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STEREO- AND REGIO-CONTROLLED FUNCTIONALIZATION OF CYCLOHEPTENE USING ORGANOMOLYBDENUM CHEMISTRY

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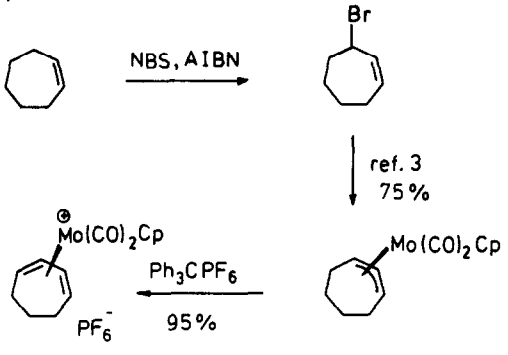
Abstract: Cycloheptene is readily converted to the cationic cycloheptadiene-$Mo(CO)_2Cp$ complex, which reacts with a range of nucleophiles; hydride abstraction from the product π-allyl-$Mo(CO)_2Cp$ complexes give substituted cycloheptadiene complexes which react with a second nucleophile stereospecifically, and decomplexation of the π-allyl complexes gives substituted cycloheptene derivatives with defined relative stereochemistry.

Because of its powerful stereochemical directing effect, use of a transition metal moiety to activate olefinic ligands toward nucleophilic attack promises to give unique access to a variety of stereochemically defined intermediates for organic synthesis. Double nucleophile addition to olefinic complexes is especially attractive and has already been demonstrated for dienyl-$Fe(CO)_3$[1], arene-$Mn(CO)_3$[2] and cyclohexadiene-$Mo(CO)_2Cp$[3] cations. In this paper we document our preliminary results on the controlled functionalization of cycloheptene *via* its derived diene-$Mo(CO)_2Cp$ complex 1, readily prepared as shown in Scheme 1.[4] These experiments were undertaken to determine whether organomolybdenum chemistry could be applied in this awkward ring size, thereby enhancing the latter's potential for synthetic application.

Scheme 1



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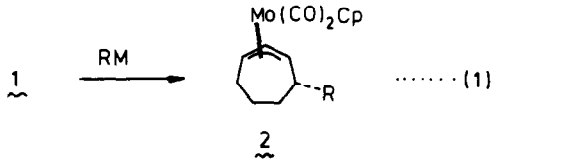
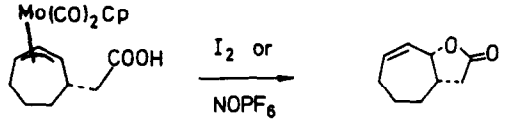
The complex 1 was found to react with a variety of carbon nucleophiles to give products 2 in high yield (equation 1, Table). For such reactions to find a place in organic synthesis methodology, the complexes 2 must either be converted to organic products, or they must be capable of further functionalization. To illustrate the former, we converted the phenyl-

sulfonylacetate 2e in two steps to the carboxylic acid 2f [(i) Na,Hg amalgam[5]; (ii) KOH, MeOH, THF, H_2O, 20°C, 36h, 76% overall yield]. We have previously shown[3(b)] that the cyclohexenyl analogs of 2 undergo lactonization and demetallation on treatment with excess iodine. Similar treatment of 2f (3.5 equiv. I_2, CH_3CN, 60 min, 20°C) gave the desired lactone 3 in 85% yield, but this was contaminated by 5-10% of impurity which was not identified. Instead, treatment of 2f with nitrosonium hexafluorophosphate ($NOPF_6$, Et_3N, CH_3CN, 0°C, 45 mins), followed by standard aqueous work up, ether extraction and chromatography afforded pure lactone 3 (85% yield). The initially formed alkene-Mo(CO)(NO)Cp complex is presumably demetallated by exposure to air during the work up.



1 2 ·····(1)

(a) R = Me
(b) R = $CH_2CH{=}CH_2$
(c) R = C_6H_4OMe-p
(d) R = $CH(CO_2Me)_2$
(e) R = $CH(SO_2Ph)CO_2Me$
(f) R = CH_2CO_2H
(g) R = CN

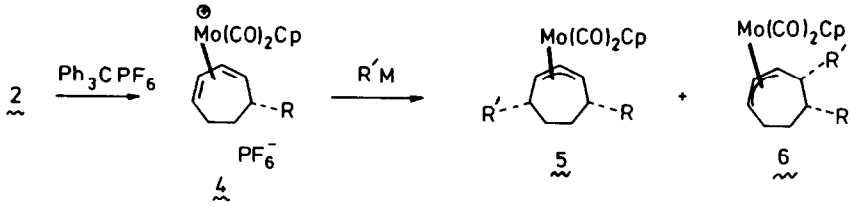


2f 3

The second requirement, further functionalization, was tested for three complexes, 2a, 2b and 2c. Hydride abstraction (Ph_3CPF_6, CH_2Cl_2, 0°C, 60 min) proceeded smoothly in each case, giving high yields of 4a (80%), 4b (90%) and 4c (90%). Subsequent nucleophile addition to these complexes also proceeded with good stereo- and regiocontrol in most cases to give complexes 5 together with, in some cases, 6 (see Table). However, this reaction is profoundly influenced by the steric requirement of the nucleophile and of the substituent (R) in cations 4. Of particular note is the fact that, whereas 4a gives only complex 5e on reaction with $NaCH(SO_2Ph)CO_2Me$, a mixture of 5 and 6 is obtained on reaction with $NaCH(CO_2Me)_2$, MeMgBr, NaCN or p-$MeOC_6H_4MgBr$ (see Table). However, the availability of complex 4c allows the latter problem to be overcome, since this compound reacts with MeMgBr to give 5i (equivalent to 5c) in high yield (less than 5% impurity, presumably 6i by 200 MHz NMR spectroscopy). Complexes 4b and 4c were found to react satisfactorily with $NaCH(CO_2Me)_2$ to give single products (Table). The double activation/nucleophile addition therefore has potential generality in this ring size.

Controlled decomplexation was established starting with the disubstituted complex 5e which was converted to carboxylic acid 5f, m.p. 140°C, in 65% overall yield as described

above. Treatment of 5f with iodine (I_2, CH_3CN) under a variety of conditions gave the lactone 7, but this was contaminated with substantial amounts of impurity (see also results on acid 2f). This problem was nicely overcome by using $NOPF_6$, as above, when the lactone 7 was obtained as the sole product in 90% yield. We have previously shown[3(c)] that cyclohexenyl-$Mo(CO)_2Cp$ complexes which do not contain pendant nucleophiles are converted to allylic



(a) R = Me
(b) R = $CH_2CH{=}CH_2$
(c) R = C_6H_4OMe-p

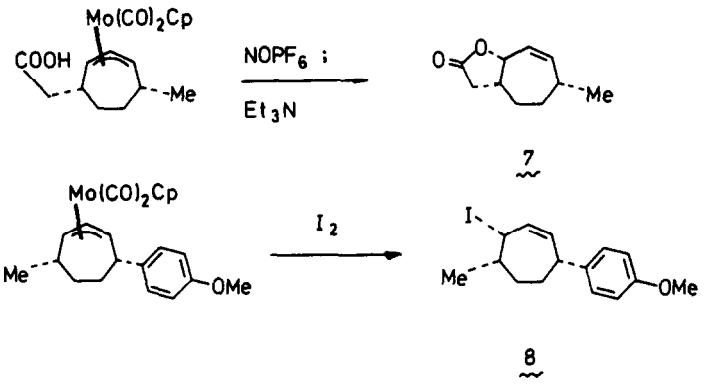
(a) R = R' = Me
(b) R = Me, R' = CN
(c) R = Me, R' = C_6H_4OMe-p
(d) R = Me, R' = $CH(CO_2Me)_2$
(e) R = Me, R' = $CH(SO_2Ph)CO_2Me$
(f) R = Me, R' = CH_2CO_2H
(g) R = $CH_2CH{=}CH_2$, R' = $CH(CO_2Me)_2$
(h) R = C_6H_4OMe-p, R' = $CH(CO_2Me)_2$
(i) R = C_6H_4OMe-p, R' = Me

TABLE Carbon Nucleophile Additions to Diene Complexes 1 and 4

Diene Complex	RM or R'M	Product(s), m.p.	Product ratio	Yield%
1	MeMgBr	2(a) 70°C	n.a.	85%
1	$CH_2{=}CHCH_2MgBr$	2(b) 71°C	n.a.	90%
1	p-$MeOC_6H_4MgBr$	2(c)[a]	n.a.	90%
1	$NaCH(CO_2Me)_2$	2(d) oil	n.a.	95%
1	$NaCH(SO_2Ph)CO_2Me$	2(e) oil	2:1(diastereomers)	98%
1	NaCN	2(g) 95°C	n.a.	90%
4(a)	MeMgBr	5(a) + 6(a)	2:1	85%
4(a)	NaCN	5(b) + 6(b)	5:1	82%
4(a)	p-$MeOC_6H_4MgBr$	5(c) + 6(c)	3:2	85%
4(a)	$NaCH(CO_2Me)_2$	5(d) + 6(d)	2:1	85%
4(a)	$NaCH(SO_2Ph)CO_2Me$	5(e)	diastereomers	98%
4(b)	$NaCH(CO_2Me)_2$	5(g)	n.a.	98%
4(c)	$NaCH(CO_2Me)_2$	5(h)	n.a.	95%
4(c)	MeMgBr	5i	$\geq$ 20:1	85%

a) contaminated with small amounts of biaryl, from Grignard coupling, which could not be completely removed by chromatography.

iodides on treatment with iodine. In the present series, it was found that reaction of complex 5i with iodine (I_2,[3] equiv., CH_3CN, 20°C) afforded the iodide 8 as the major product.



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In summary, the intermediacy of cycloheptadiene-$Mo(CO)_2Cp$ cations provides useful methodology for the stereo- and regiocontrolled functionalization of cycloheptene. We anticipate that this, coupled with ring scission, will find application in the synthesis of a variety of natural products where stereocontrol is required at remote positions, and we are currently investigating complexes related to 5i as intermediates for synthesis of aplysiatoxins.[6]

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References and Notes

1. Pearson, A.J.; Ong. C. W.; J. Org. Chem., 1982, 47, 3780; Pearson, A. J.; Chandler, M.; J. Chem. Soc. Perkin Trans 1, 1982, 1641; Pearson, A. J.; Kole, S. L.; Chen, B.; J. Am. Chem. Soc., 1983, 105, 4483; Pearson, A. J.; Kole, S. L.; Ray, T.; J. Am. Chem. Soc., 1984, 106, 6060; Paquette, L. A.; Daniels, R. G.; Gleiter, R.; Organometallics, 1984, 3, 560.
2. Chung, Y. K.; Choi, H. S.; Sweigart, D. A.; J. Am. Chem. Soc., 1982, 104, 4245.
3. (a) Faller, J. W.; Murray, H. H.; White, D. L.; Chao, K. H.; Organometallics, 1983, 2, 400; (b) Pearson, A. J.; Khan, Md. N. I.; J. Am. Chem. Soc., 1984, 106, 1872: (c) Pearson, A. J.; Khan, Md. N. I.; Tetrahedron Lett., 1984, 25, 3507.
4. All new compounds were fully characterized by IR and 200 MHz ^1H NMR spectroscopy and combustion analysis and/or high resolution mass spectrometry where possible. Details will be given in a full paper describing this work.
5. Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R.; Tetrahedron Lett., 1976, 3477.
6. Mynderse, J. S.; Moore, R. E.; J. Org. Chem., 1978, 43, 2301; Mynderse, J. S.; Moore, R. E.; Kashiwagi, M.; Norton, T. R.; Science, 1977, 196, 538; Kato, Y.; Scheuer, P. J.; J. Am. Chem. Soc., 1974, 96, 2245; Pure Appl. Chem., 1976, 48, 29; Moore, R. E.; Blackman, A. J.; Cheuk, C. E.; Mynderse, J. S.; Matsumoto, G. K.; Clardy, J.; Woodard, R. W.; Craig, J. C.; J. Org. Chem., 1984, 49, 2484.

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