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Regiochemical Substituent Switching of Spin States in Aryl(trifluoromethyl)carbenes

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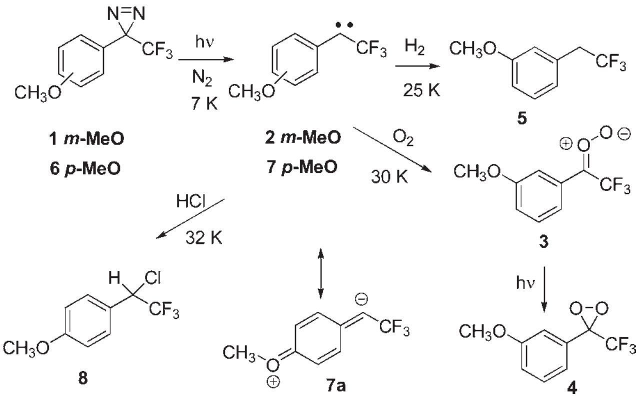
Supporting Information

ABSTRACT: Although aryl(trifluoromethyl)diazirines have achieved great popularity in photoaffinity labeling applications, the properties of the corresponding carbenes have not been as widely explored. Here, low-temperature matrix-isolation spectroscopy and reactivity studies indicate that in contrast to *m*-methoxyphenyl(trifluoromethyl)carbene and most known aryl(CF_3)carbenes, the para isomer is a ground-state singlet rather than triplet. DFT calculations support these results as well as the notion that the *p*-CH_3O group stabilizes the singlet carbene via resonance. These results may have relevance to the wide range of substituted aryl(CF_3)diazirines in photoaffinity applications.

Aryl(trifluoromethyl)diazirines enjoy great popularity in photoaffinity labeling applications.[1] Despite their widespread use, however, significant gaps exist in the understanding of the chemistry and electronics of the corresponding aryl(trifluoromethyl)carbenes.[2] In fact, the fundamental issue of ground-state multiplicity in these species has not been examined extensively either experimentally or theoretically. Electron paramagnetic resonance (EPR) spectra reported for phenyl(trifluoromethyl)-[3] and *p*-tolyl(trifluoromethyl)carbene[4] at 77 K indicate that the triplets are either the ground states or are nearly degenerate with singlet ground states. Solution trapping rates determined by laser flash photolysis allowed Platz and co-workers to estimate that the singlet tolyl(CF_3)carbene lies 0.5−1.5 kcal/mol above the triplet.[4] More recently, it has been shown both experimentally and theoretically that the singlet−triplet energy gap in 4,4′-biphenyl(CF_3)carbene depends on the polarity of the medium, with the singlet being the ground state in polar solvents.[5] Sander's group[6] and ours[7] have reported that phenyl(trifluoromethyl)carbene reacts readily with O_2 and H_2, respectively, at cryogenic temperatures; both reactions are characteristic of ground-state triplets. On the other hand, our group has recently shown that 2-benzothienyl(CF_3)carbene is a ground-state singlet.[8] Hence, how the carbene spin states are influenced by the wide array of substituents utilized in photoaffinity applications is an important but open question.[1] Herein we report experimental and theoretical studies demonstrating that the ground-state multiplicity of aryl(trifluoromethyl)carbenes may be tuned selectively via surprisingly modest substitution changes.

The known[9,10] *m*-methoxyphenyldiazirine **1** was synthesized from the corresponding ketone by a slight modification of literature procedures. Irradiation of **1** in a N_2 matrix at 7 K with 366 nm light[11] converted the diazirine cleanly to carbene **2** (Scheme 1). The IR spectra of **2** fit density functional theory (DFT) predictions at the B3LYP/6-31+G(d,p) level[12] reasonably well, though it was not possible to distinguish between the four possible conformations of the carbene or between the triplet and singlet states on this basis. The UV−vis spectrum of **2**, however, exhibited considerable structure, as is typically observed for triplet arylcarbenes (Figure 1).[13] In particular, time-dependent (TD) B3LYP calculations[12] for triplet **2** (especially the syn,syn lowest-energy conformer) paralleled the experimental UV−vis absorptions; the calculated spectrum for singlet **2** did not match that observed.

Scheme 1



The carbene was stable under further irradiation, regardless of wavelength, although minor changes in the IR and UV−vis spectra could be detected, possibly signaling conformational changes. EPR spectra[10] generated by irradiation of **1** in a perfluoro-2-*n*-butyltetrahydrofuran glass at ca. 90 K displayed typical triplet carbene signals,[4] with $|D/hc|$ and $|E/hc|$ values of 0.519 and 0.030 cm^{-1}, respectively. A second smaller set of signals corresponding to $|D/hc| = 0.532\ cm^{-1}$ and $|E/hc| = 0.031\ cm^{-1}$ were also detected, presumably arising from a different carbene conformer. These values are similar to those reported for triplet *p*-tolyl(trifluoromethyl)carbene ($|D/hc| = 0.5215\ cm^{-1}$, $|E/hc| = 0.0305\ cm^{-1}$)[4] and phenyl(trifluoromethyl)carbene ($|D/hc| = 0.5098\ cm^{-1}$, $|E/hc| = 0.0249\ cm^{-1}$).[3]

The reactivity of **2** confirmed its triplet multiplicity. Numerous studies[6] have shown that triplet carbenes react rapidly with O_2 at low temperatures, whereas singlet carbenes are unreactive under the same conditions. Warming a 0.5% O_2-doped nitrogen matrix containing **2** to 30 K readily converted the carbene primarily to carbonyl oxide **3**, which was identified through comparison of the product IR bands to those from B3LYP calculations.[10] A strong,

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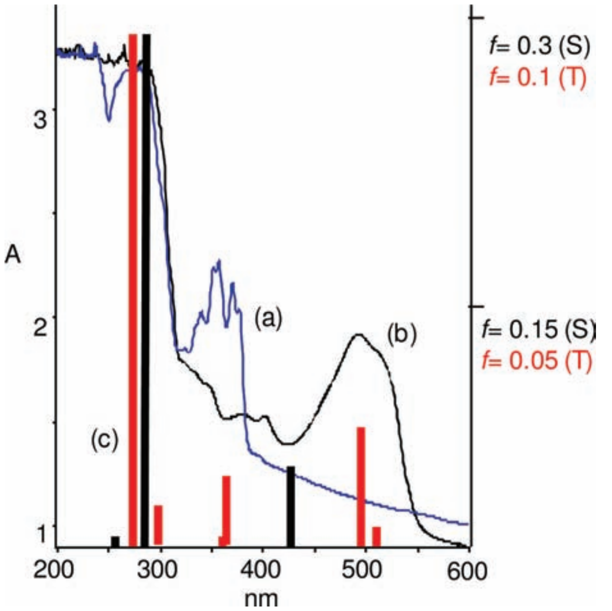


Figure 1. UV−vis spectra of *m*-diazirine **1** in N_2 at 7 K before (a, in blue) and after (b, in black) irradiation at 366 nm for ca. 12 h. (c) TD B3LYP-predicted transitions for the syn,syn conformations of singlet (black) and triplet (red) *m*-carbene **2**. Calculated *f* value scales are shown at the right.

very broad absorption was observed with a maximum at ca. 400 nm in the UV−vis spectrum, similar to that reported for the corresponding phenyl(trifluoromethyl)carbene−O_2 trapping product.[6] As demonstrated in analogous systems, subsequent irradiation of the matrix at 546 nm transformed **3** to the corresponding dioxirane **4**. Previous work in our group[7] has shown that a variety of triplet carbenes (but not singlets) add H_2 at very low temperatures, presumably via a tunneling-assisted H-abstraction/recombination process. As with triplet phenyl(trifluoromethyl)carbene,[7] annealing in an Ar matrix containing 2% H_2 to 25 K converted carbene **2** to hydrogenated product **5**. However, in contrast to singlet carbenes, **2** did not appear to react with HCl in doped matrices up to the matrix degradation temperatures of ca. 35 K.

The behavior of the corresponding *p*-methoxycarbene was dramatically different. The known[9,10] diazirine precursor **6** was synthesized in similar fashion to the meta isomer. Irradiation of **6** isolated in a N_2 matrix at 7 K using 366 nm light converted it to carbene **7**. The IR spectrum of **7** was similar to that calculated at the B3LYP level for the singlet carbene, and the fit to that predicted for the triplet carbene conformers was marginally less satisfactory.[10] The UV−vis spectrum of the carbene was dominated by an intense absorption at 330 nm, as predicted by TD B3LYP calculations for singlet carbene (289 nm, f = 0.51; Figure 2). Multiple transitions between 428 and 290 nm predicted for triplet **7** were not observed. Moreover, **7** showed a broad absorption at 820 nm (TD 972 nm), characteristic of σ−p transitions of singlet carbenes.[10,14]

The low-temperature reactivity of **7** also was consistent with singlet rather than triplet multiplicity. Regardless of concentration, **7** did not react on warming in O_2-doped matrices up to their degradation temperatures at ca. 35 K. Similarly, no reaction with H_2 could be observed under conditions where triplet carbenes react. However, warming singlet **7** in HCl-doped matrices (0.5% in N_2, 32 K) caused the IR bands of **7** to disappear and those of the corresponding trapping product **8** to grow.[10]

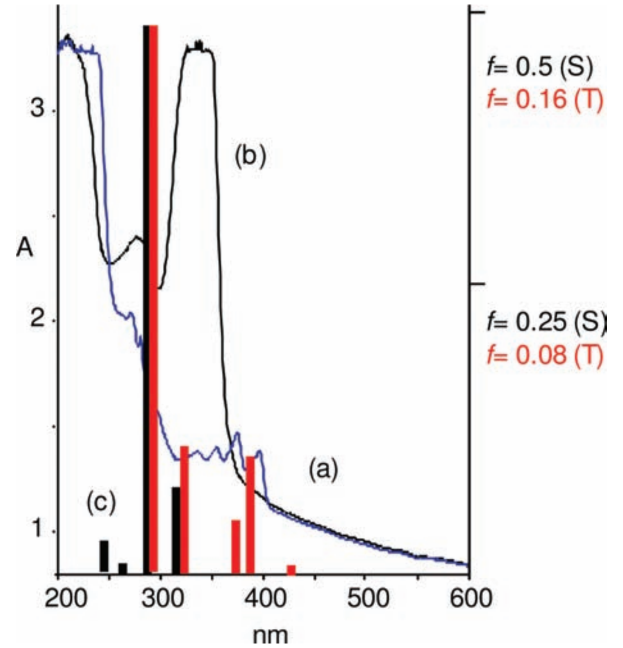


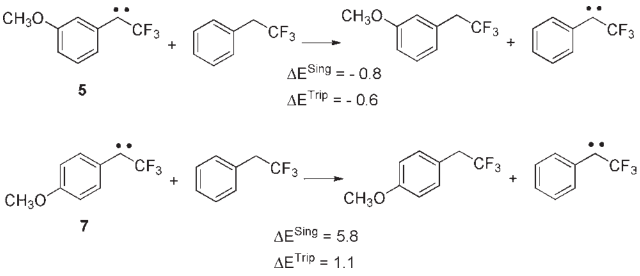
Figure 2. UV−vis spectra of *p*-diazirine **6** in N_2 at 7 K before (a, in blue) and after (b, in black) irradiation at 366 nm for ca. 12 h. (c) TD B3LYP-predicted transitions for the syn conformations of singlet (black) and triplet (red) *p*-carbene **7**. Calculated *f* value scales are shown at the right.

Finally, irradiation of **6** under the same low-temperature perfluoro-2-*n*-butyltetrahydrofuran glass conditions as for the meta isomer **1** gave no triplet EPR signals.

Calculations[12] support the experimental indications that *m*-methoxycarbene **2** is a ground-state triplet, whereas the para isomer **7** is a singlet. Others have shown that B3LYP calculations afford satisfactory approximations to arylcarbene singlet−triplet (ST) energy gaps.[15] Comparisons to results obtained using higher levels of theory as well as from experiments indicate, however, that the DFT methodology tends to overestimate the stability of triplet carbenes relative to singlets by 1−3 kcal/mol. B3LYP/6-31+G(d,p) calculations on the four planar conformations of *m*-carbene **2** gave ST energy gaps (positive values signifying triplet lowest) of 3.7−4.4 kcal/mol. A calculated overstabilization of the triplet carbene[15] by as much as 3 kcal/mol would still predict a triplet ground state. In contrast, the calculations predicted ST energy gaps of −0.4 and −0.7 kcal/mol for the syn and anti conformers, respectively, of *p*-carbene **7** (or, ca. −2.4 and −2.7 kcal/mol after correction for ca. 2 kcal/mol overstabilization of the triplet[15]).

Although lone-pair π donation is well-known to stabilize singlet carbenes,[14] it is not obvious that interaction with the *p*-methoxy group in **7** would be sufficient to lower the singlet below the triplet. Calculations have predicted that the triplet and singlet states are approximately degenerate in the corresponding parent carbene, *p*-methoxyphenylcarbene.[15b] However, we have shown recently that in comparison with H, CF_3 groups stabilize singlet carbenes relative to triplet carbenes by a small but systematic amount.[16] We have described calculational evidence that the strongly electron-withdrawing trifluoromethyl group causes rehybridization of the adjacent carbenic lone pair through a Bent's rule effect, thus selectively stabilizing singlet carbenes relative to triplets. For example, phenyl(trifluoromethyl)carbene has an ST energy gap of 4.0 kcal/mol (vs 5.4 kcal/mol for phenylcarbene) at the B3LYP/6-31+G(d,p) level.[16] Thus, the inherently small ST gap in

Scheme 2. Isodesmotic Comparison at the B3LYP/6-31+G(d,p) Level (Energies in kcal/mol)



phenyl(trifluoromethyl)carbene enables the observed substituent switching of the multiplicity in **2** versus **7**.

Others have shown the utility of isodesmotic calculations in probing the relative effects of carbene substituents on the energies of singlet versus triplet carbenes.[17] Such comparisons between *m*-methoxycarbene **2** and phenyl(CF_3)carbene (Scheme 2) suggest a negligible influence of the *m*-CH_3O group on either the triplet or singlet energies. In contrast, although the *p*-CH_3O group stabilizes triplet **7** relative to the phenylcarbene by a small amount, singlet **7** is stabilized considerably. As noted similarly by Giese and Hadad in studies of a variety of related singlet phenylcarbenes,[15b] the computed geometries and natural bond orbital (NBO) charge distributions of **2** and **7** show negligible differences related to conjugation. However, the importance of resonance structure **7a** in the singlet carbene is reflected clearly in the very different barriers for Ar—carbene and Ar—O rotation predicted for the para and meta isomers. Both rotational barriers were calculated to be significantly larger for the para singlet carbene **7** (ca. 21 and 6 kcal/mol, respectively) than for the corresponding meta singlet **2** (ca. 14 and 3 kcal/mol).[18]

In summary, we have shown that appending a *p*-methoxy group to phenyl(trifluoromethyl)carbene switches its ground state from a triplet to a singlet. In contrast, the *m*-methoxy isomer, where direct resonance interaction between oxygen and the singlet carbene is precluded, is a triplet. It is the inherently narrow ST energy gap in phenyl(trifluoromethyl)carbene that allows the ground-state multiplicity to be toggled by substituent effects.[16] Moreover, the photochemical stability of CF_3-substituted carbenes at low temperatures, relative to other substituted phenylcarbenes,[13] makes these systems particularly useful for probing substituent effects.[19] These results may have some relevance in fine-tuning the properties of aryl(CF_3)carbenes in photoaffinity applications.

■ ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Experimental details, spectra, results of DFT calculations, and complete ref 12. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) See the Supporting Information for experimental details as well as additional IR, UV—vis, and EPR spectra.

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(18) The corresponding CH_3 and CF_3 rotational barriers for triplet **2** and **7** range from 2.3 to 3.5 kcal/mol.

(19) A referee noted the interesting differences between the UV—vis spectra predicted by TD DFT for the meta and para triplet carbene isomers shown in Figures 1 and 2. As described in depth by Matzinger and Bally (ref 13b), the electronic excited states of triplet phenylcarbenes are particularly mixed configurationally and complex to interpret. As illustrated in the TD DFT molecular orbital mixing breakdowns listed for triplet carbenes **2** and **7** in the Supporting Information, the methoxy group adds yet another level of complexity that is difficult to analyze through simple orbital schemes. We are continuing to investigate the effect of substituents on the spectra of triplet and singlet aryl(trifluoromethyl)carbenes.