Regioreversed Nucleophilic Substitution of 2-(Allyloxy)benzothiazoles by Allylic Grignard Reagents governed by Anchimeric Co-ordination. A Selective and Flexible Synthesis of 1,5-Dienes

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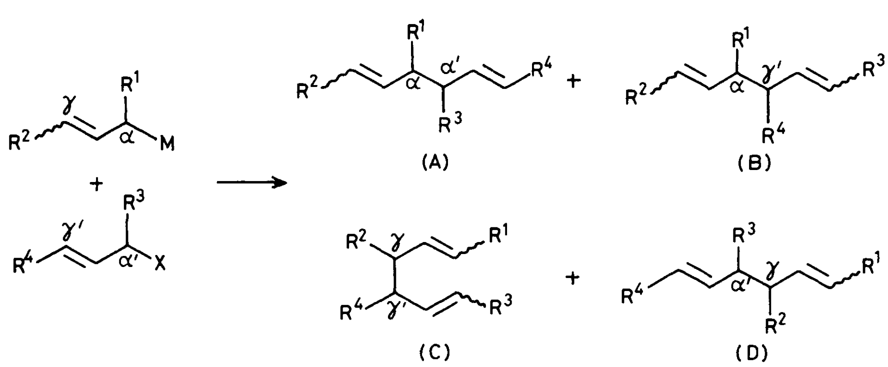
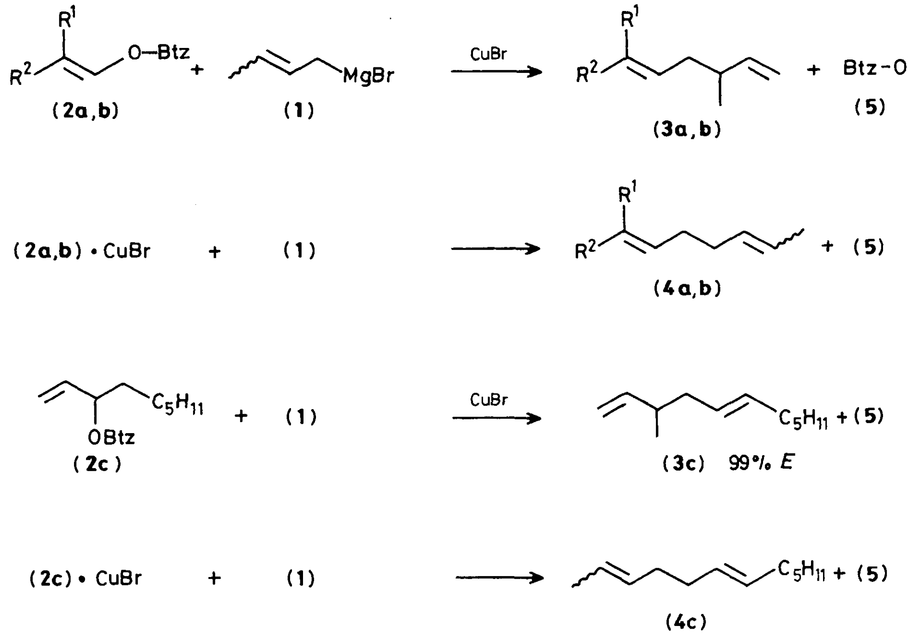
The regioselectivity in the C–C coupling process of 2-(allyloxy)benzothiazoles with allyl organomagnesium compounds is influenced by the co-ordination of the heterocycle by the organometallic reagent.

The synthesis of 1,5-dienes by cross-coupling reactions of allylic electrophiles with allylic carbon nucleophiles, although conceptually simple, is subject to severe regio- and stereochemical complications.[1] These arise from the positional ambiguity at both reaction centres since the allylic nucleophile has ambident character[2] and the allylic electrophile can react by S_N2' or S_N2 mechanisms.[3] Moreover the S_N2' process is often complicated by lack of stereoselectivity.

Recently we demonstrated[4] that the regio- and stereochemistry in allylic substitution with alkyl Grignard reagents can be governed by using 2-(allylthio)- or 2-(allyloxy)-benzothiazoles as electrophiles since these substrates may



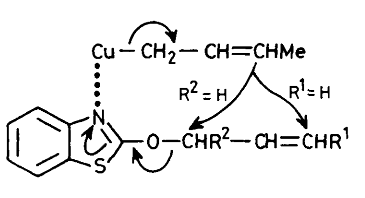
Scheme 1. X = Halogen, OAc, SO_2R, *etc.*; M = Mg, Li, Cu, BR_3, Zn, or Sn.

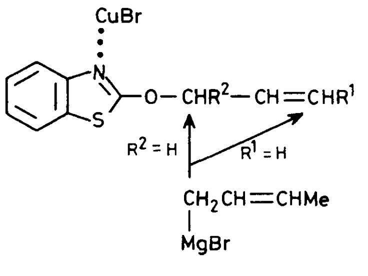


Scheme 2. (**2a**), R^1 = Me, R^2 = $Me_2C{=}CH[CH_2]_2$; (**2b**), R^1 = H, R^2 = Pr^n. Btz = benzothiazol-2-yl.

co-ordinate to the metal of the organometallic reagent. We now report that owing to the anchimeric co-ordination of 2-(allyloxy)benzothiazoles, primary allylic organomagnesium compounds lose their ambident nucleophilic character and react regioselectively to give 1,5-dienes. Thus the reaction of primary allylic ethers (**2a,b**) with but-2-enylmagnesium bromide in the presence of CuBr gives exclusively α',γ-type C–C coupling products (D, Scheme 1). On the other hand the secondary ether (**2c**) gives the γ',γ-type product (C) stereospecifically. The regiochemistry of this nucleophilic substitution can be completely reversed if the allylic organomagnesium compound reacts with the same allylic ethers but complexed with CuBr.[5] In this case, the (**2a,b**)·CuBr complexes give α',α-type products (**4a,b**) while those derived from (**2c**) give the γ',α coupling product (**4c**).

This behaviour, despite its potential importance for the synthesis of terpenes, is unprecedented. A rationale which accounts for the observed selectivity change should involve co-ordination phenomena as already observed.[5] In the first case the allylic organocopper reagent, which is an ambident nucleophile, is co-ordinated by the allylic ether and, for steric reasons, reacts in a head-to-tail or tail-to-tail fashion. On the





other hand, when the co-ordination site of the electrophile is occupied, as with the (**2a**—**c**) • CuBr complexes, the organometallic reagent reacts with the less sterically hindered position of the electrophile to give the head-to-head products (**4a,b**) or the head-to-tail product (**4c**).

The following procedures are typical. (i) CuBr (0.03 mol) was added to (**2c**) (0.01 mol) dissolved in dry tetrahydrofuran (THF) (20 ml) at 0 °C without stirring. To this suspension was added rapidly with a syringe and with stirring but-2-enylmagnesium bromide (0.02 mol) in THF. After 30 min, the usual work-up and flash-chromatography gave *trans*-3-methylundeca-1,5-diene (**3c**) in 85% yield. (ii) But-2-enylmagnesium bromide (0.02 mol) in THF was added at 0 °C with stirring to the (**2c**) • CuBr complex[5] (0.01 mol) suspended in THF (20 ml). Work-up as above gave dodeca-2,6-diene (**4c**) in 90% yield (*Z,E*:*E,E* 2:1).†

Other primary organomagnesium compounds, *e.g.* γ-dimethylallylmagnesium chloride, behave similarly, and results will be published elsewhere.

Received, 13th May 1985, Com. 652

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† Compounds (**3a**) and (**3b**) both show an ABX ^1H n.m.r. pattern: (**3a**) δ($CDCl_3$) 0.86 (d, 3H), 1.55 (s, 6H), 1.63 (s, 3H), 4.90—5.30 (m, 4H, $CH=CH_2$ and $C=CH$), and 5.78 (m, 1H); i.r. (neat) 1641, 996, and 913 cm^{-1} ($CH=CH_2$); (**3b**) δ($CDCl_3$) 0.86 (d, 3H), 0.93 (t, 3H), 4.95 (m, 2H, $CH=CH_2$), 5.42 (m, 2H, $CH=CH$), and 5.78 (m, 1H, $CH=CH_2$); i.r. (neat) 1670, 1641, 996, 969, and 913 cm^{-1}; (**4a**) δ($CDCl_3$) 4.98 (br. s, 2H) and 5.44 (m, 2H, $CH=CH$); i.r. (neat) 1672, 968, and 702 cm^{-1}; (**4b**) δ($CDCl_3$) 0.90 (t, 3H), 1.62 (m, 3H), and 5.44 (m, 4H); i.r. (neat) 1670, 965, and 702 cm^{-1}.