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# STEREOELECTRONIC STABILIZATION IN NON-CHAIR CONFORMATIONS OF SUBSTITUTED-2,3-DIHYDRO-1,4-BENZODIOXEPINS

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Abstract - 2,3-Dihydro-1,4-benzodioxepin (5) and its 3-substituted derivatives 6-9 have been studied by $^{13}C$ and $^{1}H$ dynamic NMR in two solvent systems of different polarity. The aromatic signals were found to be quite sensitive to the nature of the seven-membered cyclic geometries and were used as "conformational probes". The results show that the chair (C) conformation is the only form detected at -120°C for the parent compound 5 and its 3-methyl derivative 6 whereas the twist-boat (TB) conformation becomes predominant for three derivatives, 3,3-dimethyl 7, 3-methoxy 8 and 3,3-methylmethoxy 9, as a consequence of both steric and stereoelectronic interactions. Furthermore, in the case of 8, the detailed geometry of the TB forms detected reflects on the relative importance of competing stereoelectronic (anomeric and gauche) effects.

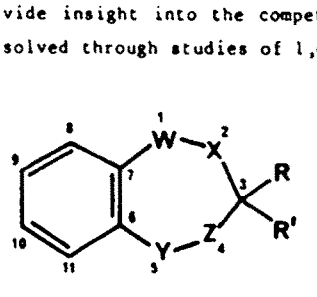
## Introduction

Conformational analysis of six-membered heterocyclic compounds has progressed tremendously during the last thirty years[1] to a point where attempts at defining the very fine details of complex phenomena such as the anomeric[2] and the gauche[2,3] effects are being made, as illustrated recently by the work of Fuchs and co-workers on substituted 1,4-dioxanes[4].

However, conformational studies in six-membered ring compounds are normally restricted to a single ring geometry, the chair (C) form, because the energy of the other possible conformer, the twist-boat (TB) form, is superior by about 5 kcal/mol[-1] so that it is therefore not detected in solution by the usual techniques.

Calculations by Favini and Nava[5] have indicated that benzocycloheptene (1) shows a reduced energy difference between the C and TB conformers. Although TB signals were not detected in the low temperature $^{1}H$ NMR spectrum of benzocycloheptene itself,[6] other studies[7-9] on some heterocyclic derivatives showed that TB signals are indeed observed in the low-temperature NMR spectra of 1,5-benzodioxepin (2) and of 2,4-benzodioxepin (3).

Considering these results and the wealth of data recently published on the 1,4-dioxane derivatives,[10] it was decided to investigate, by a combination of dynamic NMR spectroscopy and molecular mechanics calculations, the conformational properties of 2,3-dihydro-1,4-benzodioxepin (5) and its 3-substituted derivatives 6-9. The characteristics of this series of compounds is expected to provide insight into the competition between the anomeric and the gauche effects which cannot be resolved through studies of 1,4-dioxane and its derivatives.




| | | | |
|---|---|---|---|
| 1 | W,X,Y,Z=$CH_2$; R,R'=H | 7 | W,Z=O; X,Y=$CH_2$; R,R'=$CH_3$ |
| 2 | W,Y=O; X,Z=$CH_2$; R,R'=H | 8 | W,Z=O; X,Y=$CH_2$; R=H, R'=$OCH_3$ |
| 3 | W,Y=$CH_2$; X,Z=O; R,R'=H | 9 | W,Z=O; X,Y=$CH_2$; R=$CH_3$, R'=$OCH_3$ |
| 4 | W,Y=$CH_2$; X,Z=O; R=H, R'=$OCH_3$ | 10 | W=O; X,Y,Z=$CH_2$; R,R'=H |
| 5 | W,Z=O; X,Y=$CH_2$; R,R'=H | 11 | W=O; X,Y,Z=$CH_2$; R=R'=$CH_3$ |
| 6 | W,Z=O; X,Y=$CH_2$; R=H, R'=$CH_3$ | 12 | W=O; X,Y,Z=$CH_2$; R=$CH_3$, R'=$OCH_3$ |

TABLE 1. Carbon-13 Chemical Shifts[a] of Compounds 5-9 in $CHF_2Cl$[b] at High and Low Temperatures

| Compound | Temperature (°C) | Conformation | C-2 | C-3 | C-5 | C-6 | C-7 | C-8 | C-9[c] | C-10 | C-11[c] | $CH_3$ | $OCH_3$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 5 | -15° | - | 74.60 | 74.66 | 75.41 | 134.13 | 161.43 | 121.97 | 130.54 | 124.68 | 130.46 | - | - |
| | -120° | C[d] | 74.25 | 74.32 | 75.24 | 133.86 | 160.87 | 122.12 | 130.80 | 124.84 | 130.58 | - | - |
| 6 | -25° | - | 79.50 | 79.83 | 72.91 | 134.52 | 161.16 | 121.85 | 130.42 | 124.73 | 130.30 | 17.47 | - |
| | -120° | $C_e$ | 79.25 | 79.74 | 72.69 | 134.33 | 160.63 | 122.04 | 130.56 | 124.93 | 130.49 | 17.49 | - |
| 7 | -25° | - | 79.52 | 77.22 | 65.70 | 131.87 | 160.39 | 120.73 | 129.79 | 123.68 | 129.79 | 23.53 | - |
| | -120° | TB | 76.40 | 78.18 | 64.74 | 128.24 | 158.44 | 119.62 | 129.80 | 122.61 | 129.52 | 21.44<br>25.66 | - |
| | | C | 81.52 | 76.60 | 65.85 | 134.46 | 161.01 | 121.74 | 130.43 | 124.91 | 130.43 | 19.76<br>26.15 | |
| 8 | -25° | - | 73.44 | 102.27 | 63.61 | 131.69 | 160.24 | 121.07 | 130.01 | 124.07 | 129.78 | - | 55.95 |
| | -120° | $TB_{ee}$ | 70.54 | 101.41 | 62.35 | 128.18 | 158.76 | 120.33 | 129.50 | 123.19 | 129.50 | - | 55.88 |
| | | $C_e$ | 75.54 | 100.01 | 62.51 | 133.72 | 160.96 | 121.78 | 130.69 | 125.24 | 130.69 | - | 55.9[e] |
| 9 | -25° | - | 76.92 | 102.20 | 63.89 | 130.61 | 160.11 | 120.33 | 129.86 | 123.75 | 129.66 | 20.66 | 48.65 |
| | | $TB_{ee}$ | 75.01 | 102.82 | 63.60 | 128.18 | 158.78 | 120.03 | 129.61 | 123.06 | 129.55 | 20.83 | 48.89 |
| | -120° | $C_e$ | 79.00 | 100.55 | 63.33 | 134.08 | 160.84 | 121.74 | 130.77 | 125.34 | 130.52 | 20.09 | 48.9[e] |

a) All spectra were taken on a Bruker WH-400 spectrometer operating at 100.62 MHz.
b) Solutions containing 20% $CD_2Cl_2$ for locking purposes and tetramethylsilane as internal standard.
c) Assignment of C-9 and C-11 resonances could be reversed.
d) The symbols C, $C_e$, $C_a$ and TB refer to conformations described in the text.
e) The minor methoxy signal overlaps with the major one.

TABLE 2. Proton ($^1H$) Chemical Shifts[a] of Compounds 5-9 in $CHF_2Cl_{b,c}$ at High and Low Temperatures

| Compound | Temperature(°C) | Conformation | H-2e | H-2a | H-3e | H-3a | H-5e | H-5a | $CH_3$ | $OCH_3$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 5 | -5° | - | 4.07 m[d] | 4.07 m | 3.98 m | 3.98 m | 4.78 s | 4.78 s | - | - |
| | -140° | C[e] | 4.34 d | 3.86 t | 4.10 d | 3.98 t | 4.72 d | 4.68 d | - | - |
| 6 | -10° | - | 4.21 dd | 3.48 dd | - | 4.01 m | 4.74 d | 4.59 d | 1.13 d | - |
| | -100° | Ce | 4.26 d | 3.50 dd | - | 4.05 m | 4.78 d | 4.63 d | 1.14 d | - |
| 7 | -20° | - | 3.93 s | 3.93 s | - | - | 4.72 s | 4.72 s | 1.30 s | - |
| | -124° | TB | 4.36 d | 3.88 d | - | - | 4.40 d | 5.17 d | 1.39 s<br>1.23 s | - |
| | | C | 4.05 d | 3.60 d | - | - | 4.33 d | 5.05 d | 1.52 s<br>1.14 s | - |
| 8 | -10° | - | 4.08 m | 4.06 m | 4.84 m | - | 4.35 d | 5.22 d | - | 3.48 s |
| | -130° | $TB_{ee}$ | 4.2-4.3[f] | 4.2-4.3[f] | 5.08 m[g] | - | 4.43 d | 5.38 d | - | 3.47 s |
| | | Ca | 4.34 d | 3.81 d | 4.73 s | - | 4.2-4.3[f] | 5.26 d | - | 3.52 s |
| 9 | -10° | - | 4.26 d | 3.82 d | - | - | 4.23 d | 5.25 d | 1.40 s | 3.34 s |
| | -120° | $TB_{ee}$ | 4.29 d | 4.02 d | - | - | 4.37 d | 5.34 d | 1.54 s | 3.31 s |
| | | Ca | 4.23 d | 3.64 d | - | - | 4.27 d | 5.11 d | 1.26 s | 3.34 s |

a) All spectra were taken on a Bruker WH-400 spectrometer operating at 400.13 MHz.
b) Solutions contain 20% $CD_2Cl_2$ for locking purposes and tetramethylsilane as internal reference.
c) Aromatic signals in $CHF_2Cl$ solutions are masked by solvent lines and were not assigned.
d) Signal's multiplicity is described by the following abbreviations: s: singlet; d: doublet; t: triplet; m: multiplet; dd: doublet of doublet; dt: doublet of triplet.
e) The symbols C, Ce, Ca and TB refer to conformations described in the text.
f) Overlapping signals.
g) Signal corresponding to an isoclinal proton on the TB form.

## Results

Proton ($^1H$) and carbon-13 ($^{13}C$) NMR spectra of compounds 5-9 were obtained at different temperatures between -5°C and -140°C. Three solvent systems were used: a polar one consisting of $CHF_2Cl$:$CD_2Cl_2$ (80:20) for both $^{13}C$ and $^1H$ NMR spectra and two less polar mixtures, $CH_3OCH_3$:$CD_2Cl_2$ (80:20) and $CF_2Cl$:acetone-$d_6$ (94:6), for $^{13}C$ and $^1H$ NMR spectra respectively. All pertinent parameters for $CHF_2Cl$ solutions are summarized in Tables 1-2.

The 100.62 MHz $^{13}C$ proton decoupled spectrum of 5 at -15°C, in $CHF_2Cl$:$CD_2Cl_2$ (80:20), consists, for example, of nine well-resolved signals. The aromatic signals are assigned by comparison with similar signals observed[11] for 2,3,4,5-tetrahydro-1-benzoxepin 10; selective heteronuclear irradiation of the benzylic 5-protons readily identifies the C-5 signal in the coupled spectrum, and the presence of small couplings ($^3J_{CH}$) in the 74.32 ppm signal identifies it as the C-3 resonance. Lowering the temperature to -120°C only results in a slight broadening of the signals, which suggests the existence of a single chair conformation, as will be discussed in the next section. The chemical shift data are summarized in Table 1.

The 400.13 MHz $^1H$ NMR spectrum of the same compound (5) in $CHF_2Cl$ does however show some dynamic features on going from -5°C to -140°C. The spectrum at -5°C contains an $A_2$ pattern for the benzylic 5-protons and a AA'BB' pattern for the $-O-CH_2-CH_2-O-$ fragment; these signals split at lower temperatures to give, at -135°C, an AB pattern for the benzylic 5-protons and a group consisting of two broadened doublets and two broadened triplets for the $-OCH_2-CH_2-O-$ fragment. The parameters given in Table 2 result from a spectral analysis involving selective irradiation experiments.

Similar to the parent compound 5, the 100.62 MHz $^{13}C$ NMR spectrum of the monomethylated derivative 6 does not show any significant changes (in both solvent systems) as the temperature is lowered to -120°C. All signals at -120°C are attributed to a single conformation, the $C_e$ form, as will be discussed later.

Contrastingly, compounds 7-9 exhibit more complex changes in their $^{13}C$ and $^1H$ NMR spectra as the temperature is decreased, owing to the presence of a mixture of conformations at low temperatures. In addition to the chair form, each of these compounds shows the presence of signals assigned to a TB form whose NMR parameters are summerized in Tables 1 and 2. The spectral features of the methoxy derivatives 8 are illustrated as an example.

Fig. 1 shows the 100.63 MHz $^{13}C$ NMR spectrum of 8 (in $CHF_2Cl$:$CD_2Cl_2$ (80:20)) at -25°C. It consists of ten well-resolved signals, of which the aromatic resonances are readily assigned by comparaison with those of parent compound 5. The methyne (C-3) and methyl ($CH_3$) resonances are clearly identified by an off-resonance experiment, while the C-5 resonance at 63.62 ppm is distinguished from the C-2 resonance at 73.44 ppm by selective irradiation of one of the benzylic (H-5) protons in the $^1H$ NMR spectrum. All signals split as the temperature is lowered to give, at -120°C, two sets of signals of unequal intensities (55:45), which are attributed to $TB_{an}$ (major form), methoxy group "anti" to the O1-C2 bond) and $C_a$ (minor form, methoxy group in axial position) as described later. Changing the solvent system to $CH_3OCH_3$ alters only the relative proportion of the two sets of signals in favor of the $TB_{an}$ conformation (see Table 3).

## Discussion

### Conformations of the seven-membered ring in compounds 5-9

The low temperature NMR spectra of compounds 5-9, described in the previous section, contain signals for the chair and twist-boat forms; the identification of the appropriate ring geometries for each compound can be deduced from spectral analysis as explained next and summarized in Table 3.

As reported earlier[7,8], the 1,5-(2) and 2,4-(3)benzodioxepins were shown to exist in solution as mixtures of C and TB forms for which C is most abundant (79% in $CHF_2Cl$ for both 2 and 3, at -130°C). Since only one set of signals is observed in both the low temperature $^{13}C$ and $^1H$ NMR spectra of the parent compound 5, it can reasonably be attributed to a chair (C) conformation, in

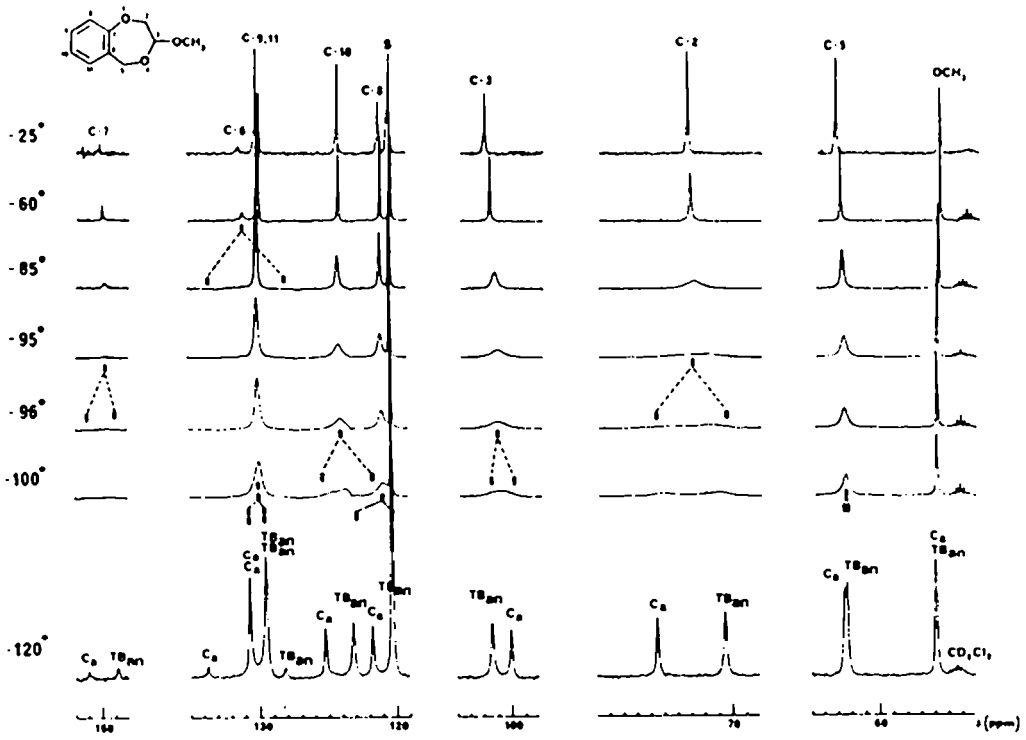



Figure 1 The 100.62 MHz $^{13}C$ NMR spectra of 8 in $CHF_2Cl:CD_2Cl_2$ (80:20) at several temperatures. $C_a$ and $TB_{an}$ refer to conformations described in the text. Broken lines link together signals corresponding to the same carbon atom position. "S" designates a solvent ($CHF_2Cl$) line.

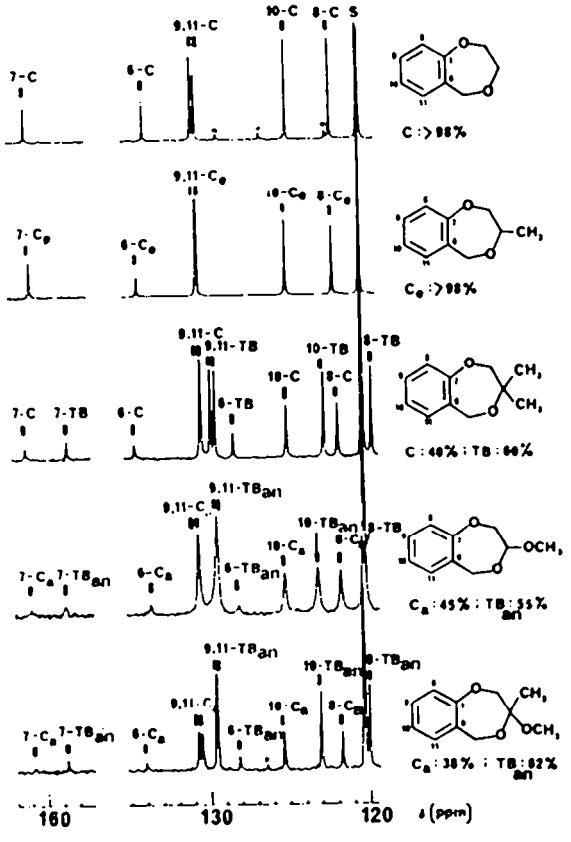



Figure 2 Aromatic portion of the 100.62 MHz $^{13}C$ NMR spectra of compounds 5-9 in $CHF_2Cl:CD_2Cl_2$ (80:20) at -120°C: C, $C_a$, $C_e$, TB and $TB_{an}$ refer to conformations described in the text. "s" denotes an impurity.

accord with the observed activation barrier of 7.6 ± 0.3 kcal/mol$^{-1}$, which is much more in line with a C ⇌ C* inversion process ($\Delta G^{\neq}$ = 7.7 ± 0.5 kcal/mol$^{-1}$ in 3 [8a]) than a TB ⇌ TB* pseudorotation process.

The seven-membered ring geometries for the substituted derivatives 6-9 are determined through analysis of their aromatic carbon signals at low temperatures, as shown in Fig. 2. Earlier work on various benzoxepins[11,12] and benzodioxepins[7,8] revealed that the chemical shifts of the $^{13}C$ aromatic signals are very sensitive to the nature of the seven-membered ring geometry while, at the same time, being rather independent of the nature of the substituents at the 3-position. These signals can then be used as conformational probes, whereby signals for the chair form generally appear downfield from those of the twist-boat form for a given system.

The chemical shift differences between the aromatic $^{13}C$ signals of the two conformations are observed to be especially large when a phenolic type oxygen atom is present in the seven-membered ring cycle, since they reflect the different effects of conjugation in each of the two forms: the smaller $C_{sp_2}$-$C_{sp_2}$-O-$C_{sp_3}$ torsion angle in the TB form produces a greater release of electrons from the oxygen atom to the π-system than in the C form, and therefore contributes to the accrued chemical shift difference between aromatic $^{13}C$ signals of those two forms.

Hence, in Fig. 2, the identification of the $^{13}C$ aromatic signals corresponding to chair geometries of compounds 6-9, is made by direct comparison with signals for the single C conformation of the parent compound 5, used as reference. The more shielded set of signals for each of compounds 7-9 is then attributed to a TB geometry. Conformational dependence of the aromatic $^{13}C$ resonances is quite large for C-6 (ortho to O1), whose chemical shift changes by as much as 6 ppm on going from C to TB.

**Substituent orientation in compounds 6, 8 and 9**

The preceding analysis of the aromatic NMR signals of compounds 6, 8 and 9 proved to be an efficient method of establishing the seven-membered ring geometries of these substituted compounds in solution. However, the aromatic signals are helpless in defining the orientation of the substituents at the 3-position because of the remoteness of the substituents from the aromatic nucleus. More classical arguments, based on general NMR parameters, must therefore be used, as described next.

For example, the orientation of the methyl and methoxy groups in the C forms of compounds 6 and 8 is deduced from the multiplicity of the 2a-proton signal, in the low-temperature $^1H$ NMR spectra of these compounds. Hence, the triplet observed for the 2a-C proton of 6 arises from strong coupling with the 2e ($^2J$) and 3a ($^3J$) protons, which points to an equatorial methyl group at the 3-position of $C_e$ conformation. On the other hand, the fact that the 2a-C proton of compound 8 exists as a doublet suggests the presence of an equatorial proton at position 3, and so the methoxy group must take an axial orientation in the chair form of 8.

For compounds 9, the absence of the 3-proton rules out such an approach and conformational information from the $^1H$ NMR spectrum is provided indirectly through a consideration of the characteristic anisotropy effects of the methoxy and methyl groups on the adjacent axial proton (in this case, 2a), as measured previously[11] in the methylmethoxy derivative 12, taken here as a model.

It is found that this substituent anisotropy effect is quite similar in the $C_a$ form of 12 ($\Delta\delta$ = -0.14 ppm)[11] and in the C form of 9 ($\Delta\delta$ = -0.17 ppm), implying that the methyl group is indeed in an equatorial position in the C form of 9, and therefore, that the methoxy group is axially oriented ($C_a$ conformation).

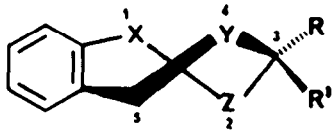
In contrast, the orientation of the methoxy substituent in the twist-boat conformations of 8 and 9 is more difficult to determine, since no reference TB signals are detected in the low-temperature NMR spectra of the parent compound 5.

For both compounds 8 and 9, two twist-boat forms are possible *a priori*, namely $TB_{an}$ (13) and $TB_g$ (14), where "an" and "g" refer respectively to the *anti* and *gauche* orientations of the external C-O bond relative to the internal $O_1$-$C_2$ bond. The single set of sharp signals assigned to the twist-boat conformation in the low-temperature NMR spectra of 8 and 9 must refer either to a single

$TB_{an}$ or $TB_g$ form, or to a mixture of those two TB forms still undergoing a rapid pseudorotation at -120°C. However, since this last proposed dynamic process is expected to be significantly slowed down at -120°C (as is the case for the dimethyl derivative 7 which shows two distinct methyl signals at -125°C), the sharpness of the TB signals at -120°C points to a single TB conformer in solution for 9, either $TB_{an}$ or $TB_g$. Each of these two forms (13 and 14) exhibits a particular orientation of the methoxy group relative to the benzylic C-5 carbon atom. Previous studies[8a] on the 3-methoxy-2,4-benzodioxepin molecule 4 revealed that the $^{13}C$ chemical shift of the C-5 signal reflect on the orientation of the methoxy group in the TB form, as these chemical shifts were indeed found to be markedly different whether the methoxy group is syn ($\delta_{C-5}$ = 62.57 ppm in structure 15) or anti ($\delta_{C-5}$ = 67.84 ppm in structure 16) to the C-5 benzylic carbon atom.

These $^{13}C$ chemical shifts are also valid probes for the TB forms, either $TB_{an}$ (13a) or $TB_g$ (14a) in compound 8, in spite of the minor structural differences between the latter and 4. Recent studies on benzoxepins,[11,12a] show that the displacement of the oxygen atom from the 2- to the 1-position in the chair forms of these compounds, changes the $^{13}C$ NMR chemical shift of the C-5 resonance by only 0.84 ppm. One can thus reasonably assume that within a 1 ppm margin, the values 62.6 ppm and 67.8 ppm for 4 represent reference $^{13}C$ NMR C-5 chemical shifts for the $TB_{an}$ and $TB_g$ conformations of 8. Therefore, the observation that the C-5 TB resonance is at 62.35 ppm for 8, at -120°C, is strongly indicative of a $TB_{an}$ conformation for this compound.

Finally, the chemical shift of 63.60 ppm for C-5 of the TB form of 9, in $CHF_2Cl$ (-120°C), compares well with the reference value (62.6 ppm), thus indicating an anti orientation of the methoxy group in 9, in accord with the sole $TB_{an}$ form (13b) in solution.




13a X,Y=O; Z=$CH_2$; R=H, R'=$OCH_3$($TB_{an}$)

13b X,Y=O; Z=$CH_2$; R=$CH_3$, R'=$OCH_3$($TB_{an}$)

14a X,Y=O; Z=$CH_2$; R=$OCH_3$, R'=H ($TB_g$)

14b X,Y=O; Z=$CH_2$; R=$OCH_3$, R'=$CH_3$ ($TB_g$)

15 X=$CH_2$; Y,Z=O; R=H, R'=$OCH_3$

16 X=$CH_2$; Y,Z=O; R=$OCH_3$, R'=H

**Conformational energies from molecular mechanic calculations**

The issue of the relative stabilities of $TB_{an}$ vs $TB_g$ for compounds 8 and 9, discussed in the previous section, together with the need for a predictive tool in the conformational analysis of seven-membered ring heterocycles, eventually led us to calculate the conformational energies of the compounds studied in this work by published molecular mechanics methods.

The MM method[13-15] has been developed considerably over the last two decades and successful extension of the method to heterocycles[16] and to conjugated systems[17] suggested that such a method could indeed be utilized to predict the relative stabilities of the various C and TB forms of compounds 5-9.

The results, using the MM285 program which includes the parametrization of the anomeric effect[18], are summarized in Table 3. Comparison between calculated enthalpy ($\Delta H^\circ$) and experimental free energy ($\Delta G^\circ$) values must be made with caution since the entropy differences ($\Delta S^\circ$) between the C and TB conformers are not known precisely in these seven-membered ring compounds. Nevertheless, the results successfully predict the global conformational preferences of the compounds studied.

Particularly interesting from this study is the large energy difference (2 kcal/mol$^{-1}$) calculated between the $TB_{an}$ and $TB_g$ forms of both the methoxy 8 and the methylmethoxy 9 derivatives; this result strongly supports the conclusions reached from the previous analysis of NMR data, that is, the existence in solution of only one TB form, namely $TB_{an}$, for both compounds 8 and 9.

TABLE 3. Relative populations of the conformations of compounds 5-9 in different solvents and comparison with calculated (MM2S5) values.

| Compound | Solvent[a] | Conformation's populations[b] % C | % TB | -ΔG°(C/TB) (kcal/mol) | Relative enthalpies of formation ($\Delta(\Delta H_f^\circ)$, kcal/mol$^{-1}$) (calculated) (MM2S5) |
|---|---|---|---|---|---|
| 5 | $CHF_2Cl$ | >98 | <2 | >1.18 | - |
| | $CF_2Cl_2$ | >98 | <2 | >1.18 | 1,1 (C/TB) |
| 6 | $CHF_2Cl$ | >98 ($C_e$) | <2 | >1.18 | |
| | $CH_3OCH_3$ | >98 ($C_e$) | <2 | >1.18 | 1,1 ($C_e/TB_g$) (2,0 ($C_e/TB_{aa}$)) |
| 7 | $CHF_2Cl$ | 40 | 60 | -0.12 | - |
| | $CH_3OCH_3$ | 40 | 60 | -0.12 | -0,5 (C/TB) |
| 8 | $CHF_2Cl$ | 45 ($C_e$) | 55 ($TB_{aa}$) | -0.06 | - |
| | $CH_3OCH_3$ | 13 ($C_e$) | 87 ($TB_{aa}$) | -0.58 | -1,1 ($C_e/TB_{aa}$) (-2,3 ($TB_g/TB_{aa}$)) |
| 9 | $CHF_2Cl$ | 38 ($C_e$) | 62 ($TB_{aa}$) | -0.15 | - |
| | $CH_3OCH_3$ | 5 ($C_e$) | 95 ($TB_{aa}$) | -0.89 | -1,0 ($C_e/TB_{aa}$) (-2,8 ($TB_g/TB_{aa}$)) |

a) All solvents contain a deuterated co-solvent ($CD_2Cl_2$ (20% (v/v)) for both $CHF_2Cl$ and $CH_3OCH_3$ and acetone-$d_6$ (6% (v/v)) for $CF_2Cl_2$) for locking purposes.

b) All integrations were carried out for $^{13}C$ NMR spectra of compounds 5-9 at -120°C (153 K).

**Stereoelectronic contributions to the conformational preferences**

As stated earlier, benzocycloheptene (1) exists as a single C form in solution. MM calculations[19] reveal that the introduction of an oxygen atom next to the benzene ring of 1 stabilizes the twist-boat form relative to the chair form ($\Delta E_{C/TB}$: 2.42 kcal/mol$^{-1}$ in 1 and 1.14 kcal/mol$^{-1}$ in 10) through better conjugation of the phenolic oxygen atom with the benzene π-system in the TB conformation.

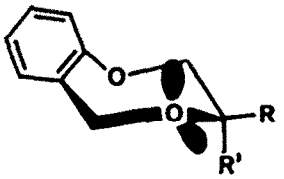
The introduction of a second oxygen atom at the 4-position of 10, leading to 2,3-dihydro-1,4-benzodioxepin (5) creates novel dipole-dipole interactions which result in the TB form being much more polar ($\mu_{TB}$: 1.91 D)[19] than the C form ($\mu_C$ = 0.46 D).[19] Dipolar interactions should therefore destabilized the TB form relatively to the C form, a phenomenon quite opposite to that occurring in all other benzodioxepins studied.[7-9,20]

However, the presence of this second oxygen atom in the seven-membered ring also changes structural forces (such as van der Waals or torsional interactions), as well as creating novel orbital interactions between the internal C-O bonds ($\sigma_{C-O}$-$\sigma_{C-O}^*$ "gauche effect"[2,3]); the latter stereoelectronic contribution is expected to depend on the value of the $O_1$-$C_2$-$C_3$-$O_4$ torsion in the C and TB conformations. Unfortunately, a quantitative determination of this effect is not possible because no TB signals are observed in the low temperature spectra of 5; the C/TB energy difference in that compound is therefore not available experimentally.

Another consequence of the replacement of the methylene group at the 4-position of 10 by an oxygen atom is to increase unfavorable steric interactions between the axial benzylic proton and a potential axial group at the 3-position, since C-O bonds are known to be shorter than C-C bonds[21]. This phenomenon is quite apparent in the methyl derivative 6, for which only the $C_e$ form is detected in solution, whereas the $C_g$ form was detected in small amounts (3%) for the 3-methyl derivative of 10.[11]

A similar situation arises with the gem-dimethyl derivative 7, where the unfavorable 1,3-diaxial interaction of the axial methyl group in the C form is relieved by a conformational change to a TB form whereby it is observed to be the major conformation in solution for 7, as also confirmed by the results of molecular mechanics calculations in Table 3.

On the other hand, the observed conformational data in solution for the methoxy derivative 8 can be rationalized through electronic and electrostatic contributions. Firstly, the antiperiplanar relationship between one lone pair of the benzylic oxygen atom and the external C-O bond, in both the $C_a$ form 17 and the $TB_{an}$ form 13a is expected to result in more stabilizing $n_\pi$-$\sigma_{C-O}^*$ orbital interactions (the so-called endo-anomeric effect[2]) in those conformations than in the $C_e$ (18) or $TB_g$ (14a) forms, in which such a favorable orientation is not possible. This factor alone should thus favour the $C_a/TB_{an}$ pair over the $C_e/TB_g$ pair. Other interactions between the $O_1$-$C_2$ and the $C_3$-O (methoxy) $\sigma$ orbitals are also operative, and should be more stabilizing for the $C_a$ and $TB_g$ forms, where the two C-O bonds in question are "gauche" to one another (the so-called attractive gauche effect[3b]); however, since the latter $\sigma_{C-O}$-$\sigma_{C-O}^*$ interactions are weaker[22] than the previously mentioned $n_\pi$-$\sigma_{C-O}^*$ orbital interactions associated with the anomeric effect, they are not expected to contribute significantly to the conformational energies for compound 8. The orbital interactions should therefore globally favor the $TB_{an}$ and $C_a$ forms over the $TB_g$ and $C_e$ forms.




17 R=H, R'=$OCH_3$ ($C_a$)

18 R=$OCH_3$, R'=H ($C_e$)

Dipolar interactions for their part are not expected to change this order of conformational stabilities, since MM calculations reveal[19] that dipole moments are of similar magnitude in the $C_a$ ($\mu$ = 1.32 D), $C_e$ ($\mu$ = 1.68 D) and $TB_g$ ($\mu$ = 1.09 D) conformations of 8. However, those same calculations also indicate that the highly unfavorable dipolar interactions in the $TB_g$ conformation ($\mu$ = 2.80 D) should destabilized this form further relative to the $TB_{an}$ and the $C_a$ forms, therefore explaining the absence of signals for this form in the low-temperature NMR spectra of 8.

One can also rationalize the population changes of the $TB_{an}$ and $C_a$ forms in compound 8 caused by the solvent changes, by means of a simple formalism[23] based on a combination of dipolar and solvation effects. Thus, in polar solvents, the more polar conformation in solution is expected to be stabilized relatively to the less polar one, through better solvation and greater attenuation of the unfavorable dipolar interactions. Those phenomena should be quite important in 8 and 9 since the presence of the polar methoxy group at the 3-position of these compounds increases their accessibility to solvent molecules. Although a recent study by Lemieux and Praly[24] and by Booth, Khedhair and Readshaw[25] on analogous six-membered ring compounds showed the importance of entropy factors, the two-term approach described above is sufficient to rationalize[17] the population increase of the $C_a$ form in 8 on going from $CH_3OCH_3$ (13%) to $CHF_2Cl$ (45%), because the $C_a$ form 17 is calculated[19] to be slightly more polar ($\mu$ = 1.32 D) than the $TB_{an}$ form ($\mu$ = 1.09 D).

Similar arguments can be invoked for the conformational preferences of the methylmethoxy derivative 9 in solution, since interactions between the polar bonds of that molecule are of the same nature as in 8. Accordingly, the introduction of the methyl group at the 3-position does not change significantly the $C_a/TB_{an}$ ratios in the two solutions, since that group occupies similar environments in those two forms.

Finally, it is noteworthy to compare the conformational preference of the 3-methoxy derivative 8 with that of 2-methoxy-1,4-dioxane. The six-membered analog is restricted to chair forms[10f] in $CDCl_3$ at +25°C ($C_a$:$C_e$ = 70:30) while 8 exist in two different ring geometries ($C_a$:$TB_{an}$ = 45:55 in $CHF_2Cl$ at -120°C), in which both methoxy orientations maximize the endo-anomeric effect. The absence of the $C_e$ form for 8 therefore shows that, in the seven-membered ring, stereoelectronic effects stabilize the $TB_{an}$ form sufficiently to make it a viable alternative to the $C_e$ conformation.

## Experimental Section

All syntheses requiring anhydrous conditions were performed under argon with techniques described elsewhere.[26] Anhydrous solvents were obtained by distilling over various drying agents: $P_2O_5$ for $CH_2Cl_2$, CaO for dimethylformamide and dimethylsulfoxide, $CaCl_2$ for benzene and xylene, and Mg for methanol. Flash chromatography was performed on 230-400 mesh silica gel (Merck) under standard conditions as described by Still and co-workers.[27] Preparative vapor phase chromatography was performed on a Varian model 920 apparatus using a 5'x3/8" stainless steel column containing 30% SE-30(P-HMDS) on Chromosorb-P. The sample to be purified is vaporized at 200°C in the injection port, passed through the separating column on a stream of helium gas (carrier gas), detected at 200°C by thermal conductivity and condensed in an acetone-dry ice bath. Column temperatures and retention times are specified when necessary.

Melting points were determined on a Thomas-Hoover (Unimelt) apparatus and were not corrected. Boiling points were determined by either simple or bulb-to-bulb (Krugelhohr) distillation for which the temperature reported represents the lowest one at which the vapors condensed on the receiving bulbs. Infrared spectra were taken on a Perkin-Elmer (Model 783) spectrometer. Low resolution mass spectra were recorded at 70 eV in the chemical ionisation mode, on a V.G. Micromass (Model 12-12) spectrometer, while those at high resolution were recorded at 70 eV, in the electron impact mode, on a modified MS-9 spectrometer. Routine $^1H$ NMR spectra were taken on a Bruker WH-90 spectrometer; solutions were typically 5% (w/v) $CDCl_3$ containing $Me_4Si$ as internal reference. The following abbreviations are used to described the signal multiplicity: s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet; br: broad.

The variable temperature $^1H$ NMR spectra at 400.13 MHz and the $^{13}C$ NMR spectra at 100.62 MHz were obtained using a Bruker WH-400 spectrometer equipped with a B-VT-1000 variable temperature unit. Calibration using a copper-constantan thermocouple inside a solvent containing NMR tube indicates that the temperatures reported are precise within ±3°C.

Proton samples in standard 5 mm tubes (degassed and sealed) were studied as 0.20M solutions in either $CHF_2Cl:CD_2Cl_2$ (80:20) or $CF_2Cl_2$:acetone-$d_6$ (94:6) solvent systems containing a small amount of TMS. The following instrumental parameters are typical: flip angle: 15°; SW: 4500 Hz; number of scans: 100-1000. Gaussian multiplication was applied on all FID's. Data size was 8K (AQ:0.91s) for low temperature spectra (-100°C to -125°C), and 16 and 32K (AQ:1.81 and 3.64s) for all others (+10°C to -100°C). All 8 and 16K FID's were zero-filled to 32K prior to the Fourier transformation.

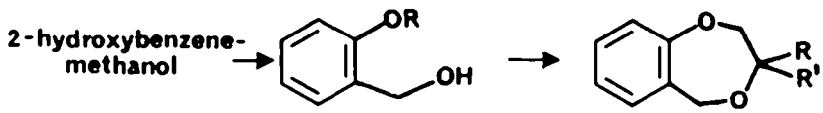
Carbon-13 samples in standard 10 mm tubes (degassed and sealed) were studied as 0.40M solutions in either $CHF_2Cl:CD_2Cl_2$ (80:20) or $CH_3OCH_3:CD_2Cl_2$ (80:20) solvent systems, containing a small amount of TMS. The following instrumental parameters are typical: flip angle: 60-70°; SW: 18000 Hz; relaxation delay: 0.20s; number of scans: 100-3000. Gaussian multiplication was applied on all FID's; data size: 16K (AQ: 0.46s), zero filled to 32K prior to Fourier transformation.

Reliable integrations from carbon-13 spectra were obtained using a 0.1-0.2 s delay between pulses and by comparing results with at least two other sets of carbon resonances of the same compound. All integration figures are therefore precise within 2%.

The rate constant for 5 was determined by NMR at the coalescence temperature using the equation $\pi((\Delta\nu)^2 + 6J^2)^{\frac{1}{2}}/\sqrt{2}$ for singlet to AB spectral change. The free-energy barrier for this compound was calculated from standard equations[28] using a transmission coefficient of one (vide infra).

Calculations by molecular mechanics methods were performed on a VAX-11/780 computer, situated at the Centre de Calcul of the Université de Montréal. Structural parameters for the conformers studied are generated by the interactive program MODEL,[29] which allows the user to create structures graphically, to modify them at will and to refine their geometries by MM2[13-15] calculations. Structures generated through this procedure are then used as input structural files for the MM285 program[16] obtained from QCPE (No. 395).

Compounds 5-9 were obtained by multistep step synthesis from 2-hydroxybenzenemethanol (Aldrich), as described in the following Scheme.




19 R=$CH_2CH_2Cl$ → 5 R,R'=H

20 R=$CH_2CH=CH_2$ → 21 R=H, R'=$CH_2SePh$ → 6 R=H, R'=$CH_3$

21 R=$CH_2C(CH_3)=CH_2$ → 23 R=$CH_3$, R'=$CH_2SePh$ → 7 R,R'=$CH_3$

22 R=$CH_2CH(OCH_3)_2$ → 8 R=H, R'=OCH3

23 R=$CH_2COCH_3$ → 9 R=$CH_3$, R'=$OCH_3$

**(2-(2-Chloroethoxy)benzenemethanol 19**

This compound was prepared following a procedure described by Kulka.[30] Distillation of the crude product under vacuum (114-115°C/0.13 mm Hg; litt. (28): 166-167°C/12 mm Hg) yielded pure 19. $^1$H NMR ($CDCl_3$): 2.79 (1H, br, -OH (exchangeable with $D_2O$)), 3.80 (2H, t, $-CH_2-Cl$), 4.23 (2H, t, $-OCH_2-$), 4.68 (2H, s, $-CH_2-O-$), 6.76-7.33 (4H, m, arom. protons); IR(neat): $\nu$($cm^{-1}$): 3600-3100 (-OH), 1610, 1590 (C=C).

**2,3-Dihydro-1,4-benzodioxepin 5**

To a solution containing 598 mg (12 mmol) of a 50% (w/w) dispersion of NaH in mineral oil in 70 $cm^3$ of anhydrous DMF, was added dropwise, under argon, a solution of 1.74 g (9 mmol) of the chloroalcohol 19 in 10 $cm^3$ of anhydrous DMF. The resulting solution was stirred and heated at 40°C during 7 h, then at room temperature during 24 h; it was then neutralized by the slow addition of 2.0 $cm^3$ of glacial acetic acid and filtered on sintered glass. The filtrate was evaporated to dryness, and then dissolved in 20 $cm^3$ of ether; this organic phase was then washed with 3 x 50 $cm^3$ brine, dried on $MgSO_4$, filtered on sintered glass and evaporated under reduced pressure to yield 1.63 g of a yellow oil which contains both the desired 5 and 2-vinyloxybenzenemethanol ($^1$H NMR ($CDCl_3$); 4.39, 4.65 (2H, AB part of an ABX pattern, $-O-CH=CH_2$), 4.66 (2H, s, $-CH_2-O-$), 5.03 (1H, br, -OH (exchangeable with $D_2O$)), 6.59 (1H, X part of an ABX pattern, $-O-CH=CH_2$), 6.86-7.42 (4H, m, aromatic protons)).

Compound 5 was isolated by preparative vapor phase chromatography (column temp.: 150°C; He flow rate: 53 $cm^3$ $min^{-1}$; retention time for 5: 6.0 min). $^{13}$C and $^1$H NMR spectra are described in Tables 1-3. Mass spectrum for 5: anal. calcd. for $C_9H_{10}O_2$: m/e: 150,0681; found m/e: 150,0644.

**2-(Propenyloxy)benzenemethanol 20**

This compound was prepared following a procedure described by Burkhard, Schmitz and Burnett.[31] A mixture of 20.00 g (201 mmol) of 2-hydroxybenzenemethanol, 13.9 $cm^3$ (201 mmol) of 3-bromopropene and 22.27 g (201 mmol) of potassium carbonate in 50 $cm^3$ of acetone thus yielded 19.03 g (72% yield) of pure 20 as a clear, dense liquid. Bp. 83-85°C/0.02 mm Hg (litt. (29): 97.5-98.0°C/ 1 mm Hg). $^1$H NMR ($CDCl_3$): 2.82 (1H, t, -OH (exchangeable with $D_2O$)), 4.53 (2H, dxt, $-O-CH_2-$), 4.67 (2H, d, $-CH_2-OH$), 5.23, 5.38 (2H, m, $=CH_2$), 6.03 (1H, m, -CH=), 6.78-7.32 (4H, m, arom. protons). IR(neat): $\nu$($cm^{-1}$): 3600-3100 (-OH), 1660 (aliph. C=C). 1610, 1600 (arom. C=C).

**N-Phenylselenophtalimide (N-PSP)**

This compound was prepared using a procedure previously described by Nicolaou et al.[32] A mixture of 43.00 g (225 mmol) of phenylselenylchloride and 45.00 g (243 mmol) of the potassium salt of phtalimide thus gave 43.12 g (63% yield) of a slightly yellow solid, whose melting point (171-175°C) and $^1$H NMR spectrum in $CDCl_3$ are identical to those described in reference 32 for N-PSP.

**3-(Phenylselenomethyl)-2,3-dihydro-1,4-benzodioxepin 21**

A mixture of 8.79 g (54 mmol) of alcohol 24.34 g (80 mmol) of N-phenylselenophtalimide 20, 0.40 g (1 mmol) of dl-camphorsulfonic acid and 400 $cm^3$ of anhydrous $CH_2Cl_2$ is stirred under argon, at 0°C during 10 min, then at room temperature for 72 h: a white, fluffy solid gradually precipitates from the solution during this period. The resultant solution is then filtered on sintered glass and evaporated under reduced pressure; the residue is dissolved in 200 $cm^3$ of hexane and the resulting solution is again filtered and evaporated to dryness, yielding a slowly crystallizing red oil. This oil was purified through flash chromatography on silica gel, using $CH_2Cl_2$/hexane (40:60) as eluant. The first fractions gave diphenyldiselenide (PhSeSePh), while subsequent fractions yielded pure 21 as white crystals. $R_F$: 0.24 ($CH_2Cl_2$/hexane: 40:60). Mp.: 77.0-78.5°C. $^1$H NMR ($CDCl_3$): 2.99 (2H, m, $-CH_2$-SePh), 3.66 (1H, dxd, H-2), 4.05 (1H, m, H-3), 4.43 (1H, dxd, H-2'), 4.71 (2H, s, H-5), 6.99-7.61 (9H, m, arom. protons). Mass spectrum for 21: (EI): 320 ($M^{+\cdot}$) (68), 120(100), 91(60). Anal. calcd. for $C_{16}H_{16}O_2Se$: m/e: 320.0315; found: m/e: 320.0336.

**3-Methyl-2,3-dihydro-1,4-benzodioxepin 6**

A stirred solution of 2.24 g (7 mmol) of compound 21 and 30.00 g of activated Raney nickel in 100 $cm^3$ of methanol is heated to reflux during 72 h; the resulting mixture is then filtered on a celite pad, and the filtrate evaporated under reduced pressure. The residue is dissolved in 50 $cm^3$ $CH_2Cl_2$, and the resulting solution is again filtered and evaporated, yielding 1.00 g (87% yield) of a clear liquid with a strong aniseed-like odor, and identified as 6. An analytically pure sample was obtained by preparative vapor phase chromatography (column temp.: 150°C; He flow rate: 50 $cm^3$, $min^{-1}$; retention time for 99: 7.0 min). $^{13}$C and $^1$H NMR spectra of 6 are described in Tables 1-3. Mass spectrum for 6: anal. calcd. for $C_{10}H_{12}O_2$: m/e: 164.0837; found: m/e: 164.0845.

**2-((2-Methyl)propenyloxy)benzenemethanol 22**

This compound was prepared from 2-hydroxybenzenemethanol, 3-chloro-2-methyl propene and potassium iodide using the same procedure as for 20. Distillation of the crude product under vacuum yielded a clear oil (13.57 g: 94% yield) identified as 22. Bp.: 90.0-92.0°C/0.35 mm Hg. $^1$H NMR ($CDCl_3$): 1.81 (3H, s, $CH_3$), 2.82 (1H, t, -OH (exchangeable with $D_2O$)), 4.43 (2H, s, $-O-CH_2-$), 4.68 (2H, d, $-CH_2-OH$), 5.02 (2H, d, $=CH_2$), 6.78-7.32 (4H, m, arom. protons).

**3-Methyl-3-phenylselenomethyl-2,3-dihydro-1,4-benzodioxepin 23**

This compound was prepared from 22 using the same selenium mediated cyclization method as for 21. Chromatography of the crude product on silica gel yielded 53% of 23 as a dense yellow oil. $R_F$: 0.30 ($CH_2Cl_2$/hexane: 40:60). Bp. 195-200°C/0.50 mm Hg. $^1$H NMR ($CDCl_3$): 1.37 (3H, s, $CH_3$), 3.13, 3.49 (2H, AB pattern, $-CH_2$-Se-), 4.09, 4.04 (2H, AB pattern, $-O-CH_2-$), 4.71 (2H, s, $-CH_2-O-$), 6.90-7.61 (9H, m, arom. protons). Mass spectrum for 23: (CI): 334 ($M^{+\cdot}$) (40), 163 ($M^{+\cdot}$-$PhSeCH_2$) (100).

**3,3-Dimethyl-2,3-dihydro-1,4-benzodioxepin 7**

This compound is prepared by a Raney nickel-mediated deselenization of compound 23, following a procedure previously described for the synthesis of compound 6. A 85% yield of the desired 7 was obtained as a clear oil after distillation. Further purification of the sample was achieved through preparative vapor phase chromatography (column temp.: 140°C; He flow rate: 41.0 $cm^3$ $min^{-1}$; retention time for 7: 6.1 min). Spontaneous crystallisation occurred in the receiving flask at -78°C, yielding pure 7 as a white solid. Mp. 44.0-46.0°C. $^{13}C$ and $^1H$ NMR spectra are described in Tables 1-3. Mass spectrum for 7: anal. calcd. for $C_{11}H_{14}O_2$: m/e: 178.0993; found: m/e: 178.0981.

**2-(2,2-Dimethoxyethoxy)benzenemethanol 24**

To a stirred mixture of 2.01 g (42 mmol) of a 50% (w/w) suspension of NaH in mineral oil and 30 $cm^3$ of anhydrous DMSO, under argon, is added in small portions 5.00 g (40 mmol) of 2-hydroxybenzenemethanol; the resulting solution is heated at 35°C until it becomes clear (5 min).To this clear solution is added, dropwise, a solution of 4.6 $cm^3$ (40 mmol) of 1,1-dimethoxy-2-chloroethane (Aldrich) in 15 $cm^3$ of anhydrous DMSO; the resulting mixture is heated at 110°C during 50 h, then brought back to room temperature and evaporated to dryness under vacuum. The residue was treated with 100 $cm^3$ of water, then extracted by 3 x 100 $cm^3$ of ethylether: the combined organic phases were then dried on $Na_2CO_3$ filtered and evaporated under reduced pressure to yield a slightly yellow oil which, upon distillation, gave pure 24 (4.78 g: 56% yield) as a clear and dense liquid. Bp. 80-82°C/1 mm Hg. $^1H$ NMR ($CDCl_3$): 3.38 (6H, s, 2X-$OCH_3$), 3.60 (1H, br, -OH (exchangeable with $D_2O$), 3.99 (2H, d, -O-$CH_2$-), 4.63 (2H, S, -$CH_2$-OH), 4.67 (2H, t, -$CH(OCH_3)_2$), 6.76-7.30 (4H, m, arom. protons). IR(neat): ν($cm^{-1}$): 3600-3100 (-OH), 1600 (arom. C=C).

**3-Methoxy-2,3-dihydro-1,4-benzodioxepin 8**

A mixture of 1.53 g (7 mmol) of 24, 50 mg (0.2 mmol), of paratoluenesulfonic acid and 125 $cm^3$ of anhydrous benzene was heated to reflux during 3 h; the clear, yellowish solution was then brought back to room temperature and evaporated to dryness. The residue was taken up in 150 $cm^3$ of ethylether and the resulting solution was dried on $K_2CO_3$: it was then filtered on sintered glass and evaporated to dryness, yielding a yellow oil which, upon distillation on a Krugelbohr apparatus (110°C/1 mm Hg), gave 0.80 g (62% yield) of pure 8 as a clear oil. Further purification was possible through the use of preparative vapour phase chromatography (column temp. 150°C; He flow rate: 24 $cm^3$ $min^{-1}$; retention time fo 8: 14.5 min). Spontaneous crystallization occurred in the receiving flask at -78°C. Mp: 48.5-49.5°C. $^{13}C$ and $^1H$ NMR spectra are described in Tables 1-3. Mass spectrum for 8: anal. calcd. for $C_{10}H_{12}O_3$: m/e: 180.0786; found: m/e: 180.0791.

**2-(Propane-2-one oxy)benzenemethanol 25**

This compound was prepared from 2-hydroxybenzenemethanol 1-chloro-2-propanone and potassium iodide using the same procedure as for 20: this procedure gave 3.86 g (53% yield) of 25 as a thick, yellow oil; any attempt to distill this compound resulted in polymerization and in the production of minor quantities of 3-methyl-1,4-benzodioxepin ($^1H$ NMR ($CDCl_3$): 1.63 (3H, d (allylic coupling: 1,2$H_3$), -$CH_3$), 5.06 (2H, s, -$CH_2$-O-), 5.73 (1H, br, s, -O-$CH$ = 6.79-7.26 (4H, m, arom)); the yellow oil was therefore utilized as such in the next step. $^1H$ NMR ($CDCl_3$) of 25: 2.20 (3H, s, -$CH_3$), 4.58 (2H, s, -O-$CH_2$-), 4.67 (2H, s, -$CH_2$-OH), 6,88-7.36 (4H, m, arom. protons).

**3-Methyl-3-methoxy-2,3-dihydro-1,4-benzodioxepin 9**

To 1.36 g (7.5 mmol) of the keto-alcohol 25 in a 200 $cm^3$ round-bottomed flask, are added 15 mg (0.1 mmol) of paratoluenesulfonic acid and 125 $cm^3$ of anhydrous methanol: the resulting mixture was then stirred and heated to reflux during 4 h. It was then cooled to room temperature and evaporated to dryness; the residue was dissolved in 30 $cm^3$ of ethylether and the resulting organic phase was dried on anhydrous $K_2CO_3$, filtered on sintered glass and evaporated under reduced pressure to give a yellow oil which was purified by flash chromatography on silica gel, using $CH_2Cl_2$ as eluent. Evaporation of the first fractions produced 0.41 g (30% yield) of the desired 9 as a slightly yellow oil, which crystallized on standing at 0°C. Mp.: 54.0-56.0°C (white solid). $^{13}C$ and $^1H$ NMR spectra of 9 are described in Tables 1-3. Mass spectrum for 9: anal. calcd. for ($M-C_2H_4^+$): $C_9H_{10}O_3$: m/e: 166,0630; found: m/e: 166,0617 (no molecular ion was detected in the spectrum).

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