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Communication

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Oxidation of Ni(II) to Ni(IV) with Aryl Electrophiles Enables Ni-Mediated Aryl–CF_3 Coupling

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Ⓢ *Supporting Information*

ABSTRACT: This communication describes the synthesis and reactivity of $Ni^{IV}(aryl)(CF_3)_2$ complexes supported by trispyrazolylborate and 4,4′-di-*tert*-butylbipyridine ligands. We demonstrate that isolable Ni^{IV} complexes can be accessed under mild conditions via the oxidation of Ni^{II} precursors with *S*-(trifluoromethyl)dibenzothiophenium triflate as well as with diaryliodonium and aryl diazonium reagents. The Ni^{IV} intermediates undergo high yielding aryl−CF_3 bond-forming reductive elimination. These studies support the potential viability of Ni^{IV} intermediates in nickel-catalyzed coupling reactions involving diaryliodonium and aryldiazonium electrophiles.

Over the past decade, nickel-catalyzed cross-coupling has emerged as an attractive method for a variety of carbon−carbon and carbon−heteroatom bond-forming reactions.[1] The mechanisms of these transformations are generally proposed to involve sequences of $1e^-$ and $2e^-$ redox events that interconvert Ni^0, Ni^I, Ni^{II}, and/or Ni^{III} intermediates.[1,2] In contrast, organometallic Ni^{IV} intermediates are rarely invoked in cross-coupling reactions. This is largely due to Kochi's pioneering mechanistic studies that implicated Ni^I and Ni^{III}-aryl intermediates in Ni-mediated carbon−carbon bond-forming processes.[2b,c]

Recently, Chatani and co-workers have suggested that Ni-catalyzed C−H arylation reactions with aryl iodide[3] and diaryliodonium[4] electrophiles proceed via $Ni^{IV}(\sigma\text{-alkyl})(\sigma\text{-aryl})$ intermediates. While these putative Ni^{IV} species were not detected directly, radical trapping experiments provided evidence against the involvement of single electron pathways. This work reopens questions about the plausibility of Ni^{IV} intermediates in catalytic transformations, particularly those involving aryl electrophiles.[5] Importantly, if such Ni^{IV} intermediates are accessible, they have the potential to exhibit complementary reactivity profiles compared to their lower valent Ni counterparts.[6] In this report, we describe the design and synthesis of organometallic model systems that demonstrate the feasibility of the $2e^-$ oxidation of Ni^{II} to Ni^{IV} with aryl electrophiles. Furthermore, our studies show that the Ni^{IV} products of these oxidation reactions participate in aryl−CF_3 bond-forming reductive elimination, a transformation that remains extremely challenging to achieve at lower valent Ni centers.[7,8]

Our initial studies focused on designing an organometallic model system that would enable us to answer two key questions: (1) Can aryl electrophiles effect the $2e^-$ oxidation of Ni^{II} precursors to Ni^{IV} products? and (2) What is the reactivity of the putative Ni^{IV}(aryl) complexes? To address these questions, we needed access to detectable and ideally isolable Ni^{IV}(aryl) species. A recent report from our group has shown that organometallic Ni^{IV} complexes can be prepared by the oxidation of Ni^{II} starting materials with electrophilic trifluoromethylating reagents (CF_3^+ in Figure 1a).[9] Both the facial tridentate ligand trispyrazolylborate (Tp) and the trifluoromethyl ligand were found to stabilize the Ni^{IV} product **A**. Thus, in the current study we targeted the Ni^{IV}-aryl complex **2**, which is supported by stabilizing Tp and CF_3 ligands (Figure 1b). We hypothesized that **2** could be accessed from two complementary pathways: (i) via the oxidation of **1** with CF_3^+ reagents (by analogy to Figure 1a)[9] or (ii) via the reaction of **3** with aryl electrophiles ($Aryl^+$).

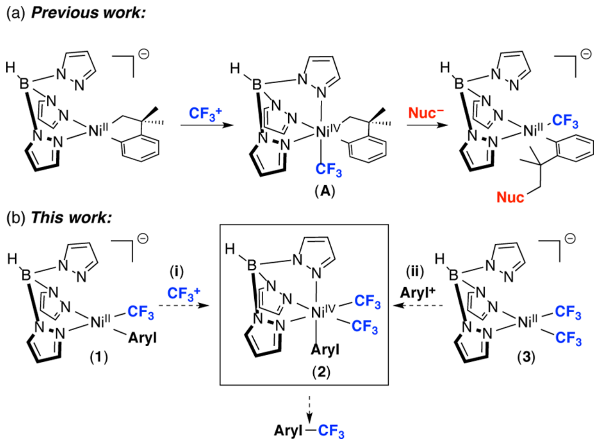

Figure 1. (a) Previous work demonstrating that Tp and CF_3 ligands stabilize Ni^{IV} complex **A**; (b) proposed synthetic routes to the target $Ni^{IV}(aryl)(CF_3)_2$ complex **2**.

We first sought to prepare **2** by the $2e^-$ oxidation of $[TpNi^{II}(Ph)(CF_3)]NBu_4$ (**1**) with *S*-(trifluoromethyl)dibenzothiophenium triflate (TDTT) (Scheme 1). The Ni^{II} precursor was synthesized in 46% isolated yield from the reaction of $(dtbpy)Ni^{II}(Ph)(CF_3)$ (dtbpy = 4,4′-di-*tert*-butylbipyridine) with NBu_4Tp. The treatment of **1** with 1.3 equiv of TDTT afforded the diamagnetic Ni^{IV} product $TpNi^{IV}(Ph)(CF_3)_2$ (**2**) in 90% isolated yield. Complex **2** was characterized by ^1H, ^{13}C, ^{11}B, and ^{19}F NMR spectroscopy. Elemental analysis

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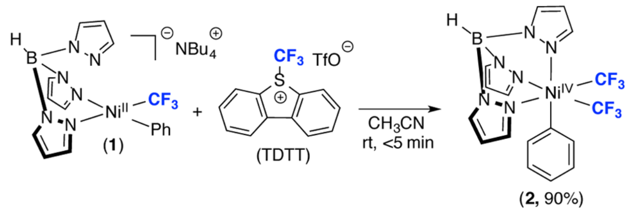
Scheme 1. Synthesis of Ni^{IV} Complex 2 via the Oxidation of 1 with TDTT



and X-ray crystallography (Figure 2) further confirmed the identity and structure of this octahedral Ni^{IV} complex.

We next examined whether 2 could be accessed via the $2e^-$ oxidation of the $Ni^{II}(CF_3)_2$ complex 3 with aryl electrophiles. Seminal studies by Vicic[10] and Mirica[11] have shown that related $Ni^{II}(CF_3)_2$ complexes react with outer-sphere $1e^-$ oxidants to yield Ni^{III} products. However, the analogous $2e^-$ oxidation of such complexes has not been disclosed.

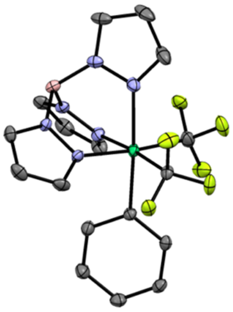
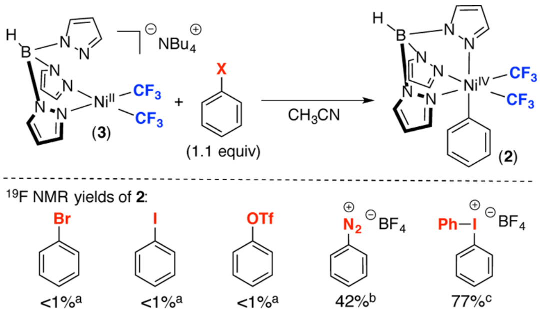


Figure 2. ORTEP of Ni^{IV} complex 2. Thermal ellipsoids are drawn at 50% probability. The rotational disorder in the CF_3 ligands and the hydrogen atoms have been removed for clarity.

The Ni^{II} starting material 3 was prepared in 94% isolated yield by the reaction of NBu_4Tp with $(MeCN)_2Ni^{II}(CF_3)_2$.[10] No reaction was observed upon the treatment of 3 with phenyl iodide, phenyl bromide, or phenyl triflate, even after heating at 70 °C for 12 h (Scheme 2).[12] However, 3 underwent rapid net $2e^-$ oxidation with the more electrophilic arylating reagents Ph_2IBF_4 and PhN_2BF_4. The reaction of 3 with 1.1 equiv of PhN_2BF_4 afforded Ni^{IV} complex 2 in 42% yield after just 10 min at 23 °C. Ph_2IBF_4 yielded the Ni^{IV} product in 77% yield after 10 min at −35 °C. These results demonstrate for the first time that $Ni^{II/IV}$ manifolds are accessible under mild conditions with aryl diazonium and diaryliodonium reagents.

Scheme 2. Synthesis of Ni^{IV} Complex 2 by the Reaction of 3 with PhX



[a]10 equiv of ArX, 70 °C, 12 h. [b]1.1 equiv of PhN_2BF_4, 23 °C, 10 min. [c]1.1 equiv of Ph_2IBF_4, −35 °C, 10 min.

We next investigated the reactivity of the Ni^{IV} product 2. Upon heating at 55 °C for 15 h in CD_3CN, 2 underwent clean $C(sp^2)-CF_3$ bond-forming reductive elimination to afford benzotrifluoride in 76% yield as determined by ^{19}F NMR spectroscopy (Figure 3).[13] The Ni^{II} byproducts of the reaction[14] are $Ni^{II}Tp_2$ (26% yield) and $(CD_3CN)_2Ni^{II}(CF_3)_2$ (29% yield).[9,15] These are presumably generated via ligand disproportionation from the initial reductive elimination product, $TpNi^{II}CF_3$. This reaction represents the first reported example of high yielding aryl−CF_3 reductive elimination from a discrete Ni complex.[16,17]

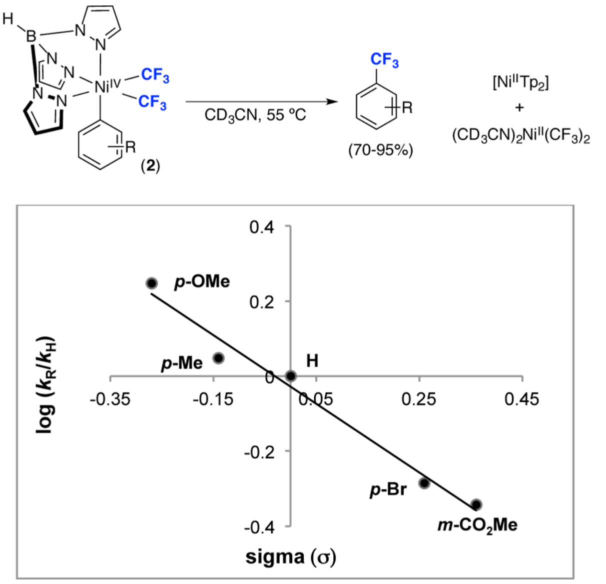


Figure 3. Hammett plot for reductive elimination from 2.

A series of Ni^{IV} complexes bearing substituted aryl ligands were prepared to investigate electronic effects on this aryl−CF_3 coupling reaction. The complexes **2-OMe**, **2-Me**, **2-Br**, and **2-CO_2Me** were synthesized via the treatment of Ni^{II} complex 3 with the appropriate Ar_2IBF_4 reagents (see Supporting Information for full details). Heating the substituted Ni^{IV} complexes at 55 °C in CD_3CN for 4−18 h afforded the corresponding benzotrifluorides in 70−95% yield as determined by ^{19}F NMR spectroscopy. The rate constant (k_{obs}) for reductive elimination from each complex at 55 °C was obtained by monitoring the reactions by ^{19}F NMR spectroscopy. A Hammett plot of the resulting data is shown in Figure 3. This plot shows a ρ value of −0.91, indicating that reductive elimination is fastest with electron-donor substituents on the aromatic ring. This effect mirrors the trend reported for aryl−CF_3 bond-forming reductive elimination from related $Pd^{IV}(aryl)(CF_3)$ complexes.[18] The electronic effect can be rationalized in two ways: (1) the larger trans-effect of electron-rich σ-aryl groups facilitates ligand dissociation to generate a reactive five-coordinate Ni^{IV} intermediate from which reductive elimination occurs, and/or (2) the electron donor substituents accelerate a nucleophilic attack by the σ-aryl ligand onto the electrophilic CF_3 group in the transition state.[19]

In a final set of experiments, we examined analogous reactions using a less stabilizing and thus potentially more catalytically relevant ligand. The bidentate ligand 4,4′-di-*tert*-

butylbipyridine (dtbpy) was selected because it is commonly used in Ni-catalyzed C−C and C−heteroatom coupling reactions.[20] The treatment of dtbpy-supported Ni^{II} complexes **4** and **5** with 1.5 equiv of TDTT and PhN_2BF_4, respectively, afforded benzotrifluoride in 57% and 67% yield as determined by ^{19}F NMR spectroscopy (Figure 4a). Notably, these transformations proceeded to completion within 10 min at room temperature. As such, they are among the fastest reported examples of aryl−CF_3 coupling at a group 10 metal center.[8] Monitoring these reactions by ^{19}F NMR spectroscopy at −25 °C showed the presence of the same transient diamagnetic intermediate in both cases.[21] The ^{19}F NMR resonances associated with this intermediate (a pair of quartets at −19.8 and −23.8 ppm, J_{FF} = 7.9 Hz; Figure 4b) are consistent with an unsymmetrical Ni^{IV} bis-trifluoromethyl complex of general structure **6**. The decay of intermediate **6** was accompanied by growth of the resonance associated with benzotrifluoride. Overall, these results strongly suggest that organometallic Ni^{IV} complexes are accessible under mild conditions using catalytically relevant bidentate nitrogen donor ligands.

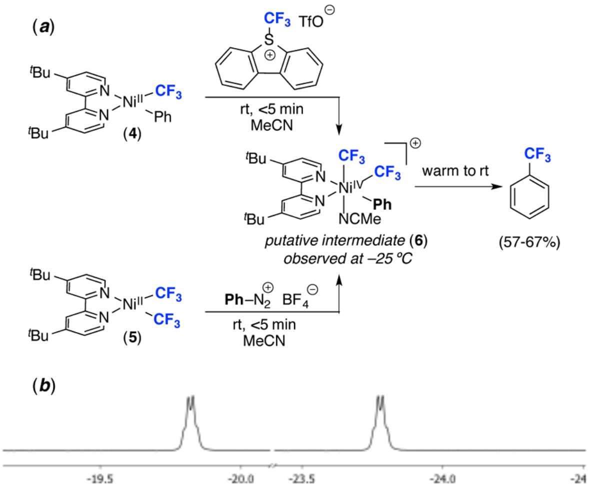


Figure 4. (a) Oxidation and subsequent aryl−CF_3 coupling from dtbpy Ni^{II} complexes **4** and **5**. (b) ^{19}F NMR spectrum showing the two signals assigned to the CF_3 resonances of Ni^{IV} intermediate **6**.

In conclusion, this communication describes studies of the formation and reactivity of $Ni^{IV}(aryl)(CF_3)_2$ complexes. We demonstrate that these Ni^{IV} compounds can be accessed under mild conditions via the net $2e^-$ oxidation of Ni^{II} precursors with diaryliodonium and aryldiazonium reagents. Furthermore, we show that the Ni^{IV} complexes undergo aryl−CF_3 bond-forming reductive elimination. The facile formation of organometallic Ni^{IV} complexes at or below room temperature suggests the viability of Ni^{IV} intermediates in a recently reported nickel-catalyzed C−H arylation reaction with Ph_2IBF_4.[4] Additional studies of related high-valent nickel systems will provide even more insights into oxidants capable of generating Ni^{IV} intermediates as well as the reactivity of these Ni^{IV} species. A fundamental understanding of these transformations will ultimately inform the development of new $Ni^{II/IV}$-catalyzed reactions.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental and spectral details for all new compounds and all reactions reported. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b04892.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Hu, X. *Chem. Sci.* **2011**, *2*, 1867. (b) Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A.-M.; Garg, N. K.; Percec, V. *Chem. Rev.* **2011**, *111*, 1346. (c) Montgomery, J. Organonickel Chemistry. In *Organometallics in Synthesis: Fourth Manual*; Lipshutz, B. H., Ed.; Wiley: Hoboken, N.J., 2013; pp 319−428. (d) Tasker, S. Z.; Standley, E. A.; Jamison, T. F. *Nature* **2014**, *509*, 299. (e) Everson, D. A.; Weix, D. J. *J. Org. Chem.* **2014**, *79*, 4793.

(2) For examples of stoichiometric C−heteroatom and C−C reductive elimination from Ni^{III}, see: (a) Burk, P.; Liu, M.; Miyashita, A.; Grubbs, R. H. *J. Am. Chem. Soc.* **1978**, *100*, 2418. (b) Tsou, T. T.; Kochi, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 1634. (c) Tsou, T. T.; Kochi, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 7547. (d) Amatore, C.; Jutand, A. *Organometallics* **1988**, *7*, 2203. (e) Matsunaga, P. T.; Hillhouse, G. L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1993**, *115*, 2075. (f) Koo, K.; Hillhouse, G. L. *Organometallics* **1995**, *14*, 4421. (g) Koo, K.; Hillhouse, G. L. *Organometallics* **1996**, *15*, 2669. (h) Jones, G. D.; McFarland, C.; Anderson, T. J.; Vicic, D. A. *Chem. Commun.* **2005**, 4211. (i) Lin, X. F.; Phillips, D. L. *J. Org. Chem.* **2008**, *73*, 3680. (j) Higgs, A. T.; Zinn, P. J.; Sanford, M. S. *Organometallics* **2009**, *28*, 6142. (k) Breitenfeld, J.; Woodrich, M.; Hu, X. *Organometallics* **2014**, *33*, 5708. (l) Zheng, B.; Tang, F.; Luo, J.; Schultz, J. W.; Rath, N. P.; Mirica, L. M. *J. Am. Chem. Soc.* **2014**, *136*, 6499. (m) Cloutier, J.-P.; Vabre, B.; Moungang-Soumé, B.; Zargarian, D. *Organometallics* **2014**, *34*, 133.

(3) Aihara, Y.; Chatani, N. *J. Am. Chem. Soc.* **2013**, *136*, 898.

(4) Iyanaga, M.; Aihara, Y.; Chatani, N. *J. Org. Chem.* **2014**, *79*, 11933.

(5) (a) Aihara, Y.; Chatani, N. *J. Am. Chem. Soc.* **2013**, *135*, 5308. (b) Terao, J.; Kambe, N. *Acc. Chem. Res.* **2008**, *41*, 1545. (c) Wu, X.; Zhao, Y.; Ge, H. *J. Am. Chem. Soc.* **2014**, *136*, 1789. (d) Yan, S.-Y.; Liu, Y.-J.; Liu, B.; Liu, Y.-H.; Zhang, Z.-Z.; Shi, B.-F. *Chem. Commun.* **2015**, *51*, 7341.

(6) For reviews discussing the complementary reactivity of Pd^{II} versus Pd^{IV} in catalysis, see: (a) Muñiz, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9412. (b) Canty, A. J. *Dalton Trans.* **2009**, 10409. (b) Xu, L.-M.; Li, B.-J.; Yang, Z.; Shi, Z.-J. *Chem. Soc. Rev.* **2010**, *39*, 712. (c) Sehnal, P.; Taylor, R. J. K.; Fairlamb, I. J. S. *Chem. Rev.* **2010**, *110*, 824. (d) Racowski, J. M.; Sanford, M. S. *Top. Organomet. Chem.* **2011**, *35*, 61. (e) Hickman, A. J.; Sanford, M. S. *Nature* **2012**, *484*, 177.

(7) (a) Dubinina, G. G.; Brennessel, W. W.; Miller, J. L.; Vicic, D. A. *Organometallics* **2008**, *27*, 3933. (b) Jover, J.; Miloserdov, F. M.; Benet-Buchholz, J.; Grushin, V. V.; Maseras, F. *Organometallics* **2014**, *33*, 6531.

(8) (a) Grushin, V. V. *Acc. Chem. Res.* **2010**, *43*, 160. (b) Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011**, *111*, 4475. (c) Furuya, T.; Kamlet, A. S.; Ritter, T. *Nature* **2011**, *473*, 470. (d) Ye, Y.; Sanford, M. S. *Synlett* **2012**, *23*, 2005.

(9) Camasso, N. M.; Sanford, M. S. *Science* **2015**, *347*, 1218.

(10) Zhang, C.-P.; Wang, H.; Klein, A.; Biewer, C.; Stirnat, K.; Yamaguchi, Y.; Xu, L.; Gomez-Benitez, V.; Vicic, D. A. *J. Am. Chem. Soc.* **2013**, *135*, 8141.

(11) Tang, F.; Rath, N. P.; Mirica, L. M. *Chem. Commun.* **2015**, *51*, 3113.

(12) The addition of halide abstractors (e.g., $AgBF_4$ or AgOAc) to these reactions resulted in the consumption of **3** and formation of at least one new paramagnetic species (likely a Ni^{III} intermediate).

(13) The presence of the radical traps styrene, TEMPO, or butylated hydroxytoluene (BHT) did not impact the yield of benzotrifluoride in the reductive elimination from **2**. This suggests that reductive elimination does not proceed via a free radical mechanism.

(14) A mixture of $[Ni(CF_3)]$ compounds is observed at the end of the reaction. After additional heating, these products converge to $NiTp_2$ and $(MeCN)_2Ni(CF_3)_2$.

(15) The maximum yield of $(CD_3CN)_2Ni(CF_3)_2$ and $NiTp_2$ are both 50% respectively.

(16) Vicic has reported the low yielding (11−22%) formation of aryl−CF_3 upon the treatment of (diphosphine)$Ni^{II}(Ph)(CF_3)$ with Zn salts and/or water over extended reaction times. The nature of the reactive Ni species is unclear in this system. See ref 7a.

(17) Another possible pathway for aryl−CF_3 coupling from **2** would be the *in situ* formation of a Ni^{III} intermediate and subsequent reductive elimination from that species. In an attempt to probe for this possibility, we conducted the stoichiometric $1e^-$ chemical reduction of **2-Me** with Cp_2Co and then examined the resulting products. Subsequent thermolysis of this reaction mixture yielded <5% of aryl−CF_3 along with organic products (CF_3H and toluene) consistent with the formation of free radical intermediates. This suggests strongly against aryl−CF_3 reductive elimination from Ni^{III} in the current system. See Supporting Information for full details.

(18) Ball, N. D.; Gary, J. B.; Ye, Y.; Sanford, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 7577.

(19) Attempts to observe Tp ligand exchange by EXSY NMR experiments and/or pyrazolyl dissociation by VT NMR line broadening studies were inconclusive. This result can be explained by either (1) ligand dissociation of the pyrazolyl arm being slower than the NMR time scale or (2) reductive elimination proceeding from a six-coordinate complex.

(20) For select examples, see: (a) Wang, S.; Qian, Q.; Gong, H. *Org. Lett.* **2012**, *14*, 3352. (b) Zultanski, S.; Fu, G. C. *J. Am. Chem. Soc.* **2013**, *135*, 624. (c) Biswas, S.; Weix, D. J. *J. Am. Chem. Soc.* **2013**, *135*, 16192. (d) Jensen, K. L.; Standley, E. A.; Jamison, T. F. *J. Am. Chem. Soc.* **2014**, *136*, 11145.

(21) The reaction of complex **5** with PhN_2BF_4 was conducted at 23 °C and then rapidly cooled down to −25 °C to resolve J_{FF} coupling.

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