

Bottleable (Amino)(Carboxy) Radicals Derived from Cyclic (Alkyl)(Amino) Carbenes

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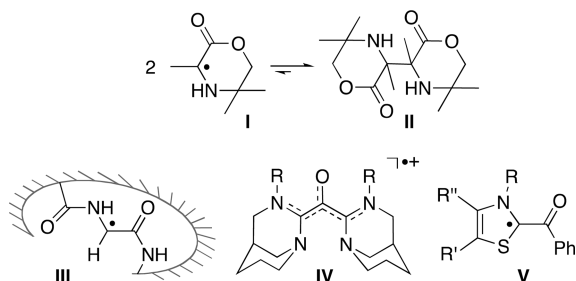
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Supporting Information

ABSTRACT: Monomeric (amino)(carboxy) radicals were synthesized in two steps: the addition of a stable cyclic (alkyl)(amino) carbene to an acyl chloride, followed by a one-electron reduction. Their stability toward dimerization also allows for the synthesis of related bi- and triradicals.

Persistent organic paramagnetic species have found numerous applications, ranging from synthetic chemistry (radical polymerization, oxidative catalysis) to medicine and material science.¹ Most of the known storable organic radicals are heteroatom-centered. Apart from a few exceptions, such as triarylmethyl radicals or highly π -delocalized phenalenyl systems, carbon-centered radicals are observable, but non-isolable as well-defined monomeric paramagnetic species.² The difference in stability is mainly due to the strength of C–C bonds, which is significantly higher (83 kcal·mol^{−1}) than those of O–O, N–N, and S–S bonds (35, 38, 54 kcal·mol^{−1} respectively)³ and, thus, favors dimerization processes. It is well-known that captodative substitution around a carbon radical center can significantly decrease the strength of the C–C bond,^{4–6} but not to the extent of allowing for isolation of well-defined monomers. The 2-oxomorpholin-3-yl radical **I** is a classical example (Scheme 1).^{7,8} Although the captodative

Scheme 1

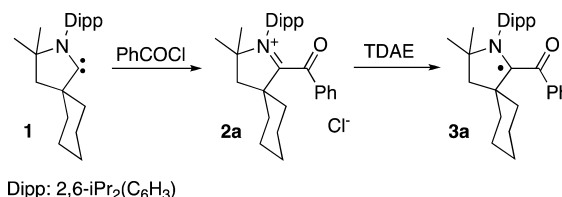


association of amino and carboxy groups is optimal, only the dimeric form **II** could be isolated. Nonetheless the dimerization is a reversible process; dissolution of **II** in well-degassed solvents yields small, but detectable, amounts of **I** with dissociation constants up to 10^{−9} M. Note that dimerization of glycyl radicals **III** can be prevented when they are sheltered in enzymes.^{9,10}

In recent years, stable carbenes¹¹ have emerged as efficient tools for the preparation of stable main-group-based radicals and diradicals.^{12,13} Recently we made the first foray into the realm of purely organic radicals. Using an anti-Bredt diaminocarbene,¹⁴ we synthesized the air-stable oxyallyl radical cation **IV**,¹⁵ in which the oxygen atom is the principal spin density carrier. On the other hand, Fukuzumi et al. reported the observation of thiazolylidene carbene-based radicals **V** by EPR. These compounds, which were generated *in situ* by electro-oxidation of the corresponding enolate, decomposed within hours at room temperature.¹⁶ Based on these results, we decided to investigate the stability of related radicals built on (alkyl)(amino)carbenes (CAACs).¹⁷ Herein, we report the synthesis and the first structural study of a monomeric (amino)(carboxy) radical. Our synthetic approach is simple and versatile, as demonstrated by the straightforward synthesis and isolation of related bi- and triradicals.

A precursor was readily synthesized by adding benzoyl chloride to a THF solution of CAAC **1** at −78 °C (Scheme 2).

Scheme 2



After workup, iminium salt **2a** was isolated in 81% yield and fully characterized, including a single crystal diffraction study (Figure 1). The cyclic voltammogram of **2a** features two reversible reduction waves ($E = -0.93$ V and -1.86 V, against Fc⁺/Fc), for the formation of the radical and the enolate, respectively (see, Supporting Information). Half an equivalent of tetrakis(dimethylamino)ethylene (TDAE) ($E \approx -1.2$ V)¹⁸ was added to a solution of **2a** in dichloromethane at −78 °C, and after workup **3a** was isolated in 94% yield, as deep red crystals.

A single crystal X-ray diffraction study revealed that the N1, C1, C2, and O1 atoms are coplanar, as expected from the captodative stabilization (Figure 1). Note that this conjugated

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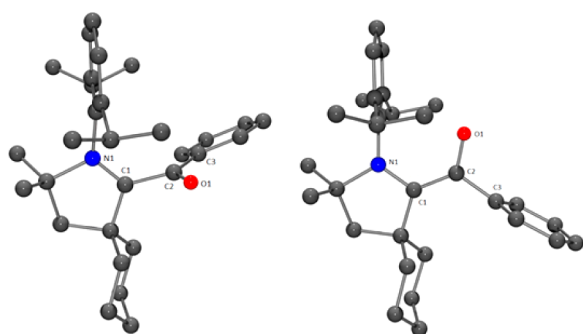


Figure 1. X-ray structure of **2a** (left) and **3a** (right). Hydrogen atoms, solvent molecules, and the chloride anion (for **2a**) were omitted for clarity.

π -system is orthogonal to the phenyl group, in contrast with the precursor **2a**, in which the iminium moiety is orthogonal to the planar benzoyl group. In addition, there is a significant shortening of the C1–C2 bond [**2a**: 1.521(2), **3a**: 1.429(2) Å] and a lengthening of the N1–C1 [**2a**: 1.292(2), **3a**: 1.3601(19) Å], C2–O1 [**2a**: 1.217(2), **3a**: 1.2587(18) Å], and C2–C3 bonds [**2a**: 1.465(2), **3a**: 1.507(2) Å].

The SOMO of **3a** (B3LYP/6-311g** level of theory) is a bonding combination of the $\pi^*(\text{CO})$ molecular orbital and the LUMO of the carbene, with significant electronic density on all conjugated atoms (Figure 2).¹⁹ The delocalization of the spin

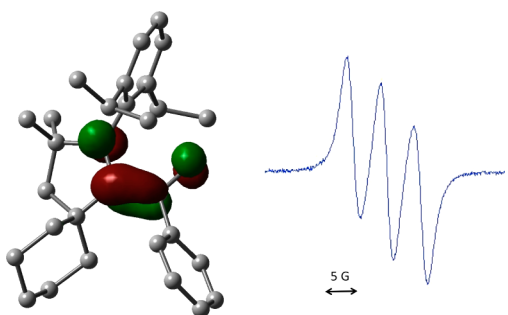


Figure 2. Left: Representation of the SOMO of **3a** (isosurfaces at 0.05 au). Right: X-band EPR spectra of **3a** in benzene at room temperature.

density across the iminium and carbonyl moieties, which is a consequence of the captodative stabilization, was confirmed by calculations (see Supporting Information for a detailed discussion). About 40% of the spin density is localized on the C1 carbon atom, which is the principal spin carrier, whereas about 28% is localized on O1, 24% on N1, 6% on C2, and less than 2% on the phenyl group.

Our synthetic strategy affords in principle an easy entry to a plethora of (amino)(carboxy) radicals from the corresponding acyl chlorides. In order to showcase the versatility of the method, we reacted CAAC **4** with terephthaloyl and trimesoyl chlorides, respectively. The resulting di- and trichloride salts **2b** and **2c** were obtained in 67% and 58% yield, respectively (Scheme 3). Reduction with TDAE afforded the corresponding bi- and triradicals **3b** and **3c**. X-ray diffraction studies revealed structures similar to that of **3a**, the phenyl linker being orthogonal to the (amino)(carboxy) radical units (Figure 3).

The X-band EPR spectra of **3a–c** in solution at room temperature are similar. They feature a triplet with close g values (2.0039, 2.0040, and 2.0040, respectively) and isotropic hyperfine coupling constants with nitrogen ($a_N = 15.4$, 16.8,

Scheme 3

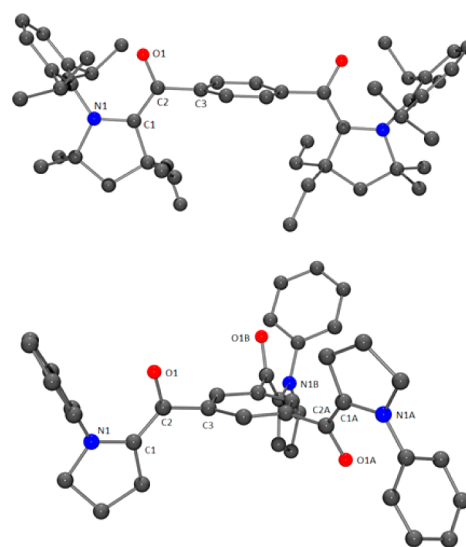
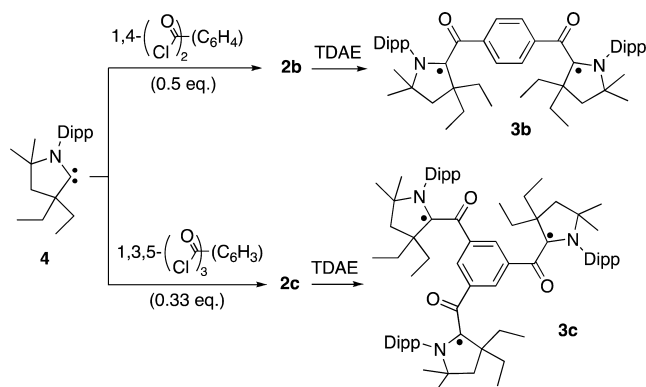


Figure 3. X-ray structure of **3b** (top) and **3c** (bottom). Hydrogen atoms and solvent molecules, as well as isopropyl and ethyl substituents in the case of **3c**, are omitted for clarity.

and 16.8 MHz, respectively). These preliminary data are in line with the expected weak electron exchange couplings in polyradicals **3b–c**, which feature nonconjugating spacers, and radical units far away from each other (C1–C1' distances range from 6.60 to 7.40 Å).²⁰

To summarize, cyclic (alkyl)(amino)carbenes afford in two simple steps (amino)(carboxy)radicals, which do not dimerize and could be characterized for the first time by X-ray diffractometry as monomeric species. Radicals **3a–c** have been stored at room temperature, in solution, and as a solid, for weeks under an inert atmosphere without any apparent decomposition. These results as a whole demonstrate that (amino)(carboxy) radicals have now to be considered as stable monomeric paramagnetic building blocks, similarly to verdazyl and nitroxyl radicals.

■ ASSOCIATED CONTENT

§ Supporting Information

Full experimental details and X-ray crystallographic data for **2a–b** and **3a–c**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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