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Enantioselective nickel-catalyzed electrochemical reductive conjugate alkenylation of α,β-unsaturated ketones†

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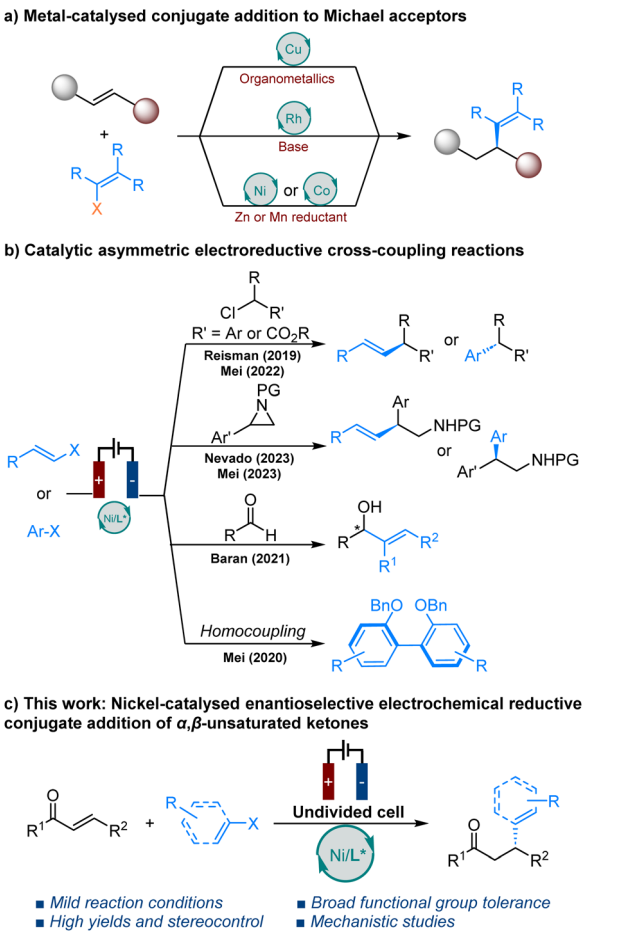
Catalytic electrochemical asymmetric catalysis is emerging as a promising strategy for the synthesis of chiral compounds. Herein, we report an asymmetric electrochemical nickel-catalysed reductive conjugate addition of alkenyl bromides/aryl iodides to α,β-unsaturated ketones in an undivided cell, leading to addition products with high yields and excellent enantioselectivities (up to 96% yield and 96% ee).

Introduction

Catalytic enantioselective conjugate addition to α,β-unsaturated carbonyl compounds, forming carbon–carbon bonds, constitutes one of the central pillars of modern-day organic synthesis.[1] This important transformation has been extensively developed in the last few decades and widely used in the synthesis of chiral products.[2] Among various catalytic systems, chiral copper-based complex catalysts have successfully promoted asymmetric conjugate additions of organometallic reagents to various Michael acceptors.[3] However, this approach requires prior synthesis of reactive organometallic reagents from the corresponding organohalides, is sensitive to both air and humidity and presents a narrow scope for both alkenylation and arylation reactions. In contrast, rhodium catalysis has been successfully applied in the asymmetric conjugate alkenylation of alkenylboronic,[4] silicon,[5] zirconium,[6] tin[7] and potassium organotrifluoroborate nucleophiles.[8] Nevertheless, most of these reactions require harsh conditions and additional steps for the synthesis of alkenyl reagents. Recently, Zhou *et al.* were the first to report on the nickel- and cobalt-catalysed enantioselective reductive conjugate addition of aryl/alkenyl halides to enones.[9–11] This transformation requires the use of super-stoichiometric amounts of zinc or manganese powder and must be carried out under an inert atmosphere in a glove box.

With the resurgence of organic electrolysis,[12] asymmetric electrocatalysis involving anodic oxidation has attracted considerable attention in recent years.[13] However, catalytic asymmetric electrochemical reduction reactions have received comparatively less attention (Scheme 1b). Chiral nickel based catalytic systems for the enantioselective coupling of alkenyl and benzyl halides,[14] α-chloroesters,[15] aryl aziridines,[16,17] and Nozaki–Hiyama–Kishi coupling[18] without the need for super-stoichiometric metal powder reductants have been developed by the groups of Reisman, Baran, Mei and Nevado.



Scheme 1 Design of enantioselective electrochemical reductive conjugate addition.

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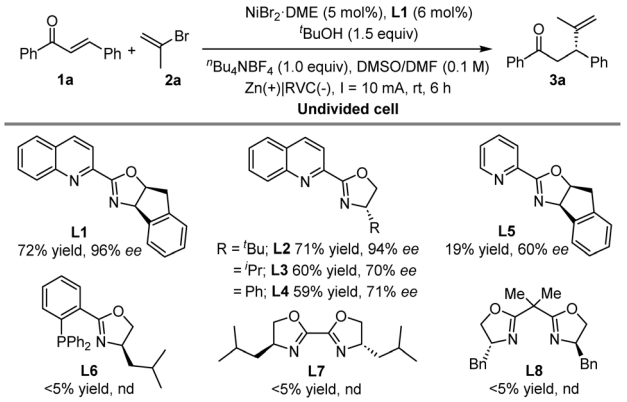
Additionally, Mei *et al.* reported enantioselective nickel-catalysed electrochemical reductive homocoupling of aryl bromides.[19] The recent report by Zhang *et al.* represents a significant advance in this area,[20] but limited examples of alkenylations emphasise the current challenges faced by this chemistry. Electroreductive alkenylations remain challenging due to the potential for side reactions, such as electrochemical difunctionalisation of alkenes, due to the presence of double bonds in both the starting materials and the resulting alkene products.[21] Herein, we present enantioselective nickel-catalysed electrochemical conjugate alkenylation of α,β-unsaturated ketones with alkenyl bromides/aryl iodides (Scheme 1c).

Results and discussion

We started our investigation (Table 1) by exploring the asymmetric electrochemical reductive conjugated addition of *trans*-chalcone **1a** with 2-bromopropene **2a** in the presence of a catalyst derived from the combination of a nickel salt and Quinox-**L1** in an undivided electrochemical cell (IKA Electrasyn 2.0). After systematic evaluation of the reaction parameters (see the ESI†), we were delighted to find that the desired product **3a** could be obtained in 72% yield and 96% ee (entry 1) when employing zinc as the anode and reticulated vitreous carbon (RVC) as the cathode in the presence of 5 mol% $NiBr_2$·DME, 6 mol% chiral quinoline–oxazoline (Quinox) ligand **L1**, 1.5 equiv. of ^{t}BuOH and 1.0 equiv. of ^{n}Bu$_4$NBF$_4$ in DMSO/DMF as solvent under 10 mA constant current electrolysis. Further investigation of different chiral quinoline–oxazoline ligands revealed that Quinox-**L2** with a bulky *tert*-butyl substituent allows for a similar outcome, while with isopropyl (**L3**) and phenyl (**L4**) substituents the corresponding product was obtained with a decreased yield and enantiopurity. Other chiral ligands such as pyridine-oxazoline (**L5**), phosphine-oxazoline (**L6**) and bis-oxazolines (**L7** and **L8**) all afforded the addition product **3a** with lower yields.

Table 1 Optimisation of the reaction conditions for the nickel-catalysed electrochemical reductive conjugate alkenylation of **1a** to **2a**[a]



Entry	Deviation from reaction conditions	Yield[b] (%)	ee[c] (%)
1	None	72	96
2	8 h instead of 6 h	41	95
3	4 h instead of 6 h	61	94
4	NaBr instead of ^{n}Bu$_4$NBF$_4$, 4 h	12	94
5	$MgBr_2$ instead of ^{n}Bu$_4$NBF$_4$, 4 h	17	92
6	^{n}Bu$_4$NBr instead of ^{n}Bu$_4$NBF$_4$, 4 h	12	94
7	^{n}Bu$_4$NPF$_6$ instead of ^{n}Bu$_4$NBF$_4$, 4 h	55	95
8	H_2O instead of ^{t}BuOH	71	94
9	EtOH instead of ^{t}BuOH	40	95
10	^{i}PrOH instead of ^{t}BuOH	74	96
11	^{i}PrOH instead of ^{t}BuOH, 0.06 M	49	95
12[d]	**^{i}PrOH instead of ^{t}BuOH, 0.2 M**	**75 (74)**	**96**

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.), **2a** (0.4 mmol, 2.0 equiv.), $NiBr_2$ DME (5 mol%), chiral ligand **L*** (6 mol%), additive (0.3 mmol, 1.5 equiv.), electrolyte (0.2 mmol, 1.0 equiv.) in DMSO/DMF (0.1 M, 2 mL, 1 : 1) under a N_2 atmosphere and 10 mA constant current in an undivided cell at room temperature. [b] The yield of **3a** was determined from the H NMR spectra of the reaction crude. Isolated yield is reported in parentheses. [c] Enantiomeric excess (ee) was determined by SFC with a chiral stationary phase. [d] In this case **1a** (0.4 mmol, 1.0 equiv.) and **2a** (0.8 mmol, 2.0 equiv.) were used.

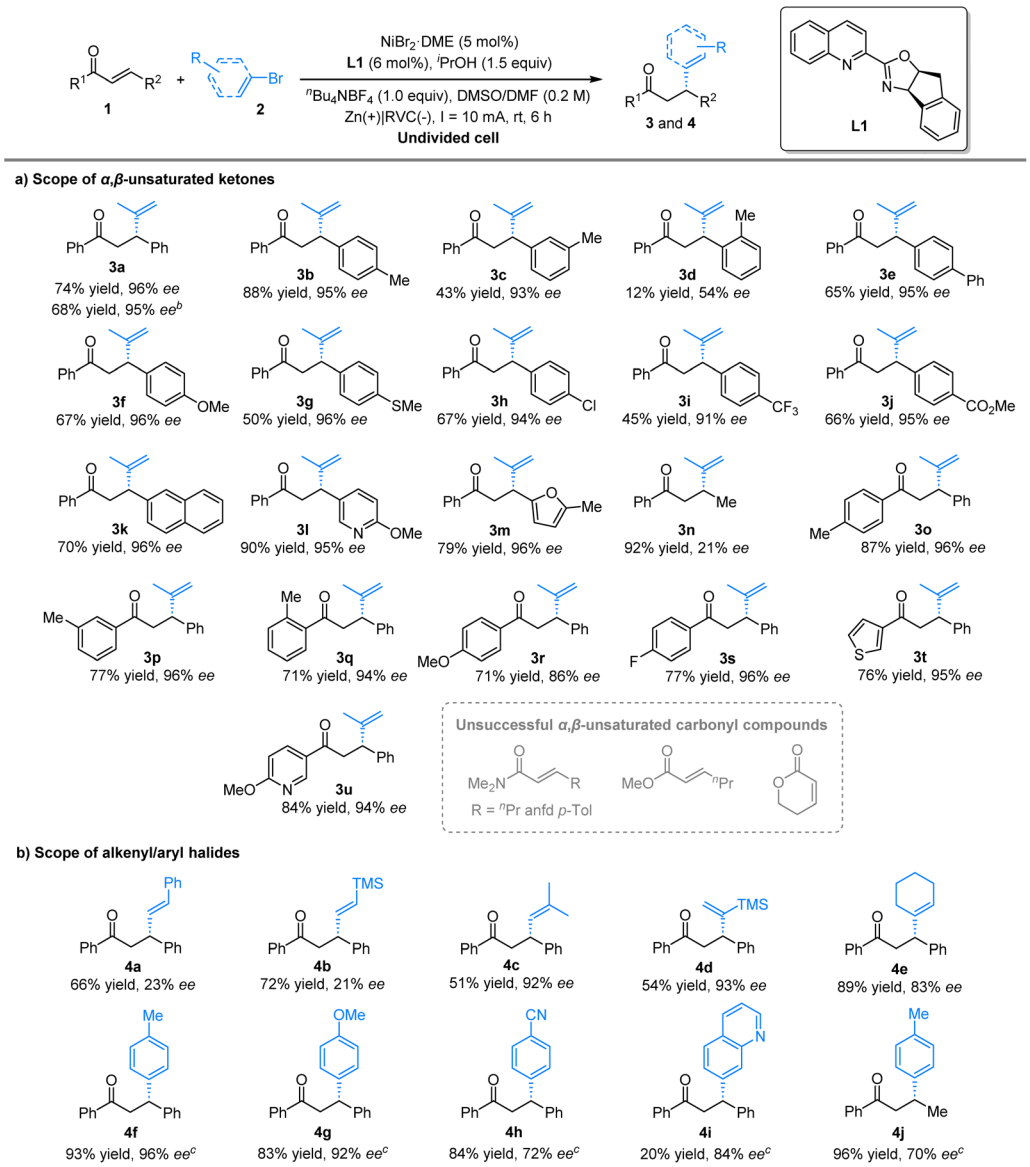
To improve the results further, we examined other reaction parameters. When the reaction was extended beyond 6 hours or stopped before 6 hours, lower yields were obtained (entries 2 and 3). The use of different supporting electrolytes such as NaBr, $MgBr_2$, ^{n}Bu$_4$NBr, or ^{n}Bu$_4$NPF$_6$ also proved detrimental to the reaction outcome (entries 4–7). At this point, we investigated the effect of additives. While reactions with H_2O and EtOH resulted in a reduced yield of **3a** (entries 8 and 9), ^{i}PrOH was found to be the most suitable additive for this reaction, yielding 74% of **3a** with 96% ee (entry 10). Reducing the concentration to 0.06 M did not improve the reaction results (entry 11). A slight increase in yield was achieved when the reaction was performed on a 0.4 mmol scale with a concentration of 0.2 M (entry 12).

Based on these results, we adopted the following optimised reaction conditions for further substrate scope studies: $NiBr_2$·DME (5 mol%) and Quinox-**L1** (6 mol%) as chiral nickel catalysts, with ^{i}PrOH (1.5 equiv.) as the additive and ^{n}Bu$_4$NBF$_4$ as the electrolyte in a DMSO/DMF (0.2 M) solvent mixture. The reaction was carried out under a N_2 atmosphere using a zinc anode and an RVC cathode in an undivided cell with 10 mA constant current electrolysis for 6 hours at room temperature.

With the optimised reaction conditions in hand, we explored the scope of this transformation with respect to α,β-unsaturated ketone substrates (Table 2(a)). First, the reaction was successfully scaled up to 1.2 mmol, yielding product **3a** in 68% yield with 95% ee. A wide range of aryl, heteroaryl, and alkyl substituents at the β-position of chalcones were well tolerated. Methyl substituents at the *meta* or *para* positions were compatible, yielding products **3b** and **3c** in 88% and 43% yields, respectively, hardly affecting the enantioselectivity. However, using the aryl moiety with an *ortho*-methyl substituent resulted in the corresponding product **3d** with a lower yield and enantiopurity (12% yield and 54% ee). In contrast, this transformation exhibited minimal sensitivity to the electronic nature of substituents on the aromatic ring.

A variety of functional groups, including phenyl (**3e**), electron-donating (**3f** and **3g**), halogen (**3h**), and electron-withdrawing (**3i** and **3j**) groups, were well tolerated, delivering the desired products in moderate to good yields (45–67%) with excellent enantiomeric excess (91–96% ee). Moreover, the

Table 2 Product scope of enantioselective nickel-catalysed electrochemical reductive conjugate addition of enones[a]



[a] Reaction conditions: **1a** (0.4 mmol, 1.0 equiv.), alkenyl bromides **2** (0.8 mmol, 2.0 equiv.), $NiBr_2 \cdot DME$ (5 mol%), chiral ligand **L1** (6 mol%), $^{i}PrOH$ (0.6 mmol, 1.5 equiv.), $^{n}Bu_4NBF_4$ (0.4 mmol, 1.0 equiv.) in DMSO/DMF (0.2 M, 2 mL, 1 : 1) under a N_2 atmosphere and 10 mA constant current in an undivided cell at room temperature for 6 h. [b] 1.2 mmol scale. [c] Aryl iodides were used. Reported yields correspond to the isolated yields. For each compound, ee values were determined by SFC on a chiral stationary phase.

method accommodated more sterically hindered substrates, such as 2-naphthyl-substituted ketone, which afforded product **3k** in 70% yield with 96% ee. The method also proved effective for enones containing heteroaromatic groups, such as pyridinyl and furfuryl, yielding products **3l** and **3m** in high yields (79–90%) with excellent enantioselectivities (96% ee). In particular, the use of *trans*-crotonophenone gave **3n** in an excellent yield of 92%, although with low enantiopurity (21% ee). The position of substituents on the phenyl ring α relative to the carbonyl moiety—whether *ortho*, *meta*, or *para*—had little impact on the outcome, resulting in products **3o–q** with high yields and excellent enantioselectivities. A variety of aryl groups containing electron-donating and -withdrawing substituents, such as methoxy (**3r**) and fluoro (**3s**), as well as heteroaryl substituents like thiophen (**3t**) and 2-methoxypyridine (**3u**), were well accommodated. However, under the standard conditions, α,β-unsaturated carboxamides and esters did not yield the corresponding alkenylated products.

We then examined the scope of alkenyl bromides using this electrochemical protocol (Table 2(b)). Both β-bromostyrene and β-(trimethylsilyl)vinyl bromide afforded products **4a** and **4b** in good yields (66–72%), albeit with low enantioselectivities (21–

23% ee). However, an alkenyl bromide bearing a β-substituent provided product **4c** in moderate yield with excellent enantiopurity. Additionally, an α-substituted alkene reacted smoothly, yielding product **4d** in 54% yield with 93% ee. Cyclohexenyl bromide gave product **4e** in 89% yield with 83% ee, while 4-iodotoluene successfully yielded the arylated product **4f** with excellent yield and enantioselectivity (93% yield and 96% ee). The reaction also accommodated both electron-donating and electron-withdrawing groups, yielding products **4g** and **4h** in good yields (83–84%) with moderate to excellent enantioselectivity (72–92% ee). Furthermore, N-heteroaryl iodides yielded product **4i** in low yields but with good enantioselectivity. In contrast, the less sterically hindered product **4j** was obtained with lower enantiopurity.

To gain further insight into the asymmetric nickel-catalysed electrochemical reductive conjugate addition, a series of control experiments were performed to verify the necessity of each reaction component (Fig. 1a). The process was completely suppressed in the absence of the nickel-ligand complex, ligand, or the electric current source, demonstrating that both the nickel-ligand catalyst and the electrical current were necessary for this transformation with no contribution from a competitive racemic background pathway. In addition, a low yield was obtained in the absence of alcohol and the deuterated product **3a** was observed when using deuterated ^{i}PrOD as the additive (Fig. 1b), suggesting that alcohol is crucial for hydrolysing nickel enolates and facilitating product formation after reductive elimination. Next, we conducted cyclic voltammetry experiments (Fig. 1c). The mixture of $NiBr_2 \cdot DME$ and **L1** in a ratio of 1 : 1 exhibits three reduction peaks (−1.13 V, −1.50 V and −1.72 V *vs.* Ag/Ag^+), corresponding to the successive formation of Ni(I), Ni(0), and $[Ni(0)\text{-}\mathbf{L1}]^{\bullet -}$ species.[22] Ni(0) can undergo oxidative addition with alkenyl bromide. The cyclic voltammetry of $NiBr_2$-**L1** was carried out in the presence of 1.0 equiv. of 2-bromopropene **2a**. New reductive peaks and the reduction of the oxidation peak (−0.68 V *vs.* Ag/Ag^+) suggest that oxidative addition of alkenyl bromide to Ni(0) occurred readily.

Next, we investigated intramolecular ^{13}C isotope effects by product analysis (Fig. 1d).[23] Determining KIEs can reveal major bonding changes in the rate-limiting step of a reaction.[24] We used high-precision NMR measurements of ^{13}C KIEs at natural isotopic abundance, developed by Singleton.[25] We conducted two independent reactions of *trans*-4-methylchalcone **1b** and **2a** under optimised reaction conditions on a 5 mmol scale and stopped the reaction at low conversions to the product **3b** (19 and 30%). The product **3b** was isolated, and its ^{13}C isotopic composition was compared to those of unreacted samples of **1b** and **2a**.

From changes in relative isotopic composition and fractional conversion, we determined ^{13}C KIEs (see details in the ESI†). We observed a primary KIE of ∼2.7% at C_β of the dihydrochalcone moiety and ∼1.7% at C_2 of the propenyl moiety, suggesting that C_β and C_2 are involved in the rate-determining step in the catalytic process. In contrast, all other carbons in the molecule exhibited near-unity KIEs, indicating their lack of involvement in the rate-determining step. The observed KIEs on both carbons strongly support that the migration of the alkenyl group from organonickel species to the electrophilic site C_β of α,β-unsaturated ketones is the rate-determining step of the catalytic cycle.

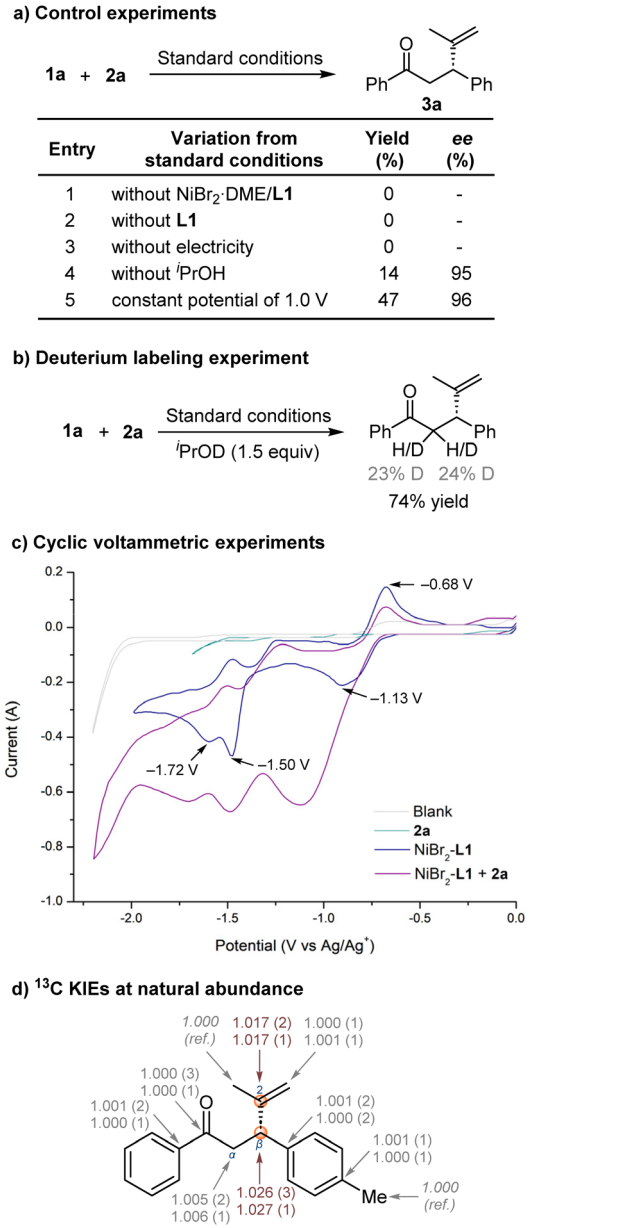
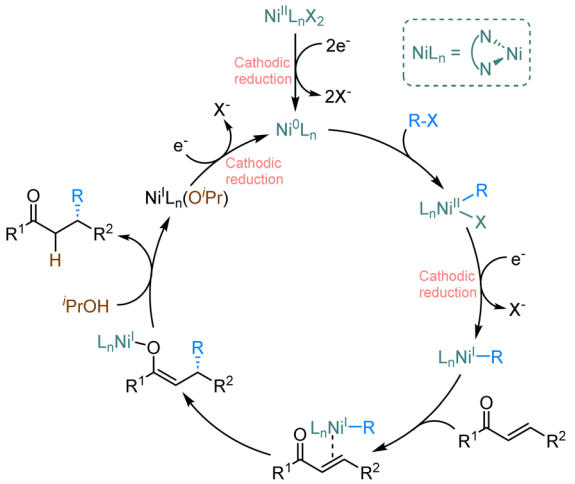


Fig. 1 Mechanistic proposal for asymmetric nickel-catalysed electrochemical reductive conjugate alkenylation. (a) Control experiments. (b) Deuterium labelling experiment. (c) Cyclic voltammetry studies of **2a**, $NiBr_2$-**L1**, and the mixture of **2a** and $NiBr_2$-**L1**. (d) Experimental ^{13}C KIEs at natural abundance for the conjugate addition of *trans*-4-methylchalcone **1b** with **2a** from product analysis. Two experiments were carried out yielding up to 19 and 30% yields of the product **2b** to determine the KIEs at dihydrochalcone and propenyl moieties. The numbers in parentheses represent the standard deviation of the last digit as determined from seven independent measurements.

Based on literature reports[9,10] and our studies, we suggest the plausible catalytic cycle (Scheme 2). Asymmetric electrochemical catalysis is initiated by the cathodic reduction of the $L_nNi(II)X_2$ precatalyst to form the active $L_nNi(0)$ catalyst that



Scheme 2 Proposed reaction mechanism for the enantioselective nickel-catalysed electrochemical reductive conjugate addition.

subsequently undergoes oxidative addition with an alkenyl halide leading to L_nNi(II)RBr. The subsequent cathodic reduction produces L_nNi(I)R, which binds the α,β-unsaturated ketone. Migratory insertion leads to the formation of a nickel *O*-enolate, likely in the rate-determining step. Subsequent hydrolysis by alcohol releases the desired product and regenerates L_nNi(I) species. Finally, the cathodic reduction of L_nNi(I) (OR) or L_nNi(I)Br completes the catalytic cycle.

Conclusions

In conclusion, we have developed asymmetric nickel-catalysed conjugate addition of alkenyl bromides and aryl iodides to α,β-unsaturated ketones in an undivided cell by merging electrochemistry and chiral nickel catalysis, affording a wide range of α,β-unsaturated ketones under mild reaction conditions. Additional investigations indicated that alkenyl halides get activated through oxidative addition to Ni(0) species and the rate-determining step of the transformation is likely reductive elimination that leads to the enolate product.

Data availability

Experimental and analytical data supporting this article are available in the ESI.†

Author contributions

Siriphong Somprasong designed the project, optimised the reaction conditions, investigated the substrate scope, analysed the data, performed the mechanistic experiments and wrote the draft of the manuscript. Bin Wan expanded the substrate scope and analysed the data. Syuzanna R. Harutyunyan supervised the project and edited the manuscript. All the authors contributed to and approved the final version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 (*a*) P. Perlmutter, *Conjugate Addition Reactions in Organic Synthesis*, Pergamon, Oxford, 1st edn, 1992; (*b*) A. Alexakis, N. Krause and S. Woodward, *Copper-Catalyzed Asymmetric Synthesis*, Wiley-VCH, Weinheim, Germany, 1st edn, 2014; (*c*) G. P. Howell, *Org. Process Res. Dev.*, 2012, **16**, 1258–1272; (*d*) L. Ge and S. R. Harutyunyan in *Catalytic Asymmetric Synthesis*, ed. T. Akiyama and I. Ojima, John Wiley & Sons, Inc., 4th edn, 2022, ch. 16, p. 617.

2 (*a*) R. W. Bates and S. Sridhar, *J. Org. Chem.*, 2008, **73**, 8104–8105; (*b*) M. K. Brown and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2008, **130**, 12904–12906; (*c*) Y.-J. Chin, S.-Y. Wang and T.-P. Loh, *Org. Lett.*, 2009, **11**, 3674–3676; (*d*) C. L. Pereira, Y.-H. Chen and F. E. McDonald, *J. Am. Chem. Soc.*, 2009, **131**, 6066–6067.

3 For selected examples of copper-catalysed asymmetric conjugate additions, see:(*a*) K.-S. Lee, M. K. Brown, A. W. Hird and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2006, **128**, 7182–7184; (*b*) F. López, A. J. Minnaard and B. L. Feringa, *Acc. Chem. Res.*, 2007, **40**, 179–188; (*c*) A. Alexakis, J. E. Bäckvall, N. Krause, O. Pàmies and M. Diéguez, *Chem. Rev.*, 2008, **108**, 2796–2823; (*d*) S. R. Harutyunyan, T. den Hartog, K. Geurts, A. J. Minnaard and B. L. Feringa, *Chem. Rev.*, 2008, **108**, 2824–2852; (*e*) T. Jerphagnon, M. G. Pizzuti, A. J. Minnaard and B. L. Feringa, *Chem. Soc. Rev.*, 2009, **38**, 1039–1075; (*f*) C. Hawner and A. Alexakis, *Chem. Commun.*, 2010, **46**, 7295–7306; (*g*) R. M. Maksymowicz, P. M. C. Roth and S. P. Fletcher, *Nat. Chem.*, 2012, **4**, 649–654; (*h*) B. Maciá, Formation of Quaternary Stereocentres by Copper-Catalysed Enantioselective Conjugate Addition Reaction, in *Progress in Enantioselective Cu(I)-catalyzed Formation of Stereogenic Centers*, ed. S. R. Harutyunyan, Springer International Publishing, Cham, 2016, pp. 41–98; (*i*) P. Ortiz, F. Lanza and S. R. Harutyunyan, 1,2-Versus 1,4-Asymmetric Addition of Grignard Reagents to Carbonyl Compounds, in *Progress in Enantioselective Cu(I)-catalyzed Formation of Stereogenic Centers*, ed. S. R. Harutyunyan, Springer International Publishing, Cham, 2016, pp. 99–134; (*j*) A. V. Brethomé, R. S. Paton and S. P. Fletcher, *ACS Catal.*, 2019, **9**, 7179–7187; (*k*) Y. Guo and S. R. Harutyunyan, *Beilstein J. Org. Chem.*, 2020, **16**, 1006.

4 (*a*) Y. Takaya, M. Ogasawara and T. Hayashi, *J. Am. Chem. Soc.*, 1998, **120**, 5579–5580; (*b*) T. Hayashi, T. Senda and M. Ogasawara, *J. Am. Chem. Soc.*, 2000, **122**, 10716–10717; (*c*) P. Mauleón and J. C. Carretero, *Chem. Commun.*, 2005, 4961–4963; (*d*) J. L. Zigterman, J. C. S. Woo, S. D. Walker, J. S. Tedrow, C. J. Borths, E. E. Bunel and M. M. Faul, *J. Org. Chem.*, 2007, **72**, 8870–8876; (*e*) N. Tokunaga and T. Hayashi, *Adv. Synth. Catal.*, 2007, **349**, 513–516; (*f*) C. Defieber, H. Grutzmacher and E. M. Carreira, *Angew Chem. Int. Ed.*, 2008, **47**, 4482–4502.

5 (*a*) S. Oi, A. Taira, Y. Honma and Y. Inoue, *Org. Lett.*, 2003, **5**, 97–99; (*b*) Y. Nakao, J. Chen, H. Imanaka, T. Hiyama, Y. Ichikawa, W. Duan, R. Shintani and T. Hayashi, *J. Am. Chem. Soc.*, 2007, **29**, 9137–9143; (*c*) R. Shintani, Y. Ichikawa, T. Hayashi, J. Chen, Y. Nakao and T. Hiyama, *Org. Lett.*, 2007, **9**, 4643–4645.

6 (*a*) S. Oi, T. Sato and Y. Inoue, *Tetrahedron Lett.*, 2004, **45**, 5051–5055; (*b*) K. C. Nicolaou, W. Tang, P. Dagneau and R. Faraoni, *Angew Chem. Int. Ed.*, 2005, **44**, 3874–3879.

7 S. J. Mahoney, A. M. Dumas and E. Fillion, *Org. Lett.*, 2009, **11**, 5346–5349.

8 (*a*) M. Pucheault, S. Darses and J.-P. Genêt, *Eur. J. Org Chem.*, 2002, 3552–3557; (*b*) A. Duursma, J.-G. Boiteau, L. Lefort, J. Boogers, A. H. de Vries, J. G. de Vries, A. J. Minnaard and B. L. Feringa, *J. Org. Chem.*, 2004, **69**, 8045–8052; (*c*) T. Cendrineau, J.-P. Genêt and S. Darses, *Org. Lett.*, 2009, **11**, 3486–3489; (*d*) X. Hu, M. Zhuang, Z. Cao and D. Du, *Org. Lett.*, 2009, **11**, 4744–4747.

9 L. Zhang, M. Zhao, M. Pu, Z. Ma, J. Zhou, C. Chen, Y.-D. Wu, Y. R. Chi and J. S. Zhou, *J. Am. Chem. Soc.*, 2022, **144**, 20249–20257.

10 M. Zhao, L. Zhang and J. S. Zhou, *ACS Catal.*, 2024, **14**, 6228–6235.

11 M. Zhao, W. Xu, Y.-D. Wu, X. Yang, J. Wang and J. S. Zhou, *J. Am. Chem. Soc.*, 2024, **146**, 20477–20493.

12 (*a*) M. Yan, Y. Kawamata and P. S. Baran, *Chem. Rev.*, 2017, **117**, 13230–13319; (*b*) Y. Yuan and A. Lei, *Acc. Chem. Res.*, 2019, **52**, 3309–3324; (*c*) P. Xiong and H.-C. Xu, *Acc. Chem. Res.*, 2019, **52**, 3339–3350; (*d*) J. L. Roeckl, D. Pollok, R. Franke and S. R. Waldvogel, *Acc. Chem. Res.*, 2020, **53**, 45–61; (*e*) K.-J. Jiao, Y.-K. Xing, Q.-L. Yang, H. Qiu and T.-S. Mei, *Acc. Chem. Res.*, 2020, **53**, 300–310; (*f*) J. C. Siu, N. Fu and S. Lin, *Acc. Chem. Res.*, 2020, **53**, 547–560; (*g*) C. Zhu, N. W. J. Ang, T. H. Meyer, Y. Qiu and L. Ackermann, *ACS Cent. Sci.*, 2021, **7**, 415–431; (*h*) Y. Yuan, J. Yang and A. Lei, *Chem. Soc. Rev.*, 2021, **50**, 10058–10086.

13 For selected examples of asymmetric electrocatalysis involving anodic oxidation, see: (*a*) D. Minato, Y. Nagasue, Y. Demizu and O. Onomura, *Angew. Chem., Int. Ed.*, 2008, **47**, 9458–9461; (*b*) K. L. Jensen, P. T. Franke, L. T. Nielsen, K. Daasbjerg and K. A. Jørgensen, *Angew. Chem., Int. Ed.*, 2010, **49**, 129–133; (*c*) N. Fu, L. Song, J. Liu, Y. Shen, J. C. Siu and S. Lin, *J. Am. Chem. Soc.*, 2019, **141**, 14480–14485; (*d*) Q. Zhang, X. Chang and C. Guo, *Angew. Chem., Int. Ed.*, 2019, **58**, 6999–7003; (*e*) X. Huang, Q. Zhang, J. Lin, K. Harms and E. Meggers, *Nat. Catal.*, 2019, **2**, 34–40; (*f*) X. Chang, Q. Zhang and C. Guo, *Angew. Chem., Int. Ed.*, 2020, **132**, 12712–12722; (*g*) U. Dhawa, C. Tian, T. Wdowik, J. C. A. Oliveira, J. Hao and L. Ackermann, *Angew. Chem., Int. Ed.*, 2020, **59**, 13451–13457; (*h*) X. Chang, J. Zhang, Q. Zhang and C. Guo, *Angew. Chem., Int. Ed.*, 2020, **59**, 18500–18504; (*i*) L. Li, Y. Li, N. Fu, L. Zhang and S. Luo, *Angew. Chem., Int. Ed.*, 2020, **59**, 14347–14351; (*j*) Z.-H. Wang, P.-S. Gao, X. Wang, J.-Q. Gao, X.-T. Xu, Z. He, C. Ma and T.-S. Mei, *J. Am. Chem. Soc.*, 2021, **143**, 15599–15605; (*k*) K. Liang, Q. Zhang and C. Guo, *Sci. Adv.*, 2022, **8**, eadd7134; (*l*) Q. Zhang, K. Liang and C. Guo, *Angew. Chem., Int. Ed.*, 2022, **61**, e202210632; (*m*) P. Xiong, M. Hemming, S. I. Ivlev and E. Meggers, *J. Am. Chem. Soc.*, 2022, **144**, 6964–6971; (*n*) K. Liang, Q. Zhang and C. Guo, *Nat. Synth.*, 2023, **2**, 1184–1193; (*o*) D. Mazzarella, C. Qi, M. Vanzella, A. Saetorel, G. Pelosi and L. Dell'Amico, *Angew. Chem., Int. Ed.*, 2024, **63**, e202401361; (*p*) J. Zhang, W. Zhu, Z. Chen, Q. Zhang and C. Guo, *J. Am. Chem. Soc.*, 2024, **146**, 1522–1531.

14 T. J. DeLano and S. E. Reisman, *ACS Catal.*, 2019, **9**, 6751–6754.

15 D. Liu, Z.-R. Liu, Z.-H. Wang, C. Ma, S. Herbert, H. Schirok and T.-S. Mei, *Nat. Commun.*, 2022, **13**, 7318.

16 X. Hu, I. Cheng-Sánchez, S. Cuesta-Galisteo and C. Nevado, *J. Am. Chem. Soc.*, 2023, **145**, 6270–6279.

17 Y.-Z. Wang, Z.-H. Wang, I. L. Eshel, B. Sun, D. Liu, Y.-C. Gu, A. Milo and T.-S. Mei, *Nat. Commun.*, 2023, **14**, 2322.

18 Y. Gao, D. E. Hill, W. Hao, B. J. McNicholas, J. C. Vantourout, R. G. Hadt, S. E. Reisman, D. G. Blackmond and P. S. Baran, *J. Am. Chem. Soc.*, 2021, **143**, 9478–9488.

19 H. Qiu, B. Shuai, Y.-Z. Wang, D. Liu, Y.-G. Chen, P.-S. Gao, H.-X. Ma, S. Chen and T.-S. Mei, *J. Am. Chem. Soc.*, 2020, **142**, 9872–9878.

20 Z. Ye, W. Ma, X. Zhang, H. Liu and F. Zhang, *Adv. Sci.*, 2024, 2405926.

21 For selected examples of electrochemical difunctionalisation of alkenes, see: (*a*) G. S. Sauer and S. Lin, *ACS Catal.*, 2018, **8**, 5175–5187; (*b*) C.-Y. Cai and H.-C. Xu, *Nat. Commun.*, 2018, **9**, 3551; (*c*) P. Xiong, H. Long, J. Song, Y. Wang, J.-F. Li and H.-C. Xu, *J. Am. Chem. Soc.*, 2018, **140**, 16387–16391; (*d*) P. Xiong, H. Long and H.-C. Xu, *Asian J. Org. Chem.*, 2019, **8**, 658–660; (*e*) N. Fu, G. S. Sauer, A. Saha, A. Loo and S. Lin, *Science*, 2017, **357**, 575–579; (*f*) S. Fu, G. S. Sauer and S. Lin, *J. Am. Chem. Soc.*, 2017, **139**, 15548–15553; (*g*) L. Zhang, G. Zhang, P. Wang, Y. Li and A. Lei, *Org. Lett.*, 2018, **20**, 7396–7399; (*h*) K.-Y. Ye, G. Pombar, N. Fu, G. S. Sauer, I. Keresztes and S. Lin, *J. Am. Chem. Soc.*, 2018, **140**, 2438–2441; (*i*) Z.-J. Wu, S.-R. Li and H.-C. Xu, *Angew. Chem., Int. Ed.*, 2018, **57**, 14070–14074; (*j*) J. C. Siu, J. B. Parry and S. Lin, *J. Am. Chem. Soc.*, 2019, **141**, 2825–2831; (*k*) N. Fu, Y. Shen, A. R. Allen, L. Song, A. Ozaki and S. Lin, *ACS Catal.*, 2019, **9**, 746–754; (*l*) M.-J. Luo, B. Liu, Y. Li, M. Hu and J.-H. Li, *Adv. Synth. Catal.*, 2019, **361**, 1538–1542; (*m*) K. Liang, Q. Zhang and C. Guo, *Sci. Adv.*, 2022, **8**, eadd7134.

22 For selected examples on cyclic voltammetric analysis for $Ni^{II}(bpy)X_2$, see: (*a*) Y. H. Budnikova, J. Perichon,

D. G. Yakhvarov, Y. M. Kargin and O. G. Sinyashin, *J. Organomet. Chem.*, 2001, **630**, 185–192; (*b*) D. G. Yakhvarov, E. G. Samieva, D. I. Tazeev and Y. G. Budnikova, *Russ. Chem. Bull.*, 2002, **51**, 796–804; (*c*) A. Klein, Y. H. Budnikova and O. G. Sinyashin, *J. Organomet. Chem.*, 2007, **692**, 3156–3166; (*d*) K. Urgin, R. Barhdadi, S. Condon, E. Leonel, M. Pipelier and V. Blot, *Electrochim. Acta*, 2010, **55**, 4495–4500.

23 For selected examples, see: (*a*) D. E. Frantz, D. A. Singleton and J. P. Snyder, *J. Am. Chem. Soc.*, 1997, **119**, 3383–3384; (*b*) D. E. Frantz and D. A. Singleton, *J. Am. Chem. Soc.*, 2000, **122**, 3288–3295; (*c*) M. J. Vetticatt and D. A. Singleton, *Org. Lett.*, 2012, **14**, 2370–2373; (*d*) S. Xiang and M. P. Mayer, *J. Am. Chem. Soc.*, 2014, **136**, 5832–5835; (*e*) S. Somprasong, M. Castiñeira Reis and S. R. Harutyunyan, *Angew. Chem., Int. Ed.*, 2023, **62**, e2022173; (*f*) S. Somprasong, M. Castiñeira Reis and S. R. Harutyunyan, *ACS Catal.*, 2024, **14**, 13030–13039.

24 H. J. A. Dale, A. G. Leach and G. C. Lloyd-Jones, *J. Am. Chem. Soc.*, 2021, **143**, 21079–21099.

25 D. A. Singleton and A. A. Thomas, *J. Am. Chem. Soc.*, 1995, **117**, 9357–9758.