Reaction Mechanism for the Formation of Dialkylated Nickel(II) Salen Involved in the Catalytic Reduction of (Bromomethyl)cyclopropane

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Cyclic voltammetry (CV) and controlled-potential electrolysis (CPE) were employed to examine the reaction between electrogenerated ligand-reduced nickel(II) salen and (bromomethyl)cyclopropane. Cyclic voltammograms for nickel(II) salen in the presence of (bromomethyl)cyclopropane exhibit characteristic features for the catalytic reduction of the substrate. Bulk electrolyses of (bromomethyl)cyclopropane at carbon cathodes in dimethylformamide catalyzed by nickel(II) salen were carried out to investigate the mechanism for the formation of dialkylated nickel(II) salen, which was analyzed and identified by high-performance liquid chromatography (HPLC). The corresponding dialkylated nickel(II) salen was further purified and collected by preparative-scale HPLC. Its complete structure was revealed by electrospray-ionization mass spectrometry (ESI-MS), ^{1}H NMR, COSY, and HECTOR NMR spectrometry. The clear-cut reaction mechanism for its formation was proposed on the basis of current and previous studies.
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Nickel(II) salen has been widely used as the catalyst for the electrochemical reduction of organic halides (RX). The corresponding catalytic reaction mechanisms were examined and proposed by various research groups.[1–5] Generally, nickel(II) salen (**1**) would undergo a one-electron reversible reduction to generate either the metal-reduced nickel(I) salen (**2**) or the ligand-reduced radical−anion (**3**, Scheme 1), which can subsequently transfer an electron to the organic halide substrate to produce a radical and a halide ion. Afterward, the substrate radicals can undergo different reactions such as coupling,[6,7] disproportionation,[6] intramolecular cyclization,[8,9] abstraction of hydrogen atom from solvent, etc. to afford a series of products. However, side reactions may also take place to cause the alkylation of nickel(II) salen. As the result, a significant amount of substrates could be lost[9] and nickel(II) salen would be deactivated.[10,11]

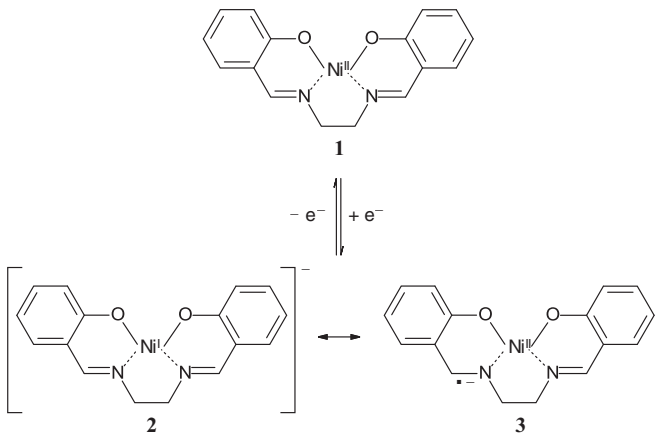
Peters and his colleagues proposed two possible routes (Route 1 or 2, Scheme 2) involving the S_N2 nucleophilic substitution and radical coupling reactions between catalyst **3** and substrates for the formation of dialkylated nickel(II) salen.[3,4] Alternatively, a derivative pathway (Route 3, Scheme 2) as well as the direct radical addition to the imino bond of nickel(II) salen (Route 4, Scheme 2)[12] cannot be ruled out. Nevertheless, a definite reaction mechanism still awaits further research.

In this study, we employed (bromomethyl)cyclopropane as the substrate for the electrochemical reduction catalyzed by nickel(II) salen. The catalytic process should lead to the formation of cyclopropylmethyl radicals, which undergo an extremely fast ring opening rearrangement to give 3-butenyl radicals at a rate constant of 8.6×10^7 s^{-1} (298 K).[13] The cyclopropyl ring could be retained in S_N2 nucleophilic substitution while the radical coupling would involve 3-butenyl radicals. Consequently, the dialkylation of nickel(II) salen will render different products (**4**−**7**, Scheme 3), depending upon which reaction route it takes. We carried out cyclic voltammetry (CV) and controlled-potential electrolysis (CPE) for the initial investigations and the electrolyzed solution was subject to HPLC analysis. Following purification by preparative-scale HPLC, the dialkylated nickel(II) salen was examined by ESI-MS, ^{1}H NMR, COSY, and HECTOR NMR spectrometry. Its structure was resolved and found to be **4**. Thus, we concluded that Route 1 (Scheme 2) should be the plausible reaction mechanism for the dialkylation of nickel(II) salen in the catalytic reduction of organic halides.

Experimental

Reagents.—(Bromomethyl)cyclopropane (Alfa Aesar, 97%) and nickel(II) salen ([[2,2′-[1,2-ethanediylbis(nitrilomethylidyne)] bis[phenolato]]-*N*,*N*′,*O*,*O*′]nickel(II), Sigma-Aldrich, 98%) were purchased and used as received. Optima grade water and acetonitrile were obtained from Fisher Chemical for HPLC analyses. Tetramethylammonium tetrafluoroborate ($TMABF_4$, Sigma-Aldrich, 97%), used as the supporting electrolyte, was stored in a vacuum oven at 60°C prior to use. Anhydrous dimethylformamide (DMF, Burdick & Jackson, 99.9%) was employed as solvent for electrochemical experiments. All deaeration procedures were carried out with Airgas zero-grade argon. CD_2Cl_2 (Cambridge Isotope Laboratories Inc., 99.9%) was utilized as the solvent in NMR spectrometry.

Cells and electrodes.—Cells for CV[14] and CPE[15] have been described previously. For CV experiments, a 3-mm-diameter glassy carbon working electrode (Part No. CHI104, CH Instruments) was used and a platinum wire was employed as the auxiliary electrode. Customized 2.4 cm diameter × 0.4 cm thick reticulated vitreous carbon disks (Duocel RVC 100 PPI, Energy Research and Generation) were used as working cathodes for CPE; these disks were cleaned and handled according to established procedures.[16] The reference electrode consists of a cadmium-saturated mercury amalgam in contact with DMF saturated with both cadmium chloride and sodium chloride[17,18]



Scheme 1.

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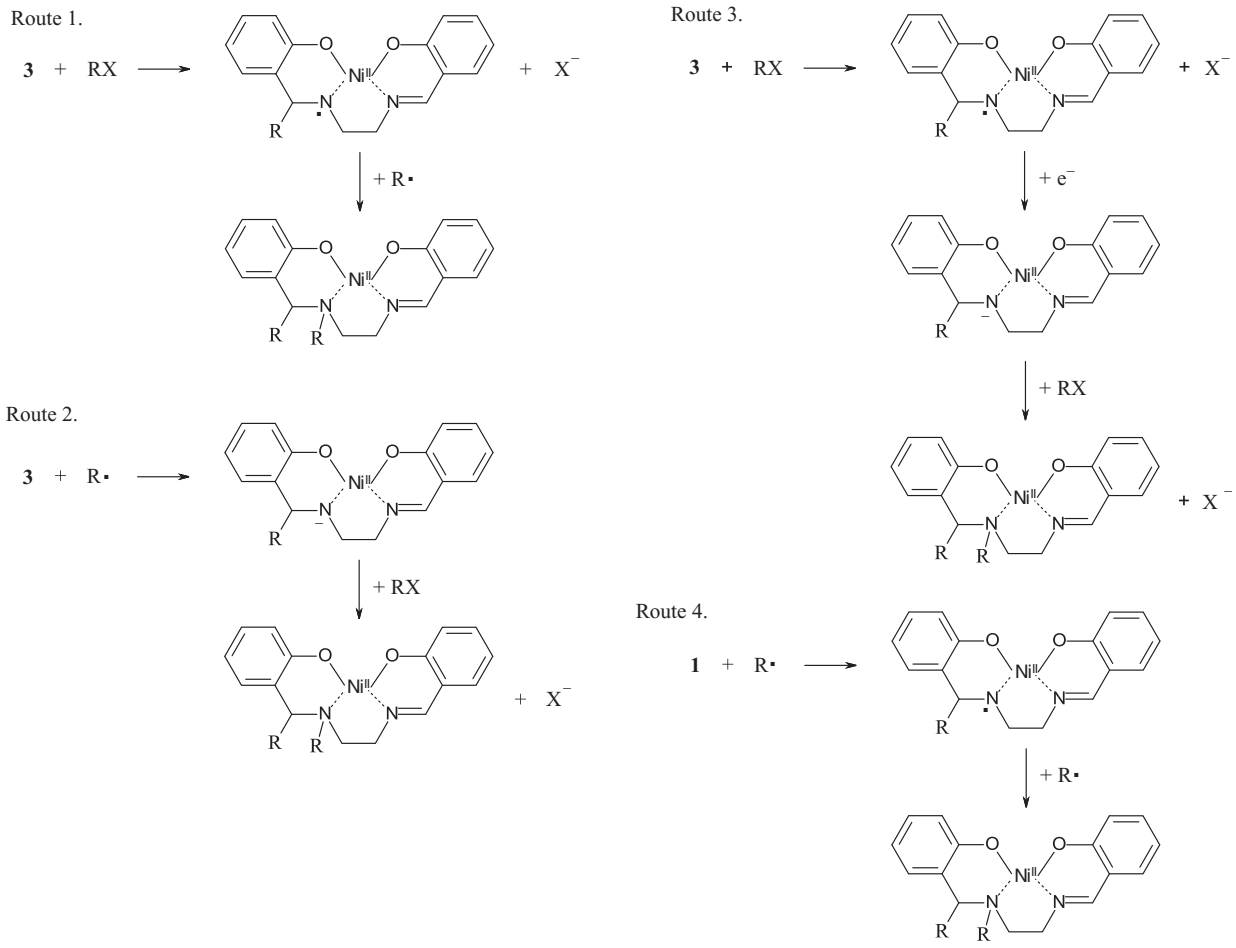


Scheme 2.

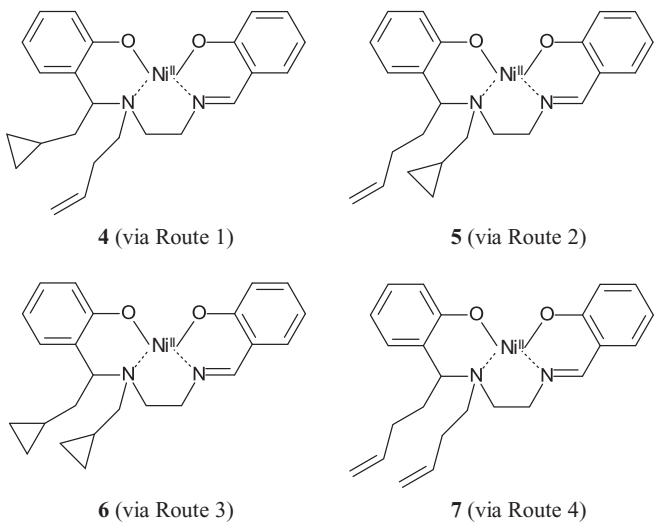
and it has a potential of −0.76 V vs. SCE at 25°C. Potentials are quoted with respect to SCE in this paper.

Instrumentation.—All CV and CPE experiments were carried out with a CH Instruments model 620B electrochemical analyzer. An Agilent Technologies model 1120 compact liquid chromatography (LC) system equipped with a 20-μL sample loop, a variable wavelength ultraviolet-visible detector (set at 254 nm), and a SUPELCOSIL LC-18 analytical HPLC column (15 cm × 4.6 mm, 3 μm particle size) was used to detect the nickel(II) salens in electrolyzed solutions. Eluent A was 1 mM ammonium acetate aqueous solution and eluent B was acetonitrile. The mobile phase was pumped at 0.4 mL min^{-1} with the elution gradient set as 10% B at 0 min, 100% B at 22.5 min, and held for another 10 min.

An Agilent Technologies PrepStar LC system equipped with a 5-mL sample loop, a semi-preparative HPLC column (Agilent-Zorbax SB-C18, 25 cm × 9.5 mm, 5 μm particle size), and the fraction collector (model 440-LC) was used to purify and collect the dialkylated nickel(II) salen. Eluent A was water and eluent B was acetonitrile. Controlled by OpenLab CDS software, the mobile phase was pumped at 2 mL min^{-1} with the elution gradient set as 10% B at 0 min, 100% B at 25 min, and held for another 3 min. A 500-μL aliquot of electrolyzed solution was injected each time and the dialkylated nickel(II) salen was detected at 254 nm and eluted at the retention time of 24.5–26 min.

The fractions containing pure dialkylated nickel(II) salen were combined and a small portion of it was subject to ESI-MS analysis. The mass spectra were recorded with a Waters Synapt G2 High Definition Mass Spectrometer. The travelling wave ion mobility (TWIM) MS experiments were performed under the following conditions: ESI capillary voltage, 5kV; sample cone voltage, 30 V; extraction cone voltage, 3.0 V; source temperature, 100°C; desolvation temperature, 100°C; cone gas (N_2) flow, 10 L/h; desolvation gas (N_2) flow, 700 L/h.

The solvents were also removed under vacuum to obtain the dialkylated nickel(II) salen in pure solid form. The compound was dissolved in CD_2Cl_2 for NMR studies. ^{1}H NMR, COSY, and HECTOR NMR spectra were collected by a Bruker Avance III 500 MHz instrument.



Scheme 3.

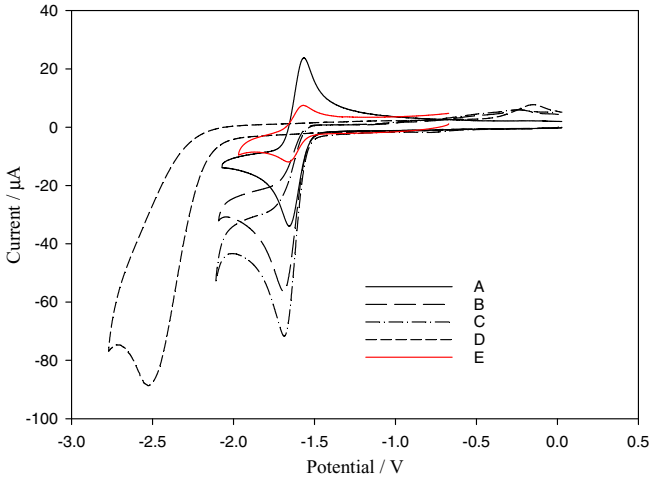


Figure 1. Cyclic voltammograms recorded with a glassy carbon electrode (3-mm-diameter) at 100 mV s^{-1} in DMF containing 0.050 M $TMABF_4$: (A) 2.0 mM of nickel(II) salen, (B) 2.0 mM of nickel(II) salen and 2.0 mM of (bromomethyl)cyclopropane, (C) 2.0 mM of nickel(II) salen and 8.0 mM of (bromomethyl)cyclopropane, (D) 2.0 mM of (bromomethyl)cyclopropane, and (E) electrolyzed solution initially containing 2.0 mM of nickel(II) salen and 20 mM of (bromomethyl)cyclopropane.

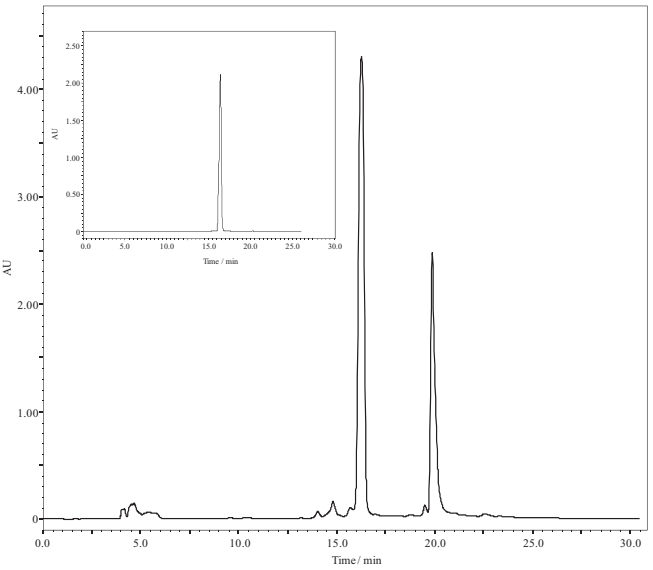


Figure 2. High-performance liquid chromatograms for a solution of 2.0 mM nickel(II) salen with 20 mM (bromomethyl)cyclopropane in DMF containing 0.050 M $TMABF_4$ after CPE at −1.80 V (full-scale) and for 1.0 mM nickel(II) salen in DMF (inset).

Results and Discussion

Cyclic voltammetry and controlled-potential electrolysis.—Fig. 1 (Curves A−D) depicts the CVs for reduction of nickel(II) salen in the absence and presence of (bromomethyl)cyclopropane, as well as for the direct reduction of the substrate, recorded at a scan rate of 100 mV s^{-1} with a glassy carbon electrode in DMF containing 0.050 M $TMABF_4$. Curve A, is a cyclic voltammogram for a 2.0 mM solution of nickel(II) salen, showing a reversible redox couple at E_{pc} of −1.66 V and E_{pa} of −1.57 V. Meanwhile, the irreversible direct reduction of (bromomethyl)cyclopropane (2.0 mM) is found to have a peak potential of −2.52 V (Curve D). When 2.0 mM of nickel(II) salen and 2.0 mM of (bromomethyl)cyclopropane are combined, as presented by Curve B, an increase in the cathodic peak current and the absence of anodic peak for the reoxidation of nickel(I) salen can be observed as the characteristics of a catalytic process. If the concentration of (bromomethyl)cyclopropane is increased to 8.0 mM, the cathodic peak current grows but not in proportion to the substrate concentration (Curve C), likely due to the sluggish regeneration of active nickel(II) salen. These electrochemical behaviors are similar to those shown in previous studies for the nickel(I) salen-catalyzed reduction of alkyl halides.[4,6,9,19–21] Some small anodic peaks also appear at −0.15 to −0.30 V for Curves B−D, possibly caused by oxidation of the products.

CPEs were carried out at −1.80 V to ensure the catalytic process for 20 mM of (bromomethyl)cyclopropane with 2.0 mM of nickel(II) salen. The average coulometric n value is 1.08 for ten runs, which is comparable to literature reuslts.[9] CV of the solution after electrolysis (Fig. 1 Curve E) suggests that a large amount of nicke(II) salen should be catalytically deactivated due to alkylation at the imino bond.[5,14] The electrolyzed solutions were saved for further analyses.

High-performance liquid chromatography (HPLC) and electrospray-ionization mass spectrometry (ESI-MS).—After CPE, a sample solution was tested by analytical HPLC to find the catalysts and the corresponding chromatogram is presented in Fig. 2. Two prominent peaks, one at the retention time of 16.5 min and the other at 20 min, can be seen. The first peak matches that for nickel(II) salen (inset, Fig. 2), whereas the second peak is for the alkylated nickel(II) salen.[3] To further identify the second peak, the electrolyzed solutions were combined and subject to preparative HPLC to collect the purified alkylated nickel(II) salen, which was then analyzed by ESI-MS.

The high definition mass spectrum reveals two peaks at m/z of 435.1656 and 869.3128, as shown in Fig. 3. Since nicke(II) salen has the formula of $C_{16}H_{14}N_2NiO_2$ and that for cyclopropylmethyl is C_4H_7, the m/z of 435.1656 peak should be due to the protonated dialkylated nickel(II) salen ($[C_{16}H_{14}N_2NiO_2 + 2C_4H_7 + H]^+$), which has an exact mass of 435.1582. On the other hand, the m/z of 869.3128 peak is owing to the dimeric species ($[2(C_{16}H_{14}N_2NiO_2 + 2C_4H_7) + H]^+$, exact mass = 869.3087). Moreover, the isotopic distributions for the two MS peaks also match well with the simulated data (Fig. 4). We concluded that the modified nicke(II) salen, observed as the second peak in HPLC after electrolysis, must be a dialkylated nickel(II) salen species. Subsequently, a variety of NMR spectrometry was employed to resolve the complete structure of this complex.

NMR spectrometry.—^{1}H NMR, COSY, and HECTOR NMR spectra were recorded to structurally characterize the dialkylated nickel(II) salen. With a comparison of previous studies,[3] we were able to discover that the exact structure of the complex is that of species **4**. ^{1}H

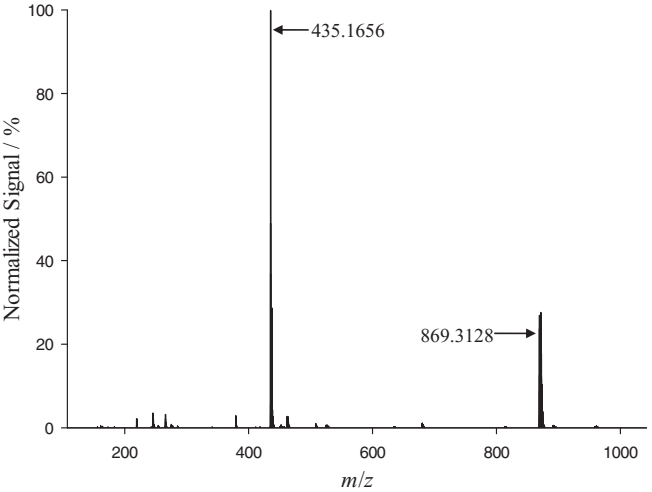


Figure 3. High definition ESI-MS for the purified dialkylated nickel(II) salen.

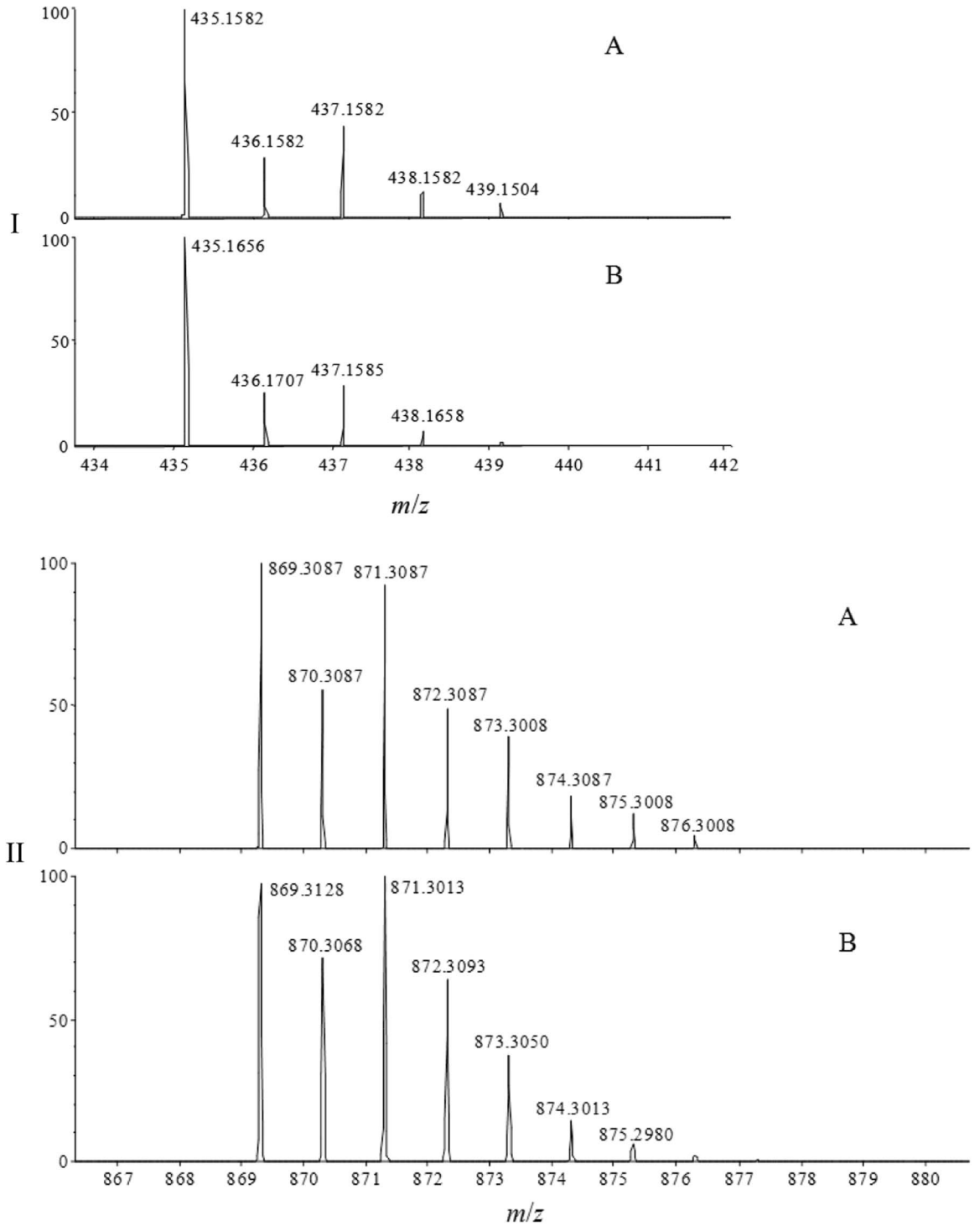
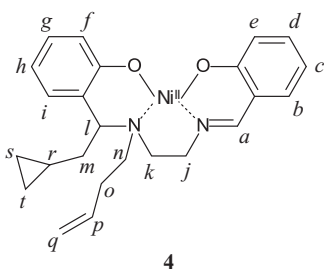


Figure 4. MS isotopic distributions for the simulated (A) and experimental (B) data of dialkylated nickel(II) salen (I) and the corresponding dimer (II).

NMR signals are as follows: (CD_2Cl_2) δ 7.46 (s, 1H, CH_a), 7.15 (t, 1H, CH_d), 7.10 (d, 1H, CH_b), 6.99 (t,1H, CH_g), 6.81 (d,1H, CH_e), 6.71 (d, 1H, CH_i), 6.64 (d, 1H, CH_f), 6.52 (t, 1H, CH_c), 6.40 (t, 1H, CH_h), 5.92 (m, 1H, CH_p), 5.13 (d, 1H, $CH_{q\text{-}trans}$), 5.04 (d, 1H, $CH_{q\text{-}cis}$), 4.26 and 3.09 (m, 1H each, CH_{2m}), 3.64 and 3.26 (td and dd, 1H each, CH_{2j}), 3.20 (m, 2H, CH_{2n}), 3.12 and 2.51 (m and dd, 1H each, CH_{2k}), 2.90 (dd, 1H, CH_l), 2.15 and 2.01 (m, 1H each, CH_{2o}), 0.98 (m, 1H, CH_r), and 0.73, 0.51, 0.44, and 0.14 (m, 1H each, CH_{2s} and CH_{2t}). We did not seek to establish the stereochemistry for some of the protons as the structure of complex **4** was revealed unambiguously.



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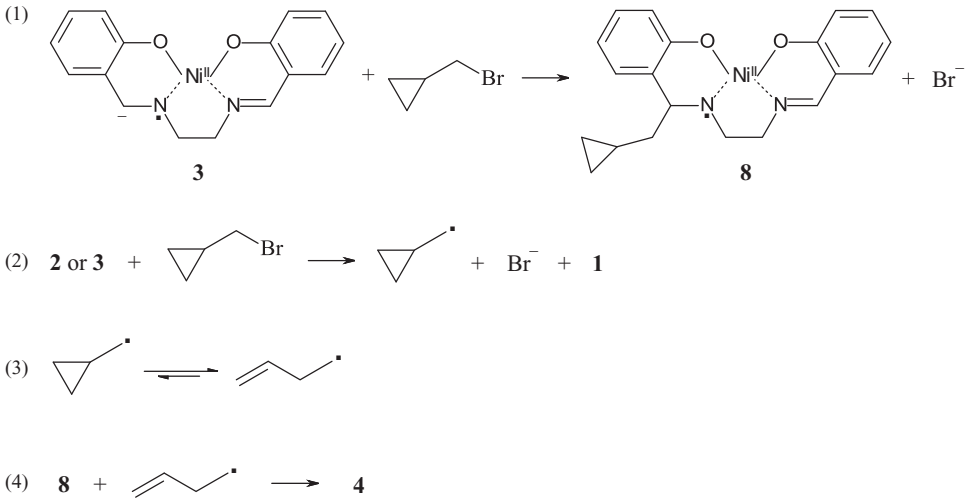

Scheme 4.

Since **4** is the only dialkylated nickel(II) salen found in the electrolyzed solution, it suggests that Route 1 (Scheme 2) should be the predominant process for alkylation of nickel(II) salen in the catalytic reduction. The other three possible pathways (Routes 2−4, Scheme 2) can be ruled out. On the basis of this and previous studies, a clean-cut mechanism would be proposed for the general reaction between the ligand-reduced nickel(II) salen (**3**) and organic halides.

Mechanistic features and conclusions.—For the nickel(II) salen radical−anion (**3**), which is electrogenerated by one-electron reduction of nickel(II) salen (Scheme 1), the negative charge should mainly reside at the carbon atom of the imino bond while the electron would be located at the nitrogen atom (Scheme 4). This structure has also been suggested by theoretical calculations in a previous study.[4] The S_N2 nucleophilic substitution (reaction 1, Scheme 4) will first take place between **3** and (bromomethyl)cyclopropane to give the intermediate radical (**8**) and bromide ion. On the other hand, most of the substrate molecules are catalytically reduced by either **2** or **3** to cyclopropylmethyl radicals (reaction 2, Scheme 4), which can immediately undergo ring opening rearrangement to generate 3-butenyl radicals (reaction 3, Scheme 4). Finally, radical **8** will couple with 3-butenyl radical to form the dialkylated nickel(II) salen **4** (reaction 4, Scheme 4).

In summary, the catalytic reduction of (bromomethyl)cyclopropane leads to the dialkylation of nickel(II) salen as the side reaction. The structure of complex **4** has been resolved and its formation is undoubtedly due to a two-step process involving S_N2 nucleophilic substitution followed by radical coupling. The analogous mechanism can be applied to reactions between the ligand-reduced nickel(II) salen (**3**) and various organic halides.

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