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Isolation and X-ray Crystal Structure of an Electrogenerated TEMPO–N_3 Charge-Transfer Complex

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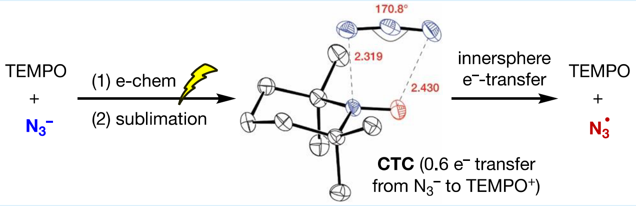
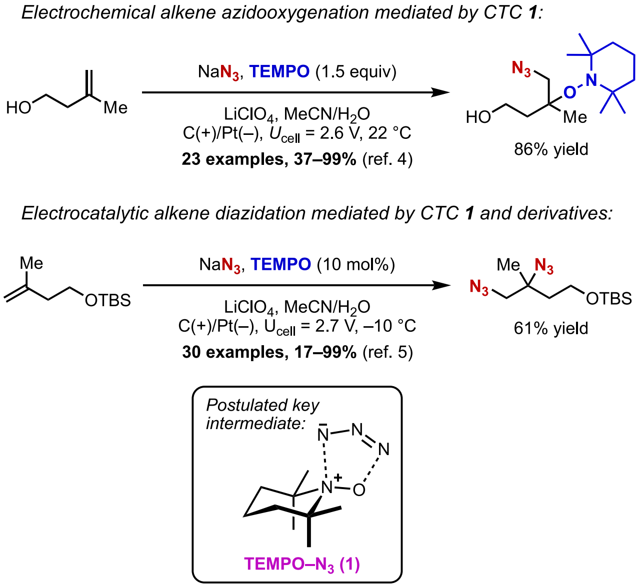
ABSTRACT: Advances in radical-based catalytic reactions have created a demand for understanding their mechanistic underpinnings. Here, we present the isolation, structural elucidation, and theoretical analysis of a catalytically relevant charge-transfer species formed between the azidyl radical and (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO). The unusual bond angles and pancake bonding between these two fragments highlight the weak bonding interactions present in this complex. This X-ray structure validates computational predictions as well as mechanistic proposals of TEMPO-mediated radical azidation reactions.



Charge-transfer complexes (CTCs) are noncovalent adducts comprised of an electron donor and an electron acceptor associated via weak molecular interactions arising from transfer of charge.[1] These species have been postulated as key intermediates in many redox organic transformations, frequently mediating single-electron transfer events between an organic substrate and a redox agent. In particular, recent advances in radical chemistry feature the strategic exploitation of the unique characteristics of CTCs in the contexts of photoredox catalysis,[2,3] electrocatalysis,[4,5] and biocatalysis,[6,7] enabling new modes of reactivity that were previously challenging to access. Despite their emerging role in radical catalysis, the short lifetimes of these CTCs have made their solid-state and solution-state structural determination difficult. Literature examples of CTC crystal structures[8−11] are most commonly reported for species that make use of polyaromatic precursors where π-stacking biases ordered packing. Such designer complexes have prominent applications in materials chemistry but are rarely relevant to catalysis.[12] Here, we report for the first time an X-ray crystal structure of an anodically generated (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO)–N_3 CTC, a metastable crystalline adduct that is shown to be a crucial intermediate in the organocatalyzed electrochemical diazidation[5] and azidooxygenation[4] of alkenes.

Scheme 1. Electrochemical Alkene Difunctionalization Mediated by the TEMPO–N_3 CTC (1)



The TEMPO–N_3 CTC was first postulated during our investigation of the electrochemical azidooxygenation of alkenes (Scheme 1).[4] Spectroscopic and voltammetric studies revealed the formation of a CTC upon electrochemical generation of oxoammonium ion TEMPO$^+$ followed by its association with N_3^-. The formation of a reactive adduct of TEMPO and N_3 has also been postulated in previous studies,[1,3,13] but few structural characterization or reactivity studies of such an adduct were reported.[14] Due to the instability of the CTC (half-life in acetonitrile (MeCN) solution ≈ 7 min at room temperature),[4] structural insight relied on DFT calculations, which suggested four possible

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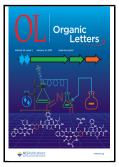

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structures, with **1** being the lowest in energy and most consistent with spectroscopic data (Figure 1).[4] Nonetheless, definitive determination of the structure of **1** proved challenging due to difficulties in obtaining high quality single crystals using traditional crystallization methods, and this structural information remained a key missing piece in the mechanism of the electrochemical azidation reactions we discovered. In addition, our theoretical prediction presents an unexpected and fascinating structure wherein the TEMPO and N_3 moieties are associated entirely via noncovalent interactions with partially formed chemical bonds and unusual bond angles. Although DFT provides a tentative structural prediction, given the unusual transition-state-like structure and the metastable nature of the complex, definitive assignment of the CTC structure is crucial. The elucidation of the complex structure will be a first of its kind and provide insights into the mechanism of charge transfer involving two of the most common molecules in radical chemistry.

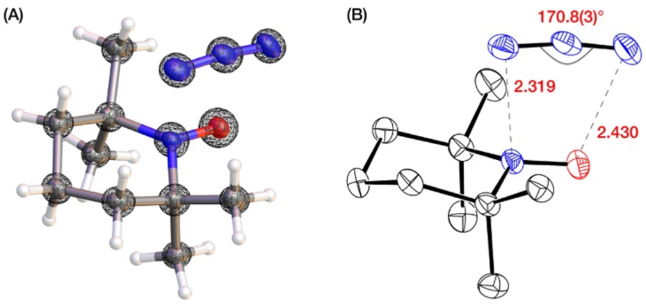

Figure 1. Experimental crystal structures of CTC **1**. (A) X-ray crystal structure of **1**, Cu Kα (1.5418 Å), with electron density map shown contoured at +3.12 rmsd (2.1526 e Å^{-3}). (B) ORTEP diagram of the X-ray structure of **1** with ellipsoids shown at the 30% probability level, with H atoms omitted for clarity.

To provide a more definitive structural confirmation, we attempted to collect diffraction data from the CTC using electron crystallography.[15] Cryo-electron micrographs of lyophilized reaction mixtures revealed highly crystalline domains. Indeed, preliminary diffraction studies provided a partial structure of the TEMPO−N_3 adduct consistent with the calculated CTC **1**, but unambiguous structural characterization was hampered by low-quality data and confounding diffraction from crystalline impurities present in the reaction mixture.

To prepare the CTC in a pure form, we devised an electrolysis experiment, in which a constant current of 5 mA/cm^3 (geometrical current density) was passed through a solution of TEMPO and NaN_3 in MeCN and H_2O using a carbon felt anode and a Pt cathode. The addition of H_2O as a cosolvent rendered this experiment free of any exogenous electrolyte (e.g., $LiClO_4$). By using aqueous NaN_3 as the electrolyte, the subsequent purification and crystallization process was significantly simplified. The electrolysis mixture, presumably consisting of TEMPO−N_3 CTC **1** and NaOH, was then subjected to a rapid workup procedure to remove NaOH. Upon solvent evaporation, the resultant mixture of CTC **1** and its decomposition product TEMPO was further purified via vacuum sublimation. During the Kugelrohr fractional sublimation, we discovered that TEMPO and TEMPO−N_3 sublime at markedly different temperatures (19 and 50 °C, respectively, at a constant pressure of 200 mTorr). This difference allowed us to isolate dark, opaque, shock-sensitive crystals that were 30−100 μm in diameter, much too large and far too sensitive for milling to proper size for electron crystallography. Importantly, dissolution of this material in MeCN regenerated the distinct spectroscopic features (λ_{max} = 380 nm) diagnostic of the TEMPO−N_3 CTC.[4] **Warning: This solid is shock-sensitive and can rapidly decompose in a range of solvents and crystallography oils.** The CTC displays enhanced stability in the solid state (decomposition visually observed after ∼3−4 h at room temperature) likely because the main decomposition pathway via radical fragmentation is retarded in the crystal state. Thus, X-ray crystallography data collection is possible.

We then subjected these crystals to Cu Kα X-ray diffraction and obtained a high-resolution structural solution of the TEMPO−N_3 CTC (**1**) (0.79 Å) (Figure 1A; data deposited to Cambridge Crystallographic Data Centre: CCDC 2035577). The X-ray data provide unequivocal confirmation of the structure predicted by quantum mechanical DFT calculations (Figure 2A), with the azide moiety positioned directly over the oxoammonium N═O bond.

The crystal structure of **1** features a nonlinear azide with an unusual N−N−N bond angle of 170.8(3)°, a geometry distinct from canonically linear azidyl radicals and azide anions. Although slightly bent metal azides (174°−177°) have been reported,[16,17] this structure is a unique example of azide

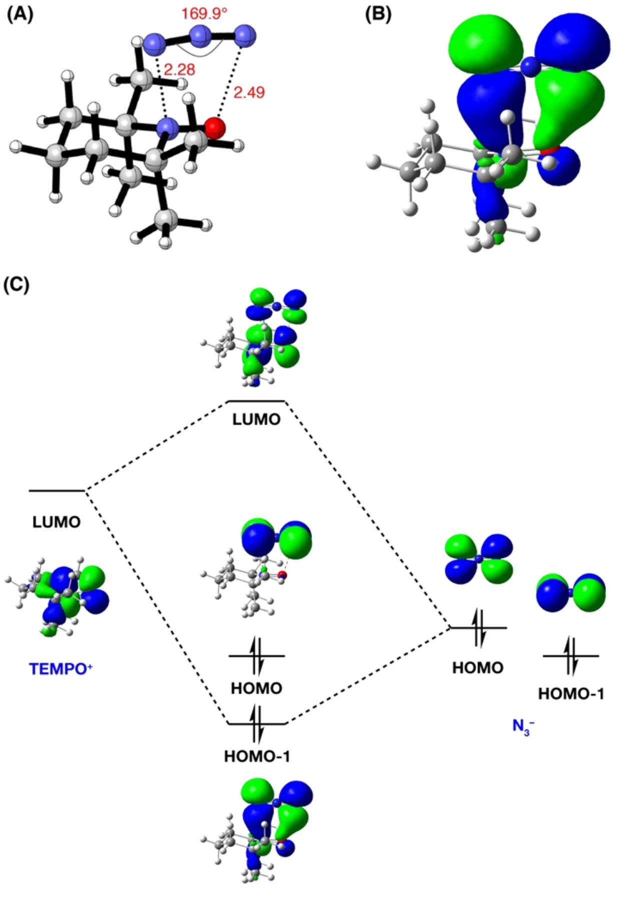

Figure 2. DFT predicted structure at B3LYP-D3/6-311++G(d,p) level of density functional theory. (B) Electronic structure (HOMO−1) of **1** calculated at B3LYP-D3/6-311++G(d,p) level of theory. See Supporting Information for other key molecular orbitals. (C) Molecular orbital construction of CTC **1** at B3LYP-D3/6-311++G(d,p).

nonlinearity engendered by a charge-transfer complex. In addition to this unique structural feature, two additional observations provide evidence of dynamic charge transfer and partial covalent bonding between N_3 and TEMPO. First, the interatomic distances between the terminal nitrogen atoms on the azide and the atoms of the oxoammonium moiety (2.319 and 2.430 Å) are contracted within the sum of the van der Waals radii, but substantially longer than a formal covalent bond. Interestingly, these distances are closely related to those found in transition states of alkyl and aryl azide cycloaddition reactions (2.1−2.5 Å).[18,19] Second, the aminoxyl N−O bond length of 1.238 Å of TEMPO−N_3 (**1**) lies in between the N−O single bond (1.28 Å) in TEMPO and the N═O double bond (1.18 Å) of $TEMPO^+$.[20] These properties are characteristic of 4-center, 2-electron "pancake bonding" between two open-shell species.[21,22] The NBO bond orders of the partially formed bonds between TEMPO and N_3 motifs are 0.24 (for NN) and 0.14 (for NO), which are also characteristic of such 4-center, 2-electron bonding.

Although crystal structures of ($TEMPO^+X^-$)-type CTCs have been reported by mixing TEMPO with a strong oxidant (e.g., Br_2 or quinone derivatives), these structures display an N−O bond distance of ca. 1.19 Å that is characteristic of $TEMPO^+$ with no apparent structural distortions or molecular interactions between the oxoammonium ion and the counteranion (X^-) beyond ion pairing.[23,24] These features indicate near-complete charge transfer from TEMPO to the oxidant and thus are distinct from the TEMPO−N_3 CTC that we report herein.

Due to the propensity of the CTC to decompose into TEMPO and N_2 in solution, analyzing the electronic structure of the complex by electron spin resonance spectroscopy proved to be experimentally difficult. DFT calculations predicted a closed-shell species rather than a triplet radical pair. We performed additional DFT calculations at a higher level of density functional theory and a more complete basis set (B3LYP-D3/6-311++G(d,p)), which provided a more accurate prediction of the structural features of **1** (Figure 2A) compared with a previous report.[4] In this structure, the HOMO of the complex resembles one of the degenerate azide HOMOs (HOMO−1) and resides exclusively on the azide, while the orthogonal orbital (HOMO) is stabilized by mixing with the LUMO of $TEMPO^+$ (which is the SOMO of TEMPO) (Figure 2B and C). The stunning resemblance between the crystal and DFT-predicted structures indicates that the CTC is a closed-shell species that arises from the interaction between the SOMOs of TEMPO and the azidyl radical.[25] The DFT-predicted charge distribution revealed a significant degree of charge redistribution, with 0.62 electron transfer from N_3^- to $TEMPO^+$, or 0.38 electron transfer from TEMPO to $N_3^\bullet$, depending on the reference starting point of CTC formation. Thus, despite being a closed-shell complex, CTC **1** lies closer in electronic structure to an interacting radical pair than an ion pair. Dissociation of **1** to the two component radicals (TEMPO and $N_3^\bullet$) is computationally estimated to require only 6−10 kcal/mol, accounting for the ability of this complex to generate radicals to facilitate the catalytic processes described previously.[4,5]

In conclusion, we report the X-ray crystal structure of a TEMPO−N3 CTC (**1**). Given the metastable nature of the complex, the combination of electrochemical generation and sublimation proved critical to obtaining single crystals of sufficient purity and quality. The structure, reminiscent of a [3 + 2] cycloaddition transition state, features an unusual azide moiety that is significantly distorted from linearity to facilitate the 4-center, 2-electron bonding in CTC. The experimentally determined structure unequivocally confirms DFT prediction, complete with partial bonding indicative of weak covalent interactions stabilizing the complex, and easily dissociated to a reactive radical pair. The definitive structural elucidation of the CTC lends further support to our proposed mechanism of the electrochemical alkene azidation reactions that it mediates. Furthermore, the structural assignment together with theoretical information provided insights into the mechanism of charge transfer between TEMPO and N_3 radicals. Given the critical role of CTCs in mediating radical redox organic transformations, we anticipate our study will have broader mechanistic implications in this area and provide a theoretical foundation for the discovery of new reactions mediated by aminoxyl radicals.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c03966.

Materials and methods; crystallographic data; computed reaction coordinate diagram; visualization of interacting molecular orbitals; coordinates of optimized compounds (PDF)

Accession Codes

CCDC 2035577 (**1**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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