JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Article

pubs.acs.org/JACS

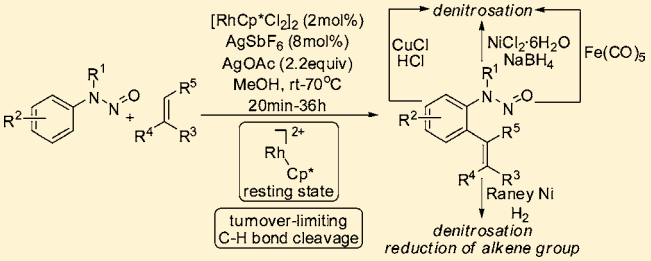
Rhodium(III)-Catalyzed *N*-Nitroso-Directed C−H Olefination of Arenes. High-Yield, Versatile Coupling under Mild Conditions

Baoqing Liu, Yang Fan, Yang Gao, Chao Sun, Cheng Xu, and Jin Zhu*

Department of Polymer Science and Engineering, School of Chemistry and Chemical Engineering, State Key Laboratory of Coordination Chemistry, Nanjing National Laboratory of Microstructures, Nanjing University, Nanjing 210093, China

Supporting Information

ABSTRACT: *N*-Nitroso compounds are a versatile class of organic structures that allow expedient access to a diversity of synthetically useful architectures through demonstrated reactivities. We report herein the development of a Rh(III)-catalyzed *N*-nitroso-directed methodology for the *ortho*-olefination of arenes. The heightened reactivity endowed by the *N*-nitroso group translates to mild reaction conditions, high reaction yields, and synthetic compatibility of otherwise elusive substrates (e.g., an unactivated olefin, 1-octene). Comprehensive mechanistic studies on the electronic effect, deuterium exchange, kinetic isotope effect, kinetic profile, and numerous Rh(III) complexes have established $[RhCp^*]^{2+}$ as the catalyst resting state, electrophilic C−H activation as the turnover-limiting step, and a five-membered rhodacycle as a catalytically competent intermediate. The ability to elaborate the *N*-nitroso moiety to an amine functionality provides a seminal example of the innumerable synthetic possibilities offered by this transformable directing group.



INTRODUCTION

Catalytic C−H functionalization has emerged as a valued atom- and step-economical strategy for the elaboration of organic molecules.[1] In particular, transition-metal-based systems have been the key driver of synthetic tool development by virtue of their diversified reaction manifolds.[2,3] In this regard, the directing group approach is uniquely powerful for site-selective C−H activation through docking-imparted high effective molarity and therefore enables the kinetic bias-driven achievement of a desired reaction course.[3] An illustrative example that showcases the synthetic utility of such a regiocontrolled approach is C−H olefination of arenes (oxidative Heck coupling or the Fujiwara−Moritani reaction).[4] Indeed, many directing groups (e.g., amide,[5] pyrazole,[6] imine,[7] ketone,[8] carboxylic acid,[9] and ester[10]) have been identified as effective handles for the proximal site coupling of C−C bonds. However, in spite of tremendous progress, further development is in demand because essentially all the systems reported thus far are synthetically restrictive, as, for example, manifested in the following aspects: harsh reaction conditions (e.g., high reaction temperature and highly acidic medium), challenge with respect to the removal/transformation of undesired external directing group, and limited substrate scope.

In search for a directing group system with desired synthetic features, we have turned our attention to the *N*-nitroso moiety. *N*-Nitroso compounds are a versatile class of organic structures that allow expedient access to a diversity of synthetically useful architectures through demonstrated reactivities.[11] For example, *N*-nitrosamines could be reduced to hydrazines and amines,[11] derivatized on α-carbons (electrophilic substitution through stabilized α-carbanion intermediates, an umpolung reactivity compared to the parent amines),[11] converted to diazonium salts (extremely useful reagents for further functionalization through Sandmeyer reactions, Schiemann reaction, hydroxylation reaction, etc.),[12] and rearranged to *C*-nitroso compounds (Fischer−Hepp rearrangement).[11] With an electron-withdrawing group tethered (e.g., *N*-nitrosamides, *N*-nitrosoureas, *N*-nitrosoguanidines, and *N*-nitrosocarbamates),[13] distinct chemical transformations are also possible (e.g., conversion of *N*-nitrosamides to esters[14]). Importantly, *N*-nitrosamines are known to interact with metal centers in a variety of coordination modes (all involving the nitroso group because of localized high-lying filled orbitals), including η^1-*O*-binding, η^1-*N*-binding, bridged μ-η^1:η^1-*N*,*O*-binding, and cyclometalated η^2-*N*,*C*-binding.[15] These diversified interaction patterns should in principle allow regulation of chemical reactivities of metalated intermediates in the target catalytic cycle and therefore achievement of desired catalytic efficiency in the respective transformation.[3b] Herein, we report on the development of an *N*-nitroso directing group method for Rh(III)-catalyzed C−H olefination of arenes. The utility of the *N*-nitroso group has enabled the achievement of heightened reactivity, which translates to mild conditions, high yields, and synthetic versatility (broad substrate scope). Comprehensive mechanistic studies have allowed the set of elementary steps to be elucidated, thus providing key insights into this *N*-nitroso-derived handy yet powerful synthetic system. In addition, as an

Received: October 12, 2012
Published: December 11, 2012

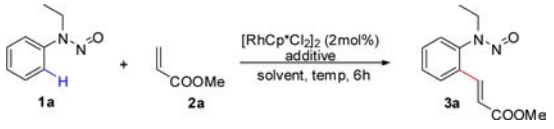
   dx.doi.org/10.1021/ja3099245 | *J. Am. Chem. Soc.* 2013, 135, 468−473

initial proof of directing group transformation, highly efficient denitrosation has been demonstrated under conditions that allow for either the retention or reduction of installed alkene motif.

RESULTS AND DISCUSSION

Reaction Development. Since anilines represent important structural motifs/synthetic precursors in dye and pharmaceutical industries, *N*-nitrosoanilines were selected for reaction development. In particular, the first set of experiments was aimed at the examination of the reaction between model substrates *N*-ethyl-*N*-nitrosoaniline (**1a**) and methyl acrylate (**2a**) using $[RhCp^*Cl_2]_2$ as the catalyst precursor. A hypothetically viable turnover of the Rh(III)/Rh(I) redox catalytic cycle likely entails the participation of an oxidant (for regeneration of Rh(III)), a base (for assistance in C−H bond cleavage), and a metathesis reagent/chloride abstractor (for enhancement of electrophilicity of Rh(III)). Initial screening of the reaction conditions in the absence of $AgSbF_6$ only led to the low conversion of **1a** (<20%, entries 1−4, Table S1, Supporting Information) and low-yield production of a denitrosated molecule **dn-3a**. With the participation of $AgSbF_6$, the conversion of **1a** became substantially higher (>90%), but still, **dn-3a** was predominantly formed in low yield under most of the evaluated conditions (entries 5−9, Table S1, Supporting Information). Only in one case (entry 10, Table S1, Supporting Information), a nitroso-retained, *ortho*-olefinated molecule **3a** (*E* isomer) was furnished as the major product. Note that, in **1a** and **3a**, as well as in other *N*-nitrosamines, contribution from the polar resonance form of the *N*-nitroso group results in hindered rotation around the N−N bond and therefore potential existence of *syn* (defined here when the *N*-alkyl group is *cis* to the *N*-nitroso oxygen atom) and *anti* isomers (Scheme S1, Supporting Information).[16] The relative ratio of the two isomers is thermodynamically dictated exclusively by their inherent stabilities. The equilibrium of two isomers will not affect the synthetic utility of the olefination reaction reported herein because typically the products after subsequent *N*-nitroso transformations are the authentic synthetic targets. Successful olefination of **1a** with **2a** provides the basis for further optimization of the reaction conditions (Table 1). The reaction proceeds optimally in the presence of both $AgSbF_6$ and AgOAc. Thus, whereas DMF, MeCN, and toluene are all suitable solvents to effect the desired transformation (entries 3−5, Table 1), a room temperature (rt) reaction in MeOH (entries 6−8, Table 1) allows the achievement of a 92% isolated yield for **3a**. Note that the reaction time should be stringently controlled because of the susceptibility of the product toward further *ortho*-olefination. A control experiment indicates that no olefination could be observed for *N*-ethylaniline under otherwise identical reaction conditions, highlighting the importance of the *N*-nitroso group.

Table 1. Reaction Development[a,b]

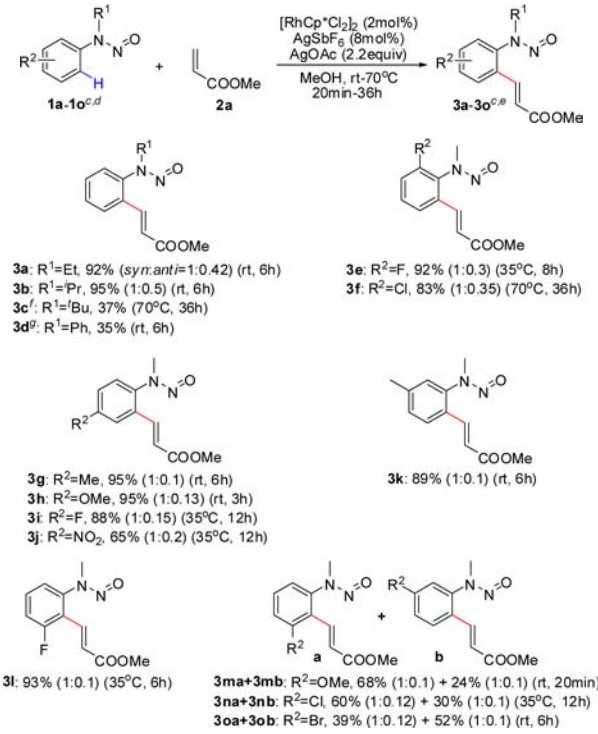


entry	additive	solvent	temp	yield
1	$Cu(OAc)_2{\cdot}H_2O$	MeOH	60 °C	68%
2	$AgSbF_6/Cu(OAc)_2{\cdot}H_2O$	MeOH	60 °C	78%
3	$AgSbF_6$/AgOAc	DMF	100 °C	83%
4	$AgSbF_6$/AgOAc	MeCN	60 °C	84%
5	$AgSbF_6$/AgOAc	toluene	80 °C	68%
6	$AgSbF_6$/AgOAc	MeOH	60 °C	86%
7	$AgSbF_6$/AgOAc	MeOH	30 °C	88%
8	$AgSbF_6$/AgOAc	MeOH	rt	92%

[a]Conditions: *N*-nitrosamine (1 equiv), olefin (1.5 equiv), all the additives (2.2 equiv) except $AgSbF_6$ (8 mol%). [b]Isolated yields.

Synthetic Scope. With a viable olefination reaction in hand, we next examined the scope of *N*-nitrosoanilines by employing **2a** as the coupling partner (Table 2). A wide range of *N*-nitrosoaniline derivatives are compatible with the protocol, furnishing the majority of products (*E* isomers) in high yields under mild synthetic conditions (rt to 35 °C). Regardless of the electronic nature of the aromatic substituent, olefination proceeds selectively by *N*-nitroso-directed *ortho* reactivity. Thus, the reaction works very well for *N*-methyl-*N*-nitrosoanilines possessing either electron-donating methyl and methoxy groups (**1g**, **1k**, **1h**, and **1m**) or electron-withdrawing halogen atoms (**1e**, **1i**, **1l**, **1f**, **1n**, and **1o**). The tolerance of the bromo substituent by our synthetic scheme (**1o**) diverges from the reaction involving a Pd(II)/Pd(0) catalytic cycle,[17] thus offering a valuable handle for further synthetic elaborations. The nitro group is also tolerated (**1j**), albeit affording the product in a reduced yield. Substrates bearing *m*-methyl and *m*-

Table 2. *N*-Nitrosamine Scope[a,b]



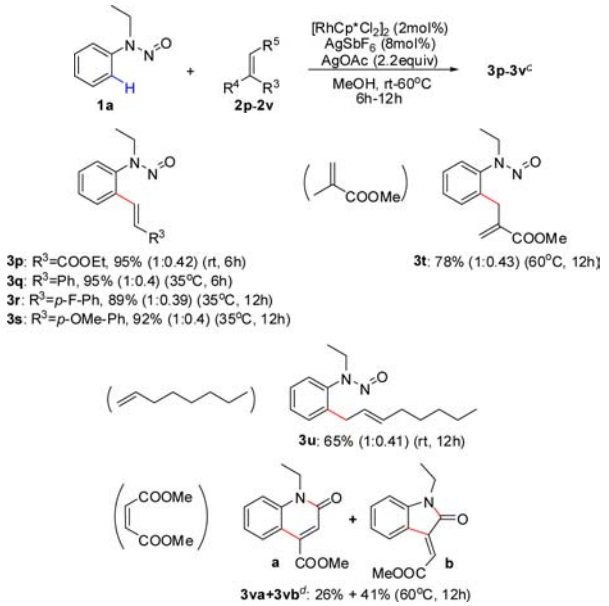
[a]Conditions: *N*-nitrosamine (1 equiv), olefin (1.5 equiv). [b]Isolated yields. [c]The *syn* and *anti* notations refer to the isomers resulting from the restricted rotation around the *N*-nitroso N−N bond; *syn*: when the *N*-alkyl group (except for **3d**, *N*-phenyl group) is *cis* to the *N*-nitroso oxygen atom. [d]For *N*-nitrosamine substrates, all exist predominantly in the *syn* form with three notable exceptions (**1b**, *syn*/*anti* = 1:0.57; **1c**, *anti*; **1f**, *syn*/*anti* = 1:0.1). [e]All the products are in the *E* form with respect to the alkene group except **3g** (*E*/*Z* = 1:0.08). All the *syn*/*anti* ratios in the products are listed in the table. [f]**3c** is in the *anti* form. [g]**3d** is in the *syn* form.

dx.doi.org/10.1021/ja3099245 | J. Am. Chem. Soc. 2013, 135, 468−473

fluoro substituents provide the respective products in a regioselective manner (**1k** and **1f**). Regiocontrolled olefination is not observed for *m*-methoxy-, *m*-chloro-, and *m*-bromo-derivatized substrates (**1m**, **1n**, and **1o**). Complications in olefination patterns for *meta*-substituted *N*-nitrosoanilines reflect a subtle interplay between electronic (e.g., as a secondary chelation site[18]) and steric effects exerted by the *meta*-substituents. An array of *N*-alkyl substituents is tolerated, with the bulkiness of the substituent dictating the reactivity. Thus, substrates containing ethyl and isopropyl groups (**1a** and **1b**) react equally well, but a *tert*-butyl group (**1c**) significantly retards the reaction. The product yield is also low for *N*-phenyl-*N*-nitrosoaniline (**1d**), due to competitive multiple-olefination side reactions.

We next proceeded to establish the scope of the olefin coupling partner by reacting with **1a** (Table 3). A variety of

Table 3. Olefin Scope[a,b]



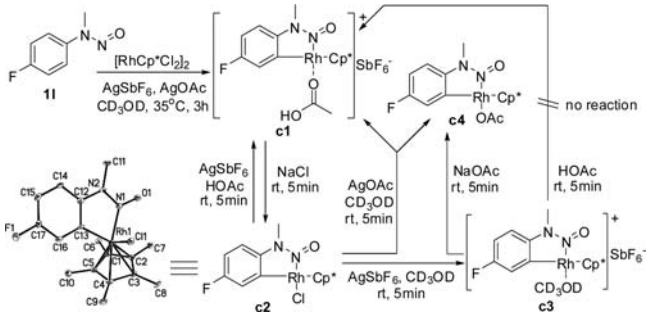
[a]Conditions: *N*-nitrosamine (1 equiv), olefin (1.5 equiv). [b]Isolated yields. [c]The products are in the *E* form with respect to the alkene group for **3p**−**3s** and **3u**. [d]**3vb** is assigned as the *E* isomer based on the nuclear Overhauser effect spectroscopy experiment.

monosubstituted olefins, ethyl acrylate (**2p**), styrene (**2q**), *p*-*F*-styrene (**2r**), and *p*-methoxystyrene (**2s**) are suitable substrates for the reaction. 1,1-Disubstitution could also be tolerated, and with the engagement of methyl methacrylate (**2t**), a product bearing an alkene group not in conjugation with the aromatic ring is generated. Most significantly, an unactivated olefin, for example, 1-octene (**2u**), could be employed in the transformation to afford a nonconjugated product. β-Hydride elimination from the benzylic hydrogen atoms is apparently disfavored for the reactions involving **2t** and **2u** owing to the restriction of conformation. Therefore, our synthetic protocol enables the construction of distinct olefinated products that could not be accessed by the conventional Heck-type methods.[19] For a 1,2-disubstituted olefin, dimethyl maleate (**2v**), an additional amide bond is formed, allowing the generation of two ring-closed isomeric products in good combined yield.

Electronic Effect, Deuterium Exchange, and Kinetic Isotope Effect. The broad substrate scope offered by our *N*-nitroso-based synthetic method has prompted us to gain a detailed understanding of the reaction mechanism. The role of the electronic effect was probed by performing a competition olefination experiment in an equimolar mixture of electronically different *N*-nitrosoaniline derivatives, **1m** and **1l** (eq S1, Supporting Information). The electron-rich **1m** is more reactive, suggesting that electrophilic aromatic substitution (EAS), rather than concerted metalation−deprotonation (CMD), is responsible for C−H activation.[2g] We next performed deuterium labeling experiments to further investigate the catalytic C−H activation and subsequent steps. Through studies on various substrates (**1a**, **1g**, **1h**, **1m**, **1l**, and **1i**) (eqs S2−S16, Supporting Information), three scenarios apparently emerged depending on the electronic property of the aromatic substituent: irreversible *ortho*-rhodation (electron-withdrawing, **1i**); quasi-irreversible *ortho*-rhodation (**1a**); and reversible *ortho*-rhodation followed by irreversible migratory insertion (electron-donating, **1m**). Thus, in the absence of olefins, although virtually no deuterium was incorporated into **1i** under either catalytic (eq S11, Supporting Information) or stoichiometric (eq S12, Supporting Information) conditions, deuterium could be apparently identified in **1a** through prolonged catalysis (eq S6, Supporting Information) or under stoichiometric conditions (eq S13, Supporting Information). For **1m**, deuterium labeling could be observed only in the absence of **2a** (eqs S9 and S15, Supporting Information); in the presence of such a coupling partner, no deuterium incorporation in either the products or the remaining **1m** was discernible (eq S16, Supporting Information). The intermolecular kinetic isotope effect (KIE) was measured to be 4.5 (eq S17, Supporting Information), consistent with the turnover-limiting C−H activation step.[20]

Rh(III) Complexes and Catalytically Competent Rhodacycle. We further sought to probe the nature of the C−H activation process by the isolation of a catalytically competent rhodacycle. Thus, **1i** reacts stoichiometically with the Rh(III) catalytic species to form a complex **c1** (with weakly coordinated HOAc, Scheme 1 and eq S18, Supporting

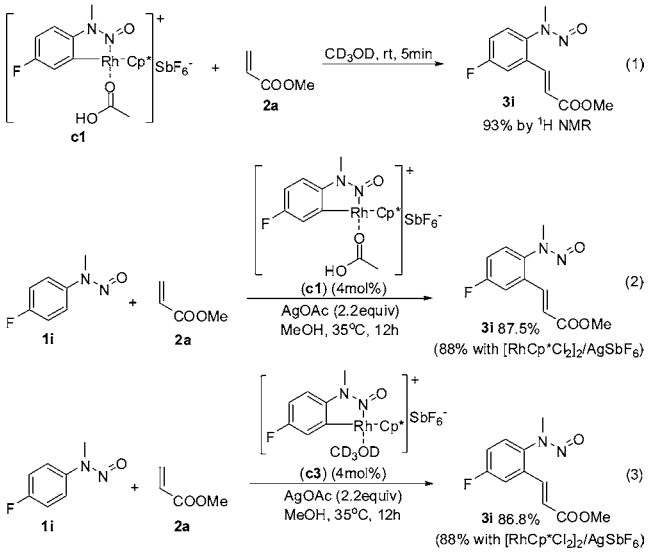
Scheme 1. Synthesis and Interconversions of Rh(III) Complexes



Information). The five-membered rhodacycle structure of **c1** was unambiguously determined by single-crystal analysis of a chloride complex (**c2**) (Scheme 1, eq S19, and Figure S19-2, Supporting Information). Complex **c2** could be facilely converted back to complex **c1** by the abstraction of chloride (Scheme 1 and eq S20, Supporting Information). In addition, a variety of transformations are possible starting from **c2** (Scheme 1 and eqs S21−24, Supporting Information), leading to **c3** (with weakly coordinated CD_3OD) and **c4** (with strongly

dx.doi.org/10.1021/ja3099245 | J. Am. Chem. Soc. 2013, 135, 468−473

coordinated OAc^-). Among those complexes, **c1** could react stoichiometrically with **2a** at rt to afford **3a** in high yield within 5 min (eq 1). This is substantially faster than the **c1** formation



reaction, which provides further support for the proposal of C−H activation as the turnover-limiting step. **c1** and **c3** are also capable of effecting the catalytic olefinatio with an approximately identical efficiency (eqs 2, 3, and S25, Supporting Information), suggesting the intermediacy of these complexes (with or without weakly coordinated neutral species) in the catalytic cycle.

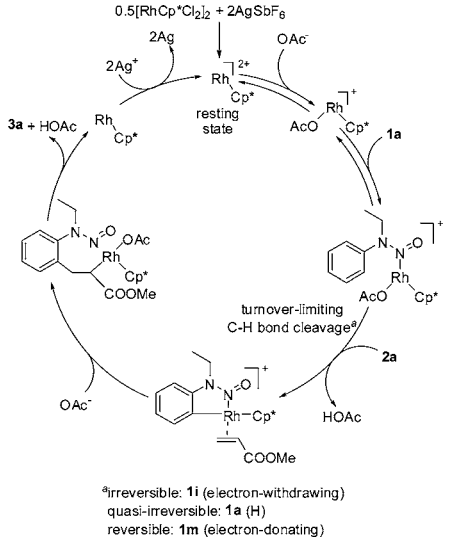
Kinetic Profile and Catalyst Resting State. Kinetic studies were then performed for the establishment of a plausible set of elementary steps in the catalytic cycle. The reaction is first order in $[RhCp^*Cl_2]_2$, first order in $AgSbF_6$, zero order in AgOAc, first order in the *N*-nitrosoaniline derivative (**1a**), and exhibits a saturation kinetics for olefin (**2a**) (Figures S27-1 to S31-2, Supporting Information, and eq 4):

$$\text{rate} = k\cdot[[RhCp^*Cl_2]_2]^1\cdot[AgSbF_6]^1\cdot[AgOAc]^0\cdot[\mathbf{1a}]^1\cdot[\mathbf{2a}]^s \quad (4)$$

Importantly, during the kinetic studies, a high-concentration, persistent Rh(III)-based species (δ ~1.688 for Cp*, Figure S32, Supporting Information; the exact chemical shift is dependent on ionic strength and therefore slightly varied during a catalytic run, Figures S32 and S33, Supporting Information) was identified through ^{1}H NMR in the catalytic system. In accord with the kinetic profile, and through an independent synthesis of $RhCp^*(OAc)_2$ (**c5**)[21] and study of its ligand dissociation behavior in CD_3OD (δ ~1.668 for Cp* of $[RhCp^*]^{2+}$ without coordinated OAc^- but shifted to ~1.537 for Cp* of $[RhCp^*]^{2+}$ with coordinated OAc^-), the catalyst resting state is assigned as $[RhCp^*]^{2+}$ (with or without weakly coordinated neutral species but without coordinated OAc^-) (Figures S34 and S35, eq S26, and Tables S2 and S3, Supporting Information). The assignment is further supported by titration studies of $[RhCp^*Cl_2]_2/AgSbF_6$ with AgOAc (Figure S36, Supporting Information) and NaOAc (Figure S37, Supporting Information).

Proposed Catalytic Mechanism. Taken together, the above results point toward the following reaction sequence in the catalytic cycle (Scheme 2): generation of catalyst resting state $[RhCp^*]^{2+}$ by $[RhCp^*Cl_2]_2$ and $AgSbF_6$, reversible

Scheme 2. Proposed Catalytic Cycle

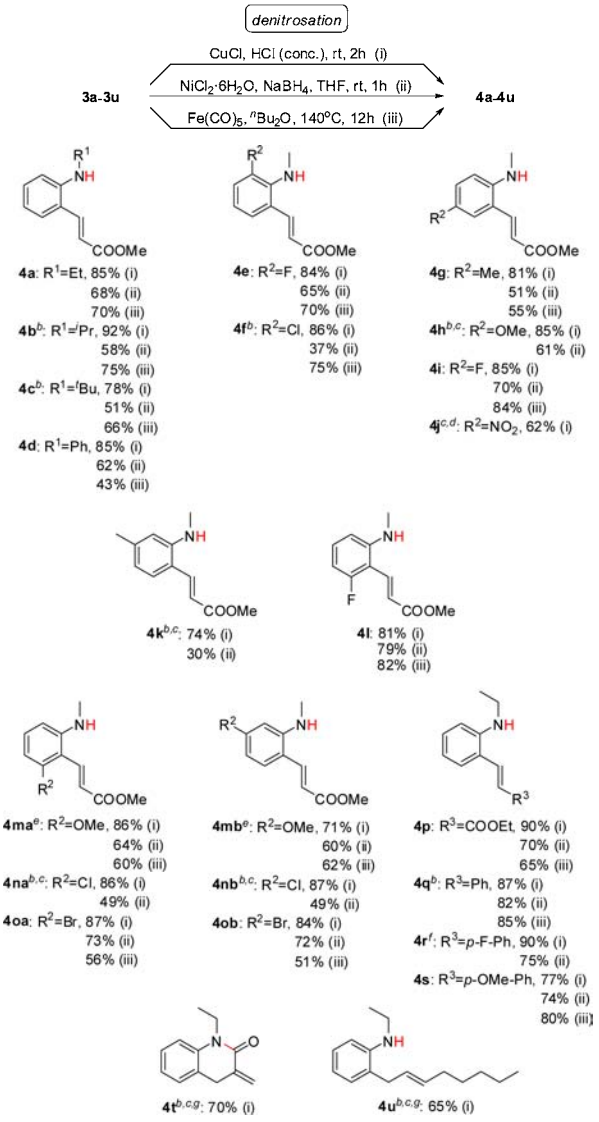


coordination of OAc^- (zero-order kinetics on AgOAc because of the essentially constant supply of a fixed concentration of OAc^- by the precipitate) and *N*-nitrosoaniline derivative, turnover-limiting electrophilic *ortho*-rhodation (C−H bond cleavage assisted by OAc^- and olefin), migratory insertion of olefin, β-hydride elimination and reductive elimination to release olefinated product and Rh(I), and reoxidation of Rh(I) to Rh(III) by Ag^+ to close the catalytic cycle. The slower catalytic reaction rate in the presence of excess NaOAc is consistent with the intermediacy of $[RhCp^*(OAc)]^+$ (with or without weakly coordinated neutral species), rather than $RhCp^*(OAc)_2$, in the catalytic cycle. The *ortho*-rhodation step is facilitated by olefin (positive-order kinetics before saturation) by virtue of its role in the displacement of HOAc. The saturation kinetics for olefin could be rationalized by either the thermodynamically uphill formation of a low-concentration metalated intermediate right prior to the turnover-limiting step and/or the accumulation of an off-cycle olefin-coordinated (e.g., with catalyst resting state) species reservoir.

Transformation of Directing Group. As a further check of the synthetic versatility associated with our protocol, we next examined the amenability of the *N*-nitroso group to further elaborations. Indeed, the *N*-nitroso group could be transformed to an amine group highly efficiently under either mild CuCl/HCl,[22] $NiCl_2\cdot 6H_2O/NaBH_4$,[23] $Fe(CO)_5$,[24] or more forced Raney Ni/H_2[25] conditions (Tables 4 and 5). The CuCl/HCl conditions privilege denitrosation as the exclusive mode of reaction without affecting alkene and other functionalities, including the nitro group (Table 4). Both $NiCl_2\cdot 6H_2O/NaBH_4$ and $Fe(CO)_5$ could in general be used to supplant CuCl/HCl (Table 4), thus offering reaction condition versatility for varied synthetic contexts. The Raney Ni/H_2 conditions enable the simultaneous reduction of both *N*-nitroso and alkene groups (Table 5). Thus, *ortho*-alkylation is the ultimate observed pattern of reaction for ester-free olefinated substrates. For ester-containing substrates, further ring closure from intramolecular secondary coupling occurs if sterically allowed. Halogen atoms could be retained or removed depending on the substitution feature.

dx.doi.org/10.1021/ja3099245 | J. Am. Chem. Soc. 2013, 135, 468−473

Table 4. Denitrosation of Olefinated *N*-Nitrosamines[a]

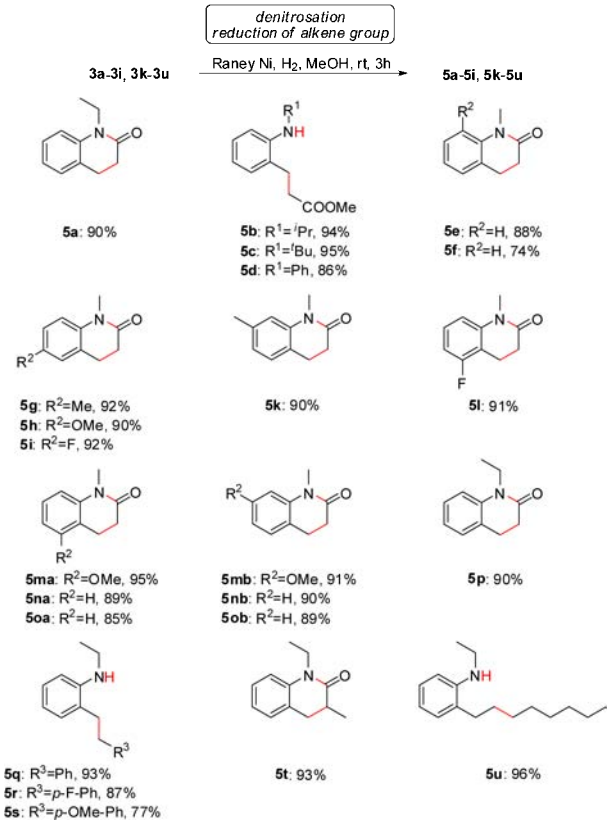


[a]Isolated yields. [b]A mixed solvent of THF/MeOH (10:1) instead of pure THF is used for condition ii. [c]Not efficient for the formation of the depicted target product under condition iii. [d]Not efficient for the formation of the depicted target product under condition ii. [e]Reaction time: 5−10 min. [f]Simultaneous removal of fluorine under condition iii, affording **4riii** (65%). [g]Simultaneous reduction of alkene group under condition ii, affording **4tii** (80%) and **4uii** (55%), respectively.

CONCLUSION

In summary, a mild, high-yield, and versatile Rh(III)-catalyzed *N*-nitroso-directed aryl *ortho*-olefination method has been developed. Notably, the unique coordination characteristics of the *N*-nitroso group have enabled the synthetic utility of otherwise elusive substrates (e.g., an unactivated olefin, 1-octene). Comprehensive mechanistic studies support a reaction pathway involving $[RhCp^*]^{2+}$ as the catalyst resting state and electrophilic C−H activation as the turnover-limiting step. A catalytically competent five-membered rhodacycle has been structurally characterized, revealing a key intermediate in the catalytic cycle. The ability to elaborate the *N*-nitroso moiety to an amine functionality (with aniline derivative as the product) provides a seminal example of the innumerable synthetic possibilities offered by this transformable directing group.

Table 5. Simultaneous Denitrosation and Alkene Reduction of Olefinated *N*-Nitrosamines[a]



[a]Isolated yields.

ASSOCIATED CONTENT

Supporting Information

General methods and reaction development; synthesis and characterization of *N*-nitrosamine substrates, olefination products, denitrosation products, and Rh(III) complexes; competition, deuterium exchange, kinetic isotope effect, kinetic, and resting state assigment experiments; reversibility studies; NMR spectra for all compounds; ORTEP drawing of **c2**; and crystallographic data as a CIF file. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

jinz@nju.edu.cn

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

J.Z. gratefully acknowledges support from the National Natural Science Foundation of China (21274058) and the National Basic Research Program of China (2013CB922101, 2011CB935801)

REFERENCES

(1) (a) White, M. C. *Science* **2012**, *335*, 807−809. (b) Brückl, T.; Baxter, R. D.; Ishihara, Y.; Baran, P. S. *Acc. Chem. Res.* **2012**, *45*, 826−839.

(2) (a) Hickman, A. J.; Sanford, M. S. *Nature* **2012**, *484*, 177−185. (b) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890−931. (c) Labinger, J. A.;

dx.doi.org/10.1021/ja3099245 | *J. Am. Chem. Soc.* 2013, 135, 468−473

Bercaw, J. E. *Nature* **2002**, *417*, 507−514. (d) Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417−424. (e) Hartwig, J. F. *Nature* **2008**, *455*, 314−322. (f) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094−5115. (g) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315−1345. (h) Wencel-Delord, J.; Dröge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740−4761.

(3) (a) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879−5918. (b) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788−802. (c) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814−825. (d) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936−946. (e) Campbell, A. N.; Stahl, S. S. *Acc. Chem. Res.* **2012**, *45*, 851−863. (f) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624−655.

(4) (a) Fujiwara, Y.; Moritani, I.; Danno, S.; Asano, R.; Teranishi, S. *J. Am. Chem. Soc.* **1969**, *91*, 7166−7169. (b) Fujiwara, Y.; Moritani, I.; Matsuda, M. *Tetrahedron* **1968**, *24*, 4819−4824. (c) Moritani, I.; Fujiwara, Y. *Tetrahedron Lett.* **1967**, *8*, 1119−1122.

(5) (a) Rakshit, S.; Grohmann, C.; Besset, T.; Glorius, F. *J. Am. Chem. Soc.* **2011**, *133*, 2350−2353. (b) Patureau, F. W.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 9982−9983. (c) Boele, M. D. K.; van Strijdonck, G. P. F.; de Vries, A. H. M.; Kamer, P. C. J.; de Vries, J. G.; can Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2002**, *124*, 1586−1587.

(6) Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 7094−7099.

(7) Tsai, A. S.; Brasse, M.; Bergman, R. G.; Ellman, J. A. *Org. Lett.* **2011**, *13*, 540−542.

(8) Patureau, F. W.; Besset, T.; Glorius, F. *Angew. Chem., Int. Ed.* **2011**, *50*, 1064−1067.

(9) (a) Wang, D.-H.; Engle, K. M.; Shi, B.-F.; Yu, J.-Q. *Science* **2010**, *327*, 315−319. (b) Shi, B.-F.; Zhang, Y.-H.; Lam, J. K.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 460−461. (c) Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2010**, *49*, 6169−6173.

(10) Park, S. H.; Kim, J. Y.; Chang, S. *Org. Lett.* **2011**, *13*, 2372−2375.

(11) Challis, B. C.; Challis, J. A. *N*-nitrosamines and *N*-nitrosoimines. In *The Chemistry of Amino, Nitroso and Nitro Compounds and Their Derivatives*; Patai, S., Ed.; John Wiley & Sons: Chichester, U.K., 1982; pp 1151−1223.

(12) Klein, D. *Organic Chemistry*; John Wiley & Sons: Hoboken, NJ, 2012.

(13) Wang, P. G.; Xian, M.; Tang, X.; Wu, X.; Wen, Z.; Cai, T.; Janczuk, A. J. *Chem. Rev.* **2002**, *102*, 1091−1134.

(14) (a) Glatzhofer, D. T.; Roy, R. R.; Cossey, K. N. *Org. Lett.* **2002**, *4*, 2349−2352. (b) White, E. H. *J. Am. Chem. Soc.* **1955**, *77*, 6014−6022.

(15) (a) Lee, J.; Chen, L.; West, A. H.; Richter-Addo, G. B. *Chem. Rev.* **2002**, *102*, 1019−1065. (b) Xu, N.; Goodrich, L. E.; Lehnert, N.; Powell, D. R.; Richter-Addo, G. B. *Inorg. Chem.* **2010**, *49*, 4405−4419.

(16) (a) D'Agostino, J. T.; Jaffé, H. H. *J. Am. Chem. Soc.* **1970**, *92*, 5160−5166. (b) D'Agostino, J. T.; Jaffé, H. H. *J. Org. Chem.* **1971**, *36*, 992−995.

(17) Le Bras, J.; Muzart, J. *Chem. Rev.* **2011**, *111*, 1170−1214.

(18) Sonoda, M.; Kakiuchi, F.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 3117−3128.

(19) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009−3066.

(20) Simmons, E. M.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2012**, *51*, 3066−3072.

(21) (a) Li, L.; Brennessel, W. W.; Jones, W. D. *Organometallics* **2009**, *28*, 3492−3500. (b) Boyer, P. M.; Roy, C. P.; Bielski, J. M.; Merola, J. S. *Inorg. Chim. Acta* **1996**, *245*, 7−15.

(22) Jones, E. C. S.; Kenner, J. *J. Chem. Soc.* **1932**, 711−715.

(23) Kano, S.; Tanaka, Y.; Sugino, E.; Shibuya, S.; Hibino, S. *Synthesis* **1980**, 741−742.

(24) Alper, H.; Edward, J. T. *Can. J. Chem.* **1970**, *48*, 1543−1549.

(25) Enders, D.; Hassel, T.; Pieter, R.; Renger, B.; Seebach, D. *Synthesis* **1976**, 548−550.