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CONCERNING THE REACTIVITY OF 1,2:3,4-DIEPOXIDES TOWARDS NUCLEOPHILES

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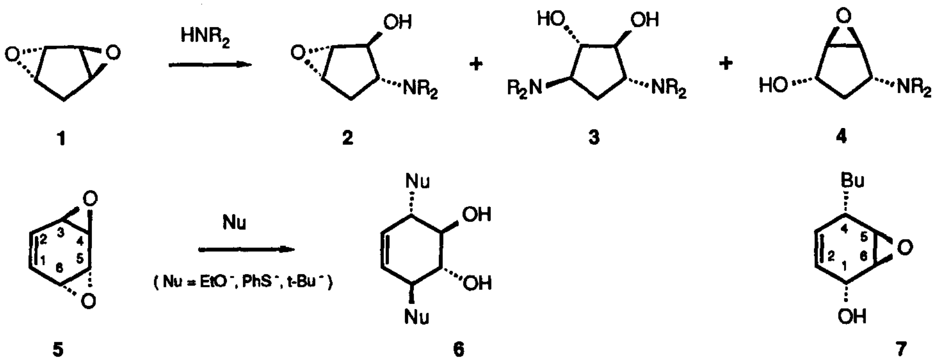
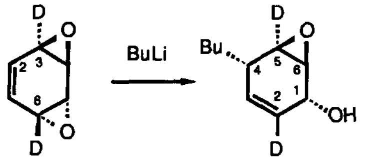
Summary: anti-Benzenedioxide reacts with various nucleophiles to give the products resulting from the attack at both epoxy functions. With butyllithium, however, the formation of a product with a central epoxide is observed. This product is not the result of an epoxide migration but rather of the attack of the nucleophile at the double bond.

1,2:3,4-Diepoxides are of interest as model compounds for natural products[1] and as intermediates in the synthesis of biologically active substances.[2] Their behavior towards nucleophiles has so far only been studied marginally. Independent reaction of the two epoxy functions was observed.[3] In contrast to this, Kozlov et al.[4] found that when anti-diepoxycyclopentane (1)[5] was allowed to react with secondary amines, a product 4 with a central epoxide was obtained in addition to the expected substances 2 and 3. This compound 4 was obviously formed by nucleophilic opening of one of the epoxides and subsequent epoxide migration. This is the only case where the formation of such a central epoxide has been described.

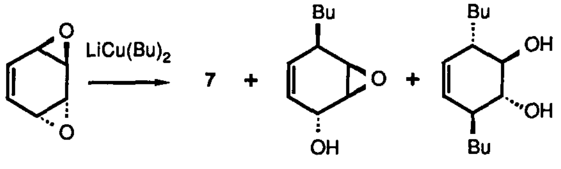


In order to investigate whether this type of reaction is general with 1,2:3,4-diepoxides, we treated some compounds of this class of substances with various nucleophiles. When anti-benzenedioxide (5)[6] was treated with secondary amines, no reaction could be discerned at all. O- and S-nucleophiles lead to simple opening of the two epoxy functions independently from each other, giving products of type 6. However, when butyllithium was used, a single product 7 with a central epoxide was obtained. Yet, 7 can be formed in several ways: either by nucleophilic attack at C(3) with simultaneous or subsequent Payne rearrangement[7] or by attack at C(2) and migration of the double bond (S_N2'-reaction).[8-10] A third possibility, the attack of the nucleophile at C(4) and subsequent rearrangement of the allylic alcohol thus formed, would lead to a product with the same constitution as 7 but with the butyl group cis to the epoxide. This third pathway can here be ruled out, since the rearrangement of the allylic alcohol would only occur in acidic milieu, which was not used in our experiments.

The way of formation of this product 7 was investigated with the aid of the deuterium labelled anti-benzenedioxide 8. This compound was prepared in analogy to the procedure of Altenbach and Vogel,[11] but the reduction of the intermediate dibromocyclohexenedione was carried out with $NaBD_4$ rather than with $NaBH_4$. Reaction of 8 with butyllithium gave a product 9 where the two deuterium labels were not in the expected positions 1 and 4 but rather in 2 and 5. Thus, compound 9 must have been formed by attack of the nucleophile at C(2) and not at C(3) of 8. Kozlov's observation of a central epoxide thus still represents a unique case.



8 9



5 10 11

The determination of the relative configuration at C(4) of 7 proved to be rather difficult. Therefore, we tried to prepare both C(4)-epimers, 7 and 10 by reaction of anti-benzenedioxide (5) with $LiCu(Bu)_2$. The reaction of vinyloxiranes with methyllithium and the corresponding cuprates is known to yield mixtures of isomers which - besides a few exceptions[8] - contain predominantly the trans-isomer.[9,10] We obtained a product mixture consisting of the cis-isomer 7, the trans-isomer 10 and the diadduct 11 in a ratio of 36:55:6. NOE difference spectra proved the cis- and trans-configurations of 7 and 10, respectively: with compound 7 weak NOE's could be observed for H-C(4) upon irradiation of H-C(1) and for H-C(1) upon irradiation of H-C(4); in 10 no such NOE's were detected. It is interesting to note that our case is again one of those exceptions where an alkyllithium compound reacts with a vinyloxirane to give predominantly the cis-product.

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