Solution Catalytic Cycle of Incompatible Steps for Ambient Air Oxidation of Methane to Methanol

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ABSTRACT: Direct chemical synthesis from methane and air under ambient conditions is attractive yet challenging. Low-valent organometallic compounds are known to activate methane, but their electron-rich nature seems incompatible with O2 and prevents catalytic air oxidation. We report selective oxidation of methane to methanol with an O2-sensitive metalloradical as the catalyst and air as the oxidant at room temperature and ambient pressure. The incompatibility between C−H activation and O2 oxidation is reconciled by electrochemistry and nanomaterials, with which a concentration gradient of O2 within the nanowire array spatially segregated incompatible steps in the catalytic cycle. An unexpected 220 000-fold increase of the apparent reaction rate constants within the nanowire array leads to a turnover number up to 52 000 within 24 h. The synergy between nanomaterials and organometallic chemistry warrants a new catalytic route for CH4 functionalization.

INTRODUCTION

It is attractive to directly use air and natural gas, mostly methane (CH4) as raw materials for the synthesis of methanol (CH3OH), an important commodity chemical. High-valent, electron-deficient organometallic compounds have been attempted as the centers for C−H activation and the immediate oxidants, presuming that the metal complexes can be reoxidized by air to fulfill a catalytic cycle. Because of the low reactivity of its C−H bond, CH4 functionalization proceeds at elevated temperatures which incurs possible overoxidation into other products. Alternatively, electron-rich organometallic compounds are capable of selectively activating CH4 at low temperature. This intriguing us to establish a hypothetical catalytic cycle at ambient conditions, in which a reductive or homolytic step of CH4 activation is followed by air oxidation to yield CH3OH with minimal overoxidation. However, as the step of CH4 activation may not be favored thermodynamically and O2 can oxidatively quench the catalytic species, external energy input is needed for catalyst regeneration, and a spatial control of these incompatible reactions is required.

In biology, incompatible biochemical reactions coexist within one organelle by localizing conflicting reactions. One example is the fixation of dinitrogen (N2) in aerobic bacteria (Figure 1B). O2-sensitive nitrogenase for N2 fixation is reversibly activated by the reducing equivalents generated from the tricarboxylic acid (TCA) cycle with O2 as the terminal electron acceptor. The tandem reactions of aerobic respiration and N2 fixation are only possible with the buildup of an O2 gradient, which yields the methylated and hydride species ((TMP)Rh−CH3, Ib; (TMP)Rh−H, Ic, respectively) (Figure 2A). The sterically bulky TLP ligand and the requirement of a four-centered transition state warrant a selectivity toward H activation and air oxidation should be connected for the catalysis yet spatially separated with mitigated oxidative quenching (Figure 1C). While these requirements are challenging in a homogeneous solution, we posit that they can be satisfied with the use of a nanowire array electrode and electrochemistry. When an electrode is biased at a potential more negative than the redox potentials of O2 and the catalyst, redox-active catalysts can be regenerated by electrochemistry. Moreover, the electrochemical reduction of O2 will establish a local O2 gradient in the solution near the electrode surface. This effect is much more pronounced for nanomaterials and porous electrodes in general, effectively creating an O2-free domain within nanomaterials suitable for chemical steps incompatible with O2. In support of this argument, our previous work demonstrated that a nanowire array electrode can create an O2-free domain that allows anaerobic microbial reduction of CO2. Establishing a similar O2 gradient and regenerating the CH4-activating catalyst with electrochemically active nanowires (Figure 1C), here we report a catalytic cycle for ambient air oxidation of CH4 to CH3OH with O2-sensitive, electron-rich Rh tetramesityl porphyrin metalloradical, (TMP)RhII (1a, Figure 2A), as the catalyst.

RESULTS AND DISCUSSION

At ambient conditions, 2 equiv of 1a reversibly activate 1 equiv of CH4 with a large equilibrium constant (K = 2.2 × 105 at 298 K), which yields the methylated and hydride species ((TMP)Rh−CH3, Ib; (TMP)Rh−H, Ic, respectively) (Figure 2A). The sterically bulky TLP ligand and the requirement of a four-centered transition state warrant a selectivity toward...
CH\textsubscript{4} by two orders of magnitude versus other larger substrates including CH\textsubscript{3}OH.\textsuperscript{21} However, in a homogeneous solution, such a reactivity with CH\textsubscript{4} is not translatable to catalysis when paired with oxidants such as O\textsubscript{2}. 1a and O\textsubscript{2} react to form a Rh\textsuperscript{III} superoxo species under a fast equilibrium (\(K' = 8.4 \times 10^4\) at 298 K, Figure 2A),\textsuperscript{22} and this reaction outcompetes the kinetically slow process of CH\textsubscript{4} activation (\(k_{\text{f,bulk}} = 0.132\ M^{-2}\cdot s^{-1}\) at 296 K).\textsuperscript{19} Despite this, we argue that electrochemistry can regenerate 1a in situ from its oxidized counterparts thereby potentially allowing the activation of CH\textsubscript{4} with 1a in air. Rh\textsuperscript{III} tetramesityl porphyrin iodide ((TMP)Rh\textsuperscript{−}I, 1d) was synthesized based on literature (Figure S1).\textsuperscript{19} In an argon (Ar) environment and noncoordinating solvent, 1,2-difluorobenzene (1,2-DFB),\textsuperscript{23} with 0.1 M tetrabutylammonium perchlorate (TBAClO\textsubscript{4}), a cyclic voltammogram (CV) of 1d on a platinum (Pt) working electrode displays quasi-reversible behavior at an electrode potential \(E_{\text{app}} = -1.26\ V\) vs standard calomel electrode (SCE) (Figure 2B), consistent with a previous report that the Rh\textsuperscript{II} species can be regenerated by electrochemistry.\textsuperscript{24,25} In the presence of O\textsubscript{2}, a catalytic cathodic wave was observed on a glassy carbon electrode preceding the Rh\textsuperscript{III}/Rh\textsuperscript{II} redox couple (\(E_{\text{app}} < -0.7\ V\) vs SCE) (green trace in Figure 2B), while the CV trace in the absence of 1d yielded no such activity (Figure S2). Previous literature report the generation of superoxide and peroxide as the immediate products both in solution or electrochemically when O\textsubscript{2} and Rh\textsuperscript{II} porphyrin are in a stoichiometric ratio.\textsuperscript{22,26,27} Here our experimental data in air suggest that additional catalytic irreversible reduction of O\textsubscript{2} is feasible when the amount of O\textsubscript{2} is in surplus.

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The capability of generating reactive oxygen species [O] electrochemically with Rh porphyrin leads us to explore whether those [O] can activate 1b and yield CH\textsubscript{3}OH. Stoichiometric reactions between different hydroperoxide species and 1b, a stable compound prepared in air (Figure S3), were performed at a 1:1 ratio under ambient conditions (see Supporting Information). The reaction between t-butyl hydroperoxide and 1b was tracked via $^1$H NMR and indicated the formation of CH\textsubscript{3}OH at the expense of the methyl group in 1b (Figure S4). This suggests that the methylated species 1b is capable of releasing CH\textsubscript{3}OH by hydroperoxide. Moreover, we found that a 3-h electrolysis of 1b at \(E_{\text{app}} = -1.4\ V\) vs SCE yielded a stoichiometric amount of CH\textsubscript{3}OH (Table S1, entry 1). A gas chromatograph equipped with a mass spectrometer (GC-MS), allowing for a clear separation of electrolyte and catalyst from product determination, was used to detect the product after establishing a calibration curve (Figure S5). This indicates that the electrochemically generated [O] from O\textsubscript{2} reduction can be a serendipitous oxidant which yields CH\textsubscript{3}OH after the step of CH\textsubscript{4} activation. During the aforementioned electrolysis, on average 2.3 equiv of electrons are consumed per CH\textsubscript{3}OH molecule synthesized, indicating that [O] is possibly of a hydroperoxide nature. However, not all of the generated [O] will lead to CH\textsubscript{3}OH formation, conveying that the value of 2.3 electrons acts as an upper boundary for the reaction during electrolysis.

Given the literature and our experimental data, we propose to establish a solution catalytic cycle of incompatible reactions at ambient conditions in air (Figure 2C), which is impossible in homogeneous solution but potentially feasible when...
combining electrochemistry and nanomaterials. A silicon (Si) nanowire array was proposed to offer a similar and even enhanced effect as that of a porous electrode with respect to induced concentration gradients.16,17 By utilizing nanowire array morphology as the working electrode in the presence of 1d and O2, the oxidant [O] will be electrochemically generated in situ from O2 with the creation of an O2 gradient. The created O2 gradient enables a nanoscopic separation of incompatible reaction steps. In a localized anaerobic environment near the base of the wire array (pink area in Figure 2C), electrochemically regenerated 1a activates CH4 and yields 1b, which diffuses out and oxidatively hydroxylates to yield CH3OH in the aerobic region (blue area in Figure 2C).

Numerical simulations based on electrochemistry models support the feasibility of the proposed catalytic cycle in the wire array. Finite-element simulations using the COMSOL Multiphysics program were conducted for different electrode geometries based on the experimentally available information (see Supporting Information).16,17 including the fast electrochemical equilibrium of RhIII/RhII redox couple, the reported chemical reactivities,18,19 and the molecular diffusion coefficients determined by diffusion ordered spectroscopy (DOSY) with 1H nuclear magnetic resonance (NMR) (Figure S6). Figure 3A displays the calculated concentrations of 1a, 1d, and O2, denoted as [1a], [1d], and [O2], respectively, versus the distance away from electrode surface (z) on a planar electrode at E_appl = −1.4 V vs SCE. An anaerobic domain of predominantly CH4-reactive 1a, pink colored in Figure 3A, is minimal as compared to the extensive aerobic domain (light blue) where CH4-unreactive 1d is predominant. In contrast, for an exemplary wire array of 50 μm length, 4 μm diameter, and 15 μm periodicity (i.e., distance between adjacent wires) under the same condition, an extended anaerobic region is visible toward the base of the array and potentially favors CH4 activation (Figure 3B). These results support our hypothesis that a nanowire array electrode can spatially define an anaerobic region for CH4 activation, which is microscopically adjacent to an aerobic one ready for CH3OH formation. Variation of the physical parameters such as the reactivities between O2 and 1a as well as the charge-transfer rate of O2 reduction (Figure S7) does not alter the effectiveness of the wire array for establishing concentration gradients, indicating the robustness of this design.

Spatially resolved optical measurements confirmed the predicted concentration gradients of 1a and 1d within the wire array electrode. The Si wire array, used as a model system, was prepared by reactive ion etching after photolithography (Figure S8, Supporting Information).20 The geometry was based on the same one used in the numerical simulation (Figure 3B) to help validate the conclusions drawn from the simulations. Electrochemical characterizations suggest that the prepared Si wire arrays are electrochemically active toward O2 reduction with the presence of 1d (Figure S9). As the lifetime of the excited triplet (τ_T) for 1d (>2 μs) is much longer than the one of 1a (~200 ns),21 under optical excitation 1d exhibits much stronger phosphorescence emission from 630 to 750 nm as compared to 1a (Figure S10). Thus, in a mixed solution containing both 1a and 1d, the local concentration percentage of 1d, and subsequently the percentage of 1a, can be tracked by monitoring the phosphorescence intensity after normalizing.
to the intensity when only 1d is in the solution (I/I₀) (Figure 3C). An electrochemical setup was constructed under a confocal microscope with 526 nm excitation to situ map the phosphorescence intensity near the electrode surface in air (Figure S11, Supporting Information). Figure 3D displays the values of I/I₀ at different z values for both planar (black) and wire array (red) Si electrodes when E_app = −1.5 V vs SCE. Near a planar electrode, the values of I/I₀ remain constant, and it suggests that the local concentration of 1d was not significantly perturbed (Figures 3D and S12). For a Si wire array (Figure S8) that possesses the exact same geometry simulated in Figure 3B, the values of I/I₀ decrease toward the base of wire array, indicating a local depletion of 1d and subsequently an accumulation of 1a. The accumulation of CH₄-reactive 1a is also suggested in the steady-state cross-sectional heatmaps of phosphorescence. A distinguishably lower emission intensity profile was observed when E_app = −1.5 V vs SCE in the wire array (Figure 3E), as compared to the case at the open-circuit condition (Figure 3F). The fidelity between simulation (Figure 3A,B) and experimental results (Figure 3E,F) confirms that the wire array spatially generates an O₂-free domain in air with a localized accumulation of 1a, which is reactive toward ambient CH₄ activation.

Selective ambient air oxidation of CH₄ to CH₃OH was observed with 1d as the precatalyst when E_app = −1.4 V vs SCE on a Si wire array electrode. A Si nanowire array, prepared by electroless wet etching, with a wire length of ~15 µm and diameter of ~100 nm (Figure 4A) was applied as the working electrode for a three-electrode configuration in a customized electrochemical reactor (Figure S13). A gas mixture with a defined ratio between CH₄ and air (P(CH₄)/P_air) was delivered at a constant rate under ambient pressure. In a 1,2-DFB solution of 1 mM 1d and P(CH₄)/P_air = 35, a 3-h bulk electrolysis on a Si nanowire electrode (E_app = −1.4 V vs SCE) yielded 0.37 ± 0.20 mM CH₃OH (n = 3, Figure 2B, Table S1, entry 2). The observed CH₃OH can be directly attributed to the reactivity of 1a and not the platinum (Pt) counter electrode as a similar performance is observed when a graphitic carbon cloth is substituted as the counter electrode (Table S1, entry 3). Longer electrolysis up to 24 h led to a higher concentration of CH₃OH up to 6.45 ± 0.92 mM (Table S1, entries 4–6). Since experimentally there was some fluctuation of electrochemical current as the electrolysis was conducted at a constant potential, a fairer comparison between experiments of different durations is based on the moles of CH₃OH normalized to the average electrochemical current. The CH₃OH yield normalized by the current (n(CH₃OH)/I) is a near linear function of the electrolysis duration (Figure 4C), which suggests a continuous catalytic reaction without much catalyst degradation. On average, 2.1 ± 0.3 equiv of electrons, a value averaged based on entries 2–6 in Table S1, corresponds to the formation of 1 equiv of CH₃OH. The calculated value in the bulk electrolysis of 1d in a CH₄/air mixture is lower than the theoretical value of 4 should hydroperoxide be the only

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**Figure 4.** Ambient air oxidation of alkanes to primary alcohols enabled by nanomaterials and electrochemistry. (A) Si nanowire array imaged by a scanning electron microscope. Scale bar, 2 µm. (B) General conditions used for catalytic ambient air CH₄ oxidation to CH₃OH. (C) The amount of generated CH₃OH normalized to the average electric current (n(CH₃OH)/I), as a function of the electrolysis duration. (D) Mass spectra for the electrolyte solution after 3-h bulk electrolysis. Red, ¹³CH₄ as the substrate; blue, CH₄ of natural isotope abundance. (E) Catalytic reactivities for different alkane substrates. BDE, bond dissociation energy; TON, turnover number based on catalyst in solution; TON⁺, turnover number based on catalyst in reaction layer; k_{on,s} and k_{on,bulk} kinetic rate constants of C–H activation by 1a calculated in nanowire array and reported in the literature, respectively. (F) The relationship between n(CH₃OH)/I in a 3-h electrolysis and the lengths of nanowire array. A planar electrode was considered as an array of 0 µm wire length.
reactive oxygen species. This suggests that reactive oxygen species other than hydroperoxide, such as superoxide, likely contribute to the oxidation of 1b and the formation of CH₃OH. As hydroperoxide is known to react reversibly with 1a in a similar fashion as O₂, a spatial distribution of reactive oxygen species generated by the O₂ also contributes to the observed reactivity. Interestingly, no other C₁ or C₂ liquid products were observed, and the generation of CO or CO₂ was not detectable in the outgas by GC-MS (Figure S14). While overoxidation may pose an issue since 1a is known to activate CH₃OH,¹⁷ the absence of other products but CH₃OH formation in the electrolysis suggests a strong selectivity for CH₄, possibly due to the 100-times faster rate of CH₄ activation as compared to CH₂OH by 1a²¹,³¹ as well as the relatively high solubility of CH₄ in the solvent (9.54 mM at 1 bar CH₄ based on ¹H NMR).

Electrolysis in the absence of either 1d, air, or CH₄ led to the disappearance of CH₃OH formation (Table S1, entries 7–9, respectively). Introducing ¹³C-labeled CH₄ as the substrate in lieu of the one with natural ¹³C abundance resulted in the surge of m/z = 33 peak in the mass spectrum (Figure 4D, Table S1, entry 10). This suggests the formation of a ¹³CH₃OH** fragment in the spectrum from the yielded ¹³CH₃OH (Figure S15). Our observations are consistent with a selective catalysis of CH₃OH formation with CH₄ as the substrate and O₂ as the oxidant. The turnover number (TON), defined as the ratio between product concentration and the concentration of precatalyst 1d in solution, was calculated to be 0.37 for the 3-h electrolysis and 6.45 for the 24-h electrolysis (Figure 4E and Table S1). Such a definition of TON values obviates the fact that only the catalyst molecules within the nanowire array are responsible for CH₄ activation in our proposed mechanism. Therefore, we also calculated an alternative turnover number (TON’), which is defined as the ratio between the moles of generated product and the moles of 1d precatalyst within the nanowire array. This TON’ relevant to electrochemical catalysts was²⁸ found to be 2972 for the 3-h electrolysis and up to 807 for a 24-h experiment (Figure 4E and Table S1). The calculated values of turnover numbers are comparable to those reported values of other catalysts for CH₄ functionalization (Tables S2 and S3), while our process is operating at room temperature and ambient pressure with air as the oxidant and CH₃OH as the product.

We further applied this ambient catalytic system to other substrates including ethane (C₂H₆), propane (C₃H₈), and toluene (PhCH₃). In all cases, selective oxidation to primary alcohols was observed (Table S1, entries 11–13), and their corresponding TON and TON’ are shown in Figure 4E. When t-butylibenzene was introduced as the substrate, no oxidation products were observed, which is in line with a previous report about the reactivity of RhIII porphyrin species³² (Table S1, entry 14). The reaction kinetics for different substrates was also compared in the developed catalytic system. As catalytic reactions of different substrates were conducted under different substrate concentrations in solution (see Supporting Information), the observed kinetic rate constants other than the turnover numbers were employed for evaluation. Given that the step of C–H activation is shown to be turnover-limiting (vide infra), we calculated the rate constants of C–H activation in a nanowire array, kₐ,nano, based on the observed rate of alcohol accumulation (Figure 4E). Despite the large differences of bond dissociation energies (BDE) of the cleaved C–H bonds (Figure 4E), kₐ,nano, which is independent of substrate concentration, appears to decrease even as BDE is simultaneously decreasing. Such a dependence of kₐ,nano over different substrates conveys the significant effect of steric constraint from 1a as reported before.¹⁸,¹⁹

Electrochemically generated 1a is the active species for CH₄ activation, and the nanowire array is responsible for 1a’s sustained presence and activity in air. We found that halving the concentration of 1d in bulk electrolysis led to a decrease of reaction rate by 4.3 times (Table S1, entry 15). This is consistent with the second-order kinetics on 1a for CH₄ activation (Figure 2A) and implies that C–H activation is turnover-limiting in the proposed catalytic cycle (Figure 2A). When we substituted the precatalyst 1d in the bulk electrolysis with a RhIII octaethyl porphyrin iodide ((OEP)Rh-I, 2) synthesized based on the literature (Figure S16),³³ no CH₃OH was produced (Table S1, entry 16). While 2 exhibits a similar electrochemical response as 1d with a slight shift of redox potential (Figure S17), the less bulky OEP supporting ligand is reported to favor the formation of the [(OEP)Rh⁺]dimer, which is unreactive toward CH₄.¹⁸ The observed difference of reactivities between 1d and 2 as precatalysts suggests that it is the electrochemically generated 1a that activates CH₄. Moreover, the catalytic ambient air oxidation of CH₄ to CH₃OH stopped, and no CH₃OH was observed when the nanowire array electrode was replaced with a planar wireless electrode, a wire array with larger spacing among wires, or an increased O₂ partial pressure at Pₐ/ₐO₂ = 1 (Table S1, entry 17, 18, and 19, respectively). Such observations are indeed consistent with our simulation results that a higher concentration of O₂, planar wireless electrode, or a less dense nanowire array all mitigate the anaerobic domain, the population of 1a, and thereby the reactivity toward CH₄ (Figure S18). Moreover, on the other hand, a 3-h electrolysis with P(CH₄)/PₐO₂ > 1000 yielded 0.25 mM CH₃OH (Table S1, entry 20), illustrating the existence of a fine window of O₂ partial pressure, which will result in optimal CH₃OH generation. These control experiments also indirectly support previous reports regarding the incompatibility of 1a with the O₂ in air.²²

Along the same lines, the effect of nanowire length was also investigated to ascertain its role in catalysis and CH₃OH formation. Additional nanowire arrays of 10 and 27 μm in length were prepared (Figure S19). The yields of CH₃OH for a 3-h electrolysis were 0.19 (Table S1, entry 21), 0.37, and 0.45 (Table S1, entry 22) for a planar electrode and nanowires of 10, 15, and 27 μm, respectively. The corresponding n(CH₃OH)/I values are plotted as a function of nanowire length in Figure 4F. As the length of the nanowire increases, the anaerobic domain in which C–H activation occurs expands, resulting in accelerated catalysis and subsequently more CH₃OH formation. Such an increase of reaction rate plateaued between nanowires of 15 and 27 μm in length, suggesting that the system reached the intrinsic limit based on its mechanism, and an additional length of nanowire is not beneficial for reaction productivity anymore. Lastly, a spent nanowire electrode, defined as a nanowire array that was previously utilized for a CH₃OH-yielding electrolysis, exhibited no activity toward CH₄ (Table S1, entry 23), and measurement of X-ray photoelectron spectroscopy (Figure S20) found no residual Rh species on the nanowire’s surface after electrolysis. It shows that the catalytic system is robust with minimal catalyst degradation, and any
obtainable Rh nanoparticle formation on the surface of the nanowires is not responsible for the observed reactivity. Interestingly, the rate of CH₄ activation by 1a was significantly increased in the nanowire array as compared to the one in bulk solution. kₒ,bulk = 2.9 × 10⁴ L²·mol⁻²·s⁻¹ for CH₄ activation, about 220 000 times the value in bulk solution (kₒ,bulk = 0.132 L²·mol⁻²·s⁻¹). A similar enhancement, by a factor of about 870 000, was observed when toluene was the substrate. As the C–H activation step of 1a undergoes an entropically disfavored four-centered transition state, high concentration and favorable intermolecular orientation between neighboring Rh centers will increase the reaction kinetics of CH₄ activation. We speculated that the negative charges from the native oxide on the Si nanowire’s surface as well as the relatively low dielectric constant of 1,2-DFB promote the adsorption of precatalyst 1d near the nanowire’s surface. While this effect will not alter the reactivity between 1a and O₂ as suggested in our experiments (comparing entry 2, 19, and 20 in Table S1), it will lead to a high local concentration of 1a, potentially create favorable intermolecular orientation between neighboring Rh centers, and subsequently increase its rate of CH₄ activation. Such a putative argument is supported by the observation that the rate of CH₃OH formation was minimal when the negative charges on the Si surface were passivated with terminal trimethylsilyl groups (Table S1, entry 24). It implies that confining homogeneous organometallic reactions within the space of a nanowire array can accelerate the reaction rate significantly, an effect possibly similar to the one observed when an organometallic catalyst is encapsulated in a supramolecular cavity. Overall, the introduction of electrochemistry and nanomaterials enables a catalytic ambient air oxidation of CH₄ to CH₃OH with the use of a low-valent electron-rich organometallic compound that is otherwise unsuitable as a catalyst in a homogeneous solution. The concept of spatially separating incompatible reaction steps at the nanoscale for a complete catalytic cycle provides new options for designing catalysis for a broad range of chemical transformations.

**ASSOCIATED CONTENT**

Supporting Information
The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscentsci.9b00625.

Full experimental details, detailed synthetic procedures, electrochemical characterizations, numerical simulation, product quantification, and additional tables and figures (PDF)

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C.L. supervised the project. C.L. and B.S.N. designed experiments and wrote the paper. B.S.N. synthesized the compounds with the assistance from E.D.C. and J.C.Q. B.S.N. conducted electrochemical characterizations and product quantification. L.S. conducted numerical simulations and experiments of confocal microscopy. All the authors discussed the results and assisted during the manuscript preparation.

**Notes**

The authors declare no competing financial interest.

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