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Reaction of Allylic Phosphoranes with Iron Porphyrin Carbenoids: Efficient, Selective, and Catalytic Intermolecular Formal Carbenoid Insertion into Olefinic C−H Bonds

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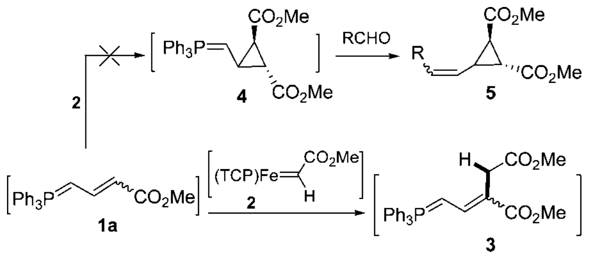
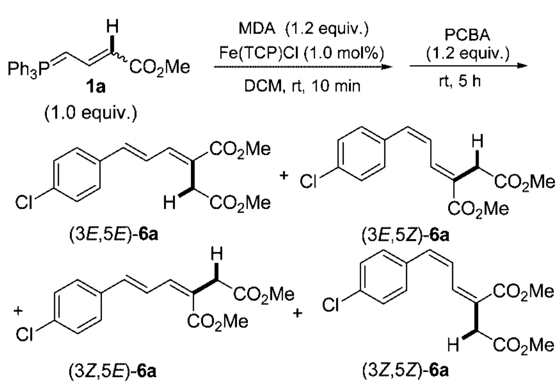
An ylide, $L_nM^+{-}C^-HR$, can be generally regarded as a carbanion bearing a unique leaving group.[1] Traditionally, ylides can react with electrophilic carbonyl compounds, imines, and electron-deficient olefins, giving alkenes and epoxides, aziridines, and cyclopropanes, respectively.[1−3] The reactions of ylides with other electrophiles, such as trialkylboranes, have also been developed.[4] In our study of the chemistry of ylides in organic synthesis,[5] we are interested in developing reactions of allyllic ylides for stereoselective synthesis of vinylcyclopropanes. However, these methods generally suffer from substrate limitations.[1] Since electrophilic iron carbenoid **2** affords cyclopropanes when subjected to olefins,[6] we envisioned that crotonate-derived phosphorus ylide **1a** can react with **2** to give ylide **4**, which can be further trapped with aldehydes to provide easy, diverse access to disubstituted vinylcyclopropanes (Scheme 1). Thus, we tried the reaction of **1a** with **2** and found that it afforded ylide **3** via intermolecular carbenoid insertion into the olefinic C−H bond (Scheme 1). In this communication, we wish to report the preliminary results for this reaction and its application in the synthesis of 1,1,4-trisubstituted 1,3-butadienes.[7]

Initially, the reaction of ylide **1a** with methyl diazoacetate (MDA) was tested in the presence of a catalytic amount of tetra(4-chlorophenyl)porphyrin iron chloride [Fe(TCP)Cl]. The reaction, after trapping with 4-chlorobenzaldehyde (PCBA), gave only the four isomers of diene **6a** shown in Scheme 2,[8] and no cyclopropane was observed. A possible pathway for the reaction involving a Wittig reaction of ylide **1a** with PCBA to form the diene followed by carbenoid insertion is excluded, since no reaction was observed when (2*E*,4*E*)-methyl 5-(4-chlorophenyl)penta-2,4-dienoate was treated with MDA in the presence of Fe(TCP)Cl under the same conditions as in Scheme 2. These results suggested that a new ylide **3** was generated, probably via an insertion of iron carbenoid **2** into the olefinic C−H bond of ylide **1a**, stimulating us to explore the insight of the C−H bond insertion of the allylic ylide. The two most likely mechanisms, involving direct carbenoid insertion into the olefinic C−H bond (path A) and tandem cyclopropanation/ring opening (path B), are shown in Scheme 3.[9] Although the cyclopropanation of 1,2-disubstituted alkenes with iron carbenoid **2** does not work,[6a] we believe that the reaction most likely proceeds through the formation of cyclopropane **4** followed by ring-opening (path B),[10] since both the reaction of ylide **1a** with *tert*-butyl diazoacetate (BDA) and the reaction of ylide **1b** with MDA gave the same product distribution[8] in the cross experiments shown in Scheme 4. Furthermore, we trapped the intermediate **4** successfully. Fortunately, when an in situ mixture of PCBA and MDA was added to ylide **1a** in CH_2Cl_2 in the presence of [Fe(TCP)Cl], vinylcyclopropane **5a** (*E*/*Z* 15:85) was isolated in 6% yield (Scheme 5). To further confirm this mechanism, we synthesized the intermediate ylide **4** and found that it could undergo the ring-opening reaction rapidly. These results clearly confirm that path B works in this reaction.

Scheme 1. Reaction of Ylide **1a** with Iron Carbenoid **2**

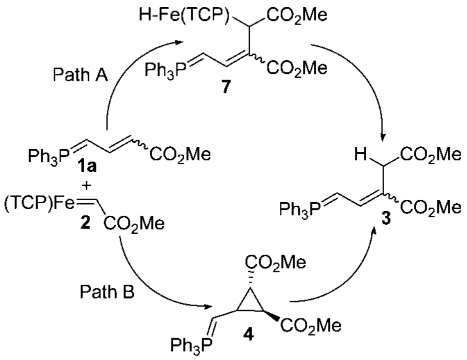


Scheme 2. Catalytic Carbenoid Insertion into the Olefinic C−H Bond of Allylic Ylide **1a**



Total yield of **6a**: 84%
(3*E*,5*E*)/(3*E*,5*Z*)/(3*Z*,5*E*)/(3*Z*,5*Z*) = 53/39/4.2/3.8 (by ^{1}H NMR)

Scheme 3. Proposed Paths for Carbenoid Insertion into the Olefinic C−H Bond of Allylic Ylide **1a**



To make the current reaction practical, we tried to improve the stereoselectivity of the Wittig reaction and use the corresponding phosphonium salt instead of ylide **1a**. The challenge is tolerance of the in-situ-produced iron carbenoid to the basic reaction

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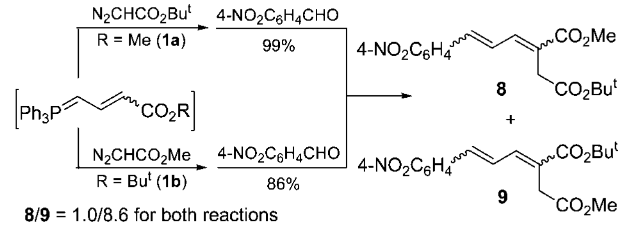
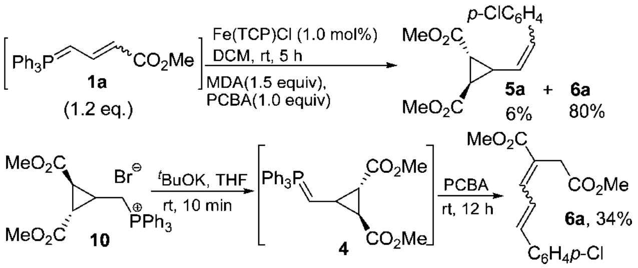
Scheme 4. Cross Experiments of the C−H Bond Insertion



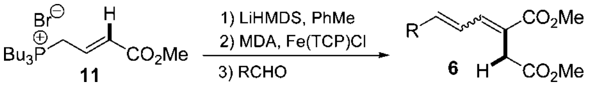
8/**9** = 1.0/8.6 for both reactions
Conditions: Fe(TCP)Cl (1.0 mol%), CH$_3$CN, rt, 10 min; then rt, 5 h.

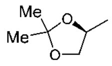
Scheme 5. Trapping of Intermediate **4** and Its Ring-Opening Reaction



conditions. After several trials, it was found that the one-pot reaction works well and that the stereoselectivity of the Wittig reaction is improved greatly when tributylphosphine-derived salt **11** is employed. The generality of the present reaction was examined by investigating a variety of aldehydes. As shown in Table 1, both aromatic and aliphatic aldehydes are suitable substrates to afford products **6** with high stereoselectivity. Although this is a one-pot procedure involving a three-step transformation, acceptable yields were obtained in all cases. Notably, the optically active aldehyde *O*,*O*-isopropylidene-D-glyceraldehyde furnished product **6j** without loss of ee (Table 1, entry 10) under mild conditions.

Table 1. One-Pot Synthesis of 1,3-Butadienes via Catalytic Carbenoid Insertion of Allylic Ylide[a]



entry	R	Time (h)	**6** (%)[b]	3*E*,5*E*/3*E*,5*Z*[c]
1	4-ClC$_6$H$_4$	6	62 (**6a**)	92/8
2	4-BrC$_6$H$_4$	7	61 (**6b**)	94/6
3	4-NO$_2$C$_6$H$_4$	7	54 (**6c**)	97/3
4	4-CNC$_6$H$_4$	6	53 (**6d**)	92/8
5	C$_6$H$_5$	7	61 (**6e**)	95/5
6	4-MeC$_6$H$_4$	20	67 (**6f**)	94/6
7	*E*-PhCH=CH	23	45 (**6g**)	90/10
8	Cy	25	72 (**6h**)	92/8
9	Ph(Me)CH	24	66 (**6i**)	94/6
10[d]		4	65 (**6j**)	75/25
11	C$_5$H$_{11}$	24	69 (**6k**)	87/13

[a] For detailed procedures, see the Supporting Information. [b] Isolated yield. [c] Determined by ^{1}H NMR, other isomers <5%. [d] 3*E*,5*E*-**6j** (96% ee), determined by chiral HPLC.

In summary, a highly efficient, selective, and catalytic intermolecular formal carbenoid insertion reaction into olefinic C−H bonds of allylic phosphoranes has been described. The mechanistic investigation showed that the insertion involves cyclopropanation of the allylic ylide with the iron carbenoid followed by ring opening of the resulting cyclopropane ylide. On the basis of this observation, a one-pot reaction of tributylphosphine-derived salt **11** with MDA and aldehydes under mild conditions has been developed, providing easy access to 1,1,4-trisubstituted 1,3-butadienes with high stereoselectivity.

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Supporting Information Available: Detailed experimental procedures, characterization data for all of the new compounds, and molecular structures in PDB format. This material is available free of charge via the Internet at http://pubs.acs.org.

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