Pergamon

Tetrahedron Letters 43 (2002) 3041–3044

TETRAHEDRON
LETTERS

Cycloaddition of styrene derivatives with quinone catalyzed by ferric ion; remarkable acceleration in an ionic liquid solvent system

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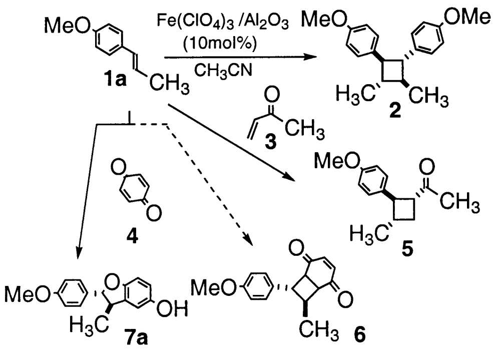
Received 22 January 2002; revised 20 February 2002; accepted 22 February 2002

Abstract—Ferric ion-catalyzed cycloaddition of styrene derivatives with quinone gave 2,3-dihydrobenzofuran derivatives in excellent yields with *trans* selectivity; remarkable acceleration was observed when the reaction was carried out in an ionic liquid solvent system. © 2002 Elsevier Science Ltd. All rights reserved.

Iron is recognized as an economical and pollution free metal source, however, iron-catalyzed reaction has been only limited.[1] Recently, we demonstrated that alumina supported iron(III) perchlorate ($Fe(ClO_4)_3$)[2] catalyzed [2+2]cycloaddition of (*trans*)-anethol (**1**) and gave the corresponding cyclobutane **2** in an excellent yield (Scheme 1).[2] Because the reaction was believed to have been caused by one-electron oxidation mediated by an iron(III) cation,[3] we further investigated the possibility of the cross coupling reaction of (*trans*)-anethol (**1**) with methyl vinyl ketone (**3**); the desired [2+2]cross coupling product **5** was obtained, however, it was unsuccessful in improving the chemical efficiency (Scheme 1). On the other hand, the cross coupling reaction of **1** with 1,4-benzoquinone **4** proceeded smoothly and the cycloaddition product was obtained in an excellent yield (>90%), although the compound was unprecedented 2,3-dihydrobenzofuran derivative **7a**[4,5] and none of the [2+2]cycloaddition product **6** was obtained (Scheme 1). Further study showed that this reaction was greatly accelerated when carried out in an ionic liquid[6] solvent system. Here, we report that efficient synthesis of 2,3-dihydrobenzofuran derivatives is accomplished using an iron(III) cation, which is derived from iron(II) tetrafluoroborate ($Fe(BF_4)_2$) in situ by the reaction of styrene derivatives with 1,4-benzoquinone in butylmethylimmidazolium hexafluorophosphate ($[bmim]PF_6$)[7] as solvent with excellent stereoselectivity.



Scheme 1.

First, we evaluated the reaction of anethol **1a** and 1,4-benzoquinone **4** with 3 mol% of alumina-supported $Fe(ClO_4)_3$[2] in acetonitrile (CH_3CN) at rt; the results are summarized in Table 1. 2,3-Dihydrobenzofuran **7a** was obtained with high *trans* selectivity (*trans*:*cis* = 13:1)[8] in 93% yield (entry 1 in Table 1). It was reported that the same compound **7a** was obtained in 68% yield by a Lewis acid-promoted reaction of (*E*)-**1a** with **4**, but an excess amount (1.2 equivalent) of Ti(IV) salt (a mixture of $TiCl_4$:$Ti(OiPr)_4$ = 1.8:1) was necessary for the reaction.[4,5] In the present reaction, the same compound was obtained through a truly catalytic reaction using $Fe(ClO_4)_3$. Interestingly, cycloadduct (*trans*)-**7a** was obtained when (*Z*)-**1a** was subjected to the reaction, though both the chemical and reaction rates dropped significantly (entry 2). Styrene derivative **1b** gave the corresponding cycloadducts **7b** with a moderate chemical yield (entry 3). Styrene derivatives **1c** and **1d** which

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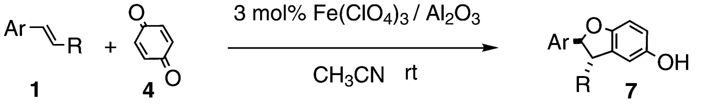
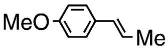
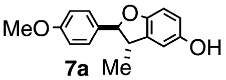
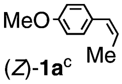
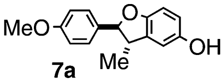
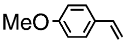
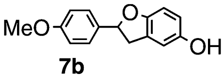
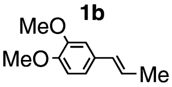
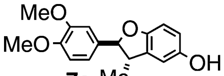
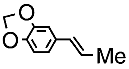
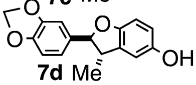
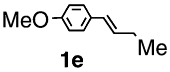
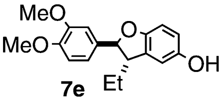
PII: S0040-4039(02)00405-7

Table 1. Results of cycloaddition of styrene derivatives with 1,4-benzoquinone

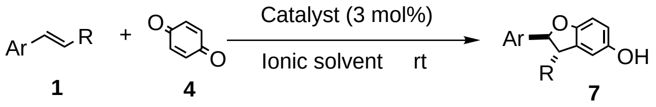


(1)

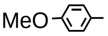
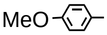
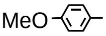
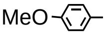
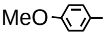
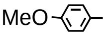
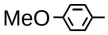
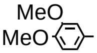
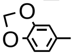
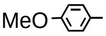
Entry	Substrate	Time / h	Product	Yield / %[a] (*trans*:*cis*)[b]
1	 (*E*)-**1a**	2.5	 **7a**	93% (13:1)
2	 (*Z*)-**1a**[c]	24	 **7a**	33% (14:1)
3	 **1b**	2.5	 **7b**	52%
4	 **1c**	4	 **7c**	94% (8:1)
5	 **1d**	4	 **7d**	91% (30:1)
6	 **1e**	2	 **7e**	80% (18:1)

[a] Isolated yield. [b] Determined by ^1H NMR analysis. [c] 83% purity.

Table 2. Iron salt-catalyzed cycloaddition in the ionic liquid solvent



(2)

Entry	**1** Ar	**1** R	Catalyst	Solvent	Time	**7** Yield/ %[a]	**7** *trans*/*cis*
1		Me	$Fe(ClO_4)_3/Al_2O_3$	$[bmim]PF_6$	**10 min**	90	15:1
2		Me	$FeCl_3$	$[bmim]PF_6$	**10 min**	91	11:1
3		Me	$FeCl_2$	$[bmim]PF_6$	4 h	94	12:1
4		Me	$FeSO_4\cdot 7H_2O$	$[bmim]PF_6$	24 h	0	---
5		Me	$Fe(BF_4)_2\cdot 6H_2O$	$[bmim]PF_6$	**10 min**	98	11:1
6		Me	$Fe(BF_4)_2\cdot 6H_2O$	$[bmim]BF_4$	3 h	68	43:1
7		Me	$Fe(BF_4)_2\cdot 6H_2O$	[bmim]OTf	24 h	0	---
8		Me	$Fe(BF_4)_2\cdot 6H_2O$	$[bmim]PF_6$	**3 min**	98	8:1
9		Me	$Fe(BF_4)_2\cdot 6H_2O$	$[bmim]PF_6$	**10 min**	86	20:1
10		Et	$Fe(BF_4)_2\cdot 6H_2O$	$[bmim]PF_6$	**10 min**	63	8:1

[a] Isolated yield.

have electron rich substituents gave the cycloadduct **7c** and **7d** with excellent yields of 94 and 91%, respectively (entries 4 and 5).

The working hypothesis of the present reaction is illustrated in Fig. 1. The Fe^{3+} ion oxidized styrene **1a** to form radical cation species **1a*** and Fe^{2+} ion, which is oxidized by quinone **4** to regenerate Fe^{3+} ion with radical anion **4***, and the catalytic cycle is completed as shown in Fig. 1; cycloadduct **7a** is thus obtained by the result of rearrangement of [2+2]cycloadduct **6a*** (Path A)[9] or [2+3]cycloaddition of **1a*** with **4*** through **6a**** (Path B).

It was anticipated that the cycloaddition reaction could proceed more rapidly in a polar solvent system if cycloadduct **7a** was produced through the reaction pathway, as illustrated in Fig. 1. Ionic liquids are a new class of solvents which have attracted growing interest over the past few years due to their unique physical and chemical properties.[6] We therefore next investigated the reaction in the ionic liquid solvent system (Table 2).[10] A remarkable acceleration was obtained when the reaction was carried out in [bmim]PF_6 and desired cycloadduct **7a** was obtained by only 10 min reaction with excellent yield (entry 1), while it took several hours to complete the same reaction if the reaction was carried out in CH_3CN solvent. Investigation to switch the counter anion part of the catalyst gave interesting results; iron(III) chloride also catalyzed the reaction very successfully (entry 2), and even iron(II) dichloride worked very well as catalyst (entry 3). However, iron(II) sulfate ($FeSO_4$) provided no cycloadduct compound (entry 4). We finally found that iron(II) tetrafluoroborate ($Fe(BF_4)_2$) was the best catalyst in this reaction; the desired compound **7a** was obtained in 98% yield after just 10 min reaction (entry 5).

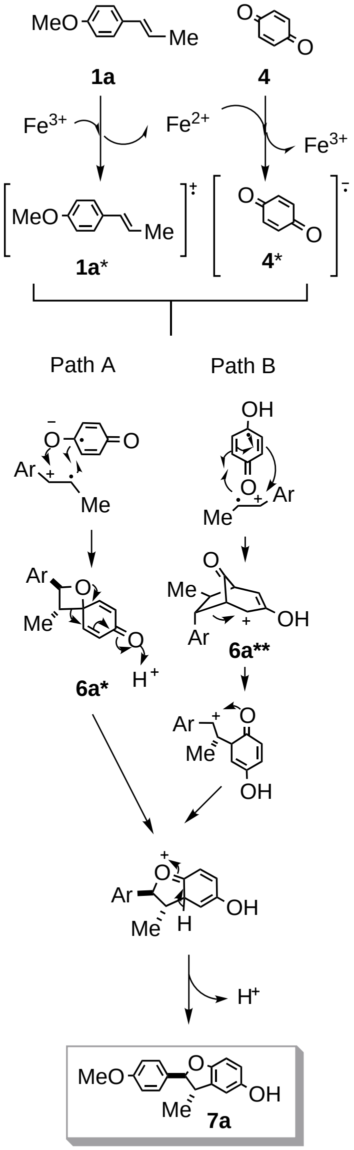


Figure 1. Working hypothesis of the present reaction.

It was suspected that the reaction was promoted by the acid. In fact, benzofuran **7a** was obtained in ca. 80% yield when the reaction was carried out in an acidified [bmim]PF_6 by partial hydrolysis with water, while no product **7a** was obtained in pure [bmim]PF_6 solvent without catalyst. It is well known that iron(II) cation is oxidized easily by quinone to generate an iron(III) cation; we therefore believe that the initial step of the cycloaddition reaction might be initiated by a one-electron oxidation of anethol **1**, as hypothesized in Fig. 1.[11] We were then interested in the proper combination of the counter anion of ionic liquid solvent with [bmim] cation using $Fe(BF_4)_2$ as catalyst, and found that the reaction rate was strongly dependent on the anionic part of the immidazolium salt. The best results were recorded when [bmim]PF_6 was employed as solvent (entry 7); a significant drop in the reaction rate was obtained when the reaction was carried out in [bmim]BF_4[12] (entry 6), and no product was obtained in [bmim]OTf[13] (entry 7). It should be emphasized that very rapid reaction was accomplished in the [bmim]PF_6 solvent system; desired cycloadducts **7c**, **7d**, and **7e** were obtained in good yield only by 3–10 min reactions (entries 8–10).[14]

In conclusion, we demonstrated that $Fe(BF_4)_2$-catalyzed cycloaddition of styrene derivatives **1** with 1,4-benzoquinone **4** in [bmim]PF_6 solvent afforded 2,3-dihydrobenzofuran derivatives **7** in excellent yields. This is not only the least recorded amount of catalyst but also the record of extremely rapid reaction in this type of reaction. Further determination of the scope and limitations of this reaction will make it even more beneficial.

Acknowledgements

This research was supported by a Grant-in-Aid for Scientific Research on Priority Areas (A) 'Exploitation of Multi-Element Cyclic Molecules' from the Ministry of Education, Culture, Sports, Science and Technology, Japan. The authors are grateful to the SC-NMR Laboratory of Okayama University for the NMR measurements.

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3. It was proposed that [2+2]cycloaddition proceeds through an electron transfer (ET) pathway: (a) a review see: Ledwith, A. *Acc. Chem. Res.* **1972**, *5*, 133; (b) for the most recent example, see: Reddy, G. D.; Wiest, O. *J. Org. Chem.* **1999**, *64*, 2860.
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5. (a) Engler, T. A.; Combrink, K. D.; Letavic, M. A.; Lynch, K. O., Jr.; Ray, J. E. *J. Org. Chem.* **1994**, *59*, 6567; (b) Engler, T. A.; Combrink, K. D.; Ray, J. E. *J. Am. Chem. Soc.* **1988**, *110*, 7931.
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7. [bmim]PF_6: Huddleston, J. G.; Willauer, H. D.; Swatloski, R. P.; Visser, A. E.; Rogers, R. D. *Chem. Commun.* **1998**, 1765.
8. The ratio of *trans–cis* was determined by ^{1}H NMR analysis.
9. It was proposed that 2,3-dihydrobenzofuran **7a** was produced by [2+2]cycloaddition of anethol with 1,4-benzoquinone and subsequent rearrangement by Engler et al.[4,5]
10. The acidity of all ionic liquid solvents employed was confirmed to be neutral prior to their use in each reaction.
11. Although we hypothesize that iron(III) salt works as a one electron transfer catalyst, as illustrated in Fig. 1, another mechanism may also be possible; Fe^{3+} ion may coordinate with the neutral quinone **4** and accelerating electron transfer reaction to anethol.
12. [bmim]BF_4 and [bmim]PF_6: Suarez, P. A. Z.; Dullius, J. E. L.; Einloft, S.; de Souza, R. F.; Dupont, J. *Polyhedron* **1996**, *15*, 1217.
13. [bmim]OTf: Bonhote, P.; Dias, A.-P.; Papageorgiou, N.; Kalyanasundaram, K.; Grötzel, M. *Inorg. Chem.* **1996**, *35*, 1168.
14. Typical experimental procedure: To a mixture of 1,4-benzoquinone **4** (44.0 mg, 0.407 mmol) and (*trans*)-anethol **1a** (62.0 mg, 0.419 mmol) in [bmim]PF_6 (0.8 mL) was added an $Fe(BF_4)_2 \cdot 6H_2O$ (4.0 mg, 0.012 mmol) in one portion at rt. The mixture was stirred for 10 min and was diluted with ether (4 mL), then extracted with ether (2 mL×5). The solvent was removed under reduced pressure to give a crude mixture which was purified by TLC (EtOAc/hexane = 20%) to give the desired 2,3-dihydrobenzofrane **7a** in 98% yield (102 mg, 0.398 mmol) as a light yellow oil.