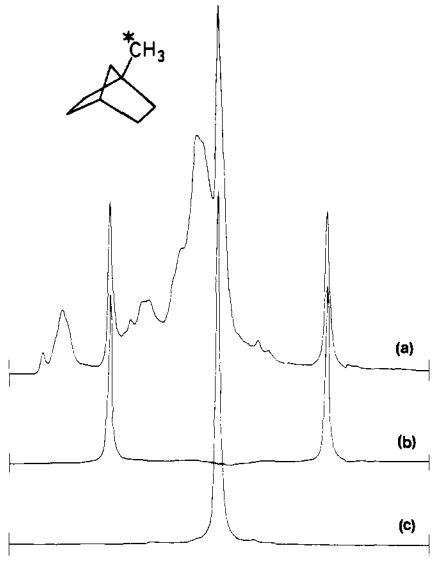

Figure 3. ^1H spectra[3] at 30 °C of pure (external D lock) 1-methylnorbornane, approximately 60% ^{13}C-enriched at the methyl group. The sweep width is 250 Hz. Sixty-four scans were collected. (a) Normal spectrum, (b) using sequence 2 without ^{13}C decoupling during acquisition, and (c) using sequence 2 with ^{13}C decoupling during acquisition.

As illustrated in Figure 2 for ethylene glycol, sequence 2 enables cancellation of the unwanted signals to better than 0.2% even for our imperfect magnet. (The ^{13}C satellites are split by homonuclear coupling unlike the central resonance and thus have a normal amplitude of about 0.1% of the central line.) Integration across the center line is considerably less than 0.2% of the uncanceled signal.

The application of the sequence to an enriched sample is shown in Figure 3. Although the ^{13}C satellites are clearly resolved in Figure 3a, the ^{12}CH-canceled spectrum [Figure 3b and the decoupled ^{12}CH-canceled spectrum (Figure 3c)] clearly illustrate what can be achieved for enriched samples where the ^{13}C satellites are normally overlapped by other resonances.

^{13}C-enriched quaternary carbons can be studied by setting τ to approximately correspond to a long-range J value. Indeed, use of larger τ values provides a general method of studying long-range ^{13}C–^1H coupling in enriched compounds if ^{13}C decoupling is not employed during acquisition. However, the greatest potential use of these sequences is in studying both short- and long-range ^{13}C–^1H coupling by two-dimensional NMR of unenriched compounds. Incrementation of τ to provide a second J dimension and ^{13}C decoupling during acquisition will produce a resonance in the J dimension for each ^{13}C–^1H coupling at $J/2$ Hz. Although these peaks will be split by proton homonuclear coupling, there will be a large gain in sensitivity over ^{13}C two-dimensional J spectra,[2] and the problem of complicated ^{13}C–^1H coupled multiplets is avoided. Since the proton homonuclear coupling occurs in both dimensions, it will assist in resolution.

Acknowledgment. This research was supported by major equipment grants from the Australian Research Grants Committee. Enriched 1-methylnorbane was provided by Dr. E. Della, Flinders University.

(2) Thomas, D. M.; Bendall, M. R.; Pegg, D. T.; Doddrell, D. M.; Field, J. *J. Magn. Reson.*, in press.
(3) Spectra were obtained by using a Bruker HX-90 spectrometer upgraded with an Aspect-2000 computer and associated CXP-series pulse modulation electronics. A 5-mm insert was used which contained a coil doubly tuned to ^{13}C and ^1H. A second coil was used for the D lock.

A New Approach to the Conformational Analysis of Seven-Membered Rings

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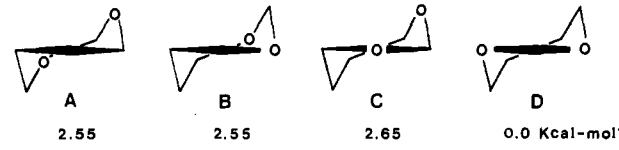
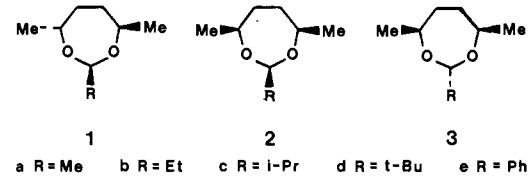
Progress in the conformational analysis of seven-membered rings has been slow, chiefly because pseudorotation of these rings is facile.[1,2] Evidence about the nature of the conformational energy surfaces for such systems and about such factors as axial–equatorial energy differences has come mainly from force-field calculations, with experimental support[1,3] for the nature of the lowest minima. Considerable advances were made in the conformational analysis of six-membered rings through the examination of the properties of derivatives with one or sometimes two groups present to lock the ring in a particular conformation.[4,5] We show here that the introduction of three groups results in comparable simplification of the conformational situation for seven-membered rings. We illustrate the procedure by using 2,4,7-trisubstituted-1,3-dioxepanes because these compounds are easily synthesized[6] and equilibrated.

For cycloheptane, there are 14 degenerate lowest energy conformations, the twist-chairs (TC), which pseudorotate into each other through 14 degenerate maxima, the chairs (calculated barrier,[1] 1.3 kcal mol^{-1}). Fourteen boat (B) and twist-boat (TB) conformations (calculated stabilities[1] relative to the TC, 3.42 and 3.39 kcal mol^{-1}, respectively) also pseudorotate into each other and are accessible from the TC conformation via an inversion process (barrier[1] 9.7 kcal mol^{-1}). For 1,3-dioxepane, there are four types of TC conformations, A–D, shown with their calculated stabilities.[1] Chair conformations are again local maxima so they will not be considered further here.



Three stereoisomers (**1**, **2**, and **3**) are produced when three



substituents are introduced at positions 2, 4, and 7 of 1,3-dioxepane, if those at 4 and 7 are identical. The relative energies of the TC conformations of the three stereoisomers with all groups methyl (**1a**, **2a**, **3a**) were evaluated approximately by making the following assumptions: (1) The four types of 1,3-dioxepane TC conformations have the energies calculated by Bocian and Strauss.[1] (2) The introduction of a methyl group at a particular position in a conformation increases the energy of the conformation by the amount calculated[2] for a similar introduction for cycloheptane. This *A* value is decreased by one-quarter of its value whenever

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(2) Hendrickson, J. B. *J. Am. Chem. Soc.* **1967**, *89*, 7036–7061.
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(6) The 2-substituted-4,7-dimethyl-1,3-dioxepane diastereomers were synthesized from a commerical mixture of 2,5-hexanediol isomers and the various aldehydes and were separated by preparative gas–liquid chromatography on a 20-ft column of 30% Carbowax 20M on Chromosorb W.

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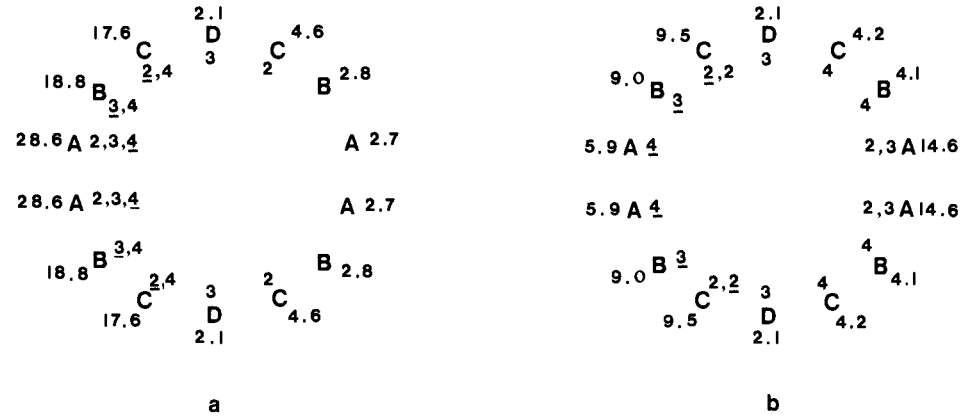

Figure 1. Pseudorotational itinerary of (a) **2a** and (b) **3a**. The letters indicate the type of 1,3-dioxepane TC conformation. A number inside the circle indicates that the conformation has an axial methyl group, and the magnitude of the number indicates the type of position the methyl adopts with respect to the pseudoaxis of C_2 symmetry of the conformation. An underlined number indicates that the axial group is the 2-methyl group. The numbers outside the circle are the energies of the conformation (kcal mol^{-1}) relative to the most stable conformation of **1a**, calculated as in the text.

a major nonbonded interaction of the axial methyl group is with oxygen.[7] If the axial methyl group is on the acetal carbon, the energy increase is doubled.[11] (3) The energy increase for an axial–axial interaction between methyl groups is taken to be the sum of the *A* values.[13] On this basis, **1a** should exist almost entirely in one D-type conformation, since the next most stable TC conformation is 2.8 kcal mol^{-1} higher in energy. Figure 1 shows the pseudorotational itineraries and calculated energies relative to this D conformation of **1a** for **2a** and **3a**. On the basis of these energies, the chief contributors to the conformational mixture present in **2a** should be two A-, two B-, and two D-type conformations, while **3a** should exist mainly in two D conformations. Qualitative evidence about the nature of the major conformations present can be obtained from the ^{13}C NMR spectra. Replacement of an equatorial 4-methyl group by an axial one in 2-substituted-4,6-dimethyl-1,3-dioxanes moves the ^{13}C NMR shift of C-2 upfield by 7.1 and 6.9 ppm, respectively, for the 2-methyl[15] and 2-phenyl[16] derivatives, respectively, and also moves the shift of that methyl group upfield by 2.2 ppm.[16] If the energies calculated as above are approximately correct, the chemical shifts of C-2 in **3** should be upfield of those in **1** by similar amounts, since both sets of derivatives should exist chiefly in D conformations and **1** should have all substituents equatorial whereas **3** should have a 4- or 7-methyl group axial. The observed upfield shifts were 5.8, 6.3, 7.3, 8.5, and 4.7 ppm for the **a**, **b**, **c**, **d**, **e** derivatives, respectively. In addition, the chemical shifts of the methyl groups at 4 and 7 showed upfield shifts of 2.5–3.4 ppm. Both of these factors are consistent with a methyl group of **3** assuming considerable axial character. In contrast, the shifts for C-2 for **2** are downfield of **1**—3.5, 3.3, 2.9, 3.2, and 4.0 ppm for **a**, **b**, **c**, **d**, and **e**, respectively—the shifts for the 4- and 7-methyl groups in **2** are nearly the same as for **1**. This evidence indicates that **2** exists chiefly in conformations without axial substituents (i.e., not in the two D conformations).

The sets of compounds **2** and **3** were equilibrated in acetonitrile with boron trifluoride etherate as catalyst at temperatures ranging from −46 to +64 °C. For all derivatives, at least five points were measured over a temperature range of at least 50 °C, and each point was the average of several measurements. Relative concentrations of the equilibrated derivatives were obtained by gas chromatography. Thermodynamic parameters derived from the results are presented in Table I. Since the D conformations of **2** and **3** must have identical energies,[17] the much greater stability of **2** supports the conclusion drawn from the ^{13}C NMR evidence that conformations of type D are minor contributors to the conformational mixture present for **2**. The statistical entropy difference between **2** and **3** can be calculated on the following basis: (1) only two A and two B conformations are present for **2**, and these are present in proportion to their calculated energies; (2) only the two D conformations are present for **3**. The value obtained, 1.37 eu, is similar to the observed values for the alkyl derivatives, **a**–**d**.[18] Thus, it is likely that the chief contributors to **2** are the two A and two B conformations, whereas **3** exists chiefly in the two D conformations.

Table I. Thermodynamic Parameters for the Equilibration 3 ⇄ 2[a]

derivative	ΔH°, kcal mol^{-1}	ΔS°, eu	ΔG°,[b] kcal mol^{-1}
a	−1.38 ± 0.03	0.82 ± 0.08	−1.628 ± 0.004
b	−1.30 ± 0.16	1.44 ± 0.55	−1.73 ± 0.02
c	−1.29 ± 0.06	1.18 ± 0.22	−1.62 ± 0.01
d	−0.84 ± 0.05	2.6 ± 0.20	−1.64 ± 0.01
e	−1.50 ± 0.01	0.19 ± 0.03	−1.558 ± 0.001

[a] In acetonitrile using 0.5 M solutions with 0.005 M boron trifluoride etherate as catalyst. [b] At 300 °C.

The A and B conformations of **2** have been shown here to be ~1.3 kcal mol^{-1} (average enthalpy difference) more stable than the D conformation of **2**, in marked contrast to the calculated differences of 0.6 or 0.7 kcal mol^{-1} favoring the D conformation. Some of this ~1.9 kcal mol^{-1} difference between the observed and calculated results may arise from the *A* value calculated here for the one axial group (2.4 kcal mol^{-1} for the axial methyl group in the D conformations of **2** and **3**). Nevertheless, the A- and B-type conformations of 1,3-dioxepane must be considerably more stable relative to the D-type conformation than previously calculated,[1] by at least 1 kcal mol^{-1}. Since the D conformation was observed to be the only conformation present[20] for 1,3-dioxepane itself, there is an upper limit of ~1.6 kcal mol^{-1} on the error in the calculated stabilities. Thus the evidence presented here in-

(7) The *A* value for a methyl group in cyclohexane is 1.7 kcal mol^{-1} [8] while the comparable values for a methyl group in 3-methyltetrahydropyran[9] (one nonbonded interaction with oxygen) and 5-methyl-1,3-dioxane[10] are 1.27 and 0.9 kcal mol^{-1}, respectively.

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(11) The *A* value for a 2-methyl group in 1,3-dioxane is ~4.0 kcal mol^{-1}.[12]

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(13) The 1,3-diaxial methyl–methyl interaction value in cyclohexane is 3.7 kcal mol^{-1},[14] approximately double the methyl *A* value.

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(17) It is assumed that there is no interaction between the substituents in the D conformations of both compounds.

(18) Different rotameric populations in the different conformations probably affect the entropy values for the 2-phenyl derivatives as for 2-phenyl-1,3-dioxanes.[19]

(19) Bailey, W. F.; Cannon, H.; Eliel, E. L.; Wiberg, K. B. *J. Am. Chem. Soc.* **1978**, *100*, 2202–2209.

(20) Less than 15% of a minor conformation would probably not have been detected.

dicates that the A and B conformations of 1,3-dioxepane are 1-1.6 kcal mol^{-1} less stable than the D conformation rather than the ~2.6 kcal mol^{-1} previously calculated.[1]

Evaluation of the energies of the boat and twist-boat conformations of **2a** and **3a**, making the same assumptions as previously, indicated that for both **2a** and **3a** there are two enantiomeric TB conformations which are considerably more stable than any others of this type and also similar in energy to the most stable TC conformations. However, neither the ^{13}C NMR evidence nor the equilibrium results are compatible with a significant proportion of TB conformations.[21] We therefore conclude that the TB conformations of 1,3-dioxepane are considerably less stable than calculated, perhaps by as much as 2 kcal mol^{-1}.

Thus, the examination of the conformational properties of 2,4,7-trisubstituted-1,3-dioxepanes gave considerable information about the conformational properties of 1,3-dioxepane.

The scheme outlined here can provide conformational informational about any seven-membered ring. For instance, examination of the pseudorotational itineraries in Figure 1 shows that equilibrium of the same stereoisomers of cycloheptane would yield the axial-equatorial energy difference.

Acknowledgment. T.B.G. is grateful to the NSERC of Canada for support. We thank Dr. Charles Rodgers of Bruker Canada for the 250-MHz NMR spectra.

(21) Variable-temperature 250-MHz ^1H NMR spectra of **3b-d**, compounds in the series (3) most likely to exist in TB or B conformations, down to 118 K showed that pseudorotation had slowed (ΔG^* 6.4-7.0 kcal mol^{-1} from coalescence measurements) but gave no indication of the presence of other than TC conformations.

Oxidation of Olefins by Potassium Permanganate. Mechanism of α-Ketol Formation

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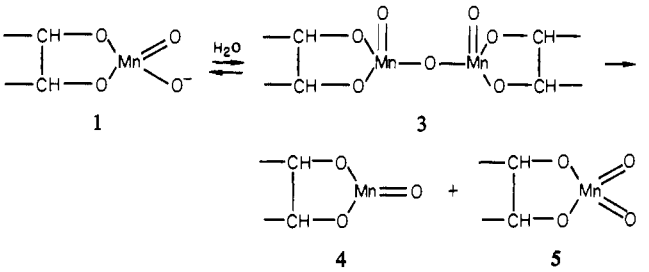
The oxidation of an olefin by potassium permanganate in aqueous media can lead, inter alia, to an α-glycol,[1] a 2-equiv oxidation, or α-ketol,[2] a 4-equiv oxidation. The glycol is a major product at pH >9 (cyclic olefins)[3] or pH >12 (acyclic olefins);[1] the ketol is a major product in the pH range 4-8[2,4] and is not formed via the glycol.[5] At pH values intermediate between the optimum for glycol formation and the optimum for ketol formation, both products are observed, and the ketol/glycol ratio can be increased by an increase in the initial permanganate/olefin ratio.[5b] With the periodate-permanganate reagent,[6] oleic acid is oxidized exclusively to ketol, even at pH 12.[5b] These various observations suggest that the glycol and the ketol arise from a common intermediate, which may react with hydroxyl ions to form the lower oxidation level product or with hydroxyl ions and permanganate (or periodate) to form the higher oxidation level product.

The cyclic hypomanganate ester **1**[7] is considered to be an intermediate in the formation of the glycol and to undergo hydrolysis with fission of the Mn-O bonds, on the basis of the stereochemistry of the reaction,[8] ^{18}O-labeling experiments,[9] and kinetic studies.[10,11] The kinetic results support the view that the glycol and the ketol are formed from a common intermediate, since the second-order rate constant is the same at pH 6.8 and 13.[10] It follows, therefore, that the ketol arises by oxidative hydrolysis of the cyclic ester **1**.



The oxidative and hydrolytic reactions of inorganic hypomanganate (MnO_4^{3-}) with permanganate, periodate, and water have been studied in some detail.[12] The reaction with water (eq 1-3) leads to disproportionation[12a,b] and oxygen exchange[12c] via

$$MnO_4^{3-} + H_2O \rightleftarrows HMnO_4^{2-} + OH^- \quad (1)$$

$$2HMnO_4^{2-} \rightleftarrows Mn_2O_7^{4-}\ (\mathbf{2}) + H_2O \quad (2)$$

$$Mn_2O_7^{4-} \rightleftarrows Mn(IV)O_3^{2-} + Mn(VI)O_4^{2-} \quad (3)$$

the dimeric species **2**. Extrapolation to pH 7 of the data of ref 12b indicates that, at 25 °C, the observed second-order rate constant for disproportionation will be greater than 10^{12} M^{-1} s^{-1}. This is much larger than the rate constants for the oxidation of hypomanganate by permanganate (eq 4) and periodate (eq 5) (2.8

$$MnO_4^{3-} + MnO_4^- \rightarrow 2MnO_4^{2-} \quad (4)$$

$$MnO_4^{3-} + H_3IO_6^{2-} \rightarrow MnO_4^- + IO_3^- + 3OH^- \quad (5)$$

× 10^6 M^{-1} min^{-1} and 20 × 10^6 M^{-1} min^{-1}, respectively, at 35 °C).[12d] An analogous protonation and dimerization of the ester **1** leads to **3** which, upon electron transfer (cf. eq 3), disproportionates to the Mn(IV) ester **4** and the Mn(VI) ester **5**. A species corresponding to **4** has apparently been observed by several groups of workers[13] and found to undergo oxidation to **5** in the presence of excess permanganate.[13b] These considerations suggest that, in neutral media, the Mn(V) ester **1** is transformed rapidly into the Mn(VI) ester **5**.

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