SN′ Reactions involving Organocuprate Reagents

By CHRISTOPHER B. CHAPLEO, MARK A. W. FINCH, THOMAS V. LEE, and STANLEY M. ROBERTS*
(*The Ramage Laboratories, Department of Chemistry and Applied Chemistry, Salford University, Salford, Lancs.* M5 4WT)
and ROGER F. NEWTON*
[*Chemical Research Department, Glaxo-Allenburys Research (Ware) Ltd., Ware, Herts.* SG12 0DJ]

Summary The allyl halides (**1**) and (**14**) and the allyl epoxide (**5**) react with butylcuprate reagents through an *SN′ anti* process preferentially: with the same reagents the hindered halide (**10**) gives the product derived from an *SN′ syn* reaction.

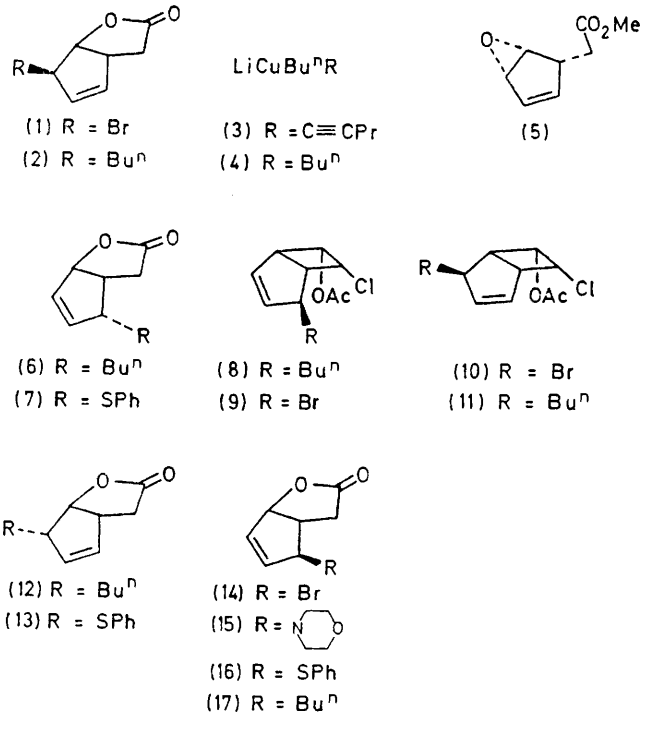
THE bromolactone (**1**)[1] reacted with an equimolar amount of the heterocuprate reagent (**3**) or the homocuprate reagent (**4**) at −78 °C to give the rearranged 6-*endo*-butyl-lactone (**6**) (60%)† contaminated with a small amount (*ca.* 5%) of the isomeric butyl-lactone (**12**). In complementary fashion the lactone (**12**) was obtained (45%)† together with a small amount (*ca.* 12%) of the stereoisomer (**6**) on reaction of the cuprate reagent (**3**) and the 6-*exo*-bromolactone (**14**) at low temperature.

The bias of the lactone (**1**) towards an *SN′ anti* mode of reaction was peculiar to cuprate reagents: thus morpholine reacted with (**1**) to give the amine (**15**) (60%)† derived from an *SN′ syn* process, while reaction of the same lactone with sodium thiophenoxide gave a mixture of the phenylthiolactones (**16**) (83%), (**7**) (4%), and (**13**) (3%).†

The *SN′ anti* process was also favoured on treatment of the allyl epoxide (**5**)[2] with the cuprate reagents (**3**) and (**4**): reaction of (**5**) with the reagent (**3**) at −78 °C in ether gave a mixture of the butyl-lactones (**17**) and (**2**) (ratio 5:2) (64%)† while reaction of (**5**) with reagent (**4**) gave (**17**) and (**2**) in the ratio 4:1 (65%).†

Paradoxically, the dihalogenoester (**10**)[3] reacted with the cuprate reagent (**3**) in ether at −78 °C to give the rearranged *syn*-substituted product (**8**) (95%).† Similarly, a mixture containing equal amounts of the acetates (**10**) and (**9**) gave, after reaction with the copper reagent (**3**), a high yield of a 1:1 mixture of the butylbicycloheptenones (**8**) and (**11**). These results suggest that the bromoester (**9**) is also alkylated with *syn*-stereochemistry.

Recent work has established that SN_2' reactions can proceed with *syn*- or *anti*-stereochemistry.[4] Only under appropriate steric and/or electronic influences will the

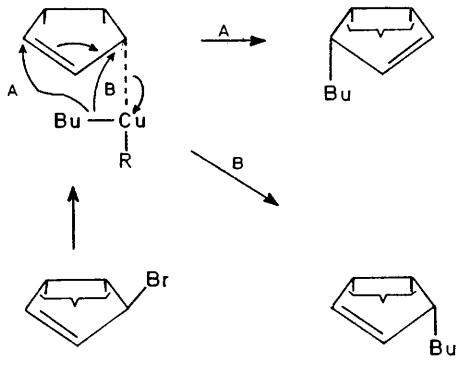


syn-mode of reaction become exclusive.[5] The reactions of the lactone (**1**) with morpholine and thiophenoxide ion have shown that in this molecule the lactone ring discourages nucleophilic attack from the *endo*-cavity. These results, combined with the high selectivity of the reactions involving the cuprate reagents and the allyl bromides (**1**), (**9**), (**10**), and (**14**), suggest that the latter reactions do *not* proceed *via* an initial one-electron reduction to form a delocalized radical[6] since this would lead to alkylation

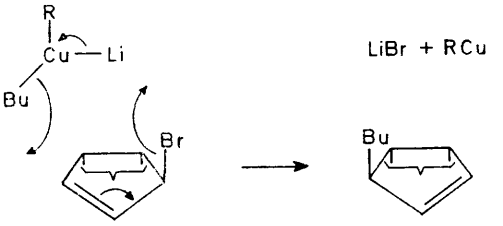
† Yields refer to isolated products after chromatography and are not optimized: the lactones were identified by ^1H and ^{13}C n.m.r. spectroscopy and isomer ratios were determined by these spectroscopic techniques and by g.l.c. analysis.

taking place from the unhindered *exo*-face in a regiorandom fashion.

In fact, our results concur with previous studies in which it has been shown that cycloallyl epoxides,[7] esters,[4,8] and ethers[9] usually react with cuprate reagents to give rearranged and/or unrearranged products with complete inversion of configuration. We propose that the allyl bromides (**1**), (**14**), and the allyl epoxide (**5**) suffer nucleophilic substitution by the cuprate reagents with inversion of configuration to give either an allyl copper(III) intermediate,[10] or a π-allyl complex which maintains stereochemical integrity[9] (Scheme 1). Migration of the alkyl ligand can take place with (path A) and without (path B) rearrangement of the double bond. Obviously, the *SN'* *syn* delivery (path A)[11] is much preferred at the low reaction temperatures that we employed.



SCHEME 1



SCHEME 2

Furthermore we suggest that when the initial nucleophilic attack by the cuprate reagent is rendered impossible by steric crowding as in the esters (**9**) and (**10**), an SN_2' process can take place circumventing a cycloalkenylcopper intermediate (Scheme 2). In this case alkylation takes place with *syn*-stereochemistry.

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