Hydrogen Bonds

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Hydrogen Bonding Switches the Spin State of Diphenylcarbene from Triplet to Singlet**

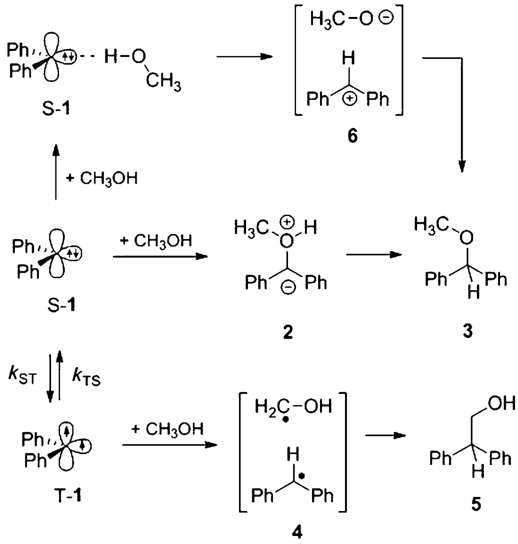
*Paolo Costa and Wolfram Sander**

Dedicated to Professor Wolfgang Kirmse

Abstract: *Spin specificity is one of the most important properties of carbenes in their reactions. Alcohols are typically used to probe the reactive spin states of carbenes: O–H insertions are assumed to be characteristic of singlet states, whereas C–H insertions are typical for the triplets. Surprisingly, the experiments presented here suggest that the spin ground state of diphenylcarbene* ***1*** *switches from triplet to singlet if the carbene is allowed to interact with methanol. Carbene* ***1*** *and methanol form a strongly hydrogen-bonded singlet ground state complex that was synthesized in low-temperature matrices and characterized by IR spectroscopy. This methanol complex is only metastable, and even at 3 K slowly rearranges to form the product of O–H insertion through quantum chemical tunneling. Thus, the ground state triplet (in the gas phase) carbene* ***1*** *forms exclusively the products expected from a singlet carbene. Whereas the assumption of spin specific reactions of carbenes is correct, the spin state itself can be changed by solvent interactions, and therefore widely accepted conclusions drawn from earlier experiments have to be revisited.*

Carbenes are molecules with divalent carbon atoms that play key roles as organic reactive intermediates, as ligands in metal organic chemistry, and as highly potent organocatalysts.[1–3] The chemistry of carbenes is controlled by their spin state, which is either triplet or singlet,[2,4] and this spin-dependent reactivity of carbenes forms the basis of carbene chemistry. In particular, reactions of carbenes with alcohols were extensively studied to develop general rules for the spin-selective chemistry of carbenes:[5,6] Triplet carbenes undergo insertion into C–H bonds,[7] whereas singlet carbenes insert into the O–H bonds of alcohols.[8]

Diphenylcarbene **1** is an archetypal triplet-ground-state arylcarbene, and its reaction with methanol has been extensively studied by time resolved[8–12] and low-temperature[13] spectroscopy (Scheme 1). Eisenthal et al. were able to directly determine k_{ST}, the rate for the intersystem crossing (ISC) from the singlet state S-**1** to the triplet state T-**1**, by picosecond fluorescence spectroscopy.[10,14,15] The lifetime of S-**1** is limited by ISC to 340 ps in acetonitrile and to only 95 ps in the less polar isooctane. By assuming that isopropene and methanol are selective scavengers for T-**1** and S-**1**, respectively, the singlet triplet gap ΔG_{ST} was determined to $-3.36\,\mathrm{kcal\,mol^{-1}}$ in acetonitrile and to $-4.75\,\mathrm{kcal\,mol^{-1}}$ in isooctane, thus in both solvents the triplet state is considerably more stable than the singlet state.[14] The smaller S-T gap in acetonitrile compared to isooctane was rationalized by the better stabilization of the more polar singlet state in the solvent of higher polarity.[16]



Scheme 1. Mechanism of the reaction of diphenylcarbene **1** with methanol.

However, these results were challenged by Griller et al.[11,17] From the temperature dependence of the quenching of **1** by methanol, activation barriers E_a were determined to $1.66\,\mathrm{kcal\,mol^{-1}}$ in acetonitrile and to $3.61\,\mathrm{kcal\,mol^{-1}}$ in isooctane. These barriers are considerably lower than the barriers that are estimated for an essentially diffusion-controlled reaction of **1** with methanol. The conclusion was that the assumption of a spin-selective reaction of **1** with methanol—which forms the basis for the determination of k_{TS}—is flawed, and **1** is able to react directly with methanol from its triplet state. This implies that the ISC occurs along the reaction coordinate rather than at a stationary point.

Because of its fundamental importance, we re-investigated the reaction between **1** and methanol under the conditions of matrix isolation using low-temperature IR and

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[*] P. Costa, Prof. Dr. W. Sander
Lehrstuhl für Organische Chemie II, Ruhr-Universität Bochum
44781 Bochum (Germany)
E-mail: wolfram.sander@rub.de
Homepage: http://www.rub.de/aksander

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EPR spectroscopy. Additional EPR experiments were performed in methanol glass.

Visible-light photolysis (530 nm) of diphenyldiazomethane (DPDM) in frozen methanol at 4 K produces diphenylcarbene **1** in high yields. The formation of **1** in its triplet state can be directly followed by EPR spectroscopy. At temperatures below 30 K the EPR signals of T-**1** are persistent, and even after several hours no decrease in intensity is observed. Warming the methanol glass above 60 K, however, results in a slow decrease of the signals of T-**1** and concurrent formation of a triplet radical pair **4**. Platz et al. reported that T-**1** reacts in frozen 2-propanol at 77 K preferentially through C–H abstraction–recombination to form an alcohol as C–H insertion product.[13] Analysis of the decay kinetics and the very large C–H/D kinetic isotope effect prompted these authors to claim that H atom tunneling is rate determining for the C–H insertion into alcohols. However, in a later publication it was described that the formal C–H insertion results from secondary photochemistry of **T**-1 rather than from a thermal reaction.[13b] In our experiments, we find that the rates for the reaction of T-**1** with methanol are getting exceedingly slow below 40 K (see Table S1). A tunnelling reaction from the lowest vibrational state is expected to be independent of temperature, which is in obvious contradiction to the observation described here.

To gain more insight into the mechanism of the reaction between **1** and methanol we performed experiments in argon matrices doped with 1% methanol. As expected, 530 nm irradiation of DPDM in these matrices at 3 K produced triplet carbene T-**1** in high yields. The IR and EPR spectra of T-**1** obtained under these conditions are in excellent agreement with previously published spectra.[13,18,19] At temperatures below 20 K the diffusion of species matrix-isolated in argon is efficiently inhibited,[20] and thus bimolecular reactions cannot occur. To allow the diffusion of small molecules in solid argon, it is necessary to anneal the matrix at temperatures between 25 and 35 K for several minutes (at higher temperatures argon rapidly evaporates). To our surprise, T-**1** rapidly reacted with methanol if the matrix was allowed to warm from 3 K to 25 K. The reaction of T-**1** could be monitored by both EPR and IR spectroscopy. The EPR signals of T-**1** decrease by more than 40% within 5 min, but no new signals are formed, indicating that the reaction product is diamagnetic (Figure 1 and Figures S3 and S4 in the Supporting Information). This is puzzling, since in methanol glass at the same temperature no reaction of T-**1** is found even after several hours.

IR spectroscopy allowed us to directly monitor the reaction of T-**1** with methanol and formation of diamagnetic products (Figure 2). The IR spectra clearly show that the reaction of T-**1** with methanol exclusively leads to the product of O–H insertion, ether **3**, whereas the expected product of C–H insertion, alcohol **5**, is not formed. Apparently, the results of these experiments are not in agreement with the generally accepted rules of spin-selective reactivity of carbenes. Careful analysis of the IR spectra revealed that ether **3** is not directly formed and that a metastable intermediate with a very strong absorption at 1327.8 cm^{-1} is the primary product of the reaction between T-**1** and methanol. This labile intermediate rearranges to the final product **3** even at temperatures as low as 3 K. Several isotopomers were synthesized by allowing T-**1** to react with CH_3OH, CH_3OD, and CD_3OH (Figure 2 and Figures S5–S10), and [^{13}C]-T-**1** (carbene center labeled with ^{13}C) to react with CH_3OD. The band at 1327.8 cm^{-1} shows a very strong ^{13}C isotopic shift of $-23.2\ \text{cm}^{-1}$. While using CD_3OH results in no significant isotopic shift of this band, with CH_3OD a blue-shift of $+2\ \text{cm}^{-1}$ is observed, suggesting that the carbene center directly interacts with the O–H/D group of methanol.

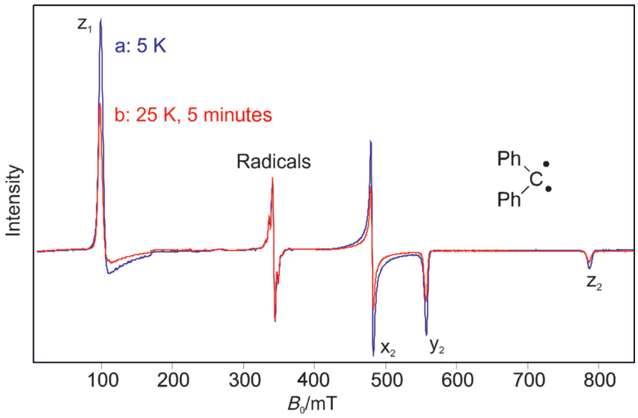

Figure 1. EPR spectra showing the reaction of T-**1** in an argon matrix doped with 1% methanol. a) Matrix at 5 K showing the triplet spectrum of **1** with the zero-field splitting (zfs) parameters $D=0.417\ \text{cm}^{-1}$, $E=0.019\ \text{cm}^{-1}$. b) After annealing for 5 minutes at 25 K 42% of the signal intensity of T-**1** is lost. The signals of the radicals are formed during the initial photolysis of the precursor and do not change in intensity during annealing.

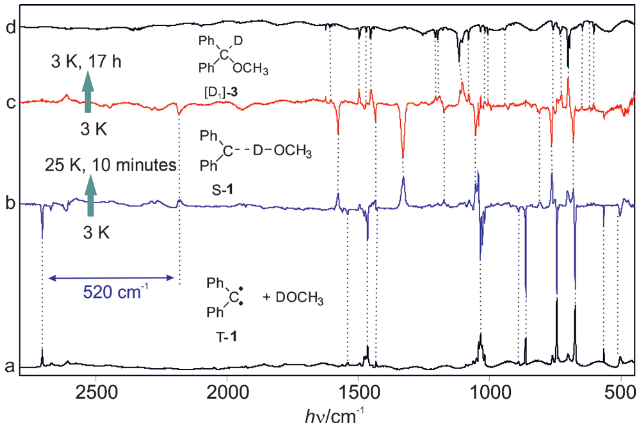

Figure 2. IR spectra showing the formation of the complex between S-**1** and CH_3OD. a) T-**1** in Ar doped with 1% CH_3OD at 3 K. b) Difference IR spectrum of the same matrix showing changes after annealing for 10 minutes at 25 K. Bands pointing downwards assigned to T-**1** and CH_3OD are disappearing, and bands pointing upwards assigned to the complex between S-**1** and CH_3OD are appearing. c) Difference IR spectrum of the same matrix showing changes after 17 h at 3 K, and bands pointing downwards are assigned to the complex between S-**1** and CH_3OD. Bands pointing upwards are assigned to [D_1]-**3**. d) IR spectrum of [D_1]-**3** matrix-isolated in argon at 3 K.

The labile intermediate shows an O–H stretching vibration at 2802 cm^{-1} (Figure S7), which corresponds to a huge red-shift of 864 cm^{-1} if compared to matrix-isolated CH_3OH. The O–D red-shift is 520 cm^{-1} (Figure 2). This evidences that the intermediate is a very strongly hydrogen-bonded complex between carbene **1** and methanol. Since this complex is EPR silent, we conclude that the singlet state S-**1** is acting as hydrogen bond acceptor for methanol rather than the triplet state T-**1**. This is confirmed by DFT calculations, which predict an IR spectrum of the S-**1**–methanol complex that is in excellent agreement with the experimental spectrum.

The highly polar S-**1** state is stabilized by hydrogen-bonding with methanol by -7.7 kcal mol^{-1}, whereas T-**1** forms only a weak van der Waals complex with a binding energy of -1.8 kcal mol^{-1} (B3LYP/6-311++G(d,p)+ZPE, Figure 3). Thus, a single molecule of methanol stabilizes S-**1** enough to make it thermodynamically more stable than T-**1** even in an unpolar environment such as solid argon.

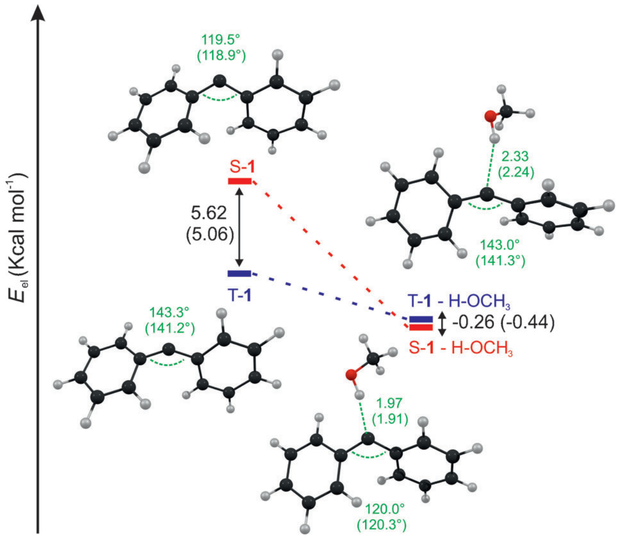

Figure 3. Relative energies of T-**1**, S-**1**, and their most stable complexes with methanol. Calculations performed at the (U)B3LYP/6-311++G(d,p) and (U)B3LYP-D3/6-311++G(d,p) (in parenthesis) levels of theory. The bond angles at the carbene centers and the non-bonding C···HO distances are shown in green.

To elucidate the reaction mechanism, we measured the kinetics of the rearrangement of the complex between S-**1** and CH_3OH, CH_3OD, and CD_3OH at 3 and at 12 K. First-order kinetics was found, and with CH_3OH and CD_3OH the rate was determined to $6.8\times10^{-5}\pm0.2$ s^{-1}, whereas with CH_3OD a rate of $1.3\times10^{-5}\pm0.2$ was observed, corresponding to a kinetic isotope effect (KIE) of 5. Between 3 and at 12 K the rates are independent of temperature, and thus the Arrhenius activation barrier for the rearrangement is zero. This is strong evidence for a tunneling mechanism.

The most likely mechanism for the formation of ether **3** from the S-**1**–methanol complex is proton transfer to form the ion pair **6** followed by combination of the ions to give **3**. This is in accordance with the observation of Kirmse et al. that in solution diarylcarbenes react with alcohols to give diarylcarbenium ions.[8] Kohler and co-workers measured a time constant for this proton transfer of only 9 ps in methanol.[12] DFT calculations in the gas phase predict that the reaction of the S-**1**–methanol complex to **3** is highly exothermic (-55 kcal mol^{-1}, B3LYP/6-311++G(d,p)+ZPE, Figure S12) and the ion pair **6** rather corresponds to a transition state than a reaction intermediate. In an unpolar argon matrix, we do not expect the ion pair to be an intermediate. However, in polar solvents the ion pair should be long-lived enough to be detected spectroscopically.

The results presented here require to re-evaluate previously published data on spin selective reactions of carbenes. Although the reaction of **1** with methanol is indeed spin specific as outlined in Scheme 1, the basic assumption that **1** and related carbenes have triplet ground states in all solvents is wrong. The singlet state of a carbene can become more stable than the triplet state by hydrogen bonding with a single molecule of alcohol, even if ΔG_{ST} is larger than -5 kcal mol^{-1} in the gas phase. Since many triplet carbenes have singlet–triplet gaps in this range, we expect that this type of singlet-state stabilization is of general importance for carbene reactions not only with alcohols, but also with other solvents and reagents that can act as hydrogen bond donors. This effect is due to specific solvation and goes beyond the general stabilization of the polar singlet states of carbenes with respect to the less polar triplet states with increasing solvent polarity.

Interestingly, while the reaction of T-**1** in methanol-doped argon at 25 K is fast, no reaction is observed in bulk methanol at the same temperature, and the EPR spectra show very strong signals of T-**1**. This could be related to methanol molecules involved in the hydrogen-bond network in solid methanol being weaker hydrogen-bond donors than matrix-isolated methanol molecules. Since for the S-**1**–methanol complex in the gas phase the singlet state is calculated to be only 0.5 kcal mol^{-1} more stable than the triplet state, in bulk methanol the order of stability might be reversed. This opens a whole range of new possibilities for controlling the spin state of carbenes by rational design of solvent systems, for example, solvent mixtures with only low concentrations of methanol or more hydrophobic alcohols as solvents.

The concept presented here of switching the ground state multiplicity of a molecule by solvent interactions represents an unique way to control chemical reactivity. This new principle not only contributes to the understanding of carbene reactivity in solution, but more importantly, it paves the way to design new carbene reactions by tailoring the solvent system.

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