CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.201101190

In(OTf)$_3$-Catalyzed Highly Chemo- and Regioselective Head-to-Tail Heterodimerization of Vinylarenes with 1,1-Diarylethenes

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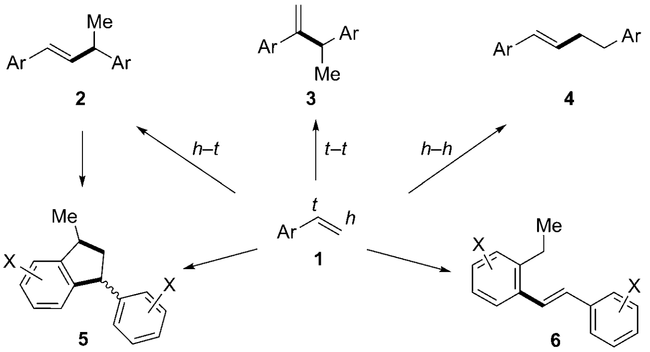
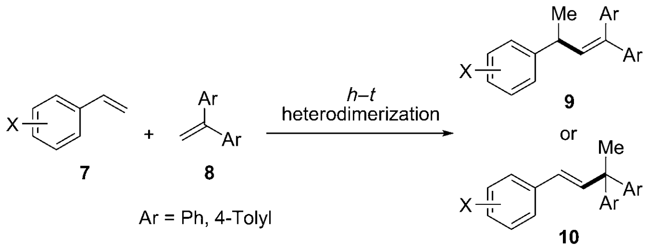
Dedicated to Professor Wei-Yuan Huang on the occasion of his 90th birthday

The dimerization of alkenes highlights an important industrial process for accessing longer chain alkenes from abundant and inexpensive petrochemical feedstocks.[1] Homodimerization may be considered simpler than heterodimerization between two different partners and yet a mixture of homodimers is often generated due to versatile dimerization modes.[1,2] As illustrated in Scheme 1, catalytic homodimerization of vinylarenes **1**, such as styrene (Ar = Ph), gives the alkenes **2**–**4** through head-to-tail (h–t),[3] tail-to-tail (t–t),[4] and head-to-head (h–h)[5] homodimerization, respectively. Moreover, compounds **1** undergo cyclodimerization to produce the indan derivatives **5**.[6] With recent advancements in catalyst development and an increasing understanding of the reaction mechanisms, selective head-to-tail homodimerization of **1** has been achieved.[3] For example, the combination of a transition metal complex with a Lewis acid,[7] such as Pd(OAc)$_2$/PPh$_3$/In(OTf)$_3$ (OTf = triflate), forms an efficient catalyst, affording dimers **2** at 20–50 °C in 73–98 % yields.[3a] The Lewis acid is thought to activate **1** towards nucleophilic attack by the Pd^0 complex, followed by insertion of another vinylarene with the formation of a palladium oxidative adduct. Alternatively, cationic iron(III) salts, formed in situ from FeCl$_3$ and AgOTf or AgNTf$_2$, afford dimers **2** at 80 °C in 51–97 % yields.[3e] Selective formation of dimers **3** through tail-to-tail homodimerization has also been reported[4] and the N-heterocyclic carbene (NHC) nickel(II) hydride complex [(IPr)NiH]OTf (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene) promotes both homo- and heterodimerization of **1** in high chemo- and regioselectivity.[4d] A ruthenium(0) complex, $[\mathrm{Ru}(\eta^6\text{-cot})(\eta^2\text{-dmfm})_2]$ (cot = 1,3,5-cyclooctatriene, dmfm = dimethyl fumarate), has been found to be efficient for the formation of alkenes **4** at 80–100 °C in alcoholic solvents in 53–66 % isolated yields.[5] Moreover, a rhodium(I) complex, [RhCl(cod)]$_2$ (cod = 1,5-cyclooctadiene), in combination with *t*BuOH and Na$_2$CO$_3$ at 160 °C facilitates the formation of *trans*-stilbenes **6** (24–63 % yields) from vinylarenes **1** through cleavage of the *ortho* C–H bond.[8]



Scheme 1. The homodimerization pathways of **1**: a) the formation of **2**–**4** through head-to-tail (h–t), tail-to-tail (t–t), and head-to-head (h–h) dimerization modes; b) the formation of *cis* and *trans* indans **5** through cyclodimerization, involving **2** as the intermediate; and c) the formation of *trans*-stilbenes **6** through dimerization by cleavage of the *ortho* C–H bond.

To the best of our knowledge, 1,1-diarylethenes **8** (Scheme 2) usually give indan products similar to **5** through cyclodimerization in the presence of Lewis acids, such as



Scheme 2. Possible products of the Lewis acid catalyzed heterodimerization of vinylarenes **7** with 1,1-diarylethenes **8**.

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201101190.

$EtAlCl_2$,[9a] $RuCl_3{\cdot}nH_2O$,[9b] $InBr_3$,[9c] and $BiCl_3$,[9d] or aminium hexachloroantimonates.[10] There is one example of aminium salt promoted heterodimerization of 1,1-diphenylethene **8a** (Ar = Ph) with vinylferrocene, which occurs in 62 % yield, along with a 10 % yield of the head-to-tail dimer of vinylferrocene.[10d] We report, herein, a general and efficient head-to-tail heterodimerization of vinylarenes **7** with 1,1-diarylethenes **8** catalyzed by $In(OTf)_3$, affording alkenes **9** in good to excellent yields with high chemo- and regioselectivity (Scheme 2). Our results support a Lewis acid mediated cationic mechanism and the role of **8** in this highly selective heterodimerization[11,12] is discussed.

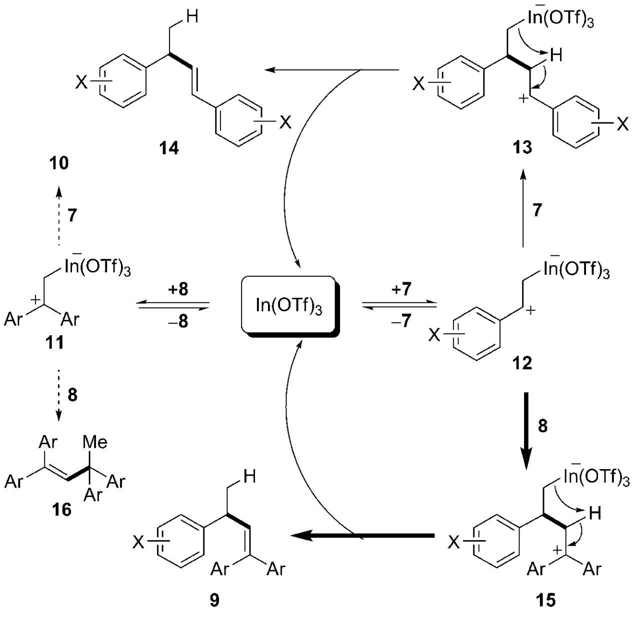
During our screening of $FeCl_3$-catalyzed reactions, we found that styrene underwent homodimerization to give the head-to-tail dimer **2** (Ar = Ph) in 22–65 % yields in the presence of $FeCl_3{\cdot}6H_2O$ (10 mol %) in 1,4-dioxane at 80–120 °C (Table 1, entries 1, 3, and 4). The temperature-dependent conversion of styrene suggests a relatively weak Lewis acidity of $FeCl_3$.[3e] We also found 1,4-dioxane to be a better solvent than THF and PEG-400 (entries 1 vs. 2 and entries 4 vs. 5, Table 1) when using a lower catalyst loading or for obtaining a higher yield of the dimer. Other solvents including toluene, CH_2Cl_2, $ClCH_2CH_2Cl$, dimethylacetamide (DMA), and DMF were totally ineffective, giving none of the dimer product. The conversion of styrene approached completion at temperatures above 100 °C, indicating that formation of polymeric materials is the competitive pathway. We examined Cr^{3+}, Zn^{2+}, and Cu^{2+} salts for catalysis of the same dimerization at 120 °C and found that both the styrene conversion and the dimer yield were reduced (entries 6–8, Table 1). These results imply that, to a large extent, Fe^{3+} is the true catalyst for the formation of the dimerization product in entry 4, Table 1 and other metal impurities, if any are present, are not likely to be involved in the catalysis. Additionally, three metal triflates were tested in the styrene dimerization (entries 9–11, Table 1). Among them, $In(OTf)_3$ was found to be a slightly better catalyst in terms of both reaction time and yield, affording **2** (Ar = Ph) in 82 % yield in 19 h.

Table 1. The Lewis acid catalyzed formation of **2** (Ar = Ph) from styrene.[a]

	Lewis acid ([mol %])	*T* [°C]	*t* [h]	Conversion [%]	Yield [%][b]
1	$FeCl_3{\cdot}6H_2O$ (10)	80	48	39	22
2	$FeCl_3{\cdot}6H_2O$ (50)	80[c]	24	40	25
3	$FeCl_3{\cdot}6H_2O$ (10)	100	36	95	62
4	$FeCl_3{\cdot}6H_2O$ (10)	120	22	100	65
5	$FeCl_3{\cdot}6H_2O$ (10)	120[d]	24	100	48
6	$CrCl_3$ (10)	120	24	40	trace
7	$Zn(OTf)_2$ (10)	120	24	56	trace
8	$Cu(OTf)_2$ (10)	120	19	20	20
9	$Sn(OTf)_2$ (10)	120	24	100	83
10	$In(OTf)_3$ (10)	120	19	100	82
11	$Yb(OTf)_3$ (10)	120	19	100	66

[a] Reaction conditions: styrene (1.0 mmol) and Lewis acid (10–50 mol %) in 1,4-dioxane (1 mL) at 80–120 °C in a sealed vial. [b] Isolated yield of **2**. [c] In THF. [d] In PEG-400.

These results on the $In(OTf)_3$-catalyzed homodimerization of styrene suggest that the $In(OTf)_3$-activated benzylic carbocation **12a** (X = H) can regioselectively add to vinylarene **7a** (X = H) to form a new carbocation **13a** (X = H) without the action of palladium(0),[3a] albeit at higher temperatures (Scheme 3). Therefore, we envisioned a heterodimerization process by selecting terminal alkenes that could compete with **7** in the addition reaction with **12** and for which the homodimerization process would be much slower. We found that 1,1-diarylethenes **8** meet these criteria according to their electronic and steric properties: 1) the tertiary carbocation **11**, formed from **8** and $In(OTf)_3$, is very stable and yet sterically bulky, preventing reactions with alkenes **7** and **8** to give the hetero- and homodimerization products **10** and **16**; and 2) the formation of the diaryl-stabilized tertiary carbocation **15** is much faster than the formation of benzylic counterpart **13**, allowing the selective formation of **15** from **12** and **8**, followed by decomposition of **15** to form heterodimers **9** with regeneration of the Lewis acid, $In(OTf)_3$.



Scheme 3. The possible mechanisms of the highly selective heterodimerization reaction.

Our experiments using 1,1-diphenylethene (**8a**) and a series of styrene derivatives **7** support this reasoning (Table 2). If a 1:2 mixture of styrene and 1,1-diphenylethene along with $In(OTf)_3$ (10 mol %) was heated in 1,4-dioxane at 120 °C for 24 h the heterodimer **9aa** was isolated in 80 % yield, along with a 15 % yield of homodimer **14a** (X = H; entry 1, Table 2). Most of the excess of 1,1-diphenylethene was recovered after the reaction and its homodimer **16a** (Ar = Ph) was not obtained. The reactions of 3- and 4-halophenylethenes with 1,1-diphenylethene under the same reaction conditions afforded **9af–ai** in 70–81 % yields (entries 6–

Table 2. The synthesis of heterodimerization products **9** from **7** and **8**.[a]

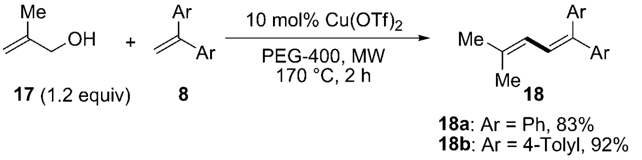
	7: X		*T* [°C]	Ar = Ph yield [%][b]	Ar = tolyl yield [%][b]
1	H	**7a**	120	**9aa**: 80 (15)[c]	**9ba**: 90
2	2-Me	**7b**	140	**9ab**: 91	**9bb**: 94
3	2-F	**7c**	140	**9ac**: 94	**9bc**: 96
4	2-Br	**7d**	140	**9ad**: 93	**9bd**: 95
5	2-Cl	**7e**	140	**9ae**: 94	**9be**: 90
6	3-Br	**7f**	120	**9af**: 76	**9bf**: 82
7	3-Cl	**7g**	120	**9ag**: 70	**9bg**: 83
8	4-Br	**7h**	120	**9ah**: 75	**9bh**: 93
9	4-Cl	**7i**	120	**9ai**: 81 (17)[c]	**9bi**: 94
10	4-Me	**7j**	120	**9aj**: 71	**9bj**: 84
11	4-MeO	**7k**	120	**9ak**: trace[d]	**9bk**: trace[d]

[a] Reaction conditions: **7** (0.5 mmol), **8a** (Ar = Ph, 1.0 mmol) or **8b** (Ar = 4-tolyl, 0.75 mmol), and $In(OTf)_3$ (10 mol %) in 1,4-dioxane (1 mL) at 120–140 °C for 24 h in a sealed vial. Byproduct **14** was observed in entries 1 and 6–10. [b] Isolated yield of **9**. [c] Isolated yield of byproduct **14** given in parentheses. [d] Polymerization might occur.

9, Table 2). Formation of homodimers **14** was observed in all reactions and **14i** (X = 4-Cl) was isolated in a 17 % yield for entry 9, Table 2. For the electron-rich styrene **7j** (X = 4-Me), the desired heterodimer **9aj** was produced in 71 % yield, although homodimer **14j** (X = 4-Me) was not observed, presumably due to the formation of an oligomer/polymer (entry 10, Table 2). The polymerization pathway became dominant for styrene **7k** (X = 4-MeO) and no separable products were obtained (entry 11, Table 2).[3e] In contrast, 4-vinylpyridine failed to react via either hetero- or homodimerization even at 140 °C and was recovered after heating for 24 h (data not shown in Table 2). Moreover, the reactivity of 2-substituted styrenes deserves special comment. The additional steric hindrance arising from the *ortho* substituent makes it difficult for carbocation **12** to react with both **7** and **8** at 120 °C. After raising the temperature to 140 °C, the heterodimerization took place in much higher selectivity to furnish **9ab–ae** in 91–94 % isolated yields (entries 2–5, Table 2).

We also examined the reaction of 4-chlorophenylethene (**7i**) with 1,1-diphenylethene (**8a**) in 1,4-dioxane (120 °C, 24 h) by using Brønsted acids [H_2SO_4 (80 mol %), HCl (100 mol %), and CF_3CO_2H (20 mol %)]. Heterodimer **9ai** was isolated in a 15 % yield under H_2SO_4 catalysis, whereas only trace amounts were detected for reactions with the other two Brønsted acids. These data clearly demonstrate the importance of the bulky indium coordination sphere in carbocations **11** and **12** for deactivating **11** and directing the heterodimerization process (**12**→**15**→**9**). Presumably the indium-bound carbocations are much less reactive than their corresponding metal-free counterparts so that the undesired homo- and cyclodimerization of vinylarenes **7**[3f,4c,6] and 1,1-diarylethenes **8**[9,10] are eliminated or suppressed. We further enhanced the selective formation of carbocation **15** by incorporating electron-rich aryl groups, such as 4-tolyl, generally providing a roughly 10 % increase in the yield for the heterodimers **9ba** and **9bf–bj** (entries 1 and 6–10, Table 2). This also allowed the ratio of **7** to **8b** (Ar = 4-tolyl) to be reduced to 1:1.5. These results are consistent with the cationic mechanisms depicted in Scheme 3.

To explore the reaction of 1,1-diarylethenes **8** with other alkenes (Scheme 4), we found that allyl alcohol **17** (2 equiv) reacted with 1,1-diphenylethene (**8a**) to form the diene **18a** (Ar = Ph) in PEG-400 at 120 °C after 24 h in the presence of a Lewis acid (50 mol %). The isolated yield of **18a** increases in the order AgOTf (18 %) < $Sc(OTf)_3$ (32 %) < $In(OTf)_3$ (47 %) < $Sn(OTf)_3$ (58 %) < $FeCl_3{\cdot}6H_2O$ (67 %) < $Cu(OTf)_3$ (88 %). Other solvents, including DMA, DMF, DMSO, toluene, and 1,4-dioxane, were examined with $FeCl_3{\cdot}6H_2O$ (50 mol %) at 120 °C for 24 h, but diene product **18a** was barely formed under these conditions except for a 46 % yield obtained for the reaction in 1,4-dioxane. If the reaction was carried out under microwave heating at 170 °C for 2 h, the loading of $Cu(OTf)_3$ could be reduced to 10 mol % and product **18a** was formed in 83 % yield. Moreover, by using electron-rich **8b** (Ar = 4-tolyl), the yield of diene **18b** was improved to 92 %.[13]



Scheme 4. The $Cu(OTf)_2$-catalyzed reaction of allyl alcohol **17** with 1,1-diarylethenes **8** under microwave heating.

In conclusion, we have established a general and efficient hydroalkenylation of vinylarenes **7** through addition to an olefinic C–H bond in 1,1-diarylethenes **8**, catalyzed by $In(OTf)_3$, to furnish trisubstituted alkenes **9** in good to excellent yields. The highly chemo- and regioselective head-to-tail heterodimerization likely takes place through a cationic mechanism initiated by the indium-bound carbocation **12**. This cation, as compared to its corresponding metal-free counterparts, contributes to the heterodimerization in a synergetic manner with 1,1-diarylethenes **8**. The unique carbocation stabilizing ability and steric bulk of the diaryl groups in **8** are the indispensable factors responsible for the high selectivity. Our results present a new method for highly selective alkene heterodimerization[4d,10d,11,12b–d] without relying on the action of transition metals.

Acknowledgements

The Laboratory of Asymmetric Catalysis and Synthesis is established under the Cheung Kong Scholars Program of The Ministry of Education of China. This work is supported by Zhejiang University and the Zhejiang University Education Foundation.

Keywords: alkenes · carbocations · C–H activation · hydroalkenylation · Lewis acids

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[13] An inseparable indene byproduct (7–8%) was found in **18a** and **b**, as confirmed by NMR and LC-MS analysis. The details can be found in the Supporting Information.

Received: April 18, 2011
Published online: June 7, 2011