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COMMUNICATIONS

Iron Porphyrin-Catalyzed Olefination of Ketenes with Diazoacetate for the Enantioselective Synthesis of Allenes

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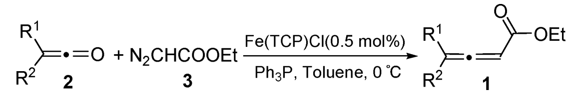
The Wittig reaction and its variants are the most powerful approaches for constructing carbon−carbon double bonds in organic synthesis due to their unambiguous positioning and good stereoselectivity.[1] Of the recent developments,[2−4] much attention has been paid to ylide olefination of aldehydes[3] and ketones[4] under neutral conditions by transition metal complex-catalyzed decomposition of diazo compounds to generate ylide in situ. In our studies on ylide reactions in organic synthesis,[2b−e,5] we are interested in developing an efficient method for the synthesis of allenes via olefination of ketenes, unstable carbonyl compounds,[6] with diazoacetate in the presence of transition metal complex. Fortunately, we found that such an olefination process could be achieved smoothly in the presence of PPh_3 and 0.5 mol % of tetra(*p*-chlorophenyl)porphyrin iron chloride (Fe(TCP)Cl). In particular, when chiral phosphine was used, optically active allenes could be prepared with high enantioselectivities in high yields. In this communication, we wish to report the preliminary results.

Allenes are of great importance due to their occurrence[7] in natural products and biologically active compounds, and they are valuable intermediates[8] in organic synthesis. Although many synthetic methods have been developed, a practical and mild process, in particular, for the synthesis of optically active ones,[9] is still a challenge. Gratifyingly, it was found that allenic ester **1a** could be synthesized in nearly quantitative yield when the reaction of 2-phenylprop-1-en-1-one with ethyl diazoacetate was carried out in toluene at 0 °C in the presence of PPh_3 and 0.5 mol % of Fe(TCP)Cl (Table 1, entry 1). Further studies showed that a variety of ketenes with different structures are good substrates for this olefination. As shown in Table 1, pure disubstituted ketenes gave good to excellent yields (entries 1−8). Disubstituted ketenes, prepared in situ from acyl chlorides without further purification, also worked well to afford the trisubstituted allenes in good yields (entries 9 and 10). A one-pot strategy has also been developed for some unstable ketenes. For example, 4-monosubstituted and 4,4-disubstituted allenic esters **1k**−**1o** could be obtained in good yields when Et_3N and acyl chloride were added sequentially[10] into the ylide generated in situ from phosphine and diazoacetate (entries 11−15). Thus, various 4-monosubstituted and 4,4-disubstituted allenic esters could be synthesized (even in gram scale, entry 2 in Table 1) by the current protocol.

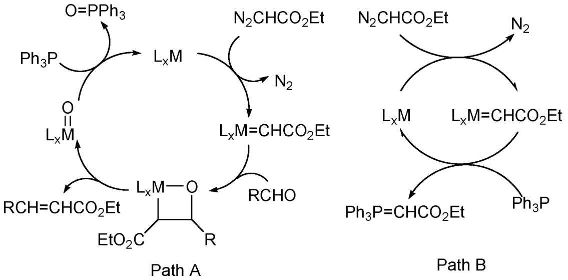
Table 1. Olefination of Ketenes with EDA Catalyzed by Fe(TCP)Cl[a]



entry	R¹	R²	method	1	yield (%)[b]
1	Ph	Me	A	**1a**	99
2	Ph	Et	A	**1b**	99 (94[d])
3	Ph	*i*-Pr	A	**1c**	99
4	Ph	*n*-Bu	A	**1d**	98
5	*p*-Cl−C_6H_4	Et	A	**1g**	98
6	*p*-MeO−C_6H_4	Et	A	**1h**	92
7	*o*-Me−C_6H_4	Et	A	**1i**	95
8	COOEt	*i*-Bu	A	**1j**	83
9[c]	Ph	allyl	A	**1e**	53
10[c]	Ph	3-butenyl	A	**1f**	75
11	*n*-C_5H_{11}	H	B	**1k**	77
12	*n*-$C_{10}H_{21}$	H	B	**1l**	80
13	Ph	H	B	**1m**	56
14	Br	Me	B	**1n**	59
15	*n*-Bu	Et	B	**1o**	74

[a] For detailed procedures of methods A and B, please see the Supporting Information. [b] Isolated yield. [c] Ketenes were prepared in situ. [d] In 7 mmol scale, and 0.25 mol % of Fe(TCP)Cl was used.

Scheme 1. Possible Pathways for the Olefination of Aldehydes via Transition-Metal-Catalyzed Decomposition of Diazoacetate



For the olefination of aldehydes with diazo compounds catalyzed by transition metal complex, there are two mechanistic pathways in the literature,[3,4] as shown in Scheme 1, depending on the metal complex. In the case of Fe(TCP)Cl employed, Woo and his coworkers[3g,4a] documented that the mechanism involved the formation of a free ylide (Path B in Scheme 1). On the basis of this mechanistic insight, it is envisaged that chiral allenes could be prepared enantioselectively just by the use of chiral phosphine instead of triphenylphosphine. To our delight, a variety of optically active allenic esters could be synthesized with excellent enantioselectivities (93−98% ee) in high yields by employing chiral diphosphine compound **4** under the optimal conditions, as shown in Table 2.[11] These results also proved clearly that the mechanism of the present olefination involves the generation of an ylide through catalytic transfer of an iron(II) carbene ligand to phosphine.

Compound **4** is a diphosphine, and the molar ratio of EDA to **4** used in the current reaction is 2:1. Therefore, both monoylide **6a** and diylide **6b** are possible intermediates of this reaction. To elucidate the real intermediate, ylides **6a** and **6b** were synthesized

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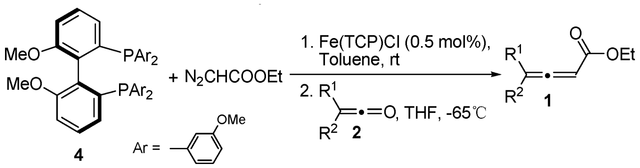
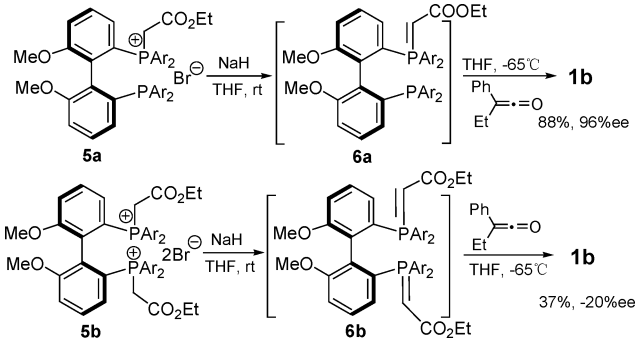
Table 2. Enantioselective Synthesis of Allenes[a]



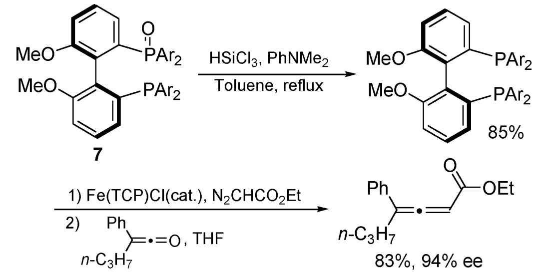
entry	R^1	R^2	1	yield (%)[b]	ee (%)[c]
1	Ph	Me	**1a**	72	93
2	Ph	Et	**1b**[d]	90	97
3	Ph	*n*-Pr	**1r**	87	93
4	*o*-Me−C$_6$H$_4$	Et	**1i**	86	97
5	*p*-MeO−C$_6$H$_4$	Et	**1h**	81	96
6	*p*-Cl−C$_6$H$_4$	Et	**1g**	83	97
7	*p*-Br-C$_6$H$_4$	Et	**1s**	80	98

[a] For detailed procedures, please see the Supporting Information. [b] Isolated yield. [c] Determined by chiral HPLC. [d] **1b** was assigned as *S*-configuration by comparing its optical rotation with the literature.

Scheme 2. Effects of Ylides on the Synthesis of Chiral Allene **1b**



Scheme 3. Phosphine Recovered and Reused



from their corresponding salts **5a** and **5b**, respectively. It was found that ylide **6a** gave the desired product **1b** in 88% yield with 96% ee, which is consistent with the experimental observation (entry 2, Table 2). However, diylide **6b** afforded the enantiomer of **1b** in 37% yield with −20% ee. These results, together with the fact that 83% of monophosphine oxide **7** was isolated in the reaction of 2-phenylpent-1-en-1-one with ylide generated in situ (entry 3 in Table 2), showed clearly that the monoylide **6a** is the intermediate and further confirmed the mechanism Woo et al. proposed. Noticeably, the recovered chiral phosphine oxide could be readily reduced by HSiCl$_3$ and reused. For example, **1r** could be obtained with 94% ee in 83% yield using the recovered compound **4** as the phosphine (Scheme 3), comparable to the results when phosphine **4** was first used (entry 3 in Table 2).

In summary, we have developed an efficient method for the synthesis of allenes under neutral conditions by olefination of ketenes with EDA in the presence of Ph$_3$P and catalytic Fe(TCP)-Cl for the first time. We have also realized its asymmetric version and found that, by employing chiral phosphine instead of PPh$_3$, chiral allenes could be synthesized with high enantioselectivities (93−98% ee) in good yields, providing an easy access to optically active allenic esters. In addition, the results described here confirmed that the mechanism involves ylide olefination. The high enantioselectivity, the neutral condition, and the fact that the phosphine could be recovered and reused make the current method potentially useful in organic synthesis.

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Supporting Information Available: Detailed experimental procedures and characterization data for all new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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