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Scalable pinacol coupling reaction utilizing inorganic electride [Ca₂N]⁺·e⁻ as an electron donor†

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The scalable pinacol coupling reaction in >99% yield is achieved utilizing the inorganic electride [Ca₂N]⁺·e⁻ as an electron donor in organic solvents. The bond cleavages of the [Ca₂N]⁺ layers by methanol play a vital role in transferring anionic electrons to electrophilic aldehydes, accompanying the formations of Ca(OMe)₂ and ammonia.

Electrides are ionic crystals with cavity-trapped electrons, which serve as anions.[1] In a complex array of subnanometer-sized cavities, channels or layers, anionic electrons localize and interact mutually. These provide a rich area for theoretical studies of quantum confinement systems and have a broad range of applications in chemical synthesis, catalysis, and electronic devices.[1b,2] The first crystalline electride, Cs⁺ (18-crown-6)₂·e⁻, is the organic compound grown from the solution that contains solvated electrons in alkali metal-ammonia solutions and macrocyclic ligands, such as crown ether or cryptands, strongly binding to cations of alkali metals.[1c] Likewise with the solvated electrons, the organic electrides are also thermally and chemically unstable and decompose in an inert atmosphere and air above approximately −30 °C, hampering the practical applications of electrides as functional materials.

In 2003, the first room temperature stable inorganic [Ca₂₄Al₂₈O₆₄]⁴⁺·4e⁻ electride was synthesized by utilizing the complex oxide 12CaO·7Al₂O₃,[3] which is a constituent of commercial alumina cements and has a positively charged lattice framework composed of 3-dimensionally connected subnanometer-sized cages with an inner diameter of ~0.4 nm. This discovery accelerated the investigation of the physical properties of the [Ca₂₄Al₂₈O₆₄]⁴⁺·4e⁻ electride, revealing an extremely low work function of 2.4 eV[2c] and a metal-insulator transition[4], as well as superconductivity[5]. Very recently, two-dimensional (2D) electride was reported in layer structured dicalcium nitride with a chemical formula of [Ca₂N]⁺·e⁻.[6] This

2D electride shows the characteristic feature of delocalized anionic electrons within the interlayer spacing of ~0.4 nm, rendering the metallic state with the electron concentration of ~1.37×10²² cm⁻³, which is comparable to typical alkali metals. As expected in electrides, the [Ca₂N]⁺·e⁻ also shows the low work function value of 2.6 eV along the in-plane direction.

It is intriguing to note that both the solvated electrons in alkali metal-ammonia solutions and the anionic electrons in electrides have played an important role in synthetic organic chemistry as effective electron donors. From early years, solvated electrons have been applied to Birch[7] and Bouveault-Blanc reductions[8] as a potent reducing agent, forming a free radical anion. Recently, it has been demonstrated that the [Ca₂₄Al₂₈O₆₄]⁴⁺·4e⁻ electride acts as an efficient electron donating promoter for metal catalysts in ammonia synthesis. However, in contrast to the solvated electrons, it is noted that the electrides can offer an interesting opportunity for chemical reactions at room temperature and under mild reactive conditions by selecting an appropriate medium for electron transfer. Taking this into consideration, the [Ca₂₄Al₂₈O₆₄]⁴⁺·4e⁻ electride was applied to the pinacol coupling reaction in an aqueous media at room temperature.

Central to organic synthetic chemistry are the methods for carbon-carbon bond formation associated with electron transfer in a free radical process.[9,10] Numerous reagents and catalysts for carbon-carbon bond formations have been utilized as electron donors. Generally, alkali and alkaline earth metals are regarded as state-of-the-art electron sources to produce the solvated electrons. As the surrogate of alkali and alkaline earth metals, the [Ca₂₄Al₂₈O₆₄]⁴⁺·4e⁻ electride was first employed for the pinacol coupling reaction.[11,12] However, in such a reaction, the water is preferentially required for destroying the cage structure and transferring anionic electrons. Although the electron released from the cage structure initiates the reactions in aqueous media, electrons are also partially consumed to

generate the H_2 and OH^- from water, limiting reactivity, yield and even scalability. This indicates that the selection of an appropriate solvent, according to the type of electrides, is significantly important for an effective electron transfer in a radical formation process.

Meanwhile, there have been no reports on the application of the 2D $[Ca_2N]^+\cdot e^-$ electride in synthetic organic reactions. Since the $[Ca_2N]^+\cdot e^-$ electride has a low work function (2.6 eV) and a high electron concentration of $\sim 1.37\times 10^{22}$ cm^{-3}, it would be effective in transferring electrons into organic solvents. Furthermore, the opened layer structured $[Ca_2N]^+\cdot e^-$ electride can provide a better accessibility to anionic electrons when compared to the closed cage structured $[Ca_{24}Al_{28}O_{64}]^{4+}\cdot 4e^-$ electride. Here, we demonstrate that 2D $[Ca_2N]^+\cdot e^-$ electride is significantly effective in donating and transferring the electrons to organic compounds in the presence of alcoholic solvents with the formation of $Ca(OMe)_2$ and evolution of ammonia, leading to the effective carbon-carbon bond formation in the pinacol coupling reaction (Fig. 1). Furthermore, an efficient electron donating and transferring of $[Ca_2N]^+\cdot e^-$ electride in alcoholic solvents allows for the gram-scale reaction.
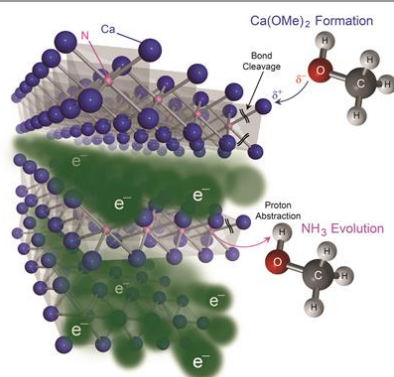

Fig. 1 Schematic illustration of a plausible mechanism for the pinacol coupling reaction utilizing $[Ca_2N]^+\cdot e^-$ electride as an electron donor in methanol, producing $Ca(OMe)_2$ and NH_3.

We carried out the pinacol coupling reaction of *p*-chlorobenzaldehyde **1a** as an electron acceptor in alcoholic solvents at room temperature. During the reaction, the black colour of the $[Ca_2N]^+\cdot e^-$ electride powders gradually changed to grey, and finally to white. This reveals that the anionic electrons of the $[Ca_2N]^+\cdot e^-$ electride are completely consumed in organic substrates. As shown in Table 1, the reaction proceeded more efficiently as the electride equivalent(s) increased (Table 1, entries 1–4). The reaction was sluggish when the solvent was switched from methanol to ethanol, resulting in a lower yield of 29% (Table 1, entry 5). Interestingly, the chemical yield of product **2a** increased with decreasing pKa values of alcohols in the following order: methanol > ethanol > *iso*-propanol = *tert*-butanol (Table 1, entries 4–7).

Furthermore, no reaction took place in the absence of either methanol or ethanol. For example, no product was detected in an aprotic polar solvent such as THF (Table 1, entry 8). Under

dilute conditions, the *dl*-selectivity of the product is slightly improved while retaining chemical yield (Table 1, entries 9–10). Gratifyingly, the dramatically increased yield was achieved via the introduction of a mixed solvent system with THF and MeOH (Table 1, entry 11). The potential $[Ca_2N]^+\cdot e^-$ electride for both reactivity and selectivity was compared by employing calcium metal and $[Ca_{24}Al_{28}O_{64}]^{4+}\cdot 4e^-$ electride (Table 1, entries 12–13). With calcium metal, a low yield of 24% was achieved, whereas the $[Ca_{24}Al_{28}O_{64}]^{4+}\cdot 4e^-$ electride was not able to participate in the co-organic solvent system, indicating no transfer of anionic electrons (Table 1, entries 12–13). These observations clearly indicate that the anionic electrons in the $[Ca_2N]^+\cdot e^-$ electride are transferred to the *p*-chlorobenzaldehyde and are responsible for the carbon-carbon bond formations. Importantly, the use of dilute methanol as a co-solvent is the most critical reaction parameter for enhancing the reaction rate and chemical yield in the use of $[Ca_2N]^+\cdot e^-$ electride.

Table 1 Optimization of the reaction conditions for the pinacol coupling reaction utilizing the $[Ca_2N]^+\cdot e^-$ electride.[a]
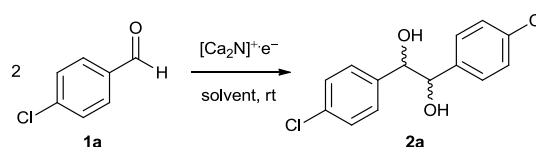
Entry	Electride (equiv.)	Solvent [M]	Time (h)	Yield[b] (%)	dl:meso[c]
1	0.5	MeOH [0.5]	0.5	29	2.5:1
2	1	MeOH [0.5]	0.5	67	1.4:1
3	1.5	MeOH [0.5]	0.5	79	1.4:1
4	2	MeOH [0.5]	0.5	83	1.4:1
5	2	EtOH [0.5]	1.5	29	3.2:1
6	2	iPrOH [0.5]	16	N.D.	-
7	2	tBuOH [0.5]	16	N.D.	-
8	2	THF [0.5]	24	N.D.	-
9	2	MeOH [0.25]	0.5	82	1.4:1
10	2	MeOH [0.125]	0.5	84	1.7:1
11	2	MeOH:THF(1:1) [0.125M]	1.5	>99	2:1
12[d]	2	MeOH:THF(1:1) [0.125M]	1	24	-
13[e]	2	MeOH:THF(1:1) [0.125M]	45	N.D.	-

[a] Reaction conditions: **1a** (0.5mmol), $[Ca_2N]^+\cdot e^-$ (0.5–2.0 equiv.), solvent (2–4 mL), rt. [b] Isolated Yield. [c] Determined by ^1H NMR spectroscopy. [d] Use of calcium metal. [e] Use of $[Ca_{24}Al_{28}O_{64}]^{4+}\cdot 4e^-$ electride.

With the established optimal condition, we examined the substrate scope of both aromatic or aliphatic aldehydes and a ketone (Table 2). Aldehydes bearing electron-deficient substituent on aromatic rings gave high yields of product **2a–f** (Table 2, entries 1–6). It is notable that the experimental maximum yield (>99%) of product **2a** was obtained. In the case of un-substituted aldehydes, a moderate yield of corresponding 1,2-*vic*-diol products **2g–h** was achieved (Table 2, entries 7–8).

Electron-rich substrates also produced the corresponding products **2i**–**j** in moderate yields (Table 2, entries 9–10). Aliphatic aldehyde such as pivalaldehyde can be also used for this reaction with a higher equivalent of electrides (Table 2, entry 11). Additionally, the reaction of ketone, such as acetophenone that is a less reactive functional group than aldehyde, also smoothly proceeded to yield the 1,2-*vic*-diol product **2l** (74% yield, Table 2, entry 12).

The observed moderate *dl-meso* selectivity results from the dimerization of radical anions and the formation of the strongly-bound ion-pairs between negatively charged oxygen and calcium ion after the first electron transfer (Scheme 1). *dl*-Product is slightly favoured compared to *meso*-product owing to minimize steric hindrance of R groups. Specifically, 2-naphthaldehyde gave the best *dl*-selectivity by the introduction of more bulky R groups.

Table 2 Reaction scope for the pinacol coupling reaction utilizing the $[Ca_2N]^{+} \cdot e^{-}$ electride in THF-MeOH co-solvent.[a]

| Entry	R^1	R^2	Product	Time (h)	Yield[b] (%)	dl:meso[c]
1	4-Cl-C$_6$H$_4$	H	**2a**	1.5	>99	1.5:1
2	4-F-C$_6$H$_4$	H	**2b**	9	71	1.9:1
3	3-CF$_3$-C$_6$H$_4$	H	**2c**	2	81	1.7:1
4	3-Br-C$_6$H$_4$	H	**2d**	9	61	1.8:1
5	3-Cl-C$_6$H$_4$	H	**2e**	8	79	1.5:1
6	2-Cl-C$_6$H$_4$	H	**2f**	8	78	1.2:1
7	Ph	H	**2g**	3	63	2.4:1
8	2-Naphthyl	H	**2h**	9	51	5.9:1
9	3-Me-C$_6$H$_4$	H	**2i**	9	63	1.6:1
10	3-MeO-C$_6$H$_4$	H	**2j**	8	66	1.8:1
11[d]	Trimethyl	H	**2k**	0.5	38	1.1:1
12	Ph	Me	**2l**	6	74	2.5:1

[a] Reaction conditions: aldehyde or ketone (0.5 mmol), $[Ca_2N]^{+} \cdot e^{-}$ (2 equiv.), THF : MeOH (v/v = 1:1, 0.125 M), rt. [b] Isolated Yield. [c] Determined by ^{1}H NMR spectroscopy. [d] Varying reaction conditions {$[Ca_2N]^{+} \cdot e^{-}$ (4 equiv.), THF : MeOH (v/v = 1:3, 0.125 M), rt.}
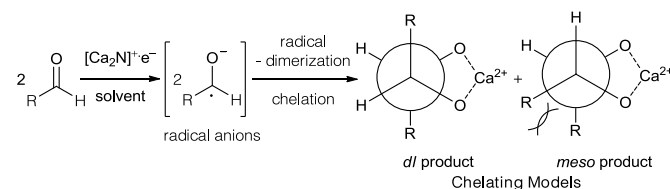
Scheme 1 Proposed mechanism for the selectivity in the pinacol coupling reaction utilizing $[Ca_2N]^{+} \cdot e^{-}$ electride.

Next, we expanded to the large-scale preparation of various 1,2-*vic*-diols (Scheme 2). Each reaction was repeated on 10 mmol scale (20 times greater than the experiments described in Table 2). It is noteworthy that higher yields were achieved by

modifying the co-solvent ratio from MeOH:THF (1:1) to MeOH:THF (3:1) compared to small-scale experiments described in Table 2. Moreover, to verify the superior performance of our protocols, we compared them with previous reports that used alkali and alkaline earth metals[12e,13] as an electron source in pinacol coupling reactions (Fig. 2). It is clear that the reaction using the $[Ca_2N]^{+} \cdot e^{-}$ electride is the most effective among the reactions in terms of yield, selectivity and scalability.
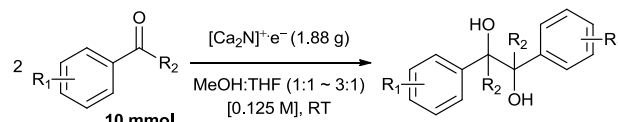
2a : R$_1$= 4-Cl, R$_2$=H, 96% yield, *dl:meso* = 64:36, 1 h, MeOH:THF (1:1)
2i : R$_1$= 3-Me, R$_2$=H, 76% yield, *dl:meso* = 63:37, 1 h, MeOH:THF (3:1)
2j : R$_1$= 3-OMe, R$_2$=H, 85% yield, *dl:meso* = 59:41, 4 h, MeOH:THF (3:1)
2l : R$_1$= H, R$_2$=Me, 60% yield, *dl:meso* = 73:27, 3 h, MeOH:THF (3:1)

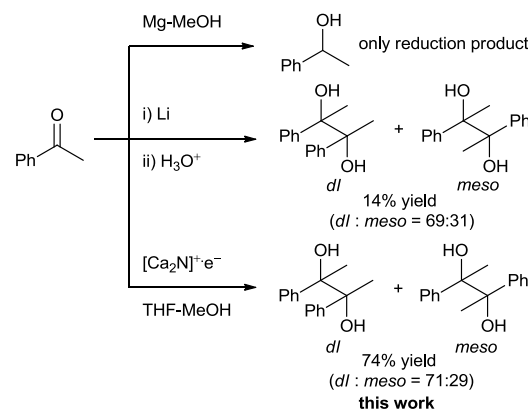**Scheme 2** Gram-scale synthesis of **2a, 2i, 2j, 2l** using $[Ca_2N]^{+} \cdot e^{-}$.

Fig. 2 Comparisons of reactivity and selectivity using alkali (Li), alkaline earth (Mg) metals and $[Ca_2N]^{+} \cdot e^{-}$ electride for carbon-carbon bond forming reactions.

We consider that the pinacol coupling reactions of aldehydes or ketone with $[Ca_2N]^{+} \cdot e^{-}$ electride presumably proceeded through the coupling of ketyl radical anions, which were generated by electron transfer from electride to carbonyl moieties. Most importantly, the methanol of the co-solvent played vital roles in the electron transfer by the cleavage of calcium-nitrogen bonds in the $[Ca_2N]^{+}$ layer, producing two different outcomes: i) formation of Ca(OMe)$_2$ by bonding of 2MeO$^-$ from methanol with Ca^{2+} of $[Ca_2N]^{+} \cdot e^{-}$, ii) formation of ammonia by bonding of protons from methanol with N^{3-} of $[Ca_2N]^{+} \cdot e^{-}$, simultaneously releasing the anionic electrons. As shown in Fig. 3(a), it is verified that X-ray diffraction (XRD) pattern of isolated Ca(OMe)$_2$ after the completion of the reaction is identical to that of standard sample (purchased Ca(OMe)$_2$ from Sigma-Aldrich).

To confirm the evolution of the ammonia during the reactions, we performed ion-chromatography (IC) measurements with the completed reaction mixtures. Samples for IC measurements were prepared by the following

procedures: each sample was taken from the individual reaction mixtures of THF and THF/MeOH using micro-glass filters without the acidic work-up procedure. For a more accurate analysis, they were diluted with deionized water. As shown in Fig. 3(b), the ammonium ion (NH^{4+}) peak was detected in the THF/MeOH co-solvent, whereas the NH^{4+} peak was not detected in the pure THF solvent. These observations strongly support a plausible mechanism (Fig. 1) for the donation of anionic electrons of $[Ca_2N]^+ \cdot e^-$ electride to the aldehydes.

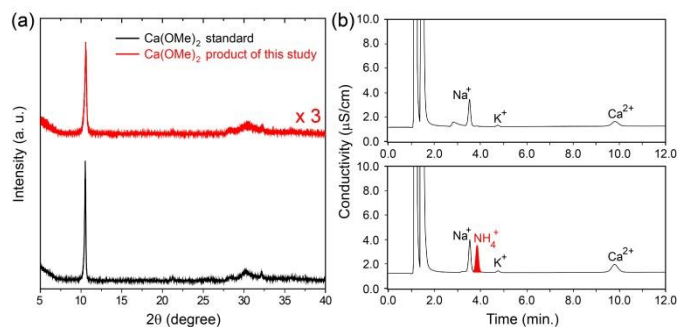**Fig. 3** (a) XRD patterns of $Ca(OMe)_2$ standard powders (black line) and resulting $Ca(OMe)_2$ product from the reaction mixtures (red line). All measurements are performed under nitrogen atmosphere. (b) IC analysis of ammonia from THF-mediated reaction mixture (top panel) and from THF/MeOH-mediated reaction mixture (bottom panel).

In conclusion, we have demonstrated that the $[Ca_2N]^+ \cdot e^-$ electride acts as an efficient electron donor for the carbon-carbon bond forming reaction via a free radical process. The appropriate solvent selection for the $[Ca_2N]^+ \cdot e^-$ electride allows for the efficient electron transfer to aldehydes. Moreover, we also identified the evolution of ammonia and the formation of $Ca(OMe)_2$ by the decomposition of $[Ca_2N]^+ \cdot e^-$ electride, thereby releasing anionic electrons to promote the pinacol coupling reaction. Our protocols can be utilized on a large-scale production of 1,2-*vic*-diol via ketyl radical anion dimerization of aldehydes, which are governed by electron donation from $[Ca_2N]^+ \cdot e^-$ electride in alcoholic solvent.

Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental procedures for the pinacol coupling reactions, characterization of products, ^{1}H NMR and ^{13}C NMR Spectra of the Products, and Calibrations and Results of Ion Chromatography. See DOI: 10.1039/c000000x/

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