Research Article

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Ligand Effects Hot Paper

How to cite: Angew. Chem. Int. Ed. 2024, 63, e202409315 doi.org/10.1002/anie.202409315

Reductive Elimination From Tetra-Alkyl Cuprates $[Me_nCu(CF_3)_{4-n}]^-$ (*n*=0-4): Beyond Simple Oxidation States

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Abstract: In recent years, the electronic structures of organocuprates in general and the complex $[Cu(CF_3)_4]^$ in particular have attracted significant interest. A possible key indicator in this context is the reactivity of these species. Nonetheless, this aspect has received only limited attention. Here, we systematically study the series of tetra-alkyl cuprates $[Me_nCu(CF_3)_{4-n}]^-$ and their unimolecular reactivity in the gas phase, which includes concerted formal reductive eliminations as well as radical losses. Through computational studies, we characterize the electronic structures of the complexes and show how these are connected to their reactivity. We find that all $[Me_{\it n}Cu(CF_3)_{4-{\it n}}]^-$ ions feature inverted ligand fields and that the distinct reactivity patterns of the individual complexes arise from the interplay of different effects.

Introduction

Among the different high-valent organocuprates, $[Cu(CF_3)_4]^-$ is the one that has attracted most attention. This complex was first synthesized by Naumann et al., who

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proposed a d⁸ configuration for the copper center with its nearly square-planar coordination geometry (Scheme 1).^[1] $[Cu(CF_3)_4]^-$ proved remarkably stable,^[2] in contrast to most fluorine-free high-valent organocuprates.^[3] Based on quantum chemical calculations, Snyder attributed this unexpectedly high stability to a special bonding situation in $[Cu(CF_3)_4]^{-[4]}$ In contrast to the typical electronic configuration in transition-metal complexes, he supposed the symmetry-adapted orbitals of the ligands, i.e., the CF₃ groups, to lie energetically above the 3d orbitals of the metal center. Since then, such an ordering of the orbital energies has been commonly referred to as an inverted ligand field.^[5] For the case of $[Cu(CF_3)_4]^-$, an inverted ligand field implies the presence of a copper center in a d¹⁰ configuration. Simplified ways to view this scenario are descriptions, according to which three coordinating CF₃⁻ anions and one CF_3^+ cation bind to copper (Scheme 1, bottom middle; the charges are averaged for the individual CF₃ groups). Alternatively, the binding of two CF₃⁻ anions and two CF₃⁻ radicals would also be compatible with a d¹⁰ configuration on copper (Scheme 1, bottom right). From the very beginning, Snyder's analysis has been discussed controversially.^[6] This controversy has not been settled to date, despite extensive theoretical calculations and X-ray absorptionspectroscopic measurements.^[7] The descriptions put forward for $[Cu(CF_3)_4]^-$ in the current literature range from a Cu(III)/d⁸ complex^[7c] to a Cu(I)/d¹⁰ complex with an inverted ligand field^[7g] up to the questioning of the existence of genuine Cu(III)/d⁸ compounds in general.^[7b]

In comparison to CF_3 , simple methyl groups have higher orbital energies. Thus, the sequential exchange of CF_3 for Me may possibly be expected to give rise to inverted ligand fields in $[Me_nCu(CF_3)_{4-n}]^-$ complexes as well. Nonetheless,



Scheme 1. Ambiguities in the formal oxidation state assignments as pointed out by Snyder (top).^[4] Conceptual descriptions of Cu(III)/d⁸ and Cu(I)/d¹⁰ configurations (bottom). Note that for the Cu(I)/d¹⁰ scenarios (bottom right) the charges are averaged.

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 $[Me_nCu(CF_3)_{4-n}]^-$ and related $[R_nCu(CF_3)_{4-n}]^-$ species, R =alkyl, are widely considered d⁸ complexes and the question of their having normal or inverted ligand fields has only been addressed in a few cases. This neglect and almost complete lack of systematic evaluation is surprising, given that $[RCu(CF_3)_3]^-$ and $[RCuMe_3]^-$ are known as key intermediates in synthetically important cross-coupling and Michael-type addition reactions.^[3,8] Systematic studies on the effects of CF₃ vs Me group substitution have only been accomplished in very few cases. Liu and co-workers probed the reactivity of $[RCu(CF_3)_3]^-$ complexes, $R = alkyl_1^{[9]}$ including [MeCu(CF₃)₃]⁻, a compound previously reported by Li and co-workers^[10] and recently examined theoretically by Lancaster and co-workers.^[11] Additional insight was gained from studies on formal reductive eliminations of R-CF₃, R=alkyl, alkenyl, and aryl,^[9,12] as well as related polyfluorinated coupling products^[13] from high-valent copper complexes.

Here, we seek to achieve a comprehensive understanding of the electronic structure and reactivity of high-valent probing full organocuprates by the series of $[Me_nCu(CF_3)_{4-n}]^-$ complexes, $0 \le n \le 4$. In this way, we can systematically assess how the exchange of CF₃ for Me groups and the gradual transformation from $[Cu(CF_3)_4]^-$ to $[CuMe_4]^-$ affect the metal-ligand binding. We base our analysis on a combination of gas-phase fragmentation experiments and high-level quantum chemical calculations. The former have already proven very useful for characterizing several high-valent cuprates,^[14] including $[Cu(CF_3)_4]^{-,[15]}$ $[MeCu(CF_3)_3]^{-,[15c]}$ and $[Me_4Cu]^{-,[16]}$ In particular, the results of the gas-phase experiments are directly comparable with the predictions of the theoretical calculations and, thus, can serve as a rigorous proof of the reliability of the latter. We take special care to address the implications of inverted ligand fields because it has been proposed that formal reductive eliminations of high-valent copper species may indeed proceed in an approximately redox-neutral manner.^[7b,11,17] This problem is of particular significance for formal Cu(III) complexes not containing any CF₃ groups due to the singular importance of these species as intermediates in synthesis and catalysis.

Results and Discussion

For the preparation of $[Me_nCu(CF_3)_{4-n}]^-$ complexes, we solutions of [(bpy)Cu(CF₃)₃] treated (bpy = 2, 2' bipyridine)^[18] in tetrahydrofuran (THF) with an excess of MeLi or MeMgBr (see Supporting Information for details). The anionic constituents of the sample solutions were transferred into a three-dimensional quadrupole ion trap via negative-ion mode electrospray ionization (ESI, Figures S1-S7). The different $[Me_nCu(CF_3)_{4-n}]^-$ complexes^[19] then were mass-selected, accelerated to higher kinetic energies, and allowed to collide with the He atoms present in the ion trap. A subsequent m/z scan identified the resulting fragment ions and, thus, revealed the unimolecular reactivity of the cuprates (Figures S8-S12). A comparison of the reactions observed shows a clear trend (Figure 1): While radical losses predominate for $[Cu(CF_3)_4]^-$, they occur only to a minor extent for $[MeCu(CF_3)_3]^-$ and could not be detected for the remaining complexes.^[12g,20] Instead, the latter exclusively undergo concerted formal reductive eliminations. Furthermore, both competing reaction types proceed in a selective fashion. Thus, the primary radical loss from $[MeCu(CF_3)_3]^$ results exclusively in the expulsion of the Me, but no CF₃ group. Likewise, the concerted reductive eliminations from the heteroleptic cuprates preferentially involve the Me groups. Accordingly, the resulting fragment ions exhibit a



Figure 1. Unimolecular reactivity of high-valent cuprates $[Me_nCu(CF_3)_{4-n}]^-$. Top: Competing radical losses (red) and formal reductive eliminations (blue) observed upon collision-induced dissociation (CID). Middle: Fractions of the competing reactions observed (given uncertainties correspond to one standard deviation or the maximum error derived from > 5 single CID experiments in each case). Minor additional primary fragmentation channels, such as the elimination of CF₂, are not considered. Bottom: Theoretically predicted barriers associated with radical losses (red) and formal reductive eliminations (blue). For $[Me_2Cu(CF_3)_2]^-$, the barriers for the fragmentation of the *cis* isomer are given. The relative rate constants and, thus, fractions of the competing reactions supposedly correlate inversely with the corresponding barriers.

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higher CF₃:Me ratio than their corresponding precursor ions.

We studied the reactivity patterns computationally at the DLPNO-CCSD(T)/PBE0^[21] level of theory (for full computational details, see the Supporting Information) and calculated the barriers of the different fragmentation reactions (Tables S1- S7 and Figure 1, bottom). For the radical losses, the barriers are supposed to equal the simple bonddissociation enthalpies. Furthermore, we base our discussion upon $\Delta H/\Delta H^{\ddagger}$ instead of $\Delta G/\Delta G^{\ddagger}$ values because the former better describe the behavior of the microcanonical ensembles probed in our gas-phase experiments.^[22] The predicted barriers very well agree with our experimental observations. For the complexes $[Me_nCu(CF_3)_{4-n}]^-$, $n \ge 2$, we find the barriers associated with the formal reductive elimination of Me_2 to be $\geq 40 \text{ kJ mol}^{-1}$ lower than those associated with the loss of a methyl radical, in accordance with the exclusive observation of the former fragmentation channel in our experiments. Likewise, the formal reductive elimination of MeCF₃ from $[MeCu(CF_3)_3]^-$ is energetically preferred over the loss of a methyl radical. However, the difference in barrier heights amounts to only $\Delta\Delta H^{\ddagger} = 39 \text{ kJ mol}^{-1}$. The decreased energetic preference of the formal reductive elimination as well as the highly ordered nature of the related transition state (TS) explain why the radical-loss channel starts to compete in this case. For the homoleptic $[Cu(CF_3)_4]^-$, the barriers associated with the formal reductive elimination of C_2F_6 and the homolytic bond cleavage are almost identical. Accordingly, the less ordered nature of the TS of the trifluoromethyl-radical loss (corresponding to the separate fragments) is expected to favor this fragmentation channel, in full agreement with our experimental findings. Nonetheless, the expulsion of a CF₃ radical from $[Cu(CF_3)_4]^-$ is energetically significantly more demanding than the reductive eliminations from the $[Me_nCu(CF_3)_{4-n}]^{-1}$ complexes with $n \ge 1$, which explains the increased stability of the former.

As the experimentally observed trends are reproduced well by the computations and, thus, lend support to the validity of the latter, we now turn to the question of their origin. First, we addressed the problem whether the electronic structures of these cuprates show variations related to the presence/absence of an inverted ligand field. A simple means to tackle this question is the analysis of the composition of the σ -antibonding LUMO, which should be of predominant ligand character in case of an inverted ligand field (less than 50% metal character is defined by Lancaster and co-workers as a threshold).^[7b] For the series of cuprates studied here, the values range from 32.9% to 36.7 % d-orbital-character when going from $[Cu(CF_3)_4]^-$ to $[Me_4Cu]^-$ (Figure 2A, for depictions and additional details see the Supporting Information). This result already indicates that an inverted ligand field is present for the entire series of complexes. Likewise, it suggests that an analysis into the origin of the observed reactivity trends must go beyond the problem of the possible involvement of inverted ligand fields. The relationship between inverted ligand fields and oxidation states has been recently discussed by two of us elsewhere.^[17c]



Figure 2. (A) Canonical LUMO for $[Cu(CF_3)_4]^-$ of σ-antibonding nature. (B) Localized Cu–C σ-bonds (IBOs) for $[Cu(CF_3)_4]^-$. (C) Dominant valence bond structures of $[Me_nCu(CF_3)_{4-n}]^-$ complexes. Arrows indicate spin-coupled pairs of electrons. Orbital depictions are based on PBE0-D3(BJ)/def2-TZVP Kohn–Sham wave functions.

To substantiate this finding further, we used energy decomposition analyses (EDA)^[23] for evaluating whether these complexes are best described as having d^8 , d^9 , or d^{10} configurations. Following a previous study analyzing $[Cu(CF_3)_4]^{-,[17b]}$ we focus on the orbital interaction energy, which can be considered a measure of the energetic difference between the molecular wave function and the orbitals of the fragments resulting from a given split-up of the complex under investigation. The lower the absolute value of this orbital interaction energy, the more closely the corresponding fragments resemble the electronic structure of the intact molecular complex. For all of the $[Me_nCu(CF_3)_{4-n}]^-$ cuprates, we find d¹⁰ configurations to exhibit the lowest values (Tables S8-S12). This result suggests once more that the Cu centers of these complexes are of similarly reduced nature. Further support for this conclusion comes from the analysis of the intrinsic bond orbitals (IBOs)^[24] for these complexes and their Cu-C bonds in particular. As we have argued before,^[17b] the results from the EDA are consistent with the partial charge distributions of the IBOs for the four Cu–C σ -bonds summing up to ~2 electrons worth of charge on Cu. Hence, they lead to electronic configurations, which can be described as quasi d¹⁰ (Figures 2B and S20, Table S13). Although the partial charges located on the Cu center on the one hand and on the ligands on the other remain almost constant in total, the partial charge distributions of the individual bonds vary significantly for the different cuprates. We will come back to this variation later when analyzing reactivity patterns.

The present findings are also corroborated by valencebond (VB) calculations,^[25] which again show that the oxidation level is similar in all cases. For all complexes, the key structures are those with Cu(0) and Cu(+I) centers (Figure 2C) accounting for >80% combined weight (for additional details, see the Supporting Information). Contri-

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butions of the Cu(III) oxidation state do not exceed 11%. Upon substitution of the CF₃ for Me groups, a slight increase in the weights of the higher oxidation states (Cu(+I), Cu(+II), and Cu(+III)) is discernible, whereas those of the lower oxidation states (Cu(-I) and Cu(0)) decrease accordingly. Hence, the complexes are of comparable oxidation level and the observed differences in reactivity must have an alternative origin.

In their recent analysis of the unimolecular reactivity of $[Cu(CF_3)_4]^-$ and $[MeCu(CF_3)_3]^-$, Lancaster and co-workers ascribed the difference in the reactivity of these complexes to deviating electrostatics.^[11] The partial charge distributions of the IBOs of the Cu-C σ -bonds derived from our calculations point into a similar direction (Figure 3). While throughout these partial charges add up to ~2 on Cu, the way that these values are achieved differs significantly (see above). For the highly symmetrical $[Cu(CF_3)_4]^-$ complex, we find that all Cu–C σ-bonds have a partial charge distribution of 0.46 on Cu and 1.46 on C. This well-balanced picture is severely disturbed in the complex $[MeCu(CF_3)_3]^-$, in which partial charge distributions of 0.38 on Cu and 1.51 on C for the Cu-CF₃ bonds trans to each other, 0.24 on Cu and 1.58 on C for the Cu–CF₃ bond *trans* to the Me group, and 0.92 on Cu and 1.06 on C for the Cu-Me bond are predicted. This finding already indicates that the Cu-Me bond is primed for the electron pair to relocate to Cu in the C-C bond forming step, with the Me group being transferred as an electrophile and the CF₃ group retaining its electron pair and acting as the nucleophile. Thus, it explains the formation of $MeCF_3$ and the absence of C_2F_6 as product.



Figure 3. Ensemble of the four localized Cu–C σ -bonds (IBOs) for $[Me_nCu(CF_3)_{4-n}]^-$ complexes and the resulting sum of the Cu-centered partial charge distributions originating from σ -bonding. Orbitals depictions and values are based on PBE0-D3(BJ)/def2-TZVP Kohn–Sham wave functions.

However, if such a bonding scenario were required for C–C bond formation, we should not have observed the release of Me₂ from the complex [Me₄Cu]⁻, whose partial charge distribution of 0.49 on Cu and 1.42 on C does not show any bias in bond polarities and barely deviates from the bonding picture in [Cu(CF₃)₄]⁻. The different behavior of [Me₄Cu]⁻ and [Cu(CF₃)₄]⁻ becomes obvious from the calculated energy barriers for the competing reaction paths. For the former, the activation enthalpy of $\Delta H^{\ddagger} = 153$ kJ mol⁻¹ for the formal reductive elimination is much lower than the *BDE* = 198 kJ mol⁻¹ associated with homolytic Cu–C bond cleavage whereas no such pronounced preference is predicted for the latter ($\Delta H^{\ddagger} = 216$ kJ mol⁻¹ and *BDE* = 217 kJ mol⁻¹).

For obtaining further insight into the origin of the different energy barriers of the elimination of Me₂ and C₂F₆, we turned to VB and activation-strain model calculations for the TSs. In the former, we studied structures representing a neutral CX₃-CX₃ together with a negatively charged $[Cu](CX_3)(CX_3)$ fragment (A–D, Figure 4), a negatively charged CX_3 - CX_3 with a neutral $[Cu](CX_3)(CX_3)$ fragment (E-F), and a doubly negatively charged CX₃-CX₃ with a positively charged $[Cu](CX_3)(CX_3)$ fragment (G). The cumulative weight of the structures E-F (see the Supporting Information for more details) is substantially higher for the elimination of C₂F₆ than for that of Me₂. This finding indicates that the CF₃ groups more effectively stabilize the negative charge than their Me counterparts, while changes to the oxidation level (reduction) of the metal take place after passing through the TS. The superior ability of the CF_3 groups to stabilize the negative charge can be attributed to the high electronegativity of fluorine and the resulting strong negative inductive effects. For this reason, the number of CF₃ groups remaining attached to the Cu center is maximized. We had already previously put forward similar arguments to explain the selectivity observed in gas-phase fragmentation experiments of other high-valent cuprates.^[15c,16] Furthermore, the VB calculations suggest that the dipolar structures C and D have more weight than their charge-balanced analogue **B**. This finding is in accordance with the importance of uneven partial charge distributions of the IBOs (see above).

The results of the activation strain model calculations give a complementary view on the reactions (Table S14). With the energy of the fragments in the reactant as reference, the strain contributions for the released CX_3 - CX_3



Figure 4. Valence bond structures considered for the transition states.

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and $[Cu](CX_3)(CX_3)^-$ fragments are negative (Figure 5). Hence, strain is released during the reaction and the structure of the fragments resembles those of the products more closely than those of the reactants. The negative strain contributions are counterbalanced by positive interaction energies, which indicate that the bonding between the two fragments is weaker than in the reactants. In all cases, the positive interaction energies overcompensate the negative strain contributions and, thus, give rise to positive reaction barriers. A comparison of the eliminations of C₂F₆ and Me₂ shows that the former are characterized both by more negative strain contributions and more positive interaction energies. Due to the larger absolute quantities of the interaction energies, the C2F6 eliminations are associated with higher barriers. As discussed above, we ascribe the higher bonding interaction in the reactant between the C₂F₆ and the [Cu] fragment to the stronger stabilization of the negative charge by the CF_3 groups than by the Me groups. The distinct barriers of the C₂F₆ and Me₂ eliminations are most evident for the case of cis-[Me₂Cu(CF₃)₂]⁻, which allows a direct comparison of the two competing reaction pathways. For this complex, the elimination of Me2 is not only intrinsically favorable, but additionally facilitated by the electron-withdrawing effect of the two CF_3 groups, which remain attached to the Cu center and stabilize its negative charge (see above). Accordingly, this reaction has a barrier as low as ~100 kJ mol⁻¹. In contrast, the elimination of C_2F_6 is intrinsically unfavorable and, at the same time, lacks a significant stabilization because the two Me groups bound to Cu are not effective in withdrawing the extra electron density from the metal center. As a result, the reaction barrier reaches a value of $\sim 280 \text{ kJmol}^{-1}$. For the elimination of MeCF₃, we find an intermediate behavior with a barrier of $\sim 180 \text{ kJ mol}^{-1}$.



Figure 5. Evaluation of transition states of formal reductive eliminations according to the activation strain model. Fragments are defined with respect to the formed products $[Cu(CX_3)_2]^-$ and C_2X_6 . The positive section of the blue bar defines the barrier height.

Conclusions

For better understanding the electronic structures of highvalent organocuprates and probing their implications for the unimolecular reactivity of these species, we have studied $[Me_nCu(CF_3)_{4-n}]^-$ complexes, $0 \le n \le 4$, by a combination of gas-phase experiments and quantum chemical calculations. While the homoleptic cuprate $[Cu(CF_3)_4]^-$ preferentially undergoes homolytic Cu-C bond cleavage, all other complexes react predominantly or exclusively via formal reductive eliminations of C-C-coupling products. These eliminations proceed in a highly selective way in that they result in neutral coupling products enriched in Me and anionic cuprate fragments enriched in CF3 groups. Our quantum chemical calculations reproduce these trends well. The entire series of $[Me_nCu(CF_3)_{4-n}]^-$ complexes are characterized by inverted ligand fields and more reduced Cu centers than their formal oxidation state of +III would suggest, which appears to be a common feature of all tetra-alkyl cuprates.

Although the overall number of electrons assignable to the Cu center is very similar in all cases, the distribution of the electrons among the different ligands varies considerably. For all heteroleptic complexes, the individual Cu-C bonds are polarized to different degrees, the negative partial charge of the electron-withdrawing CF₃ groups always exceeding that of their methyl counterparts. Thus, the CF₃ groups can act as nucleophilic component in a coupling reaction affording MeCF₃, which is the main product formed from $[MeCu(CF_3)_3]^-$. Another consequence of the electronwithdrawing effect of the CF₃ groups is their tendency to remain bound to the Cu center, where they help to stabilize the negative charge. This stabilization is one of the main factors resulting in the observed selectivity in favor of methyl-rich elimination products. For cis-[Me₂Cu(CF₃)₂]⁻, the barrier for the elimination of Me₂ indeed is more than 180 kJ mol⁻¹ lower than that for the elimination of C₂F₆. The intrinsically lower tendency of CF₃ groups to combine in a concerted reductive elimination also explains why the homoleptic complex [Cu(CF₃)₄]⁻ preferentially undergoes homolytic bond cleavages. At the same time, the lack of an energetically favorable fragmentation pathway via a concerted reductive elimination accounts for the increased stability of $[Cu(CF_3)_4]^-$, which so far had not been understood satisfactorily.

For future studies it will be important to probe changes of the electronic structure during reactions computationally. As our present findings demonstrate, a variety of factors need to be considered for understanding selectivities and product distributions. In particular, the effect of electronsharing covalency and bond polarization requires further attention.

Acknowledgements

B.Z. and K.K. thank Prof. Franc Meyer for enlightening discussions and gratefully acknowledge funding by the Deutsche Forschungsgemeinschaft (KO 2875/12-1, INST

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186/1326-1 FUGG) and the Niedersächsische Ministerium für Wissenschaft und Kultur. This work was sponsored by NWO Exact and Natural Sciences for the use of supercomputer facilities (NWO-2022.004/L1). This research used resources (Summit) of the Oak Ridge Leadership Computing Facility at the Oak Ridge National Laboratory, which is supported by the Office of Science of the U.S. Department of Energy under Contract No. DE-AC05-00OR22725 (DD). We thank the Center for Information Technology of the University of Groningen for their support and for providing access to the Peregrine/Habrok high performance computing cluster. J.E.M.N.K. acknowledges funding from the Dutch Research Council (NWO-740.018.014, Start-Up Grant). Open Access funding enabled and organized by Projekt DEAL.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: cuprates • gas-phase reactions • ligand effects • quantum chemistry • trifluoromethyl

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Manuscript received: May 16, 2024 Accepted manuscript online: July 29, 2024 Version of record online: September 17, 2024

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