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C-H Borylation Catalysis of Heteroaromatics by a Rhenium Boryl Polyhydride

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accessible and catalyze the C-H borylation of heteroaromatic substrates. Reaction of $[K(DME)(18-c-6)][ReH_4(Bpin)(\eta^2-HBpin) (\kappa^2$ -H₂Bpin)] **1** with 1,3-bis(diphenylphosphino)propane (dppp) produced [K(18-c-6)][ReH₄(η^2 -HBpin)(dppp)] 2 through substitution of two equivalents of HBpin, and protonation of 2 formed the neutral complex [ReH₆(Bpin)(dppp)] 3. Combined X-ray crystallo-



graphic and DFT studies show that 2 is best described as a σ -borane complex, whereas 3 is a boryl complex. Significantly, the boryl complex 3 acted as a catalyst for the $C(sp^2)$ -H borylation of a variety of heteroarenes (14 examples including furan, thiophene, pyrrole and indole derivatives) and displayed similar reactivity to the iridium analogues.

KEYWORDS: heteroarene, hydride, borane, phosphine, homogeneous catalysis, crystallography, AIRSS

INTRODUCTION

The synthesis of transition metal complexes containing metalboron bonds is of particular interest due to the relevance of these complexes as intermediates in catalytic C-X (X = H or halogen) borylation to prepare synthetically valuable boronic esters.¹⁻⁴ The borylation of unactivated $C(sp^2)$ -H bonds can be catalyzed by a number of transition metal boryl complexes of Ir, $^{5-10}$ Rh, $^{6,11-13}$ Co, $^{14-16}$ Fe, $^{17-20}$ Ni, $^{21-23}$ and Pt. 24 The most widely used catalysts are Ir complexes typically of the form $[Ir(Bpin)_3(L)_2]$, where L is a neutral monodentate or bidentate ligand, and invoke an Ir(III)/Ir(V) redox couple. The most commonly used catalyst systems use bulky bipyridine or phenanthroline ligands, first developed by Hartwig and co-workers.^{25,26} Smith and co-workers demonstrated the use of the bidentate phosphine complex, [Ir- $(Bpin)_3(dppe)]$, as a catalyst for the selective C–H borylation of arenes in the presence of haloarenes; the catalyst was formed in situ from the reaction of $[(\eta^5 \text{-indene}) \text{Ir}(\text{COD})]$ with dppe and HBpin. The related 5-coordinate complexes [Ir- $(Bpin)_3(L)$ (where L = dtbpe or dippe) have also been shown to mediate C-H borylation of arenes, albeit stoichiometrically.²⁷ Further studies of the stoichiometric reactivity of $[Ir(Bpin)_3(dippe)]$ reveal a series of borylene, hydrido, and hydrido boryl complexes that can be formed under catalytic C-H borylation conditions.²⁸

Recently, we reported the rhenium polyhydride borane anion $[\text{ReH}_4(\text{Bpin})(\eta^2\text{-HBpin})(\kappa^2\text{-H}_2\text{Bpin})]^-$ 1, synthesized by the exhaustive deoxygenation of perrhenate, $[ReO_4]^-$, with HBpin, and showed that it is a catalyst for the hydroboration of N-heteroaromatic substrates.²⁹ Reaction of 1 with H-B-9-BBN resulted in reductive borane substitution to form a related dihydroborate complex. These simple methods provided straightforward access to reactive rhenium complexes containing boron-centered ligands that can be further functionalized. Interestingly, 1 also underwent stoichiometric $C(sp^2)-H$ borylation of toluene with high meta-selectivity; unfortunately, attempts to adapt these conditions for catalytic C-H borylation by addition of stoichiometric boron reagents or sacrificial H₂ acceptors were unsuccessful. It was, therefore, envisaged that strongly σ -donating, neutral ligands such as phosphines would help to stabilize the high oxidation state hydrido-boryl complexes involved in C-H bond activation and subsequent C-B bond formation. Rhenium-catalyzed C-H borylation has, to the best of our knowledge, only been reported using low oxidation-state complexes. For example, Hartwig and co-workers reported the C-H borylation of alkanes and arenes using $Cp*Re(CO)_3$ and B_2pin_2 under

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photochemical conditions and an atmosphere of CO (Scheme 1A).³⁰ Murai and Takai reported the $C(sp^3)$ -H borylation of

Scheme 1. Examples of Rhenium-Catalyzed Borylation of C–H Bonds

A) Photochemical Alkane C(sp³)-H Borylation (Hartwig 1999)

$$H_{n}^{n}C_{4}H_{9} + H_{0}^{n}C_{4}H_{9} + H_{0}^{n}C_{4}H_{9}$$

B) Directed Dehydrogenative Borylation of C(sp³)-H Bonds (Murai & Takai 2015)



C) Dehydrogenative C(sp²)-H Borylation of Unactivated Arenes (This Work)



tertiary amines at the α -position, facilitated by a pyridyl directing group under thermal conditions using [ReBr-(CO)₃(THF)]₂ as the catalyst and H-B-9-BBN as the boron source (Scheme 1B).³¹ However, no examples of C(sp²)–H borylation of arenes were reported using this catalyst system.

Herein, we report that the reaction of $[K(DME)(18-c-6)][ReH_4(Bpin)(\eta^2-HBpin)(\kappa^2-H_2Bpin)]$ 1 with dppp leads to HBpin ligand substitution to give the Re(V) phosphine complex $[K(18-c-6)][ReH_4(\eta^2-HBpin)(dppp)]$ 2. Complex 2 reacts with 2,6-lutidinium chloride to give the neutral Re(VII) boryl complex $[ReH_6(Bpin)(dppp)]$ 3, which acts as a catalyst for the C–H borylation of heteroarenes (Scheme 1C). To the best of our knowledge, this work represents the first example of a high oxidation-state Re complex acting as a catalyst for this reaction and draws comparisons to existing reactivity shown by established iridium examples.

RESULTS AND DISCUSSION

An equivalent of bis(diphenylphosphino)propane (dppp) was added to a solution of 1 in DME at -20 °C, which, on warming slowly to room temperature and stirring for 72 h, produces a single phosphine-ligated complex 2 with liberation of two equivalents of HBpin. Complex 2 was then reacted with 1 equivalent of 2,6-lutidinium chloride, which results in protonation without H₂ evolution to form the neutral complex [ReH₆(Bpin)(dppp)] 3 (Scheme 2). The ¹H NMR spectrum of 3 displays a triplet at -5.57 ppm for 6 hydrides, and the ³¹P NMR spectrum exhibits a broad signal at 6.24 ppm. As with 2, these resonances are unchanged at -80 °C. A broad signal at 47.3 ppm is seen in the ¹¹B NMR spectrum of 3 and corresponds to a Re-Bpin environment.

Single-crystal X-ray diffraction analysis of 3 shows the P and B atoms arranged in a distorted trigonal planar geometry (Figure 2). The hydrides were located in the difference Fourier map and display an average Re–H bond length of 1.50(3) Å, which is comparable to other terminal hydride bond lengths.

Scheme 2. Reaction of 1 with dppp to Produce the Neutral Phosphine Complex 3 via the Anionic Complex 2



The Re-B bond length is 2.188(3) Å, and B1-H1 distance is 1.69(3) Å, both of which are within the range of other high oxidation-state, elongated σ -borane or hydrido boryl complexes.^{32,33} The usual caveats of locating hydrides with confidence from the X-ray structure apply here. As such, possible hydride positions were identified using ab initio random structure searching (AIRSS, see Supporting Information for details) with the initial positions of the heavier atoms derived from the crystal structure and geometric constraints on prospective initial hydride positions to ensure H_2 is not formed.^{34,35} This approach generates a series of structures with various combinations of hydride, boryl, σ -borane, and hydroborate ligands that are then ranked in increasing energy (Supporting Information). From a data set of 24 optimized structures obtained, a series of 21 closely related, low-energy structures (within 5 kJ mol⁻¹) reveal a geometry that matches the solid-state structure (Figure 1). Given the long B1-H1



Figure 1. X-ray crystal structure (left) and calculated structure (right) of 3 (toluene solvate and all hydrogen atoms except for the Re hydrides are omitted; displacement ellipsoids are drawn at 50% probability). X-ray crystal structure selected distances (Å) and angles (deg): Re1–B1, 2.188(3); Re1–H, 1.50(3) avg.; B1–H1, 1.69(3); Re1–P1, 2.4053(9); Re1–P2, 2.4106(9); P2–Re1–P1, 96.22(3); P1–Re1–B1, 127.9(1); P2–Re1–B1, 135.9(1).

distances in both the solid-state and calculated structures and that the crystals of 3 are colorless, it is evident that 3 is best described as a boryl hexahydride complex (i.e., Re^{VII}).

The time course of the reaction between 1 and dppp was monitored by NMR spectroscopy in d_{s} -THF and revealed full conversion of 1 to a monodentate complex (major) and a bidentate complex (minor) after 2 h. The monodentate complex corresponds to a doublet at -8.05 ppm in the ¹H NMR spectrum and a broad signal at 52.9 ppm in the ¹¹B NMR spectrum. This monodentate complex, then, slowly converts to the bidentate complex, which is characterized by a triplet at -8.16 ppm in the ¹H NMR spectrum and a broad signal at 53.8 ppm in the ¹¹B NMR spectrum. Correlations between the hydride signals and two signals at 24.5 and 11.6 ppm in the ³¹P NMR spectrum are observed in the ¹H-³¹P HMBC NMR spectrum. This suggests that the second equivalent of HBpin is significantly less labile than the first. A screen of phosphine ligands showed that the range of ligands that can successfully and selectively coordinate to 1 is narrow (Supporting Information).

When dimethoxyethane (DME) is used as the reaction solvent, $[K(18-c-6)][ReH_4(\eta^2-HBpin)(dppp)]$ **2** is isolated by crystallization from the reaction mixture as large yellow blocks. However, **2** is unstable once isolated from the reaction mixture and decomposes rapidly upon drying under vacuum or at ambient temperature/pressure to give multiple phosphinecoordinated rhenium hydride complexes. This could be due to dissociation of HBpin or H₂ to form an unstable 16-electron complex, which reacts unselectively with itself or with the solvent. The X-ray crystal structure of **2** (Figure 2) reveals a



Figure 2. X-ray crystal structure (left) and calculated structure (right) of 2 (all hydrogen atoms except for the Re hydrides are omitted; displacement ellipsoids are drawn at 50% probability). X-ray crystal structure selected distances (Å) and angles (deg): Re1–B1, 2.149(4); Re1–H, 1.54(4) avg.; B1–H1, 1.48(4); H5–K1, 2.74(5); H4–K1, 3.19(5); Re1–P1, 2.3571(9).; Re1–P2, 2.3465(9); P2–Re1–P1, 93.28(3); P2–Re1–B1, 141.5(1); B1–Re1–P1, 91.36(9).

rhenium pentahydride anion in which the P and B atoms are arranged in a distorted T-shape geometry with an elongated Re–B bond (Re1–B1 = 2.149(4) Å), which could reflect contributions from σ -borane structures because of the close B1–H1 distance (1.48(4) Å). The hydrides were located in the difference Fourier map and refined freely. The structure also exhibits a close Re–H–K contact (H5–K1 = 2.74(5) Å), which is similar to the those seen in other potassium salts of rhenium polyhydride anions.³⁶ Once again, possible hydride positions were identified using AIRSS where, of the data set of 26 optimized structures generated, the same lowest energy geometry is obtained 18 times, in which the only significant difference to the X-ray structure is a closer K1–H4 contact (2.956 Å compared with 3.19(5) Å). The calculated structure contains an elongated B1–H1 distance compared with the solid-state structure (1.522 Å), although this bond distance remains in the range reported for σ -borane complexes and is within one esd range of the X-ray structure (Figure 2).^{32,37} The hydride positions are consistent with those from the X-ray structure, indicating a high level of confidence for their assignment.

The ready synthesis of the well-defined Re(VII) boryl complex 3 prompted its exploration as a catalyst for the $C(sp^2)$ -H borylation of arenes (Scheme 3). Optimized

Scheme 3. Substrate Scope for the Catalytic Dehydrogenative C–H Borylation of Heteroarenes^a



^{*a*}Reaction conditions: heteroarene 4 (0.50 mmol), HBpin (0.75 mmol), catalyst 3 (0.0125 mmol), THF (2.5 mL), 80 °C for 16 h. NMR yields determined by ¹H NMR spectroscopy by integration against mesitylene (10 μ L, 0.0719 mmol), isolated yields in parentheses. ^{*b*}Three equivalents of HBpin (1.50 mmol).

conditions were established for the C–H borylation of 2methylfuran 4a using 2 mol % of 3 and 1.5 equivalent of HBpin in THF at 80 °C for 16 h (see Supporting Information for full details); this gives the borylated furan 5a with high regioselectivity for the C5-Bpin isomer over the C4-Bpin isomer (>95% conversion, 95:5). No product is seen using B₂pin₂ as the boron source for this reaction. Increasing the catalyst loading results in an enhanced rate of reaction and lowering the loading of HBpin from 1.5 to 1.0 equivalent decreases conversion. In contrast, catalytic borylation reactivity is not observed using complexes 1 or 2 showing that the neutral, phosphine-coordinated complex 3 displays significant differences in reactivity.

Mono- and disubstituted furans 4a-4c are tolerated under these reaction conditions with good selectivity for the C5-Bpin regiosiomer. Furan 4b reacts with 3 equiv of HBpin to give the doubly borylated products exclusively. Thiophene substrates are also converted to borylated products although the yields are lower than seen for furans. Thiophene 4d gives a mixture of 2-boryl and 2,5-diboryl thiophenes. Monosubstituted thiophenes 4e-4i are converted with high selectivity for the 5boryl products. 3,4-Ethylenedioxythiophene (EDOT) 4g and 2,2'-bithiophene 4i give a mixture of monosubstituted (major) and disubstituted (minor) boronic ester products. Pyrroles and indoles 4i-4n are tolerated and give high yields and regioselectivities. Notably, substrates containing carbon halide bonds (C-Cl/Br) 4m and 4n favor C-H borvlation over Miyaura borylation of the C-X bond. N-Methyl and N-Boc protected pyrroles and indoles only show trace conversion. Similarly, di-ortho-substituted heteroaromatics show significantly reduced conversion to the boronic ester products. No $C(sp^3)$ -H, N-H, or dppp borylation is seen in these reactions.

The time course of a catalytic borylation of 4a was monitored by ¹H NMR spectroscopy in d_8 -THF (Figure 3).



Figure 3. Analysis by ¹H NMR spectroscopy of the Re hydride species during the catalytic C–H borylation of 2-methylfuran 4a. Reaction conditions: heteroarene 4 (0.20 mmol), HBpin (0.3 mmol), catalyst 3 (0.004 mmol), d_8 -THF (0.5 mL), 80 °C for 16 h.

Over 16 h, the hydride signal at -6.08 ppm corresponding to complex 3 diminishes, and two new signals at -6.27 (t) and -6.34 (p) ppm are observed. Both signals correspond to catalyst deactivation and are identified as arising from the heptahydride complex [ReH₇(dppp)] 7 and the dinuclear octahydride complex [ReH₄(dppp)]₂ 8, respectively (Figure 3). Heptahydride 7 has been previously reported and was synthesized independently to confirm this assignment.³⁸ The complex was originally reported to be inert to H₂ loss when heated under reflux in THF in the presence of PPh₃, pyridine, and hydrosilanes. Interestingly, we find that 7 acts as a catalyst for C–H borylation, albeit at a significantly reduced rate compared with 3, achieving only 48% NMR yield after 16 h (Scheme 4A). In contrast, in situ ¹H/¹¹B/³¹P NMR spectroscopy shows that dinuclear complex 8 is inactive in C–H

Scheme 4. Mechanistic investigation of catalytic C–H borylation



borylation catalysis and inert to hydride substitution by HBpin, reinforcing its role in a deactivation pathway.

Complex 7 is presumably formed during standard catalytic conditions from boryl complex 3 by coordination of H_{2} , liberated by C-H borylation of the substrate, to a transiently formed $\text{ReH}_5(\text{dppp})$. When heptahydride 7 was heated in the presence of an excess of HBpin a small amount of boryl complex 3 is seen in the ¹H NMR spectrum, along with dinuclear 8 and an unknown complex 9, which has a hydride resonance at -8.52 ppm (Scheme 4B). To assess the effect of H₂ evolution and its role within catalysis, the borylation of 3hexylthiophene 4e was conducted under standard conditions in a Teflon-tapped NMR tube and compared with a reaction under static vacuum to enable the H₂ formed during the reaction to escape into the headspace of the NMR tube. The progress of both reactions and Re hydride speciation was monitored by in situ ¹H NMR spectroscopy (Supporting Information). By comparing the yield of borylated product 5e in each reaction over time, it is clear that both reactions follow the same profile until \sim 240 min, upon which they diverge with the rate of reaction for the standard reaction slower than that of the reaction under partial static vacuum. At 1000 min the final yield of 5e is 37% for the standard reaction and 44% for the vacuum reaction, indicating the deleterious effect of H₂ on catalysis. Quantification of the Re hydride species present by integration of the relevant hydride signals in the ¹H NMR spectra show a much higher proportion of heptahydride 7 in the standard reaction; this is as expected, given the higher concentration of H₂ in this reaction compared with the reaction under static vacuum. Given the decreased catalytic activity of heptahydride 7 compared with boryl 3, the increased concentration of 7 supports the observed decrease in the rate of reaction. The standard reaction also appears to have a higher relative concentration of dimer 8 compared with the reaction under static vacuum, which again supports the lower rate of reaction by loss of active Re hydride species through this deactivation pathway. Significantly, the changes in speciation correlate with the observed evolution of H_2 (4.55 ppm in the ¹H NMR spectra) during the course of the reaction, with a consistently lower concentration of H₂ seen in solution in the reaction under static vacuum compared with the standard reaction.

The dinuclear complex 8 is the sole product formed on heating 3 or 7 at 80 °C in toluene and crystallizes directly from the reaction mixture (Scheme 4C). The ¹H NMR spectrum of isolated 8 matches that corresponding to the hydride resonance at -6.34 (p), observed under standard catalytic conditions. It should be noted that the formation of 8 by heating 3 at 80 °C for 16 h in toluene results in stoichiometric borylation of toluene to give a 74:26 regioisomeric mixture of the meta and para borylated products in 48% NMR yield against an internal standard. The borylation of carboarenes is limited to stoichiometric reactivity using 3. The X-ray crystal structure of 8, which has two chemically equivalent but crystallographically independent molecules in the asymmetric unit (Figure 4), confirms that it is a dimeric complex with four



Figure 4. X-ray crystal structure of 8 (one of the two molecules in the asymmetric unit is shown, all hydrogen atoms except for the Re hydrides are omitted; displacement ellipsoids are drawn at 50% probability). Selected distances (Å) and angles (deg): Re1-H^t, 1.47(4) avg.; Re1-H^b, 1.89(4) avg.; Re1-Re1', 2.5383(5); Re1-P1, 2.327(1); Re1-P2, 2.3265(8); P1-Re1-P2, 96.62(3); P1-Re1-Re1', 133.81(3); P2-Re1-Re1', 129.57(3); P1-Re1-Re1'-P1', 180.00(5).

bridging hydrides between the Re atoms and two terminal hydrides on each Re atom; the hydride atoms were located in the difference Fourier map and refined freely. Similar dinuclear complexes have been synthesized bearing monodentate or tridentate phosphines; $^{39-41}$ however, to the best of our knowledge, complex 8 is the first example with a bidentate phosphine.

The reactivity of Re polyhydrides is largely determined by their ability to generate vacant coordination sites by liberation of H₂, either thermally or photochemically, and they have been shown to participate in C–H bond activation chemistry.⁴² It is likely that complex 3 participates in a similar manner to activate the C–H bonds of the heteroarenes. However, under catalytic conditions, there is potential for the boryl complex 3 to sequentially lose equivalents of H₂ and add equivalents of HBpin to form higher-order boryl complexes, which may be catalytically relevant. To investigate this, a solution of the boryl complex 3 and HBpin (20 equiv) in d₁₂-cyclohexane was heated at 80 °C and monitored by NMR spectroscopy (Scheme 4D). After 3 h, a broad singlet is seen at -8.50 ppm in the ¹H NMR spectrum corresponding to a phosphinecoordinated Re hydride complex 9 (Scheme 4B and D), as well as several minor signals between -6.00 and -7.50 ppm; H₂ evolution is also observed (singlet at 4.55 ppm). The formation of 9 does not coincide with the observation of an obvious Re-B resonance in the ¹¹B NMR spectrum. A similar, but shorter-lived complex is seen if the reaction is undertaken in d_8 -THF, but it is not present under standard catalysis conditions. It was not possible to isolate complex 9 as it is unstable under vacuum and its formulation is difficult to discern as integration of the ¹H NMR spectrum is inconclusive due to some decomposition. It is likely, however, that 9 is a higher-order boryl complex, for example Re- $H_4(Bpin)_3(dppp)$ ²⁸ Complex 9 is found to be active in the catalytic borylation of 3-hexylthiophene 4e: complex 9 was generated in situ by the reaction between 3 and HBpin for 3 h in d_{12} -cyclohexane, after which addition of 4e and further heating for 16 h results in the borylated product 5e in 36% yield. Complex 9 does not react with 4e at room temperature but, after 20 min heating in the presence of thiophene 4e, it is almost fully consumed with the only hydride species seen being 3. From this point, the reaction follows a similar profile to standard catalytic reaction conditions using 3. Complex 9 is only observed in significant quantities in the presence of a large excess of HBpin and in the absence of substrate, therefore it may only be formed transiently under standard catalytic conditions. These results suggest that 9 is likely a higher-order boryl complex such as ReH₄(BPin)₃(dppp), which may act similarly to the known iridium tris(boryl) complexes in hydroborylation catalysis.43-45

On the basis of these results a catalytic cycle is proposed with complex 9 as an off-cycle intermediate present in very low concentrations and in equilibrium with 3 (Scheme 5A): (1) Elimination of an equivalent of H₂ from precatalyst 3 forms a coordinatively unsaturated boryl complex Int-A; (2) oxidative addition of the arene substrate gives a Re aryl intermediate Int-**B**; (3) reductive elimination of the boronic ester product and formation of a coordinatively unsaturated pentahydride complex Int-C; and (4) addition of an equivalent of HBpin and elimination of H_2 reforms Int-A. The reaction of precatalyst 3 with an excess of HBpin will lead to the formation of the higher-order boryl 9 and the reaction of 3 with H₂ will form heptahydride 7. Catalyst deactivation can occur through the dimerization of 3 or 7 to form 8. We cannot discount a mechanism involving 9 as an active species for C-H borylation, where it is present as an on-cycle intermediate. The formation of 9 under high HBpin concentrations may also limit the formation of the off-cycle heptahydride 7. Computational studies on the reaction intermediates and potential reaction pathways may provide more definitive insight into the reaction mechanism.

CONCLUSIONS

Two new Re boron-polyhydride complexes 2 and 3 have been synthesized and characterized from the previously reported 1. The boryl complex 3 is an effective catalyst for the C–H borylation of heteroarenes proceeding with good yields and regioselectivities. An investigation of the mechanism of this reaction identifies potential reactive intermediates and deactivation pathways. This work represents a new application of high-oxidation-state Re complexes in C–H functionalization catalysis and may have applications to related transformations, for example C–H silylation and germylation. Further work to Scheme 5. Proposed Catalytic Cycle for the C–H Borylation of Heteroarenes



optimize the ligand structure to inhibit the formation of heptahydride 7 and dimer 8 could develop a class of catalysts that can compete with established Ir examples. Exploration of ligand scaffolds other than phosphines may also enable the catalytic C–H borylation of more challenging $C(sp^2)$ –H bonds of carboarenes and pyridines, and $C(sp^3)$ –H bonds of alkanes and is subject to ongoing investigations in our laboratory.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acscatal.1c00869.

Syntheses and characterization, NMR spectra, crystallographic details, AIRSS/CASTEP details for **2**, **3** and **8**, synthetic and spectroscopic details (PDF)

Crystallographic data for 2 (CCDC 2060777) (CIF) Crystallographic data for 3 (CCDC 2060776) (CIF)

Crystallographic data for 8 (CCDC 2060778) (CIF) AIRSS/CASTEP data for 2 and 3 (ZIP)

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All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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