6. *2,3-Dihydro-3-hydroxy-7-methyl-5*H,*8*H-*thiazolo[3,2-*a*]pyrrolo[2,3-*d*]pyrimidin-5-on* (**10**). Eine Lösung von 18 g **8** [4] in 110 ml 1 N Natronlauge wurde bei etwa 80° mit 28 ml 30-proz. wässeriger Chloracetaldehydlösung versetzt und noch 15 Min. bei 80° gerührt, wobei **10** auskristallisierte. Ausbeute: 94%. $C_9H_9N_3O_2S$ (223,3), Smp. 283–286°.

7. *2,3-Dihydro-3-hydroxymethyl-7-methyl-5*H,*8*H-*thiazolo[3,2-*a*]pyrrolo[2,3-*d*]pyrimidin-5-on* (**11**). 36,2 g **8** [4] und 12 g NaOH wurden unter leichtem Erwärmen in 1,3 l Wasser gelöst und nach dem Abkühlen auf Raumtemperatur mit 21,3 g Epichlorhydrin versetzt. Nach kurzer Zeit begann Kristallisation von **11**. Ausbeute: ca. 50%. $C_{10}H_{11}N_3O_2S$ (237,3), Smp. 293–295°.

8. *7-Methyl-5*H,*8*H-*thiazolo[3,2-*a*]pyrrolo[2,3-*d*]pyrimidin-5-on* (**12a**). In einer Sublimierapparatur wurden 16 g **10** mit 32 g Kaliumhydrogensulfat unter 15 Torr auf 300–340° erhitzt, wobei **12a** aus dem Gemisch sublimierte. $C_9H_7N_3OS$ (205,2), Smp. > 320°.

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180. Evidence for a Synfacial Nucleophilic Displacement with Allylic Rearrangement. Mechanistic Conclusions

Preliminary Communication[1])

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(27. VI. 71)

Summary. Reduction of *exo*-2-methyl-3,4-dichlorobicyclo[3.2.1]oct-2-ene and the *exo*-2-phenyl-3,4-dibromo analogue with lithium aluminium hydride proceeds mainly with allylic rearrangement. Moreover, hydride enters and bromide leaves synfacially. The stereochemistry of the process is discussed in the light of the favourable energy of a quasi-cyclic transition state in which reagent and halide are complexed.

It has recently been suggested that the concerted S_N2' mechanism may be mythical as there appear to be no unambiguous examples [1]. Certainly, controversy and ambiguity have characterised the history of this mechanism since its formulation [2] [3]. A difficulty inherent in the analysis of bimolecular allylic substitutions is that multiple processes may be involved. Consequently, clearcut examples of such reactions which can be precisely designated as S_Ni', S_N2' etc. are rare.

In this preliminary paper we report firstly evidence for a synfacial nucleophilic displacement by hydride on an allylic bromide proceeding with allylic rearrangement, which is accompanied by a small amount of direct displacement at the allylic carbon. Secondly, we comment on the faciality of the rearrangement with respect to the apparent dilemma of attributing the S_N2' or S_Ni' designation.

The substrate chosen, the bicyclo[3.2.1]octenyl halide system, is well-suited for the study of cyclohexenyl reactivity [4]. In particular, *exo*-2-methyl-3,4-dichlorobi-

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[1]) The full paper will be submitted to Helv.

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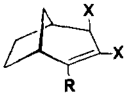
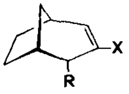
cyclo[3.2.1]oct-2-ene (**1**) and its *exo*-2-phenyl-3,4-dibromo analogue (**4**) were treated with metal hydrides and the products examined.

The action of lithium aluminium hydride (LAH) on **1** in boiling ether gave two products **2** and **3** in the ratio of 4:1 in 73% yield. By similar treatment with LAH, the phenyl analogue **4** gave **5** and **6** in a ratio of 9:1 also in high yield (77%). Thus, the



1 R = Me, X = Cl
4 R = Ph, X = Br



2 R = Me, X = Cl
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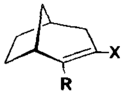
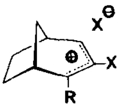


3 R = Me, X = Cl
6 R = Ph, X = Br

overall reaction is reductive substitution with mainly allylic rearrangement. Further, in both major products **2** and **5**, the allylic substituents *viz.* the methyl and phenyl groups respectively, have the *endo* disposition. The interpretation of these reductions is not straightforward, as non-rearranged product is also formed. Three mechanisms need to be considered. Attack by free hydride on the intimate allylic ion pair **7** could have taken place preferentially at the tertiary carbon atom [5]. This possibility is



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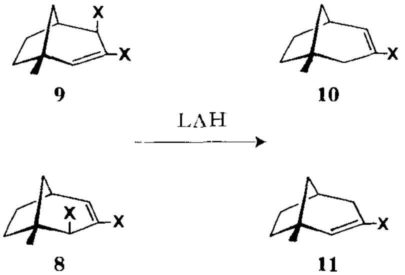
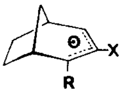
difficult to discount, especially as it had previously been shown that a 20:80 mixture of the bicyclo-octenyl dibromides **8** and **9** gave an 84:16 mixture of allylically rearranged and non-rearranged products **10** and **11** on reduction [6]. Arguments concerning the stereochemistry of the process however are not affected by this possibility.

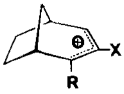


A second possibility is the simultaneous operation of S_N2' and S_N2 mechanisms, separately leading to major (**2** and **5**) and minor products (**3** and **6**). Thirdly, the results could be explained by a common S_N1' mechanism since the allylic cations derived from **1** and **4** could conceivably be attacked by hydride ion to give rearranged and unrearranged products in the ratios observed.

In order to clarify this last possibility, **1** was treated with tri-*n*-butyl tin hydride (TBTH). Rearranged (**2**) and unrearranged (**3**) products were obtained in the ratio of 1:4, the inverse of that found for the LAH reduction. A similar reversal (1:9) was found in the TBTH reduction of **4**. Since the action of TBTH on halides is known [7] to generate the corresponding radical intermediate, which subsequently abstracts hydrogen from a second reagent molecule, it is reasonable to assume that the behaviour of radicals **12** and **13** towards reagent should resemble that of the corresponding allylic cations **14** and **15**. Consequently, the intermediacy of such species can be ruled out for the LAH reduction.

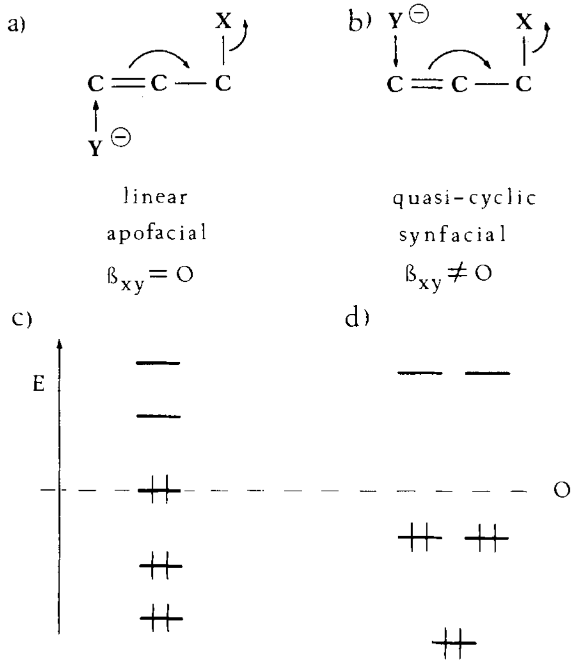


12 R = Me, X = Cl
13 R = Ph, X = Br



14 R = Me, X = Cl
15 R = Ph, X = Br

The results indicate that the chief mechanistic feature of the reduction with allylic rearrangements is the synfacial displacement of halide by hydride. The term synfacial is used to signify the involvement of *two* groups on the same face of the molecule, in contrast to the term suprafacial which refers to a possible trajectory of a *single* atom or group with respect to a surface. Two related questions now arise; (i) why is the reaction synfacial and not apofacial (entering and leaving groups disposed on opposite faces of the molecule); (ii) what is the distinction between an *S*$_N$i′ (necessarily synfacial) process and a synfacial *S*$_N$2′ process.



MO energy levels c) *and* d) *for the apofacial* (a) *and synfacial* (b) *transition states of an* S$_N$2′*-type process*

An answer is forthcoming from a simple qualitative consideration of the transition states possible for six reacting electrons in a basis set of five atomic orbitals (AO). Two limiting arrays of AO's may be envisaged, linear and quasi-cyclic which correspond to the apo- and syn-facial processes (see Fig.). In the linear arrangement (Fig., a) there is no interaction between the terminal AO's, and consequently the resulting MO's will be like those of the pentadienyl anion (Fig., c). On the other hand, in the quasi-cyclic arrangement (Fig., b), the proximity of the atoms X and Y renders mutual orbital interaction likely and thus the corresponding MO's will resemble those of the cyclopentadienyl anion (Fig., d). Thus, provided the reacting groups X and Y can have a satisfactory orbital interaction, the synfacial process will be energetically favoured. Moreover, this conclusion implies that the designation S_Ni′ is more appropriate than is S_N2' for such a process.

In a perfectly general way the relative energies of the syn- and apo-facial processes should depend on the nature of X and Y and should be affected by geometric, electrostatic and configurational factors [8]. Indeed, conformational effects have been invoked to explain the preferred apofaciality of the acetolysis of a 4β-bromo-5β-cholestan-3-one [9].

Electrostatic repulsion between X and Y should disfavour the synfacial process. The opposite effect, favourable interaction between incoming and leaving groups, has already been postulated by *Ingold* [2] who argued that the classic example of an S_N2' process, namely the reaction of piperidine with cyclohexenyl 2,6-dichlorobenzoate [10], should, owing to hydrogen bonding between entering and leaving groups, be reclassified as S_Ni′.

Similar effects involving electrostatic bonding between departing bromide and aluminohydride anion have been proposed by *Hatch* [11] to account for the stereospecificities of certain LAH reductions, with allylic rearrangement, of allyl bromides.

We conclude that the synfaciality of our reductions is similarly a consequence of complexation between the allylic halogen substituent and the electrophilic metal atom, lithium or aluminium. Furthermore, in concurrence with *Bordwell* [1] we suggest that the myth [1] concerning synfacial S_N2' displacements should not be perpetuated and that such processes should henceforth be regarded as S_Ni′. Further experiments are under way to determine the stereochemical requirements of apofacial and synfacial allylic rearrangements.

All new compounds gave acceptable elemental values on analysis and their spectroscopic properties were consistent with the proposed structures.

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