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LEAVING GROUP DEPENDENT STEREOCHEMISTRY OF THIOALLENE FORMATION WITH PHENYLTHIOCOPPER PHOSPHINE COMPLEXES

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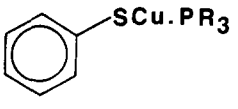
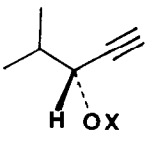
A Chiral secondary propargylic triflate (5) reacts with phenylthiocopper phosphine complexes (1) and (2) to give propargyl and allenic sulphides with complete inversion of configuration, but the corresponding mesylate (4) reacts with both complexes to give racemic products.

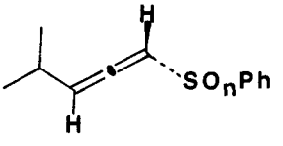
One of the most important routes to allenes involve the reaction of alkyl cuprates with propargylic halides, sulphonates and sulphinates.[2] These reactions generally proceed with complete inversion of the propargyl system and anti stereochemistry.[3] However the cuprous bromide catalysed reactions of propargylic alcohols with HBr give clean bromoallene products, but with syn stereochemistry.[4] In this communication we report on the stereochemistry and regiochemistry of the reactions of two phenylthiocopper species with two chiral propargylic sulphonate esters.



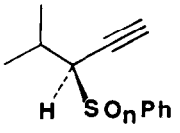
1. R = OCH_3
2. R = Ph



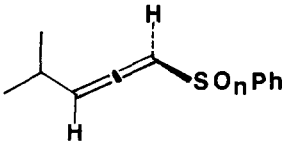
3. X = H
4. X = SO_2CH_3
5. X = SO_2CF_3



6. n = 1
7. n = 2



8. n = 0
9. n = 2



10. n = 0
11. n = 2

We have reported previously[5] that phenylthiocopper trimethylphosphite complex (1) reacts with propargylic halides and mesylates to yield mainly propargylically inverted thioallenes. The corresponding triphenylphosphine complex (2) behaves similarly. In order to determine the stereochemistry of these reactions we examined the displacement reactions of two derivatives of [R], 4-methyl-pent-1-yn-3-ol (3), sulphonate esters (4) and (5), with complexes (1) and (2). The alcohol derivatives were chosen because the alcohol can be obtained readily in high, known, enantiomeric excess by chiral synthesis.[6] By a simple S_N2 reaction, or a 2,3-sigmatropic rearrangement, [R]-alcohol (3) can be converted into both possible regioisomeric products with

known configurations. The reactions of complex (1) with mesylates appear to give high allene:acetylene ratios under kinetic conditions, whereas the similar ratios obtained with propargylic halides in TMEDA, were obtained under equilibrating conditions, the allene:acetylene ratio increasing with time.

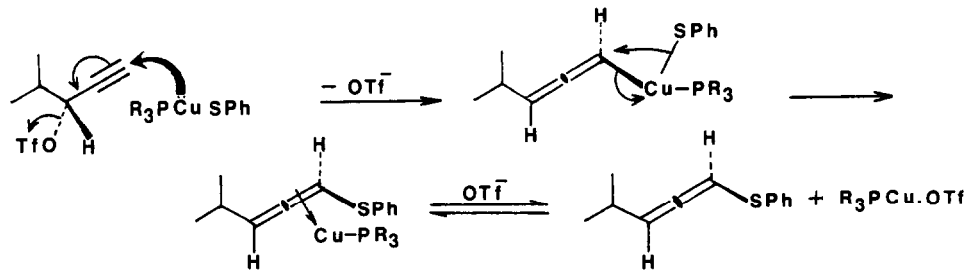
[R], 4-methylpent-1-yn-3-ol (3) was produced by the method Midland[6] in 92% enantiomeric excess. On treatment with phenylsulphenyl chloride and triethylamine[7] (0°, CH_2Cl_2) alcohol (3) gave the [R]-allenyl sulphoxide (6), as a 10:1 mixture of diastereoisomers at sulphur, in 80-90% yield. To eliminate problems involved with chirality at sulphur[8] the sulphoxide was oxidised to corresponding [R]-sulphone (7), (mCPBA, CH_2Cl_2, 0°→25°) which has only an axis as chiral element. An ORD spectrum taken on this showed a negative curve $[\alpha]_D$-14.7°, $[\alpha]_{300}$ - 106°, (92% e.e.) in accordance with Brewster's rules[8,9]. (Since the sulphones were generally more stable, and easier to purify, than the corresponding sulphides all ORD comparisons were carried out on them as 1-2 gpl solutions in ethanol).

As direct displacement at C_3 of ynol (3) can also occur, to give sulphide (8), the reaction of mesylate (4) with sodium thiophenoxide was examined. Mesylate (4) proved to be very unreactive towards thiophenoxide ion, being recovered completely unchanged even with DMF (3h, 25°) as solvent. In contrast the corresponding triflate (5), generated and reacted <u>in situ</u> (3 eq. NEt_3, Tf_2O, CH_2Cl_2-78°, then PhSH,-78°→25°), proved to be very reactive, giving clean [S]-acetylene (8), in 90% yield. Oxidation (2eq. mCPBA, 0°→25°, CH_2Cl_2) gave [S]-sulphone (9), $[\alpha]_D$-3.0°, $[\alpha]_{300}$-19.7°.

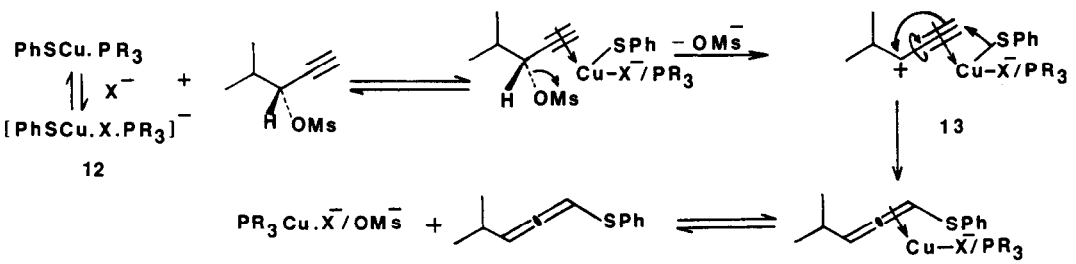
The reaction of phosphite complex (1) with <u>in situ</u> generated mesylate (4) was examined initially. This is a very straightforward procedure, giving good yields, and high allene:acetylene ratios (~20:1 in this case), which do not alter with time, suggesting that no equilibration occurs under these circumstances. Under these conditions (NEt_3, CH_2Cl_2, 0°, MsCl, then PhSCu.$P(OMe)_3$, 0°, 5 min) [R]-alcohol (3) gave a 66% yield of allene (10), which on oxidation (2 eq. mCPBA, CH_2Cl_2, 0°→25°) to sulphone (11), proved to be completely racemic. The same result, racemisation, was obtained, with lower yields, on shortening the reaction time to 2 minutes, or on adding complex (1) to the reaction mixture prior to mesylation. Previous experiments had suggested that the presence of halide ion can have a powerful effect on the course of these reactions, especially with oxygen leaving groups. Presumably halide ion ligands to the cuprous ion to produce the anionic "ate" complex $[PhSCu.X.PR_3]^-$ (12) which is probably the active species in the above reactions. We therefore investigated the reactions between purified mesylate (4) and complexes (1) and (2). In $CDCl_3$ mesylate (4) reacted very slowly with complex (1), taking 2 hours to be completely consumed at 25°. However the yield of allene (10) peaked at around 15% after 20 minutes, and extensive decomposition then occurred. In contrast, mesylate (4) reacted quite rapidly with complex (2) (15 minutes, 25°) to give 38% of allene (10) and 20% of acetylene (8), but on oxidation both sulphones proved to be racemic again. Repeating this reaction in the presence of chloride ion increased the allene:acetylene ratio to 5:1, but did not show the rate enhancement, seen with complex (1), and no attempt was made to determine its stereochemistry.

Complexes (1) and (2) both reacted rapidly with the <u>in situ</u> generated triflate (5),

(Tf_2O,NEt_3, CH_2Cl_2,-78°, then $PhSCu.PR_3$,78°→0°). Complex (1) gave a 5:1 ratio of allene:acetylene, but the reaction mixture was rather dirty, and, allene (10 was obtained in 28% yield. After oxidation (2 eq. mCPBA, CH_2Cl_2, 0°→20°) the sulphone (11) showed a positive ORD curve, values within 2% of those obtained for the (-) sulphone (7), ($[\alpha]_D$ + 17°, $[\alpha]_{300}$ + 104°). Thus this reaction went with clean anti stereochemistry. Under the same conditions complex (2) gave 20% of allene (10) and 13% of allene (8), both with clean inversion of configuration. These reactions presumably involve dicoordinated metal complexes rather than anionic tricoordinated complexes, and the low yields may be due to the reactivity of the byproduct cuprous triflate complexes.



Scheme 1



Scheme 2

The isolation of unracemised [S]-allene (10) strongly suggests that the results obtained under similar conditions with mesylate (4) are not due to copper catalysed racemisation[10] of the allene, since it is very improbable that cuprous mesylate would cause complete racemisation within two minutes whilst cuprous, triflate causes no detectable racemisation. The relative chemical inertness of mesylate (4) makes it very improbable that it racemised prior to reaction, so we conclude that it is the displacement process which occurs with racemisation.

We believe that the different stereochemical outcomes of the reactions of (4) and (5) can be explained by considering their different electrophilicities, as demonstrated by their thiophenoxide reactions. Complexes (1) and (2) are much less reactive than normal cuprates as they have two stabilising ligands for the copper ion. Therefore they are not reactive enough to undergo oxidative addition to mesylate (4), but can do so with the much more electrophilic triflate (5), as shown in Scheme 1. The attack on (5) occurs with clean anti stereochemistry[2], and the subsequent transfer of the phenylthio ligand from copper to carbon proceeds in a syn

fashion[11] to C_1 (or C_3) leading to [R]-allene and [S] acetylene. Mesylate (4) may follow the pathway shown in Scheme 2. Initially a copper alkyne complex[12] (13) is formed. This can ionise very readily[13] to give cationic complex (14),[4] which racemises, by rapid rotation about the C_2-C_3 bond, more quickly than the relatively slow transfer of the good sulphur ligand from copper to carbon.

As a synthetic procedure, the reactions described in this paper allow for the conversion of a single enantiomer of a propargyl alcohol into either enantiomer of a chiral axis compound with complete stereospecificity.

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References

1. CMAC Undergraduate Research Fellow.
2. M. Kalli, P. D. Landor and S. R. Landor, J. Chem. Soc. Perkin I, 1973, 1347. P. Rona and P. Crabbe J. Amer. Chem. Soc., 1969, 91, 3289. P. Vermeer, H. Westmijze, H. Kleijn and L. A. Van Dijck, Rec. Trav. Chim. Pays-Bas, 1978, 97 56. P. Vermeer J. Meijer and L. Brandsma ibid, 1975, 94, 112.
3. C. J. Elsevier, J. Meijer, H. Westmijze, P. Vermeer and L. A. Van Dijck, J. Chem. Soc. Chem. commun., 1982, 84. In this paper the previous reports of syn stereochemistry in steroidal systems were shown to be due to misassignment of product stereochemistry using the Lowe-Brewster rules.
4. S. R. Landor, B. Demetriou, R. J. Evans, R. Grzeskowiak and P. Davey, J. Chem. Soc., Perkin II, 1972, 1995.
5. A. J. Bridges, Tetrahedron Lett., 1980, 4401. See also L. Brandsma and H. D. Verkruijsse in ''Synthesis of Acetylenes Allenes and Cumulenes,'' Elseviewr, 1981, 195.
6. M. M. Midland, J. Org. Chem., 1975, 40, 2250. M. M. Midland, D. C. McDowell, R. L. Hatch and A. Tramontano, J.Amer. Chem. Soc., 1980, 102, 867.
7. L. Horner and V. Binder, Annalen, 1972, 757, 33. R. C. Cookson and P. J. Parsons J. Chem. Soc. Chem. Commun., 1978, 822.
8. M. Cinquini, S. Colonna, F. Cozzi and C. J. M. Stirling, J. Chem. Soc. Perkin I, 1976, 2061.
9. G. Lowe, J. Chem. Soc. Chem. Commun., 1965, 411.
10. A. Claesson and L.-I. Olsson J. Chem. Soc. Chem. Commun., 1979, 524.
11. R. A. J. Smith and O. J. Hannah Tetrahedron, 1979, 35, 1183.
12. G. A. Chukhadhyan, G. A. Gevorkyan and V. P. Kukolev J. Gen. Chem.(USSR)., 1976, 46, 905.
13. K. M. Nicholas and R. Pettit J. Organomet. Chem. 1972, 44, C21.

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