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Complexation of dichlorocarbene by methylanisoles

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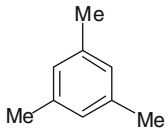
ABSTRACT

Dichlorocarbene generated by laser flash photolysis of dichlorodiazirine readily forms UV–vis active π- and *O*-ylidic complexes with methylanisole derivatives.

We recently reported that dichlorocarbene (CCl_2), generated by laser flash photolysis (LFP) of dichlorodiazirine, formed π- and *O*-ylidic complexes with aryl ethers such as anisole, 1,3-dimethoxybenzene, and 1,3,5-trimethoxybenzene.[1] Detected by UV–vis spectroscopy, these complexes significantly retarded the addition of CCl_2 to tetramethylethylene (TME). Structures, energetics, and spectral assignments for the complexes were provided by computational studies based on density functional theory.

Mesitylene (**1**) and durene (**2**) also retarded the addition of CCl_2 to TME, by factors of 15 and 21, respectively, but we did not observe the UV absorptions computed for their CCl_2 complexes in the 300–350 nm region.[1] The sensitivity of our LFP detection system may possibly be reduced in this spectral region due to strong background absorption by dichlorodiazirine (λ_{max} 324, 359 nm in pentane).[2]



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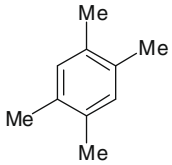

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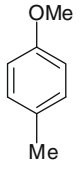
It occurred to us that the substitution of a methoxy group for a proton on arenes such as **1** or **2** would shift the electronic spectra of their CCl_2 complexes toward the red, into the 400–500 nm region, where they might be more readily detected. For example, the UV–vis spectrum of the CCl_2/anisole complex features *O*-ylidic and π-complex absorptions at 460 and 500 nm, respectively.[1] In the event, this proved a successful strategy, enabling us to describe here the CCl_2 complexes of 4-methylanisole (**3**), 2,4-dimethylanisole (**4**), 2,4,6-trimethylanisole (**5**), and 2,3,5,6-tetramethylanisole (**6**).



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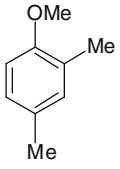

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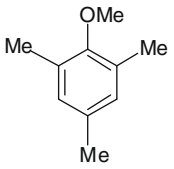

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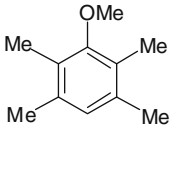

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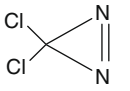
Compounds **3** and **4** were commercially available, while trimethylanisole **5** was obtained by methylation of 2,4,6-trimethylphenol with dimethyl carbonate and a catalytic quantity of tetrabutylammonium iodide (93 °C, 19 h).[3] Tetramethylanisole **6** was similarly prepared from the corresponding phenol using 2,3,5,6-tetramethylphenol obtained by *ortho*-methylation of 2,3,5-trimethylphenol with ethyl(iodomethyl)zinc.[4] Compounds **5** and **6** were characterized by ^{1}H and ^{13}C NMR spectroscopy (see Figs. S-1–S-4 in the Supplementary data), and by mass spectrometry.

LFP of dichlorodiazirine (**7**)[2] in 1:1 (v/v) pentane solutions of methylanisoles **3**–**6** affords the UV–vis spectra shown in Figure 1. Each spectrum exhibits two distinct absorption peaks in the 450–550 nm region, which we attribute to CCl_2 complexes.



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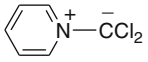

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Table 1 records the wavelengths of these species, and includes the previously reported *O*-ylidic and π-complexes of the parent anisole.[1]

We note that both absorptions, in each spectrum of Figure 1, shift to longer wavelengths in response to each additional methyl substituent imposed on the parent anisole structure. CCl_2 usually[5] (although not always[6]) behaves as an electrophile, so that this observation accords with enhanced electron donation by the methylanisole derivative to an electrophilic CCl_2, buttressed by the successive methyl group substitutions.

Theoretical considerations generally support this view: calculations based on density functional theory (see the Supplementary data for details) provide structures and energetics for the transient CCl_2/methylanisole species and largely rationalize their absorption spectra. Computed complexation enthalpies are low for all identified complexes, spanning a range from −2.6 to −4.3 kcal/mol, whereas the (standard) free energies are well into the positive realm (~4–5 kcal/mol, PBE/6-311+G(d); see Table S-1 in the Supplementary data). Thus, the binding of individual complexes is weak. However, there are many CCl_2/methylanisole configurations with slightly variant carbene-ligand orientations and/or interaction distances, all of approximately equal energies, and so the net number of complexes formed is sufficiently large to be detected.

The binding enthalpies tend to become more favorable as the degree of methylation increases, in particular for the π-type complexes, whereas the binding enthalpies of the *O*-ylidic complexes lie within a smaller range of −2.6 to −3.5 kcal/mol. Generally, binding increases with increasing electron richness of the aromatic ring, but we find no simple relationship between net atomic charge (C or O) at a particular methylanisole binding site and binding enthalpy. (See Fig. S-9 in the Supplementary data for net atomic charges of the methylanisoles.)

Table 1
Absorption maxima of CCl_2-methylanisole complexes[a]

Ligand	λ_{max} (nm)	
Anisole[b]	460	500
3	484	516
4	488	520
5	508	532
6	516	548

[a] In 1:1 (v/v) pentane/ligand solutions.
[b] From Ref. 1.

Illustrative examples of typical *O*-ylidic and π-complexes are shown in Figure 2, using 2,4-dimethylanisole as the representative ligand. In the *O*-ylidic complexes (Fig. 2, left-hand structure), the C(carbene)-O distance is in the 2.4–2.6 Å range, and the O atom rehybridizes toward tetrahedral coordination. The smallest C(carbene)-C(phenyl) interaction distances in the π-complexes (Fig. 2, center) are slightly longer at 2.6–2.9 Å; C(carbene) is always located vertically above a C(phenyl) atom, and one of the Cl atoms points toward the center of the phenyl ring.

The electronic transitions of lowest energy computed for each complex (TD-B3LYP/6-311+G(d)//PBE/6-311+G(d)) are also listed in Table S-1. As detailed previously,[1] the *O*-ylidic species was computed to be the thermodynamically most stable of the parent CCl_2/anisole complexes (ΔG = 3.7 kcal/mol), while the relative stabilities

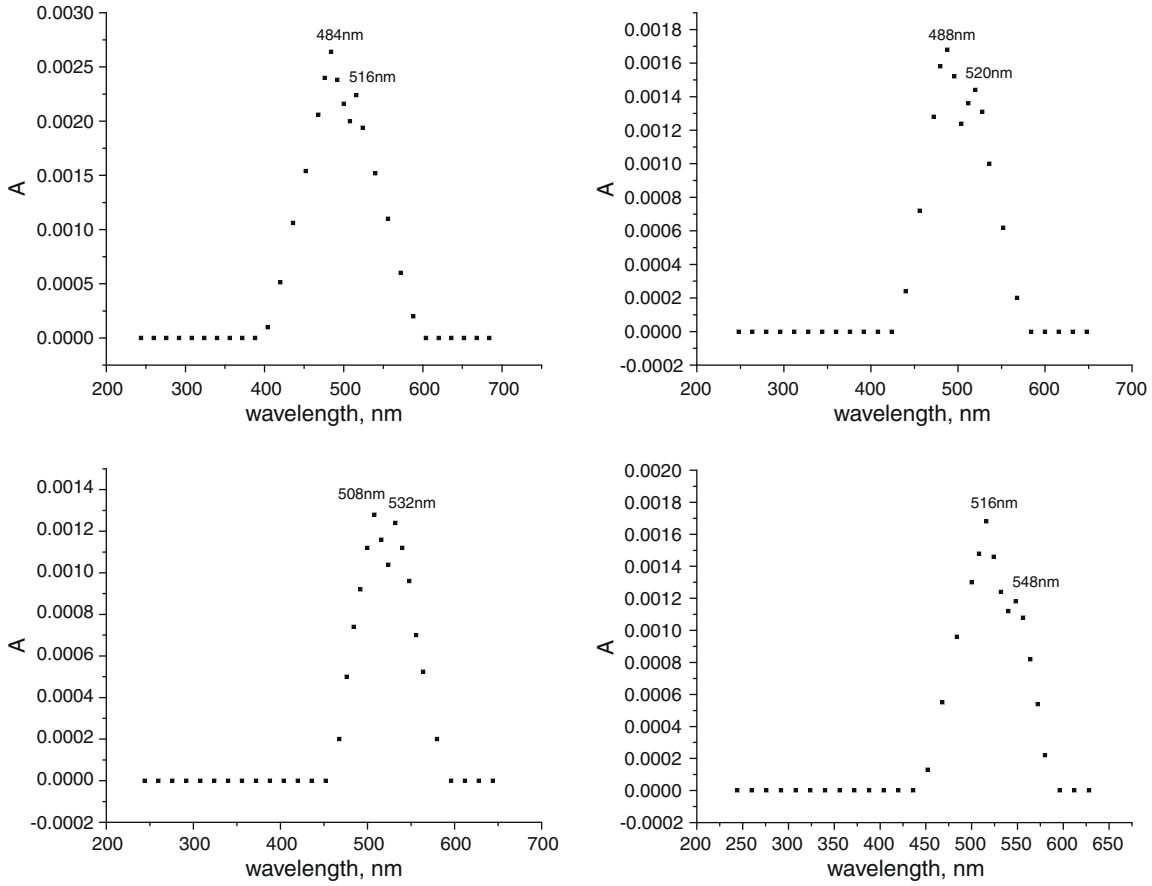

Figure 1. Complexes of CCl_2 with (upper left) 4-methylanisole (**3**); (upper right) 2,4-dimethylanisole (**4**); (lower left) 2,4,6-trimethylanisole (**5**); (lower right) 2,3,5,6-tetramethylanisole (**6**). All spectra were determined in 1:1 (v/v) pentane-ligand solutions, under nitrogen, 150 ns after the laser flash. The axes of each graph are labeled 'A' (for absorbance) and 'wavelength, (nm).'

of the three different π-complexes were about equal ($\Delta G \sim 4.4$–5.0 kcal/mol). The experimental absorption around 460 nm for CCl_2/anisole was assigned to the *O*-ylidic complex for which a strong absorption band with significant O→p(CCl_2) character was predicted at 486 nm (f = oscillator strength = 0.11). The absorption observed at 500 nm was assigned to the π-complexes collectively; individual absorbances [π(anisole)→p(CCl_2)] were predicted at 513 nm ($f \sim 0.1$) for both the C2 and C4 coordinated complexes and at 534 nm ($f = 0.08$) for C6 coordination.[1]

In the present study, the absorptions of the CCl_2/4-methylanisole complexes are red-shifted by about 20 nm relative to the anisole complexes. The *O*-ylidic CCl_2/**3** complex is computed to be the most stable and to absorb at 507 nm ($f = 0.14$), so that we assign this species as responsible for the observed absorption at 484 nm (see Fig. 1). We have located π-complexes at every possible phenyl ring location (Table S-1), and sites C5 and C6 are particularly favorable for CCl_2 binding. The resulting complexes absorb at 544 nm ($f = 0.09$, C5) and 557 nm ($f = 0.08$, C6), respectively, consequently, we assign these complexes as the dominant contributors to the absorption observed at 516 nm (Fig. 1).

For CCl_2 and 2,4-dimethylanisole (**4**), the calculations find the **π**-complexes at the C1 and C6 binding sites to be the most stable (cf., Fig. 2, center); both sets of complexes are predicted to absorb around 570 nm with substantial intensities ($f \sim 0.1$), and we assign these complexes to the experimental absorption peak at 520 nm in Figure 1. The *O*-ylidic complex (Fig. 2, left) and π-complexes formed at C5 absorb about 30–35 nm further to the blue in the 535–540 nm region (both absorptions have $f = 0.12$), and we assign these complexes to the observed absorption peak at 488 nm in Figure 1.

In ligands **5** and **6,** the methyl group of the methoxy unit rotates to assume a position perpendicular to the aryl ring plane because of steric hindrance from the adjacent methyl groups on C2 and C6, thus diminishing π-donation by the methoxy group. Although the orbital energies of the upper occupied π-orbitals of the arene become less negative (i.e., are destabilized) from anisole to the methylanisoles **3** and **4**, the rotation of the methoxy group leads to a reversal of this trend for the HOMO's of **5** and **6** (Table S-2 in the Supplementary data). The energy of the donor orbital enters directly into the expression for the electronic transition energy and, as a result, the CCl_2 complexes of **5** and **6** are *computed* to experience blue shifts relative to analogous complexes formed with **3** and **4**. In contrast, the *observed* absorptions for the CCl_2 complexes of **5** and **6** are red shifted by 10–30 nm, relative to complexes with **4** (cf. the spectra in Fig. 1 and the data in Table 1). For CCl_2 and **5** we located complexes of equal stability ($\Delta G \sim 3.8$ kcal/mol) at C1 and C3 (the C1 complex is shown in Fig. 2, right) which should absorb at 490 nm and 511 nm, respectively, with $f \sim 0.1$. The *O*-ylidic complex is computed to be slightly less stable ($\Delta G \sim 4.4$ kcal/mol) and absorb slightly further to the blue at 464 nm ($f \sim 0.1$). Similarly, for CCl_2 and **6**, we compute **π**-complexes at C1 and C4 which absorb at 506 nm and 486 nm, respectively, with $f \sim 0.1$. Two absorptions of the *O*-ylidic complex should center around 455 nm with overall intensities similar to those of the π-complexes.

Table 2
Rate constants for the addition of CCl_2 to TME[a]

Solvent or additive	k_{add} (M^{-1} s^{-1})	k_{pent}/k_{add}
Pentane[b]	4.7×10^9	1.0
Anisole[c]	2.6×10^8	18
3	1.0×10^8	47
4	7.8×10^7	60
5	5.5×10^7	85
6	4.9×10^7	96

[a] At 25 °C; [pyridine] = 0.12 mM for anisole, **3**, and **4**; 2.4 mM for **5** and **6**.
[b] Rate constant from Ref. 8.
[c] Rate constant from Ref. 1.

In summary, for CCl_2 complexes with methylanisoles **5** and **6**, the calculations predict three absorption peaks in the 460–510 nm region of similar intensities and nearly equidistant spacing (~20 nm), whereas experiment shows only two distinct peaks in the 510–550 nm region (cf., Fig. 1 and Table 1). We are thus unable to make specific assignments of the CCl_2/**5** or CCl_2/**6** absorption spectra to individual complexes.

In keeping with previous observations,[1] complexation of CCl_2 with methylanisoles **3**–**6** diminishes the rate constants for the addition of CCl_2 to TME. We used the pyridine ylide method[1,7] to determine rate constants for the addition of CCl_2 to TME in pentane and in the presence of anisole and the methylanisoles; cf. Table 2.

The apparent rate of the formation of the CCl_2-pyridinium ylide **8**, measured at 404 nm in pentane or a pentane-additive solution, increased upon the addition of TME at a constant concentration of pyridine. A correlation of the observed rate constants for the formation of **8** versus [TME] was linear and its slope gave k_{add} for the addition of CCl_2 to TME.[7a] In this way, we determined that CCl_2 generated by LFP of diazirine **7** adds to TME in pentane with $k_{add} = 4.7 \times 10^9$ M^{-1} s^{-1}.[8] Repetition of this experiment in 1:1 anisole-pentane gave $k_{add} = 2.6 \times 10^8$ M^{-1} s^{-1}; see Figure 8 of Ref. 1 and Table 2, above.

Similarly, we measured k_{add} for the CCl_2-TME addition in 1:1 solutions of pentane and methylanisoles **3**–**6**. The results appear in Table 2, and the corresponding correlations of k_{obs} with [TME] are shown in Figs. S-5–S-8 of the Supplementary data. Table 2 reveals that successive methylations of anisole lead to increased retardation of CCl_2 addition to TME. One interpretation holds that CCl_2 complexes with increasingly methylated anisole derivatives are not only more stable, but also slower to transfer their complexed carbene to TME, possibly due to a combination of steric and stabilization effects. Alternatively, if complexation is reversible, the more

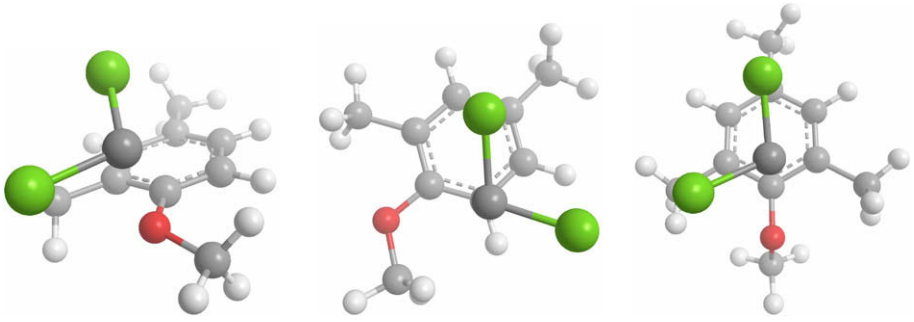

Figure 2. Perspective and depth-fading illustration of CCl_2/methylanisole complexes: *O*-ylidic CCl_2/2,4-dimethylanisole complex (left); CCl_2/2,4-dimethylanisole π-complex at C6 (center); CCl_2/2,4,6-trimethylanisole π-complex at C1 (right).

highly methylated anisoles may sequester more CCl_2 at equilibrium, thus leaving less free CCl_2 available for addition to TME.

Tri- and tetramethylanisoles **5** and **6** are more potent than their non-methoxy analogs, mesitylene (**1**) and durene (**2**), at retarding CCl_2 addition to TME: the ratios of k_{add} for **1** versus **5** and **2** versus **6** are 5.8 and 3.1, respectively.[9] These disparities probably reflect the additional stabilization conferred upon the mesitylene or durene CCl_2 complexes by substitution of the electron-donating methoxy group which converts them to complexes of **5** and **6**, respectively.

In conclusion, CCl_2 generated by LFP of dichlorodiazirine forms readily visualized π- and *O*-ylidic complexes with methylanisoles **3**–**6**. These complexes are UV–vis active and are substantiated by DFT computations. Complexation of CCl_2 by the methylanisoles retards the addition of the carbene to TME by factors of about 50–100.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.01.023.

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9. Values of k_{add} for **1** (3.3×10^8 M^{-1} s^{-1}) and **2** (1.5×10^8 M^{-1} s^{-1}) appear in Ref. 1.