Tetrahedron Letters No. 24, pp 2261 - 2262.
©Pergamon Press Ltd. 1979. Printed in Great Britain.
0040-4039/79/0608-2261$02.00/0

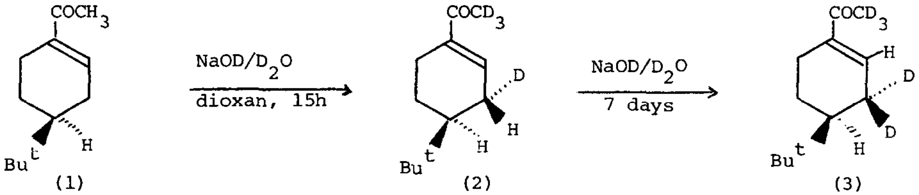
STERIC CONTROL IN THE BASE CATALYSED H-D EXCHANGE OF AN α,β-UNSATURATED KETONE

Bruce A.W. Coller, W. Roy Jackson, Anna Stragalinou and Jürgen U.G. Strauss,
Department of Chemistry, Monash University, Clayton, Victoria, Australia, 3168.

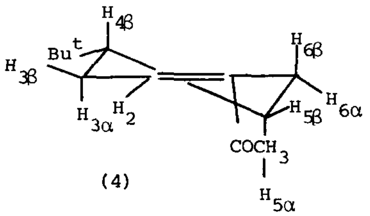
For the base catalysed H-D exchange of the equatorial hydrogen and the axial hydrogen in 4-t-butyl-1-acetylcyclohex-1-ene (1) in CH_3OD containing CH_3ONa, k_{eq}/k_{ax} is 3.8:1. This is clearly a result of steric rather than stereoelectronic factors.

A recent publication has demonstrated that stereoelectronic control predominates in the base catalysed H-D exchange of the α-protons in twistan-4-one.[1] Similarly, the base catalysed enolisation of androst-4-end-3,17-dione and the addition of DCl to 3-ethoxycholesta-3,5-diene have been shown to give the products of stereoelectronic control.[2] Each of these latter examples involves reaction at the axial 6β-position even though this involves attack on the more hindered 6β-face of the steroid molecule.

We wish to report that in contrast the stereochemistry of base catalysed H-D exchange in the cyclic enone 4-t-butyl-1-acetylcyclohex-1-ene (1), is dominated by steric rather than stereoelectronic factors. When (1) was reacted with NaOD/D_2O in dioxan at 90° for 15h four of the five potentially exchangeable protons had been replaced by deuterium in the products. Reaction under the same conditions for a further 7 days led to essentially complete exchange of the five protons as in (3). ^1H and ^2H spectra were recorded for the products (2) and (3). The ^1H spectrum of (1) was assigned as follows on the basis of extensive decoupling experiments, δ, 0.90 (s, 9H, Bu^t), 2.30 (s, 3H, CH_3CO), 6.02 (dd, 1H, H-2), 1.0 (m, 2H, H-5's), 1.14 (m, 1H, H-4β), 1.73-1.92 (m, 3H, H-3α, H-3β, H-6β), 2.40 (dd, H, H-6α). The coupling constants $J_{6\alpha,6\beta}$ 14.5Hz, $J_{5\alpha,6\alpha}$ 4.5Hz, $J_{4\beta,5\alpha}$ 11.5Hz, $J_{3\alpha,4\beta}$ 11.5Hz, $J_{3\beta,4\beta}$ 5.0Hz, $J_{2,3\alpha}$ 3.1Hz and $J_{2,3\beta}$ 1.4Hz were assigned. The significant differences between $J_{3\alpha,4\beta}$ and $J_{3\beta,4\beta}$ are consistent with a fairly rigid cyclohexene chair conformation (4). The tetradeuterio substituted compound (2)



(1) (2) (3)



(4)

showed the olefinic proton as a doublet with J3.1Hz and $H_{4\beta}$ as a triplet with J=11.4Hz. Retention of the pseudo-axial-axial coupling of 11.4Hz suggested that the pseudo-equatorial 3β-proton had been preferentially exchanged. The multiplet centred on 1.8 p.p.m. had decreased in intensity by the equivalent of one proton and confirmation of this chemical shift was obtained from a ^{2}H spectrum which showed a peak at 1.85 p.p.m. in addition to that due to the $COCD_3$ group. The ^{1}H n.m.r. of the pentadeuterio compound (3) now showed the absorption for $H_{4\beta}$ as a doublet with $J_{4\beta,5\alpha}$ 11.4Hz together with some fine splitting due to long range coupling in further agreement with these proposals.

The stereochemical results strongly suggest that the stereoelectronic preference for pseudo-axial exchange cannot overcome the steric resistance to attack of base on the axial hydrogen atom by the adjacent, cis-t-butyl group. The kinetics of exchange for a solution of (1) (0.07M) in CH_3OD containing sodium methoxide (0.485M) were measured at 35.6°[4]. The rate constants for exchange of the equatorial hydrogen and the axial hydrogen were k_{eq} $0.333h^{-1}$ and k_{ax} $0.086h^{-1}$. The ratio of these rate constants $k_{rel} = k_{eq}/k_{ax} = 3.8$ is dramatically less than that quoted for the exchange of the two α-protons in twistan-4-one ($k_{rel} \sim 290$)[1] or for the 6-protons in the steroidal example[2] ($k_{rel} = 64$). It thus appears that although in the cyclic enone (1) steric effects lead to a preferential exchange of equatorial hydrogen strong stereoelectronic preference for axial exchange exists and is only just overcome.

Attempts were made to measure the relative rates of exchange of (1) with the bulkier bases NaOPh in CH_3OD and $Bu^{t}OK$ in $Bu^{t}OD$. Unfortunately the kinetic data could not be interpreted in terms of simple H-D exchange reactions.

References and Footnotes

1. R.R. Fraser and P.J. Champagne, J.Amer.Chem.Soc., 1978, 100, 657.
2. K. Henderson and F.J. McQuillin, J.C.S.Chem.Comm., 1978, 15; S.K. Malhotra and H.J. Ringold, J.Amer.Chem.Soc., 1965, 87, 3228.
3. Spectra were recorded at 290MHz for ^{1}H and at 41.44MHz for ^{2}H by Dr. Alan Jones and his colleagues at the National N.M.R. Centre, Canberra, A.C.T.
4. Rate constants are reported as pseudo-first order rate constants. Mass spectra were recorded on samples from quenched aliquots using a VG-Micromass spectrometer operating in the unfocussed mode. Average values were taken after correction for natural isotopic abundances. The formation of a d_3 derivative, i.e. $COCD_3$, was shown to be virtually complete in less than one minute and the formation of d_4 derivative was monitored by the diminution in intensity of the $d_3$peak. The rate constant for d_5 formation was calculated by means of a graph of d_5 peak height versus a graphical integral of the d_4 peak height, $[d_5] = k\int[d_4]dt$, a procedure previously described by R.P. Bell and B.A.W. Coller, Trans.Faraday Soc., 1964, 60, 1087.

(Received in UK 2 April 1979)