

[2+2]-Cycloaddition Reaction of Styrene Derivatives Using an Fe(III) Salt Catalyst

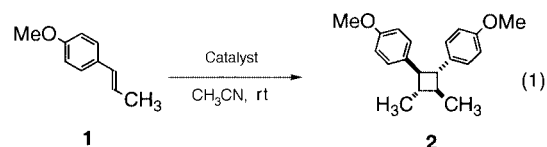
Hiroyuki Ohara, Toshiyuki Itoh,* Masaharu Nakamura,† and Eiichi Nakamura†

Department of Chemistry, Faculty of Education, Okayama University, Okayama 700-8530

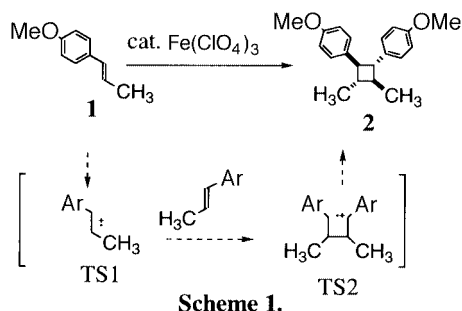
†Department of Chemistry, Graduate School of Science, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033

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Iron(III) perchlorate catalyzed cyclodimerization of *trans*-anethole gave *trans,anti,trans*-cyclobutane stereospecifically in good yield. Alumina supported iron(III) perchlorate was an especially efficient one-electron oxidation reagent.



Iron is recognized as an economical and environmentally benign metal source, but only limited reaction has been reported for iron-catalyzed reaction.¹ Recently we demonstrated a novel intramolecular cyclization of a cyclopropanone dithioacetal by treatment of a catalytic amount of iron(III) perchlorate ($\text{Fe}(\text{ClO}_4)_3$) in acetonitrile under aerobic conditions.² It was believed that the reaction started from oxidative severance of the cyclopropane ring caused by the single electron oxidation mediated by $\text{Fe}(\text{ClO}_4)_3$; this formed a radical cation and subsequent cyclization with the olefinic part giving *cis*-fused oxabicyclo[3.3.0]octane-1,1-trimethylenethioacetals.² We have investigated further the possibility of iron(III)-mediated reaction starting from the single electron oxidation and have attempted to use iron(III)-catalyzed oxidation for the cyclodimerization system. The chemistry of both photodimerization and metal-catalyzed cyclodimerization has a long history, although the level of results has remained low.³ Because it is established that iron(III)-catalyzed cyclodimerization of aromatic enamines proceeds cation radical intermediate,⁴ we anticipated that cyclodimerization of *trans*-anethole **1** might be possible using $\text{Fe}(\text{ClO}_4)_3$ via a single electron oxidation process following our working hypothesis through TS1 and TS2 as illustrated in Scheme 1.⁵ Here we report that [2+2]-cyclodimerization of *trans*-anethole **1** is accomplished using alumina-supported $\text{Fe}(\text{ClO}_4)_3$ to afford cyclobutane **2**⁶ in an excellent yield with stereospecificity.



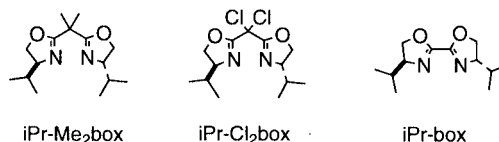
Scheme 1.

First, we investigated the reaction of *trans*-anethole **1** with $\text{Fe}(\text{ClO}_4)_3$ under aerobic conditions (eq 1). Desired dimerized compound **2** was obtained in 68% yield with perfect *trans-anti-trans* selectivity when *trans*-anethole **1** was treated with 10 mol% of $\text{Fe}(\text{ClO}_4)_3$ in CH_3CN at rt for 24 h (Entry 1 in Table 1). Dimeric compound **2** was obtained even when 5 mol% of

Table 1. $\text{Fe}(\text{ClO}_4)_3$ catalyzed cyclodimerization of *trans*-anethole

Entry	Catalyst	Conditions	Yield/% ^a
1	$\text{Fe}(\text{ClO}_4)_3$, 10 mol%, air	CH_3CN (0.5 M), 24 h	68
2	$\text{Fe}(\text{ClO}_4)_3$, 5 mol%, air	CH_3CN (1.0 M), 24 h	52
3	$\text{Fe}(\text{ClO}_4)_3$, 5 mol%	CH_3CN (1.0 M), 24 h	52
4	$\text{Fe}(\text{ClO}_4)_3 \cdot 9\text{H}_2\text{O}$, 10 mol%	CH_3CN (0.5 M), 24 h	21
5	$\text{Fe}(\text{ClO}_4)_3$, 10 mol%, 2,6-lutidine, 12 mol%	CH_3CN (0.5 M), 24 h	49
6	$\text{Fe}(\text{ClO}_4)_3$, 10 mol%, bipyridine, 10 mol%	CH_3CN (1.0 M), 17 h	53
7	$\text{Fe}(\text{ClO}_4)_3$, 10 mol%, iPr-Me ₂ box 12 mol%	CH_3CN (1.0 M), 24 h	23 ^b
8	$\text{Fe}(\text{ClO}_4)_3$, 10 mol%, iPr-Cl ₂ box 10 mol%	CH_3CN (1.0 M), 12 h	78 ^c
9	$\text{Fe}(\text{ClO}_4)_3$, 10 mol%, iPr-box 10 mol%	CH_3CN (0.8 M), 24 h	45 ^c

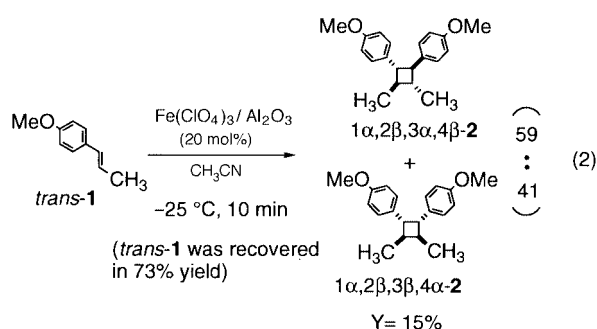
^aIsolated yield. ^b7% ee of the product was obtained. % ee was determined by HPLC (Chiralcel OD), Hexane: i-PrOH=350:1, monitored at 269 nm. ^cThe product was a racemic form.



the catalyst was employed, though the chemical yield dropped slightly (Entry 2). Although we initially anticipated that the reaction would need an oxidant to complete the catalytic cycle, the reaction required no aerobic conditions and dimer **2** was obtained in the same yield when the reaction was carried out in the absence of air (Entry 3). On the other hand, the yield of **2** dropped significantly when $\text{Fe}(\text{ClO}_4)_3 \cdot 9\text{H}_2\text{O}$ was employed as catalyst even when the reaction was carried out using dried

CH₃CN as solvent (Entry 4). It was clearly recognized that reaction efficiency of the metal-catalyzed reaction was dependent on the ligand. Hence the reactions were conducted in the presence of several types of ligands (Entries 5–9). Among the five types tested, the best result was recorded when the reaction was carried out using 10 mol% of dichloro-bisoxazoline ligand (iPr-Cl₂box) and desired dimer **2** was obtained in 78% yield (Entry 8). However, no enantioselectivity was observed even when an optically active ligand was employed for these reactions. Dimer **2** was obtained with only 7% ee when the reaction was carried out in the presence of optically active iPr-Me₂box ligand (Entry 7). From these results, it seems that the dimerization reaction takes place without influence of the ligand via the radical cation pathway as hypothesized initially in Scheme 1, though the ligand employed obviously affects the Fe³⁺–Fe²⁺ oxidation reduction system.

In addition, a mixture (59:41) of *anti*-(1 α ,2 β ,3 α ,4 β)-**2** and *syn*-(1 α ,2 β ,3 β ,4 α)-**2** was obtained in 15% yield and the starting material was recovered in 73% yield when our reaction was carried out at low temperature and stopped at 10 min (eq 2). This result was the same as that reported by the dimerization of *trans*-anethole **1** mediated by tris(*p*-bromophenyl)aminium hexachloroantimonate.^{3g} GC analysis revealed that *syn*-dimer **2** was completely isomerized to *anti*-dimer **2** with forming of a small amount of *trans*-anethole **1** when an acetonitrile solution of mixture of *anti*-**2** and *syn*-**2** (59:41) was treated with 10 mol% of Fe(ClO₄)₃ at rt for 6 h. It therefore is concluded that perfect stereoselectivity of the present reaction was attributable to the formation of thermodynamically stable dimer *anti*-**2** during the equilibrium between the cycloadduct **2** and the substrate **1** which was produced by the cycloreversion of dimer **2**.^{3g}



It was well recognized that efficiency of the catalyst was dependent on the proper supporting materials. We next investigated these supporting materials; neither celite nor silica gel accelerated or improved the chemical yield (Entries 1 and 2, Table 2). We finally found that the alumina supported Fe(ClO₄)₃ catalyst gave excellent results, though requiring a long reaction time.⁷ The desired dimeric compound **2** was obtained in the highest yield of 92% using only 3 mol% of the catalyst (Entry 3 in Table 2). To the best of our knowledge, this is the least amount ever recorded of catalyst used for this type of reaction.

In conclusion, we demonstrated that alumina supported Fe(ClO₄)₃ catalyzed cyclodimerization of *trans*-anethole **1** to afford (1 α ,2 β ,3 α ,4 β)-1,2-bis(4-methoxyphenyl)-3,4-dimethylcyclobutane (**2**)^{3e,g} in excellent yield. Further investigation of the scope and limitations of this reaction, especially switching

Table 2. Cyclodimerization of *trans*-anethole in the presence of a porous solid supported Fe(ClO₄)₃

Entry	Catalyst	Conditions	Yield of 2
1	Fe(ClO ₄) ₃ / Celite (3 mol%)	CH ₃ CN (1.0 M), rt, 66 h	33%
2	Fe(ClO ₄) ₃ / SiO ₂ (3 mol%)	CH ₃ CN (1.0 M), rt, 66 h	39%
3	Fe(ClO ₄) ₃ / Al ₂ O ₃ (3 mol%)	CH ₃ CN (1.0 M), rt, 66 h	92%

the counter anion from perchlorate to a safer anion species, will make it even more beneficial.

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References and Notes

- 1 A review see. P. Laszlo, *Acc. Chem. Res.*, **19**, 121 (1986).
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- 3 A review see. a) N. L. Bauld, *Tetrahedron*, **45**, 5307 (1989). Photodimerization: b) K. Mizuno, C. Pac, and H. Sakurai, *Chem. Lett.*, **1973**, 309. c) C. Pac, K. Mizuno, T. Sugioka, and H. Sakurai, *Chem. Lett.*, **1973**, 187. d) C. Pac, T. Sugioka, K. Mizuno, and H. Sakurai, *Bull. Chem. Soc. Jpn.*, **46**, 238 (1973). e) F. D. Lewis and M. Kojima, *J. Am. Chem. Soc.*, **110**, 8660 (1988). D F. D. Lewis and M. Kojima, *J. Am. Chem. Soc.*, **110**, 8664 (1988). Tris(*p*-bromophenyl)aminium hexachloroantimonate: g) N. L. Bauld and R. Pabon, *J. Am. Chem. Soc.*, **105**, 633 (1983).
- 4 a) F. A. Bell, R. A. Crellin, and A. Ledwith, *J. Chem. Soc., D*, **1969**, 251. b) D. W. Reynolds, K. T. Lorenz, H-S. Chiou, D. J. Bellville, R. A. Pabon, and N. L. Bauld, *J. Am. Chem. Soc.*, **109**, 4960 (1987).
- 5 It was proposed that [2+2]-cycloaddition proceeds through an electron transfer (ET) pathway: a) for a review see: A. Ledwith, *Acc. Chem. Res.*, **5**, 133 (1972). b) for the most recent example see: G. D. Reddy and O. Wiest, *J. Org. Chem.*, **64**, 2860 (1999).
- 6 Some spectroscopic properties of (1 α ,2 β ,3 α ,4 β)-**2**^{3e}: ¹H NMR (200 MHz, CDCl₃): δ 7.13 (d, 4H, *J* = 8.7 Hz), 6.82 (d, 4H, *J* = 8.7 Hz), 3.77 (s, 6H), 2.80 (m, 2H), 1.82 (m, 2H), 1.18 (d, 6H, *J* = 6.0 Hz); ¹³C NMR (50 MHz, CDCl₃) δ 157.9, 135.9, 127.7, 113.7, 55.2, 52.4, 43.2, 18.9.
- 7 Catalyst was prepared as follows: neutral alumina (714 mg, Aldrich) was added to a solution of Fe(ClO₄)₃·nH₂O (286 mg) in freshly distilled CH₃CN (0.5 mL) and the solvent was removed at 60 °C under reduced pressure using a rotary evaporator. The mixture was dried under vacuum and the resulting uniformly orange powder was used for the reaction. The catalyst should be handled with care because it has been reported that iron(III) perchlorate salt detonates with violence when subjected to mechanical or thermal shock. However, our catalyst is believed to be safe due to the support by neutral alumina. The content of Fe(III) ion was determined by iodometry titration in aqueous solution.