

One-step Synthesis of *cis*-5,6-Dideuterio-*cis*-cyclo-octene and Its Thermal Stability towards Concerted, Intramolecular Transfer of Hydrogen

By A. J. Bellamy, Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ

cis-5,6-Dideuterio-*cis*-cyclo-octene has been synthesised in one step from cyclo-octa-1,5-diene by reduction with dideuteriodi-imide. On prolonged pyrolysis at 250°, intramolecular transfer of the vicinal 5- and 6-protons to the double bond does not occur; thus no 1,2-dideuterio-*cis*-cyclo-octene is formed.

SEVERAL examples of the concerted, intermolecular transfer of two vicinal hydrogen atoms to a double bond are known,¹ but few intramolecular examples have been reported.² In all known examples of this type of reaction a decrease in free energy at the origin of migration occurs (see ref. 1). However, given a suitable configuration and/or conformation, a thermally neutral, intramolecular hydrogen transfer might conceivably occur.

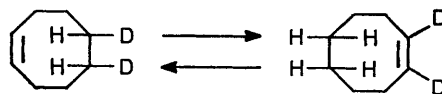
Transannular transfer of a single hydrogen atom is common in the cyclo-octane series.³ Molecular models suggest that *cis*-cyclo-octene might be able to adopt a suitable conformation for the concerted transfer of two vicinal 5- and 6-protons to the double bond. In the extreme-boat conformation of *cis*-cyclo-octene, the internuclear distances between the *endo*-5- and 6-protons and C(1) and C(2) respectively, are both *ca.* 2.2 Å. However, in this conformation there are severe non-bonded interactions between the 4- and 7-protons and the 3- and 8-protons as well as many eclipsed interactions. A twist-boat conformation would relieve most of these non-bonded interactions to some degree; in such a conformation, the same hydrogen-carbon internuclear distances are *ca.* 2.2 and *ca.* 2.5 Å. In both conformations the 5- and 6-protons appear close enough to the double bond to make transfer possible, but the attainment of these conformations may be sterically difficult.

Since an intramolecular transfer of hydrogen in *cis*-cyclo-octene would produce no observable chemical change, *cis*-5,6-dideuterio-*cis*-cyclo-octene was studied.

¹ S. Hunig, H. R. Muller, and W. Thier, *Angew. Chem. Internat. Edn.*, 1965, **4**, 271; W. von E. Doering and J. W. Rosenthal, *J. Amer. Chem. Soc.*, 1967, **89**, 4534; I. Fleming and E. Wildsmith, 'Orbital Symmetry Correlations in Organic Reactions,' Chemical Society Symposium, Cambridge, 1969.

Transfer of the *cis*-vicinal deuterium atoms in this compound would again produce no observable chemical change, but transfer of the *cis*-vicinal 5- and 6-protons would give 1,2-dideuterio-*cis*-cyclo-octene. Such a transfer would be detectable by n.m.r. spectroscopy.

The material studied was in fact a mixture of *cis*-5,6-dideuterio-*cis*-cyclo-octene (72.7%), 5-deuterio-*cis*-cyclo-octene (23.6%), and *cis*-cyclo-octene (3.7%). Neglecting secondary isotope effects, complete equilibration of *cis*-5,6-dideuterio-*cis*-cyclo-octene with 1,2-dideuterio-*cis*-cyclo-octene by a concerted transfer of hydrogen should favour the 5,6-isomer by a factor of two. Thus, for the material used, the ratio olefinic : allylic : other protons (1.95 : 3.95 : 6.39 in the starting



material) should change to 1.44 : 4.00 : 6.87 in the equilibrated material. However, heating the *cis*-5,6-dideuterio-compound at 250° during 7 days produced no significant change in the n.m.r. spectrum. Concerted transfer of hydrogen does not therefore occur in this system at this temperature. At higher temperatures polymerisation becomes significant.

Preparation of cis-5,6-Dideuterio-cis-cyclo-octene.—5,6-Dideuterio-*cis*-cyclo-octene has been prepared by Cope *et al.*⁴ in a three-stage synthesis from *cis,cis*-cyclo-octa-1,5-diene monoepoxide. The *cis*-cyclo-octene obtained

² K. MacKenzie, *J. Chem. Soc.*, 1965, 4646.

³ A. C. Cope, M. M. Martin, and M. A. McKerver, *Quart. Rev.*, 1966, **20**, 119.

⁴ A. C. Cope, G. A. Berchtold, P. E. Peterson, and S. H. Sharman, *J. Amer. Chem. Soc.*, 1960, **82**, 6366.

contained 74% of the [$^2\text{H}_2$]-compound (deuterium atoms expected to be in a *cis*-configuration because of the method of synthesis), 13% of the [$^2\text{H}_1$]- and 13% of the [$^2\text{H}_3$]-compound [the third deuterium atom was at C(5)]. A more convenient preparation of *cis*-5,6-dideuterio-*cis*-cyclo-octene involves reduction of *cis,cis*-cyclo-octa-1,5-diene with dideuteriodi-imide. Since di-imide is a *cis*-reducing agent,⁵ the *cis*-cyclo-octene formed must have the two 5- and 6-deuterium atoms in a *cis*-relationship. *cis*-Cyclo-octene is reduced by di-imide more rapidly than *cis,cis*-cyclo-octa-1,5-diene; thus use of a large excess of the diene is necessary for efficient production of *cis*-cyclo-octene.

From the ratio of products, and the isotopic abundance in the isolated cyclo-octene and cyclo-octane, it was calculated that there had been an uptake of 88.1 mmol of deuterium atoms and 15.9 mmol of hydrogen atoms. Of the hydrogen, only 2.5 mmol could come from the acetic [^2H]acid used to generate the di-imide from potassium azodicarboxylate. The most likely source for most of the hydrogen is the potassium azodicarboxylate, which contained *ca.* 0.3% hydrogen even after prolonged drying. To determine what proportion of this hydrogen was exchangeable, a weighed amount of potassium azodicarboxylate was dissolved in aqueous deuteriated methanol of known isotopic composition. Integration of the hydroxy-proton signal in the n.m.r. spectrum and comparison with the ^{13}C side-band of the signal for the methanolic methyl group gave the amount of exchangeable hydrogen liberated by the potassium azodicarboxylate. We calculated that 21.8 mmol of exchangeable hydrogen was present in the amount of the salt used in the reduction, more than enough to account for the reduction results.

A reduction product of higher deuterium content could probably be obtained by precipitating the salt from deuteriated solvents, ensuring that any exchangeable hydrogen in the salt was replaced by deuterium, but this was not necessary for the present work.

EXPERIMENTAL

N.m.r. spectra were determined using a Varian HA 100 spectrometer, and mass spectra using an A.E.I. MS 902 double-focusing spectrometer. G.l.c. analyses were performed with a 50 m, 0.25 mm i.d. capillary column coated with Apiezon L, operating at 40°.

*Potassium Azodicarboxylate.*⁶—Azofornamide (70 g) was added with stirring to aqueous potassium hydroxide (175 ml; 1:1 w/w) at 0°. The solid partially dissolved, ammonia was evolved, and the product was precipitated. The latter was filtered off under nitrogen when the evolution of ammonia had ceased, and dried (water pump). It was then dissolved in the minimum volume of water (*ca.* 400 ml) at 0°, and immediately filtered into ethanol (*ca.* 1.6 l) at 0°. The precipitated yellow potassium azodicarboxylate was filtered off, washed twice with methanol at 0°, dried at the pump, and finally dried *in vacuo* (H_2SO_4); yield

* All silver nitrate solutions were saturated with ether.

† A control experiment showed that 17% of the cyclo-octene was lost during the silver nitrate treatment. The extraction was followed by g.l.c.

100 g (Found: C, 12.3, 12.2; H, 0.3, 0.25; N, 13.85, 13.9. Calc. for $\text{C}_8\text{N}_2\text{K}_2\text{O}_4$: C, 12.35; H, 0.0; N, 14.4%). After further drying *in vacuo* at 100° (P_2O_5) a 0.5 g sample had lost 5 mg in weight, and gave the following analytical figures: C, 9.7, 9.55, 9.85; H, 0.3, 0.4, 0.25; N, 13.4, 13.45, 13.05%. [These figures suggest that some decomposition of the salt had occurred (lit.,⁶ C, 12.45; H, 0.5; N, 14.15%).]

Reduction of cis,cis-Cyclo-octa-1,5-diene.—The diene was purified before use by the formation of its silver nitrate complex.⁷ Regeneration by steam-distillation gave material which was 99.98% pure by g.l.c., and contained less than 0.001% *cis*-cyclo-octene. The purified diene (50.8 g, 0.47 mol) was added to a suspension of potassium azodicarboxylate (19.3 g, 0.10 mol) in dry ether (200 ml). The apparatus was flushed with nitrogen, then acetic [^2H]acid (5.0 g, 0.082 mol; 98.5% [$^2\text{H}_1$]) in dry ether (20 ml) was added at the rate of 2–3 drops min^{-1} with vigorous stirring. After stirring for 24 h, a further quantity of acetic [^2H]acid in ether (5.0 g in 20 ml) was added at the same rate. The reduction was followed by g.l.c. (see the Table). After 180 h, the solid was filtered off

Product ratios in the reduction of *cis,cis*-cyclo-octa-1,5-diene

t/h	Cyclo-octadiene	Cyclo-octene	Cyclo-octane
24	96.0	3.6	0.4
84	93.7	5.4	0.9
132	92.1	6.4	1.5
180	91.0	7.0	2.0

and washed with dry ether (100 ml), and the organic solution was dried (Na_2CO_3 ; 6 h). To remove the excess of cyclo-octa-1,5-diene, the solution was first extracted with aqueous silver nitrate* (100 ml) and water (350 ml), the latter to dissolve the large amount of complex formed in this extraction, and then with saturated aqueous silver nitrate (3×100 ml). The resulting ethereal solution, free from cyclo-octa-1,5-diene,† was dried (MgSO_4), filtered, and evaporated to give cyclo-octene (75%) and cyclo-octane (25%).

The mixture was separated by preparative g.l.c. [0.1 ml samples, 10 ft \times 0.25 in column, Gas Chrom P (40–60 mesh) with a 30% coating of 30% silver nitrate in glycerol, 75°, helium carrier gas, 30 lb in^{-2}]. The separated products were shown to have the following isotopic composition by low-voltage mass spectrometry: cyclo-octene, [$^2\text{H}_2$] 72.7%, [$^2\text{H}_1$] 23.6%, [$^2\text{H}_0$] 3.7%; cyclo-octane, [$^2\text{H}_4$] 53.7%, [$^2\text{H}_3$] 34.4%, [$^2\text{H}_2$] 10.0%, and [$^2\text{H}_1$] 1.9%.

The n.m.r. spectrum (CCl_4 solution) of the cyclo-octene showed the following absorptions: τ 4.45 (1.95H, m, olefinic), 7.9 (3.95H, m, allylic), and 8.55 (6.39H, m, other) (the integrations were based on an isotopic composition of 73% [$^2\text{H}_2$] and 24% [$^2\text{H}_1$] in the third region). Integration of the spectrum of undeuteriated cyclo-octene gave values of 1.96H, 3.97H, and 8.03H, respectively. Another reduction, where the mixing of reagents was carried out in a dry-box, gave products with the following isotopic composition: cyclo-octene, [$^2\text{H}_2$] 79.4%, [$^2\text{H}_1$] 19.4%, [$^2\text{H}_0$] 1.2%; cyclo-octane, [$^2\text{H}_4$] 66.1%, [$^2\text{H}_3$] 29.0%.

⁵ E. J. Corey, D. J. Pasto, and W. L. Mock, *J. Amer. Chem. Soc.*, 1961, **83**, 2957.

⁶ J. Thiele, *Annalen*, 1892, **271**, 127.

⁷ A. C. Cope, C. L. Stevens, and F. A. Hochstein, *J. Amer. Chem. Soc.*, 1950, **72**, 2510; A. C. Cope and F. A. Hochstein, *ibid.*, p. 2515.

[$^2\text{H}_2$] 4.9%. The isotopic abundance in cyclo-octane is very close to that calculated for the reduction of both double bonds by using the isotopic abundance found for the reduction of the first double bond. This indicates that the isotopic abundance in the di-imide must be uniform throughout the reaction.

Determination of the Amount of Exchangeable Hydrogen in Potassium Azodicarboxylate.—Deuterium oxide (4.005 g; 99.7% [$^2\text{H}_2$]) and methan[$^2\text{H}_1$]ol (1.304 g; 98.5% [$^2\text{H}_1$]) were mixed in a dry-box, and the hydrogen content was determined by integrating the hydroxy-proton signal and comparing it with the ^{13}C side-band of the methyl group signal in the n.m.r. spectrum. Potassium azodicarboxylate (1.011 g) was added slowly to deuterium oxide-methan[$^2\text{H}_1$]ol (2.734 g) in a dry-box, and the resulting solution was again analysed by n.m.r. After correction for the hydrogen present in the solvent, this indicated that 1.14 mmol of exchangeable hydrogen atoms were present in

1.011 g of the salt (*i.e.*, 21.8 mmol of exchangeable hydrogen atoms in the 19.3 g of potassium azodicarboxylate used in the large-scale reduction of cyclo-octa-1,5-diene).

Pyrolysis of cis-5,6-Dideuterio-cis-cyclo-octene.—The cyclo-octene (73 mg), in a sealed tube, was heated at (a) 180° and (b) 250° during 170 h. The product, pure cyclo-octene (by g.l.c.), was dissolved in CCl_4 and analysed by n.m.r. The average of several integrated spectra gave the following ratios of protons (based on an average of 12.31 protons per molecule):

$T/^\circ\text{C}^a$	Olefinic	Allylic	Other
b	1.95	3.95	6.39
180	1.96	4.02	6.32
250	1.90	4.04	6.35

^a Polymerisation became significant at 300 °C. ^b Starting material.

[1/1365 Received, August 3rd, 1971]