Nickel-Catalyzed Anti-Markovnikov Hydroarylation of Unactivated Alkenes with Unactivated Arenes Facilitated by non-Covalent Interactions

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Abstract: Anti-Markovnikov additions to alkenes have been a longstanding goal of catalysis, and anti-Markovnikov addition of arenes to alkenes would produce alkylarenes that are distinct from those formed by acid-catalyzed processes. Existing hydroarylations are either directed or occur with low reactivity and low regioselectivities for the linear alkylarene. Herein, we report the first undirected hydroarylation of unactivated alkenes with unactivated arenes that occurs with high regioselectivity for the anti-Markovnikov product. The reaction occurs with a Ni catalyst ligated by a highly sterically hindered N-heterocyclic carbene (NHC, L₄ or L₅). Catalytically relevant arene- and alkene-bound Ni complexes have been characterized, and the rate-limiting step was shown to be reductive elimination to form the C-C bond. DFT calculations, combined with second-generation, absolutely-localized molecular orbital energy decomposition analysis (ALMO-EDA), suggest that the difference in activity between catalysts containing large and small carbenes results more from stabilizing intramolecular, non-covalent interactions in the secondary coordination sphere than from steric hindrance.
Linear alkylbenzenes are fundamental precursors to a variety of industrially relevant surfactants, detergents, plastics, and fine chemicals\textsuperscript{1} with a global market value over $7.75 billion.\textsuperscript{2} Although termed “linear alkylbenzenes,” the commercial process forms mixtures of isomeric and homologous branched alkylbenzenes from rearrangement of carbocationic intermediates in the alkylation step.\textsuperscript{3} Because the branched alkylarenes are more resistant to biodegradation;\textsuperscript{4} their use as surfactants and detergents has led to extensive river, lake, and ocean pollution.\textsuperscript{5–6}

Anti-Markovnikov, transition-metal catalyzed hydroarylation could form truly linear alkylbenzenes, but the reaction of unactivated alkenes with simple unactivated arenes lacking a directing group\textsuperscript{7–10} has not been reported with high selectivity for the linear product (Fig. 1A). Iridium, ruthenium and platinum systems reported by Periana,\textsuperscript{11–14} Gunnoe,\textsuperscript{15–16} and Goldberg\textsuperscript{17} all catalyze the reaction of benzene (1) with propylene (2) to provide alkylarenes 3 and 4 with moderate activity, but to give nearly 1:1 ratios of constitutional isomers (Fig. 1B). Gunnoe recently reported a two-step synthesis of linear alkylarenes by Rh-catalyzed oxidative alkenylation and hydrogenation, but the process involves two steps and stoichiometric copper as oxidant.\textsuperscript{18–19}

The regioselectivity of published, undirected hydroarylations is controlled by the regioselectivity of insertion of the alkene into the metal-aryl bond (1,2 vs. 2,1 addition).\textsuperscript{13, 16, 20–22} By this mechanism, high selectivity for the linear product requires that insertion must form a branched alkylmetal intermediate, but such an intermediate is typically less stable than the linear alkylmetal isomer. Moreover, the rates of these processes are likely limited by the counterbalancing electronic effects on the oxidative addition of an aryl C-H bond, which is often faster to more electron rich metal centers than electron-poor metal centers,\textsuperscript{23} and migratory insertion, which is often faster into metal-ligand bonds of more electron-poor metal centers than of more electron-rich metal centers.\textsuperscript{24}
A catalytic cycle that operates by an alternative mechanism could enable higher levels of regioselectivity for the linear product and bypass the counterbalancing electronic effects on multiple steps. Previous research from our groups led to a nickel-catalyzed, linear-selective
hydroarylation with electron-deficient arenes,\textsuperscript{25} and various electronically activated heteroarenes,\textsuperscript{26} but the reactions of electron-neutral arenes, such as benzene or alkylarenes, occurred with low turnovers. Thus, an analysis of the factors controlling activity was needed to achieve the first addition of an unactivated arene to a terminal alkene in good yields with high linear selectivity. In the most favorable case, this reaction would occur with a catalyst based on an earth-abundant, non-precious metal.

We report undirected, nickel-catalyzed hydroarylations of electron-neutral arenes with unconjugated terminal alkenes that occur in good yields with exceptionally high \( l:b \) selectivity (>50:1 in most cases, Fig. 1C) catalyzed by a nickel complex containing an outsized N-heterocyclic carbene. The reaction occurs by formation of an alkynickel aryl intermediate by an unusual ligand-to-ligand hydrogen transfer (LLHT) to a coordinated alkene\textsuperscript{25, 27} and rate-determining reductive elimination. Deep computational studies imply that attractive interactions of the large NHC ligand, rather than steric hindrance, leads to the high activity of the nickel-carbene complex.

**Results and Discussion:**

**Reaction development.** Initial studies\textsuperscript{25} showed that the combination of \( \text{Ni(COD)}_2 \) and the common NHC ligand IPr (L\textsubscript{1}) led to the addition of benzene (1) to 1-decene (5) with a high linear-to-branched ratio \( l:b \) of 19:1, but with less than one turnover. To increase the turnover numbers, we evaluated the hydroarylation of 1-decene (5) with benzene (1) catalyzed by L–Ni(\( \eta^6-C_6H_6 \)) complexes as the catalyst precursor (Fig. 2A).\textsuperscript{28} The yields were more reproducible, particularly at low catalyst loadings (\textit{vide infra}), when catalytic amounts of NaH and Na(acac) were added. While the reaction catalyzed by L\textsubscript{1}–Ni(\( \eta^6-C_6H_6 \)) provided only trace amounts of hydroarylation product 6, the reaction catalyzed by the complex of the more sterically encumbered ligand IPr*
(L2)\textsuperscript{29} and its more σ-donating analog IPr\textsuperscript{*OMe} (L3) occurred with several turnovers.\textsuperscript{30} Further altering the substitution of the aromatic rings on the sidearms of the NHC with \textit{m}-xylyl groups (L4, \textit{m}-XylIPr\textsuperscript{*OMe})\textsuperscript{31} or with \textit{m}-diethylphenyl groups (L5, \textit{m}-DepIPr\textsuperscript{*OMe}) led to a catalyst that reacted with much higher yields of the hydroarylation product (56\% for L4 and 54\% for L5 after 24 h). Alkene isomerization during the reaction by an independent process\textsuperscript{25} decreased the concentration of terminal alkene and reaction rates over time (Fig. S4-S5), but the catalyst was stable, and 75\% and 84\% isolated yields of 6 were obtained with L4 or L5 as ligand after 5 days (Fig. 2B). The \textit{l}:\textit{b} selectivity when using L4 or L5 remained an unprecedently high >50:1 (see above, Fig. 1B).

The addition of benzene occurred to a series of unactivated alkenes (Fig. 2B) with \textit{l}:\textit{b} selectivity >50:1 or undetected branched isomer in all cases. Because L4–Ni(\textit{η}\textsuperscript{6}–C\textsubscript{6}H\textsubscript{6}) and L5–Ni(\textit{η}\textsuperscript{6}–C\textsubscript{6}H\textsubscript{6}) catalyze parallel isomerization of alkenes, reactions initiated with internal alkenes, such as \textit{trans}-4-octene (7), also occurred with benzene (1) to form the 1-alkylarene product in good yield. Consistent with this observation, a mixture of \textit{cis}- and \textit{trans}- 2-hexene (8) and 3-hexene (9) isomers reacted to give the linear alkylarene product in 98\% yield. Terminal alkenes bearing substitution at the α-position that inhibit or prevent isomerization reacted to full conversion within 24 h. For example, the alkene 10 bearing a tertiary carbon at the α-position and alkene 11 bearing a quaternary carbon at the α-position reacted to give the resulting alkylarene products in >90\% yield. Both protected primary alcohols (12) and vinyl siloxanes (13) were tolerated under these reaction conditions.
Fig. 2. Reaction development and scope (A) Identifying NHC ligands to achieve hydroarylation. (B) Scope of alkene reaction partner for the hydroarylation reaction. (C) Hydroarylation of alkene 14 at reduced catalyst loading and/or basic additives. (D) Scope of arene reaction partner for the hydroarylation reaction. (E) ORTEP diagram of L4-Ni(η⁶-C₆H₆) (thermal ellipsoids at the 50% probability level), calculated %V₄ values, and steric map calculations. For clarity, all hydrogen
atoms have been omitted from the ORTEP diagram and NHC sidearms are represented in wire-format. a Determined by GC/NMR analysis of the crude reaction mixture. b 18 equivalents of arene were added. c 3 equivalents of arene were added. d NaH and Na(acac) were excluded. e Mesitylene was added as the reaction solvent.

The reaction of \( t \)-butylethylene (14) with benzene occurred in nearly quantitative yield after only 1 h under the standard conditions (Fig. 2C, Entry 1). The reaction with 3 mol% catalyst without added NaH and Na(acac) provided the product in yield that was the same as that with added NaH and Na(acac) (Fig. 2C, Entry 2). However, with basic additives, the reaction with only 0.3 mol% catalyst formed the addition product in 85% yield (TON = 283, Fig. 2C, Entry 3). The basic additives likely remove trace water that affects reactions with low loadings; the reaction with 0.3 mol% catalyst without NaH and Na(acac) formed the alkylarene in only 6% yield (Fig. 2C, Entry 4; for further details, see the Supplementary Information).

The hydroarylation of unactivated alkenes also occurred with a variety of electron-neutral, electron-rich, and electron-deficient arenes (Fig. 2D). The reaction of alkene 14 with toluene provided linear alkylarene 15 in good yield as a mixture of 3- and 4-alkylarene isomers. Alkene 11 reacted with xylene isomers at the most sterically accessible position to give products 16 and 17 in moderate yields. Reactions with more electron-deficient fluoroarenes proceeded in high yield (18-21). The intramolecular reaction of arene 22 containing a pendant alkene provided tetrahydronapthalene 23 in 86% yield by \(^1\)H NMR spectroscopy. In contrast, no cyclized product was observed from the potential intramolecular reaction to form a 5-membered ring.

**Investigation of the reaction mechanism.** Having developed a method for the hydroarylation reaction between unactivated arenes and alkenes that occurs in good yields with high anti-Markovnikov regioselectivity, we sought to understand the origins of the high activity of the catalysts containing ligands L4 and L5. To do so, we determined experimentally the resting
state of the catalyst with unhindered and hindered alkenes and the rate-determining step of the reaction, and we used a computational energy decomposition analysis\textsuperscript{32} to reveal the intramolecular interactions leading to high activity stemming from the large ligands.

Arene-bound NHC-ligated Ni complexes were prepared on the gram scale by the addition of free carbene ligand to a Ni\textsuperscript{0} source in C\textsubscript{6}H\textsubscript{6} as solvent under H\textsubscript{2} pressure.\textsuperscript{28,33} The solid-state structures of these complexes (Fig. 2E for L\textsubscript{4}–Ni(η\textsuperscript{6}–C\textsubscript{6}H\textsubscript{6})) illustrate the steric impact of the NHC ligand. In contrast to the symmetrical coordination of benzene in L2–Ni(η\textsuperscript{6}–C\textsubscript{6}H\textsubscript{6}), the angle between the carbene carbon and the benzene ligand in L\textsubscript{4}–Ni(η\textsuperscript{6}–C\textsubscript{6}H\textsubscript{6}) is significantly distorted from linearity (169.4°). This difference suggests that steric hindrance of the NHC ligand prevents a complete η\textsuperscript{6} interaction.

To quantify the steric properties of L\textsubscript{4} further, the percent buried volume (%\textit{V}_{Bur})\textsuperscript{34-35} and steric map of L\textsubscript{4} were calculated.\textsuperscript{36} With Nolan and Cavallo’s standard parameters for the radius (\(r\)) of the sphere surrounding the metal center of 3.5 Å, the proximal %\textit{V}_{Bur} of L\textsubscript{4} was smaller than that of L\textsubscript{1} by 3%.\textsuperscript{37} However, with a radius of 5.5 Å to account for the remote steric environment of L\textsubscript{4}, the %\textit{V}_{Bur} of L\textsubscript{4} was greater than that of L\textsubscript{1} by >10%. This difference is slightly greater than the difference between IPr and its N-2,6-dimethylphenyl analog known as IMes (8% difference in buried volume within 3.5 Å for L-AuCl)\textsuperscript{34} and correlates with the large difference in activity between the catalyst containing L\textsubscript{1} and that containing L\textsubscript{4} for the hydroarylation reaction. However, the large size of L\textsubscript{4} and L\textsubscript{5} cannot be solely responsible for the high reactivity of the catalyst containing L\textsubscript{4} for alkene hydroarylation because the reactivity of complexes of L\textsubscript{2} and L\textsubscript{3} possessing similar steric properties (see the Supplementary Information for all %\textit{V}_{Bur} values) are closer to that of the catalyst containing L\textsubscript{1} than to that containing L\textsubscript{4}.
Monitoring the reaction catalyzed by the complex with a $^{13}$C label in the carbene carbon ($^{13}$C-L4) by NMR spectroscopy revealed the resting states of the hydroarylation reactions with alkenes of varying sizes. The $^{13}$C NMR spectrum at 100 °C of the hydroarylation reaction between 1-$d_6$ and the long-chain alkene 5 contained a resonance at δ 204.7 (Fig. 3A), matching that of bis-alkene complex 24 generated independently in solution by combining 2.2 equiv of alkene 5 with $^{13}$C-L4–Ni($^{\eta^6}$-C$_6$H$_6$) (Fig. S7-8). The bis-propylene analog 25 was isolated in 50% yield from the reaction of L4–Ni($^{\eta^6}$-C$_6$H$_6$) and propylene (2) (Fig. 3B) and fully characterized by NMR spectroscopy and single-crystal X-ray diffraction. The $^{13}$C NMR spectrum obtained at 25 °C of the reaction of the more hindered $t$-butylethylene 14 contained a single resonance at 198.7 ppm (Fig. S11) and the color of the solution was yellow, matching the spectrum and color of the alkene complex 26 generated in situ from $^{13}$C-L4–Ni($^{\eta^6}$-C$_6$H$_6$) and 14 (vide infra). However, the $^{13}$C NMR spectrum at 100 °C contained a resonance at 196.2 ppm, and the color was red, matching those of $^{13}$C-L4–Ni($^{\eta^6}$-C$_6$D$_6$). Studies of the relative stabilities of the alkene and arene complexes (Fig. 3C) showed that both L4–Ni($^{\eta^6}$-C$_6$H$_6$) and the alkene complex 26 were present at equilibrium at lower concentrations (0.007–0.2 M) of alkene, but the mono-alkene dinitrogen complex 26, which was identified by NMR, IR spectroscopies and single-crystal X-ray diffraction (Fig. 3E), was the only species observed at higher concentrations of alkene (0.3–0.5 M). Thus, the catalytically active species in reactions of the unhindered alkenes (such as 5) are the bis-alkene complexes, whereas those in reactions of hindered alkenes (such as 14) at elevated temperatures are an equilibrium mixture of mono-alkene and arene complexes.
Fig. 3. Observation and isolation of catalyst resting states (A) Observation of catalyst resting state in hydroarylation reaction of 1-\(d_6\) with unhindered alkene 5 by \(^{13}\)C NMR spectroscopy. (B) Preparation and ORTEP diagram of 25. (C) \(^{13}\)C NMR spectra for the addition of 14 to a solution of \(^{13}\)L4-Ni(\(\eta^6\)-C\(_6\)H\(_6\)) in C\(_6\)D\(_6\). (E) Expression for the equilibrium between arene-bound and alkene-bound \(^{13}\)L4-Ni complexes and a plot of the ratio of Ni complexes with respect to [14]. (E) Preparation and ORTEP diagram of 26. For clarity, all hydrogen atoms have been omitted from the ORTEP diagrams and NHC sidearms are represented in wire-format.
To reveal the steps of the catalytic cycle, the initial rates of the hydroarylation of benzene (1) with both unhindered alkene 5 and hindered alkene 11 were measured at varying alkene concentrations (Fig. 4A). The initial rate of the hydroarylation reaction with terminal alkene 5 was inverse 1st order in the concentration of 5 (Fig. 4A, top), indicating that one equivalent of the unhindered alkene 5 dissociates from the bis-alkene resting state 24 prior to the binding of arene and the rate-determining step of the reaction. The order in hindered alkene 11 depended on the concentration of 11 (Fig. 4A, bottom), which is consistent with the equilibrium between catalytic resting states as a function of the identity and concentration of alkene described above (see Fig. 3D). The 1st order dependence of the reaction rate on [11] at low [11] indicates that replacement the zero-order dependence of the reaction rate on [11] at high [11] indicates that the resting state shifts to the mono-alkene complex 27 and the highest-energy transition state contains an aryl or arene unit.

Two sets of experiments revealed reversible steps within the catalytic cycle. The reaction of 1-d6 with alkene 11 led to 43% incorporation of deuterium into the alkenyl hydrogen atom in unreacted 11 after 60% conversion (Fig. 4B). Second, the kinetic isotope effect (KIE) determined from separate reactions of alkene 11 with either 1 or 1-d6 was only 1.3 ± 0.1 (Fig. 4C). The results of both experiments imply that transfer of the arene hydrogen to the alkene by one or multiple steps is reversible.
Fig. 4. Mechanistic experiments (A) Dependence of the initial rate of the hydroarylation on alkene concentration with (top) unhindered alkene 5 or (bottom) hindered alkene 11. (B) Deuterium scrambling observed in the hydroarylation of 1-\(d_6\) with 11. (C) Separate vessel KIE experiment for the hydroarylation of alkene 11.
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Computational studies by DFT provided further insight into the mechanism of C−H bond cleavage (Fig. 5A, see the Supplementary Information for computational details). C−H activation could occur by oxidative addition of the C−H bond in benzene or by an alternative mechanism involving direct transfer of the C-H bond of a coordinated arene to the bound alkene called ligand-to-ligand hydrogen transfer (LLHT). Previous computational studies on nickel-catalyzed
hydroarylation of alkynes, hydroarylation with more acidic arenes, and hydroarylation with less hindered ligands have indicated that the barrier to direct oxidative addition of the C−H bonds in benzene and other arenes to NHC-ligated Ni\(^0\) complexes is higher than those of a one-step transfer of the hydrogen from a coordinated arene to the coordinated \(\pi\)-system of the alkene or alkyne.\(^{31}\)

The barrier we computed for the LLHT process with the catalyst containing \(\textbf{L4} (^{14}\text{TS}_{\text{LLHT}}, 21.3\) kcal/mol), relative to the combination of benzene and the bis-alkene ground state (GS), was 5.2 kcal/mol lower in energy than that for the LLHT process with the catalyst containing the less hindered \(\textbf{L1} (^{11}\text{TS}_{\text{LLHT}}, 26.5\) kcal/mol) and 3 kcal/mol lower than the barrier for oxidative addition of the aryl C−H bond.

However, the highest-energy transition state of the catalytic process deduced from experiment (\textit{vide supra}) and computation is reductive elimination to form the alkyl-aryl C−C bond from T-shaped \(\textbf{28}\), not the LLHT. The computed barrier (relative to the ground state) for reductive elimination from the alkyl aryl complex bound by \(\textbf{L4} (^{14}\text{TS}_{\text{RE}})\) is 29.2 kcal/mol and 3.9 kcal/mol lower than the computed barrier for reductive elimination from the alkyl aryl complex bound by \(\textbf{L1} (^{11}\text{TS}_{\text{RE}})\). This difference is consistent with the much faster rates and higher turnover numbers for the reactions catalyzed by \(\textbf{L4}–\text{Ni}(\eta^6–\text{C}_6\text{H}_6)\) than for reactions catalyzed by \(\textbf{L4}–\text{Ni}(\eta^6–\text{C}_6\text{H}_6)\).

One might envision this difference in barriers to result from a steric effect on the rate of reductive elimination. However, computation of the geometry and non-covalent interactions provided a much different picture of the origin of high activity of the complexes of \(\textbf{L4}\) versus those of the smaller \(\textbf{L1}\). Most striking, the geometrical parameters around the Ni center in \(^{14}\text{TS}_{\text{RE}}\) were almost identical to those in \(^{11}\text{TS}_{\text{RE}}\) (Fig. 5B), suggesting that an effect beyond simple steric effects within the transition state controls the rate.
Fig. 5. **Computational investigations** (A) Computed reaction pathways for the hydroarylation reaction with L1 and L4. (B) DFT-optimized geometries for TS\textsubscript{RE} (C) Energy decomposition analysis for TS\textsubscript{RE} and comparisons between ligands. ΔE\textsubscript{dist} is the difference in energy between the most stable form of the free ligand and free nickel fragment and the energy of the two components in their geometries of the complex. ΔΔE\textsubscript{dist} is the difference in distortion energies between the ground state and transition state, and ΔΔΔE\textsubscript{dist} is the difference in ΔE\textsubscript{dist} for the pairs of ligands. ΔE\textsubscript{int} is the interaction energy of the two fragments in their distorted geometries and is decomposed as the sum of ΔE\textsubscript{Pauli}, ΔE\textsubscript{elstat}, ΔE\textsubscript{disp}, ΔE\textsubscript{ct}, and ΔE\textsubscript{pol}. In a similar manner, ΔE values are the difference in energies between the GS and the TS, and ΔΔΔE values are the difference in component ΔΔΔE for pairs of ligands. (D) Overall mechanistic proposal for the Ni-catalyzed hydroarylation of unactivated alkenes.
To decipher the origin of the different barrier for reductive elimination from the complexes containing \textbf{L1} and \textbf{L4}, we used the ligand-substrate interaction model pioneered by Houk\textsuperscript{40} and the second-generation absolutely-localized molecular orbital energy decomposition analysis (ALMO-EDA) developed by Head-Gordon\textsuperscript{32}. Selected energy values from this analysis for complexes of the four ligands \textbf{L1-L4} are summarized in Fig. 5C. A comparison of the difference in distortion energies between pairs of complexes shows that the peripheral methyl groups in \textbf{L4} ($\Delta\Delta\Delta E_{\text{dist}} \text{L4-L3} = -1.5 \text{ kcal/mol}$), in addition to the aromatic rings ($\Delta\Delta\Delta E_{\text{dist}} \text{L2-L1} = -1.1 \text{ kcal/mol}$), lead to distortion energies that favor reaction with \textbf{L4} over reaction with the other ligands ($\Delta\Delta\Delta E_{\text{dist}} \text{L4-L1} = -2.4 \text{ kcal/mol}$). For all of the four NHC ligands, the NHC fragment is less distorted from the free carbene in the transition state for reductive elimination than it is in the ground state. However, this difference between the distortion energy of the carbene in the transition state and ground state is greatest for \textbf{L4} and contributes to a lower barrier for reaction of complexes containing \textbf{L4} than for reactions containing \textbf{L1-L3} (Table S6).

This energy-decomposition analysis also shows that the aryl groups on ligands \textbf{L2-L4}, which are not present in \textbf{L1}, lead to interaction energies that cause the barriers for reactions catalyzed by complexes of \textbf{L4} (and \textbf{L2} and \textbf{L3}) to be lower than those by complexes of the more common ligand \textbf{L1} ($\Delta\Delta\Delta E_{\text{int}} \text{L4-L1} = -4.3 \text{ kcal/mol}$). An analysis of the major contributions to the difference between the interaction energies in the transition state for reductive elimination with one ligand and those in the transition state for reductive elimination with another ligand can be seen from Fig. 5C. The largest differences between these values for \textbf{L4} vs \textbf{L1} are the Pauli repulsive (steric effects), electrostatic, and London dispersion terms. Assessment of each pairwise difference in these contributions to interaction energies for reactions catalyzed by complexes of the series of ligands reveals the structural elements of the ligands that lead to these values. This
analysis shows that the Pauli repulsion term strongly influences the barrier and results principally from the larger steric impact of \( \text{L4} \). Particularly striking is that this Pauli term increases the barrier for reaction with the large ligand, relative to that for reaction with the smaller ligand, rather than decreasing the barrier (\( \Delta \Delta \Delta E_{\text{Pauli L4-L1}} = 5.2 \text{ kcal/mol} \)). Typically, one presumes that steric effects cause reductive elimination involving the coupling of two ligands from a single metal center to be faster for complexes of more hindered ancillary ligands.\(^{41}\)

In contrast, attractive electrostatic and London dispersion terms reduce the energy of the transition state containing \( \text{L4} \) versus the ground state more than they reduce this difference in energy for the complexes containing the other ligands. More specifically, the values in Fig. 5C show that that presence of the eight aryl groups in ligands \( \text{L2, L3, and L4} \) lead to electrostatic interactions that are approximately 4 kcal/mol larger than the electrostatic interactions in the complexes of \( \text{L1} \) (\( \Delta \Delta \Delta E_{\text{elstat L2-L1}} = -4.9 \text{ kcal/mol} \) and \( \Delta \Delta \Delta E_{\text{elstat L4-L1}} = -3.7 \text{ kcal/mol} \)). A similar pairwise comparison of the London dispersion effects show that the difference in value between the system containing \( \text{L4} \) and the system containing \( \text{L1} \) (\( \Delta \Delta \Delta E_{\text{disp L4-L1}} = -4.3 \text{ kcal/mol} \)) results mainly from the presence of the sixteen methyl groups on \( \text{L4} \) that are not present in \( \text{L1-L3} \).

While the results above demonstrate that the peripheral methyl groups in \( \text{L4} \) cause the difference between stabilizing dispersive interactions in the ground and transition states containing \( \text{L4} \) to be larger than this difference between those containing \( \text{L3} \) (\( \Delta \Delta \Delta E_{\text{disp L4-L3}} = -2.9 \text{ kcal/mol} \)), we further probed the origin of this difference in dispersive interactions with ligands \( \text{L3 and L4} \). The methyl groups in \( \text{L4} \) could participate in stabilizing dispersive interactions with each other and with other groups in the complex or they could cause the positions of the aryl groups and the structure of the core of the complexes of \( \text{L4} \) to be altered from those of \( \text{L1-L3} \) in a way that leads to a larger difference in dispersion interactions between the ground and transition states bearing
L4. To distinguish between these two possibilities, we performed the same energy decomposition analysis of the ground and transition states with L3 (lacking the peripheral methyl groups), but placing the atoms in the same positions as those in the lowest-energy geometry of L4. The results of this analysis are included in the Supplementary Information and show that the differences in dispersion interactions between the ground and transition states of the complexes containing L4 and L3 in the same geometry (the minimum-energy geometry of L4, ΔΔΔE_{disp L4-L3 in L4 geometry} = -2.9 kcal/mol, Table S12) are similar to those the ground and transition states containing L4 and L3 in their respective minimum-energy geometries. In other words, the stabilizing dispersion interactions in the complexes of L4 are due to direct interactions with the methyl groups, not to changes to the ligand geometry imparted by the methyl groups in L4. Finally, a graphical plot of the non-covalent interactions\(^{42-43}\) present in L4^TS_{RE} (Fig. S17) corroborates the presence of significant stabilizing interactions involving the methyl groups.

**Conclusion.** Thus, the first highly anti-Markovnikov hydroarylation of unactivated alkenes with unactivated arenes has been accomplished, and many of these reactions occur in good yields. Even internal alkenes react to give linear alkylarene products. The unparalleled selectivity and activity in this reaction was enabled by a nickel catalyst containing an extremely large N-heterocyclic carbene ligand that undergoes C-H activation by a mechanism to form a linear alkyl-metal complex and undergoes reductive elimination to form the new carbon-carbon bond in the alkylarene product with rates that are enhanced by intramolecular, non-covalent interactions. Our computational studies imply that the conventional view of how steric bulk favors reductive elimination does not apply to this system. Instead of accelerating the reductive elimination by steric repulsion, the multiple aryl groups in ligand L4 of the most active catalyst lead to favorable electrostatic interactions, and the large number of methyl groups in L4 leads to favorable London
dispersion interactions and lower distortion energy. We anticipate that this reactivity and analysis of its origins should aid the development of new methods for functionalization of alkenes with additional strong, unactivated C-H or X-H bonds catalyzed by complexes of nickel ligated by N-heterocyclic carbenes, as well as by complexes of metals other than nickel with appropriate properties of the ancillary ligands.

**References and Notes:**


(37) Because no crystal structure for L1-Ni(η6-C6H6) has been reported, the calculation for percent buried volume with L1 was performed with the DFT-optimized structure of L1-Ni(η6-C6H6).


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Supplementary Materials:

Materials and Methods
Supplementary Text
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References