Pergamon

Tetrahedron Letters, Vol. 37, No. 18, pp. 3087-3088, 1996

0040-4039/96 $15.00 + 0.00

S0040-4039(96)00367-X

Studies on Asymmetric Conversion of Arenes to Functionalized Cyclohexenones *via* Chiral Auxiliary-Promoted Nucleophilic Additions to Arene-Chromium Complexes

Anthony J. Pearson,* Alexander V. Gontcharov, and (in part) Paul D. Woodgate†

Department of Chemistry, Case Western Reserve University, Cleveland, OH 44106, USA;
†Department of Chemistry, University of Auckland, Auckland, New Zealand

Abstract Reactions of alkoxyarene-chromium tricarbonyl complexes, having chiral alkoxy groups, with isobutyronitrile anion, followed by standard work-up produces substituted alkoxycyclohexadienes with diastereomeric excesses of up to 76%. Conversion to cyclohexenones allows recovery of the chiral alcohol auxiliary. The absolute stereochemistry of the product from the optimum procedure was determined by using Mosher's method on the derived cyclohexenol. Copyright © 1996 Elsevier Science Ltd

Addition of nucleophiles to arene-transition metal complexes provides useful methodology for the conversion of aromatic compounds to functionalized cyclohexenones.[1,2] However, there have been very few reports on developing an asymmetric version of such nucleophilic additions.[3,4] We recently reported[5,6] that *trans*-2,5-dimethylpyrrolidine can serve as an efficient chiral auxiliary in nucleophilic additions to arene manganese tricarbonyl complexes, where diastereoselectivities of up to 95:5 can be obtained. Problems that have arisen during the attempted conversion of the intitial cyclohexadienyl adducts to cyclohexenones prompted us to undertake the study described in this Letter (a full account of our arene-manganese work will be published elsewhere).

Chromium complexes **1** and **2** were prepared in excellent yield by reaction of the corresponding (fluoroarene)chromium tricarbonyl derivatives with the potassium alkoxides (Scheme I). Addition of $LiCMe_2CN$ gave an anionic dienyl adduct, which was converted *in situ* into the cyclohexadiene complex by treating with trifluoroacetic acid. The resulting solution was worked up with aqueous ammonia, according to standard procedures, to afford the free dienol ethers **3a, b** and **4a, b** as mixtures of diastereomers, the ratios of which were determined by integration of the corresponding ^1H NMR signals and are presented in Table 1.

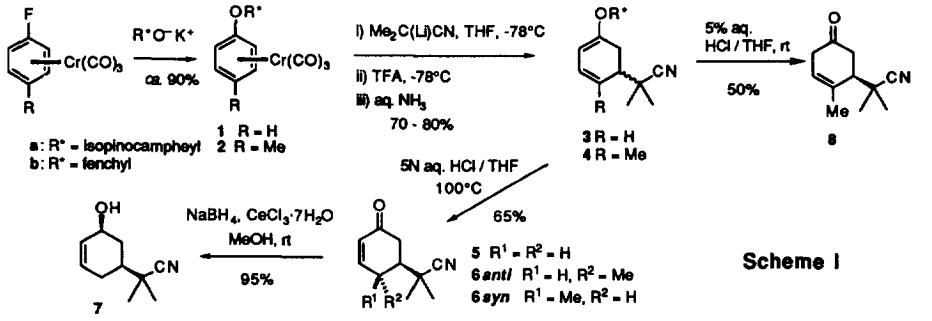
Table 1 Reactions of $LiCMe_2CN$ with complexes **1** and **2**

Complex	d.e. (%)	Yield (%)*
1a	39	40
1b	40	67
2a	56	84
2b	76	59

*Not optimized

Hydrolysis of the dienol ethers **3a** and **3b** with 5N aq. HCl in THF at 100°C gave enantiomerically enriched cyclohexenone **5**. The chiral alcohol is liberated during this operation and may be recovered. To determine the absolute stereochemistry of the major and minor enantiomers, cyclohexenone **5** was reduced to the allylic alcohol **7**, the absolute stereochemistry of which was readily established by using Mosher's

method.[7,8] Hydrolysis of **4a** and **4b** under similar conditions gave *ca.* 1:1 mixtures of enones **6*syn*** and **6*anti***, with the methyl group *syn* or *anti* to the isobutyronitrile substituent, respectively. Hydrolysis of **4a** and **4b** under milder conditions (THF/5% aq. HCl, room temp.) gave the enantiomerically enriched non-conjugated enone **8**.



Scheme I

Such significant diastereoselectivities (7.5:1 in the case of **2b**) are unexpected because the chiral auxiliary is somewhat remote from the reaction site and is an ether, for which one normally does not expect appreciable conformational restriction. It should be noted, however, that according to literature data[9] addition of nucleophiles to arene-chromium complexes is reversible, so that the basis for the stereo-differentiation in the present case may have a thermodynamic nature (unlike arene-manganese systems, where carbon nucleophile addition is kinetically controlled) and the diastereomer ratios should reflect the difference in the relative energies of the two diastereomeric addition products.

Acknowledgements: We are grateful to the National Institutes of Health, General Medical Sciences (GM 36925), for the financial support of this research.

References

(1) Pike, R. D.; Sweigart, D. A. *Synlett* **1990**, 565.

(2) Semmelhack, M. F. In *Comprehensive Organic Synthesis*; B. M. Trost and I. Fleming, Eds.; Pergamon Press: Oxford, 1991; Vol. 4; pp 517-549.

(3) Miles, W. H.; Brinkman, H. R. *Tetrahedron Lett.* **1992**, *33*, 584.

(4) Kündig, E. P.; Ripa, A.; Bernadinelli, G. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1071.

(5) Pearson, A. J.; Zhu, P. Y.; Youngs, W. J.; Bradshaw, J. D.; McConville, D. B. *J. Am. Chem. Soc.* **1993**, *115*, 10376.

(6) Pearson, A. J.; Milletti, M. C.; Zhu, P. Y. *J. Chem. Soc., Chem. Commun.* **1995**, 853.

(7) Dale, A. D.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(8) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

(9) Semmelhack, M. F.; Hall, H. T., Jr.; Farina, R.; Yoshifuji, M.; Clark, G.; Bargar, T.; Hirotsu, K.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 3535.

(*Received in USA* 3 *January* 1996; *revised* 19 *February* 1996; *accepted* 20 *February* 1996)