# $^{13}C$ Chemical-Shift Assignments in Cyclooctyl Derivatives from the Spectra of Deuterioisotopomers. Deuterium Isotope Effects on Chemical Shifts and Conformational Equilibria

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The $^{13}C$ NMR spectra of some derivatives of (*Z*)-cyclooctene, cyclooctanols and cyclooctanone have been assigned by consideration of substituent effects, $^{1}H$–$^{13}C$ correlated spectra, and $^{2}H$ isotope effects. Some four-bond downfield $^{2}H$ effects (+ $^{4}\Delta$) on certain chemical shifts have been measured and attributed to conformational equilibrium perturbations and *trans*-annular $^{1}H$–$^{1}H$ interactions. The data provide a basis for further assignments in these systems.

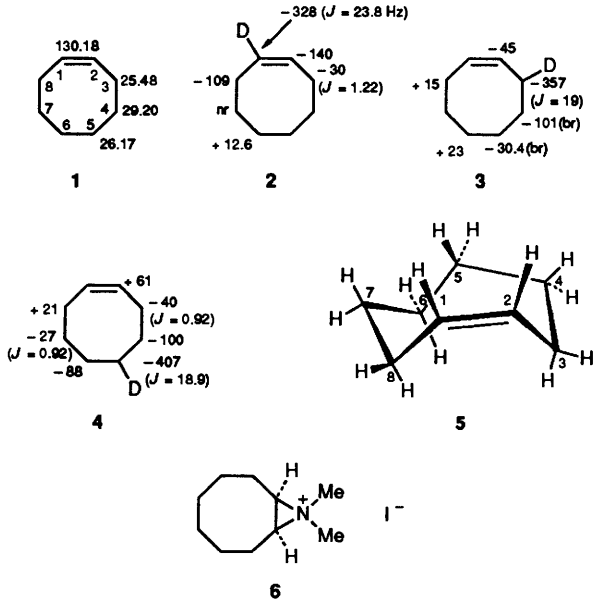
In connection with our studies of certain organometallic derivatives of (*Z*)- and (*E*)-cyclooctene,[1] unambiguous assignments of the $^{13}C$ NMR spectra of a range of cyclooctyl precursors and reaction products were required. However, the surprising dearth of secure data for these systems necessitated a more extensive study, and the results therefrom, coupled with the recent data of Read and Shaw,[2] provide a basis for further assignments of the spectra of cyclooctyl compounds.

## Discussion

(*Z*)-*Cyclooctene*.—The $^{13}C$ NMR spectrum of cyclooctene was reported originally by Roberts and Dorman,[3] and their assignments were based on shielding parameters. From an examination of the [3-$^{2}H_1$] and [5-$^{2}H_1$] derivatives, Read and Shaw[2] have corrected these assignments, but the reported values of $^{2}H$ effects on certain parameters seemed unreasonably small,† and some interesting longer range effects were not detected at the operating frequency employed (62.9 MHz). We have examined the 100 MHz $^{13}C$ spectra of cyclooctene and the [1-$^{2}H_1$], [3-$^{2}H_1$], and [5-$^{2}H_1$] isotopomers, compounds **1**, **2**, **3** and **4**, respectively. Molar proportions of the deuteriated and non-deuteriated compounds were distinctly different, so that authentic measures of $^{2}H$-induced effects would be obtained.

Deuterioisotopomers **2** and **3** resulted from cleavage of the corresponding trimethylstannanes with $CF_3CO_2D$ (in $CDCl_3$), and compound **3** was obtained alternatively by $LiAlD_4$ reduction of 3-bromocyclooctene. This latter procedure applied to 5-bromocyclooctene provided the [5-$^{2}H_1$] derivative **4**. When necessary, samples were purified by preparative GC.

The spectrum of compound **3** (admixed with controlled amounts of cyclooctene **1**) completely assigns the spectrum of cyclooctene **1**. C-3 Suffers a large one-bond isotope effect ($^{1}\Delta$ −357 ppb) and appears as a triplet, with $^{1}J_{CD}$ 19.05 Hz, whereas the signal at $\delta_C$ 29.24 experiences a two-bond isotope effect ($^{2}\Delta$ −101 ppb), such magnitude being similar to those observed previously in comparable systems.[4,5] Thus the assignments for cyclooctene are shown on structure **1**, and agree with those of Read and Shaw.[2] We also observe more remote Δ-values in the spectrum of compound **3**, such as $^{3}\Delta$ (to C-5) of −30 ppb. Most intriguing are the positive (downfield) four-bond $^{2}H$ effects ($^{4}\Delta$) to C-6 (+23 ppb) and C-8 (+15 ppb). $^{2}H$ Effects on $^{13}C$ chemical shifts are generally shielding,[4,5] but reports of positive Δ-values exist for $^{2}\Delta$, $^{3}\Delta$ and $^{4}\Delta$ cases.[6,7] While some effects are 'intrinsic', others are ascribed to $^{2}H$-induced perturbations of otherwise degenerate conformational equilibria, variations in C–H and C–D hyperconjugation, or hydrogen-bonding effects.[5,8] However, positive $^{4}\Delta$-values have been




measured in rigid systems such as norbornane[5] where conformational processes[9] cannot be relevant.

Our data for the effects of $^{2}H$ substitution on the spectra of cyclooctene are summarised on structures **2**, **3** and **4** above, such comparisons relating to internal (unlabelled) cyclooctene. Δ-Values are expressed throughout in parts per billion (ppb). The $^{1}\Delta$- and $^{2}\Delta$-values are all negative and comparable in magnitude with those reported for other cycloalkyl systems,[4,5] and require no further comment. We did not resolve any $^{2}J$-couplings fully (which are normally ~0.5 Hz)[5] but signals of carbons adjacent to $^{2}H$ were noticeably broadened (br = broadened). In favourable cases, $^{3}J$ were resolved, with measured values being 0.92 Hz in compound **4** and 1.22 Hz in compound **2**, where the dihedral angles are very favourable.[5]

A plausible explanation of the positive $^{4}\Delta$-values observed is associated with $^{2}H$ perturbation of the conformational equilibria.[9] The dynamic processes operative in cyclooctene have been studied by Anet and St. Jacques[10] and may be described as a ring reversion with a time-average plane of symmetry through the double bond ($\Delta G^{\ddagger}$ 8.2 kcal mol$^{-1}$)‡ and a more readily

† These authors report $^{1}\Delta$ to be −159 ppb and $^{2}\Delta$ (to C-4) to be −32 ppb, but Dr. Read has informed us that because of a computational error, the apparently low Δ-values should be multiplied by 2.5. Δ-Values so obtained are in satisfactory agreement with those reported herein.
‡ 1 cal = 4.184 J.

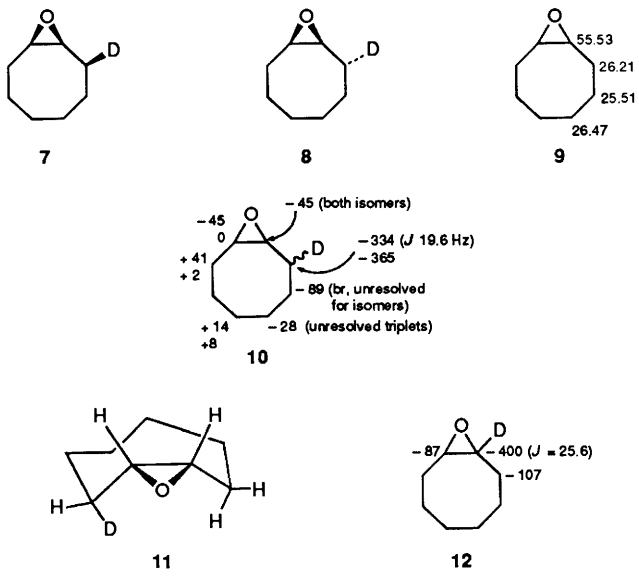
occurring process ($\Delta G^{\ddagger}$ 5.8 kcal mol$^{-1}$) characterised by a two-fold axis of symmetry. The operation of both processes results in the presence of only three methylene proton sets (NMR time-scale), and the predominant conformation (from low-temperature studies) is considered to be the unsymmetrical 'chair–boat' arrangement **5** which lacks symmetry elements and incorporates non-bonded interactions between the hydrogens on C-3, -8 and with those on C-5, -6 (see structure **5**). Indeed, the relatively high-field position for C-3, -8 in cyclooctene ($\delta_C$ 25.48) almost certainly reflects non-bonding interactions in those regions. An appreciation of the relevant H···H distances in (*Z*)-cyclooctene may be inferred from the crystal structure[11] of *cis*-9,9-dimethyl-9-azoniabicyclo[6.1.0]nonane iodide **6**, with the approximation that the torsional constraints in the three-membered ring resemble those in (*Z*)-cyclooctene.

Monodeuteriation at any site lifts the degeneracy of the overall conformational equilibrium, and it would be expected that $^2$H would occupy, preferentially, sites that are subject to non-bonded congestion. The reasons for this have been detailed elsewhere,[9] and the consequence is that 'steric shielding' of carbons *via* C–$H_a$···$H_b$– interactions is reduced by the preferential location of $^2$H in the environment from which steric shielding originates, *i.e.* at $H_b$. Thus a shift of the carbon resonance to lower field would be expected.[9] Although 'intrinsic' $^2$H effects are also operative, these appear to be insignificant over more than three bonds, and thus may not contribute to the measured $^4\Delta$-value.[12] However, $^3\Delta$-values that pertain to a congested region will be the resultant of a shielding 'intrinsic' effect of $^2$H, and a deshielding 'steric isotope' or conformational isotope effect. In such cases, the measured $^3\Delta$-value may be smaller than is usual.[5]

The data displayed on structures **2**, **3** and **4** are in harmony with this general analysis. For example, in structure **3**, $^2$H incorporation at the allylic position (C-3) induces positive $^4\Delta$ at C-6 and the other allylic position, C-8, and non-bonding H···H interactions occur between these positions and 3-H. (See structure **5**.) In structure **4**, $^2$H location at C-6 (using numbering on structure **5**) induces a positive $^4\Delta$ to C-3 (21 ppb), but not at C-8, where a 1,3-'diaxial type' H–H interaction operates. In this situation, the intrinsic shielding $^3\Delta$ apparently is greater than any isotope deshielding. A large $^4\Delta$ (+61 ppb) (from $^2$H at C-6 or what is equivalent, $^2$H at C-5 to C-2, see **5**) has also been measured, and is reciprocated by placement of $^2$H at a vinylic site (+12.6 ppb) as in structure **2**. There is no measurable $^3\Delta$ to C-7 in structure **2**, and the $^2$H–C-1–C-8–C-7 dihedral angle is ~90°, the least favourable array for $^3\Delta$, according to Gunther.[4]

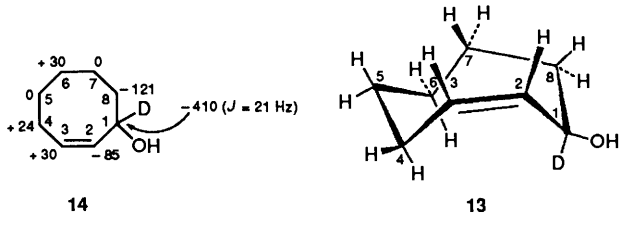
*Epoxycyclooctanes*(cis-*Cyclooctene Oxide*).—On the basis that the torsional constraints in epoxides are very similar to those in the corresponding alkene,[13] and given that dynamic NMR measurements on *cis*[1,3,3-$^2H_3$]cyclooctene oxide indicate utilisation of a conformational profile analogous to that proposed for (*Z*)-cyclooctene,[14] we expected that $^2$H effects on certain chemical shifts in appropriate $^2$H-substituted cyclooctene oxides would resemble those described above for $^2$H-substituted (*Z*)-cyclooctenes.

Epoxidation of compound **3** provided a 1:1 mixture of the *cis* and *trans* epoxides **7** and **8**, the $^{13}$C NMR spectrum of which provided the assignments for the parent epoxide **9**. In comparison with the shifts on structure **1** for cyclooctene, the notable difference concerns the shift of $C_{4,7}$ which is *ca.* 4 ppm to higher field in compound **9**, and may be a result of the γ-oxygen group. $^2$H-Induced shifts were also measured (by addition of unlabelled epoxide) and several were resolved for the two isomers. These values (in ppb) are shown on structure **10**. There is a 4 ppb chemical-shift difference at C-7 for the



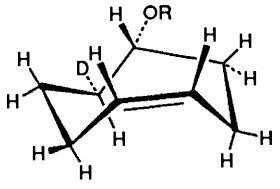

isomers, but the signs relative to added unlabelled epoxide could not be measured because of resolution limitations. The data on structure **10** show a general resemblance to those on structure **3**, consistent with conformational similarities for the systems.[14] One isomer (*i.e.*, either **7** or **8**) exhibits a $^4\Delta$ (to C-4) of +41 ppb, whereas in the other isomer, the value is ≯2 ppb, *i.e.* limit of resolution. The former isomer would, on the basis of the above discussions for cyclooctene, have $^2$H *vic-cis* to oxygen, as portrayed in structure **11**. The [1-$^2H_1$] isomer **12** was also examined, but longer range shifts were not resolved, but there is a general resemblance with the data on structure **2**.

*Cyclooctenols.*—If the above analysis is basically sound, $^4\Delta$-effects would be expected to be substantial in systems where $^2$H very preferentially occupied a congested position, by virtue of the greater steric demand of a second substituent. Thus [1-$^2H_1$]cyclooct-2-enol would presumably exist mainly in arrangement **13**, with 'outside OH', and the significant $^4\Delta$ at C-4 and C-6 are thus expected and somewhat greater to comparable positions than in structure **3**. The full listing of Δ-values is shown on structure **14**, and the very small $^3\Delta$ (to C-7) is again consistent with the dihedral angle dependence (~90°). The $^{13}$C shifts of this alcohol were assigned from $^2$H effects and a $^{13}$C-$^1$H correlated spectrum.

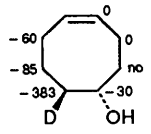



Support for the above conclusions was sought from the spectra of other derivatives. Ring opening of the mono epoxide of cycloocta-1,5-diene with $LiAlD_4$ provided one diastereoisomer of [8-$^2H_1$]cyclooct-4-enol, with $^2$H and OH presumably *trans*, and structure **15** would be a reasonable representation of the dominant conformation. With respect to conformer **15**, we expect $^4\Delta$ would be extremely small, as both $^2$H and OR occupy 'outside' uncongested positions, and this is confirmed by the values shown on structures **16** and **17**. Cyclooct-3-enol results from the regiospecific ring opening of the mono epoxide of cycloocta-1,3-diene with $LiAlH_4$, and the $^1$H NMR spectrum

was fully assigned by homonuclear decoupling. A $^{13}C$-$^{1}H$ correlated spectrum then provided full assignment of the $^{13}C$ NMR spectrum. Use of $LiAlD_4$ as before provided [2-$^{2}H_1$]cyclooct-3-enol, and models suggest structure **18** as the preferred conformation. Therefore incorporation of $^{2}H$ is expected to induce very minor changes as far as $^{4}\Delta$ is concerned, as the size of the hydroxy group is determining.* This is borne out by the results shown on structure **19**, with only $^{1}\Delta$ and $^{2}\Delta$ being resolved.



15 R = OTs, H



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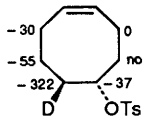

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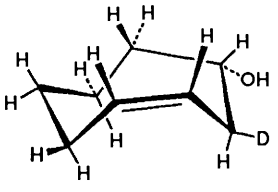

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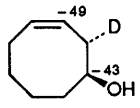

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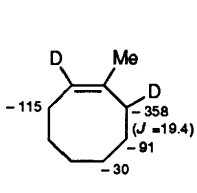
*The Methylcyclooctenes.*—The effect of replacing H with Me on the $^{13}C$ shifts of hydrocarbon systems has received much attention and this is particularly so in alicyclic systems, because of the conformational control the methyl group may exercise. The α- and β-effect of Me can be substantial and downfield, depending on the system, whereas the γ-effect depends on the geometry of the butane-like fragment.[16] In connection with another study, we required full assignments of the $^{13}C$ spectra of certain methylcyclooctenes, and consequently we have prepared the 1-, 3-, 4- and 5-methylcyclooctenes and assigned their spectra by chemical-shift considerations and deuterium isotope effects.

1-Methylcyclooctene resulted from dehydration ($KHSO_4$) of 1-methylcyclooctanol, whereas a mixture of 1-methyl-[2-$^{2}H_1$]-cyclooctene and 1-methyl-[8-$^{2}H_1$]cyclooctene was provided by dehydration of 1-methyl-[2-$^{2}H_1$]cyclooctanol formed by addition of MeMgI to [2-$^{2}H_1$]cyclooctanone. Similar treatment of [2,2,8,8-$^{2}H_4$]cyclooctanone led to 1-methyl-[2,8,8-$^{2}H_3$]-cyclooctene. Comparison of the spectra of these samples, separate and admixed, led to the asssignments for 1-methylcyclooctene shown in Table 1, and the effects of $^{2}H$ substitution on chemical shifts are displayed in structures **20** and **21**.

3-Methylcyclooctene (from 3-bromocyclooctene and ($Me_2$-CuLi) provides a well separated $^{1}H$ NMR spectrum at 400 MHz, which was assigned by homonuclear decoupling. A $^{13}C$–$^{1}H$ correlated spectrum then led to assignment of the $^{13}C$ spectrum. These assignments were confirmed by the spectrum of 3-methyl-[8-$^{2}H_1$]cyclooctene **22** which was obtained as a



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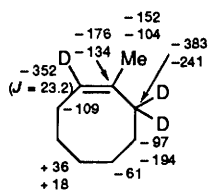

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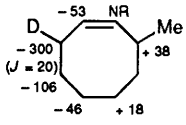

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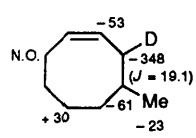

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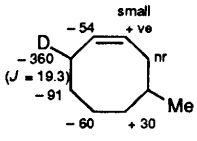

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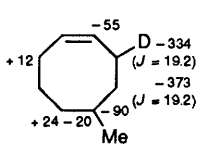

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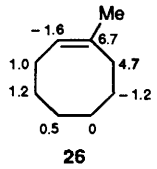
mixture with 4-methyl-[3-$^{2}H_1$]cyclooctene **23** from the $CF_3CO_2D$ cleavage of certain allylic stannanes.[17] In this way the chemical shifts and assignments for 4-methylcyclooctene were also determined. In a similar way, a mixture of 4-methyl-[8-$^{2}H_1$] cyclooctene **24** and 5-methyl-[3-$^{2}H_1$]cyclooctene **25** was obtained, and thus the assignments for 5-methylcyclooctene were established, knowing of course the identity of the signals for the co-occurring 4-methylcyclooctene. (In the $CF_3CO_2D$ cleavages of allylic stannanes, $^{2}H_1$-incorporation is normally $< 100\%$ and this provides convenient internal measures of $^{2}H$-effects in the spectra).[18] The chemical-shift assignments of the methylcyclooctenes are given in Table 1, and the $^{2}H$-effects (ppb) on the spectra are shown in structures **20**–**25**.

With respect to structure **20**, the level of $^{2}H$-incorporation was low (exchange during the dehydration of the tertiary alcohol) and the $^{2}H$ present is distributed between positions 2 and 8. Compound **21** is mainly the $^{2}H_3$-derivative as drawn, but significant levels of $^{2}H_2$-analogue are also present. In structure **20**, $^{4}\Delta$ at C-5 was not resolved, but in the more enriched derivative **21** only two $^{4}\Delta$-effects, of +18 and +36 ppb, are clearly resolvable and this is consistent with the argument relating to the presence of such effects in compounds **2** and **3**. (In structure **21** pairs of effects correspond to the two predominating deuteriated derivatives.) Overall, the effects of $^{2}H$ substitution shown in structures **20**–**25** require little comment except to note the significant positive $^{4}\Delta$ operating at *trans*-annular positions where H···H non-bonded distances are reasonably short. We had hoped that the magnitude of $^{4}\Delta$ in the various methyl[$^{2}H_1$]cyclooctenes would provide a basis for distinguishing the diastereoisomeric pairs within each system (*i.e.*, $^{2}H$ *cis* or *trans* to Me) but this may not be as decisive as we had hoped.

The chemical shifts induced by Me (substituent-induced shifts, SIS) in the four methylcyclooctenes are shown below in structures **26**–**29**.



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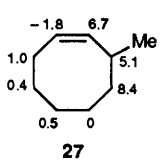

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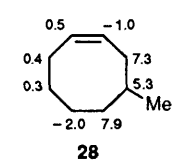

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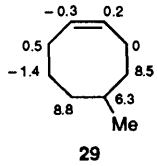

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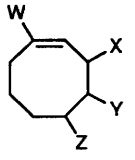
* Internal H-bonding from the hydroxy group to the π-bond is not considered to be important for these cyclic enols in chloroform solution. See, however, ref. 15. (We are grateful to a referee for raising this possibility.)

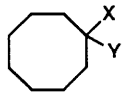
**Table 1** $^{13}C$ Chemical shifts of some cyclooctyl derivatives

| Compound | Carbon number 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | Other |
|---|---|---|---|---|---|---|---|---|---|
| **37a** | 130.18 | 130.18 | 25.48 | 29.20 | 26.17 | 26.17 | 29.20 | 25.48 | |
| **37b** | 136.91 | 124.10 | 26.52 | 30.36 | 26.65 | 26.20 | 28.00 | 30.21 | 23.43 |
| **37c** | 128.26 | 136.75 | 30.52 | 38.57 | 26.07 | 26.65 | 29.56 | 26.48 | 22.11 |
| **37d** | 130.65 | 129.11 | 32.82 | 34.45 | 34.09 | 24.17 | 29.48 | 25.88 | 22.00 |
| **37e** | 129.84 | 130.42 | 25.45 | 37.72 | 32.44 | 34.95 | 27.85 | 26.00 | 25.07 |
| **37f** | 144.37 | 140.44 | 27.04 | 29.16 | 26.55* | 25.88* | 29.33 | 30.35 | −9.88 |
| | (488) | (31.2) | (62.9) | (6.1) | (no) | (no) | (11.6) | (39.4) | (3.25) |
| **37g** | 125.59 | 133.84 | 26.65 | 31.53 | 29.25 | 25.40 | 29.01 | 25.97 | −11.03 |
| | (57.2) | (33.6) | (365) | (13) | (70) | (no) | (14) | (7.5) | (309) |
| **37h** | 128.50 | 132.34 | 27.57 | 32.44 | 28.44 | 25.73 | 29.11 | 26.05 | 128.21, 128.43, 137.34, 138.25 |
| | (nl) | (~35) | (402) | (17) | (73) | (no) | (13) | (~7) | (11), (45), (32), (nl) |
| **37i** | 128.38 | 135.03 | 69.28 | 38.51 | 23.65 | 25.87 | 29.01 | 26.24 | |
| **37j** | 129.42 | 132.69 | 56.99 | 40.17 | 25.28* | 25.63* | 28.88 | 26.07 | |
| **37k** | 129.67 | 133.19 | 48.83 | 40.79 | 26.05* | 25.59* | 28.92 | 26.48 | |
| **37l** | 132.18 | 126.00 | 33.89 | 72.02 | 34.93 | 21.14 | 28.21 | 25.60 | |
| **37m** | 129.83 | 129.15 | 22.58 | 37.17 | 72.26 | 36.07 | 24.70 | 25.42 | |
| **37n** | 129.58 | 129.58 | 21.82 | 34.32 | 84.62 | 33.63 | 24.29 | 25.25 | 21.41, 127.44, 128.98, 134.42, 144.25 |
| **37o** | 129.46* | 129.10* | 25.20† | 39.65 | 55.80 | 37.01 | 26.93 | 25.11† | |
| **38a** | 71.83 | 34.47 | 22.53 | 27.24 | 25.14 | 27.24 | 22.53 | 34.47 | |
| **38b** | 73.28 | 37.98 | 22.51 | 28.18 | 29.72 | 28.18 | 22.51 | 37.98 | 24.77 |
| **38c** | 217.62 | 41.52 | 25.27 | 26.81 | 24.36 | 26.81 | 25.27 | 41.52 | |

For $CDCl_3$ solvent. Centre of $CDCl_3$ triplet taken as $\delta_C$ 77.00. For structures of compounds, refer to diagrams **37** and **38** and numbering system shown. Assignments for **37c**, **37h** and **37l** based on $^1H$-$^{13}C$ correlated spectra. Values in parentheses are $^{119}Sn$–$^{13}C$ couplings. Values for $^{117}Sn$–$^{13}C$ are *ca.* 4% lower. no = not observed. nl = not located. Assignments for **38a** based on the [1-$^2H_1$]isotopomer in which $^1\Delta$ −489 ppb ($^1J_{CD}$ 21.4 Hz) and $^2\Delta$ −104 ppb. *,† Signals may be interchanged across a row.




**37**




**38**

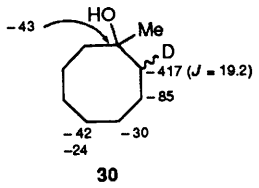
| | W | X | Y | Z |
|---|---|---|---|---|
| **37a** | H | H | H | H |
| **37b** | Me | H | H | H |
| **37c** | H | Me | H | H |
| **37d** | H | H | Me | H |
| **37e** | H | H | H | Me |
| **37f** | $SnMe_3$ | H | H | H |
| **37g** | H | $SnMe_3$ | H | H |
| **37h** | H | $SnPh_3$ | H | H |
| **37i** | H | OH | H | H |
| **37j** | H | Cl | H | H |
| **37k** | H | Br | H | H |
| **37l** | H | H | OH | H |
| **37m** | H | H | H | OH |
| **37n** | H | H | H | OTs |
| **37o** | H | H | H | Br |

| | X | Y |
|---|---|---|
| **38a** | H | OH |
| **38b** | Me | OH |
| **38c** | O | |

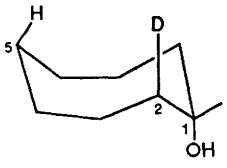
Positive α- and β-effects are manifested in all cases except compound **26**, where the *cis*-nature of Me and 2-H leads to a substantial shielding (−6.1 ppm) of C-2. Similarly, again in compound **26**, the downfield β-effect at C-8 (+4.7) is smaller than normal,[16] presumably due to a low torsional angle (~30°) between Me and one of the C-8 hydrogens. Reciprocally, the somewhat smaller β-effect at C-2 in compound **27** (*i.e.*, 6.7 ppm) is explained. Regarding γ-effects in these isomers, these are measurable at C-7 in compound **26** (−1.20), at both C-2 and C-6 in compound **28** (−1.0 and −2.0 ppm, respectively) and at C-7 (−1.4 ppm) in compound **29**. Compared with the γ-effects of *equatorial* Me (~0 ppm) and *axial*-Me in cyclohexane (−6 ppm),[16] the above effects are modest and reflect conformations characterised by predominantly 'equatorial' methyl groups.

1-*Methylcyclooctanol*.—The addition of MeMgI to [2-$^2H_1$]cyclooctanone (acquired by deuterolysis of the trimethylsilylenol ether of cyclooctanone) provided 1-methylcyclooctanol specifically labelled at C-2. The $^{13}C$ spectrum of this material (admixed with some unlabelled compound) provided the assignments for the alcohol shown in Table 1, as well as the $^2H$-effects on chemical shifts shown in structure **30**. The formation of diastereoisomeric alcohols in roughly equal amounts would be expected, and this is supported by the presence of two (unresolved) triplets to the high-field side of the (unlabelled) C-2 signal (see structure **30**). This was confirmed by the resolution of two $^4\Delta$ at C-5, of −42 and −24 ppb.

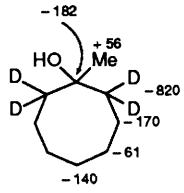
On the basis that substituent location is probably favoured at either C-1 or C-4/6 in the boat-chair arrangement, structure **31** is a reasonable approximation to one of the likely important conformations of compound **30**, and we expected that the 'axial' $^2H$ at C-2 would result in a positive $^4\Delta$ at C-5, rather than the observed −42 and −24 ppb for the two diastereoisomers. A $^3\Delta$ at C-8 was not resolved.




30




31

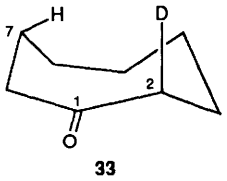



32

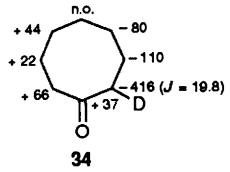
1-methyl-[2,2,8,8-$^2H_4$]cyclooctanol was obtained (from [2,2,8,8-$^2H_4$]cyclooctanone) and the $^2$H-effects shown in structure **32** demonstrate the additivity of the $^2$H-effects, when compared with the data for compound **30**. This correspondence implies a negligible $^2$H-effect on any conformational equilibria for 1-methylcyclooctanol, and suggests one strongly predominating arrangement for it. The positive $^3\Delta$ for the methyl carbon in structure **32** probably reflects *gauche* $^2$H · · · Me interactions.

*Cyclooctanone.*—Partial assignment of the $^{13}$C spectrum of cyclooctanone was reported by Weigart and Roberts[19] but distinction between the C-3 and C-4 signals was not possible. (The C-5 signal is less intense than that of C-3 or C-4 for symmetry reasons). Subsequently Milosavljevic reported[20] the spectrum of [5-$^2H_1$]cyclooctanone, obtained by oxidation of [1-$^2H_1$]cyclooctanol. More recently, Read and Shaw[2] provided unambiguous assignments from the spectra of a 1:1 mixture of [4-$^2H_1$]- and [5-$^2H_1$]-cyclooctanone isotopomers. Our interest in examining the spectra of $^2$H-substituted cyclooctanones was based on expected $^2$H-effects on the conformational equilibria, given the favoured boat-chair conformation **33** of this ketone in which significant H · · · H non-bonded interactions exist.[10] The most severe involve 'axial'-type hydrogens at positions 2, 4 and 7, and on this basis [2-$^2H_1$]cyclooctanone **34** may adopt preferentially a conformation approximating to structure **33** which is capable of averaging by pseudorotation. We also prepared and examined [2,2,8,8-$^2H_4$]cyclooctanone and the $^2$H-effects for the deuteriated derivatives are shown in structures **34** and **35**. Notice that in compound **35** isotope effects on the conformational equilibria would not apply because of symmetry, but in compound **34** the degeneracy of the equilibria is removed. If $^2$H-effects are additive in compound **35**, as appears reasonable, 'intrinsic' isotope effects of −340, −91, −40 and +7 ppb for $^1\Delta$, $^2\Delta$, $^3\Delta$ and $^4\Delta$ respectively, are obtained, and these can be applied to the data for compound **34**. The results are shown in structure **36** and the isotope shifts are roughly symmetrical with respect to the shifts for the unlabelled cyclooctanone. An analysis of this type has been applied to cyclodecanone,[21] which utilises an unsymmetrical boat-chair-boat conformation. In both compounds **34** and **35** the carbonyl signal experiences a positive two-bond effect (+ $^2\Delta$) normally ascribed to reduced hyperconjugative stabilisation of the polar carbonyl group by the adjacent C–D bond relative to C–H.[22]

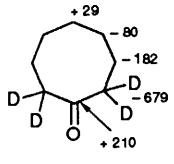
A listing of the $^{13}$C chemical shifts of the cyclooctyl derivatives examined in this work is presented in Table 1, and these data, along with those of Read and Shaw,[2] provide a basis for further analysis of the $^{13}$C NMR spectra of cyclooctyl derivatives. In this connection, we shall report results for derivatives of the (*E*)-cyclooctene system in the near future.



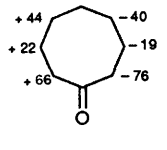

33




34




35




36

## Experimental

$^1$H NMR spectra were recorded at 400 MHz in the FT mode on a JEOL JNM-GX400 spectrometer and chemical shifts were referenced to internal tetramethylsilane (0.0 ppm) or residual $CHCl_3$ solvent (7.24 ppm). $^{13}$C NMR spectra were recorded at 100 MHz and chemical shifts were referenced to the central peak of the solvent signal ($CDCl_3$) at 77.00 ppm. Combined gas chromatography–mass spectrometry (GC-MS) was conducted on a Hewlett-Packard Model 5992B instrument using OV1 or BP5 capillary columns. Preparative GC was performed on a Shimadzu gas chromatograph Model GC-9A equipped with OV101 and C-20M columns. Accurate mass determinations were conducted on a Kratos mass spectrometer at Flinders University, South Australia, by Dr. M. J. Thompson and Ms R. Parry.

*Synthesis of Compounds.*—3-Bromocyclooctene, 3-chlorocyclooctene, cyclooct-2-enol and cyclooctanone are known compounds.[2,23] [3-$^2H_1$]cyclooctene was acquired either by $LiAlD_4$ reduction of 3-bromocyclooctene or by cleavage of cyclooct-2-enyltrimethylstannane with $CF_3CO_2D$ in $CDCl_3$. [1-$^2H_1$]Cyclooctene similarly resulted from acid cleavage of cyclooct-1-enyltrimethylstannane.[17] Detailed discussion of these and related stannanes will be presented elsewhere.[24] Reduction of 5-bromocyclooctene[25] with $LiAlD_4$ in bis-(2-ethoxyethyl) ether at 80 °C for several days afforded the required [5-$^2H_1$]cyclooctene along with other products. A pure sample was obtained by preparative GC. 1-Methylcyclooctanol is a known compound[26] and dehydration ($KHSO_4$) led to 1-methylcyclooctene, which together with the 3-, 4- and 5-methylcyclooctene have been synthesised and characterised by Cope and Woo.[26] Cyclooct-3-enol and cyclooct-4-enol (and the tosyl ester of the latter), are known compounds[27] and exhibited properties and spectra in accord with the structures. Use of $LiAlD_4$ in the ring-opening step of the monoepoxides of cycloocta-1,3-diene and cycloocta-1,5-diene led to the regiospecifically monodeuteriated derivatives discussed in the text. [1-$^2H_1$]Cyclooct-2-enol resulted cleanly from $LiAlD_4$ reduction of cyclooct-2-enone and exhibited appropriate spectra.[2]

*Cyclooct-3-enol.*—The monoepoxide of cycloocta-1,3-diene was reduced with $LiAlH_4$ in the standard way to provide, by regiospecific epoxide opening, cyclooct-3-enol having physical properties in agreement with those reported[27] (Found: $M^+$, 126.1041. Calc. for $C_8H_{14}O$: M, 126.1044) [Found: ($NH_3$, CI) *m/z* 126.1290. ($C_8H_{14}O + NH_4^+ - H_2O$) requires *m/z*, 126.1282]; $\delta_H$(400 MHz): 1.32 (1 H, m, 7-H), 1.5 (3 H, m, 6-$H_2$ and 8-H), 1.65 (1 H, m, 7-H), 1.78 (1 H, m, 8-H), 1.88 (1 H, s, OH), 2.06 (1 H, m, 5-H), 2.32 (2 H, dd 2-$H_2$), 3.75 (1 H, m, 1-H) and 5.65 [2 H, m, 3- and 4-H (lower field than 3-H)]. For the $^{13}$C NMR data see Discussion and Table 1.

The extent of $^2$H-incorporation in the compounds examined was clear from the $^{13}$C NMR data, and reduction of ketones with $LiAlD_4$ normally resulted in >99% $^2$H-incorporation. For the measurement of $^2$H-effects on the spectra, it is necessary to observe clearly the signals of the unlabelled material, and in cases of very high $^2$H levels, some unlabelled compound was deliberately added, in controlled amounts. Irrespective of the method used in acquiring the labelled compound, the level of $^2$H-incorporation was not <80%.

## Acknowledgements

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