# $^{13}C$ Chemical Shift Assignments in Cyclo-octene, Cyclo-octanone, and Cyclo-oct-2-enol from the Spectra of Monodeuterioisotopomers

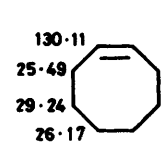
**Gordon Read* and Janet Shaw**
*Department of Chemistry, University of Exeter, Exeter EX4 4QD*

The $^{13}C$ n.m.r. spectra of [3-$^2H_1$]- and [5-$^2H_1$]-cyclo-octenes indicate that the assigned shifts for C-4 and C-5 in the cycloalkene must be transposed. The spectra of [4-$^2H_1$]- and [5-$^2H_1$]-cyclo-octanones consolidate earlier evidence for the assignment of shifts in the case of the cyclic ketone. The $^{13}C$ n.m.r. spectra of [1-$^2H_1$]-, [5-$^2H_1$]-, [6-$^2H_1$]-, [7-$^2H_1$]-, and [8-$^2H_1$]-cyclo-oct-2-enols afford unambiguous evidence for the origins of the signals in the spectrum of the unlabelled cyclo-octenol.

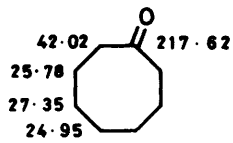
Prior to a detailed mechanistic study on rhodium-catalysed oxygenations of cyclo-octene, using [5-$^2H_1$]cyclo-octene as the substrate,[1] it was considered necessary to assign unequivocally the $^{13}C$ chemical shifts in the cyclic alkene and its oxygenated products, namely cyclo-octanone and cyclo-oct-2-enol. To our knowledge the only assignment in the literature for cyclo-octene is that of Dorman *et al.*[2] which is based on shielding parameters. The $^{13}C$ spectrum of cyclo-octanone has been studied, together with those of other cycloalkanones, by Weigert and Roberts,[3] but on the basis of additivity relationships it was not possible to distinguish the C-3 and C-4 signals. In a brief note[4] Wehrli *et al.* made this distinction on the basis of the spectrum of [5-$^2H_1$]cyclo-octanone. The deuteriated material was obtained in undisclosed yields by thermal and photolytic lead tetra-acetate oxidations of [1-$^2H_1$]cyclo-octanol. No detailed examination of the origins of the chemical shifts in cyclo-oct-2-enol appears to have been made. In this paper we report the syntheses and $^{13}C$ spectra of monodeuterioisotopomers of each of these compounds. The spectra unequivocally establish the origin of each carbon signal.

The [3-$^2H_1$]- and [5-$^2H_1$]-cyclo-octenes were synthesized, with greater than 98% isotopic purity, by reduction of 3-bromo- and 5-bromo-cyclo-octene with $LiAlD_4$ in bis(2-ethoxyethyl) ether. On comparing these products with unlabelled cyclo-octene by high-field $^{13}C$ n.m.r. spectroscopy at 62.9 MHz, the former showed a shift of −0.159 p.p.m. and a 19 Hz C–D splitting for the signal at 25.49 p.p.m. and the latter a similar α-shift and splitting for the signal at 26.17 p.p.m. In both labelled compounds a β-shift of −0.032 p.p.m. could be detected in the signal at 29.24 p.p.m. These findings require a reversal of the earlier assignments[2] of the 26.17 p.p.m. signal to C-4 and the 29.24 p.p.m. signal to C-5 and lead to the full assignments for cyclo-octene as shown in (**1**). A check that the assignments of $^{13}C$ shifts for cycloheptene[2] were not also in error was made by preparing [3-$^2H_1$]cycloheptene from 3-bromocycloheptene. The signals in the $^{13}C$ n.m.r. spectrum of this compound show an α-shift (−0.159 p.p.m.), a β-shift (−0.032 p.p.m.) and a barely detectable γ-shift (−0.002 p.p.m.), respectively from those found at 29.24, 27.55, and 32.28 p.p.m. in the unlabelled material. The assignments given by Roberts to the spectrum of this cycloalkene are therefore confirmed.

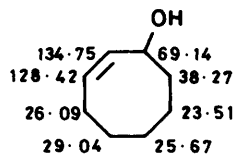
In order to distinguish unequivocally the C-3 and C-4 centres in the spectrum of cyclo-octanone, the [5-$^2H_1$]cyclo-octene was hydrated and oxidised to give a 1:1 mixture of the [4-$^2H_1$]- and [5-$^2H_1$]-cyclo-octanone isotopomers. As expected, in this mixture the characteristically smaller C-5 signal was partly α-shifted (−0.397 p.p.m., $J_{C,D}$ 19.1 Hz) and partly β-shifted (− 0.095 p.p.m.) relative to the C-5 signal at 24.95 p.p.m. in the unlabelled ketone. When compared with the signal at 27.35 p.p.m. from the unlabelled ketone, the corresponding signal from the mixture was split into unshifted, α-shifted (−0.397 p.p.m., $J_{C,D}$ 19.2 Hz), and β-shifted (−0.095 p.p.m.) components, entirely consistent with a C-4 origin. These findings support the conclusions of Wehrli, giving the assignment for the cyclo-octanone signals as shown in (**2**).



(1)



(2)



(3)

The eight carbons in cyclo-oct-2-enol are unique. The C-1, C-2, and C-3 signals may be readily assigned on the basis of their chemical shifts but confident distinctions cannot be simply made between the five remaining $sp^3$-hybridised centres. To allow such distinctions monodeuteriated isotopomers were synthesized as follows. [1-$^2H_1$]Cyclo-oct-2-enol was readily prepared in greater than 98% isotopic purity by reduction of cyclo-oct-2-enone with $LiAlD_4$. The [8-$^2H_1$]cyclo-oct-2-enol was obtained by reduction of [8-$^2H_1$]cyclo-oct-2-enone (isotopic purity 47%) which was formed on stirring the undeuteriated ketone in deuteriated ethanol for 72 h at room temperature in the presence of Amberlite 45(OH) resin. The level of the [8-$^2H_2$] compound obtained was less than 5%. Interestingly, in the absence of the resin, ethanol addition to the double bond accompanied the proton–deuteron exchange in this reaction to give [8-$^2H_1$]-3-ethoxycyclo-octanone as the major deuteriated product. *N*-Bromosuccinimide bromination of [5-$^2H_1$]cyclo-octene followed by displacement of the allylic bromide by mild hydrolysis using a suspension of $NaHCO_3$ in aqueous acetone afforded a 1:2:1 mixture of [5-$^2H_1$]-, [6-$^2H_1$]-, and [7-$^2H_1$]-cyclo-oct-2-enols.

In addition to the expected α-shift (−0.175 p.p.m.) relative to the 69.14 p.p.m. signal of the unlabelled cycloalkenol, the $^{13}C$ spectrum of [1-$^2H_1$]cyclo-oct-2-enol showed a β-shift (−0.048 p.p.m.) relative to the 38.27 p.p.m. signal, linking this to C-8.

This assignment was confirmed by the spectrum of the [8-$^2H_1$]-isotopomer which showed an α-shift (−0.159 p.p.m.) for the 38.27 p.p.m. signal. This spectrum also showed a β-shift (−0.0318 p.p.m.) for the 23.51 p.p.m. signal which must originate, therefore, from C-7. The complex spectrum from the mixture of [5-$^2H_1$]-, [6-$^2H_1$]-, and [7-$^2H_1$]-isotopomers, nominally in the ratio 1:2:1, showed α-shifted components in the 23.51, 25.67, and 29.04 p.p.m. signals. The fractions of each signal associated with these α-shifts were 0.19, 0.32, and 0.16, respectively. Whilst each of these values is almost certainly an underestimate by about 30%[5] of the true fraction of deuterium directly bound to each carbon, the relative values are significant. The 25.67 p.p.m. signal with the largest fraction of α-shifted component is therefore assigned to C-6. The 23.15 p.p.m. signal has already been assigned to C-7 to leave C-5 as the origin of the 29.04 p.p.m. signal. A secondary isotopic influence in one of the synthetic steps may be responsible for the apparent difference in concentrations of the [5-$^2H_1$]- and [7-$^2H_1$]-isotopomers. The remaining signal corresponding to 26.09 p.p.m. in the unlabelled cyclo-oct-2-enol shows no α-shift. However, *ca.* 0.2 of the total signal appears as a partially resolved β-shift (−0.064 p.p.m.) in full accord with this signal originating from C-4 carbons in an isotopomeric mixture containing *ca.* 20% of [5-$^2H_1$]cyclo-oct-3-enol. The complete assignment of $^{13}C$ signals for cyclo-oct-2-enol is therefore that shown in (**3**).

With the exception of [1-$^2H_1$]cyclo-oct-2-en-1-ol, each synthesized monodeuteriated cyclo-oct-2-enol will be composed of approximately equal concentrations of two stereoisomeric isotopomers with the orientation of the deuterium atom and hydroxy group *cis* in one case and *trans* in the other. This isotopomeric difference is clearly detectable in the case of the [6-$^2H_1$] compound. The 62.89 MHz $^{13}C$ spectrum shows two sets of three-line signals from C-6 differing in chemical shift by 0.05 p.p.m. A similar set of signals, but with a smaller difference in chemical shift (0.02 p.p.m.), is seen in the spectrum of the [5-$^2H_1$] compound. However, the [7-$^2H_1$]cyclo-oct-3-enol shows no such splitting and it is assumed that the spectral differences found in the cases of the [5-$^2H_1$] and [6-$^2H_1$] species stem primarily from transannular influences of the hydroxylic oxygen. Broadening of the three line signals from C-8 is seen in the 25.15 MHz spectrum of [8-$^2H_1$]cyclo-oct-2-enol corresponding to a difference in chemical shift between the *cis* and *trans* isotopomers of *ca.* 0.04 p.p.m.

## Experimental

I.r. measurements were recorded on a Perkin-Elmer 398 spectrometer. N.m.r. measurements were made using either a JEOL-PFT-100 instrument on a Bruker AM250 spectrometer with $CDCl_3$ (Nuclear Magnetic Resonance Ltd.) as solvent. Gas liquid chromatography was carried out using a Pye Unicam GCD gas chromatograph for analytical work and a Pye 105 instrument for preparative work. For g.l.c.–m.s., samples were gas chromatographed using a Pye 104 before being passed into a Micromass 16F instrument.

*cis*-Cyclo-octene (Aldrich) and *cis*-cycloheptene (Aldrich) were distilled from $LiAlH_4$ under $N_2$ and stored at 0 °C in the dark. Bis(2-ethoxyethyl) ether (Aldrich) was freshly distilled from $LiAlH_4$ before use. $LiAlD_4$ (98 atom% D) and EtOD (99.5 atom% D) were supplied by Aldrich.

*Measurement of Isotopic Abundance.*—Samples of the compound were introduced directly from a 2.2 m 10% PEGA column into the mass spectrometer. To compensate for mass discrimination on the column (in the cases of partly monodeuteriated samples) not less than 10 measurements of the range of mass units embracing the molecular ion were taken at uniform intervals as the compound passed through the mass spectrometer.

The ratios $r$ and $s$ were first determined for non-deuteriated samples where:

$$r = \frac{\Sigma\ (\text{galvanic response } M - 1)}{\Sigma\ (\text{galvanic response } M)}$$

and

$$s = \frac{\Sigma\ (\text{galvanic response } M)}{\Sigma\ (\text{galvanic response } M + 1)}$$

The fraction of monodeuteriated component, in any sample, was derived from the expression $(s - s')[s(1 - r) - s'(1 - s)]^{-1}$ where $s'$ is the ratio $s$ for the deuteriated sample.

[3-$^2H_1$]*Cyclo-octene.*—Freshly distilled 3-bromocyclo-octene[6] (4.90 g, 0.026 mol) in bis(2-ethoxyethyl) ether (50 $cm^3$) was added to a stirred suspension of $LiAlD_4$ (0.50 g, 0.013 mol) in bis(2-ethoxyethyl) ether (80 $cm^3$) over a period of 5 min. Nitrogen was passed over the flask and the reaction mixture was maintained at 100 °C for 12 h. Hydroquinone (5 mg) was added to the flask and the product was isolated directly from the reaction mixture by distillation using 90 cm Normag spinning band column. The [3-$^2H_1$]cyclo-octene (1.30 g, 0.012 mol), b.p. 135—140 °C, had an isotopic purity of >99% by mass spectroscopy; $\nu_{max.}$(film) 3 008, 2 992, 2 972, 2 850 (C–H), and 1 648 $cm^{-1}$ (C=C); $\delta_H$ 1.50 (8 H, m, 4 × $CH_2$), 2.15 (3 H, m, $CH_2CH$=CH–$CH$D), and 5.62 (2 H, m, 2 × –CH=). For the $^{13}C$ n.m.r. data, see the Discussion.

[3-$^2H_1$]*Cycloheptene.*—3-Bromocycloheptene[7] (1.85 g, 0.01 mol) was converted into [3-$^2H_1$]cycloheptene (0.51 g, 0.005 mol), b.p. 110—111 °C, by essentially the same procedure as that given above for the analogous cyclo-octene. The isotopic purity was found to be 98% by mass spectroscopy; $\nu_{max.}$(film) 3 013, 2 919, 2 848 (C–H), and 1 644 $cm^{-1}$ (C=C); $\delta_H$ 1.55 (6 H, m, 3 × $CH_2$), 2.10 (3 H, m, $CH_2CH$=CH–$CH$D), and 5.80 (2 H, m, 2 × –CH–) $\delta_C$ 132.50, 132.40 (C-1), 32.15, 32.10 (C-5), 29.15, 28.00 (t, 10 Hz) (C-3), and 27.45, 27.35 (C-4).

[5-$^2H_1$]*Cyclo-octene.*—5-Bromocyclo-octene[8] (33.0 g, 0.17 mol) in dry distilled bis(2-ethoxyethyl) ether (120 $cm^3$) was added to a stirred suspension of $LiAlD_4$ (5.0 g, 0.12 mol) in the same solvent (70 $cm^3$). Dry $N_2$ was passed over the flask and the reaction mixture was maintained at 70—80 °C for 2.5 days. Vacuum distillation of the reaction solution using a 90 cm Normag spinning band column gave, as the first fraction, [5-$^2H_1$]cyclo-octene of 98% isotopic purity (12.04 g, 0.105 mol), b.p. 47—49 °C at 18 mm Hg; $\nu_{max.}$(film) 3 007, 2 914, 2 840 (C–H), and 1 650 $cm^{-1}$ (C=C); $\delta_H$ 1.49 (7 H, m, 3 × $CH_2$ and CHD), 2.15 (4 H, m, 2 × –$CH_2$CH=), and 5.64 (2 H, m, 2 × –$CH_2$). See the Discussion for the $^{13}C$ n.m.r. data.

[4-$^2H_1$]- *and* [5-$^2H_1$]-*Cyclo-octanones.*—Following the general method of Brown and Geoghegan,[9] [5-$^2$H]cyclo-octane of 98% isotopic purity (3.30 g, 0.03 mol) was added to a fine suspension of $Hg(OCOMe)_2$ in water (30 $cm^3$) and THF (30 $cm^3$) and the mixture was stirred at room temperature. After 3 h, aqueous NaOH (3M; 30 $cm^3$) was carefully added with cooling followed by $NaBH_4$ in 3M NaOH (0.5M; 30 $cm^3$). When the mercury had precipitated, the aqueous phase was saturated with NaCl. The THF layer was separated and combined with the ethereal extracts of the aqueous phase. After the solution was dried ($MgSO_4$) and the solvent evaporated, a crude mixture of [4-$^2H_1$]- and [5-$^2H_1$]-cyclo-octanols (2.55 g, 0.02 mol) was

obtained. The alcohols, in ether (30 $cm^3$), were oxidised with chromic acid in 1.2M $H_2SO_4$ (0.62M; 18 $cm^3$) for 1 h at 3 °C and 12 h at room temperature.[10] Evaporation of the combined ethereal layer and aqueous layer ethereal extracts, which had been washed (aqueous $NaHCO_3$–water) and dried ($MgSO_4$), gave the crude cycloalkanones which were purified by distillation (b.p. 82—84 °C at 16 mmHg) followed by flash chromatography [ethyl acetate—light petroleum b.p. (60—80 °C) (3 : 7)]. The 1:1 mixture of [4-$^2H_1$]- and [5-$^2H_1$]-cyclooctanones showed $\nu_{max.}$(film) 2 923, 2 852 (C–H), and 1 692 $cm^{-1}$ (C=O). See the Discussion for the $^{13}C$ n.m.r. data.

[1-$^2H_1$]*Cyclo-oct-2-enol*.—Cyclo-oct-2-enone (1.26 g, 0.01 mol) in dry ether (5 $cm^3$) was added dropwise to a suspension of $LiAlD_4$ (0.25 g, $6 \times 10^{-3}$ mol) in dry ether (50 $cm^3$) and the mixture was stirred for 0.5 h at 0 °C under nitrogen and then at room temperature for a further 1.5 h. The excess of reagent was destroyed with 1M $H_2SO_4$. The aqueous layer was saturated with NaCl and the ethereal layer was separated, combined with ethereal extracts of the aqueous phase, washed, dried ($MgSO_4$), and evaporated to give the crude alkenol. The product was purified by vacuum distillation to give [1-$^2H_1$]cyclo-oct-2-enol (0.82 g, 0.0064 mol), b.p. 96—98 °C at 12 mmHg, isotopic purity >98%; $\nu_{max.}$(film) 3 360 (OH), 3 010, 2 920, 2 845 (C–H), and 1 650 $cm^{-1}$ (C=C); $\delta_H$ 1.49 + 1.89 (7 H + 1 H, m + m, methylenes), 2.1 (3 H, m, $-CH_2-CH=$ + O*H*), and 5.5—5.7 (2 H, m, 2 × –CH=). See the Discussion for the $^{13}C$ n.m.r. data.

[5-$^2H_1$]-, [6-$^2H_1$]-, *and* [7-$^2H_1$]-*Cyclo-oct-2-enols*.—[5-$^2H_1$]Cyclo-octene (2.50 g, 0.022 mol, isotopic abundance 85%), *N*-bromosuccinimide (4.00 g, 0.022 mol), and benzoyl peroxide (0.01 g) were refluxed in $CCl_4$ (15 $cm^3$) under $N_2$ for 24 h. The reaction was cooled and the succinimide was filtered off, the solution was washed (aqueous $NaHCO_3$, then water) and evaporated to give an isotopomeric mixture of the crude allyl bromides. A solution of this mixture in acetone (40 $cm^3$)–water (20 $cm^3$), together with a suspension of $NaHCO_3$ (4.0 g, 0.046 mol) was vigorously stirred under reflux for 2 h. The reaction was cooled and filtered, the solvents were removed, and the products (0.86 g, 0.007 mol), b.p. 93—103 °C at 12 mmHg, were isolated by vacuum distillation. Further purification by preparative g.l.c. (2.5 m 10% OV 17 column at 155 °C) gave [5-$^2H_1$]-, [6-$^2H_1$]-, and [7-$^2H_1$]-cyclo-oct-2-enols; $\delta_H$ 1.49 + 1.89 (6 H + 1 H, m + m, methylenes + CHD–), 2.10 (2 H, m, $-CH_2-CH=$), 2.80 (1 H, s, OH), 4.60 (1 H, m, C*H*–OH), and 5.60 (2 H, m, 2 × –CH=). See the Discussion for the $^{13}C$ n.m.r. data.

[8-$^2H_1$]*Cyclo-oct-2-enol*.—A solution of cyclo-oct-2-enone (1.69 g, 0.014 mol) in 99.5% EtOD (16 $cm^3$) was stirred with Amberlite IR-45 (OH) resin (0.80 g) at ambient temperature in a stoppered flask for 3 days. The extent of exchange was monitored at intervals throughout this period by g.l.c.–m.s. The partly deuteriated ketone (1.53 g, 0.012 mol) was recovered from the ethanolic solution, dissolved in dry ether (10 $cm^3$) and reduced with $LiAlH_4$ (0.25 g, 6.5 mmol) in ether (50 $cm^3$) at 0 °C under nitrogen for 0.5 h and at ambient temperature for 1.5 h. The product was isolated as described above for the [1-$^2H_1$]-isotopomer to give [8-$^2H_1$]cyclo-oct-2-enol (0.92 g, 0.008 mol), b.p. 102—104 °C at 15 mmHg, isotopic purity 47%; $\nu_{max.}$(film) 3 355 (OH) 3 010, 2 918, 2 845 (C–H), and 1 650 $cm^{-1}$ (C=C); $\delta_H$ 1.49 + 1.89 (7.5 H + 1 H, m + m, methylenes + –CHD), 2.10 (2 H, m, $-CH_2-CH=$), 2.21 (1 H, s, OH), 4.65 (1 H, m, C*H*–OH), and 5.5 (2 H, m, –CH=). See the Discussion for the $^{13}C$ n.m.r. data.

## Acknowledgements

The authors gratefully acknowledge the award of an S.E.R.C. postgraduate studentship (to J. S.).

## References

1 G. Read and J. Shaw, unpublished work.
2 D. E. Dorman, M. Jautelat, and J. D. Roberts, *J. Org. Chem.*, 1971, **36**, 2757.
3 F. J. Weigert and J. D. Roberts, *J. Am. Chem. Soc.*, 1970, **92**, 1347.
4 S. Milosavljević, D. Jeremić, M. Lj. Mihailović, and F. W. Wehrli, *Org. Magn. Reson.*, 1981, **17**, 299.
5 M. J. Garson and J. Staunton, *Chem. Soc. Rev.*, 1979, **8**, 539.
6 A. C. Cope and L. L. Estes, *J. Am. Chem. Soc.*, 1950, **72**, 1128.
7 L. F. Hatch and G. Bachmann, *Chem. Ber.*, 1964, **97**, 132.
8 K. Ziegler and H. Wilms, *Justus Liebigs Ann. Chem.*, 1950, **567**, 1.
9 H. C. Brown and P. J. Geoghegan, Jr., *J. Org. Chem.*, 1970, **35**, 1844.
10 H. C. Brown, C. P. Garg, and K. T. Liu, *J. Org. Chem.*, 1971, **36**, 387.

*Received* 21*st December* 1987; *Paper* 7/2225