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Ligand mediated iron catalyzed dimerization of terminal aryl alkynes: scope and limitations†‡

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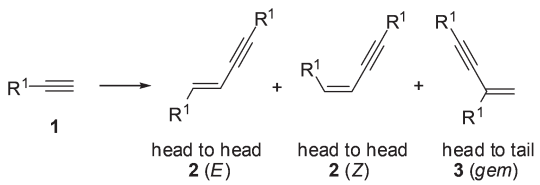
Regioselective dimerization of terminal aryl alkynes to produce conjugated enynes has been achieved using $FeCl_3$ and KO^{t}Bu in the presence of either DMEDA or dppe. The reaction proceeds smoothly in toluene at 145 °C for 2 h to give the corresponding head-to-head dimers in good to excellent yields (54 to 99%) with high *E*-selectivity (67 : 33 to 83 : 17 *E*/*Z*). Both strongly electron-donating and electron-withdrawing groups are compatible with this procedure. The bidentate phosphine (dppe) ligand exhibits better catalytic activity than the bidentate amine (DMEDA). The aliphatic acetylene fails to react under this catalytic system which suggests that potassium tertiary butoxide activates the conjugated system of aryl acetylene through cation–pi interaction and pi–pi interaction. A radical inhibitor (galvinoxyl or TEMPO) completely suppresses the reaction. Employing $FeCl_2$ as a catalyst instead of $FeCl_3$, only phenyl acetylene afforded the corresponding head to head dimer in good yield. Mechanistic pathways for both $FeCl_3$ catalyzed dimerization of aryl alkynes and $FeCl_2$ catalyzed dimerization of phenyl acetylene have been proposed.

Introduction

Conjugated enynes are the key structural unit in many natural and bioactive molecules, drug intermediates and organic materials.[1–3] Conjugated enynes can be used as precursors for the synthesis of polysubstituted benzenes[4] and stereospecific 1,3-dienes[5] and natural products.[6] Thus, the past few decades have witnessed substantial efforts in the direction of developing versatile strategies to synthesize the enyne synthons. Commonly used practical methods in the literature include alkynylation of alkene metal,[7] metal-catalyzed coupling between an alkene and an organometallic alkyne,[8] Sonogashira type coupling[9] between terminal alkyne and vinyl halide and the dimerization of terminal alkynes.[10–20] The synthesis of enynes by dimerization of terminal alkynes is a straightforward and an atom-economical[21] process (Scheme 1).

However, a highly selective synthesis of conjugated enynes by a dimerization is challenging due to the competitive formation of the other three possible (*E*), (*Z*), and *gem*-enyne isomers (Scheme 1).[10–20] Catalysts based on transition metals[10–17] (Zr,[10] Hf,[11] Re,[12] Ru,[13] Rh,[14] Ir,[15] Ni[16] and Pd[17]), lanthanides,[18] actinides[19] and main group elements[20] have been developed for the dimerization of terminal alkynes. Although these methods have been utilized extensively and effectively, some limitations exist because of the difficulties in synthesizing the organometallic substrates, toxicity and the recovery of expensive noble metal catalyst for an industrial scale preparation.



Scheme 1 Dimerization of terminal alkyne.

Recently iron-based catalytic systems have attracted significant growing interest because iron salts are readily available, inexpensive, and environmentally benign.[22–25] Iron salts have been used as important alternatives to established transition metal-catalyzed carbon–carbon and carbon–hetero atom bond formation reactions.[22–25] Realizing the importance of the enyne motif and its potential application we thought it would be useful if a protocol for the facile transformation of alkyne to enyne can be designed using the cheap iron salts as catalysts.

It is noteworthy that iron/copper promoted oxidative homocoupling reaction of terminal alkynes has been reported to give the corresponding diynes (Scheme 2, eqn (ii))[26] and an

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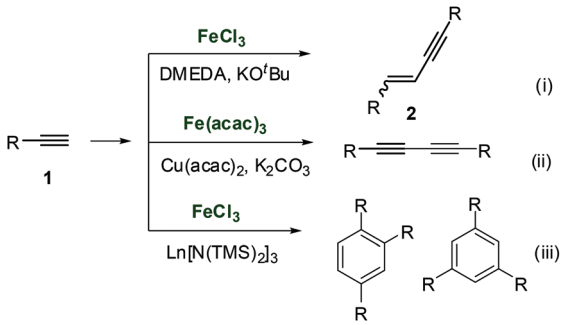
†This paper is dedicated to Professor Rabindranath Mukherjee on the occasion of his 60th birthday.

‡Electronic supplementary information (ESI) available: Analytical data and NMR spectra of all synthetic compounds. See DOI: 10.1039/c3ob42365d



Scheme 2 Dimerization and trimerization of terminal alkyne using iron salts.

iron salt/organolanthanide-based bimetallic catalytic system has been efficiently used for cyclotrimerization of terminal alkynes (Scheme 2, eqn (iii)).[27] We have recently presented the first report of an iron catalyzed highly regioselective protocol for the dimerization of terminal alkynes using N^1,N^2-dimethylethane-1,2-diamine (DMEDA) as a ligand in the presence of KO^{t}Bu (Scheme 2, eqn (i)).[28]

Recently Bolm and Buchwald reported that $FeCl_3$ catalyzed reactions may be influenced by trace amounts of copper impurities.[29] However, iron/copper promoted oxidative homo-coupling reaction of terminal alkynes has been reported to give the corresponding diynes (Scheme 2, eqn (ii)).[26] Herein we explore various aspects of this head to head dimerization of terminal aryl alkynes, from the effect of electronic and steric properties of ligands, to the scope and limitations to mechanistic manifolds.

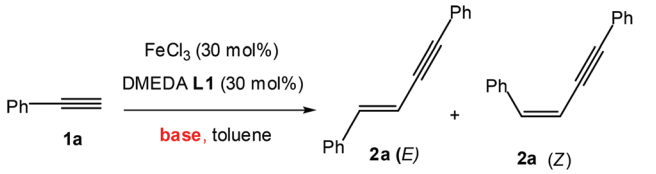
Results and discussion

In our previous work,[28] we employed 30 mol% of $FeCl_3$ in the presence of 30 mol% of DMEDA and 3 equivalents of KO^{t}Bu for the dimerization of terminal alkynes. The reaction was performed in toluene at 145 °C for 2 h (Table 1). To improve the yield and selectivity, it was decided to study the effect of bases first keeping other parameters fixed.

Screening of bases

Bases tend to affect the dimerization reactions to a major extent. In the absence of a base, no reaction took place (Table 1, entry 1). The use of cesium chloride dramatically improved the yield to 48% (entry 2) with a good selectivity (89 : 11). When potassium carbonate (K_2CO_3) was employed as the base, the reaction took even longer time (72 h) without an appreciable increase in yield of the dimers with decreased stereoselectivity (entry 3). Potassium phosphate (K_3PO_4) after 3 days gave *E*/*Z* selectivity comparable to that of the cesium carbonate (Cs_2CO_3); however, the yield of **2a** was very low (35%, entry 4). The reaction was sluggish in the presence of 3 equivalents of lithium tertiary butoxide (LiO^{t}Bu) and sodium tertiary butoxide (NaO^{t}Bu) (entries 5 and 6). Surprisingly, when 2 equivalents of potassium tertiary butoxide (KO^{t}Bu) were used

Table 1 Screening of bases for iron catalyzed dimerization of phenyl acetylene **1a**



Entry	Base (equiv.)	Temp. (°C), time (h)	Ratio[a] of **2a** (*E*/*Z*)	Yield[b] (%) of **2a** (*E*/*Z*)
1	No base	145, 48	No reaction	No base
2	Cs_2CO_3 (3)	145, 48	89 : 11	48
3	K_2CO_3 (3)	145, 72	67 : 33	50
4	K_3PO_4 (3)	145, 72	86 : 14	35
5	LiO^{t}Bu (3)	145, 2	Not determined	<5
6	NaO^{t}Bu (3)	145, 2	Not determined	<5
7	KO^{t}Bu (2)	145, 2	78 : 22	65
8	KO^{t}Bu (3)	145, 2	78 : 22	73
9	KO^{t}Bu (3)	65, 15	75 : 25	51
10	KO^{t}Bu (3)	145, 7	60 : 40	67
11	KO^{t}Bu (0.4)	145, 15	55 : 45	63
12	DABCO (3)	145, 72	No reaction	
13	Et_3N (3)	145, 72	No reaction	
14	Et_3N[c]	130, 72	No reaction	

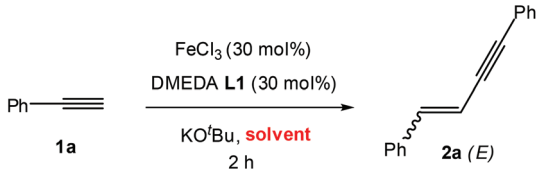
[a] *E* : *Z* ratios were determined by ^{1}H NMR analysis of the crude reaction mixture. [b] Isolated yields after chromatography. [c] Using Et_3N as a solvent.

(entry 7), within 2 hours the reaction afforded the dimer **2a** in moderately good yield (65%) with high selectivity (78 : 22). Use of 3 equivalents of KO^{t}Bu was then used to provide the dimer **2a** in good yield (73%) with identical selectivity (entry 8). However, when the reaction was carried out at lower temperature (65 °C), even after 15 h the yield could not reach up to the expectation, although the selectivity was still high (entry 9). After screening of different bases (entries 1–7), potassium *tert*-butoxide (3 equiv.) was found to be the most effective (entry 7). Our hypothesis to further increase the yield by keeping the reaction for a longer time failed, as both the yield and selectivity of product **2a** was decreased with further increase of the reaction time (entry 10). The reaction was found to proceed using 40 mol% KO^{t}Bu (entry 11) to give **2a** in 63% yield. No product was detected using nitrogen containing bases like DABCO (entry 12) and Et_3N (entries 13 and 14).

Solvent optimization

Different solvents were then screened with the aim of further improving the reaction outcome (Table 2). Solvents such as THF (entry 1), DMF (entry 2), DMSO (entry 3) and dioxane (entry 4) gave the desired product **2a** in low yields with moderate stereoselectivity, whereas no product was detected using CH_2Cl_2 (entry 5) and MeCN (entry 6). Among the studied aromatic solvents (entries 7–9), toluene gave the best results with facile dimerization of **1** with high yield and regioselectivity. Lower yield of the product **2a** was obtained using 1,2-dichlorobenzene (entry 8) and xylene (entry 9), albeit a nearly similar

Table 2 Screening of solvents for iron catalyzed dimerization of phenyl acetylene **1a**[a]



Entry	Solvent	Temp. (°C)	Ratio[a]	Yield[b] (%) of **2a** (*E*/*Z*)
1	THF	85	61 : 29	67
2	DMF	145	75 : 25	55
3	DMSO	145	74 : 26	50
4	Dioxane	145	72 : 28	45
5	CH_2Cl_2	85	No reaction	
6	MeCN	145	No reaction	
7	Toluene	145	78 : 22	73
8	1,2-Dichlorobenzene	145	76 : 24	65
9	Xylene	145	75 : 25	63
10	Neat	145	71 : 29	45

[a] *E* : *Z* ratios were determined by ^{1}H NMR analysis of a crude reaction mixture. [b] Isolated yields after chromatography.

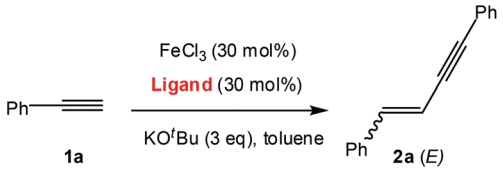
selectivity to toluene as a solvent. Under solvent free conditions the dimer **2a** was obtained in 45% yield (entry 10).

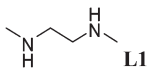
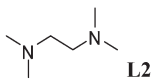
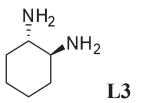
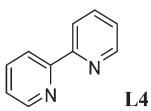
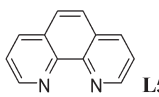
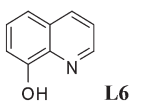
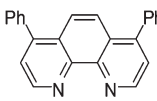
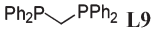
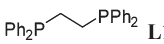
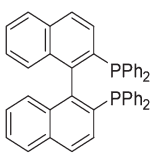
Choice of the ligand

With the aim of improving the reaction outcome, various ligands were examined in the iron catalyzed dimerization of phenyl acetylene (Table 3). Surprisingly only iron could drive the selectivity as in the absence of any ligand (entry 1, Table 3), an *E*-selective dimerization was observed with low yield (42%). We initially screened the nitrogen based ligands (entries 2–8). In all the cases, the use of bulkier ligands resulted in lower yields. When TMEDA (**L2**) was used instead of DMEDA (**L1**), the yield slightly decreased (60%). When a chiral ligand cyclohexane-1,2-diamine was used (**L3**), the selectivity was not at all affected, although the yield was slightly lower, possibly owing to its bulk (entry 4). The product **2a** was isolated in moderate yields when aromatic ligands such as 2,2′-bipyridine, **L4** (entry 5), and 1,10-phenanthroline, **L5** (entry 6), were used. We thought that perhaps the use of the aromatic ligand would facilitate the reaction as the reagents have aromatic rings. But unfortunately, the yield did not improve, rather it decreased even more, presumably because of its higher bulk. 8-Hydroxyquinoline, **L6**, gave compound **2a** with a slightly better selectivity (entry 7); however, the yield was very low (58%). Use of the bathophenanthroline ligand **L7** also failed to give good yield (entry 8). When triphenylphosphine, **L8**, was used as the ligand, the product was obtained in 50% yield with a slightly decreased selectivity (entry 9). Using the bidentate ligand 1,1-bis(diphenylphosphino)-methane (dppm) **L9**, the enyne was isolated in a good yield (85%). Notably, when the phosphene analogue of DMEDA, *i.e.* 1,1-bis(diphenylphosphino)ethane (dppe) **L10**, was used, the best reaction conditions were achieved with the highest yield (90%) and good selectivity (81 : 19).

When ligand bulk was increased by introducing 2,2′-bis-(diphenylphosphino)-1,1′-binaphthyl (BINAP) **L11**, the reaction

Table 3 Iron catalyzed dimerization of phenyl acetylene **1a** using different ligands[a]



Entry	Ligand (30 mol%)	Ratio[a] (*E*/*Z*)	Yield[b] (%) of **2a**
1	No ligand	77 : 23	42
2	 **L1**	78 : 22	73
3	 **L2**	75 : 25	60
4	 **L3**	77 : 23	68
5	 **L4**	75 : 25	45
6	 **L5**	76 : 24	43
7	 **L6**	83 : 17	58
8	 **L7**	77 : 23	60
9	PPh_3 **L8**	71 : 29	50
10	 **L9**	80 : 20	85
11	 **L10**	81 : 19	90
12	 **L11**	79 : 21	70

[a] Ratios were determined by ^{1}H NMR analysis of the unpurified reaction mixture. [b] Isolated yields after chromatography.

yield decreased. All the observations point to the following conclusions. (1) The ligand has a primary role in improving the yield. (2) The selectivity is primarily decided by the catalyst. On the basis of selectivity, reaction times and yields, the best result was achieved using 30 mol% $FeCl_3$, 30 mol% dppe, and 3 equiv. of KO^{t}Bu in toluene at 145 °C for 2 h.

Substrate scope and limitations

We found that a series of aryl acetylenes **1** smoothly underwent dimerization to produce the head-to-head dimers **2** in good to excellent yield (Table 4). Both strongly electron-donating and electron-withdrawing groups were compatible with this procedure. The yields of the dimerization ranged from 54 to 99% and the ratio of *E* and *Z* head-to-head dimers varied from 67 : 33 to 83 : 17 in favor of *E* isomer. Whenever the yields were compared in the presence of DMEDA (**L1**) and dppe (**L10**), the yield was the same or higher for **L10** over **L1**. For example, the dimerization of 4-fluorophenylacetylene **1b** in toluene gave a 67 : 33 mixture of the *E* and *Z* head-to-head dimers in the presence of **L1** with 71% yield (entry 4), whereas in the presence of **L10**, the yield improved to 80% (entry 5). The 4-bromo phenylacetylene **1c** was successfully reacted under the effect of DMEDA (**L1**) conditions (entry 7) to give the corresponding product **2c** in 67% yield. When dimerization of aryl acetylene **1d** was carried out in the absence of the ligand, the corresponding product **2d** was obtained in 29% yield as a nearly 1 : 1 ratio of *E*/*Z* isomers (data not shown in the table),[28] while in the presence of ligand **L1** (entry 8), the product **2d** was obtained in an improved yield (55%) and selectivity (*E*/*Z* = 67 : 33). And when ligand **L10** was used, the reaction yield even improved (60%, entry 9), which confirms the key role of the ligand in iron catalyzed dimerization.

When *m*-fluoro **1e** was employed (entry 11) under the same conditions, the dimer **2e** was obtained in moderate yield (55%). The product **2e** was obtained in improved yield (65%), when ligand **L10** was used instead of **L1** (entry 12). But 1-ethynyl-3,5-difluorobenzene (**1f**) was converted to the corresponding dimers with a slightly higher yield (59%) than the *meta* derivative **1e** with an *E*/*Z* ratio of 3 : 1 in the presence of **L1** (entry 13). When ligand **L1** was employed, the *ortho* fluoro derivative **1g** furnished good yield (65%) of the dimerized product **2g** (entry 14). The order was 4-fluoro > 4-bromo > 2-fluoro > 3,5-difluoro > 3-fluoro. The orthotrifluoromethyl derivative **1h** gave the corresponding dimer in moderate yield (54%, entry 15).

Then a set of methyl substituents were analyzed under the dimerization conditions to get further insight into the reaction. Methyl derivative at *para* positions of phenyl acetylenes **1i** accelerated the reaction (entries 16 and 17) as evidenced by quantitative yield (99%) irrespective of the ligands. The *meta* analogue **1j** resulted in the corresponding dimer in moderate yield (73%) in the presence of **L1** (entry 18). So, the order is 4-methyl > 3-methyl. However, a reduced yield (57–58%) was observed with the *tert*-butyl group at the *para* position of phenyl acetylene (**1k**) with a similar 2 : 1 stereoselectivity in the presence of either **L1** or **L10** (entries 19 and 20).

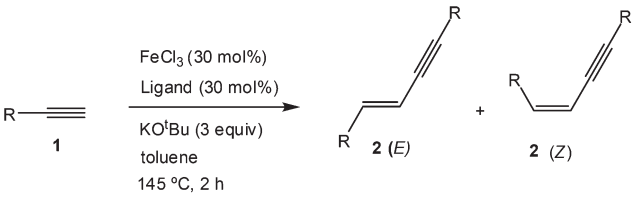
The *para* SMe substituted phenyl acetylene **1l** afforded lower yield (60%) of the corresponding dimers **2l** in the presence of **L1** (entry 21); however, the yield improved (68%) upon employing **L10** (entry 22). The methoxy substituent behaved similar to that of the methyl substituted derivatives. 4-Methoxy phenylacetylenes **1m** furnished the corresponding dimer **2m** in near quantitative yield (*E*/*Z* = 2.5 : 1, entries 23 and 24). Its *ortho* analogue **1o** also resulted in the dimer **2o** with a high yield (entries 28 and 29). For *para* and *ortho* methoxy derivatives, the yields were similar for both the ligands. However, when the *meta* derivative **1n** was employed, the yield was reduced dramatically to 57% in the presence of **L1** (entry 25). The yield was improved to 63% using **L10** (entry 26). The yield in the case of 3,5-dimethoxy derivative **1p** (entry 30) was lower than that of the 3,5-difluoro derivative **1f** in the presence of **L1** (entry 13). So, for the methoxy family, the order is 4-methoxy > 2-methoxy ≫ 3-methoxy > 3,5-dimethoxy. The *para* SMe substituted phenyl acetylene **1l** afforded a lower yield (60%) of the corresponding dimers **2l** in the presence of **L1** (entry 21); however, the yield improved (68%) upon employing **L10** (entry 22).

The reaction of 2-ethynyl-6-methoxynaphthalene (**1q**) afforded the desired products in 65% yield with high selectivity (entry 31). Similarly, bulky alkyne 9-ethynylanthracene **1r** reacted to afford the enynes in moderate yield (57%) and decreased selectivity (entry 32). Notably, 4-*N*,*N*-dimethyl derivative **1s** did not proceed when **L1** was employed (entry 33); however, it went smoothly in the presence of ligand **L10** to give moderate yield (56%, entry 34). Heteroaromatic thiophene alkyne **1t** in the presence of ligand **L10** gave moderate yield with high *E* selectivity (entry 35). The reaction of ester **1u** (entry 36) and the amide **1v** (entry 37) at the *para* position did not take place in the presence of either of the ligands. Most surprisingly, under the reaction conditions employed, aliphatic alkyne **1w** did not yield the corresponding dimer at all (entry 38). When iron(II) chloride was employed as a catalyst instead of iron(III) chloride, only phenyl acetylene reacted to give the dimer in acceptable yields (Table 4, entry 3). Interestingly, none of the phenyl acetylene derivatives **1** could successfully undergo the dimerization reaction using $FeCl_2$ either using **L1** or **L2**. Since the result was independent of the type of the group, *i.e.* electron donating or withdrawing, the above phenomenon was solely attributed to the steric factor. Notably, the phosphene ligand dppe **L10** proved to be more effective than DMEDA **L1**, even for the iron(II) chloride catalyst. The phenyl acetylene derivatives could undergo dimerization reaction in the presence of dppe as the ligand, although the yield was low (10–23%, entries 6, 10, and 27).

Radical quenching experiment

When 0.5 equiv. of galvinoxyl (radical inhibitor) was added to the reaction system, the yield of **2a** significantly dropped to 30% (Table 5, entry 1). The reaction completely stopped in the presence of 1 equiv. of galvinoxyl (entry 2). Similarly in the presence of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO), no dimer **2a** was isolated (entry 3). These results indicate that the

Table 4 Iron catalyzed dimerization of aryl acetylenes **1**[a]



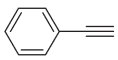
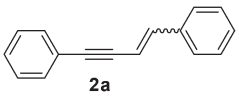
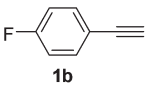
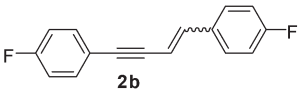
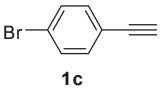
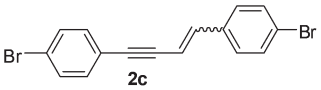
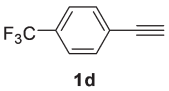
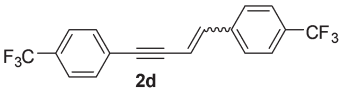
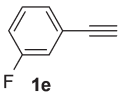
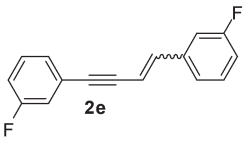
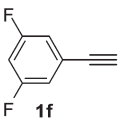
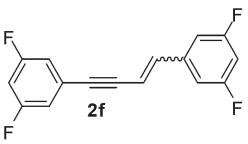
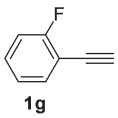
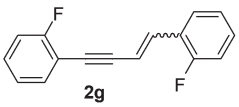
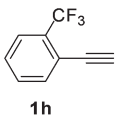
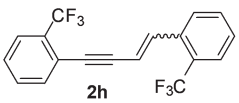
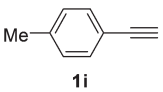
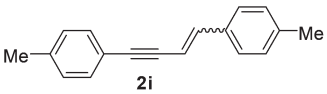
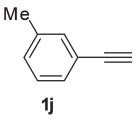
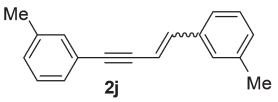
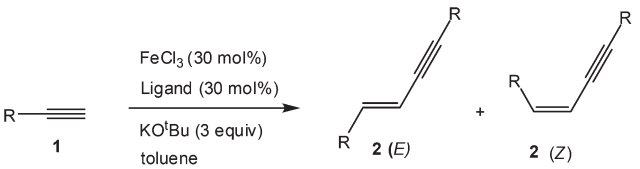
Entry	Alkyne **1a**	Product	Yield[a] (%), *E*/*Z*[b]
1 2 3	 **1a**	 **2a**	**L1**, 73% yield, 78 : 22 *E*/*Z* **L10**, 90% yield, 81 : 19 *E*/*Z* **L1**, 63% yield, 67 : 33 *E*/*Z*[c]
4 5 6	 **1b**	 **2b**	**L1**, 71% yield, 67 : 33 *E*/*Z* **L10**, 80% yield, 71 : 29 *E*/*Z* **L10**, 20% yield, 71 : 29 *E*/*Z*[c]
7	 **1c**	 **2c**	**L1**, 67% yield, 67 : 33 *E*/*Z*
8 9 10	 **1d**	 **2d**	**L1**, 55% yield, 67 : 33 *E*/*Z* **L10**, 60% yield, 70 : 30 *E*/*Z* **L10**, 10% yield, 70 : 30 *E*/*Z*[c]
11 12	 **1e**	 **2e**	**L1**, 55% yield, 73 : 27 *E*/*Z* **L10**, 65% yield, 73 : 27 *E*/*Z*
13	 **1f**	 **2f**	**L1**, 59% yield, 75 : 25 *E*/*Z*
14	 **1g**	 **2g**	**L1**, 65% yield, 83 : 17 *E*/*Z*
15	 **1h**	 **2h**	**L1**, 54% yield, 68 : 32 *E*/*Z*
16 17	 **1i**	 **2i**	**L1**, 99% yield, 73 : 27 *E*/*Z* **L1**, 99% yield, 73 : 27 *E*/*Z*
18	 **1j**	 **2j**	**L1**, 73% yield, 67 : 33 *E*/*Z*

Table 4 *(Contd.)*



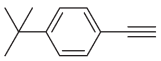
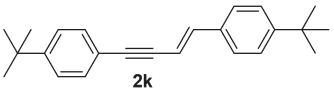
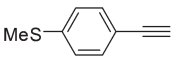
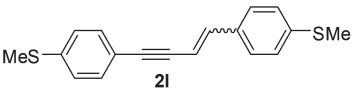
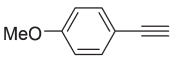
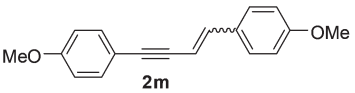
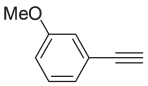
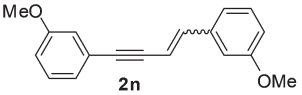
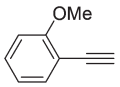
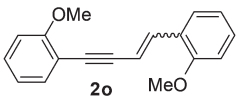
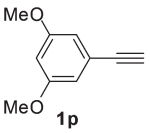
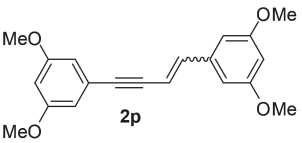
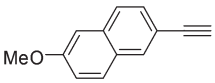
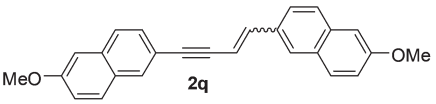
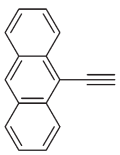
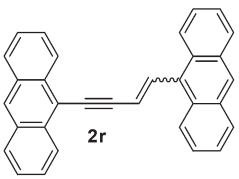
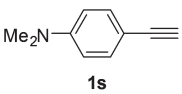
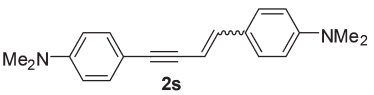
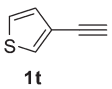
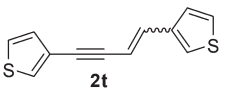
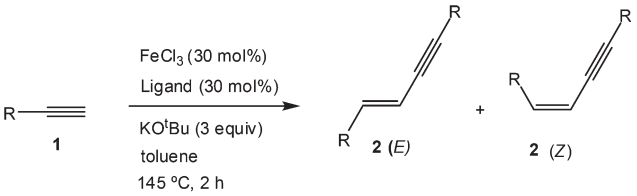
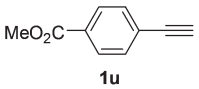
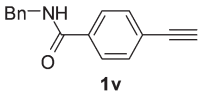
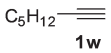
Entry	Alkyne **1a**	Product	Yield[a] (%), *E*/*Z*[b]
19 20	 **1k**	 **2k**	**L1**, 57% yield, 73 : 27, *E*/*Z* **L10**, 58% yield, 75 : 25 *E*/*Z*
21 22	 **1l**	 **2l**	**L1**, 60% yield, 75 : 25 *E*/*Z* **L10**, 68% yield, 77 : 23 *E*/*Z*
23 24	 **1m**	 **2m**	**L1**, 97% yield, 70 : 30 *E*/*Z* **L10**, 98% yield, 75 : 25 *E*/*Z*
25 26 27	 **1n**	 **2n**	**L1**, 57% yield, 75 : 25, *E*/*Z* **L10**, 63% yield, 77 : 23, *E*/*Z* **L10**, 23% yield, 75 : 25, *E*/*Z*
28 29	 **1o**	 **2o**	**L1**, 91% yield, 71 : 29, *E*/*Z* **L10**, 93% yield, 75 : 25, *E*/*Z*
30	 **1p**	 **2p**	**L1**, 55% yield, 78 : 22 *E*/*Z*
31	 **1q**	 **2q**	**L1**, 65% yield, 78 : 22 *E*/*Z*
32	 **1r**	 **2r**	**L1**, 57% yield, 69 : 31 *E*/*Z*
33 34	 **1s**	 **2s**	**L1**, no reaction **L10**, 56% yield, 77 : 28 *E*/*Z*
35	 **1t**	 **2t**	**L10**, 57% yield, 71 : 29 *E*/*Z*

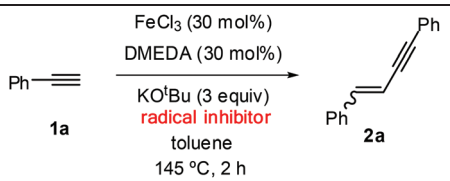
Table 4 *(Contd.)*



Entry	Alkyne **1a**	Product	Yield[a] (%), E/Z[b]
36	 **1u**	No reaction	
37	 **1v**	No reaction	
38	 **1w**	No reaction	

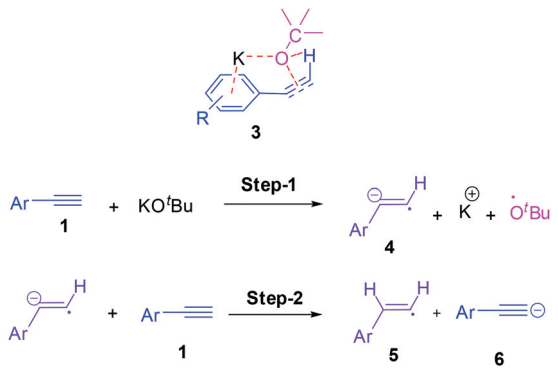
[a] Ratios were determined by ^{1}H NMR analysis of unpurified reaction mixture. [b] Isolated yields after chromatography. [c] Using $FeCl_2$ (99.99%) as the catalyst.

Table 5 Effect of radical inhibitor



Entry	Additive/equiv.	Ratio of **2**[a] (E/Z)	Yield (%) of **2**[b]
1	Galvinoxyl/0.5	77 : 23	30
2	Galvinoxyl/1		No reaction
3	Tempo/1		No reaction

[a] Ratios were determined by ^{1}H NMR analysis of the unpurified reaction mixture. [b] Isolated yields after chromatography.

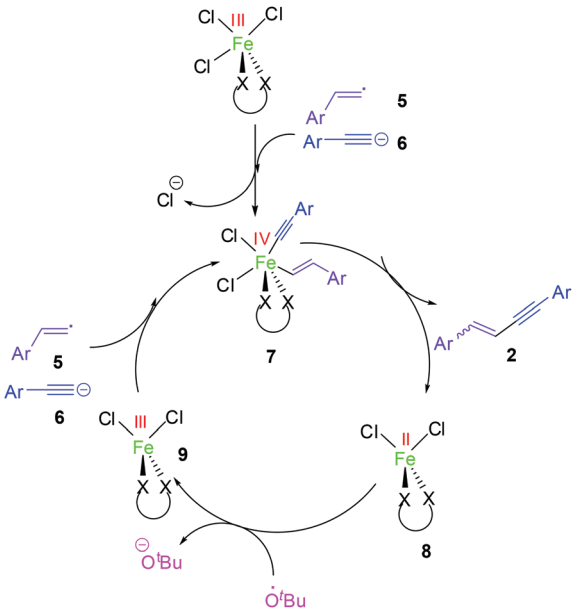


Scheme 3 First two steps of the iron dimerization reaction.

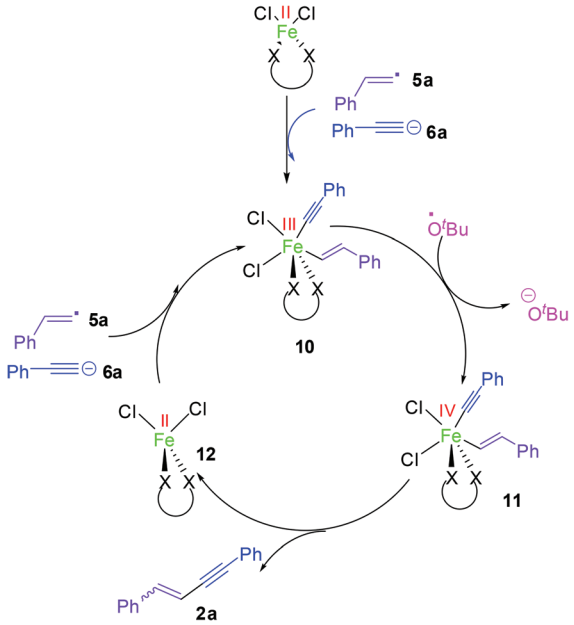
radical process may be a possible pathway in this reaction, unlike the protocol reported previously by others in the presence of other catalysts. On the basis of all the above observations, a plausible mechanism is proposed.

Mechanism

We propose that the potassium tertiary butoxide interacts with the conjugated system of aryl acetylene through cation–pi interaction and pi–pi interaction as shown in the transition state **3** to promote the reactivity of the inactive aryl acetylene (Scheme 3). Subsequently, the increased reactivity of the transition state **3** results in two important species, one tertiary butoxide radical and another radical anion **4**. The radical anion **4** then reacts with the second molecule of aryl acetylene **1** and abstracts the acidic hydrogen to give the corresponding alkene radical **5** and the aryl acetylide **6** (Scheme 3). The reaction yields employing bases of similar structures validate the formation of transition state **3** (Table 1). In addition to potassium tertiary butoxide, potassium carbonate (K–O–), cesium carbonate (Cs–O–) and potassium phosphate (K–O–) also proceed through the mechanism to give the corresponding product. So, bases sharing bond connectivity similar to potassium tertiary butoxide undergo the reaction. Notably, NaO^{t}Bu and LiO^{t}Bu did not yield anything, which can be explained as follows. Both the phenyl acetylene and toluene have an aromatic ring; however, toluene being the solvent molecule has a much higher probability of forming cation–pi interaction with the cations. Smaller cations such as lithium and sodium have the highest efficiency of forming cation–pi interaction;[30] also they are most easily solvated. So, the interplay between cation–pi interaction energy and desolvation energy decides the most effective catalyst among all. The high desolvation energy restricts their binding to the benzene ring of the phenyl acetylene, which explains the inability of the tertiary butoxide salt of lithium and sodium to push the reaction forward. Organic



Scheme 4 Iron(III) cycle for the dimerization of aryl acetylene.



Scheme 5 Iron(II) cycle for the dimerization of phenyl acetylene **1a**.

bases having structures different from the above class like DABCO and Et_3N did not yield anything.

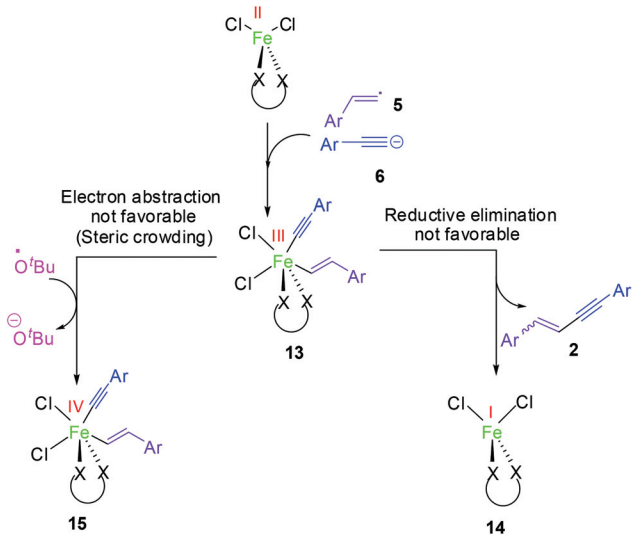
Notably, only aryl acetylene gave the enyne product and the aliphatic acetylene did not. We think that the transition state **3** solely decides which reactant to favor. As the observations suggest, the cation–pi interaction plays an important role in stabilizing the transition state. In the case of aliphatic acetylene, the cation–pi interaction is absent, which then inhibits further progress of the reaction.

In the presence of iron(III) chloride, the outcome of Step 2, *i.e.* the alkene radical **5** and aryl acetylide **6** attack to form the reactive species **7** (Scheme 4). Subsequently, this tetravalent hexacoordinated species **7** undergoes reductive elimination to give the Fe(II) species **8** and the desired enyne product **2**. The tertiary butoxide radical further abstracts an electron from the divalent iron center **8** to generate the corresponding Fe(III) species **9** and the alkene radical **5**. The aryl acetylide **6** then attacks the tetra-coordinated species **9** regenerating **7** to complete the cycle. The yield is based on the hypothesis that more the nucleophilicity of the acetylide, more the probability of attacking the Fe(III) center to regenerate the catalyst, and hence the better is the yield. So, in accordance with our proposition, phenyl acetylene bearing *ortho* or *para* electron donating groups almost gives the corresponding product in a quantitative amount. The phosphene ligand gave better results for alkyne containing electron withdrawing groups, which also corroborates our hypothesis. Electron withdrawing groups at *ortho* and *para* positions decrease its ability to attack and coordinate to the metal center. The strong pi-acceptor ligand dppe compensates for it. Being attached to the metal center, it increases the effective local charge (oxidation state) of the metal, to which the radical **5** and anion **6** components containing electron withdrawing groups at *ortho* and *para* positions can efficiently attack, and the better is the yield. Thus, the ligand plays a crucial role in carrying out the reaction.

The inability of iron(II) chloride to dimerize derivatives of phenyl acetylene also fits our model (Scheme 5). In the case of Fe(II) chloride, the alkene radical **5a** and the aryl acetylide **6a** attack to form the Fe(III) species **10**. The generated tertiary butoxide radical subsequently abstracts an electron from the Fe(III) species **10**, thus resulting in the formation of the tetravalent iron species **11**. Reductive elimination from **11** gives the enyne product **2a**. The alkene radical **5a** and aryl acetylide **6a** subsequently attacks the tetra-coordinated species regenerating **10** to complete the cycle.

Then the question arises: why does only phenyl acetylene give the enyne product in the presence of $FeCl_2$ but its derivatives do not? The answer behind this is the steric crowding. In the case of the Fe(III) catalytic cycle (Scheme 4) the tertiary butoxide radical abstracts an electron from a tetra-coordinated species **8**, whereas in the case of the Fe(II) catalytic cycle the tertiary butoxide radical has to abstract the electron from a hexacoordinated species **10** (Scheme 5).

Whenever we employ phenyl acetylene derivatives (Scheme 6), we effectively increase the steric bulk of the complex (irrespective of the electron donating or withdrawing groups), which makes it even more difficult or impossible for the tertiary butoxide radical to abstract the electron from **13** to form **15**. As a result, the Fe(II) species interacts with the alkene radical to generate a Fe(III) species **13**, which on reductive elimination has to form a Fe(I) species **14**, which is neither stable nor favorable. When the phosphene ligand was used instead of DMEDA, low yield was observed. In the case of dppe **L10**, either the alkene radical or aryl acetylide interacts with the benzene ring of the ligand *via* weak pi–pi stacking, which brings either of the groups closer to the ligand, finally



Scheme 6 Schematic diagram for the two unlikely options for the dimerization of phenyl acetylene derivatives in the iron(II) cycle.

resulting in the availability of space for tertiary butoxide radical to attack the Fe center and abstract the electron. As a result, the reaction proceeds, but with a low yield.

Conclusions

In summary, we have described novel iron catalyzed regio- and stereoselective dimerization of terminal aryl alkynes to give the corresponding head-to-head dimers in moderate to excellent yields. Phenyl acetylene bearing *ortho* or *para* electron donating groups almost gave the corresponding product in quantitative yield. Mechanistic evidence suggests that the transformation proceeds through the activation of aryl acetylene *via* cation–pi interaction and pi–pi interaction with potassium tertiary butoxide to produce alkene radical and aryl acetylide. In the presence of iron(III) chloride, the alkene radical and aryl acetylide attacks to form the reactive tetravalent hexacoordinated species which then undergoes reductive elimination to give the desired enyne product **2**. Notably, the phosphene analogue dppe gave marginally better results as compared to DMEDA. We further identified that $FeCl_2$ could only promote the dimerization of phenyl acetylene. This novel catalytic system provides an alternative to toxic and expensive transition metals for a variety of conjugated enyne compounds.

Experimental

General information

All experiments were carried out under an inert atmosphere of argon in flame-dried microwave vials. Solvents were dried using standard procedures. Starting materials were obtained from commercial suppliers and used as received. Products were purified by flash chromatography on silica gel (100–200 mesh). NMR spectra were recorded in $CDCl_3$. ^1H NMR spectra were recorded at 500 MHz and 400 MHz instruments at 278 K. Signals are quoted as δ values in ppm using residual protonated solvent signals as the internal standard ($CDCl_3$: δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a JEOL-400 (100 MHz) or a Brüker AVANCE 500 MHz (125 MHz) with complete proton decoupling. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane with the solvent as the internal reference ($CDCl_3$: δ 77.26 ppm). Infrared (FTIR) spectra were recorded by the KBr disk and KBr plate techniques for solid and liquid samples, ν_{max} cm^{-1}. HRMS analyses were performed by +ve mode electrospray ionization.

General procedure for dimerization of aryl acetylenes 1

To a 10 mL oven dried microwave vial were added KO^{t}Bu (3 equiv.), anhydrous toluene (4 mL $mmol^{-1}$) and anhydrous $FeCl_3$ (0.3 equiv.). Then, the resulting mixture was submitted to argon/vacuum cycles stirring under an atmosphere of argon. Subsequently DMEDA **L1** (0.3 equiv.) or dppe **L10** (0.3 equiv.) followed by aryl acetylene **1** (1 equiv.) were added. Then, the resulting mixture was stirred at 145 °C for 2 h. After cooling, the solvent was evaporated and the crude residue was purified by flash column chromatography on silica gel using distilled *n*-hexanes–EtOAc (100 : 0 to 90 : 10) as an eluent to give the desired enynes **2**. The ^1H and ^{13}C NMR spectroscopic data of the enyne compounds **2a–g**,[28] **2h**,[13b] **2i–j**,[28] **2k** (*E*),[13f] **2k** (*Z*),[31] **2m–2q**,[28] **2r** (*E*),[17d] **2r** (*Z*),[32] **2s** (*E*),[14b] **2s** (*Z*),[31] **2t** (*E*),[17i] and **2t** (*Z*)[18d] matched with those reported in the literature (see ESI‡).

(4,4′-(But-1-en-3-yne-1,4-diyl)bis(4,1-phenylene))bis (methylsulfane) 2l

Light yellow oil; ESI-MS: calcd for $C_{18}H_{16}S_2$ $[M]^+$: 296.0693; found, 296.0767. (*E*)-isomer (**2l**): FT-IR (neat): 3401, 3016, 2925, 2853, 2395, 2193, 1934, 1607, 1581, 1486, 1268, 1178, 1152, 1075; ^1H NMR (400 MHz): 7.38–7.32 (m, 4H), 7.21–7.17 (m, 4H), 6.97 (d, J = 15.9 Hz, 1H), 6.33 (d, J = 16.5 Hz, 1H), 2.49 (s, 6H); ^{13}C NMR (100 MHz): 140.4, 139.3, 139.2, 133.1, 131.7, 126.6, 126.3, 125.8, 119.6, 107.2, 91.7, 89.1. (*Z*)-isomer (**2l**): data from a mixture of *E*/*Z* = 84 : 16; ^1H NMR (400 MHz): δ = 7.85 (d, J = 8.5 Hz, 2H), 7.41–7.33 (m, 2H, merged with *trans* isomer), 7.23–7.17 (m, 4H, merged with *trans* isomer), 6.63 (d, J = 12.2 Hz, 1H), 5.86 (d, J = 11.6 Hz, 1H), 2.51, (s, 3H), 2.50 (s, 3H).

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