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Noncatalytic Heck coupling reaction using supercritical water

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Heck coupling of iodobenzene with styrene can be promoted in supercritical water without using catalyst, and the conversion reaches over 70% within 10 min in the presence of base, such as KOAc, in which case the yield of stilbene is 55.6% (both *trans*- and *cis*-stilbene).

The Heck reaction is an extremely valuable method for carbon–carbon bond formation and is now widely used in the fine chemical and pharmaceutical manufacturing industries.[1,2] However, its practical production has been restricted due to the disadvantages of using environmentally damaging solvents and transition metal catalysts, such as palladium, and of problems associated with catalyst–product separation and side reactions such as decomposition, which would take place during the distillation after the reaction. Recently, environmentally benign approaches to the Heck reaction have been developed, such as the application of water with a water-soluble ligand,[3] phase-transfer catalysts,[4,5] as well as supercritical CO_2[6,7] and ionic liquids[8] as solvent media.

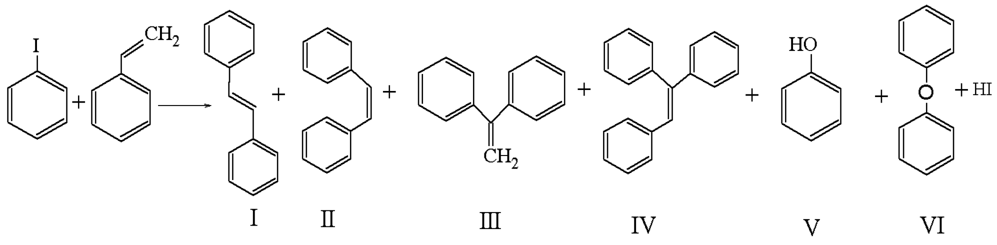
Supercritical water (scH_2O) should be a more useful replacement for organic solvents because water is the most environmentally acceptable solvent and its physicochemical properties can be changed widely with pressure and temperature. For example, the static relative permittivity of water is 78.5 at 298 K, and dramatically decreases to about 6.0 at the supercritical point.[9] As a result, nonpolar organic compounds are very soluble or miscible in scH_2O. This nature, along with high diffusivity and low viscosity, is expected to allow it to function as an ideal alternative to organic solvents.[10]

The Heck arylation of alkenes has been carried out in hot compressed water (533 K) and also in scH_2O (673 K) in the presence of Pd catalysts.[11–14] In the case of Pd-catalysed reaction of iodobenzene and styrene, the yield of coupling products was less than 25% and the catalysts were deactivated rapidly. Further, the influence of water on the selectivity and the reaction mechanism has scarcely been elucidated.[15] We have recently demonstrated a remarkable stimulation of rearrangement or disproportionation using scH_2O even in the absence of any acid or base catalysts.[16,17] This might be due to the acid and base difunctionality of scH_2O. In this paper we attempted to conduct noncatalytic arylation of styrene with iodobenzene using scH_2O. It will be shown that high reaction rate and high selectivity are possible in water near its critical point.

The experiments were performed by using an Inconnel 625 batch reactor system with an internal volume of 10.2 cm^3. Triply distilled high-purity water was used for all experiments and degassed by N_2 gas prior to use. A predetermined amount of substrates and base (1.0 mmol each) and water were loaded into the reactor in argon atmosphere. The reactor vessel was immersed and vigorously shaken in a molten salt bath. The heat-up time to raise the reactor temperature from 293 K to the reaction temperature was within 30 s. Pressure was calculated using a steam table. After a preselected reaction time of 10 min, the reactor was withdrawn from the molten salt bath and rapidly quenched in an ice–water bath. All of the products were extracted with dichloromethane and identified by GC-MS and ^{1}H-NMR, and each concentration was determined by using GC-FID. The product yield was calculated based on styrene.

We first found that coupling of styrene and iodobenzene can be promoted even in the absence of any catalysts in scH_2O, in which several alkylarenes, such as stilbene (I and II) and 1,1-diphenylethylene (III), were formed as shown in Scheme 1, besides hydrogen iodide. Furthermore, the effect of base on the Heck reaction in scH_2O was investigated. Experiments were carried out in the presence of NEt_3, NaOAc, KOAc, K_2CO_3, Na_2CO_3, $NaHCO_3$, or NaOH base. The results are shown in Table 1. The kind of base had a strong influence on both the conversion and the selectivity in scH_2O. That is, KOAc base was the most effective for synthesizing coupling compounds such as stilbene (I and II). The conversion of iodobenzene and styrene reached over 70% and the yield of stilbene (both *trans*- and *cis*-stilbene) was 55.6%. In addition, white crystals of *trans*-stilbene can be easily separated from water.

In the absence of base or in the presence of NEt_3 base, high conversion of styrene was obtained; however, only small amounts of the coupling products were formed and the main products were polymeric compounds. Furthermore, ethylbenzene and diphenylethane compounds that were the hydrogenated products of styrene and the coupling products (I, II, and III) were obtained in about 10 and 6% yields, respectively. It would be predicted that the hydrogenation would be caused by the resulting hydrogen iodide, because the hydrogenation of styrene to ethylbenzene in scH_2O was shown to proceed only when hydrogen iodide was present. Moreover, in the absence of hydrogen iodide the formation of a small amount of 1-phenylethyl alcohol from styrene in scH_2O was confirmed, and so one cannot deny the donation of hydrogen from scH_2O itself for the hydrogenation. When relatively strong bases K_2CO_3, Na_2CO_3, $NaHCO_3$, and NaOH were used, the conversion of iodobenzene was high and phenol was the chief product. Homocoupling of iodobenzene to biphenyl has not been observed in scH_2O regardless of the base used.



Scheme 1 Heck reaction of iodobenzene and styrene.

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Table 1 Effect of base on coupling of iodobenzene and styrene at 650 K and 25 MPa

Base	Initial pH value	Conversion (%) Styrene	Conversion (%) Iodobenzene	Yield (%) I	II	III	IV	V	VI
—[a]	6.5	100.0	39.7	5.0 (3.3)	0	0 (1.3)[c]	0 (1.8)	0	0
NEt$_3$[b]	10.8	94.1	45.1	13.9 (2.0)	0 (3.0)	0 (1.8)	0	0	0
NaOAc	7.2	65.4	65.6	35.3	8.5	1.9	2.0	6.3	0
KOAc	7.2	72.5	77.5	45.1	10.5	2.3	3.0	0	0
Na$_2$CO$_3$	10.0	64.6	100.0	23.1	4.7	1.2	0.5	44.3	5.2
K$_2$CO$_3$	10.0	39.0	93.1	8.7	2.0	0	0	58.2	7.7
NaHCO$_3$	9.0	55.2	95.0	8.5	1.7	0	0	52.8	4.1
NaOH	12.0	41.4	100.0	6.2	1.5	0	0	59.4	11.5

[a] Ethylbenzene 10.2%. [b] Ethylbenzene 10.5%. [c] The numbers in parentheses are yields of corresponding hydrogenated products.

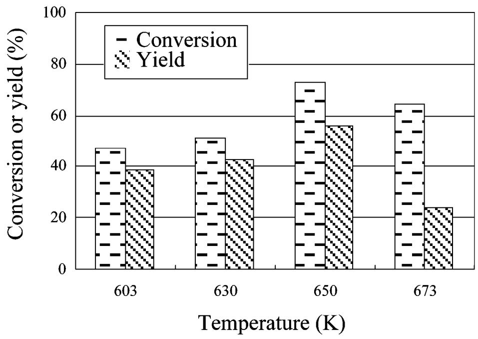

Fig. 1 Influence of temperature on the conversion and the yield of stilbene at 25 MPa in the presence of KOAc.

Fig. 1 shows the temperature dependence of the conversion and the yield of stilbene at 25 MPa in the presence of KOAc. One can see an interesting temperature dependence in which both the conversion and the yield increased, reaching maximum conversion and yield at 650 K near the critical temperature of water, and then decreased with increasing temperature.

The change of hydrogen bonding is presumed to be a key factor for understanding the above results. Our Raman[18] and IR[17] measurements of the hydrogen bonding of sub- and supercritical water suggest that the tetrahedral configurations disappear near the critical point, where the monomer or dimer or trimer structures are predominant. This result was further supported by a recent first-principle molecular dynamics study.[19] The ion product (K_w) monotonously decreases with increasing temperature above 573 K at 25 MPa,[20] and so the proton or hydroxide ion (OH^-) concentration anticipated from the K_w concept is not so high near the critical temperature at 25 MPa. However, in scH_2O the OH^- or proton adjacent to substrate molecules cannot migrate throughout the hydrogen bonding network near the critical point, and hence the OH^- or proton species could react spontaneously with substrate molecules to form a transient intermediate owing to lower activation energies for bond breakage and formation. At least 10 water molecules are considered to be required for appreciable interaction between the hydrogen bonding network and proton.[21] Moreover, the local proton and OH^- concentrations would be high when the transferring ions cannot escape.

Considering the experimental results, a general mechanism for the coupling reaction in scH_2O is postulated as follows. The OH^- removes the β-H of styrene, giving a carbanion. Then the nucleophilic carbanion attacks iodobenzene at the electrophilic carbon, resulting in the formation of coupled products. The hydrogen iodide formed during the reaction facilitates the polymerisation of styrene and the hydrogenation of styrene and both coupling products. The addition of a relatively mild base, such as NaOAc and KOAc (see Table 1, initial pH value is less than 8.0), can not only neutralize hydrogen iodide, but also promote the removal of iodine *via* an intermediate composed of an ion–dipole bond between cation and iodine.[22] As for the formation of phenol, hydrolysis of chlorobenzene in NaOH solution under high temperature (633–663 K) and high pressure (28–30 MPa) has been used commercially for the production of phenol.[23] We confirmed that phenol is obtained in over 50% yield by hydrolysis of iodobenzene in the presence of a relatively strong base.

In summary, the unusual properties of water near its critical point provide a novel method for extending the Heck reaction into water. The choice of base had a significant effect on product selectivity. The best result was obtained using KOAc, which is a relatively mild base. The conversion reached 70% and the yield of stilbene was 55.6% (both *trans*- and *cis*-stilbene) within 10 min.

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