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INVERSION OF CONFIGURATION IN A FUSED CYCLOPROPANE RING OPENING BY HYDROCHLORIC ACID

by

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Opening of a cyclopropane ring by electrophiles can in principle occur via an inversion or via a retention mechanism. It has been found that with the proton as electrophile the opening proceeds with retention of configuration in the case of bicyclobutanes[1] and cyclopropanols[2]. With halogen as electrophilic agent both inversion[2] and retention[1] have been observed, depending on the substrate.

We wish to report an example of electrophilic addition of hydrogen chloride to a cyclopropane ring occurring via inversion of configuration at the carbon atom attacked initially*. Introduction of gaseous hydrogen chloride in a 10-20% solution of 1,2,3,4,5,6-hexamethyl-exo-tricyclo [4.1.0.$0^{2,5}$]hept-3-ene[4] $\underline{1}$ in CH_2Cl_2 or $CHCl_3$ at room temperature gives immediately a quantitative conversion to 1,2,3,4,5-endo-,7-syn-hexamethyl, 7-anti-chlorobicyclo[2.2.1]hept-2-ene $\underline{2a}$.

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* A few other examples of "end-on" protonation of a cyclopropane ring have recently been published[3].

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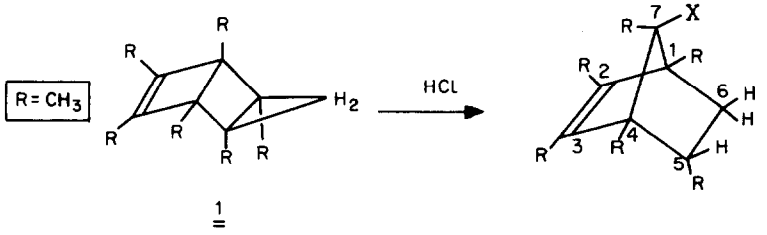


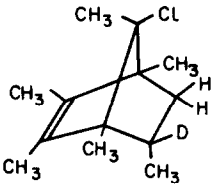
1

2a (X = Cl)
2b (X = OH)

The structure of compound 2a is assigned on the basis of the molecular weight, the NMR spectrum - - signals at 0.57 (dd, H-6-en), J(6-en-6-ex), 11.0, J(6 en-5 ex)3.5 Hz), 0.67(d, CH_3-5, J 6.8 Hz), 1.00(s, CH_3-1,4), 1.21(s, CH_3-7), 1.53(s, CH_3-2,3), 1.91(dd, H-6-ex, J(6 en-6 ex)11.0, J(6 ex-5 ex) 9.0 Hz) and ~2.2 ppm(m, H-5) - and on the conversion of 2a into 2b by chromatography of a solution of 2a in pentane/CH_2Cl_2 over moist Al_2O_3 or SiO_2. The NMR spectrum of compound 2b in chloroform-signals at 0.56(dd, H-6-en, J(6 en-6 ex)10.7, J(6 en-5 ex)3.5 Hz), 0.70(d, CH_3-5, J 6.6 Hz), 0.90(s, CH_3-7), 0.94 and 0.95(s, CH_3-1,4), ~1.2(7-OH), 1.56(s, CH_3-2,3), 1.83(dd, H-6-ex), J(6 en-6 ex)10.7, J(6 ex-5 ex)9.0 Hz) and ~2.0 ppm(m, H-5) - was also measured in the presence of tris(dipivalomethanato) europium complex[5], which facilitated the decoupling experiments for the methine and methylene protons. The configuration of endo-methyl and exo-proton at carbon 5 in compounds 2a and 2b is established by the following facts: (i) only one endo-proton (high-field[6] signal at 0.57(0.56) ppm) and two exo-protons (low-field signals at 1.91 and 2.2(1.83 and 2.0) ppm)[6] are present;

(ii) the chemical shift enhancement in the spectrum of 2b on addition of $Eu(DPM)_3$ which will be complexed to the oxygen lone-pair electrons[5b] - is about twice as large for the multiplets at 1.83 and 2.0 ppm as for the multiplet at 0.56 ppm, which is consistent with two exo and one endo protons. Interestingly, the chemical shift enhancement is equally low for the 2,3-CH_3 and 5-endo CH_3 groups (being about half of that for the 1,4-CH_3 groups), which agrees with the anti-position of X towards the carbon-carbon double bond (if X were syn to this bond, then complexing with $Eu(DPM)_3$ would have resulted in a larger effect on the chemical shifts of the 2,3-CH_3 groups. Compare ref. 5b);

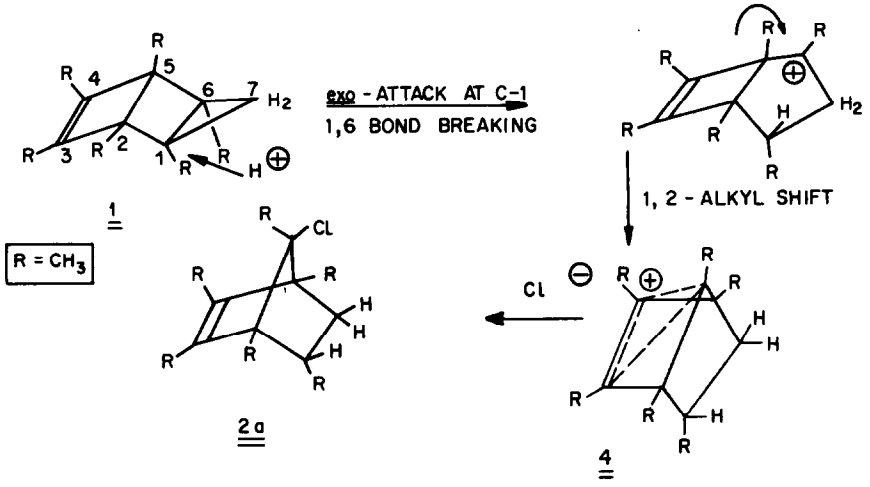
(iii) addition of DCl to 1 in $CDCl_3$ solution at room temperature gives compound 3:



3

which differs from compound 2a in the following NMR signals: 0.56(d, J = 11.0 Hz), 0.69 (s) and 1.96 ppm (broadened d, J = 11.0 Hz), while no absorption at ~2.2 ppm was found*.

These results can be explained by the following inversion (at C-1) mechanism:



1 2a 4

A retention (at C-1) mechanism would lead to the exo-isomer.

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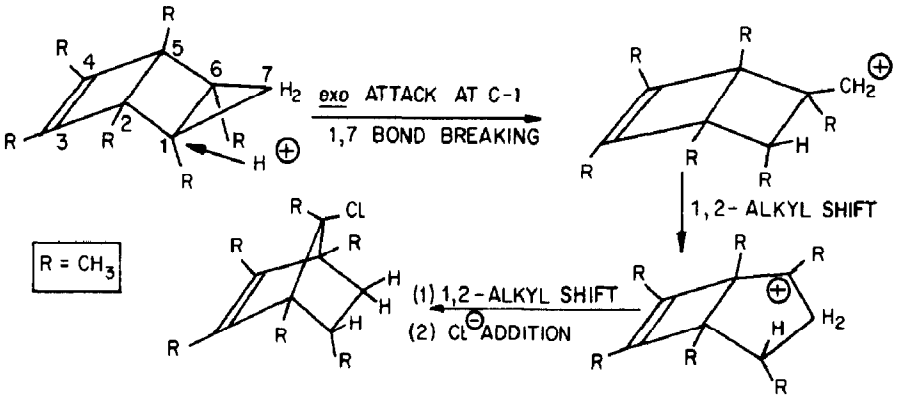
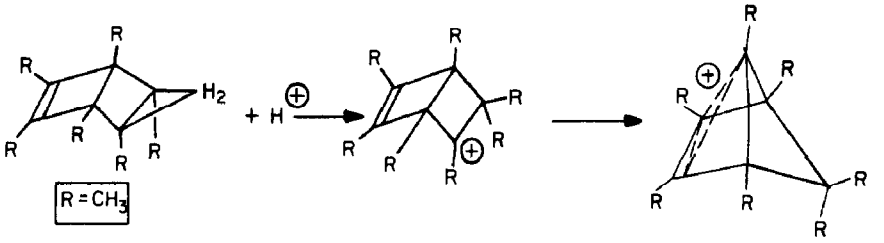
* Depending on the experimental conditions, a partial H-D exchange between the methylene protons of compound 1 and DCl was sometimes observed[7].

A conceivable alternative retention (at C-1) mechanism that would still explain the formation of compound 2a

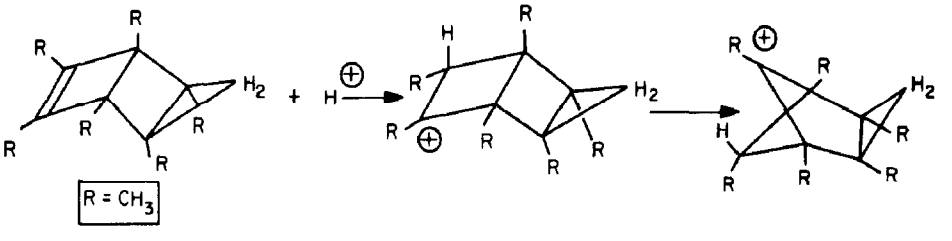


can be excluded because it involves a highly unstable primary cyclobutylcarbonium ion. It should be emphasized that also the following two processes[8]:

proton addition at C-7

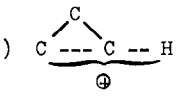
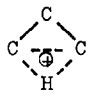


and proton addition at the carbon-carbon double bond

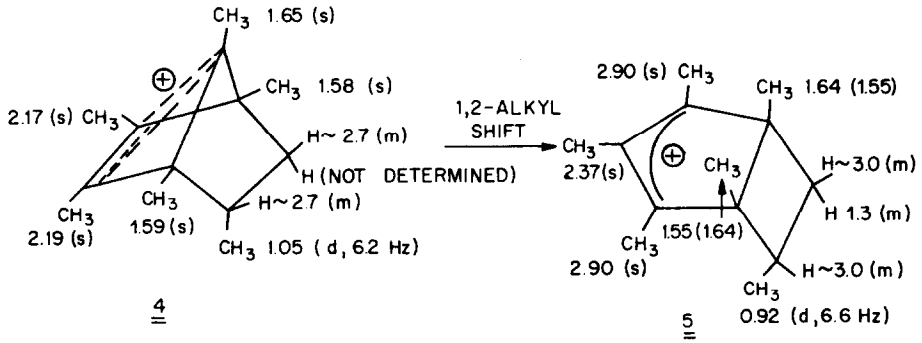


do not occur to any measurable extent.

The reason for the occurrence of the inversion mechanism in the cyclopropane ring-opening of compound 1 may be a steric one. Molecular models indicate that there is more severe hindrance from the endo than from the exo side, which could explain the preference of a (quasi)

linear transition state (intermediate)  over a triangular one 

All attempts to generate the postulated intermediate ion 4 as a stable entity by protonation of 1 at low temperatures (to -100 °C) in superacids as $FHSO_3$-SO_2ClF, $FHSO_3$-SbF_5-SO_2F_2, HF-BF_3 were unsuccessful. However, $Cl^{\ominus}$ abstraction from 2a by SbF_5-SO_2ClF (1:1 v/v) or $FHSO_3$-SbF_5 (2:1 v/v) at -70 °C readily afforded ion 4, which was identified by its NMR spectrum* (see ref. 9)



4 5

At 0 °C ion 4 reacts quantitatively in about one hour to give ion 5, which is a cyclobutane ring-fused ubi-cation[10]. The thermodynamic stability of (polymethyl)cyclopentenyl cations[11] is obviously so large that the inherent increase in strain by forming a fused cyclobutane ring is overcompensated. Very recently, a similar reaction of a protonated 7-norbornenone has been reported**. (see ref. 12).

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* Chemical shifts (in ppm) measured relative to internal tetramethyl ammonium chloride and converted to δ_{TMS} values by using δ_{TMS} = -3.20 ppm for the reference ion.

** The unidentified compound obtained[9b] on rearrangement of 7-methyl-7-norbornenyl cation probably has also a cyclobutane ring-fused cyclopentenyl cation structure.

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