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LEWIS ACID CATALYSED CYCLOADDITION OF 1,3-BISTRIMETHYLSILYLOXYCYCLOHEXADIENES TO 2-CHLORO-ACRYLONITRILE. NOVEL REARRANGEMENT OF THE RESULTING ADDUCTS TO CYCLOHEXENONES

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Summary: Lewis acid catalysed cycloaddition of the dienes (**1**) and (**2**) to 2-chloroacrylonitrile occurs in high yield and with stereoselectivity to give the corresponding adducts (**3**) and (**4**) which can be rearranged upon treatment with fluoride ion to the bicyclic cyclohexenones (**5**) - (**8**).

The Diels-Alder adducts of 1-methoxycyclohexadienes and ketene equivalents (*e.g.*, 2-chloroacrylonitrile) can be converted into substituted cyclohexenones by Baeyer-Villiger fragmentation.[1] We were attracted to investigate the cycloaddition of ketene equivalents with 1,3-bis-silyloxycyclohexadienes which had previously been shown to be effective Diels-Alder partners with acrylonitrile, albeit under forcing conditions.[2] The dienes (**1**) and (**2**) were prepared by the methods of Simchen[3] and Ainsworth.[4] Following previous precedent[2] the cycloaddition of dienophiles to the dienes (**1**) and (**2**) was first studied at 65 °C. With 2-chloroacrylonitrile and (**1**) the adducts (**3a**) and (**3b**)[5] were obtained in 65% yield in a ratio of 10:1 after work-up with methanolic potassium carbonate.[6] However a superior yield (97%) of a 1.1-1.2:1 mixture of isomers was obtained by carrying out the reaction at room temperature in the dienophile as solvent. The inferior yield at higher temperatures is almost certainly due to the preferential thermal rearrangement of the *exo*-chloro silyl enol ether adduct corresponding to (**3b**). Previous studies in the methoxy series have demonstrated that the *exo*-chloro bicyclic enol ethers undergo a rearrangement to the corresponding bicyclo[3.2.1] derivatives.[7,8]

Similarly diene (**2**) and 2-chloroacrylonitrile at 65 °C afforded in 53% yield the products (**4a**)-(**4d**)[5] with a *syn*-methyl (syn to the ketone) [(**4a**) + (**4b**)] to *anti*-methyl ratio [(**4c**) + (**4d**)] of 3:1. At room temperature the yield was 80% with the ratio (**4a**):(**4b**):(**4c**):(**4d**) 10:7:1.2:1, *i.e.* an overall syn:anti ratio of 8:1 (as estimated from integration of signals due to the methyl group in the ^{1}H N.M.R. spectrum, and by g.c analysis). The ^{1}H N.M.R. spectra of the individual isomers of (**4**) resembled very closely those recorded and rigorously assigned for the coresponding bridgehead methoxy analogues.[1,8]

The effect of added stoichiometric quantities of Lewis acid on the syn/anti ratio of compounds (**4**) was quite dramatic. Both $TiCl_4$ and Me_2AlCl enhanced the preference for the *syn* adducts (**4a**) and (**4b**) (after work-up with aqueous HCl). The most dramatic result was obtained using Me_2AlCl in toluene at -78 °C when a quantitative yield of products was obtained with the ratio (**4a,b**):(**4c,d**) in excess of 25:1 with a slight (4:1)

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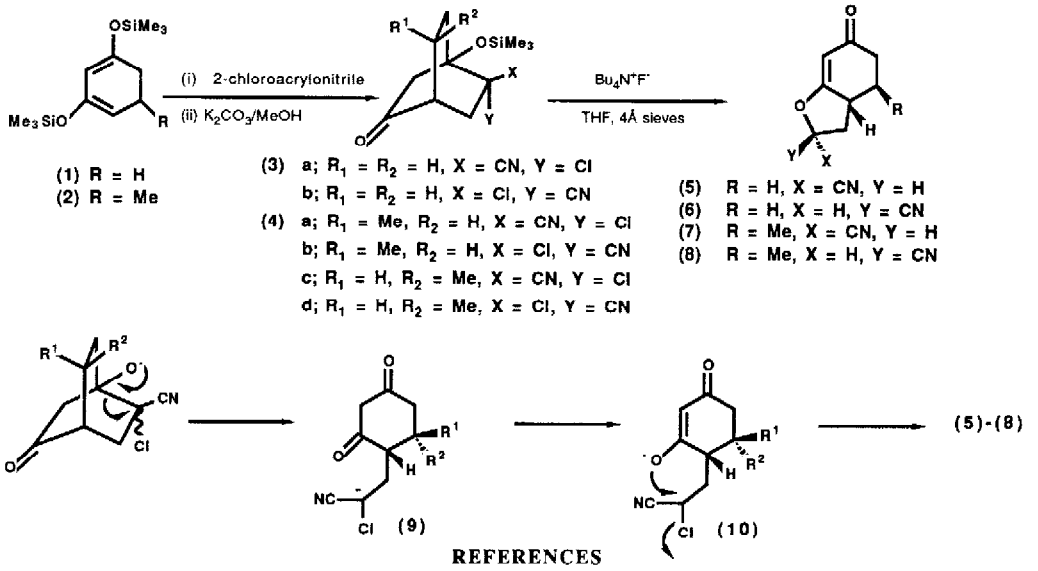
preference for the *exo*-cyano isomer (**4a**):(**4b**). This is a most impressive example of increased face selectivity in cycloadditions catalysed by organoaluminium species,[9, 10] and offers potential for asymmetric induction.[11]

The silyl ethers (**3**) and (**4**) could be desilylated to the corresponding tertiary alcohol derivatives using *tetra*-n-butylammonium fluoride in THF.[12] These products were accompanied by the novel rearranged cyclohexenones (**5**,**6**) and (**7**,**8**) respectively. Optimum yields of the rearranged products were achieved using the fluoride reagent in the presence of 4Å molecular sieves. Thus (**3a**,**b**) gave (**5**) and (**6**) in 89% yield in a 1:1 ratio and likewise (**4a**,**b**) afforded (**7**) and (**8**) (1:1) in 42% yield.[5] Stereochemical assignments at the nitrile are based on analysis of the vicinal coupling constants with the neighbouring methylene group. The rearrangement involves cleavage of the bicycle to the corresponding cyclohexanedione (**9**) followed by recyclisation of the enolate (**10**) with displacement of chloride. The rearrangement demands the presence of a carbonyl group in the starting bicycle, and the product stereochemistry is independent of the epimeric ratio of starting chloronitriles; both observations support the proposed pathway.

In summary, the *syn*-selective Lewis acid-catalysed cycloaddition reactions of (**2**) and the novel rearrangement of (**3**)-(**4**) to (**5**)-(**8**) offer scope for new synthetic approaches to cyclohexenones.[13]



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