Tetrahedron Letters,Vol.25,No.33,pp 3507-3510,1984 0040-4039/84 $3.00 + .00
printed in Great Britain

STEREOCONTROLLED FUNCTIONALIZATION OF CYCLOHEXENE USING ORGANOMOLYBDENUM CHEMISTRY

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Abstract. Cyclohexadiene-$Mo(CO)_2Cp$ cations react stereospecifically with stabilised enolate nucleophiles to give π-allyl complexes which are converted to substituted allylic iodides on treatment with iodine.

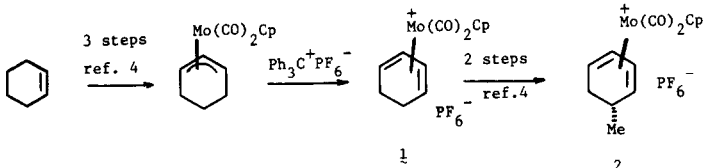
Attachment of a transition metal moiety to an olefinic ligand results in activation of the olefin toward nucleophilic attack, thereby providing methods for carbon-carbon bond formation which complement those already available to the synthetic organic chemist. [1] In cases where the metal remains attached to the ligand after bond formation (i.e., non-catalytic reactions) it is possible to utilize the metal moiety to effect further transformations, whose regio- and stereochemical outcome is controlled. In this respect, we have already described efficient vicinal stereocontrol using cyclohexadienyliron cations[2] and 1,3-stereocontrol in the seven-membered ring using cycloheptadienyliron complexes. [3] Faller's group have demonstrated 1,3-stereocontrol using cyclohexadiene-$Mo(CO)_2Cp$ cations[4] and Sweigart has reported 1,2-stereocontrol on arenemanganese and derived complexes. [5]

For organic synthesis purposes the cylohexadiene-molybdenum complexes, readily prepared from cyclohexene as outlined in Scheme 1, have considerable potential, offering functionalization modes complementary to e.g., dienyliron complexes. The major problem is the manipulation of π-allyl-$Mo(CO)_2Cp$ complexes, such as **5**, resulting from nucleophile addition. The replacement of CO by NO+ previously described[4,5] provides one answer to this problem, but is not useful when sensitive functional groups are present, nor does it allow controlled functionalization in the ring. We recently described[6] an iodolactonisation procedure, allowing conversion of π-allyl-$Mo(CO)_2Cp$ complexes 3 directly to γ-lactones 4. We have further investigated the reaction of these types of complex with iodine, resulting in conversion to allylic iodies, and these results are reported in the present communication.

Complexes **5**(a)-**5**(d) and **6** were prepared by the reaction of the known[4] diene complexes **1** and **2** with enolate nucleophiles (e.g., $NaCH(SO_2Ph)CO_2Me$ to give **5**(a)), and complex **5**(e) was prepared by reaction of **1** with p-methoxyphenylmagnesium bromide. All of these reactions proceed in high yield (>80%) and the reactions with methyl-substituted complex **2** were stereo-

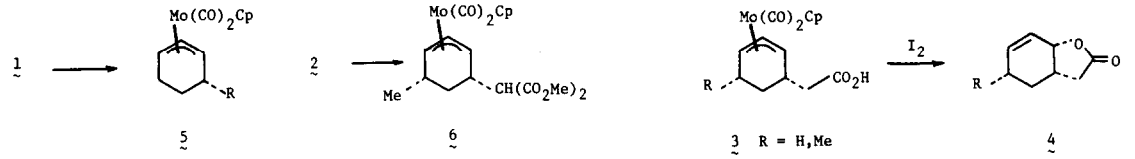
specific according to 200 MHz ^{1}H NMR spectroscopy,[7] the second nucleophile attacking cis to the methyl group.

Surprisingly, we observed that 5(a) was obtained as an approximately 8:1 mixture, and 5(b) as a 2:1 mixture of diastereomers. Structure determination of individual isomers was prevented by their tendency to epimerise on attempted chromatographic separation. Reaction of 1 with methyl 2-oxocyclopentane carboxylate anion gave a crude product whose ^{1}H and ^{13}C NMR spectra (200 and 50 MHz, respectively) showed the presence of a single diastereomer. The purified crystalline compound was subjected to X-ray analysis,[8] revealing the relative stereochemistry 5(c) (Scheme 2). Reaction of the methyl-substituted diene complex 2 with these enolates gave poorer diastereoselectivity, as did reaction of 1 with the enolate from 5-methoxy-2-methoxycarbonyl-1-indanone, giving 5(f). We currently have no explanation for the remarkable highly diastereoselective formation of 5(c), 5(a) and (less so) 5(b), and we await the results of further investigations for a fuller understanding of these effects.



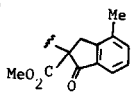
1 2

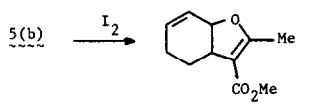
SCHEME 1



5 6 3 R = H,Me 4

(a) R = $CH(SO_2Ph)CO_2Me$
(b) R = $CH(COMe)CO_2Me$
(c) R = $\overline{CH(CO_2Me)COCH_2CH_2CH_2}$
(d) R = $CMe(CO_2Me)_2$
(e) R = p - $MeOC_6H_4$
(f) R =



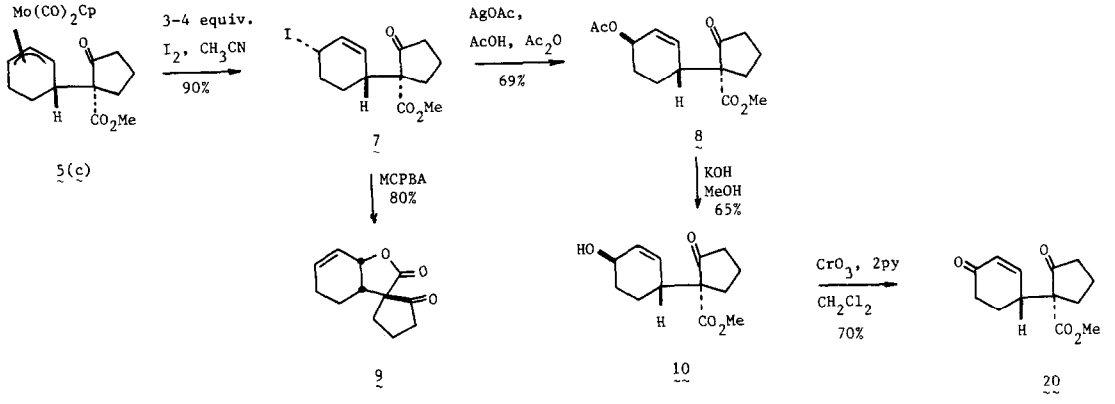


11

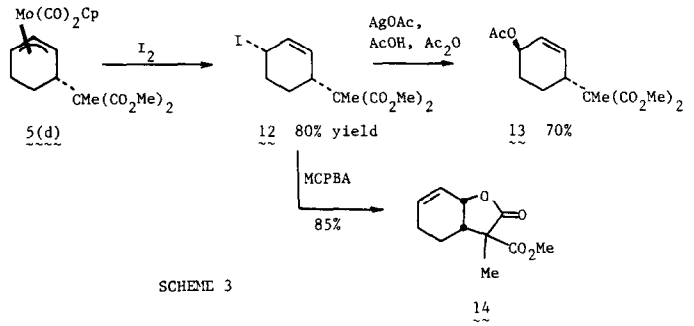
Reaction of the product π-allyl-$Mo(CO)_2Cp$ complexes with iodine (3-4 equiv. in CH_3CN, 20°C, 0.5 h) in most cases led directly to allylic iodides stereospecifically, as shown in Schemes 2 and 3 and Equations 1 and 2. The monosubstituted complexes reacted with high regioselectivity, iodide becoming attached at the substituent-remote terminus, whilst disubstituted complexes led to mixtures, depending on the steric bulk of the second substituent. In some cases, e.g. the acetoacetate derivative 5(b), cyclofunctionalization occurred to give, e.g. 11, analogous to our earlier reported lactonisation.[6]

The stereochemistry assigned to the allylic iodides was supported by the following observation. Careful treatment of iodide 12 with m-chloroperoxybenzoic acid (2 equiv., EtOAc, H_2O, 2:1, $NaHCO_3$, 20°C, 1h)[9] resulted in the formation of γ-lactone 14 identical to the one

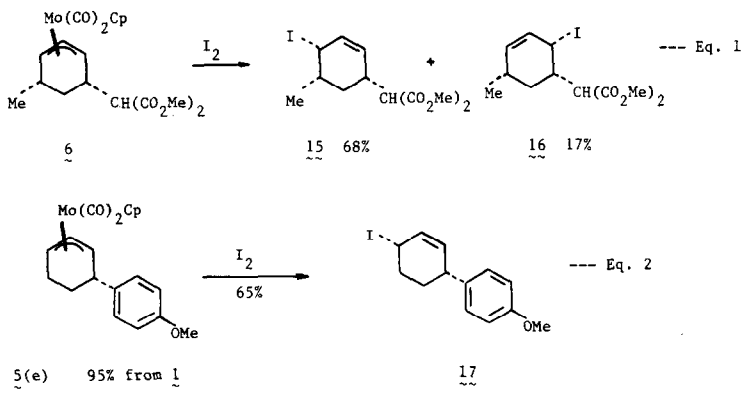
we previously obtained by direct cyclofunctionalization[6] (cf 3 → 4). It has been previously reported[9] that this transformation proceeds *via* rearrangement of an intermediate iodoso compound, which can be expected to occur with stereochemical retention analogous to the well-known [2,3]sigmatropic rearrangements of allylic sulfoxides[10] and selenoxides.[11]



SCHEME 2

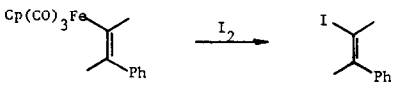


SCHEME 3



The stereochemistry of the iodine reaction is mechanistically interesting, since it was not known at the outset whether iodine would be "inserted" *cis* to metal *via* reductive elimination of an intermediate metal iodide species, or whether attack by I^- occurs *trans* to the metal in a cationic allyl-$MoI(CO)_2Cp$ intermediate, to give a η^2-olefin complex which is then

oxidized by the excess iodine to liberate the substituted alkene. Apparently, the latter pathway is followed, in contrast to the cleavage of e.g., vinyl-Fp derivatives such as 18 which is known[12] to give the vinyl iodide 19.



18 19

The allylic iodides produced in these reactions can be manipulated in other ways. Treatment of 7 or 12 with silver acetate (in AcOH, Ac_2O, 110°C, 2h) resulted in clean conversion to allylic acetates 8 and 13, presumably with inversion of the iodide configuration. Hydrolysis of acetate 8, followed by Collins' oxidation of the product alcohol gave a single enone 20 in good yield. It may be noted that 20 possesses the correct relative stereochemistry compared to similar intermediates produced using organoiron chemistry and which we have previously converted to trichothecene derivatives.[13] With this methodology for the controlled manipulation of π-allyl-$Mo(CO)_2Cp$ now in hand we are in a position to examine the application of a wide range of complexes to organic synthesis.

Acknowledgements

We are grateful to the National Institutes of Health for financial support (GM 30757 and 32114) and to the National Science Foundation (CHE 80-24633) and NIH (RR-01689) for grants allowing purchase of the Varian XL 200 NMR spectrometers used in this research.

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(Received in USA 3 May 1984)