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STEREOPECIFICITY IN FORMATION OF A BICYCLO[3,2,0]HEPTANONE FROM A 2-HYDROXYMETHYLCYCLOHEXANONE TOSYLATE

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In 1963 Wiberg and Klein[1] observed that the ketosulphonate (1) by action of base yielded two cyclobutanones (4) and (6), and postulated the intermediacy of (9) for the formation of (6). This type of reaction was again confirmed by Barco et al.[2] According to their mechanism an optically active ketosulphonate at the starred carbon must completely lose its activity in a bicyclo[3,2,0]heptanone. While recent publication[3] of acid and thermal rearrangement of (-)-crythansenone to (+)-2,4,4-trimethylbicyclo[3,2,0]hept-2-en-7-one suggested an alternate possibility that during the reaction (4) might rearrange to (6) with retention of its activity.

Here we show that the rearrangement of (1) to (6) proceeds stereospecifically, but the acid catalysed rearrangement of (4), though it actually occurs, gives the different bicyclo[3,2,0]heptanone (8).

The compounds (12)[4], m.p. 183-185°, and (13)[4], m.p. 211-213°, are epimeric at C_4 apart from other part of the molecule. On treatment with potassium t-butoxide in t-butanol for 5 min. either compound furnished single cyclobutanones [(14), m.p. 223-225°, IR 1770 cm^{-1}, and (15), m.p. 264-268°, IR 1770 cm^{-1}] in excellent yield, respectively. The products showed opposite Cotton effects [ORD, $[\phi]^{trough}_{324\ nm}=-8059$, CD, $\Delta\varepsilon_{309nm}=-1.25$ for (14), and ORD, $[\phi]^{peak}_{325\ nm}=+8676$, CD, $\Delta\varepsilon_{309\ nm}=+0.99$ for (15)] indicating that they are antipodal regarded to the bicyclo[3,2,0]heptanone systems. This proves that the rearrangement proceeded stereospecifically with complete retention of the configuration at C_4. The structure proofs are as follows. i) The NMR spectrum of (14) showed a broad singlet of 2H at δ 2.47 and a quartet of 1H at δ 3.33 (J=5 and 4 Hz) corresponding to $-C\underline{H}_2-CO-$ and $>C\underline{H}-CO-$, and that of (15) exhibited multiplets at δ 2.2$\sim$3.3 corresponding to three hydrogens. ii) Those signals disappeared after heating the compounds with NaOD in D_2O-dioxan indicating that they have three deutrium-exchangable hydrogens respectively. iii) Hydride reduction of them afforded the corresponding cyclobutanols whose acetates showed multiplet $>C_{(3)}\underline{H}-OAc$ signals respectively. These facts rejected the possibility that the cyclobutanones have bicyclo[3,1,1] system. Following transformations further confirmed the assigned structures. By oxidation with dilute H_2O_2-NaOH[5] at 0°C, (14) yielded a single γ-lactone (16), IR 1760 cm^{-1}, which on LAH reduction gave an alcohol (17;OH instead of OAc). Similar oxidation of (15) yielded a mixture of two γ-lactones (18) (major) and (19) (minor) (IR, 1770 cm^{-1}) which were converted to alcohols and characterized as acetates, (20) m.p. 174-176° and (21) m.p. 201-202°. The NMR spectra of the γ-lactones and the acetates (17), (20), and (21) agreed well with the assigned structures [NMR(δ): (17), $>C\underline{H}-OAc$, 5.00(1H, m.), $-CH_2-C\underline{H}_2-OAc$, 4.16(2H, t. J=8 Hz); (20), $>C_{(2)}\underline{H}-OAc$, 4.95 (1H, q. J=3 and 5 Hz), $-CH_2-C\underline{H}_2-OAc$, 4.10(2H, t. J=8 Hz); (21), $>CH-C\underline{H}_2-OAc$, 4.18(2H, m.), $-\overset{|}{\underset{|}{C}}-C\underline{H}_2-OAc$, 4.15(2H, broad s.)].

Next we reinvestigated the reaction of (1) in order to test the possibility of rearrangement (4) to (6). The mixture of (4) and (6) (IR, 1776 cm^{-1}) was more conveniently obtained from (1) by action of potassium t-butoxide in t-butanol instead of sodium hydroxide in methanol.[1] The ratio of (4) and (6) was 2:3 shown by GLPC and by the intensity ratio of methyl peaks at δ 1.09 and 1.46 in the NMR spectrum of the mixture. This ratio was constant from the earliest stage of the reaction though either peak increased their intensities as reaction proceeds and did not change by prolonged heating; the fact which indicates that the base affects neither to (4) nor (6). Treatment of this mixture with acid (e.g. oxalic acid, hydrochloric acid) changed the former methyl peak to δ 1.27 but the latter peak (1.46) remained unchanged. The ratio of these peaks was 2:3, though the product (IR, 1778 cm^{-1}) gave overlapped peaks in the GLPC. Alkaline hydrogen peroxide oxidation quantitatively transformed

Fig. 1

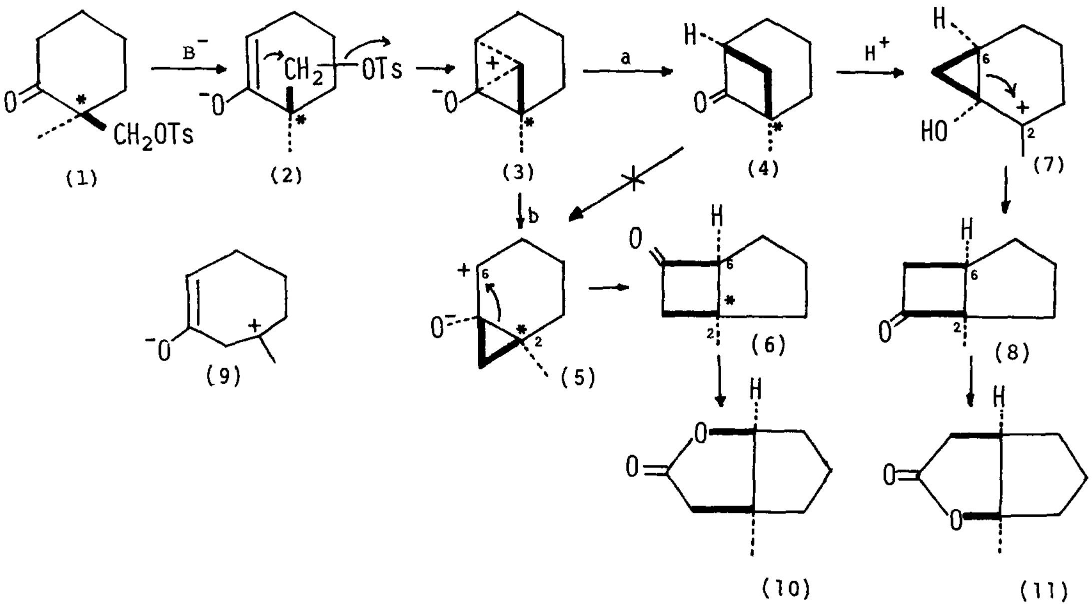
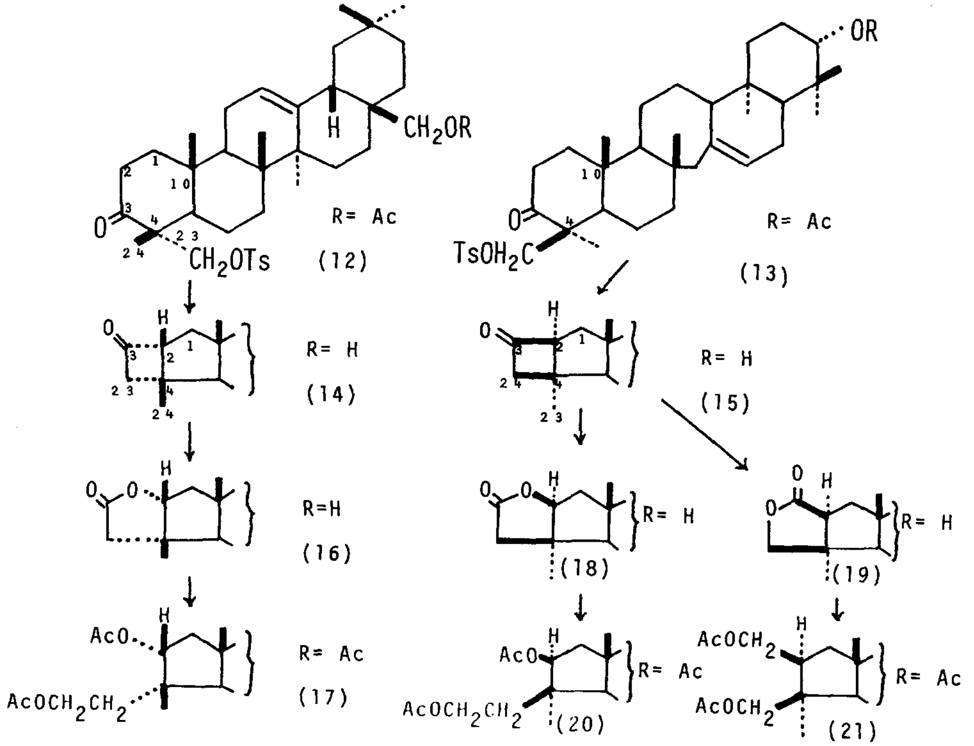

B⁻
CH2OTs
OTs
a
H⁺
b
HO
(1)
(2)
(3)
(4)
(5)
(6)
(7)
(8)
(9)
(10)
(11)

Fig. 2


CH2OR
OR
CH2OTs
TsOH2C
R= Ac
(12)
(13)
R= H
(14)
(15)
R=H
(16)
(18)
(19)
R= Ac
(17)
(20)
(21)
AcO
AcOCH2CH2
AcOCH2

this mixture to the γ-lactones (IR, 1766 cm^{-1}) having the NMR methyl peaks at δ 1.49 and 1.26 in ratio of 2:3. A singlet at δ 2.52 and a triplet at δ 4.51 are attributable to $-\overset{|}{\underset{|}{C}}-C\underline{H}_2-COO-$ and to $-COO-\overset{|}{C}\underline{H}-$ of (10) respectively, but no other signal due to geminal proton to lactone oxygen was observed suggesting that the other lactone has the structure (11). This assignment is supported by the appreciable down-field shift (∿0.22 ppm) of the methyl peak. The above results imply that (4) rearranged by acid to (8) whilst (6) remained unchanged.

We therefore conclude that by alkaline treatment of (1) two cyclobutanones (4) and (6) are independently produced from the common intermediate (3) shown in Fig. 1. The homoallylic conjugation of the derived cation (2) with the enolate will be easily achieved, then the cleavage of a̲ leads to bicyclo[3,1,1]heptanone system and the cleavage of b̲ leads to cyclopropanolate (5) which rearranges to bicyclo[3,2,0]heptanone system with retention of the configuration at C_2. In triterpenoid series non-bonded interactions due to the presence of 10-Me prevent the reaction of course a̲, thus the reaction is directed toward relief of the interaction to give bicyclo[3,2,0] systems, (14) and (15), as single products.

In acid catalysed rearrangement of bicyclo[3,1,1]heptanone (4), the tertiary carbonium ion (7), in which configuration at C_6 is still retained, is apparently more stable than the secondary ion (5, OH instead of O^-), thus leads to the different bicyclo[3,2,0]heptanone (8).

REFERENCES

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3. W. F. Erman, J. Am. Chem. Soc., 91, 779 (1969).
4. Syntheses of these compounds will be reported elsewhere.
5. We found that this reagent selectively oxidizes cyclobutanones to the corresponding γ-lactones rapidly even in cold condition. The practical application of this method will be reported separately.