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Observations on the regio- and stereoselective trapping of organozinc carbenoids by acetoxybutadienes: a useful route to functionalised vinylcyclopropanes

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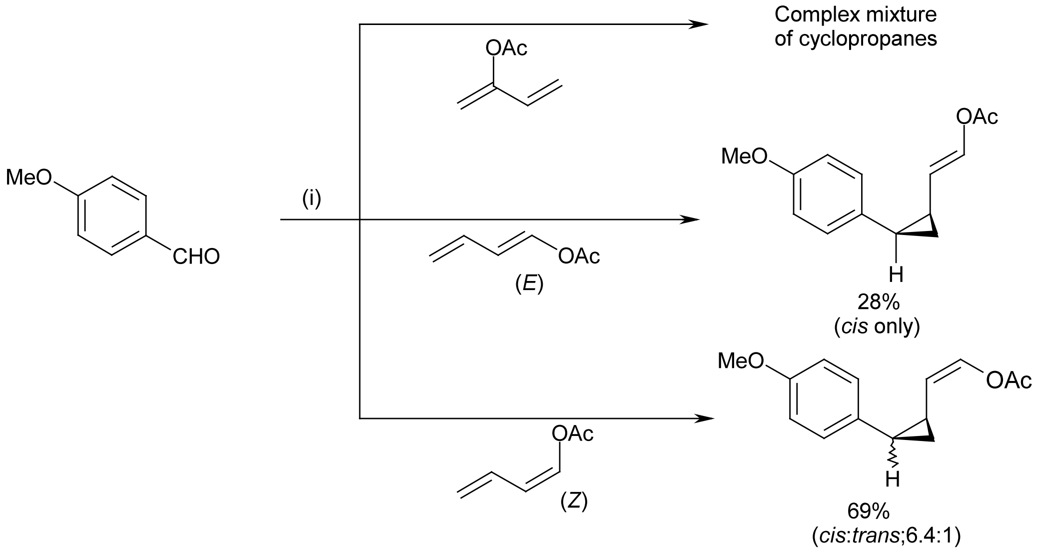
Abstract—Regiospecific trapping of organozinc carbenoids generated from carbonyl compounds with *Z*-1-acetoxybutadiene provides a useful preparative route to functionalised vinyl and divinylcyclopropanes. © 2002 Elsevier Science Ltd. All rights reserved.

We have previously shown that a useful range of organozinc carbenoids can be simply generated from the reaction of readily available carbonyl compounds with metallic zinc in the presence of a silicon electrophile, and that these reactive intermediates can then undergo a variety of classical carbenoid reactions including C–H insertion to give alkenes, dicarbonyl coupling *via* a carbonyl ylide, and inter- and intramolecular cyclopropanation.[1]



Scheme 1. *Reagents and conditions*: (i) Zn, (10.0 equiv.), $Me_2Si(Cl)(CH_2)_2Si(Cl)Me_2$ (1.5 equiv.), acetoxybutadiene (2.0 equiv.), Et_2O, reflux, N_2.

Keywords: organozinc; carbenoids; vinylcyclopropanes; divinylcyclopropanes.

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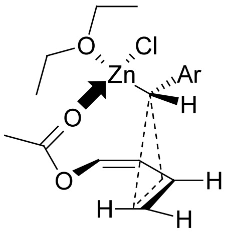
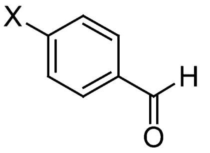
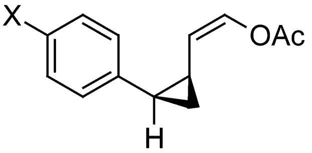
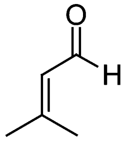
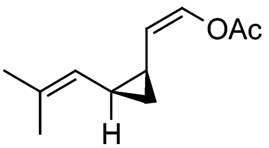
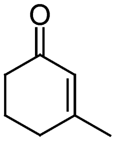
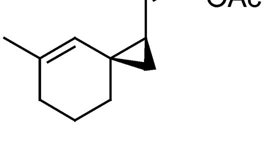
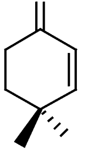
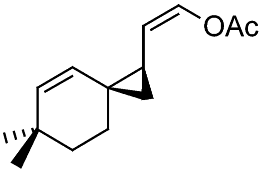


Figure 1.

Since the trapping of an organometallic carbenoid by a diene offers possibilities for the construction of highly functionalised and synthetically valuable vinylcyclopropane derivatives,[2] it was therefore of interest to examine the behaviour of our organozinc carbenoids with such substrates. In the first instance, we elected to carry out a preliminary study of the reactivity of the organozinc carbenoid derived from *para*-methoxybenzaldehyde with the three isomeric acetoxybutadiene derivatives, as shown in Scheme 1. Examination of these results clearly reveals an intriguing pattern of reactivity, both in terms of regio- and stereoselectivity, and also of efficiency.

Thus, although electronic factors are generally considered to dominate in carbenoid additions to 2–alkoxy-substituted butadienes with consequent mono-cyclopropanation occurring almost exclusively in the 1,2 position,[3a,b] the present reaction provided a complex mixture of both regio– and stereoisomeric cyclopropanes, as evidenced by NMR. The relatively indiscriminate behaviour of this organozinc carbenoid was substantiated to some extent by a simple competition experiment using the carbenoid from *para*-methoxybenzaldehyde and an equimolar mixture of cyclohexene and isopropenyl acetate, which led to isolation of similar yields of cyclopropanated products (cyclohexene, 44%, isopropenyl acetate, 37%). Contrastingly, whilst the reactions of both the *E* and the *Z* isomers of 1-acetoxybutadiene led to attack at the less hindered double bond, as has been observed for both rhodium[3b,4] and palladium[5] carbenoids generated from diazo precursors, it was of particular interest to note

Table 1.

Entry	X	Carbonyl compound	Products	Isomer ratio[a]	Yield (%)[b]
1	OMe			6.4:1	69
2	CH_3			4.6:1	44
3	H			3.1:1	35
4	Cl			2.7:1	28
5				6.1:1	42
6				5.4:1	26
7				Only	35

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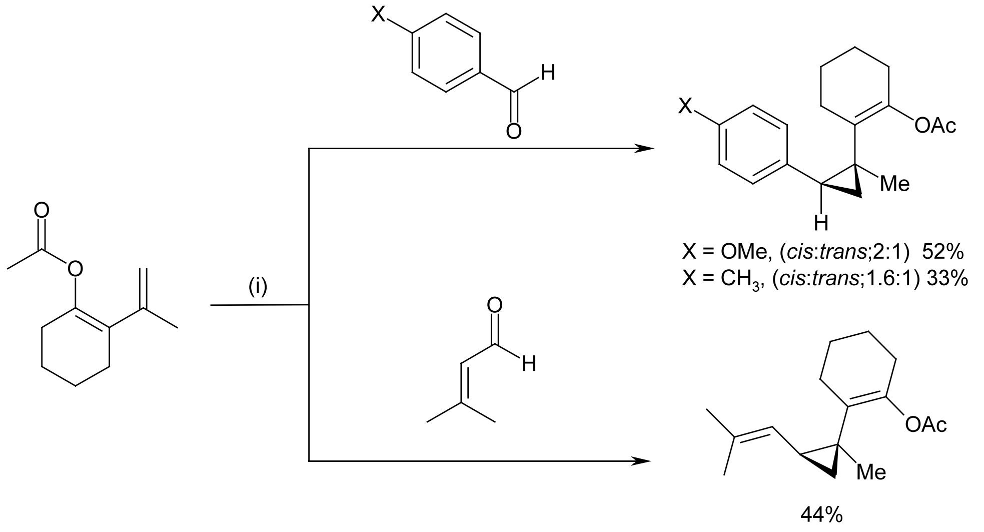
[a] Determined using NMR spectroscopy. For convenience the major *cis* isomer is shown.

[b] Isolated yields based on the use of 1.0 equiv. of carbonly compound and 2.0 equiv. of *Z*-1-acetoxybutadiene.



Scheme 2. *Reagents and conditions*: (i) Zn, (10.0 equiv.), $Me_2Si(Cl)(CH_2)_2Si(Cl)Me_2$ (1.5 equiv.), enol acetate (2.0 equiv.), Et_2O, reflux, N_2.

that the *Z*-isomer furnished a much higher yield of the vinylcyclopropane product. As expected, both the *E* and *Z* isomers of 1-acetoxybutadiene were highly *cis* stereoselective with respect to the cyclopropane.

From a mechanistic standpoint these observations are clearly reminiscent of the ability of the hydroxyl group in an allylic alcohol to control stereoselectivity in the Simmons-Smith cyclopropanation[6] reaction and, in the present instance, may be indicative of a strongly directing influence from the acetoxy group. It is also relevant to note that the present reaction of organozinc carbenoids differs from the aforementioned cyclopropanation[4] of 1-acetoxybutadienes using diazo compounds, in which similar yields were obtained irrespective of whether *Z* or *E*-1-acetoxybutadiene was used. With these thoughts in mind, a plausible rationale invoking the acetoxy group as a co-ordinating ligand for zinc can be constructed as shown in Fig. 1.

Having established the above pattern of reactivity, our attention was then directed towards the use of *Z*-1-acetoxybutadiene with a variety of other carbonyl compounds, which can be used for the generation of organozinc carbenoids. The results of this study are presented in Table 1 and reveal several points of interest. Thus, as we have noted and rationalised for the cyclopropanation of simple alkenes,[1] comparison within the series of aromatic aldehydes (entries 1–4) confirms that electron releasing substituents not only facilitate carbenoid generation but also favour formation of the more hindered *cis* isomer. This stereochemical trend is also mirrored in the behaviour of the α,β unsaturated substrates (entries 5–7) which lead to usefully differentiated divinylcyclopropanes.

Finally, we have also extended this study to another *cisoid* acetoxybutadiene system of even greater steric demand. The results for a small selection of carbonyl compounds using the enol acetate derived from 2-isopropylidene cyclohexanone are shown in Scheme 2 and confirm that the trends established in the parent system are also operative.

In summary, the above results provide a simple, mild and inexpensive method for the preparation of vinyl and divinylcyclopropanes possessing a stereochemically distinct *Z*-enol acetate moiety for further stereospecific elaboration, either via controlled enolate chemistry or in reactions involving the divinylcyclopropane rearrangement.[7] The fact that, of the three isomeric acetoxybutadienes, only the *Z*-1-acetoxybutadiene displays a useful degree of regiospecific and highly stereoselective behaviour in cyclopropanation reactions is certainly of mechanistic interest and also highlights the dangers of attempting to draw comparisons with the reactions of other transition metal carbenoids generated from alternative precursors.

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References

1. For recent overviews on the generation and reactivity of organozinc carbenoids derived from carbonyl compounds see: (a) Motherwell, W. B. *J. Organomet. Chem.* **2001**, *624*, 41; (b) Motherwell, W. B. *Pure Appl. Chem.* **2002**, *74*, 135.
2. Hudlicky, T.; Reed, J. W. Rearrangements of vinylcyclopropanes and related systems in *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I. Eds. (Paquette, L. A. Vol. Ed.) Pergamon Press: Oxford, New York, Seoul, Tokyo; 1991; Vol. 5, 8.1, pp 899–970.

3. (a) Girard, C.; Amice, P.; Barnier, J. P.; Conia, J. M. *Tetrahedron Lett*. **1974**, 3329; (b) Doyle, M. P.; Dorow, R. L.; Tamblyn, W. H.; Buhro, W. E. *Tetrahedron Lett*. **1982**, *23*, 2261.
4. Cantrell, W. R., Jr.; Davies, H. M. L. *J. Org. Chem*. **1991**, *56*, 723.
5. Tomilov, Y. V.; Kostitsyn, A. B.; Shulishov, E. V.; Nefedov, O. M. *Synthesis* **1990**, 246.
6. For reviews which emphasise hydroxyl directed cyclopropanation with zinc carbenoids see: (a) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoine, C. M. *Org. Reactions* **1973**, *20*, 1–131; (b) Furukawa, J.; Kawabata, N. *Adv. Organomet. Chem*. **1974**, *12*, 83–134; (c) Zeller, K.-P.; Gugel, H. Houben-Weyl: *methoden der organischen chemie;* Regitz, M. Ed; Georg Thieme Verlag: Stuttgart; 1989, Band EXIXb, 195; (d) Motherwell, W. B.; Nutley, C. J. *Contemp. Org. Synthesis* **1994**, *1*, 219–241.
7. Piers, E. Rearrangements of divinylcyclopropanes, in *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I. Eds. (Paquette, L. A. Vol Ed.) Pergamon Press: Oxford, New York, Seoul, Tokyo, 1991; Vol 5, 8.2, pp 971–998.