1,4-Asymmetric induction in the formation of cyclohexadienones by chirality transfer from a transiently installed chromium–stereospecific electrocyclic ring closure of a metal complexed vinyl ketene

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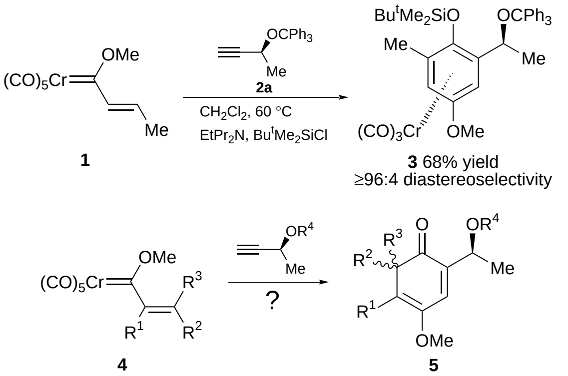
The cyclohexadienone annulation of a β,β-disubstituted vinyl chromium carbene complex and a chiral prop-2-ynylic ether results in high 1,4-asymmetric induction at the newly formed quaternary carbon; the stereochemical information from the prop-2-ynylic ether is initially transfered to the chromium coordination sphere and then to the quaternary carbon of the cyclohexa-2,4-dienone.

We recently reported the first examples of an asymmetric synthesis of an arene chromium tricarbonyl from a benzannulation reaction.[1,2] The formation of the arene complex **3** occurs *via* 1,2-induction from the prop-2-ynylic carbon to the chiral centre of the complexed arene (Scheme 1). This success prompted us to investigate the cyclohexadienone annulation of β,β-disubstituted vinyl carbene complexes **4** with chiral prop-2-ynyl ethers.[3] We report here that this reaction occurs with significant 1,4-asymmetric induction and that the sense of induction provides the first experimental determination of the stereoselectivity associated with the elctrocyclic ring closure of a metal complexed vinyl ketene intermediate.

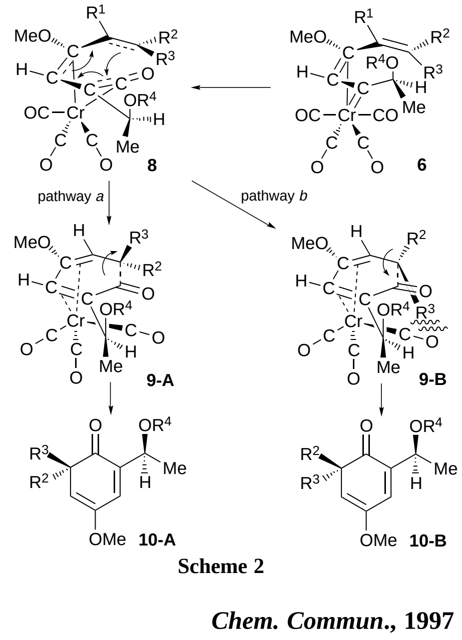
The expectation that a 1,4-asymmetric induction would occur with high fidelity was not at all clear for several reasons. First, the vinyl carbene complex **4** may undergo *cis*–*trans* isomerization. Although rates of isomerization for β,β-disubstituted complexes have not been reported, it is known that the *cis*-propenyl complex (**4**, R^3 = Me, R^2, R^1 = H) will isomerize to the *trans*-propenyl complex **1** at a rate competitive with its reaction with pent-1-yne.[4] This unpropitious result does not bode well for the stereoselective synthesis of the cyclohexadienone **5**. Additionally, the stereochemistry associated with the electrocyclic ring closure of the vinyl ketene complex has not been previously discussed or examined experimentally.[5] According to the most likely mechanism,[5,6] the ring closure occurs *via* a six electron electrocyclic reaction of the vinyl ketene complex **8** (Scheme 2). However, since the arene complex **3** must be derived from the vinyl carbene intermediate **6** and not its diastereoisomer **7** (not shown), and since only a single diastereoisomer of **3** is formed, it is likely that only one diastereoisomer of the vinyl ketene complex is formed. Therefore, while the selective formation of **3** reveals that the chiral centre on the prop-2-ynylic alkyne must induce a stereoselective coordination of the chromium, the selective formation of cyclohexadienone **5** requires that the chromium in ketene complex **8** induces a selective electrocyclic ring closure. This could occur by either pathway *a* or *b* as indicated in Scheme 2.



Scheme 1

The reactions of carbene complexes **11** and **12** with alkyne **2** are both stereoselective and stereospecific (Table 1). Complex *E*-**11** gives cyclohexadienone **13** with an α-ethyl group (92 : 8) while the *Z*-isomer gives cyclohexadienone **14** with a β-ethyl group (91 : 9). The reaction of complex **12** is also stereospecific. The isomerically pure *E*-**12** gave a 90 : 10 mixture of **15** and **16** and a 60 : 40 mixture[8] of *E*-**12** and *Z*-**12** gave a 68 : 32 mixture of **15** and **16**. In both cases, the substituent R^3 *syn* to the carbene unit is selectivity incorporated *syn* to the trityloxy group when the product is drawn as shown. If the alkoxy substituent R^4 is changed from CPh_3 to TBS the selectivity drops from 9 : 1 to 4.6 : 1. This appears to be due to electronics rather than sterics.[1,9] When a heptane solution of *E*-**11** was heated at 90 °C for 14 h no isomerization could be detected. Likewise, when *E*-**12** was heated in heptane at 85 °C for 11 h no isomerization could be detected. These results suggest that the carbene complexes do not isomerize under the reaction conditions.

The stereochemical assignments for the dienones were made on the basis of an X-ray structure of dienone **15a**.† Correlation of the ^{1}H NMR spectra of **15a** and **16a** with **13** and **14** then leads to the assignment of the major product from the reaction of complex *E*-**11** as the cyclohexadienone **13**. In a similar fashion



Scheme 2

the stereochemistry of the major product from the reaction of *E*-**12** with **2b** was assigned as **15b**. The stereochemistry of the cyclohexadienone products allows for an assignment of the direction of the electrocyclic ring closure. The favoured pathway is thus with the rotation of the substituent R^3 up and away from the metal centre in the vinyl ketene complex **8** to give the cyclohexadienone metal complex **9-A**. Downward rotation of R^3 (pathway *b*) is apparently disfavoured due to severe close-contacts with the metal and its ligands. The overall stereo-induction begins with the prop-2-ynylic chiral centre which leads to a stereospecific coordination of the chromium to the lower face of the vinyl ketene complex **8**. This in turn leads to stereo-induction in the formation of the quaternary carbon centre formed in the ring closing step. This represents an overall 1,4-induction with a stereochemical relay *via* a transiently installed metal centre.

An alternative mechanism for the observed stereo-induction involves a 16 e$^-$ η^2-vinyl carbene complex which could be derived from decoordination of the double bond in **6**, followed by the formation of the vinyl ketene complex **8** according to the allochemical mechanism.[10] This would involve a 1,2-induction in the formation of an η^2-coordinated vinyl ketene complex. This possibility is not considered here because of evidence which suggests that the allochemical mechanism is not operative when hexane is the solvent.[6a] The less than complete stereoselection observed in these reactions may not necessarily be due to rotation of R^3 through the metal centre in the vinyl ketene complex **8**. Rather, it may reflect the level of stereoselection associated with the introduction of the metal to a particular face of the vinyl carbene species in intermediate.‡

In the light of the synthetic importance of both the benzannulation reaction and the cyclohexadienone annulation, further studies on the mechanism of these reactions are being pursued. Additionally, synthetic applications for the stereospecific cyclohexadienone annulation are being explored.

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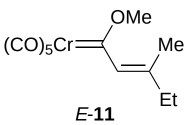
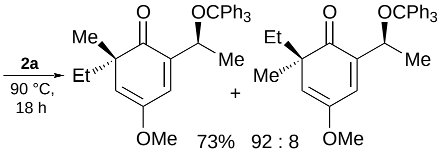
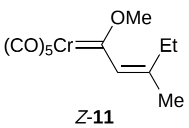
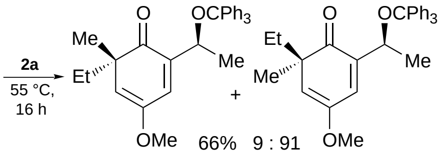
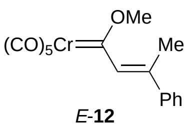
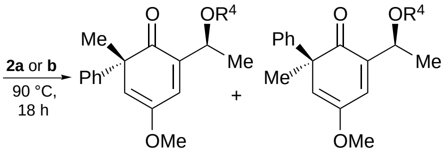
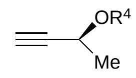
Table 1 1,4-Induction with stereoisomerically pure vinly carbene complexes[a2]

Carbene complex[b]	Cyclohexadienones
 *E*-**11** (68%)	 73% 92 : 8 **13** **14**
 *Z*-**11** (56%)	 66% 9 : 91 **13** **14**
 *E*-**12** (57%)	 **15** **16**
 **2a** R^4 = CPh$_3$ **b** R^4 = SiMe$_2$Bu^t	72% 90 : 10 R^4 = CPh$_3$
	68% 80 : 20^c R^4 = CPh$_3$
	65% 68 : 32^d R^4 = CPh$_3$
	73% 82 : 18 R^4 = SiMe$_2$Bu^t
	49% 66 : 34^c R^4 = SiMe$_2$Bu^t

[a] Reaction carried out under argon with carbene complex (0.01 mol dm^{-3}) and alkyne (1.3 equiv.) in heptane; *E*-**11** 90 °C, 18 h; *Z*-**11** 55 °C, 16 h; *E*-**12** 90 °C, 18 h. [b] Made from the corresponding vinyl iodides in the indicated yields. The vinyl iodides were made by the method of Negishi (ref. 7) each with greater than 98% diastereoisomeric purity as determined by capillary GC and ^{1}H NMR spectroscopy. The isomeric purity of the carbene complexes was determined by ^{13}C NMR spectroscopy to be $\geqslant$ 98% for *E*-**11** and *Z*-**11** and $\geqslant$ 97% for *E*-**12**. [c] Reaction performed in the presence of 3.0 equiv. of Bu$_3$P. [d] Reaction of a 60 : 40 mixture of *E* and *Z* isomers of complex **12** which was prepared in 8% yield by Michael addition in a manner similar to that reported for a related complex, ref. 8.

Footnotes

† *Crystal data* for **15a**: C$_{35}$H$_{32}$O$_3$, monoclinic, a = 17.457(7), b = 8.689(3), c = 21.408(9) Å, space group $C2$, V = 3082(2) Å^3, Z = 4, D_c = 1.079 g cm^{-3}, crystal dimensions 0.2 × 0.2 × 0.2 mm, radiation: Mo-Kα (λ = 0.71073 Å), 2θ scan range 4.0–42.0°, standard reflection: 3 standards, 197 reflections; independent reflections: 1793; R = 0.1108, R_w = 0.1395, GOF 1.84. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/289.

‡ The cyclohexadienone **13** does not isomerize under the reaction conditions. A sample of **13** and **14** (84.3 : 15.7) was heated in heptane for 23 h at 85 °C and recovered quantitatively with no change in composition (84.1 : 15.9).

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