahedron Lett.* **1992**, *33*, 5753–5756.
- [16] A. Chrostowska, F. Gracian, J. M. Sotiropoulos, G. Pfister-Gouillouzo, K. Wojciechowski, *Eur. J. Org. Chem.* **2000**, 313–318.
- [17] J. Morawietz, W. Sander, M. Träubel, *J. Org. Chem.* **1995**, *60*, 6368–6378.
- [18] W. Sander, J. Morawietz, *Tetrahedron Lett.* **1993**, *34*, 1913–1916.
- [19] H. Tomioka, *Pure Appl. Chem.* **1997**, *69*, 837–840.
- [20] M. A. Lewis, D. Graff Yoerg, J. N. Bolton, J. A. Thompson, *Chem. Res. Toxicol.* **1996**, *9*, 1368–1374.
- [21] H. W. Moore, R. Czerniak, *Med. Res. Rev.* **1981**, *1*, 249–280.
- [22] A. A. L. Gunatilaka, *Triterpenoid Quinonemethides and Related Compounds (Celastrols)*, in: *Progress in the Chemistry of Organic Natural Products* (Eds.: W. Herz, G. W. Kirby, R. E. Moore, W. Steglich, Ch. Tamm), Springer, Vienna, New York, **1996**, vol. 67, chapter 1, p. 1–123.
- [23] P. Pande, J. Shearer, J. Yang, W. A. Greenberg, S. E. Rokita, *J. Am. Chem. Soc.* **1999**, *121*, 6773–6779.
- [24] Y. Shi, P. Wan, *Chem. Commun.* **1997**, 273–274.
- [25] Y. Shi, P. Wan, *Chem. Commun.* **1995**, 1217–1218.
- [26] A number of possible products with $m = 150$ were synthesized, among them 2-amino-*N*-ethylbenzylamine, 2-(ethylamino)-

- benzylamine, and *N*-ethyl-*N*-methyl-*o*-phenylenediamine. None of the compounds was identical to the product formed in the photolyses.
- [27] [27a] G. Bucher, H. G. Korth, *Angew. Chem.* **1999**, *111*, 209–211; *Angew. Chem. Int. Ed.* **1999**, *38*, 215–218. – [27b] G. Bucher, *Angew. Chem.* **1999**, *111*, 1247; *Angew. Chem. Int. Ed.* **1999**, *38*, 1192.
- [28] G. I. Kokorev, *J. Gen. Chem. USSR* **1990**, *60*, 408–409; *Zh. Obshch. Khim.* **1990**, *60*, 469–471.
- [29] C. Betschart, B. Schmidt, D. Seebach, *Helv. Chim. Acta* **1988**, *71*, 1999–2021.
- [30] D. M. Hall, E. E. Turner, *J. Chem. Soc.* **1945**, 694–699.
- [31] T.-Y. Liang, G. B. Schuster, *J. Am. Chem. Soc.* **1987**, *109*, 7803–7810.
- [32] H. Zhai, M. S. Platz, *J. Phys. Org. Chem.* **1996**, *10*, 22–26.
- [33] E. Leyva, M. J. T. Young, M. S. Platz, *J. Am. Chem. Soc.* **1986**, *108*, 8307–8309.
- [34] M. J. T. Young, M. S. Platz, *J. Org. Chem.* **1991**, *56*, 6403–6406.
- [35] The compound with $m/z = 249$ shows the following decay pattern: $m/z = 249$ [M^+] (ca. 10%), 176 /175 [$M^+ - HNEt_2, -H$] (ca. 30%), 161 [$176 - NH$] (ca. 25%), 147 [$175 - C_2H_4$] (100%). The base peak with $m/z = 147$ corresponds to the 2-amino-*N*-ethylbenzonitrilium cation. The very low yield of **11** may be due to hydrolysis of this rather labile compound, yielding 2-aminobenzaldehyde (**6**). Several attempts were made to synthesize **11** independently. While it was possible to obtain an aminal from 2-nitrobenzaldehyde by refluxing the aldehyde in neat diethylamine for 48 h, all attempts to reduce this compound to **11** failed. Under all conditions tried (catalytic hydrogenation, various catalysts and solvents, presence of diethylamine), the aminal functionality was reduced before the nitro group. 2-Aminobenzaldehyde (**6**), on the other hand, did not react with diethylamine, polymerizing instead.
- [36] B. A. DeGraff, D. W. Gillespie, R. J. Sundberg, *J. Am. Chem. Soc.* **1974**, *96*, 7491.
- [37] In the case of *n*-propylamine quenching, all traces could be fitted to first-order kinetics. Here, quenching of **X** and the “slow” transient obviously takes place with a very similar rate constant. Again, a rate constant of the order of $6 \cdot 10^4 \text{ M}^{-1} \text{ s}^{-1}$ is consistent with an assignment of the slow component to didehydroazepine **5**.
- [38] M. J. Travers, D. C. Cowles, E. P. Clifford, G. B. Ellison, *J. Am. Chem. Soc.* **1992**, *114*, 8699–8701.
- [39] R. N. McDonald, S. J. Davidson, *J. Am. Chem. Soc.* **1993**, *115*, 10857–10862.
- [40] N. P. Gritsan, T. Yuzawa, M. S. Platz, *J. Am. Chem. Soc.* **1997**, *119*, 5059–5060.
- [41] R. Born, C. Burda, P. Senn, J. Wirz, *J. Am. Chem. Soc.* **1997**, *119*, 5061–5062.
- [42] N. P. Gritsan, Z. Zhu, C. M. Hadad, M. S. Platz, *J. Am. Chem. Soc.* **1999**, *121*, 1202–1207.
- [43] N. P. Gritsan, A. D. Gudmundsdottir, D. Tigelaar, M. S. Platz, *J. Phys. Chem. A* **1999**, *103*, 3458–3461.
- [44] N. P. Gritsan, D. Tigelaar, M. S. Platz, *J. Phys. Chem. A* **1999**, *103*, 4465–4469.
- [45] G. B. Schuster, M. S. Platz, *Photochemistry of Phenyl Azide*, in: *Advances in Photochemistry* (Eds.: D. H. Volman, G. Hammond, D. C. Neckers), John Wiley & Sons Inc., **1992**, vol. 17, p. 69–143.
- [46] Heinzelmann has reported on the formation of simple iminoquinone methides by acid-induced tautomerization of 2-aminobenzaldimines. In the light of the results presented in this study, this assignment has to be incorrect. Most probably, the compounds wrongly identified as neutral iminoquinone methides in fact are the conjugate acids of the iminoquinone methides, which are the 2-aminobenzaldiminium cations; W. Heinzelmann, *Helv. Chim. Acta* **1978**, *61*, 618–625.
- [47] P. Subramanian, J. Rajaram, V. Ramakrishnan, J. C. Kuriacose, *Indian J. Chem.* **1991**, *30A*, 913–919.
- [48] D. Griller, M. T. H. Liu, J. C. Scaiano, *J. Am. Chem. Soc.* **1982**, *104*, 5549–5551.
- [49] R. S. Sheridan, R. A. Moss, B. K. Wilk, S. Shen, M. Wlostowski, M. A. Kesselmayr, R. Subramanian, G. Kmiecik-Lawrynowicz, K. Krogh-Jespersen, *J. Am. Chem. Soc.* **1988**, *110*, 7563–7564.
- [50] R. A. Moss, S. Shen, L. M. Hadel, G. Kmiecik-Lawrynowicz, J. Wlostowska, K. Krogh-Jespersen, *J. Am. Chem. Soc.* **1987**, *109*, 4341–4349.
- [51] X.-M. Du, H. Fan, J. L. Goodman, M. A. Kesselmayr, K. Krogh-Jespersen, J. A. LaVilla, R. A. Moss, S. Shen, R. S. Sheridan, *J. Am. Chem. Soc.* **1990**, *112*, 1920–1926.
- [52] W. Kirmse, M. Guth, S. Steenken, *J. Am. Chem. Soc.* **1996**, *118*, 10838–10849.
- [53] G. W. Robinson, *J. Phys. Chem.* **1991**, *95*, 10386–10391.
- [54] F. G. Bordwell, J.-P. Cheng, G.-Z. Ji, V. Satish, X. Zhang, *J. Am. Chem. Soc.* **1991**, *113*, 9790–9795.
- [55] R. A. Kenley, S. E. Jackson, Y. Shunko, J. S. Winterle, *J. Pharm. Sci.* **1986**, *75*, 648–653.
- [56] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, Jr., M. A. Montgomery, R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Menucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Ciolowski, J. V. Ortiz, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, J. A. Pople, *Gaussian 98, Revision A.6*, Gaussian Inc., Pittsburgh, PA., **1998**.
- [57] *Titan Vers. 1.0.1*, Schrödinger, Inc., Portland, **1999**.
- [58] A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652.

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