

Singlet carbene stability: linear free-energy analysis of substituent effects

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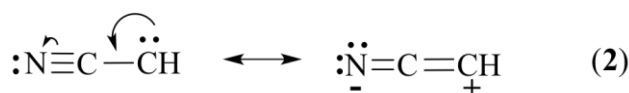
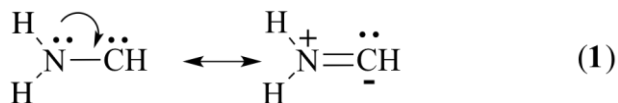
Abstract

The energies of a series of substituted methylene and methylcarbene singlet states were computed by quantum mechanical calculations at the CCSD(T)/cc-pVDZ//M06-2X/cc-pVDZ level. Stabilization energies relative to singlet methylene were correlated with polarizability, polar and resonance Hammett sigma constants using multiple regression analysis. The results revealed that most of the carbenes gave rise to inverse polar effects. It is concluded that separation of polar and resonance effects *via* linear free energy methods (LFE) fails for singlet carbenes with substituents directly attached to carbene carbons.

Keywords: Singlet carbene stability, linear free energy correlations, quantum computations

Introduction

The unique ability of carbenes to both donate and accept electron pairs has long been appreciated. Thus, singlet aminocarbene is stabilized by resonance donation of an electron pair from nitrogen into the empty carbon p-orbital (Eq. 1). By the same token, singlet cyanocarbene can be stabilized by donation of electron density from the filled p-orbital of the carbenic carbon into the π orbital network of the CN triple bond (Eq. 2).



The relative importance of the inductive properties of the substituents has received less attention. Since both the amino group and the cyano group are characterized as electron-withdrawing groups there is competition between the two electronic contributions. Likewise, fluorocarbene can also be stabilized by resonance donation of fluorine lone pairs but it is also a powerful electron-withdrawing group due to its high electronegativity.¹⁻⁴

The major objective of this study is to carry out a systematic LFE analysis of simple singlet carbenes stabilities using isodesmic equation **3** where R = H or CH₃ to determine whether the results would reveal accurate quantitative measures of the relative importance of resonance vs. other electronic contributions to carbene singlet stability.



Earlier authors have reported limited studies that suggest that this approach might be viable.⁵⁻⁷ Gronert, Keeffe and More O'Ferrall⁵ recently published studies of substituted phenylcarbene stabilities using a LFE approach that reported the complementary effects of resonance and inductive effects on carbene stabilization enthalpies (CSEs). Similarly, Keeffe and More O'Ferrall also reported good correlations of relative stabilities of a limited series of substituted simpler carbenes.⁶ Loudan, Moss and Houk have found good correlations with carbene stability for electron donating groups and R⁺ (electron donating resonance) constants.⁷

Results and Discussion

A series of substituted carbenes and methylcarbenes were optimized using the Gaussian09⁸⁻¹¹ package and the M06-2X hybrid functional of Zhao and Truhlar¹² and the cc-pVDZ basis set of Woon and Dunning.¹³ All structures were shown to be lowest energy conformers and proved to be electronic minima by normal coordinate analyses. Relative enthalpies and free energies were computed using equation **3** and are listed in Table 1.

The final analyses relied on higher level computations carried out at the CCSD(T)/cc-pVDZ //M06-2X/cc-pVDZ level. Comparisons of relative energies are listed in Table 2 including a list of the sigma values used in linear regression analyses.¹⁴

What is striking about relative energies of substituted methylenes and methylcarbenes is the fact that in every case, save one, each substituent resulted in stabilization of a given carbene despite large differences in expected resonance and inductive contributions. Even strongly electron withdrawing groups that do not have available lone pairs, e.g. N(CH₃)₃⁺, S(CH₃)₂⁺, are weakly stabilizing for methylcarbene, possibly by hyperconjugative interactions. Trimethylsilyl and t-butyl are both electron-donating groups that do not contain lone pairs and are weakly stabilizing. π -Electron acceptor substituents, e.g. cyano and nitro are weakly stabilizing, with acetyl a somewhat better electron acceptor. Both trifluoromethyl substituted carbenes were

destabilized relative to methylene and methylcarbene: -3.05 and -1.36 kcal/mol, respectively. The only other difference was the reversal of the relative stabilities of the trimethylsilyl systems.

Table 1. Relative stabilization enthalpies and free energies of substituted singlet methylenes and methylcarbenes: M06-2X/cc-pVDZ computed from Equation 3

Carbene: RCH	$\Delta(\Delta H)^a$	$\Delta(\Delta G)^a$	$\Delta(\Delta H)^a$	$\Delta(\Delta G)^a$
	R=H	R=H	R=CH3	R=CH3
RCH	0	0	0	0
RCF	31.38	31.21	25.77	25.29
RCCl	24.02	23.86	18.48	17.95
RCBr	22.87	22.71	17.38	16.74
RCCF ₃	-2.36	-2.22	-1.15	-1.64
RCNH ₂	61.16	60.10	52.99	51.97
RCOCH ₃	49.51	48.82	41.48	43.47
RCCH ₃	13.83	13.09	11.08	10.42
RCC ₆ H ₅	19.40	17.58	12.75	12.21
RCCN	11.55	11.45	9.42	8.68
RCC=O(CH ₃)	15.58	15.23	9.77	9.92
RCSCH ₃	45.78	44.64	35.80	34.34
RCOH	49.70	48.58	42.33	41.44
RCSi(CH ₃) ₃	2.38	4.65	1.97	1.51
RCOC=O(CH ₃)	35.99	34.65	35.79	34.91
RCS(CH ₃) ₂ ⁺	13.46	13.94	9.64	9.79
RCC(CH ₃) ₃	<i>b</i>	<i>b</i>	8.56	7.95
RCNCH ₃) ₃ ⁺	<i>b</i>	<i>b</i>	4.88	4.68
RCN(CH ₃) ₂	62.55	62.51	50.98	51.36
RCCCH	22.66	22.74	18.63	18.77
RCNHC=O(CH ₃)	52.40	51.47	45.36	47.12
RCNO ₂	<i>b</i>	<i>b</i>	11.94	11.45
RCSH	40.91	39.56	29.57	28.76
RCC=O(H)	<i>b</i>	<i>b</i>	42.33	41.44
RCCH=CH ₂	18.82	18.18	14.50	14.00
RCSO(CH ₃)	38.34	37.45	24.56	24.20
RCCO ₂ CH ₃	9.46	8.76	6.39	5.90
RCC=O(CN)	8.22	7.77	8.52	8.10
RCC=O(F)	7.25	6.57	5.98	5.35

^a kcal/mol ^b rearranges

Table 2. Relative stabilization energies of substituted methylenes and methylcarbenes: CCSD(T)/cc-pVDZ //M06-2X/cc-pVDZ

Carbene: RCH	$\Delta(\Delta E)^a$		σ_α^b	σ_F^c	$\sigma_{R^+}^d$
	R=H	R=CH3			
RCH	0	0	0	0	0
RCF	30.59	26.57	0.13	0.44	-0.25
RCCI	23.72	19.24	-0.43	0.45	-0.17
RCBr	22.34	18.21	-0.59	0.45	-0.15
RCCF ₃	-3.05	-1.36	-0.25	0.44	0.00
RCNH ₂	57.47	51.67	-0.16	0.14	-0.52
RCOCH ₃	47.46	41.88	-0.17	0.25	-0.42
RCCH ₃	10.34	9.87	-0.35	0.00	-0.08
RCC ₆ H ₅	17.16	12.56	-0.81	0.10	-0.22
RCCN	10.89	9.40	-0.46	0.60	0.00
RCC=O(CH ₃)	13.51	8.78	-0.55	0.26	0.00
RCSCH ₃	43.93	36.13	-0.68	0.25	-0.27
RCOH	47.99	42.71	-0.03	0.30	-0.38
RCSi(CH ₃) ₃	0.65	1.28	-0.72	-0.02	0.00
RCOC=O(CH ₃)	33.46	29.25	NA	NA	NA
RCS(CH ₃) ₂ ⁺	10.63	8.99	NA	NA	NA
RCC(CH ₃) ₃	NA	7.42	-0.75	0.00	-0.06
RCNCH ₃) ₃ ⁺	NA	4.31	NA	NA	NA
RCN(CH ₃) ₂	58.93	50.28	-0.44	0.10	-0.64
RCCCH	20.72	18.59	-0.60	0.23	0.00
RCNHC=O(CH ₃)	50.01	47.17	NA	NA	NA
RCNO ₂	NA	13.53	-0.26	0.65	0.00
RCSH	39.25	30.24	-0.55	0.28	-0.25
RCC=O(H)	NA	7.38	-0.46	0.31	0.00
RCCH=CH ₂	16.63	14.32	-0.50	0.06	-0.16
RCSO(CH ₃)	37.87	26.91	-0.65	0.40	0.00
RCCO ₂ CH ₃	9.14	6.62	-0.49	0.24	0.00
RCC=O(CN)	8.18	7.26	-0.60	0.66	0.00
RCC=O(F)	6.69	5.76	NA	NA	NA

Sigma values are taken from Hansch, Leo and Taft Table IX.¹⁴ ^a kcal/mol. ^c polar. ^b polarizability. ^d resonance

In addition, fluorcarbene was examined at the CCSD(T)/cc-pVQZ level to test the importance of more comprehensive basis sets. The resulting stabilization energy was 28.5 kcal/mol vs 30.5

kcal/mol (**Table 2**). Application of this protocol to more complex systems was not considered feasible. See Supplemental Information for data.

Regression analysis of data in **Table 2** for substituted methylenes led to equation **4** ($R^2 = 0.89$; $SD=6.4$).

$$\Delta(\Delta E) = 1.90 - 3.99 \sigma_{\alpha} + 12.6 \sigma_{\text{F}} - 96.6 \sigma_{\text{R}^+} \quad (4)$$

Similarly, regression analysis of the relative energies of the methyl-substituted carbenes in **Table 2** gave equation **5** ($R^2 = 0.90$; $SD=0.19$).

$$\Delta(\Delta E) = 3.0 - 0.24 \sigma_a + 11.8 \sigma_{\text{F}} - 82.1 \sigma_{\text{R}^+} \quad (5)$$

Both equations lead to the conclusion that resonance effects are dominant and stabilizing factors. The algebraic signs of the polarizability and field effects are contrary to expectations for substituents directly attached to an electron-deficient carbon. For example, the data for fluorocarbene according to Equation 4 leads to the conclusion that the field contribution (+5.5 kcal/mol) for the strongly electronegative fluorine atom is in the opposite direction from the commonly accepted trend, i.e. destabilizing. Complete tables of the relative contributions of each of the three terms are given in the Supplementary Materials. The fact that earlier LFE studies^{5,6} generated correlations with appropriate algebraic signs for polarizability and field effects is attributable the mitigating effects of the aromatic rings with phenylcarbenes and/or smaller sample size in the latter case.

As an alternative approach, dual parameter correlations were sought with variations of **F** (field) and **R** (resonance) parameters originally developed by Swain, et al.^{15,16} and modified by Taft, et al.¹⁷ These workers developed parameters that assigned non-zero values to sigma constants for π systems that might be expected to partially delocalize the lone pair on carbene centers. For example, the cyano and carbomethoxy groups were assigned positive R values ranging from 0.15 to 0.71 and 0.11 to 0.67, respectively. i.e. electron-withdrawing. Regression analyses were performed on the $\Delta(\Delta E)$ values in **Table 2** and four different sets of F and R values. None of the correlations proved to be satisfactory in terms of r^2 and/or standard deviations (see Supplemental Information). In each case ρ_{F} values were uniformly positive leading to inverse field energy contributions to carbene stability. As an example, the regression equation produced for substituted methylenes using F and R values from **Table V** in Taft's compilation¹⁷ is shown in equation **6** ($R^2 = 0.92$; $SD=6.1$).

$$\Delta(\Delta E) = 3.7 + 32.6 F - 31.8 R \quad (6)$$

None of our other efforts to correlate the stabilization energies with various computed properties were fruitful, e.g. NBO natural charges on carbene centers, carbene-X bond lengths or Wiberg CH-X bond indices.^{18,19} Likewise, NBO perturbation analyses which were expected to

reveal 2nd order perturbation stabilizations involving lone pair donations to unoccupied p orbitals on carbene centers were also not forthcoming. For example results with aminocarbene, fluorocarbene, and all others with neighboring lone pairs did not itemize these interactions, but treated the C-X bonds as double bonds. Methylcarbene displayed a partially “empty” p-orbital with 0.16 e occupancy and 46.9 kcal/mol second-order perturbation energy with the adjacent parallel C-H bond.² Similarly, the interaction of the bonding C-Si orbital (occupancy = 0.076 e) that is parallel to the “empty” p-orbital on the carbene center gives rise to a second order perturbation energy of 13.4 kcal/mol. Other systems containing adjacent π -substituents, e.g. acetylene, cyano, vinyl, cyanoacyl, led to weak second order stabilization perturbation interactions between the partially filled carbene lone pair orbitals and the adjacent π^* orbitals, in part a reflection of the increase in energy required for promotion of the electrons in carbene sp^2 orbitals to p orbitals.²⁰ The C-C-N bond of cyanomethylene is almost linear (173°) due to partial delocalization of the carbon lone pair into the π system. Molecular orbital representation of the HOMO-2 for this system shows continuous delocalization over the three atoms. Nitro-substituted methylcarbene, in contrast, prefers an orthogonal conformation of the NO₂ group relative to the carbon lone pair an indication that the lone pair does not delocalize into the nitro framework. Another example is ethynylcarbene in which the partially filled p-orbital (0.255e) of the carbene center showed an interaction energy of 14.7 kcal/mol with a π^* orbital of the acetylenic system. Other carbenes with neighboring π systems, e.g. acetylcabene did not report the consequences of the lone pair interactions with the carbene center. The lone pair on the carbene carbon of trifluoromethylcarbene was partially delocalized into a neighboring C-F* anti bond that gave rise to a perturbation energy of 9.22 kcal/mol. The unoccupied p-orbital did not lead to a significant 2nd order perturbation contribution to the energetics of this molecule. Ultimately, NBO methods provided interesting information about individual systems, but were not useful in enlightening our overall understanding of relative substituent effects.

Conclusions

This work has demonstrated that published correlations of carbene properties using standard LFE methodology are not generally applicable for carbenes that have substituents *directly* attached to the electron-deficient center. In this situation, polar and resonance effects are not independent of one another and “ σ -donation and π -back-bonding act synergistically.”²¹

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Supplementary Information

Absolute enthalpies and free energies for all species are listed along with zero-point corrections. Data used to compute CCSD(T) relative energies are included. Several examples of attempted correlations with other sets of sigma constants.

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