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Catalytic Synthesis of *n*-Alkyl Arenes through Alkyl Group Cross-Metathesis

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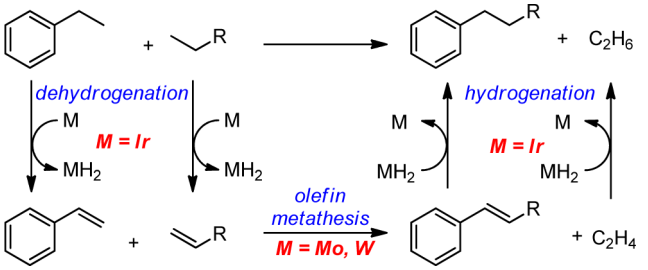
Supporting Information

ABSTRACT: *n*-Alkyl arenes were prepared in a one-pot tandem dehydrogenation/olefin metathesis/hydrogenation sequence directly from alkanes and ethylbenzene. Excellent selectivity was observed when (^{tBu}PCP)IrH$_2$ was paired with tungsten monoaryloxide pyrrolide complexes such as W(NAr)(C_3H_6)(pyr)(OHIPT) (**1a**) [NAr = 2,6-*i*-$Pr_2C_6H_3$; pyr = pyrrolide; OHIPT = 2,6-(2,4,6-*i*-$Pr_3C_6H_2)_2C_6H_3O$]. Complex **1a** was also especially active in *n*-octane self-metathesis, providing the highest product concentrations reported to date. The thermal stability of selected olefin metathesis catalysts allowed elevated temperatures and extended reaction times to be employed.

Selective functionalizations of C−H bonds are highly sought because of the abundance of hydrocarbon feedstocks.[1] *n*-Alkanes would be ideal starting materials in many reactions if C−H bond activation in an alkane were possible. One goal could be the synthesis of *n*-alkyl arenes (e.g., 1-phenyloctane), which are precursors for surfactants with high detersive power at elevated temperatures and low concentrations.[2] The largest group of linear alkylbenzenes, produced on a million ton per year scale for the synthesis of surfactants,[3] are typically branched alkyl arenes (e.g., 2-phenyloctane) generated by Friedel−Crafts alkylation of benzene with olefins.[4] *n*-Alkyl arenes cannot be produced in this fashion, and while the anti-Markovnikov arylation of olefins[5] is a potential catalytic method for their synthesis, a more efficient route would proceed directly from an abundant alkane as a starting material. Dehydroaromatization is one strategy for the synthesis of specific *n*-alkyl arenes from *n*-alkanes in a single step,[6] but this requires a stoichiometric amount of an olefin to serve as a hydrogen acceptor.

An Ir dehydrogenation/hydrogenation catalyst and a W or Mo complex competent for olefin metathesis have been shown to work in tandem to generate a broad distribution of *n*-alkanes from a single *n*-alkane.[7,8] We have been exploring the possibility of what could be called alkyl group cross-metathesis (AGCM) to generate *n*-alkyl arenes from ethylbenzene and an alkane (Scheme 1; only terminal olefins are shown). While ethylbenzene has never been used previously in an alkane metathesis reaction, (PCP)Ir-catalyzed dehydrogenation of ethylbenzene has been reported.[9] In alkane metathesis, the overall distribution of products is influenced by several factors, including the terminal selectivity of the alkane dehydrogenation

Scheme 1. The Alkyl Group Cross-Metathesis Reaction



step[10] and the rate at which intermediate olefins are isomerized, either by Ir complexes[11] or by the products of Mo or W decomposition.[12] Competitive metathesis homocoupling of intermediate olefins could compete with cross-metathesis and further increase the number of products.

Catalyst longevity is another major challenge in the development of a practical alkane metathesis protocol. The high temperatures (at least 125 °C) and multiday reaction times required for alkane metathesis deactivate Mo and W olefin metathesis catalysts more rapidly than Ir pincer complexes. In this work, we found that certain monoaryloxide pyrrolide (MAP) complexes of Mo and W, previously studied in the context of *Z*-selective metathesis reactions,[13−15] are thermally quite stable. In concert with Ir pincer complexes, they provide high total product concentrations in the metathesis of *n*-octane. These MAP complexes are also robust catalysts for AGCM of alkanes and ethylbenzene, as described herein.

A previous screen of Mo and W alkylidene complexes identified several active catalysts for *n*-octane metathesis and established that W complexes provide higher total product concentrations than the analogous Mo species.[16] Unfortunately, the thermal stability of the most active complexes at 150 °C was poor. Therefore, we turned to complexes containing sterically demanding phenoxide ligands, which we hypothesized might improve the stability by discouraging bimolecular decomposition.[17]

The results of an evaluation of olefin metathesis catalysts for the metathesis of *n*-octane are shown in Table 1. The most encouraging results were obtained with complexes that incorporate the 2,6-(2,4,6-*i*-$Pr_3C_6H_2)_2C_6H_3O$ (OHIPT) ligand. The OHIPT-containing compounds **1a**,[13a] **1b**,[14] and W(N-*t*-

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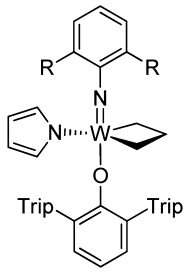
Table 1. Total Product Concentrations Obtained in the Metathesis of *n*-Octane[a]

metathesis catalyst	total product (mM)
W(NAr)(C_3H_6)(pyr)(OHIPT) (**1a**)	3920, 4910[b]
W(NAr′)(C_3H_6)(pyr)(OHIPT) (**1b**)	2400
Mo(NAr)(C_3H_6)(pyr)(OHIPT)	2450
W(NC_6F_5)(CH-*t*-Bu)(Me_2Pyr)(OHMT)	3660, 3750[b]
W(NC_6F_5)(CH-*t*-Bu)(Me_2Pyr)(OHIPT)	~0
W(N-*t*-Bu)(CH-*t*-Bu)(pyr)(OHIPT)	2790
W(O)(CH-*t*-Bu)(OHMT)$_2$	1600
W(NAr)($CHCMe_2Ph$)[$OC(CF_3)_3$]$_2$	2260
W(NAr)($CHCMe_2Ph$)($OSiPh_3$)$_2$	2770, 1420[b]
W(O)(CH-*t*-Bu)(Me_2Pyr)(OHIPT)	~0
W(NAr)(CH-*t*-Bu)(Me_2Pyr)(OHMT)	~0

[a]Conditions: 125 °C, 4 days in J. Young tubes with 16 mM metathesis catalyst, 10 mM (^{tBu}POCOP)Ir(C_2H_4), and 28.8 mM mesitylene (internal standard). See the Supporting Information (SI) for details. Abbreviations: Ar = 2,6-*i*-$Pr_2C_6H_3$; Ar′ = 2,6-$Me_2C_6H_3$; pyr = pyrrolide; Me_2Pyr = 2,5-dimethylpyrrolide; OHMT = 2,6-(2,4,6-$Me_3C_6H_2$)$_2C_6H_3O$); OHIPT = 2,6-(2,4,6-*i*-$Pr_3C_6H_2$)$_2C_6H_3O$. [b]150 °C, 2 days.

Bu)(CH-*t*-Bu)(pyr)(OHIPT)[18] are superior catalysts. W(O)(CH-*t*-Bu)(MePyr)(OHIPT),[19] W(NC_6F_5)(CH-*t*-Bu)(Me_2Pyr)(OHIPT), and W(NAr)(CH-*t*-Bu)(Me_2Pyr)(OHMT) [Me_2Pyr = 2,5-dimethylpyrrolide; OHMT = 2,6-(2,4,6-$Me_3C_6H_2$)$_2C_6H_3O$] are essentially inactive. Surprisingly, W(NC_6F_5)(CH-*t*-Bu)(Me_2Pyr)(OHMT) is an excellent catalyst for the metathesis of *n*-octane at 125 °C, in contrast to W(NC_6F_5)(CH-*t*-Bu)(Me_2Pyr)(OHIPT). We previously found that W and Mo *bisalkoxide* complexes containing the pentafluorophenylimido (NC_6F_5) group are poor catalysts for alkane metathesis.[20]



1a; R = i-Pr
1b; R = Me

Trip = 2,4,6-i-$Pr_3C_6H_2$

The activity of **1a** at various temperatures and reaction times was explored further. A higher total product concentration was obtained when the reaction temperature was increased from 125 to 150 °C and the reaction time was decreased from 4 to 2 days (Table 1). Higher efficiency at higher temperatures is not a general phenomenon; for example, W(NAr)($CHCMe_2Ph$)($OSiPh_3$)$_2$ provided lower product concentrations at higher reaction temperatures (2770 mM at 125 °C, 4 days vs 1420 mM at 2 days, 150 °C). W(NC_6F_5)(CH-*t*-Bu)(Me_2Pyr)(OHMT) also showed good stability at higher temperatures, generating 3750 mM total product over 2 days at 150 °C.

With thermally robust olefin metathesis catalysts in hand, we began to investigate the metathesis of *n*-octane in ethylbenzene (1:4 v/v). A broad distribution of *n*-alkylbenzenes [1-phenylpropane (PhC3) to 1-phenyloctane (PhC8)] was obtained with **1a** and (^{tBu}POCOP)Ir(C_2H_4) at 150 °C over 2 days (Figure 1). Various *n*-alkanes [up to tetradecane (C14)] were also formed as side products. Alkylbenzenes were the major products in the C10−C14 range when (^{tBu}POCOP)Ir-

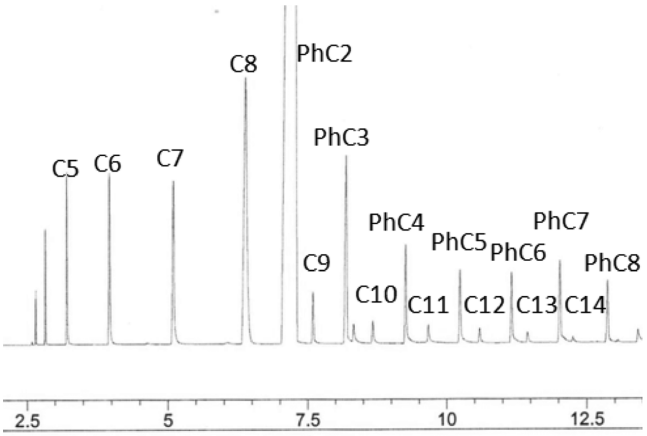


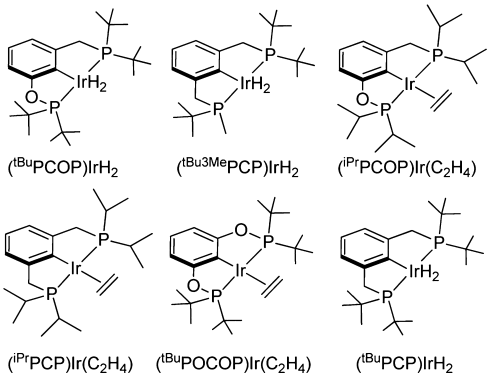
Figure 1. GC trace of the alkane metathesis of 1:4 (v/v) *n*-octane/ethylbenzene at 150 °C for 2 days using 16 mM **1a** and 10 mM (^{tBu}POCOP)Ir(C_2H_4).

(C_2H_4) was employed, but despite the high selectivity for alkylbenzenes over alkanes, there was no selectivity for *specific* alkylbenzenes with this Ir catalyst. In addition, a large fraction of the alkanes were in the C5−C7 range. Other Ir complexes produced more PhC8, even when the reaction temperature was increased to 180 °C (Table 2). The (^{tBu}PCP)IrH_2 complex

Table 2. Total Concentrations (mM) of Tetradecane (C14), 1-Phenyloctane (PhC8), and 1-Phenylheptane (PhC7) Obtained by AGCM Using Various Dehydrogenation Catalysts[a]

catalyst	C14	PhC8	PhC7
(^{tBu}PCOP)IrH_2	60	230	150
(^{tBu3Me}PCP)IrH_2	40	210	140
(^{iPr}PCOP)Ir(C_2H_4)	20	150	100
(^{iPr}PCP)Ir(C_2H_4)	10	190	80
(^{tBu}POCOP)Ir(C_2H_4)	20	70	100
(^{tBu}PCP)IrH_2	20	240	60

[a]Conditions: 24 h, 180 °C in J. Young tubes with 0.3 mL of *n*-octane, 0.4 mL of ethylbenzene, 11 mM **1a**, 7 mM Ir catalyst, and mesitylene (internal standard). See the SI for details.



provided 240 mM PhC8 in the cross-metathesis of *n*-octane and ethylbenzene over 24 h (Scheme 2). The selectivity for alkylbenzenes over alkanes was maintained even when only a slight excess of ethylbenzene was used (*n*-octane:ethylbenzene = 3:4 v/v). After PhC8, 1-phenylheptane (PhC7) was the next major *n*-alkyl arene product in the C10−C14 range (60 mM). Additionally, 20 mM C14 was generated. Because the AGCM reactions described here proceeded only to low conversion

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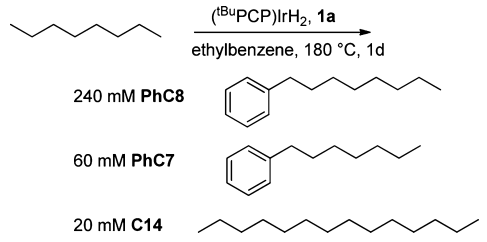
Scheme 2. Major Products in the AGCM of 3:4 v/v *n*-Octane/Ethylbenzene



(relative to ethylbenzene), only traces of diphenyl products $Ph(CH_2)_nPh$ (formed by cross-metathesis on both termini of one alkane) were produced.

Various olefin metathesis catalysts were screened using (^{tBu}PCP)IrH$_2$ as the dehydrogenation catalyst (Table 3).

Table 3. Total Concentrations (mM) of Tetradecane (C14), 1-Phenyloctane (PhC8), and 1-Phenylheptane (PhC7) Obtained by AGCM Using (^{tBu}PCP)IrH$_2$ and Various Metathesis Catalysts[a]

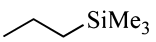
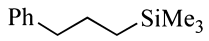
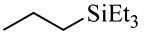
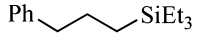
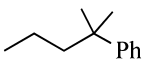
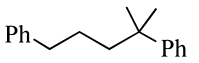
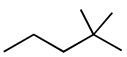
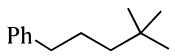
catalyst	C14	PhC8	PhC7
W(NAr)(C_3H_6)(pyr)(OHIPT) (**1a**)	20	240	60
	20[b]	280[b]	100[b]
W(NAr′)(C_3H_6)(pyr)(OHIPT) (**1b**)	20	350	100
Mo(NAr)(C_3H_6)(pyr)(OHIPT)	20	80	10
W(NC_6F_5)(CH-*t*-Bu)(Me_2Pyr)(OHMT)	<10	160	40
W(N-*t*-Bu)(CH-*t*-Bu)(pyr)(OHIPT)	<10	<10	<10
Mo(NAr)($CHMe_2Ph$)(OR_{F6})$_2$	50	240	20
W(NAr)($CHMe_2Ph$)($OC(CF_3)_3$)$_2$	<10	30	<10
W(NAr)($CHMe_2Ph$)($OSiPh_3$)$_2$	50	220	60

[a]Conditions: 24 h, 180 °C in J. Young tubes with 0.3 mL of *n*-octane, 0.4 mL of ethylbenzene, 11 mM metathesis catalyst, 7 mM (^{tBu}PCP)IrH$_2$, and mesitylene (internal standard). See the SI for details. OR_{F6} = $OC(CF_3)_2CH_3$. See Table 1 for other abbreviations. [b]22 mM metathesis catalyst.

Complex **1b** provided the highest conversion to PhC8 under these conditions (350 mM), corresponding to a W turnover number (TON) of 31 and an Ir TON of 50. **1b** also provided the highest selectivity for *n*-alkyl arene versus C14 (~17:1 PhC8:C14). While bisalkoxide complexes were also active for AGCM, they generated more *n*-alkane side products. However, Mo(NAr)($CHMe_2Ph$)(OR_{F6})$_2$ [OR_{F6} = $OC(CF_3)_2CH_3$] demonstrated the greatest selectivity for PhC8 versus PhC7 of any catalyst (12:1). This result is consistent with the high levels of C14 selectivity previously observed using Mo(NAr)($CHMe_2Ph$)(OR_{F6})$_2$ for the metathesis of *n*-octane.[8,16]

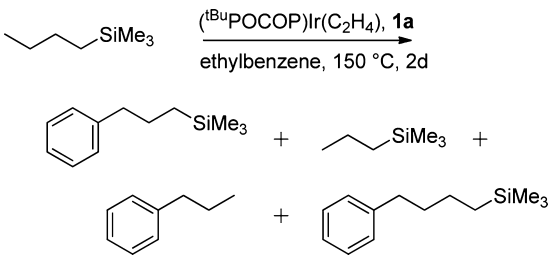
Branched alkanes, which are less prone to isomerization or dehydrogenation at internal positions, can also undergo AGCM reactions. The substrates shown in Table 4 reacted with ethylbenzene at 180 °C in the presence of (^{tBu}POCOP)Ir(C_2H_4) and **1a**. Bibenzyl was the only major byproduct of these reactions as a consequence of homoalkane metathesis of ethylbenzene. Only trace amounts of products derived from isomerization were observed with the substrates in Table 4. Less hindered alkanes prone to isomerization led to broader distributions of products. For example, *n*-propyltrimethylsilane in ethylbenzene afforded trimethyl(3-phenylpropyl)silane in 24% yield over 2 days at 180 °C with only bibenzyl as a side product. When *n*-butyltrimethylsilane was employed, trimethyl(3-phenylpropyl)silane, *n*-propylbenzene, and *n*-propyltrimethylsilane were all formed along with trace amounts of trimethyl(4-phenylbutyl)silane, as determined by GC–MS analysis (Scheme 3).

Table 4. Branched Substrates for AGCM with Ethylbenzene[a]

Substrate	Product	Yield (Conc)
		25% (400 mM)
		11% (180 mM)
		18% (290 mM)
		6% (100 mM)

[a]Conditions: 2 days, 180 °C in J. Young tubes with 16 mM **1a**, 10 mM (^{tBu}POCOP)Ir(C_2H_4), and mesitylene (internal standard).

Scheme 3. AGCM of *n*-Butyltrimethylsilane and Ethylbenzene



Substrates containing a heteroatom [e.g., methyl propionate, *n*-propyl(trimethoxy)silane] deactivated one or both catalysts. Ir complexes are known to be deactivated in the presence of C–O,[21] C–I,[22] and C–F[23] bonds. However, these bond cleavages may be reversible under some conditions. The known reversible activation of arene C–H bonds by (PCP)Ir[24] clearly does not inhibit AGCM.

Although the conditions required for appreciable conversion in AGCM are relatively harsh, tungsten alkylidenes were observed in the residue remaining after 2 days in a 180 °C reaction. A proton NMR spectrum of the nonvolatile components of a completed catalytic reaction revealed two ^{1}H NMR resonances in the alkylidene region. One integrated to 25% of the original W catalyst loading (vs an internal standard) and was assigned to W(NAr)(CHPh)(pyr)(OHIPT) (δ_{CHPh} = 10.25 ppm, C_6D_6) on the basis of a comparison with the alkylidene complex formed through addition of styrene to **1a**. The identity of the other alkylidene (δ_{CHR} = 10.61 ppm; 0.2 μmol, or 2.5% of the original W catalyst) is currently not known.

We conclude that certain W and Mo complexes catalyze alkyl group cross-metathesis reactions at relatively high temperatures. Sterically demanding aryloxide ligands appear to make the complexes more thermally stable. These robust catalysts can be employed in AGCM to provide *n*-alkyl arenes directly from ethylbenzene and alkanes in a one-pot process that is relatively selective for the formation of alkyl arenes over alkanes. Beyond providing a new route to *n*-alkyl arenes, this work more broadly demonstrates that a dehydrogenation/olefin metathesis sequence can provide AGCM products with good selectivity, even between alkyl chains in different substrates. An understanding of the inherent biases of each catalyst toward alkyl

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groups in various substrates should allow other AGCM variations to be designed.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details for all metal complexes, substrates, and products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507. (b) Crabtree, R. H. *J. Organomet. Chem.* **2004**, *689*, 4083. (c) Giri, R.; Shi, B.-F.; Engle, K. M.; Maugel, N.; Yu, J.-Q. *Chem. Soc. Rev.* **2009**, *38*, 3242. (d) Hashiguchi, B. G.; Bischof, S. M.; Konnick, M. M.; Periana, R. A. *Acc. Chem. Res.* **2012**, *45*, 885.

(2) Baumgartner, F. N. *Ind. Eng. Chem.* **1954**, *46*, 1349.

(3) Kocal, J. A.; Vora, B. V.; Imai, T. *Appl. Catal., A* **2001**, *221*, 295.

(4) Kosswig, K. Surfactants. In *Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH: Weinheim, Germany, 2000.

(5) (a) Foley, N. A.; Lee, J. P.; Ke, Z.; Gunnoe, T. B.; Cundari, T. R. *Acc. Chem. Res.* **2009**, *42*, 585. (b) Luedtke, A. T.; Goldberg, K. I. *Angew. Chem., Int. Ed.* **2008**, *47*, 7694. (c) Oxgaard, J.; Periana, R. A.; Goddard, W. A., III. *J. Am. Chem. Soc.* **2004**, *126*, 11658. (d) Bhalla, G.; Bischof, S. M.; Ganesh, S. K.; Liu, X. Y.; Jones, C. J.; Borzenko, A.; Tenn, W. J., III; Ess, D. H.; Hashiguchi, B. G.; Lokare, K. S.; Leung, C. H.; Oxgaard, J.; Goddard, W. A., III; Periana, R. A. *Green Chem.* **2011**, *13*, 69. (e) Oxgaard, J.; Muller, R. P.; Goddard, W. A., III; Periana, R. A. *J. Am. Chem. Soc.* **2004**, *126*, 352. (f) Matsumoto, T.; Periana, R. A.; Taube, D. J.; Yoshida, H. *J. Mol. Catal. A: Chem.* **2002**, *180*, 1. (g) Lail, M.; Bell, C. M.; Conner, D.; Cundari, T. R.; Gunnoe, T. B.; Petersen, J. L. *Organometallics* **2004**, *23*, 5007.

(6) Ahuja, R.; Punji, B.; Findlater, M.; Supplee, C.; Schinski, W.; Brookhart, M.; Goldman, A. S. *Nat. Chem.* **2011**, *3*, 167.

(7) Haibach, M. C.; Kundu, S.; Brookhart, M.; Goldman, A. S. *Acc. Chem. Res.* **2013**, *46*, 947.

(8) Goldman, A. S.; Roy, A. H.; Huang, Z.; Ahuja, R.; Schinski, W.; Brookhart, M. *Science* **2006**, *312*, 257.

(9) Gupta, M.; Kaska, W. C.; Jensen, C. M. *Chem. Commun.* **1997**, 461.

(10) Liu, F.; Pak, E. B.; Singh, B.; Jensen, C. M.; Goldman, A. S. *J. Am. Chem. Soc.* **1999**, *121*, 4086.

(11) Biswas, S.; Huang, Z.; Choliy, Y.; Wang, D. Y.; Brookhart, M.; Krogh-Jespersen, K.; Goldman, A. S. *J. Am. Chem. Soc.* **2012**, *134*, 13276.

(12) Marinescu, S. C.; King, A. J.; Schrock, R. R.; Singh, R.; Müller, P.; Takase, M. K. *Organometallics* **2010**, *29*, 6816.

(13) (a) Jiang, A. J.; Zhao, Y.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 16630. (b) Marinescu, S. C.; Levine, D. S.; Zhao, Y.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 11512.

(14) Flook, M. M.; Jiang, A. J.; Schrock, R. R.; Müller, P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 7962.

(15) (a) Meek, S. J.; O'Brien, R. V.; Llaveria, J.; Schrock, R. R.; Hoveyda, A. H. *Nature* **2011**, *471*, 461. (b) Yu, M.; Ibrahem, I.; Hasegawa, M.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 2788. (c) Kiesewetter, E. T.; O'Brien, R. V.; Yu, E. C.; Meek, S. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2013**, *135*, 6026. (d) Wang, C.; Yu, M.; Kyle, A. F.; Jacubec, P.; Dixon, D. J.; Schrock, R. R.; Hoveyda, A. H. *Chem.—Eur. J.* **2013**, *19*, 2726. (e) Townsend, E. M.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 11334.

(16) Bailey, B. C.; Schrock, R. R.; Kundu, S.; Goldman, A. S.; Huang, Z.; Brookhart, M. *Organometallics* **2009**, *28*, 355.

(17) Schrock, R. R. *Chem. Rev.* **2009**, *109*, 3211.

(18) Jeong, H.; Axtell, J. C.; Török, B.; Schrock, R. R.; Müller, P. *Organometallics* **2012**, *31*, 6522.

(19) Peryshkov, D. V.; Schrock, R. R.; Takase, M. K.; Müller, P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 20754.

(20) Yuan, J.; Schrock, R. R.; Müller, P.; Axtell, J. C.; Dobereiner, G. E. *Organometallics* **2012**, *31*, 4650.

(21) Kundu, S.; Choi, J.; Wang, D. Y.; Choliy, Y.; Emge, T. J.; Krogh-Jespersen, K.; Goldman, A. S. *J. Am. Chem. Soc.* **2013**, *135*, 5127.

(22) Ghosh, R.; Emge, T. J.; Krogh-Jespersen, K.; Goldman, A. S. *J. Am. Chem. Soc.* **2008**, *130*, 11317.

(23) Choi, J.; Wang, D. Y.; Kundu, S.; Choliy, Y.; Emge, T. J.; Krogh-Jespersen, K.; Goldman, A. S. *Science* **2011**, *332*, 1545.

(24) Kanzelberger, M.; Singh, B.; Czerw, M.; Krogh-Jespersen, K.; Goldman, A. S. *J. Am. Chem. Soc.* **2000**, *122*, 11017.