Highly enantioselective chiral base mediated [2,3]-Wittig rearrangement

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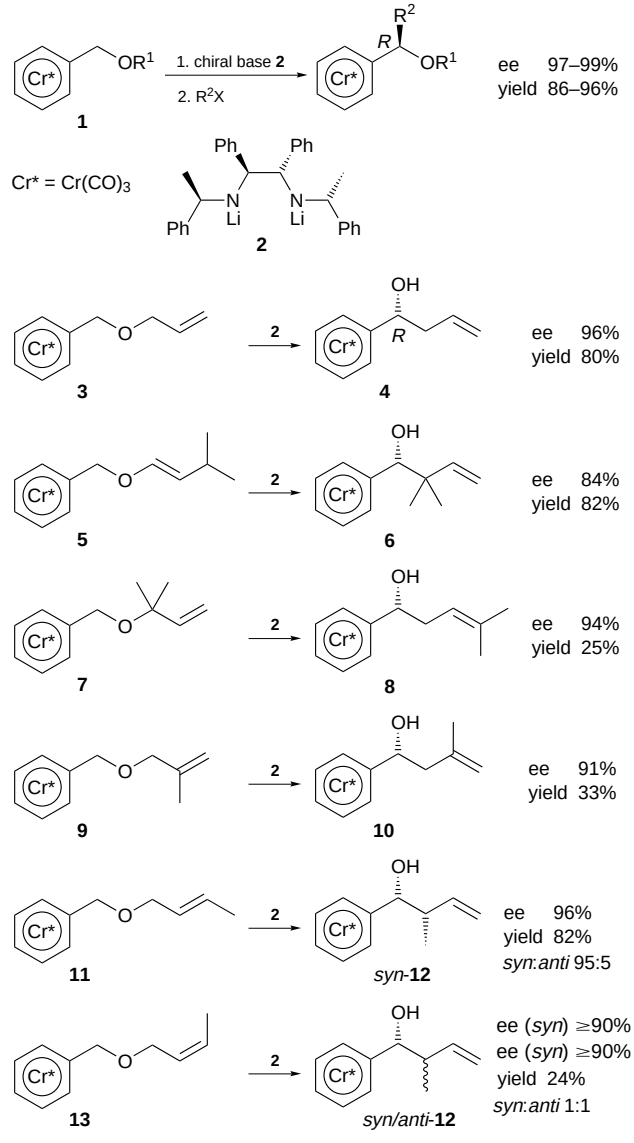
A chiral non-racemic base promoted [2,3]-Wittig rearrangement of a series of (allyloxymethylbenzene)tricarbonylchromium(0) complexes proceeds with remarkably high enantioselectivity.

The [2,3]-Wittig (sigmatropic) rearrangement is a useful carbon–carbon bond-forming reaction.[1] As such, asymmetric versions of it are a desirable goal and research in recent years has produced several approaches to such systems.[2] The greatest success has been achieved using chiral auxiliaries.[3] For example, rearrangement of a range of α-allyloxy ketone hydrazones derived from a non-racemic chiral hydrazine proceeded in excellent yield (89–100%), with very good *syn*/*anti* selectivity (80–94% de) and good enantioselectivity (63–90% ee).[3a] Enantioselective versions of the [2,3]-Wittig rearrangement involving an achiral substrate and a chiral non-racemic base are synthetically more attractive but this approach has been much less successful, providing very moderate yields, diastereoselectivities and enantioselectivities.[4] The best results to date for a linear† system were obtained very recently using diprop-2-ynyl ethers as substrates.[4a] These rearranged in modest yield (29–57%) and with moderate enantioselectivity (46–62% ee) on treatment with a base derived from norpseudoephedrine. In view of the moderate success achieved so far for the chiral non-racemic base mediated [2,3]-Wittig rearrangement, we reveal herein a rearrangement that proceeds with relatively high enantioselectivity (84–96% ee) and, with appropriate substitution, very good yield (80–82%).

Our recent observation that the benzylic methylene group in tricarbonylchromium(0) complexes of alkyl benzyl ethers **1** may be functionalised asymmetrically in high yield and enantiomeric excess by treatment with the chiral non-racemic base **2** and an external electrophile,[6] together with earlier reports that tricarbonylchromium(0) complexes of allyl benzyl ethers undergo [2,3]-Wittig rearrangements,[7] suggested to us that the action of base **2** on allyl benzyl ether complexes may lead to a highly enantioselective [2,3]-Wittig rearrangement. Accordingly a series of allyl benzyl ether complexes were synthesised using standard procedures‡ and the outcome of their reactions with base **2** determined (Scheme 1).

Initially the reaction of parent complex **3** with base **2** was examined. Complex **3** was added dropwise to a mixture of 1.1 equiv. of base **2**[8] and 1 equiv. of LiCl in THF at −78 °C. The reaction mixture was allowed to warm to −50 °C over 2 h and then stirred at −50 °C for a further 5 h. Addition of methanol and work-up gave a yellow oil that was identified as the [2,3]-Wittig rearrangement product **4** by comparison of its spectroscopic data with literature values.[7d] The enantiomeric purity of **4** was readily assessed by chiral HPLC (Chiralpak AD) and, to our delight, was found to be 96%. In order to determine the absolute configuration of product **4**, the tricarbonylchromium(0) unit was removed (*hν*, 83% yield) and the $[\alpha]_D$ of the resulting alcohol compared with literature values.[9] This revealed that the absolute configuration of **4** was *R*, a result consistent with the sense of asymmetric induction observed for the functionalisation of complexes **1** with external electrophiles.[6]

The effect of substituents on the chemical yields and enantioselectivity of the [2,3]-Wittig rearrangement were examined next starting with substituent patterns that would lead to products containing just one chiral centre. Complexes **5**, **7** and **9** rearranged to give the novel§ alcohol complexes **6**, **8** and **10** with very good enantioselectivity (84–94%).¶ Although the chemical yield of **6** was good (82%), the yields of **8** and **10** were relatively poor (25 and 33% respectively) probably reflecting, for **8**, the hindered trajectory presented to the base by **7** and, for **10**, the extra electron donating substituent on an already electron-rich centre[10] in the transition state leading to **10**.



Scheme 1

Finally complexes **11** and **13** were reacted with base **2** in order to determine the level of stereochemical control this asymmetric [2,3]-Wittig rearrangement would exert over the generation of two adjacent chiral centres. The (*E*)-but-2-enyl complex **11** rearranged smoothly to give a good yield (82%) of alcohol **12**. The diastereomeric ratio of the product complex was found to be 95 : 5 and the relative stereochemistry of the major isomer was identified as *syn* by comparison of the ^{1}H NMR spectroscopic data of **12** and its decomplexation product with literature values obtained from a racemic sample.[7c] Chiral HPLC analysis revealed that the ee of **12** was 96%. In contrast the (*Z*)-but-2-enyl complex **13** rearranged to give a relatively poor yield of a 1 : 1 mixture of diastereomers,‖ although it was noted that the ee of each of the diastereomers was ⩾90%.

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Footnotes and References

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† The best result recorded to date for a *cyclic* system is the conversion of a 13-membered prop-2-ynylic ether into a 10-membered prop-2-ynylic alcohol in 69% ee and 82% yield using lithium bis[(*S*)-1-phenylethyl]amide.[5] This success was attributed to special conformational effects as the same base gave a poorer result with a 17-membered homologue (30% ee, 78% yield), and racemic products when applied to acyclic α-(allyloxy)acetic acids and amides.[5]

‡ The novel complexes **5** and **7**, and the known complexes **11** and **13**[7c] were synthesised by heating $Cr(CO)_6$ with the appropriate allyl benzyl ether (62–78%), whilst the uncharacterised complex **3**[7d] and the novel complex **9** were made by reacting (hydroxymethylbenzene)tricarbonylchromium(0) with NaH–allyl bromide (86%) and $ZnCl_2$–2-methylprop-2-en-1-ol (54%) respectively.

§ The novel complexes **3**, **5**–**10** and **12** all gave satisfactory microanalytical and spectroscopic (IR, ^{1}H NMR, ^{13}C NMR, *m/z*) data.

¶ The absolute stereochemistry of products **6**, **8**, **10** and **12** has been assigned by analogy with the rearrangement of complex **3** to **4** under the influence of base **2**.

‖ The clean rearrangement of the (*E*)-but-2-enyl complex **11** to a *syn* product and the uncontrolled rearrangement of the (*Z*)-but-2-enyl complex **12** is consistent with results obtained with racemic complexes[7] and contrasts with the (*Z*)-*syn* selectivity normally observed for the [2,3]-Wittig rearrangement of but-2-enyl systems.[1,7,10]

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