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Iodine mediated/Brønsted acid-catalyzed dimerization of vinylarenes: a tandem reaction through Ritter trapping to produce *N*-(4-iodo-1,3-diarylbutyl) acetamides†

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In the presence of *p*-toluenesulfonic acid and iodine, styrene derivatives undergo head-to-tail dimerization followed by trapping with nitriles to yield the corresponding Ritter-type products.

The development of sustainable processes is one of the main targets in modern chemistry.[1] Particularly, construction of complex structures from simple starting materials in a tandem process through an efficient catalytic transformation is a powerful tool for saving energy and resources.[2] Catalytic dimerization of aryl alkenes is one of the current interesting and useful reactions to construct a new C–C bond,[3] and in consequence of our interest in the development of new sustainable process in organic synthesis,[4] we report a method to build up a new series of compounds *N*-(4-iodo-1,3-diarylbutyl)acetamides through iodine mediated and *p*-toluenesulfonic acid promoted head-to-tail dimerization of vinylarenes.

Recently, when we investigated the $Yb(OTf)_3$ catalyzed reaction of styrene with I_2 in MeCN (1 mL, commercial reagent grade), a new product *N*-(4-iodo-1,3-diphenylbutyl)acetamide **3a**, in which carbon skeleton was resulted from the head-to-tail dimerization of styrene was obtained in a yield of 55%. The ratio of two diastereoisomers was 1 : 0.8 and the structure had been determined by IR, NMR, HRMS spectroscopic data and X-ray diffraction.[6] The ORTEP drawing is shown in Fig. 1. The interesting structure and the high efficient domino process prompted us to further optimize the current reaction conditions. Hence, a study of reaction conditions with variation of acid and temperature is summarized in Table 1. Lewis acids $ZnCl_2$ and $SnCl_2$ gave slightly lower yields (49% and 48% respectively, Table 1, entries 3 and 4). It was found that Brønsted acid also worked on this transformation. *p*-Toluenesulfonic acid (PTSA) showed the

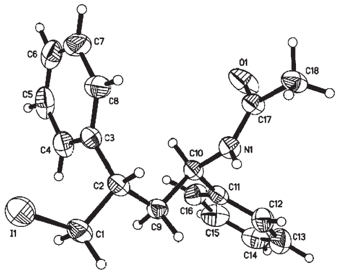
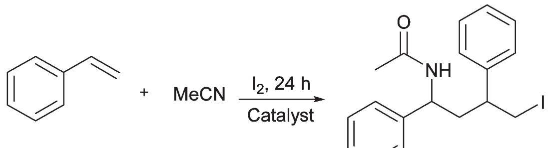


Fig. 1 The ORTEP drawing of compound **3a**: *N*-((1*R*,3*S*)-4-iodo-1,3-diphenylbutyl)acetamide).[5]

Table 1 Optimization of the reaction conditions for the dimerization reaction of styrene[a]



1a **2a** **3a**

Entry	Catalyst	Temperature (°C)	Yield[b] (%)
1	—	0 to rt	0[c]
2	$Yb(OTf)_3$	0 to rt	55 (1 : 0.8)
3	$ZnCl_2$	0 to rt	49 (1 : 0.8)
4	$SnCl_2$	0 to rt	48 (1 : 0.9)
5	CH_3COOH	0 to rt	44 (1 : 0.8)
6	HCl	0 to rt	48 (1 : 0.8)
7	PTSA	0 to rt	68 (1 : 0.7)
8	PTSA	rt	50 (1 : 0.7)
9	PTSA	0	59 (1 : 0.7)
10[d]	PTSA	0 to rt	17 (1 : 0.7)
11[e]	PTSA	0 to rt	68 (1 : 0.7)
12[f]	PTSA	0 to rt	68 (1 : 0.7)
13[g]	PTSA	0 to rt	44 (1 : 0.7)

[a] Conditions: 1 mmol styrene, 1 mmol iodine, 0.1 mmol catalyst, solvent: 1 mL acetonitrile. [b] Isolated yield; the ratio of the two diastereoisomers determined by ^1H NMR was given in parenthesis. [c] SM was recovered. [d] 0.05 mmol PTSA. [e] 0.125 mmol PTSA. [f] Anhydrous MeCN + 0.6 mmol H_2O. [g] 1 mL DCM, 2 mmol acetonitrile.

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† Electronic supplementary information (ESI) available: Experimental procedures, characterization data and copies of ^1H and ^{13}C NMR spectra for all new compounds. CCDC 838337. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2ob25142f

Table 2 Dimerization of vinylarenes catalysed by PTSA[a]

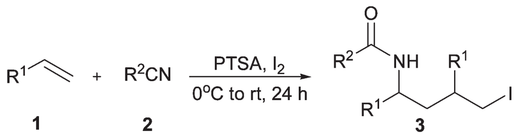
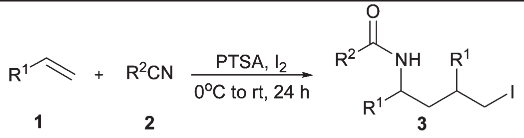
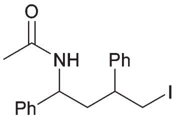
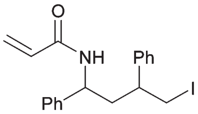
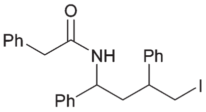
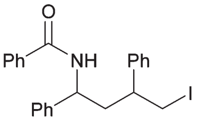
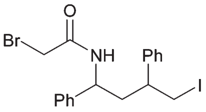
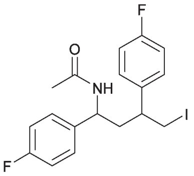
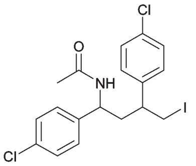
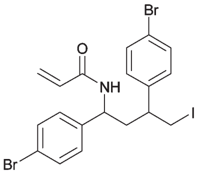
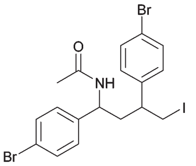
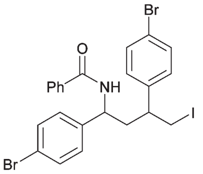
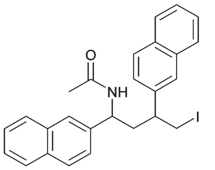
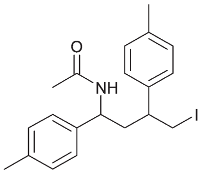
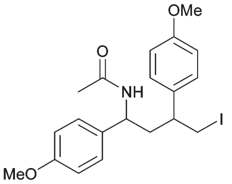


Table 2 *(Contd.)*



Entry	R^1, R^2	Product	3	Yield[b] (%)
1	R^1 = Ph R^2 = CH_3		**3a**	68 (1 : 0.7)
2	R^1 = Ph R^2 = $CH_2{=}CH$		**3b**	90 (1 : 0.8)
3	R^1 = Ph R^2 = $PhCH_2$		**3c**	72 (1 : 1)
4	R^1 = R^2 = Ph		**3d**	64 (1 : 1)
5	R^1 = Ph R^2 = $BrCH_2$		**3e**	27 (1 : 0.5)
6	R^1 = 4-FC_6H_4 R^2 = CH_3		**3f**	71 (1 : 1)
7	R^1 = 4-ClC_6H_4 R^2 = CH_3		**3g**	62 (1 : 1)
8	R^1 = 4-BrC_6H_4 R^2 = $CH_2{=}CH$		**3h**	74 (1 : 0.5)
9	R^1 = 4-BrC_6H_4 R^2 = CH_3		**3i**	42 (1 : 0.7)
10	R^1 = 4-BrC_6H_4 R^2 = Ph		**3j**	54 (1 : 0.9)
11[c]	R^1 = 2-Naphtyl R^2 = CH_3		**3k**	38 (1 : 0.8)
12[d]	R^1 = 4-MeC_6H_5 R^2 = CH_3		**3l**	30 (1 : 1)
13	R^1 = 4-$MeOC_6H_5$ R^2 = CH_3		**3m**	Trace

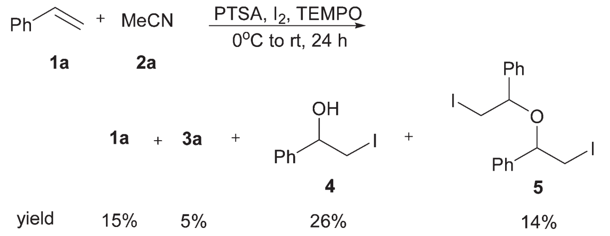
[a] Standard reaction conditions: 1 mmol **1**, 0.1 mmol PTSA and 1 mmol iodine in 1 mL nitrile, 0 °C to rt, 24 h. [b] Isolated yields; the ratio of two diastereoisomers determined by ^1H NMR was given in parenthesis. [c] 1 mL DCM was added. [d] The reaction was carried out in 30 mol% $SnCl_2$ instead of PTSA.

best yield at 68% (Table 1, entry 7) for the desired product **3a** and the polymer of styrene was the major byproduct.

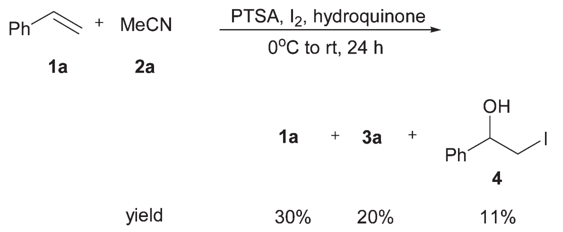
Investigating the effect of catalyst loading revealed that 10 mol% PTSA afforded the product in much lower yield and 25 mol% PTSA gave almost the same yield as 20 mol% (Table 1, entries 10 and 11). The studies on the reaction temperature showed that 0 °C to rt was optimal. The presence of 1.2 equiv of water in the reaction mixture gave the same result of using commercial reagent grade CH_3CN (Table 1, entry 12). The use of dichloromethane (DCM) as solvent led to a lower yield in 44% (Table 1, entry 13). Hence, the best conditions are shown in Table 1, entry 7.

The generality of this reaction was then examined and these results were listed in Table 2. The scope of the reaction disclosed herein appeared to be quite broad with regard to the nitrile partner, and a variety of nitriles were found to react with styrenes. Especially for acrylonitrile **2b**, a 90% yield of desired product **3b** was obtained. Moreover, the effect of substituents on the aromatic ring was also investigated. The corresponding product **3** was formed in moderate to good yields when the aromatic ring contained an electron-withdrawing group. However, the electron-rich vinylarenes reacted reluctantly (Table 2, entries 11–13), and the corresponding 2-iodo-1-arylethanol and polymer of aryl alkenes were collected as byproducts.

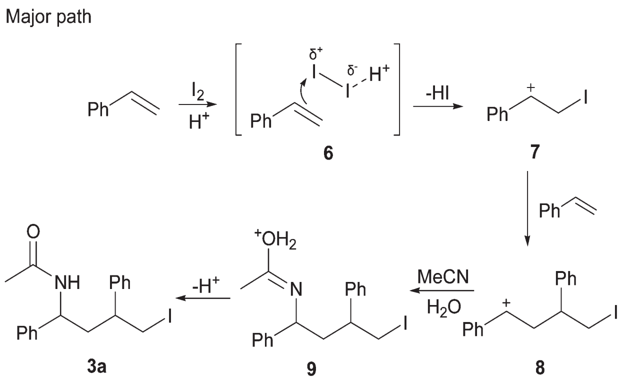
When TEMPO (1 mmol) was added in this reaction system, it was found that the yield of the desired product **3a** dropped to 5%



Scheme 1 Products of the reaction carried out in the presence of TEMPO.



Scheme 2 Products of the reaction carried out in the presence of hydroquinone.



Scheme 3 Proposed mechanism for the iodine mediated/Brønsted acid-catalyzed dimerization reaction.

along with the recovery of 15% of styrene **1a**. Other than compounds **4** and **5**, some unidentified products were also observed (Scheme 1). For the reaction in the presence of hydroquinone (1 mmol), the desired product **3a** was obtained in 20% yield with 30% of styrene recovered. Meanwhile, **4** and some unidentified compounds were also observed in the mixture (Scheme 2).

At the current stage, the precise reaction mechanism is not clear yet. It was tentatively proposed that the major reaction pathway might be initiated by an electrophilic halogenation reaction at a carbon–carbon double bond,[7] followed by a cationic dimerization to produce **8**, which was subsequently trapped by the solvent acetonitrile in a manner analogous to the Ritter reaction[8] to furnish the desired dimer **3a** (Scheme 3). In addition, the radical process might not be neglected, based on the control reaction results in Schemes 1 and 2.

Conclusions

We have developed a new iodine mediated and PTSA catalyzed head-to-tail dimerization reaction of vinylarenes, through which a series of functionalized products could be synthesized from readily available starting materials in one step. The preliminary results suggested that the major reaction pathway might be a combination of cationic dimerization and Ritter reaction for the domino process, while a competitive radical procedure might be involved also. Further studies towards a deeper insight into the reaction mechanism, substrate scope and the stereoselective synthesis are currently ongoing in our group.

Acknowledgements

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Notes and references

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5 CCDC 838337 (**3a**) contains the supplementary crystallographic data for this paper†.

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