Air-Persistent Monomeric (Amino)(carboxy) Radicals Derived from Cyclic (Alkyl)(Amino) Carbenes

Janell K. Mahoney,[†] David Martin,*[,†,‡] Fabrice Thomas,[‡] Curtis E. Moore,[§] Arnold L. Rheingold,[§] and Guy Bertrand*[,†]

[†]UCSD-CNRS Joint Research Laboratory (UMI 3555), Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093-0343, United States

[‡]UMR CNRS 5250, Département de Chimie Moléculaire, Université Joseph Fourier B. P. 53, 38041 Cedex 9 Grenoble, France

[§]UCSD Crystallography Facility, San Diego, La Jolla, California 92093-0343, United States

S *Supporting Information*

ABSTRACT: A series of monomeric (amino)(carboxy) radicals featuring carbonyl substituents with increasing electron-withdrawing properties (**3a**, phenyl; **3b**, 3,5-bis(trifluoromethyl)phenyl; **3c**, perfluorophenyl; **3d**, heptafluoropropyl; **3e**, 2H-pyrroliumyl) were synthesized in two or three steps from stable cyclic (alky)(amino)carbenes (CAACs). Although (amino)(carboxy) radicals had been previously considered as highly air-sensitive, some of these compounds feature half-lives of hours (**3d**), and even days (**3c** and **3e**) in well-aerated solutions. DFT calculations show that (amino)(carboxy) radicals evolve from C-centered radical to ambidentate C,O-radicals when increasing the electron-withdrawing properties of the carbonyl substituent. This is paralleled with a destabilization of the peroxide resulting from the addition of dioxygen to the radical. This latter reaction is even predicted to be endothermic for substituents with Hammett constant $\sigma_p > 0.2$.
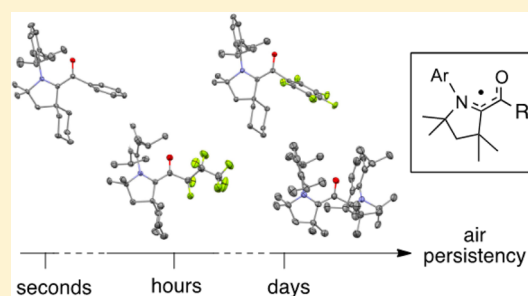
■ INTRODUCTION

The discovery by Gomberg in 1900 of the first persistent organic radicals, namely, tri(aryl)methyl radicals, is a major landmark of modern chemistry.[1,2] Since this pioneering work, this class of odd-electron compounds has evolved toward highly stable versions featuring perchlorinated tri(aryl)methyl patterns, which have found various applications in the design of multifunctional materials.[3,4] Paradoxically, apart from few exceptions,[5] most carbon-centered radicals are still considered only as intermediates of interest for organic reactions, and not as typical stable paramagnetic building blocks.[6] This is in marked contrast with the variety of stable heteroatom-based radicals, such as nitroxides, thiazyls, and verdazyls.[5] Two common features of C-radicals are clearly detrimental for the design of materials: (i) their reluctance to remain well-defined monomeric species, due to the C−C bond strength (typically 80 kcal·mol^{-1}, compared to 30−40 kcal·mol^{-1} for O−O or N−N bonds);[7] (ii) their propensity to react with dioxygen to afford peroxide radicals and related derivatives.

Since the 1960s, it has been well established that captodative substitution disfavors the formation of C−C dimers,[8,9] up to the point that small amounts of monomeric radicals can be detected in solution. The 2-oxomorpholin-3-yl radical **I** is a classical example, with a dissociation constant of about 10^{-9} M at room temperature (Figure 1).[10−12] Additionally, several enzymes harboring persistent glycyl radicals **II** were reported a decade ago.[13,14] These results suggested that a suitable

Figure 1. 2-Oxomorpholin-3-yl radical **I** and its dimer, enzymes harboring persistent glycyl radicals **II**, and recently isolated monomeric (amino)(carboxy)radical **3a**.

combination of electronic and steric factors could be used to prevent dimerization. Indeed, we recently took advantage of the stabilizing effect of cyclic (alkyl)(amino)carbenes (CAACs)[15] for paramagnetic species[16] to synthesize the first isolable monomeric (amino)(carboxy)radical **3a** and related di- and triradicals.[17] On the other hand, the design of air-persistent variants remains a challenge. Indeed, although **3a** and related polyradicals are perfectly stable under inert atmosphere, they decay within minutes when exposed to air. Interestingly, it has to be noted that radicals of type **I** could be considered as
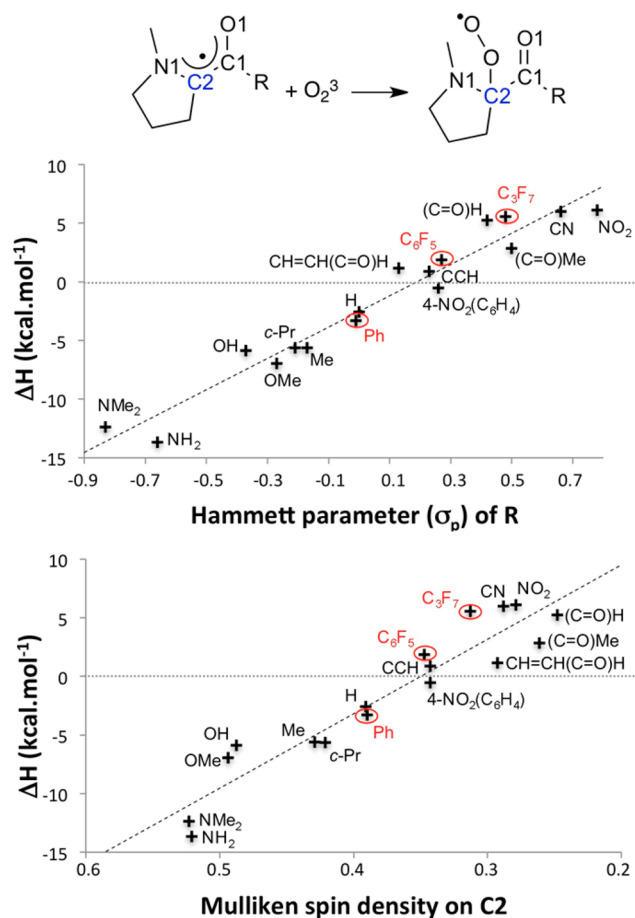
"unreactive" toward dioxygen when their reaction with O_2 is slower than the time-scale of their dimerization, which is at best a millisecond at room temperature.[12] Additionally, glycyl enzymes **II**, which catalyze anaerobic processes, are air-sensitive, indicating that even substantial steric protection may not be sufficient to prevent the oxidation of sheltered captodative carboradicals.[14]

Herein we report a theoretical and experimental study on the influence of the electronic effects upon the reactivity with dioxygen from air of isolable monomeric (amino)(carboxy) radicals derived from CAACs. We show that air-persistent variants—with half-lives in aerated solution at room temperature of several hours, and even days in the most favorable cases—can be rationally designed.

RESULTS AND DISCUSSION

In order to design air-persistent (amino)(carboxy) radicals, we examined the reaction of triplet oxygen with model compounds at the B3LYP/6-311(d,p) level of theory. We considered a series of representative examples of CAAC-derived (amino)-(carboxy) radicals with R substituents at the carboxy moiety covering a broad range of electronic properties. A good correlation was found between the enthalpy of the reaction and the Hammett parameter σ_p[18] of R (Figure 2, top). The formation of the corresponding peroxide radical is favored by

electron donating substituents (low σ_p). Conversely, the exothermicity of the process decreases as the electron withdrawing capabilities of R increase, to such a point that the reaction is predicted to be endothermic for the most electron-withdrawing groups ($\sigma_p > 0.2-0.3$).

It can be intuitively assumed that the formation of the peroxide radical is favored when the "C-centered" character of the radical increases. Again, there is a fair correlation between the enthalpy of the reaction and the spin density on C2 (Figure 2, bottom). As shown in Figure 3, the tuning of the electronic
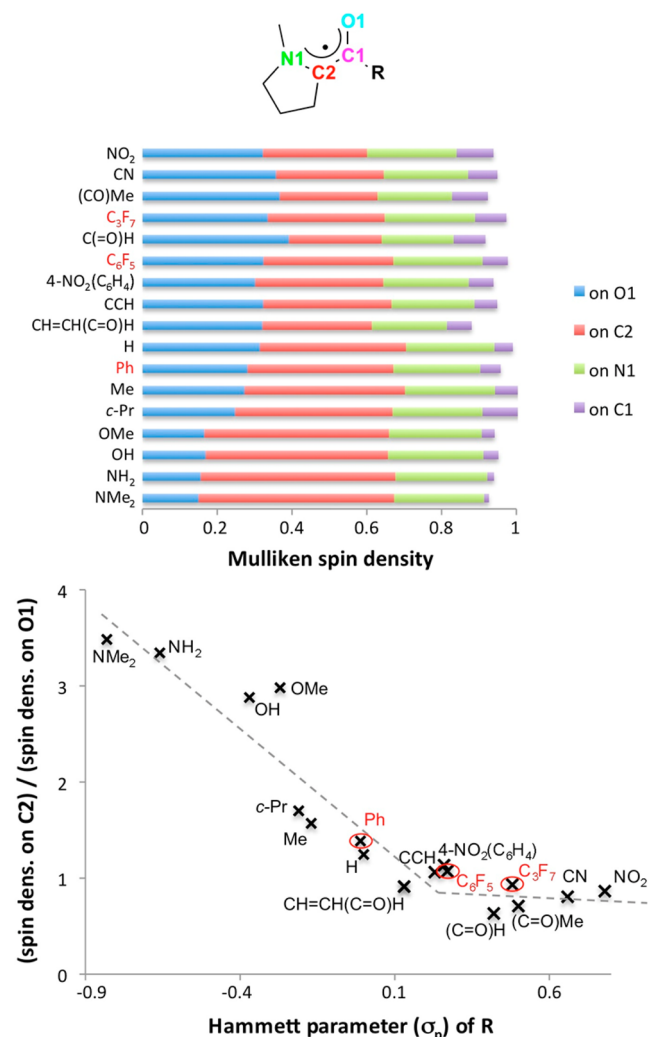
Figure 3. Top: Calculated Mulliken spin densities in (amino)-(carboxy) radicals featuring R substituents, with increasing Hammett parameters σ_P from bottom to top. Bottom: Plot of the ratio of the Mulliken spin densities on C2 and O1 against σ_P. Substituents highlighted in red are those of the experimentally isolated radicals **3**.

Figure 2. Plot of the enthalpy of the reaction of $O_2{}^3$ with model (amino)(carboxy) radicals against the Hammett parameter σ_p of R (top), and against Mulliken spin density on C2 (bottom). Substituents highlighted in red are those of the experimentally isolated radicals **3**.

properties of R essentially affects the spin density on O1 and C2. The remaining spin density, which is localized on C1 and N1 (25−33%), is only slightly influenced. Radicals with strongly donating amino groups ($\sigma_p < -0.6$) bear more than 50% of the spin density on C2, and only 15% on O1. Increasing the electron-withdrawing character of R results in a gradual transfer of spin density from C2 to O1. A plateau is reached around $\sigma_p \approx 0.2$ and in the case of strong electron-withdrawing R groups the spin densities on both O1 and C2 tends to be around 30−35%.

Scheme 1
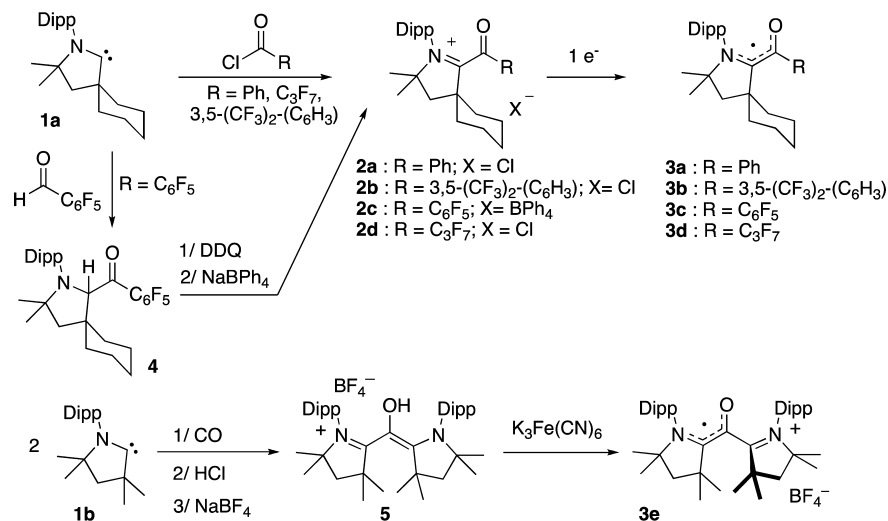
Table 1. Structural Parameters, Redox Potentials, EPR Hyperfine Coupling Constants and Mulliken Spin Densities of Radicals 3a–e (Calculated Values[b] are in Parentheses)

	3a	3b	3c	3d	3e
R	Ph	3,5-$(CF_3)_2(C_6H_3)$	C_6F_5	C_3F_7	2H-pyrroliumyl
bond lengths (pm)					
O1–C1	125.9/125.8[a]	(125.1)	125.0	125.8	126.0
C1–C2	142.9/142.8[a]	(143.2)	142.2	142.9	142.6
C2–N1	136.0/136.5[a]	(136.9)	136.2	135.3	136.1
angle and torsions (deg)					
C1–C2–N1	121.7/120.6[a]	(121.2)	121.4	119.3	120.0
O1–C1–C2-N1	2.3/8.8[a]	(7.4)	2.7	3.9	4.5
$E_{1/2}$ vs Fc/Fc$^+$(V)					
1$^+$/1	−0.93	−0.65	−0.41	−0.30	+0.25
1/1$^-$	−1.86	−1.74[d]	−1.73[d]	−1.51[d]	−1.03
g factor	2.0039	2.0043	2.0031	2.0032	2.0032
isotropic EPR hyperfine coupling (MHz)					
A(^{14}N)	15.4	17.1	17.2	17.3	8.9 (average)[c]
(1 nucleus)	(14.4)	(14.8)	(14.9)	(14.5)	(13.2 and 3.7)
A(^{19}F)[e]	–	–	8.2	30.8	–
(2 nuclei)	–	–	(7.3)	(35.5)	–
Mulliken spin density[e]					
on O1	(28.0)	(28.9)	(30.5)	(32.7)	(35.5)
on C1	(5.4)	(6.7)	(6.8)	(10.0)	(14.8)
on C2	(41.9)	(38.8)	(36.6)	(31.4)	(18.7)
on N1	(24.6)	(25.4)	(25.7)	(25.0)	(23.0)

[a]Values given for each of the two independent molecules in the unit cell. [b]Calculations at the B3LYP/TZVP level of theory. [c]Assuming a fast exchange between two equivalent conformers, see text. [d]Irreversible. [e]Values calculated on optimized structure at the B3LYP/TZVP level with the zeroth order regular approximation (ZORA).

In summary, our computational study indicates that CAAC-derived (amino)(carboxy) radicals evolve from marked C-centered radical to ambidentate C,O-radicals as the electron-withdrawing properties of the carbonyl substituent increase. This is paralleled with a thermodynamic protection of the radical from dioxygen where the formation of the corresponding peroxide is predicted to be endothermic for $\sigma_p > 0.2$. Importantly, high σ_p values should also kinetically disfavor the formation of the peroxide by virtue of the Hammond postulate.

In order to experimentally ascertain the influence of electronic effects on the air-persistency of (amino)(carboxy) radicals, we considered the series of radicals 3a–e with carbonyl moieties featuring substituents with increasing electron with-

drawing properties: phenyl, 3,5-bis(trifluoromethyl)phenyl, perfluorophenyl, heptafluoropropyl, and 2H-pyrrolium. The iminium precursors 2a,b and 2d were readily prepared by addition of the appropriate acyl chloride to a hexane solution of CAAC 1a[19] (Scheme 1). Iminium 2c was obtained by addition of 2,3,4,5,6-pentafluorobenzaldehyde to CAAC 1a, followed by oxidation of the resulting α-(amino)ketone 4 with DDQ and treatment with sodium tetraphenylborate. Lastly, following the procedure[20,21] used with "anti-Bredt" N-heterocyclic carbene,[22] compound 5 was synthesized by addition of excess carbon monoxide to a THF solution of CAAC 1b at −78 °C, subsequent addition of one equivalent of hydrogen chloride, and anion exchange with sodium tetrafluoroborate. Note that

the less hindered CAAC **1b** has to be used instead of **1a**, since CAACs, and other electrophilic carbenes with bulkier substituents are known to react with CO to give ketenes.[23]

Cyclic voltammograms of **2a−d** feature two 1-electron reductions indicating the successive formation of a radical and an enolate, respectively (Table 1). As expected, electron-withdrawing groups shift the first oxidation to higher reduction potentials. Thus, whereas **3a** and **3b** were successfully synthesized by reduction of **2a−b** with half an equivalent of tetrakis(dimethylamino)ethylene (TDAE; $E_{1/2} \approx -1.2$ V vs Fc/Fc$^+$), the reduction of the electron-poor iminiums **2c,d**, to afford radicals **3c,d**, required the milder decamethylferrocene (Fe[Cp*]$_2$; $E_{1/2} \approx -0.59$ V). Lastly, **3e** was prepared from **5** using potassium ferricyanide, a procedure adapted from that reported by Mayer et al.[24] for preparing the 2,4,6-tri-*tert*-butylphenoxy radical from the corresponding phenol. Not surprisingly, cyclic voltammetry indicates that **3e** undergoes reversible 1-electron oxidation and reduction at +0.25 and −1.03 V, respectively, with these values being the highest of the series.

Radicals **3a−e** were isolated in 54−94% yields, and single crystals of **3a** and **3c−e** were subjected to X-ray diffraction studies, which confirmed the expected monomeric structure (see Figure 4, Table 1, and Supporting Information for
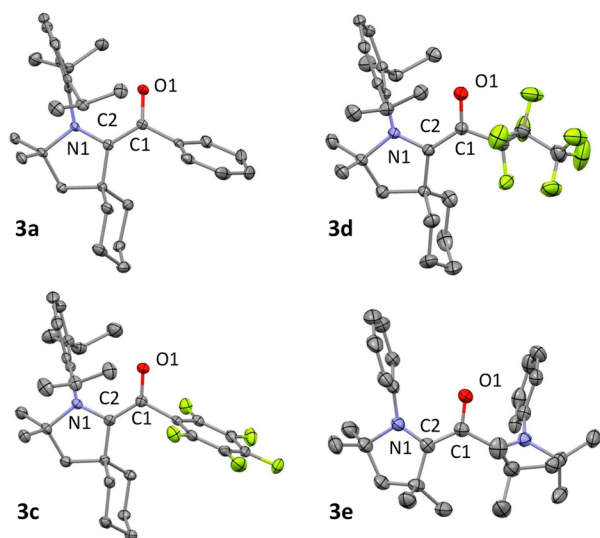
Figure 4. Solid-state structure of **3a** and **3c−e** with thermal ellipsoids drawn at 50% probability level. Hydrogen atoms, molecules of solvent, as well as the counteranion and isopropyl groups of **3e** are omitted for clarity.

structural details). As expected, N1, C1, C2, and O1 atoms were found to be coplanar, as a result of the delocalization of the unpaired electron over the conjugated captodative system, with the second substituent (CAAC unit or aryl ring) being twisted away from coplanarity (torsion 57°−85°).

The X-band EPR spectra of **3a−e** were recorded in dry dichloromethane at room temperature under an inert atmosphere of argon (Figure 5). They feature close g factors (2.003−2.004, see Table 1) and isotropic hyperfine coupling constants with nitrogen (a_N = 15−17 MHz). In the case of **3c** and **3d**, coupling with two equivalent fluorine atoms is also observed (a_F = 8 and 31 MHz, respectively). DFT calculations fairly reproduce these experimental values (Table 1).[25] Interestingly, the hyperfine coupling constants that are

predicted for **3e** at the same level of theory (a_N = 13.2 MHz for the conjugated amino group, and only 3.7 MHz for the other nitrogen) fit well in this series and are coherent with the averaged experimental value (8.9 MHz), which results from a dynamic process that is fast at the EPR time scale. Indeed, the calculated Gibbs energy of activation for the exchange of magnetic environment between the two different amino moieties is only 11 kJ mol^{-1} (see the Supporting Information).

Mulliken spin densities calculated for **3a−e** follow the trends previously observed at a lower level of theory with the simpler models of Figure 3. The spin density remains essentially unchanged on C1 and N1 across the series, most variations occurring on O1 and C2 (Table 1). Radical **3a** has 42% spin density on C2 and 28% on O1. This difference slowly diminishes when increasing the electron-withdrawing capabilities of the R substituent on the carbonyl group. While **3b** (39% on C2, 29% on O1) and **3c** (37% on C2, 31% on O1) can still be considered as C-centered, **3d** has equally shared spin density on both atoms (31% on C2, 33% on O1). In the extreme, radical cation **3e** features significantly more spin density on O1 (36%) than on C2 (19%).

Next, the air-sensitivity of radicals **3a−e** was evaluated by bubbling air into each EPR sample over the course of a minute. Note that **3a** is so air-sensitive that it could not be detected by EPR after this procedure. Thus, in order to monitor its decomposition, a new sample was exposed very briefly to air (few seconds). Even under these conditions, the concentration of **3a** decreased according to a pseudo first-order kinetic with a half-life of about 1 min at room temperature (Figure 6). Radical **3b** and **3c** have a half-life of about 13 min and 1.5 day, respectively, in well-aerated solutions of dichloromethane. It is interesting to note that washing a solution of **3c** in aerated dichloromethane with water does not increase the rate of its decay, confirming that the radical is significantly more sensitive toward dioxygen than moisture. Radical **3d** is still remarkably air persistent (half-life: 3 h), but strikingly it is more air-sensitive than **3c**, although it should benefit from a better electron-withdrawing per(fluoro)-n-propyl substituent. These results clearly indicate that steric hindrance also plays a role in hindering the reaction of (amino)(carboxy) radicals with O$_2$. Indeed, we found that **3e**, featuring the electron-withdrawing and bulky 2*H*-pyrroliumyl substituent has a lifetime of about a week in aerated technical dichloromethane solution, and can be stored as a solid in a regular vial under air for more than a year.[26]

■ CONCLUSION

Similarly to many captodative C-radicals, (amino)(carboxy) radicals have long been considered to readily undergo dimerization and to be very reactive toward oxygen. However, our study demonstrates that (amino)(carboxy) radicals derived from CAACs exist as monomers both in solution and in the solid state. Moreover, having an electron withdrawing carboxy substituent results in highly air-persistent radicals; their half-life in air can even be prolonged up to several days when sterically hindered substituents are used. Radical **3c**, which features a moderately electron withdrawing and bulky group (C$_6$F$_5$, Hammett σ_p = +0.26), is tame enough to be handled in solution in open air over several hours with no significant decomposition. Given the plethora of available electron-withdrawing substitution patterns, diverse new models can be envisioned. We are currently exploring the possibilities for such new and unforeseen families of organic air-persistent radicals.
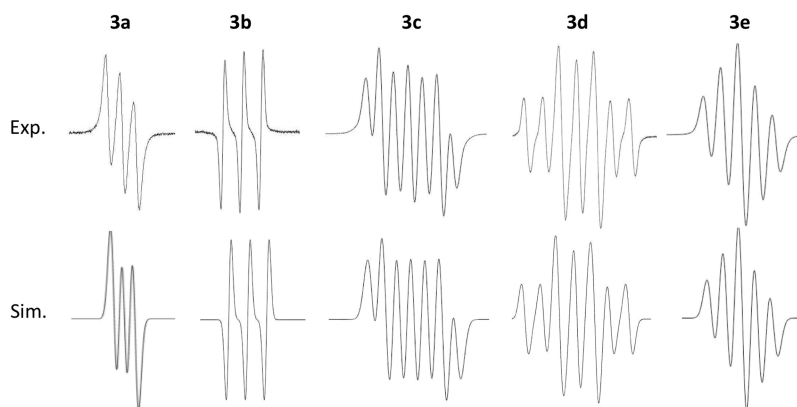
Figure 5. Top: Experimental EPR spectra in solution in dichloromethane at room temperature. Bottom: corresponding simulated spectra with isotropic hyperfine coupling constants as reported in Table 1.
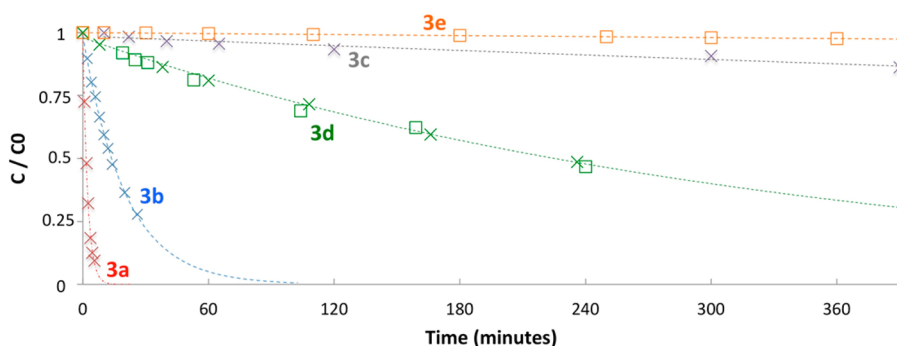
Figure 6. Decay of radicals **3a–e** in solution in dichloromethane after exposure to air (×) or after exposure to air and water (□).

■ EXPERIMENTAL SECTION

General Considerations. The synthesis of radicals and of their precursors were performed under an inert atmosphere of dry argon, using standard Schlenk and drybox techniques, dry and oxygen-free solvents. Commercially available 3,5-bis(trifluoromethane)benzoyl chloride was distilled before use. Heptafluorobutyryl chloride was first distilled and then subjected to ten freeze−pump−thaw cycles to remove any excess hydrochloric acid. Compounds **1a−b**, **2a**, and **3a** were prepared as previously reported.[17,19] ^{1}H, ^{13}C, ^{19}F, and ^{11}B NMR spectra were recorded on Bruker Avance 300, Varian VX 500, and Jeol ECA 500 spectrometers. All spectra were obtained at 25 °C in the solvent indicated. Chemical shifts are given relative to $SiMe_4$ and referenced to the residual solvent signal (^{1}H, ^{13}C) or relative to an external standard (^{19}F, F_3COOH; [11]B, $BF_3 \cdot Et_2O$). Melting points were measured with an Electrothermal MEL-TEMP apparatus. Electrochemical experiments were performed with an analyzer from CH Instruments (model 620E) with platinum working and auxiliary electrodes. The reference electrode was built from a silver wire inserted in a small glass tube fitted with a porous Vycor frit and filled with an $AgNO_3$ solution in acetonitrile (0.01 M). Ferrocene was used as a standard, and all reduction potentials are reported with respect to the $E_{1/2}$ of the Fc^+/Fc redox couple. EPR spectra were recorded on a Bruker EMX+ spectrometer. EPR g factors were calibrated with 2,2-diphenyl-1-picrylhydrazyl (DPPH, g = 2.0036) as a standard.

Iminium Chloride 2b. 3,5-bis(trifluoromethane)benzoyl chloride (0.44 mL, 2.42 mmol), was added to hexane solution of CAAC **1a** (582 mg, 2.42 mmol), which resulted in the immediate formation of a heavy white precipitate. After stirring for 10 min, the solvent was removed in vacuo, and the precipitate was washed with diethyl ether (3 × 20 mL). Yield: 807 mg (55%). mp: 168−170 °C. MS (m/z): [M$^+$] calcd for $C_{32}H_{38}F_6NO^+$, 566.2853; found, 566.2851. ^{1}H NMR (CDCl$_3$, 300 MHz): 8.76 (s, 2H), 8.15 (s, 1H), 7.43 (t, J = 3 Hz, 1H), 7.22 (d, J = 3 Hz, 2H), 3.08 (bs, 2H), 3.26 (bs, 2H), 2.72 (bs, 2H), 1.80−1.83 (m, 3H), 1.78 (s, 6H), 1.49−1.59(m, 5H), 1.32 (d, J = 3

Hz, 6H), 0.80 (s, 6H). ^{13}C NMR (CDCl$_3$, 125 MHz): 194.5 (C), 184.9 (C), 145.8 (C), 144.4 (C), 133.9 (C), 133.6 (C, q, $^2J_{C-F}$ = 35 Hz), 132.3 (CH), 131.6 (C), 131.2 (CH), 129.9 (CH), 127.3 (C), 126.6 (CH), 125.1 (C), 122.1 (C, q, $^1J_{C-F}$ = 272.5 Hz), 87.6 (C), 57.5 (C), 41.5 (CH$_2$), 35.3 (CH$_2$), 29.5 (CH$_3$), 29.3 (CH), 26.7 (CH$_3$), 25.0 (CH$_3$), 24.3 (CH$_2$), 22.6 (CH$_2$). ^{19}F NMR (CDCl$_3$, 282 MHz): −62.63 (CF$_3$).

Radical 3b. Tetrakis(dimethylamino)ethylene (31 μL, 0.133 mmol) was added to a dichloromethane (3.0 mL) solution of the iminium chloride **2b** (200 mg, 0.332 mmol). The mixture was stirred for 10 min, and the solvent removed in vacuo. Extraction with toluene (1 × 5.0 mL) and removal of the solvent in vacuo yielded **3b** as a red solid. Yield: 122 mg (81%). mp: 145−147 °C.

Compound 4. 2,3,4,5,6-Pentafluorobenzaldehyde (1.89 g, 9.68 mmol) in THF was slowly added via cannula to a THF solution of CAAC **1a** (3.15 g, 9.68 mmol). After 20 min, the solution was opened to air and stirred for 1 h. The solvent was then removed under vacuum. Column chromatography using a 5:95 ethyl acetate/hexanes solution yielded **4** as an orange oil. Yield: 3.81 g (76%). MS (m/z): [M$^+$] calcd for $C_{30}H_{35}F_5NO$, 520.2633; found, 520.2630. ^{1}H NMR (CDCl$_3$, 300 MHz): 7.19 (t, J = 6 Hz, 1H), 7.10 (d, J = 6 Hz, 2H), 4.68 (s, 1H), 4.08 (sept., J = 6 Hz, 1H), 3.16 (sept., J = 6 Hz, 1H), 3.28 (d, J = 12 Hz, 1H), 2.02 (bs, 1H), 1.97 (bs, 1H), 1.95 (d, J = 12 Hz, 1H), 1.62 (bs, 4H), 1.52 (s, 3H), 1.42 (m, 3H), 1.26 (d, J = 6 Hz, 6H), 1.17 (d, J = 6 Hz, 3H), 0.99 (d, J = 6 Hz, 6H). ^{13}C NMR (CDCl$_3$, 125 MHz): 198.7 (C), 152.4(C), 149.0 (C), 140.1 (C), 126.8 (CH), 124.6 (CH), 124.4 (CH), 86.1 (CH), 64.3 (C), 51.7 (CH$_2$), 47.8 (C), 42.2 (CH$_2$), 34.5 (CH$_2$), 32.1 (CH$_3$), 28.0 (CH), 27.9 (CH$_3$), 27.4 (CH), 25.8 (CH$_2$), 25.7 (CH$_3$), 25.3 (CH$_3$), 25.0 (CH$_3$), 24.9 (CH$_3$), 24.3 (CH$_2$), 23.6 (CH$_2$). ^{19}F NMR (C$_6$D$_6$, 282 MHz): −138.7 (d, J = 16.9 Hz, 2F), −149.9 (t, J = 19.7 Hz, 1F), −160.2 (m, 2F).

Iminium 2c. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (423 mg, 1.86 mmol) dissolved in ether was added via addition funnel to an ether solution of **4** (970 mg, 1.86 mmol). The mixture was stirred overnight. The solvent was then removed via filtration, and the purple

precipitate washed with ether (3 × 20 mL). The solid was then dissolved in dichloromethane and added to an aqueous solution of sodium tetraphenylborate (1.273 g, 3.72 mmol). The biphasic mixture was stirred vigorously for 1 h. The layers were then separated. The organic layer was washed with brine (3 × 20 mL) and subsequently dried with magnesium sulfate. After removal of volatiles in vacuo, **2c** was dissolved in dichloromethane and yellow crystals were obtained by layering diethyl ether. Yield: 503 mg (32%). mp: 151−153 °C. MS (*m/z*): [M$^+$] calcd for $C_{30}H_{35}F_5NO^+$, 520.2633; found, 520.2637. ^{1}H NMR (CDCl$_3$, 300 MHz): 7.46 (bm, 9H), 7.26 (d, *J* = 6 Hz, 2H), 7.05 (t, *J* = 6 Hz, 8H), 6.91 (t, *J* = 6 Hz, 4H), 2.49 (sept, *J* = 3 Hz, 2H), 1.95 (s, 2H), 1.91 (d, *J* = 9 Hz, 2H), 1.73 (bd, *J* = 9 Hz, 3H), 1.55 (bt, *J* = 9 Hz, 3H), 1.34 (m, 2H), 1.29 (d, *J* = 3 Hz, 6H), 1.21 (s, 6H), 1.01 (d, *J* = 3 Hz, 6H). ^{13}C NMR (CDCl$_3$, 125 MHz): 189.9 (C), 177.3 (C), 164.3 (q, C, $J_{C−B}$ = 48.8 Hz), 148.1 (C), 146.0 (C), 145.3 (C), 139.3 (C), 137.2 (C), 136.4 (CH), 133.0 (CH), 127.0 (CH), 125.6 (CH), 121.7 (CH), 87.1 (C), 57.8 (C), 43.3 (CH$_2$), 35.1 (CH$_2$), 29.6 (CH), 29.0 (CH$_3$), 26.0 (CH$_3$), 25.4 (CH$_3$), 24.1 (CH$_2$), 21.3 (CH$_2$). ^{19}F NMR (CDCl$_3$, 282 MHz): −134.0 (bs, 2F), −134.5 (bs, 1F), −155.7 (t, 2F, *J* = 16.9 Hz). ^{11}B NMR (CDCl$_3$, 96 MHz): −7.77 (s).

Radical 3c. Iminium tetraphenylborate **2c** (58 mg, 0.069 mmol) and decamethylferrocene (22.6 mg, 0.069 mmol) were combined under argon. Dichloromethane (5.0 mL) was added and the solution stirred for 30 min. Removal of the solvent in vacuo and extraction with hexanes yielded **3c** as an orange powder. Single crystals were obtained by cooling a concentrated toluene solution to −40 °C. Yield: 24 mg (67%). mp: 186−189 °C.

Iminium Chloride 2d. Heptafluorobutyryl chloride (0.20 mL, 1.31 mmol) was added to a hexane solution of CAAC **1a** (0.340 g, 1.19 mmol) which resulted in the immediate formation of a yellow solid. After stirring for 20 min, the solvent was removed under vacuum and the precipitate washed with pentane (4 × 10 mL). Yellow crystals were grown by slow diffusion of pentane in a chloroform solution of **2d** at −40 °C. Yield: 345 mg (52%). mp: 112−114 °C. MS (*m/z*): [M$^+$] calcd for $C_{27}H_{35}F_7NO^+$, 552.2607; found, 522.2599. ^{1}H NMR (CDCl$_3$, 300 MHz): 7.57 (t, *J* = 6 Hz, 1H), 7.34 (d, *J* = 6 Hz, 2H), 3.12 (s, 2H), 2.60 (sept, *J* = 6 Hz, 2H), 2.23 (bs, 1H), 2.19 (bs, 1H), 1.87 (bs, 3H), 1.84 (s, 6H), 1.68−1.53 (m, 4H), 1.48 (s, 1H), 1.30 (d, J =6 Hz, 6H), 1.12 (d, *J* = 6 Hz, 6H). ^{13}C NMR (CDCl$_3$, 125 MHz): 189.1 (C), 181.2 (C, t, *J* = 36 Hz)), 145.0 (C), 133.3 (CH), 127.7 (C), 127.3 (CH), 116.7 (C, qt, $^1J_{C−F}$ =287.5 Hz, $^2J_{C−F}$ = 32.5 Hz), 108.0 (C, t, sext., $^1J_{C−F}$ =268.8 Hz, $^2J_{C−F}$ = 32.5 Hz) 107.1 (C, tt, $^1J_{C−F}$ =287.5 Hz, $^2J_{C−F}$ = 32.5 Hz), 90.8 (C), 58.1 (C), 43.9 (CH$_2$), 34.4 (CH$_2$), 29.8 (), 29.7 (CH$_3$), 26.5 (CH), 25.0 (CH$_3$), 24.2 (CH$_2$), 21.0 (CH$_2$). ^{19}F NMR (CDCl$_3$, 282 MHz): −80.5 (t, *J* = 8.46 Hz, 3F), −115.0 (bs, 2F), −125.3 (bs, 2F).

Radical 3d. Iminium chloride **2d** (100 mg, 0.179 mmol) and decamethylferrocene (58.4 mg, 0.179 mmol) were combined under argon, and dichloromethane was added to the flask. The solution was stirred for 20 min and the solvent was removed under vacuum. Extraction with toluene and removal of the solvent under vacuum yielded **3d** as a yellow powder. Single crystals were grown by cooling a concentrated hexane solution of **3d** to −40 °C. Yield: 87.9 mg (94%). mp: 128−130 °C.

Iminium 5. CO(g) was bubbled through a cooled solution of **1b** (336 mg, 1.17 mmol) in THF (5 mL) for 1 h. A solution of HCl in diethyl ether (2 M, 0.30 mL, 0.6 mmol) was added dropwise, and the solution was warmed to room temperature. After removing the solvent under vacuum, the residue was extracted in toluene and the solvent removed in vacuo. The resulting residue was dissolved in dichloromethane and a solution of sodium tetrafluoroborate (321 mg, 2.92 mmol) in water (5 mL) was added. The mixture was stirred vigorously for 1 h before the layers were separated and the organics were washed with brine, dried over magnesium sulfate and the solvent removed. Crystals were grown by slow diffusion of diethyl ether in a dichloromethane solution of **5**. Yield: 148 mg (38%). mp: 254−256 °C. MS (*m/z*): [M$^+$] calcd for $C_{41}H_{63}N_2O^+$, 599.4940; found, 599.4935. ^{1}H NMR (CDCl$_3$, 500 MHz): 7.24 (t, *J* = 7.7 Hz, 2H), 7.14 (d, *J* = 7.7 Hz, 2H), 7.04 (d, *J* = 7.7 Hz, 2H), 2.75 (sept., *J* = 6.5 Hz, 2H), 2.49 (sept., *J* = 6.5 Hz, 2H), 2.47 (d, *J* = 13.5 Hz, 2H), 2.30

(d, *J* = 13.5 Hz, 2H), 2.08 (s, 6H), 1.75 (s, 6H), 1.34 (s, 6H), 1.31 (d, *J* = 6.5 Hz, 6H), 1.22 (d, *J* = 6.5 Hz, 6H), 1.16 (s, 6H), 1.09 (d, *J* = 6.5 Hz, 6H), 0.24 (d, *J* = 6.5 Hz, 6H). ^{13}C NMR (CDCl$_3$, 125 MHz): 176.3 (C), 146.1 (C), 144.0 (C), 135.2 (C), 129.2 (CH), 125.4 (CH), 125.0 (CH), 118.13 (C), 72.2 (C), 58.4 (CH$_2$), 46.4 (C), 32.8 (CH$_3$), 30.7 (CH$_3$), 30.6 (CH$_3$), 29.9 (CH), 28.9 (CH), 28.7 (CH$_3$), 28.3 (CH$_3$), 25.0 (CH$_3$), 24.7 (CH$_3$), 23.6 (CH$_3$). ^{19}F NMR (CDCl$_3$, 470 MHz): −78.39 (s, 3F). Note that the triflate salt can be obtained by using tri(fluoro)methanesulfonic acid instead of hydrogen chloride. Yield: 73%. mp: 182−185 °C.

Radical 3e. CO(g) was bubbled through a cooled solution of **1b** (336 mg, 0.24 mmol) in toluene (5 mL) for 1 h. Then, a solution of HCl in diethyl ether (2 M, 0.06 mL, 0.12 mmol) was added dropwise and the solution warmed to room temperature. A solution of potassium ferricyanide (198 mg, 0.6 mmol) in water was added to the flask. The biphasic mixture was stirred vigorously for 10 min. The phases were then separated, and the organic phase was washed with brine (3 × 10 mL) and dried with magnesium sulfate. After removing the solvent, the blue powder was dissolved in water and a solution of saturated sodium tetrafluoroborate was added to the reaction flask. After stirring for 20 min, the product was extracted with dichloromethane. The organic phase was washed with water (3 × 10 mL) and dried over magnesium sulfate, and the solvent removed under reduced pressure. Suitable single crystals were grown through diffusion of diethyl ether into a dichloromethane solution of the product. Yield: 116 mg (84%). mp: 220−222 °C. MS (*m/z*): [M$^+$] calcd for $C_{41}H_{62}N_2O^+$, 598.4812; found, 598.4854.

Decay of Radicals 3a−e in Aerobic Conditions. An EPR sample of the radical in distilled dichloromethane was poured into an open-to-air vial. The volume of the solution was filled to 3 mL, and air was vigorously bubbled over 1 min; an aliquot was taken, and the evolution of the concentration of the radical was monitored by EPR. In the case of **3d**, the remaining solution was steadily washed with 3 mL of distilled water over a minute. The organic phase was recovered, and a sample was monitored by EPR.

■ ASSOCIATED CONTENT

ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra; cyclic voltammograms; X-ray crystallographic data; DFT calculations: conformational study of compound **3e**, Cartesian coordinates, and absolute energies for all optimized geometries. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b04414.

■ AUTHOR INFORMATION

Corresponding Authors
*guybertrand@ucsd.edu
*david.martin@ujf-grenoble.fr

Notes
The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

■ REFERENCES

(1) Gomberg, M. *J. Am. Chem. Soc.* **1900**, 22, 757−771.

(2) Gomberg's historical discovery was officially designated as a United States national historic chemical landmark by the ACS in 2000; see http://www.acs.org/content/acs/en/education/whatischemistry/landmarks/freeradicals.html.

(3) (a) Ballester, M.; Riera, J.; Castaner, J.; Badia, C.; Monso, J. M. *J. Am. Chem. Soc.* **1971**, *93*, 2215. (b) Ballester, M. *Acc. Chem. Res.* **1985**, *18*, 380.

(4) For a recent review on organic radicals as building blocks for functional molecular materials, see: Ratera, I.; Veciana, J. *Chem. Soc. Rev.* **2012**, *41*, 303.

(5) *Stable Radicals: Fundamental And Applied Aspects Of Odd-Electron Compounds*; Hicks, R. G., Ed.; Wiley: Chichester, 2010.

(6) (a) *Radicals in organic chemistry*; Renaud, P.; Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001. (b) Easton, C. J. *Chem. Rev.* **1997**, *97*, 53.

(7) Sanderson, R. T. *Chemical Bonds and Bond Energy*; Academic Press: New York, 1976.

(8) For the captodative stabilization of radicals (also known as push–pull or merostabilization), see: (a) Baldock, R. W.; Hudson, P.; Katritzky, A. R. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1422. (b) Balaban, A. T.; Caproiu, M. T.; Negoita, N.; Baican, R. *Tetrahedron* **1977**, *33*, 2249. (c) Viehe, H. G.; Mértnyi, E.; Stella, L.; Janousek, Z. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 917. (d) Viehe, H. G.; Janousek, Z.; Mértnyi, R.; Stella, L. *Acc. Chem. Res.* **1985**, *18*, 148. (e) Zipse, H. *Top. Curr. Chem.* **2006**, *263*, 163.

(9) (a) Leroy, G.; Peeters, D.; Sana, M.; Wilante, C. *Substituent Effects in Radical Chemistry*; Viehe, V. H., Janousek, Z., Mértnyi, R., Eds.; Reidel: Boston, 1986; pp 1–48. (b) Katritzky, A. R.; Zerner, M. C.; Karelson, M. M. *J. Am. Chem. Soc.* **1986**, *108*, 7213. (c) Pasto, D. J. *J. Am. Chem. Soc.* **1988**, *110*, 8164. (d) Bordwell, F. G.; Lynch, T.-Y. *J. Am. Chem. Soc.* **1989**, *111*, 7558. (e) Wright, J. S.; Shadnia, H.; Chepelev, L. L. *J. Comput. Chem.* **2009**, *30*, 1016.

(10) (a) Koch, T. H.; Olesen, J. A.; DeNiro, J. *J. Am. Chem. Soc.* **1975**, *97*, 7285. (b) Himmelsbach, R. J.; Barone, A. D.; Kleyer, D. L.; Koch, T. H. *J. Org. Chem.* **1983**, *48*, 2989. (c) Gaudiano, G.; Sweeney, K.; Haltiwanger, R. C.; Koch, T. H. *J. Am. Chem. Soc.* **1984**, *106*, 7628. (d) Benson, O., Jr.; Demirdji, S. H.; Haltiwanger, R. C.; Koch, T. H. *J. Am. Chem. Soc.* **1991**, *113*, 8879. (e) Benson, O., Jr.; Gaudiano, G.; Haltiwanger, R. C.; Koch, T. H. *J. Org. Chem.* **1988**, *53*, 3036.

(11) For other related isolated dimers, see also: (a) Kleyer, D. L.; Haltiwanger, R. C.; Koch, T. H. *J. Org. Chem.* **1983**, *48*, 147. (b) Welle, F.; Verevkin, S. P.; Keller, M.; Beckhaus, H.-D.; Rüchardt, C. *Chem. Ber.* **1994**, *127*, 697.

(12) Such radicals have been described as "dynamically stable"; see discussion in: Frenette, M.; Aliaga, C.; Font-Sanchis, E.; Scaiano, J. C. *Org. Lett.* **2004**, *6*, 2579 and references cited herein.

(13) For reviews on radical based proteins, see: (a) Stubbe, J.; van der Donk, W. A. *Chem. Rev.* **1998**, *98*, 705. (b) Buckel, W.; Golding, B. T. *Annu. Rev. Microbiol.* **2006**, *60*, 27.

(14) (a) Frey, M.; Rothe, M.; Wagner, A. F.; Knappe, J. *J. Biol. Chem.* **1994**, *269*, 12432. (b) Mulliez, E.; Fontecave, M.; Gaillard, J.; Reichard, P. *J. Biol. Chem.* **1993**, *268*, 2296. (c) Leuthner, B.; Leutwein, C.; Schulz, H.; Horth, P.; Haehnel, W.; Schiltz, E.; Schägger, H.; Heider, J. *Mol. Microbiol.* **1998**, *28*, 615. (d) O'Brien, J. R.; Raynaud, C.; Croux, C.; Girbal, L.; Soucaille, P.; Lanzilotta, W. N. *Biochemistry* **2004**, *43*, 4635. (e) Martins, B. M.; Blaser, M.; Feliks, M.; Ullmann, G. M.; Buckel, W.; Selmer, T. *J. Am. Chem. Soc.* **2011**, *133*, 14666. (f) Jarling, R.; Sadegh, M.; Drozdowska, M.; Lahme, S.; Buckel, W.; Rabus, R.; Widdel, F.; Golding, B. T.; Wilkes, H. *Angew. Chem., Int. Ed.* **2012**, *51*, 1334.

(15) For reviews on CAACs: (a) Soleilhavoup, M.; Bertrand, G. *Acc. Chem. Res.* **2015**, *48*, 256. (b) Melaimi, M.; Soleilhavoup, M.; Bertrand, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 8810. (c) Droege, T.; Glorius, F. *Angew. Chem., Int. Ed.* **2010**, *49*, 6940. (d) Martin, D.; Melaimi, M.; Soleilhavoup, M.; Bertrand, G. *Organometallics* **2011**, *30*, 5304.

(16) For isolated carbene-main group element-centered radicals: (a) Back, O.; Donnadieu, B.; Parameswaran, P.; Frenking, G.; Bertrand, G. *Nat. Chem.* **2010**, *2*, 369. (b) Kinjo, R.; Donnadieu, B.; Bertrand, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 5930. (c) Back, O.; Celik, M. A.; Frenking, G.; Melaimi, M.; Donnadieu, B.; Bertrand, G. *J. Am. Chem. Soc.* **2010**, *132*, 10262. (d) Back, O.; Donnadieu, B.; von Hopffgarten, M.; Klein, S.; Tonner, R.; Frenking, G.; Bertrand, G. *Chem. Sci.* **2011**, *2*, 858. (e) Kinjo, R.; Donnadieu, B.; Celik, M. A.; Frenking, G.; Bertrand, G. *Science* **2011**, *333*, 610. (f) Percival, P. W.; McCollum, B. M.; Brodovitch, J.-C.; Driess, M.; Mitra, A.; Mozafari, M.; West, R.; Xiong, Y.; Yao, S. *Organometallics* **2012**, *31*, 2709. (g) Mondal, K. C.; Roesky, H. W.; Schwarzer, M. C.; Frenking, G.; Tkach, I.; Wolf, H.; Kratzert, D.; Herbst-Irmer, R.; Niepötter, B.; Stalke, D. *Angew. Chem., Int. Ed.* **2013**, *52*, 1801. (h) Abraham, M. Y.; Wang, Y.; Xie, Y.; Gilliard, R. J., Jr.; Wei, P.; Vaccaro, B. J.; Johnson, M. K.; Schaefer, H. F., III; Schleyer, P. v. R.; Robinson, G. H. *J. Am. Chem. Soc.* **2013**, *135*, 2486. (i) Mondal, K. C.; Roesky, H. W.; Schwarzer, M. C.; Frenking, G.; Niepötter, B.; Wolf, H.; Herbst-Irmer, R.; Stalke, D. *Angew. Chem., Int. Ed.* **2013**, *52*, 2963. (j) Mondal, K. C.; Samuel, P. P.; Tretiakov, M.; Singh, A. P.; Roesky, H. W.; Stückl, A. C.; Niepötter, B.; Carl, E.; Wolf, H.; Herbst-Irmer, R.; Stalke, D. *Inorg. Chem.* **2013**, *52*, 4736. (k) Martin, C. D.; Soleilhavoup, M.; Bertrand, G. *Chem. Sci.* **2013**, *4*, 3020. (l) Mondal, K. C.; Roesky, H. W.; Stueckl, A. C.; Ehret, F.; Kaim, W.; Dittrich, B.; Maity, B.; Koley, D. *Angew. Chem., Int. Ed.* **2013**, *52*, 11804. (m) Roy, S.; Stückl, A. C.; Demeshko, S.; Dittrich, B.; Meyer, J.; Maity, B.; Koley, D.; Schwederski, B.; kaim, W.; Roesky, H. W. *J. Am. Chem. Soc.* **2015**, *137*, 4670−4673.

(17) Mahoney, J. K.; Martin, D.; Moore, C. E.; Rheingold, A. L.; Bertrand, G. *J. Am. Chem. Soc.* **2013**, *135*, 18766.

(18) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

(19) (a) Lavallo, V.; Canac, Y.; Prasang, C.; Donnadieu, B.; Bertrand, G. *Angew. Chem., Int. Ed.* **2005**, *44*, 5705. (b) Jazzar, R.; Dewhurst, R. D.; Bourg, J.-B.; Donnadieu, B.; Canac, Y.; Bertrand, G. *Angew. Chem., Int. Ed.* **2007**, *46*, 2899. (c) Jazzar, R.; Bourg, J.-B.; Dewhurst, R. D.; Donnadieu, B.; Bertrand, G. *J. Org. Chem.* **2007**, *72*, 3492. (d) Back, O.; Henry-Ellinger, M.; Martin, C. D.; Martin, D.; Bertrand, G. *Angew. Chem., Int. Ed.* **2013**, *52*, 2939.

(20) Martin, D.; Moore, C. E.; Rheingold, A. L.; Bertrand, G. *Angew. Chem., Int. Ed.* **2013**, *52*, 7014.

(21) For 2:1 adducts of stable carbenes with CO, see also: (a) Siemeling, U.; Färber, C.; Bruhn, C.; Leibold, M.; Selent, D.; Baumann, W.; von Hopffgarten, M.; Goedecke, C.; Frenking, G. *Chem. Sci.* **2010**, *1*, 697. (b) Schulz, T.; Färber, C.; Leibold, M.; Bruhn, C.; Baumann, W.; Selent, D.; Porsch, T.; Holthausen, M. C.; Siemeling, U. *Chem. Commun.* **2013**, *49*, 6834.

(22) (a) Martin, D.; Lassauque, N.; Donnadieu, B.; Bertrand, G. *Angew. Chem., Int. Ed.* **2012**, *51*, 6172. (b) Martin, D.; Lassauque, N.; Steinman, F.; Manuel, G.; Bertrand, G. *Chem.—Eur. J.* **2013**, *19*, 14895.

(23) (a) Lavallo, V.; Canac, Y.; Donnadieu, B.; Schoeller, W. W.; Bertrand, G. *Angew. Chem., Int. Ed.* **2006**, *45*, 3488. (b) Hudnall, T. W.; Bielawski, C. W. *J. Am. Chem. Soc.* **2009**, *131*, 16039.

(24) Manner, V. W.; Markle, T. F.; Freudenthal, J. H.; Roth, J. P.; Mayer, J. M. *Chem. Commun.* **2008**, 256.

(25) EPR parameters and Mulliken spin densities were calculated on optimized structures with the ORCA suite of programs: Neese, F. *Wiley Interdiscip. Rev.: Comput. Mol. Sci.* **2012**, *2*, 73.

(26) Part of our study was performed in 2015 on a sample of crystalized **3e** that we synthesized in mid-2013, and had been stored in a regular vial under air.